WHAT'S HAPPENING IN

Neurology®
Neuroimmunology & Neuroinflammation

Neurology.org/NN

Abstracts

Articles appearing in the May 2019 issue

MuSK myasthenia gravis monoclonal antibodies: Valency dictates pathogenicity

Objective To isolate and characterize muscle-specific kinase (MuSK) monoclonal antibodies from patients with MuSK myasthenia gravis (MG) on a genetic and functional level.

Methods We generated recombinant MuSK antibodies from patient-derived clonal MuSK-specific B cells and produced monovalent Fab fragments from them. Both the antibodies and Fab fragments were tested for their effects on neural agrin-induced MuSK phosphorylation and acetylcholine receptor (AChR) clustering in myotube cultures.

Results The isolated MuSK monoclonal antibody sequences included IgG1, IgG3, and IgG4 that had undergone high levels of affinity maturation, consistent with antigenic selection. We confirmed their specificity for the MuSK Ig-like 1 domain and binding to neuromuscular junctions. Monovalent MuSK Fab, mimicking functionally monovalent MuSK MG patient Fab-arm exchanged serum IgG4, abolished agrin-induced MuSK phosphorylation and AChR clustering. Surprisingly, bivalent monospecific MuSK antibodies instead activated MuSK phosphorylation and partially induced AChR clustering, independent of agrin.

Conclusions Patient-derived MuSK antibodies can act either as MuSK agonist or MuSK antagonist, depending on the number of MuSK binding sites. Functional monovalency, induced by Fab-arm exchange in patient serum, makes MuSK IgG4 antibodies pathogenic.

NPub.org/N2/9314a

Real-world persistence and benefit–risk profile of fingolimod over 36 months in Germany

Objective To assess the long-term real-world benefit–risk profile of fingolimod in patients with relapsing MS in Germany.

Methods This analysis used data from the noninterventional real-world study, Post-Authorization Non-interventional German sAfety study of GilEnyA (PANGAEA), to assess prospectively the persistence, effectiveness, and safety of fingolimod over 36 months (±90 days) in Germany. For inclusion in the effectiveness analysis (n = 2,537), patients were required to have received fingolimod for the first time in PANGAEA, to have at least 12 months of data, and to have completed each 12-month follow-up period. For the safety analysis (n = 3,266), patients were additionally allowed to have received fingolimod before enrollment.

Results At baseline, 94.7% of patients in the effectiveness analysis had received a previous disease-modifying therapy. After 36 months, 70.4% of patients were still receiving fingolimod. Over this period, annualized relapse rates decreased to 0.265 (95% CI: 0.244–0.286) from 1.79 (95% CI: 1.75–1.83), and mean Expanded Disability Status Scale scores remained stable (mean change from baseline: +0.049 [95% CI: −0.015 to +0.114]). In total, 16% of patients had 6-month confirmed disability improvement, 12.5% had 6-month confirmed disability worsening, and 52.4% were free from relapses and 6-month confirmed disability worsening. Adverse events (AEs) and serious AEs were experienced by up to 23.4% and 3.9% of patients, respectively, during any of the 12-month follow-up periods. The frequency and nature of AEs were in line with previous findings.

Conclusions Using systematically collected data from PANGAEA, this analysis demonstrates the sustained effectiveness, high persistence, and manageable safety profile of fingolimod over 36 months.

NPub.org/N2/9314b

Most-Read Articles

As of February 22, 2019

Aquaporin-4 autoimmunity

V. Lennon, A. Zekeridou. 2015;2: e110. doi.org/10.1212/NXI.0000000000000110

Normal volumes and microstructural integrity of deep gray matter structures in AQP4+ NMOSD

C. Finke, J. Heine, F. Pache, et al. 2016;3:e229. doi.org/10.1212/NXI.0000000000000229

Reduction of CD8$^+$ T lymphocytes in multiple sclerosis patients treated with dimethyl fumarate

C.M. Spencer, E.C. Crabtree-Hartman, K. Lehmann-Horn, B.A.C. Cree, S.S. Zamvil. 2015;2: e76. doi.org/10.1212/NXI.0000000000000076

Treatment of spontaneous EAE by laquinimod reduces Tfh, B cell aggregates, and disease progression

M. Varrin-Doyer, K.L. Pekarek, C.M. Spencer, et al. 2016;3:e272. doi.org/10.1212/NXI.0000000000000272

Microglial activation, white matter tract damage, and disability in MS

E. Rissanen, J. Tuisku, T. Vahlberg, et al. 2019;3:e443. doi.org/10.1212/NXI.0000000000000443

Copyright © 2019 American Academy of Neurology

Copyright © 2019 American Academy of Neurology. Unauthorized reproduction of this article is prohibited.

Neurology®

What's happening in *Neurology® Neuroimmunology & Neuroinflammation*
Neurology 2019;93;623
DOI 10.1212/WNL.0000000000008201

This information is current as of September 30, 2019

Updated Information & Services	including high resolution figures, can be found at: http://n.neurology.org/content/93/14/623.full
Permissions & Licensing	Information about reproducing this article in parts (figures,tables) or in its entirety can be found online at: http://www.neurology.org/about/about_the_journal#permissions
Reprints	Information about ordering reprints can be found online: http://n.neurology.org/subscribers/advertise

Neurology ® is the official journal of the American Academy of Neurology. Published continuously since 1951, it is now a weekly with 48 issues per year. Copyright © 2019 American Academy of Neurology. All rights reserved. Print ISSN: 0028-3878. Online ISSN: 1526-632X.

AMERICAN ACADEMY OF NEUROLOGY®