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Findings From OLIKOS: Baseline Immunoglobulin and B-Cell Concentrations in Patients Who Switch From Ocrelizumab to Ofatumumab

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SUMMARY

1 OLIKOS is the first prospective study to assess maintained clinical efficacy, participant retention and satisfaction, and safety and tolerability of monthly ofatumumab, administered via autoinjector pen, in patients with RMS previously treated with ocrelizumab or rituximab

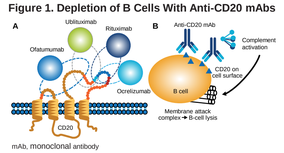
2 At baseline, 19 of 102 patients had IgG concentrations less than the lower limit of normal; however, mean IgG and IgM concentrations were within normal reference ranges. Mean CD19⁺ B-cell concentrations in OLIKOS patients were well below the normal reference range; however, B cells were detectable in 61 of 102 patients

3 Future analyses will include historical as well as on-study trends in Ig concentrations and on-study B-cell concentrations

INTRODUCTION

- Anti-CD20 therapies reduce annualized relapse rates and inflammatory lesion activity while delaying time to confirmed disability worsening in relapsing multiple sclerosis (RMS) by depleting B cells[1-3]
  - Ofatumumab (OMB) binds to a distinct epitope on 2 noncontinuous regions of CD20 on the surface of B cells[4] (**Figure 1A**). Complement-dependent cytotoxicity is induced by activation of the classical complement pathway in response to monoclonal antibody binding at the cell surface[4] (**Figure 1B**)

Figure 1. Depletion of B Cells With Anti-CD20 mAbs



- Ocrelizumab and rituximab are administered intravenously (IV), whereas OMB is administered subcutaneously (SC) via autoinjector pen, facilitating patient self-administration at home
- OLIKOS (NCT04486716) is a single-arm, prospective, multicenter, phase 3b study designed to assess the maintained efficacy and safety of, and patient satisfaction with, OMB in patients with RMS transitioning from IV anti-CD20 therapy
- OLIKOS is designed to address the important clinical question of what the effects of OMB are on immunoglobulin (Ig) concentrations in patients previously exposed to intermittent IV anti-CD20 therapy

OBJECTIVE

- Describe baseline Ig and B-cell concentrations, along with other baseline demographic and clinical characteristics, for patients enrolled in OLIKOS

METHODS

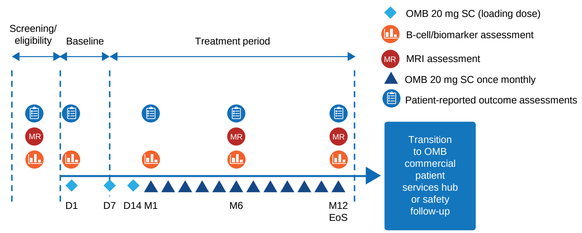
STUDY DESIGN

- OLIKOS enrolled patients aged 18 to 60 years with RMS per 2017 revised McDonald criteria who had received ≥2 consecutive IV courses of anti-CD20 therapy (ocrelizumab or rituximab), with the last dose 4 to 9 months before OLIKOS baseline. Patients also had Expanded Disability Status Scale (EDSS) score ≤5.5 and were neurologically stable for 1 month before study drug administration
- Participants were enrolled from 21 centers in the United States. All baseline labs were conducted via the central lab (LabCorp)
- Patients with suboptimal response to their anti-CD20 therapy or who discontinued it due to select treatment-emergent adverse events (TEAEs) were excluded
- Patients receive open-label OMB 20 mg SC once monthly for 12 months following an initial loading regimen of 20-mg SC doses on Days 1, 7, and 14 (**Figure 2**)
- The primary endpoint is the proportion of patients with no change or reduction in the number of gadolinium-enhancing lesions observed by magnetic resonance imaging from baseline to Month 12
- Secondary endpoints include OMB retention, immune biomarker changes, treatment satisfaction, and TEAEs (all at Months 6 and 12)

STUDY POPULATIONS

- The full analysis set (FAS) comprised all patients who received ≥1 dose of OMB 20 mg SC. The safety set (SAF) is identical to the FAS

Figure 2. Study Design



D, Day; EoS, end of study; M, Month; MRI, magnetic resonance imaging; SC, subcutaneous

RESULTS

- As of January 2023, OLIKOS has screened 145 patients. Following 34 screen failures, 111 patients were enrolled and received OMB 20 mg; these patients were included in the FAS/SAF analysis sets. The population analyzed for this poster included 121 screened patients, 19 screen failures, and 102 enrolled patients

BASELINE CHARACTERISTICS

- The mean age at baseline for patients in OLIKOS was 43.5 years (**Table 1**)
- Most patients were White (77.5%) and female (66.7%) (**Table 1**)

Table 1. Demographics and Baseline Characteristics

Characteristic	OMB 20 mg (N=102)
Mean (SD) age, years	43.5 (8.2)
Sex, n (%)	
Male	34 (33.3)
Female	68 (66.7)
Race, n (%)	
White	79 (77.5)
Black or African American	19 (18.6)
Asian	3 (2.9)
Unknown	1 (1.0)
Ethnicity, n (%)	
Hispanic or Latino	29 (28.4)
Not Hispanic or Latino	71 (69.6)
Not reported	2 (2.0)

OMB, ofatumumab; SD, standard deviation
n: Number of patients with a measurement (for continuous variables); N: Number of patients in the full analysis set. Percentages are computed using N as the denominator

- Most OLIKOS patients had relapsing-remitting MS upon study entry (98%), with a mean (standard deviation [SD]) time since diagnosis of 9.36 (7.21) years (**Table 2**)
- Mean (SD) baseline EDSS score of OLIKOS patients was 2.93 (1.29) (**Table 2**)
- Just 1 OLIKOS patient had previously received rituximab, whereas the other 101 patients had previously received ocrelizumab (**Table 3**)
- The average duration of previous rituximab or ocrelizumab therapy for OLIKOS patients was 33.90 and 26.65 months, respectively, with a mean (SD) time between patients' last infusion of rituximab or ocrelizumab and their baseline visit of -6.62 (not applicable) or -6.20 (1.62) months, respectively (**Table 3**)
- The patient who previously received rituximab discontinued treatment based on patient/guardian decision. Among those who received previous ocrelizumab, the most common reason for disease-modifying therapy discontinuation was patient/guardian decision (49.0%) (**Figure 3**)

Table 2. MS Baseline Characteristics and Disease History

Characteristic	OMB 20 mg (N=102)
Mean (SD) baseline EDSS score	2.93 (1.29)*
Number of Gd+ T1 lesions	
Mean (SD)	0.01 (0.10)†
Median	0.00
T1 lesions present at baseline (yes), n (%)	1 (1.0)
Mean (SD) duration of MS since diagnosis, years	9.36 (7.21)
Type of MS at study entry, n (%)	
RRMS	100 (98.0)
SPMS	2 (2.0)

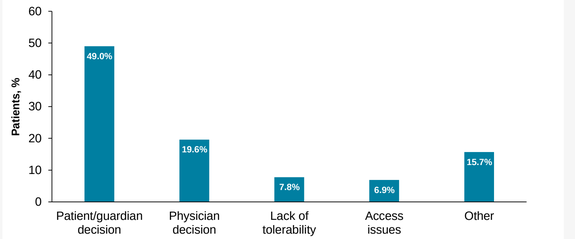
EDSS, Expanded Disability Status Scale; Gd+, gadolinium-enhancing; MS, multiple sclerosis; OMB, ofatumumab; RRMS, relapsing-remitting multiple sclerosis; SD, standard deviation; SPMS, secondary progressive multiple sclerosis
*n=101; †n=95
EDSS score ranges from 0 (normal) to 10 (death due to MS), in 0.5-unit increments. Duration of MS since diagnosis (years) is derived ([first dose date – MS diagnosis start date + 1] / 365.25). n: Number of patients with a measurement (for continuous variables); N: Number of patients in the full analysis set. Percentages are computed using N as the denominator

Table 3. Previous Use of MS Disease-Modifying Therapies

Characteristic	OMB 20 mg (N=102)
Previous MS IV anti-CD20 therapy	
Rituximab, n (%)	1 (1.0)
Ocrelizumab, n (%)	101 (99.0)
Mean (SD) duration of previous IV anti-CD20 therapy, months	
Rituximab	33.90 (NA)
Ocrelizumab	26.65 (15.21)
Time between last infusion and baseline visit, months	
Rituximab	
Mean (SD)	-6.62 (NA)
Ocrelizumab	
Mean (SD)	-6.20 (1.62)
Median (range)	-6.03 (-11.6 to -1.3)

IV, intravenous; MS, multiple sclerosis; NA, not applicable; OMB, ofatumumab; SD, standard deviation
A patient can be counted in multiple categories. For duration of previous IV and time between last infusion and baseline visit: n: Number of patients with a measurement (for continuous variables); N: Number of patients in the safety set

Figure 3. Reasons for Discontinuation of Previous Ocrelizumab Treatment



- Mean baseline IgG) and IgM concentrations were within the normal reference ranges (**Table 4**)
- Mean CD19⁺ B-cell concentrations were well below the normal reference range at baseline (**Table 4**)

Table 4. Baseline Hematology Parameters

Parameter	OMB 20 mg (N=102)
IgG concentration, g/L	
Mean (SD)	9.74 (2.82)
Median (range)	9.47 (4.58-17.00)
Reference range	7.00-16.00
IgM concentration, g/L*	
Mean (SD)	0.61 (0.34)
Median (range)	0.54 (0.20-1.71)
Reference range	0.40-2.30
CD19⁺ B-cell concentration, cells/μL†	
Mean (SD)	25.29 (58.35)
Median (range)	1.00 (0-325)
Reference range	107-698

IgG, immunoglobulin G; IgM, immunoglobulin M; OMB, ofatumumab; SD, standard deviation
*n=92; †n=99
n: Number of patients with a measurement (for continuous variables); N: Number of patients in the safety set

ABBREVIATIONS: D, Day; **EDSS**, Expanded Disability Status Scale; **EoS**, end of study; **FAS**, full analysis set; **Gd+**, gadolinium-enhancing; **Ig**, immunoglobulin; **IgG**, immunoglobulin G; **IgM**, immunoglobulin M, **IV**, intravenous; **M**, Month; **mAb**, monoclonal antibody; **MRI**, magnetic resonance imaging; **MS**, multiple sclerosis; **NA**, not applicable; **OMB**, ofatumumab; **RMS**, relapsing multiple sclerosis; **RRMS**, relapsing-remitting multiple sclerosis; **SAF** (safety analysis set; **SC**, subcutaneous; **SD**, standard deviation; **SPMS**, secondary progressive multiple sclerosis; **TEAE**, treatment-emergent adverse event

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