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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

Le H. Hua,[1] Brandon Brown,[2] Elizabeth Camacho,[2] Benjamin M. Greenberg,[3] Roland G. Henry,[4] Rebecca Piccolo,[2] Enrique Alvarez[5]

[1]Cleveland Clinic Lou Ruvo Center for Brain Health, Las Vegas, NV, USA; [2]Novartis Pharmaceuticals Corporation, East Hanover, NJ, USA; [3]Department of Neurology, University of Texas Southwestern Medical Center, Dallas, TX, USA; [4]UCSF Weill Institute for Neurosciences, Department of Neurology, University of California, San Francisco, San Francisco, CA, USA; [5]The Rocky Mountain MS Center at the University of Colorado, Anschutz Medical Campus, Aurora, CO, USA

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. **In this interim analysis, ofatumumab 20 mg SC maintained efficacy at 6 months as demonstrated by no Gd+ T1 lesions**
3. **From Baseline to Month 6, mean IgM and IgG concentrations remained within the normal reference ranges and mean CD19+ B-cell concentration decreased from 25.4 to 0.5 cells/µL. No new safety signals were identified**

INTRODUCTION

- Anti-CD20 therapies reduce annualised 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 non-continuous 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, multicentre, 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

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

METHODS

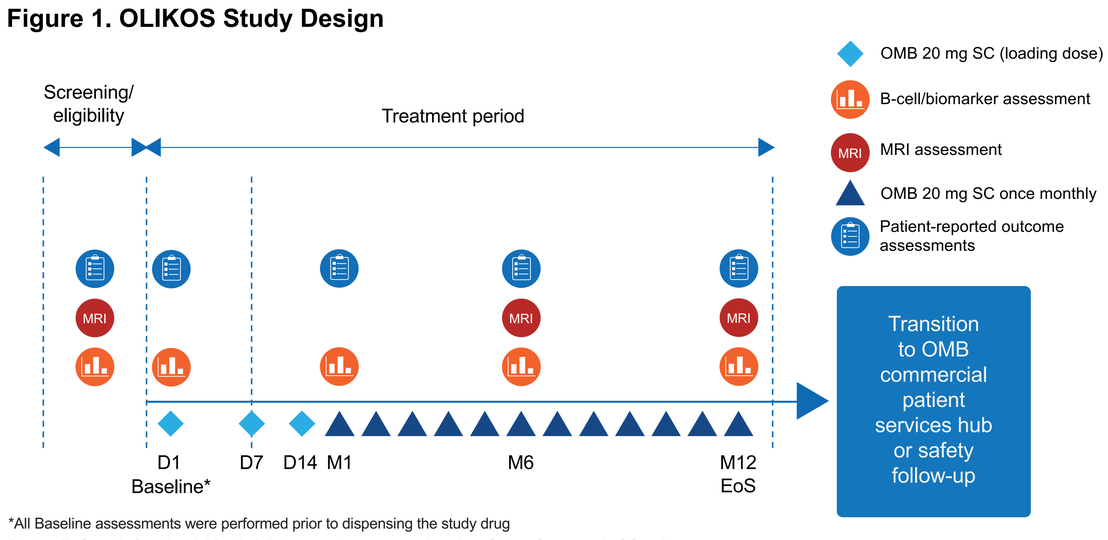
STUDY DESIGN

- 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 centres 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



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

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

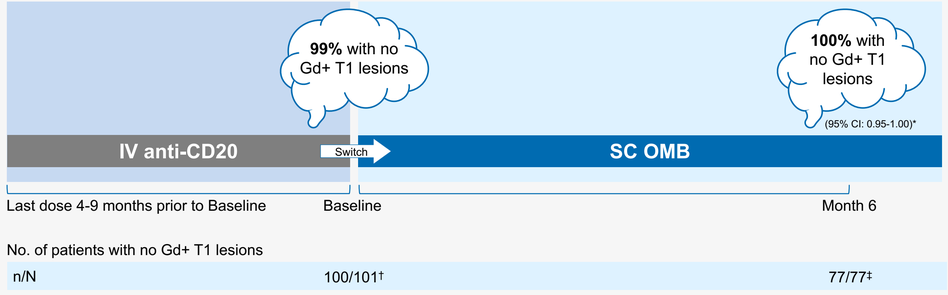
Characteristic	OMB 20 mg SC (N=102)
Age, years, mean (SD)	43.5 (8.2)
Female, n (%)	69 (67.6)
Race, n (%)	
White	78 (76.5)
Black or African American	20 (19.6)
Asian	3 (2.9)
Unknown	1 (1.0)
Ethnicity, n (%)	
Not Hispanic or Latino	70 (68.6)
Hispanic or Latino	30 (29.4)
Not reported	2 (2.0)
BMI, kg/m², mean (SD)	29.3 (7.3)
Baseline EDSS score, mean (SD)	2.9 (1.4)
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; SD, standard deviation; 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+ type 1 (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



*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. Non-responder imputation was applied for missing data. Only patients with evaluable MRI assessment within the pre-defined interval are included in the analysis
CI, confidence interval; Gd+ T1, gadolinium-enhancing, type 1; IV, intravenous; MRI, magnetic resonance imaging; No., number; OMB, ofatumumab; SC, subcutaneous

SAFETY RESULTS

- TEAEs occurred at the same frequency as in the phase 3 clinical trials, 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 coronavirus disease 2019 (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

HAEMATOLOGY 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**)
- At 6 months, mean CD19+ B-cell concentration decreased from 25.39 cells/uL at Baseline to 0.54 cells/uL

Table 3. Change in Haematology 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; SD, standard deviation
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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