Profile of patients with multiple sclerosis on oral disease-modifying therapies while enrolled in North American Registry for Care and Research in Multiple Sclerosis (NARCRMS)

RWD128

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Introduction

- Multiple sclerosis (MS) is an autoimmune, inflammatory, and neurodegenerative disease of the central nervous system[1]
- Guidelines recommend that disease-modifying therapies (DMTs) be considered for patients based on the evidence that these medications can reduce relapse, slow disease progression, and improve patient outcomes[1-3]
- DMTs are available in oral and non-oral (eg, injectable) formulations[1]
- As treatment options in MS expand, there is a need to characterize patients with MS by their medication's route of administration

Objective

- **Primary:** Characterize patients with MS who were receiving daily oral DMTs at enrollment in the North American Registry for Care and Research in Multiple Sclerosis (NARCRMS)
- **Secondary:** Compare patients with MS receiving daily oral DMTs at enrollment with
  - Overall MS cohort in NARCRMS
  - Patients receiving non-oral DMTs at enrollment

Methods

Study design

- A retrospective cohort study was conducted using registry data from NARCRMS between 2016 and 2021

NARCRMS

- NARCRMS is a physician/clinician-based registry and longitudinal database of MS patients from MS Centers across the United States and Canada
- Implemented in 2016, NARCRMS is a project of the Consortium of MS Centers and a collaborative partnership between industry, academic centers, general practice, and patients
- At the time of this analysis (July 2021), the registry included 889 patients with MS with up to 3 years of follow-up data from 26 sites

Population inclusion criteria

- Overall cohort
  - Patients aged 18–65 years with relapsing or progressive MS
  - Patients with a clear date of onset within 15 years
  - Patients with Expanded Disability Status Scale (EDSS) scores ≥6.5 at enrollment
- Oral cohort
  - Patients receiving any of the daily oral DMTs at enrollment: Tecfidera (dimethyl fumarate), Gilenya (fingolimod), and Aubagio (teriflunomide)
    - Zeposia (ozanimod) and Mayzent (siponimod) were not found at enrollment for any patients
  - Patients with enrollment consent date and available oral medication start and end dates
- Non-oral cohort
  - All patients not included in the oral cohort (ie, patients receiving Copaxone [glatiramer acetate], Rebif [interferon beta-1a], Avonex [interferon beta-1a], Betaseron [interferon beta-1b], Glatopa [glatiramer acetate], Extavia [interferon beta-1b], Zinbryta [daclizumab], Tysabri [natalizumab], Ocrevus [ocrelizumab], Lemtrada [alemtuzumab], Rituxan [rituximab], or other non-oral DMTs)
  - Patients with enrollment consent date and available oral medication start and end dates

Population exclusion criteria

- Patients with any concomitant confounding disorders, including neuromyelitis optica and idiopathic isolated transverse myelitis, and/or known autoimmune disorders that can cause neurologic disorders

Variables of interest

- The following were assessed at enrollment and annual follow-up visits:
  - Patient demographics data (collected at enrollment only)
  - Health-related productivity data recorded via Health-Related Productivity Questionnaire
  - EDSS scores (a measure for quantifying disability in MS and monitoring changes in the level of disability over time; EDSS scale scores range from 0 to 10 in increments of 0.5, with higher scores indicating higher levels of disability)

Statistical analyses

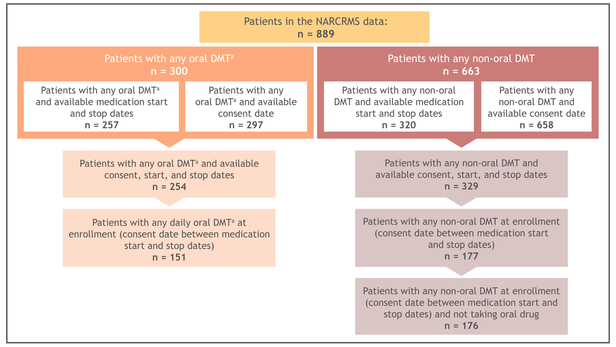
- Descriptive statistics were conducted to describe patient profiles for all cohorts (overall, oral, and non-oral)
- Statistical comparisons were carried out using Chi-square tests or Fisher's exact test for categorical variables, and Wilcoxon rank sum test or Student's *t*-test for continuous variables

Results

Patient attrition

- The overall study population comprised the 889 patients with MS in NARCRMS at the time of data analysis (**Figure 1**)
  - Oral cohort: 151 patients receiving oral DMTs at enrollment
  - Non-oral cohort: 176 patients receiving non-oral DMTs at enrollment

Figure 1. Patient attrition



[a]Dimethyl fumarate, fingolimod, teriflunomide, or cladribine. Patients taking cladribine were excluded from analysis. At enrollment, 86 patients were taking dimethyl fumarate, 46 were taking fingolimod, and 18 were taking teriflunomide.
DMT, disease-modifying therapy; NARCRMS, North American Registry for Care and Research in Multiple Sclerosis.

Patient demographics

- The majority of patients in each cohort was female and White and had a mean age of ~34 years at MS diagnosis (**Table 1**)
- No statistically significant differences were noted between cohorts

EDSS scores

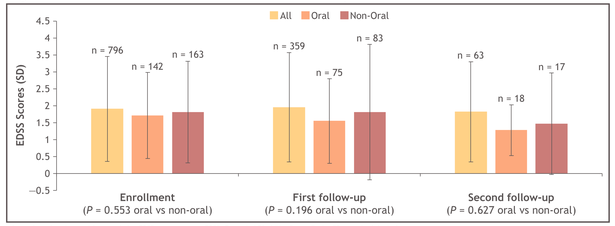
- **Figure 2** presents EDSS scores at enrollment and follow-up visits
- Overall vs oral cohorts
  - Mean EDSS scores at enrollment did not differ between the overall and oral cohorts (1.9 and 1.7, respectively)
  - At first and second follow-up, scores were significantly higher in the overall cohort
    - Year 1: 1.96 and 1.55 ($P = 0.016$)
    - Year 2: 1.82 and 1.28 ($P = 0.04$)
- Oral vs non-oral cohort: Mean EDSS scores did not differ significantly at enrollment or follow-up

Table 1. Patient demographics

	All[a]		Oral DMT		Non-oral DMT		*P* value (oral vs non-oral DMT)
Cohorts	**N**	**%**	**n**	**%**	**n**	**%**	
Total patients	**889**		**151**		**176**		
Sex							
n[b]	851		151		176		
Female	635	74.6	117	77.5	133	75.6	0.697
Male	213	25.0	34	22.5	43	24.4	
Transgender male	3	0.4	0	0	0	0	
Age at diagnosis of MS							
n[b]	779		141		164		0.681
Mean	34.6		34.3		33.9		
SD	9.8		9.7		9.8		
Race (self-identified)							
n[b]	851		151		175		
Caucasian/White	729	85.7	136	90.0	154	88.0	0.704
African American/Black	91	10.7	10	6.6	16	9.1	
Other	31	3.6	5	3.3	5	2.9	
Marital status							
n[b]	858		151		176		
Married	481	56.1	91	60.3	93	52.8	
Single (never married)	234	27.3	38	25.2	50	28.4	0.516
Divorced/separated	95	11.1	18	11.9	23	13.1	
Living with partner	43	5.0	4	2.7	8	4.6	
Widowed	5	0.6	0	0	2	1.1	
Highest completed level of education							
n[b]	856		151		176		
Less than high school	4	0.5	1	0.7	0	0	
High school graduate (through grade 12)	192	22.4	35	23.2	35	19.9	0.322
Bachelor's, vocational, or associate's degree	483	56.4	79	52.3	102	58.0	
Master's degree and higher	177	20.7	36	23.8	39	22.1	
Smoking status (cigarettes/cigars/ pipes/E-cigarettes)							
n[b]	855		151		175		0.189
No	533	62.3	85	56.3	111	63.4	
Yes	322	37.7	66	43.7	64	36.6	

[a]Includes patients not receiving a DMT. [b]n is the number of patients with non-missing data and the denominator for the percentage calculation for each medical history variable.
DMT, disease-modifying therapy; MS, multiple sclerosis; SD, standard deviation.

Figure 2. EDSS scores at enrollment and follow-up visits



n is number of patients with non-missing EDSS score at entry. EDSS, Expanded Disability Status Scale; SD, standard deviation.

Health-related productivity and resource utilization

- Employment rates did not differ significantly between the overall (73.2%) and oral (70.8%) cohorts
- Both cohorts had a large proportion of patients receiving disability income at first follow-up (overall, 87.6%; oral, 90.0%)
  - 35.3% of overall patients and 45.0% of oral DMT patients who had worked the week prior reported that MS affected work output

Strengths and Limitations

Strengths

- Data from the NARCRMS registry provides a real-world picture of clinical management of patients with MS
- Registries have the potential to provide data to inform future study design, planning, and power calculations for real-world effectiveness studies

Limitations

- Retrospective studies based on observational data can only show associations as opposed to causation, since it is possible that not all confounders have been adjusted for
- Registry data reflect the purpose for which they were collected and the environment from which they were collected; as such, they rely on healthcare workers and others to record patient information completely and accurately
- Treatment was assessed at enrollment, and patients may have switched or discontinued their treatment at any time during the follow-up

Conclusions

- Previous work has shown that there are differences in disease activity, presentation, and disease burden, which were not captured here
- Results suggest, based on the variables collected, that real-world patients with MS receiving oral DMTs at enrollment are similar to MS patients overall and to those receiving non-oral treatment (disease activity parameters were not assessed)
- As MS registries are growing and more treatment options become available, capturing high-quality, long-term data is becoming increasingly important

References

1. Nicholas JA, et al. *BMC Neurol* 2020;20:1-15. **2.** Rae-Grant A, et al. *Neurology* 2018;90:789-800. **3.** Finkelsztejn A. *Perspect Medicin Chem* 2014;6:65-72.

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Disclosures

- **HZ** and **TP**: Employees and shareholders of Bristol Myers Squibb
- **XC**: Employee and shareholder of Bristol Myers Squibb at the time of study

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