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Ofatumumab in different RMS patient populations in everyday clinical practice in Germany

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INTRODUCTION

- Ofatumumab, a fully human anti-CD20 monoclonal antibody administered monthly subcutaneously, selectively depletes CD20⁺ B- and T-cells and is approved for treating relapsing multiple sclerosis (RMS) in adults[1].
- The Phase 3 ASCLEPIOS I/II trials demonstrated the superiority of ofatumumab (up to 30 months) compared to teriflunomide in reducing the clinical and MRI disease activity, while maintaining a favorable safety profile in patients with RMS[2]
- Extended treatment with ofatumumab for up to 5 years showed sustained differences in efficacy outcomes and a well-tolerated safety profile during the ALITHIOS open-label extension study[2,3]
- Data from clinical routine is currently obtained in two ongoing non-interventional studies (NIS) in Germany that, among other things, evaluate effectiveness, safety and tolerability of ofatumumab:
  - The AIOLOS-study: "A non-interventional study evaluating injectable treatments (ofatumumab, glatiramer acetate and interferon-β1) in patients with RMS" (#NCT05344469)
  - The KAIROS-study: "Ofatumumab in patients with relapsing remitting multiple sclerosis (RRMS) who previously received another disease-modifying therapy (DMT)" (#NCT05566756)

METHODS

Study design

AIOLOS study:

- Prospective, open label, multicenter, two-armed NIS expected to enroll 800 **treatment-naïve patients without evidence of a highly active course of RMS.** Enrollment is restricted to ≤2.5 EDSS and no more than five years may have passed since first symptom(s) leading to MS diagnosis.
- Patients enrolled in the AIOLOS study are either treated with **Ofatumumab** or other first-line injectable DMTs (interferon β-1a, β-1b or glatiramer acetate).
- The planned observational period per patient is two years.

KAIROS study:

- Prospective, open label, multicenter NIS with 300 enrolled patients with remitting RMS **who previously received any European Union approved** DMT for RMS but **switched to Ofatumumab**.
- Reasons for the switch may be lack of efficacy of previous DMT based on physicians' discretion or other reasons (e.g. safety or tolerability considerations, patient wish, non-adherence with previous DMT or physician's choice).
- After obtaining informed consent patients will enter in the observation period of one year and a follow-up phase (only in case of increased Expanded Disability Status Scale (EDSS) score within six months from the End of study visit).

Statistic analysis

- The interim analyses of the studies include descriptive data of the **ofatumumab patients** enrolled until 2nd January 2024 which do not violate any in- or exclusion criteria and have at least their initial study treatment documented.
- The mean observational time for this interim analysis was 6.5 months since baseline for patients enrolled to AIOLOS and 3.9 months for patients enrolled to KAIROS.
- All safety data reported from the first dose of ofatumumab until up to 100 days after the last dose were considered to be treatment-emergent and were included into the analyses.

RESULTS

Demographic and baseline data

- Demographic data of the analysis populations is shown in **Table 1**. Females were substantially higher represented than males (67.3% in the AIOLOS and 75.5% in the KAIROS trial).
- Mean time between diagnosis and start of ofatumumab was 0.3±0.5 years for the treatment-naive AIOLOS patients, while the switch patients of KAIROS showed a mean time of 9.7±7.5 years. KAIROS patients had 2.5±1.7 other DMTs before switching to ofatumumab (**Table 1**).

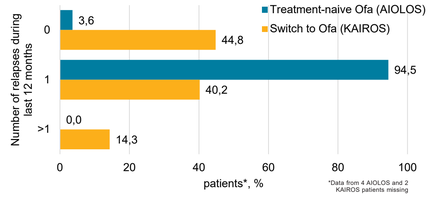
Table 1. Demographics and Baseline characterstics

	Treatment-naïve Ofa (AIOLOS)	Switch to Ofa (KAIROS)
Number of patients	220	286
Sex, female (n, %)	148 (67.3)	216 (75.5*)
Age, years (Mean ± SD)	36.2±10.4	41.0±11.3
Time between first symptoms and diagnosis (years) (Mean ± SD)	0.6±1.9	2.1±4.8
Time between diagnosis and start of ofatumumab treatment (years) (Mean ± SD)	0.3±0.5	9.7±7.5
Previously DMT-treated patients (n, %)	0 (0.0)	286 (100.0)
Number of pretreatments prior to ofatumumab initiation (Mean ± SD)	n/a	2.5±1.7
Last DMT prior to ofatumumab initiation (n,%)*		
• Interferon beta-1a & -1b, peg-interferon, glatiramer acetate	n/a	56 (19.5)
• Dimethyl fumarate, diroximel fumarate, teriflunomide	n/a	84 (29.4)
• Fingolimod, siponimod, ponesimod, ozanimod, cladribine	n/a	63 (22.0)
• Alemtuzumab, natalizumab, ocrelizumab, rituximab†	n/a	82 (28.7)
Number of relapses during the last 12 months prior to BL (Mean ± SD)	1.0±0.2	0.7±0.8
EDSS score (Mean ± SD)	1.3±0.8	2.7±1.8
Duration of observational time (months) (Mean ± SD)	6.5±5.0	3.9±3.7

*Data for two patients missing, ^Data for one patient missing, †off-label; DMT: Disease modifying therapy, EDSS: Expanded Disability Status Scale, Ofa: Ofatumumab, SD:standard deviation, n.a.: not available

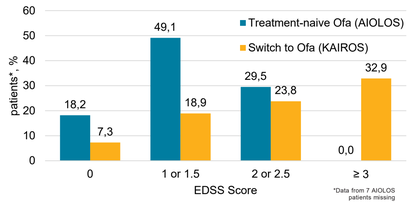
- The number of relapses 12 months prior to baseline was substantially different in the AIOLOS and KAIROS study (**Figure 1**). Almost every patient in the AIOLOS study (208 patients, 94.5%) had one relapse, whereas almost half of the patients in the KAIROS study had no relapse during this time period (128 patients, 45.1%).

Figure 1. Baseline characteristics: Number of relapses during the last 12 months prior to baseline



- The Expanded Disability Status Scale (EDSS) score differs between the subjects of the AIOLOS and KAIROS study (**Figure 2**), in part due to the different in- and exclusion criteria of the studies (AIOLOS enrollment was restricted to ≤2.5 EDSS).
- The majority of AIOLOS patients (67.3%, n=153) had a score of 1.5 or less compared to only 26.2% (n=75) of KAIROS patients.

Figure 2. Baseline characteristics: EDSS



Safety

- The cumulative exposure for AIOLOS patients was 121.2 years and for KAIROS patients 93.2 years.
- Overall, 49.1% (108 patients) experienced adverse events (AEs) in the AIOLOS study, whereas 33.2% (95 patients) experienced AEs in the KAIROS study (**Table 2**). The Exposure-adjusted incidence rate (EAIR) per 100 patient-years for AEs was 89.1 (AIOLOS) and 101.9 (KAIROS).
- In both AIOLOS and KAIROS most patients suffered from AEs originating from system organ class (SOC) 'General disorders and administration site conditions' with Influenza like illness being the most frequent condition affecting 15.9% vs. 9.4% of the patients (**Table 3**).

- Four patients (1.4%) in the KAIROS study and five patients (2.3%) in the AIOLOS study experienced serious adverse events (SAEs). The Exposure-adjusted incidence rate per 100 patient-years for SAEs was 4.3 (KAIROS) and 4.1 (AIOLOS).
- Most SAEs in the KAIROS study were allocated to SOC 'Infections and Infestations' with two patients affected by three SAEs (COVID-19 [2x], bacterial pneumonia [1x]). No tendency could be found in the AIOLOS study with the SAEs being sensorimotor disorder (1x), pyrexia (1x), breast cancer (1x), panic attack (1x) and anaphylactic reaction (1x) (**Table 3**).
- The SAE anaphylactic reaction on the day of the 1st treatment in the AIOLOS study was suspected to be in relationship with ofatumumab treatment. The patient experienced bronchospasms, dyspnoea, laryngeal/tracheal/tongue oedema, stridor, pruritus, rash, skin oedema and urticaria on the day of ofatumumab injection. The event was classified as moderate, and the patient fully recovered within one day. Ofatumumab treatment was thereafter discontinued.

- In the pivotal ASCLEPIOS I&II studies, 791 patients (83.6%) in the ofatumumab group reported an adverse event and 9.1% of the patients treated with ofatumumab reported a serious adverse event for a median follow-up of 1.6 years[2].

Table 2. Safety and Tolerability

	Treatment-naïve Ofa (AIOLOS) n (%) [95% CI] (N=220)	Treatment-naïve Ofa (AIOLOS) EAIR (patient years: 121.2)	Switch to Ofa (KAIROS) n (%) [95% CI] (N=286)	Switch to Ofa (KAIROS) EAIR (patient years: 93.2)
Patients with ≥1 AE	**108 (49.1) [42.3; 55.9]**	89.1	**95 (33.2) [27.8; 39.0]**	101.9
Patients with ≥1 SAE	**5 (2.3)⁺ [0.7; 5.2]**	4.1	**4 (1.4)‡ [0.4; 3.5]**	4.3
Patients with AEs leading to treatment discontinuation	**2 (0.9) [0.1; 3.2]**	n.a.	**1 (0.3) [0.0; 1.9]**	n.a.
Patients with ≥1 injection site reaction(s)†	**6 (2.7) [1.0; 5.8]**	5.0	**7 (2.4) [1.0; 5.0]**	7.5
Patients with ≥1 injection systemic reaction(s)†	**63 (28.6) [22.8; 35.1]†**	52.0	**56 (19.6) [15.1; 24.7]†**	60.1

A patient with multiple occurrences of an AE is counted only once in this AE category.
EAIR: Exposure-adjusted incidence rate per 100 patient-years, + one SAE with suspected relationship to ofatumumab treatment (preferred term: anaphylactic reaction); ‡ none with suspected causality; † injection reaction within 24 h after injection as assessed by treating physician

Table 3. Adverse events and Serious adverse events

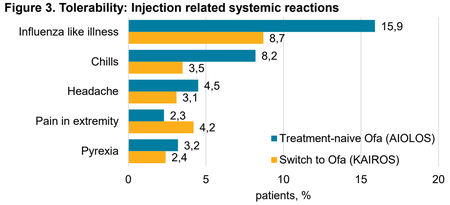
	Treatment- naïve Ofa (AIOLOS) n (%) [95% CI] (N=220)	Treatment- naïve Ofa (AIOLOS) EAIR (patient years: 121.2)	Switch to Ofa (KAIROS) n (%) [95% CI] (N=286)	Switch to Ofa (KAIROS) EAIR (patient years: 93.2)
Most common AEs affecting ≥2% of the AIOLOS or KAIROS patients [by SOC and PT]				
General disorders and administration site conditions	**64 (29.1) [23.2; 35.6]**	**52.8**	**46 (16.1) [12.0; 20.9]**	**49.3**
Influenza like illness	35 (15.9) [11.3; 21.4]	28.9	27 (9.4) [6.3; 13.4]	29.0
Chills	20 (9.1) [5.6; 13.7]	16.5	10 (3.5) [1.7; 6.3]	10.7
Pyrexia	8 (3.6) [1.6; 7.0]	6.6	9 (3.1) [1.4; 5.9]	9.7
Fatigue	7 (3.2) [1.3; 6.4]	5.8	3 (1.0) [0.2; 3.0]	3.2
Infections and infestations	**27 (12.3) [8.2; 17.4]**	**22.3**	**36 (12.6) [9.0; 17.0]**	**38.6**
Nasopharyngitis	7 (3.2) [1.3; 6.4]	5.8	1 (3.8) [1.9; 6.8]	11.8
COVID-19	10 (4.5) [2.2; 8.2]	8.3	6 (2.1) [0.8; 4.5]	6.4
Musculoskeletal and connective tissue disorders	**15 (6.8) [3.9; 11.0]**	**12.4**	**29 (10.1) [6.9; 14.2]**	**31.1**
Pain in extremity	7 (3.2) [1.3; 6.4]	5.8	15 (5.2) [3.0; 8.5]	16.1
Nervous system disorders	**31 (14.1) [3.9; 11.0]**	**25.6**	**20 (7.0) [4.3; 10.6]**	**21.4**
Headache	15 (6.8) [3.9; 11.0]	12.4	11 (3.8) [1.9; 6.8]	11.8
Skin and subcutaneous tissue disorders	**11 (5.0) [2.5; 8.8]**	**9.1**	**8 (2.8) [1.2; 5.4]**	**8.6**
Alopecia	5 (2.3) [0.7; 5.2]	4.1	2 (0.7) [0.1; 2.5]	2.1
Most common SAEs affecting ≥0.5% of the AIOLOS or KAIROS patients [by SOC and PT]				
General disorders and administration site conditions	**1 (0.5) [0.0; 2.5]**	**0.8**	**0**	n.a.
Pyrexia	1 (0.5) [0.0; 2.5]	0.8	0	n.a.
Nervous system disorders	**1 (0.5) [0.0; 2.5]**	**0.8**	**0**	n.a.
Sensorimotor disorder	1 (0.5) [0.0; 2.5]	0.8	0	n.a.
Neoplasms benign, malignant and unspecified (incl. cysts and polyps)	**1 (0.5) [0.0; 2.5]**	**0.8**	**0**	n.a.
Breast cancer	1 (0.5) [0.0; 2.5]	0.8	0	n.a.
Psychiatric disorders	**1 (0.5) [0.0; 2.5]**	**0.8**	**0**	n.a.
Panic attack	1 (0.5) [0.0; 2.5]	0.8	0	n.a.
Immune system disorders	**1 (0.5) [0.0; 2.5]**	**0.8**	**0**	n.a.
Anaphylactic reaction	1 (0.5) [0.0; 2.5]	0.8	0	n.a.
Infections and infestations	**0**	n.a.	**2 (0.7) [0.1; 2.5]**	**2.1**
COVID-19	0	n.a.	2 (0.7) [0.1; 2.5]	2.1

A patient with multiple AEs within a primary system organ class (bold font above) is counted only once.
EAIR: Exposure-adjusted incidence rate per 100 patient-years

Tolerability Injection related systemic reactions

- The most common injection related systemic reaction (occurrence within 24 h after injection as assessed by the treating physician) in the AIOLOS study was influenza like illness with 15.9% corresponding to 35 patients (95%-CI: 11.3; 21.4], **Figure 3**). Far less likely were chills, pyrexia, headache and pain in extremity. Likewise, in the KAIROS study influenza like illness represented the most common adverse events with 25 patients (8.7%; [95%-CI: 5.7; 12.6]).
- In the pivotal ASCLEPIOS I&II studies, injection-related reactions (defined as reactions occurring within 24 hours after injection) were reported the most common adverse events (20.2%), and comprised the symptoms pyrexia (7.0%), headache (5.3%), chills (3.7%), myalgia (3.9%) and others[2,4].
- Most injection related systemic reactions (>80% in the AIOLOS and 100% in KAIROS study) were experienced within the first month of ofatumumab treatment initiation. In the ASCLEPIOS I&II studies it has been observed that most injection related systemic reactions occurred after the 1st injection with decreasing occurrences at the subsequent injections[2].

Figure 3. Tolerability: Injection related systemic reactions



KEY FINDINGS & CONCLUSIONS

- Real-world interim data of both treatment-naïve patients (AIOLOS NIS) and patients switching to Ofatumumab (KAIROS NIS) provide insights on effectiveness, safety, and tolerability of ofatumumab in everyday clinical care in Germany.
- Patients of the two real-world studies show differences in various baseline characteristics such as age, time since diagnosis, number of prior relapses and EDSS score and represent the **broad spectrum of patients with MS treated with Ofatumumab in Germany**.
- The here presented data underline that the **ofatumumab safety profile** seen in the pivotal ofatumumab trials (ASCLEPIOS I&II) is **confirmed** in different patient populations in clinical practice:
  - Despite the diversity between the two analyzed real-world patient populations, the incidence rates of AEs per patient year are comparable.
  - Five patients in the AIOLOS study (2.3%) and four patients in the KAIROS study (1.4%) experienced a serious adverse event (SAE). Only one of the SAEs was suspected to have a relationship to ofatumumab treatment.
  - Most injection related systemic reactions were experienced within the first month of ofatumumab treatment initiation.

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Disclosures

Gereon Nelles served on scientific advisory boards by Biogen, BMS, Merck, Novartis and Roche. He received speaking honoraria from Biogen, BMS, Janssen Cilag, Merck, Novartis and Roche. **Felix Bischof** received personal compensation from Merck Serono, Biogen, Novartis, TEVA, Roche, Sanofi-Aventis/Genzyme, Celgene/Bristol-Myers Squibb and Janssen. None related to this report. **Josef Redolfi** and **Carola Wagner** are employees of the Novartis Pharma GmbH and work also for the Novartis Pharma Vertriebs GmbH, Nuremberg, Germany.

References

1. KESIMPTA® (ofatumumab) summary of product characteristics, 2021. Available on http://www.ema.europa.eu (accessed January 29th, 2024); 2. Hauser S et al. N Engl J Med 2020; 383:546-557; 3. Kappos L et al. Poster presented at EAN 2023, #EPR-097; 4. Novartis data on file