For your adult patients with generalized myasthenia gravis (gMG) who are anti-acetylcholine receptor (AChR) antibody-positive[1]

ULTOMIRIS®
(ravulizumab-cwvz)
injection for intravenous use
300 mg/3 mL vial

Could complement C5 inhibition target the underlying driver of damage in your patients with gMG?[2]

See how targeting C5 may help protect synaptic structure at the NMJ.[2,a]

See MG-ADL exploratory endpoint data by time-from-diagnosis subgroups.

The precise mechanism by which ULTOMIRIS® exerts its therapeutic effect in gMG patients is unknown, but is presumed to involve reduction of terminal complement complex C5b-9 deposition at the NMJ.[1]

[a]Based on a study conducted using rat models. See study details on page 3.

C5, complement component 5; C5b-9, complement system membrane attack complex; MG-ADL, Myasthenia Gravis Activities of Daily Living; NMJ, neuromuscular junction.

Brittany, ULTOMIRIS patient living with gMG.
Brittany has received compensation from Alexion Pharmaceuticals, Inc.

INDICATION

ULTOMIRIS is indicated for the treatment of adult patients with generalized myasthenia gravis (gMG) who are anti-acetylcholine receptor (AChR) antibody-positive.

SELECT IMPORTANT SAFETY INFORMATION

WARNING: SERIOUS MENINGOCOCCAL INFECTIONS

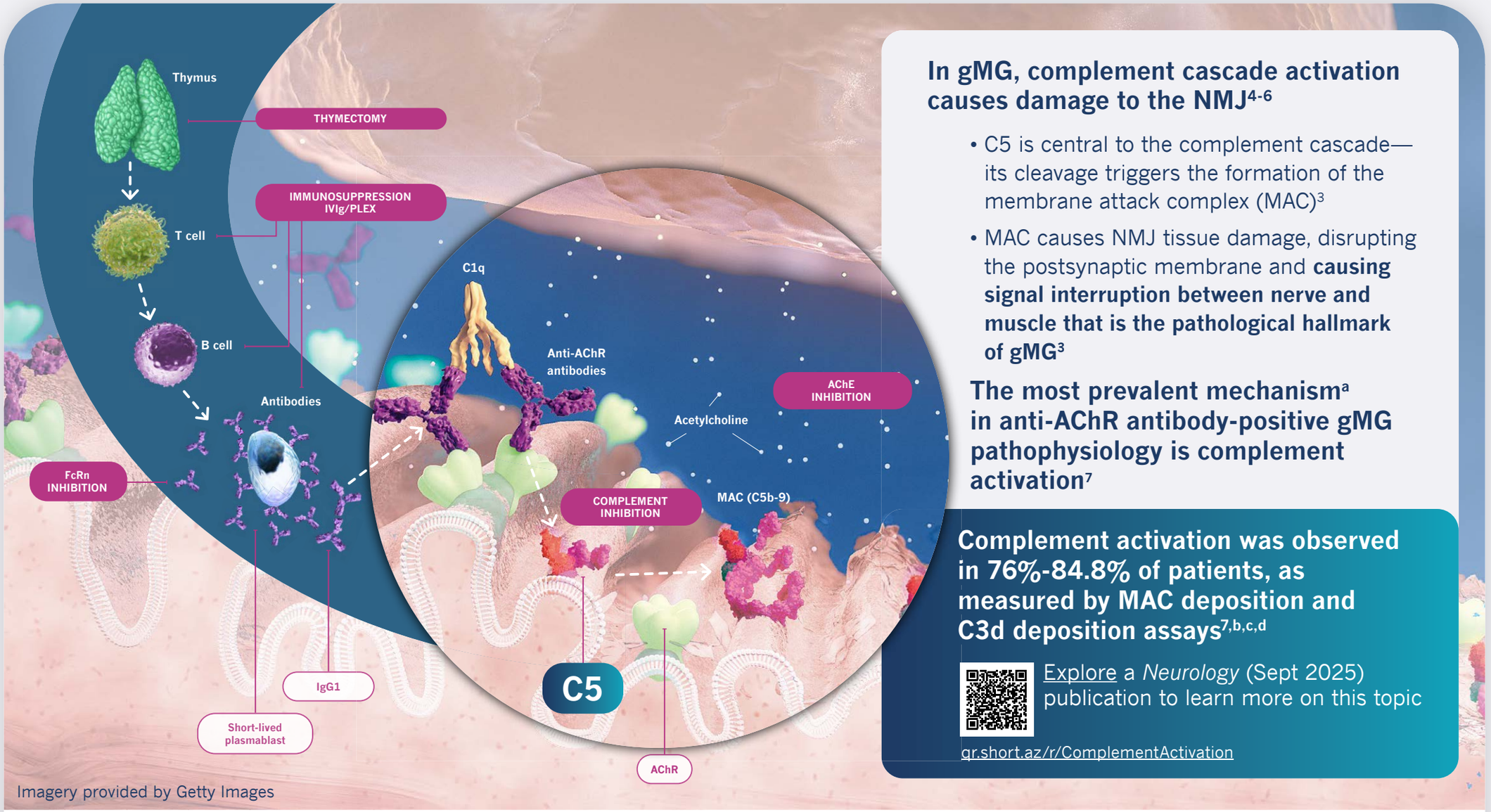
ULTOMIRIS, a complement inhibitor, increases the risk of serious infections caused by *Neisseria meningitidis* [*see Warnings and Precautions (5.1)*] Life-threatening and fatal meningococcal infections have occurred in patients treated with complement inhibitors. These infections may become rapidly life-threatening or fatal if not recognized and treated early.

- **Complete or update vaccination for meningococcal bacteria (for serogroups A, C, W, Y, and B) at least 2 weeks prior to the first dose of ULTOMIRIS, unless the risks of delaying ULTOMIRIS therapy outweigh the risk of developing a serious infection. Comply with the most current Advisory Committee on Immunization Practices (ACIP) recommendations for vaccinations against meningococcal bacteria in patients receiving a complement inhibitor. See *Warnings and Precautions (5.1)* for additional guidance on the management of the risk of serious infections caused by meningococcal bacteria.**
- **Patients receiving ULTOMIRIS are at increased risk for invasive disease caused by *Neisseria meningitidis*, even if they develop antibodies following vaccination. Monitor patients for early signs and symptoms of serious meningococcal infections and evaluate immediately if infection is suspected.**

Because of the risk of serious meningococcal infections, ULTOMIRIS is available only through a restricted program under a Risk Evaluation and Mitigation Strategy (REMS) called ULTOMIRIS and SOLIRIS REMS [*see Warnings and Precautions (5.2)*].

Please see additional Important Safety Information throughout and accompanying full Prescribing Information for ULTOMIRIS, including Boxed WARNING regarding serious and life-threatening or fatal meningococcal infections.

Complement C5 is a central driver of ongoing neuromuscular disruption in gMG[3]



Imagery provided by Getty Images

In gMG, complement cascade activation causes damage to the NMJ[4-6]

- C5 is central to the complement cascade—its cleavage triggers the formation of the membrane attack complex (MAC)[3]
- MAC causes NMJ tissue damage, disrupting the postsynaptic membrane and **causing signal interruption between nerve and muscle that is the pathological hallmark of gMG[3]**

The most prevalent mechanism[a] in anti-AChR antibody-positive gMG pathophysiology is complement activation[7]

Complement activation was observed in 76%-84.8% of patients, as measured by MAC deposition and C3d deposition assays[7,b,c,d]

Explore a *Neurology* (Sept 2025) publication to learn more on this topic

qr.short.az/r/ComplementActivation

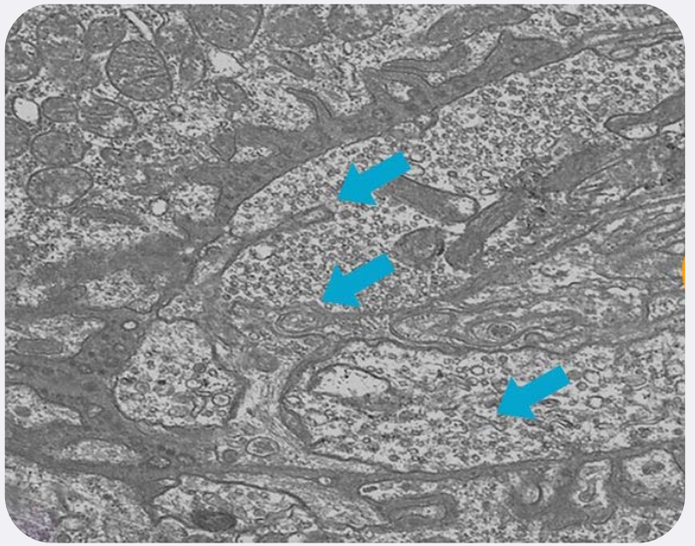
[a]Three pathogenic mechanisms were studied: complement activation, antigenic modulation, and the blockage of AChRs.[7]
[b]Clinicians do not assess for autoantibody heterogeneity to determine which treatment patients would respond to best.[7]
[c]Longitudinal serum analyses (N=210) from 50 AChR+ gMG patients assessed AChR autoantibody isotypes, IgG subclasses, and 3 pathogenic mechanisms via live cell-based assays, over 2 years.[7]
[d]Complement activity was assessed by measuring MAC deposition—the terminal product of the complement pathway—on the membrane of AChR-expressing cells. To account for MAC-induced cell lysis, which may have underestimated complement activity, these results were further validated using a complementary C3d detection assay. Primary and secondary staining techniques were used with negative and positive controls included in each assay. Complement activity was quantified by calculating the normalized mean fluorescence intensity (ΔMFI) as follows: $\Delta MFI = MFI_{AChR\text{-}GFP\text{-}positive} - MFI_{AChR\text{-}GFP\text{-}negative}$.[7]

AChE, acetylcholinesterase; AChR, acetylcholine receptor; C1q, complement component 1q; C3d, complement component 3d; C5, complement component 5; C5b-9, complement system membrane attack complex; FcRn, neonatal fragment crystallizable receptor; GFP, green fluorescent protein; gMG, generalized myasthenia gravis; IgG, immunoglobulin G; IgG1, immunoglobulin G1; IVIg, intravenous immunoglobulin; NMJ, neuromuscular junction; PLEX, plasma exchange.

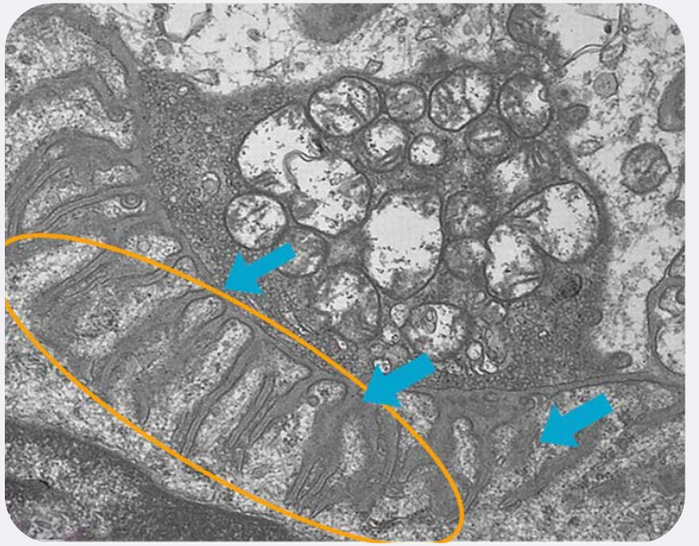
Rat models have shown that anti-C5 monoclonal antibody treatment may help protect the neuromuscular junction (NMJ)[2]

Treatment with an anti-C5 monoclonal antibody may have helped protect the integrity of the NMJ, including normal junctional folds and synaptic structure[2]

NMJs in untreated rats compared with NMJs in rats treated with an anti-C5 mAb[2,a]



NMJs in untreated rats were abnormal, with shortened or no junctional folds, widened junctional space, widened synaptic cleft, or electron-dense material consistent with sloughed synaptic membrane.



NMJs from anti-C5 mAb-treated rats had minimal changes, with relatively normal junctional folds and space and normal synaptic clefts with some membrane blebbing.

Inhibiting C5 helps preserve synaptic integrity and neuromuscular signaling[2]

Precisely targeting C5 could potentially deliver mechanistic impact in gMG based on a rat study[1,2,8,a]

[a]The effect of anti-C5 mAb was evaluated over 7 days in an experimental myasthenia gravis rat model induced with AChR mAb-3.[2]

AChR, acetylcholine receptor; C5, complement component 5; gMG, generalized myasthenia gravis; mAb, monoclonal antibody; mAb-3, monoclonal antibody type 3.

Early intervention in gMG may be critical to helping patients[9,10]

Across 2 studies, up to 89% of patients reached peak disease severity within the first year[11,12,a]

Early progression is common and treatment delays may miss the critical window for intervention[11,12]

Unpredictable gMG symptom fluctuations can be life-threatening[13]

Uncontrolled gMG can ultimately lead to clinical events such as **crises or exacerbations**[13]

gMG can rapidly disrupt daily life[14]

Fluctuations occur consistently and impact a range of physical symptoms, affect emotion and physical well-being, and alter work and family life[14]

[a]Based on 2 studies—a retrospective study of 1976 patients diagnosed with MG between 1940 and 2000 at 2 centers in the US and a retrospective analysis of medical records from 199 inpatients and outpatients diagnosed with gMG between January 1, 2000, and December 31, 2018, with sufficient follow-up data up to 10 years at 2 centers in Austria.[11,12]

gMG, generalized myasthenia gravis; MG, myasthenia gravis.

Even low levels of anti-AChR antibodies can activate complement, destroy NMJ morphology, and disrupt neuromuscular transmission[7,15]

> **Complement-mediated destruction of the NMJ results in morphological changes and simplification, leading to loss of function of AChRs, which are critical for muscle contraction.**
> This results in fatigable muscle weakness associated with anti-AChR antibody-positive gMG."

– Dr Kevin C O'Connor,
Associate Professor of Neurology and Immunobiology at Yale School of Medicine

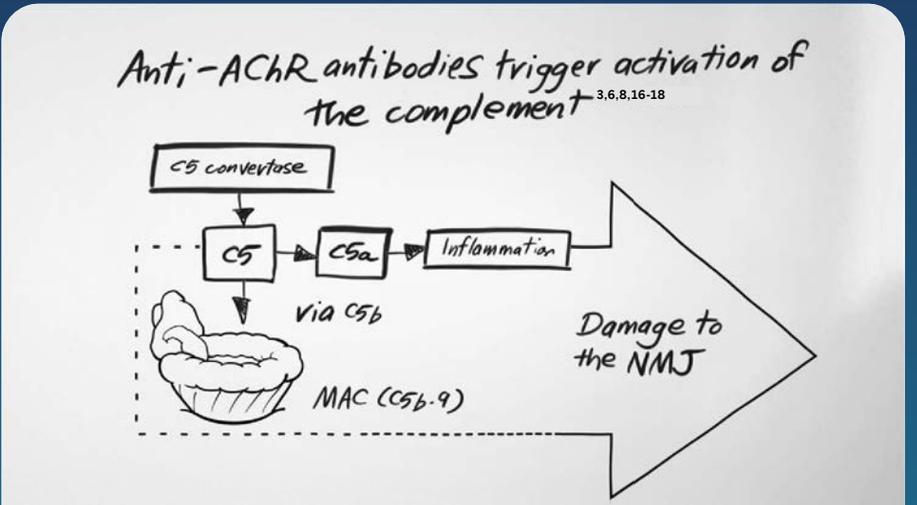


Image created by Alexion Pharmaceuticals, Inc., for illustrative purposes only.

Watch Dr Kevin O'Connor explain how complement-mediated NMJ damage shapes his treatment strategy.

qr.short.az/r/Complement

Could inhibiting C5 activation help target the complement-mediated driver of NMJ damage in your gMG patients?[2]

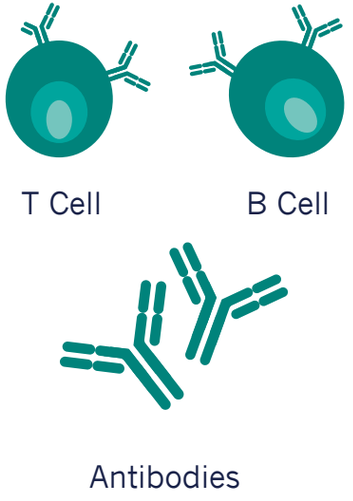
AChR, acetylcholine receptor; C5, complement component 5; C5a, complement component 5a; C5b, complement component 5b; C5b-9, complement system membrane attack complex; gMG, generalized myasthenia gravis; MAC, membrane attack complex; NMJ, neuromuscular junction.

ULTOMIRIS® does not broadly suppress immune function, as it selectively inhibits the terminal complement pathway[1,8]

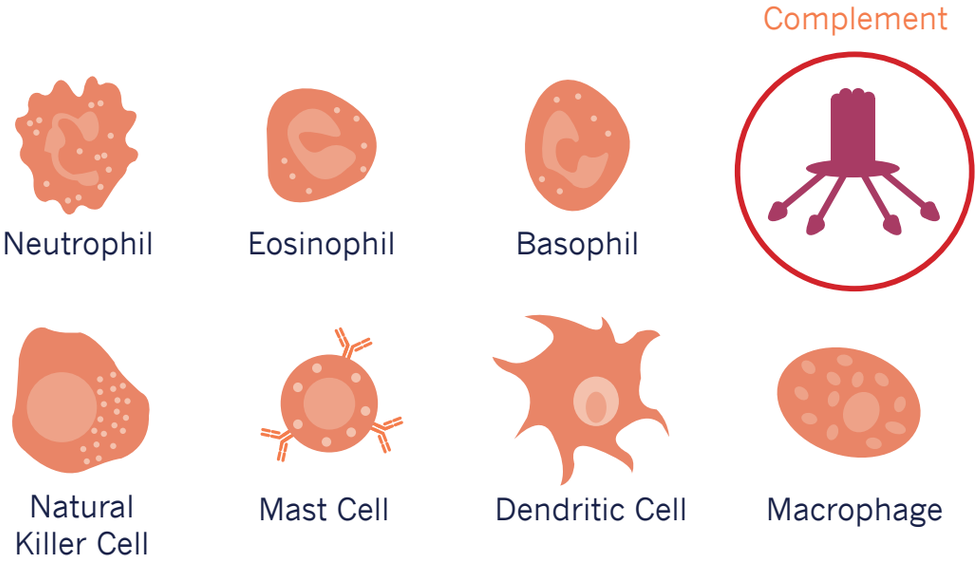
ULTOMIRIS® (ravulizumab-cwvz) injection for intravenous use 300 mg/3 mL vial

Selective inhibition may limit impact on adaptive immunity[1,19]

Adaptive immunity[20,21]



Innate immunity[20,21]



Adapted from: Creative-Diagnostics.com

Targeted therapy

ULTOMIRIS selectively targets C5. Some other gMG treatments broadly suppress the immune system, leaving patients vulnerable to an array of infections.[1,8,22]

C5, complement component 5; gMG, generalized myasthenia gravis.

SELECT IMPORTANT SAFETY INFORMATION

CONTRAINDICATIONS

- Initiation in patients with unresolved serious *Neisseria meningitidis* infection.

ULTOMIRIS blocks terminal complement activation[1]

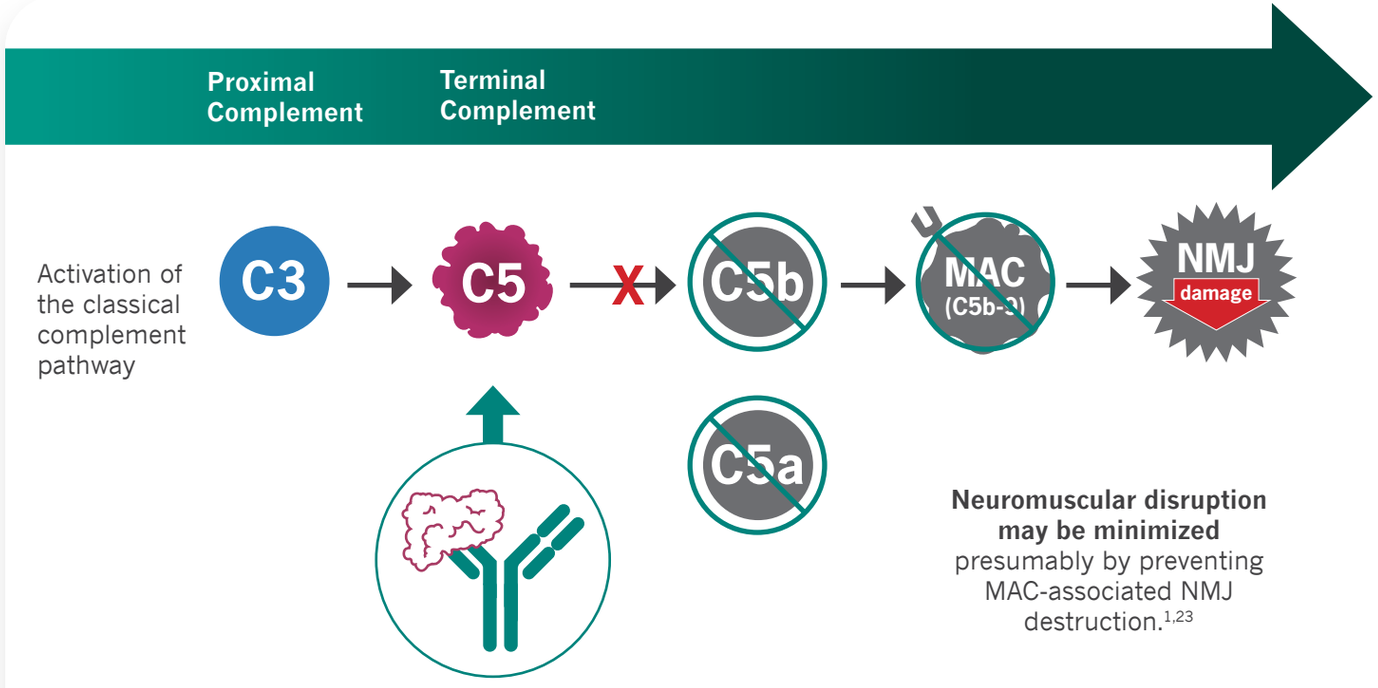
Therefore, patients may have increased susceptibility to infections, especially with encapsulated bacteria, such as infections caused by *Neisseria meningitidis* but also *Streptococcus pneumoniae, Haemophilus influenzae*, and to a lesser extent, *Neisseria gonorrhoeae*. Patients receiving ULTOMIRIS are at increased risk for infections due to these organisms, even if they develop antibodies following vaccination.

Please see additional Important Safety Information throughout and accompanying full Prescribing Information for ULTOMIRIS, including Boxed WARNING regarding serious and life-threatening or fatal meningococcal infections.

ULTOMIRIS® is designed to prevent MAC formation and protect the neuromuscular junction (NMJ)[1,8,23]

ULTOMIRIS® (ravulizumab-cwvz) injection for intravenous use 300 mg/3 mL vial

The binding of ULTOMIRIS to complement C5 **inhibits cleavage into C5a and C5b**, preventing a key driver of NMJ damage.[1,8]



Neuromuscular disruption may be minimized presumably by preventing MAC-associated NMJ destruction.[1,23]

ULTOMIRIS selectively binds to complement C5 to block its activation. **The effect on B cells and other immune responses may be minimized.**[1,19,23-25]

ULTOMIRIS leaves the proximal complement cascade intact, which can help protect the body against an array of bacteria and viruses.[1,19,23-25]

Patients on ULTOMIRIS may have increased susceptibility to other infections[1]

Why do patients need to be vaccinated specifically against meningococcal infections?

Patients may have increased susceptibility to certain bacterial infections, specifically *Neisseria meningitidis*[1,a]

To reduce the risk of infection, patients must be vaccinated against meningococcal infections at least 2 weeks prior to initiating ULTOMIRIS, per ACIP recommendations. If urgent ULTOMIRIS therapy is indicated in a patient who is not up to date with meningococcal vaccines according to ACIP recommendations, provide the patient with antibacterial drug prophylaxis and administer these vaccines as soon as possible.[1]

The precise mechanism by which ULTOMIRIS exerts its therapeutic effect in gMG is unknown but is presumed to involve reduction of terminal complement complex C5b-9 deposition at the NMJ.[1]

[a]*Neisseria meningitidis* is a bacteria that can cause meningitis or meningococcal infections. Unlike most other bacteria, it cannot be cleared by the proximal complement cascade.[24]

ACIP, Advisory Committee on Immunization Practices; C3, complement component 3; C5, complement component 5; C5a, complement component 5a; C5b, complement component 5b; C5b-9, complement system membrane attack complex; gMG, generalized myasthenia gravis; MAC, membrane attack complex.

SELECT IMPORTANT SAFETY INFORMATION

WARNINGS AND PRECAUTIONS

Serious Meningococcal Infections

ULTOMIRIS, a complement inhibitor, increases a patient's susceptibility to serious, life-threatening, or fatal infections caused by meningococcal bacteria (septicemia and/or meningitis) in any serogroup, including non-groupable strains. Life-threatening and fatal meningococcal infections have occurred in both vaccinated and unvaccinated patients treated with complement inhibitors.

Please see additional Important Safety Information throughout and accompanying full Prescribing Information for ULTOMIRIS, including Boxed WARNING regarding serious and life-threatening or fatal meningococcal infections.

ULTOMIRIS® (ravulizumab-cwvz) injection for intravenous use 300 mg/3 mL vial

ULTOMIRIS trial design and key safety information

Studied in one of the longest clinical trials for a gMG treatment, in a broad population of patients[23,28]

CHAMPION-MG was a randomized, multicenter, double-blind, placebo-controlled trial with an open-label extension (OLE). Patients were randomized 1:1 to receive either ULTOMIRIS (n=86) or placebo (n=89) for 26 weeks and were subsequently allowed to enter the OLE period for up to 4 years.[1,23,28]

Patients on concomitant medications to treat gMG were permitted to continue on therapy at stable doses throughout the course of the study, and those medications could be adjusted as necessary during the OLE.[1,28]

Adverse reactions reported in ≥5% and at greater frequency than placebo in ULTOMIRIS-treated patients

Adverse Reactions[1]	ULTOMIRIS (n=86), n (%)	Placebo (n=89), n (%)
GASTROINTESTINAL DISORDERS		
Diarrhea	13 (15)	11 (12)
Abdominal pain	5 (6)	0
INFECTIONS AND INFESTATIONS		
Upper respiratory tract infection	12 (14)	7 (8)
Urinary tract infection	5 (6)	4 (4)
MUSCULOSKELETAL AND CONNECTIVE TISSUE DISORDERS		
Back pain	7 (8)	5 (6)
NERVOUS SYSTEM DISORDERS		
Dizziness	8 (9)	3 (3)

164 weeks (RCP + OLE): safety outcomes reported in the ULTOMIRIS-treated population (N=169).[28]

Most common adverse reactions (≥10%) with ULTOMIRIS: COVID-19 (36%), headache (23%), diarrhea (17%), arthralgia (14%), back pain (13%), nausea (13%), nasopharyngitis (12%), urinary tract infection (12%), fatigue (11%), and dizziness (10%).[28]

AChR, acetylcholine receptor; ACIP, Advisory Committee on Immunization Practices; C5, complement component 5; gMG, generalized myasthenia gravis; RCP, randomized controlled period.

SELECT IMPORTANT SAFETY INFORMATION

WARNINGS AND PRECAUTIONS (continued)

Serious Meningococcal Infections (continued)

Revaccinate patients in accordance with ACIP recommendations considering the duration of ULTOMIRIS therapy. Note that ACIP recommends an administration schedule in patients receiving complement inhibitors that differs from the administration schedule in the vaccine prescribing information.

Please see additional Important Safety Information throughout and accompanying full Prescribing Information for ULTOMIRIS, including Boxed WARNING regarding serious and life-threatening or fatal meningococcal infections.

PRIMARY ENDPOINT

Proven to deliver improvement in MG activities of daily living (MG-ADL)[1,28]

ULTOMIRIS® (ravulizumab-cwvz) injection for intravenous use 300 mg/3 mL vial

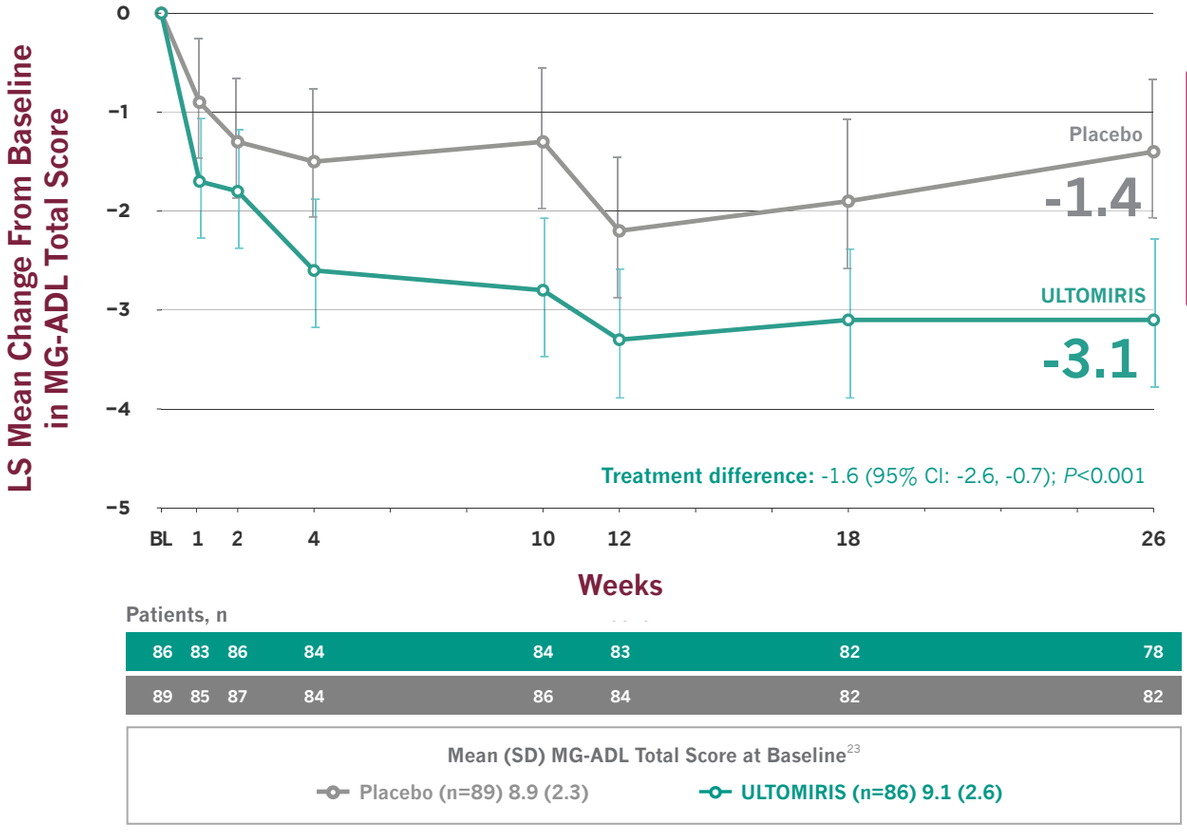
For your adult patients with generalized myasthenia gravis (gMG) who are anti-acetylcholine receptor (AChR) antibody-positive

Among patients in the ULTOMIRIS® treatment arm,

Improvements in MG-ADL total scores were observed within 1 week of treatment and sustained through Week 26[1,28]

Based on MG-ADL assessment of symptoms in the 26-week trial, which measures how gMG affects daily functions through 8 commonly impacted signs and symptoms.[1]

ULTOMIRIS demonstrated efficacy vs placebo at Week 26 (-3.1 vs -1.4, respectively [*P*<0.001])[1,23]



More than 2x greater improvement vs placebo[1,23]

Many patients continued with concomitant medications for gMG throughout the 26 weeks of the study.[1,28]

CHAMPION-MG STUDY LIMITATIONS:

Data shown are least-squares means and 95% confidence intervals (CIs), using a mixed model for repeated measures; 95% CIs were not adjusted for multiplicity.[1,23]

Time to response was part of the planned efficacy analysis, but the primary endpoint was at Week 26. Therefore, results should be interpreted with caution.

ACIP, Advisory Committee on Immunization Practices; BL, baseline; LS, least squares; MG, myasthenia gravis; SD, standard deviation.

SELECT IMPORTANT SAFETY INFORMATION

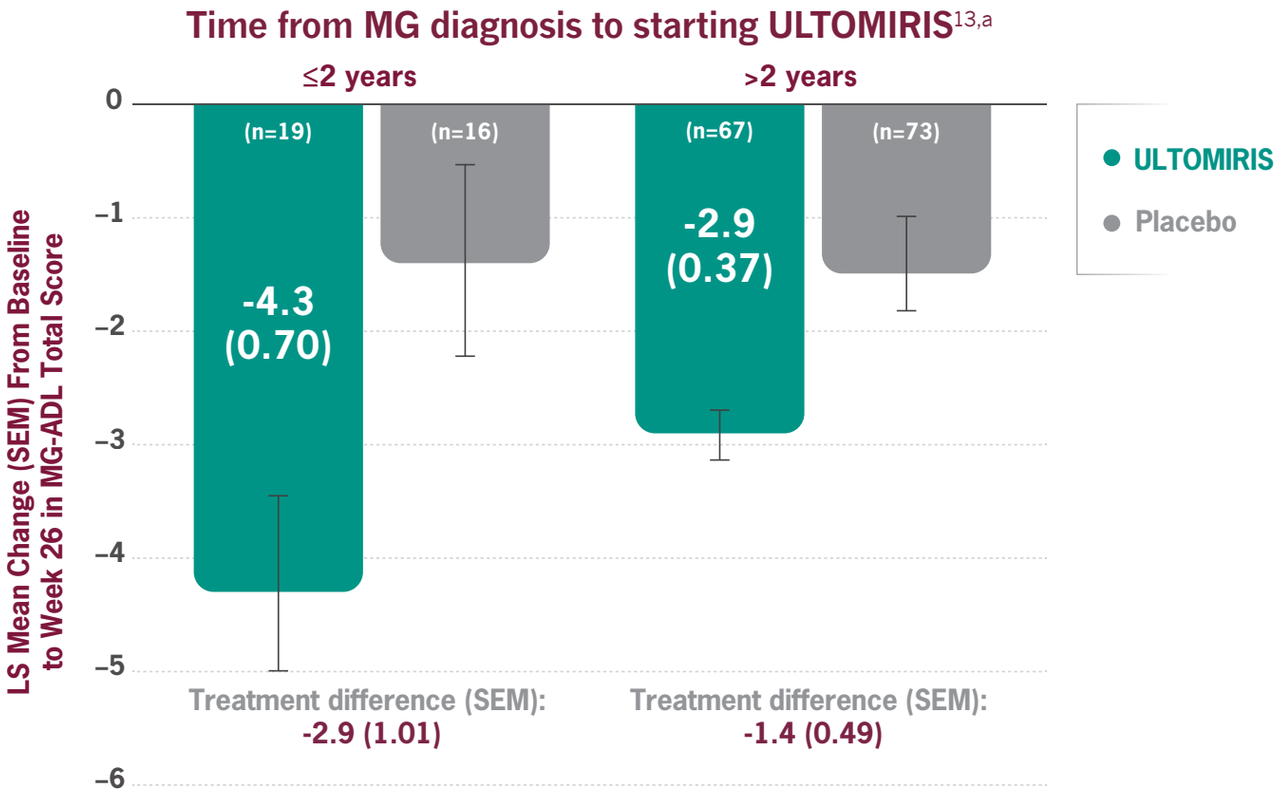
WARNINGS AND PRECAUTIONS (continued)

Serious Meningococcal Infections (continued)

If urgent ULTOMIRIS therapy is indicated in a patient who is not up to date with meningococcal vaccines according to ACIP recommendations, provide antibacterial drug prophylaxis and administer meningococcal vaccines as soon as possible.

Please see additional Important Safety Information throughout and accompanying full Prescribing Information for ULTOMIRIS, including Boxed WARNING regarding serious and life-threatening or fatal meningococcal infections.

Impact of early use of ULTOMIRIS® on MG-ADL total score changes



CHAMPION-MG STUDY LIMITATIONS:

Change in MG-ADL total score reduction with earlier use was not a prespecified endpoint. Differences between the 2 ULTOMIRIS arms were not statistically significant. Results and clinical outcomes should be interpreted with caution.[28]

[a]The numbers of patients indicated in the figure are the numbers of patients included in the MMRM analysis. MG-ADL data were available at both baseline and 26 weeks for 30 patients in the ≤2-year subgroup (17 receiving ravulizumab, 13 receiving placebo) and 130 patients in the >2-year subgroup (61 receiving ravulizumab, 69 receiving placebo). The MMRM analysis used all available longitudinal data for inference, assuming missing at random for missing assessments. Estimates are based on MMRM that includes treatment group, stratification factor region, age at baseline and MG-ADL total score at baseline, study visit, study visit by treatment group interaction, time from diagnosis by treatment group, time from diagnosis by study visit interaction, and time from diagnosis by study visit by treatment group interaction.[13]

[b]In a post hoc analysis of 175 patients at Week 26.[13]

gMG, generalized myasthenia gravis; LS, least squares; MG, myasthenia gravis; MG-ADL, Myasthenia Gravis Activities of Daily Living; MMRM, mixed model for repeated measures; SEM, standard error of the mean.

Patients who started ULTOMIRIS within 2 years of gMG diagnosis were observed to have experienced a 4.3-point reduction in MG-ADL total score from baseline. Patients who started after 2 years were observed to have experienced a 2.9-point reduction from baseline.[13,a,b]

SELECT IMPORTANT SAFETY INFORMATION

WARNINGS AND PRECAUTIONS (continued)

Serious Meningococcal Infections (continued)

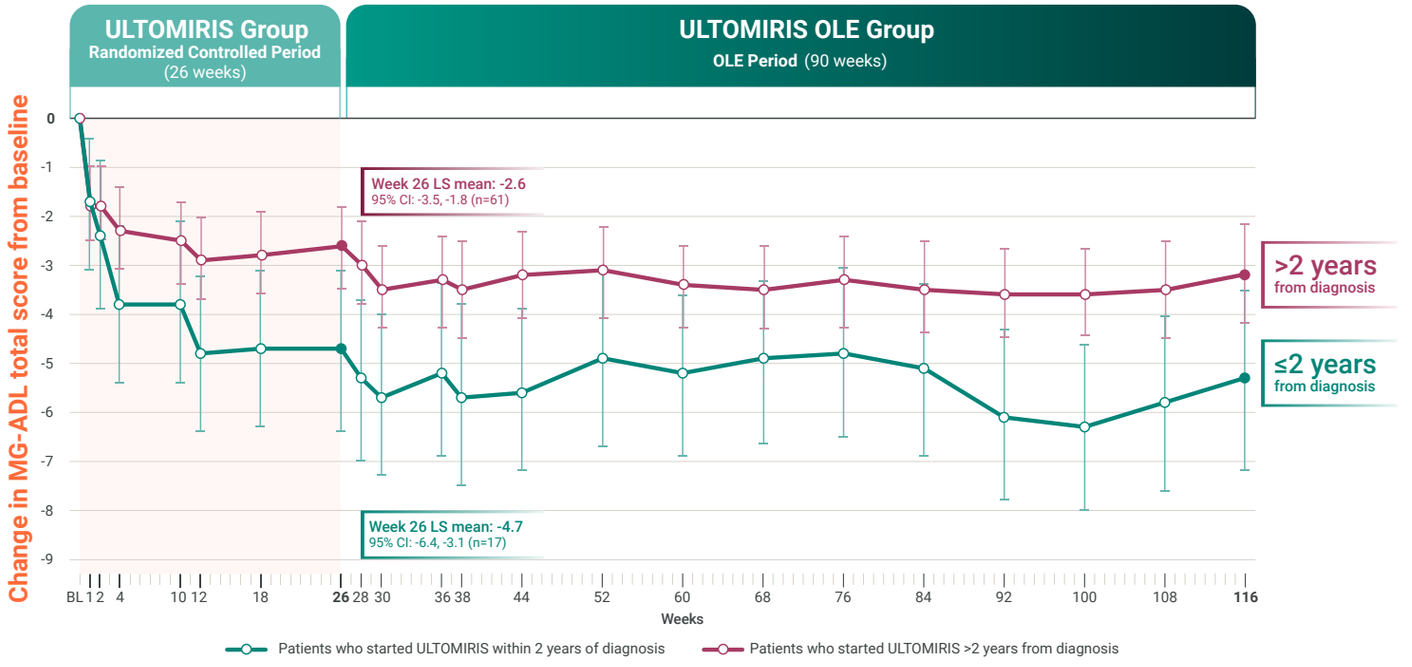
Various durations and regimens of antibacterial drug prophylaxis have been considered, but the optimal durations and drug regimens for prophylaxis and their efficacy have not been studied in unvaccinated or vaccinated patients receiving complement inhibitors, including ULTOMIRIS. The benefits and risks of treatment with ULTOMIRIS, as well as those associated with antibacterial drug prophylaxis in unvaccinated or vaccinated patients, must be considered against the known risks for serious infections caused by *Neisseria meningitidis.*

Please see additional Important Safety Information throughout and accompanying full Prescribing Information for ULTOMIRIS, including Boxed WARNING regarding serious and life-threatening or fatal meningococcal infections.

Changes in MG-ADL total score over time with ULTOMIRIS®, by time from diagnosis[29,a]

ULTOMIRIS → ULTOMIRIS arm

Changes in MG-ADL total score over time, by time from diagnosis to first dose of ULTOMIRIS



		Randomized Controlled Period (26 weeks)							OLE Period (82 weeks)												
		Week 1	Week 2	Week 4	Week 10	Week 12	Week 18	Week 26	Week 28	Week 30	Week 36	Week 38	Week 44	Week 52	Week 60	Week 68	Week 76	Week 84	Week 92	Week 100	Week 108	Week 116
≤2 years from diagnosis: (N=19)	n	19	19	19	19	19	19	17	16	16	18	18	17	16	16	15	15	15	15	15	15	15
	LS mean (SEM)	-1.7 (0.69)	-2.4 (0.74)	-3.8 (0.79)	-3.8 (0.82)	-4.8 (0.81)	-4.7 (0.81)	-4.7 (0.84)	-5.3 (0.84)	-5.7 (0.82)	-5.2 (0.88)	-5.7 (0.92)	-5.6 (0.85)	-4.9 (0.90)	-5.2 (0.83)	-4.9 (0.84)	-4.8 (0.89)	-5.1 (0.88)	-6.1 (0.88)	-6.3 (0.85)	-5.8 (0.90)	-5.3 (0.93)
	95% CI for LS mean	(-3.1, -0.4)	(-3.9, -0.9)	(-5.4, -2.2)	(-5.4, -2.1)	(-6.4, -3.2)	(-6.3, -3.1)	(-6.4, -3.1)	(-7.0, -3.7)	(-7.3, -4.0)	(-6.9, -3.4)	(-7.5, -3.8)	(-7.2, -3.9)	(-6.7, -3.1)	(-6.9, -3.6)	(-6.6, -3.3)	(-6.5, -3.0)	(-6.9, -3.4)	(-7.8, -4.3)	(-8.0, -4.6)	(-7.6, -4.0)	(-7.2, -3.5)
>2 years from diagnosis: (N=67)	n	64	67	65	65	64	63	61	59	59	59	58	57	57	54	54	54	52	50	48	43	40
	LS mean (SEM)	-1.8 (0.36)	-1.8 (0.39)	-2.3 (0.42)	-2.5 (0.43)	-2.9 (0.43)	-2.8 (0.43)	-2.6 (0.44)	-3.0 (0.44)	-3.5 (0.43)	-3.3 (0.47)	-3.5 (0.49)	-3.2 (0.45)	-3.1 (0.48)	-3.4 (0.44)	-3.5 (0.44)	-3.3 (0.47)	-3.5 (0.47)	-3.6 (0.47)	-3.6 (0.45)	-3.5 (0.49)	-3.2 (0.51)
	95% CI for LS mean	(-2.5, -1.0)	(-2.5, -1.0)	(-3.1, -1.4)	(-3.4, -1.7)	(-3.7, -2.0)	(-3.6, -1.9)	(-3.5, -1.8)	(-3.8, -2.1)	(-4.3, -2.6)	(-4.3, -2.4)	(-4.5, -2.5)	(-4.1, -2.3)	(-4.1, -2.2)	(-4.3, -2.6)	(-4.3, -2.6)	(-4.3, -2.4)	(-4.4, -2.5)	(-4.5, -2.7)	(-4.5, -2.7)	(-4.5, -2.5)	(-4.2, -2.2)

At 26 weeks, patients who started **ULTOMIRIS within 2 years** of gMG diagnosis were observed to have experienced a **4.7-point reduction in MG-ADL** total score from baseline, compared with a 2.6-point reduction in patients who started more than 2 years after diagnosis.[29]

At 116 weeks, only patients who participated in the OLE and **started ULTOMIRIS within 2 years** of gMG diagnosis were observed to have experienced a **5.3-point reduction in MG-ADL** total score from baseline, compared with a 3.2-point reduction in patients who started more than 2 years after diagnosis.[29]

CHAMPION-MG OLE STUDY LIMITATION:

Results or clinical outcomes should be interpreted with caution since the study was designed to evaluate safety and lacked a control group.

[a]Data for this post hoc analysis were only available through 116 weeks.[29]

BL, baseline; CI, confidence interval; gMG, generalized myasthenia gravis; LS, least squares; MG-ADL, Myasthenia Gravis Activities of Daily Living; SEM, standard error of the mean.

SELECT IMPORTANT SAFETY INFORMATION

WARNINGS AND PRECAUTIONS (continued)

Serious Meningococcal Infections (continued)

Vaccination does not eliminate the risk of serious meningococcal infections, despite development of antibodies following vaccination.

Please see additional Important Safety Information throughout and accompanying full Prescribing Information for ULTOMIRIS, including Boxed WARNING regarding serious and life-threatening or fatal meningococcal infections.

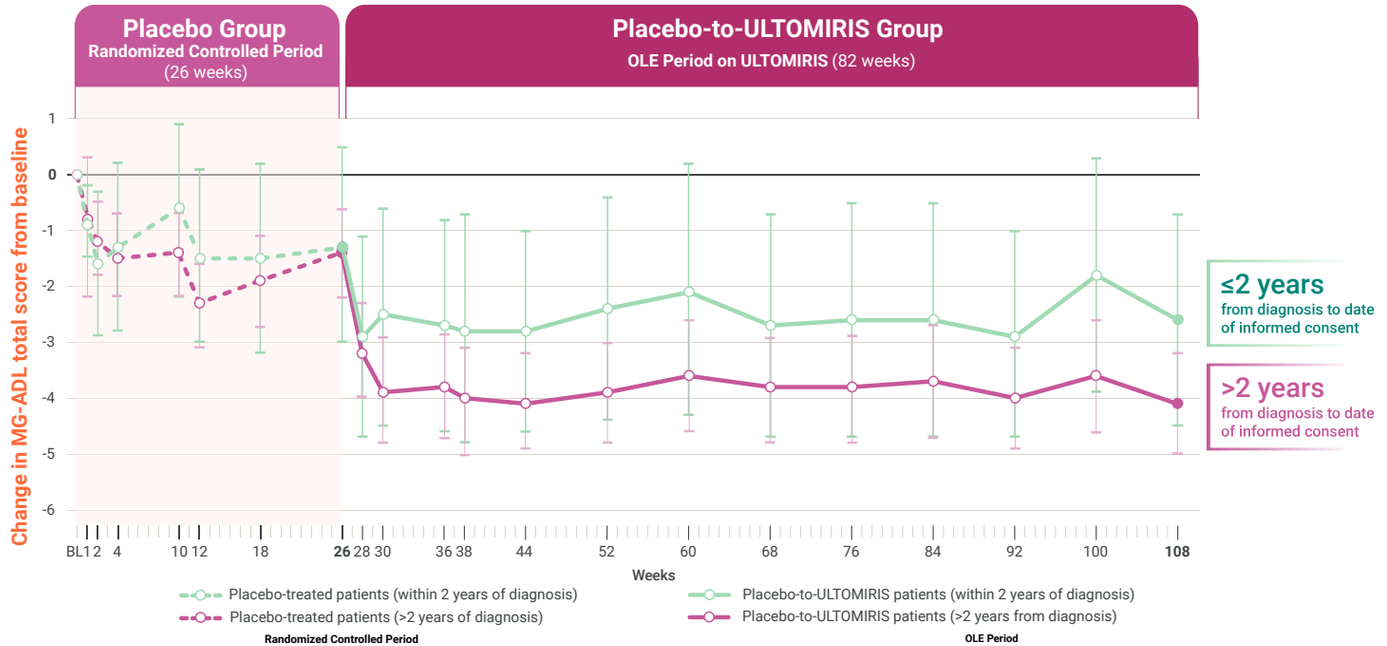
Changes in MG-ADL total score for the placebo-to-ULTOMIRIS® group

(placebo: time from diagnosis to informed consent date)[29,30,a]

ULTOMIRIS® (ravulizumab-cwvz) injection for intravenous use 300 mg/3 mL vial

Placebo → ULTOMIRIS arm

Changes in MG-ADL total score over time, by time from diagnosis to informed consent date



		Randomized Controlled Period (26 weeks)							OLE Period (82 weeks)												
		Week 1	Week 2	Week 4	Week 10	Week 12	Week 18	Week 26	Week 28	Week 30	Week 36	Week 38	Week 44	Week 52	Week 60	Week 68	Week 76	Week 84	Week 92	Week 100	Week 108
≤2 years from diagnosis: (N=16)	n	15	15	13	14	14	13	13	12	11	13	10	11	10	11	11	11	11	11	11	11
	LS mean (SEM)	-0.9 (0.64)	-1.6 (0.64)	-1.3 (0.76)	-0.6 (0.79)	-1.5 (0.78)	-1.5 (0.86)	-1.3 (0.89)	-2.9 (0.90)	-2.5 (1.00)	-2.7 (0.96)	-2.8 (1.03)	-2.8 (0.91)	-2.4 (1.01)	-2.1 (1.13)	-2.7 (1.00)	-2.6 (1.04)	-2.6 (1.04)	-2.9 (0.92)	-1.8 (1.05)	-2.6 (0.97)
	95% CI for LS mean	(-2.2, 0.3)	(-2.9, -0.3)	(-2.8, 0.2)	(-2.2, 0.9)	(-3.0, 0.1)	(-3.2, 0.2)	(-3.0, 0.5)	(-4.7, -1.1)	(-4.5, -0.6)	(-4.6, -0.8)	(-4.8, -0.7)	(-4.6, -1.0)	(-4.4, -0.4)	(-4.3, 0.2)	(-4.7, -0.7)	(-4.7, -0.5)	(-4.7, -0.5)	(-4.7, -1.0)	(-3.9, 0.3)	(-4.5, -0.7)
>2 years from diagnosis: (N=72)	n	70	72	71	71	70	69	69	68	69	69	67	68	66	66	65	63	61	58	57	53
	LS mean (SEM)	-0.8 (0.32)	-1.2 (0.32)	-1.5 (0.37)	-1.4 (0.38)	-2.3 (0.37)	-1.9 (0.40)	-1.4 (0.42)	-3.2 (0.43)	-3.9 (0.46)	-3.8 (0.45)	-4.0 (0.48)	-4.1 (0.43)	-3.9 (0.46)	-3.6 (0.51)	-3.8 (0.46)	-3.8 (0.48)	-3.7 (0.48)	-4.0 (0.44)	-3.6 (0.49)	-4.1 (0.46)
	95% CI for LS mean	(-1.5, -0.2)	(-1.8, -0.5)	(-2.2, -0.7)	(-2.2, -0.7)	(-3.1, -1.6)	(-2.7, -1.1)	(-2.2, -0.6)	(-4.0, -2.3)	(-4.8, -2.9)	(-4.7, -2.9)	(-5.0, -3.1)	(-4.9, -3.2)	(-4.8, -3.0)	(-4.6, -2.6)	(-4.8, -2.9)	(-4.8, -2.9)	(-4.7, -2.7)	(-4.9, -3.1)	(-4.6, -2.6)	(-5.0, -3.2)

In the first 26 weeks, patients were randomized to either placebo or ULTOMIRIS. After completion of the randomized controlled period, patients were eligible to enter the OLE. All patients were treated with ULTOMIRIS in the OLE period.[1,23]

CHAMPION-MG OLE STUDY LIMITATION:

Results or clinical outcomes should be interpreted with caution since the study was designed to evaluate safety and lacked a control group.

"Informed consent" is the point at which patients voluntarily agreed to participate in research after being fully informed about the study.

[a]Data for this post hoc analysis were only available through 108 weeks.[29]

BL, baseline; CI, confidence interval; LS, least squares; MG-ADL, Myasthenia Gravis Activities of Daily Living; SEM, standard error of the mean.

SELECT IMPORTANT SAFETY INFORMATION

WARNINGS AND PRECAUTIONS (continued)

Serious Meningococcal Infections (continued)

Closely monitor patients for early signs and symptoms of meningococcal infection and evaluate patients immediately if infection is suspected. Inform patients of these signs and symptoms and instruct patients to seek immediate medical care if they occur. Promptly treat known infections.

Please see additional Important Safety Information throughout and accompanying full Prescribing Information for ULTOMIRIS, including Boxed WARNING regarding serious and life-threatening or fatal meningococcal infections.

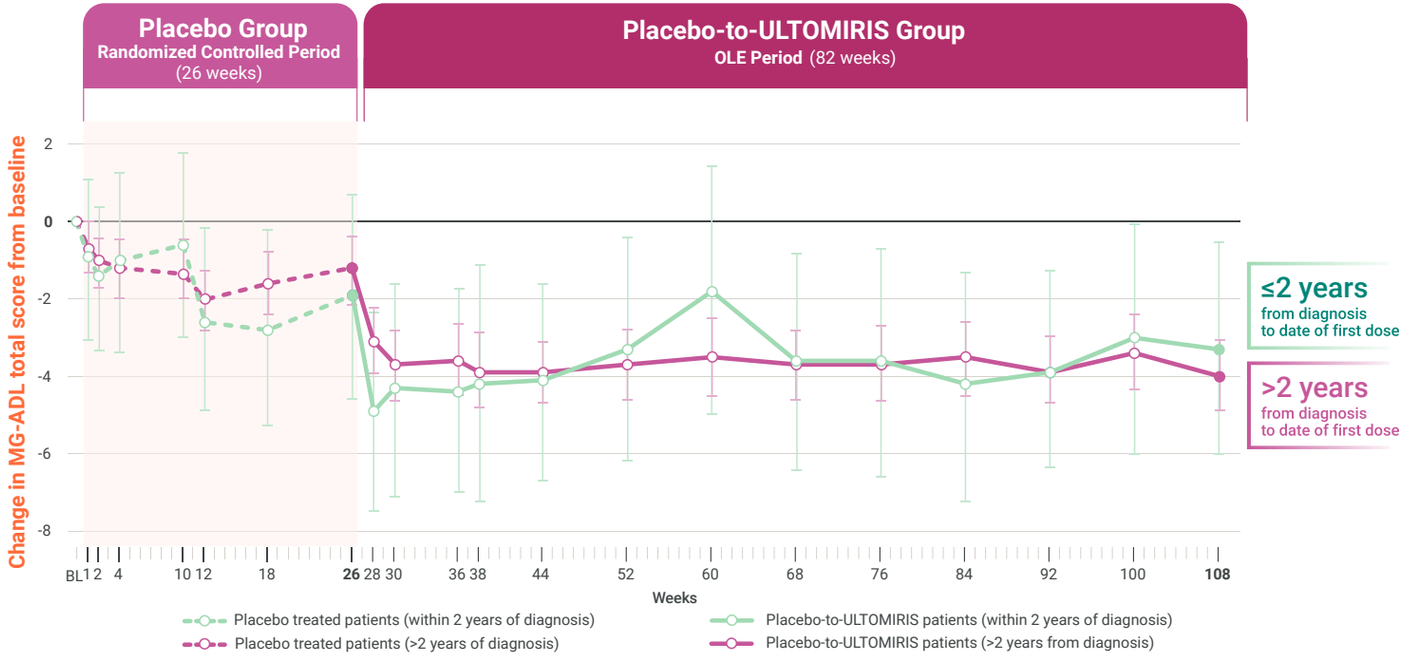
Changes in MG-ADL total score for the placebo-to-ULTOMIRIS® group

(placebo: time from diagnosis to date of first ULTOMIRIS dose)[29,a]

ULTOMIRIS® (ravulizumab-cwvz) injection for intravenous use 300 mg/3 mL vial

Placebo → ULTOMIRIS arm

Changes in MG-ADL total score over time, by time from diagnosis to first dose of ULTOMIRIS



		Randomized Controlled Period (26 weeks)							OLE Period (82 weeks)												
		Week 1	Week 2	Week 4	Week 10	Week 12	Week 18	Week 26	Week 28	Week 30	Week 36	Week 38	Week 44	Week 52	Week 60	Week 68	Week 76	Week 84	Week 92	Week 100	Week 108
≤2 years from diagnosis: (N=6)	n	5	6	5	6	6	6	6	5	5	6	3	5	4	5	5	5	5	5	5	5
	LS mean (SEM)	-0.9 (1.03)	-1.4 (0.94)	-1.0 (1.17)	-0.6 (1.20)	-2.6 (1.18)	-2.8 (1.29)	-1.9 (1.33)	-4.9 (1.26)	-4.3 (1.40)	-4.4 (1.33)	-4.2 (1.51)	-4.1 (1.27)	-3.3 (1.46)	-1.8 (1.62)	-3.6 (1.42)	-3.6 (1.48)	-4.2 (1.49)	-3.9 (1.29)	-3.0 (1.51)	-3.3 (1.38)
	95% CI for LS mean	(-3.0, 1.1)	(-3.3, 0.4)	(-3.4, 1.3)	(-3.0, 1.8)	(-4.9,-0.2)	(-5.3,-0.2)	(-4.6, 0.7)	(-7.5,-2.4)	(-7.1,-1.6)	(-7.0,-1.7)	(-7.2,-1.1)	(-6.7,-1.6)	(-6.2,-0.4)	(-5.0, 1.4)	(-6.4,-0.8)	(-6.6,-0.7)	(-7.2,-1.3)	(-6.4,-1.3)	(-6.0,-0.0)	(-6.0,-0.5)
>2 years from diagnosis: (N=77)	n	75	77	76	77	77	76	76	75	75	76	74	74	72	72	71	69	67	64	63	59
	LS mean (SEM)	-0.7 (0.33)	-1.0 (0.32)	-1.2 (0.37)	-1.3 (0.38)	-2.0 (0.38)	-1.6 (0.40)	-1.2 (0.42)	-3.1 (0.42)	-3.7 (0.45)	-3.6 (0.44)	-3.9 (0.47)	-3.9 (0.42)	-3.7 (0.46)	-3.5 (0.50)	-3.7 (0.45)	-3.7 (0.47)	-3.5 (0.47)	-3.9 (0.43)	-3.4 (0.48)	-4.0 (0.45)
	95% CI for LS mean	(-1.3,-0.0)	(-1.7,-0.4)	(-2.0,-0.5)	(-2.0,-0.5)	(-2.8,-1.3)	(-2.4,-0.8)	(-2.1,-0.4)	(-3.9,-2.2)	(-4.6,-2.8)	(-4.5,-2.7)	(-4.8,-2.9)	(-4.7,-3.1)	(-4.6,-2.8)	(-4.5,-2.5)	(-4.6,-2.8)	(-4.6,-2.7)	(-4.5,-2.6)	(-4.7,-3.0)	(-4.3,-2.4)	(-4.9,-3.1)

In the first 26 weeks, patients were randomized to either placebo or ULTOMIRIS. After completion of the randomized controlled period, patients were eligible to enter the OLE. All patients were treated with ULTOMIRIS in the OLE period.[1,23]

CHAMPION-MG OLE STUDY LIMITATION:

Results or clinical outcomes should be interpreted with caution since the study was designed to evaluate safety and lacked a control group.

For the placebo-to-ULTOMIRIS groups, the definition of "time from diagnosis" was evaluated for time from diagnosis to each of: 1) date of informed consent and 2) date of first ULTOMIRIS dose.

[a]Data for this post hoc analysis were only available through 108 weeks.[29]

BL, baseline; CI, confidence interval; LS, least squares; MG-ADL, Myasthenia Gravis Activities of Daily Living; SEM, standard error of the mean.

SELECT IMPORTANT SAFETY INFORMATION

WARNINGS AND PRECAUTIONS (continued)

Serious Meningococcal Infections (continued)

Meningococcal infection may become rapidly life-threatening or fatal if not recognized and treated early. Consider interruption of ULTOMIRIS in patients who are undergoing treatment for serious meningococcal infection depending on the risks of interrupting treatment in the disease being treated.

Please see additional Important Safety Information throughout and accompanying full Prescribing Information for ULTOMIRIS, including Boxed WARNING regarding serious and life-threatening or fatal meningococcal infections.

INDICATION & IMPORTANT SAFETY INFORMATION

ULTOMIRIS®
(ravulizumab-cwvz)
injection for intravenous use
300 mg/3 mL vial

INDICATION

ULTOMIRIS is indicated for the treatment of adult patients with generalized myasthenia gravis (gMG) who are anti-acetylcholine receptor (AChR) antibody-positive.

IMPORTANT SAFETY INFORMATION

WARNING: SERIOUS MENINGOCOCCAL INFECTIONS

ULTOMIRIS, a complement inhibitor, increases the risk of serious infections caused by *Neisseria meningitidis* [*see Warnings and Precautions (5.1)*] Life-threatening and fatal meningococcal infections have occurred in patients treated with complement inhibitors. These infections may become rapidly life-threatening or fatal if not recognized and treated early.

- **Complete or update vaccination for meningococcal bacteria (for serogroups A, C, W, Y, and B) at least 2 weeks prior to the first dose of ULTOMIRIS, unless the risks of delaying ULTOMIRIS therapy outweigh the risk of developing a serious infection. Comply with the most current Advisory Committee on Immunization Practices (ACIP) recommendations for vaccinations against meningococcal bacteria in patients receiving a complement inhibitor. See *Warnings and Precautions (5.1)* for additional guidance on the management of the risk of serious infections caused by meningococcal bacteria.**
- **Patients receiving ULTOMIRIS are at increased risk for invasive disease caused by *Neisseria meningitidis*, even if they develop antibodies following vaccination. Monitor patients for early signs and symptoms of serious meningococcal infections and evaluate immediately if infection is suspected.**

Because of the risk of serious meningococcal infections, ULTOMIRIS is available only through a restricted program under a Risk Evaluation and Mitigation Strategy (REMS) called ULTOMIRIS and SOLIRIS REMS [*see Warnings and Precautions (5.2)*].

CONTRAINDICATIONS

- Initiation in patients with unresolved serious *Neisseria meningitidis* infection.

WARNINGS AND PRECAUTIONS

Serious Meningococcal Infections

ULTOMIRIS, a complement inhibitor, increases a patient's susceptibility to serious, life-threatening, or fatal infections caused by meningococcal bacteria (septicemia and/or meningitis) in any serogroup, including non-groupable strains. Life-threatening and fatal meningococcal infections have occurred in both vaccinated and unvaccinated patients treated with complement inhibitors.

Revaccinate patients in accordance with ACIP recommendations considering the duration of ULTOMIRIS therapy. Note that ACIP recommends an administration schedule in patients receiving complement inhibitors that differs from the administration schedule in the vaccine prescribing information. If urgent ULTOMIRIS therapy is indicated in a patient who is not up to date with meningococcal vaccines according to ACIP recommendations, provide antibacterial drug prophylaxis and administer meningococcal vaccines as soon as possible. Various durations and regimens of antibacterial drug prophylaxis have been considered, but the optimal durations and drug regimens for prophylaxis and their efficacy have not been studied in unvaccinated or vaccinated patients receiving complement inhibitors, including ULTOMIRIS. The benefits and risks of treatment with ULTOMIRIS, as well as those associated with antibacterial drug prophylaxis in unvaccinated or vaccinated patients, must be considered against the known risks for serious infections caused by *Neisseria meningitidis*.

Vaccination does not eliminate the risk of serious meningococcal infections, despite development of antibodies following vaccination.

Closely monitor patients for early signs and symptoms of meningococcal infection and evaluate patients immediately if infection is suspected. Inform patients of these signs and symptoms and instruct patients to seek immediate medical care if they occur. Promptly treat known infections. Meningococcal infection may become rapidly life-threatening or fatal if not recognized and treated early. Consider interruption of ULTOMIRIS in patients who are undergoing treatment for serious meningococcal infection depending on the risks of interrupting treatment in the disease being treated.

Please see accompanying full Prescribing Information for ULTOMIRIS, including Boxed WARNING regarding serious and life-threatening or fatal meningococcal infections.

IMPORTANT SAFETY INFORMATION (continued)

WARNINGS AND PRECAUTIONS (continued)

ULTOMIRIS and SOLIRIS REMS

Due to the risk of serious meningococcal infections, ULTOMIRIS is available only through a restricted program called ULTOMIRIS and SOLIRIS REMS.

Prescribers must enroll in the REMS, counsel patients about the risk of serious meningococcal infection, provide patients with the REMS educational materials, assess patient vaccination status for meningococcal vaccines (against serogroups A, C, W, Y, and B) and vaccinate if needed according to current ACIP recommendations two weeks prior to the first dose of ULTOMIRIS. Antibacterial drug prophylaxis must be prescribed if treatment must be started urgently, and the patient is not up to date with both meningococcal vaccines according to current ACIP recommendations at least two weeks prior to the first dose of ULTOMIRIS. Patients must receive counseling about the need to receive meningococcal vaccines and to take antibiotics as directed, signs and symptoms of meningococcal infection, and be instructed to carry the Patient Safety Card at all times during and for 8 months following ULTOMIRIS treatment.

Further information is available at www.UltSolREMS.com or 1-888-765-4747.

Other Infections

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

ULTOMIRIS blocks terminal complement activation; therefore, patients may have increased susceptibility to infections, especially with encapsulated bacteria, such as infections caused by *Neisseria meningitidis* but also *Streptococcus pneumoniae*, *Haemophilus influenzae*, and to a lesser extent, *Neisseria gonorrhoeae*. Patients receiving ULTOMIRIS are at increased risk for infections due to these organisms, even if they develop antibodies following vaccination.

Thromboembolic Event Management

The effect of withdrawal of anticoagulant therapy during treatment with ULTOMIRIS has not been established. Treatment should not alter anticoagulant management.

Infusion-Related Reactions

Administration of ULTOMIRIS may result in systemic infusion-related reactions, including anaphylaxis and hypersensitivity reactions. In clinical trials, infusion-related reactions occurred in approximately 1 to 7% of patients, including lower back pain, abdominal pain, muscle spasms, drop or elevation in blood pressure, rigors, limb discomfort, drug hypersensitivity (allergic reaction), and dysgeusia (bad taste). These reactions did not require discontinuation of ULTOMIRIS. If signs of cardiovascular instability or respiratory compromise occur, interrupt ULTOMIRIS and institute appropriate supportive measures.

ADVERSE REACTIONS

Most common adverse reactions in adult patients with gMG (incidence ≥10%) were diarrhea and upper respiratory tract infection. Serious adverse reactions were reported in 20 (23%) of patients treated with ULTOMIRIS and in 14 (16%) patients receiving placebo. The most frequent serious adverse reactions were infections reported in at least 8 (9%) patients treated with ULTOMIRIS and in 4 (4%) patients treated with placebo. Of these infections, one fatal case of COVID-19 pneumonia was identified in a patient treated with ULTOMIRIS and one case of infection led to discontinuation of ULTOMIRIS.

DRUG INTERACTIONS

Plasma Exchange, Plasmapheresis, and Intravenous Immunoglobulins

Concomitant use of ULTOMIRIS with plasma exchange (PE), plasmapheresis (PP), or intravenous immunoglobulin (IVIg) treatment can reduce serum ravulizumab concentrations and requires a supplemental dose of ULTOMIRIS.

Neonatal Fc Receptor Blockers

Concomitant use of ULTOMIRIS with neonatal Fc receptor (FcRn) blockers (e.g., efgartigimod) may lower systemic exposures and reduce effectiveness of ULTOMIRIS. Closely monitor for reduced effectiveness of ULTOMIRIS.

USE IN SPECIFIC POPULATIONS

Pregnancy Exposure Registry

There is a pregnancy exposure registry that monitors pregnancy outcomes in women exposed to ULTOMIRIS during pregnancy. Healthcare providers and patients may call 1-833-793-0563 or go to www.UltomirisPregnancyStudy.com to enroll in or to obtain information about the registry.

To report SUSPECTED ADVERSE REACTIONS, contact Alexion Pharmaceuticals, Inc. at 1-844-259-6783 or FDA at 1-800-FDA-1088 or www.fda.gov/medwatch.

Please see accompanying full Prescribing Information for ULTOMIRIS, including Boxed WARNING regarding serious and life-threatening or fatal meningococcal infections.

For your adult patients with gMG who are anti-acetylcholine receptor (AChR) antibody-positive[1]

ULTOMIRIS® (ravulizumab-cwvz)
injection for intravenous use
300 mg/3 mL vial

ULTOMIRIS® offers adult patients:

2x

More than 2x greater improvement in MG-ADL total score from baseline at Week 26 vs placebo (-3.1 vs -1.4, respectively [*P*<0.001])[1,23]

Based on MG-ADL assessment of symptoms in the 26-week trial, which measures how gMG affects daily functions through 8 commonly impacted signs and symptoms[1]

A targeted MOA—specifically binds to C5 to prevent MAC formation, a key driver of NMJ damage, while avoiding broad immune suppression, so the effect on B cells and other immune responses may be minimized[1,3,19,23]

An established safety profile[1]

Most common adverse reactions occurring in ≥10% of patients taking ULTOMIRIS were diarrhea and upper respiratory tract infection[1]

Consider early meningococcal vaccination for patients who may benefit from C5 inhibition at some point in their treatment journey

Due to changes to vaccination recommendations, primary meningococcal vaccinations may take 6 months.

Learn more about ULTOMIRIS at UltomirisHCP.com/gMG

C5, complement component 5; gMG, generalized myasthenia gravis; MAC, membrane attack complex; MG-ADL, Myasthenia Gravis Activities of Daily Living; MOA, mechanism of action; NMJ, neuromuscular junction.

SELECT IMPORTANT SAFETY INFORMATION

WARNING: SERIOUS MENINGOCOCCAL INFECTIONS

ULTOMIRIS, a complement inhibitor, increases the risk of serious infections caused by *Neisseria meningitidis* [*see Warnings and Precautions (5.1)*] Life-threatening and fatal meningococcal infections have occurred in patients treated with complement inhibitors. These infections may become rapidly life-threatening or fatal if not recognized and treated early.

- **Complete or update vaccination for meningococcal bacteria (for serogroups A, C, W, Y, and B) at least 2 weeks prior to the first dose of ULTOMIRIS, unless the risks of delaying ULTOMIRIS therapy outweigh the risk of developing a serious infection. Comply with the most current Advisory Committee on Immunization Practices (ACIP) recommendations for vaccinations against meningococcal bacteria in patients receiving a complement inhibitor. See *Warnings and Precautions (5.1)* for additional guidance on the management of the risk of serious infections caused by meningococcal bacteria.**
- **Patients receiving ULTOMIRIS are at increased risk for invasive disease caused by *Neisseria meningitidis*, even if they develop antibodies following vaccination. Monitor patients for early signs and symptoms of serious meningococcal infections and evaluate immediately if infection is suspected.**

Because of the risk of serious meningococcal infections, ULTOMIRIS is available only through a restricted program under a Risk Evaluation and Mitigation Strategy (REMS) called ULTOMIRIS and SOLIRIS REMS [*see Warnings and Precautions (5.2)*].

References: 1. ULTOMIRIS. Prescribing Information. Alexion Pharmaceuticals, Inc. **2.** Zhou Y, et al. *J Immunol.* 2007;179(12):8562-8567. **3.** Howard JF Jr. *Ann N Y Acad Sci.* 2018;1412(1):113-128. **4.** Kusner LL, et al. *Ann N Y Acad Sci.* 2012;1274(1):127-132. **5.** Meriggioli MN, et al. *Lancet Neurol.* 2009;8(5):475-490. **6.** Conti-Fine BM, et al. *J Clin Invest.* 2006;116(11):2843-2854. **7.** Khani-Habibabadi F, et al. *Neurol Neuroimmunol Neuroinflamm.* 2025;12(5):e200436. **8.** Rother RP, et al. *Nat Biotechnol.* 2007;25(11):1256-1264. **9.** Michailidou I, et al. *Front Immunol.* 2025;16:1526317. **10.** Dalakas MC, et al. *Expert Rev Clin Immunol.* 2022;18(7):691-701. **11.** Grob D, et al. *Muscle Nerve.* 2008;37(2):141-149. **12.** Tomschik M, et al. *Neurology.* 2020;95(10):e1426-e1436. **13.** Howard JF Jr, et al. *Muscle Nerve.* 2024;69(5):556-565. **14.** Jackson K, et al. *Neurol Ther.* 2023;12(1):107-128. **15.** Obaid AH, et al. *Neurol Neuroimmunol Neuroinflamm.* 2022;9(4):e1169. **16.** Merle NS, et al. *Front Immunol.* 2015;6:262. **17.** Walport MJ. *N Engl J Med.* 2001;344(14):1058-1066. **18.** Dunkelberger JR, Song WC. *Cell Res.* 2010;20(1):34-50. **19.** Ricklin D, et al. *Nat Immunol.* 2010;11(9):785-797. **20.** Innate and Adaptive Immunity. Creative Diagnostics. Accessed December 4, 2025. https://www.creative-diagnostics.com/innate-and-adaptive-immunity.htm **21.** National Institute of Allergy and Infectious Diseases. Features of an immune response. Updated January 16, 2014. Accessed October 6, 2025. https://www.niaid.nih.gov/research/immune-response-features **22.** Howard JF, et al. *Lancet Neurol.* 2021;20(7):526-536. **23.** Vu T, et al. *NEJM Evid.* 2022;1(5):1-12. **24.** Murphy K, et al. *Janeway's Immunobiology.* 10th ed. W.W. Norton; 2022:1-2396. **25.** Vu T, et al. *J Neurol.* 2023;270(6):3129-3137. **26.** Kulasekararaj AG, et al. *Blood.* 2019;133(6):540-549. **27.** Lee JW, et al. *Blood.* 2019;133(6):530-539. **28.** Vu T, et al. *Eur J Neurol.* 2025;32(4):e70158. **29.** Data on file. Alexion Pharmaceuticals, Inc. **30.** National Institutes of Health. The basics. Updated April 24, 2025. Accessed October 6, 2025. https://www.nih.gov/health-information/nih-clinical-research-trials-you/basics

Please see additional Important Safety Information throughout and accompanying full Prescribing Information for ULTOMIRIS, including Boxed WARNING regarding serious and life-threatening or fatal meningococcal infections.

ALEXION
AstraZeneca Rare Disease

US/ULT-g/1049 V1 12/2025