Early treatment with ofatumumab increases the likelihood of stabilizing disease in patients with relapsing-remitting multiple sclerosis.

Keywords
disease progression, ofatumumab, multiple sclerosis, disease modifying therapies, relapse activity

Abstract

Introduction
The methods of multiple sclerosis (MS) treatment are evolving rapidly with numerous classes of disease-modifying therapies (DMTs). A more aggressive approach to early and effective treatment of MS with defined treatment target increases the chance of achieving a state of no no evidence of disease activity (NEDA). Currently, B cell–depleting monoclonal antibodies have been proven as high effective strategy for the treatment of relapsing-remitting MS (RRMS). Ofatumumab (OFA), anti-CD-20 monoclonal antibody is effective in treatment of RRMS, as it positively affects relapse rates, magnetic resonance imaging (MRI) measures of disease activity and disability progression.

Material and methods
A retrospective observational study conducted in six MS clinical centers in Poland, including a cohort of patients with RRMS treated with OFA over a two-year period was presented.

Results
The results of this study showed a statistically significant decrease in the relapse activity of the disease in the course of a year of OFA therapy. The percentage of patients free of relapses increased from 45% before treatment to 88% after one year of follow-up. Moreover, the disability assessment index measured by the Expanded Disability Status Scale (EDSS) remained stable after a two years of follow-up.

Conclusions
In the presented study the high efficacy of OFA therapy in reducing recurrent disease activity as well as in inhibiting disability progression, with a favorable safety profile was confirmed. Moreover, it was emphasized that to achieve the best possible inhibition of disease activity and its progression, it is necessary to implement the treatment as soon as possible after the diagnosis.

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Introduction

Multiple sclerosis (MS) is a chronic and progressive demyelinating disease of the brain and spinal cord that responds to immunosuppression [1]. Despite progres in the treatment of relapsing-remitting MS (RRMS) thanks to the approval of numerous therapies over the past decade, reducing disease relapses and disability progression remains a challenge for many patients.

Currently, B cell–depleting monoclonal antibodies that principally act through modulation of peripheral immune responses were proven as high effective strategy for the treatment of RRMS [2]. Immediate initiation of the treatment with highly effective drugs is currently the most effective way to treat patients with MS. However, we still encounter many MS patients who initially treated with drugs of lower efficacy do not obtain satisfactory results in the long run.

Ofatumumab (OFA), an anti-CD-20 monoclonal antibody, was approved in 2020 in the European Union and has been shown to be highly effective in inhibiting disease activity and progression in randomized, controlled clinical trials [3]. It has been demonstrated that OFA is effective in treatment of RRMS, as it positively affects relapse rates, magnetic resonance imagining (MRI) measures of disease activity and disability progression. Furthermore, it can reduce risk of progression to clinically definite MS in patients with a first clinical demyelinating event.

In phase II studies (APLIOS, APOLITOS and MIRROR) subcutaneous OFA therapy in patients with RRMS was associated with a significant reduction in the number of new active (contrast-enhanced, Gd+) demyelinating lesions compared to baseline or placebo. [4-6] This was confirmed by the results of two multicenter, double-blind, randomized, active comparator-controlled (teriflunomide) phase III studies (ASCLEPIOS I (n=927) and ASCLEPIOS II (n=955), which enrolled patients aged 18–55 years, diagnosed with RRMS or secondary progressive MS (SPMS) [7]. Furthermore, long-term data from the open-label ALITHIOS study confirmed the durable efficacy of continuous OFA treatment for five and six years in patients with RRMS [8-10]. In the long-term analysis, there was a significant reduction in the frequency of relapses, a reduction in the number of new MRI lesions, and a high percentage of patients achieving no evidence of disease activity (NEDA-3). In patients who switched from teriflunomide to OFA, a marked reduction in relapses and resonance activity was observed after the change of treatment. A significant difference in annualized

relapse rate (ARR) between teriflunomide and OFA was observed in the first 2 years of follow-up. After changing treatment to OFA, no statistically significant were noted in the group of patients previously taking teriflunomide. ARR remained low in the OFA group continuously from the initiation of the treatment. However, effectiveness of OFA in the real-world setting remains to be fully elucidated.

The aim of the presented study was to assess the efficacy and safety of OFA treatment in patients with RRMS in real clinical practice in six Polish MS treatment centers. To the best of our knowledge, this is the first multi-center real world evidence (RWE) study in Poland. The hypothesis of the presented analysis, based on available clinical trials and RWE, was to indicate the high effectiveness of OFA in reducing the relapse activity of the disease and inhibiting its progression, especially in patients whose treatment was initiated immediately after the diagnosis of MS was set.

Materials and methods

Study design

This retrospective observational study was conducted in six MS clinical centers in Poland, involving a cohort of patients with RRMS who started treatment with OFA between May 2022 and August 2024. The inclusion criteria were the following: patients with RRMS, age over 18, receiving OFA treatment. The exclusion criteria were: patients with other forms of MS, patients under 18 years of age, patients taking disease modifying therapies (DMTs) other than OFA, the presence of cancer, pregnancy and breastfeeding. Epidemiologic data at baseline were applied to evaluate outcomes. All diagnoses were in accordance with the McDonald criteria (2017 update) [11]. The following data were collected: demographics, duration of the disease, number of previous MS therapies, the last DMT used before starting OFA treatment and the reason of switching; number of relapses within 12 months before OFA initiation and at 12, 24 months after starting treatment; Expanded Disability Status Scale (EDSS) scores before OFA initiation and at 12, 24 months; lymphocyte counts before OFA initiation and at 2, 6, 12, 14, 18, 24 months; MRI assessments within 12 months before OFA initiation and at 12, 24 months; adverse events (AE), discontinuation of OFA treatment, change to another DMT within the two years of treatment.

Definitions

Active MRI lesions were defined as gadolinium enhanced (Gd+) lesions or new/enlarging T2 lesions. No evidence of disease activity (NEDA-3) was defined as no relapses, no disability progression, and no active MRI lesions. According to previous reports, changes in EDSS scores were classified as improvement or worsening as follows: for patients with a baseline EDSS of 0, a change of at least 1.5 points; for patients with a baseline EDSS of 0.5 to 4.5, a change of at least 1 point; and for patients with a baseline EDSS of ≥ 5, a change of at least 0.5 points. EDSS changes that did not meet the criteria for improvement or worsening were classified as stable EDSS [12].

The degrees of lymphopenia were defined as follows: grade I (< 1.0–0.8 × 109/L); grade II (< 0.8–0.5 × 109/L); grade III (< 0.5–0.2 × 109/L); and grade IV (< 0.2 × 109/L) [13]. The incidence of lymphopenia in patients whose lymphocyte counts were measured two months after the first treatment or later was evaluated, taking into account the lowest lymphocyte count recorded for each patient.

We considered naive patients as those who had not previously received any therapy, whereas previously treated patients were those who had used other DMTs prior to OFA.

Statistical Methods

The descriptive part of statistical analysis included the numbers of each group and their structure indicators. As the variables analyzed were not normally distributed, the median and quartile range (IQR) values were provided in the descriptive analysis. The analysis of the significance of differences in the numbers of each subgroup was performed using Chi2 Pearson test.

Multivariate logistic regression was used to find possible correlations and level of the effects of independent variables upon the parameters of interest, adjusted where necessary. The Odds ratios (OR) and 95% confidence intervals (CI) were calculated respectively. A value of $p < 0.05$ was considered statistically significant. Statistical analysis was performed using STATISTICA 13.0 software (StatSoft, Kraków, Poland).

RESULTS

Patients' characteristics

The study recruited 430 patients with RRMS from 6 MS treatment centers in Poland. Among the patients, 66.5% were women, the mean age at diagnosis was 29.5 years. Until the August of 2024, on average their disease lasted 6.90 (median 5.28) years. Mean time between diagnosis and treatment initiation was 1.71 years, however, the median time was 0.25 year. Between treatment start and OFA onset – 3.90 years (median 2.79) and between diagnosis and OFA treatment onset 5.61 years (median 3.90). 27,44 % of patients were treatment-naïve.

Most patients had been previously treated (72.56%), 63,02% received 1 or 2 DMT; 9,54% - 3 or more DMT. Most often patients were treated with dimethyl fumarate (48,87%), IFN-1a/ IFN-1b/GA (30,8%) and teriflunomide (12,54%). Treatment-naïve patients and those previously treated with other therapies were not compared with each other in this study. The reason of switching treatment for OFA was mostly the ineffectiveness of the previous therapy (36,13%) and side effects (29.19%). Among patients with data available (n=234), 87.6% had type 2 oligoclonal bands in cerebrospinal fluid (CSF).

Baseline characteristics of the group are presented in Table 1.

Table 1. Baseline characteristics of patients treated with OFA (n=430)

Baseline characteristics of patients	
Age (years); mean (SD)	36,3 (9,667)
Women (%)	66.5%
Mean age at diagnosis (years)	29,5 (8,475)
Clinical characteristic of patients	
Disease duration from diagnosis to treatment (weeks); mean (SD)	89,2 (197,24)
EDSS (mean)	2.14 (1,199)
ARR one years before OFA treatment (mean)	O,64 (0.653)
ARR in first year of treatment	0,14 (0.381)
Number of previous therapies	
0	27.44%
1-2	63.02%

3 or more	9,54%
Name of previous therapies	
DMF	48,87%
S1P modulators	2,89%
Teriflunomide	12,54%
Monoclonal antibodies	2,89%
IFN-1a/ IFN-1b/GA	30,87%
Other	1,93%
NEDA 3 after the first year of treatment with ofatumumab	**72,73%**
Laboratory tests	
Lymphocyte count before treatment; mean (SD)	1,9 (0,676)
Lymphocyte count after 12 months of treatment; mean (SD)	1,6 (0,602)
Patients vaccinated against COVID-19 (%)	59 (54,13%)
Patients who underwent COVID-19 infection (%)	29 (26,60%)
Present oligoclonal bands in CSF	87.6%
Reason of switching to OFA	
Ineffectiveness of previous treatment	36,13%
AE	24,19%
MRI progression	15,81%
Relapse	11,61%
Doctor decision	9,03%
Progression in EDSS	3,23%

EDSS – Expanded Disability Status Scale, ARR – Annual Relapse Rate, MRI – Magnetic Resonance Imaging, DMT – disease modifying therapy, AE – Adverse Events, OCB – oligoclonal bands, CSF – cerebro-spinal fluid

Treatment efficacy

The results of the presented study show a statistically significant decrease in the relapse activity of the disease during one ~~a~~ year of OFA therapy. The percentage of patients free of relapses increased from 45%, before treatment, to 88% after one year of follow-up [Figure 1.]. Moreover, the disability assessment index measured by mean EDSS remained stable after a year of follow-up and was 2. With regard to the reduction of radiological activity of the described treatment, the percentage of patients without new demyelinating lesions in T2-weighted MRI increased from 59.52% before the start of treatment, to 89.77% after 6 months of treatment and 73.96% after a year of follow-up. NEDA-3 index after the first year of

treatment was obtained by 72.7% of patients, including 68% of women and 83% of men [Table2]. Moreover, logistic regression analysis showed that men were 2.3 times more likely to achieve NEDA-3 (OR=2.309, CL95=[1.064;5.012], p=0.031).

Table 2. Percentage of patients who achieved NEDA-3 (no evidence of disease activity), defined as no relapses, no disability progression, and no active MRI lesions, by subgroup (women vs men).

	NEDA-3	
	n	**%**
Total	136	72,73
Women	87	67,97
Men	49	83,05
p -value		0,0314

This was most likely related to the fact that in the population analyzed men were included in OFA treatment sooner than women. Interestingly, a significantly longer period of time from MS diagnosis to treatment initiation was observed among women (mean 100 weeks versus 67.5 weeks in men) (p=0.00514). This may suggest that a significant factor that has an influence on the chance of achieving NEDA-3 after the first year of OFA treatment is the duration of the disease – the earlier the DMT is initiated, the greater the chance of achieving NEDA-3 by the patient (p=0.005) [Figure 2.]. The analysis of the correlation of the period of time from diagnosis to the initiation of DMTs treatment confirmed the hypothesis that a significant factor increasing the chance of obtaining NEDA-3 after the first year of OFA treatment, is the duration of the disease – the longer the difference in the period between diagnosis and initiation of DMTs treatment, the lower the chance of obtaining NEDA-3. Similarly, a significant factor decreasing the chance of obtaining NEDA-3 after the first year of OFA treatment, is the delay between diagnosis and initiation of OFA treatment. Although the influence of patient's age and the length of the delay in OFA treatment proved to be statistically significant in logistic regression (p=0.045 and p=0.005, respectively), the size of the odds ratio in both cases does not allow to demonstrate the type of correlation (OR=0.967 and OR=0.999). It should be noted that in the regression analysis, age and delay were treated as continuous (numeric) variables. On the other hand, the analysis of the effect of delay as a variable coded into intervals showed that the shorter the delay period from diagnosis to the moment of initiation of OFA treatment, the higher the percentage of NEDA-3 obtained. The relationship was statistically significant (p=0.005).

Safety profile of therapy

The study also confirmed the beneficial safety profile of OFA therapy. No new safety signals were detected. AE were reported in 56 patients (18.60%) during two years of the treatment, including flu-like symptoms and weakness (Table 3.). These symptoms were mild in most patients and occurred mostly after the first dose of OFA. These events did not require additional interventions and did not lead to discontinuation of the drug. All patients completed two years treatment and did not start another treatment during follow-up period.

Table 3. Adverse events during follow-up period

Adverse events (AE)	n	%
No AE	245	81.40
Influenza-like symptoms	42	13.95
Weakness	14	4.65

The lymphocyte count 2 months after the first dose (mean 1.76) was statistically significantly lower than before the start of therapy (mean 1.90) ($p<0.0000$) [Figure 3.]. However, after a 6-month follow-up period, it returned almost to the baseline (mean 1.83) ($p>0.05$). 86.67% of patients had normal lymphocyte counts across the study, 9.39% had grade 1 lymphopenia, 3.64% grade 2 lymphopenia, 0.30% grade 3 lymphopenia and no grade 4 lymphopenia. Lymphopenia of grade 3 and higher was only observed utill month 4. COVID-19 infection was noted in 29 out of 107 patients. 59 out of 109 patients were vaccinated.

Discussion

The presented analysis was the first multicenter RWE study to assess the efficacy and safety of OFA in the Polish population, which made it innovative. The obtained results confirmed the high efficacy and safety of OFA therapy in a one-year follow-up.

The results of the proposed analysis proved the effectiveness of OFA therapy in reducing relapsing and radiological disease activity. Our data further demonstrated a measurable benefit of initiating treatment with OFA with respect to confirmed disability progression, as after one year of the treatment, the patients remained stable in EDSS assessment.

It was also indicated, that the best result of the treatment can be achieved in patients who start the therapy as soon as possible after the diagnosis of the disease has been set. The suboptimal effectiveness of OFA was noted in patients whose treatment was initiated with a delay after the diagnosis of MS was made. Therefore, early treatment with OFA is recommended to patients with active relapsing MS. These findings supported previous studies indicating the most effectiveness of immune B-cell–depleting therapies in naïve patients with RMS [9].

In relation to the safety profile, no new safety signals or side effects were detected during the follow-up period. The most common AE was flu-like symptoms that occurred after the first dose of treatment and did not require any intervention. This was consistent with previous analyses, mainly from clinical trials and confirmed the high safety profile of OFA therapy.

Similarly to our results, ASCLEPIOS I and ASCLEPIOS II studies showed, that OFA therapy, compared to the one based on teriflunomide, was associated with a significantly lower ARR [7]. In addition, a reduced risk of confirmed disability worsening (CDW) was observed at 3 and 6 months. Furthermore, OFA therapy was more effective in reducing new demyelinating lesions on MRI – there was an almost complete reduction of active demyelinating lesions. A similar effect of OFA compared to teriflunomide was observed in all analyzed subgroups (age, gender, body weight, disease activity, previous DMTs).

Additionally, a post hoc analysis of the ASCLEPIOS study assessed the effectiveness of OFA in a subgroup of treatment- naïve patients diagnosed with RRMS within the last 3 years [14]. Compared with patients receiving teriflunomide, OFA reduced ARR by 50.3% (0.09 vs. 0.18; $p<0.001$), the number of Gd+ lesions by 95.4% (0.02 vs. 0.39: $p<0.001$), and the number of new/enlarging T2 lesions/year by 82.0% (0.86 vs. 4.78, $p<0.001$).

The latest data from the open-label ALITHIOS study showed sustained efficacy of OFA treatment for up to six years in recently diagnosed patients – defined as those initiating treatment within three years of initial diagnosis – and previously untreated patients [9-10]. In patients whose OFA therapy was initiated from the beginning of diagnosis, a 44% reduction in ARR was achieved, and a 96.4% and 82.7% reduction in MRI changes (Gd+ and T2), respectively. Similarly, a 24.5% and 21.6% reduction in CDW at 3 and 6 months, respectively was noted, compared with patients who replaced teriflunomide therapy with OFA. The ARR in treatment – naïve RRMS patients was reduced from 0.104 to 0.050 (52.0% reduction), corresponding to an adjusted ARR of one relapse per 20 years. The 3- and 6-

month rates of progression independent of relapse activity (PIRA) in previously untreated patients were also lower compared to patients who have changed their treatment. A rapid increase in the percentage of patients achieving NEDA-3 was also observed, which was maintained during the six years of follow-up. This is in accordance with our results, which indicated that the earlier OFA treatment was initiated after diagnosis, the higher the chance of achieving NEDA-3.

RWE analyses are also consistent with the results from our study. Two non-interventional studies are ongoing in Germany to assess the efficacy, safety and tolerability of OFA - AIOLOS (study with previously untreated patients) and KAIROS (study with patients previously taking other DMTs) [15-16]. In the AIOLOS analysis, 384 patients (78.6% OFA | 21.4% interferon beta/glatiramer acetate (IFNβ/GA)) were enrolled by 75 centers. Relapses in the IFNβ/GA cohort tended to be more severe, and more often required hospitalization or corticosteroid treatment. In addition, more patients in the IFNβ/GA cohort than in the OFA cohort experienced serious adverse events and AEs leading to study discontinuation.

Moreover, a retrospective secondary study of MSBase registry data conducted in Australia by Van der Wait et al., which included both naïve and transition/previous therapy patients showed that the relapse-free rate in OFA group at 1 year was 94.7% and 92.9% at 2 years [17]. Furthermore, in a Swedish registry of 111 MS patients treated with OFA reduced ARR from 0.690 to 0.019 during a one-year follow-up was observed [18]. In addition patients remained stable on the EDSS scale. Similar reductions in relapse activity and disability inhibition were confirmed in the study by Chisari et al., which recruited patients with RRMS from seven Italian MS centers who were treated with OFA [20]. In contrast to the other studies, no significant differences were found between the previously treated and switched groups. Furthermore, no serious AEs were reported, the most common of which was fever on first administration (80.3%) as in our analysis.

According to the presented results, the analysis by Harding et al. demonstrated that in a real-world setting, long-term outcomes are more favorable with early intensive therapy compared with first-line moderately effective DMTs [19]. It is consistent with the He et al. study, which showed that highly effective therapy initiated within 2 years of disease onset is associated with less disability after 6-10 years than that initiated later in the course of the disease [21].

Our study had several limitations. First, due to the nature of the study (RWE) and the relatively recent approval of OFA for the treatment of RRMS in Europe (2020), the follow-up period was only one year. Therefore, our study can be considered a pilot study, especially since data are still being collected in all centers and further results will be presented in subsequent publications. In addition, it was currently a retrospective study, but as mentioned above, due to the continuous updating of data, we will be able to evaluate patients prospectively. Moreover, the vast majority of the analyzed patients had been previously treated with another DMT (over 72%), which could have influenced the assessment of the efficacy of OFA. Additionally, naïve patients and patients previously treated with other therapies were not currently compared with each other, which is planned in the next stages of the analysis. Nevertheless, in our opinion, the proposed study constitutes a significant contribution to the evaluation of the effectiveness and safety of OFA treatment analyzed in the Polish population. Already at this stage, the presented RWE analysis provided reliable results on the assessed therapy, which are consistent with previous clinical studies and RWE from other countries. Moreover, the perspective of further data collection gives possibility for even more detailed, prospective and long-term observation of patients using OFA treatment.

Conclusions

To sum up, the results of the presented study confirmed the high effectiveness of OFA therapy in reducing the relapsing activity of the disease, as well as in inhibiting the progression of disability, with a favorable safety profile. They also indicated the necessity to start treatment as soon as possible after diagnosis in order to achieve the best possible inhibition of the disease activity and progression. Early access to highly effective treatment methods, such as OFA, may help reduce the burden of disease, the risk of RRMS progression and contribute to long-term improvement of quality of life. Moreover, the presented study was one of the few multicenter RWE studies that are currently available in the literature. The analysis seemed to be limited by the short observation period. Therefore, there is a need to continue obtaining data for long-term assessment of the efficacy and safety of OFA therapy in real medical practice.

Figure 1. Efficacy of ofatumumab therapy in reducing relapse activity of the disease. The percentage of patients free of relapses increased from 45% before treatment to 88% after one year of follow-up.

Figure 2. Assessment of the correlation of the length of the period between the diagnosis of multiple sclerosis (MS) and the implementation of disease-modifying treatment (DMT) with ofatumumab (OFA) with the percentage of patients achieving disease inactivity (no evidence of disease activity - NEDA-3) defined as no relapses, no disability progression, and no active MRI lesions.

Figure 3. The lymphocyte count in subsequent months of ofatumumab (OFA) therapy.

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Ethical approval

The study was approved by the Ethics Committee of the Polish Military Medical Chamber.

Conflict of interest

The authors declare no conflict of interest.

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Patients with relapsing-remitting multiple sclerosis recruited from 6 centers in Poland between May 2022 and August 2024

Inclusion criteria

- patients with relapsing remitting multiple sclerosis
- age over 18
- receiving ofatumumab treatment

Exclusion criteria

- patients with other forms of multiple sclerosis
- patients under 18 years of age
- patients taking disease modifying therapies other than ofatumumab
- the presence of cancer
- pregnancy
- breastfeeding

430 patients with relapsing remitting multiple sclerosis

- Expanded Disability Status Scale (EDSS) scores
- Annualized Relapse Rates (ARR)
- New demyelinating lesions in T2-weighted magnetic resonance imagining (MRI)
- No evidence of disease activity (NEDA)
- Adverse events (AE)
- Lymphocyte counts
- Oligoclonal bands in cerebrospinal fluid (CSF)

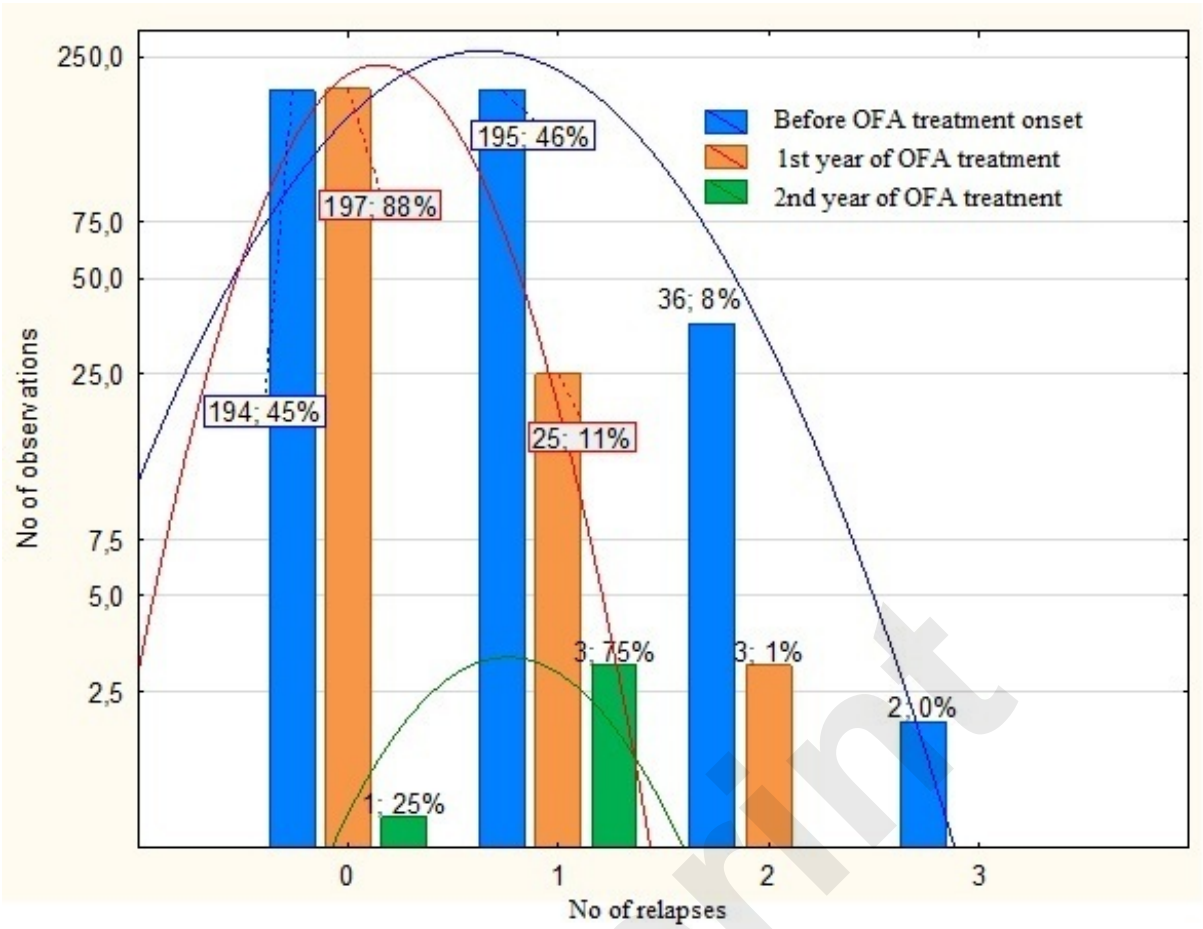
Table 1. Baseline characteristics of patients treated with OFA (n=430)

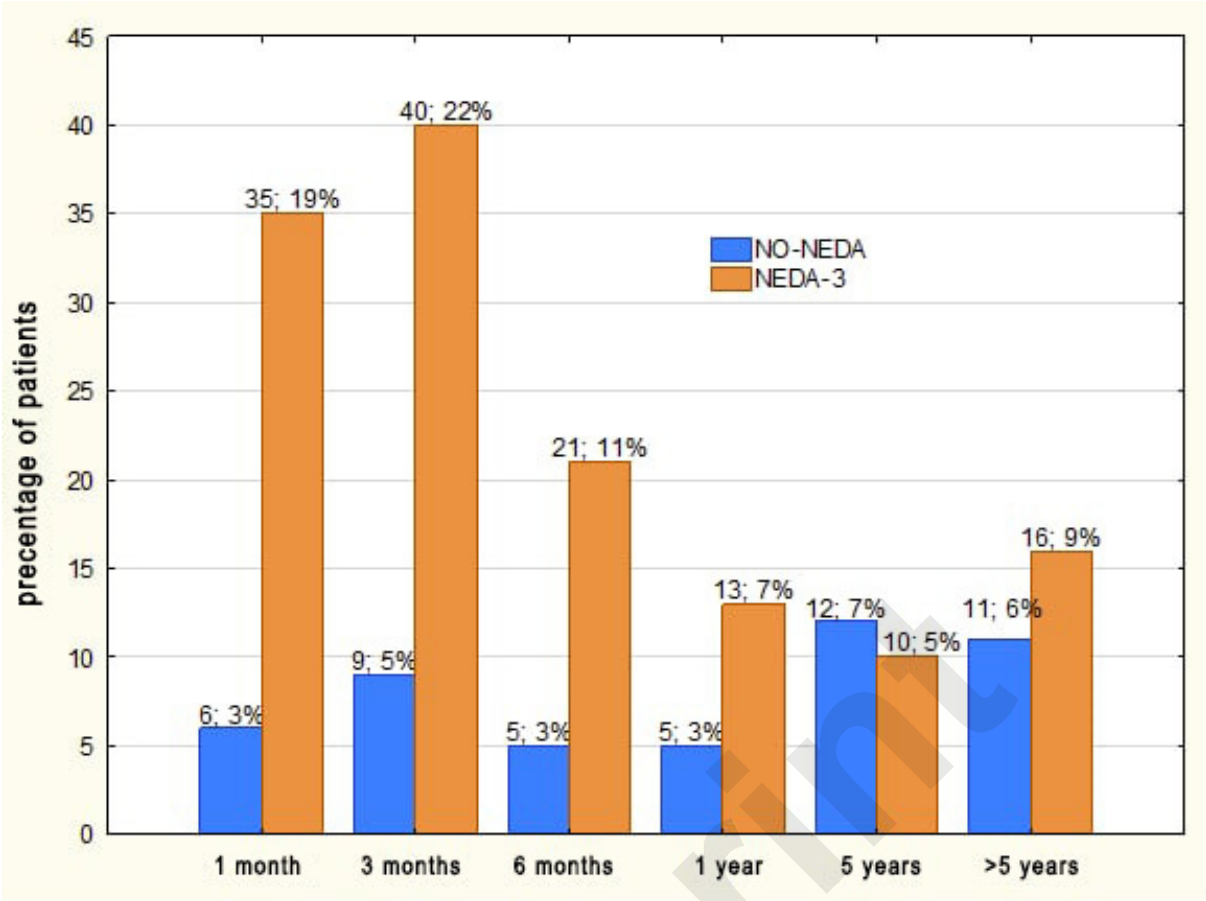
Baseline characteristics of patients	
Age (years); mean (SD)	29,5
Women (%)	66.5%
Mean age at diagnosis (years)	28.7
Clinical characteristic of patients	
Disease duration from diagnosis to treatment (weeks); mean (SD)	89,2
EDSS (mean)	2.0
ARR one years before OFA treatment (mean)	O,64
ARR in first year of treatment	0,14
No Drugs used before OFA %	27,4%
0	27.44%
2-3	63.02%
4 or more	2.32%
DMF	48%
S1P modulators	2,9%
Teriflunomide	12,5%
mAb	2,9%
IFN-1a/ IFN-1b/GA	30,8%
other	1,9%
NEDA 3 after the first year of treatment with ofatumumab	72,33%
Laboratory tests	
Lymphocyte count before treatment; median (IQR)	1,8
Lymphocyte count after 12 months of treatment; median (IQR)	1,65
Patients vaccinated against COVID-19 (%)	59 (54,13%)
Patients who underwent COVID-19 infection (%)	29 (27,1%)
Present oligoclonal bands in CSF	87.6%
Reason of switching to OFA	
Ineffectiveness of previous treatment	36%
AE	24%
MRI progression	15,*%
Relapse	11,6%
Progression in EDSS	3,2%
Doctor decision	9%

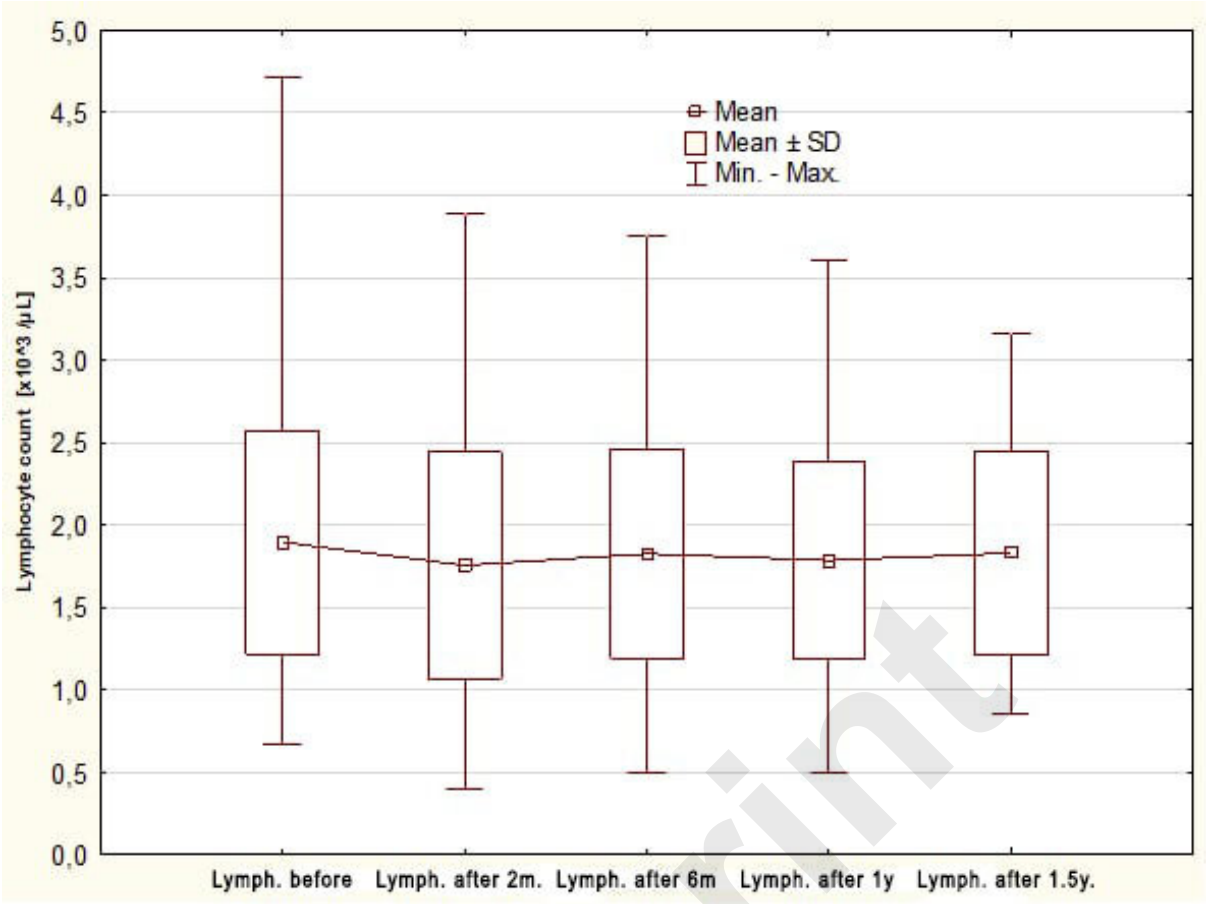
EDSS – Expanded Disability Status Scale, ARR – Annual Relapse Rate, MRI – Magnetic Resonance Imaging, DMT – disease modifying therapy, AE – Adverse Events, OCB – oligoclonal bands, CSF – cerebro-spinal fluid

Table 2. Adverse events during follow-up period

Adverse events (AE)	n	%
No AE	245	81.40
Influenza-like symptoms	42	13.95
Weakness	14	4.65


250,0
75,0
50,0
25,0
7,5
5,0
2,5
No of observations
194; 45%
197; 88%
195; 46%
25; 11%
36; 8%
1; 25%
3; 75%
3; 1%
2; 0%
0
1
2
3
No of relapses
Before OFA treatment onset
1st year of OFA treatment
2nd year of OFA treatnent


precentage of patients
45
40
35
30
25
20
15
10
5
0
NO-NEDA
NEDA-3
6; 3%
35; 19%
9; 5%
40; 22%
5; 3%
21; 11%
5; 3%
13; 7%
12; 7%
10; 5%
11; 6%
16; 9%
1 month
3 months
6 months
1 year
5 years
>5 years


Mean
Mean ± SD
Min. - Max.
Lymphocyte count [x10^3 /µL]
5,0
4,5
4,0
3,5
3,0
2,5
2,0
1,5
1,0
0,5
0,0
Lymph. before
Lymph. after 2m.
Lymph. after 6m
Lymph. after 1y
Lymph. after 1.5y.