Poster presented at the 9th Joint ECTRIMS-ACTRIMS Meeting, 11–13 October 2023 Milan, Italy.

Real-world effectiveness, tolerability, and safety of ofatumumab at 12-month follow-up

P1559

Moein Amin,[1] Tucker Harvey,[2] Brandon Moss,[1] Ming-Hui Tai,[3] Abhijit Gadkari,[3] Brandon Brown,[3] Devon S. Conway,[1] Carrie M. Hersh[4]

[1]Mellen Center for MS Treatment and Research, Cleveland Clinic, Cleveland, OH; [2]Quantitative Health Sciences, Cleveland Clinic, Cleveland, OH; [3]Novartis Pharmaceuticals Corporation, East Hanover, NJ; [4]Lou Ruvo Center for Brain Health, Cleveland Clinic, Las Vegas, NV

INTRODUCTION

- Ofatumumab (OMB) is a highly effective disease-modifying therapy (DMT) approved for relapsing multiple sclerosis (MS).
- OMB is a fully humanized monoclonal antibody (mAB) targeting CD-20, 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 two 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.

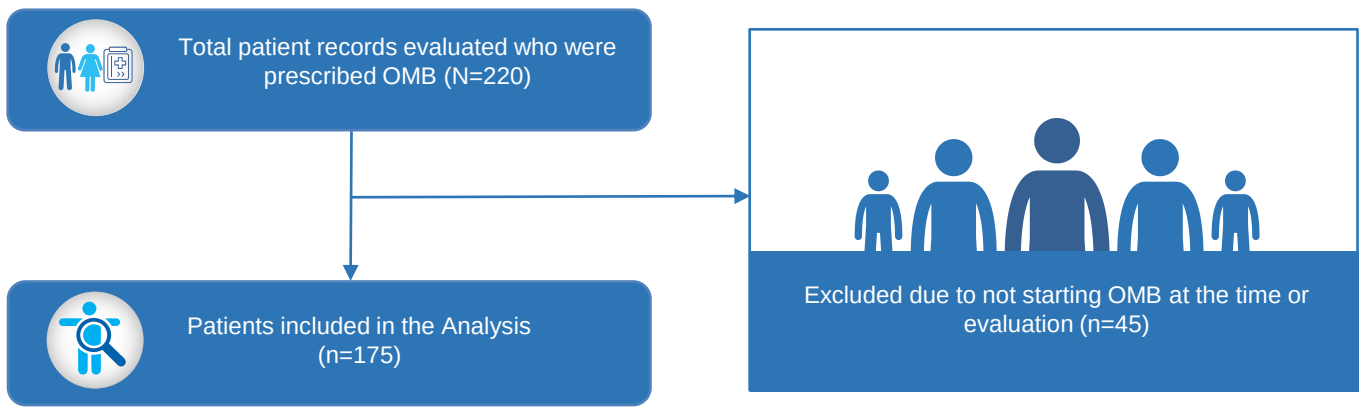
OBJECTIVE

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

METHODS

- Electronic medical records (EMR) were reviewed for patients prescribed OMB from October 2020 to August 2022 at two comprehensive MS centers (Cleveland Clinic, Mellen Center, Cleveland, OH; Lou Ruvo Center for Brain Health, Las Vegas, NV).
- Adult patients (≥18 years) prescribed OMB from October 2020-August 2022, having a diagnosis of clinically isolated syndrome or MS, and a follow-up of 12 months in the EMR system were incuded.
- Patients participating in OMB clinical trials (e.g., ARTIOS, OLIKOS) were excluded.
- Patients who did not receive at least one dose of OMB were excluded (**Figure 1**).

Figure 1. Study flowchart of inclusion/exclusion criteria.



- Data were reviewed for a period of up to 12 months after the first dose or until discontinuation of OMB.
- Data sources included electronic medical records and Multiple Sclerosis Performance Test (MSPT) assessments.[3]
- Data were collected at 3 time points: Baseline (up to 12 months prior to starting OMB) and 6-month (±3 months) and 12-month follow-up (±3 months).
- 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 neuro-performance measures) and radiographic outcomes collected at baseline, 6 months, and 12 months.
- Statistical analyses included all patients who started OMB regardless of discontinuation status. Mean and standard deviation (SD) for normally distributed variables and median and interquartile range (IQR) 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 (GLMM). Binary outcomes for these variables (presence or absence of each event) were compared using logistic GLMM. P-values <0.05 were considered statistically significant. For each calculation, observations with missing values were excluded. Percentages were calculated using total number of events available as the denominator.

RESULTS

- A total of 175 patients who met 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)

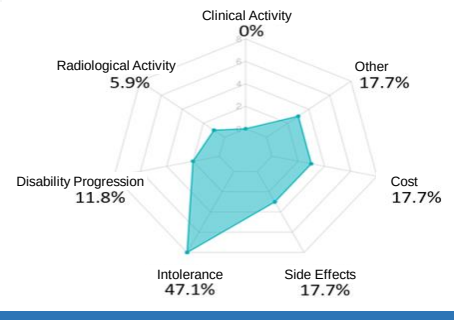
Variable	Statistical summary
Age, years: mean (SD), range	44.9 (10.4), 21-72
Sex: female n (%)	129 (73.7)
Race: n (%)	
White	142 (81.1)
Black	22 (12.6)
Multiracial/Multicultural	4 (2.3)
Asian	1 (0.6)
Unknown	6 (3.4)
Disease duration, years: mean (SD), range	13.6 (9.6), 0-48
Most recent disease course: n (%)	
RRMS/CIS	140 (80.0)
SPMS	27 (15.4)
PPMS	8 (4.6)
PDDS: n (%)[1]	
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; IQR: interquartile range; PDDS: patient determined disease steps; PPMS: primary progressive MS; RRMS: relapsing-remitting MS; SD: standard deviation; SPMS: secondary progressive MS.

[1]PDDS data at baseline were only available for 74 patients.

- 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 ofatumumab during each time window (plot demonstrating overall cumulative incidence)



	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

- 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 (IRR) were headache [24 (13.7%) in the first 6 months and 5 (2.9%) between 7-12 months] and fatigue [15 (8.6%) in the first 6 months and 4 (2.3%) between 7-12 months].
- The incidence of IRR decreased consistently with subsequent injections and were noted primarily from the initial injections (i.e., 1st, 2nd, and 3rd injection) – 25%, 15%, and 11%, respectively. Only 8 patients (5%) reported IRR between months 7-12.
- Sixty-two (35%) patients experienced an infection, with 24% having upper respiratory infection (URI), 8% urinary tract infection (UTI), and 3.4% other types. Total IgG levels remained stable and the proportion of patients with IgG below lower limit of normal did not differ between time intervals (p=0.892).
- If the reaction was known and expected with OMB, it was categorized as “side effects,” but 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 months period, and cumulative over 12 months when available. For each variable, the number of subjects with available information is listed

	Baseline	6 months	12 months	Cumulative 0-12 months	p value*
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 (100.0)	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; *p value comparing overall differences across all intervals.

- 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).

CONCLUSIONS

- In our cohort of 175 patients who started 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 IRR and subsided over time with continued treatment. Only 35% of patients experienced an infection, most commonly URI and UTI, 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 in patients on OMB.
- Our study provides data in support of the safety and efficacy of OMB in a broader group of patients compared to 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.

References: 1. Hauser SL, et al. N Engl J Med. 2020;383(6):546-557. **2.** Hauser SL, et al. Mult Scler J. 2022;28(10):1576-1590. **3.** Rudick RA, et al. J Vis Exp. 2014;88:e51318.

Disclosures: MA: Has received Novartis and Biogen fellowship awards. **TH:** None. **BM:** Has received research support from Genentech, consulting fees from Biogen, and has stock in Pfizer. Ming-Hui Tai, Abhijit Gadkari and Brandon Brown are employees of Novartis. **DSC:** Has received research support paid to his institution from Novartis, Biogen, EMD Serono, BMS, Horizon, and the National Institutes of Health. He has received consulting fees from Novartis and Alexion and speaking fees from Biogen. **CMH:** Has received speaking, consulting, and advisory board fees from Genentech, Genzyme, Biogen, Novartis, EMD-Serono, Bristol Myers Squibb, TG Therapeutics, and Alexion. She has received research support paid to her institution by Biogen, Novartis, Genentech, Patient-Centered Outcomes Research Institute (PCORI) and NIH – NINDS 1U01NS111678-01A1 sub-award.

Funding: This study was funded by Novartis Pharmaceuticals Corporation.

Presenter email address: AMINM@ccf.org