SWISSMASIA: Swiss Study of the Impact of Siponimod on SPMS Patients in a Long-term Non-interventional Study

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Introduction

- Siponimod (Mayzent®), a selective modulator of sphingosine-1 phosphate receptors 1 and 5 (S1P1 and S1P5), received Swiss marketing authorization in October 2020 for the treatment of adult secondary progressive multiple sclerosis (SPMS) patients with active disease[1,2,3]
- While the pivotal randomized, phase III EXPAND study demonstrated the safety and efficacy of siponimod in a representative SPMS population, long-term data in routine clinical practice are still missing[3]

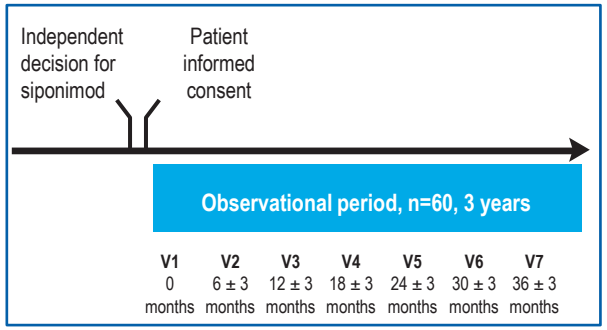
Objective

- To present the study design of the multicenter, non-interventional SWISSMASIA study (Swiss study of the Impact of Mayzent [Siponimod] on secondary progressive multiple sclerosis patients, NCT04895202)
- SWISSMASIA aims to describe the long-term effectiveness and safety of siponimod in clinical routine using clinical and patient-reported outcomes.

Methods

Study design

- SWISSMASIA is a multicenter, non-interventional study conducted in Switzerland with the aim to assess the real-world use of siponimod treatment in SPMS patients with inflammatory disease activity
- The design of SWISSMASIA is based on the German Non-Interventional study AMASIA[4] which will allow for pooled data analysis. Paired comparisons of siponimod-treated patients in the present study with AMASIA, which compares to PANGAEA 2.0 EVOLUTION SPMS patients under previous standard therapy[4] are intended to describe the siponimod treatment effect on clinical parameters, quality of life and socio-economic factors
- A total of 60 SPMS patients with active disease treated with siponimod per the Swiss label and local clinical practice will be enrolled in the study. The observation period will run over 3 years and visits will be recorded every 6 months (± 3 months) according to clinical routine



Inclusion criteria

- Adult patients with a documented diagnosis of SPMS with inflammatory disease activity who are going to be treated with siponimod under routine medical care and in accordance with the Swiss label
- Patients willing to provide written informed consent
- Patients willing and able to complete the questionnaires

Exclusion criteria

- Use of investigational drugs during the study OR within 3 months before enrolment OR within 5 half-lives of the investigational drug before enrolment OR until the expected pharmacodynamic effect has returned to baseline, whichever is longer
- Prior or already ongoing treatment with siponimod
- Patients treated outside of the Swiss label for siponimod
- Subjects who are not able to provide consent due to incapable judgement

Sample size

- Based on the results of the fingolimod non-interventional study,[5] accounting for an adherence of 83% after 3 years, a total of 60 patients should be recruited in the study. Within the recruitment period, patients dropping out of the study can be replaced by newly recruited patients

Primary endpoint

- Change in the Expanded Disability Status Scale (EDSS) score after 36 months of siponimod treatment from baseline

Secondary endpoints

- Proportion of patients with 6-month confirmed disability progression (6mCDP) by EDSS score after 36 months of siponimod treatment
- Proportion of patients with 6mCDP using the Symbol Digit Modalities Test (SDMT)
- Treatment effect of siponimod on walking speed as measured using the Timed 25 Foot Walk Test (T25FWT)
- Treatment effect of siponimod on the clinical course of SPMS, relapses, and magnetic resonance imaging (MRI) parameters vs baseline
- Treatment effect of siponimod on quality of life based on the 5-dimension EuroQOL (EQ-5D) after 36 months vs baseline
- Treatment effect of siponimod on fatigue (measured using the Fatigue Scale for Motor and Cognitive Functions [FSMC], Beck Depression Inventory [BDI], and Epworth Sleepiness Scale (ESS) questionnaires) and upper limb function (measured using the Nine-Hole Peg test) after 36 months vs baseline
- Exposure-adjusted percentage of patients with non-serious and serious adverse events

Exploratory endpoints

- Percentage of MSProDiscuss usage in clinical routine and correlation of the MSProDiscuss score with disease progression
- Percentages of patients receiving a reduced dose of 1 mg vs 2 mg siponimod according to the information provided by the CYP2C9 genotype
- Sampling and storage of blood/plasma samples collected during standard visits at the central facility for retrospective analysis for established disease biomarkers
- Outcome differences based on paired comparisons of siponimod-treated patients from SWISSMASIA with participants in the PANGAEA study

Statistical methods

- Documented variables in this non-interventional study will be evaluated using appropriate statistical methods and reported. Due to the observational character of this study, primarily descriptive methods will be used

Results

- SWISSMASIA was approved by the competent ethics committee on August 4, 2021 (BASEC-Number: 2021-01005), and the first patient was enrolled on November 19, 2021. First results are expected in 2024.

Conclusion

- The efficacy and safety of siponimod in SPMS was demonstrated in phase III EXPAND study (NCT01665144). This study will generate real world effectiveness and safety data from Swiss patients

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