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An assessment of adherence among multiple sclerosis patients newly initiating treatment with a self-injectable versus oral disease-modifying drug

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Introduction

- Multiple sclerosis (MS), a chronic, recurrent inflammatory disease of the white and gray matter of the central nervous system (CNS), is characterized by inflammatory attacks on CNS myelin, which result in a variety of symptoms such as blurred vision, walking and coordination problems, bladder or bowel dysfunction, numbness, and cognitive impairment.[1]
- Relapsing–remitting MS, which accounts for approximately 85% of MS diagnoses, is characterized by defined attacks or relapses that result in worsening of neurological function, with partial to complete recovery between attacks.[1]
- Several disease-modifying drugs (DMDs) have been developed to reduce relapse rates and delay disability progression.[1]
- Adherence to DMD treatment is associated with improved clinical outcomes, including a lower risk of MS relapse.[2,3]
- As the MS DMD class expands with oral entrants, it is important to understand how oral therapy may affect treatment adherence.

Objective

- To compare adherence to DMDs among patients with MS initiating an oral DMD versus patients initiating a self-injectable DMD.

Methods

Study design and patients

- Patients were identified from a retrospective database (IMS PharMetrics Plus) between July 1, 2010 and June 30, 2013 and were divided into two treatment cohorts based on the DMD route of administration: Cohort 1 (oral DMD users) and Cohort 2 (self-injectable DMD users). In both cohorts, patients had ⩾1 medical claim (at any service location) with a diagnosis for MS (International Classification of Diseases, Ninth Revision, Clinical Modification code 340.xx).
- Eligible patients had ⩾1 prescription for either an oral or a self-injectable DMD after the MS diagnosis; the date of the first prescription was the index date. Included patients had no use of any DMD during the 12 months prior to the index date and had continuous eligibility for the 12 months before and after the index date. Patients were aged 18 to 64 years at the index date.
- Oral and self-injectable DMDs included in the study are listed in **Table 1**.

Table 1. Oral and self-injectable DMDs.

DMD type	Brand name	Generic name
Oral	Aubagio[®a]	Teriflunomide
Oral	Gilenya[®b]	Fingolimod
Oral	Tecfidera[®c]	Dimethyl fumarate
Self-injectable	Avonex[®c]	Interferon beta-1a
Self-injectable	Betaseron[®d]	Interferon beta-1b
Self-injectable	Copaxone[®e]	Glatiramer acetate
Self-injectable	Extavia[®f]	Interferon beta-1b
Self-injectable	Rebif[®g]	Interferon beta-1a

DMD, disease-modifying drug.
[a]Genzyme Corporation, Cambridge, MA, USA.
[b]Novartis Pharma Stein AG, Stein, Switzerland.
[c]Biogen Idec Inc., Cambridge, MA, USA.
[d]Bayer HealthCare Pharmaceuticals Inc., Whippany, NJ, USA.
[e]Teva Neuroscience, Inc., Overland Park, KS, USA.
[f]Bayer HealthCare Pharmaceuticals Inc., Montville, NJ, USA.
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Follow-up outcomes

DMD adherence

- A continuous measure representing the annual medication possession ratio (MPR) during the follow-up period was evaluated to measure adherence to the index DMD route of administration (ie, oral or self-injectable).
  - The annual MPR was calculated as total number of treated days of follow-up divided by total number of days from first treated day until end of follow-up. A day with any DMD medication was considered a treated day, as multiple medications (ie, all orals or all self-injectables) could be used.
  - The calculation was restricted to ambulatory days (ie, days when the patient was not in the hospital).
- A binary measure representing adherence (MPR ⩾0.8) versus nonadherence (MPR <0.8) to therapy was used.

DMD discontinuation and switching

- A categorical measure representing three mutually exclusive treatment outcomes was evaluated and defined as follows:
  - *Discontinuation* was defined as the absence of the index DMD for a 90-day period during follow-up, without evidence of another DMD during that time.
  - *Switching* was defined as the presence of any other (non-index) DMD during a 90-day period without the index DMD during follow-up.
  - *Remaining* on the index DMD was defined as no absence of the index DMD for a 90-day gap during follow-up.
- A continuous measure of average time to discontinuation was assessed among patients who discontinued their index DMD.
- A categorical measure representing the DMD type to which patients switched (oral, self-injectable, or other [natalizumab or mitoxantrone]) was evaluated among patients who switched.

Descriptive analysis

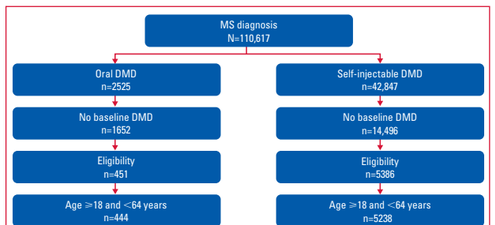
- Baseline demographic and clinical characteristics were evaluated for patients in both cohorts.
- All descriptive analyses included mean, median, standard deviation, minimum, maximum, and interquartile ranges for continuous measures, and proportions for binary and categorical measures.
- All measures concerning DMD adherence, discontinuation, and switching were evaluated for patients in both cohorts. Patients without valid days of supply values (ie, non-missing and >0) on relevant prescriptions were excluded from analyses of adherence, discontinuation, and switching.
- Statistical testing of differences between cohorts was evaluated with Fisher's exact and Wilcoxon rank-sum tests for binary/categorical and continuous measures, respectively.

Multivariate analysis

- Logistic regression was used to evaluate the likelihood of nonadherence to the index DMD therapy class (ie, MPR <0.8).
- Covariates included patient demographics (age, sex, baseline comorbidities) and the index treatment type (oral vs self-injectable).

Results

- A total of 444 patients with an oral DMD and 5238 patients with a self-injectable DMD met the inclusion criteria and were included in the assessment (**Figure 1**).



DMD, disease-modifying drug; MS, multiple sclerosis.
Figure 1. Patient selection flowchart.

- Baseline patient characteristics for both treatment cohorts, including age ranges, Charlson Comorbidity Index (CCI) score, and select common MS comorbidities, are shown in **Table 2**.
  - Mean age was similar between the two groups (44.05 [oral] vs 43.00 [self-injectable] years).
  - A greater proportion of patients with oral DMDs were from the South, and a greater proportion of patients with self-injectable DMDs were from the Northeast (34.2% vs 28.4% and 32.8% vs 27.5%, respectively; p<0.05).
  - Mean CCI score was higher among patients with self-injectable DMDs compared with those with oral DMDs (0.55 vs 0.42).
  - The most common comorbidity in both cohorts was hypertension, present in approximately 21–23% of patients.
  - Anxiety was more common among self-injectable DMD users (12.5% vs 9.0% of oral DMD users; p<0.05), while depression was more common among oral DMD users (8.1% vs 5.5% of self-injectable DMD users; p<0.05).

Table 2. Baseline demographic and clinical characteristics of patients with MS newly initiating a DMD.

Characteristic	Oral DMD	Self-injectable DMD	p value
n	444	5238	–
Age, years, mean (SD)	44.05 (9.72)	43.00 (10.39)	0.0418
Age group, years, n (%)			0.0562
18–34	79 (17.8)	1205 (23.0)	–
35–44	140 (31.5)	1631 (31.1)	–
45–54	154 (34.7)	1601 (30.6)	–
55–64	71 (16.0)	801 (15.3)	–
Female, n (%)	335 (75.5)	4045 (77.2)	0.4103
Region, n (%)			0.0183
Northeast	122 (27.5)	1719 (32.8)	–
Midwest	150 (33.8)	1717 (32.8)	–
South	152 (34.2)	1487 (28.4)	–
West	20 (4.5)	315 (6.0)	–
CCI score, mean (SD)	0.42 (0.92)	0.55 (1.06)	0.0023
Select comorbidities, n (%)			
Anxiety	40 (9.0)	655 (12.5)	0.0343
Arthritis (RA/OA)	29 (6.5)	391 (7.5)	0.5097
Depression	36 (8.1)	289 (5.5)	0.0324
Diabetes	28 (6.3)	411 (7.8)	0.2672
Gastrointestinal disease[a]	83 (18.7)	876 (16.7)	0.2911
Hypertension	94 (21.2)	1219 (23.3)	0.3481
Thyroid disease	59 (13.3)	820 (15.7)	0.1946

CCI, Charlson Comorbidity Index; DMD, disease-modifying drug; MS, multiple sclerosis; OA, osteoarthritis; RA, rheumatoid arthritis; SD, standard deviation.
[a]Including constipation, diarrhea, dysphagia, gastroesophageal reflux disease, and irritable bowel syndrome.

- In both cohorts, the majority of patients who switched to another DMD switched to a self-injectable. No patients in the oral DMD cohort switched to another oral DMD, although only 25 patients in the oral group had switched. Factors influencing adherence and discontinuation are compared in **Table 3**.
  - Over the follow-up period, overall mean MPR in each cohort was similar (0.71 [oral] vs 0.70 [self-injectable]).
  - The proportion of patients adherent to therapy did not differ significantly between the oral DMD cohort (58.2%) and the self-injectable DMD cohort (54.8%; p=not significant [NS]).
  - A higher proportion of patients in the oral DMD cohort remained on their index DMD over the follow-up period compared with the self-injectable cohort (70.2% vs 64.6%; p=0.0130).
  - A similar proportion of patients in the self-injectable DMD cohort discontinued their index DMD compared with patients in the oral DMD cohort (27.0% vs 24.2%; p=NS).
  - Significantly more patients in the self-injectable DMD cohort switched to another DMD compared with patients in the oral DMD cohort (8.4% vs 5.6%; p=0.0464).
  - Among patients who discontinued their index DMD, the average time to discontinuation was similar in both cohorts (116.92 [oral] vs 116.32 [self-injectable] days; p=NS).

Table 3. Adherence and discontinuation characteristics among patients with MS newly initiating a DMD.

Characteristic	Oral DMD	Self-injectable DMD	p value
n	444	5238	–
MPR			
n with data available	443	5196	–
Mean (SD)	0.71 (0.28)	0.70 (0.29)	0.1709
Adherent to therapy[a]			
n with data available	443	5196	–
n (%)	258 (58.2)	2850 (54.8)	0.1791
Treatment outcome, n (%)			
n with data available	443	5201	–
Remained on index therapy	311 (70.2)	3359 (64.6)	0.0130
Discontinued index therapy[b]	107 (24.2)	1405 (27.0)	0.1990
Switched to other DMD[c]	25 (5.6)	437 (8.4)	0.0464
Time to discontinuation, days			
n patients who discontinued	107	1405	–
Mean (SD)	116.92 (82.48)	116.32 (78.89)	0.4763
Type of DMD switched to, n (%)			0.0216
n patients who switched	25	437	–
Self-injectable	20 (80.0)	264 (60.4)	–
Oral	0 (0.0)	83 (19.0)	–
Other	5 (20.0)	90 (20.6)	–

DMD, disease-modifying drug; MPR, medication possession ratio; MS, multiple sclerosis; SD, standard deviation.
[a]Defined as MPR ⩾0.8.
[b]Defined as absence of the index DMD for >90 days during the follow-up period without switching to another DMD during those 90 days.
[c]Defined as switching from the index DMD to another DMD.

Predictors of nonadherence

- Factors predictive of DMD nonadherence are shown in **Table 4**.
  - Male (vs female) sex and all age groups older than the 18-to-34-year group were significantly associated with a higher probability of adherence to the index DMD type (odds ratios [ORs] for nonadherence: 0.812 and 0.696–0.812, respectively; p<0.05 for all comparisons).
  - The presence of depression was associated with a significantly higher likelihood of being nonadherent to therapy (OR: 1.722; p<0.0001).
  - Index DMD type was not a significant predictor of DMD nonadherence (OR: 1.144; p=0.1821).

Table 4. Multivariate analysis of predictors of adherence.

Covariate	OR estimate	Lower 95% CI	Upper 95% CI	p value
Male (vs female)	0.812	0.715	0.923	0.0014
Age group, years (vs 18–34)				
35–44	0.812	0.702	0.939	0.0050
45–54	0.754	0.650	0.875	0.0002
55–64	0.696	0.579	0.837	0.0001
Select comorbidities (vs none)				
Anxiety	0.933	0.790	1.103	0.4166
Arthritis (RA/OA)	0.976	0.793	1.201	0.8175
Depression	1.722	1.363	2.176	<0.0001
Diabetes	1.156	0.941	1.420	0.1684
Gastrointestinal disease	1.112	0.962	1.284	0.1506
Hypertension	1.077	0.940	1.233	0.2865
Thyroid disease	1.050	0.904	1.218	0.5243
Self-injectable index DMD (vs oral DMD)	1.144	0.939	1.395	0.1821

CI, confidence interval; DMD, disease-modifying drug; OA, osteoarthritis; OR, odds ratio; RA, rheumatoid arthritis.

Limitations

- A fixed MPR was utilized over a variable MPR (eg, denominator ending at last treated day), which may impact results by underestimating adherence in either cohort.
- Although we attempted to identify patients new to DMD therapy by requiring no DMD claim during the 12-month baseline period, it is possible that patients could have been treated with DMDs prior to the baseline and discontinued for that period. Additionally, patients in the sample were not necessarily newly diagnosed patients with MS.

Conclusions

- In unadjusted analyses, adherence to therapy appeared relatively similar between the cohorts of patients with MS initiating treatment with an oral versus a self-injectable DMD.
- While a higher proportion of patients in the self-injectable DMD cohort switched therapies (p<0.05), a higher proportion also remained on the index therapy (p<0.05), and there was no statistically significant difference in switching rates (p=NS).
- In adjusted analyses, male sex and older age were significantly associated with a lower risk of nonadherence, whereas comorbid depression was associated with a higher risk of nonadherence.
- Index DMD was not a significant predictor of DMD nonadherence.

References

1. Menzin J, *et al. J Manag Care Pharm* 2013;19 (1 Suppl A):S24–40.
2. Tan H, *et al. Adv Ther* 2011;28:51–61.
3. Ivanova JI, *et al. J Med Econ* 2012;15:601–9.

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Disclosures

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