Cost of patients with multiple sclerosis newly initiating subcutaneous interferon β-1a vs oral disease-modifying drugs – a real-world assessment

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Introduction

- In order to achieve the 'Triple Aim' of optimizing health system performance, healthcare payers and providers must simultaneously improve patient quality of care, improve the health of populations, and lower healthcare expenditures.
- Real-world evidence (RWE) involves patient healthcare data collected outside of the randomized controlled trial environment to provide information on relevant health outcomes, including cost of care.[1] This evidence provides insights into unmet needs, interventional pathways, and the clinical and economic effects on patients and the healthcare systems involved.
- Administrative claims datasets provide information on outcomes and healthcare expenditures in actual clinical care settings in a broader patient population.[2,3]
- Self-injectable disease-modifying drugs (DMDs) have historically been the most commonly used DMDs. In recent years, newer DMDs, including oral formulations (ie, dimethyl fumarate, fingolimod, and teriflunomide), have been approved. However, there is limited RWE for the estimated comparative effectiveness of oral DMDs.
  - No published RWE studies directly comparing subcutaneous interferon beta-1a (scIFNβ1a) with oral DMDs were identified in the published literature.
  - Existing studies have often combined scIFNβ1a with other interferons and/or with glatiramer acetate.[4,5]

Objective

- To utilize real-world data to evaluate healthcare expenditures of patients with multiple sclerosis (MS) newly initiating scIFNβ1a versus oral DMDs (ie, dimethyl fumarate, fingolimod, and teriflunomide).

Methods

Data source

- This was a retrospective database study using IMS Health Real World Data (RWD) Adjudicated Claims – US data from January 1, 2012 to June 30, 2014.
- The IMS RWD Adjudicated Claims – US database is an anonymous, HIPAA-compliant, national managed care database that represents approximately 70 million enrollees from over 65 health plans.
- IMS RWD Adjudicated Claims – US data include demographic variables (age, sex, region of the US), eligibility by month, healthcare resource use, and the adjudicated payment for inpatient, outpatient, and pharmaceutical services.

Patient population

- Inclusion criteria selected patients who were between 18 and 65 years of age at index or during the period of observation (65 years of age represents the most frequent age for transition to Medicare), with at least one medical claim with a diagnosis for MS (International Classification of Diseases, Ninth Revision, Clinical Modification [ICD-9-CM] code: 340.xx) and at least one prescription for scIFNβ1a, dimethyl fumarate, fingolimod, or teriflunomide after MS diagnosis between January 1, 2012 and June 30, 2013.
- The date of the first DMD prescription was the index date.
- In order to examine patients new to treatment (treatment naïve), any patient with a DMD during the 12 months prior to the index date was excluded.
- Continuous eligibility for the 12 months before and 12 months after the index date was required.

DMD treatment outcomes – healthcare expenditures

- Healthcare expenditures were assessed during the first year following treatment initiation and were adjusted to October 2014 US dollars using the Medical Services component of the Consumer Pricing Index.
- Healthcare expenditures excluding DMD treatment costs were also evaluated and compared among groups.

Descriptive/univariate analyses

- Baseline demographic and clinical characteristics were compared among the scIFNβ1a and oral DMD cohorts (ie, dimethyl fumarate, fingolimod, and teriflunomide).
- For descriptive (ie, unadjusted) analyses, categorical variables were summarized using frequencies and percentages, and continuous variables were summarized using means (with confidence intervals), standard deviations, and medians.
- Pairwise Chi-square tests were conducted using scIFNβ1a as the reference group (ie, all pairwise comparison with scIFNβ1a). Continuous variables were tested with *t*-tests using scIFNβ1a as the reference group.

Multivariable analyses

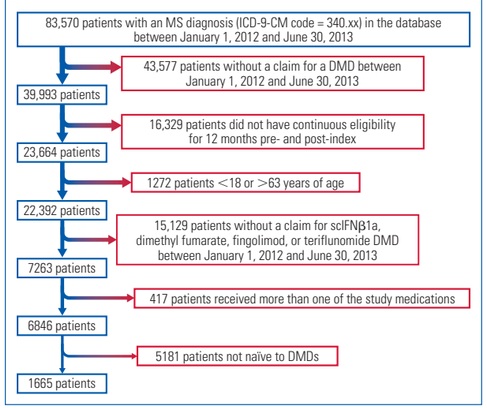
- Generalized linear models with gamma distribution and log link assessed healthcare expenditures with scIFNβ1a versus dimethyl fumarate, fingolimod, or teriflunomide.
- Covariates included patient demographics (ie, age, sex, region) and clinically meaningful measures of disease severity (ie, 90-day pre-index indicators for relapse, neurologist/established patient visits, and magnetic resonance imaging [MRI]).
  - 90 days was selected as a time period that would be likely to have utilization that was associated with the initiation of DMD therapy.
- Models were evaluated for interactions with each individual DMD treatment.

Results

Patient selection

- A total of 1665 patients (686 scIFNβ1a, 406 dimethyl fumarate, 455 fingolimod, and 118 teriflunomide) met the inclusion criteria (**Figure 1**).

Figure 1. Patient selection flowchart.



DMD, disease-modifying drug; ICD-9-CM, International Classification of Diseases, Ninth Revision, Clinical Modification; MS, multiple sclerosis; scIFNβ1a, subcutaneous interferon beta-1a.

Baseline characteristics

- Baseline patient demographic and clinical characteristics for the treatment cohorts are shown in **Table 1**.
  - Patients initiating scIFNβ1a were statistically significantly younger compared with patients initiating oral DMDs.
  - A significantly greater proportion of patients initiating scIFNβ1a were from the Midwest compared with patients initiating teriflunomide. A significantly greater proportion of patients initiating dimethyl fumarate and teriflunomide were from the Northeast compared with patients initiating scIFNβ1a. A significantly greater proportion of patients initiating dimethyl fumarate were from the West and a significantly lower proportion were from the South compared with scIFNβ1a patients.
  - Patients initiating scIFNβ1a had a significantly lower comorbidity score during the year prior to initiating treatment compared with patients initiating dimethyl fumarate.
  - A significantly smaller proportion of patients initiating scIFNβ1a had: depression or gastrointestinal disease compared with patients initiating oral agents; arthritis or thyroid disease compared with patients initiating teriflunomide; and anxiety compared with patients initiating dimethyl fumarate.
- Clinically meaningful measures of patient baseline severity are presented in **Table 2**.
  - A significantly greater proportion of patients initiating scIFNβ1a had 90-day pre-index relapses compared with patients initiating fingolimod.
  - A significantly greater proportion of patients initiating dimethyl fumarate had 90-day pre-index neurologist/established patient visits compared with patients initiating scIFNβ1a.
  - A significantly greater proportion of patients initiating scIFNβ1a had 90-day pre-index MRIs compared with patients initiating fingolimod and teriflunomide.

DMD treatment outcomes – healthcare expenditures

- Generalized linear models predicting healthcare expenditures during the first year on treatment after adjustment for demographics and clinically meaningful disease severity indicators are shown in **Table 3**.
- After adjustment for demographics and clinically meaningful disease severity indicators, the estimated least squares mean total healthcare expenditure for scIFNβ1a ($57,558) was statistically significantly lower than for dimethyl fumarate ($69,798; p<0.0001) and fingolimod ($69,478; p<0.0001).
- After adjustment for demographics and clinically meaningful disease severity indicators, the estimated total healthcare expenditure without DMD-related expenditures for scIFNβ1a ($13,562) was statistically significantly lower compared with dimethyl fumarate ($20,987; p<0.0001), fingolimod ($15,840; p=0.0234), and teriflunomide ($17,148; p=0.0350).

Table 1. Baseline demographic and clinical characteristics of patients with MS newly initiating scIFNβ1a, dimethyl fumarate, fingolimod, or teriflunomide.

Characteristic	scIFNβ1a	Dimethyl fumarate	Fingolimod	Teriflunomide
n	686	406	455	118
Age, years, mean (SD)	42.1 (10.3)	**46.4 (9.8)****	**45.2 (9.6)****	**48.2 (7.3)****
Female, n (%)	516 (75.2)	312 (76.8)	336 (73.8)	93 (78.8)
Region, n (%)				
Northeast	176 (25.7)	**131 (32.3)***	115 (25.3)	**44 (37.3)***
Midwest	263 (38.3)	135 (33.3)	152 (33.4)	**33 (28.0)***
South	207 (30.2)	**96 (23.6)***	162 (35.6)	32 (27.1)
West	40 (5.8)	**44 (10.8)****	26 (5.7)	9 (7.6)
CCI score, mean (SD)	0.54 (1.13)	**0.70 (1.28)***	0.43 (0.85)	0.58 (0.88)
Select comorbidities, n (%)				
Anxiety	66 (9.6)	**67 (16.5)****	50 (11.0)	17 (14.4)
Arthritis (RA/OA)	40 (5.8)	30 (7.4)	26 (5.7)	**15 (12.7)***
Depression	86 (12.5)	**89 (21.9)****	**82 (18.0)***	**25 (21.2)***
Diabetes	45 (6.6)	36 (8.9)	29 (6.4)	8 (6.8)
Gastrointestinal disease[a]	91 (13.3)	**87 (21.4)****	**86 (18.9)***	**27 (22.9)***
Hypertension	137 (20.0)	92 (22.7)	100 (22.0)	26 (22.0)
Thyroid disease	94 (13.7)	71 (17.5)	68 (14.9)	**27 (22.9)***

Bolded values denote significance.
CCI, Charlson Comorbidity Index; MS, multiple sclerosis; OA, osteoarthritis; RA, rheumatoid arthritis; scIFNβ1a, subcutaneous interferon beta-1a; SD, standard deviation.
[a]Including constipation, diarrhea, dysphagia, gastroesophageal reflux disease, and irritable bowel syndrome.
*p<0.05 using pairwise Chi-square test or independent sample *t*-test versus scIFNβ1a as the standard (no adjustment for multiplicity); **p<0.005 using pairwise Chi-square test or independent sample *t*-test versus scIFNβ1a as the standard (no adjustment for multiplicity).

Table 2. Clinically meaningful measures of patient baseline severity: 90-day pre-index relapses, neurologist/established patient visits, and MRIs.

Characteristic	scIFNβ1a	Dimethyl fumarate	Fingolimod	Teriflunomide
n	686	406	455	118
90-day pre-index relapses, n (%)	204 (29.7)	105 (25.9)	**105 (23.1)***	34 (28.8)
90-day pre-index neurologist/established patient visits, n (%)	532 (77.6)	**347 (85.5)****	352 (77.4)	97 (82.2)
90-day pre-index MRI, n (%)	317 (46.2)	163 (40.1)	**104 (22.9)****	**40 (33.9)***

Bolded values denote significance.
MRI, magnetic resonance imaging; scIFNβ1a, subcutaneous interferon beta-1a.
*p<0.05 using pairwise Chi-square test versus scIFNβ1a as the standard (no adjustment for multiplicity); **p<0.005 using pairwise Chi-square test versus scIFNβ1a as the standard (no adjustment for multiplicity).

Table 3. Generalized linear models predicting healthcare expenditures of patients with MS newly initiating scIFNβ1a, dimethyl fumarate, fingolimod, or teriflunomide.[a]

	scIFNβ1a	Dimethyl fumarate	Fingolimod	Teriflunomide
Total healthcare expenditures				
LS mean	$57,558	**$69,798**	**$69,478**	$55,414
95% CI	$54,924–$60,319	**$66,006–$73,808**	**$65,727–$73,442**	$50,025–$61,383
p value vs scIFNβ1a		**<0.0001**	**<0.0001**	0.4977
Total healthcare expenditures without DMDs				
LS mean	$13,562	**$20,987**	**$15,840**	**$17,148**
95% CI	$12,336–$14,910	**$18,807–$23,418**	**$14,186–$17,687**	**$13,971–$21,047**
p value vs scIFNβ1a		**<0.0001**	**0.0234**	**0.0350**

Bolded values denote significance. Healthcare expenditures have been adjusted to October 2014 US dollars using the Medical Services component of the Consumer Pricing Index.
CI, confidence interval; DMD, disease-modifying drug; LS, least squares; MRI, magnetic resonance imaging; MS, multiple sclerosis; scIFNβ1a, subcutaneous interferon beta-1a.
[a]A generalized linear model with a gamma distribution and log link controlling for patient demographics (ie, age, sex, region) and clinically meaningful measures of disease severity (ie, 90-day pre-index indicators for relapse, neurologist/established patient visits, and MRI) was used for this analysis. LS means are reported.

Limitations

- The ICD-9-CM code for MS does not distinguish between different MS types, such as relapsing–remitting or primary progressive MS.
- It is possible that patients were treated with DMDs prior to the 1-year baseline period. Additionally, patients in the sample may not have necessarily been newly diagnosed patients with MS.
- While adjustments were made for key differences, not all confounders may have been accounted for.
- There is a possible lack of generalizability given the inherent characteristics of claims databases and the use of an individual cohort.

Conclusions

- **In this real-world assessment of treatment-naïve patients with MS, after adjustment for demographics and clinically meaningful disease severity indicators, total healthcare expenditures during the first year following treatment initiation were statistically significantly lower for scIFNβ1a patients compared with patients initiating dimethyl fumarate or fingolimod.**
- **In addition, after adjustment for demographics and clinically meaningful disease severity indicators, healthcare expenditures excluding DMD-related costs were statistically significantly lower for scIFNβ1a compared with patients initiating dimethyl fumarate, fingolimod, and teriflunomide.**
- **The results of this study demonstrate the economic impact of scIFNβ1a versus dimethyl fumarate, fingolimod, and teriflunomide.**
- **Ongoing assessment of DMD treatments using real-world data is important for comparative effectiveness research.**

References

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Disclosures

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*A business of Merck KGaA, Darmstadt, Germany.

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