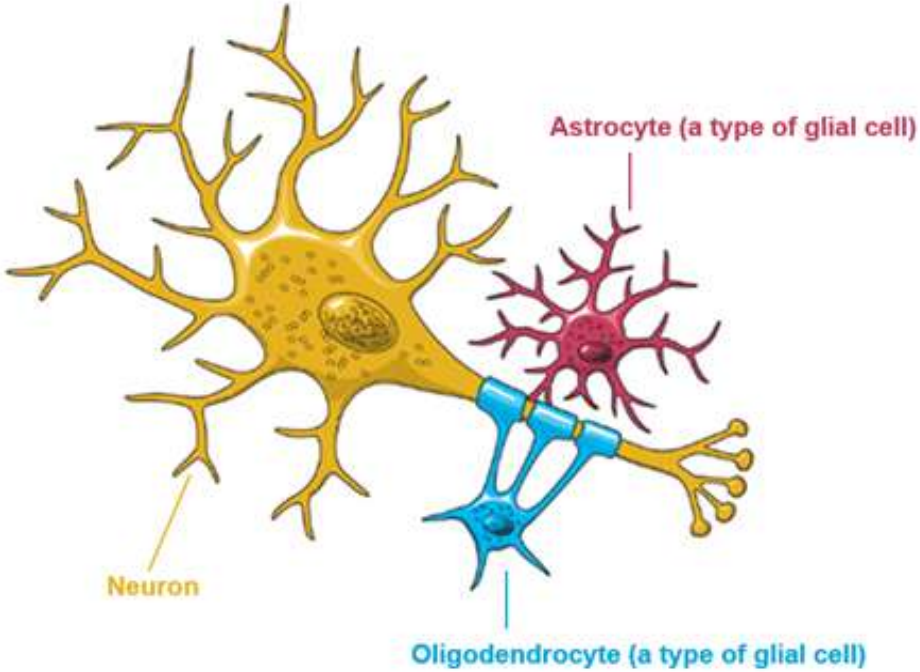
RĪGAS STRADIŅA UNIVERSITĀTE

aslimnīca
RĪGAS AUSTRUMU KLĪNISKĀ UNIVERSITĀTES SLIMNĪCA

KOMPLEMENTS
un
NEIROLOĢISKĀS SLIMĪBAS

doc. Viktorija Ķēniņa
neirologs-imunologs
7. Vispārējās neiroloģijas nodaļas vadītāja

SAPRAST = ĀRSTĒT EFEKTĪVI



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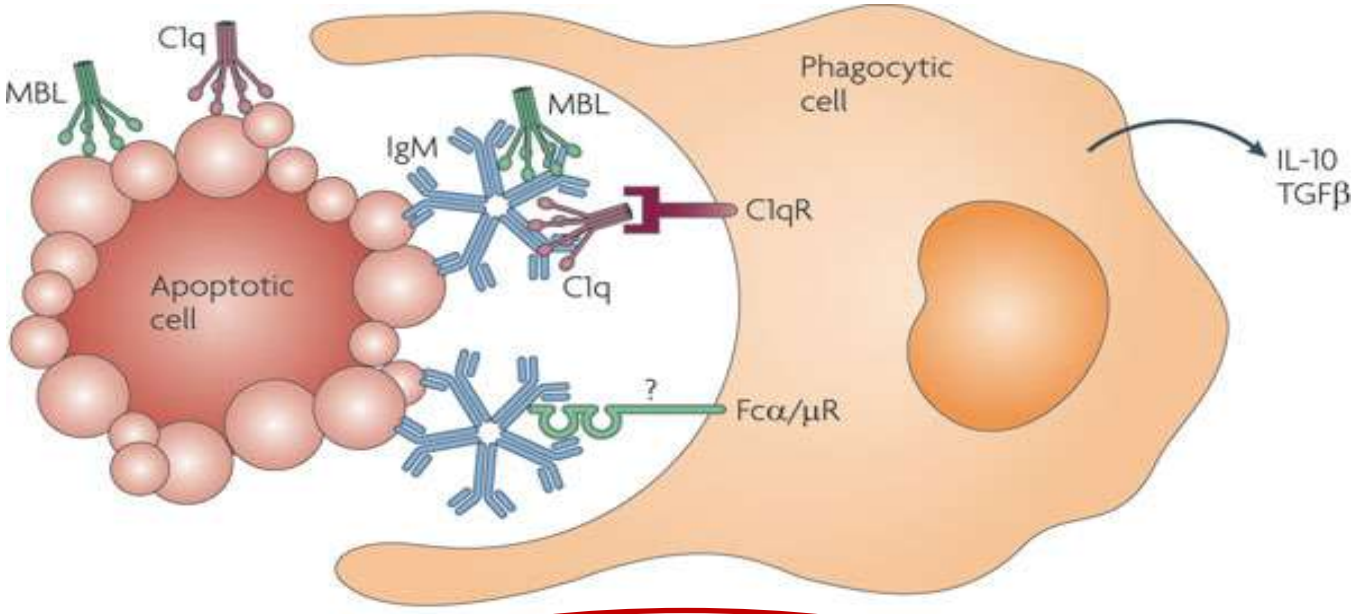


NEIROPROTEKCIJA

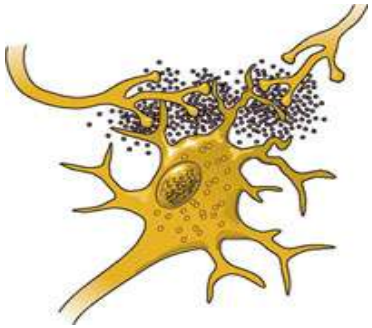
SINAPTISKĀ PLASTICITĀTE

NEIROĢENĒZE

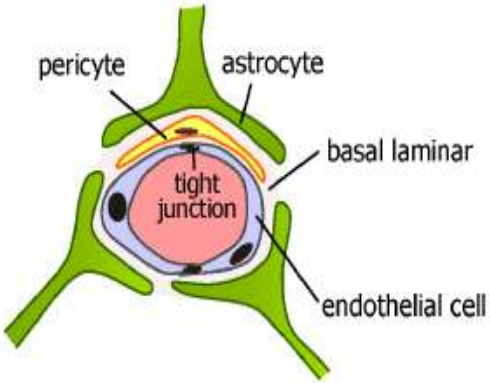
KOMPLEMENTA AKTIVĀCIJA

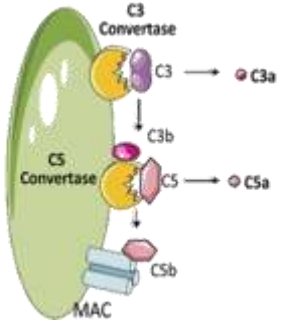
AKSONĀLS BOJĀJUMS

NEIRONU ZUDUMS

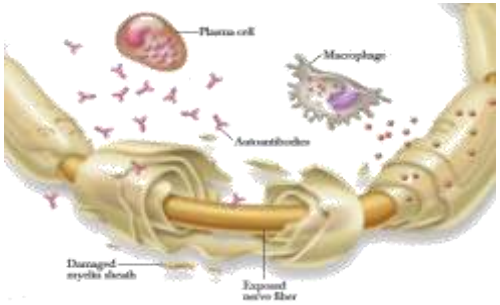


MUGURAS SMADZEŅU BARJERAS BOJĀJUMS

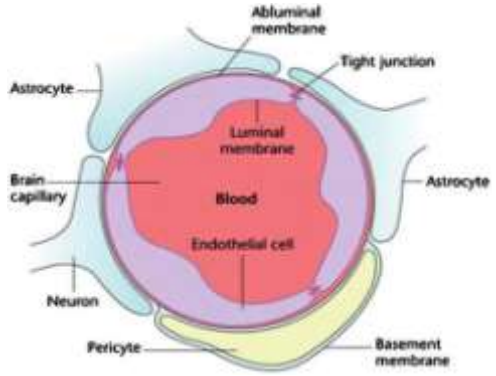




DEMIELINIZĀCIJA



HEMATOENCEFĀLISKĀS BARJERAS BOJĀJUMS



KOMPLEMENTA AKTIVĀCIJA

GIJĒNA – BARĒ SY

AUTOIMŪNIE ENCEFALĪTI

NEUROMIELITIS OPTICA

AUTOIMŪNĀS EPILEPSIJAS

NEIROMIOTONIJA

MIASTĒNIJA

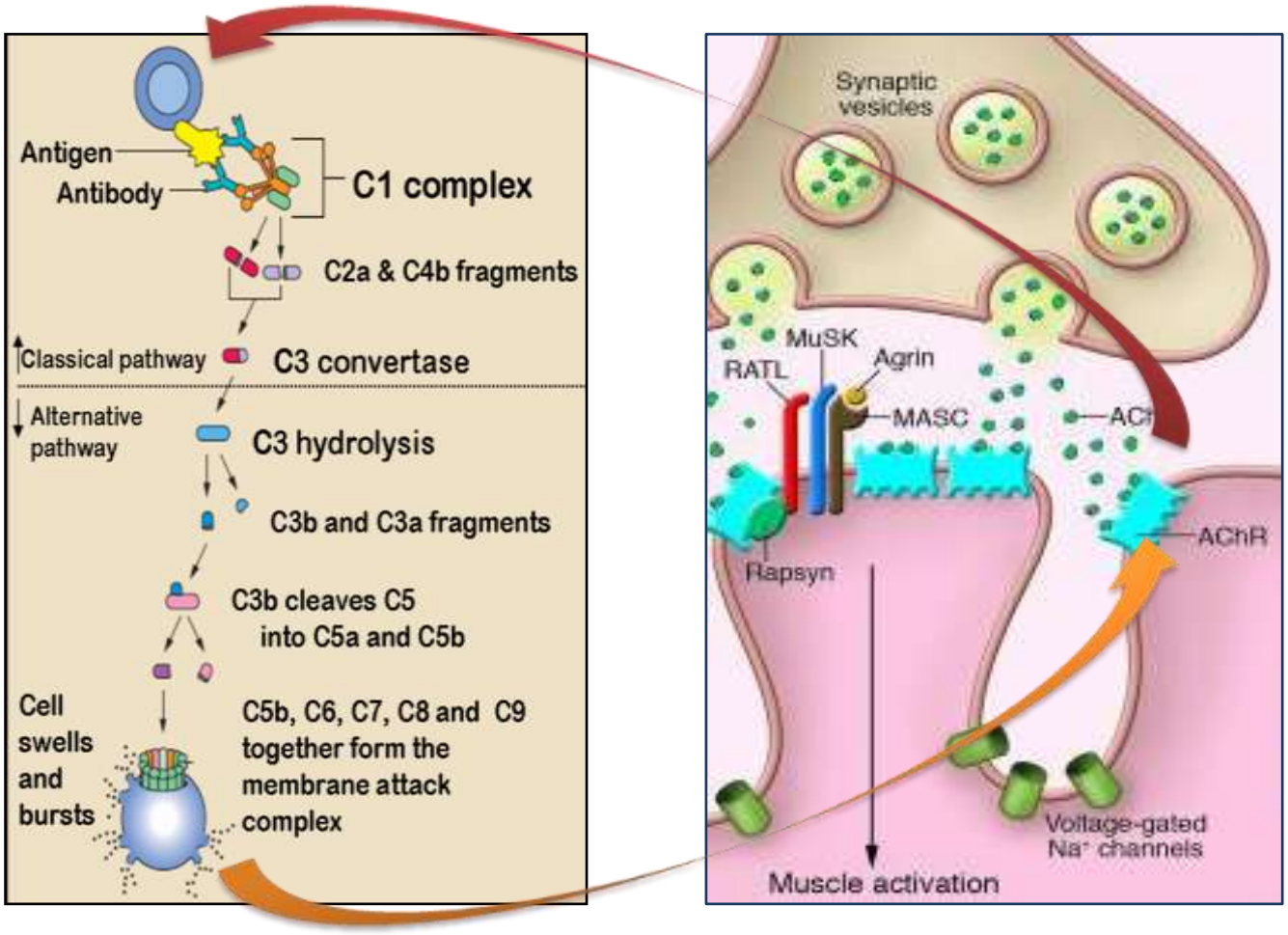
MULTIPLĀ SKLEROZE

AUTOIMŪNĀS DEMENCES

LAMBERTA- ĪTONA SY

NEISSERIA INFEKCIJAS ← **DEFICĪTS** → *BAKTERIĀLA MENINGĪTA IZNĀKUMS*

KOMPLEMENTA LOMA



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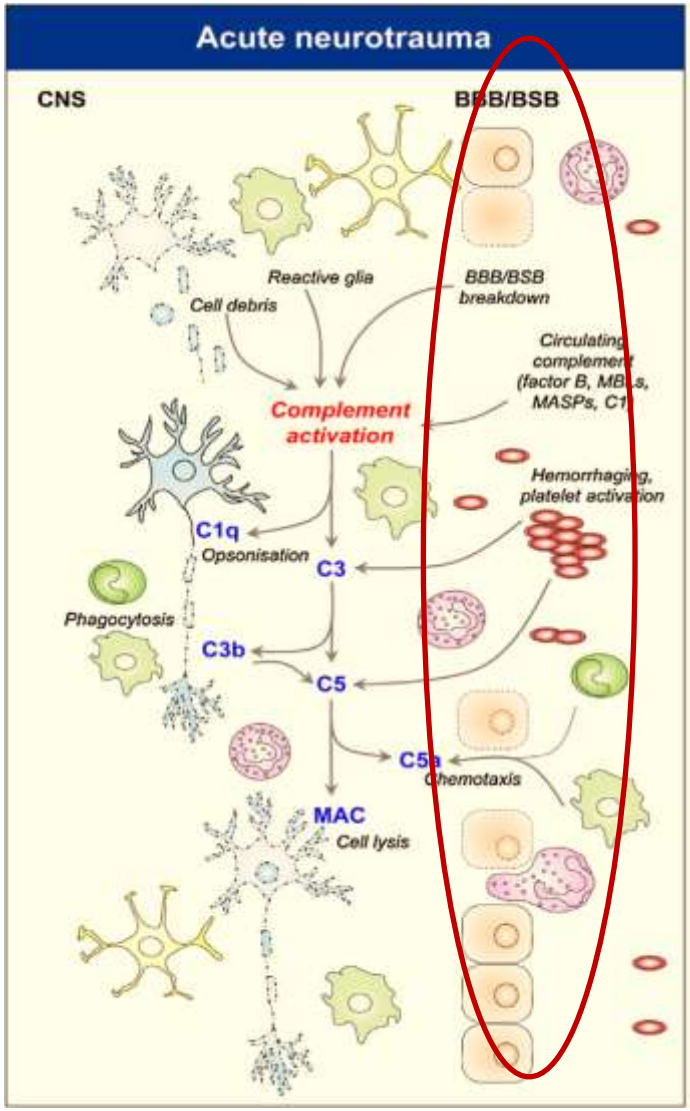

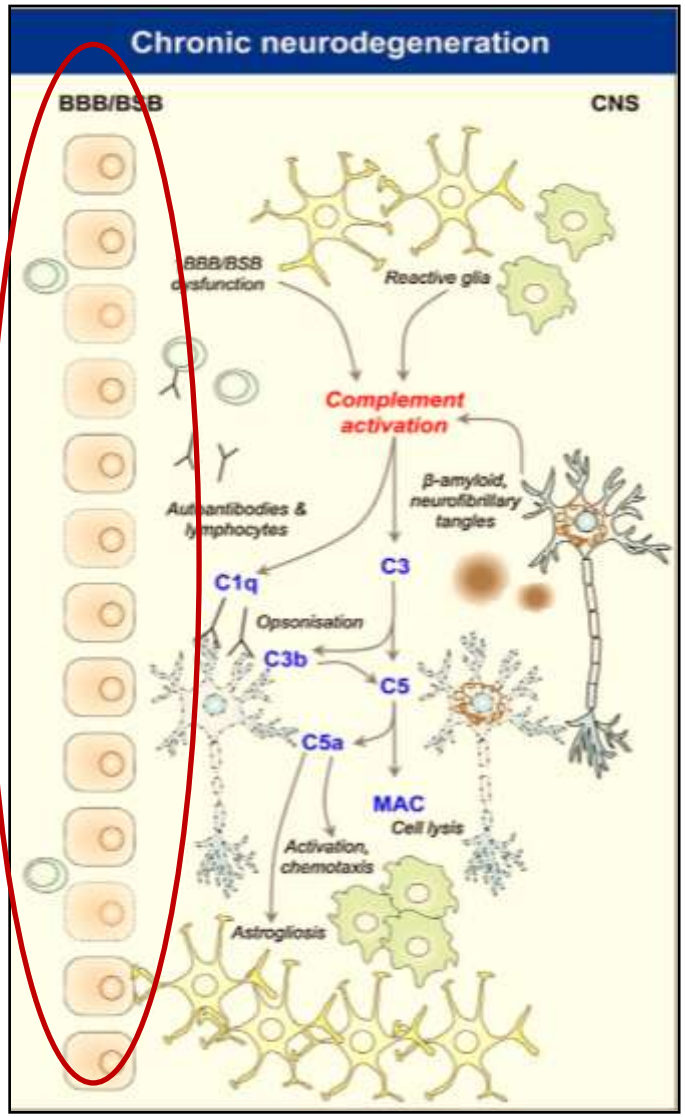

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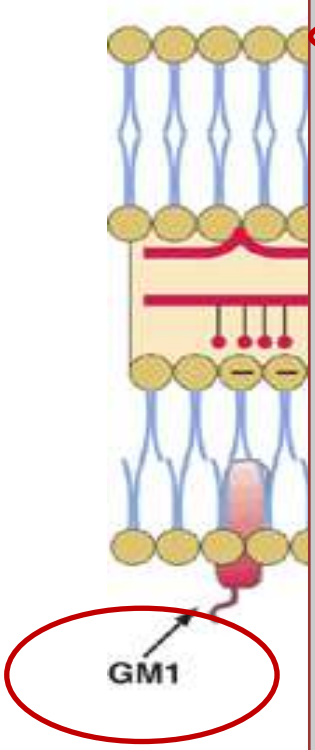


Neurol Neuroimmunol Neuroinflamm. 2015 Jun 25;2(4):e119. doi: 10.1212/NXI.0000000000000119. eCollection 2015.

Complement activity is associated with disease severity in multifocal motor neuropathy.

Vlam L[1], Cats EA[1], Harschnitz O[1], Jansen MD[1], Piepers S[1], Veldink JH[1], Franssen H[1], Stork AC[1], Heezius E[1], Rooijakkers SH[1], Herpers BL[1], van Strijp JA[1], van den Berg LH[1], van der Pol WL[1].

⊕ Author information

Abstract

OBJECTIVE: To investigate whether high innate activity of the classical and lectin pathways of complement is associated with multifocal motor neuropathy (MMN) and whether levels of innate complement activity or the potential of anti-GM1 antibodies to activate the complement system correlate with disease severity.

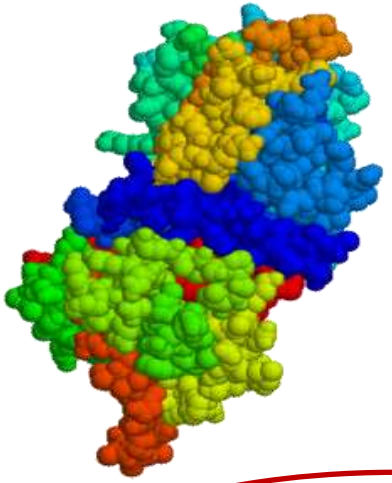
METHODS: We performed a case-control study including 79 patients with MMN and 79 matched healthy controls. Muscle weakness was documented with Medical Research Council scale sum score and axonal loss with nerve conduction studies. Activity of the classical and lectin pathways of complement was assessed by ELISA. We also determined serum mannose-binding lectin (MBL) concentrations and polymorphisms in the MBL gene (MBL2) and quantified complement-activating properties of anti-GM1 IgM antibodies by ELISA.

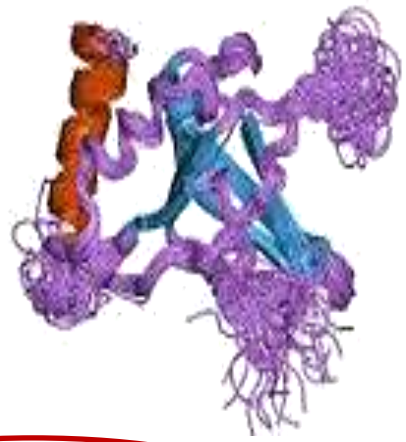
RESULTS: Activity of the classical and lectin pathways, MBL2 genotypes, and serum MBL concentrations did not differ between patients and controls. Complement activation by anti-GM1 IgM antibodies was exclusively mediated through the classical pathway and correlated with antibody titers ($p < 0.001$). Logistic regression analysis showed that both high innate activity of the classical pathway of complement and high complement-activating capacity of anti-GM1 IgM antibodies were significantly associated with more severe muscle weakness and axonal loss.

CONCLUSION: High innate activity of the classical pathway of complement and efficient complement-activating properties of anti-GM1 IgM antibodies are determinants of disease severity in patients with MMN. These findings underline the importance of anti-GM1 antibody-mediated complement activation in the pathogenesis and clinical course of MMN.

PMID: 26161430 PMCID: PMC4484896 DOI: 10.1212/NXI.0000000000000119

TERAPIJA





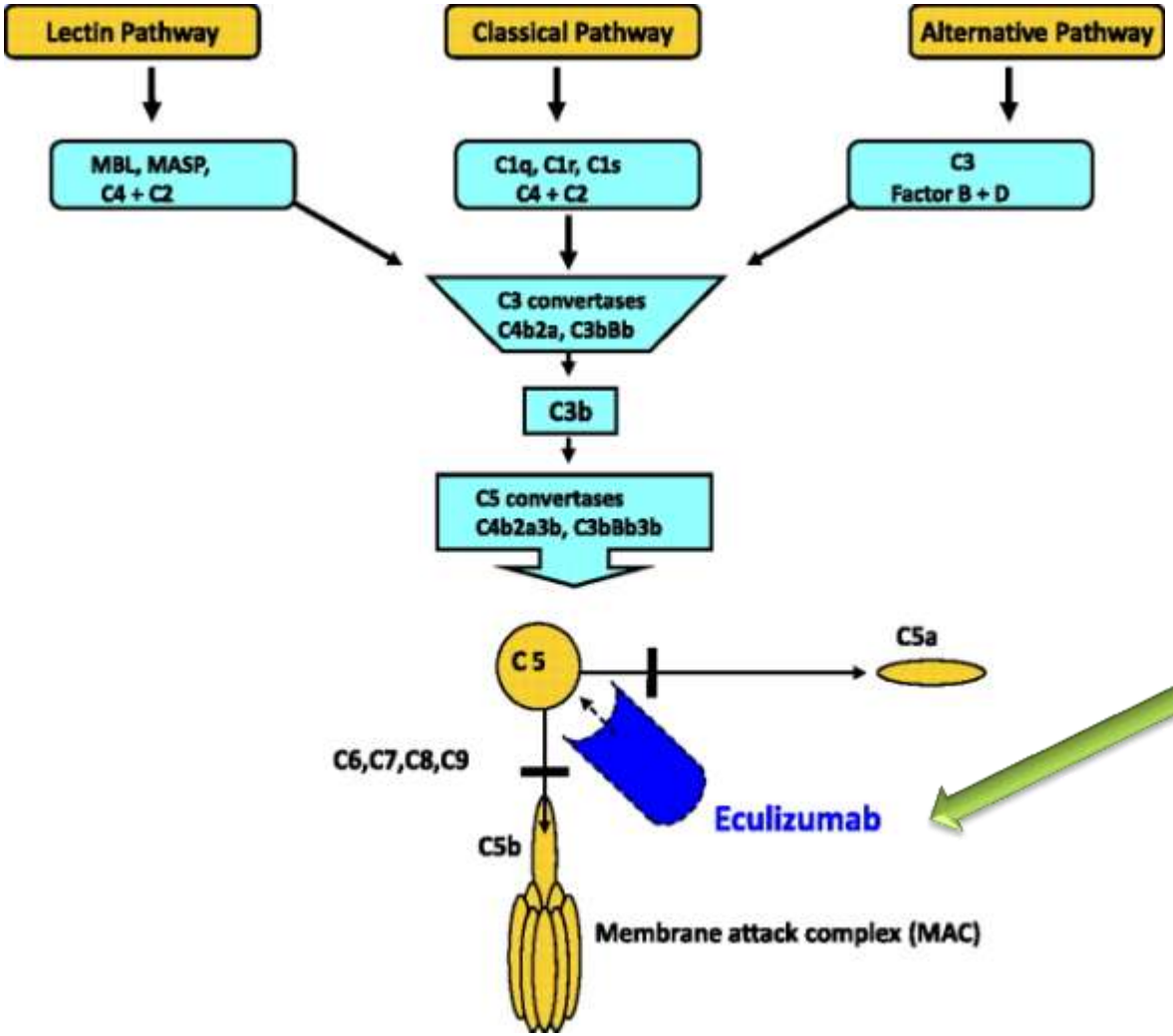
C1 inhibitors
(Cinryze,
Berinert)

C5 monoklonālā antiviela
(Eculizumabs)

Hereditārā angioedema

Neiroloģiskās slimības

KOMPLEMENTA LOMA



C5 MONOKLONĀLĀ ANTIVIELA

NMO

MG

KOMPLEMENTA LOMA

Muscle Nerve. 2013 Jul;48(1):76-84. doi: 10.1002/mus.23839. Epub 2013 Apr 30.

A randomized, double-blind, placebo-controlled phase II study of eculizumab in patients with refractory generalized myasthenia gravis.

Howard JF Jr[1], Barohn RJ, Cutter GR, Freimer M, Juel VC, Mozaffar T, Mellion ML, Benatar MG, Farrugia ME, Wang JJ, Malhotra SS, Kissel JT; MG Study Group.

⊕ Collaborators (55)

⊕ Author information

Abstract

INTRODUCTION: Comple
neuromuscular transmissi
complement complex by s

METHODS: This study wa
generalized MG (gMG).

RESULTS: Six of 7 patien
myasthenia gravis (QMG)
between eculizumab and p
baseline was found to be s

CONCLUSION: The data s

Lancet Neurol. 2013 Jun;12(6):554-62. doi: 10.1016/S1474-4422(13)70076-0. Epub 2013 Apr 26.

Eculizumab in AQP4-IgG-positive relapsing neuromyelitis optica spectrum disorders: an open-label pilot study.

Pittock SJ[1], Lennon VA, McKeon A, Mandrekar J, Weinshenker BG, Lucchinetti CF, O'Toole O, Wingerchuk DM.

⊕ Author information

Abstract

BACKGROUND: Complement activation after binding of an IgG autoantibody to aquaporin 4 (AQP4) is thought to be a major determinant of CNS inflammation and astrocytic injury in neuromyelitis optica. The aim of this study was to investigate the use of eculizumab--a therapeutic monoclonal IgG that neutralises the complement protein C5--in neuromyelitis optica spectrum disorders.

METHODS: Between Oct 20, 2009, and Nov 3, 2010, we recruited patients from two US centres into an open-label trial. Patients were AQP4-IgG-seropositive, aged at least 18 years, had a neuromyelitis optica spectrum disorder, and had at least two attacks in the preceding 6 months or three in the previous 12 months. Patients received meningococcal vaccine at a screening visit and 2 weeks later began eculizumab treatment. They received 600 mg intravenous eculizumab weekly for 4 weeks, 900 mg in the fifth week, and then 900 mg every 2 weeks for 48 weeks. The coprimary endpoints were efficacy (measured by number of attacks [new worsening of neurological function lasting for more than 24 h and not attributable to an identifiable cause]) and safety. Secondary endpoints were disability (measured by expanded disability status scale), ambulation (Hauser score), and visual acuity. At follow-up visits (after 6 weeks and 3, 6, 9, and 12 months of treatment; and 3 and 12 months after discontinuation), complete neurological examination was undertaken and an adverse event questionnaire completed. This trial is registered with ClinicalTrials.gov, number NCT00904826.

FINDINGS: We enrolled 14 patients, all of whom were women. After 12 months of eculizumab treatment, 12 patients were relapse free; two had had possible attacks. The median number of attacks per year fell from three before treatment (range two to four) to zero (zero to one) during treatment ($p<0·0001$). No patient had worsened disability by any outcome measure. Median score on the expanded disability status scale improved from 4·3 (range 1·0-8·0) before treatment to 3·5 (0-8·0) during treatment ($p=0·0078$). Two patients improved by two points and three improved by one point on the Hauser score; no change was recorded for the other patients. Visual acuity had improved in at least one eye by one point in four patients, and by two points in one patient; no change was recorded for other patients. One patient had meningococcal sepsis and sterile meningitis about 2 months after the first eculizumab infusion, but resumed treatment after full recovery. No other drug-related serious adverse events occurred. Eight attacks in five patients were reported within 12 months of eculizumab withdrawal.

INTERPRETATION: Eculizumab seems to be well tolerated, significantly reduce attack frequency, and stabilise or improve neurological disability measures in patients with aggressive neuromyelitis optica spectrum disorders. The apparent effects of eculizumab deserve further investigation in larger, randomised controlled studies.

FUNDING: Alexion Pharmaceuticals.

«TAKE HOME»

Komplementa aktivācija - neirodeģeneratīvās, autoimūnās un traumatiskās CNS un PNS slimības

Katras slimības gadījumā komplementa loma atsķirīga

Anti- komplementa terapija- jauna iespēja palīdzēt pacientiem

PALDIES!