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KAIROS: A non-interventional study of ofatumumab in patients with relapsing remitting multiple sclerosis who previously received another disease-modifying therapy.

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SUMMARY

1. The KAIROS study aims to address the lack of real-world data from patients switching to ofatumumab from other DMTs and to characterize patient populations based on the reason for therapy switch. This includes patients switching due to safety issues or intolerance of the prior therapy, considered as in-label patients based on the Kesimpta EPAR report[1].
2. This prospective, multicenter, non-interventional study in Germany involves around 300 patients at 40 centers who switched to ofatumumab from other RMS therapies for various reasons. Here, we present the data of the first interim analysis including the baseline data of 168 patients.
3. Prospective primary data are collected via questionnaires and an electronic case report form (eCRF) over a treatment period of one year (max. 1.5 years). In addition to safety data, the medical history of the participants including disease duration, EDSS, MRI parameters and relapses is documented.

INTRODUCTION

- Ofatumumab is a fully humanized anti-CD20 monoclonal antibody that selectively depletes CD20+ B and T cells.
- In the pivotal studies ASCLEPIOS I and II (COMB157G2301 and -2), ofatumumab demonstrated a significant reduction in inflammatory activity as well as a reduction in disability progression in patients with relapsing multiple sclerosis (RMS) compared to teriflunomide.[2]
- However, there are no clinical routine data of patients switching from other therapies to ofatumumab.

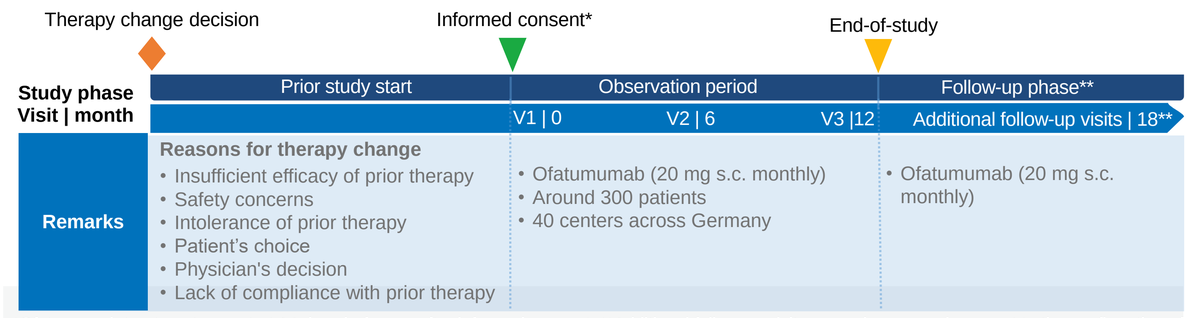
OBJECTIVE

- The aim of the KAIROS study is to characterize patient populations switching to ofatumumab based on the reason for their therapy switch. In addition, important clinical parameters for effectiveness, safety and tolerability as well as effects on quality of life, therapy satisfaction, adherence and socio-economic parameters are examined in clinical practice.

METHODS

- KAIROS study design is shown in the **Figure 1**.
- Around 300 RMS patients diagnosed per McDonald Criteria (2017), who previously received any approved DMT are eligible for enrollment.
- The decision to transition to ofatumumab therapy as routine medical treatment was taken independently of study participation and prior to the study start.
- After obtaining informed consent patients will enter in the observation period of one year (max. 1.5 years) and a follow-up phase (only in case of increased EDSS score within 6 months from the End of study visit).
- Prospective primary data are collected via questionnaires and an electronic case report form (eCRF).
- Medical history of the participants including disease duration, EDSS, MRI parameters and relapses is documented.

Figure 1: Study design



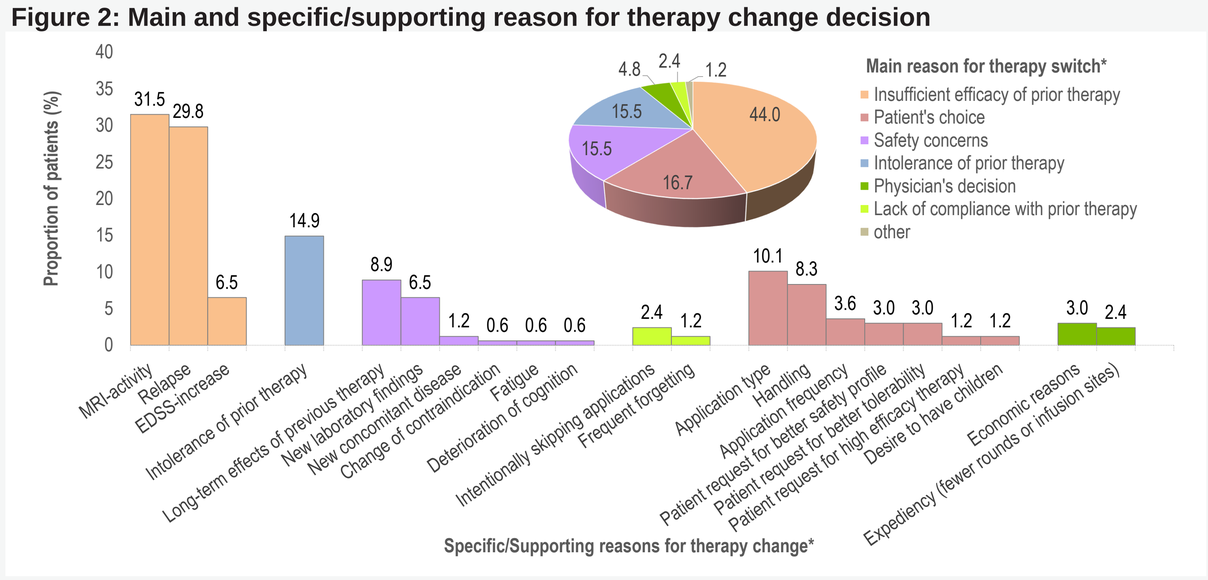
*Ofatumumab treatment may start 14 days before or after informed consent. **Additional follow-up visits can only occur subsequent to the confirmation of disease worsening, as indicated by an increased EDSS score within 6 months from the End of study (visit 3)

RESULTS

REASONS FOR THERAPY CHANGE DECISION

- The majority of patients (44.0%) in the analysis set (n=168) switched to ofatumumab due to insufficient efficacy of the prior therapy as shown in the **Figure 2**. Among these patients MRI-activity (31.5%) and relapse rate (29.8%) were the major indicators of the inefficient efficacy.
- About 15.5% switched therapies due to safety concerns associated with their prior treatment including long-term effects of previous therapy and/or new laboratory findings necessitating a change. Similar percentage of patients opted for therapy change based on their own preferences and desires (16.7%) or intolerance of the prior therapy (15.5%).
- In only a minority of cases, physicians played a central role in recommending therapy changes due to economic reasons or expediency (4.8%) or the patients switched therapies due to challenges with adhering to their previous treatment regimen (2.4%).

Figure 2: Main and specific/supporting reason for therapy change decision



* Multiple specific/supporting reasons for therapy change decision are possible for individual patients.

PATIENT CHARACTERISTICS

- Patient characteristics at the time of screening classified on the basis of reasons for therapy switch are shown in **Table 1**. The majority of patients in the analysis were female (77 %) with the mean age of approximately 41 years.
- With a mean age of 38.4 years the “efficacy” switchers (n=74) represent the youngest group in the analysis set.
- Baseline EDSS scores were available for 147 patients. On average, patients displayed an EDSS of 2.7 ± 1.86 before transitioning to ofatumumab.

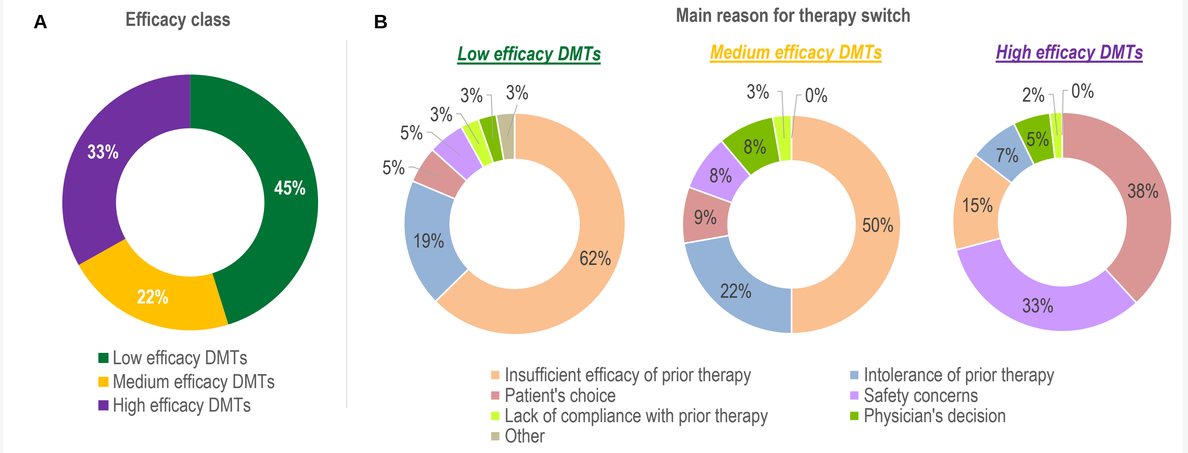
Table 1. Patient characteristics

Main reason for therapy switch to ofatumumab	Efficacy of prior therapy (n=74)	Intolerance of prior therapy (n=26)	Safety (n=26)	Compliance (n=4)	Patient’s choice (n=28)	Physician’s decision (n=8)	Others (n=2)	Total (n=168)
Gender, %								
Female/male	77.0/23.0	88.5/11.5	69.2/30.8	75.0/25.0	71.4/28.6	87.5/12.5	100.0/0.0	77.4/22.6
Age at study inclusion in years*								
Mean±SD	38.4±11.5	39.7±11.7	42.4±10.4	43.3±11.3	44.9±12.5	46.6±8.3	45.0±18.4	40.9±11.6
Age (classes) in years, %								
18 to 30 years	29.7	19.2	3.8	0.0	10.7	0.0	0	18.5
>30 to ≤40 years	29.7	38.5	50.0	50.0	32.1	25.0	50.0	35.1
>40	40.5	42.3	46.2	50.0	57.1	75.0	50.0	46.4
Working status, %								
Working	74.3	69.2	76.9	75.0	57.1	62.5	100.0	70.8
Unfit for work	4.1	7.7	0.0	0.0	3.6	0.0	0.0	3.6
Retired	12.2	11.5	23.1	0.0	32.1	37.5	0.0	17.9
Other	9.5	11.5	0.0	25.0	7.1	0.0	0.0	7.7
Number of DMTs taken prior to study start, n								
Mean±SD	2.4±1.9	2.6±1.4	3.0±1.9	2.5±1.3	3.8±2.2	2.1±1.1	2.5±2.1	2.7±1.9
EDSS at baseline								
Mean±SD	2.68±1.59	2.30±1.69	2.43±1.65	1.17±1.04	3.46±2.46	3.63±1.77	0.00±0.00	2.74±1.86

LAST DISEASE MODIFYING THERAPY PRIOR TO STUDY START

- For 166 (98.8 %) the last disease modifying therapy before switching to ofatumumab was documented.
- Collectively the DMTs previously administered included 16 medications classified in three efficacy classes (high/medium/low)*: Proportion of patients receiving the three efficacy classes of DMTs are shown in **Figure 3A**; 33% of the patients received high efficacy DMTs (purple), 45% medium efficacy DMTs (yellow) and 22% low efficacy DMTs (green).
- Reasons for switching to ofatumumab were reflected proportionally in patients receiving low (45%, green) or medium (22%, yellow) efficacy class DMTs as prior therapies with insufficient efficacy being the most frequent reason (62% and 50%, respectively) (**Figure 3B**).
- Patients receiving high efficacy DMTs (33%, purple) as prior therapy switched to ofatumumab mainly due to their own preference (38%) and safety concerns of the previous therapy (33%) (**Figure 3B**).

Figure 3: Last disease modifying therapy prior to study start



* Low efficacy DMTs: Interferone, Glatiramer acetate, Teriflunomid, Fumarat based therapies | Medium efficacy DMTs: S1P Receptor modulators, Cladiribin | High efficacy DMTs: Alemtuzumab, Natalizumab, Ocrelizumab, Rituximab

SAFETY

- At the cut-off date of this interim analysis patients received ofatumumab for up to 9 month. Until the cut-off date, 28.5 % of patients experienced adverse events (AEs). The most frequent system organ class (SOCs) and the preferred terms observed within these SOCs are presented in **Table 2**.
- Most patients (15.4%) suffered from AEs originating from SOC ‘General disorders and administration site conditions’ with Influenza like illness being the most frequent condition (10.1%)
- Two serious adverse events (SAE) (0.6%) were reported. None of the SAEs (Choledocholithiatis/Bile duct stone and Covid-19) is suspected to be related to treatment.

Table 2. Adverse events (analysis set, n = 168)

System organ class Condition	non-serious adverse events events, n | patients, n (%)*
Any serious adverse events‡	**2 | 1 (0.6)**
Any non-serious adverse events	**103 | 48 (28.6)**
General disorders and administration site conditions Influenza like illness	**42 | 26 (15.4)** 21 | 17 (10.1)
Infections and infestations Urinary tract infection	**20 | 18 (10.7)** 4 | 4 (2.3)
Musculoskeletal and connective tissue disorders Pain in extremity	**16 | 11 (6.5)** 10 | 7 (4.1)
Nervous system disorders Headache	**11 | 6 (3.6)** 6 | 4 (2.4)

* percentages based on all documented patients (n=168); ‡ none with suspected causality

CONCLUSIONS

- Real world safety data of ofatumumab remains consistent with observations in the double-blind Phase 3 ASCLEPIOS I/II trials.
- In a clinical routine setting, the majority of patients (44%) switched from a low efficacy therapy to ofatumumab highlighting the positive Benefit/Risk profile of Ofatumumab.
- More than two thirds of patients who received prior HET switched mainly due to their own preference (e.g. application type or handling) or safety concerns underlining the benefits of ofatumumab as low dose, subcutaneously (s.c.) administered anti-CD20 mAb with the potential for limiting the trade-offs between high efficacy therapy and safety.
- The KAIROS study represents real world evidence that will contribute to a better understanding of RMS management in the medical community.

REFERENCES: 1. Kesimpta EPAR – Public assessment report EMA/160608/2021 **2.** Hauser et al., N Engl J Med 2020; 383:546-557

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