



Changes in Immunoglobulin in Patients with Multiple Sclerosis Treated with Anti-CD20 Monoclonal Antibodies

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Objective

- To explore changes in immunoglobulin G (IgG) and immunoglobulin M (IgM) lab values over time while on treatment with ocrelizumab and rituximab for multiple sclerosis (MS).

Introduction

- Ocrelizumab and rituximab are B-cell depleting antibodies used in the treatment of multiple sclerosis (MS).
- A decrease in IgG serum concentration has been associated with B cell depletion which may pose an increased risk of infection.

Methods

Sample and Data Collection:

MS patients who were prescribed ocrelizumab or rituximab at the Rocky Mountain MS Center were identified through Health Data Compass, a health data warehouse at University of Colorado that integrates electronic medical records patient data, billing data and a variety of state data sources including all-payer claims databases. Patients were randomly selected and included if they were:

- Age 18 or over at the time of MS diagnosis
- Initiated ocrelizumab or rituximab after 2017
- Were anti-CD20 naive at time of initiation of ocrelizumab or rituximab
- Had at least one IgG lab value in the 12 months prior to ocrelizumab or rituximab treatment initiation
- Had at least one IgG lab value while on ocrelizumab or rituximab treatment

Data were supplemented through retrospective chart review of clinician reported data collected from electronic medical records.

Outcomes:

Change in IgG (mg/dl) and IgM (mg/dl) levels over time since newly initiating ocrelizumab or rituximab treatment

Analysis:

Demographic and disease history variables were examined using summary statistics. Lab values for IgG and IgM were analyzed with longitudinal regression (repeated measures model) on the logarithmic scale to assess changes over time.

Results

	Ocrelizumab (N=118)		Rituximab (N=140)	
	Mean or N	SD or %	Mean or N	SD or %
Type of MS				
RRMS	97	82.20%	98	70.00%
SPMS	12	10.17%	29	20.71%
PPMS	9	7.63%	13	9.29%
Disease Duration from Diagnosis (Years, SD)	7.53	7.91	6.17	8.54
Age (Years, SD)	42.81	10.84	42.92	13.03
Sex-Female	82	69.49%	96	68.57%
Race				
White	99	83.90%	100	71.43%
Black	4	3.39%	19	13.57%
Asian	0	0.00%	2	1.43%
Other	11	9.32%	16	11.43%
Unknown	4	3.39%	3	2.14%
Ethnicity				
Non-Hispanic	108	91.53%	115	82.14%
Hispanic	9	7.63%	20	14.29%
Unknown	1	0.85%	5	3.57%
# of previous DMTs	1.50	1.47	1.11	1.50
Most Recent Previous DMT				
Interferons	9	7.63%	14	10.00%
Glatiramer Acetate	16	13.56%	13	9.29%
Natalizumab	7	5.93%	14	10.00%
Fingolimod	16	13.56%	12	8.57%
Dimethyl Fumarate	25	21.19%	14	10.00%
Other	8	6.78%	5	3.57%
None	37	31.36%	68	48.57%
Time on Previous DMT (Months) (median, IQR)	38.60	[14.13, 72.93]	28.45	[12.17, 62.77]
Time Since Previous DMT (Months) (median, IQR)	0.63	[0.23, 7.20]	1.65	[0.48, 12.32]
Reason for Discontinuing Previous DMT*				
Disease Activity	37	45.68%	35	48.61%
Adverse Events/Tolerability	34	41.98%	18	25.00%
Insurance/Cost	1	1.23%	6	8.33%
Other	9	11.11%	13	18.06%

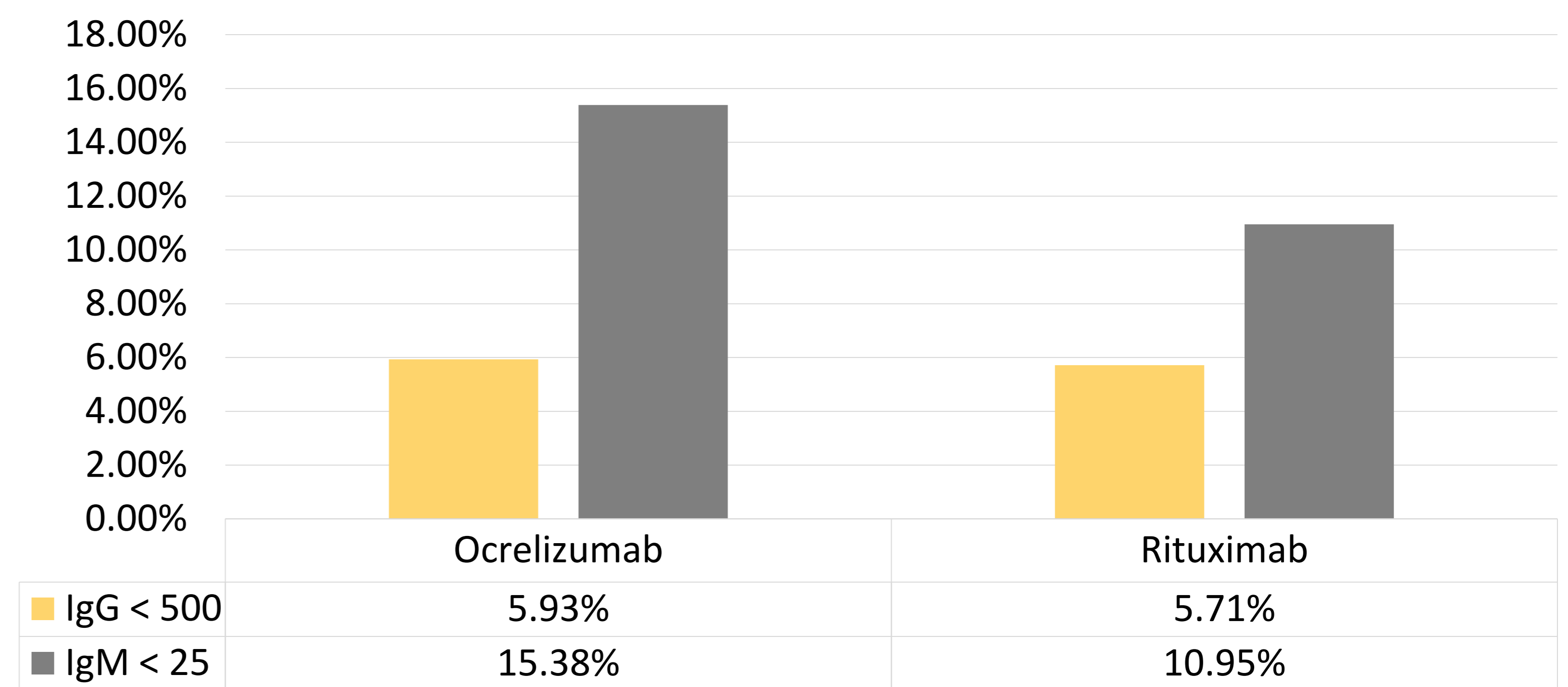
*Percentages calculated out of those who were on a DMT previously
RRMS: relapsing-remitting MS; SPMS: secondary progressive MS; PPMS: primary progressive MS; SD: standard deviation; DMT: disease modifying therapy; IQR: interquartile range

Results

	Ocrelizumab (N=118)		Rituximab (N=140)	
	Mean	SD	Mean	SD
Follow-Up Time (months)	44.94	17.31	40.19	17.22
Number of Infusions	6.70	2.81	6.16	2.84
Cumulative dose (mg) (median, IQR)	4200	[2400, 5400]	3100	[2250, 4500]
	Geometric Mean	95% Confidence Interval	Geometric Mean	95% Confidence Interval
Baseline IgG (mg/dl) *	957.71	(922.24, 994.54)	940.34	(901.80, 980.53)
Baseline IgM (mg/dl) *	101.90	(92.32, 112.47)	101.11	(91.68, 111.51)

*Calculated using all available baseline lab values with 12 months prior to ocrelizumab or rituximab therapy
SD: standard deviation; IQR: interquartile range; IgG: immunoglobulin G; IgM: immunoglobulin M

Figure 1. Percent of Patients with Low Immunoglobulin Values



Note: Ocrelizumab sample sizes: IgG (N=118), IgM (N=117); Rituximab sample sizes: IgG(N=140), IgM (N=137)

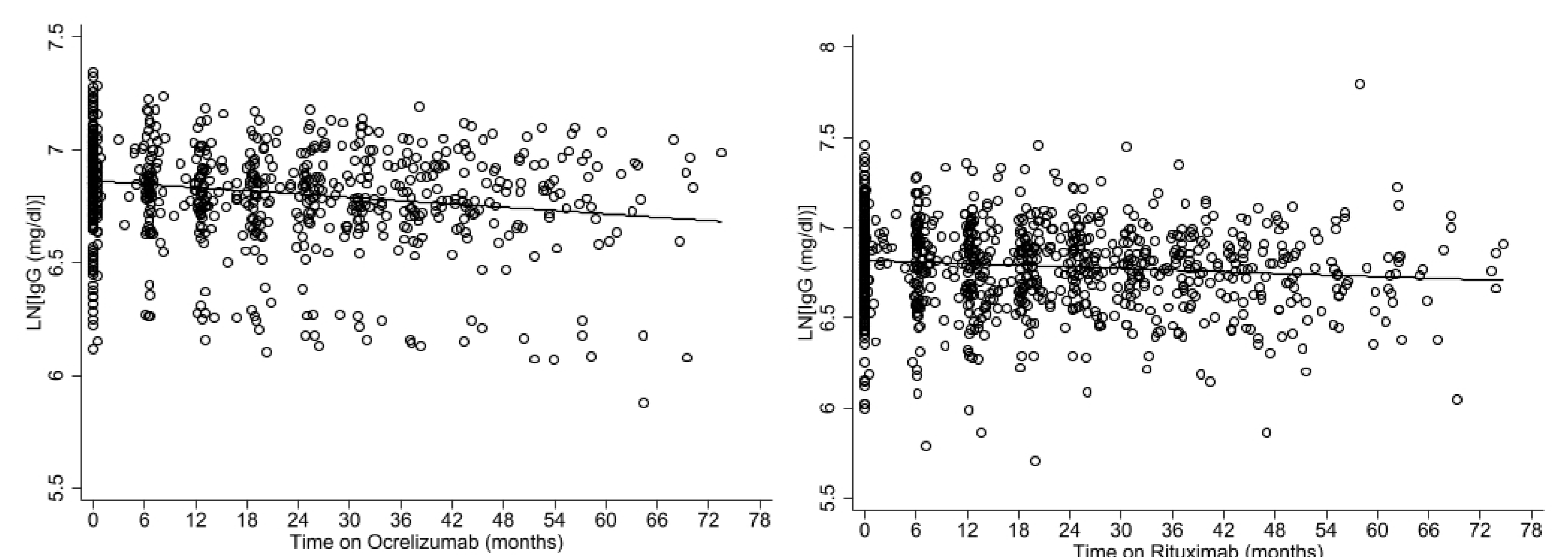
- 5.93% of patients on ocrelizumab had at least one IgG lab value below 500 mg/dl while on therapy.
- 5.71% of patients on rituximab had at least one IgG lab value below 500 mg/dl while on therapy.

DMT	Immunoglobulin	Percent Change Per Year	95% Confidence Interval	P-Value
Ocrelizumab	IgG	-2.93	(-4.30, -1.55)	<0.0001
	IgM	-17.82	(-20.34, -15.23)	<0.0001
Rituximab	IgG	-1.81	(-2.88, -0.73)	0.0011
	IgM	-19.00	(-21.42, -16.52)	<0.0001

DMT: disease modifying therapy; IgG: immunoglobulin G; IgM: immunoglobulin M

- For patients on ocrelizumab, IgG values are estimated to decrease 2.93% (95% Confidence Interval: -4.30, -1.55) per year on treatment.
- For patients on rituximab, IgG values are estimated to decrease 1.81% (95% Confidence Interval: -2.88, -0.73) per year on treatment.

Figure 2. Log linear fit for IgG while on ocrelizumab (left) and rituximab (right) over time.



Conclusion & Discussion

- Our study presents immunoglobulin data MS patients treated with ocrelizumab and rituximab who were anti-CD20 treatment naive at time of initiation.
- A log linear fit appears to fit the trend of the immunoglobulin data well.
- Decreases in IgG values for ocrelizumab and rituximab are significant, however decreases per year are slight.
- Few patients were below an IgG value of 500 mg/dl for both ocrelizumab and rituximab.
- Future studies should investigate whether predictors are associated with decreases in IgG values.



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