Soliris® (eculizumab), a complement inhibitor, is the first FDA-approved therapy for adults with anti-aquaporin-4 (AQP4) antibody-positive neuromyelitis optica spectrum disorder (NMOSD)[1]

Results from the Soliris PREVENT study in anti-AQP4 antibody-positive NMOSD[1]*

The PREVENT study met its primary endpoint, demonstrating Soliris is superior to placebo based on time to first adjudicated relapse (relative risk reduction, 94%; HR, 0.058; 95% CI: 0.017, 0.197; *P*<0.0001).

94% **reduction in risk of relapse in patients treated with Soliris compared to placebo (*P*<0.0001).**

SHE IS ONE OF THE 98%

OF PATIENTS TREATED WITH SOLIRIS WHO WERE RELAPSE-FREE AT 48 WEEKS VS 63% WITH PLACEBO[1,2]

Abbreviations: CI, confidence interval; HR, hazard ratio.

*Study description: The objective of this phase 3, randomized, double-blind, placebo-controlled trial, called PREVENT (Prevention of Relapses in Neuromyelitis Optica), was to evaluate the efficacy and safety of Soliris (N=96) vs placebo (N=47) in patients with anti-AQP4 antibody-positive NMOSD.[1,2]

This is a hypothetical patient.

INDICATION & IMPORTANT SAFETY INFORMATION FOR SOLIRIS® (eculizumab)

INDICATION

Neuromyelitis Optica Spectrum Disorder (NMOSD)

Soliris is indicated for the treatment of neuromyelitis optica spectrum disorder (NMOSD) in adult patients who are anti-aquaporin-4 (AQP4) antibody positive.

SELECT IMPORTANT SAFETY INFORMATION

WARNING: SERIOUS MENINGOCOCCAL INFECTIONS

Life-threatening and fatal meningococcal infections have occurred in patients treated with Soliris and may become rapidly life-threatening or fatal if not recognized and treated early.

- **Comply with the most current Advisory Committee on Immunization Practices (ACIP) recommendations for meningococcal vaccination in patients with complement deficiencies.**
- **Immunize patients with meningococcal vaccines at least 2 weeks prior to administering the first dose of Soliris, unless the risks of delaying Soliris therapy outweigh the risk of developing a meningococcal infection. (See *Serious Meningococcal Infections* for additional guidance on the management of the risk of meningococcal infection).**
- **Vaccination reduces, but does not eliminate, the risk of meningococcal infections. Monitor patients for early signs of meningococcal infections and evaluate immediately if infection is suspected.**

Soliris is available only through a restricted program under a Risk Evaluation and Mitigation Strategy (REMS). Under the Soliris REMS, prescribers must enroll in the program. Enrollment in the Soliris REMS program and additional information are available by telephone: 1-888-SOLIRIS (1-888-765-4747) or at www.solirisrems.com.

Please see additional Important Safety Information throughout and accompanying full Prescribing Information for Soliris, including Boxed WARNING regarding serious meningococcal infections.

SOLIRIS®
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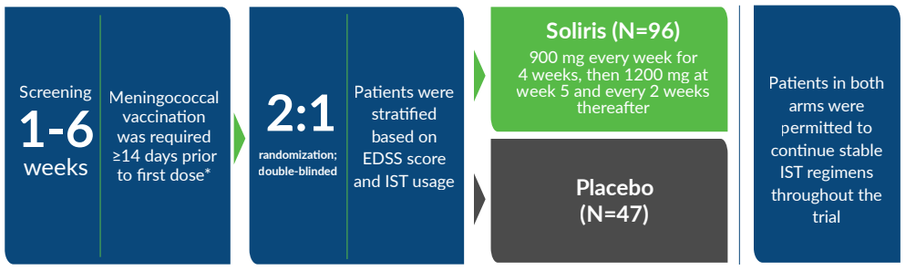
Injection for Intravenous Use
300 mg/30 mL vial

CLINICAL TRIAL OVERVIEW

PREVENT evaluated the ability of Soliris® (eculizumab) to help prevent future relapses[1,2]

PREVENT was a randomized, double-blind, placebo-controlled trial in 143 adults with anti-AQP4 antibody-positive NMOSD[1-3]



*All patients must have been vaccinated against *Neisseria meningitidis* if not already vaccinated. Patients must have been vaccinated at least 14 days prior to receiving the first dose of study drug or been vaccinated and received treatment with appropriate antibiotics until 14 days after vaccination.[1,2]

Abbreviations: EDSS, Expanded Disability Scale Status; IST, immunosuppressive therapy.

Patients who completed PREVENT or experienced an on-trial relapse were eligible to enroll in an open-label extension trial.[2]

SELECT IMPORTANT SAFETY INFORMATION

Contraindications

- Patients with unresolved serious *Neisseria meningitidis* infection
- Patients who are not currently vaccinated against *Neisseria meningitidis*, unless the risks of delaying Soliris treatment outweigh the risks of developing a meningococcal infection

Warnings and Precautions

Serious Meningococcal Infections Risk and Prevention

The use of Soliris increases a patient's susceptibility to serious meningococcal infections (septicemia and/or meningitis).

(continued on following pages)

PREVENT measured time to first adjudicated on-trial relapse and additional outcomes

Primary endpoint[1]

- Time to first adjudicated on-trial relapse

Primary analysis[1]

- Risk reduction at 48 weeks
- Total number of adjudicated relapses by treatment group
- Kaplan-Meier curve for time to first adjudicated relapse by treatment group

On-trial relapse was defined as new onset of neurologic symptoms or worsening of existing neurologic symptoms that[2]:

- Presented as objective change (clinical sign) on the neurologic examination
- Persisted for more than 24 hours
- Were confirmed by the treating physician
- Were attributable to NMOSD rather than other causes
- Were preceded by at least 30 days of clinical stability

All relapses were retrospectively adjudicated by a panel of 3 experts (2 neurologists and 1 neuro-ophthalmologist) who were blinded to the treatment assignment.[2]

Changes in imaging were not considered relapses without related clinical findings.[2]

Prespecified subgroup analysis[1,2]

- Time to first adjudicated on-trial relapse in patients who were not receiving IST at baseline (24% of patients)

Additional outcome measures[1,2]

- Annualized relapse rate (ARR)
- Neurologic function
- Disease-related disability
- NMOSD interventions
- Safety and tolerability

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Patients studied in PREVENT were anti-AQP4 antibody-positive and had a history of relapse

Key inclusion criteria[1,2]

- Age ≥18 years
- Confirmed diagnosis of NMO or NMOSD (defined by Wingerchuk 2006 or Wingerchuk 2007 criteria, respectively)
- Positive serologic test for anti-AQP4 antibodies
- Historical relapses
  - ≥2 in the last 12 months, or
  - 3 in the last 24 months, with ≥1 in the 12 months prior to screening
- EDSS score ≤7
- On a stable dosage of IST*

*Patients were not required to be on IST.[1]

Key exclusion criteria[1,2]

- Use of rituximab or mitoxantrone within 3 months prior to screening
- Use of intravenous immunoglobulin (IVIg) within 3 weeks prior to screening
- Use of prednisone >20 mg/day or equivalent
- Unresolved meningococcal disease
- Any systemic bacterial or other infection considered clinically significant or not treated with appropriate antibiotics

Patient demographics and baseline characteristics[2,3]

	Soliris (N=96)	Placebo (N=47)
Female, n (%)	**88 (92)**	**42 (89)**
Race, n (%)		
Asian	37 (38.5)	15 (31.9)
Black or African American	9 (9.4)	8 (17.0)
White	46 (47.9)	24 (51.1)
Other or unknown	4 (4.2)	0 (0)
IST at baseline, n (%)		
None	21 (22)	13 (28)
Glucocorticoids alone	16 (17)	11 (23)
Azathioprine with or without glucocorticoids	37 (39)	13 (28)
Mycophenolate mofetil with or without glucocorticoids	17 (18)	8 (17)
Other drug with or without glucocorticoids[a]	5 (5)	2 (4)
Disease status at baseline		
Median score on EDSS (range)[b]	4 (1.0-7.0)	4 (1.0-6.5)
Mean ARR during previous 24 months ± SD	1.94 ± 0.90	2.07 ± 1.04

[a]Other drugs include cyclosporine, cyclophosphamide, methotrexate, mizoribine, and tacrolimus.
[b]Scores on the EDSS range from 0 (no disability) to 10 (death).

SELECT IMPORTANT SAFETY INFORMATION

Risk and Prevention (continued)

Vaccinate or revaccinate for meningococcal disease according to the most current ACIP recommendations for patients with complement deficiencies. Immunize patients without a history of meningococcal vaccination at least 2 weeks prior to receiving the first dose of Soliris. If Soliris must be initiated immediately in an unvaccinated patient, administer meningococcal vaccine(s) as soon as possible and provide 2 weeks of antibacterial drug prophylaxis. Discontinue Soliris in patients who are undergoing treatment for serious meningococcal infections.

Please see additional Important Safety Information throughout and accompanying full Prescribing Information for Soliris, including Boxed WARNING regarding serious meningococcal infections.

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Soliris® (eculizumab) significantly reduced the risk of relapse vs placebo

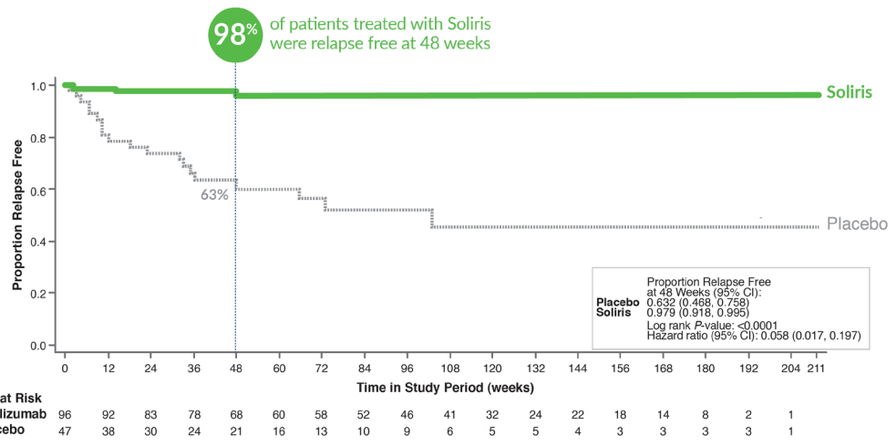
The PREVENT study met its primary endpoint, demonstrating that Soliris is superior to placebo based on time to first adjudicated relapse (*P*<0.0001)[1]

PRIMARY ENDPOINT

The time to the first adjudicated on-trial relapse was significantly longer in Soliris-treated patients compared to placebo-treated patients (relative risk reduction, 94%; HR, 0.058; 95% CI: 0.017, 0.197; *P*<0.0001).[1]

PRIMARY ANALYSIS

Percentage of patients who were relapse-free (full trial population)[1,2]



Kaplan-Meier plot of relapse-free survival estimates among patients who were receiving Soliris or placebo for NMOSD in the analysis of the primary endpoint modified intent-to-treat population.[1,2]

94% reduction in risk of relapse in patients treated with Soliris compared to placebo (*P*<0.0001).[1]

Significant relative reduction in adjudicated annualized relapse rate (ARR)

SECONDARY ENDPOINT

96% reduction in adjudicated ARR with Soliris vs placebo (adjusted ARR, 0.02 vs 0.35; HR, 0.045; 95% CI: 0.01, 0.15; *P*<0.0001).[1*]

*Adjudicated ARR is based on Poisson regression adjusted for randomization strata and historical ARR in 24 months prior to screening.[1,2]

OTHER EFFICACY ANALYSES

Compared to placebo, patients treated with Soliris had reduced annualized rates of[1]:

Hospitalization	IV corticosteroid adminstration to treat acute relapses	Plasma exchange treatments
0.04 SOLIRIS vs 0.31 placebo	0.07 SOLIRIS vs 0.42 placebo	0.02 SOLIRIS vs 0.19 placebo
87% Relative reduction vs placebo	**83%** Relative reduction vs placebo	**89%** Relative reduction vs placebo

SELECT IMPORTANT SAFETY INFORMATION

REMS

Prescribers must counsel patients about the risk of meningococcal infection, provide the patients with the REMS educational materials, and ensure patients are vaccinated with meningococcal vaccine(s).

Please see additional Important Safety Information throughout and accompanying full Prescribing Information for Soliris, including Boxed WARNING regarding serious meningococcal infections.

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Safety in anti-AQP4 antibody-positive NMOSD in a 3+ year study[1,2]

Adverse reactions reported in 5% or more of Soliris® (eculizumab)-treated patients in NMOSD study 1 and at a greater frequency than in placebo-treated patients[1]

	Soliris (N=96)	Placebo (N=47)
	N (%)	N (%)
Events/Patients	1295/88	617/45
Blood and lymphatic system disorders		
Leukopenia	5 (5)	1 (2)
Lymphopenia	5 (5)	0 (0)
Eye Disorders		
Cataract	6 (6)	2 (4)
Gastrointestinal disorders		
Diarrhea	15 (16)	7 (15)
Constipation	9 (9)	3 (6)
General disorders and administration site conditions		
Asthenia	5 (5)	1 (2)
Infections and infestations		
Upper respiratory tract infection	28 (29)	6 (13)
Nasopharyngitis	20 (21)	9 (19)
Influenza	11 (11)	2 (4)
Pharyngitis	10 (10)	3 (6)
Brochitis	9 (9)	3 (6)
Conjunctivitis	9 (9)	4 (9)
Cystitis	8 (8)	1 (2)
Hordeolum	7 (7)	0 (0)
Sinusitis	6 (6)	0 (0)
Cellulitis	5 (5)	1 (2)
Injury, poisoning, and procedural complications		
Contusion	10 (10)	2 (4)
Metabolism and nutrition disorders		
Decreased appetite	5 (5)	1 (2)
Musculoskeletal and connective tissue disorders		
Back pain	14 (15)	6 (13)
Arthralgia	11 (11)	5 (11)
Musculoskeletal pain	6 (6)	0 (0)
Muscle spasms	5 (5)	2 (4)
Nervous system disorders		
Dizziness	14 (15)	6 (13)
Paraesthesia	8 (8)	3 (6)
Respiratory, thoracic, and mediastinal disorders		
Oropharyngeal pain	7 (7)	2 (4)
Skin and subcutaneous tissue disorders		
Alopecia	5 (5)	2 (4)

SELECT IMPORTANT SAFETY INFORMATION

Other Infections

Serious infections with *Neisseria* species (other than *N. meningitidis*), including disseminated gonococcal infections, have been reported.

Patients may have increased susceptibility to infections, especially with encapsulated bacteria. Additionally, *Aspergillus* infections have occurred in immunocompromised and neutropenic patients. Use caution when administering Soliris to patients with any systemic infection.

Infusion Reactions

Administration of Soliris may result in infusion reactions, including anaphylaxis or other hypersensitivity reactions. Interrupt Soliris infusion and institute appropriate supportive measures if signs of cardiovascular instability or respiratory compromise occur.

Please see additional Important Safety Information throughout and accompanying full Prescribing Information for Soliris, including Boxed WARNING regarding serious meningococcal infections.

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Immunize patients with both types of meningococcal vaccines at least 2 weeks before starting treatment with Soliris® (eculizumab)[1,4]

The use of Soliris increases a patient's susceptibility to serious meningococcal infections[1]

MenACWY[5]		MenB-4C[5]		MenB-FHbp[5]
2 DOSES	+	2 DOSES	OR	3 DOSES
At least 2 months apart		At least 1 month apart		0, 1-2, and 6 months[b]
Revaccinate every 5 years[a] as long as the risk persists		MenB vaccines are not interchangeable. You must administer the same product for all doses in series. Revaccination recommendations are not currently available from ACIP. Consult the vaccine manufacturer or the vaccine prescribing information for additional information.		

[a]The Centers for Disease Control and Prevention Advisory Committee on Immunization Practices (ACIP) recommends revaccination every 5 years if risk remains.[5]

[b]For MenB-FHbp, if dose 2 was administered 6 months after dose 1, dose 3 is not needed.[5]

Abbreviation: Advisory Committee on Immunization Practices, ACIP

- Initiate vaccine regimen at least 2 weeks prior to administering the first dose of Soliris, unless the risks of delaying therapy outweigh the risk of developing a meningococcal infection[1]
- If urgent Soliris therapy is indicated in an unvaccinated patient, administer the first dose of both meningococcal vaccines as soon as possible and provide 2 weeks of antibacterial drug prophylaxis[1]
- Vaccination reduces, but does not eliminate, the risk of meningococcal infections. Monitor patients for early signs of meningococcal infections, and evaluate immediately if infection is suspected[1]

Please reference the most up-to-date ACIP recommendations for the most current and complete information for meningococcal vaccination in persons who are taking Soliris or have persistent complement component deficiencies.

SELECT IMPORTANT SAFETY INFORMATION

Adverse Reactions

The most frequently reported adverse reactions in the NMOSD placebo-controlled trial (≥10%) are: upper respiratory infection, nasopharyngitis, diarrhea, back pain, dizziness, influenza, arthralgia, pharyngitis, and contusion.

Enroll in the REMS program to get your patient started on Soliris

Because of the risk of meningococcal infections, Soliris is available only through a restricted program under a Risk Evaluation and Mitigation Strategy (REMS)[1]

Under the Soliris REMS, prescribers must enroll in the program. Prescribers must counsel patients about the risk of meningococcal infection, provide the patients with the REMS educational materials, and ensure patients are vaccinated with meningococcal vaccine(s).

Enrollment in the Soliris REMS program and additional information are available by telephone: 888-SOLIRIS (888-765-4747) or at www.solirisrems.com.

Ongoing maintenance treatment with Soliris consists of biweekly, 35-minute infusions[1]

Patients can receive Soliris at an infusion center or in their own homes (with insurance approval). Treatment begins with an induction phase, followed by a maintenance phase.

Dosing for adult patients with anti-AQP4 antibody-positive NMOSD[1]*

INDUCTION PHASE		MAINTENANCE PHASE†
900 mg given as IV infusion once weekly for 4 weeks	1200 mg given as IV infusion once at week 5	1200 mg given as IV infusion every 2 weeks thereafter

Abbreviation: IV, intravenous.

*Administer Soliris at the recommended dosage regimen time points or within 2 days of these time points.[1]

†This assumes that the patient has completed the 5-week induction phase.[1]

For adult patients with NMOSD, supplemental dosing of Soliris is required in the setting of concomitant plasmapheresis or plasma exchange, or fresh frozen plasma infusion (PE/PI).[1]

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PATIENT SUPPORT

Alexion offers complimentary support for eligible patients

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OneSource@alexion.com

Visit:
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References: 1. Soliris [package insert]. Boston, MA: Alexion Pharmaceuticals, Inc; 2019. **2.** Pittock SJ, Berthele A, Fujihara K, et al. Eculizumab in aquaporin-4-positive neuromyelitis optica spectrum disorder. *N Engl J Med.* 2019;381(7):614-625. **3.** Pittock SJ, Berthele A, Fujihara K, et al. Eculizumab in aquaporin-4-positive neuromyelitis optica spectrum disorder [suppl]. *N Engl J Med.* 2019. **4.** Meningococcal vaccination: what everyone should know. Centers for Disease Control and Prevention website. https://www.cdc.gov/vaccines/vpd/mening/public. Accessed May 2, 2019. **5.** Kim DK, Hunter P; for the Advisory Committee on Immunization Practices. Recommended adult immunization schedule, United States, 2019. *Ann Intern Med.* 2019;170(3):182-192.

Please see additional Important Safety Information throughout and accompanying full Prescribing Information for Soliris, including Boxed WARNING regarding serious meningococcal infections.

ALEXION®

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