Baseline Characteristics of AMASIA: First Real World Data of Siponimod Treated Patients with Secondary Progressive Multiple Sclerosis

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Background and objective

- 85% of MS patients are initially diagnosed with RRMS[1]
- 60% will convert to SPMS within 20 years due to evolvement of the disease over time[2,3]
- Hallmarks of SPMS include progressive motor disability and cognitive decline[4-7]
- Siponimod (Mayzent®), a selective sphingosine-1-phosphate receptor modulator, has been approved by the EMA for the treatment of active SPMS, evidenced by relapses or imaging features of inflammatory activity
- 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
- 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) is the first prospective non-interventional study to assess long-term effectiveness and safety of siponimod in clinical routine and the impact on quality of life and socioeconomic conditions

MS: Multiple Sclerosis; RRMS: relapsing-remitting MS; SPMS: secondary progressive MS; EMA: European Medicines Agency; RCT: randomized controlled trial;

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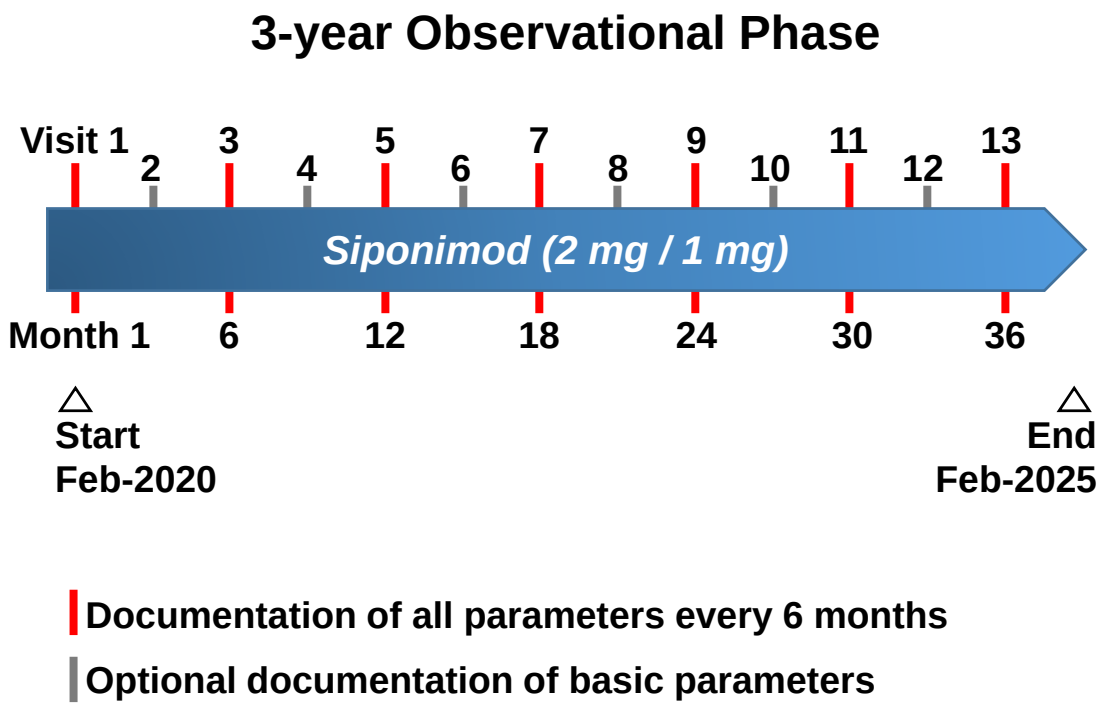
Methods

Study design, patients and assessment parameters

Figure 1. Study design



Patients

- 1,500
- Age ≥18
- Diagnosis of SPMS with active disease
- Siponimod treatment (2 mg or 1 mg)

Observational phase

- 3 years (from Feb-2020 to Feb-2025) in up to 250 centers across Germany

Frequency of study visits

- 6 months (optional: 3 months)

Assessments

- Clinic: Laboratory, ophthalmic and physical evaluation
- MS-activity: MRI, MS-AS, EDSS
- Functional domains: SDMT, EDSS
- Patient's perspective: UKNDS, FSMC, EuroQol-5D
- Physician`s perspective: CGI, progression questionnaire
- Socioeconomic factors: MS-HRS

EDSS: Expanded Disability Status Scale; FSMC: Fatigue Scale For Motor And Cognitive Functions; MRI: Magnetic Resonance Imaging; MS-AS: MS Activity Scale Score; MS-HRS: Multiple Sclerosis Health Resource Survey; MSProDiscuss™: progression questionnaire; SDMT: Symbol Digit Modalities Test; UKNDS: United Kingdom Neurological Disability Scale || Figure adapted from Ziemssen et al. (2020) JMIR Research Protocols (Epub ahead of print)

Results

Demography and Baseline Characteristics

Data analysis / Statistics

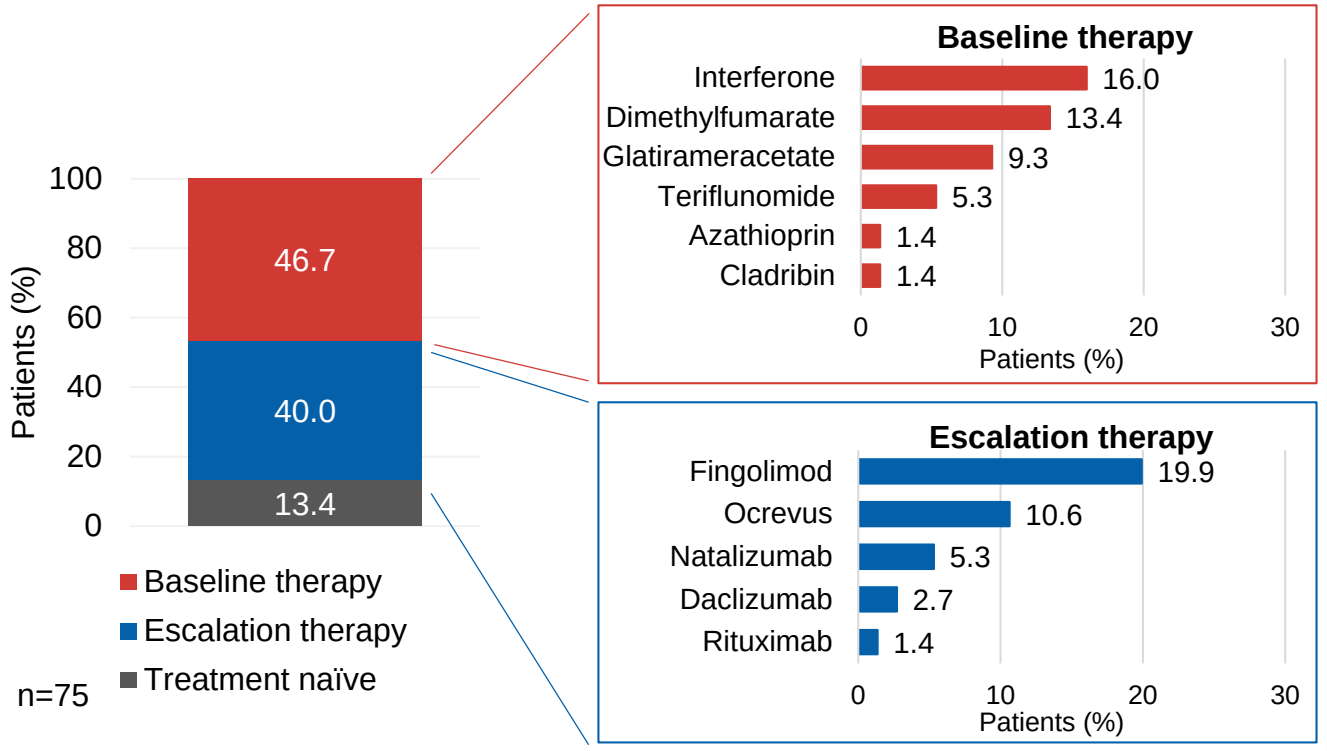
- As of July 16, 2020 93 patients were enrolled in AMASIA and included in this interim analysis
- Data were analyzed as observed by descriptive statistics

Table 1. Demography & Baseline characteristics

Variable	AMASIA	EXPAND active SPMS subgroup*
Number of patients, n	93	779
Age, years (mean ± SD)	52.7±8.1	46.6±8.26
Female, %	60.2	63.8
Time since first symptoms of MS, years (mean ± SD)	20.3±9.2	15.6±7.99
Time since conversion to SPMS, years (mean ± SD)	2.3±3.9	3.2±3.28
Patients with relapses in the previous 2 years before screening, %	51.3	75.8

**Represents population of the EMA label*

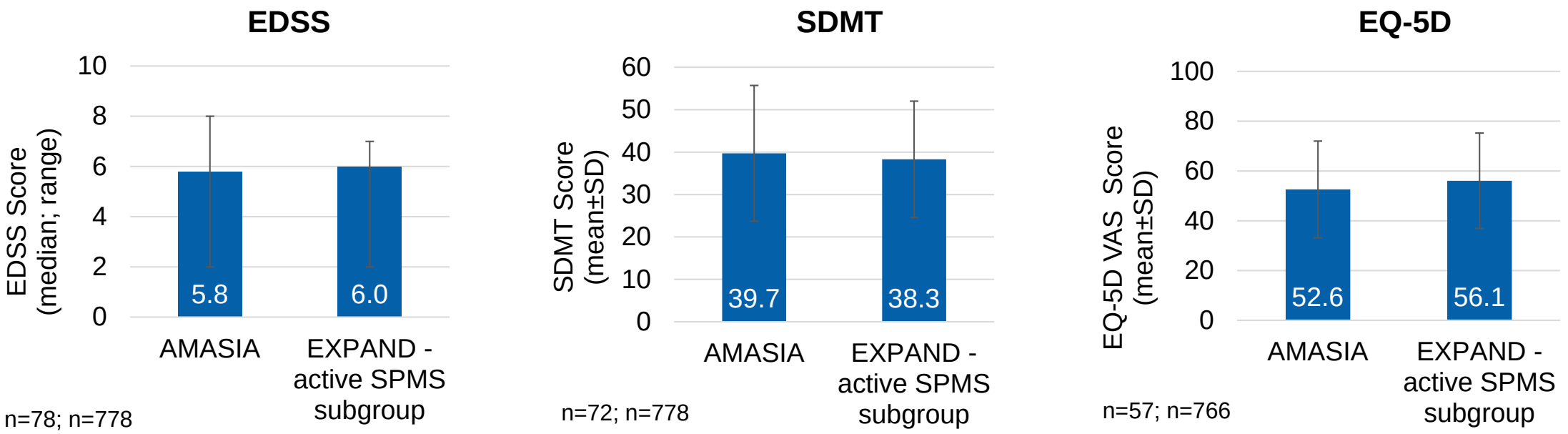
Figure 2. Last treatment before siponimod (AMASIA)



Results

Disability, cognitive and behavioral impairments

Figure 3. Disability cognitive/behavioral impairment assessed by EDSS, SDMT and EQ-5D



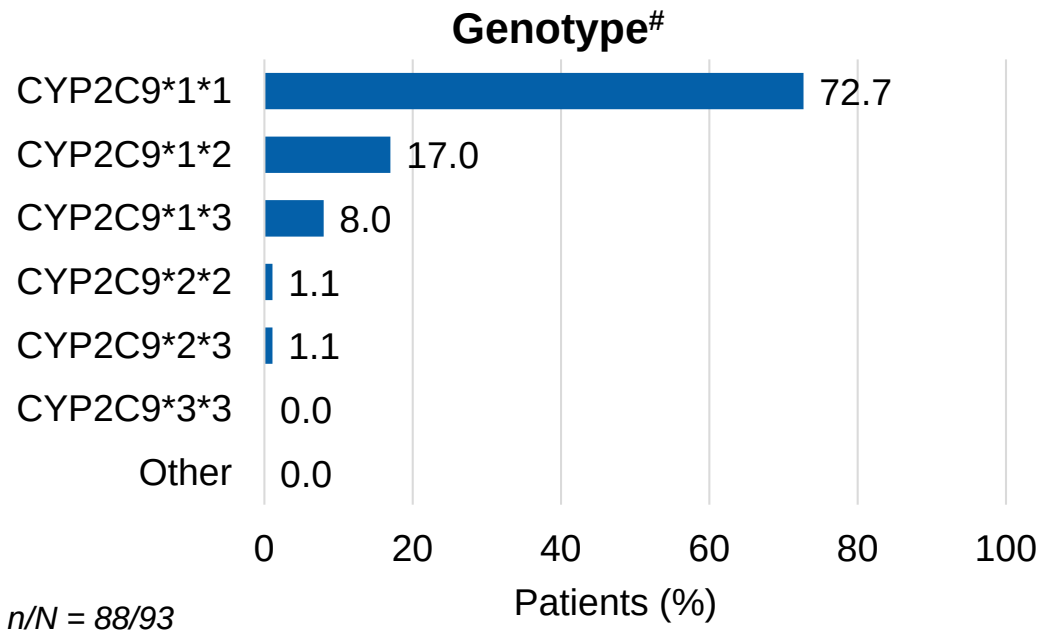
Real word data confirms SPMS population observed in EXPAND – comparable disability, cognitive impairment and even lower quality of life in a real world setting

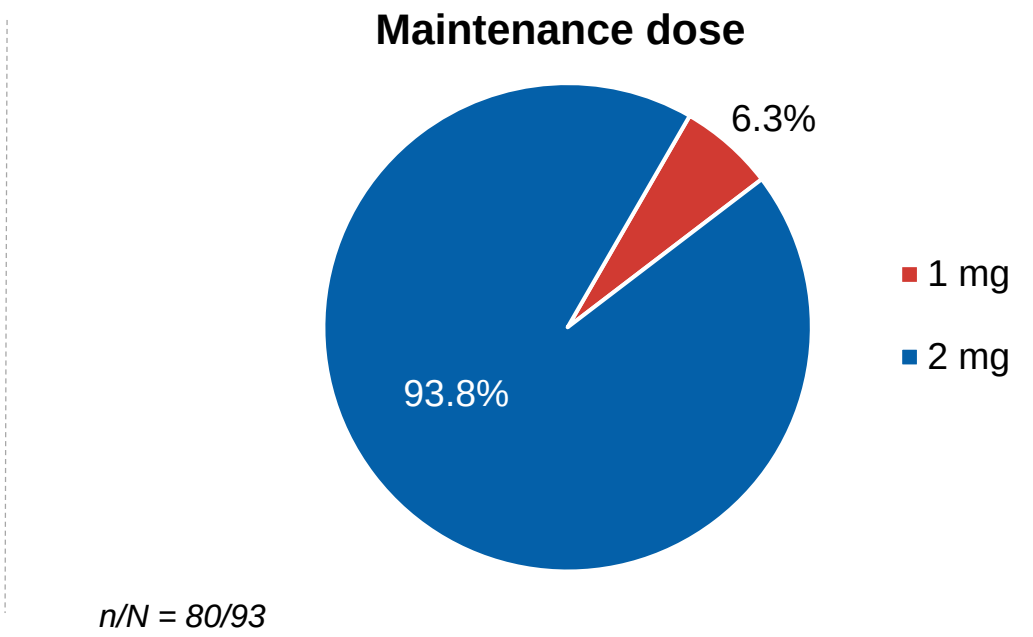
EDSS: Expanded Disability Status Scale | SDMT: Symbol Digit Modalities Test | EQ-5D: EuroQol-5D

Results

SPMS genotype and siponimod dose

Figure 4. Distribution of CYP2C9-Genotype and resulting siponimod dose





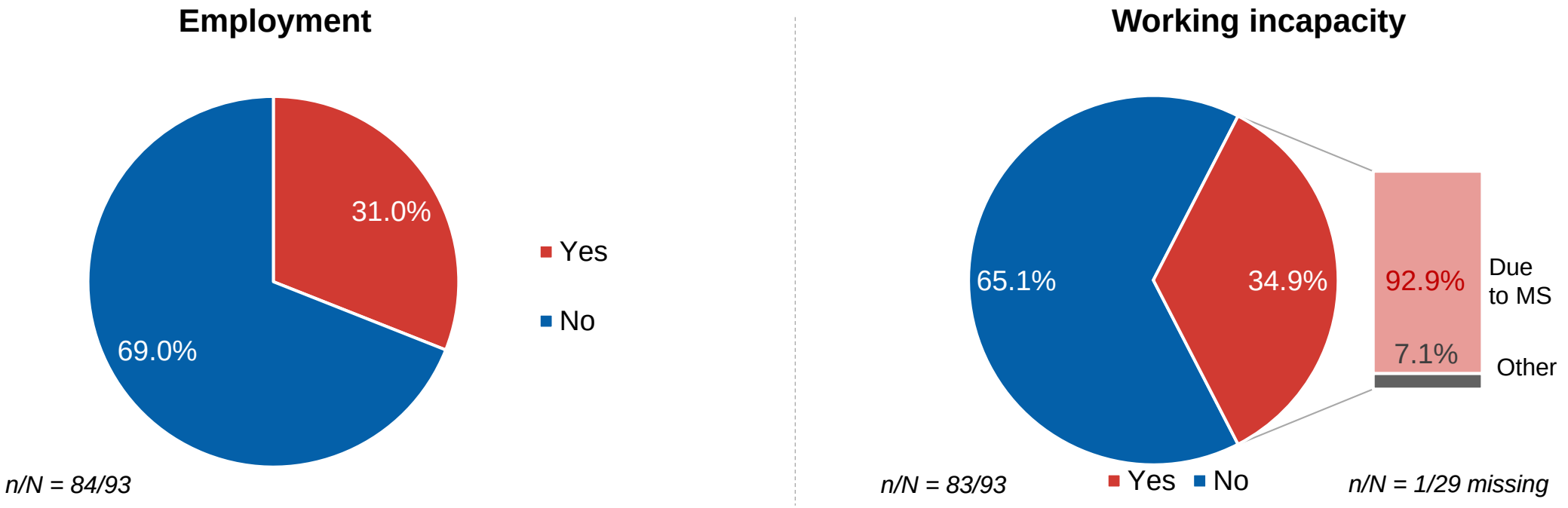
The most frequent genotype in AMASIA is CYP2C9*1*1.

#Siponimod is metabolized by CYP2C9. Activity of the enzyme is strongly affected by CYP2C9 genetic polymorphism. In compliance with SmPC, siponimod dose is selected according to the individual CYP2C9 genotype and is contraindicated for patients with homozygote genotype CYP2C9*3*3.
CYP2C9*3*3 patients are excluded from the study.

Results

Employment and working status

Figure 5. Employment and working incapacity

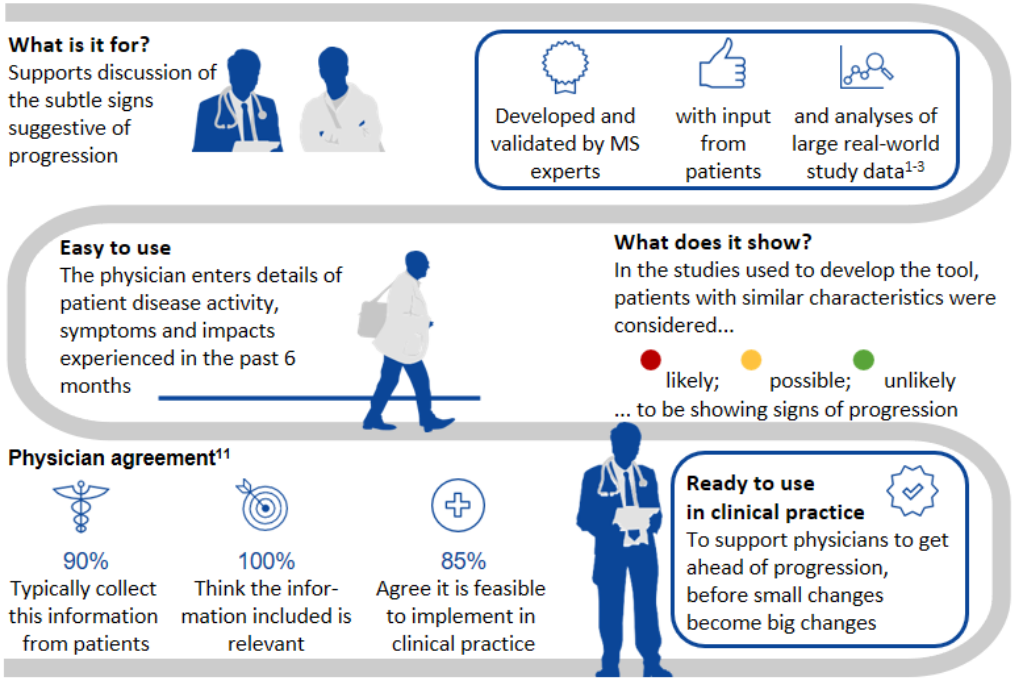


A high proportion (69%) of siponimod-treated SPMS patients is not employed and more than one third (34.9%) of the patients is incapable of working, mainly due to MS (92.9%)

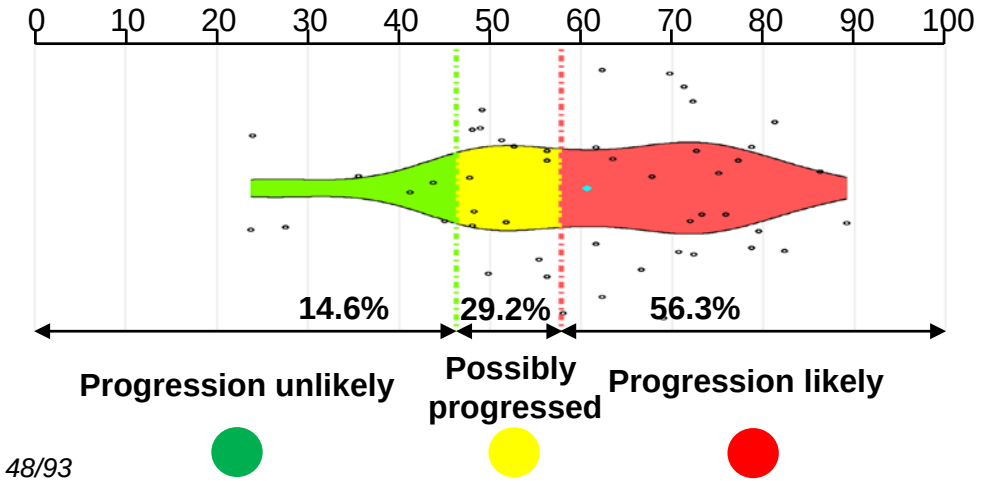
Results

Progression questionnaire: MSProDiscuss™

Figure 6. Assessment of disease progression by MSProDiscuss™ [1-6]



MSProDiscuss algorithm indicates 29.2% of the patients being in an early stage and 56.3% of the patients being in a more advanced stage of progression



n/N = 48/93

According to the MSProDiscuss™ algorithm, AMASIA represents an early SPMS population treated with siponimod.

MSProDiscuss™ is for educational and discussion purposes only. MSProDiscuss™ does not provide medical advice, diagnosis, prediction, prognosis or treatment. MSProDiscuss™ and its content are being provided for general information purposes only. Any medical advice, diagnosis or treatment should be made by the appropriate healthcare professional. The development of MSProDiscuss™ was funded by Novartis Pharma. MSProDiscuss™ is hosted by www.neuro-compass.education, a free independent medical education resource

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Conclusions

- AMASIA provides insight into the use of siponimod in clinical routine for the first time
- Compared to the active SPMS subgroup in the pivotal EXPAND trial, the real-world population of AMASIA is slightly older with a longer overall MS disease duration, but has a shorter time since conversion to SPMS
- Equally advanced disability and cognitive impairment and a lower quality of life were observed in AMASIA vs. EXPAND
- Prior to siponimod, more than half of the patients received baseline therapy or were untreated
- Based on their CYP2C9 genotype, > 90 % of patients are normal metabolizers (maintenance dose, siponimod 2 mg once daily)
- Applying the MSProDiscuss™ algorithm, most participants appear to be at an early stage of SPMS
- AMASIA patients are strongly affected by SPMS, leading to high rates of unemployment and inability to work

The combination of clinical parameters and patient reported outcomes including quality of life and socioeconomics allows a more detailed insight in the siponimod treated SPMS patient population in clinical routine in Germany.

This study represents real-world evidence that will contribute to a better understanding of SPMS management in the medical community

Thank you