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Widen the world for your patients with PNH

Case 1

Reason for Visit[a]

- Is concerned about managing a busy work and travel schedule around biweekly infusions with eculizumab
- Wants to discuss whether she is a candidate for a reduced infusion frequency with ULTOMIRIS

Patient History[a]

- 56-year-old woman with PNH diagnosis
- History of anemia and Budd-Chiari syndrome
- Stable condition on labeled-maintenance dosing of eculizumab for the past 2 years

PNH, paroxysmal nocturnal hemoglobinuria.

[a]This patient narrative was deidentified and adapted from an actual patient case.

Please see accompanying full Prescribing Information for ULTOMIRIS, including Boxed WARNING regarding serious and life-threatening meningococcal infections/sepsis. Please see Important Safety Information on inside flap.

US/ULT-P/0024

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INDICATION

ULTOMIRIS is indicated for the treatment of adult patients with paroxysmal nocturnal hemoglobinuria (PNH).

SELECT IMPORTANT SAFETY INFORMATION

WARNING:
SERIOUS MENINGOCOCCAL INFECTIONS

Life-threatening meningococcal infections/sepsis have occurred in patients treated with ULTOMIRIS. Meningococcal infection 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 ULTOMIRIS, unless the risks of delaying ULTOMIRIS therapy outweigh the risk of developing a meningococcal infection. See *Warnings and Precautions* 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.**

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

CONTRAINDICATIONS

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

WARNINGS AND PRECAUTIONS

Serious Meningococcal Infections

Risk and Prevention

Life-threatening meningococcal infections have occurred in patients treated with ULTOMIRIS. The use of ULTOMIRIS increases a patient's susceptibility to serious meningococcal infections (septicemia and/or meningitis). Meningococcal disease due to any serogroup may occur.

Vaccinate or revaccinate for meningococcal disease according to the most current ACIP recommendations for patients with complement deficiencies. Immunize patients without history of meningococcal vaccination at least 2 weeks prior to the first dose of ULTOMIRIS. If ULTOMIRIS must be initiated immediately in an unvaccinated patient, administer meningococcal vaccine(s) as soon as possible and provide 2 weeks of antibacterial drug prophylaxis. In clinical studies, 59 patients with PNH were treated with ULTOMIRIS less than 2 weeks after meningococcal vaccination. All of these patients received antibiotics for prophylaxis of meningococcal infection until at least 2 weeks after meningococcal vaccination. The benefits and risks of antibiotic prophylaxis for prevention of meningococcal infections in patients receiving ULTOMIRIS have not been established. In PNH clinical studies, 3 out of 261 PNH patients developed serious meningococcal infections/sepsis while receiving treatment with ULTOMIRIS; all 3 had been vaccinated. These 3 patients recovered while continuing treatment with ULTOMIRIS. Consider discontinuation of ULTOMIRIS in patients who are undergoing treatment for serious meningococcal infection.

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SELECT IMPORTANT SAFETY INFORMATION (CON'T)

REMS
Under the ULTOMIRIS REMS, prescribers must enroll in the program due to the risk of meningococcal infections. Prescribers must counsel patients about the risk of meningococcal infection/sepsis, provide the patients with the REMS educational materials, and ensure patients are vaccinated with meningococcal vaccines.

Other Infections
Patients may have increased susceptibility to encapsulated bacteria infections, especially infections caused by *Neisseria meningitidis* but also *Streptococcus pneumoniae, Haemophilus influenzae,* and to a lesser extent, *Neisseria gonorrhoeae*. If ULTOMIRIS is administered to patients with active systemic infections, monitor closely for worsening infection.

Monitoring Disease Manifestations after ULTOMIRIS Discontinuation
After discontinuing treatment with ULTOMIRIS, closely monitor for signs and symptoms of hemolysis, identified by elevated LDH along with sudden decrease in PNH clone size or hemoglobin, or reappearance of symptoms such as fatigue, hemoglobinuria, abdominal pain, shortness of breath (dyspnea), major adverse vascular event (including thrombosis), dysphagia, or erectile dysfunction. Monitor any patient who discontinues ULTOMIRIS for at least 16 weeks to detect hemolysis and other reactions. If signs and symptoms of hemolysis occur after discontinuation, including elevated LDH, consider restarting treatment with ULTOMIRIS.

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 infusion-related reactions. In clinical trials, 5 out of 296 patients treated with ULTOMIRIS experienced infusion-related reactions (lower back pain, drop in blood pressure, infusion-related pain, elevation in blood pressure and limbs discomfort) during ULTOMIRIS administration which did not require discontinuation. Interrupt infusion and institute supportive measures if signs of cardiovascular instability or respiratory compromise occur.

ADVERSE REACTIONS
Adverse reactions reported in 5% or more of patients treated with ULTOMIRIS vs. Eculizumab was Upper respiratory tract infection (39% vs. 39%), Headache (32% vs. 26%), Diarrhea (9% vs. 5%), Nausea (9% vs. 9%), Pyrexia (7% vs. 8%), Pain in extremity (6% vs. 5%), Abdominal pain (6% vs. 7%), Dizziness (5% vs. 6%), Arthralgia (5% vs. 5%).

Serious adverse reactions were reported in 15 (6.8%) patients receiving ULTOMIRIS. The serious adverse reactions in patients treated with ULTOMIRIS included hyperthermia and pyrexia. No serious adverse reaction was reported in more than 1 patient treated with ULTOMIRIS.

One fatal case of sepsis was identified in a patient treated with ULTOMIRIS.

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

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ALEXION®

Diagnostic Journey

2 years

Patient history (Age: 53)

Clinical presentation
Anemia, severe upper quadrant abdominal pain

Lab Values

Hb: 10 g/dL
Reticulocytes: 4.9%
WBC: 3.9 x 10^9/L
PLTs: 100 x 10^9/L
LDH: 900 U/L
Bilirubin: 3 mg/dL
AST: 90 U/L
ALT: 75 U/L
D-dimer: 2400 ng/mL
Coombs Test: Negative result
Spiral CT of the Abdomen: Hepatic vein thrombosis (Budd-Chiari syndrome)

Diagnosis
PNH
Owing to evidence of Coombs-negative hemolytic anemia, HSFC—performed on peripheral blood—identified PNH clone (granulocytes, 67%)

Management
Eculizumab (concurrent with meningococcal vaccination and 2 weeks of prophylactic antibiotics) and anticoagulant therapy were started

Adverse events
Headache

3 months

Clinical presentation
The patient has remained clinically stable on labeled-maintenance doses of eculizumab for the past 2 years (ie, LDH levels within normal limits, asymptomatic)

Lab values
PNH granulocyte clone: 68%

Management
Eculizumab; anticoagulant therapy discontinued per patient request

The effect of withdrawal of anticoagulant therapy during eculizumab treatment has not been established. Therefore, treatment with eculizumab should not alter anticoagulant management.

Adverse events
No adverse event reported

4 months

Current visit (Age: 56) switched to ULTOMIRIS

Clinical presentation
The patient remains clinically stable on eculizumab but has expressed interest in less frequent infusions. She comes in for a routine visit and to discuss whether she is a candidate for a reduced infusion frequency with ULTOMIRIS

Lab values before switching to ULTOMIRIS

Hb: 10.8 g/dL
Reticulocytes: 5.1%
WBC: 3.5 x 10^9/L
PLTs: 135 x 10^9/L
LDH: 225 U/L
Bilirubin: 1.0 mg/dL

Management
ULTOMIRIS was started

Adverse events
Headache

10 months

Clinical presentation
The patient was safely and effectively switched from eculizumab to ULTOMIRIS and has been clinically stable for the past 6 months

6-Month post-ULTOMIRIS lab values

Hb: 11 g/dL
Reticulocytes: 5.2%
WBC: 4.2 x 10^9/L
PLTs: 140 x 10^9/L
LDH: 225 U/L
Bilirubin: 1.0 mg/dL
PNH granulocyte clone: 72%

Adverse events
Nausea

Reference ranges		
	ALT, U/L: 6-29	**LDH, U/L:** 246
	AST, U/L: 10-35	**PLT, x 10^9/L:** 140-400
	Bilirubin, mg/dL: 0.2-1.2	**Reticulocytes, %:** 0.5-1.5
	D-dimer, ng/mL: <500	**WBC, x 10^9/L:** 3.8-10.8
	Hb (female), g/dL: 11.7-15.5	

Individual results may vary.

Reference ranges for Hb, PLT, WBC, D-dimer, bilirubin, AST, and ALT from Quest Diagnostics; reference range for reticulocytes from MedlinePlus; reference for LDH from study 302.

ALT, alanine aminotransferase; AST, aspartate aminotransferase; CT, computed tomography; Hb, hemoglobin; HSFC, high-sensitivity flow cytometry; lab, laboratory; LDH, lactate dehydrogenase; PLTs, platelets; PNH, paroxysmal nocturnal hemoglobinuria; WBC, white blood cell.

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

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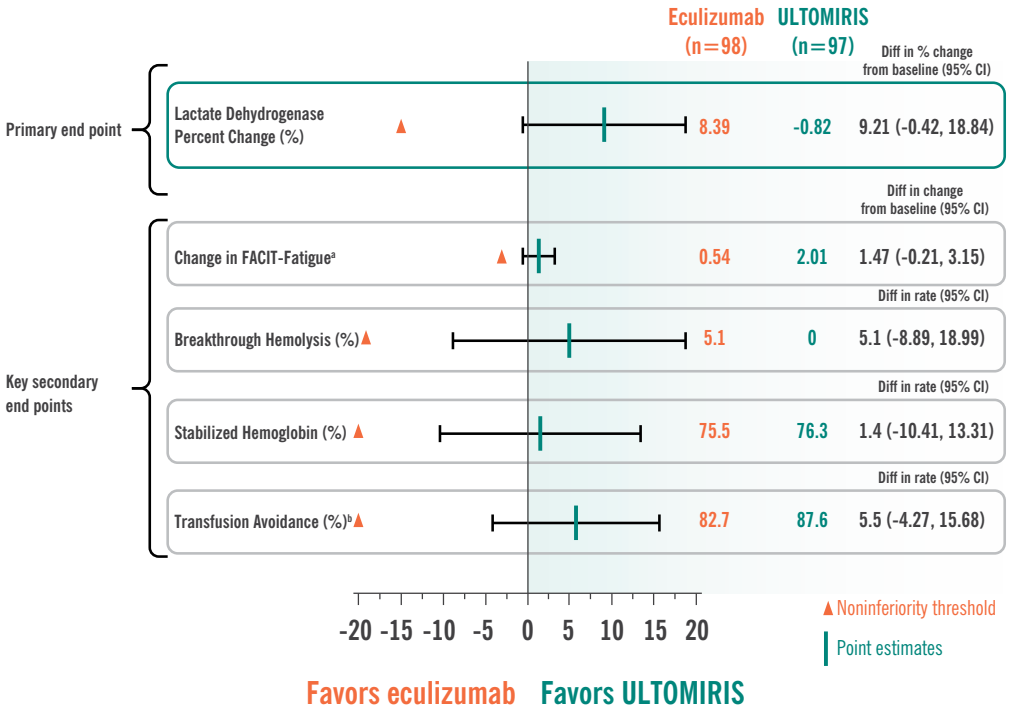
In the Switch Study (302), ULTOMIRIS was noninferior to eculizumab on all primary and key secondary efficacy end points[1,2]

The ULTOMIRIS Switch Study (302) (ALXN1210-PNH-302; NCT03056040) was a 26-week, multicenter, open-label, randomized, active-controlled, noninferiority, phase 3 study conducted in 195 patients with PNH who were clinically stable after having been treated with eculizumab for at least the past 6 months.[1,2]

Efficacy Results Across Primary and Key Secondary End Points[1,2]



[a]There was no observable difference in fatigue between ULTOMIRIS and eculizumab after 26 weeks of treatment compared with baseline, as measured by the FACIT-Fatigue instrument. Patient-reported fatigue may be an under- or over-estimation, because patients were not blinded to treatment assignment. [b]For the transfusion avoidance endpoint, treatment differences (95% CIs) are based on estimated differences in percent with 95% CI.

- ULTOMIRIS demonstrated immediate and complete inhibition of serum C5 by the end of the first infusion, and this effect was sustained throughout the treatment period in all patients.[1]
- Breakthrough hemolysis occurred in 0% of ULTOMIRIS-treated patients and 5.1% of eculizumab-treated patients (difference in rate, 5.1% [95% CI, -8.9 to 19.0]).[1]
- Patients with PNH were safely and effectively switched from eculizumab every-2-weeks to ULTOMIRIS every-8-weeks.[1]
- The safety profile of ULTOMIRIS was similar to that of eculizumab. The 4 most common adverse events occurring in ≥5% of patients in the ULTOMIRIS and eculizumab groups were, respectively, headache (26.8% vs 17.3%), nasopharyngitis (21.6% vs 20.4%), upper respiratory tract infection (18.6% vs 10.2%), and diarrhea (9.3% vs 7.1%).[1]

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FACIT, Functional Assessment of Chronic Illness Therapy; Hb, hemoglobin; LDH, lactate dehydrogenase; PNH, paroxysmal nocturnal hemoglobinuria.

1. Kulasekararaj AG, et al. *Blood*. 2019;133(6):540-549. **2.** ULTOMIRIS [Prescribing Information]. Alexion Pharmaceuticals, Inc; Boston, MA: October 2020.

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Widen the world for your patients with PNH

Case 2

Reason for Visit[a]

- Presents for routine visit for PNH
- Wants to discuss how to manage current Q2W infusion regimen with eculizumab in light of increased overseas travel as part of new job

Patient History[a]

- 32-year-old man with PNH diagnosed 13 years ago
- 2 episodes of Budd-Chiari syndrome
- Clinically stable condition on eculizumab for the past 9 years
- 1 breakthrough hemolysis event in the past year

PNH, paroxysmal nocturnal hemoglobinuria; Q2W, every-2-weeks.

[a]The narrative was deidentified and adapted from an actual patient case from the extension phase of the ULTOMIRIS Switch Study (302) clinical trial.

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INDICATION

ULTOMIRIS is indicated for the treatment of adult patients with paroxysmal nocturnal hemoglobinuria (PNH).

SELECT IMPORTANT SAFETY INFORMATION

WARNING:
SERIOUS MENINGOCOCCAL INFECTIONS

Life-threatening meningococcal infections/sepsis have occurred in patients treated with ULTOMIRIS. Meningococcal infection 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 ULTOMIRIS, unless the risks of delaying ULTOMIRIS therapy outweigh the risk of developing a meningococcal infection. See *Warnings and Precautions* 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.**

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CONTRAINDICATIONS

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

WARNINGS AND PRECAUTIONS

Serious Meningococcal Infections

Risk and Prevention

Life-threatening meningococcal infections have occurred in patients treated with ULTOMIRIS. The use of ULTOMIRIS increases a patient's susceptibility to serious meningococcal infections (septicemia and/or meningitis). Meningococcal disease due to any serogroup may occur.

Vaccinate or revaccinate for meningococcal disease according to the most current ACIP recommendations for patients with complement deficiencies. Immunize patients without history of meningococcal vaccination at least 2 weeks prior to the first dose of ULTOMIRIS. If ULTOMIRIS must be initiated immediately in an unvaccinated patient, administer meningococcal vaccine(s) as soon as possible and provide 2 weeks of antibacterial drug prophylaxis. In clinical studies, 59 patients with PNH were treated with ULTOMIRIS less than 2 weeks after meningococcal vaccination. All of these patients received antibiotics for prophylaxis of meningococcal infection until at least 2 weeks after meningococcal vaccination. The benefits and risks of antibiotic prophylaxis for prevention of meningococcal infections in patients receiving ULTOMIRIS have not been established. In PNH clinical studies, 3 out of 261 PNH patients developed serious meningococcal infections/sepsis while receiving treatment with ULTOMIRIS; all 3 had been vaccinated. These 3 patients recovered while continuing treatment with ULTOMIRIS. Consider discontinuation of ULTOMIRIS in patients who are undergoing treatment for serious meningococcal infection.

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SELECT IMPORTANT SAFETY INFORMATION (CON'T)

REMS
Under the ULTOMIRIS REMS, prescribers must enroll in the program due to the risk of meningococcal infections. Prescribers must counsel patients about the risk of meningococcal infection/sepsis, provide the patients with the REMS educational materials, and ensure patients are vaccinated with meningococcal vaccines.

Other Infections
Patients may have increased susceptibility to encapsulated bacteria infections, especially infections caused by *Neisseria meningitidis* but also *Streptococcus pneumoniae, Haemophilus influenzae,* and to a lesser extent, *Neisseria gonorrhoeae*. If ULTOMIRIS is administered to patients with active infections, monitor closely for worsening infection.

Monitoring Disease Manifestations after ULTOMIRIS Discontinuation
After discontinuing treatment with ULTOMIRIS, closely monitor for signs and symptoms of hemolysis, identified by elevated LDH along with sudden decrease in PNH clone size or hemoglobin, or reappearance of symptoms such as fatigue, hemoglobinuria, abdominal pain, shortness of breath (dyspnea), major adverse vascular event (including thrombosis), dysphagia, or erectile dysfunction. Monitor any patient who discontinues ULTOMIRIS for at least 16 weeks to detect hemolysis and other reactions. If signs and symptoms of hemolysis occur after discontinuation, including elevated LDH, consider restarting treatment with ULTOMIRIS.

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 infusion-related reactions. In clinical trials, 5 out of 296 patients treated with ULTOMIRIS experienced infusion-related reactions (lower back pain, drop in blood pressure, infusion-related pain, elevation in blood pressure and limbs discomfort) during ULTOMIRIS administration, which did not require discontinuation. Interrupt infusion and institute supportive measures if signs of cardiovascular instability or respiratory compromise occur.

ADVERSE REACTIONS
Adverse reactions reported in 5% or more of patients treated with ULTOMIRIS vs. Eculizumab was Upper respiratory tract infection (39% vs. 39%), Headache (32% vs. 26%), Diarrhea (9% vs. 5%), Nausea (9% vs. 9%), Pyrexia (7% vs. 8%), Pain in extremity (6% vs. 5%), Abdominal pain (6% vs. 7%), Dizziness (5% vs. 6%), Arthralgia (5% vs. 5%).

Serious adverse reactions were reported in 15 (6.8%) patients receiving ULTOMIRIS. The serious adverse reactions in patients treated with ULTOMIRIS included hyperthermia and pyrexia. No serious adverse reaction was reported in more than 1 patient treated with ULTOMIRIS.

One fatal case of sepsis was identified in a patient treated with ULTOMIRIS.

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ALEXION®

Diagnostic Journey

2004

Patient history

Age: 19

Clinical presentation
Anemia, elevated bilirubin

Lab values
Coombs Test: Negative result

Diagnosis
PNH
Owing to evidence of Coombs-negative hemolytic anemia, HSFC—performed on peripheral blood—identified PNH clone

Management
Supportive measures with iron, vitamin B12, and folic acid supplementation

2005-2007

Age: 20

2005 Clinical presentation
Abdominal pain

Lab tests
Abdominal CT: Ascites, hepatosplenomegaly

Diagnosis
Budd-Chiari syndrome

Management
Low molecular weight heparin (LMWH)

2005-2007 Ongoing management
Between late 2005 and 2007, the patient had intermittent bouts of fatigue and required 5 RBC transfusions in addition to continued LMWH

Folic acid, vitamin B12, and iron supplementation were added to his regimen

2008

Age: 23

Clinical presentation
Recurrence of hepatosplenomegaly, now with jaundice, ascites, and a deep vein thrombosis

Lab values
Hb: 7.5 g/dL
WBC: 5 x 10^9/L
LDH: 1264 U/L
Hematocrit: 22.9%
D-dimer: >4000 ng/mL

Diagnosis
Recurrent thrombotic events despite anticoagulation therapy

Management
Patient received eculizumab concurrent with meningococcal vaccination and 2 weeks of prophylactic antibiotics. No further RBC transfusions needed. LMWH therapy was continued

Adverse events
Patient experienced headache after the first eculizumab infusion

Early 2017

Current visit (Age: 32)

Clinical presentation
The patient experienced a breakthrough hemolysis event associated with gastroenteritis in the previous year but has been clinically stable on labeled-maintenance dosing of eculizumab for >6 months. However, the patient feels his Q2W dosing schedule is not compatible with his current lifestyle

Management
Because of his medical history, he was a candidate for the ULTOMIRIS Switch Study (302) of patients with PNH who were treated with and clinically stable on eculizumab for ≥6 months[a]

Enrollment in Study 302
The patient was initially randomized to the eculizumab arm

Adverse events
Upper respiratory tract infection

Study prescreen lab values
Hb: 11.0 g/dL
PLTs: 360 x 10^9/L
LDH: 127 U/L
WBC: 10 x 10^9/L
PNH granulocyte clone: 99%

Late 2017

3-Month follow-up

Clinical presentation
Gastroenteritis, dyspnea on exertion

Lab values
Hb: 10.4 g/dL
PLTs: 400 x 10^9/L
LDH: 590 U/L
WBC: 11 x 10^9/L

Adverse Events
No additional adverse events reported

6-Month follow-up

Clinical Presentation
Dyspnea on exertion

Lab values
Hb: 10.4 g/dL
PLTs: 400 x 10^9/L
LDH: 363 U/L
WBC: 17 x 10^9/L

Adverse events
Nasopharyngitis

Patient enters OLE period[b]

2018

6-Month OLE follow-up

Age: 33

Switched to ULTOMIRIS
In February 2018, the patient was switched to the ULTOMIRIS arm in the extension phase of study 302

6-Month post-ULTOMIRIS Lab Values
Hb: 11.7 g/dL
PLTs: 380 x 10^9/L
LDH: 188 U/L
WBC: 21 x 10^9/L
PNH granulocyte clone: 99%

The patient was safely and effectively switched from eculizumab Q2W to ULTOMIRIS Q8W, and he perceives an improved quality of life with his reduced dosing frequency with ULTOMIRIS

Throughout the OLE study, the patient did not experience a breakthrough hemolysis event and showed durable response to percentage change in LDH level from baseline. He also remained transfusion independent, as his Hb count remained stabilized. Anticoagulation therapy was continued

Adverse events
No additional adverse events reported

Reference Ranges		
	D-dimer: <500 ng/mL	**LDH, U/L:** 246 U/L
	Hb (male), g/dL: 13.2-17.1	**PLT, x 10^9/L:** 140-400
	Hematocrit: 38.5%-50%	**WBC, x 10^9/L:** 3.8-10.8

Individual results may vary.

Reference ranges for Hb, PLT, WBC, hematocrit, D-dimer, and bilirubin from Quest Diagnostics; reference for LDH from study 302.

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

CT, computed tomography; FACIT, Functional Assessment of Chronic Illness Therapy; Hb, hemoglobin; HSFC, high-sensitivity flow cytometry; lab, laboratory; LDH, lactate dehydrogenase; OLE, open-label extension; PLTs, platelets; PNH, paroxysmal nocturnal hemoglobinuria; Q2W, every-2-weeks; Q8W, every-8-weeks; RBC, red blood cell; WBC, white blood cell.

[a]The ULTOMIRIS Switch Study (302) (ALXN1210-PNH-302; NCT03056040) was a 26-week, multicenter, open-label, randomized, active-controlled, noninferiority, phase 3 study conducted in 195 patients with PNH who were clinically stable after having been treated with eculizumab for at least the past 6 months. Patients randomly assigned to the ULTOMIRIS treatment group (n=97) received weight-based dosing: a loading dose on day 1 followed by maintenance doses of ULTOMIRIS (on day 15 and Q8W thereafter). Patients randomly assigned to the eculizumab treatment group (n=98) received 900 mg Q2W. The primary efficacy end point was hemolysis, as directly measured by percentage change in LDH levels from baseline to day 183. Key secondary efficacy end points were proportion of patients with breakthrough hemolysis, change from baseline in quality of life, transfusion avoidance, and proportion of patients with stabilized Hb levels.[1] At the end of the 26-week treatment period, all patients had the option to switch to ULTOMIRIS for an extension period.[1,2] [b]This was an extension of the ULTOMIRIS Switch Study (302), where all patients received weight-based dosing of ULTOMIRIS. Results have been reported through 52 weeks of treatment. The primary efficacy end point was percentage change in LDH levels from baseline, and key secondary end points included the proportion of patients with breakthrough hemolysis, transfusion avoidance, improvement in FACIT-Fatigue total score, and stabilized Hb levels. Additional end points included change in plasma free C5 levels from baseline and safety evaluations.[2]

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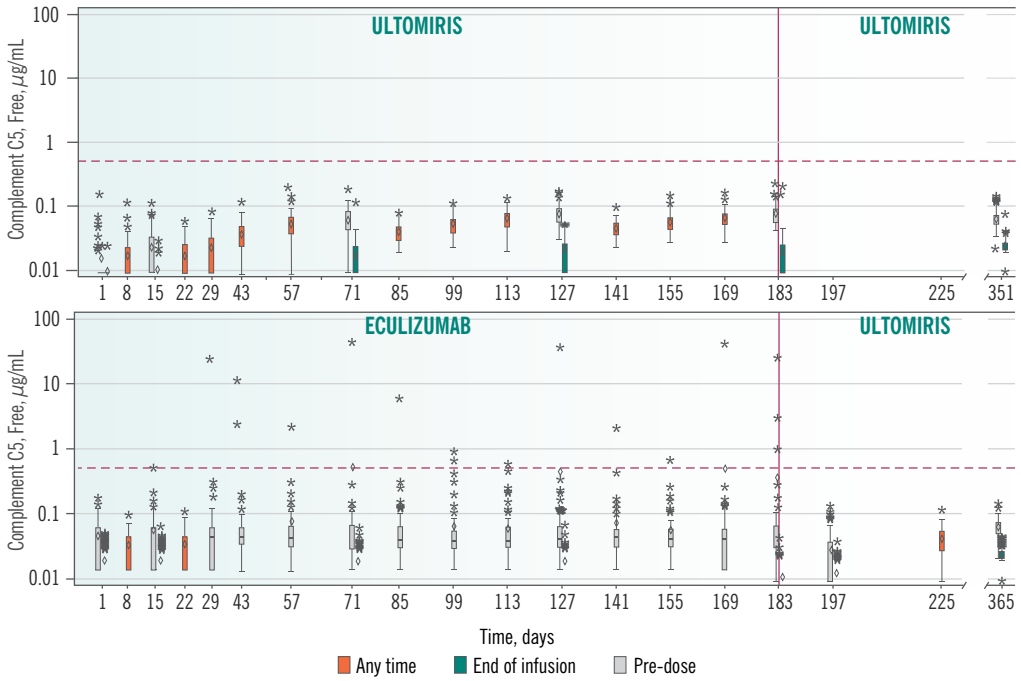
Free C5 Concentrations Over Time in Patients Treated With ULTOMIRIS and Eculizumab[2]

Complete free C5 inhibition demonstrated in ULTOMIRIS-treated patients with PNH who were clinically stable on eculizumab[2]

Box Plots Over Time: Free C5 Concentrations, μg/mL (Extension Set)[a,b]



[a]The median is indicated by a horizontal line in the middle of each box. The mean is indicated by a diamond. The 75th and 25th percentiles (interquartile range) are indicated by the top and the bottom borders of the box, respectively. The whiskers represent the 1.5 interquartile range of the lower and upper quartiles, respectively. Outliers are represented by asterisks beyond the whiskers. Dashed horizontal lines indicate serum-free C5 concentration of 0.5 μg/mL.
[b]A Gyros-based fluorescence assay was used for patients who received ULTOMIRIS, and an electrochemiluminescence immunoassay was used for patients who received eculizumab.

- During the extension phase of the Switch Study (302), patients who continued ULTOMIRIS maintenance therapy (n=96) or were switched from eculizumab to ULTOMIRIS (n=95) demonstrated a durable response for percentage change in LDH levels up to 52 weeks, with mean LDH levels maintained at 1.0 x upper limit of normal (<246 U/L).[2]
- The percentage of patients avoiding transfusion remained stable. During the 26-week treatment period, 88% of patients in the ULTOMIRIS arm avoided transfusion vs 87% during the 52-week period. In the eculizumab switch arm, 83% of patients avoided transfusion during the 26-week treatment period vs 83% during the 52-week period.[1,2]
- The proportion of patients with Hb stabilization was 76% in each arm during the 26-week treatment period vs 81% during the 52-week period.[1,2]
- All patients in the ULTOMIRIS arm maintained free C5 of <0.5 μg/mL at all time points through the 52-week period. In patients initially randomized to eculizumab, the switch to ULTOMIRIS showed improved free C5 control, with no patients having free C5 of ≥0.5 μg/mL after the switch.[2]
- The number of patients experiencing breakthrough hemolysis during the extension period with ULTOMIRIS (weeks 27-52) was 3 patients in the ULTOMIRIS arm and 1 patient in the eculizumab arm after switching to ULTOMIRIS. No breakthrough hemolysis events were associated with free C5 of ≥0.5 μg/mL (threshold for complete C5 inhibition).[2]
- During weeks 27 and 52, fatigue was the most common adverse event (incidence ≥10%) reported in the ULTOMIRIS arm (13 patients [13.5%]), and fatigue (13 [13.7%]) and headache (10 [10.5%]) were most commonly reported in the eculizumab switch arm.[2]
- Serious adverse events were experienced by 8 patients (8%) who continued ULTOMIRIS maintenance therapy and in 5 patients (5%) who switched from eculizumab to ULTOMIRIS.[2]

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Hb, hemoglobin; LDH, lactate dehydrogenase; OLE, open-label extension; PNH, paroxysmal nocturnal hemoglobinuria.

1. Kulasekararaj AG, et al. *Blood.* 2019;133(6):540-549. **2.** Kulasekararaj AG, et al. 61st ASH Annual Meeting and Exposition; December 7-10, 2019; Orlando, FL; Poster 2231.

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