Poster P486

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KAIROS: Ofatumumab in Patients With Relapsing Remitting Multiple Sclerosis who Previously Received Another Disease-Modifying Therapy

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KEY FINDINGS & 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, about half of the patients (49%) switched from a low efficacy therapy to ofatumumab highlighting the positive Benefit/Risk profile of ofatumumab.
- More than three quarters of patients who received a prior high efficacy therapy switched mainly due to their own preference (e.g., application type or handling) or safety concerns of the previous DMT, 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.

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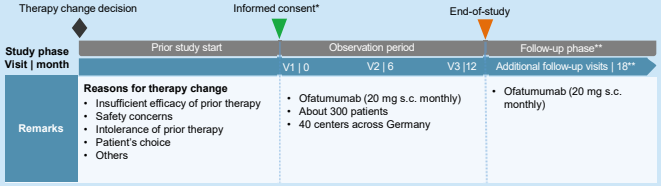
INTRODUCTION

- Ofatumumab (OMB157, Kesimpta®) 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.[1]
- However, there are no real-world insights of patients switching from other therapies to ofatumumab. The KAIROS study aims to characterize this patient population based on the reason for therapy switch and to provide insights into current therapeutic strategies.
- KAIROS is a prospective non-interventional study in Germany involving around 300 patients at 40 sites. Here, we present the data of the second interim analysis including the baseline data of 286 patients.

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 Expanded Disability Status Scale (EDSS) score within six 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 after the confirmation of disease worsening, as indicated by an increased EDSS score within 6 months from the End of study (visit 3); s.c., subcutaneous

RESULTS

PATIENT CHARACTERISTICS

- Patient characteristics at the time of screening classified based on reasons for therapy switch are shown in **Table 1**. Most of the patients in the analysis were female (75.5 %) with the mean age of approximately 41 years. With a mean age of 38.8±10.9 years the "efficacy" switchers (n=138) represent the youngest group in the analysis set and showed the highest number of relapses within the last 12 months prior to switch (1.0±0.8).
- Baseline EDSS scores were available for 237 patients. On average, patients displayed an EDSS of 2.7±1.8 before switching to ofatumumab. Highest EDSS score (3.3±2.2) was observed for patients switching DMT due to their own choice. These group also showed highest number of DMTs taken prior to switch (3.4±2.1 DMTs).

Table 1. Patient characteristics

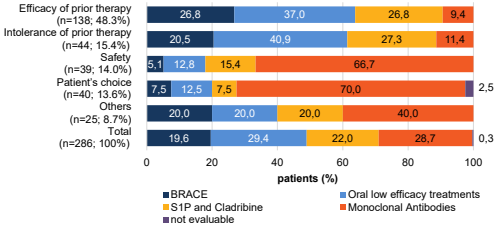
Main reason for therapy switch to ofatumumab	Efficacy of prior therapy (n=138)	Intolerance of prior therapy (n=44)	Safety (n=39)	Patient choice (n=40)	Others (n=25)	Total (n=286)
Sex, %						
Female/male	72.5/26.8*	84.1/15.9	71.8/28.2	75.0/25.0	84.0/12.0*	75.5/23.8**
Age at study inclusion (years)						
Mean±SD	38.8±10.9	41.0±11.2	43.3±10.9	43.4±13.0	45.5±9.8	41.0±11.3
EDSS (4 months before to two months after start of treatment)						
Mean±SD	2.56±1.56	2.38±1.81	2.48±1.69	3.28±2.21	2.92±1.81	2.66±1.76
Number of relapses during the last 12 months prior to baseline visit						
Mean±SD	1.0±0.8	0.5±0.6	0.4±0.6	0.4±0.6	0.5±0.9	0.7±0.8
Number of DMTs taken prior to study start						
Mean±SD	2.3±1.7	2.5±1.5	2.6±1.7	3.4±2.1	2.2±1.3	2.5±1.7

* Data for one patient missing, ** Data for two patients missing || DMT, disease modifying treatment; EDSS, Expanded Disability Status Scale; SD, standard deviation

REASONS FOR SWITCHING TO OFATUMUMAB

- Most of the patients (48.3%) in the analysis set (n=286) switched to ofatumumab due to insufficient efficacy of the prior disease modifying treatment (DMT) as shown in the **Figure 2**. Among these patients, most patients (63.8%) received an interferon or glatiramer acetate-based therapy (BRACE) or oral low efficacy treatments prior to switch.
- For 15.4% of the patients, a switch to ofatumumab was due to intolerance of the previous DMT; 61.4% of the patients in this group received BRACE or oral low efficacy treatments prior to the switch.
- For 14.0% of the patients, the main reason to switch to ofatumumab was patient choice (e.g., due to application type and handling). Most of these patients (70.0%) received other monoclonal antibodies as previous DMT.
- About 13.6% switched to ofatumumab due to safety concerns associated with their prior treatment, of which two thirds (66.7%) received other monoclonal antibodies as previous DMT.
- Overall, about half of the patients (49.0%) received BRACE or oral low efficacy treatments before switching to ofatumumab. About every fifth patient switch from either Sphingosin-1-Phosphat (S1P)-Receptor modulators or cladribine (22.0%) to ofatumumab and about every fourth patient (28.4%) from other antibodies (**Figure 2 || Total**).

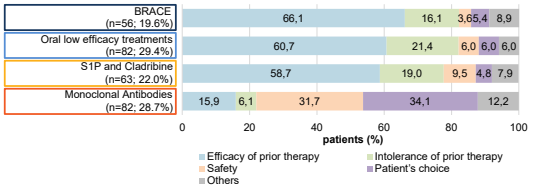
Figure 2: Reason for therapy change decision and last DMT prior to change



❖ BRACE: all interferons (interferon beta-1a, interferon beta-1b, peg-interferon beta-1a) and glatiramer acetate
❖ Oral low efficacy treatments: dimethyl fumarate, diroximel fumarate, teriflunomide
❖ S1P & Cladribine: fingolimod, siponimod, ponesimod, ozanimod and cladribine
❖ Monoclonal antibodies: alemtuzumab, natalizumab, ocrelizumab, rituximab
❖ Not evaluable: one patient in the patient choice group could not be evaluated

- Whereas for BRACE, oral low efficacy treatments and S1P or Cladribine the main reason for switching to ofatumumab was low efficacy (58.7%- 66.1%) or intolerance (16.1%- 21.4%) of the previous DMT, a switch from monoclonal antibodies was likely due to patient preference (34.1%) or safety reasons (31.7%), **Figure 3**.

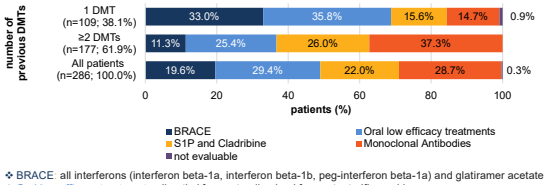
Figure 3: Reason for therapy switch vs. last DMT prior to study start



PATIENTS SWITCHING EARLY TO OFATUMUMAB (= FIRST SWITCH)

- In total, 109 patients (38.1%) received one DMT and 177 patients (61.9%) ≥2 DMTs prior switching to ofatumumab, **Figure 4**.
- Most of the first switch patients received BRACE or oral low efficacy treatments (68.8%) before switching to ofatumumab, about every seventh patient either S1P or Cladribine (15.6%) or monoclonal antibodies (14.7%) and 0.9% other drugs.
- In contrast, for 36.7% of the patients with ≥2 DMTs, the last DMT prior to therapy switch to ofatumumab was BRACE or oral low efficacy treatments. A similar fraction switched from another monoclonal antibody (37.3%) and about a quarter of patients received either S1P or Cladribine (26.0%) as the last DMT before switching to ofatumumab.
- The fraction of patients receiving BRACE or oral low efficacy treatments as the last therapy before switching to ofatumumab is about 1.9-times larger in first-switch patients compared to patients receiving ≥2 DMTs (68.8% vs. 36.7%).

Figure 4: Last DMT prior to ofatumumab depends on number of previous DMTs



❖ BRACE: all interferons (interferon beta-1a, interferon beta-1b, peg-interferon beta-1a) and glatiramer acetate
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❖ Not evaluable: one patient in the patient choice group could not be evaluated

SAFETY

- Until the cut-off date of this interim analysis patients received ofatumumab for 4.0±3.7 months.
- Overall, 33.2% of the patients (n=95) experienced adverse events (AEs). Most patients (16.1%) 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 9.4% of the patients (**Table 2**).
- Four patients (1.4%) experienced serious adverse events (SAE). Most SAEs were allocated to SOC 'Infections and Infestations' with two patients affected by three SAEs (COVID-19 [2x], bacterial pneumonia [1x]). None of the SAEs was suspected to be related to treatment.

Table 2. Adverse events (analysis set, n = 286)

Frequency of adverse events	events, n | patients, n (%)*
Any adverse event (AE)	**103 | 95 (33.2)**
Any serious adverse event (SAE)‡	**8 | 4 (1.4)**
Most common AEs [by SOC and PT]**	**n (%) [95% CI]**
General disorders and administration site conditions	**46 (16.1) [12.0; 20.9]**
Influenza like illness	27 (9.4) [6.3; 13.4]
Chills	10 (3.5) [1.7; 6.3]
Pyrexia	9 (3.1) [1.4; 5.9]
Infections and infestations	**36 (12.6) [9.0; 17.0]**
Nasopharyngitis	11 (3.8) [1.9; 6.8]
Musculoskeletal and connective tissue disorders	**29 (10.1) [6.9; 14.2]**
Pain in extremity	15 (5.2) [3.0; 8.5]
Nervous system disorders	**20 (7.0) [4.3; 10.6]**
Headache	11 (3.8) [1.9; 6.8]

* percentages based on all documented patients (n=286); **affecting ≥3% of the patients; ‡ none with suspected causality

Disclosures

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. **Marie Groth** and **Josef Redolfi** are employees of Novartis Pharma Vertriebs GmbH.

References

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