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Abstracts

Articles appearing in the September 2019 issue

Long-term safety and efficacy of subcutaneous immunoglobulin IgPro20 in CIDP: PATH extension study

Objective To investigate the long-term safety and efficacy of weekly subcutaneous IgPro20 (Hizentra, CSL Behring) in chronic inflammatory demyelinating polyneuropathy (CIDP).

Methods In a 48-week open-label prospective extension study to the PATH study, patients were initially started on 0.2 g/kg or on 0.4 g/kg weekly and—if clinically stable—switched to 0.2 g/kg weekly after 24 weeks. Upon CIDP relapse on the 0.2 g/kg dose, 0.4 g/kg was (re) initiated. CIDP relapse was defined as a deterioration by at least 1 point in the total adjusted Inflammatory Neuropathy Cause and Treatment score.

Results Eighty-two patients were enrolled. Sixty-two patients initially received 0.4 g/kg, 20 patients 0.2 g/kg weekly. Seventy-two received both doses during the study. Sixty-six patients (81%) completed the 48-week study duration. Overall relapse rates were 10% in 0.4 g/kg–treated patients and 48% in 0.2 g/kg–treated patients. After dose reduction from 0.4 to 0.2 g/kg, 51% (27/53) of patients relapsed, of whom 92% (24 of 26) improved after reinitiation of the 0.4 g/kg dose. Two-thirds of patients (19/28) who completed the PATH study without relapse remained relapse-free on the 0.2 g/kg dose after dose reduction in the extension study. Sixty-two patients had adverse events (AEs) (76%), of which most were mild or moderate with no related serious AEs.

Conclusions Subcutaneous treatment with IgPro20 provided long-term benefit at both 0.4 and 0.2 g/kg weekly doses with lower relapse rates on the higher dose. Long-term dosing should be individualized to find the most appropriate dose in a given patient.

Classification of evidence This study provides Class IV evidence that for patients with CIDP, long-term treatment with SCIG beyond 24 weeks is safe and efficacious.

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Pharmacokinetics and pharmacodynamics of natalizumab in pediatric patients with RRMS

Objective This phase I study investigated pharmacokinetic (PK) and pharmacodynamic (PD) profiles of natalizumab in pediatric patients with relapsing-remitting MS (RRMS).

Methods Pediatric patients with RRMS who were prescribed natalizumab 300 mg IV every 4 weeks were enrolled. Blood samples were collected on days 1, 2, 8, 15, and 22 and at weeks 4, 8, 12, and 16 to estimate PK parameters; PD properties were evaluated by measuring α4-integrin saturation and lymphocyte counts over time. Natalizumab's safety profile was also evaluated.

Results PK parameters were similar to those reported in adult patients; natalizumab concentrations peaked approximately 1 day after infusion in most of the participants (Cmax 142.9 μg/mL, AUClast 47389.4 hr*μg/mL), followed by a biphasic decline with a rapid distribution phase and a slow elimination phase, with a terminal half-life of 215.1 hours. In terms of PD, both time course and magnitude of α4-integrin saturation and increase in lymphocyte counts were similar to those observed in adults. During the 16-week study follow-up, 3 adverse events attributed to natalizumab were observed; no unexpected safety events occurred.

Conclusions PK profile, α4-integrin saturation, lymphocyte counts, and safety observed in these pediatric patients are comparable to those reported in adults.

Classification of evidence This study provides Class I evidence that natalizumab PK/PD parameters and safety profile are similar in adults and pediatric patients in the short term. Longer studies, also including a larger number of younger subjects (aged 10–12 years), are required to further inform about long-term PK and PD parameters in pediatric patients with MS.

NPub.org/N2/9416b

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F. Luessi, S. Engel, A. Spreer, S. Bittner, F. Zipp. 2018;5:e481. doi.org/10.1212/NXI.0000000000000481

Intrathecal B-cell accumulation and axonal damage distinguish MRI-based benign from aggressive onset in MS

S. Engel, M. Friedrich, M. Muthuraman, et al. 2019;6:e595. doi.org/10.1212/NXI.0000000000000595

Pilot study of a ketogenic diet in relapsing-remitting MS

J.N. Brenton, B. Banwell, A.G.C. Bergqvist, et al. 2019;6:e565. doi.org/10.1212/NXI.0000000000000565

Dimethyl fumarate-induced lymphopenia in MS due to differential T-cell subset apoptosis

M. Ghadiri, A. Rezk, R. Li, et al. 2017;4:e340. doi.org/10.1212/NXI.0000000000000340

Dimethyl fumarate as a first- vs second-line therapy in MS: Focus on B cells

E. Staun-Ram, E. Najjar, A. Volkowich, A. Miller. 2018;5:e508. doi.org/10.1212/NXI.0000000000000508

