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Dopamine Dysregulation Syndrome in Parkinson's Disease and its Management with Advanced Therapies

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Background: Dopamine Dysregulation Syndrome (DDS) is an adverse non-motor complication of dopamine replacement therapy in Parkinson's Disease. The current literature on DDS is limited, and it remains underdiagnosed and challenging to manage. **Methods:** We performed a retrospective chart review and classified patients according to risk factors that have been identified in the literature, UPDRS scores, intervention and outcome. Univariate analyses were performed to quantify these characteristics. **Results:** Prior psychiatric illness was identified in 70% of patients, impulse control disorder in 89% and substance abuse in 3.7%. Interventions included reduction of dopamine therapy (88.9%), deep brain stimulation (DBS) of the subthalamic nucleus (STN, 48.1%) or globus pallidus interna (GPi, 7.4%), and levodopa-carbidopa intestinal gel (LCIG) infusion (11.1%). Baseline UPDRS IV before treatment and MDS III after treatment were not significant between intervention groups (p=0.09 and p=0.13 respectively). Overall 88.9% patients improved at follow up, with medication only (75%), STN DBS (100%), GPi DBS (100%) and LCIG (33%). Relapse rate was 18.2%, in the STN group only. **Conclusions:** Our results suggest that GPi DBS, in concurrence with dopaminergic medication reduction, is the most effective intervention. STN DBS might be also beneficial although the associated medications reduction causes DDS relapse in a subgroup of patients.

Multiple Sclerosis

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Long term MS clinical outcomes predicted by baseline serum neurofilament light levels

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Background: Prognostic biomarkers are badly needed to direct MS treatment intensity early in the condition Levels of serum neurofilament light chains (sNfL) result from the destruction of central nervous system axons in MS and correlate with the aggressiveness of the disease. **Methods:** In this prospective cohort study, we identified patients with serum collected within 5 years of first MS symptom onset with more than 15 years of clinical follow-up. Levels of sNfL were quantified in patients and matched controls using digital immunoassay. **Results:** Sixty-seven patients had a median follow-up period of 17.4 years (range:15.1-26.1). Median serum NfL levels in baseline samples of MS patients was 10.1 pg/ml, 38.5% higher than median levels in 37 controls (7.26pg/ml, p=0.004). Baseline NfL level was most helpful as a predictive marker to rule out progression; patients with levels less 7.62pg/ml were 4.3 times less likely to develop an EDSS score of $^{3}4$ (p=0.001) and 7.1 times less likely to develop progressive MS (p=0.054). Patients with the highest NfL levels (3rd-tertile, >13.2 pg/ml) progressed most rapidly with an EDSS annual rate of 0.16 (p=0.004), remaining significant after adjustment for sex, age, and disease-modifying treatment (p=0.022). **Conclusions:** This study demonstrates that baseline sNfL is associated with long term disease progression.

P.044

Infection risk in patients with NMOSD or gMG receiving eculizumab: findings from two phase 3 studies and their extensions

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Background: PREVENT (NCT01892345) and REGAIN (NCT01997229) were phase 3, randomized, double-blind studies with open-label extensions (NCT02003144 [interim data], NCT02301624), comparing the safety and efficacy of eculizumab and placebo in patients with AQP4+ NMOSD and AChR+ gMG, respectively. This analysis compared infection rates in patients receiving eculizumab or placebo, with/without concomitant immunosuppressant therapy (IST). **Methods:** Patients were vaccinated against *Neisseria meningitidis* and randomized to eculizumab (maintenance dose, 1200 mg/2 weeks) or placebo, with stable-dose concomitant ISTs permitted. We report *post hoc* analysis of pooled infection rates for subgroups determined by number of baseline ISTs (0, 1, 2 or ≥ 3 ISTs) in these studies. **Results:** Rates (Table) and types of infection were similar in eculizumab and placebo groups. **Conclusions:** In these complement-mediated neurological indications, overall risk and types of infections were similar in eculizumab and placebo groups, regardless of concomitant IST use. This is consistent with the established safety profile for eculizumab in other indications.

	Infection rates/100 PY (N)				Serious infection rates[a]/100 PY (N)			
	NMOSD		gMG		NMOSD		gMG	
	Eculizumab	Placebo	Eculizumab	Placebo	Eculizumab	Placebo	Eculizumab	Placebo
No ISTs	192.1(35)	192.2(13)	238.2(2)	305.6(2)	1.4(35)	8.0(13)	0.0(2)	0.0 (2)
1IST	183.6(55)	154.1(22)	230.6(41)	253.1(18)	13.9(55)	7.0(22)	16.3(41)	34.5(18)
2 ISTs	195.1(47)	266.7(12)	171.7(78)	192.5(41)	15.1(47)	47.6 (12)	13.4(78)	24.1(41)
≥ 3 ISTs[b]	–	–	98.0(2)	100.1(2)	–	–	14.0(2)	0.0(2)

Infection rates shown per 100 PY to standardize for differences in treatment exposure.

[a]A serious adverse event (experience) or reaction was defined as any untoward medical occurrence that at any dose: results in death; is life-threatening; requires inpatient hospitalization or prolongation of existing hospitalization; results in persistent or significant disability/incapacity; is a congenital anomaly/birth defect; is an important medical event.

[b]No patients with NMOSD were receiving ≥ 3 ISTs at baseline.

gMG, generalized myasthenia gravis; IST, immunosuppressant therapy; N, total number of patients in category; NMOSD, neuromyelitis optica spectrum disorder; PY, patient-years.