The Differential Impact of Ocrelizumab Versus Rituximab on Lymphocyte Count, Immunoglobulins, and Infection Rate

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Background

- Ocrelizumab and rituximab are anti-CD20 monoclonal antibodies which have demonstrated efficacy in treating MS, NMOSD, and other related neurological conditions.
- While effective, safety concerns of these treatments, namely excessive immunosuppression, remains a concern. Limited data exist exploring differences in the safety profile between these two agents.

Objective

- To evaluate differences in immunosuppressive safety profile between the anti-CD20 agents ocrelizumab and rituximab.

Methods

- An observational, cohort study was completed among patients of the University Hospitals Neurological Institute receiving ocrelizumab or rituximab for the treatment of MS, NMOSD, or other related neurological disorders from January 2018-January 2022.
- An exploratory analysis was performed investigating the differences in lymphocyte count, immunoglobulins, B-cell concentrations, and infection rates between the two therapies.

Results

- One hundred eighty four patients (mean age 48.3 ± 13.6, 67% females) were included.
- Thirty two patients received rituximab and 152 patients received ocrelizumab.
- Patients receiving ocrelizumab were exclusively treated for multiple sclerosis, whereas rituximab was utilized for a number of neurological indications (Table 1).

Table 1. Indications for Use of Ocrelizumab and Rituximab

	Ocrelizumab (n=152)	Rituximab (n=32)
Diagnosis	RRMS (n=92) PPMS (n=43) SPMS (n=17)	NMOSD (n=19) Recurrent optic neuritis (n=4) Neurosarcoidosis (n=3) RRMS (n=2) Recurrent transverse myelitis (n=2) Pachymeningitis (n=1) Recurrent autoimmune encephalitis (n=1)

Table 2. Differences of Clinical Factors Among Patients Receiving Ocrelizumab or Rituximab

Clinical factors, n (%)	Ocrelizumab (n= 152)	Rituximab (n=32)	Statistical Test	p-value
Age	48.1 ± 13.5	49.3 ± 14.3	t = 0.4373	0.6624
Age ≥ 50 years	71 (46.71%)	14 (43.75%)	0.0932	0.7613
Female	97 (63.81%)	26 (81.25%)	3.6256	0.0569
Time on Therapy (days)	778.09 ± 465.20	1073.31 ± 535.0	t = 3.17	**0.0018**
Hypogammaglobulinemia	14 (9.21%)	8 (25.00%)	6.2605	**0.0123**
Matched for Time on Therapy¶	9 (9.2%)	8 (25.0%)	5.309	**0.0212**
Lymphopenia	64 (47.0%)	17 (56.7%)	0.4631	0.4962
Neutropenia	6 (3.97%)	2 (6.25%)	0.3273	0.5672
Early B-cell repopulation (≥1% CD19)	51 (42.9%)	11 (40.7%)	0.0403	0.8408
B-Cell Concentration (%)	1.46 ± 2.6	2.03 ± 4.0	t = 0.9177	0.3603
Serious infection	16 (10.53%)	5 (15.63%)	0.6797	0.4097
Non-serious infections	25 (16.45%)	6 (18.75%)	0.1000	0.7518
Total Infections	41 (26.9%)	11 (34.3%)	0.7143	0.3980
Baseline IgG	1113.7 ± 409.0	985.9 ± 450.8	t = 0.8125	0.4198
Nadir IgG	922.5 ± 289.0	910.2 ± 372.3	t = 0.1987	0.8427
% Reduction in IgG	17.2%	7.7%		
Baseline IgA	222.8 ± 88.9	176.5 ± 79.4	t = 0.8125	0.4198
Nadir IgA	191.5 ± 104.5	180.2 ± 141.1	t = 0.5000	0.6178
Baseline IgM	99.2 ± 73.9	62.0 ± 25.1	t = 1.115	0.2716
Nadir IgM	56.4 ± 50.9	44.3 ± 39.6	t = 0.5000	0.6178
Baseline ALC	1.80 ± 0.90	1.80 ± 1.31	t = 0.0022	0.9983
Nadir ALC	1.09 ± 0.62	0.93 ± 0.52	t = 1.3891	0.1667
Baseline ANC	4.93 ± 2.94	9.16 ± 5.86	t = 5.3506	**0.0001**
Nadir ANC	3.25 ± 1.29	3.28 ± 1.80	t = 0.1345	0.8932

1. Values reported in mean ± standard deviation unless otherwise indicated
2. Immunoglobulin values reported in mg/dL; lymphocyte count and neutrophil count reported in $x10^9$ cells/L

¶ 98 ocrelizumab patients included in the matched analysis (1055.03 ± 322.30 days on therapy). Included only patients that had been on ocrelizumab therapy for at least 18 months

Results

- Patients receiving rituximab were on average receiving therapy longer than those patients receiving ocrelizumab. (1073 ± 535 vs. 778 ± 465 days; p=.0018) (Table 2)
- Patients receiving rituximab were more likely to experience hypogammaglobulinemia (IgG <600 mg/dL) during treatment, even after adjusting for therapy duration (25.0% vs. 9.20%; p=0.0212) (Table 2)
- No differences were observed between groups in on-treatment B cell concentration (p=0.3603), lymphocyte count (p=0.1667), or incidence of severe infections (p=0.4097) (Table 2)

Conclusion

- Patients receiving rituximab were more likely to have experienced hypogammaglobulinemia during treatment than those receiving ocrelizumab.
- Rates of serious and non-serious infection were similar between those receiving ocrelizumab and rituximab.
- On treatment lymphocyte count and B-cell concentrations did not differ between treatment groups.

References

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