Sponsor
Novartis Pharmaceuticals

Generic Drug Name
Ofatumumab (OMB)

Trial Indication(s)
Multiple sclerosis (MS)

Protocol Number
COMB157GUS11

Protocol Title
Characterization of Early Patients Initiating Ofatumumab for Treatment of Multiple Sclerosis in the Real-world

Clinical Trial Phase
IV

Phase of Drug Development
NA

Study Start/End Dates
Study start date: 13/12/2020

Study Completion date: 31/12/2021

Reason for Termination

NA

Study Design/Methodology

This was a retrospective cohort study utilizing secondary data from IQVIA's open-source pharmacy claims database selecting patients with prescription claims for ofatumumab or other DMTs of interest. The date of first ofatumumab prescription claim or other DMT of interest was defined as the index date. No post-index requirements were imposed.

The initial data were extracted in October 2020. The data and results were refreshed in April 2021 and July 2021 to allow for assessment of changes in characteristics at 6 and 9 months post-launch.

Key dates for the study:

Time window	Original data extract	Data refresh #1	Data refresh #2
Study period	8/1/2019 – 10/31/2020	8/1/2019 – 2/28/2021	8/1/2019 – 5/31/2021
Index window	8/1/2020 – 10/31/2020	8/1/2020 – 2/28/2021	8/1/2020 – 5/31/2021
Index date	Date of first ofatumumab claim (or other DMT of interest for non-ofa cohorts)		
Pre-index period	Fixed 12-months prior to index date		
Post-index period	None	None	Variable

Centers

Novartis Investigative Site

Objectives:

Primary objective(s)

- To describe the pre-index treatment status (DMT-naïve vs. DMT experienced) of patients initiating ofatumumab.

Secondary objective(s)

- To evaluate the demographic, clinical, and treatment characteristics in patient initiating ofatumumab
- To describe a geographical heat map of patients initiating ofatumumab
- To assess ofatumumab persistence

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

NA

Statistical Methods

The results were reported descriptively for each cohort. Mean, median, and standard deviation were generated as measures of central tendency and variance for continuous variables. For categorical variables, data were summarized using frequencies and percentages.

Study Population: Key Inclusion/Exclusion Criteria

Inclusion criteria

- Patients with ≥1 prescription for ofatumumab or other DMTs of interest (siponimod, ocrelizumab, dimethyl fumarate, or glatiramer acetate) in the LRx/Dx database were included. For the ofatumumab cohort, the date of the first observed ofatumumab prescription within the index window served as the index date. For patients with no ofatumumab use during the index window, the date of the first observed claim for the other DMTs of interest was index date.
    - For the non-ofatumumab cohort, patients were required to be new users of their index medication (i.e., no claims for the index DMT observed during the 12-month pre-index period).
- Patients with ≥1 medical claim in Dx with a diagnosis of MS within the 24-months prior to the index date or any time after index.
- Patients aged ≥ 18 years at the time of the index date.
- To confirm continuous data availability in the LRx and Dx database, the most frequency visited must have consistently submitted to the LRx /Dx database for a period of at least 12 months pre-index.
- Patients with linkage to Dx data by patient ID.

Exclusion criteria

No exclusion criteria were applied to patients in the study.

Participant Flow
Overall, a total of 3,600 patients with a pharmacy claim for ofatumumab were identified in the LRx database between 8/1/2020 and 5/31/2021. After applying all study eligibility criteria, 2,101 patients remained in the study.

Baseline Characteristics
Refer to Secondary outcomes results (Demographics)

Primary Outcome Result(s)
The primary measure was pre-index treatment status of patients initiating ofatumumab, measured as proportion (n, %) of DMT-naïve and DMT-experienced patients among patients initiating ofatumumab based on DMT use in the 12-month pre-index period.
Overall, 41.6% of patients used DMTs in the year prior to ofatumumab initiation, whereas only 15.6% of the non-ofatumumab cohort had DMTs prior to initiation of the index medication.

Secondary Outcome Result(s)
In the latest refresh, 1,270 (60.4%) ofatumumab patients were aged 45 years or older (median age of 49 years) and 1,554 (74.0%) were female. The age distribution aligned with the non-ofatumumab cohort (median age of 48 years) overall. Over time there appeared to be a slight increase in the proportion of older patients (aged 55 years and older) utilizing ofatumumab.
Patients were primarily from the South (46.8%) and Midwest (20.7%) regions of the US. Differences were observed in the geographical distribution of ofatumumab patients and the other DMTs of interest. A shift in the geographic distribution was observed over time, with an increase and decrease in the proportion of patients from the Midwest and South, respectfully.
Patients were generally healthy with limited comorbid conditions; 1,667 (79.8%) patients had a CCI score of 0. The most observed comorbidity was osteoarthritis (29.8%) followed by hypertension (17.0%). CCI and the comorbidity profile was similar between of the ofatumumab and non-ofatumumab patients.

Ofatumumab persistence
The study used an open-source database, which does not have patient continuous eligibility information. Persistence estimate is not feasible using this dataset at this point.

Characteristics of MS in patients treated with ofatumumab

MS Characteristics	All ofa patients N=2,101	DMT-naïve N=1,226	DMT-experienced N=875
MS relapses in the prior year			
None	1,717 (81.7%)	993 (81.0%)	724 (82.7%)
1	273 (13.0%)	167 (13.6%)	106 (12.1%)
2+	111 (5.3%)	66 (5.4%)	45 (5.1%)
Common MS-related symptoms			
Anxiety	255 (12.1%)	161 (13.1%)	94 (10.7%)
Fatigue	232 (11.0%)	137 (11.2%)	95 (10.9%)
Muscle weakness	120 (5.7%)	72 (5.9%)	48 (5.5%)
Sensory problems	297 (14.1%)	201 (16.4%)	96 (11.0%)
UTI	154 (7.3%)	81 (6.6%)	73 (8.3%)
Baseline MS disability level			
Mild	1,360 (64.7%)	762 (62.2%)	598 (68.3%)
Moderate	519 (24.7%)	319 (26.0%)	200 (22.9%)
Severe	222 (10.6%)	145 (11.8%)	77 (8.8%)

Pre-index concomitant medications, vaccinations and scans, overall and stratified by prior DMT use

Pre-Index Characteristics	All ofa patients N=2,101	DMT-naïve N=1,226	DMT-experienced N=875
Pre-medication use	54 (2.6%)	27 (2.2%)	27 (3.1%)
Steroid pre-medication	44 (2.1%)	21 (1.7%)	23 (2.6%)
Antihistamine pre-medication	15 (0.7%)	7 (0.6%)	8 (0.9%)
Concomitant medications			
Angiotensin II receptor blockers	163 (7.8%)	100 (8.2%)	63 (7.2%)
Anti-anxiety	735 (35.0%)	427 (34.8%)	308 (35.2%)
Antidepressant	1,105 (52.6%)	641 (52.3%)	464 (53.0%)
SSRI	569 (27.1%)	327 (26.7%)	242 (27.7%)
SNRI	382 (18.2%)	223 (18.2%)	159 (18.2%)
Tetracyclic/Tricyclics	240 (11.4%)	145 (11.8%)	95 (10.9%)
Monoamine oxidase inhibitors	0 (0.0%)	0 (0.0%)	0 (0.0%)
Other	381 (18.1%)	232 (18.9%)	149 (17.0%)
Antidiabetics	213 (10.1%)	131 (10.7%)	82 (9.4%)
Beta blockers	269 (12.8%)	168 (13.7%)	101 (11.5%)
NSAIDs	506 (24.1%)	293 (23.9%)	213 (24.3%)
Opioids	646 (30.7%)	376 (30.7%)	270 (30.9%)
Statins	380 (18.1%)	213 (17.4%)	167 (19.1%)
Hepatitis B virus screening	201 (9.6%)	121 (9.9%)	80 (9.1%)
Quantitative serum immunoglobulin screening	215 (10.2%)	129 (10.5%)	86 (9.8%)
Pre-index flu shot	258 (12.3%)	149 (12.2%)	109 (12.5%)
Post-index flu shot	57 (2.7%)	28 (2.3%)	29 (3.3%)
Number of pre-index brain/spinal MRI scan			
None	1,473 (70.1%)	839 (68.4%)	634 (72.5%)
1	214 (10.2%)	128 (10.4%)	86 (9.8%)
2	349 (16.6%)	219 (17.9%)	130 (14.9%)
3+	65 (3.1%)	40 (3.3%)	25 (2.9%)

Healthcare resource utilization

Pre-Index HCRU	All ofa patients N=2,101	DMT-naïve N=1,226	DMT-experienced N=875
Number of patients with an inpatient visit	298 (14.2%)	212 (17.3%)	86 (9.8%)
Number of inpatient visits (among those with at least 1)			
1	217 (72.8%)	151 (71.2%)	66 (76.7%)
2	47 (15.8%)	34 (16.0%)	13 (15.1%)
3+	34 (11.4%)	27 (12.7%)	7 (8.1%)
Number of patients with an ED visit	535 (25.5%)	341 (27.8%)	194 (22.2%)
Number of ED visits (among those with at least 1)			
1	318 (59.4%)	209 (61.3%)	109 (56.2%)
2	115 (21.5%)	68 (19.9%)	47 (24.2%)
3+	102 (19.1%)	64 (18.8%)	38 (19.6%)
Number of patients with an outpatient visit	1,939 (92.3%)	1,123 (91.6%)	816 (93.3%)
Number of outpatient visits (among those with at least 1)			
1	120 (6.2%)	82 (7.3%)	38 (4.7%)
2	140 (7.2%)	85 (7.6%)	55 (6.7%)
3+	1,679 (86.6%)	956 (85.1%)	723 (88.6%)
Number of patients with a pharmacy claim	2,101 (100.0%)	1,226 (100.0%)	875 (100.0%)
Number of pharmacy claims (among those with at least 1)			
1	25 (1.2%)	20 (1.6%)	5 (0.6%)
2	29 (1.4%)	29 (2.4%)	0 (0.0%)
3+	2,047 (97.4%)	1,177 (96.0%)	870 (99.4%)

Post-index healthcare resource utilization accrued while on ofatumumab

Post-Index HCRU	All ofa patients N=2,101	DMT-naïve N=1,226	DMT-experienced N=875
Number of patients with an inpatient visit	70 (3.3%)	46 (3.8%)	24 (2.7%)
Number of inpatient visits (among those with at least 1)			
1	52 (74.3%)	36 (78.3%)	16 (66.7%)
2	9 (12.9%)	4 (8.7%)	5 (20.8%)
3+	9 (12.9%)	6 (13.0%)	3 (12.5%)
Number of patients with an ED visit	175 (8.3%)	108 (8.8%)	67 (7.7%)
Number of ED visits (among those with at least 1)			
1	130 (74.3%)	82 (75.9%)	48 (71.6%)
2	32 (18.3%)	17 (15.7%)	15 (22.3%)
3+	13 (7.4%)	9 (8.3%)	4 (6.0%)
Number of patients with an outpatient visit	1,318 (62.7%)	751 (61.3%)	567 (64.8%)
Number of outpatient visits (among those with at least 1)			
1	384 (29.1%)	235 (31.3%)	149 (26.3%)
2	226 (17.1%)	131 (17.4%)	95 (16.8%)
3+	708 (53.7%)	385 (51.3%)	323 (57.0%)
Number of patients with a pharmacy claim	2,101 (100.0%)	1,226 (100.0%)	875 (100.0%)
Number of pharmacy claims (among those with at least 1)			
1	198 (9.4%)	131 (10.7%)	67 (7.7%)
2	145 (6.9%)	89 (7.3%)	56 (6.4%)
3+	1,758 (83.7%)	1,006 (82.1%)	752 (85.9%)

Time between ofatumumab claims occurring before and after a COVID-19 vaccination

Overall, 23 (19.7%) and 46 (39.3%) of ofatumumab patients with COVID-19 had an inpatient or ED visit, respectfully, within 30 days after the COVID-19 diagnosis

Limitations
This was an early post-marketing study using two patient level data assets. Due to the limited data available, sample size was relatively small, and a limited number of patients had longer follow-up times (6+ months). No statistical comparisons were made to estimate differences between cohorts. The databases used in this study are considered open-source, with no patient-level enrollment information available; patients may have gaps in their data given this lack of enrollment information.

Safety Results
No safety data were collected during the study.

Other Relevant Findings
NA

Conclusion
This is the first comprehensive real-world study of multiple sclerosis patients treated with ofatumumab. The study provided an early look of demographic and clinical characteristics of patients initiating ofatumumab as a treatment for MS. Future studies comparing clinical and economic outcomes in patients treated with ofatumumab versus major competitors are warranted.

Date of Clinical Study Report
17 March 2022