Sponsor

Novartis

Generic Drug Name

Ofatumumab

Trial Indication(s)

Multiple Sclerosis

Protocol Number

COMB157AUS21

Protocol Title

Effectiveness of Ofatumumab in Real-world Practice

Clinical Trial Phase

Not applicable

Phase of Drug Development

Not applicable

Study Start/End Dates

Study Start Date: 24 October 2023 (Final Protocol)

Study Completion Date: 15 January 2024 (Full Stats Analysis Final)

Reason for Termination

Not applicable

Study Design/Methodology

This study used a retrospective single cohort pre-post design on Optum® Clinformatics® Data Mart (CDM) data from 20 August 2019 to 31 December 2023 (study period). Patients with a diagnosis of multiple sclerosis (MS) treated with ofatumumab (OMB) between 20 August 2020 (FDA approval date) and 01 July 2023 (patient identification window) were included in the study population. The date of the first OMB claim within the patient identification window was defined as the index date. Outcomes, including annualized relapse rate (ARR) and MS-related healthcare resource utilization (HCRU), were measured across two distinct periods. The pre-index period was defined as the fixed 12-month period prior to the index date, during which demographic and clinical characteristics were also assessed. The post-index period was defined as the variable period of ≥6 months after the index date, extending until the earliest between the end of persistent OMB use (defined as last day of OMB supply before a gap of ≥60 days or switch to another disease modifying therapy [DMT]), discontinuation of enrollment, or end of study period on 31 December 2023.

Centers

Not applicable. This study used the Optum® CDM database.

Objectives:

Primary objective(s)

Describe the clinical effectiveness of OMB among anti-CD20 naïve patients diagnosed with MS and treated with OMB.

Secondary objective(s)

1. Describe the changes in MS-related HCRU among anti-CD20 naïve patients diagnosed with MS and treated with OMB.
2. Describe demographic and clinical characteristics of anti-CD20 naïve patients diagnosed with MS and treated with OMB.
3. Replicate primary objective and secondary objectives 1-2 among all patients treated with OMB, regardless of prior anti-CD20 use.

Test Product (s), Dose(s), and Mode(s) of Administration

Patients had received OMB per their dosing regimen prior to this observational study.

Statistical Methods

Descriptive statistics were used to characterize pre-index demographic and clinical characteristics. Continuous variables were summarized using mean (standard deviation [SD]). Categorical variables were described using frequencies and percentages. ARRs and rates of MS-related HCRU per person-year (PPY) and their 95% confidence intervals (CIs) were obtained from intercept-only negative binomial (NB) models with an offset for the natural log of person-time. Results are presented as rate PPY (95% CI; N events / N person-years). To compare rates PPY in the pre- and post-index periods, incidence rate ratios (IRR) were obtained from NB models with period (post- vs. pre-index) as a predictor variable, standard errors adjusted for clustering by patient ID, and no covariate adjustment. Covariate adjustment was not applied in the analysis as patient-level confounders were controlled by the within-individual pre-post design.

Study Population: Key Inclusion/Exclusion Criteria

Inclusion criteria:

1. Aged 18 years or older as of the index date corresponding to the initial claim for OMB therapy.
2. One claim or more for OMB therapy recorded during the patient identification period (index date = date of the first claim for OMB).
3. One claim or more with a diagnosis of MS (International Classification of Diseases, Tenth Revision [ICD-10] code G35.xx) any time before the index date and up to 6 months after the index date.
4. Continuous healthcare plan enrollment from ≥12 months prior to the index date (pre-index period) to ≥12 months following the index date (post-index period).
5. Persistent use of OMB therapy throughout the post-index period, defined as the absence of a discontinuation of OMB or switch to another MS treatment.

Exclusion criteria:

None.

Participant Flow

A total of 779 patients meeting eligibility criteria were included in the OMB MS sample. Of these patients, 662 and 117 met the criteria for the anti-CD20-naïve and anti-CD20-experienced sub-cohorts, respectively.

Baseline Characteristics

Refer to Secondary Outcome Results.

Primary Outcome Result(s)

Relapse in the pre- and post-index periods

	OMB MS sample N = 779			Anti-CD20-naïve sub-cohort N = 662			Anti-CD20-experienced sub-cohort N = 117		
	Pre-index period	**Post-index period**	**P-value**	**Pre-index period**	**Post-index period**	**P-value**	**Pre-index period**	**Post-index period**	**P-value**
N person-years	779	1060	--	662	899	--	117	161	--
N events	317	103	--	176	81	--	141	22	--
ARR (95% CI)	0.407 (0.356,0.465)	0.104 (0.081,0.132)	--	0.266 (0.224,0.315)	0.096 (0.074,0.125)	--	1.205 (1.022,1.421)	0.141 (0.077,0.257)	--
IRR (95% CI)	0.246 (0.195, 0.310)		<0.001	0.351 (0.267, 0.461)		<0.001	0.114 (0.069, 0.187)		<0.001

Abbreviations: ARR: annualized relapse rate; CI: confidence interval; IRR: incidence rate ratio; MS: multiple sclerosis; OMB: ofatumumab.

Secondary Outcome Result(s)

Demographic and clinical characteristics in the pre-index period

	OMB MS sample	Anti-CD20-naïve sub-cohort	Anti-CD20-experienced sub-cohort
	N = 779	N = 662	N = 117
Age, mean (SD)	48.16 (11.03)	48.30 (11.06)	47.40 (10.83)
Age groups, n (%)			
18-34 years	81 (10.40)	67 (10.12)	14 (11.97)
35-44 years	250 (32.09)	215 (32.48)	35 (29.91)
45-54 years	235 (30.17)	198 (29.91)	37 (31.62)
55-64 years	163 (20.92)	136 (20.54)	27 (23.08)
65+ years	50 (6.42)	46 (6.95)	4 (3.42)
Gender, n (%)			
Female	580 (74.45)	487 (73.56)	93 (79.49)
Male	199 (25.55)	175 (26.44)	24 (20.51)
Race, n (%)			
White	536 (68.81)	461 (69.64)	75 (64.10)
Black or African American	106 (13.61)	91 (13.75)	15 (12.82)
Hispanic	69 (8.86)	53 (8.01)	16 (13.68)
Asian	13 (1.67)	10 (1.51)	3 (2.56)
Missing	55 (7.06)	47 (7.10)	8 (6.84)
Region[1], n (%)			
Midwest	183 (23.49)	158 (23.87)	25 (21.37)
Northeast	92 (11.81)	83 (12.54)	9 (7.69)
South	350 (44.93)	295 (44.56)	55 (47.01)
West	154 (19.77)	126 (19.03)	28 (23.93)
Payer type[1], n (%)			
Commercial	528 (67.78)	456 (68.88)	72 (61.54)
Medicare	250 (32.09)	205 (30.97)	45 (38.46)
Multiple	1 (0.13)	1 (0.15)	0 (0.00)
Year of index date			
2020	18 (2.31)	17 (2.57)	1 (0.85)
2021	294 (37.74)	244 (36.86)	50 (42.74)
2022	297 (38.13)	253 (38.22)	44 (37.61)
Deyo-Charlson Comorbidity Index, mean (SD)	1.44 (1.92)	1.44 (1.90)	1.44 (2.02)

	OMB MS sample	Anti-CD20-naïve sub-cohort	Anti-CD20-experienced sub-cohort
	N = 779	N = 662	N = 117
Psychiatric diagnostic group, mean (SD)	1.08 (1.19)	1.06 (1.18)	1.18 (1.24)
Top five selected comorbidities, n (%)			
Osteoarthritis	471 (60.46)	410 (61.93)	61 (52.14)
Dyslipidemia	265 (34.02)	235 (35.50)	30 (25.64)
Depression	263 (33.76)	215 (32.48)	48 (41.03)
Hypertension	258 (33.12)	225 (33.99)	33 (28.21)
Sleep disorders	190 (24.39)	159 (24.02)	31 (26.50)
Top 5 MS-related symptoms and secondary conditions, n (%)			
Anxiety	252 (32.35)	210 (31.72)	42 (35.90)
Fatigue or malaise	251 (32.22)	212 (32.02)	39 (33.33)
Sensory problems	206 (26.44)	185 (27.95)	21 (17.95)
Eye symptoms	137 (17.59)	126 (19.03)	11 (9.40)
Urinary tract infection	115 (14.76)	87 (13.14)	28 (23.93)
MS disability[2], n (%)			
No EDSS-related symptoms	657 (84.34)	562 (84.89)	95 (81.20)
Mild	14 (1.80)	14 (2.11)	0 (0.00)
Moderate	39 (5.01)	32 (4.83)	7 (5.98)
Severe	69 (8.86)	54 (8.16)	15 (12.82)
DMTs used in the pre-index period, n (%)			
Any DMT	491 (63.03)	374 (56.50)	117 (100.00)
Low/moderate efficacy therapy[3]	326 (41.85)	321 (48.49)	5 (4.27)
High efficacy therapy[3]	176 (22.59)	59 (8.91)	117 (100.00)
No DMT	288 (36.97)	288 (43.50)	0 (0.00)

Abbreviations: DM: durable medical equipment; DMT: disease-modifying therapy; EPO: Exclusive Provider Organization; HMO: Health Maintenance Organization; IND: individual; MS: multiple sclerosis; OMB: ofatumumab; POS: point of service; PPO: Preferred Provider Organization; SD: standard deviation.

Notes:

[1] Some patients had multiple enrollment records with differing region and/or insurance overlapping with index date. In such cases, patients were recorded as having 'Multiple' regions or insurance types.

[2] MS disability level is based on observance of EDSS-related symptoms and DME use observed in claims data weighted by severity score. Disability levels and definitions, based on Berkovich et al. (2021), are as follows: Severe = Defined as having ≥1 EDSS-related symptom with severity score = 3 in any functional system; Moderate: Defined as having ≥1 EDSS-related symptom with severity score = 2 in any functional system, or having ≥2 functional systems with severity score = 1; Mild: Defined as having only one EDSS-related symptom with severity score = 1 or having no EDSS-related symptoms observed during the measurement period.

	OMB MS sample	Anti-CD20-naïve sub-cohort	Anti-CD20-experienced sub-cohort
	N = 779	N = 662	N = 117

[3] Low/moderate efficacy therapies include cladribine, dimethyl fumarate, diroximel fumarate, fingolimod, glatiramer acetate, interferon beta-1a, interferon beta-1b, monomethyl fumarate, peginterferon beta-1a, ozanimod, siponimod, and teriflunomide. High efficacy therapies include natalizumab, ocrelizumab, and rituximab.

MS-related healthcare resource utilization in the pre- and post-index periods

	OMB MS sample N = 779			Anti-CD20-naïve sub-cohort N = 662			Anti-CD20-experienced sub-cohort N = 117		
	Pre-index period	Post-index period	P-value	Pre-index period	Post-index period	P-value	Pre-index period	Post-index period	P-value
N person-years	779	1060	--	662	899	--	117	161	--
MS-related hospitalizations									
N events	126	17	--	98	16	--	28	1	--
Rate PPY (95% CI)	0.162 (0.126, 0.207)	0.017 (0.010, 0.028)	--	0.148 (0.115, 0.191)	0.019 (0.011, 0.031)	--	0.239 (0.112, 0.513)	0.006 (0.001, 0.044)	--
IRR (95% CI)	0.103 (0.059, 0.179)		< 0.001	0.124 (0.070, 0.218)		< 0.001	0.027 (0.003, 0.231)		< 0.001
Days of MS-related hospitalization									
N events	301	125	--	273	106	--	28	19	--
Rate PPY (95% CI)	0.386 (0.199, 0.750)	0.118 (0.099, 0.141)	--	0.412 (0.205, 0.828)	0.118 (0.097, 0.143)	--	0.239 (0.028, 2.014)	0.118 (0.075, 0.185)	--
IRR (95% CI)	0.359 (0.179, 0.720)		0.004	0.324 (0.164, 0.642)		0.001	0.494 (0.276, 0.884)		0.018
MS-related ED visits									
N events	128	138	--	88	102	--	40	36	--
Rate PPY (95% CI)	0.164 (0.123, 0.219)	0.130 (0.095, 0.177)	--	0.133 (0.097, 0.183)	0.109 (0.079, 0.152)	--	0.342 (0.184, 0.637)	0.257 (0.107, 0.619)	--
IRR (95% CI)	0.789 (0.569, 1.092)		0.153	0.822 (0.539, 1.253)		0.363	0.741 (0.461, 1.192)		0.216
MS-related outpatient visits									
N events	5107	4830	--	4227	4024	--	880	806	--
Rate PPY (95% CI)	6.556 (6.210, 6.920)	4.596 (4.357, 4.848)	--	6.385 (6.010, 6.784)	4.507 (4.257, 4.771)	--	7.521 (6.727, 8.410)	5.103 (4.393, 5.928)	--
IRR (95% CI)	0.701 (0.653, 0.753)		< 0.001	0.706 (0.652, 0.765)		< 0.001	0.677 (0.579, 0.792)		< 0.001

Abbreviations: CI: confidence interval; ED: emergency department; HCRU: healthcare resource utilization; IRR: incidence rate ratio; MS: multiple sclerosis; OMB: ofatumumab; PPY: per person-year.

Safety Results

Not applicable

Adverse Events by System Organ Class

Not applicable

Most Frequently Reported AEs Overall by Preferred Term n (%)

Not applicable

Serious Adverse Events and Deaths

Not applicable

Other Relevant Findings

Not applicable

Conclusion

In a real-world sample of patients with multiple sclerosis (MS), the rate of relapse was reduced by four times following ofatumumab (OMB) initiation. Similarly, rates of MS-related hospitalization, days of hospitalization, and outpatient visits decreased significantly following ofatumumab initiation. Results align with clinical trial evidence of ofatumumab's efficacy in reducing relapse incidence in MS and suggest that the clinical benefits of OMB translate to reduced healthcare resource utilization (HCRU) for patients. Taken together, the results highlight the benefits of OMB for patients, payers, and the healthcare system.

Date of Clinical Study Report

15 October 2024