Chair's Select Abstracts - Adult Neurology and Neurophysiology

A.01

Relieving the burden of myasthenia gravis: eculizumab reduces exacerbation, hospitalization and rescue therapy rates

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Background: Patients with anti-acetylcholine receptor antibody-positive (AChR+) generalized myasthenia gravis (MG) unresponsive to conventional treatment experience greater disease burden than responsive patients. This is partly due to exacerbations, which may result in significant healthcare resource utilization. Eculizumab is well tolerated and gives clinically meaningful benefits in these patients. We evaluated the effect of long-term eculizumab treatment on exacerbations, hospitalizations and rescue therapy in the REGAIN study and its open-label extension. **Methods:** Exacerbations were defined as clinical worsening/deterioration, MG crises or rescue therapy usage; pre-study exacerbations/hospitalizations were defined from patient records. Event rates adjusted for patient-years were calculated for all patients in the pre-study year, patients receiving placebo during REGAIN, and patients receiving eculizumab during REGAIN and its open-label extension (median exposure, 27.5 months [range, 22 days–42.8 months]); rates were compared using a Poisson regression model. **Results:** Eculizumab treatment reduced exacerbations by 65% (p=0.0057), hospitalizations by 71% (p=0.0316) and rescue therapy use by 66% (p=0.0072) versus placebo. Eculizumab treatment reduced exacerbations by 74% and hospitalizations by 83% (both p<0.0001) versus the pre-study year. **Conclusions:** Long-term eculizumab treatment reduces disease burden and healthcare resource utilization, demonstrating continuing improvements in clinical endpoints that lead to additional meaningful outcomes for patients with AChR+ generalized MG. (NCT01997229, NCT02301624).

A.02

Serum biomarkers of MS disease activity in patients treated with bone marrow transplant

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Background: There is an unmet need for blood-based biomarkers that can reliably detect MS disease activity. Serum Biomarkers of interest includ Neurofilament-light-chain (NfL), Glial-fibrillary-strocyte-protein(GFAP) and Tau. Bone Marrow Transplantation (BMT) is reserved for aggressive forms of MS and has been shown to halt detectable CNS inflammatory activity for prolonged periods. Significant pre-treatment tissue damage at followed by inflammatory disease abeyance should be reflected longitudinal sera collected from these patients. **Methods:** Sera were collected from 23 MS patients pre-treatment, and following BMT at 3, 6, 9 and 12-months in addition from 33 non-inflammatory neurological controls. Biomarker quantification was performed with SiMoA. **Results:** Pre-AHSCT levels of serum NfL and GFAP but not Tau were elevated compared to controls (p=0.0001), and NfL correlated with lesion-based disease activity (6-month-relapse, MRI-T2 and Gadolinium-enhancement). 3-months post-treatment, while NfL levels remained elevated, Tau/GFAP paradoxically increased (p=0.0023/0.0017). These increases at 3m correlated with MRI 'pseudoatrophy' at 6-months. NfL/Tau levels dropped to that of controls by 6-months (p=0.0036/0.0159). GFAP levels dropped progressively after 6-months although even at 12-months remained higher than controls (p=0.004). **Conclusions:** NfL was the closest correlate of MS disease activity and treatment response. Chemotherapy-related toxicity may account for transient increases in NfL, Tau and MRI brain atrophy post-BMT.

A.03

Cholinergic Neurons in Nucleus Subputaminalis in Primary Progressive Aphasia

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Background: Primary Progressive Aphasia (PPA) involves an isolated impairment of language function at disease onset. The cholinergic system is implicated in language and cholinergic deficits are seen in brains of individuals with PPA. One major source of cholinergic innervation is the nucleus basalis of Meynert (NBM) within which lies the nucleus subputaminalis (NSP). We quantified cholinergic neurons in the NBM and NSP of PPA and controls. Also explored was whether individuals with PPA who subsequently developed different clinical and neuropathological profiles, showed similar cholinergic deficits in the NSP. **Methods:** Cytoarchitecture of the basal forebrain was studied using Nissl staining in control (n=5) and PPA (n=5) brains. Choline acetyltransferase immunohistochemical staining labelled cholinergic neurons, quantified using Neurolucida software. **Results:** Compared to matched controls, PPA showed reduction of cholinergic neurons in the NBM, $t(4) = 4.224$, $p = 0.013$; Cohen's d=1.89 and the NSP, $t(4) = 4.013$, $p = 0.016$; Cohen's d= 1.79. The average percent of cholinergic neuronal loss was higher in the NSP (64.66%) compared to NBM (17.66%). **Conclusions:** Regardless of underlying pathology, all cases presenting with PPA showed marked loss of cholinergic neurons in the NSP providing further evidence for the importance of this nucleus in language function.