

Recommendations on NMOSD Treatment in Latin America: Consensus-based RAND/UCLA methodology

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Introduction

Despite the progress in NMOSD treatment, there are various scenarios where therapeutic management should be personalized, including AQP4 seropositive versus seronegative patients, treatment initiation in naive patients, and management of suboptimal treatment responses. Furthermore, there are access challenges in Latin America (LATAM), including limited diagnostic resources, high treatment costs, and regulatory issues. These barriers hinder timely access to therapies, impacting the ability of NMOSD patients in LATAM to effectively manage their condition (Ref). It is crucial to consider the best practice therapeutic decision-making, including emerging long-term preventive therapies, to ensure patients in LATAM and elsewhere can effectively manage their disease. There are few guidelines or consensus addressing NMOSD treatment management. In an effort to optimize the management and treatment of NMOSD patients, a group of specialized neurologists in LATAM gathered and reviewed the existing related data. They developed recommendations on NMOSD treatment in LATAM, taking into account the unique challenges and considerations of the region.

Methodology

During 2022 and 2023, LATAM neurologists dedicated to the diagnosis and care of NMOSD patients assembled to set up a working group to discuss the treatment approaches in NMOSD patients. LATAM experts were selected by LG and RA based on their experience in managing patients with NMOSD in different countries of LATAM. Following the RAND/UCLA Appropriateness Method one steering group (LG, and RA), external advisors (KF and VR) and one working panel chose by the steering group (19 LATAM neurologists) conducted a consensus process.

Panelists were asked to manifest agreement or disagreement for each statement using a 9-point Likert scale, according to their experience and knowledge. An affirmation was appropriate when at least 70% of the answers ranged between 7 and 9 points, inappropriate when 70% ranged from 1 to 3 points, or otherwise doubtful.

The statements were divided between general recommendations (14/31) and clinical scenarios (17/31). The scenarios were based on treatment-naïve NMOSD AQP4 positive patients (4/17); treatment-Naive seronegative NMOSD patients (4/17); treatment switching (5/17) and safety (4/17).

Conclusions

Consensus recommendations were developed on the most important areas of NMOSD treatment by a panel of experts in LATAM. These statements are a valuable tool to guide decision-making and improve patient outcomes, serving as the foundation for developing standardized practice guidelines in our region.

Statements

General recommendations

Patients diagnosed with NMOSD (mainly AQP4 positive) should start a disease modifying treatment (DMT) as soon as possible.

Before starting a DMT, it is recommended to do an infection screening according to the local epidemiology of each Latin American country

Before starting a DMT, family planning should always be considered in every woman with child bearing potential

The patient should participate in the treatment selection considering the risks and benefits of individual treatments

It is recommended that infusions of intravenous monoclonal antibodies (such as, eculizumab, inebilizumab, ravulizumab and rituximab) should be done in a center with experience with these treatments

The DMT choice should consider the health care system of each country in the region in order to guarantee the access and adherence to the treatment

The DMT choice should consider the presence of other autoimmune comorbidities

The DMT choice should always be defined after the determination of the serological status of the aquaporin 4 antibody (AQP4) with the best available test.

Newly diagnosed patients treated with oral steroids should continue oral maintenance till DMT becomes fully effective. The tapering period of the oral steroids depends on the subsequent DMT and the time of its maximum biological effect

Patients older than 65 years old can be treated with DMT, always considering the risks and benefits of these treatment in the elderly population

Recently new treatments for NMOSD AQP4+ patients such as eculizumab, satralizumab, inebilizumab and ravulizumab have demonstrated high efficacy in relapse prevention in randomized controlled trials

Effectiveness data of treatments such as eculizumab, satralizumab, inebilizumab and ravulizumab could be extrapolated to Latin American population with the diagnosis of NMOSD AQP4+

Despite their common use, azathioprine, mycophenolate mofetil, tocilizumab and rituximab are off-label treatments for NMOSD patients irrespective of their serological AQP4 status

To date there is no evidence demonstrating comparative efficacy between new treatments (such as eculizumab, satralizumab, inebilizumab and ravulizumab) and rituximab or tocilizumab in patients with NMOSD AQP4+

Naïve NMOSD Aqp4 positive patients

If the treatments such as eculizumab, satralizumab, inebilizumab, and ravalizumab were to be approved by local regulatory agencies, they should be the first therapeutically choice after the diagnosis of NMOSD AQP4+

Off label immunosuppressants as rituximab or tocilizumab should be the therapeutically option in NMOSD Aqp4+ patients in places where the new treatments are still not available or affordable to the individual or to the health system.

Off-label immunosuppressants such as mycophenolate mofetil, azathioprine, or oral prednisone should be the therapeutic option in patients with NMOSD Aqp4+ if previously recommended treatments are not available.

It is not recommended to combine two or more immunosuppressant drugs to treat NMOSD AQP4+ patients

Monitoring of disease activity is recommended to assess the effectiveness of DMTs.

Naive seronegative NMOSD patients

The panel acknowledges that the level of evidence to recommend DMT in patients diagnosed with seronegative NMOSD is lower compared to the level of evidence for seropositive NMOSD patients.

Treatments such as eculizumab, satralizumab, inebilizumab, and ravalizumab, have not shown to be effective for the treatment of patients with AQP4 seronegative NMOSD in randomized controlled clinical trials.

To date, there are no randomized clinical trials that demonstrate efficacy in patients with AQP4 seronegative NMOSD

Despite not having data of high methodological quality, it is recommended to start treatment with rituximab, mycophenolate mofetil or azathioprine in patients diagnosed with AQP4 seronegative NMOSD

Previous therapy

NMOSD patients treated with any DMT and that have clinical activity (relapse), it is recommended to change treatment to a different mechanism of action to the initial therapy.

NMOSD patients treated with any DMT who suffers moderate or serious adverse events, it is recommended to change treatment to a different mechanism of action to the initial therapy with a different security profile according to the patient (keep in mind age, comorbidities, concomitant medications)

It is recommended that NMOSD Aqp4+ and seronegative patients using off label immunosuppressants that are clinically stable and without adverse events, remain in their current treatment

NMOSD Aqp4+ patients treated with any DMT and that have a clinical activity (relapse), treatments such as eculizumab, satralizumab, inebilizumab, and ravalizumab approved by local regulatory agencies, should be the first therapeutic choice.

In NMOSD Aqp4+ patients, when switching between eculizumab, satralizumab, inebilizumab and ravulizumab, the new therapy can be started immediately after stopping the previous therapy always taking into consideration the mechanism and duration of action

Security

The clinical trial data in NMOSD with eculizumab, ravalizumab, satralizumab and inebilizumab regarding security data cannot be completely extrapolated to the Latin American population with the diagnosis of NMOSD Aqp4+ in view that the region has a different epidemiology, and the potential genomic differences.

It is recommended to constant monitoring of infections (opportunistic) always considering the local infections of each country of the region

It is recommended that all patients eligible for DMT, should complete a vaccine scheme according to the local policies and epidemiology, at least 2 weeks before starting the treatment for inactivate vaccines and 4 weeks for attenuated viral vaccine.

It is recommended to include a meningococcal vaccinations scheme in patients that are will receive eculizumab and ravulizumab

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Treatments for NMOSD approved by countries

