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OLIKOS Study: 6-Month Interim Efficacy and Safety in Patients With Relapsing Multiple Sclerosis Who Switched to Subcutaneous Ofatumumab From Intravenous Anti-CD20 Therapies

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KEY FINDINGS & CONCLUSIONS

- In this interim analysis of the phase 3b OLIKOS study, ofatumumab 20 mg subcutaneous maintained efficacy at 6 months as demonstrated by no gadolinium-enhancing type 1 lesions in patients switching from intravenous anti-CD20 therapies
- From Baseline to Month 6, mean immunoglobulin M and immunoglobulin G concentrations remained within the normal reference ranges and median CD19+ B-cell concentration decreased from 1.00 to 0.00 cells/µL
- Treatment-emergent adverse events occurred at the same frequency as in phase 3 clinical trials, with no new safety signals identified

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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] Complement-dependent cytotoxicity is induced by activation of the classical complement pathway in response to monoclonal antibody binding at the cell surface[5]
- 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 may provide additional information on the effects that OMB has on immunoglobulin (Ig) concentrations in patients previously exposed to intermittent IV anti-CD20 therapy

OBJECTIVE

- To describe interim efficacy and safety results for patients enrolled in OLIKOS who completed the first 6 months of the study

METHODS

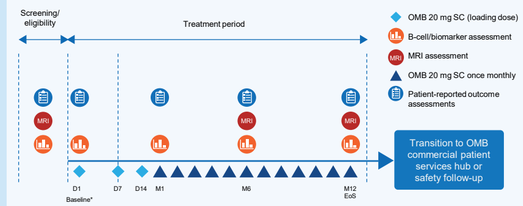
Study Design

- OLIKOS enrolled patients aged 18 to 60 years with RMS per the 2017 revised McDonald criteria[6] who had received ≥2 consecutive IV courses of anti-CD20 therapy (ocrelizumab or rituximab), with the last dose being 4 to 9 months before OLIKOS Baseline. Patients also had Expanded Disability Status Scale score ≤5.5 and were neurologically stable for 1 month before study drug administration
- Patients were enrolled from 21 centers in the United States. All Baseline laboratory assessments were conducted via the central laboratory (Labcorp)
- Exclusion criteria included suboptimal response to anti-CD20 therapy and discontinuation of anti-CD20 due to select treatment-emergent adverse events (TEAEs); patients were required to be stable on their previous therapy and switched for reasons other than safety or lack of efficacy
- Patients are receiving 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 1**)
- The primary endpoint is the proportion of patients with no change or reduction in the number of gadolinium-enhancing (Gd+) lesions observed by magnetic resonance imaging (MRI) 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) comprises all patients who received ≥1 dose of OMB 20 mg SC. The safety set (SAF) is identical to the FAS

Figure 1. OLIKOS Study Design



D, Day; EoS, end of study; M, Month; MRI, magnetic resonance imaging; OMB, ofatumumab; SC, subcutaneous
*All Baseline assessments were performed prior to dispensing the study drug

RESULTS

- A total of 145 patients were screened for inclusion in OLIKOS
- Following 34 screen failures, 111 patients were enrolled; of these, 102 received OMB 20 mg and were included in the FAS/SAF
- Of the 102 patients included in the FAS/SAF, 18 had MRI assessments outside of the 6-month window and 7 had no MRI data
- As of August 2023, 77 patients had evaluable MRI data for the primary endpoint within the 6-month window

Baseline Characteristics (Table 1)

Table 1. Patient Demographics and Baseline Clinical Parameters

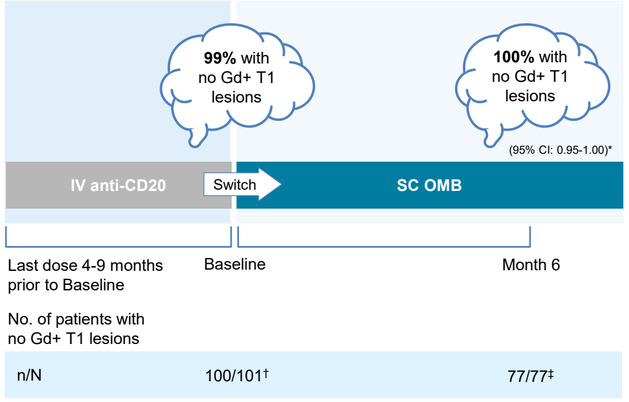
Characteristic	OMB 20 mg SC (N=102)
Age, years, mean (SD)	43.5 (8.2)
Female, n (%)	69 (67.6)
Race, n (%)	
White	78 (76.5)
Black or African American	20 (19.6)
Asian	3 (2.9)
Unknown	1 (1.0)
Ethnicity, n (%)	
Not Hispanic or Latino	70 (68.6)
Hispanic or Latino	30 (29.4)
Not reported	2 (2.0)
BMI, kg/m², mean (SD)	29.3 (7.3)
Baseline EDSS score	
Mean (SD)	2.9 (1.4)
Median (range)	2.9 (0.0-5.5)
Gd+ T1 lesions*, n	
Mean (SD)	0.01 (0.1)
Median	0
Gd+ T1 lesions present at Baseline (yes), n (%)	1 (1.0)
Duration of MS since diagnosis, years, mean (SD)	9.4 (7.1)
Type of MS at study entry, n (%)	
RRMS	100 (98.0)
SPMS	2 (2.0)
Previous MS IV anti-CD20 therapy, n (%)	
Rituximab	1 (1.0)
Ocrelizumab	101 (99.0)
Duration of previous IV anti-CD20 therapy, months, mean (SD)	
Rituximab	33.90 (NA)
Ocrelizumab	26.71 (15.15)
Time between last infusion and Baseline visit, months	
Rituximab	
Mean (SD)	-6.62 (NA)
Ocrelizumab	
Mean (SD)	-6.26 (1.62)
Median (range)	-6.13 (-11.6 to -1.3)

BMI, body mass index; EDSS, Expanded Disability Status Scale; FAS, full analysis set; Gd+ T1, gadolinium-enhancing type 1; IV, intravenous; MS, multiple sclerosis; NA, not applicable; OMB, ofatumumab; RRMS, relapsing-remitting multiple sclerosis; SAF, safety set; SC, subcutaneous; SPMS, secondary progressive multiple sclerosis
*n=101
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 FAS/SAF. Percentages are computed using N as the denominator

Primary Efficacy Endpoint

- In this interim analysis, in the subgroup of patients with evaluable MRI assessments (n=77), 100% met the primary efficacy endpoint at Month 6 (**Figure 2**)
- No Gd+ T1 lesions were identified in the 18 patients with MRI assessments outside of the 6-month window (range, 1-64 days)

Figure 2. Number of Patients With No Change or Reduction in the Number of Gd+ T1 Lesions From Baseline to Month 6



Gd+ T1, gadolinium-enhancing, type 1; IV, intravenous; MRI, magnetic resonance imaging; No., number; OMB, ofatumumab; SC, subcutaneous
*The 95% CI was computed using normal approximation method. †MRI was performed after Baseline for 1 patient. ‡Includes patient with Gd+ T1 lesion at Baseline
Response was defined as no change or a reduction in the number of Gd+ T1 lesions. Nonresponder imputation was applied for missing data. Only patients with evaluable MRI assessment within the predefined interval are included in the analysis

Safety Results

- TEAEs occurred at the same frequency as phase 3 clinical trials,[7] including low rates of injection-related reactions, with no new safety signals identified (**Table 2**)
- The most common injection site and injection systemic reactions were injection site pain (3.9%) and headache (4.9%), respectively (**Table 2**)
- The most frequent TEAEs (incidence >4%) were COVID-19 (14.7%), fatigue (9.8%), headache (8.8%), urinary tract infection (6.9%), pruritus (5.9%), and dizziness (4.9%)

Table 2. TEAEs

Characteristic, n (%)	OMB 20 mg SC (N=102)
Any TEAE	77 (75.5)
Serious TEAE	1 (1.0)
Drug-related TEAE	32 (31.4)
Discontinued study due to TEAE	1 (1.0)
Drug interruptions due to TEAE	3 (2.9)
Injection site reaction	8 (7.8)
Injection systemic reaction	16 (15.7)

OMB, ofatumumab; SC, subcutaneous; TEAE, treatment-emergent adverse event
TEAEs causing study drug discontinuations or interruptions refer to those with "action taken with study treatment" answered as "drug withdrawn" or "drug interrupted", respectively

Hematology Parameters

- Mean Baseline IgG and IgM concentrations were within the normal reference ranges, and mean Baseline CD19+ B-cell concentrations were well below the normal reference range (**Table 3**)
- Mean IgG and IgM levels remained within the normal reference ranges at Month 6 (**Table 3**)
- Although some patients' IgG/IgM levels were outside of the normal reference range, no values of clinical concern were reported
- At Baseline, 8 (7.8%) of patients had CD19+ B-cell concentrations within the normal reference range. However, all patients showed depleted B-cell concentrations after switching to ofatumumab

Table 3. Change in Hematology Parameters From Baseline to Month 6

Parameter	Baseline	Month 6	Change
IgG concentration, n	102	95	95
Mean (SD), g/L	9.88 (2.84)	9.80 (2.92)	-0.10 (0.71)
Median (range), g/L	9.62 (4.58-17.00)	9.58 (4.59-17.89)	-0.03 (-2.83 to 1.41)
IgM concentration, n	102	95	95
Mean (SD), g/L	0.58 (0.35)	0.52 (0.34)	-0.05 (0.08)
Median (range), g/L	0.49 (0.10-1.71)	0.46 (0.10-1.77)	-0.04 (-0.45 to 0.14)
CD19+ B-cell concentration, n	101	90	90
Mean (SD), cells/µL	25.39 (58.20)	0.54 (1.38)	-25.81 (58.86)
Median (range), cells/µL	1.00 (0-325)	0.00 (0-8)	-1.00 (-324 to 8)

IgG, immunoglobulin G; IgM, immunoglobulin M
n: Number of patients with a measurement (for continuous variables). At Month 6, only patients with a value at both Baseline and that time point are included. IgG reference range: 7.00-16.00 g/L; IgM reference range: 0.40-2.30 g/L; CD19+ B-cell concentration reference range: 107-698 cells/µL

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