PANGAEA 2.0 EVOLUTION: Unraveling patient and treatment characteristics for SPMS and at risk for SPMS patients in clinical routine

Tjalf Ziemssen¹, Benedict Rauser²

Poster Number: P0896

¹Zentrum für klinische Neurowissenschaften, Universitätsklinikum Carl Gustav Carus, Dresden, Germany
²Novartis Pharma GmbH, Nuremberg, Germany
Disclosure || Background and objective

**DISCLOSURE**

Tjaaf Ziemssen received speaking honoraria and financial support for research activities from Almirall, Biogen, Celgene, Novartis, Roche, Teva, and Sanofi. Benedict Rauser is an employee of the Novartis Pharma GmbH, Nuremberg, Germany. This non-interventional study was funded by Novartis Pharma GmbH, Nuremberg, Germany. Medical writing support was provided by CROLLL GmbH, Nuremberg, Germany. The final responsibility for the content lies with the authors.

- 85% of MS patients are diagnosed with RRMS¹
- 60% will convert to SPMS within 20 years due to evolvement of the disease over time²,³
- Currently, there are no reliable biomarkers or immunologic, pathologic or imaging based diagnostic markers to predict the transition of RRMS to SPMS⁴,⁵
- Unclear criteria to define the transition from RRMS to SPMS lead to late and mostly retrospective diagnosis of SPMS⁴,⁵
- Diagnosis of SPMS is still difficult due to a lack of clear diagnostic criteria³
- The PANGAEA 2.0 study is a post-authorization, non-interventional, German, treatment benefit study in MS patients. The study aims to better understand the disease progression of MS and especially the conversion from RRMS to SPMS with the goal to develop new diagnostic tools. A new study arm was added to PANGAEA 2.0, termed PANGAEA 2.0 EVOLUTION focusing on RRMS-patients with high-risk for SPMS and SPMS patients.

**Objective**

Aim of this interim analysis is to show differences in demographic and baseline characteristics of RRMS-patients with risk for SPMS vs SPMS-patients and present first follow-up data.

---

Methods

Study design

As of July 21, 2020 453 patients were enrolled in PANGAEA 2.0 EVOLUTION and included in this analysis.

Figure 1. Study design

Current DMT or no treatment for last 12 months

Arm IIA

Physician’s decision

Arm IIB

1000 patients, up to 2 years observation

EE0 E1 E2 E3 E4

SPMS

Evaluation visits every 6 months

EE0 E1 E2 E3 E4

RRMS at risk for SPMS

FPFV

03/2019

LPLV

12/2021

Inclusion criteria

• Age 18 to 65
• EDSS 3.0 – 6.5
• Prior RRMS diagnosis (McDonald criteria 2010)
• Current diagnosis based on physician’s evaluation:
  – SPMS
  – RRMS at risk for SPMS
• On current DMT or no treatment for the last 12 months

Exclusion criteria

• Patients likely not being able to participate in this study for 24 months based on physicians evaluation
## Results

### Demography and Baseline Characteristics

<table>
<thead>
<tr>
<th>Variable</th>
<th>High risk for SPMS</th>
<th>SPMS</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number of patients</td>
<td>n</td>
<td></td>
</tr>
<tr>
<td>Age years [mean ± SD]</td>
<td>49.8 ± 8.5</td>
<td>53.6 ± 7.3</td>
</tr>
<tr>
<td>Sex female [n (%)]</td>
<td>187 (72.5%)</td>
<td>119 (75.3%)</td>
</tr>
<tr>
<td></td>
<td>71 (27.5%)</td>
<td>39 (24.7%)</td>
</tr>
<tr>
<td>Disease and treatment history</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Time since diagnosis years [mean ± SD]</td>
<td>13.9 ± 8.1</td>
<td>17.1 ± 9.0</td>
</tr>
<tr>
<td>Time since first symptoms years [mean ± SD]</td>
<td>16.7 ± 8.9</td>
<td>21.1 ± 8.9</td>
</tr>
<tr>
<td>Time from first symptoms to diagnosis years [mean ± SD]</td>
<td>2.9 ± 5.4</td>
<td>4.0 ± 6.8</td>
</tr>
<tr>
<td>Number of pretreatments mean ± SD</td>
<td>2.0 ± 1.7</td>
<td>2.0 ± 1.4</td>
</tr>
<tr>
<td>Last treatment at inclusion</td>
<td></td>
<td></td>
</tr>
<tr>
<td>No treatment at inclusion (total)</td>
<td>23.6%</td>
<td>16.5%</td>
</tr>
<tr>
<td>Baseline therapies (total)</td>
<td>50.8%</td>
<td>59.4%</td>
</tr>
<tr>
<td>Azathioprin</td>
<td>0.4%</td>
<td>1.9%</td>
</tr>
<tr>
<td>Cladribin</td>
<td>0.0%</td>
<td>0.0%</td>
</tr>
<tr>
<td>Dimethylfumarate</td>
<td>12.0%</td>
<td>5.7%</td>
</tr>
<tr>
<td>Glatirameracetate</td>
<td>11.6%</td>
<td>10.1%</td>
</tr>
<tr>
<td>Interferone</td>
<td>20.9%</td>
<td>25.9%</td>
</tr>
<tr>
<td>Mitoxantron</td>
<td>1.6%</td>
<td>13.9%</td>
</tr>
<tr>
<td>Teriflunomide</td>
<td>4.3%</td>
<td>1.9%</td>
</tr>
<tr>
<td>Escalation therapies (total)</td>
<td>21.7%</td>
<td>16.4%</td>
</tr>
<tr>
<td>Daclizumab</td>
<td>2.7%</td>
<td>0.0%</td>
</tr>
<tr>
<td>Fingolimod</td>
<td>10.5%</td>
<td>3.8%</td>
</tr>
<tr>
<td>Lemtrada</td>
<td>0.4%</td>
<td>0.6%</td>
</tr>
<tr>
<td>Ocrevus</td>
<td>1.9%</td>
<td>3.2%</td>
</tr>
<tr>
<td>Rituximab</td>
<td>0.0%</td>
<td>2.5%</td>
</tr>
<tr>
<td>Tysabri</td>
<td>6.2%</td>
<td>6.3%</td>
</tr>
<tr>
<td>Cannot be defined (total)</td>
<td>3.9%</td>
<td>7.6%</td>
</tr>
</tbody>
</table>

- SPMS patients are older (53.6 ± 7.3 vs. 49.8 ± 8.5)
- SPMS patients have a longer disease history (time since first symptoms: 21.1 ± 8.9 vs. 16.7 ± 8.9)
- Higher proportion of patients without treatment in high risk for SPMS cohort at baseline compared to SPMS patients (23.6% vs. 16.5%)
- Compared to SPMS patients, a lower proportion of high risk for SPMS patients receive baseline therapies (50.8% vs. 59.4%)
- Only a minority of patients receives escalation therapies at baseline (High risk for SPMS: 21.7% vs SPMS: 16.4%)
Results

EDSS and relapse activity

Disease burden: SPMS patients have a higher EDSS score, lower annualized relapse rate

Figure 2. Assessment of disease burden by EDSS and annualized relapse rate

EDSS score at baseline

High-risk for SPMS

SPMS

Annualized relapse rate

n=212

n=134

n=95 | 84*

n=60 | 53*

Values are mean ± 95% CI

Values show estimate ± 95% CI; estimates for ARR are calculated for the first six months of the study for the Follow-up Set; *Number of observations used

EDSS: Expanded Disability Status Scale (the higher the score the higher the impairment)
## Results

### Cognition and Fatigue

Impairment of cognition and motor fatigue are more pronounced in SPMS patients. Cognitive fatigue is comparable in both populations.

*Note: Whereas “impairment in cognition” refers to a decrease in patient’s mental processing speed, “cognitive fatigue” describes mental impairment caused by the patient’s state of exhaustion. FSMC: Fatigue Scale for Motor and Cognitive Functions (the higher the score the higher the impairment); SDMT: Symbol Digit Modalities Test (the lower the numbers the higher the impairment).*
Results

Quality of Life || Working status

Quality of life assessments show higher impairment in SPMS patients

EQ-5D: EuroQol 5-dimension - visual analog scale: (the lower the number the higher the impairment); MSIS-29: Multiple sclerosis impact scale - 29 items (the higher the score the higher the impairment)

SPMS patients face higher unemployment rate and incapacity to work due to MS when compared to patients at high-risk for SPMS
**Results**

**Progression questionnaire - MSProDiscuss™**

**Figure 6. Assessment of progression by MSProDiscuss™ 1-6**

- MSProDiscuss algorithm confirms SPMS classification by physicians, assesses broader distribution in ‘at risk for SPMS’ population

- High-risk for SPMS
  - n=258
  - 23.3% Likely progression
  - 26.2% Possibly progressed
  - 50.5% Unlikely progression

- SPMS
  - n=158
  - 7.2% Likely progression
  - 11.5% Possibly progressed
  - 81.3% Unlikely progression

**Algorithm highly correlates with physicians’ decision to classify SPMS patients**

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.

**Results**

Patients’ and physicians’ disability assessment

Both UKNDS and EDSS show SPMS patients having higher disease burden which is mainly due to impairments in motoric and urogenital/gastrointestinal domains. In general, evaluations from patients’ and physicians’ perspective were in accordance.

Values are mean ± 95% CI; UKNDS domains “sexuality” and “other” were not compared as EDSS domain “other” was not evaluated;
n(UKNDS [High-risk SPMS/SPMS]) || EDSS [High-risk SPMS/SPMS]): Total: ([171/110] || [212/134]); Movement: ([185/120; 187/120] || [212/136; 212/135]); Cognition: ([188/119] || [212/135]); Mood: ([187/120]) || ([212/135]); Fatigue: ([186/119] || [212/135]); Visus: ([186/120] || [212/134]); Speech and swallow: ([181/120; 182/118] || [212/135]); Bladder and bowel: ([185/120; 185/120] || [212/136]); Sensitivity and pain: ([181/117] || [212/136]); || EDSS: Expanded Disability Status Scale; UKNDS: United Kingdom neurological disability scale
Conclusions

- SPMS patients are older, have a longer disease history, more often received an induction therapy, while patients with high risk for SPMS received more often escalation therapies
- SPMS patients have higher EDSS score, but less relapses than risk patients
- Quality of life is more diminished in SPMS patients compared to patients at high risk for SPMS
- MSProDiscuss algorithm correlates with physicians’ decision to classify SPMS patients in clinical routine
- Cognition and motor fatigue are more impaired in SPMS patients, while cognitive fatigue is similar in both populations
- Unemployment and retirement due to MS is increased in SPMS patients

Interim results of PANGAEA 2.0 EVOLUTION show different progressive patient profiles in a real world setting.

A longitudinal observation aims to identify key symptoms associated with the underlying progression and helps to define a more accurate and unified diagnosis for progression and SPMS and subsequently a better long-term outcome for these patients.