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Natalizumab-associated progressive multifocal leukoencephalopathy occurring at low positive anti-JC virus antibody level

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Background: Risk of progressive multifocal leukoencephalopathy (PML), a serious adverse event of natalizumab therapy, is higher with positive anti-JC virus antibody status, greater cumulative exposure to natalizumab and prior immunosuppressant use. Plavina et al. (2014) showed that plasma or serum anti-JC virus antibody index value may allow further PML risk stratification. Among anti-JC virus antibody positive multiple sclerosis patients with no prior immunosuppressant treatment receiving natalizumab, anti-JC virus antibody index >6 months prior to PML diagnosis was significantly higher among those who developed PML with 96% consistently having an anti-JC virus antibody index >0.9. *Methods:* We describe a case of natalizumab-associated PML with low positive anti-JC virus index value prior to diagnosis. *Results:* A 53 year old man with 20 year history of relapsing remitting multiple sclerosis was diagnosed with PML following 46 infusions of natalizumab. Glatiramer acetate was his only prior immunomodulatory therapy. Routine MRI surveillance resulted in diagnosis of PML following detection of a confluent right anterior frontal T2 hyperintense lesion extending across the corpus callosum. Six months prior, routine MRI surveillance demonstrated a small right frontal T2 hyperintensity with no diffusion restriction while serum anti-JC virus antibody index was 0.69. *Conclusions:* Natalizumab-associated PML may develop despite low positive anti-JC virus index value.

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Disease phenotype analyses of relapsing-remitting multiple sclerosis in Canada and Saudi Arabia

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Background: Multiple sclerosis (MS) exhibits a spectrum of clinical findings, especially in relapsing-remitting MS (RR-MS). To assess the effects of geographic location and ethnicity on RR-MS phenotype, we investigated RR-MS patients in Canada and Saudi Arabia. *Methods:* A retrospective cross-sectional analysis of patients receiving active care in MS Clinics was performed in Medina, Saudi Arabia and Edmonton, Alberta. Demographic and clinical data was collected for each patient. *Results:* 98 patients with treated RR-MS were recruited (n=51, Medina; n=47, Edmonton); 40 patients were Caucasian (Edmonton) while 46 patients were Bedouin (Medina). Although the disease duration was longer in the Edmonton (5.7+2.3 yr) compared to the Medina group (4.4+1.4 yr) (p<0.05), the mean age of RR-MS onset, relapse rate and EDSS change were similar. The female:male ratio was comparable in Edmonton (35:12) and Medina (32:19), as was the risk of optic neuritis. The likelihood of an infratentorial lesion-associated presentation differed (Edmonton, n=23; Medina; n=13) among groups (p<0.05). Spinal cord lesions on MRI were more frequent in Edmonton (n=18) compared to Medina

(n=1) patients (p<0.05). *Conclusions:* Despite differences in location, ethnicity, and a predominance of infratentorial lesion burden the Edmonton group, the RR-MS phenotype displayed similar disease severity and trajectory in these cohorts.

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The low adherence and disability outcomes of disease-modifying drugs in Multiple Sclerosis in Saskatchewan, a cohort study, 1997-2014

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Background: The beneficial effects of the injected disease-modifying drugs (DMDs) in relapsing-remitting Multiple Sclerosis have been previously reported. However the results related to disability outcomes and the reduction of disease progression in the pivotal trials and few longer studies are variable and inconclusive. *Objectives:* To determine the utilization and the disability outcomes of the DMDs on relapsing-remitting Multiple Sclerosis over fifteen years. *Methods:* A prospective open-label cohort of 262 clinical definite patients, 78 men and 184 women, with two attacks in the past two years and a disability level DSS≤5.5 were enrolled consecutively from December 1997 to November 1999. A descriptive analysis of the cohort and individual drugs outcomes were performed. The results were compared to natural history studies of Multiple Sclerosis as controls. *Results:* At 15 years, one-seventh, 38/262 (14.5%) remain on the initial prescription, Betaseron, 15/131 (11.5%), Copaxone, 16/102 (15.5%) and Rebif 7/28 (25%), Avonex 0/1. 223(63.6%) had discontinued at a mean duration of 5.5(SD=4.7) years. 95/262 (36.4%) remain on a drug after switches. The DSS levels of the individual DMDs were analyzed. *Conclusion:* One-seventh of participants remained on their first prescription. Because of low adherence, the impact of DMDs on disease progression in the longer term cannot be verified.

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Prolonged-release fampridine as adjunct therapy to active enabled motor training in multiple sclerosis patients: a pilot, double-blind, placebo-controlled study

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Objectives: To investigate if MS subjects treated with PRF 10mg BID will show a greater benefit from active enabled motor training compared with placebo. *Methods:* Single center, phase 4, pilot, placebo-controlled, double-blind 18 weeks study. Fifteen patients were randomized to receive PRF 10mg BID and fifteen to received placebo BID. All patients participated in active enabled motor training of 3 sessions of 1 hour/week for 6 weeks. Patients were evaluated at -4, 0, 6 and 14 weeks using the timed 8 meters walk (8MW), the 6 minute walk (6MW) and the timed sit to stand (STS). *Results:* The PRF treated group achieved a higher mean percent improvement from baseline in all tasks at both 6 and 14 week time points. The difference reached statistical significance (mean difference of 14.29, p=0.046) for the 8MW at the 14 week time point. A higher incidence of responders (>20% improvement from baseline) was seen in the PRF treated group at 6 weeks on the 8MW (odds ratio [OR] of 2.31) and