Disease-Modifying Therapy Choice in People With Multiple Sclerosis in the Era of Covid-19: Characterizing Outcomes in Patients Who Switched From Anti-CD20 Therapies to Diroximel Fumarate

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OBJECTIVE

- **To evaluate and track changes in functional ability and overall disease stability in relapsing MS patients who have been switched from B-cell depleting DMT to diroximel fumarate (DRF) by examining changes found in peripheral immune parameters, cognitive assessment battery (CAB), ocular coherence tomography (OCT) testing, and clinical and patient-reported outcomes (PROs).**

CONCLUSIONS

- **PwMS who were switched from ocrelizumab to DRF in routine care due to concerns over immune suppression during the global pandemic remained relapse free, showed stability with PRO QoL, cognitive outcomes, OCT, and peripheral immune parameters.**
- **PwMS who switched to DRF showed a significant increase in CD19+ B-cells in the blood over the 1-year period.**
- **DRF may be a reasonable option for MS patients switching from anti-CD20 DMTs.**

Introduction

- Disease-modifying therapy (DMT) selection in MS is typically considered based on route of administration, adherence, frequency of treatment, efficacy, and safety.
- Other considerations related to DMT choice, such as the ability to mount an effective response to vaccination, must also be considered, especially in the era of a viral pandemic.
- B-cell depleting therapies are reported to be associated with reduction of protective immunoglobulin synthesis, increased rate of infections in those with immune deficiencies and impaired humoral immune response to vaccination. In addition, infections have been seen to cause pseudo relapses and contribute to overall accumulation of disability.
- Should de-escalation be considered due to concerns of immune deficiency, infection risk, impaired vaccine response, immunosenescence or other factors, a fumarate class DMT may be an alternative option for disease control with a potentially reduced risk of infections and improved ability to mount antibody responses to both infections and vaccines.

Methods

- Retrospective collection of relapse rate, blood work, CAB, OCT and PROs at baseline and 1 year post switch in PwMS who were switched from anti-CD20 therapies to DRF during routine care.
- Eligibility:
  - Must be ≥18 years old with relapsing type MS (RRMS); must have been clinically stable for ≥1 year on anti-CD20, with an EDSS 0-5.5.
  - Excluded if: history of head injury, seizures, or neurological conditions involving the CNS other than MS; history of drug or alcohol abuse; active psychosis; IgG <300 mg/dL; or ALC <0.5 x 10^9/L.
  - T-test to test for statistically significant differences ($p<0.05$).

Results

- 25 PwMS switched from ocrelizumab to DRF (average age 52 ± 9 years; 64% female).
- Mean duration of treatment with ocrelizumab: 26 ± 8 months.
- No patients relapsed on DRF during follow-up.
- All patients remained persistent on DRF at 1 year.
- Peripheral immune parameters (N=25): no significant ($p>0.05$) change in IgG, IgA, IgM, IgG subclasses 1-4, CD4 or abs, CD8 % or abs, or CD4/CD8 ratio; however, CD19 % showed a significant difference ($p<0.05$) between baseline taken on ocrelizumab and 1 year on DRF (Table 1).
- PROs (N=17): no significant difference ($p>0.05$) from baseline on ocrelizumab therapy to 1 year on DRF (Figure 1).
- CAB (N=17): no significant difference ($p>0.05$) from baseline on ocrelizumab to 1 year on DRF (Figure 2).
- OCT (N=12): no significant difference ($p>0.05$) from baseline on ocrelizumab to 1 year on DRF (Table 2).

Table 1. Blood work Results: Baseline Versus 1 Year Post Switch to DRF

	Baseline on OCRE													1 Year Post Switch to DRF											
	IgG	IgA	IgM	IgG 1	IgG 2	IgG 3	IgG 4	CD4 %	CD4 Abs	CD8 %	CD8 Abs	CD4/ CD8	CD19 %	IgG	IgA	IgM	IgG 1	IgG 2	IgG 3	IgG 4	CD4 %	CD4 Abs	CD8 %	CD8 Abs	CD4/ CD8	CD19 %
Avg	873	203	85	464	263	41	24	56	743	20	264	4	1	846	216	48	452	264	32	25	52	733	21	270	4	8
SD	222	171	116	146	100	18	15	12	305	9	149	2	2	195	188	38	138	99	9	17	11	339	17	199	3	10

Figure 1. Longitudinal PROs: Baseline Versus 1 Year Post Switch to DRF

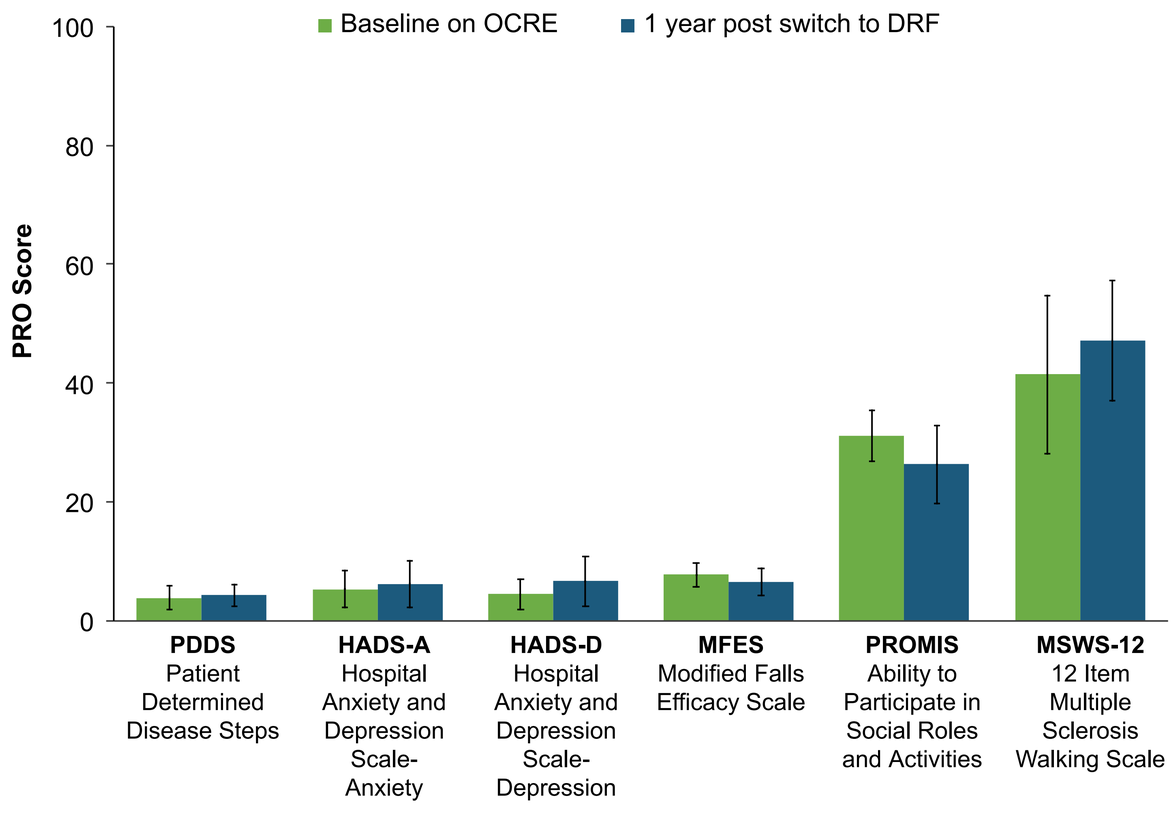
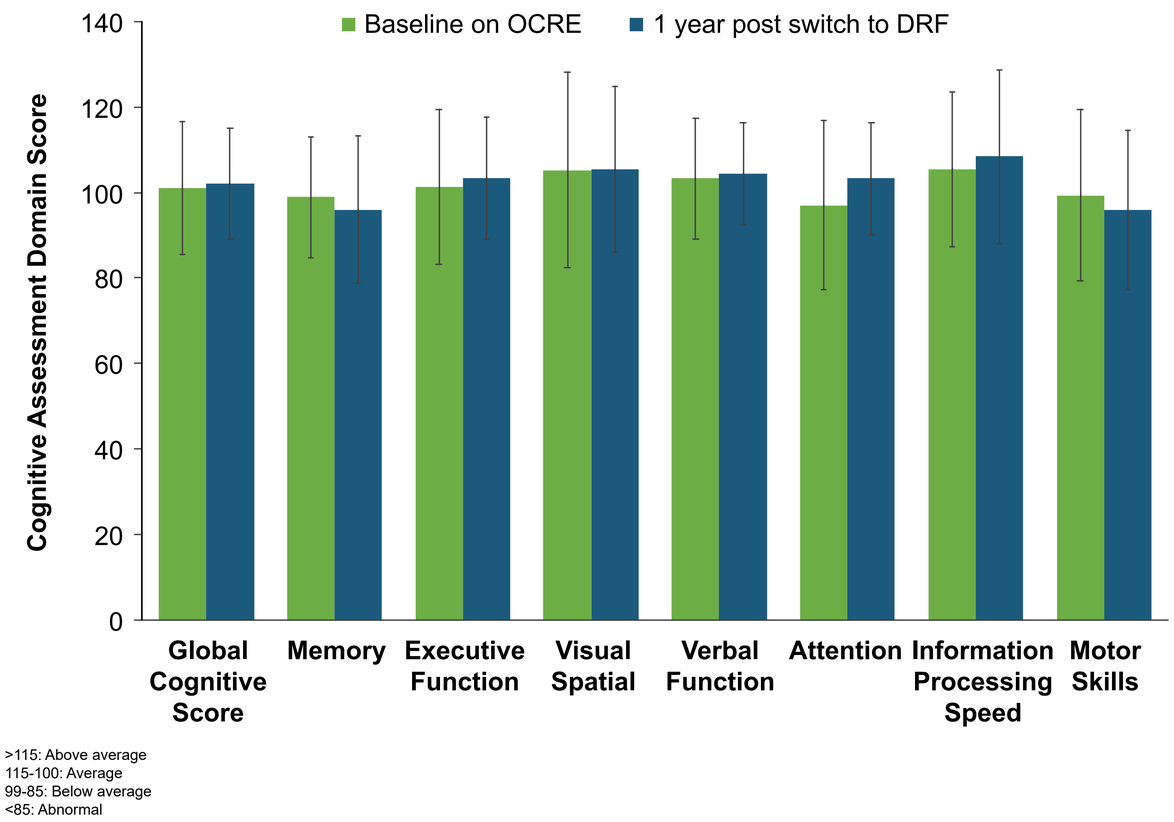


Figure 2. Longitudinal Cognition Scores: Baseline Versus 1 Year Post Switch to DRF



>115: Above average
115-100: Average
99-85: Below average
<85: Abnormal

Table 2. OCT: Baseline Versus 1 Year Post Switch to DRF

	Baseline on OCRE (n=12)	1 Year Post Switch to DRF (n=12)
Mean OD RNFL	89.5	89.3
Mean OS RNFL	91.1	91.3

References 1. Golub RM. *JAMA*. 2008;300(1):98-99. 2. Fontanarosa PB, Bauchner H. *JAMA*. 2012;307(8):849-850. 3. DeAngelis CD, et al. *JAMA*. 2005;293(23):2927-2929. Disclosures JTP: honoraria from Avanair, Biogen, Genzyme, Novartis, and Teva; research support from Biogen and Roche; KJP: advisory boards for Bayer, Biogen, BPL, Octapharma, and Pfizer; educational support and travel grants from Biogen, Novo Nordisk, Octapharma, and Pfizer. Acknowledgments This study was sponsored by Biogen (Cambridge, MA, USA): funding was provided by Biogen.