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DMT47

Baseline Characteristics and 6-Month Tolerability, Safety and Persistence in a Real-World Cohort of Multiple Sclerosis Patients Initiating Ofatumumab

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CONCLUSIONS

1. This retrospective study provides insights into the patient characteristics, 6-month tolerability, safety, and persistence in a real-world cohort of MS patients who initiated OMB.
2. At 6 months, there were no unexpected tolerability or safety concerns and persistence remained high with OMB.

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INTRODUCTION

- Ofatumumab (OMB; Kesimpta®) is a highly effective disease-modifying therapy (DMT) approved in August 2020 in the US for the treatment of relapsing multiple sclerosis (RMS).
- The efficacy and safety of OMB vs teriflunomide has been demonstrated in two pivotal clinical trials (ASCLEPIOS I & II).[1] However, real-world data are needed to understand the utilization and safety of OMB in a broader population outside of a clinical trial.

OBJECTIVE

- The purpose of this study was to describe baseline characteristics and 6-month tolerability, safety and persistence in a real-world cohort of patients with MS starting OMB.

METHODS

STUDY DESIGN

- This was a non-interventional, retrospective review of a longitudinal electronic medical record (EMR) dataset (collected as part of the Cleveland Clinic registry) of MS patients initiating OMB in real-world practice.

DATA SOURCE

- The Cleveland Clinic database is a large registry of over 6,000 MS patients and has standardized methods of collecting data in aggregate into a large database.

INCLUSION AND EXCLUSION CRITERIA

- Adult patients (≥18 years) prescribed OMB from October 2020-August 2022, having a diagnosis of clinically isolated syndrome or MS (at two Cleveland Clinic comprehensive MS centers), and a follow-up of 6 months, were identified and their EMR data were retrospectively reviewed.
- Patients participating in OMB clinical trials (e.g., ARTIOS, OLIKOS) were excluded.

ANALYSES

- Categorical variables were reported using frequencies (%) of relevant subgroups, and numerical variables were summarized using means (SD: standard deviation) or medians (IQR: interquartile range).
- Baseline was defined as up to 12 months pre-OMB, and 6-month follow-up was defined as 6 ± 3 months post-OMB initiation.
- OMB was defined as a switch therapy when patients started OMB within 3 months of discontinuing a prior DMT.
- All data collection, data management, and statistical analyses were completed by the Cleveland Clinic investigators.

VARIABLES ASSESSED

- Patient demographics and MS disease characteristics
- Key comorbidities
- Previous DMT status (DMT naive or experienced)
- Prior DMTs received and reasons for discontinuation
- 6-month tolerability and adverse effects
- 6-month discontinuation and reasons for discontinuation

ETHICS

- The Cleveland Clinic Institutional Review Board approval was obtained for the conduct of this study.

RESULTS

STUDY POPULATION

- A total of 175 patients were included in the analyses.

PATIENT BASELINE CHARACTERISTICS

- The mean age of patients at baseline was 44.9 years (SD: 10.4; range: 21-72 years). The majority of the patients were female (73.7%), Caucasian (81.1%), non-Hispanic (92%), and had relapsing-remitting MS (77.7%) (**Table 1**).
- The mean disease duration was 13.6 years (SD: 9.6; range: 0-48 years). The majority of patients (86.9%) had received a median of two agents (IQR: 1-4 agents) prior switching to OMB, 67.8% of patients switched from prior DMT to OMB without a treatment gap (i.e. 3 months).
- Of the patients with available brain MRI data at baseline, 54 (34%) had new T2 lesions and 27 (17%) had new gadolinium enhancing (GdE) lesions.
- Over half of the patients (55.9%) reported using a moderate or low-efficacy drug as their most recent DMT. The most common reasons for switch were adverse effects (36.2%) followed by breakthrough disease (34.9%), and inconvenience (15.1%) (**Figure 1**). The median time between prior DMT and OMB was 5.3 months (IQR: 1-12.5 months).
- DMTs before OMB change were monoclonal antibodies (44.1%), fumarates (21.1%), sphingosine-1-phosphate receptor modulators (15.8%), teriflunomide (7.2%), and interferon beta-1a (4.6%).

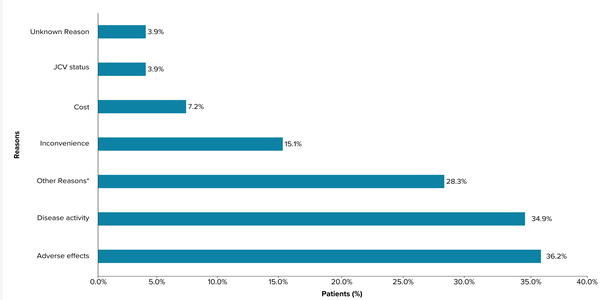
Table 1. Patient demographic, baseline clinical and treatment characteristics

	Total (N=175)
Age (years), mean (SD)	44.9 (10.4)
Female, n (%)	129 (73.7)
Disease duration, mean (SD)	13.6 (9.6)
Race, n (%)	
Caucasian	142 (81.1)
Black	22 (12.6)
Others	11 (6.3)
Ethnicity, n (%)	
Hispanic	8 (4.6)
Not Hispanic	161 (92)
Missing	6 (3.4)
Current MS course, n (%)	
CIS	3 (1.7)
PPMS	4 (2.3)
PRMS	4 (2.3)
RRMS	136 (77.7)
SPMS	27 (15.4)
Missing	1 (0.6)
Key comorbidities, n (%)	
Hypertension	34 (19.4)
Hyperlipidemia	25 (14.3)
Diabetes, Type 2	12 (6.9)
Other	69 (39.4)
Relapses in the year prior to starting OMB, n (%)	
0	136 (77.7)
1	36 (20.6)
2	3 (1.7)

	Total (N=175)
PDDS, n (%)	
Normal	23 (13.1)
Mild disability	11 (6.3)
Moderate disability	8 (4.6)
Severe disability[a]	32 (18.3)
Missing	101 (57.7)
Prior DMT experienced, n (%)	
No	23 (13.1)
Yes	152 (86.9)
High-efficacy DMTs (monoclonal antibodies)[a], n (%)	67 (44.1)
Moderate/low-efficacy DMTs, n (%)	85 (55.9)
Fumarates[b]	32 (21.1)
S1PR Modulators[c]	24 (15.8)
Teriflunomide	11 (7.2)
Interferon β-1a[d]	7 (4.6)
Glatiramer acetate	8 (5.3)
Others[e]	3 (1.9)
New brain T2 lesions, n (%)**	
0	104 (65.8)
1-3	32 (20.3)
>3	22 (13.9)
New brain GdE lesions, n (%)***	
0	133 (83.1)
1-3	22 (13.7)
>3	5 (3.1)

[a]alemtuzumab (0.7%), natalizumab (6.6%), ocrelizumab (35.5%) and rituximab (1.3%); [b]dimethyl fumarate (19.7%), monomethyl fumarate (0.7%) and diroximel fumarate (0.7%); [c]fingolimod (11.2%), siponimod (2.6%) and ozanimod (2.0%); [d]peglFNβ-1a(2.0%), interferon β-1a (2.7%); [e]Included one patient each on cyclophosphamide, cladribine, methylprednisolone
*Includes gait disability (7.4%), early cane (2.9%), late cane (1.1%), bilateral support (5.1%) and wheelchair or scooter (1.7%). ** N=158, ***N=160
CIS, clinically isolated syndrome; DMTs, disease-modifying therapies; GdE: Gadolinium-enhancing; MS, multiple sclerosis; PDDS, Patient Determined Disease Steps; PPMS, primary progressive MS; PRMS, progressive relapsing MS; RRMS, relapsing remitting MS; S1PR, sphingosine-1-phosphate receptor; SD, standard deviation; SPMS, secondary progressive MS.

Figure 1. Reasons for discontinuing prior DMTs (N=152)

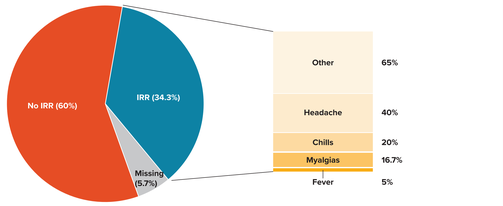


*Other reasons included completion of therapy (i.e. completion of planned treatment course such as cyclophosphamide and alemtuzumab), infusion-related concerns (accessibility, fatigue, transfer), infection concerns, intolerance to steroid pretreatment, family planning, pregnancy, wearing off effect, QT prolongation, and low ALC.
ALC, absolute lymphocyte count, DMTs, disease-modifying therapies; JCV, John Cunningham Virus

TOLERABILITY OF INJECTION (6-MONTH)

- Injection-related reactions (IRR) were commonly reported with the first injection (71.7% of the patients who reported IRR during the follow-up). The types of IRR reported in the study are presented in **Figure 2**.

Figure 2. Incidence of injection-related reactions with OMB (N=60)**



*Other reasons included abdominal pain, angioedema, bladder retention, flu, flushing, GI symptoms, insomnia, leg cramps, light-headedness, mood changes, nausea, palpitations, pruritis, rhinorrhea, shakiness in less than 10 patients. Fatigue occurred in more than 10 patients (n=15). **OMB patients who experienced IRR.
The data for types of IRR are not mutually exclusive.
GI, gastrointestinal; IRR, injection-related reactions; OMB, ofatumumab

SAFETY (6-MONTH)

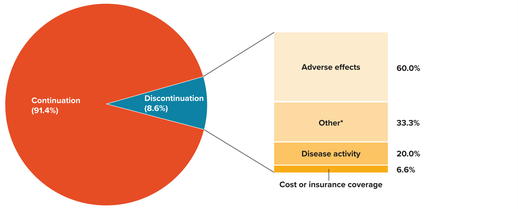
- At 6 months, 11 (6.3%) patients reported urinary tract infection, while 24 (13.7%) and 5 (2.9%) patients reported upper respiratory tract infection and other infections, respectively.
- No unexpected safety events were observed.

TREATMENT CONTINUATION/DISCONTINUATION (6-MONTH)

- Overall, 91.4% (n=160) continued OMB. For those who discontinued OMB (8.6%, n=15), the mean duration was 101 days (SD: 78.9, range: 7-275 days).

- Of the 15 patients who discontinued, the most common reason was adverse effects followed by other reasons, and disease activity (**Figure 3**).

Figure 3. Percentage of patients who continued/discontinued OMB and reasons for their discontinuation at 6-month follow-up



*Other reasons included leg feeling heavy, leg wound and infection, logistic issues, patient felt no difference in condition, poor compliance.
The data for reasons for discontinuation are not mutually exclusive.

DISCUSSION & LIMITATIONS

- Results from this clinical practice cohort suggest that safety and tolerability of OMB in an MS population with real-world characteristics were consistent with those observed in ASCLEPIOS trials. Furthermore, 6-month persistence with OMB remained high.
- This study utilized real-world observational data, and in some cases, visit data may not have been available at exactly 6 and 12 months. A 3-month window was permitted for each time point, which may have had some impact on data interpretation.
- Data for this study came from two tertiary MS centers. As such, generalizability of the findings may be affected, although this effect would be expected to be small for safety and tolerance outcomes.

REFERENCES: 1. Hauser et al. *N Engl J Med*.2020; 383: 546-557.

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