Characterization of patient and treatment characteristics in SPMS and at risk for SPMS patients in clinical routine: The PANGAEA 2.0 EVOLUTION study

Benedict Rauser[1]; T. Ziemssen[2]
[1] Novartis Pharma GmbH, Nuremberg, Germany
[2] Zentrum für klinische Neurowissenschaften, Universitätsklinikum Carl Gustav Carus, Dresden, Germany

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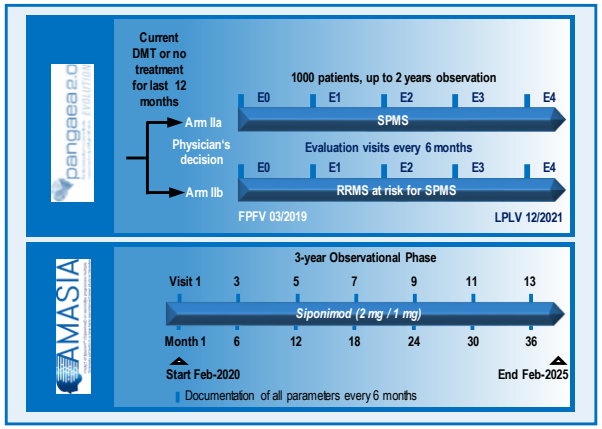
BACKGROUND

- 85% of MS patients are diagnosed with relapsing remitting multiple sclerosis (RRMS)[1] and 60% will convert to secondary progressive multiple sclerosis (SPMS) within 20 years due to evolvement of the disease over time[2,3].
- Inconsistent criteria to define the transition from RRMS to SPMS and previous lack of treatment options led to late and mostly retrospective diagnosis of SPMS[4,5].
- The PANGAEA 2.0 study is a post-authorization, non-interventional 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 (**Figure 1**).
- Here we compare baseline characteristics of 616 EVOLUTION patients with baseline data of 315 patients from the AMASIA study, i.e. patients deemed by the physician to require a specific treatment for active SPMS (siponimod). AMASIA is the first prospective non-interventional study to assess long-term effectiveness and safety of siponimod in clinical routine.

Figure 1. Study design of PANGAEA 2.0 Evolution and AMASIA



OBJECTIVE

- The 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 follow-up data after 12 months.

METHODS

- In the prospective non-interventional study PANGAEA 2.0 EVOLUTION approximately 600 patients with either SPMS or RRMS at high risk for SPMS are followed independently of treatment for up to two years.
- As there are no standard criteria for the transition state from RRMS to SPMS, physicians independently assign patients to the 'high risk for SPMS' cohort after a comprehensive evaluation of the patient's symptoms according to their daily practice
- At 6-month intervals routine clinical measurements, quality of life (QoL) and socioeconomic parameters are documented.
- In the non-interventional study AMASIA 1,500 SPMS patients on Siponimod will be documented over 3 years.

RESULTS

- As of Jan 28, 2021 658 patients were enrolled in PANGAEA 2.0 EVOLUTION and as of Jan 14, 2021 321 patients were enrolled in AMASIA; 616 patients of PANGAEA 2.0 Evolution and 315 patients of AMASIA satisfied all eligibility criteria and were included in this analysis.

Demography and baseline characteristics

- Demography and baseline characteristics are depicted in **Table 1.**

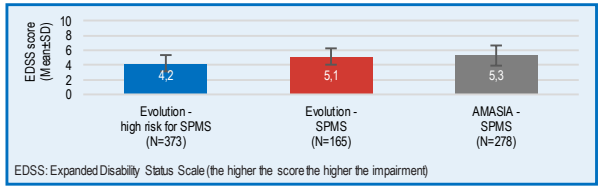
Table 1. Baseline characteristics of patients included in this interim analysis.

Variable	Evolution – High risk for SPMS	Evolution – SPMS	AMASIA – SPMS
Number of patients; n	427	189	315
Age; years [mean±SD]	49.5±9.1	53.6±7.2	54.6±8.1
Female; [n (%)]	306 (71.7)	142 (75.1)	212 (67.3)
Disease and treatment history			
Time since MS diagnosis; years [mean±SD]	13.8±7.9	17.2±9.4	17.1±9.3
Relapses within last 24 months prior to study inclusion; n [mean±SD]	0.47±0.89	0.33±0.75	0.89±1.29
Number of pretreatments; n [mean±SD]	1.6±1.6	2±1.4	2.3±1.7
Last treatment at inclusion			
No treatment at inclusion (total)	**20.8%**	**10.6%**	**9.5%**
Baseline therapies (total)	46.1%	46.1%	44.8%
Dimethylfumarate	9.1%	7.4%	10.2%
Glatirameracetate	11.7%	10.6%	8.9%
Interferone	21.6%	26.5%	20.3%
Teriflunomide	3.7%	1.6%	5.4%
Escalation therapies (total)	**21.8%**	**29.7%**	**32.8%**
Alemtuzumab	0.5%	1.1%	1%
Azathioprine	0.2%	1.1%	1.6%
Cladribin	0.0%	0.0%	0.6%
Daclizumab	3.5%	1.1%	1.3%
Fingolimod	8%	6.9%	11.7%
Mitoxantron	2.1%	14.3%	7%
Natalizumab	7.3%	4.2%	3.2%
Ocrelizumab	0.2%	0.5%	5.4%
Rituximab	0.0%	0.5%	1%
Cannot be defined | unknown | other (total)	**7.0%**	**8.0%**	**8.8%**

Disability

- At baseline, SPMS patients from PANGAEA 2.0 Evolution showed a EDSS score higher than patients at high risk for SPMS. Score was highest for patients from AMASIA (**Figure 2**).

Figure 2. Assessment of disease burden by EDSS

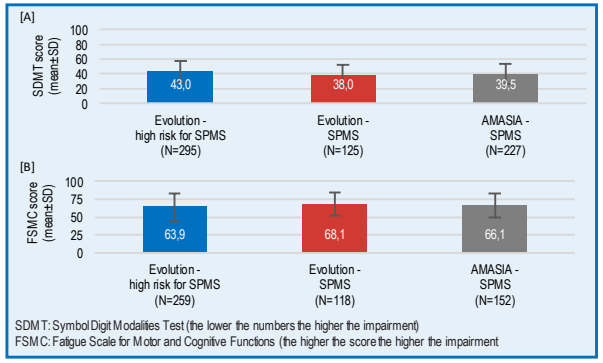


EDSS: Expanded Disability Status Scale (the higher the score the higher the impairment)

Cognition and fatigue

- Impairment of cognition (assessed by SDMT) and motor fatigue (assessed by FSMC) are more pronounced in SPMS patients (**Figure 3A & Figure 3B**).

Figure 3. Assessment of cognition by SDMT and MS-related fatigue by FSMC

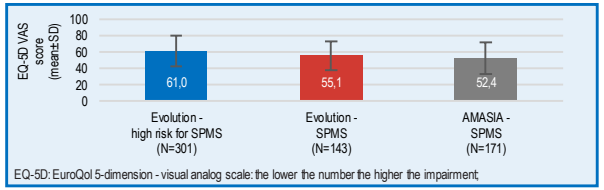


SDMT: Symbol Digit Modalities Test (the lower the numbers the higher the impairment)
FSMC: Fatigue Scale for Motor and Cognitive Functions (the higher the score the higher the impairment

Quality of life

- Quality of life assessed by EQ-5D VAS showed higher impairment in SPMS patients at baseline (**Figure 5**).

Figure 5: Assessment of quality of life by EQ-5D (VAS)

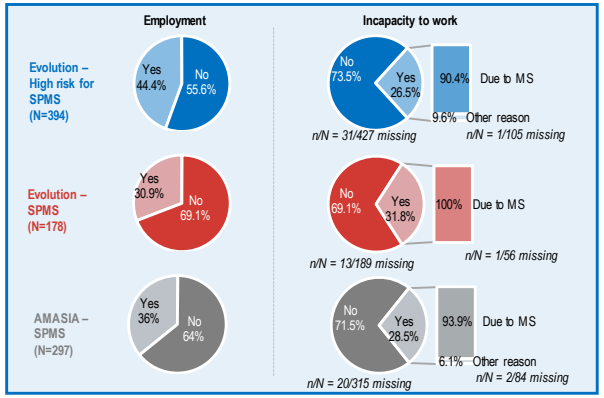


EQ-5D: EuroQol 5-dimension - visual analog scale: the lower the number the higher the impairment;

Working status

- SPMS patients face higher unemployment rate and incapacity to work due to MS when compared to patients at high-risk for SPMS (**Figure 6**).

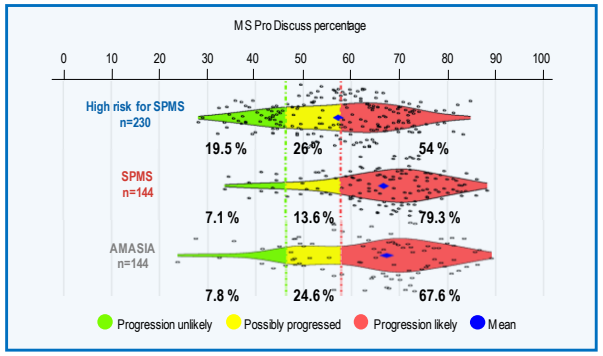
Figure 6: Assessment of working status and incapacity



Progression questionnaire – MSProDiscuss™

- The MSProDiscuss™ algorithm was used to assess disease progression[6-11]. The MSProDiscuss™ algorithm confirms SPMS classification by physicians and revealed a broader distribution in the 'at high-risk for SPMS' population (**Figure 7**).

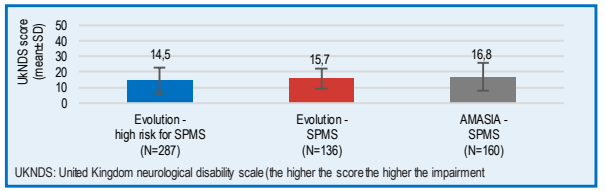
Figure 7: Assessment of progression by MSProDiscuss™



Patients' disability assessment

- UKNDS indicates SPMS patients having higher disease burden (**Figure 8**).

Figure 8. Assessment of disability by UKNDS

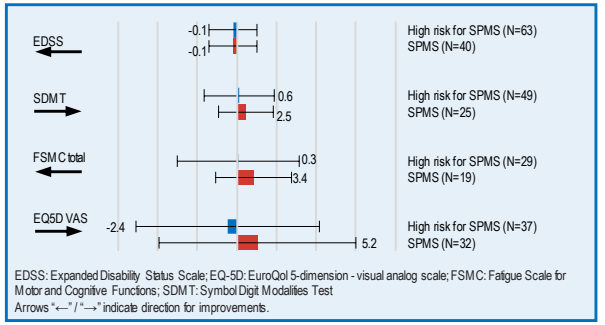


UKNDS: United Kingdom neurological disability scale (the higher the score the higher the impairment

12-Month follow-up data of PANGAEA 2.0 Evolution

- 12-Month follow-up data of PANGAEA 2.0 show higher improvements for patients with SPMS vs patients with high risk for SPMS in SDMT score and EQ5D VAS, but increasing disability in FSMC total score (**Figure 9**).

Figure 9. Evolution Follow-up data - Absolute change from baseline to month 12



EDSS: Expanded Disability Status Scale; EQ-5D: EuroQol 5-dimension - visual analog scale; FSMC: Fatigue Scale for Motor and Cognitive Functions; SDMT: Symbol Digit Modalities Test
Arrows "←" / "→" indicate direction for improvements.

CONCLUSION AND OUTLOOK

- Baseline data of PANGAEA 2.0 Evolution and AMASIA show that SPMS patients are still diagnosed late in the disease progression.
- ➢ Subgroup analyses in the EXPAND study have shown that especially younger patients with an early SPMS diagnosis benefit from a treatment with Siponimod[13], which highlights the need for an earlier diagnosis.
- ➢ Together both studies, Evolution and AMASIA, will contribute to a better understanding of SPMS diagnosis and management in the medical community.

REFERENCES

1. Rio J, et el. 2011; *Curr Opin Neurol.* 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 FC, et al. *Neurology.* 2014 | 5. Shirani A, et al. *Neurotherapeutics.* 2016; 13(1): 58–69 | 6. Ziemssen T, et al. Poster P2.156 presented at AAN 2016 | 7. Simsek D, et al. Poster P241 presented at ECTRIMS 2015 | 8. Piani-Meier D, et al. Poster EP1401 presented at ECTRIMS 2017 | 9. Tolley C, et al. JMIR Med Inform. 2020;8(4):e17592 | 10. Ziemssen T, et al. J Med Internet Res. 2020;22(2):e16932 | 11. Ziemssen T, et al. Mult Scler Relat Disord. 2020;38:101861 | 12. Penner et al 2009 Multiple Sclerosis 15(12) 1509–1517 | 13. Kappos et al 2018 The Lancet S0140-6736(18)30475-6

DISCLOSURES

B. Rauser is an employee of the Novartis Pharma GmbH, Nuremberg, Germany.
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