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Real-World Persistence of Ofatumumab vs Self-Injectable or Oral Disease-Modifying Therapies in Patients With Multiple Sclerosis

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KEY FINDINGS & CONCLUSIONS

- In this real-world study with 12 months of follow-up, patients treated with ofatumumab demonstrated higher persistence compared to those treated with platform self-injectable disease-modifying therapies (DMTs) and those treated with oral DMTs

INTRODUCTION

- Multiple sclerosis (MS) is a chronic demyelinating and neurodegenerative disease of the central nervous system that affects about 1 million adults in the United States (US)[1,2]
- More than 20 disease-modifying therapies (DMTs) are available in the US that significantly reduce relapse rates and new MRI lesions and slow disability worsening and disease progression[3,4]
- Ofatumumab (OMB) was approved in the US in August 2020 as the first self-administered monthly subcutaneous B-cell depleting therapy for relapsing MS[5]
- The ALITHIOS extension study showed that nearly 9 out of 10 patients remained on OMB over the long term (up to 4 years)[6]

OBJECTIVE

- This study examined real-world data on the persistence and adherence of OMB and how it compares with platform self-injectable and oral DMTs

METHODS

Study Design

- This retrospective cohort study utilized data from IQVIA PharMetrics® Plus (a longitudinal health plan database of medical and pharmacy claims in the US)
- Adults diagnosed with MS and treated with OMB, a platform self-injectable DMT (glatiramer acetate, interferon β-1a/-1b, or peginterferon β-1a), or an oral DMT (dimethyl fumarate, diroximel fumarate, monomethyl fumarate, fingolimod, siponimod, ozanimod, teriflunomide, or cladribine) between August 2020 and November 2021 and who had ≥6 months of follow-up were included
- Eligible patients were at least 18 years of age on the index date and had continuous enrollment in a health plan with medical and pharmacy benefits for ≥12 months prior to and 6 months after therapy initiation
- First pharmacy claim for index treatment was defined as the index date

Study Endpoints

- Persistence was defined as the number of days from the index date until discontinuation of the index therapy or a switch to a new DMT
- Discontinuation was defined as having a >60- (for self-injectable DMTs) or >90-day (for oral DMTs) gap in supply of the index medication, defined as a gap between the last supply date (based on expected duration of treatment or days' supply) and the next claim date for the index therapy

Statistical Analysis

- 1:1 greedy nearest neighbor propensity score (PS) matching was used to reduce indication bias in this real-world data set. A standardized mean difference <|0.1| indicated balance between cohorts
- Patients in the OMB cohorts were matched to patients in the platform self-injectable cohort or the oral DMT cohort. Patients were matched on age, sex, region, Deyo-Charlson comorbidity index, psychiatric diagnostic group score, number of pre-index MS relapses, MS disability, and prior DMT use
- A stratified Cox regression model was used to compare persistence in patients treated with OMB vs platform self-injectable or oral DMTs after adjusting for differences in patient characteristics that remained unbalanced after PS matching
- Inverse probability of treatment weighting was performed to test the robustness of the study findings and further details will be discussed in a future publication

RESULTS

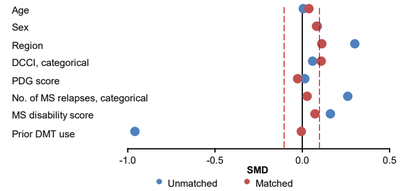
Patient Demographics and Clinical Characteristics

- In all cohorts, the mean duration of follow-up after the index date was more than 1 year

OMB vs Self-Injectable DMTs

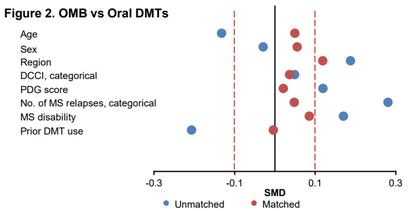
- A total of 1168 patients met the inclusion criteria (OMB, n=576; platform self-injectable DMT, n=592). After matching, 333 patients remained in each cohort
- Before PS matching, the OMB cohort had a higher proportion of patients in the 45-54–year age group, patients who lived in the South, and patients indexed in 2021. The OMB cohort also had more pre-index relapses (0.61 vs 0.38, respectively) and a higher proportion of patients with moderate MS disability and cerebellar and pyramidal symptoms vs patients on platform self-injectable DMTs
- After matching, demographic and clinical characteristics were generally balanced between the 2 cohorts (**Table 1**, **Figure 1**). Region, categorical DCCI score, index year, and patients with cerebellar and pyramidal symptoms remained unbalanced after PS matching*

Figure 1. OMB vs Self-Injectable DMTs



DCCI, Deyo-Charlson comorbidity index; DMT, disease-modifying therapy; MS, multiple sclerosis; OMB, ofatumumab; PDG, psychiatric diagnostic group; SMD, standardized mean difference
Dashed vertical lines indicate SMD cutoffs used to determine covariable balance
*For PS matching, the matching variables were selected a priori and are listed in the methods section; however, balance was assessed in all baseline measures after matching

Figure 2. OMB vs Oral DMTs



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Dashed vertical lines indicate SMD cutoffs used to determine covariable balance
*For PS matching, the matching variables were selected a priori and are listed in the methods section; however, balance was assessed in all baseline measures after matching

OMB vs Oral DMTs

- A total of 3040 patients met the inclusion criteria (OMB, n=576; oral DMT, n=2464). After PS matching, 576 patients remained in each cohort
- Before PS matching, patients in the OMB cohort were younger and more likely to live in the South, indexed in 2021, and have higher psychiatric burden. The OMB cohort also had more pre-index MS relapses, moderate MS disability, and cerebellar and pyramidal symptoms vs the oral DMT cohort
- After PS matching, all variables were generally balanced between cohorts, except for index year, chronic obstructive pulmonary disorder, cerebellar and pyramidal symptoms, and tremor (**Table 1**, **Figure 2**)

Table 1. Baseline Patient Characteristics in the PS Matched Cohort

	OMB vs self-injectable DMTs		OMB vs oral DMTs	
	OMB (N=333)	Platform self-injectable DMTs (N=333)	OMB (N=576)	OMB DMTs (N=576)
Mean (SD) age, years	46.3 (10.2)	45.9 (11.3)	46.7 (10.3)	46.2 (10.1)
Female, n (%)	259 (77.8)	270 (81.1)	447 (77.6)	460 (79.9)
Region, n (%)				
Northeast	69 (20.7)	78 (23.4)	114 (19.8)	104 (18.1)
Midwest	92 (27.6)	93 (27.9)	175 (30.4)	152 (26.4)
South	126 (37.8)	127 (38.1)	233 (40.5)	264 (45.8)
West	46 (13.8)	35 (10.5)	54 (9.4)	56 (9.7)
Insurance type, n (%)*				
Commercial	316 (94.9)	314 (94.3)	544 (94.4)	541 (93.9)
Medicaid	3 (0.9)	4 (1.2)	4 (0.7)	1 (0.2)
Medicare	14 (4.2)	15 (4.5)	28 (4.9)	34 (5.9)
Index year, n (%)				
2020	31 (9.3)	101 (30.3)	51 (8.9)	162 (28.1)
2021	302 (90.7)	232 (69.7)	525 (91.1)	414 (71.9)
PDG				
Mean (SD)	0.87 (1.1)	0.90 (1.1)	0.9 (1.1)	0.9 (1.0)
DCCI				
Mean (SD)	0.6 (1.0)	0.5 (1.0)	0.5 (1.0)	0.5 (1.0)
Prior DMT use, n (%)	141 (42.3)	140 (42.0)	384 (66.7)	383 (66.5)
Number of MS relapses prior to index DMT,† n (%)				
0	210 (63.1)	214 (64.3)	336 (58.3)	329 (57.1)
1	92 (27.6)	90 (27.0)	170 (29.5)	182 (31.6)
2+	31 (9.3)	29 (8.7)	70 (12.2)	65 (11.3)
MS disability,‡ n (%)				
None	110 (33.0)	112 (33.6)	178 (30.9)	192 (33.3)
Mild	48 (14.4)	48 (14.4)	72 (12.5)	63 (10.9)
Moderate	126 (37.8)	132 (39.6)	237 (41.2)	244 (42.4)
Severe	49 (14.7)	41 (12.3)	89 (15.5)	77 (13.4)
Top 5 MS-related symptoms and secondary conditions, n (%)				
Anxiety	101 (30.3)	106 (31.8)	175 (30.4)	176 (31.6)
Pyramidal symptoms*,§	110 (33.0)	77 (23.1)	187 (32.5)	147 (25.5)
Fatigue	89 (26.7)	93 (27.9)	164 (28.5)	159 (27.6)
Cerebellar symptoms*,§	86 (25.8)	64 (19.2)	142 (24.7)	112 (19.4)
IBS	46 (13.8)	50 (15.0)	100 (17.4)	106 (18.4)

DCCI, Deyo-Charlson comorbidity index; DMT, disease-modifying therapy; EDSS, Expanded Disability Status Scale; IBS, irritable bowel syndrome; IV, intravenous; MS, multiple sclerosis; OMB, ofatumumab; PS, propensity score; PDG, psychiatric diagnostic group
*p<0.05, characteristic remained unbalanced between matched cohorts for OMB vs oral DMTs; †MS relapse was defined as having ≥1 inpatient visit with a primary diagnosis (diagnosis ≥1 of MS or ≥1 outpatient claim visit with a diagnosis code for MS in any position and ≥1 claim for oral or IV corticosteroid use on or within 7 days after the outpatient visit. Corticosteroid use within 5 days before or after a DMT infusion (alemtuzumab, ocrelizumab, natalizumab) was not flagged as a relapse; ‡MS disability was defined as having evidence of EDSS-related MS symptoms or DMT use during the measurement period†; §p<0.05, characteristic remained unbalanced between matched cohorts for OMB vs self-injectables

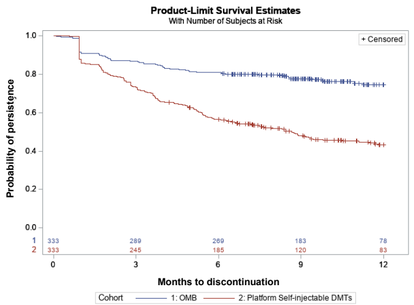
MS Treatment History

- On average, 42.2.% of the self-injectable treated patients and 66.6% of the oral DMT–treated patients had prior DMT use
  - For the OMB vs self-injectable DMTs cohort, glatiramer acetate (11.3% vs 15.7%), ocrelizumab (28.4% vs 13.6%), and dimethyl fumarate (15.6% vs 29.3%) were the most common self-injectable, intravenous, and oral DMT, respectively, used immediately prior to the index oral DMT
  - For the OMB vs oral DMTs cohort, the most common DMTs used immediately prior to OMB initiation were ocrelizumab (28.6% vs 7.6%), dimethyl fumarate (19.0% vs 44.6%), and glatiramer acetate (10.9% vs 17.2%), respectively, whereas dimethyl fumarate, glatiramer acetate, and ocrelizumab were the most common DMTs used immediately prior to the index oral DMT

Treatment Discontinuation – OMB vs Self-Injectable DMTs

- Among patients on OMB, 80.8% and 74.5% of patients were persistent at 6 and 12 months post index vs 56.7% and 43.2% patients in the platform self-injectable DMT cohort, respectively (p<0.0001) (**Figure 3**)
  - This indicates a 72% improvement in persistence over platform self-injectables at 12 months
- Patients on OMB had a 55% lower risk of treatment discontinuation than patients on platform self-injectable DMTs after adjusting for demographic and clinical characteristics that remained unbalanced after matching

Figure 3. KM Curve for Time to Treatment Discontinuation Defined as a >60-Day Gap in Supply of the Index Medication or Switch to a New DMT (OMB vs Platform Self-Injectable DMTs Matched Cohort)

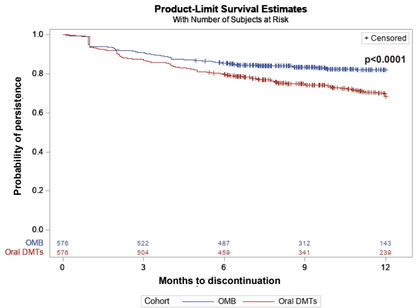


DMT, disease-modifying therapy; KM, Kaplan–Meier; OMB, ofatumumab

Treatment Discontinuation – OMB vs Oral DMTs

- Unadjusted analysis (using the >90-day gap definition) showed that among patients on OMB, the probabilities of remaining on treatment at 6 and 12 months post index were 85.4% and 82.0% vs 79.7% and 68.4% in the oral DMT cohort, respectively (p<0.0001) (**Figure 4**)
  - Univariate analyses using a >60-day gap definition also showed that OMB had better persistence vs oral DMTs. The probabilities of remaining on therapy at 6 and 12 months post index were:
    - >60-day gap: OMB; 81.9%, 76.3% vs 77.8%, 64.6%, respectively (p=0.0020)
- Patients treated with OMB had a 31% lower risk of treatment discontinuation within the first 12 months of therapy than patients treated with oral DMTs

Figure 4. KM Curve for Time to Treatment Discontinuation Defined as a >90-Day Gap in Supply of the Index Medication or Switch to a New DMT (OMB vs Oral DMTs Matched Cohort)



DMT, disease-modifying therapy; KM, Kaplan–Meier; OMB, ofatumumab

LIMITATIONS

- The study sample consists primarily of commercially insured patients in the US and may not be generalizable to other payer populations
- Generalizability is also limited due to a sizable number of patients on oral DMT being excluded from the 1:1 PS matching
- Analyses using claims data are dependent on the accuracy and specificity of entered diagnostic codes
- Early discontinuation may be overestimated if treatment occurred outside the purview of the claims data source (eg, under a different payer structure including cash payments or within a clinical trial)
- Certain clinical and radiographic measurements of disease severity and sociodemographic variables are unavailable in claims data, increasing susceptibility to hidden bias

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Disclosures

Carrie M. Hersh is an employee of the Cleveland Clinic Lou Ruvo Center for Brain Health and has worked as a consultant for Novartis Pharmaceuticals Corporation. **Magdaliz Gorritz**, **Chi Chang Chen**, **Rifat Tuly**, and **Yifan Gu** are employees of IQVIA and have worked as consultants for Novartis Pharmaceuticals Corporation. **Qiujun (Samantha) Shao**, **Abhijit Gadkari**, and **Brandon Brown** are employees of Novartis Pharmaceuticals Corporation

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