Plain Language Summary of Publication

Eculizumab or ravulizumab treatment effect in people with neuromyelitis optica spectrum disorder: a plain language summary of three studies

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Journal of Comparative Effectiveness Research

First draft submitted: 11 September 2024; Accepted for publication: 15 January 2025; Published online: 12 February 2025

Summary

What is this summary about?

Neuromyelitis optica spectrum disorder (NMOSD for short) is a rare autoimmune health condition, meaning that the body's natural defense system (the **immune system**) attacks the body's own tissues. This summary describes NMOSD and the results of three studies of the effects of treatment with two medicines called eculizumab and ravulizumab. Eculizumab and ravulizumab are approved to treat people with a type of NMOSD called **AQP4-Ab+ NMOSD**. The three studies included in this summary are the PREVENT and CHAMPION-NMOSD clinical studies and a study done in everyday clinical practice in Japan.

What are the key conclusions from these studies?

The PREVENT study was a phase 3 study (a large study testing safety and effectiveness of a treatment before it is approved) with three parts. The PREVENT main study compared eculizumab to a placebo (a treatment with no active ingredients, used to test how well a new treatment works). A long-term follow-up study assessed the safety and effectiveness of eculizumab over time, without a placebo group. Another long-term follow-up focused on people taking eculizumab alone, without other **immunosuppressive treatments**. The CHAMPION-NMOSD study was another phase 3 study testing ravulizumab, a treatment based on eculizumab but given less often, using the placebo group from the PREVENT study for comparison. A **daily clinical practice** study with eculizumab in Japan looked at how eculizumab works in everyday medical practice (outside of controlled clinical trials) after the medication was already approved.

The studies found eculizumab and ravulizumab to be safe and effective for preventing **relapses** in AQP4-Ab+ NMOSD. More than 95% of people treated with these medicines stayed relapse-free during the months or years of the studies follow-up periods. Most people reported side effects that were mild or moderate. The most common side effects were headache, runny nose or sore throat (nasopharyngitis), and infections in the upper respiratory system. The daily practice study confirmed that eculizumab works well in everyday medical practice.

What do the findings of the study mean?

These studies suggest that eculizumab and ravulizumab are safe and effective treatments for people with AQP4-Ab+ NMOSD. Eculizumab may help reduce or stop the need for other treatments that weaken the immune system (immunosuppressive therapies). These treatments help people maintain their ability to carry out daily activities and their quality of life.

Immune system: The body's defense system that fights infections and diseases
AQP4-Ab+ NMOSD: Refers to a common subtype of NMOSD called neuromyelitis optica spectrum disorder (NMOSD) where the immune system targets a protein called aquaporin-4 (AQP4). "Ab+" means **antibody** positive, meaning this antibody can be detected in the blood
Antibody: A protein made by the immune system to identify and fight infections or harmful substances in the body
Immunosuppressive treatments: Medicines that reduce the activity of the immune system to prevent it from attacking the body
Daily clinical practice: Refers to how medicines work in everyday life, outside of controlled clinical trials
Relapse: When symptoms of a disease return after a period of improvement

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How to say (double click on the sound icon to play the sound)

Aquaporin: ah-kwuh-POHR-in
Area postrema: AIR-ee-uh poh-STREE-muh
Astrocyte: AS-troh-syte
Corticosteroids: KOR-tih-ko-STEER-oyds
Eculizumab: ek-yoo-LIH-zoo-mab
Inebilizumab: ih-NEB-ih-LIZ-yoo-mab
Meningococcal infections: muh-NIN-joh-KAH-kul in-FEK-shuns
Myelitis: MY-uh-LY-tis
Monoclonal antibody: MON-noh-KLOH-nul AN-tee-BOH-dee
Myelin: MY-uh-lin
Narcolepsy: NAR-koh-lep-see
Neuromyelitis optica spectrum disorder: newr-oh-my-e-LY-tis OP-tik-a SPEK-truhm duh-SAW-duh
Neurons: NEW-ronz
Placebo: pluh-SEE-boh
Optic neuritis: OP-tik nuh-RY-tis
Relapse: REE-laps
Ravulizumab: RAV-yoo-LIZ-yoo-mab
Remission: ruh-MISH-un
Satralizumab: SAY-truh-LIZ-yoo-mab

Who is this article for?

This article may be useful for:

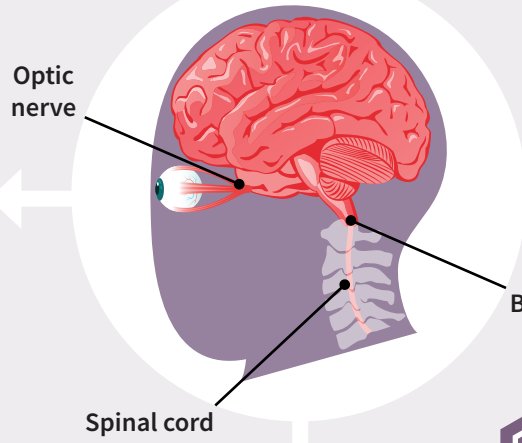
- People with AQP4-Ab+ NMOSD, their family members, and other caregivers.
- Patient associations or other organizations supporting people with NMOSD.
- Healthcare providers (such as physicians and nurses) who treat people with NMOSD.
- Healthcare providers or policymakers who draft recommendations for the management of NMOSD.

What is NMOSD?

- NMOSD, previously known as Devic's disease, is a rare autoimmune condition where the own immune system mistakenly attacks parts of the central nervous system, mainly:
  - The optic nerve (the nerve that sends signals from the eye to the brain)
    - » This can cause **optic neuritis** (inflammation of the optic nerve), damaging sight.
  - The spinal cord (the bundle of nerves in the backbone that connect the brain to the rest of the body)
    - » This can cause **myelitis** (inflammation of the spinal cord), leading to body sensitivity and muscle related symptoms.
  - The brainstem (the part of the brain that connects to the spinal cord and controls basic functions like breathing and swallowing)
    - » Damage here can cause what is called "**area postrema** syndrome" (after the inflammation of a specific area in the brainstem), leading to hiccups, nausea, vomiting and/or sleep disorders.
- The symptoms of NMOSD vary depending on the area of the central nervous system affected.

Optic neuritis: Inflammation of the nerve that connects the eye to the brain, causing vision problems
Myelitis: Inflammation of the backbone spinal cord that can cause weakness, pain, or paralysis
Area postrema: A part of the brainstem that can trigger vomiting or nausea

Central nervous system areas affected in NMOSD and their associated symptoms



Symptoms caused by inflammation in the optic nerve may include

- Loss or blurring of vision in one or both eyes
- Loss of color vision
- Pain worsened by eye movement

Symptoms caused by inflammation in the brainstem may include

- Uncontrollable and persistent hiccups
- Unexplained nausea or vomiting
- **Narcolepsy**

Symptoms caused by inflammation to the spinal cord may include

- Weakness, numbness, or loss of sensation
- Loss of bowel or bladder control or difficulty emptying the bladder
- Spasticity (increased muscle tone or stiffness in the arms or legs
- Shooting pain or tingling in the neck, back, or abdomen
- Painful spasms

? **Narcolepsy:** A sleep disorder that causes extreme tiredness and sudden episodes of falling asleep

- Symptoms of NMOSD typically occur as sudden episodes, called attacks (relapses), lasting from days to weeks. These attacks, if untreated, can cause lasting damage to the nervous system and lead to cumulative severe disability.
- Although NMOSD is a chronic condition, these attacks happen suddenly because the own immune system becomes episodically overactive, leading to bursts of inflammation in the optic nerve, spinal cord, or brainstem.
- Attacks are often followed by periods of stability (**remissions**), which can last from weeks to years.
  - Around 90% of individuals with NMOSD experience severe attacks, followed by remissions.
  - Approximately 50% of people with NMOSD experience an attack within the first year after their initial episode.
  - About 90% of people with NMOSD will experience an attack within 5 years.
- Each attack increases the risk of permanent damage, potentially leading to:
  - Complete loss of vision in one or both eyes.
  - Difficulty walking or requiring assistance with mobility

? **Remission:** A period when symptoms of a disease improve or disappear

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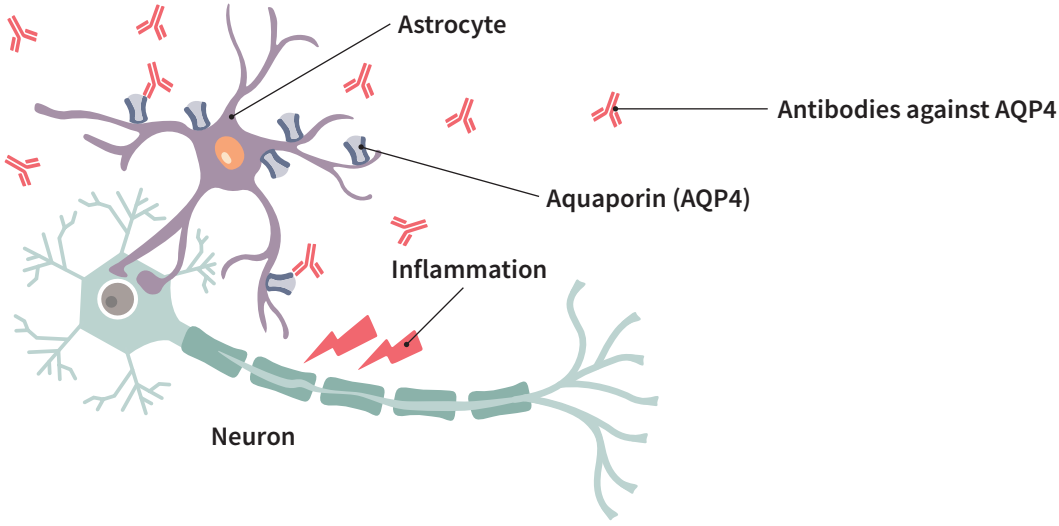
What happens in the body during NMOSD?

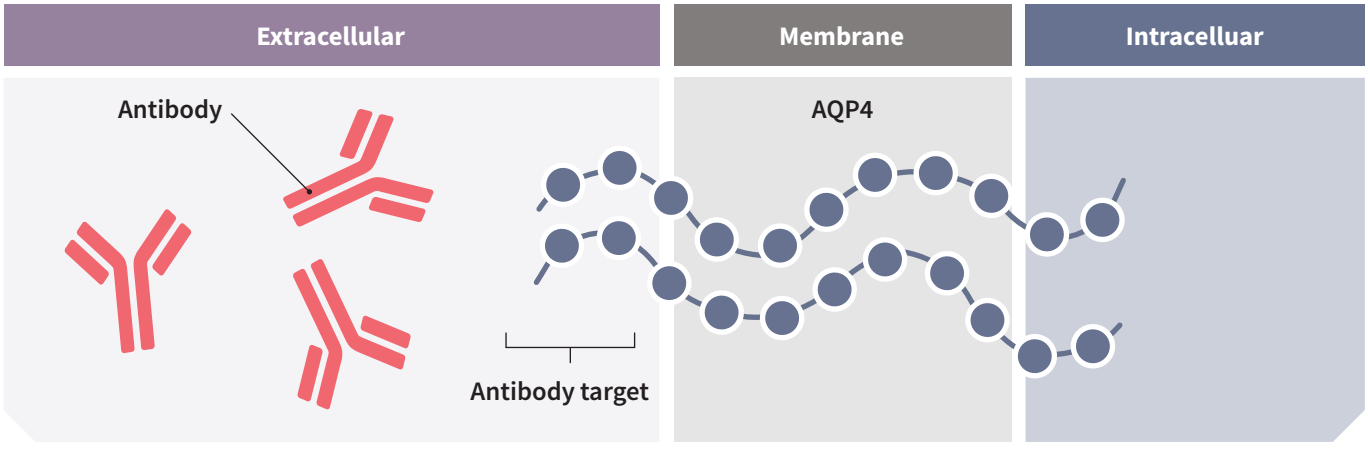
- Normally, the immune system produces antibodies to fight infections and foreign substances, like viruses that cause the common cold or bacteria that cause a sore throat.
- In NMOSD, the immune system produces antibodies that attack an own protein called aquaporin-4 (AQP4).
  - These antibodies are found in around 8 in 10 people with NMOSD.
  - AQP4 is found on the surface of astrocytes, star-shaped cells in the brain and spinal cord that support nerve cells.
  - AQP4 helps control the flow of water in and out of cells.
  - **Astrocytes** in the optic nerve, spinal cord, and brainstem have large amounts of AQP4, making these areas more likely to be damaged.
  - Damage to astrocytes causes inflammation.

Astrocyte: A type of cell in the brain and spinal cord that helps support and protect neurons

How NMOSD antibodies attack astrocytes and cause inflammation



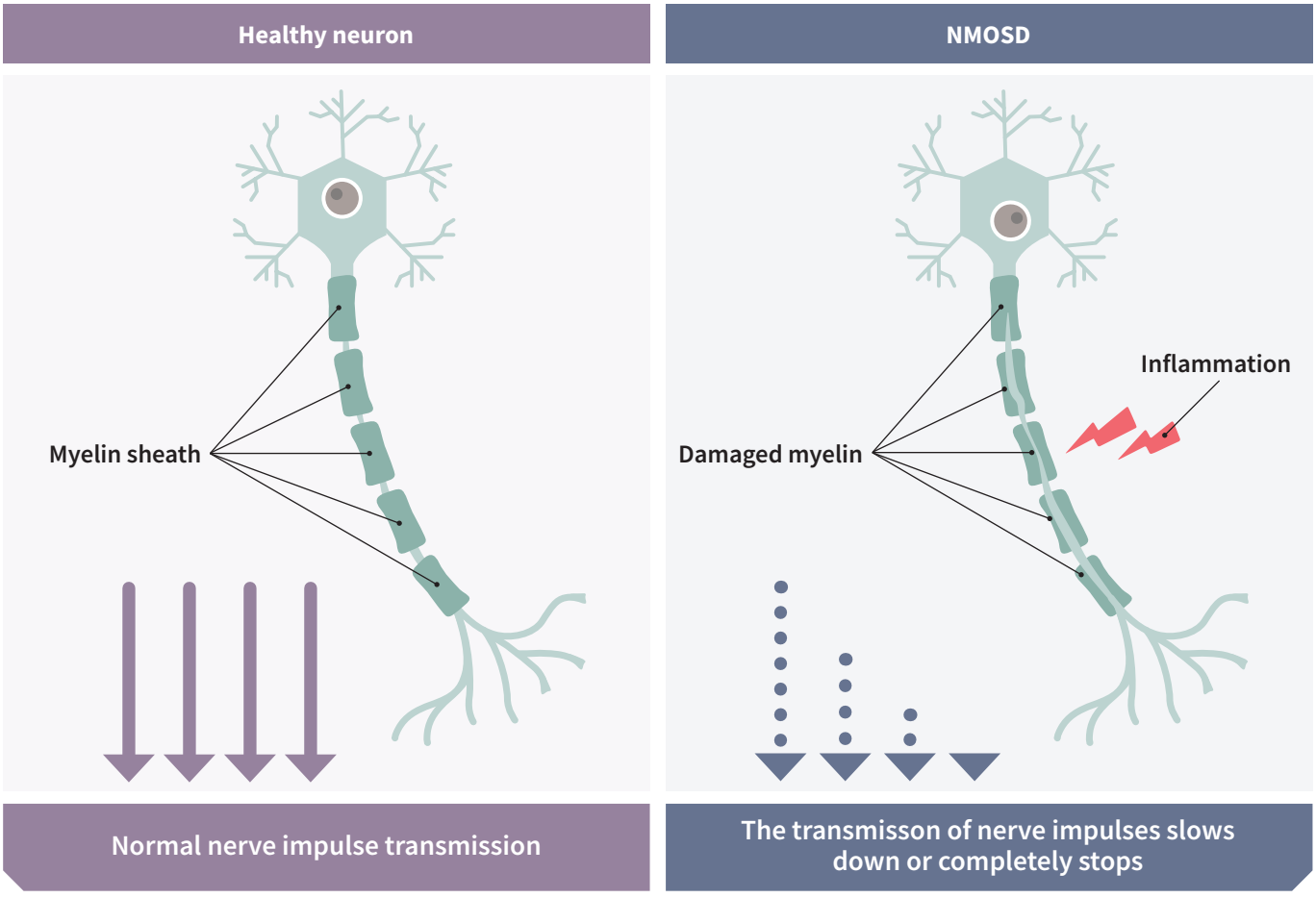
Antibody attaching to AQP4 on the surface of an astrocyte



- **Inflammation** due to astrocyte damage breaks down the protective covering around **neurons** (called the **myelin sheath**). This can cause the nerve impulses to slow down or stop altogether.

Inflammation: Swelling, redness, or pain caused when the body's immune system responds to injury or illness
Myelin sheath: A protective layer that covers nerves and helps them send signals quickly
Neuron loss: Damage or death of nerve cells (neurons), which can affect how the brain or spinal cord works

How NMOSD damages neurons and slows or stops nerve impulses



- In people with NMOSD, if AQP4 antibodies are detected in the blood, the condition is called AQP4-Ab+ NMOSD. This confirms that the immune system is attacking the AQP4 cells protein.
- Without treatment, around half of people with NMOSD would become blind in one or both eyes and need help with walking within 5 years of developing the condition.
- One of the main goals of treating NMOSD is to quickly treat attacks when they happen to reduce damage to nerves and prevent long-term problems. Another key goal is to avoid future attacks to protect patients' ability to do daily activities and maintain their quality of life.
- This approach focuses on managing the condition rather than curing it, as this is not possible as for today. Not treating would lead people with NMOSD to face severe disability or life-threatening relapses.

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Who does NMOSD affect?

- NMOSD is rare, affecting around 1–10 people per 100,000 worldwide.
- Around 8 in 10 people with NMOSD are women. This may be due to differences in immune system function between males and females influenced by genetics and hormones.
- NMOSD usually starts between the ages of 30 and 40 years. Less than 5% of people with the condition are children.
- Asians and people of African ancestry are at higher risk compared to individuals of European ancestry, possibly due to genetic factors.

How is NMOSD treated?

- Treatment for an attack of NMOSD is usually a short course of medicine to reduce inflammation. For example, a patient undergoing an NMOSD attack might receive 5 to 10 days of a high-dose corticosteroid (medicines that reduce inflammation and are often used to treat inflammatory conditions).
- Another treatment sometimes used for acute attacks is plasma exchange.
  - This treatment removes and replaces a person's blood. It aims to remove the antibodies that cause inflammation in NMOSD.
  - **Plasma exchange** can be used together with high-dose **corticosteroids**.
- Treatment for an acute attack is followed by long-term treatment with medicines to reduce the function of the immune system (known as immunosuppressive treatments).
  - This aims to prevent further attacks.
  - However, long-term immunosuppressive treatments can have side effects which may be serious.
- More recently, treatments that target the immune system in a more specific way have become available.

  Examples of these treatments are eculizumab, ravulizumab, satralizumab or inebilizumab.

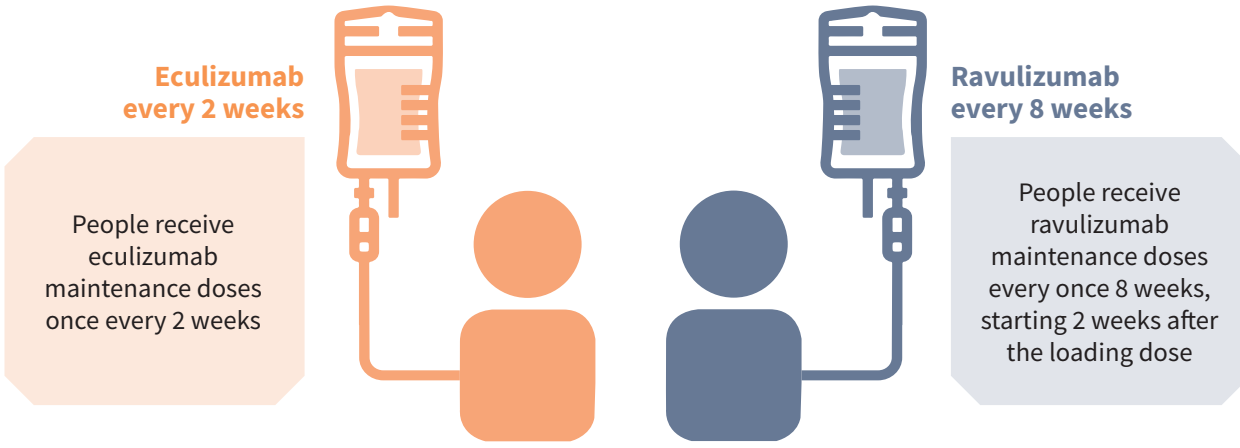
Plasma exchange: A treatment that removes harmful substances from the blood by replacing plasma
Corticosteroids: Medicines that reduce inflammation and are often used to treat **inflammatory diseases**
Inflammatory disease: A condition where inflammation happens for no clear reason or lasts for a long time

What are eculizumab and ravulizumab?

- Eculizumab and ravulizumab are treatments that belong to a group of medicines called **monoclonal antibodies**.
- Monoclonal antibodies are specially made proteins designed to target specific parts of the body.
- Ravulizumab is a medicine derived from eculizumab, designed to work in a similar way; however, it has been engineered to last longer in the body, allowing for less frequent dosing compared to eculizumab.
- Eculizumab and ravulizumab are designed to block a protein in the immune system called **complement 5** (C5 for short).

Monoclonal antibodies: Special laboratory-made proteins that target specific parts of the immune system to treat diseases
C5 (complement protein): A protein in the **complement system**, part of the immune system that helps fight infections but can cause damage in some diseases
Complement system: A group of proteins in the immune system that help the body fight infections and remove damaged cells.

- Blocking C5 helps stop the immune system from causing inflammation and damaging the optic nerve, brain and spinal cord in NMOSD.
- People receive eculizumab and ravulizumab as a liquid slowly injected into a vein. Treatment starts with a higher initial dose, called a loading dose, to quickly block C5 and stop the immune system from causing damage. This is followed by regular lower doses, called maintenance doses, to keep C5 blocked and prevent further inflammation and nerve damage:



- C5 inhibitors like eculizumab and ravulizumab, after their mode of action, can increase the risk of a group of serious infections called meningococcal infections.
  - **Meningococcal infections** are rare but serious bacterial infections of the brain, spinal cord, and bloodstream. Everyone who is starting treatment with eculizumab or ravulizumab must be vaccinated against the different types of meningococcal infections at least 2 weeks before starting treatment.
  - Anyone who needs urgent treatment with a C5 inhibitor but is not up to date with their meningococcal vaccinations may receive preventive antibacterial treatment. They should then receive the vaccine as soon as possible.
- People receiving C5 inhibitors and their healthcare providers must be informed about this risk. They must stay vigilant for any symptoms that may indicate a possible meningococcal infection.
- Eculizumab was **approved for the treatment** of AQP4-AB+ NMOSD by the United States Food & Drug Administration (FDA) in June 2019 and by the European Medical Agency (EMA) in March 2020.
- Ravulizumab was approved for the treatment of AQP4-AB+ NMOSD by the FDA in December 2022 and by the EMA in July 2023.

Meningococcal infections: Serious infections caused by bacteria that can affect the brain, spinal cord, or bloodstream

Therapy approval: When a treatment is officially allowed for use after proving it is safe and effective

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Which studies looked at eculizumab or ravulizumab for people with AQP4-Ab+ NMOSD?

Three key studies looked at eculizumab and ravulizumab for people with AQP4-Ab+ NMOSD.

1 The PREVENT study with eculizumab

- This was a phase 3 clinical trial (a large study done to test how safe and effective a treatment is before it can be approved for use).
- The study compared eculizumab with a placebo (a treatment with no active ingredients).
- After the main study ended, participants continued taking eculizumab in a longer follow-up phase to check its long-term safety and effectiveness. This phase did not include a comparison with placebo.
- A separate analysis of this last follow-up phase focused on people who took eculizumab alone, without any immunosuppressive treatments.

2 The CHAMPION-NMOSD study with ravulizumab

- This was another phase 3 clinical trial.
- Ravulizumab, a medicine based on eculizumab requiring less frequent takes, was tested.
- Instead of creating a new placebo group, researchers compared the results of ravulizumab to the placebo group from the PREVENT study.

3 The daily practice study with eculizumab in Japan

- This study examined how well eculizumab works in daily life clinical practice (how a treatment performs in everyday medical settings, outside of a controlled clinical trial).
- It focused on patients in Japan after the treatment was approved for use.

How did the researchers measure how effective the treatments were in these studies?

- The researchers looked at the following measures to see how effective the treatments were:
  - In the clinical studies (known as efficacy).
  - In the daily life study (known as effectiveness).

- The proportion of people who had a relapse (attack) during the study:

➡ Experts assessed all relapses, confirming that reported events were genuine, met specific criteria, and were documented appropriately.

- The average number of relapses (attacks) experienced per year by participants:

➡ Each reported relapse was reviewed and confirmed by an independent group of experts.

- Changes in the level of disability
  - Researchers examined whether people's level of disability changed for better or worse during treatment compared to the start of the study.
  - They used a scale called the Expanded Disability Status Scale (EDSS for short). This is based on a thorough neurological examination that assesses a wide range of functions, including movement, sensation, coordination, vision, bowel and bladder function, and thinking and memory.
  - Decreasing scores indicate worsening disability.

- Quality of life:

→ Researchers looked at whether people's quality of life changed during treatment compared with the start of the study with specific questionnaires measuring different key quality of life aspects

What did the PREVENT study of eculizumab find?

Who took part in the study?

PREVENT main study

143 Adults

18 Countries

96 Participants eculizumab

Participants placebo **47**

66% Immunosuppressive treatments

- 143 adults with NMOSD from 18 countries participated in the study.
- 90% of participants (130 people) were woman.
- 96 participants received eculizumab, and 47 participants received a placebo.
- The average age at the start of the study was approximately 44 years
- Participants had experienced an average of 2 attacks per year in the two years before joining the study.
- 66% of participants were recieving some form of immunosuppressive treatment.

PREVENT main study + long-term follow-up

137 Adults eculizumab

- 137 of the previous study phase people received eculizumab.
- This included 41 people who switched from placebo to eculizumab at the end of the main study.

PREVENT main study + long-term follow-up with eculizumab alone

33 Adults eculizumab

- 33 of the long term follow-up study participants received eculizumab alone, without any immunosuppressive treatments.
- This included 12 people who switched from placebo to eculizumab at the end of the main study.

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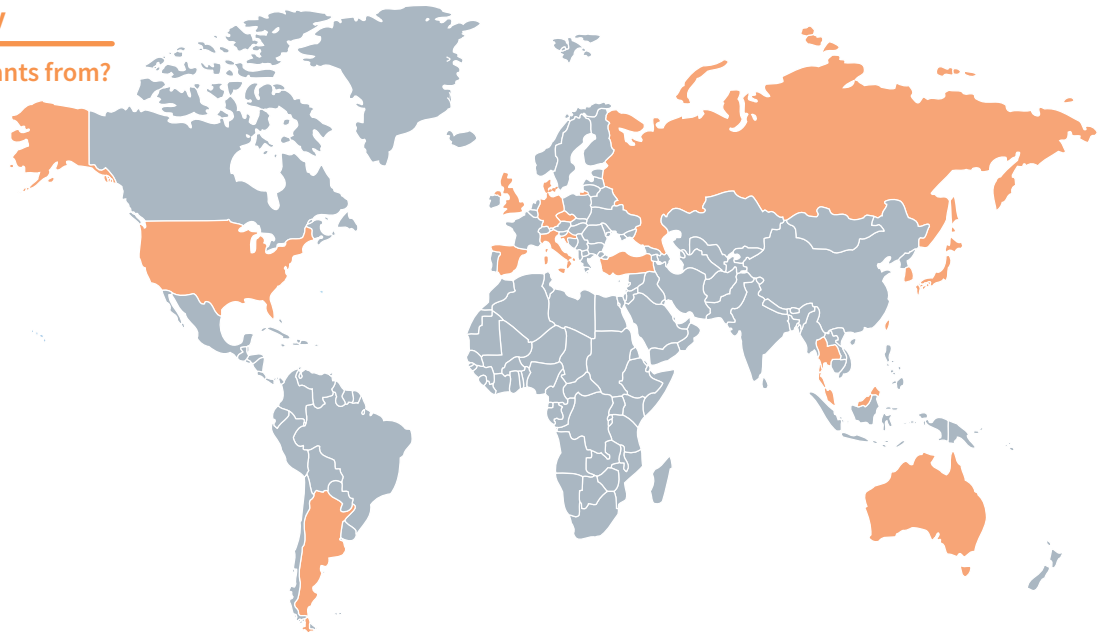
PREVENT main study

Where are the participants from?

44
Americas

51
Europe

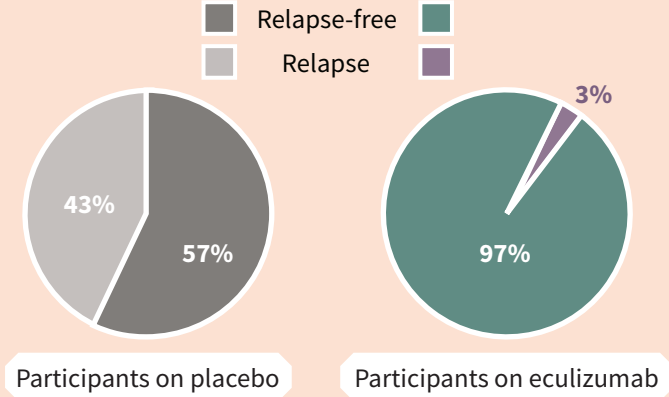
48
Asia–Pacific



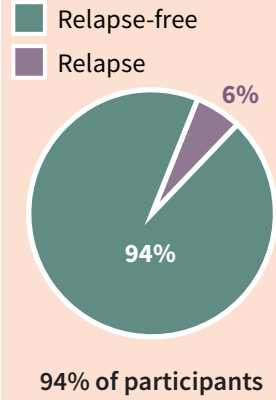
How effective was treatment with eculizumab?

Number of relapses

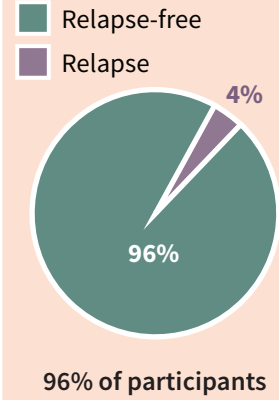
PREVENT main study (143 participants)	PREVENT main study + long-term follow-up (137 participants)	PREVENT main study + long-term follow-up with eculizumab alone (33 participants)
Relapses occurred in 3 of 96 participants (3%) in the eculizumab group, while it was 20 of 47 (43%) in the placebo group after an average of 36 weeks	After around 3.7 years of follow-up relapses occurred in 8 of 137 patients on eculizumab (6%)	After around 3.7 years of follow-up relapses occurred in 1 out of 33 patients on eculizumab alone (4%)



97% of participants on eculizumab and 57% of those on placebo remained free from relapses



94% of participants on eculizumab remained free from relapses



96% of participants on eculizumab alone remained free from relapses

Number of relapses per year

PREVENT main study	PREVENT main study + long-term follow-up	PREVENT main study + long-term follow-up with eculizumab alone
The average number of relapses per year was 0.02 for people who received eculizumab and 0.35 for people who received placebo.	The average number of relapses per year was 0.025 with eculizumab compared with 0.35 in the group assigned to placebo in the PREVENT main study.	The average number of relapses per year was 0.012 compared with 0.625 in the group assigned to placebo alone in the PREVENT main study.

Changes in the level of disability

PREVENT main study	PREVENT main study + long-term follow-up	PREVENT main study + long-term follow-up with eculizumab alone
Overall, people who received eculizumab had a small decrease in their EDSS score (-0.18). People who received placebo had a slight increase in their EDSS score (+0.12) in the placebo group. However, this difference was too small to be considered meaningful.	The trends toward improvement in EDSS with eculizumab observed during the PREVENT main study were maintained during the long term follow-up.	Between the start and end of the PREVENT main study, 95% of participants receiving eculizumab alone showed no worsening in EDSS scores, compared to 62% of participants receiving placebo alone. The observed effect in the eculizumab alone group was maintained during the longer follow-up.

Quality of life

PREVENT main study	PREVENT main study + long-term follow-up	PREVENT main study + long-term follow-up with eculizumab alone
Participants receiving eculizumab showed a trend of improved quality of life, as measured by various questionnaires, but this improvement was not significantly different from that observed in participants receiving placebo.	The trends toward improvement in quality of life with eculizumab observed during the PREVENT main study were maintained during the long term follow-up.	Eculizumab alone improved quality of life more than placebo alone, as measured by various questionnaires, in the PREVENT main study. This improvement remained sustained during the long term follow-up.

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What were the main side effects that occurred? (not necessarily related to treatment)

PREVENT main study	PREVENT main study + long-term follow-up	PREVENT main study + long-term follow-up with eculizumab alone
Comparing with participants on placebo, participants in the eculizumab group had:	The most common side effects were:	The most common side effects were:
• More Infections in the upper respiratory system (31 vs 19 per 100 **patient-years**) • More headaches (55 vs 38 per 100 patient-years)	• Headache: 29% of participants • Infections in the upper respiratory system: 28% • Runny nose and sore throat (nasopharyngitis): 26% • Urinary infection: 22% • Joint pain 18% • Back pain: 17.5% • Diarrhea: 17.5% • Feeling sick (nausea): 17.5%	• Runny nose and sore throat (nasopharyngitis): 39% • Headache: 30% • Infections in the upper respiratory system: 24% • Urinary tract infections: 18%
No meningococcal infections were reported. One person died whilst receiving treatment with eculizumab. They had a chest infection.	No meningococcal infections or deaths were reported during the longer follow-up.	No meningococcal infections or deaths were reported during the longer follow-up.

? **Patient-year:** A way to measure time in studies; one patient-year means one person followed for one year

What did the CHAMPION-NMOSD study of ravulizumab find?

Who took part in the study?

58 Adults

11 Countries

50% Immunosuppressive treatments

- A total of 58 adults with NMOSD from 11 countries participated in the study.
- 90% of participants (52 people) were women.
- The average age at the start of the study was approximately 47 years.
- Participants had experienced an average of 2 attacks per year in the 2 years before joining the study.
- 50% of participants were recieving some form of immunosuppressive treatment.

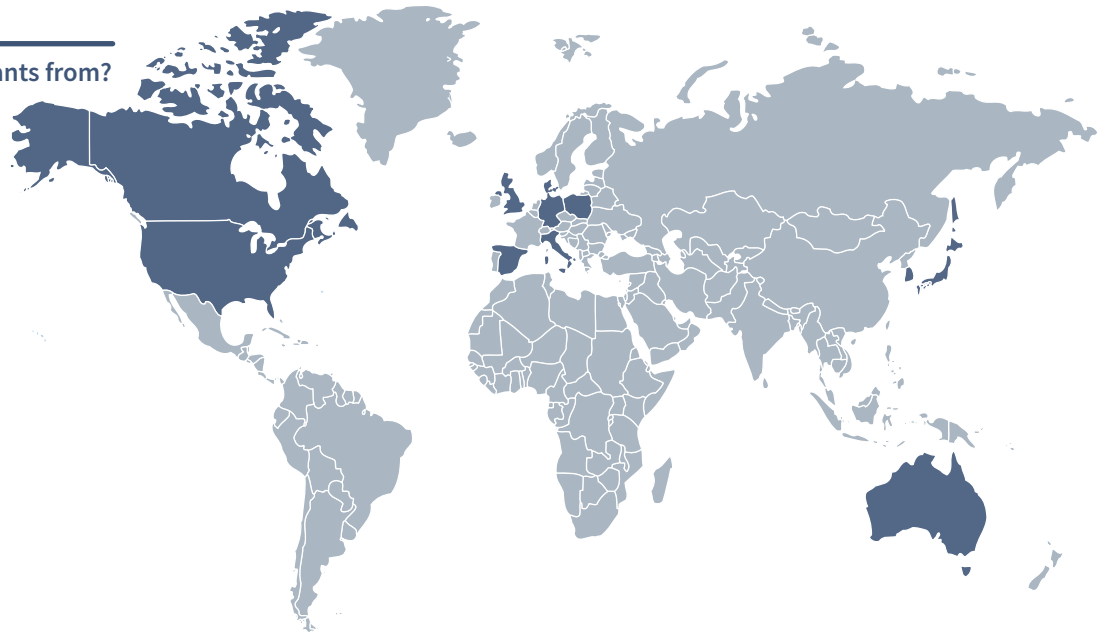
CHAMPION study

Where are the participants from?

21
Americas

17
Europe

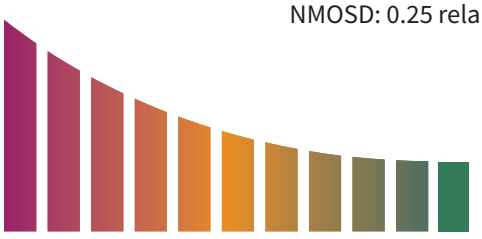
20
Asia–Pacific



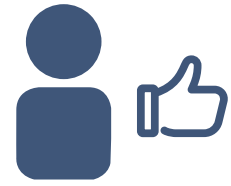
How effective was treatment with ravulizumab?

- On average, researchers followed people in the CHAMPION-NMOSD study for about 68 weeks (approximately 17 months). In the PREVENT placebo group, the average follow-up time was 36 weeks (about 8 months).
- Because the follow-up time was different for the two groups, the number of relapses was measured per "patient-year." A patient-year combines the total time all participants were followed. For example, 10 patients followed for 1 year equals 10 patient-years.
- After over 84 patient-years of follow-up, no patients treated with ravulizumab had any relapses. In comparison, over 46.9 patient-years of follow-up, 20 patients from the 47 in the PREVENT placebo group had relapses. This means that ravulizumab reduced the risk of relapse by 98.6%.

- The number of relapses per year for people treated with ravulizumab was 0 (no relapses), which was better than the rate typically seen in people with NMOSD: 0.25 relapses per year (1 relapse for every 4 people in one year).



- Regarding the level of disability, only 6 out of 58 patients (10%) treated with ravulizumab experienced worsening in their EDSS scores, while 90% had no clinical worsening.



- There was no meaningful difference in quality of life between people treated with ravulizumab and those in the PREVENT placebo group.

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What were the main side effects that occurred?

- The most common side effects reported with ravulizumab in CHAMPION-NMOSD were:
  - COVID-19: 24%
  - Headache: 24%
  - Back pain 12%
  - Joint pain 10%
  - Urinary infection 10%
- Most side effects during ravulizumab treatment were mild (did not affect daily activities) or moderate (somewhat bothersome but manageable).
- Two patients taking ravulizumab experienced meningococcal infections. Both patients recovered with no lasting effects. One patient discontinued treatment while the other chose to continue ravulizumab treatment after recovery.
- No deaths were reported with ravulizumab.

What did the daily practice study with eculizumab in Japan find?

Who took part in the study?

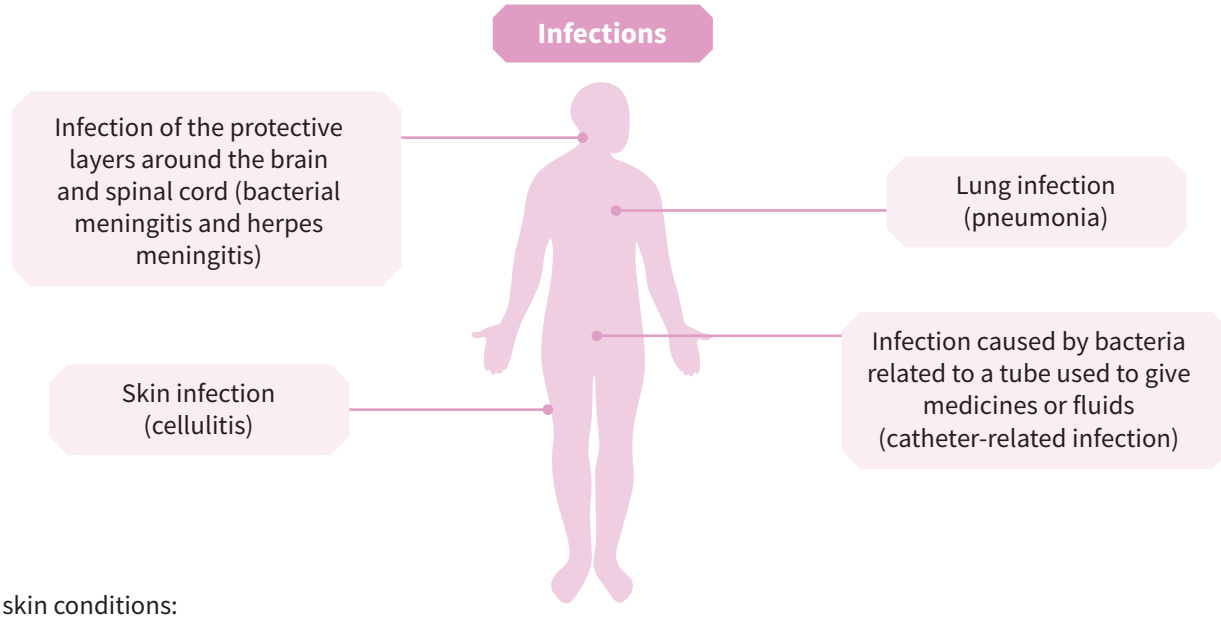
- The researchers recorded information about the side effects of eculizumab for 71 people and its effectiveness for 68 people with NMOSD.
- 94% of participants were woman.
- The average age at the start of the study was approximately 50 years.
- Around 70% of participants had had NMOSD for at least 2 years.
- Participants had experienced a total of 101 relapsesin the 2 years before receiving eculizumab.
- 22 people (43%) had 1 relapse
- 14 people (27.5%) had 2 relapses
- 9 people (18%) had 3 relapses
- 6 people (12%) had 4 relapses

How effective was treatment with eculizumab?

- Three-quarters of people (51 out of 68, or 75%) in the effectiveness analysis had at least one relapse in the 2 years before starting eculizumab treatment.
- At the time of analysis after eculizumab treatment start, 1 person had experienced a relapse, and around 98% of people were relapse-free.
- The number of relapses per year after starting eculizumab was 0.02 per patient-year compared with 0.74 per patient-year before starting eculizumab.
- Before starting eculizumab, more than half (54%) of patients in the effectiveness analysis were taking immunosuppressive treatments. After 6–12 months of eculizumab treatment, this proportion had decreased to 47.5%.
- For people who were taking prednisolone (a medicine from the corticosteroid group that helps reduce swelling and inflammation), their average daily dose was reduced by 67%.
  - On average, people were taking 16 mg of the corticosteroid prednisolone 16.0 milligrams per day at 24–20 weeks before starting eculizumab. At 100–104 weeks after starting eculizumab, they were taking 5.3 milligrams of prednisolone per day on average.

What were the main side effects that occurred?

- 19 of 71 participants (27%) experienced side effects.
- 10 participants experienced one or more side effects possibly related to treatment:



  - 2 skin conditions:
    - Hair loss (alopecia)
    - Red or irritated skin (erythema)
  - 2 muscle and joint conditions:
    - Muscle pain (myalgia)
    - An immune system disorder (systemic lupus erythematosus)
  - 2 people had a fever (pyrexia).
  - 1 case each of:
    - Swollen eyelid
    - High blood pressure in the lungs (pulmonary hypertension)
    - Diarrhea
    - Kidney problems (renal impairment)
    - High levels of C-reactive protein (a sign of inflammation in the body).
- No-one developed a meningococcal infection.
- 1 person who stopped taking eculizumab due to increased pressure in the blood vessels in their lungs died more than 7 months after they had stopped taking eculizumab.
- 12 people stopped eculizumab. The reasons for stopping treatment were:
  - Side effects, for 3 people. 2 people had fever, and 1 person had high pressure in the blood vessels in their lungs.
  - Their doctor decided it was the best choice, for 6 patients.
  - The person with NMOSD decided it was the best choice, for 5 people.
  - Other reasons, for 1 person.

10.57264/cer-2024-0177

What do the results of these studies mean?

These studies suggest that eculizumab and ravulizumab are safe and effective treatments for people with AQP4-Ab+ NMOSD.

Relapses prevention

- Preventing relapses is the main goal of treatment because relapses cause lasting damage.
- More than 95% of people treated with eculizumab or ravulizumab stayed relapse-free for many months or years, as shown in the three studies reviewed.
- Both treatments appear to work equally well to prevent relapses.

Reduction or elimination of immunosuppressive therapies

- The PREVENT study and its extension, as well as in the daily clinical practice study conducted in Japan showed that some patients using eculizumab did not need other medications like immunosuppressive treatments. Others were able to significantly reduce their dose.
- This fact is especially helpful for people with AQP4-Ab+ NMOSD who are at risk of side effects or cannot take immunosuppressive treatments.

Maintaining day-to-day functioning and quality of life

- Eculizumab and ravulizumab help people with NMOSD maintain their ability to carry out daily activities. This is likely because these treatments prevent relapses, which cause tissue damage and disability.
- As shown in the PREVENT study and CHAMPION-NMOSD study, no worsening of disability was seen, as measured by the EDSS score.
- Additionally, the results suggest a trend toward maintaining or improving quality of life for patients treated with these therapies.

Safety profile

- Most side effects were mild or moderate. The most common ones were headache, runny nose with sore throat (nasopharyngitis), and infections in the upper respiratory system.
- Meningococcal vaccination was effective in preventing infections.
- No patients treated with eculizumab developed meningococcal infections, as shown in the PREVENT study and in the study in daily life conducted in Japan.
- 2 patients treated with ravulizumab developed menigococcal infections but recovered fully, as observed in the CHAMPION-NMOSD study.

Daily clinical practice effectiveness

- Eculizumab seems to work just as well controlling NMOSD in daily clinical practice as in clinical trials, as demonstrated by the study in real life conducted in Japan.

Where can readers find more information about these studies?

You can find the full scientific articles that this summary is based on at the following links You can access these articles for free.

PREVENT main study

- This article is called: Eculizumab in aquaporin-4-positive neuromyelitis optica spectrum disorder.
- The full citation of this article is: Pittock SJ, Berthele A, Fujihara K, *et al.* Eculizumab in aquaporin-4-positive neuromyelitis optica spectrum disorder. *N. Engl. J. Med.* 381:614–625 (2019).
- You can read the article for free at: https://www.nejm.org/doi/full/10.1056/NEJMoa1900866

PREVENT main study + long-term follow-up

- This article is called: Long-Term Safety and Efficacy of Eculizumab in Aquaporin-4 IgG-Positive NMOSD.
- The full citation of this article is: Wingerchuk DM, Fujihara K, Palace J, *et al.* Long-term safety and efficacy of eculizumab in aquaporin-4 IgG-positive NMOSD. *Ann. Neurol.* 89(6):1088–1098 (2021).
- You can read the article for free at: https://onlinelibrary.wiley.com/doi/full/10.1002/ana.26049

PREVENT main study + long terms follow-up with eculizumab alone

- This article is called: Eculizumab monotherapy for NMOSD: Data from PREVENT and its open-label extension.
- The full citation of this article is: Pittock SJ, Fujihara K, Palace J, *et al.* Eculizumab monotherapy for NMOSD: Data from PREVENT and its open-label extension. *Multiple Sclerosis Journal* 28(3):480–486 (2022).
- You can read the article for free at: https://journals.sagepub.com/doi/full/10.1177/13524585211038291

CHAMPION-NMOSD study with ravulizumab

- This article is called: Ravulizumab in Aquaporin-4–Positive Neuromyelitis Optica Spectrum Disorder
- The full citation of this article is: Pittock SJ, Barnett M, Bennett JL, *et al.* Ravulizumab in aquaporin-4-positive neuromyelitis optica spectrum disorder. *Ann. Neurol.* 93(6):1053–1068 (2023).
- You can read the article for free at: https://onlinelibrary.wiley.com/doi/10.1002/ana.26626

Daily practice study with eculizumab in Japan

- This article is called: Long-term safety and effectiveness of eculizumab in patients with aquaporin-4 antibody-positive neuromyelitis optica spectrum disorder: a 2-year interim analysis of post-marketing surveillance in Japan.
- The full citation of this article is: Nakashima I, Nakahara J, Yokote H, *et al.* Long-term safety and effectiveness of eculizumab in patients with aquaporin-4 antibody-positive neuromyelitis optica spectrum disorder: a 2-year interim analysis of post-marketing surveillance in Japan. *Ther. Adv. Neurol. Discord.* 16:17562864231181177 (2023)
- You can read the article for free at: https://journals.sagepub.com/doi/10.1177/17562864231181177

Who sponsored the studies?

All studies were sponsored by Alexion, AstraZeneca Rare Disease.

Financial disclosure

Funding for this publication was sponsored by Alexion, AstraZeneca Rare Disease.

Competing interests disclosure

Dr Alfredo Damasceno declares to have received advisory board and/or research/travel grants from: Alexion, Bayer, Biogen, Horizon, Janssen, Merck, Novartis, Roche, Sanofi and Teva. Dr Mariano Marrodan has received fees for educational presentations and/or conference attendance from Merck-Serono Argentina, Biogen-Idec Argentina, Novartis Argentina, Gador, AstraZeneca, Raffo and Roche Argentina.

Writing disclosure

Editorial assistance for this PLSP was provided by Dr. Pablo Rivas and Kerry Dechant, ISMPP CMPP™, on behalf of Content Ed Net (Madrid, Spain) with funding from Alexion, AstraZeneca Rare Disease.