A First Look at the Characteristics of Patients with Multiple Sclerosis Initiating Siponimod Therapy in the United States

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Disclosures

Roshani Shah, Gina M. Cox, and Kristen M. Johnson are employees of Novartis Pharmaceuticals Corporation, East Hanover, NJ, USA.

Magdaliz Gorritz, Rolin L. Wade, Jasjit K. Multani, and Hsiu-Ching Chang are employees of IQVIA Inc., Plymouth Meeting, PA, USA.

Karishma Shelley was an employee of Thomas Jefferson University, Philadelphia, PA and was providing services to Novartis Pharmaceutical at time of the study.

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Background and objective

- In March 2019, siponimod was approved in the United States (US) for the treatment of relapsing forms of multiple sclerosis (MS) in adults, including clinically isolated syndrome, relapsing-remitting disease, and active secondary progressive disease[1].
- The approved indication is broader than the secondary progressive MS (SPMS) patient population studied in the EXPAND study, the largest Phase 3 clinical trial in SPMS patients that demonstrated siponimod significantly reduced risk of confirmed disease progression, including physical disability and cognitive decline[2].

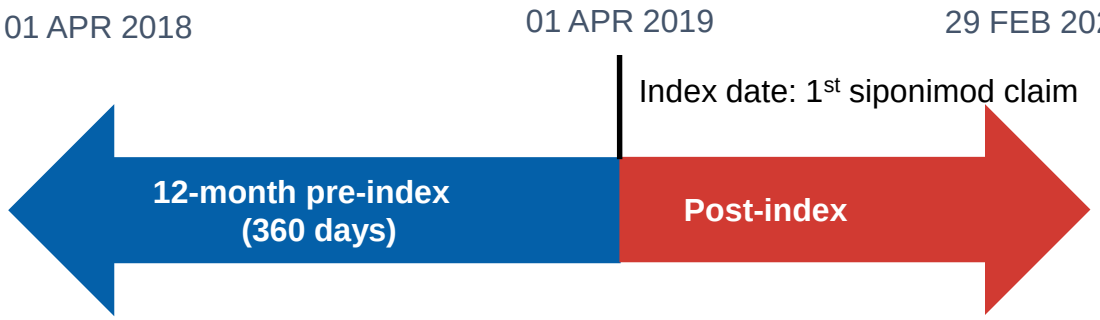
Objective	**To describe characteristics of siponimod users in the first 10 months following US approval using linked pharmacy and medical administrative claims data.**

1. Novartis Pharmaceuticals Corporation. Mayzent (siponimod) [package insert]. US Food and Drug Administration; 2. Kappos L, et al. *The Lancet.* 2018; 391: 1263-73.

Methods: Study design, outcomes, and statistical analysis

- Study design:
  - Retrospective study of patients initiating siponimod between 01 APR 2019 and 29 FEB 2020 with a 12-month baseline period (Figure 1).
- Data source:
  - IQVIA's open source pharmacy claims database (LRx) linked to medical claims database (Dx)
- Summary statistics:
  - Continuous variables: mean, standard deviation (SD)
  - Categorical variables: frequency, proportions
- Variables measured at baseline:
  - Demographic characteristics
  - Comorbid conditions
  - Charlson Comorbidity Index (CCI)
  - Disability level[1]
  - MS relapse
  - Pre-index durable medical equipment (DME) use
  - Pre-index MS medications

Figure 1: Study schema



Disease disability level[1] was based on the presence of claims with EDSS-related ICD-9/10 diagnosis codes or use of DME, defined using the following hierarchy:

- Severe: defined as having ≥1 EDSS-related symptom with severity score=3 in any functional system
- Moderate: defined as having ≥1 EDSS-related symptom with severity score=2 in any functional system, or having ≥ 2 functional systems with severity score=1
- Mild: defined as having only one EDSS-related symptom with severity score=1 or having no EDSS-related symptoms observed during the measurement period.

1. Berkovich R, et al. *Multiple Sclerosis Journal*. 2019; 25: 113-4 (Proxy disability level were assessed using MS symptoms (mild, moderate, severe) based on Berkovich et al. 2019.

DME: Durable medical equipment; EDSS: Expanded disability status scale; ICD: International Classification of Diseases; MS: Multiple sclerosis; SD: Standard deviation

Results

Patient attrition based on study inclusion and exclusion criteria

Figure 2: Patient Attrition

Patients with ≥1 claim for siponimod in LRx between 01 APR 2019 and 29 FEB 2020 (the date of the first observed claim within this window served as the index date)	N=2,272
Patients aged ≥18 years at index date	N=2,249
Patients with non-missing gender	N=2,249
Patients receiving prescriptions from pharmacies that consistently reported data in the 12-month pre-index period	N=2,189
Linkage to the Dx database	N=1,968
Patients with ≥2 medical claims with a diagnosis of MS in Dx at least 30 days apart within the 12-month pre-index period	N=1,081

Dx: IQVIA Medical Claims Database; LRx: IQVIA Longitudinal Prescription Database; MS: Multiple sclerosis

Results

Baseline characteristics

- A total of 1,081 siponimod patients were identified and included in the analysis.
- Most of the patients (63.1%) were in the 45-64 year age group at siponimod initiation, were generally female (75.9%), and from a Southern US geographic region (31.0%) (Figure 3A, 3B).
- The mean (SD) Charlson Comorbidity Index score was 0.7 (1.1).
- Depression, UTIs, and fatigue were the most common MS-related comorbidities observed (Figure 3C).
- A MS relapse occurred in 28% of patients in the prior year.

Figure 3A: Age (years)

Mean (SD): 53.4 (11.4) years

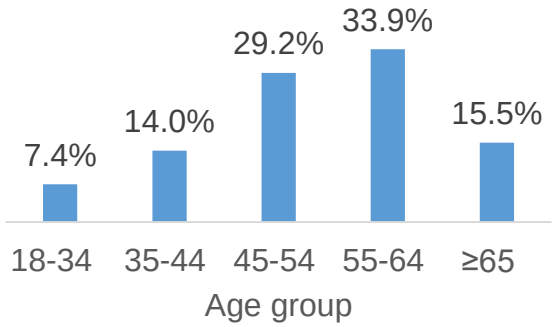


Figure 3B: Geographic region (US)

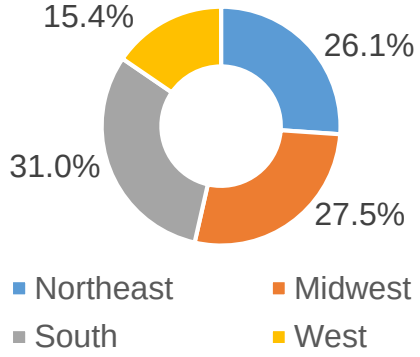
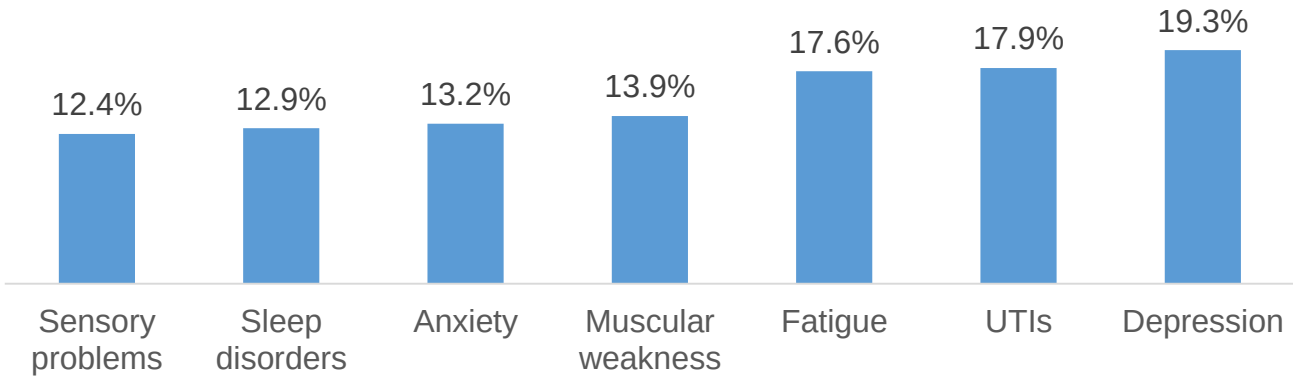


Figure 3C: Proportion of patients with MS-related comorbidities



MS: Multiple sclerosis; SD: Standard deviation; US: United States; UTI: Urinary tract infection

Results

Baseline characteristics (continued)

- Most patients (n=651; 60.2%) had no evidence of DMT use in the prior year (Table 1).
- Among 430 patients with DMT use in the prior year:
  - 57.9% were still on a DMT in 60 days prior to initiating siponimod, suggesting these patients were switching DMTs (Table 1).
  - The most common DMTs used prior to siponimod were dimethyl fumarate (21%), fingolimod (20%), and glatiramer acetate (19%) (Table 1).
  - Majority of the siponimod patients switched from oral medications (57%), 32% had switched from platform DMTs†, and 11% from infusion (Table 1).

Table 1: DMT use in prior one year (N=1,081)

No DMT	651 (60.2%)
Any DMT	430 (39.8%)
Oral*	246 (57.2%)
Dimethyl fumarate	91 (21.2%)
Fingolimod	88 (20.5%)
Teriflunomide	67 (15.6%)
Infusible*	48 (11.2%)
Natalizumab	36 (8.4%)
Ocrelizumab	7 (1.6%)
Rituximab	5 (1.2%)
Platform DMTs	136 (31.6%)
Glatiramer acetate	81 (18.8%)
Interferon beta-1a	37 (8.6%)
Interferon beta-1b	10 (2.3%)
Pegylated interferon beta-1a	8 (1.9%)
Previous DMT <60 days prior to siponimod initiation	249 (57.9%)

*There were no patients on alemtuzumab and cladribine in the prior one year; †interferons/glatiramer acetate
DMT: Disease modifying therapy; MS: Multiple sclerosis

Results

Baseline characteristics (continued)

- At siponimod initiation, the majority (>60%) of patients had moderate or severe disability[1] (Figure 4).
- Durable medical equipment (DME) use was observed in 118 (11%) patients, mostly for wheelchairs (36%) and walkers (32%) (Table 2).

Figure 4: Baseline disability level among patients initiating siponimod[1$]

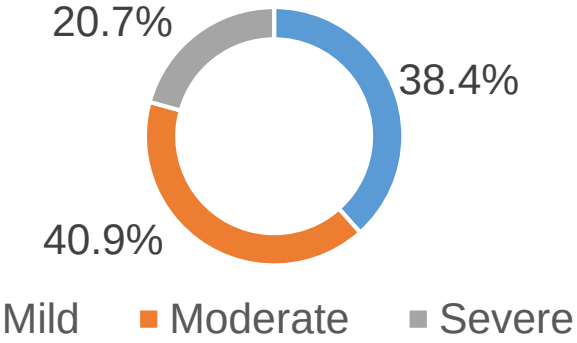


Table 2: Durable medical equipment use (N=118)

Brace	24 (20.3%)
Cane	1 (0.8%)
Crutches	1 (0.8%)
Walker	38 (32.2%)
Wheelchair	43 (36.4%)
Hospital bed	26 (22.0%)

1. Berkovich R, et al. *Multiple Sclerosis Journal*. 2019; 25: 113-4 (Proxy disability level was assessed using MS symptoms (mild, moderate, severe) based on Berkovich et al. 2019.
[$]Measured by the occurrence of EDSS-related symptoms as defined in the methods. EDSS: Expanded disability status scale

Limitations

- The IQVIA LRx and Dx databases are ‘open’ source databases, therefore continuous enrollment of medical and pharmacy benefits could not be confirmed. It is possible that healthcare services were not recorded if the patient sought care outside of the network that contributes data to LRx/Dx.
- These databases comprise data from ambulatory pharmacies and physician offices. Thus, generalizability to populations treated in inpatient or institutional settings such as long-term care facilities may be limited.
- For Dx, medical claims data comes from claims that are used for reimbursement. Any information that is not needed for reimbursement is unlikely to be included.
- This was an early post-marketing study, and patients selected for early use of a newly approved product may not be representative of the larger MS population.
- Due to limited data available, sample size in this study is small and no post-index evaluation was conducted.
- Finally, there were some missing data points for redundant e.g. there was no data for cladribine use in prior year since cladribine was approved for use in the US in March 2019.

Dx: IQVIA Medical Claims Database; LRx: IQVIA Longitudinal Prescription Database; MS: Multiple sclerosis; US: United States

Conclusions

- This is the first study from the US reporting patient demographics, clinical characteristics, and pre-index treatment patterns of early siponimod initiators using an open source patient level data asset. The study indicates that the early siponimod patient population is generally consistent with that reported in the pivotal trial[1].
- The study suggests that siponimod is being used in an older MS patient population with moderate-to-severe disability. Most patients had no DMT use in the year prior to siponimod initiation, suggesting siponimod fulfills an unmet need in this population.

1. Kappos L, et al. *The Lancet*. 2018; 391: 1263-73.
DMT: Disease modifying therapy; MS: Multiple sclerosis; US: United States