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Abstracts

Articles appearing in the September 2018 issue

Autoimmune septin-5 cerebellar ataxia

Objective To report a form of autoimmune cerebellar ataxia in which antibodies target septin-5, a guanosine triphosphate (GTP)–binding neural protein involved in neurotransmitter exocytosis.

Methods Archived sera and CSF specimens with unclassified synaptic antibodies were re-evaluated by tissue-based indirect immunofluorescence assay. Autoantigens were identified by Western blot and mass spectrometry. Recombinant protein assays (Western blot, cell-based, and protein screening array) confirmed antigen specificity.

Results Serum and CSF from 6 patients produced identical synaptic immunoglobulin G (IgG) staining patterns of synaptic regions (neuropil) of the mouse cerebrum and cerebellum. The molecular layer of the cerebellum and the thalamus demonstrated stronger immunoreactivity than the midbrain, hippocampus, cortex, and basal ganglia. The antigen revealed by mass spectrometry analysis of immunoprecipitated cerebellar proteins and confirmed by recombinant protein assays was septin-5. All 4 patients with records available had subacute onset of cerebellar ataxia with prominent eye movement symptoms (oscillopsia or vertigo). None had cancer detected. Improvements occurred after immunotherapies (2) or spontaneously (1). One patient died.

Conclusion Septin-5 IgG represents a biomarker for a potentially fatal but treatable autoimmune ataxia.

NPub.org/N2/9204a

Cladribine tablets added to IFN-β in active relapsing MS: The ONWARD study

Objective To evaluate the safety and efficacy of cladribine tablets in patients still experiencing active relapsing multiple sclerosis (MS) despite interferon (IFN)–β treatment.

Methods This was a 96-week phase II study, randomizing patients treated with IFN-β to cladribine tablets 3.5 mg/kg/IFN-β or placebo/IFN-β. Patients were to receive cladribine tablets 3.5 mg/kg/IFN-β or placebo/IFN-β in a 2:1 ratio (n = 172) with safety and exploratory efficacy outcomes being assessed.

Results Adverse events (AEs) and serious AEs were similar across treatment groups, except lymphopenia. Fifty of 124 (40.3%) cladribine/IFN-β recipients vs 0% of placebo/IFN-β recipients reported lymphopenia as an AE, with grade 3/4 lymphopenia (laboratory lymphocyte count <500 cells/mm^3) experienced by 79/124 (63.7%) vs 1 (2.1%), respectively. Patients treated with cladribine tablets 3.5 mg/kg/IFN-β were 63% less likely to have a qualifying relapse than placebo/IFN-β recipients, and cladribine tablets 3.5 mg/kg/IFN-β reduced most MRI measures of disease activity.

Conclusions In patients with active relapsing MS despite IFN-β treatment, cladribine tablets 3.5 mg/kg/IFN-β reduced relapses and MRI lesion activity over 96 weeks compared with placebo/IFN-β but led to an increased incidence of lymphopenia.

Classification of evidence This study provides Class I evidence that for patients with active relapsing MS despite IFN-β treatment, cladribine tablets added to IFN-β reduced relapses and MRI lesion activity over 96 weeks and increased the incidence of lymphopenia.

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Characteristics of optic neuropathy in Behçet disease

Akdal G, Toydemir HE, Saatci AO, et al. 2018;3:e490. doi.org/10.1212/NXI.0000000000000490

Cladribine tablets added to IFN-β in active relapsing MS

Montalban X, Leist TP, Cohen BA, et al. 2018;5:e477 doi.org/10.1212/NXI.0000000000000477

Lipoic acid in secondary progressive MS: A randomized controlled pilot trial

R. Spain, K. Powers, C. Murchison, et al. 2017;4:e374. doi.org/10.1212/NXI.0000000000000374

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Moreno MA, Or-Geva N, Aftab BT, et al. 2018;4:e466. doi.org/10.1212/NXI.0000000000000466