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Ofatumumab, interferon ß1 and glatiramer acetate as first-line treatment in everyday practice: the AIOLOS study

Gereon Nelles[1], Bert Wagner[2], Stephan Richter[2], Andreas Kowalik[3] and Carola Wagner[4]

[1]Neuromed-Campus, Werthmannstr. 1c, 50935 Cologne, Germany
[2]mind mvz GmbH, Charlottenstraße 14, 70182 Stuttgart, Germany
[3]Kriegsbergstr. 60, 70174 Stuttgart, Germany
[4]Novartis Pharma Vertriebs GmbH, Roonstr. 25, 90429 Nuremberg, Germany

CONCLUSIONS

1. **Enrolled Ofatumumab patients show a very short period between first symptoms, RMS diagnosis and start of ofatumumab therapy.**
2. **Most enrolled ofatumumab patients had only one relapse before enrollment and an EDSS of ≤1.5 at baseline representing a similar patient pool to SoC.**
3. **For 91% of patients in the "ofatumumab arm" main reason for the therapy decision was the expected efficacy.**
4. **Ofatumumab treated patients reported no impacts on quality of life till FU1 as measured by FSIQ-RMS.**
5. **Three adverse events were reported in the ofatumumab cohort, whereas one SAEs was reported in the SoC cohort with a total study population of 133 patients in both cohorts.**
6. **This study represents real-world evidence that will contribute to a better understanding of RMS management in the medical community.**

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Presenter email address: gereon.nelles@uni-due.de

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INTRODUCTION

- Ofatumumab, a fully human monoclonal antibody against CD20, is the first subcutaneous B-cell depleting treatment of active relapsing multiple sclerosis (RMS). While safety and efficacy of ofatumumab versus teriflunomide were shown in a representative RMS population as part of the approval studies ASCLEPIOS I and II (COMB157G2301 and -2)[1], data from clinical routine are still missing, even though market research analysis showed that in Germany, 45% of Ofatumumab treated patients were treatment naive[3].

OBJECTIVE

- This non-interventional study AIOLOS ("A non-interventional study evaluating injectable treatments [ofatumumab, glatiramer acetate and interferon-β1] in patients with relapsing multiple sclerosis") aims to evaluate subcutaneously or intramuscular administered therapies (ofatumumab, interferon-ß1 [IFN-ß1] or glatiramer acetate [GA]) as first-line treatment in treatment-naïve RMS patients with mild/moderate disease activity in routine clinical practice.

METHODS

Study design

- This is a prospective, open label, multicenter, two-armed, non-interventional study (NIS) conducted in Germany, expected to enroll 800 patients treated with subcutaneously or intramuscular administered first-line disease-modifying drugs for RMS (ofatumumab, IFN-ß1 or GA) approved in Germany. Two treatment arms are being observed:
  - ofatumumab versus
  - standard of care (SoC) first-line therapy (IFN-ß1 or GA).
- The primary objective of this study is the retention rate of the two treatment arms after 24 months.

Patient population

- In order to ensure a comparable patient population in both study arms, only adult treatment-naïve patients without evidence of a highly active course of the disease and within 3 years after first symptoms leading to MS diagnosis are included.

Assessments

- Clinic: Laboratory and physical evaluation
- MS-activity: Magnetic Resonance Imaging (MRI), Expanded Disability Status Scale (EDSS)
- Patient's perspective: Fatigue Symptoms and Impacts Questionnaire Relapsing Multiple Sclerosis (FSIQ-RMS), Patient Health Questionnaire 8 (PHQ-8), Generalized Anxiety Disorder Scale 7 (GAD-7), Multiple Sclerosis Treatment Concerns Questionnaire (MSTCQ)
- Socioeconomic factors: Multiple Sclerosis Health Resource Survey (MS-HRS)

Statistic analysis

- Here we present interim baseline data, patient-reported outcomes on fatigue, tolerability and safety data. The interim analysis includes data of the patients enrolled to date which do not violate any in- or exclusion criteria, have at least their initial study treatment documented and in case they withdrew, have allowed further use of their study data.

RESULTS

Patient disposition

- As of May 2nd, 2023 180 patients were enrolled in AIOLOS. Of these, 110 patients were enrolled into the "ofatumumab arm" and 30 into the "SoC arm", **Figure 1**.
- In total, 133 patients were included in this analysis, 104 in the "ofatumumab arm" and 29 in the "SoC arm". 40 patients were not included in this analysis given that no initial therapy was documented yet, and 7 patients violated at least one in- or exclusion criteria.
- 36 sites contributed to the "ofatumumab arm" for this study, whereas 16 sites contributed to the "SoC arm".

Demographic and baseline data

- Demographic data of the analysis population is provided in **Table 1.** Females were substantially higher represented than males (64.4% vs. 35.6% in the "ofatumumab arm" and 86.2% vs. 13.8% in the "SoC arm").

Figure 1: Patient disposition (interim analysis)

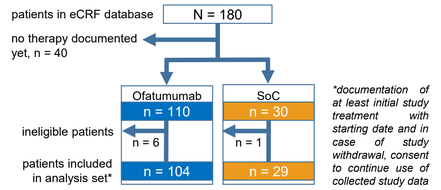


Table 1: Demography & Baseline characteristics

Variable	Ofatumumab cohort	SoC cohort
Number of patients, n	104	29
Initial therapy*		
Ofatumumab	104 (100)	-
Glatiramer acetate	-	20 (69.0)
Interferon beta	-	9 (31.0)
Age, years (mean ± SD)	36.4 ± 10.2	36.4 ± 11.6
Sex, female (%)	64.4	86.2
Age (classes in years, n (%)		
18 to 30 years	37 (35.6)	9 (31.0)
>30 to ≤40 years	37 (35.6)	15 (51.7)
>40	30 (28.8)	5 (17.2)
Working status, n (%)		
Working	90 (86.5)	23 (79.3)
Retired	1 (1.0)	2 (6.9)
Other	13 (12.5)	4 (13.8)

Figure 2: Duration between baseline and follow-up visits

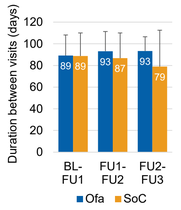


Table 2: Symptoms onset, diagnosis and last relapses

	Ofatu-mumab cohort	SoC cohort
Time between first symptoms and diagnosis, years (mean ± SD)	0.7 ± 2.2	1.0 ± 1.4
Time between diagnosis and start of treatment, years (mean ± SD)	0.3 ± 0.4	0.4 ± 0.6
Time between last relapse and start of therapy, months (mean ± SD)	4.46 ± 4.59	3.53 ± 3.12

MS medical history and disease activity status at baseline

- Time between onset of first symptoms and diagnosis was between eight and twelve months and time between diagnosis and start of treatment was about four to five months, **Table 2**.
- On average, last relapse prior to start of therapy was 4.46 ± 4.59 months ago in the "ofatumumab cohort" and 3.53 ± 3.12 months ago in the "SoC cohort", **Table 2**.
- Mean duration between visits (baseline, follow-up 1 and 2) was approx. 80 to 90 days, **Figure 2**.
- The baseline EDSS scores were comparable between both study arms (1.21 ± 0.8 for "ofatumumab arm" and 1.17 ± 0.8 for "SoC arm"). 22.1% of patients in the "ofatumumab arm" and 20.7% in the "SoC arm" had an EDSS score of 0, while 49% in the "ofatumumab cohort" and 37.9% in the "SoC cohort" had a score of 1 or 1.5. Furthermore, 25% of patients in the "ofatumumab cohort" and 31% in the "SoC cohort" had an EDSS score of 2 or 2.5, as shown in **Figure 3**.

Figure 3: EDSS score at baseline

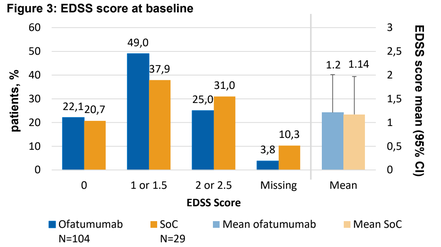
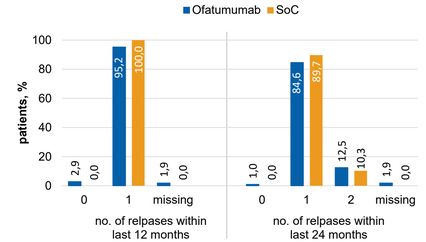
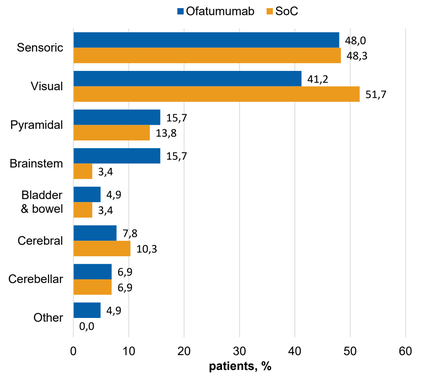


Figure 4: Number of relapses prior baseline



- Over 95% of the patients experienced one relapse during the past twelve months and for over 84% of patients this was the only relapse within the last 24 months prior to start of therapy, **Figure 4**.

Figure 5: MS symptoms before baseline visit



- More patients in the "ofatumumab cohort" showed MS symptoms affecting the brainstem compared to the "SoC cohort" (15.7% vs. 3.4%). More patients in the "SoC cohort" showed symptoms regarding the visual organ system compared to the "ofatumumab cohort" (51.7% vs. 41.2%), **Figure 5**.

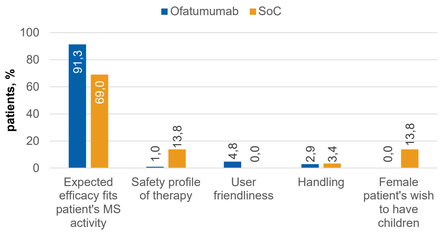
MRI

- Overall, for 78.8% of patients in the "ofatumumab cohort" and for 48.3% in the "SoC cohort" a retrospective MRI was documented at baseline.
- Information on lesion number was only provided in up to one third of the documented MRIs (T1 Gd+ lesion information unknown/missing: 56.1% in the "ofatumumab cohort" and 78.6% in the "SoC cohort". T2 lesions information unknown/missing: 57.3% in the "ofatumumab cohort" and 71.4% in the "SoC cohort").The majority of patients had no lesion or were categorized in the group of 1-5 T1 Gd+ lesions ("ofatumumab cohort" 41.5% und "SoC cohort" 21.4%). In the "ofatumumab cohort", 18.3% of patients had no or 1-5 T2 lesions, 14.6% 6-9 T2 lesions and 9.8% >10 T2 lesions. In the "SoC cohort" all 4 patients documented had no or 1-5 T2 lesions (28.5%).
- 42 patients (51.2%) in the "ofatumumab cohort" and three patients (21.4%) in the "SoC cohort" showed (a) spinal lesion(s), whereas in 19 patients (23.2%) in the "ofatumumab cohort" and in seven patients (50%) in the "SoC cohort" no spinal lesion was present. For the remaining 21 patients (25.6%) in the "ofatumumab cohort" and 4 patients (28.6) in the "SoC cohort" this information was unknown/missing.

Initial therapy

- Main reason for initial therapy decision is that the expected efficacy fits patients MS activity (91.3% in the "ofatumumab cohort" and 69% in the "SoC cohort"), **Figure 6.**

Figure 6: Main reasons for initial therapy decision



Secondary parameters - FSIQ-RMS

- Results of FSIQ-RMS at baseline are given in **Table 3**. Higher scores represent greater (impact of) fatigue. A change of 6.3 points in the FSIQ-RMS symptom scale is considered a meaningful change threshold.[2]
- Change in scores from baseline to FU1 showed worsening in three domains of patients in the "SoC arm" (n=7). No meaningful changes in scores from baseline to FU1 were observed in the "ofatumumab arm".

Table 3: FSIQ-RMS at baseline

	Ofatumumab (N=33)		SoC (N=7)	
	score	Change from BL to FU1	score	Change from BL to FU1
Symptoms daily score	27.1	2.1	32.0	**13.9**
Symptoms weekly score	7.2	0.0	7.0	2.1
Weekly impacts sub-domains (physical)	13.4	1.7	13.4	**7.5**
Weekly impacts sub-domains (cognitive/ emotional)	17.4	-2.0	18.4	4.4
Weekly impacts sub-domains (coping)	21.4	1.7	19.1	**6.3**

Adverse Events

- Until the cut-off date, 40.3% of patients in the "ofatumumab cohort" and 37.9% of patients in the "SoC cohort" experienced adverse events (AEs). Most frequent AEs affecting ≥5% of patients are presented in **Table 4**.
- Three serious adverse events (SAE) (2.9%) were reported in the "ofatumumab cohort", and one SAEs (3.4%) was reported in the "SoC cohort". None of the SAEs is suspected to have a relationship to a treatment.
- 'Injection site reactions' occurred in 1.9% of patients in the "ofatumumab cohort" and in 10.3% of patients in the "SoC cohort". 'Injections systemic reactions' occurred in 27.9% of patients in the "ofatumumab cohort" and in 3.4% of patients in the "SoC cohort". The majority of injection reactions occurred in the first month of treatment.

Table 4: Adverse events

	Ofatumumab cohort (n=104): n (%)* [95%-CI]	SoC cohort (n=29): n (%)* [95%-CI]
Any serious adverse event	**3 (2.9) [0.6; 8.1]**	**1 (3.4) [0.1; 17.8]**
Any adverse event	**42 (40.4) [30.9; 50.5]**	**11 (37.9) [20.7; 57.7]**
General disorders and administration site conditions	**28 (26.9) [18.7; 36.5]**	**3 (10.3) [2.2; 27.4]**
Chills	12 (11.5) [6.1; 19.3]	0
Influenza like illness	12 (11.5) [6.1; 19.3]	1 (3.4) [0.1; 17.8]
Injection site reaction	1 (1.0) [0.0; 5.2]	2 (6.9) [0.8; 22.8]
Nervous system disorders	**10 (9.6) [4.7; 17.0]**	**3 (10.3) [2.2; 27.4]**
Headache	7 (6.7) [2.7; 13.4]	0
Infections and infestations	**9 (8.7) [4.0; 15.8]**	**5 (17.2) [5.8; 35.8]**
COVID-19	3 (2.9) [0.6; 8.2]	3 (10.3) [2.2; 27.4]

**percentages based on all documented patients (n=104 in ofatumumab cohort, n=29 in SoC cohort)*

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2. Hudgens S., Boyanova N., Davies E. W., Jamieson C., Keenan A., Value in Health, Volume 23, Supplement 1, 2020, Page S278, ISSN 1098-3015)
3. Treatment naive: no DMT >12 months; IQVIA LRx (Mrz 21 – Feb 23)

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