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Real-world persistence of ofatumumab versus oral disease modifying therapies (DMTs) in patients with multiple sclerosis (MS)

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SUMMARY

1 **This real-world retrospective study evaluated and compared DMT discontinuation among MS patients treated with OMB versus oral DMTs.**

2 **Univariate analysis showed higher persistence in patients treated with OMB versus oral DMTs; these results held even after adjusting for baseline differences when using the 90-day gap definition.**

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INTRODUCTION

- Multiple sclerosis (MS) is a chronic, irreversible autoimmune disease of the central nervous system[1] that affects close to 1 million US adults.[2]
- Currently, no curative treatment exists for MS. However, several disease-modifying therapies (DMTs) are available that have been shown to significantly reduce relapse rates, slow disability worsening, and disease progression.[3]
- Ofatumumab (OMB) was approved in the US in Aug 2020 as the first B-cell therapy to be self-administered subcutaneously once-monthly for relapsing MS.[4]
- The ALITHIOS extension study showed that nearly 9 out of 10 patients remained on OMB over the long term (up to ≥4 years).[5]

OBJECTIVE

- To compare persistence of OMB versus oral DMTs

METHODS

STUDY DESIGN

- This retrospective cohort study utilized the IQVIA PharMetrics® Plus data (a longitudinal health plan database of medical and pharmacy claims in the US).
- Adult patients diagnosed with MS and treated with OMB or an oral DMT (dimethyl fumarate, fingolimod, teriflunomide, cladribine, siponimod, ozanimod, diroximel fumarate, monomethyl fumarate, ponesimod) from Aug 2020 to Nov 2021 were identified and indexed on the first therapy. Patients were followed from the index date until discontinuation of the initial therapy or switch to another line of therapy, or 12-months post-index for persistent patients.
- Eligible patients were ≥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.

KEY OUTCOMES

- **Discontinuation** was defined as having a >90-day gap in supply of the index medication (i.e., 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) or switching to a new DMT. Analyses were also performed using a >45- and 60-day gap.
- **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. It was measured during the post-index period which included the index date.

STATISTICAL ANALYSIS

- Patients in the OMB cohort were 1:1 matched to patients in the oral DMT cohort using greedy nearest neighbor propensity score matching. Patients were matched on age, sex, region, Deyo-Charlson comorbidity index, psychiatric diagnostic group (PDG) score, number of pre-index MS relapses, MS disability, and use of prior DMTs.
- Kaplan-Meier analysis was used to compare unadjusted persistence between cohorts.
- A stratified Cox regression model was used to compare persistence in patients treated with OMB versus oral DMTs after adjusting for differences in patient characteristics that remained unbalanced after matching.

RESULTS

BASELINE CHARACTERISTICS

- A total of 3,040 patients met inclusion criteria (OMB n=576, oral DMT n=2,464). After matching, 576 patients remained in each cohort.
- Before matching, patients in the OMB cohort were younger and more likely to live in the South, index in 2021, and have higher psychiatric burden. The OMB cohort also had more pre-index MS relapses, more moderate MS disability, and more cerebellar and pyramidal symptoms compared to the oral DMT cohort.
  - After matching, all variables were balanced between cohorts except for index year, COPD, cerebellar and pyramidal symptoms and tremor (**Table 1**).

Table 1. Baseline Patient Characteristics

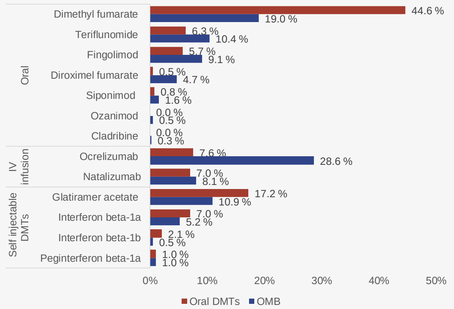
	OMB (N=576)	Oral DMTs (N=576)	p-value
Age (mean, SD)	46.7 (10.3)	46.2 (10.1)	0.3712
Female sex (n,%)	447 (77.6%)	460 (79.9%)	0.3258
Region (n, %)			0.2555
Northeast	114 (19.8%)	104 (18.1%)	
Midwest	175 (30.4%)	152 (26.4%)	
South	233 (40.5%)	264 (45.8%)	
West	54 (9.4%)	56 (9.7%)	
Index year (n, %)			**<0.0001**
2020	51 (8.9%)	162 (28.1%)	
2021	525 (91.1%)	414 (71.9%)	
DCCI, continuous	0.5 (1.0)	0.5 (1.0)	0.8337
PDG, continuous	0.9 (1.1)	0.9 (1.0)	0.7024
Number of MS relapses[1] prior to index DMT (n,%)			0.5580
0	336 (58.3%)	329 (57.1%)	
1	170 (29.5%)	182 (31.6%)	
2+	70 (12.2%)	65 (11.3%)	
MS disability[2] (n,%)			0.2052
None	178 (30.9%)	192 (33.3%)	
Mild	72 (12.5%)	63 (10.9%)	
Moderate	237 (41.2%)	244 (42.4%)	
Severe	89 (15.5%)	77 (13.4%)	
Prior DMT use (n, %)	384 (66.7%)	383 (66.5%)	0.9387
Pyramidal symptoms	187 (32.5%)	147 (25.5%)	**0.0101**
Cerebellar symptoms	142 (24.7%)	112 (19.4%)	**0.0394**

Abbreviations: DMT, disease-modifying therapy; MS, multiple sclerosis; OMB, ofatumumab; SD, standardized difference
[1]Defined as ≥1 MS-related inpatient visit or ≥1 MS-related outpatient visit and ≥1 claim for oral or IV corticosteroid use on or within 7 days after the outpatient visit. Corticosteroid use within 5 days of DMT infusion (alemtuzumab, ocrelizumab, natalizumab) was not flagged as a relapse.
[2]MS disability was proxied using the claims-based disability score and was defined as having claims with diagnosis codes for EDSS-related MS symptoms or DME use during the measurement period.[6]

MS TREATMENT HISTORY

- On average, 66.6% of patients had prior DMT use in the matched cohort.
- Ocrelizumab, dimethyl fumarate and glatiramer acetate were the most common DMTs used immediately prior to OMB initiation, while dimethyl fumarate, glatiramer acetate and ocrelizumab were the most common DMTs used immediately prior to the index oral DMT (**Figure 1**).

Figure 1. Summary of Prior DMTs Before Index Treatment



Abbreviations: DMT, disease-modifying therapy; OMB, ofatumumab; SD, standardized difference

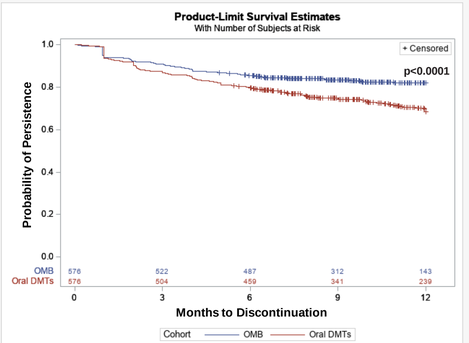
TREATMENT DISCONTINUATION – UNIVARIATE ANALYSIS

- Unadjusted analysis (using the 90-day gap definition) showed that among patients on OMB, the probabilities of remaining on treatment at 6-, 9-, and 12-months post-index were 85.4%, 83.4%, and 82.0% versus 79.7%, 74.5%, and 68.4% in the oral DMT cohort, respectively (p<0.0001) (**Figure 2**).
- Univariate analyses using a >45- and 60-day gap definition also showed that OMB had better persistence compared to oral DMTs. The probabilities of remaining on therapy at 6-, 9-, and 12 months post-index were:
  - 45-day gap: OMB; 79.0%, 75.5%, 71.8% versus oral DMTs; 76.2%, 69.6%, 61.0%, respectively (p=0.0124).
  - 60-day gap: OMB; 81.9%, 78.6%, 76.3% versus 77.8%, 71.7%, 64.6%, respectively (p=0.0020).

TREATMENT DISCONTINUATION – MULTIVARIATE ANALYSIS

- Results from the stratified Cox proportional hazards model show that, after adjusting for unbalanced confounders, the difference in persistence (based on the 90-day gap) between OMB and oral DMTs remained statistically significant (p=0.0134).

Figure 2. KM Curve for Time to Treatment Discontinuation Defined as ≥90-day gap in Therapy of the Index Medication or Switched to a new DMT (OMB vs Oral DMTs Matched Cohort)

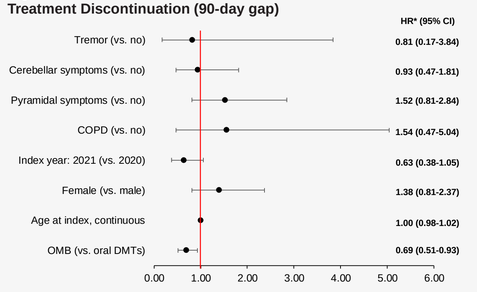


Months persistent (90-day gap)	# patients still on treatment[1] (at risk) (OMB cohort)	Survival probability[2] (OMB cohort)	# patients still on treatment[1] (at risk) (Oral DMT cohort)	Survival probability[2] (Oral DMT cohort)
3-months	522	90.6%	504	86.6%
6-months	487	85.4%	459	79.7%
9-months	312	83.4%	341	74.5%
12-months	143	82.0%	239	68.4%

Abbreviations: DMT, disease-modifying therapy; KM, Kaplan-Meier; OMB, ofatumumab; SD, standardized difference
[1]Patients still on treatment include patients who did not discontinue or switch therapies and patients who were not censored for other reasons at each time point.
[2]The denominator for the survival probabilities are dynamic. Patients still at risk for discontinuation (i.e., patients who have not already discontinued or switched and those who are not censored are included in the denominator for each time point.

- 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 3**).

Figure 3. Stratified Cox Proportional Hazards Model of Time to Treatment Discontinuation (90-day gap)



Abbreviations: CI, confidence interval; COPD, chronic obstructive pulmonary disease; DMT, disease-modifying therapy; HR, hazard ratio; OMB, ofatumumab
* Hazard ratio <1.0 indicates that the factor is less likely to attribute to discontinuation

Limitations

- The study sample consists primarily of commercially insured patients in the US and may not be generalizable to other payer populations.
- 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, e.g., under a different payer structure including cash payments or within a clinical trial.
- Certain clinical and radiographic measurements of disease severity and socio-demographic variables are unavailable in claims data.

AFFILIATIONS: MG, CCC, RT and YG are employees of IQVIA Inc. and worked as consultants to Novartis Pharmaceuticals Corporation. QS, AG and BB are employees of Novartis Pharmaceuticals Corporation. CMH is an employee of the Cleveland Clinic Lou Ruvo Center for Brain Health and worked as a consultant to Novartis Pharmaceuticals Corporation.

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