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

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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 (ImpAct of Mayzent\(^{®}\) [Siponimod] on secondAry progressive multiple Sclerosis patients in a long-term non-Interventional study in GermAny) 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
Methods
Study design, patients and assessment parameters

**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

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

*Represents population of the EMA label
Results

Disability, cognitive and behavioral impairments

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

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.
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™

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