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Real-World Effectiveness, Tolerability, and Safety of Ofatumumab at 12-Month Follow-Up

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KEY FINDINGS & CONCLUSIONS

- In our cohort of 175 patients who started ofatumumab (OMB) treatment, OMB demonstrated good clinical and radiographic effectiveness and was well tolerated with excellent patient adherence through 12-month follow-up
- Adverse events were reported in less than half of patients, with the most common being injection-related reaction, and subsided over time with continued treatment. Only 35% of patients experienced an infection, most commonly upper respiratory infection and urinary tract infection, as expected from clinical trials
- There was a notable reduction in the proportion of patients experiencing clinical relapses and radiological disease activity during the first 12 months of OMB treatment
- Our study provides data in support of the safety and efficacy of OMB in a broader group of patients compared with those studied in clinical trials
- Some limitations of this study include its retrospective nature, considerable missingness in several outcomes, and inconsistent patient follow-up and data acquisition. Our results need further validation in a larger multicenter real-world study with longer follow-up

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INTRODUCTION

- Ofatumumab (OMB) is a highly effective disease-modifying therapy approved for relapsing multiple sclerosis (MS)
- OMB is a fully humanized monoclonal antibody targeting CD20, a transmembrane antigen present on a variety of human B lineage cells
- The efficacy and safety of OMB for relapsing-remitting MS was demonstrated in 2 large randomized clinical trials, ASCLEPIOS I and II,[1] and long-term data are available from a single-arm open-label extension study, ALITHIOS[2]
- However, real-world effectiveness, tolerability, and safety data for OMB are limited

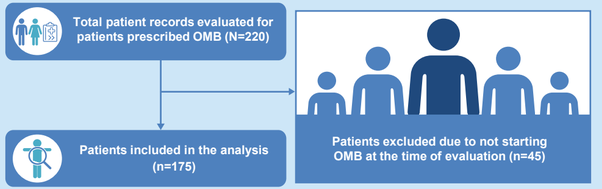
OBJECTIVE

- In this study, we describe the 12-month effectiveness, tolerability, and safety data for OMB in a real-world MS population

METHODS

- Electronic medical records (EMRs) were reviewed for patients prescribed OMB from October 2020 to August 2022 at 2 comprehensive MS centers (Cleveland Clinic, Mellen Center, Cleveland, OH, USA; Lou Ruvo Center for Brain Health, Las Vegas, NV, USA)
- Adult patients (≥18 years) prescribed OMB with a diagnosis of clinically isolated syndrome or MS and a follow-up of 12 months in the EMR system were included
- Patients participating in OMB clinical trials (eg, ARTIOS, OLIKOS) were excluded
- Patients who did not receive at least 1 dose of OMB were excluded (**Figure 1**)
- Data were reviewed for a period of up to 12 months after the first dose or until discontinuation of OMB
- Data sources included EMRs and Multiple Sclerosis Performance Test assessments[3]
- Data were collected at 3 time points: Baseline (up to 12 months prior to starting OMB) and 6- (±3 months) and 12-month (±3 months) follow-up

Figure 1. Study Flowchart of Inclusion/Exclusion Criteria



OMB, ofatumumab

- The following on-treatment intervals were defined: 0-6 months (first 6-month window), 7-12 months (second 6-month window), and 0-12 months (cumulative window)
- Demographics and disease characteristics were collected at Baseline. Clinical (including patient-reported outcomes and neurological performance measures) and radiographic outcomes were collected at Baseline, 6 months, and 12 months
- Statistical analyses included all patients who started OMB regardless of discontinuation status. Mean (SD) for normally distributed variables and median (interquartile range) for non-normally distributed variables or those with small sample sizes were reported. Event numbers between treatment periods were compared using negative binomial generalized linear mixed effects models (GLMMs). Binary outcomes for these variables (presence or absence of each event) were compared using logistic GLMMs. P-values <0.05 were considered statistically significant. For each calculation, observations with missing values were excluded. Percentages were calculated using the total number of events available as the denominator
- All data collection, handling, and statistical analyses were conducted by Cleveland Clinic investigators

RESULTS

- A total of 175 patients who met the inclusion and exclusion criteria were included in the analysis, with baseline characteristics summarized in **Table 1**

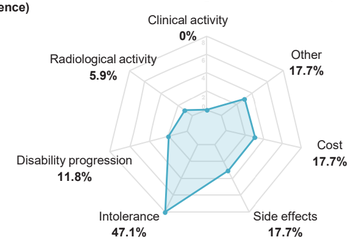
Table 1. Baseline Characteristics and Demographics of Patients Prior to Starting OMB (n=175)

Variable	Statistical summary
Age, years, mean (SD), range	44.9 (10.4), 21-72
Sex, female, n (%)	129 (73.7)
Race, n (%)	
White	142 (81.1)
Black	22 (12.6)
Multiracial/multicultural	4 (2.3)
Asian	1 (0.6)
Unknown	6 (3.4)
Disease duration, years, mean (SD), range	13.6 (9.6), 0-48
Most recent disease course, n (%)	
RRMS/CIS	140 (80.0)
SPMS	27 (15.4)
PPMS	8 (4.6)
PDDS, n (%)*	
0 (normal)	23 (31.1)
1 (mild disability)	11 (14.9)
2 (moderate disability)	8 (10.8)
3 (gait disability)	13 (17.6)
4 (early cane)	5 (6.8)
5 (late cane)	2 (2.7)
6 (bilateral support)	9 (12.2)
7 (wheelchair bound)	3 (4.1)
Comorbidities, n (%)	
Hypertension	34 (19.4)
Hyperlipidemia	25 (14.3)
Type 2 diabetes mellitus	12 (6.9)
DMT experience	
Naïve to DMT, n (%)	24 (13.7)
Number of prior DMTs, median (IQR)	2 (1, 4)
DMT switch to OMB, n (%)†	103 (58.9)
Interval between prior DMT and OMB, months, median (IQR)	5.3 (1.0, 12.5)
Most recent prior DMT, n (%)	
High efficacy	66 (37.7)
Ocrelizumab/rituximab	56 (32.0)
Natalizumab	10 (5.7)
Medium/low efficacy	85 (48.6)
Dimethyl/monomethyl/diroximel fumarate	32 (18.3)
Fingolimod/siponimod/ozanimod	24 (13.7)
Teriflunomide	11 (6.3)
Glatiramer acetate	8 (4.6)
Interferon beta	7 (4.0)
Alemtuzumab	1 (0.6)
Cyclophosphamide	1 (0.6)
Cladribine	1 (0.6)

CIS, clinically isolated syndrome; DMT, disease-modifying therapy; IQR, interquartile range; OMB, ofatumumab; PDDS, Patient-Determined Disease Steps; PPMS, primary progressive multiple sclerosis; RRMS, relapsing-remitting multiple sclerosis; SPMS, secondary progressive multiple sclerosis
*PDDS data at Baseline were only available for 74 patients
†The switch was defined as transitioning to OMB within 3 months of the last DMT scheduled dose

- Over 12 months, a total of 17 (9.7%) patients discontinued OMB, with discontinuation reasons for each 6-month period summarized in **Figure 2**

Figure 2. Reasons for Discontinuation of OMB During Each Time Window (Plot Demonstrating Overall Cumulative Incidence)



Reason for discontinuation, n	During either window (cumulative) (n=175)	During first 6-month window (n=175)	During second 6-month window (n=175)
Intolerance*	8	8	0
Side effects†	3	3	0
Cost	3	1	2
Other: convenience/patient preference	3	3	0
Disability progression	2	2	0
Radiological activity	1	1	0
Clinical activity	0	0	0

OMB, ofatumumab
*Side effects were based on adverse events that could be explained by drug pharmacology
†Intolerance was determined based on other complaints that may not have been related to drug but correlated temporally with ofatumumab use

- A total of 17 (9.7%) patients reported missing any doses during the study period, and 63 (36%) patients experienced tolerability concerns during the study period
- The most common injection-related reactions (IRRs) were headache (24 [13.7%] in the first 6 months and 5 [2.9%] between 7 and 12 months) and fatigue (15 [8.6%] in the first 6 months and 4 [2.3%] between 7 and 12 months)
- The incidence of IRRs decreased consistently with subsequent injections and were noted primarily from the initial injections (ie, first, second, and third injections—25%, 15%, and 11%, respectively). Only 8 patients (5%) reported IRRs between Months 7 and 12
- 62 (35%) patients experienced an infection, with 24% having upper respiratory infection, 8% having urinary tract infection, and 3.4% having other types of infection. Total immunoglobulin G (IgG) levels remained stable, and the proportion of patients with IgG levels below the lower limit of normal did not differ between time intervals (Baseline, 11.1%; 6 months, 12.3%; and 12 months, 11.3%) (p=0.892)
- If the reaction was known and expected with OMB, it was categorized as "side effects"; otherwise, if it was not clearly attributable to OMB use, it was categorized as "intolerance"
- Clinical and radiological disease activity outcomes for patients with available information are summarized in **Table 2**

Table 2. Clinical and Radiological Disease Activity at Baseline, Each 6-Month Period, and the Cumulative Period Over 12 Months When Available*

	Baseline	During first 6 months	During second 6 months	Cumulative, 0-12 months	P-value† (overall)
Clinical disease activity					
Number of relapses, n (%)	n=175	n=161	n=125	n=161	<0.001
0	136 (77.7)	160 (99.4)	125 (100)	160 (99.4)	
1	36 (20.6)	1 (0.6)	0 (0)	1 (0.6)	
2	3 (1.7)	0 (0)	0 (0)	0 (0)	
Any	39 (22.3)	1 (0.6)	0 (0)	1 (0.6)	<0.001
Radiological disease activity					
Number of new brain lesions, n (%)	n=158	n=87	n=67	n=122	<0.001
0	104 (65.8)	74 (85.1)	59 (88.1)	104 (85.2)	
1	16 (10.1)	10 (11.5)	5 (7.5)	15 (12.3)	
2	14 (8.9)	2 (2.3)	1 (1.5)	3 (2.5)	
3	2 (1.3)	0 (0)	0 (0)	0 (0)	
>3	22 (13.9)	1 (1.1)	3 (4.5)	4 (3.3)	
Any	52 (32.9)	13 (14.9)	9 (13.4)	18 (14.8)	0.001
Number of new brain GdE lesions, n (%)	n=160	n=86	n=66	n=124	<0.001
0	133 (83.1)	84 (97.7)	66 (100)	122 (98.4)	
1	12 (7.5)	2 (2.3)	0 (0)	2 (1.6)	
2	6 (3.8)	0 (0)	0 (0)	0 (0)	
3	4 (2.5)	0 (0)	0 (0)	0 (0)	
>3	5 (3.1)	0 (0)	0 (0)	0 (0)	
Any	27 (16.9)	2 (2.3)	0 (0)	2 (1.6)	DNC
Disability status					
PDDS, n (%)	n=74	n=60	n=54		0.104
0 (normal)	23 (31.1)	14 (23.3)	18 (33.3)	–	
1 (mild disability)	11 (14.9)	14 (23.3)	12 (22.2)	–	
2 (moderate disability)	8 (10.8)	6 (10.0)	2 (3.7)	–	
3 (gait disability)	13 (17.6)	6 (10.0)	7 (13.0)	–	
4 (early cane)	5 (6.8)	8 (13.3)	4 (7.4)	–	
5 (late cane)	2 (2.7)	2 (3.3)	1 (1.9)	–	
6 (bilateral support)	9 (12.2)	6 (10.0)	3 (5.6)	–	
7 (wheelchair)	3 (4.1)	4 (6.7)	7 (13.0)	–	

DNC, unable to calculate; GdE, gadolinium-enhancing; PDDS, Patient-Determined Disease Steps
*For each variable, the number of patients with available information is listed
†Overall p-value represents change across the measured time points, ie, during the first and second 6-month period

- Although only a limited number of patients had available disability outcomes and neurological quality of life data, there were no statistically significant changes across measures, including change in processing speed test, high and low contrast visual acuity, manual dexterity time, and walking speed tests. We did not detect a statistically significant change across the mean values for any of the neurological quality of life measures across the 3 time points in the study (data not shown)

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Disclosures

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