Scientific Foundation SPIROSKI, Skopje, Republic of Macedonia
Open Access Macedonian Journal of Medical Sciences. 2020 Nov 07; 8(B):1083-1087.
https://doi.org/10.3889/oamjms.2020.5048
eISSN: 1857-9655
Category: *B - Clinical Sciences*
Section: *Neurology*

Modern Methods of Devic's Disease Treatment

Grigolashvili Marina Archilovna*, Kim Ekaterina Danilovna, Beisembayeva Mira Baikonyrovna, Smagulov Amirzhan Muratovich, Omarova Sholpan Kabidenovna, Biduysenov Nurdaulet Kurmashovich, Belyaev Ruslan Andreevich, Abildina Akmaral Ardakovna, Abueva Zhanna Argynovna, Aimurzina Zhanargul Nagimovna, Amanzhol Aigerim Baltalykyzy

Department of Neurology, Neurosurgery, Psychiatry and Rehabilitation, Karaganda Medical University, Karaganda, Kazakhstan

Edited by: Ksenija Bogoeva-Kostovska
Citation: Archilovna GM, Danilovna KE, Baikonyrovna BM, Muratovich SA, Kabidenovna OS, Kurmashovich BN, Andreevich BR, Ardakovna AA, Argynovna AZ, Nagimovna AZ, Baltalykyzy AA. Modern Methods of Devic's Disease Treatment. Open Access Maced J Med Sci. 2020 Nov 07; 8(B):1083-1087. https://doi.org/10.3889/oamjms.2020. 5048
Keywords: Neuromyelitis optica; Devic's disease; Optical neuritis; Neuromyelitis optica treatment; Aquaporin
***Correspondence:** Grigolashvili Marina Archilovna, Associate Professor, Head of the Neurology, Neurosurgery, Psychiatry and Rehabilitation Department, Karaganda Medical University, Karaganda, Kazakhstan, 40 Gogol street. Tel: +77472502288. E-mail: grigolashvili.marina@mail.ru
Received: 04-Jun-2020
Revised: 24-Oct-2020
Accepted: 28-Oct-2020

Funding: This research did not receive any financial support
Competing Interests: The authors have declared that no competing interests exist

Abstract

BACKGROUND: Neuromyelitis optica (NMO) (also known as opticomyelitis, Devic's syndrome/disease) is an idiopathic inflammatory disorder of the central nervous system characterized by predominant involvement of the optic nerves, spinal cord, and extensive transverse myelitis. To date, there are no convincing clinical trials that would fully evaluate the efficacy and safety of drugs for the treatment and prevention of NMO exacerbation. Taking into account the malignant course that quickly leads to disability of young, economically active population, the issues of searching for effective methods of NMO treatment remain highly urgent.

AIM: The purpose of the study was to examine available modern methods of treatment and prevention of NMO exacerbation, which have potential and require further detailed clinical trials to ensure possible application of these treatment options in clinical practice.

MATERIALS AND METHODS: We have reviewed previously applied and modern methods of treatment. We have analyzed systematic reviews, clinical, randomized, and retrospective studies of scientific medical databases: PubMed, Cochrane, The Lancet, UpToDate, and reviews of world medical journals in Russian and English.

CONCLUSIONS: The authors concluded that there is a sufficient number of drugs and combinations of methods of Devic's disease treatment. We were interested in combinations of rituximab (RIT) and autologous stem cell transplantation, RIT and fetal hepatocyte transplantation, and RIT and strengthening the effect by plasmapheresis sessions. However, successful implementation of these methods in clinical practice requires conducting controlled clinical trials with a larger number of patients and longer follow-up periods.

Introduction

Neuromyelitis optica (NMO) (opticomyelitis, Devic's syndrome/disease) is an idiopathic inflammatory disease of the central nervous system (CNS) characterized by predominant involvement of the optic nerves, spinal cord, and extensive transverse myelitis longitudinally extensive transverse myelitis at the level of the thoracic, less frequently cervical segments with relative preservation of the brain [1], [2].

Devic's disease is more common among people of African and Asian descent. In countries of the Asia-Pacific Region, its prevalence is 7.6–17.3% of all demyelinating CNS disorders. In European countries, NMO accounts for <1–2%. The epidemiology of opticomyelitis should take into account the fact that some cases are often misinterpreted as multiple sclerosis, recurrent transverse myelitis, and retrobulbar neuritis. NMO is 9 times more common in women than in men [3]. Typically, the disease develops in individuals aged 35–47 years. In most cases, it is malignant, leads to severe disability and death. It is therefore necessary to determine the correct diagnosis and prescribe adequate therapy as soon as possible.

There are the following diagnostic criteria for Devic's disease (according to D.H. Miller 2008):

Large criteria (all criteria are required):

- Optical neuritis
- Transverse myelitis with spinal cord lesions occupying more than three segments of the spine (radiologically proven focal area)
- Elimination of systemic diseases with a similar clinical pattern (systemic lupus erythematosus, sarcoidosis, vasculitis, and Sjogren's syndrome).

Small criteria (at least one criterion is required):

- Changes in T2 regime that is not in the Barcoff's criteria list (included in McDonald's criteria)
- Presence of foci in the medulla oblongata (dorsal sections) that merge or do not merge with spinal cord foci
- Presence of foci in the trunk and/or hypothalamus

- Presence of "linear" foci localized in the periventricular zone or callous body region, having "Dawson's fingers" shape, without spreading into the parenchyma
- Identification of antibodies to aquaporin in blood serum or cerebrospinal fluid [4].

Relevance

To date, there are no convincing clinical trials that would fully evaluate the efficacy and safety of drugs for the treatment and prevention of NMO exacerbation. Taking into account the malignant course that quickly leads to disability of young, economically active population, the issues of searching for effective methods of NMO treatment remain highly urgent.

Goals and Objectives

The purpose of this review is to examine available modern methods of treatment and prevention of NMO exacerbation that has potential and require further extensive clinical trials.

The objective is to assess the possibility of applying these methods of treatment in clinical practice: To improve prognosis, reduce disability, and death rates.

We have reviewed previously applied and modern methods of treatment. According to the 2015 clinical protocol used in the Republic of Kazakhstan, the multiple sclerosis disease-modifying drugs (MSDMD therapy) were earlier applied in NMO treatment. The following drugs were used as the main ones: Interferons β (interferon – β-1a subcutaneously 3 times a week, interferon – β-1b 9.6 mln IU subcutaneously alternate day, and interferon – 1a 30 mcg intramuscularly once a week), glatiramer acetate, and natalizumab [5].

There are conflicting data on both the effectiveness of preventive immunomodulatory therapy (interferons beta, glatiramer acetate) and the negative effect of increased relapses. In this regard, immunosuppressive rather than immunomodulatory therapy is recommended for NMO long-term treatment [6].

To date, many countries, as well as the Republic of Kazakhstan, apply plasmapheresis (PP) courses, hormonal pulse therapy, and prednisolone supporting therapy for therapeutic purposes.

In the case of severe, rapidly progressive disease, low-efficiency glucocorticosteroid therapy, extracorporeal detoxication, patients with NMO are prescribed courses of immunosuppressive therapy: Cyclophosphamide, mitoxantrone, and azathioprine (AZA). Stem cell therapy helps to improve the quality of life, as well as supports patients in many countries.

Seven tertiary medical centers in the United States and England conducted a retrospective multi-center study with 25 patients from 7 centers to evaluate the use of RIT targeted therapy in adults with NMO. Before RIT therapy, the study participants received various immunosuppressive drugs: Mitoxantrone, prednisolone, AZA, beta-interferons, and the effect of which was not observed.

Results

With an average 19-month follow-up period, the median annual relapse rate after treatment was lower than before treatment (0 [range 0–3.2] vs. 1.7 [range 0.5–5] of relapses, $p < 0.001$). Disability has improved or stabilized in 20 of 25 patients (80%, $p = 0.02$). Two patients died during the follow-up period, 1 due to brain stem relapse, and 1 due to suspected septicemia. Infections were recorded in 20% of patients.

The use of RIT resulted in clinical and radiological remission in 80% of patients. However, despite the visible efficacy, this drug has a high risk of relapse after the successful time course of the drug, 6–12 months later. Furthermore, with chronic administration of RIT, the risk of infectious complications and oncological diseases is high, that is why the question about this method of therapy remains open [7]. The authors considered one of the options for prolongation and maintenance of remission after administration of RIT – autologous transplantation of hematopoietic stem cells and long-term administration of mycophenolate mofetil. As an example, there were two clinical cases amount patients from their center. In the first case, after the RIT course, the tactic of long-term administration of mycophenolate mofetil was chosen for further disease management. The patient continued to have remission of the underlying disease in the course of this therapy. In the second case, allo-HSCT was conducted. Moreover, an assessment of the neurological status was conducted on day 2000 after the transplantation, which showed positive dynamics in the form of motor activity recovery (walking without support). However, these cases are not indicative due to the small number of patients and a short follow-up period [8].

In the retrospective study (Plasauto EZ, Asahi Kasei Medical, Tokyo, Japan), PP was conducted in 15 patients with NMO exacerbation. The immediate effect after 6 months, change of serum levels of anti-AQP4 antibodies was observed in the course of treatment, which led to significant improvement of neurological disability in patients with NMO [9].

Monoclonal antibodies are one of the fastest-growing areas of specific therapy for autoimmune and demyelinating diseases. The main targets of monoclonal antibodies in autoimmune and demyelinating diseases are T- and B-lymphocytes, cytokines, complement, and adhesion molecules. The UBC Hospital in Vancouver, British Columbia, Canada, conducted a multi-center,

double-blind, randomized, and placebo-controlled study with 230 participants. The participants were randomized (3:1) within the period from January 6, 2015 to September 24, 2018, with 174 participants randomized to inebilizumab and 56 participants – to placebo. Only 21 (12%) of 174 participants who received inebilizumab had a relapse, compared to 22 (39%) of 56 participants who received a placebo. Thus, inebilizumab clearly has shown efficacy in reducing the risk of relapse of opticomyelitis [10].

There is strong evidence of the role of the complement system in the NMO pathogenesis and, therefore, the benefits of targeted therapy. The inflammatory process in opticomyelitis involves an obvious vasculocentric deposition of activated complement.

Selective inhibition of early stages in the classical complement pathway has a potential advantage over inhibition of later stages. Interest was expressed in the therapeutic potential of C1-inhibitor (C1-inh). In this study, experiments were performed on rats. The investigators were representatives of the Department of Medicine and Physiology, the University of California in San Francisco. Lewis rats were purchased at the Charles River Laboratory (Wilmington, Massachusetts). To investigate the activity of C1-inh complement in rats, C1-inh was injected intravenously at a dose of 600 units/kg, and the serum obtained at different times was analyzed for complement activity. The study used an artificial model of opticomyelitis in rats, the pathology of which was caused by IgG injection which led to characteristic pathological features, including damage to astrocytes, inflammation, and demyelination after 5 days. Pathological changes in this model were completely prevented by inhibiting the complement system with cobra venom toxin, indicating that the complement activity in rats is necessary for further pathological changes. It should be noted that despite the same activity of complement in rats and humans, studies conducted using experimental models of rats should be extrapolated to humans with extreme caution. The final evaluation of the potential efficacy of C1-inh will require controlled clinical trials [11].

Clinical trials on the efficacy of using fetal hepatocytes in MS treatment were conducted in Kazakhstan. After fetal neurotransplantation in 93.3% of subjects during 36 months, positive dynamics in the form of a 21.9% regression of clinical symptomatology on the eating disorder diagnostic scale was observed. Magnetic resonance imaging (MRI) showed positive dynamics manifested by the reduction of number and size of lesions with regression of surrounding perifocal edema. The application of this treatment method is effective for NMO and will help to maintain remission after administration of RIT [12].

At Shandong Provincial Hospital, in the period from December 1, 2012, to May 31, 2016, patients with NMO received AZA, mycophenolate mofetil (MMF), or low doses of RIT (RTX) for 6 months. The annual relapse rate, EDSS scores, CD19 + B-cells in peripheral blood, serum AQP-4-IgG titer, and adverse drug reactions were compared between the three groups. In the AZA group (n = 22), the MMF group (n = 30) and the RTX group (n = 20), 54.5%, 60.0%, and 65.0% of patients achieved a relapse-free state, while the EDSS score improved in 90.9%, 83.3%, and 90.0% of patients, respectively. Decreased RTX dose had a significant effect on the reduction of CD19 + B-cell count ($p < 0.01$). Compared to the AZA group, the MMF group and the RTX group obviously reduced AQP-4-IgG titer and have fewer side effects. Efficacy was found in the course AZA, MMF administration, and reduction of RIT dose. Low RTX doses were more effective than others in reducing CD19 B-cell count. MMF and low RTX doses reduced AQP-4-IgG titer and led to fewer side effects than AZA. However, a multi-center study is still needed to find a more effective therapeutic regimen [13].

An open randomized clinical study was conducted in the Neurology Department of Kashani Hospital, a part of the Isfahan University of Medical Sciences, Isfahan, Iran, in the period from 09.2015 to 12.2016. The first group received AZA; the second group received RIT. There was a significant decrease in relapses and EDSS scores among patients with opticomyelitis in response to AZA and RIT, although a more favorable response was observed in RIT patients. The number of side effects did not differ significantly between the two groups. In this study, more relapse-free patients were found in the RIT group than in the AZA group (78.8% vs. 54.3%). In addition, both ARR (1.09 vs. 0.49) and EDSS (0.98 vs. 0.44) were observed to be lower in RIT patients than in AZA patients. Based on these results, RIT is an excellent drug for preventing relapse and reducing disability in patients with opticomyelitis [14].

A double-blind, placebo-controlled, randomized 2 phase study (RENEW) was conducted in 33 clinical bases in Europe, Canada, and Australia. The study involved 82 patients aged 18–35 years with a newly diagnosed NMO. After hormonal pulse therapy with methylprednisolone, patients were randomized to two groups: Opicinumab or placebo. The follow-up period was 32 weeks. The therapy efficacy was assessed by a recovery of evoked visual potentials, improvement of functions of the damaged optic nerve, clinical positive manifestations. No statistically significant differences in changes in brain MRI were found between the groups.

Opicinumab did not lead to remyelination processes, compared to placebo. However, remyelination is still considered possible and requires further clinical trials [15].

A randomized, placebo-controlled, and double-blind study of patients with NMO was conducted in the National Institute of Neuroscience, National Center of Neurology and Psychiatry, Ogawa-Higashi, Kodaira, Tokyo, Japan. The groups of patients were randomized in a 1:1 ratio, as seropositive or seronegative to AQP4-IgG. Subjects received satralizumab in 120 mg dose or placebo. A relapse occurred in 8 patients (20%) who

received satralizumab and in 18 (43%) who received placebo (risk ratio 0.38; confidence interval 95% [CI], 0.16–0.88). The frequency of serious side effects and infections did not differ between these groups. The authors concluded that satralizumab, which was added to immunosuppressant in patients with NMO, resulted in a lower risk of relapse than placebo but were no different from placebo in its effect on pain or fatigue [16].

The efficacy of the subcutaneous administration of tocilizumab (TCZ) for NMO is unknown. In two tertiary US centers, a retrospective analysis of data from patients with NMO who received TCZ for more than 6 months between 2014 and 2019 was conducted. During treatment with TCZ, eight patients (66.6%) had no relapses, one patient (8.3%) had 1 relapse, two patients (16.6%) had 2 relapses, and one patient (8.3%) had 3 relapses. One patient who received TCZ died after severe myelitis. The administration of TCZ for NMO reduced the relapse rate in two small series of cases. However, the clinical protocol, which requires frequent intravenous injections, may have a negative impact on treatment adherence, especially in patients with disabilities, thereby reducing efficacy. Subcutaneous treatment with TCZ for opticomyelitis is similar to the effect of intravenous administration. Subcutaneous administration of TCZ also has the advantage that it is more cost-effective compared to the newer anti-IL-6 agents. The low risk of serious complications and the high efficacy of TCZ raise the question of whether it can be used as first-line therapy for opticomyelitis, especially in patients with active disease. Comparative prospective studies on the administration of this drug are justified [17].

The Johns Hopkins University, Baltimore studied PP efficacy for NMO: The first group of 192 patients; the second group of 38 patients used the immunoabsorption (IA) method. Both types of PP were found to be equally effective. This suggests that the removal of IgG antibodies is an important treatment effect of PP for NMO. It is also an important factor that the use of (PP or IA) as first-line therapy and the initiation of PP within 3 days of relapse provide good clinical results. About 40% of patients who received PP within 3 days after relapse initiation have returned to their baseline, compared to <4% of those who initiated PP within 7 days. Thus, early PP is the preferred treatment for acute NMO relapses [18].

The Saitama Medical Center, Kamoda, Kawagoe, Japan conducted a study involving 50 patients: 42 of patients had a positive result to anti-AQP4 antibodies and 8 – a negative result. It showed the efficacy of co-administration of tacrolimus and prednisolone, which clearly inhibited the relapse rate of both anti-AQP4-positive and negative NMO [19].

A multi-center, double-blind, randomized, and placebo-controlled study was conducted in hospitals and specialized clinics in 25 countries in the period from 06.01.2015 to 24.09.2018. Participants in the study were adult patients aged over 18 years, diagnosed with NMO, with 8 or fewer scores on the EDSS scale. Two hundred thirty participants were randomized to two groups: 174 participants received inebilizumab and 56 received placebo. Twenty-one (12%) of 174 participants who received inebilizumab had an acute episode; 22 (39%) of 56 participants in the placebo group had a relapse. Serious adverse events occurred in eight (5%) of 174 participants who received inebilizumab and in five (9%) of 56 participants who received a placebo.

Compared to placebo, inebilizumab reduces the risk of NMO relapse. However, inebilizumab has potential as an evidence-based treatment of patients with NMO [20].

An international randomized, placebo-controlled, and double-blind clinical study prevent was conducted in 143 patients with AQP4-IgG+ NMO. After 48 weeks of therapy, 98% of patients receiving eculizumab noted no relapse of the disease; in the placebo group – 63%. The duration of the relapse-free period in the eculizumab group was 144 weeks. Changes in the EDSS scale were not statistically significant in comparison with the control group: −0.18 versus +0.12.

As for prevention, eculizumab significantly reduced the assessed risk of relapse compared to placebo. The study was discontinued after 23 of 24 predetermined assessed relapses; these relapses occurred in 3 (3%) of 96 patients in the eculizumab group and in 20 (43%) of 47 patients in the placebo group (risk ratio [HR] 0.06; 95% CI 0.02–0.20; $p < 0.001$).

According to the study, the disability rate of those receiving eculizumab is lower than that of those receiving placebo because there was an increase in EDSS score (11.5 vs. 23.4%; $p < 0.05$) or HAI score (8.3 vs. 23.4%; $p < 0.01$) between the baseline and the end of the study. Based on a categorical analysis of clinically significant changes in SF-36 score, eculizumab significantly ($p < 0.05$) reduces the likelihood of physical component score (PCS) worsening and increases the likelihood of PCS improvement compared to placebo. Thus, eculizumab significantly reduced the risk of relapse compared to placebo in patients with AQP4-IgG+ NMO, about a quarter of whom did not receive immunosuppressive therapy. All patients showed positive dynamics in the form of improved neurological symptoms and improved quality of life. Eculizumab provides an effective, well-tolerated, and approved NMO treatment option [21].

Conclusions

We have concluded that there are a sufficient number of drugs and combinations of treatments for Devic's disease. We were interested in combinations of RIT and autologous stem cell transplantation, RIT

and fetal hepatocyte transplantation, and RIT and strengthening the effect by PP sessions. However, successful implementation of these methods in clinical practice requires conducting controlled clinical trials with a larger number of patients and longer follow-up periods. The follow-up requires a comprehensive assessment of the efficacy of treatment, the development of side effects in the administration of these combinations. We hope that many ongoing clinical trials will be justified and that the prognosis of Devic's disease will be favorable in the future.

References

1. Mironenko TV. Opticomyelitis (Devic's disease). Scientific review and own clinical observation. Int Neurol J. 2012;71(1):141-7.
2. Shakhov BE, Belova AN, Shalenkov IV. Opticomyelitis devica: Questions of diagnosis and a description of the case from practice. Med Almanac. 2012:20(1):165-70.
3. Isaikin AI, Shmidt TE, Yakhno NN. Opticomyelitis. Neurol J. 2014;5:45-51.
4. Bradl M, Reindl M, Lassmann H. Mechanisms for lesion localization in neuromyelitis optica spectrum disorders. Curr Opin Neurol. 2018;31(3):325-33. https://doi.org/10.1097/wco.0000000000000551
   PMid:29465432
5. Clinical protocol for the diagnosis and treatment of optoneuromyelitis (Devik's disease) of the Republic of Kazakhstan Protocol code: Code (s) ICD-10:G36.0 Neuromyelitis optic [Devik's disease] -2015 - http://www.rcrz.kz/docs/clinic_protocol/2015.
6. Jeffery DR. Early intervention with immunomodulatory agents in the treatment of multiple sclerosis. J Neurol Sci. 2002;197(1-2):1-8.
   PMid:11997060
7. Jacob A, Weinshenker BG, Violich I, McLinskey N, Krupp L, Fox RJ, *et al*. Treatment of neuromyelitis optica with rituximab: Retrospective analysis of 25 patients. Arch Neurol. 2008;65(11):1443-8. https://doi.org/10.1001/archneur.65.11.noc80069
   PMid:18779415
8. Kirgizov KI, Skorobogatova EV, Volkova EY. Experience of the High\Dose Chemotherapy followed by Autologous Hematopoietic Stem Cell Transplantation (Auto\HSCT) in the Patients with CNS Autoimmune Diseases; 2013.
9. Kim SH, Kim W, Huh SY, Lee KY, Jung IJ, Kim HJ. Clinical efficacy of plasmapheresis in patients with neuromyelitis optica spectrum disorder and effects on circulating anti-aquaporin-4 antibody levels. J Clin Neurol. 2013;9(1):36-42. https://doi.org/10.3988/jcn.2013.9.1.36
   PMid:23346159
10. A Double-masked, Placebo-controlled Study With Open Label Period to Evaluate MEDI-551 in Neuromyelitis Optica and Neuromyelitis Optica Spectrum Disorders.
11. Tradtrantip L, Asavapanumas N, Phuan P-W, Verkman AS (2014) Potential Therapeutic Benefit of C1-Esterase Inhibitor in Neuromyelitis Optica Evaluated In Vitro and in an Experimental Rat Model. PLoS ONE 9(9): e106824. https://doi.org/10.1371/journal.pone.0106824
12. Khamidulla AA. Modern aspects of the diagnosis and treatment of multiple sclerosis West Kazakhstan state medical university named after Marat Ospanov. J Neurosurg Neurol Kazakhstan. 2016;1(42):24-9. https://doi.org/10.18484/2305-0047.2018.4.496
13. Yang Y, Wang CJ, Wang BJ, Zeng ZL, Guo SG. Comparison of efficacy and tolerability of azathioprine, mycophenolate mofetil, and lower dosages of rituximab among patients with neuromyelitis optica spectrum disorder. J Neurol Sci. 2018;385:192-7. https://doi.org/10.1016/j.jns.2017.12.034
   PMid:29406904
14. Nikoo Z, Badihian S, Shaygannejad V, Asgari N, Ashtari F. Comparison of the efficacy of azathioprine and rituximab in neuromyelitis optica spectrum disorder: A randomized clinical trial. J Neurol. 2017;264(9):2003-9. https://doi.org/10.1007/s00415-017-8590-0
   PMid:28831548
15. Cadavid D, Balcer L, Galetta S, Aktas O, Ziemssen T, Vanopdenbosch L, *et al*. Safety and efficacy of opicinumab in acute optic neuritis: A randomised, placebo-controlled, phase 2 trial. Lancet Neurol. 2017;16(3):189-99. https://doi.org/10.1016/s1474-4422(16)30377-5
16. Yamamura T, Kleiter I, Fujihara K, Palace J. Trial of satralizumab in neuromyelitis optica spectrum disorder. N Engl J Med. 2019;381:2114-24. https://doi.org/10.1056/nejmoa1901747
17. Lotan I, Charlson RW, Ryerson LZ, Levy M, Kister I. Effectiveness of subcutaneous tocilizumab in neuromyelitis optica spectrum disorders. Mult Scler Relat Disord. 2020;39:101920. https://doi.org/10.1016/j.msard.2019.101920
18. Levy M. Plasmapheresis for acute attacks in neuromyelitis optica spectrum disorders. Neurol Neuroimmunol Neuroinflamm. 2018;5(6):e510. https://doi.org/10.1212/nxi.0000000000000510
   PMid:30345335
19. Kojima M, Oji S, Tanaka S. Tacrolimus is effective for neuromyelitis optica spectrum disorders with or without anti-AQP4 antibody. Mult Scler Relat Disord. 2019;39:101907. https://doi.org/10.1016/j.msard.2019.101907
   PMid:31931404
20. Cree AC, Bennett JL, Kim J, Weinshenker BG, Pittock SJ. Inebilizumab for the treatment of neuromyelitis optica spectrum disorder (N-MOmentum): A double-blind, randomised placebo-controlled phase 2/3 trial. Lancet. 2019;394(10206):1352-63. https://doi.org/10.3410/f.736576420.793565143
   PMid:31495497
21. Frampton JE. Correction to: Eculizumab: A review in neuromyelitis optica spectrum disorder. Drugs. 2020;80(7):729. https://doi.org/10.1007/s40265-020-01315-x
   PMid:32319075