DX51

Real-World Comparison of Relapse Rates in Patients with Multiple Sclerosis Treated with Disease-Modifying Therapies

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INTRODUCTION

- Multiple sclerosis (MS) is a chronic and debilitating disease that affects approximately 570,000 individuals in the USA, and 2.3 million worldwide.[1,2]
- Introduction of the oral disease-modifying therapies (DMTs), such as dimethyl fumarate, fingolimod and teriflunomide, has provided patients and clinicians with treatment alternatives to injectable DMTs (glatiramer acetate and interferon β).[3]
- Therapeutic outcomes in routine clinical practice have the potential to be influenced by factors that are controlled for during clinical trials, including prior disease, treatment history, comorbidities, and disease duration and severity. Evaluation of real-world outcomes, using data provided by medical reimbursement claims, is therefore important for assessing therapeutic effectiveness.
- Real-world data on the comparative effectiveness of DMTs for the management of MS in routine clinical practice are limited.

OBJECTIVE

- To compare annualized relapse rates (ARR) and DMT adherence for patients with MS initiating dimethyl fumarate, interferon β, glatiramer acetate, teriflunomide or fingolimod in routine clinical practice.

METHODS

Data Source

- Truven MarketScan Commercial Claims Databases: Administrative claims and eligibility records of 80 million commercially-insured individuals from the USA:
  - Medical services claims for inpatient and outpatient settings with associated procedures and diagnosis codes
  - Pharmacy dispensing claims
  - Demographic information including age, sex, health plan type and region of residence.
- Data were collected between January 2012 and December 2014, inclusive.

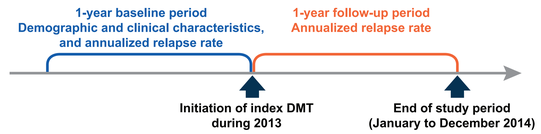
Patient Identification

- Adult patients with MS who initiated an injectable or oral DMT during 2013 were included in the analysis (Figure 1, Figure 2).
- Index date was defined as the date of the first claim for the initiated DMT. Patients were required to have full enrollment 1 year before and 1 year after the index date.

Study Measures

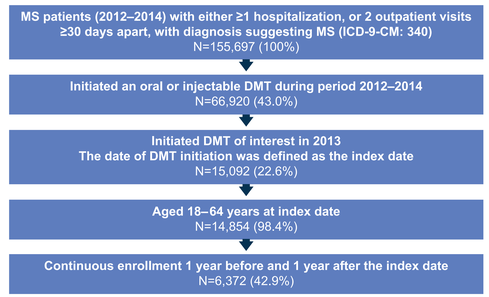
- Patient demographics included age at index date, sex, type of health plan and region of residence.
- Baseline clinical characteristics were assessed based on claims within the 1 year pre-index period and included chronic disease burden (measured by Charlson Comorbidity Index [CCI]) and MS-related symptoms.
  - CCI is a composite score calculated based on the presence of 22 chronic conditions, such as diabetes, peptic ulcer, liver disease and cancer. It was initially developed to predict 10-year mortality and has been widely used to assess chronic disease burden in large retrospective studies.
- ARR, the primary outcome of interest, was calculated based on the number of MS-related relapses (identified from inpatient and outpatient claims) within 1 year after DMT initiation.

Figure 1. Schematic figure of patient selection



DMT, disease-modifying therapy.

Figure 2. Patient selection



DMT, disease-modifying therapy; ICD-9-CM, International Classification of Diseases, Ninth Revision, Clinical Modification; MS, multiple sclerosis.

- Relapse episodes were identified based on a published claim-based algorithm[4] and clinical input from the research investigators.
- Adherence to index DMT was assessed using the proportion of days covered (PDC) in the 1 year after initiation.
  - PDC is defined as the proportion of days during a defined time period for which a patient is "covered" by prescription claims for a medication or another in its therapeutic category. In this analysis, a patient was defined as having "coverage" for a post-index period day if they had a valid prescription claim for a DMT.

Statistical Analysis

- Annual relapse rates were compared pre- and post-DMT initiation for each cohort.
- To adjust for potential confounding, a Poisson regression model was used to estimate the adjusted incidence rate ratios of relapse rate. As the largest patient group, the dimethyl fumarate cohort was used as the reference for the regression.
  - Demographic and clinical characteristics used in the Poisson model included age, sex, region of residence, CCI score, presence of seven MS-related symptoms and number of relapses in the baseline year.

RESULTS

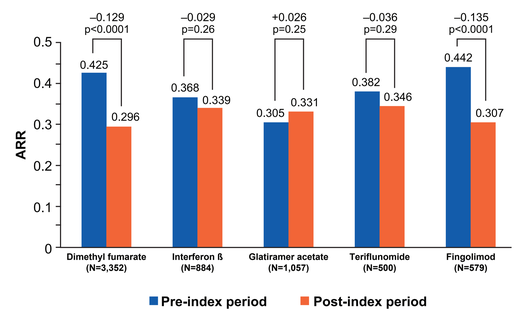
- Overall, 6,372 patients with MS were included in the analysis. Baseline differences between cohorts were observed in age, prior DMT exposure and comorbidities (measured using the CCI) (Table 1).
- Significant decreases in unadjusted relapse rates were observed in the dimethyl fumarate and fingolimod cohorts, consistent with a previous claims database analysis.[5] The largest decreases were observed in the dimethyl fumarate and fingolimod cohorts (–0.129 and –0.135, respectively; Figure 3).
- After adjusting for baseline patient demographics, clinical characteristics and prior DMT exposure, dimethyl fumarate was associated with significantly lower ARR than glatiramer acetate, interferon and teriflunomide. No significant difference was found between the dimethyl fumarate and fingolimod cohorts (Figure 4).
- Patients initiating dimethyl fumarate or fingolimod were more adherent to treatment than patients receiving teriflunomide, glatiramer acetate or interferon β in the 1 year after DMT initiation (Table 2).

Table 1. Baseline demographic and clinical characteristics

	Dimethyl fumarate (N=3,352)	Interferon β (N=884)	Glatiramer acetate (N=1,057)	Teriflun-omide (N=500)	Fingolimod (N=579)	p-value across cohorts*
Age, mean (SD) years	46.7 (9.7)	43.6† (10.8)	43.5† (10.4)	49.6† (8.9)	43.8† (10.1)	<0.0001
Female, % patients	76.6	78.6	79.0	80.0	76.2	0.2147
DMT exposure in pre-index period, % patients	68.7	13.5†	15.7†	66.0	64.2†	<0.0001
CCI score, mean (SD)	0.52 (1.06)	0.71† (1.26)	0.76† (1.33)	0.65† (1.15)	0.42† (0.91)	<0.0001
CCI score, % patients		‡	‡	‡		
0	73.6	68.7	66.7	68.4	77.9	
1	11.1	7.5	10.1	10.2	9.3	
2	10.1	15.6	13.6	13.8	8.5	
≥3	5.2	8.3	9.6	7.6	4.3	

*p<0.05 indicates that one cohort is significantly different from comparator cohorts but does not specify which cohort is different. †Pairwise comparison with dimethyl fumarate significantly different at p<0.05. ‡Pairwise comparison with dimethyl fumarate significantly different at p<0.001.
CCI, Charlson Comorbidity Index; DMT, disease-modifying therapy; SD, standard deviation.

Figure 3. Unadjusted ARR for 1 year before and 1 year after the index date



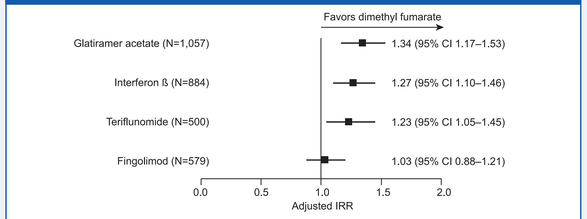
ARR, annualized relapse rate.

Table 2. Adherence to index DMT in the year after DMT initiation

	Dimethyl fumarate (N=3,352)	Interferon β (N=884)	Glatiramer acetate (N=1,057)	Teriflunomide (N=500)	Fingolimod (N=579)
PDC, mean (SD)	0.69 (0.30)	0.63* (0.32)	0.63* (0.31)	0.67* (0.31)	0.79* (0.24)
PDC ≥0.8, % patients	56.2	44.7*	43.4*	51.0†	69.4*

*Pairwise comparison with dimethyl fumarate significantly different at p<0.0001.
†Pairwise comparison with dimethyl fumarate significantly different at p<0.05.
DMT, disease-modifying therapy; PDC, proportion of days covered; SD, standard deviation.

Figure 4. Adjusted IRR of ARR in 1 year after DMT initiation relative to the dimethyl fumarate cohort (N=3,352)



Interpretation: IRR <1 means the ARR of the comparison DMT cohort is lower than the dimethyl fumarate cohort while IRR >1 means the ARR of the comparison DMT cohort is higher than the dimethyl fumarate cohort. For example, an IRR for interferon β vs. dimethyl fumarate of 1.27 means the ARR in the interferon β cohort is 27% higher than the ARR in the dimethyl fumarate cohort after adjusting for baseline differences.
ARR, annualized relapse rate; CI, confidence interval; DMT, disease-modifying therapy; IRR, incidence rate ratio.

Limitations

- Claims data are recorded for accounting purposes and not specifically for clinical research.
- Data did not provide clinical information required to assess disease severity.

CONCLUSIONS

- In this retrospective study of real-world DMT comparative effectiveness in more than 6,000 patients with MS, the largest reductions in unadjusted relapse rates after DMT initiation were observed in the dimethyl fumarate and fingolimod cohorts.
- Dimethyl fumarate is associated with significantly lower ARR than glatiramer acetate, interferon β and teriflunomide after DMT initiation. ARR after DMT initiation was comparable between the dimethyl fumarate and fingolimod cohorts.
- Despite differences in patient demographics and comorbidities between DMT clinical trial populations and these US claims data, the real-world effectiveness reported here is consistent with previous mixed and indirect treatment comparisons based on clinical trial data.[6–8]
- Insights provided by real-world data, and the implications for differences in real-world comparative effectiveness of available DMTs, should be taken into account when making decisions on appropriate therapy for the management of MS.

References

1. Campbell JD, *et al. Mult Scler Relat Disord.* 2014; 3: 227–236.
2. Browne P, *et al. Neurology.* 2014; 83: 1022–1024.
3. Oh J & O'Connor PW. *Curr Opin Neurol.* 2015; 28: 220–229.
4. Chastek BJ, *et al. J Med Econ.* 2010; 13: 618–625.
5. Cramer JA, *et al. Value Health.* 2008; 11: 44–47.
6. Bergvall N, *et al. PLoS One.* 2014; 9: e88472.
7. Hutchinson M, *et al. Curr Med Res Opin.* 2014; 30: 613–627.
8. Tramacere I, *et al. Cochrane Database Syst Rev.* 2015; 9: CD011381.

Disclosures

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