Dossier zur Nutzenbewertung gemäß § 35a SGB V

Ravulizumab (Ultomiris®)

Alexion Pharma Germany GmbH

Anhang 4-G

Neuromyelitis-optica-Spektrum-Erkrankungen

Stand: 02.06.2023

Table TFR-1.2
Time to First Adjudicated On-Trial Relapse by Sex
Censoring at Missed or Delayed Dose Due to COVID-19 Pandemic
Full Analysis Set

Sex	Variable	Statistic	Eculizumab (N=96)	Ravulizumab (N=58)	P-value (7)
Male		n	8	6	
	Patients with an Adjudicated On-Trial Relapse	n (%)	0 (0.0)	0 (0.0)	
	Follow-up time (weeks)	Median (Min, Max)	98.00 (8.43, 117.71)	69.64 (56.29, 99.86)	
	Estimated proportion of patients relapse-free at	Cumulative probability (1) (95% CI (2))			
	24 weeks		1.000 (1.000, 1.000)	1.000 (1.000, 1.000)	
	48 weeks		1.000 (1.000, 1.000)	1.000 (1.000, 1.000)	
	72 weeks		1.000 (1.000, 1.000)	1.000 (1.000, 1.000)	
	96 weeks		1.000 (1.000, 1.000)	1.000 (1.000, 1.000)	
	120 weeks		NA (NA, NA)	NA (NA, NA)	
	144 weeks		NA (NA, NA)	NA (NA, NA)	

The eculizumab group data were collected as part of the PREVENT trial, Study ECU-NMO-301.

Patients who did not experience an adjudicated on-trial relapse were censored at the earlier of the end of the study period and 35 days after a missed or >35-day delayed dose due to the COVID-19 pandemic. If a patient in the eculizumab group was followed longer than any of the patients in the ravulizumab arm, then that patient was censored at the longest ravulizumab follow-up time.

(1) Based on the Kaplan-Meier product limit method, (2) Based on the complementary log-log transformation, (3) Based on the log-rank test, (4) Based on a Cox proportional hazards model, with Firth's adjustment if no relapses observed in a treatment arm,

(5) Wald confidence interval or Profile Likelihood Confidence Limits, if no relapses observed in a treatment arm, (6) Constructed as a risk ratio: A tipping point analysis quantifying the level of confounding which could compensate the estimated treatment effect.

(7) P-value is for the interaction term of treatment:subgroup from a Cox proportional hazards model with treatment, subgroup, and treatment:subgroup interaction as covariates, with Firth's adjustment if no relapses observed in a treatment arm.

Source: adsl, adtte

Table TFR-1.2
Time to First Adjudicated On-Trial Relapse by Sex
Censoring at Missed or Delayed Dose Due to COVID-19 Pandemic
Full Analysis Set

Sex	Variable	Statistic	Eculizumab (N=96)	Ravulizumab (N=58)	P-value (7)
Male	Relapse-free time (weeks)	Percentile (1)			
		10th	NA	NA	
		25th	NA	NA	
		50th	NA	NA	
	Treatment Effect				
		p-value (3)		NA	0.6015
		Hazard ratio (4) (Ravulizumab/Eculizumab)		NA	
		95% CI (5)		(NA, NA)	
		% reduction (4) (Ravulizumab/Eculizumab)		NA	
		95% CI (5)		(NA, NA)	
		E-value			
		For estimate		NA	
		For upper 95% CL (6)		NA	

The eculizumab group data were collected as part of the PREVENT trial, Study ECU-NMO-301.

Patients who did not experience an adjudicated on-trial relapse were censored at the earlier of the end of the study period and 35 days after a missed or >35-day delayed dose due to the COVID-19 pandemic. If a patient in the eculizumab group was followed longer than any of the patients in the ravulizumab arm, then that patient was censored at the longest ravulizumab follow-up time.

(1) Based on the Kaplan-Meier product limit method, (2) Based on the complementary log-log transformation, (3) Based on the log-rank test, (4) Based on a Cox proportional hazards model, with Firth's adjustment if no relapses observed in a treatment arm,

(5) Wald confidence interval or Profile Likelihood Confidence Limits, if no relapses observed in a treatment arm, (6) Constructed as a risk ratio: A tipping point analysis quantifying the level of confounding which could compensate the estimated treatment effect.

(7) P-value is for the interaction term of treatment:subgroup from a Cox proportional hazards model with treatment, subgroup, and treatment:subgroup interaction as covariates, with Firth's adjustment if no relapses observed in a treatment arm.

Source: adsl, adtte

Table TFR-1.2
Time to First Adjudicated On-Trial Relapse by Sex
Censoring at Missed or Delayed Dose Due to COVID-19 Pandemic
Full Analysis Set

Sex	Variable	Statistic	Eculizumab (N=96)	Ravulizumab (N=58)	P-value (7)
Female		n	88	52	
	Patients with an Adjudicated On-Trial Relapse	n (%)	3 (3.4)	0 (0.0)	
	Follow-up time (weeks)	Median (Min, Max)	89.43 (2.57, 117.71)	74.29 (11.00, 117.71)	
	Estimated proportion of patients relapse-free at	Cumulative probability (1) (95% CI (2))			
	24 weeks		0.977 (0.911, 0.994)	1.000 (1.000, 1.000)	
	48 weeks		0.977 (0.911, 0.994)	1.000 (1.000, 1.000)	
	72 weeks		0.961 (0.882, 0.987)	1.000 (1.000, 1.000)	
	96 weeks		0.961 (0.882, 0.987)	1.000 (1.000, 1.000)	
	120 weeks		NA (NA, NA)	NA (NA, NA)	
	144 weeks		NA (NA, NA)	NA (NA, NA)	

The eculizumab group data were collected as part of the PREVENT trial, Study ECU-NMO-301.

Patients who did not experience an adjudicated on-trial relapse were censored at the earlier of the end of the study period and 35 days after a missed or >35-day delayed dose due to the COVID-19 pandemic. If a patient in the eculizumab group was followed longer than any of the patients in the ravulizumab arm, then that patient was censored at the longest ravulizumab follow-up time.

(1) Based on the Kaplan-Meier product limit method, (2) Based on the complementary log-log transformation, (3) Based on the log-rank test, (4) Based on a Cox proportional hazards model, with Firth's adjustment if no relapses observed in a treatment arm,

(5) Wald confidence interval or Profile Likelihood Confidence Limits, if no relapses observed in a treatment arm, (6) Constructed as a risk ratio: A tipping point analysis quantifying the level of confounding which could compensate the estimated treatment effect.

(7) P-value is for the interaction term of treatment:subgroup from a Cox proportional hazards model with treatment, subgroup, and treatment:subgroup interaction as covariates, with Firth's adjustment if no relapses observed in a treatment arm.

Source: adsl, adtte

Table TFR-1.2
Time to First Adjudicated On-Trial Relapse by Sex
Censoring at Missed or Delayed Dose Due to COVID-19 Pandemic
Full Analysis Set

Sex	Variable	Statistic	Eculizumab (N=96)	Ravulizumab (N=58)	P-value (7)
Female	Relapse-free time (weeks)	Percentile (1)			
		10th	NA	NA	
		25th	NA	NA	
		50th	NA	NA	
	Treatment Effect				
		p-value (3)		0.1547	
		Hazard ratio (4) (Ravulizumab/Eculizumab)		0.210	
		95% CI (5)		(0.002, 2.189)	
		% reduction (4) (Ravulizumab/Eculizumab)		79.0	
		95% CI (5)		(-118.9, 99.8)	
		E-value			
		For estimate		5.17	
		For upper 95% CL (6)		NA	

The eculizumab group data were collected as part of the PREVENT trial, Study ECU-NMO-301.

Patients who did not experience an adjudicated on-trial relapse were censored at the earlier of the end of the study period and 35 days after a missed or >35-day delayed dose due to the COVID-19 pandemic. If a patient in the eculizumab group was followed longer than any of the patients in the ravulizumab arm, then that patient was censored at the longest ravulizumab follow-up time.

(1) Based on the Kaplan-Meier product limit method, (2) Based on the complementary log-log transformation, (3) Based on the log-rank test, (4) Based on a Cox proportional hazards model, with Firth's adjustment if no relapses observed in a treatment arm,

(5) Wald confidence interval or Profile Likelihood Confidence Limits, if no relapses observed in a treatment arm, (6) Constructed as a risk ratio: A tipping point analysis quantifying the level of confounding which could compensate the estimated treatment effect.

(7) P-value is for the interaction term of treatment:subgroup from a Cox proportional hazards model with treatment, subgroup, and treatment:subgroup interaction as covariates, with Firth's adjustment if no relapses observed in a treatment arm.

Source: adsl, adtte

Table TFR-1.3
Time to First Adjudicated On-Trial Relapse by Age Group
Censoring at Missed or Delayed Dose Due to COVID-19 Pandemic
Full Analysis Set

Age Group	Variable	Statistic	Eculizumab (N=96)	Ravulizumab (N=58)	P-value (7)
< 45 years		n	47	25	
	Patients with an Adjudicated On-Trial Relapse	n (%)	0 (0.0)	0 (0.0)	
	Follow-up time (weeks)	Median (Min, Max)	79.71 (4.43, 117.71)	74.86 (11.00, 112.86)	
	Estimated proportion of patients relapse-free at	Cumulative probability (1) (95% CI (2))			
	24 weeks		1.000 (1.000, 1.000)	1.000 (1.000, 1.000)	
	48 weeks		1.000 (1.000, 1.000)	1.000 (1.000, 1.000)	
	72 weeks		1.000 (1.000, 1.000)	1.000 (1.000, 1.000)	
	96 weeks		1.000 (1.000, 1.000)	1.000 (1.000, 1.000)	
	120 weeks		NA (NA, NA)	NA (NA, NA)	
	144 weeks		NA (NA, NA)	NA (NA, NA)	

The eculizumab group data were collected as part of the PREVENT trial, Study ECU-NMO-301.

Patients who did not experience an adjudicated on-trial relapse were censored at the earlier of the end of the study period and 35 days after a missed or >35-day delayed dose due to the COVID-19 pandemic. If a patient in the eculizumab group was followed longer than any of the patients in the ravulizumab arm, then that patient was censored at the longest ravulizumab follow-up time.

(1) Based on the Kaplan-Meier product limit method, (2) Based on the complementary log-log transformation, (3) Based on the log-rank test, (4) Based on a Cox proportional hazards model, with Firth's adjustment if no relapses observed in a treatment arm,

(5) Wald confidence interval or Profile Likelihood Confidence Limits, if no relapses observed in a treatment arm, (6) Constructed as a risk ratio: A tipping point analysis quantifying the level of confounding which could compensate the estimated treatment effect.

(7) P-value is for the interaction term of treatment:subgroup from a Cox proportional hazards model with treatment, subgroup, and treatment:subgroup interaction as covariates, with Firth's adjustment if no relapses observed in a treatment arm.

Source: adsl, adtte

Table TFR-1.3
Time to First Adjudicated On-Trial Relapse by Age Group
Censoring at Missed or Delayed Dose Due to COVID-19 Pandemic
Full Analysis Set

Age Group	Variable	Statistic	Eculizumab (N=96)	Ravulizumab (N=58)	P-value (7)
< 45 years	Relapse-free time (weeks)	Percentile (1)			
		10th	NA	NA	
		25th	NA	NA	
		50th	NA	NA	
	Treatment Effect				
		p-value (3)		NA	0.5024
		Hazard ratio (4) (Ravulizumab/Eculizumab)		NA	
		95% CI (5)		(NA, NA)	
		% reduction (4) (Ravulizumab/Eculizumab)		NA	
		95% CI (5)		(NA, NA)	
		E-value			
		For estimate		NA	
		For upper 95% CL (6)		NA	

The eculizumab group data were collected as part of the PREVENT trial, Study ECU-NMO-301.

Patients who did not experience an adjudicated on-trial relapse were censored at the earlier of the end of the study period and 35 days after a missed or >35-day delayed dose due to the COVID-19 pandemic. If a patient in the eculizumab group was followed longer than any of the patients in the ravulizumab arm, then that patient was censored at the longest ravulizumab follow-up time.

(1) Based on the Kaplan-Meier product limit method, (2) Based on the complementary log-log transformation, (3) Based on the log-rank test, (4) Based on a Cox proportional hazards model, with Firth's adjustment if no relapses observed in a treatment arm,

(5) Wald confidence interval or Profile Likelihood Confidence Limits, if no relapses observed in a treatment arm, (6) Constructed as a risk ratio: A tipping point analysis quantifying the level of confounding which could compensate the estimated treatment effect.

(7) P-value is for the interaction term of treatment:subgroup from a Cox proportional hazards model with treatment, subgroup, and treatment:subgroup interaction as covariates, with Firth's adjustment if no relapses observed in a treatment arm.

Source: adsl, adtte

Table TFR-1.3
Time to First Adjudicated On-Trial Relapse by Age Group
Censoring at Missed or Delayed Dose Due to COVID-19 Pandemic
Full Analysis Set

Age Group	Variable	Statistic	Eculizumab (N=96)	Ravulizumab (N=58)	P-value (7)
>= 45 years		n	49	33	
	Patients with an Adjudicated On-Trial Relapse	n (%)	3 (6.1)	0 (0.0)	
	Follow-up time (weeks)	Median (Min, Max)	98.29 (2.57, 117.71)	73.14 (52.14, 117.71)	
	Estimated proportion of patients relapse-free at	Cumulative probability (1) (95% CI (2))			
	24 weeks		0.959 (0.847, 0.990)	1.000 (1.000, 1.000)	
	48 weeks		0.959 (0.847, 0.990)	1.000 (1.000, 1.000)	
	72 weeks		0.932 (0.801, 0.978)	1.000 (1.000, 1.000)	
	96 weeks		0.932 (0.801, 0.978)	1.000 (1.000, 1.000)	
	120 weeks		NA (NA, NA)	NA (NA, NA)	
	144 weeks		NA (NA, NA)	NA (NA, NA)	

The eculizumab group data were collected as part of the PREVENT trial, Study ECU-NMO-301.

Patients who did not experience an adjudicated on-trial relapse were censored at the earlier of the end of the study period and 35 days after a missed or >35-day delayed dose due to the COVID-19 pandemic. If a patient in the eculizumab group was followed longer than any of the patients in the ravulizumab arm, then that patient was censored at the longest ravulizumab follow-up time.

(1) Based on the Kaplan-Meier product limit method, (2) Based on the complementary log-log transformation, (3) Based on the log-rank test, (4) Based on a Cox proportional hazards model, with Firth's adjustment if no relapses observed in a treatment arm,

(5) Wald confidence interval or Profile Likelihood Confidence Limits, if no relapses observed in a treatment arm, (6) Constructed as a risk ratio: A tipping point analysis quantifying the level of confounding which could compensate the estimated treatment effect.

(7) P-value is for the interaction term of treatment:subgroup from a Cox proportional hazards model with treatment, subgroup, and treatment:subgroup interaction as covariates, with Firth's adjustment if no relapses observed in a treatment arm.

Source: adsl, adtte

Table TFR-1.3
Time to First Adjudicated On-Trial Relapse by Age Group
Censoring at Missed or Delayed Dose Due to COVID-19 Pandemic
Full Analysis Set

Age Group	Variable	Statistic	Eculizumab (N=96)	Ravulizumab (N=58)	P-value (7)
>= 45 years	Relapse-free time (weeks)	Percentile (1)			
		10th	NA	NA	
		25th	NA	NA	
		50th	NA	NA	
	Treatment Effect				
		p-value (3)		0.1300	
		Hazard ratio (4) (Ravulizumab/Eculizumab)		0.186	
		95% CI (5)		(0.001, 1.932)	
		% reduction (4) (Ravulizumab/Eculizumab)		81.4	
		95% CI (5)		(-93.2, 99.9)	
		E-value			
		For estimate		5.65	
		For upper 95% CL (6)		NA	

The eculizumab group data were collected as part of the PREVENT trial, Study ECU-NMO-301.

Patients who did not experience an adjudicated on-trial relapse were censored at the earlier of the end of the study period and 35 days after a missed or >35-day delayed dose due to the COVID-19 pandemic. If a patient in the eculizumab group was followed longer than any of the patients in the ravulizumab arm, then that patient was censored at the longest ravulizumab follow-up time.

(1) Based on the Kaplan-Meier product limit method, (2) Based on the complementary log-log transformation, (3) Based on the log-rank test, (4) Based on a Cox proportional hazards model, with Firth's adjustment if no relapses observed in a treatment arm,

(5) Wald confidence interval or Profile Likelihood Confidence Limits, if no relapses observed in a treatment arm, (6) Constructed as a risk ratio: A tipping point analysis quantifying the level of confounding which could compensate the estimated treatment effect.

(7) P-value is for the interaction term of treatment:subgroup from a Cox proportional hazards model with treatment, subgroup, and treatment:subgroup interaction as covariates, with Firth's adjustment if no relapses observed in a treatment arm.

Source: adsl, adtte

Table TFR-1.5
Time to First Adjudicated On-Trial Relapse by Region
Censoring at Missed or Delayed Dose Due to COVID-19 Pandemic
Full Analysis Set

Region	Variable	Statistic	Eculizumab (N=96)	Ravulizumab (N=58)	P-value (7)
Asia-Pacific		n	35	20	
	Patients with an Adjudicated On-Trial Relapse	n (%)	1 (2.9)	0 (0.0)	
	Follow-up time (weeks)	Median (Min, Max)	85.86 (14.00, 117.71)	73.93 (53.00, 95.14)	
	Estimated proportion of patients relapse-free at	Cumulative probability (1) (95% CI (2))			
	24 weeks		0.971 (0.814, 0.996)	1.000 (1.000, 1.000)	
	48 weeks		0.971 (0.814, 0.996)	1.000 (1.000, 1.000)	
	72 weeks		0.971 (0.814, 0.996)	1.000 (1.000, 1.000)	
	96 weeks		0.971 (0.814, 0.996)	NA (NA, NA)	
	120 weeks		NA (NA, NA)	NA (NA, NA)	
	144 weeks		NA (NA, NA)	NA (NA, NA)	

The eculizumab group data were collected as part of the PREVENT trial, Study ECU-NMO-301.

Patients who did not experience an adjudicated on-trial relapse were censored at the earlier of the end of the study period and 35 days after a missed or >35-day delayed dose due to the COVID-19 pandemic. If a patient in the eculizumab group was followed longer than any of the patients in the ravulizumab arm, then that patient was censored at the longest ravulizumab follow-up time.

(1) Based on the Kaplan-Meier product limit method, (2) Based on the complementary log-log transformation, (3) Based on the log-rank test, (4) Based on a Cox proportional hazards model, with Firth's adjustment if no relapses observed in a treatment arm,

(5) Wald confidence interval or Profile Likelihood Confidence Limits, if no relapses observed in a treatment arm, (6) Constructed as a risk ratio: A tipping point analysis quantifying the level of confounding which could compensate the estimated treatment effect.

(7) P-value is for the interaction term of treatment:subgroup from a Cox proportional hazards model with treatment, subgroup, and treatment:subgroup interaction as covariates, with Firth's adjustment if no relapses observed in a treatment arm.

For eculizumab arm, Americas: ARG and USA; Europe: CZE, DEU, DNK, ESP, HRV, ITA, RUS and TUR; Asia-Pacific: AUS, HKG, JPN, KOR, MYS, THA and TWN. For ravulizumab arm, Americas: CAN and USA; Europe: DEU, DNK, ESP, GBR, ITA and POL; Asia-Pacific: AUS, JPN and KOR.

Source: adsl, adtte

Table TFR-1.5
Time to First Adjudicated On-Trial Relapse by Region
Censoring at Missed or Delayed Dose Due to COVID-19 Pandemic
Full Analysis Set

Region	Variable	Statistic	Eculizumab (N=96)	Ravulizumab (N=58)	P-value (7)
Asia-Pacific	Relapse-free time (weeks)	Percentile (1)			
		10th	NA	NA	
		25th	NA	NA	
		50th	NA	NA	
	Treatment Effect				
		p-value (3)		0.4497	0.9723
		Hazard ratio (4) (Ravulizumab/Eculizumab)		0.556	
		95% CI (5)		(0.004, 10.939)	
		% reduction (4) (Ravulizumab/Eculizumab)		44.4	
		95% CI (5)		(-993.9, 99.6)	
		E-value			
		For estimate		2.37	
		For upper 95% CL (6)		NA	

The eculizumab group data were collected as part of the PREVENT trial, Study ECU-NMO-301.

Patients who did not experience an adjudicated on-trial relapse were censored at the earlier of the end of the study period and 35 days after a missed or >35-day delayed dose due to the COVID-19 pandemic. If a patient in the eculizumab group was followed longer than any of the patients in the ravulizumab arm, then that patient was censored at the longest ravulizumab follow-up time.

(1) Based on the Kaplan-Meier product limit method, (2) Based on the complementary log-log transformation, (3) Based on the log-rank test, (4) Based on a Cox proportional hazards model, with Firth's adjustment if no relapses observed in a treatment arm,

(5) Wald confidence interval or Profile Likelihood Confidence Limits, if no relapses observed in a treatment arm, (6) Constructed as a risk ratio: A tipping point analysis quantifying the level of confounding which could compensate the estimated treatment effect.

(7) P-value is for the interaction term of treatment:subgroup from a Cox proportional hazards model with treatment, subgroup, and treatment:subgroup interaction as covariates, with Firth's adjustment if no relapses observed in a treatment arm.

For eculizumab arm, Americas: ARG and USA; Europe: CZE, DEU, DNK, ESP, HRV, ITA, RUS and TUR; Asia-Pacific: AUS, HKG, JPN, KOR, MYS, THA and TWN. For ravulizumab arm, Americas: CAN and USA; Europe: DEU, DNK, ESP, GBR, ITA and POL; Asia-Pacific: AUS, JPN and KOR.

Source: adsl, adtte

Table TFR-1.5
Time to First Adjudicated On-Trial Relapse by Region
Censoring at Missed or Delayed Dose Due to COVID-19 Pandemic
Full Analysis Set

Region	Variable	Statistic	Eculizumab (N=96)	Ravulizumab (N=58)	P-value (7)
Americas		n	29	21	
	Patients with an Adjudicated On-Trial Relapse	n (%)	1 (3.4)	0 (0.0)	
	Follow-up time (weeks)	Median (Min, Max)	72.14 (4.43, 117.71)	87.71 (69.71, 117.71)	
	Estimated proportion of patients relapse-free at	Cumulative probability (1) (95% CI (2))			
	24 weeks		1.000 (1.000, 1.000)	1.000 (1.000, 1.000)	
	48 weeks		1.000 (1.000, 1.000)	1.000 (1.000, 1.000)	
	72 weeks		0.950 (0.695, 0.993)	1.000 (1.000, 1.000)	
	96 weeks		0.950 (0.695, 0.993)	1.000 (1.000, 1.000)	
	120 weeks		NA (NA, NA)	NA (NA, NA)	
	144 weeks		NA (NA, NA)	NA (NA, NA)	

The eculizumab group data were collected as part of the PREVENT trial, Study ECU-NMO-301.

Patients who did not experience an adjudicated on-trial relapse were censored at the earlier of the end of the study period and 35 days after a missed or >35-day delayed dose due to the COVID-19 pandemic. If a patient in the eculizumab group was followed longer than any of the patients in the ravulizumab arm, then that patient was censored at the longest ravulizumab follow-up time.

(1) Based on the Kaplan-Meier product limit method, (2) Based on the complementary log-log transformation, (3) Based on the log-rank test, (4) Based on a Cox proportional hazards model, with Firth's adjustment if no relapses observed in a treatment arm,

(5) Wald confidence interval or Profile Likelihood Confidence Limits, if no relapses observed in a treatment arm, (6) Constructed as a risk ratio: A tipping point analysis quantifying the level of confounding which could compensate the estimated treatment effect.

(7) P-value is for the interaction term of treatment:subgroup from a Cox proportional hazards model with treatment, subgroup, and treatment:subgroup interaction as covariates, with Firth's adjustment if no relapses observed in a treatment arm.

For eculizumab arm, Americas: ARG and USA; Europe: CZE, DEU, DNK, ESP, HRV, ITA, RUS and TUR; Asia-Pacific: AUS, HKG, JPN, KOR, MYS, THA and TWN. For ravulizumab arm, Americas: CAN and USA; Europe: DEU, DNK, ESP, GBR, ITA and POL; Asia-Pacific: AUS, JPN and KOR.

Source: adsl, adtte

Table TFR-1.5
Time to First Adjudicated On-Trial Relapse by Region
Censoring at Missed or Delayed Dose Due to COVID-19 Pandemic
Full Analysis Set

Region	Variable	Statistic	Eculizumab (N=96)	Ravulizumab (N=58)	P-value (7)
Americas	Relapse-free time (weeks)	Percentile (1)			
		10th	NA	NA	
		25th	NA	NA	
		50th	NA	NA	
	Treatment Effect				
		p-value (3)		0.3055	0.9018
		Hazard ratio (4) (Ravulizumab/Eculizumab)		0.319	
		95% CI (5)		(0.002, 5.951)	
		% reduction (4) (Ravulizumab/Eculizumab)		68.1	
		95% CI (5)		(-495.1, 99.8)	
		E-value			
		For estimate		3.79	
		For upper 95% CL (6)		NA	

The eculizumab group data were collected as part of the PREVENT trial, Study ECU-NMO-301.

Patients who did not experience an adjudicated on-trial relapse were censored at the earlier of the end of the study period and 35 days after a missed or >35-day delayed dose due to the COVID-19 pandemic. If a patient in the eculizumab group was followed longer than any of the patients in the ravulizumab arm, then that patient was censored at the longest ravulizumab follow-up time.

(1) Based on the Kaplan-Meier product limit method, (2) Based on the complementary log-log transformation, (3) Based on the log-rank test, (4) Based on a Cox proportional hazards model, with Firth's adjustment if no relapses observed in a treatment arm,

(5) Wald confidence interval or Profile Likelihood Confidence Limits, if no relapses observed in a treatment arm, (6) Constructed as a risk ratio: A tipping point analysis quantifying the level of confounding which could compensate the estimated treatment effect.

(7) P-value is for the interaction term of treatment:subgroup from a Cox proportional hazards model with treatment, subgroup, and treatment:subgroup interaction as covariates, with Firth's adjustment if no relapses observed in a treatment arm.

For eculizumab arm, Americas: ARG and USA; Europe: CZE, DEU, DNK, ESP, HRV, ITA, RUS and TUR; Asia-Pacific: AUS, HKG, JPN, KOR, MYS, THA and TWN. For ravulizumab arm, Americas: CAN and USA; Europe: DEU, DNK, ESP, GBR, ITA and POL; Asia-Pacific: AUS, JPN and KOR.

Source: adsl, adtte

Table TFR-1.5
Time to First Adjudicated On-Trial Relapse by Region
Censoring at Missed or Delayed Dose Due to COVID-19 Pandemic
Full Analysis Set

Region	Variable	Statistic	Eculizumab (N=96)	Ravulizumab (N=58)	P-value (7)
Europe		n	32	17	
	Patients with an Adjudicated On-Trial Relapse	n (%)	1 (3.1)	0 (0.0)	
	Follow-up time (weeks)	Median (Min, Max)	105.07 (2.57, 117.71)	65.00 (11.00, 86.00)	
	Estimated proportion of patients relapse-free at	Cumulative probability (1) (95% CI (2))			
	24 weeks		0.969 (0.798, 0.996)	1.000 (1.000, 1.000)	
	48 weeks		0.969 (0.798, 0.996)	1.000 (1.000, 1.000)	
	72 weeks		0.969 (0.798, 0.996)	1.000 (1.000, 1.000)	
	96 weeks		0.969 (0.798, 0.996)	NA (NA, NA)	
	120 weeks		NA (NA, NA)	NA (NA, NA)	
	144 weeks		NA (NA, NA)	NA (NA, NA)	

The eculizumab group data were collected as part of the PREVENT trial, Study ECU-NMO-301.

Patients who did not experience an adjudicated on-trial relapse were censored at the earlier of the end of the study period and 35 days after a missed or >35-day delayed dose due to the COVID-19 pandemic. If a patient in the eculizumab group was followed longer than any of the patients in the ravulizumab arm, then that patient was censored at the longest ravulizumab follow-up time.

(1) Based on the Kaplan-Meier product limit method, (2) Based on the complementary log-log transformation, (3) Based on the log-rank test, (4) Based on a Cox proportional hazards model, with Firth’s adjustment if no relapses observed in a treatment arm,

(5) Wald confidence interval or Profile Likelihood Confidence Limits, if no relapses observed in a treatment arm, (6) Constructed as a risk ratio: A tipping point analysis quantifying the level of confounding which could compensate the estimated treatment effect.

(7) P-value is for the interaction term of treatment:subgroup from a Cox proportional hazards model with treatment, subgroup, and treatment:subgroup interaction as covariates, with Firth’s adjustment if no relapses observed in a treatment arm.

For eculizumab arm, Americas: ARG and USA; Europe: CZE, DEU, DNK, ESP, HRV, ITA, RUS and TUR; Asia-Pacific: AUS, HKG, JPN, KOR, MYS, THA and TWN. For ravulizumab arm, Americas: CAN and USA; Europe: DEU, DNK, ESP, GBR, ITA and POL; Asia-Pacific: AUS, JPN and KOR.

Source: adsl, adtte

Table TFR-1.5
Time to First Adjudicated On-Trial Relapse by Region
Censoring at Missed or Delayed Dose Due to COVID-19 Pandemic
Full Analysis Set

Region	Variable	Statistic	Eculizumab (N=96)	Ravulizumab (N=58)	P-value (7)
Europe	Relapse-free time (weeks)	Percentile (1)			
		10th	NA	NA	
		25th	NA	NA	
		50th	NA	NA	
	Treatment Effect				
		p-value (3)		0.4661	
		Hazard ratio (4) (Ravulizumab/Eculizumab)		0.603	
		95% CI (5)		(0.004, 11.765)	
		% reduction (4) (Ravulizumab/Eculizumab)		39.7	
		95% CI (5)		(-1076.5, 99.6)	
		E-value			
		For estimate		2.19	
		For upper 95% CL (6)		NA	

The eculizumab group data were collected as part of the PREVENT trial, Study ECU-NMO-301.

Patients who did not experience an adjudicated on-trial relapse were censored at the earlier of the end of the study period and 35 days after a missed or >35-day delayed dose due to the COVID-19 pandemic. If a patient in the eculizumab group was followed longer than any of the patients in the ravulizumab arm, then that patient was censored at the longest ravulizumab follow-up time.

(1) Based on the Kaplan-Meier product limit method, (2) Based on the complementary log-log transformation, (3) Based on the log-rank test, (4) Based on a Cox proportional hazards model, with Firth's adjustment if no relapses observed in a treatment arm,

(5) Wald confidence interval or Profile Likelihood Confidence Limits, if no relapses observed in a treatment arm, (6) Constructed as a risk ratio: A tipping point analysis quantifying the level of confounding which could compensate the estimated treatment effect.

(7) P-value is for the interaction term of treatment:subgroup from a Cox proportional hazards model with treatment, subgroup, and treatment:subgroup interaction as covariates, with Firth's adjustment if no relapses observed in a treatment arm.

For eculizumab arm, Americas: ARG and USA; Europe: CZE, DEU, DNK, ESP, HRV, ITA, RUS and TUR; Asia-Pacific: AUS, HKG, JPN, KOR, MYS, THA and TWN. For ravulizumab arm, Americas: CAN and USA; Europe: DEU, DNK, ESP, GBR, ITA and POL; Asia-Pacific: AUS, JPN and KOR.

Source: adsl, adtte

Table TFR-1.6
Time to First Adjudicated On-Trial Relapse by Supportive IST use at baseline
Censoring at Missed or Delayed Dose Due to COVID-19 Pandemic
Full Analysis Set

IST use at baseline	Variable	Statistic	Eculizumab (N=96)	Ravulizumab (N=58)	P-value (7)
Yes		n	75	28	
	Patients with an Adjudicated On-Trial Relapse	n (%)	3 (4.0)	0 (0.0)	
	Follow-up time (weeks)	Median (Min, Max)	85.86 (2.57, 117.71)	74.00 (52.14, 101.00)	
	Estimated proportion of patients relapse-free at	Cumulative probability (1) (95% CI (2))			
	24 weeks		0.973 (0.895, 0.993)	1.000 (1.000, 1.000)	
	48 weeks		0.973 (0.895, 0.993)	1.000 (1.000, 1.000)	
	72 weeks		0.954 (0.863, 0.985)	1.000 (1.000, 1.000)	
	96 weeks		0.954 (0.863, 0.985)	1.000 (1.000, 1.000)	
	120 weeks		NA (NA, NA)	NA (NA, NA)	
	144 weeks		NA (NA, NA)	NA (NA, NA)	

The eculizumab group data were collected as part of the PREVENT trial, Study ECU-NMO-301.

Patients who did not experience an adjudicated on-trial relapse were censored at the earlier of the end of the study period and 35 days after a missed or >35-day delayed dose due to the COVID-19 pandemic. If a patient in the eculizumab group was followed longer than any of the patients in the ravulizumab arm, then that patient was censored at the longest ravulizumab follow-up time.

(1) Based on the Kaplan-Meier product limit method, (2) Based on the complementary log-log transformation, (3) Based on the log-rank test, (4) Based on a Cox proportional hazards model, with Firth's adjustment if no relapses observed in a treatment arm,

(5) Wald confidence interval or Profile Likelihood Confidence Limits, if no relapses observed in a treatment arm, (6) Constructed as a risk ratio: A tipping point analysis quantifying the level of confounding which could compensate the estimated treatment effect.

(7) P-value is for the interaction term of treatment:subgroup from a Cox proportional hazards model with treatment, subgroup, and treatment:subgroup interaction as covariates, with Firth's adjustment if no relapses observed in a treatment arm.

Source: adsl, adtte

Table TFR-1.6
Time to First Adjudicated On-Trial Relapse by Supportive IST use at baseline
Censoring at Missed or Delayed Dose Due to COVID-19 Pandemic
Full Analysis Set

IST use at baseline	Variable	Statistic	Eculizumab (N=96)	Ravulizumab (N=58)	P-value (7)
Yes	Relapse-free time (weeks)	Percentile (1)			
		10th	NA	NA	
		25th	NA	NA	
		50th	NA	NA	
	Treatment Effect				
		p-value (3)		0.2545	0.8448
		Hazard ratio (4) (Ravulizumab/Eculizumab)		0.329	
		95% CI (5)		(0.002, 3.418)	
		% reduction (4) (Ravulizumab/Eculizumab)		67.1	
		95% CI (5)		(-241.8, 99.8)	
		E-value			
		For estimate		3.70	
		For upper 95% CL (6)		NA	

The eculizumab group data were collected as part of the PREVENT trial, Study ECU-NMO-301.

Patients who did not experience an adjudicated on-trial relapse were censored at the earlier of the end of the study period and 35 days after a missed or >35-day delayed dose due to the COVID-19 pandemic. If a patient in the eculizumab group was followed longer than any of the patients in the ravulizumab arm, then that patient was censored at the longest ravulizumab follow-up time.

(1) Based on the Kaplan-Meier product limit method, (2) Based on the complementary log-log transformation, (3) Based on the log-rank test, (4) Based on a Cox proportional hazards model, with Firth's adjustment if no relapses observed in a treatment arm,

(5) Wald confidence interval or Profile Likelihood Confidence Limits, if no relapses observed in a treatment arm, (6) Constructed as a risk ratio: A tipping point analysis quantifying the level of confounding which could compensate the estimated treatment effect.

(7) P-value is for the interaction term of treatment:subgroup from a Cox proportional hazards model with treatment, subgroup, and treatment:subgroup interaction as covariates, with Firth's adjustment if no relapses observed in a treatment arm.

Source: adsl, adtte

Table TFR-1.6
Time to First Adjudicated On-Trial Relapse by Supportive IST use at baseline
Censoring at Missed or Delayed Dose Due to COVID-19 Pandemic
Full Analysis Set

IST use at baseline	Variable	Statistic	Eculizumab (N=96)	Ravulizumab (N=58)	P-value (7)
No		n	21	30	
	Patients with an Adjudicated On-Trial Relapse	n (%)	0 (0.0)	0 (0.0)	
	Follow-up time (weeks)	Median (Min, Max)	98.29 (16.43, 117.71)	73.50 (11.00, 117.71)	
	Estimated proportion of patients relapse-free at	Cumulative probability (1) (95% CI (2))			
	24 weeks		1.000 (1.000, 1.000)	1.000 (1.000, 1.000)	
	48 weeks		1.000 (1.000, 1.000)	1.000 (1.000, 1.000)	
	72 weeks		1.000 (1.000, 1.000)	1.000 (1.000, 1.000)	
	96 weeks		1.000 (1.000, 1.000)	1.000 (1.000, 1.000)	
	120 weeks		NA (NA, NA)	NA (NA, NA)	
	144 weeks		NA (NA, NA)	NA (NA, NA)	

The eculizumab group data were collected as part of the PREVENT trial, Study ECU-NMO-301.

Patients who did not experience an adjudicated on-trial relapse were censored at the earlier of the end of the study period and 35 days after a missed or >35-day delayed dose due to the COVID-19 pandemic. If a patient in the eculizumab group was followed longer than any of the patients in the ravulizumab arm, then that patient was censored at the longest ravulizumab follow-up time.

(1) Based on the Kaplan-Meier product limit method, (2) Based on the complementary log-log transformation, (3) Based on the log-rank test, (4) Based on a Cox proportional hazards model, with Firth's adjustment if no relapses observed in a treatment arm,

(5) Wald confidence interval or Profile Likelihood Confidence Limits, if no relapses observed in a treatment arm, (6) Constructed as a risk ratio: A tipping point analysis quantifying the level of confounding which could compensate the estimated treatment effect.

(7) P-value is for the interaction term of treatment:subgroup from a Cox proportional hazards model with treatment, subgroup, and treatment:subgroup interaction as covariates, with Firth's adjustment if no relapses observed in a treatment arm.

Source: adsl, adtte

Table TFR-1.6
Time to First Adjudicated On-Trial Relapse by Supportive IST use at baseline
Censoring at Missed or Delayed Dose Due to COVID-19 Pandemic
Full Analysis Set

IST use at baseline	Variable	Statistic	Eculizumab (N=96)	Ravulizumab (N=58)	P-value (7)
No	Relapse-free time (weeks)	Percentile (1)			
		10th	NA	NA	
		25th	NA	NA	
		50th	NA	NA	
	Treatment Effect				
		p-value (3)		NA	
		Hazard ratio (4) (Ravulizumab/Eculizumab)		NA	
		95% CI (5)		(NA, NA)	
		% reduction (4) (Ravulizumab/Eculizumab)		NA	
		95% CI (5)		(NA, NA)	
		E-value			
		For estimate		NA	
		For upper 95% CL (6)		NA	

The eculizumab group data were collected as part of the PREVENT trial, Study ECU-NMO-301.

Patients who did not experience an adjudicated on-trial relapse were censored at the earlier of the end of the study period and 35 days after a missed or >35-day delayed dose due to the COVID-19 pandemic. If a patient in the eculizumab group was followed longer than any of the patients in the ravulizumab arm, then that patient was censored at the longest ravulizumab follow-up time.

(1) Based on the Kaplan-Meier product limit method, (2) Based on the complementary log-log transformation, (3) Based on the log-rank test, (4) Based on a Cox proportional hazards model, with Firth's adjustment if no relapses observed in a treatment arm,

(5) Wald confidence interval or Profile Likelihood Confidence Limits, if no relapses observed in a treatment arm, (6) Constructed as a risk ratio: A tipping point analysis quantifying the level of confounding which could compensate the estimated treatment effect.

(7) P-value is for the interaction term of treatment:subgroup from a Cox proportional hazards model with treatment, subgroup, and treatment:subgroup interaction as covariates, with Firth's adjustment if no relapses observed in a treatment arm.

Source: adsl, adtte

Table TFR-1.7
Time to First Adjudicated On-Trial Relapse by Rituximab use in the prior year
Censoring at Missed or Delayed Dose Due to COVID-19 Pandemic
Full Analysis Set

Rituximab use in the prior year	Variable	Statistic	Eculizumab (N=96)	Ravulizumab (N=58)	P-value (7)
Yes		n	19	20	
	Patients with an Adjudicated On-Trial Relapse	n (%)	1 (5.3)	0 (0.0)	
	Follow-up time (weeks)	Median (Min, Max)	88.00 (4.43, 117.71)	74.79 (53.00, 112.86)	
	Estimated proportion of patients relapse-free at	Cumulative probability (1) (95% CI (2))			
	24 weeks		1.000 (1.000, 1.000)	1.000 (1.000, 1.000)	
	48 weeks		1.000 (1.000, 1.000)	1.000 (1.000, 1.000)	
	72 weeks		0.929 (0.591, 0.990)	1.000 (1.000, 1.000)	
	96 weeks		0.929 (0.591, 0.990)	1.000 (1.000, 1.000)	
	120 weeks		NA (NA, NA)	NA (NA, NA)	
	144 weeks		NA (NA, NA)	NA (NA, NA)	

The eculizumab group data were collected as part of the PREVENT trial, Study ECU-NMO-301.

Patients who did not experience an adjudicated on-trial relapse were censored at the earlier of the end of the study period and 35 days after a missed or >35-day delayed dose due to the COVID-19 pandemic. If a patient in the eculizumab group was followed longer than any of the patients in the ravulizumab arm, then that patient was censored at the longest ravulizumab follow-up time.

(1) Based on the Kaplan-Meier product limit method, (2) Based on the complementary log-log transformation, (3) Based on the log-rank test, (4) Based on a Cox proportional hazards model, with Firth's adjustment if no relapses observed in a treatment arm,

(5) Wald confidence interval or Profile Likelihood Confidence Limits, if no relapses observed in a treatment arm, (6) Constructed as a risk ratio: A tipping point analysis quantifying the level of confounding which could compensate the estimated treatment effect.

(7) P-value is for the interaction term of treatment:subgroup from a Cox proportional hazards model with treatment, subgroup, and treatment:subgroup interaction as covariates, with Firth's adjustment if no relapses observed in a treatment arm.

Source: adsl, adtte

Table TFR-1.7
Time to First Adjudicated On-Trial Relapse by Rituximab use in the prior year
Censoring at Missed or Delayed Dose Due to COVID-19 Pandemic
Full Analysis Set

Rituximab use in the prior year	Variable	Statistic	Eculizumab (N=96)	Ravulizumab (N=58)	P-value (7)
Yes	Relapse-free time (weeks)	Percentile (1)			
		10th	NA	NA	
		25th	NA	NA	
		50th	NA	NA	
	Treatment Effect				
		p-value (3)		0.2320	0.9333
		Hazard ratio (4) (Ravulizumab/Eculizumab)		0.237	
		95% CI (5)		(0.002, 4.374)	
		% reduction (4) (Ravulizumab/Eculizumab)		76.3	
		95% CI (5)		(-337.4, 99.8)	
		E-value			
		For estimate		4.74	
		For upper 95% CL (6)		NA	

The eculizumab group data were collected as part of the PREVENT trial, Study ECU-NMO-301.

Patients who did not experience an adjudicated on-trial relapse were censored at the earlier of the end of the study period and 35 days after a missed or >35-day delayed dose due to the COVID-19 pandemic. If a patient in the eculizumab group was followed longer than any of the patients in the ravulizumab arm, then that patient was censored at the longest ravulizumab follow-up time.

(1) Based on the Kaplan-Meier product limit method, (2) Based on the complementary log-log transformation, (3) Based on the log-rank test, (4) Based on a Cox proportional hazards model, with Firth's adjustment if no relapses observed in a treatment arm,

(5) Wald confidence interval or Profile Likelihood Confidence Limits, if no relapses observed in a treatment arm, (6) Constructed as a risk ratio: A tipping point analysis quantifying the level of confounding which could compensate the estimated treatment effect.

(7) P-value is for the interaction term of treatment:subgroup from a Cox proportional hazards model with treatment, subgroup, and treatment:subgroup interaction as covariates, with Firth's adjustment if no relapses observed in a treatment arm.

Source: adsl, adtte

Table TFR-1.7
Time to First Adjudicated On-Trial Relapse by Rituximab use in the prior year
Censoring at Missed or Delayed Dose Due to COVID-19 Pandemic
Full Analysis Set

Rituximab use in the prior year	Variable	Statistic	Eculizumab (N=96)	Ravulizumab (N=58)	P-value (7)
No		n	77	38	
	Patients with an Adjudicated On-Trial Relapse	n (%)	2 (2.6)	0 (0.0)	
	Follow-up time (weeks)	Median (Min, Max)	94.00 (2.57, 117.71)	71.93 (11.00, 117.71)	
	Estimated proportion of patients relapse-free at	Cumulative probability (1) (95% CI (2))			
	24 weeks		0.973 (0.898, 0.993)	1.000 (1.000, 1.000)	
	48 weeks		0.973 (0.898, 0.993)	1.000 (1.000, 1.000)	
	72 weeks		0.973 (0.898, 0.993)	1.000 (1.000, 1.000)	
	96 weeks		0.973 (0.898, 0.993)	1.000 (1.000, 1.000)	
	120 weeks		NA (NA, NA)	NA (NA, NA)	
	144 weeks		NA (NA, NA)	NA (NA, NA)	

The eculizumab group data were collected as part of the PREVENT trial, Study ECU-NMO-301.

Patients who did not experience an adjudicated on-trial relapse were censored at the earlier of the end of the study period and 35 days after a missed or >35-day delayed dose due to the COVID-19 pandemic. If a patient in the eculizumab group was followed longer than any of the patients in the ravulizumab arm, then that patient was censored at the longest ravulizumab follow-up time.

(1) Based on the Kaplan-Meier product limit method, (2) Based on the complementary log-log transformation, (3) Based on the log-rank test, (4) Based on a Cox proportional hazards model, with Firth's adjustment if no relapses observed in a treatment arm,

(5) Wald confidence interval or Profile Likelihood Confidence Limits, if no relapses observed in a treatment arm, (6) Constructed as a risk ratio: A tipping point analysis quantifying the level of confounding which could compensate the estimated treatment effect.

(7) P-value is for the interaction term of treatment:subgroup from a Cox proportional hazards model with treatment, subgroup, and treatment:subgroup interaction as covariates, with Firth's adjustment if no relapses observed in a treatment arm.

Source: adsl, adtte

Table TFR-1.7
Time to First Adjudicated On-Trial Relapse by Rituximab use in the prior year
Censoring at Missed or Delayed Dose Due to COVID-19 Pandemic
Full Analysis Set

Rituximab use in the prior year	Variable	Statistic	Eculizumab (N=96)	Ravulizumab (N=58)	P-value (7)
No	Relapse-free time (weeks)	Percentile (1)			
		10th	NA	NA	
		25th	NA	NA	
		50th	NA	NA	
	Treatment Effect				
		p-value (3)		0.3172	
		Hazard ratio (4) (Ravulizumab/Eculizumab)		0.400	
		95% CI (5)		(0.003, 4.915)	
		% reduction (4) (Ravulizumab/Eculizumab)		60.0	
		95% CI (5)		(-391.5, 99.7)	
		E-value			
		For estimate		3.16	
		For upper 95% CL (6)		NA	

The eculizumab group data were collected as part of the PREVENT trial, Study ECU-NMO-301.

Patients who did not experience an adjudicated on-trial relapse were censored at the earlier of the end of the study period and 35 days after a missed or >35-day delayed dose due to the COVID-19 pandemic. If a patient in the eculizumab group was followed longer than any of the patients in the ravulizumab arm, then that patient was censored at the longest ravulizumab follow-up time.

(1) Based on the Kaplan-Meier product limit method, (2) Based on the complementary log-log transformation, (3) Based on the log-rank test, (4) Based on a Cox proportional hazards model, with Firth's adjustment if no relapses observed in a treatment arm,

(5) Wald confidence interval or Profile Likelihood Confidence Limits, if no relapses observed in a treatment arm, (6) Constructed as a risk ratio: A tipping point analysis quantifying the level of confounding which could compensate the estimated treatment effect.

(7) P-value is for the interaction term of treatment:subgroup from a Cox proportional hazards model with treatment, subgroup, and treatment:subgroup interaction as covariates, with Firth's adjustment if no relapses observed in a treatment arm.

Source: adsl, adtte

Table TFR-1.4
Time to First Adjudicated On-Trial Relapse by Disease severity via EDSS score at baseline
Censoring at Missed or Delayed Dose Due to COVID-19 Pandemic
Full Analysis Set

EDSS score at baseline	Variable	Statistic	Eculizumab (N=96)	Ravulizumab (N=58)	P-value (7)
< 5		n	66	49	
	Patients with an Adjudicated On-Trial Relapse	n (%)	1 (1.5)	0 (0.0)	
	Follow-up time (weeks)	Median (Min, Max)	92.35 (6.57, 117.71)	73.14 (11.00, 104.86)	
	Estimated proportion of patients relapse-free at	Cumulative probability (1) (95% CI (2))			
	24 weeks		0.984 (0.893, 0.998)	1.000 (1.000, 1.000)	
	48 weeks		0.984 (0.893, 0.998)	1.000 (1.000, 1.000)	
	72 weeks		0.984 (0.893, 0.998)	1.000 (1.000, 1.000)	
	96 weeks		0.984 (0.893, 0.998)	1.000 (1.000, 1.000)	
	120 weeks		NA (NA, NA)	NA (NA, NA)	
	144 weeks		NA (NA, NA)	NA (NA, NA)	

The eculizumab group data were collected as part of the PREVENT trial, Study ECU-NMO-301.

Patients who did not experience an adjudicated on-trial relapse were censored at the earlier of the end of the study period and 35 days after a missed or >35-day delayed dose due to the COVID-19 pandemic. If a patient in the eculizumab group was followed longer than any of the patients in the ravulizumab arm, then that patient was censored at the longest ravulizumab follow-up time.

(1) Based on the Kaplan-Meier product limit method, (2) Based on the complementary log-log transformation, (3) Based on the log-rank test, (4) Based on a Cox proportional hazards model, with Firth's adjustment if no relapses observed in a treatment arm,

(5) Wald confidence interval or Profile Likelihood Confidence Limits, if no relapses observed in a treatment arm, (6) Constructed as a risk ratio: A tipping point analysis quantifying the level of confounding which could compensate the estimated treatment effect.

(7) P-value is for the interaction term of treatment:subgroup from a Cox proportional hazards model with treatment, subgroup, and treatment:subgroup interaction as covariates, with Firth's adjustment if no relapses observed in a treatment arm.

Source: adsl, adtte

Table TFR-1.4
Time to First Adjudicated On-Trial Relapse by Disease severity via EDSS score at baseline
Censoring at Missed or Delayed Dose Due to COVID-19 Pandemic
Full Analysis Set

EDSS score at baseline	Variable	Statistic	Eculizumab (N=96)	Ravulizumab (N=58)	P-value (7)
< 5	Relapse-free time (weeks)	Percentile (1)			
		10th	NA	NA	
		25th	NA	NA	
		50th	NA	NA	
	Treatment Effect				
		p-value (3)		0.3827	0.9037
		Hazard ratio (4) (Ravulizumab/Eculizumab)		0.414	
		95% CI (5)		(0.003, 8.205)	
		% reduction (4) (Ravulizumab/Eculizumab)		58.6	
		95% CI (5)		(-720.5, 99.7)	
		E-value			
		For estimate		3.07	
		For upper 95% CL (6)		NA	

The eculizumab group data were collected as part of the PREVENT trial, Study ECU-NMO-301.

Patients who did not experience an adjudicated on-trial relapse were censored at the earlier of the end of the study period and 35 days after a missed or >35-day delayed dose due to the COVID-19 pandemic. If a patient in the eculizumab group was followed longer than any of the patients in the ravulizumab arm, then that patient was censored at the longest ravulizumab follow-up time.

(1) Based on the Kaplan-Meier product limit method, (2) Based on the complementary log-log transformation, (3) Based on the log-rank test, (4) Based on a Cox proportional hazards model, with Firth's adjustment if no relapses observed in a treatment arm,

(5) Wald confidence interval or Profile Likelihood Confidence Limits, if no relapses observed in a treatment arm, (6) Constructed as a risk ratio: A tipping point analysis quantifying the level of confounding which could compensate the estimated treatment effect.

(7) P-value is for the interaction term of treatment:subgroup from a Cox proportional hazards model with treatment, subgroup, and treatment:subgroup interaction as covariates, with Firth's adjustment if no relapses observed in a treatment arm.

Source: adsl, adtte

Table TFR-1.4
Time to First Adjudicated On-Trial Relapse by Disease severity via EDSS score at baseline
Censoring at Missed or Delayed Dose Due to COVID-19 Pandemic
Full Analysis Set

EDSS score at baseline	Variable	Statistic	Eculizumab (N=96)	Ravulizumab (N=58)	P-value (7)
>=5		n	30	9	
	Patients with an Adjudicated On-Trial Relapse	n (%)	2 (6.7)	0 (0.0)	
	Follow-up time (weeks)	Median (Min, Max)	78.58 (2.57, 117.71)	76.14 (53.00, 117.71)	
	Estimated proportion of patients relapse-free at	Cumulative probability (1) (95% CI (2))			
	24 weeks		0.967 (0.786, 0.995)	1.000 (1.000, 1.000)	
	48 weeks		0.967 (0.786, 0.995)	1.000 (1.000, 1.000)	
	72 weeks		0.918 (0.704, 0.980)	1.000 (1.000, 1.000)	
	96 weeks		0.918 (0.704, 0.980)	1.000 (1.000, 1.000)	
	120 weeks		NA (NA, NA)	NA (NA, NA)	
	144 weeks		NA (NA, NA)	NA (NA, NA)	

The eculizumab group data were collected as part of the PREVENT trial, Study ECU-NMO-301.

Patients who did not experience an adjudicated on-trial relapse were censored at the earlier of the end of the study period and 35 days after a missed or >35-day delayed dose due to the COVID-19 pandemic. If a patient in the eculizumab group was followed longer than any of the patients in the ravulizumab arm, then that patient was censored at the longest ravulizumab follow-up time.

(1) Based on the Kaplan-Meier product limit method, (2) Based on the complementary log-log transformation, (3) Based on the log-rank test, (4) Based on a Cox proportional hazards model, with Firth's adjustment if no relapses observed in a treatment arm,

(5) Wald confidence interval or Profile Likelihood Confidence Limits, if no relapses observed in a treatment arm, (6) Constructed as a risk ratio: A tipping point analysis quantifying the level of confounding which could compensate the estimated treatment effect.

(7) P-value is for the interaction term of treatment:subgroup from a Cox proportional hazards model with treatment, subgroup, and treatment:subgroup interaction as covariates, with Firth's adjustment if no relapses observed in a treatment arm.

Source: adsl, adtte

Table TFR-1.4
Time to First Adjudicated On-Trial Relapse by Disease severity via EDSS score at baseline
Censoring at Missed or Delayed Dose Due to COVID-19 Pandemic
Full Analysis Set

EDSS score at baseline	Variable	Statistic	Eculizumab (N=96)	Ravulizumab (N=58)	P-value (7)
>=5	Relapse-free time (weeks)	Percentile (1)			
		10th	NA	NA	
		25th	NA	NA	
		50th	NA	NA	
	Treatment Effect				
		p-value (3)		0.3872	
		Hazard ratio (4) (Ravulizumab/Eculizumab)		0.532	
		95% CI (5)		(0.004, 6.661)	
		% reduction (4) (Ravulizumab/Eculizumab)		46.8	
		95% CI (5)		(-566.1, 99.6)	
		E-value			
		For estimate		2.46	
		For upper 95% CL (6)		NA	

The eculizumab group data were collected as part of the PREVENT trial, Study ECU-NMO-301.

Patients who did not experience an adjudicated on-trial relapse were censored at the earlier of the end of the study period and 35 days after a missed or >35-day delayed dose due to the COVID-19 pandemic. If a patient in the eculizumab group was followed longer than any of the patients in the ravulizumab arm, then that patient was censored at the longest ravulizumab follow-up time.

(1) Based on the Kaplan-Meier product limit method, (2) Based on the complementary log-log transformation, (3) Based on the log-rank test, (4) Based on a Cox proportional hazards model, with Firth's adjustment if no relapses observed in a treatment arm,

(5) Wald confidence interval or Profile Likelihood Confidence Limits, if no relapses observed in a treatment arm, (6) Constructed as a risk ratio: A tipping point analysis quantifying the level of confounding which could compensate the estimated treatment effect.

(7) P-value is for the interaction term of treatment:subgroup from a Cox proportional hazards model with treatment, subgroup, and treatment:subgroup interaction as covariates, with Firth's adjustment if no relapses observed in a treatment arm.

Source: adsl, adtte

Table ARR-1.2
Adjudicated On-Trial Annualized Relapse Rate by Treatment Group by Sex
Adjusted for Historical ARR
Full Analysis Set

Sex	Variable	Statistic	Eculizumab (N=96)	Ravulizumab (N=58)	P-value (4)
Male		n	8	6	
	Number of patients with a total relapse count of				
	0	n (%)	8 (100.0)	6 (100.0)	
	Total number of relapses	Sum	0	0	
	Total number of patient-years in study period	Sum	12.38	8.43	
	Unadjusted annualized relapse rate (1)	Rate	0.00	0.00	
		95% CI	(NA, NA)	(NA, NA)	
	Adjusted annualized relapse rate (2)	Rate	NA	NA	
		95% CI	(NA, NA)	(NA, NA)	
	Treatment effect (2)	Rate ratio (Ravulizumab/Eculizumab)		NA	--
		95% CI		(NA, NA)	
		p-value		NA	
	Patient relapse rate (3)	n	8	6	
		Mean (SD)	0.00 (0.000)	0.00 (0.000)	
		Median	0.00	0.00	
		Q1, Q3	0.00, 0.00	0.00, 0.00	
		Min, Max	0.00, 0.00	0.00, 0.00	

The eculizumab group data were collected as part of the PREVENT trial, Study ECU-NMO-301.

The ARR was determined using a time period for patients in the ravulizumab arm that more closely matches the time period for patients in the eculizumab arm: the minimum of the end of primary treatment period date and the date of the Week 6 relapse evaluation visit for the first On-Trial Relapse, excluding the time from 36 days after a missed or delayed dose due to COVID-19 related reasons until the day before the next dose.

For patients in the eculizumab group, the maximum length of study period will not exceed the maximum length of the ravulizumab study period; relapses occurring beyond that time will not be included in this analysis.

(1) Calculated as the total number of relapses during the study period for all patients, divided by the total number of patient-years in the study period. Confidence interval based on a Poisson regression with treatment group covariate.

(2) Based on a Poisson regression adjusted for historical ARR in the 24 months prior to screening.
95% CI could not be estimated when the ARR or the rate ratio was 0.

(3) The number of relapses for each patient divided by the number of years in the study period for that patient. Summary statistics across all patients are presented.

(4) P-value is for the interaction term of treatment:subgroup from a Poisson regression adjusted for historical ARR in the 24 months prior to screening with treatment, subgroup, and treatment:subgroup interaction as covariates, with Firth's adjustment if no relapses observed in a treatment arm. P-value is for the iteraction term could not be determided when there were so few cases.

Source: adsl, adeff

Table ARR-1.2
Adjudicated On-Trial Annualized Relapse Rate by Treatment Group by Sex
Adjusted for Historical ARR
Full Analysis Set

Sex	Variable	Statistic	Eculizumab (N=96)	Ravulizumab (N=58)	P-value (4)
Female		n	88	52	
	Number of patients with a total relapse count of				
	0	n (%)	85 (96.6)	52 (100.0)	
	1	n (%)	3 (3.4)	0 (0.0)	
	Total number of relapses	Sum	3	0	
	Total number of patient-years in study period	Sum	133.54	73.00	
	Unadjusted annualized relapse rate (1)	Rate	0.02	0.00	
		95% CI	(0.01, 0.07)	(NA, NA)	
	Adjusted annualized relapse rate (2)	Rate	0.02	0.00	
		95% CI	(0.01, 0.07)	(NA, NA)	
	Treatment effect (2)	Rate ratio (Ravulizumab/Eculizumab)		0.000	
		95% CI		(NA, NA)	
		p-value		0.1067	
	Patient relapse rate (3)	n	88	52	
		Mean (SD)	0.10 (0.636)	0.00 (0.000)	
		Median	0.00	0.00	
		Q1, Q3	0.00, 0.00	0.00, 0.00	
		Min, Max	0.00, 5.37	0.00, 0.00	

The eculizumab group data were collected as part of the PREVENT trial, Study ECU-NMO-301.

The ARR was determined using a time period for patients in the ravulizumab arm that more closely matches the time period for patients in the eculizumab arm: the minimum of the end of primary treatment period date and the date of the Week 6 relapse evaluation visit for the first On-Trial Relapse, excluding the time from 36 days after a missed or delayed dose due to COVID-19 related reasons until the day before the next dose.

For patients in the eculizumab group, the maximum length of study period will not exceed the maximum length of the ravulizumab study period; relapses occurring beyond that time will not be included in this analysis.

(1) Calculated as the total number of relapses during the study period for all patients, divided by the total number of patient-years in the study period. Confidence interval based on a Poisson regression with treatment group covariate.

(2) Based on a Poisson regression adjusted for historical ARR in the 24 months prior to screening.
95% CI could not be estimated when the ARR or the rate ratio was 0.

(3) The number of relapses for each patient divided by the number of years in the study period for that patient. Summary statistics across all patients are presented.

(4) P-value is for the interaction term of treatment:subgroup from a Poisson regression adjusted for historical ARR in the 24 months prior to screening with treatment, subgroup, and treatment:subgroup interaction as covariates, with Firth's adjustment if no relapses observed in a treatment arm. P-value is for the iteraction term could not be determided when there were so few cases.

Source: adsl, adeff

Table ARR-1.3
Adjudicated On-Trial Annualized Relapse Rate by Treatment Group by Age Group
Adjusted for Historical ARR
Full Analysis Set

Age Group	Variable	Statistic	Eculizumab (N=96)	Ravulizumab (N=58)	P-value (4)
< 45 years		n	47	25	
	Number of patients with a total relapse count of				
	0	n (%)	47 (100.0)	25 (100.0)	
	Total number of relapses	Sum	0	0	
	Total number of patient-years in study period	Sum	68.15	35.18	
	Unadjusted annualized relapse rate (1)	Rate	0.00	0.00	
		95% CI	(NA, NA)	(NA, NA)	
	Adjusted annualized relapse rate (2)	Rate	NA	NA	
		95% CI	(NA, NA)	(NA, NA)	
	Treatment effect (2)	Rate ratio (Ravulizumab/Eculizumab)		NA	--
		95% CI		(NA, NA)	
		p-value		NA	
	Patient relapse rate (3)	n	47	25	
		Mean (SD)	0.00 (0.000)	0.00 (0.000)	
		Median	0.00	0.00	
		Q1, Q3	0.00, 0.00	0.00, 0.00	
		Min, Max	0.00, 0.00	0.00, 0.00	

The eculizumab group data were collected as part of the PREVENT trial, Study ECU-NMO-301.

The ARR was determined using a time period for patients in the ravulizumab arm that more closely matches the time period for patients in the eculizumab arm: the minimum of the end of primary treatment period date and the date of the Week 6 relapse evaluation visit for the first On-Trial Relapse, excluding the time from 36 days after a missed or delayed dose due to COVID-19 related reasons until the day before the next dose.

For patients in the eculizumab group, the maximum length of study period will not exceed the maximum length of the ravulizumab study period; relapses occurring beyond that time will not be included in this analysis.

(1) Calculated as the total number of relapses during the study period for all patients, divided by the total number of patient-years in the study period. Confidence interval based on a Poisson regression with treatment group covariate.

(2) Based on a Poisson regression adjusted for historical ARR in the 24 months prior to screening.
95% CI could not be estimated when the ARR or the rate ratio was 0.

(3) The number of relapses for each patient divided by the number of years in the study period for that patient. Summary statistics across all patients are presented.

(4) P-value is for the interaction term of treatment:subgroup from a Poisson regression adjusted for historical ARR in the 24 months prior to screening with treatment, subgroup, and treatment:subgroup interaction as covariates, with Firth's adjustment if no relapses observed in a treatment arm. P-value is for the iteraction term could not be determided when there were so few cases.

Source: adsl, adeff

Table ARR-1.3
Adjudicated On-Trial Annualized Relapse Rate by Treatment Group by Age Group
Adjusted for Historical ARR
Full Analysis Set

Age Group	Variable	Statistic	Eculizumab (N=96)	Ravulizumab (N=58)	P-value (4)
>= 45 years		n	49	33	
	Number of patients with a total relapse count of				
	0	n (%)	46 (93.9)	33 (100.0)	
	1	n (%)	3 (6.1)	0 (0.0)	
	Total number of relapses	Sum	3	0	
	Total number of patient-years in study period	Sum	77.77	46.25	
	Unadjusted annualized relapse rate (1)	Rate	0.04	0.00	
		95% CI	(0.01, 0.12)	(NA, NA)	
	Adjusted annualized relapse rate (2)	Rate	0.03	0.00	
		95% CI	(0.01, 0.12)	(NA, NA)	
	Treatment effect (2)	Rate ratio (Ravulizumab/Eculizumab)		0.000	
		95% CI		(NA, NA)	
		p-value		0.1058	
	Patient relapse rate (3)	n	49	33	
		Mean (SD)	0.18 (0.848)	0.00 (0.000)	
		Median	0.00	0.00	
		Q1, Q3	0.00, 0.00	0.00, 0.00	
		Min, Max	0.00, 5.37	0.00, 0.00	

The eculizumab group data were collected as part of the PREVENT trial, Study ECU-NMO-301.

The ARR was determined using a time period for patients in the ravulizumab arm that more closely matches the time period for patients in the eculizumab arm: the minimum of the end of primary treatment period date and the date of the Week 6 relapse evaluation visit for the first On-Trial Relapse, excluding the time from 36 days after a missed or delayed dose due to COVID-19 related reasons until the day before the next dose.

For patients in the eculizumab group, the maximum length of study period will not exceed the maximum length of the ravulizumab study period; relapses occurring beyond that time will not be included in this analysis.

(1) Calculated as the total number of relapses during the study period for all patients, divided by the total number of patient-years in the study period. Confidence interval based on a Poisson regression with treatment group covariate.

(2) Based on a Poisson regression adjusted for historical ARR in the 24 months prior to screening.
95% CI could not be estimated when the ARR or the rate ratio was 0.

(3) The number of relapses for each patient divided by the number of years in the study period for that patient. Summary statistics across all patients are presented.

(4) P-value is for the interaction term of treatment:subgroup from a Poisson regression adjusted for historical ARR in the 24 months prior to screening with treatment, subgroup, and treatment:subgroup interaction as covariates, with Firth's adjustment if no relapses observed in a treatment arm. P-value is for the iteraction term could not be determided when there were so few cases.

Source: adsl, adeff

Table ARR-1.5
Adjudicated On-Trial Annualized Relapse Rate by Treatment Group by Region
Adjusted for Historical ARR
Full Analysis Set

Region	Variable	Statistic	Eculizumab (N=96)	Ravulizumab (N=58)	P-value (4)
Asia-Pacific		n	35	20	
	Number of patients with a total relapse count of				
	0	n (%)	34 (97.1)	20 (100.0)	
	1	n (%)	1 (2.9)	0 (0.0)	
	Total number of relapses	Sum	1	0	
	Total number of patient-years in study period	Sum	54.46	28.66	
	Unadjusted annualized relapse rate (1)	Rate	0.02	0.00	
		95% CI	(0.00, 0.13)	(NA, NA)	
	Adjusted annualized relapse rate (2)	Rate	NA	NA	
		95% CI	(NA, NA)	(NA, NA)	
	Treatment effect (2)	Rate ratio (Ravulizumab/Eculizumab)		NA	1.0000
		95% CI		(NA, NA)	
		p-value		NA	
	Patient relapse rate (3)	n	35	20	
		Mean (SD)	0.07 (0.426)	0.00 (0.000)	
		Median	0.00	0.00	
		Q1, Q3	0.00, 0.00	0.00, 0.00	
		Min, Max	0.00, 2.52	0.00, 0.00	

The eculizumab group data were collected as part of the PREVENT trial, Study ECU-NMO-301.
The ARR was determined using a time period for patients in the ravulizumab arm that more closely matches the time period for patients in the eculizumab arm: the minimum of the end of primary treatment period date and the date of the Week 6 relapse evaluation visit for the first On-Trial Relapse, excluding the time from 36 days after a missed or delayed dose due to COVID-19 related reasons until the day before the next dose.
For patients in the eculizumab group, the maximum length of study period will not exceed the maximum length of the ravulizumab study period; relapses occurring beyond that time will not be included in this analysis.
(1) Calculated as the total number of relapses during the study period for all patients, divided by the total number of patient-years in the study period. Confidence interval based on a Poisson regression with treatment group covariate.
(2) Based on a Poisson regression adjusted for historical ARR in the 24 months prior to screening.
95% CI could not be estimated when the ARR or the rate ratio was 0.
(3) The number of relapses for each patient divided by the number of years in the study period for that patient. Summary statistics across all patients are presented.
(4) P-value is for the interaction term of treatment:subgroup from a Poisson regression adjusted for historical ARR in the 24 months prior to screening with treatment, subgroup, and treatment:subgroup interaction as covariates, with Firth's adjustment if no relapses observed in a treatment arm. P-value is for the iteraction term could not be determided when there were so few cases.
For eculizumab arm, Americas: ARG and USA; Europe: CZE, DEU, DNK, ESP, HRV, ITA, RUS and TUR; Asia-Pacific: AUS, HKG, JPN, KOR, MYS, THA and TWN. For ravulizumab arm, Americas: CAN and USA; Europe: DEU, DNK, ESP, GBR, ITA and POL; Asia-Pacific: AUS, JPN and KOR.
Source: adsl, adeff

Table ARR-1.5
Adjudicated On-Trial Annualized Relapse Rate by Treatment Group by Region
Adjusted for Historical ARR
Full Analysis Set

Region	Variable	Statistic	Eculizumab (N=96)	Ravulizumab (N=58)	P-value (4)
Americas		n	29	21	
	Number of patients with a total relapse count of				
	0	n (%)	28 (96.6)	21 (100.0)	
	1	n (%)	1 (3.4)	0 (0.0)	
	Total number of relapses	Sum	1	0	
	Total number of patient-years in study period	Sum	39.93	33.07	
	Unadjusted annualized relapse rate (1)	Rate	0.03	0.00	
		95% CI	(0.00, 0.18)	(NA, NA)	
	Adjusted annualized relapse rate (2)	Rate	0.01	0.00	
		95% CI	(0.00, 0.61)	(NA, NA)	
	Treatment effect (2)	Rate ratio (Ravulizumab/Eculizumab)		0.000	1.0000
		95% CI		(NA, NA)	
		p-value		0.1696	
	Patient relapse rate (3)	n	29	21	
		Mean (SD)	0.03 (0.180)	0.00 (0.000)	
		Median	0.00	0.00	
		Q1, Q3	0.00, 0.00	0.00, 0.00	
		Min, Max	0.00, 0.97	0.00, 0.00	

The eculizumab group data were collected as part of the PREVENT trial, Study ECU-NMO-301.
The ARR was determined using a time period for patients in the ravulizumab arm that more closely matches the time period for patients in the eculizumab arm: the minimum of the end of primary treatment period date and the date of the Week 6 relapse evaluation visit for the first On-Trial Relapse, excluding the time from 36 days after a missed or delayed dose due to COVID-19 related reasons until the day before the next dose.
For patients in the eculizumab group, the maximum length of study period will not exceed the maximum length of the ravulizumab study period; relapses occurring beyond that time will not be included in this analysis.
(1) Calculated as the total number of relapses during the study period for all patients, divided by the total number of patient-years in the study period. Confidence interval based on a Poisson regression with treatment group covariate.
(2) Based on a Poisson regression adjusted for historical ARR in the 24 months prior to screening.
95% CI could not be estimated when the ARR or the rate ratio was 0.
(3) The number of relapses for each patient divided by the number of years in the study period for that patient. Summary statistics across all patients are presented.
(4) P-value is for the interaction term of treatment:subgroup from a Poisson regression adjusted for historical ARR in the 24 months prior to screening with treatment, subgroup, and treatment:subgroup interaction as covariates, with Firth's adjustment if no relapses observed in a treatment arm. P-value is for the iteraction term could not be determided when there were so few cases.
For eculizumab arm, Americas: ARG and USA; Europe: CZE, DEU, DNK, ESP, HRV, ITA, RUS and TUR; Asia-Pacific: AUS, HKG, JPN, KOR, MYS, THA and TWN. For ravulizumab arm, Americas: CAN and USA; Europe: DEU, DNK, ESP, GBR, ITA and POL; Asia-Pacific: AUS, JPN and KOR.
Source: adsl, adeff

Table ARR-1.5
Adjudicated On-Trial Annualized Relapse Rate by Treatment Group by Region
Adjusted for Historical ARR
Full Analysis Set

Region	Variable	Statistic	Eculizumab (N=96)	Ravulizumab (N=58)	P-value (4)
Europe		n	32	17	
	Number of patients with a total relapse count of				
	0	n (%)	31 (96.9)	17 (100.0)	
	1	n (%)	1 (3.1)	0 (0.0)	
	Total number of relapses	Sum	1	0	
	Total number of patient-years in study period	Sum	51.53	19.70	
	Unadjusted annualized relapse rate (1)	Rate	0.02	0.00	
		95% CI	(0.00, 0.14)	(NA, NA)	
	Adjusted annualized relapse rate (2)	Rate	0.00	0.00	
		95% CI	(NA, NA)	(NA, NA)	
	Treatment effect (2)	Rate ratio (Ravulizumab/Eculizumab)		0.000	
		95% CI		(NA, NA)	
		p-value		0.0957	
	Patient relapse rate (3)	n	32	17	
		Mean (SD)	0.17 (0.950)	0.00 (0.000)	
		Median	0.00	0.00	
		Q1, Q3	0.00, 0.00	0.00, 0.00	
		Min, Max	0.00, 5.37	0.00, 0.00	

The eculizumab group data were collected as part of the PREVENT trial, Study ECU-NMO-301.
The ARR was determined using a time period for patients in the ravulizumab arm that more closely matches the time period for patients in the eculizumab arm: the minimum of the end of primary treatment period date and the date of the Week 6 relapse evaluation visit for the first On-Trial Relapse, excluding the time from 36 days after a missed or delayed dose due to COVID-19 related reasons until the day before the next dose.
For patients in the eculizumab group, the maximum length of study period will not exceed the maximum length of the ravulizumab study period; relapses occurring beyond that time will not be included in this analysis.
(1) Calculated as the total number of relapses during the study period for all patients, divided by the total number of patient-years in the study period. Confidence interval based on a Poisson regression with treatment group covariate.
(2) Based on a Poisson regression adjusted for historical ARR in the 24 months prior to screening.
95% CI could not be estimated when the ARR or the rate ratio was 0.
(3) The number of relapses for each patient divided by the number of years in the study period for that patient. Summary statistics across all patients are presented.
(4) P-value is for the interaction term of treatment:subgroup from a Poisson regression adjusted for historical ARR in the 24 months prior to screening with treatment, subgroup, and treatment:subgroup interaction as covariates, with Firth's adjustment if no relapses observed in a treatment arm. P-value is for the iteraction term could not be determided when there were so few cases.
For eculizumab arm, Americas: ARG and USA; Europe: CZE, DEU, DNK, ESP, HRV, ITA, RUS and TUR; Asia-Pacific: AUS, HKG, JPN, KOR, MYS, THA and TWN. For ravulizumab arm, Americas: CAN and USA; Europe: DEU, DNK, ESP, GBR, ITA and POL; Asia-Pacific: AUS, JPN and KOR.
Source: adsl, adeff

Table ARR-1.6
Adjudicated On-Trial Annualized Relapse Rate by Treatment Group by Supportive IST use at baseline
Adjusted for Historical ARR
Full Analysis Set

IST use at baseline	Variable	Statistic	Eculizumab (N=96)	Ravulizumab (N=58)	P-value (4)
Yes		n	75	28	
	Number of patients with a total relapse count of				
	0	n (%)	72 (96.0)	28 (100.0)	
	1	n (%)	3 (4.0)	0 (0.0)	
	Total number of relapses	Sum	3	0	
	Total number of patient-years in study period	Sum	111.90	39.06	
	Unadjusted annualized relapse rate (1)	Rate	0.03	0.00	
		95% CI	(0.01, 0.08)	(NA, NA)	
	Adjusted annualized relapse rate (2)	Rate	0.03	0.00	
		95% CI	(0.01, 0.08)	(NA, NA)	
	Treatment effect (2)	Rate ratio (Ravulizumab/Eculizumab)		0.000	--
		95% CI		(NA, NA)	
		p-value		0.1879	
	Patient relapse rate (3)	n	75	28	
		Mean (SD)	0.12 (0.689)	0.00 (0.000)	
		Median	0.00	0.00	
		Q1, Q3	0.00, 0.00	0.00, 0.00	
		Min, Max	0.00, 5.37	0.00, 0.00	

The eculizumab group data were collected as part of the PREVENT trial, Study ECU-NMO-301.

The ARR was determined using a time period for patients in the ravulizumab arm that more closely matches the time period for patients in the eculizumab arm: the minimum of the end of primary treatment period date and the date of the Week 6 relapse evaluation visit for the first On-Trial Relapse, excluding the time from 36 days after a missed or delayed dose due to COVID-19 related reasons until the day before the next dose.

For patients in the eculizumab group, the maximum length of study period will not exceed the maximum length of the ravulizumab study period; relapses occurring beyond that time will not be included in this analysis.

(1) Calculated as the total number of relapses during the study period for all patients, divided by the total number of patient-years in the study period. Confidence interval based on a Poisson regression with treatment group covariate.

(2) Based on a Poisson regression adjusted for historical ARR in the 24 months prior to screening.
95% CI could not be estimated when the ARR or the rate ratio was 0.

(3) The number of relapses for each patient divided by the number of years in the study period for that patient. Summary statistics across all patients are presented.

(4) P-value is for the interaction term of treatment:subgroup from a Poisson regression adjusted for historical ARR in the 24 months prior to screening with treatment, subgroup, and treatment:subgroup interaction as covariates, with Firth's adjustment if no relapses observed in a treatment arm. P-value is for the iteraction term could not be determided when there were so few cases.

Source: adsl, adeff

Table ARR-1.6
Adjudicated On-Trial Annualized Relapse Rate by Treatment Group by Supportive IST use at baseline
Adjusted for Historical ARR
Full Analysis Set

IST use at baseline	Variable	Statistic	Eculizumab (N=96)	Ravulizumab (N=58)	P-value (4)
No		n	21	30	
	Number of patients with a total relapse count of				
	0	n (%)	21 (100.0)	30 (100.0)	
	Total number of relapses	Sum	0	0	
	Total number of patient-years in study period	Sum	34.02	42.36	
	Unadjusted annualized relapse rate (1)	Rate	0.00	0.00	
		95% CI	(NA, NA)	(NA, NA)	
	Adjusted annualized relapse rate (2)	Rate	NA	NA	
		95% CI	(NA, NA)	(NA, NA)	
	Treatment effect (2)	Rate ratio (Ravulizumab/Eculizumab)		NA	
		95% CI		(NA, NA)	
		p-value		NA	
	Patient relapse rate (3)	n	21	30	
		Mean (SD)	0.00 (0.000)	0.00 (0.000)	
		Median	0.00	0.00	
		Q1, Q3	0.00, 0.00	0.00, 0.00	
		Min, Max	0.00, 0.00	0.00, 0.00	

The eculizumab group data were collected as part of the PREVENT trial, Study ECU-NMO-301.

The ARR was determined using a time period for patients in the ravulizumab arm that more closely matches the time period for patients in the eculizumab arm: the minimum of the end of primary treatment period date and the date of the Week 6 relapse evaluation visit for the first On-Trial Relapse, excluding the time from 36 days after a missed or delayed dose due to COVID-19 related reasons until the day before the next dose.

For patients in the eculizumab group, the maximum length of study period will not exceed the maximum length of the ravulizumab study period; relapses occurring beyond that time will not be included in this analysis.

(1) Calculated as the total number of relapses during the study period for all patients, divided by the total number of patient-years in the study period. Confidence interval based on a Poisson regression with treatment group covariate.

(2) Based on a Poisson regression adjusted for historical ARR in the 24 months prior to screening.
95% CI could not be estimated when the ARR or the rate ratio was 0.

(3) The number of relapses for each patient divided by the number of years in the study period for that patient. Summary statistics across all patients are presented.

(4) P-value is for the interaction term of treatment:subgroup from a Poisson regression adjusted for historical ARR in the 24 months prior to screening with treatment, subgroup, and treatment:subgroup interaction as covariates, with Firth's adjustment if no relapses observed in a treatment arm. P-value is for the iteraction term could not be determided when there were so few cases.

Source: adsl, adeff

Table ARR-1.7
Adjudicated On-Trial Annualized Relapse Rate by Treatment Group by Rituximab use in the prior year
Adjusted for Historical ARR
Full Analysis Set

Rituximab use in the prior year	Variable	Statistic	Eculizumab (N=96)	Ravulizumab (N=58)	P-value (4)
Yes		n	19	20	
	Number of patients with a total relapse count of				
	0	n (%)	18 (94.7)	20 (100.0)	
	1	n (%)	1 (5.3)	0 (0.0)	
	Total number of relapses	Sum	1	0	
	Total number of patient-years in study period	Sum	27.47	27.85	
	Unadjusted annualized relapse rate (1)	Rate	0.04	0.00	
		95% CI	(0.01, 0.26)	(NA, NA)	
	Adjusted annualized relapse rate (2)	Rate	NA	NA	
		95% CI	(NA, NA)	(NA, NA)	
	Treatment effect (2)	Rate ratio (Ravulizumab/Eculizumab)		NA	1.0000
		95% CI		(NA, NA)	
		p-value		NA	
	Patient relapse rate (3)	n	19	20	
		Mean (SD)	0.05 (0.222)	0.00 (0.000)	
		Median	0.00	0.00	
		Q1, Q3	0.00, 0.00	0.00, 0.00	
		Min, Max	0.00, 0.97	0.00, 0.00	

The eculizumab group data were collected as part of the PREVENT trial, Study ECU-NMO-301.

The ARR was determined using a time period for patients in the ravulizumab arm that more closely matches the time period for patients in the eculizumab arm: the minimum of the end of primary treatment period date and the date of the Week 6 relapse evaluation visit for the first On-Trial Relapse, excluding the time from 36 days after a missed or delayed dose due to COVID-19 related reasons until the day before the next dose.

For patients in the eculizumab group, the maximum length of study period will not exceed the maximum length of the ravulizumab study period; relapses occurring beyond that time will not be included in this analysis.

(1) Calculated as the total number of relapses during the study period for all patients, divided by the total number of patient-years in the study period. Confidence interval based on a Poisson regression with treatment group covariate.

(2) Based on a Poisson regression adjusted for historical ARR in the 24 months prior to screening.
95% CI could not be estimated when the ARR or the rate ratio was 0.

(3) The number of relapses for each patient divided by the number of years in the study period for that patient. Summary statistics across all patients are presented.

(4) P-value is for the interaction term of treatment:subgroup from a Poisson regression adjusted for historical ARR in the 24 months prior to screening with treatment, subgroup, and treatment:subgroup interaction as covariates, with Firth's adjustment if no relapses observed in a treatment arm. P-value is for the iteraction term could not be determided when there were so few cases.

Source: adsl, adeff

Table ARR-1.7
Adjudicated On-Trial Annualized Relapse Rate by Treatment Group by Rituximab use in the prior year
Adjusted for Historical ARR
Full Analysis Set

Rituximab use in the prior year	Variable	Statistic	Eculizumab (N=96)	Ravulizumab (N=58)	P-value (4)
No		n	77	38	
	Number of patients with a total relapse count of				
	0	n (%)	75 (97.4)	38 (100.0)	
	1	n (%)	2 (2.6)	0 (0.0)	
	Total number of relapses	Sum	2	0	
	Total number of patient-years in study period	Sum	118.45	53.57	
	Unadjusted annualized relapse rate (1)	Rate	0.02	0.00	
		95% CI	(0.00, 0.07)	(NA, NA)	
	Adjusted annualized relapse rate (2)	Rate	0.02	0.00	
		95% CI	(0.00, 0.07)	(NA, NA)	
	Treatment effect (2)	Rate ratio (Ravulizumab/Eculizumab)		0.000	
		95% CI		(NA, NA)	
		p-value		0.1775	
	Patient relapse rate (3)	n	77	38	
		Mean (SD)	0.10 (0.673)	0.00 (0.000)	
		Median	0.00	0.00	
		Q1, Q3	0.00, 0.00	0.00, 0.00	
		Min, Max	0.00, 5.37	0.00, 0.00	

The eculizumab group data were collected as part of the PREVENT trial, Study ECU-NMO-301.

The ARR was determined using a time period for patients in the ravulizumab arm that more closely matches the time period for patients in the eculizumab arm: the minimum of the end of primary treatment period date and the date of the Week 6 relapse evaluation visit for the first On-Trial Relapse, excluding the time from 36 days after a missed or delayed dose due to COVID-19 related reasons until the day before the next dose.

For patients in the eculizumab group, the maximum length of study period will not exceed the maximum length of the ravulizumab study period; relapses occurring beyond that time will not be included in this analysis.

(1) Calculated as the total number of relapses during the study period for all patients, divided by the total number of patient-years in the study period. Confidence interval based on a Poisson regression with treatment group covariate.

(2) Based on a Poisson regression adjusted for historical ARR in the 24 months prior to screening.
95% CI could not be estimated when the ARR or the rate ratio was 0.

(3) The number of relapses for each patient divided by the number of years in the study period for that patient. Summary statistics across all patients are presented.

(4) P-value is for the interaction term of treatment:subgroup from a Poisson regression adjusted for historical ARR in the 24 months prior to screening with treatment, subgroup, and treatment:subgroup interaction as covariates, with Firth's adjustment if no relapses observed in a treatment arm. P-value is for the iteraction term could not be determided when there were so few cases.

Source: adsl, adeff

Table ARR-1.4
Adjudicated On-Trial Annualized Relapse Rate by Treatment Group by Disease severity via EDSS score at baseline
Adjusted for Historical ARR
Full Analysis Set

EDSS score at baseline	Variable	Statistic	Eculizumab (N=96)	Ravulizumab (N=58)	P-value (4)
< 5		n	66	49	
	Number of patients with a total relapse count of				
	0	n (%)	65 (98.5)	49 (100.0)	
	1	n (%)	1 (1.5)	0 (0.0)	
	Total number of relapses	Sum	1	0	
	Total number of patient-years in study period	Sum	101.56	70.31	
	Unadjusted annualized relapse rate (1)	Rate	0.01	0.00	
		95% CI	(0.00, 0.07)	(NA, NA)	
	Adjusted annualized relapse rate (2)	Rate	NA	NA	
		95% CI	(NA, NA)	(NA, NA)	
	Treatment effect (2)	Rate ratio (Ravulizumab/Eculizumab)		NA	--
		95% CI		(NA, NA)	
		p-value		NA	
	Patient relapse rate (3)	n	66	49	
		Mean (SD)	0.04 (0.310)	0.00 (0.000)	
		Median	0.00	0.00	
		Q1, Q3	0.00, 0.00	0.00, 0.00	
		Min, Max	0.00, 2.52	0.00, 0.00	

The eculizumab group data were collected as part of the PREVENT trial, Study ECU-NMO-301.

The ARR was determined using a time period for patients in the ravulizumab arm that more closely matches the time period for patients in the eculizumab arm: the minimum of the end of primary treatment period date and the date of the Week 6 relapse evaluation visit for the first On-Trial Relapse, excluding the time from 36 days after a missed or delayed dose due to COVID-19 related reasons until the day before the next dose.

For patients in the eculizumab group, the maximum length of study period will not exceed the maximum length of the ravulizumab study period; relapses occurring beyond that time will not be included in this analysis.

(1) Calculated as the total number of relapses during the study period for all patients, divided by the total number of patient-years in the study period. Confidence interval based on a Poisson regression with treatment group covariate.

(2) Based on a Poisson regression adjusted for historical ARR in the 24 months prior to screening.
95% CI could not be estimated when the ARR or the rate ratio was 0.

(3) The number of relapses for each patient divided by the number of years in the study period for that patient. Summary statistics across all patients are presented.

(4) P-value is for the interaction term of treatment:subgroup from a Poisson regression adjusted for historical ARR in the 24 months prior to screening with treatment, subgroup, and treatment:subgroup interaction as covariates, with Firth's adjustment if no relapses observed in a treatment arm. P-value is for the iteraction term could not be determided when there were so few cases.

Source: adsl, adeff

Table ARR-1.4
Adjudicated On-Trial Annualized Relapse Rate by Treatment Group by Disease severity via EDSS score at baseline
Adjusted for Historical ARR
Full Analysis Set

EDSS score at baseline	Variable	Statistic	Eculizumab (N=96)	Ravulizumab (N=58)	P-value (4)
>= 5		n	30	9	
	Number of patients with a total relapse count of				
	0	n (%)	28 (93.3)	9 (100.0)	
	1	n (%)	2 (6.7)	0 (0.0)	
	Total number of relapses	Sum	2	0	
	Total number of patient-years in study period	Sum	44.36	11.11	
	Unadjusted annualized relapse rate (1)	Rate	0.05	0.00	
		95% CI	(0.01, 0.18)	(NA, NA)	
	Adjusted annualized relapse rate (2)	Rate	0.01	0.00	
		95% CI	(0.00, 0.17)	(NA, NA)	
	Treatment effect (2)	Rate ratio (Ravulizumab/Eculizumab)		0.000	
		95% CI		(NA, NA)	
		p-value		0.4864	
	Patient relapse rate (3)	n	30	9	
		Mean (SD)	0.21 (0.990)	0.00 (0.000)	
		Median	0.00	0.00	
		Q1, Q3	0.00, 0.00	0.00, 0.00	
		Min, Max	0.00, 5.37	0.00, 0.00	

The eculizumab group data were collected as part of the PREVENT trial, Study ECU-NMO-301.

The ARR was determined using a time period for patients in the ravulizumab arm that more closely matches the time period for patients in the eculizumab arm: the minimum of the end of primary treatment period date and the date of the Week 6 relapse evaluation visit for the first On-Trial Relapse, excluding the time from 36 days after a missed or delayed dose due to COVID-19 related reasons until the day before the next dose.

For patients in the eculizumab group, the maximum length of study period will not exceed the maximum length of the ravulizumab study period; relapses occurring beyond that time will not be included in this analysis.

(1) Calculated as the total number of relapses during the study period for all patients, divided by the total number of patient-years in the study period. Confidence interval based on a Poisson regression with treatment group covariate.

(2) Based on a Poisson regression adjusted for historical ARR in the 24 months prior to screening.
95% CI could not be estimated when the ARR or the rate ratio was 0.

(3) The number of relapses for each patient divided by the number of years in the study period for that patient. Summary statistics across all patients are presented.

(4) P-value is for the interaction term of treatment:subgroup from a Poisson regression adjusted for historical ARR in the 24 months prior to screening with treatment, subgroup, and treatment:subgroup interaction as covariates, with Firth's adjustment if no relapses observed in a treatment arm. P-value is for the iteraction term could not be determided when there were so few cases.

Source: adsl, adeff

Table RL-3.2
Summary of Severity of Relapse by Patient by Sex
Full Analysis Set with An On-Trial Relapse

Sex	Variable	Statistic	Eculizumab	Ravulizumab
Male	Patients with an adjudicated on-trial relapse		0	0
	Major	n (%)	0 (0.0)	0 (0.0)
	Minor	n (%)	0 (0.0)	0 (0.0)
	Patients with an on-trial relapse (1)		1	0
	Major	n (%)	0 (0.0)	0 (0.0)
	Minor	n (%)	1 (100.0)	0 (0.0)
Female	Patients with an adjudicated on-trial relapse		3	0
	Major	n (%)	1 (33.3)	0 (0.0)
	Minor	n (%)	2 (66.7)	0 (0.0)
	Patients with an on-trial relapse (1)		13	2
	Major	n (%)	3 (23.1)	0 (0.0)
	Minor	n (%)	9 (69.2)	2 (100.0)
	Unknown	n (%)	1 (7.7)	0 (0.0)

The eculizumab group data were collected as part of the PREVENT trial, Study ECU-NMO-301.
If a patient had more than one relapse, the relapse used for time to first relapse analysis is presented in the table. If the relapse includes more than one type of relapse, the worst severity is presented in the table. Severity of a relapse as measured by OSIS was only classified for Optic Neuritis and Acute Myelitis relapses; patients with other types of relapses are reported as unknown.
(1) Includes both positively and negatively adjudicated on-trial relapses.
Source: adce, adtte

Table RL-3.3
Summary of Severity of Relapse by Patient by Age Group
Full Analysis Set with An On-Trial Relapse

Age Group	Variable	Statistic	Eculizumab	Ravulizumab
< 45 years	Patients with an adjudicated on-trial relapse		0	0
	Major	n (%)	0 (0.0)	0 (0.0)
	Minor	n (%)	0 (0.0)	0 (0.0)
	Patients with an on-trial relapse (1)		4	1
	Major	n (%)	0 (0.0)	0 (0.0)
	Minor	n (%)	4 (100.0)	1 (100.0)
>= 45 years	Patients with an adjudicated on-trial relapse		3	0
	Major	n (%)	1 (33.3)	0 (0.0)
	Minor	n (%)	2 (66.7)	0 (0.0)
	Patients with an on-trial relapse (1)		10	1
	Major	n (%)	3 (30.0)	0 (0.0)
	Minor	n (%)	6 (60.0)	1 (100.0)
	Unknown	n (%)	1 (10.0)	0 (0.0)

The eculizumab group data were collected as part of the PREVENT trial, Study ECU-NMO-301.
If a patient had more than one relapse, the relapse used for time to first relapse analysis is presented in the table. If the relapse includes more than one type of relapse, the worst severity is presented in the table. Severity of a relapse as measured by OSIS was only classified for Optic Neuritis and Acute Myelitis relapses; patients with other types of relapses are reported as unknown.
(1) Includes both positively and negatively adjudicated on-trial relapses.
Source: adce, adtte

Table RL-3.5
Summary of Severity of Relapse by Patient by Region
Full Analysis Set with An On-Trial Relapse

Region	Variable	Statistic	Eculizumab	Ravulizumab
Asia-Pacific	Patients with an adjudicated on-trial relapse		1	0
	Major	n (%)	0 (0.0)	0 (0.0)
	Minor	n (%)	1 (100.0)	0 (0.0)
	Patients with an on-trial relapse (1)		4	0
	Major	n (%)	0 (0.0)	0 (0.0)
	Minor	n (%)	4 (100.0)	0 (0.0)
Americas	Patients with an adjudicated on-trial relapse		1	0
	Major	n (%)	1 (100.0)	0 (0.0)
	Minor	n (%)	0 (0.0)	0 (0.0)
	Patients with an on-trial relapse (1)		3	2
	Major	n (%)	1 (33.3)	0 (0.0)
	Minor	n (%)	2 (66.7)	2 (100.0)
Europe	Patients with an adjudicated on-trial relapse		1	0
	Major	n (%)	0 (0.0)	0 (0.0)
	Minor	n (%)	1 (100.0)	0 (0.0)
	Patients with an on-trial relapse (1)		7	0
	Major	n (%)	2 (28.6)	0 (0.0)
	Minor	n (%)	4 (57.1)	0 (0.0)
	Unknown	n (%)	1 (14.3)	0 (0.0)

The eculizumab group data were collected as part of the PREVENT trial, Study ECU-NMO-301.
If a patient had more than one relapse, the relapse used for time to first relapse analysis is presented in the table. If the relapse includes more than one type of relapse, the worst severity is presented in the table. Severity of a relapse as measured by OSIS was only classified for Optic Neuritis and Acute Myelitis relapses; patients with other types of relapses are reported as unknown.
(1) Includes both positively and negatively adjudicated on-trial relapses.
For eculizumab arm, Americas: ARG and USA; Europe: CZE, DEU, DNK, ESP, HRV, ITA, RUS and TUR; Asia-Pacific: AUS, HKG, JPN, KOR, MYS, THA and TWN. For ravulizumab arm, Americas: CAN and USA; Europe: DEU, DNK, ESP, GBR, ITA and POL; Asia-Pacific: AUS, JPN and KOR.
Source: adce, adtte

Table RL-3.6
Summary of Severity of Relapse by Patient by Supportive IST use at baseline
Full Analysis Set with An On-Trial Relapse

IST use at baseline	Variable	Statistic	Eculizumab	Ravulizumab
Yes	Patients with an adjudicated on-trial relapse		3	0
	Major	n (%)	1 (33.3)	0 (0.0)
	Minor	n (%)	2 (66.7)	0 (0.0)
	Patients with an on-trial relapse (1)		14	1
	Major	n (%)	3 (21.4)	0 (0.0)
	Minor	n (%)	10 (71.4)	1 (100.0)
	Unknown	n (%)	1 (7.1)	0 (0.0)
No	Patients with an adjudicated on-trial relapse		0	0
	Major	n (%)	0 (0.0)	0 (0.0)
	Minor	n (%)	0 (0.0)	0 (0.0)
	Patients with an on-trial relapse (1)		0	1
	Major	n (%)	0 (0.0)	0 (0.0)
	Minor	n (%)	0 (0.0)	1 (100.0)

The eculizumab group data were collected as part of the PREVENT trial, Study ECU-NMO-301.
If a patient had more than one relapse, the relapse used for time to first relapse analysis is presented in the table. If the relapse includes more than one type of relapse, the worst severity is presented in the table. Severity of a relapse as measured by OSIS was only classified for Optic Neuritis and Acute Myelitis relapses; patients with other types of relapses are reported as unknown.
(1) Includes both positively and negatively adjudicated on-trial relapses.
Source: adce, adtte

Table RL-3.7
Summary of Severity of Relapse by Patient by Rituximab use in the prior year
Full Analysis Set with An On-Trial Relapse

Rituximab use in the prior year	Variable	Statistic	Eculizumab	Ravulizumab
Yes	Patients with an adjudicated on-trial relapse		1	0
	Major	n (%)	1 (100.0)	0 (0.0)
	Minor	n (%)	0 (0.0)	0 (0.0)
	Patients with an on-trial relapse (1)		4	2
	Major	n (%)	1 (25.0)	0 (0.0)
	Minor	n (%)	3 (75.0)	2 (100.0)
No	Patients with an adjudicated on-trial relapse		2	0
	Major	n (%)	0 (0.0)	0 (0.0)
	Minor	n (%)	2 (100.0)	0 (0.0)
	Patients with an on-trial relapse (1)		10	0
	Major	n (%)	2 (20.0)	0 (0.0)
	Minor	n (%)	7 (70.0)	0 (0.0)
	Unknown	n (%)	1 (10.0)	0 (0.0)

The eculizumab group data were collected as part of the PREVENT trial, Study ECU-NMO-301.
If a patient had more than one relapse, the relapse used for time to first relapse analysis is presented in the table. If the relapse includes more than one type of relapse, the worst severity is presented in the table. Severity of a relapse as measured by OSIS was only classified for Optic Neuritis and Acute Myelitis relapses; patients with other types of relapses are reported as unknown.
(1) Includes both positively and negatively adjudicated on-trial relapses.
Source: adce, adtte

Table RL-3.4
Summary of Severity of Relapse by Patient by Disease severity via EDSS score at baseline
Full Analysis Set with An On-Trial Relapse

EDSS score at baseline	Variable	Statistic	Eculizumab	Ravulizumab
< 5	Patients with an adjudicated on-trial relapse		1	0
	Major	n (%)	0 (0.0)	0 (0.0)
	Minor	n (%)	1 (100.0)	0 (0.0)
	Patients with an on-trial relapse (1)		8	0
	Major	n (%)	1 (12.5)	0 (0.0)
	Minor	n (%)	6 (75.0)	0 (0.0)
	Unknown	n (%)	1 (12.5)	0 (0.0)
>=5	Patients with an adjudicated on-trial relapse		2	0
	Major	n (%)	1 (50.0)	0 (0.0)
	Minor	n (%)	1 (50.0)	0 (0.0)
	Patients with an on-trial relapse (1)		6	2
	Major	n (%)	2 (33.3)	0 (0.0)
	Minor	n (%)	4 (66.7)	2 (100.0)

The eculizumab group data were collected as part of the PREVENT trial, Study ECU-NMO-301.
If a patient had more than one relapse, the relapse used for time to first relapse analysis is presented in the table. If the relapse includes more than one type of relapse, the worst severity is presented in the table. Severity of a relapse as measured by OSIS was only classified for Optic Neuritis and Acute Myelitis relapses; patients with other types of relapses are reported as unknown.
(1) Includes both positively and negatively adjudicated on-trial relapses.
Source: adce, adtte

Table RL-2.2
Summary of Adjudicated On-trial Relapse Treatment and Hospitalizations by Treatment Group by Sex
Full Analysis Set

Sex	Variable	Statistic	Eculizumab (N=96)	Ravulizumab (N=58)
Male		n	8	6
	Number of patients with an Adjudicated On-Trial relapse requiring hospitalization	n (%)	0 (0.0)	0 (0.0)
	Total number of Adjudicated On-Trial relapses requiring hospitalization	Sum	0	0
	Total number of patient-years in study period	Sum	12.38	8.43
	Annualized relapse-related hospitalization rate (1)	Rate	0.00	0.00
		95% CI	(NA, NA)	(NA, NA)
		p-value		NA
	Number of patients with an Adjudicated On-Trial relapse requiring acute treatment with			
	High-dose oral steroids	n (%)	0 (0.0)	0 (0.0)
	IV Methylprednisolone	n (%)	0 (0.0)	0 (0.0)
	Plasma Exchange	n (%)	0 (0.0)	0 (0.0)
	IVIg	n (%)	0 (0.0)	0 (0.0)
	Total number of Adjudicated On-Trial relapses requiring acute treatment with			
	High-dose oral steroids	Sum	0	0
	IV Methylprednisolone	Sum	0	0
	Plasma Exchange	Sum	0	0
	IVIg	Sum	0	0

The eculizumab group data were collected as part of the PREVENT trial, Study ECU-NMO-301.
Summaries and analyses performed using a time period for patients in the ravulizumab arm that more closely matches the time period for patients in the eculizumab arm: the minimum of the end of primary treatment period date and the date of the Week 6 relapse evaluation visit for the first On-Trial Relapse, excluding the time from 36 days after a missed or delayed dose due to COVID-19 related reasons until the day before the next dose.
For patients in the eculizumab group, the maximum length of study period will not exceed the maximum length of the ravulizumab study period; relapses occurring beyond that time will not be included in this analysis.
(1) Calculated as the total number of On-Trial relapses requiring hospitalization/treatment during the study period for all patients, divided by the total number of patient-years in the study period. P-value and confidence interval based on a Poisson regression with treatment group covariate and log of the time period as an offset variable.
95% CI could not be estimated when the ARR was 0.
Source: adsl, adce, adeff

Table RL-2.2
Summary of Adjudicated On-trial Relapse Treatment and Hospitalizations by Treatment Group by Sex
Full Analysis Set

Sex	Variable	Statistic	Eculizumab (N=96)	Ravulizumab (N=58)
Male	Annualized relapse-related (1)			
	High-dose oral steroid rate	Rate	0.00	0.00
		95% CI	(NA, NA)	(NA, NA)
		p-value		NA
	IV Methylprednisolone rate	Rate	0.00	0.00
		95% CI	(NA, NA)	(NA, NA)
		p-value		NA
	Plasma Exchange rate	Rate	0.00	0.00
		95% CI	(NA, NA)	(NA, NA)
		p-value		NA
	IVIg rate	Rate	0.00	0.00
		95% CI	(NA, NA)	(NA, NA)
	Number of relapse-related plasma exchange sessions			
		n	0	0
		Mean (SD)		
		Median		
		Q1, Q3		
		Min, Max		
		Total		

The eculizumab group data were collected as part of the PREVENT trial, Study ECU-NMO-301.
Summaries and analyses performed using a time period for patients in the ravulizumab arm that more closely matches the time period for patients in the eculizumab arm: the minimum of the end of primary treatment period date and the date of the Week 6 relapse evaluation visit for the first On-Trial Relapse, excluding the time from 36 days after a missed or delayed dose due to COVID-19 related reasons until the day before the next dose.
For patients in the eculizumab group, the maximum length of study period will not exceed the maximum length of the ravulizumab study period; relapses occurring beyond that time will not be included in this analysis.
(1) Calculated as the total number of On-Trial relapses requiring hospitalization/treatment during the study period for all patients, divided by the total number of patient-years in the study period. P-value and confidence interval based on a Poisson regression with treatment group covariate and log of the time period as an offset variable.
95% CI could not be estimated when the ARR was 0.
Source: adsl, adce, adeff

Table RL-2.2
Summary of Adjudicated On-trial Relapse Treatment and Hospitalizations by Treatment Group by Sex
Full Analysis Set

Sex	Variable	Statistic	Eculizumab (N=96)	Ravulizumab (N=58)
Female		n	88	52
	Number of patients with an Adjudicated On-Trial relapse requiring hospitalization	n (%)	2 (2.3)	0 (0.0)
	Total number of Adjudicated On-Trial relapses requiring hospitalization	Sum	2	0
	Total number of patient-years in study period	Sum	133.54	73.00
	Annualized relapse-related hospitalization rate (1)	Rate	0.01	0.00
		95% CI	(0.00, 0.06)	(NA, NA)
		p-value		0.1866
	Number of patients with an Adjudicated On-Trial relapse requiring acute treatment with			
	High-dose oral steroids	n (%)	2 (2.3)	0 (0.0)
	IV Methylprednisolone	n (%)	2 (2.3)	0 (0.0)
	Plasma Exchange	n (%)	2 (2.3)	0 (0.0)
	IVIg	n (%)	0 (0.0)	0 (0.0)
	Total number of Adjudicated On-Trial relapses requiring acute treatment with			
	High-dose oral steroids	Sum	2	0
	IV Methylprednisolone	Sum	2	0
	Plasma Exchange	Sum	2	0
	IVIg	Sum	0	0

The eculizumab group data were collected as part of the PREVENT trial, Study ECU-NMO-301.
Summaries and analyses performed using a time period for patients in the ravulizumab arm that more closely matches the time period for patients in the eculizumab arm: the minimum of the end of primary treatment period date and the date of the Week 6 relapse evaluation visit for the first On-Trial Relapse, excluding the time from 36 days after a missed or delayed dose due to COVID-19 related reasons until the day before the next dose.
For patients in the eculizumab group, the maximum length of study period will not exceed the maximum length of the ravulizumab study period; relapses occurring beyond that time will not be included in this analysis.
(1) Calculated as the total number of On-Trial relapses requiring hospitalization/treatment during the study period for all patients, divided by the total number of patient-years in the study period. P-value and confidence interval based on a Poisson regression with treatment group covariate and log of the time period as an offset variable.
95% CI could not be estimated when the ARR was 0.
Source: adsl, adce, adeff

Table RL-2.2
Summary of Adjudicated On-trial Relapse Treatment and Hospitalizations by Treatment Group by Sex
Full Analysis Set

Sex	Variable	Statistic	Eculizumab (N=96)	Ravulizumab (N=58)
Female	Annualized relapse-related (1)			
	High-dose oral steroid rate	Rate	0.01	0.00
		95% CI	(0.00, 0.06)	(NA, NA)
		p-value		0.1866
	IV Methylprednisolone rate	Rate	0.01	0.00
		95% CI	(0.00, 0.06)	(NA, NA)
		p-value		0.1866
	Plasma Exchange rate	Rate	0.01	0.00
		95% CI	(0.00, 0.06)	(NA, NA)
		p-value		0.1866
	IVIg rate	Rate	0.00	0.00
		95% CI	(NA, NA)	(NA, NA)
	Number of relapse-related plasma exchange sessions			
		n	2	0
		Mean (SD)	8.5 (2.12)	
		Median	8.5	
		Q1, Q3	7, 10	
		Min, Max	7, 10	
		Total	17	

The eculizumab group data were collected as part of the PREVENT trial, Study ECU-NMO-301.
Summaries and analyses performed using a time period for patients in the ravulizumab arm that more closely matches the time period for patients in the eculizumab arm: the minimum of the end of primary treatment period date and the date of the Week 6 relapse evaluation visit for the first On-Trial Relapse, excluding the time from 36 days after a missed or delayed dose due to COVID-19 related reasons until the day before the next dose.
For patients in the eculizumab group, the maximum length of study period will not exceed the maximum length of the ravulizumab study period; relapses occurring beyond that time will not be included in this analysis.
(1) Calculated as the total number of On-Trial relapses requiring hospitalization/treatment during the study period for all patients, divided by the total number of patient-years in the study period. P-value and confidence interval based on a Poisson regression with treatment group covariate and log of the time period as an offset variable.
95% CI could not be estimated when the ARR was 0.
Source: adsl, adce, adeff

Table RL-2.3
Summary of Adjudicated On-trial Relapse Treatment and Hospitalizations by Treatment Group by Age Group
Full Analysis Set

Age Group	Variable	Statistic	Eculizumab (N=96)	Ravulizumab (N=58)
< 45 years		n	47	25
	Number of patients with an Adjudicated On-Trial relapse requiring hospitalization	n (%)	0 (0.0)	0 (0.0)
	Total number of Adjudicated On-Trial relapses requiring hospitalization	Sum	0	0
	Total number of patient-years in study period	Sum	68.15	35.18
	Annualized relapse-related hospitalization rate (1)	Rate	0.00	0.00
		95% CI	(NA, NA)	(NA, NA)
		p-value		NA
	Number of patients with an Adjudicated On-Trial relapse requiring acute treatment with			
	High-dose oral steroids	n (%)	0 (0.0)	0 (0.0)
	IV Methylprednisolone	n (%)	0 (0.0)	0 (0.0)
	Plasma Exchange	n (%)	0 (0.0)	0 (0.0)
	IVIg	n (%)	0 (0.0)	0 (0.0)
	Total number of Adjudicated On-Trial relapses requiring acute treatment with			
	High-dose oral steroids	Sum	0	0
	IV Methylprednisolone	Sum	0	0
	Plasma Exchange	Sum	0	0
	IVIg	Sum	0	0

The eculizumab group data were collected as part of the PREVENT trial, Study ECU-NMO-301.
Summaries and analyses performed using a time period for patients in the ravulizumab arm that more closely matches the time period for patients in the eculizumab arm: the minimum of the end of primary treatment period date and the date of the Week 6 relapse evaluation visit for the first On-Trial Relapse, excluding the time from 36 days after a missed or delayed dose due to COVID-19 related reasons until the day before the next dose.
For patients in the eculizumab group, the maximum length of study period will not exceed the maximum length of the ravulizumab study period; relapses occurring beyond that time will not be included in this analysis.
(1) Calculated as the total number of On-Trial relapses requiring hospitalization/treatment during the study period for all patients, divided by the total number of patient-years in the study period. P-value and confidence interval based on a Poisson regression with treatment group covariate and log of the time period as an offset variable.
95% CI could not be estimated when the ARR was 0.
Source: adsl, adce, adeff

Table RL-2.3
Summary of Adjudicated On-trial Relapse Treatment and Hospitalizations by Treatment Group by Age Group
Full Analysis Set

Age Group	Variable	Statistic	Eculizumab (N=96)	Ravulizumab (N=58)
< 45 years	Annualized relapse-related (1)			
	High-dose oral steroid rate	Rate	0.00	0.00
		95% CI	(NA, NA)	(NA, NA)
		p-value		NA
	IV Methylprednisolone rate	Rate	0.00	0.00
		95% CI	(NA, NA)	(NA, NA)
		p-value		NA
	Plasma Exchange rate	Rate	0.00	0.00
		95% CI	(NA, NA)	(NA, NA)
		p-value		NA
	IVIg rate	Rate	0.00	0.00
		95% CI	(NA, NA)	(NA, NA)
	Number of relapse-related plasma exchange sessions			
		n	0	0
		Mean (SD)		
		Median		
		Q1, Q3		
		Min, Max		
		Total		

The eculizumab group data were collected as part of the PREVENT trial, Study ECU-NMO-301.
Summaries and analyses performed using a time period for patients in the ravulizumab arm that more closely matches the time period for patients in the eculizumab arm: the minimum of the end of primary treatment period date and the date of the Week 6 relapse evaluation visit for the first On-Trial Relapse, excluding the time from 36 days after a missed or delayed dose due to COVID-19 related reasons until the day before the next dose.
For patients in the eculizumab group, the maximum length of study period will not exceed the maximum length of the ravulizumab study period; relapses occurring beyond that time will not be included in this analysis.
(1) Calculated as the total number of On-Trial relapses requiring hospitalization/treatment during the study period for all patients, divided by the total number of patient-years in the study period. P-value and confidence interval based on a Poisson regression with treatment group covariate and log of the time period as an offset variable.
95% CI could not be estimated when the ARR was 0.
Source: adsl, adce, adeff

Table RL-2.3
Summary of Adjudicated On-trial Relapse Treatment and Hospitalizations by Treatment Group by Age Group
Full Analysis Set

Age Group	Variable	Statistic	Eculizumab (N=96)	Ravulizumab (N=58)
>= 45 years		n	49	33
	Number of patients with an Adjudicated On-Trial relapse requiring hospitalization	n (%)	2 (4.1)	0 (0.0)
	Total number of Adjudicated On-Trial relapses requiring hospitalization	Sum	2	0
	Total number of patient-years in study period	Sum	77.77	46.25
	Annualized relapse-related hospitalization rate (1)	Rate	0.03	0.00
		95% CI	(0.01, 0.10)	(NA, NA)
		p-value		0.1719
	Number of patients with an Adjudicated On-Trial relapse requiring acute treatment with			
	High-dose oral steroids	n (%)	2 (4.1)	0 (0.0)
	IV Methylprednisolone	n (%)	2 (4.1)	0 (0.0)
	Plasma Exchange	n (%)	2 (4.1)	0 (0.0)
	IVIg	n (%)	0 (0.0)	0 (0.0)
	Total number of Adjudicated On-Trial relapses requiring acute treatment with			
	High-dose oral steroids	Sum	2	0
	IV Methylprednisolone	Sum	2	0
	Plasma Exchange	Sum	2	0
	IVIg	Sum	0	0

The eculizumab group data were collected as part of the PREVENT trial, Study ECU-NMO-301.
Summaries and analyses performed using a time period for patients in the ravulizumab arm that more closely matches the time period for patients in the eculizumab arm: the minimum of the end of primary treatment period date and the date of the Week 6 relapse evaluation visit for the first On-Trial Relapse, excluding the time from 36 days after a missed or delayed dose due to COVID-19 related reasons until the day before the next dose.
For patients in the eculizumab group, the maximum length of study period will not exceed the maximum length of the ravulizumab study period; relapses occurring beyond that time will not be included in this analysis.
(1) Calculated as the total number of On-Trial relapses requiring hospitalization/treatment during the study period for all patients, divided by the total number of patient-years in the study period. P-value and confidence interval based on a Poisson regression with treatment group covariate and log of the time period as an offset variable.
95% CI could not be estimated when the ARR was 0.
Source: adsl, adce, adeff

Table RL-2.3
Summary of Adjudicated On-trial Relapse Treatment and Hospitalizations by Treatment Group by Age Group
Full Analysis Set

Age Group	Variable	Statistic	Eculizumab (N=96)	Ravulizumab (N=58)
>= 45 years	Annualized relapse-related (1)			
	High-dose oral steroid rate	Rate	0.03	0.00
		95% CI	(0.01, 0.10)	(NA, NA)
		p-value		0.1719
	IV Methylprednisolone rate	Rate	0.03	0.00
		95% CI	(0.01, 0.10)	(NA, NA)
		p-value		0.1719
	Plasma Exchange rate	Rate	0.03	0.00
		95% CI	(0.01, 0.10)	(NA, NA)
		p-value		0.1719
	IVIg rate	Rate	0.00	0.00
		95% CI	(NA, NA)	(NA, NA)
	Number of relapse-related plasma exchange sessions			
		n	2	0
		Mean (SD)	8.5 (2.12)	
		Median	8.5	
		Q1, Q3	7, 10	
		Min, Max	7, 10	
		Total	17	

The eculizumab group data were collected as part of the PREVENT trial, Study ECU-NMO-301.
Summaries and analyses performed using a time period for patients in the ravulizumab arm that more closely matches the time period for patients in the eculizumab arm: the minimum of the end of primary treatment period date and the date of the Week 6 relapse evaluation visit for the first On-Trial Relapse, excluding the time from 36 days after a missed or delayed dose due to COVID-19 related reasons until the day before the next dose.
For patients in the eculizumab group, the maximum length of study period will not exceed the maximum length of the ravulizumab study period; relapses occurring beyond that time will not be included in this analysis.
(1) Calculated as the total number of On-Trial relapses requiring hospitalization/treatment during the study period for all patients, divided by the total number of patient-years in the study period. P-value and confidence interval based on a Poisson regression with treatment group covariate and log of the time period as an offset variable.
95% CI could not be estimated when the ARR was 0.
Source: adsl, adce, adeff

Table RL-2.5
Summary of Adjudicated On-trial Relapse Treatment and Hospitalizations by Treatment Group by Region
Full Analysis Set

Region	Variable	Statistic	Eculizumab (N=96)	Ravulizumab (N=58)
Asia-Pacific		n	35	20
	Number of patients with an Adjudicated On-Trial relapse requiring hospitalization	n (%)	1 (2.9)	0 (0.0)
	Total number of Adjudicated On-Trial relapses requiring hospitalization	Sum	1	0
	Total number of patient-years in study period	Sum	54.46	28.66
	Annualized relapse-related hospitalization rate (1)	Rate	0.02	0.00
		95% CI	(0.00, 0.13)	(NA, NA)
		p-value		0.3578
	Number of patients with an Adjudicated On-Trial relapse requiring acute treatment with			
	High-dose oral steroids	n (%)	0 (0.0)	0 (0.0)
	IV Methylprednisolone	n (%)	1 (2.9)	0 (0.0)
	Plasma Exchange	n (%)	1 (2.9)	0 (0.0)
	IVIg	n (%)	0 (0.0)	0 (0.0)
	Total number of Adjudicated On-Trial relapses requiring acute treatment with			
	High-dose oral steroids	Sum	0	0
	IV Methylprednisolone	Sum	1	0
	Plasma Exchange	Sum	1	0
	IVIg	Sum	0	0

The eculizumab group data were collected as part of the PREVENT trial, Study ECU-NMO-301.
Summaries and analyses performed using a time period for patients in the ravulizumab arm that more closely matches the time period for patients in the eculizumab arm: the minimum of the end of primary treatment period date and the date of the Week 6 relapse evaluation visit for the first On-Trial Relapse, excluding the time from 36 days after a missed or delayed dose due to COVID-19 related reasons until the day before the next dose.
For patients in the eculizumab group, the maximum length of study period will not exceed the maximum length of the ravulizumab study period; relapses occurring beyond that time will not be included in this analysis.
(1) Calculated as the total number of On-Trial relapses requiring hospitalization/treatment during the study period for all patients, divided by the total number of patient-years in the study period. P-value and confidence interval based on a Poisson regression with treatment group covariate and log of the time period as an offset variable.
95% CI could not be estimated when the ARR was 0.
For eculizumab arm, Americas: ARG and USA; Europe: CZE, DEU, DNK, ESP, HRV, ITA, RUS and TUR; Asia-Pacific: AUS, HKG, JPN, KOR, MYS, THA and TWN. For ravulizumab arm, Americas: CAN and USA; Europe: DEU, DNK, ESP, GBR, ITA and POL; Asia-Pacific: AUS, JPN and KOR.
Source: adsl, adce, adeff
Run Date: 2023-04-18T16:02:02 FINAL
/alxn/a1210-nmo-307/a1210-nmo-307-amnog/Files/tables/production/programs/t-hosp.sas

Table RL-2.5
Summary of Adjudicated On-trial Relapse Treatment and Hospitalizations by Treatment Group by Region
Full Analysis Set

Region	Variable	Statistic	Eculizumab (N=96)	Ravulizumab (N=58)
Asia-Pacific	Annualized relapse-related (1)			
	High-dose oral steroid rate	Rate	0.00	0.00
		95% CI	(NA, NA)	(NA, NA)
		p-value		NA
	IV Methylprednisolone rate	Rate	0.02	0.00
		95% CI	(0.00, 0.13)	(NA, NA)
		p-value		0.3578
	Plasma Exchange rate	Rate	0.02	0.00
		95% CI	(0.00, 0.13)	(NA, NA)
		p-value		0.3578
	IVIg rate	Rate	0.00	0.00
		95% CI	(NA, NA)	(NA, NA)
	Number of relapse-related plasma exchange sessions			
		n	1	0
		Mean (SD)	10.0 (NA)	
		Median	10.0	
		Q1, Q3	10, 10	
		Min, Max	10, 10	
		Total	10	

The eculizumab group data were collected as part of the PREVENT trial, Study ECU-NMO-301.

Summaries and analyses performed using a time period for patients in the ravulizumab arm that more closely matches the time period for patients in the eculizumab arm: the minimum of the end of primary treatment period date and the date of the Week 6 relapse evaluation visit for the first On-Trial Relapse, excluding the time from 36 days after a missed or delayed dose due to COVID-19 related reasons until the day before the next dose.

For patients in the eculizumab group, the maximum length of study period will not exceed the maximum length of the ravulizumab study period; relapses occurring beyond that time will not be included in this analysis.

(1) Calculated as the total number of On-Trial relapses requiring hospitalization/treatment during the study period for all patients, divided by the total number of patient-years in the study period. P-value and confidence interval based on a Poisson regression with treatment group covariate and log of the time period as an offset variable.

95% CI could not be estimated when the ARR was 0.

For eculizumab arm, Americas: ARG and USA; Europe: CZE, DEU, DNK, ESP, HRV, ITA, RUS and TUR; Asia-Pacific: AUS, HKG, JPN, KOR, MYS, THA and TWN. For ravulizumab arm, Americas: CAN and USA; Europe: DEU, DNK, ESP, GBR, ITA and POL; Asia-Pacific: AUS, JPN and KOR.

Source: adsl, adce, adeff

Table RL-2.5
Summary of Adjudicated On-trial Relapse Treatment and Hospitalizations by Treatment Group by Region
Full Analysis Set

Region	Variable	Statistic	Eculizumab (N=96)	Ravulizumab (N=58)
Americas		n	29	21
	Number of patients with an Adjudicated On-Trial relapse requiring hospitalization	n (%)	0 (0.0)	0 (0.0)
	Total number of Adjudicated On-Trial relapses requiring hospitalization	Sum	0	0
	Total number of patient-years in study period	Sum	39.93	33.07
	Annualized relapse-related hospitalization rate (1)	Rate	0.00	0.00
		95% CI	(NA, NA)	(NA, NA)
		p-value		NA
	Number of patients with an Adjudicated On-Trial relapse requiring acute treatment with			
	High-dose oral steroids	n (%)	1 (3.4)	0 (0.0)
	IV Methylprednisolone	n (%)	0 (0.0)	0 (0.0)
	Plasma Exchange	n (%)	0 (0.0)	0 (0.0)
	IVIg	n (%)	0 (0.0)	0 (0.0)
	Total number of Adjudicated On-Trial relapses requiring acute treatment with			
	High-dose oral steroids	Sum	1	0
	IV Methylprednisolone	Sum	0	0
	Plasma Exchange	Sum	0	0
	IVIg	Sum	0	0

The eculizumab group data were collected as part of the PREVENT trial, Study ECU-NMO-301.
Summaries and analyses performed using a time period for patients in the ravulizumab arm that more closely matches the time period for patients in the eculizumab arm: the minimum of the end of primary treatment period date and the date of the Week 6 relapse evaluation visit for the first On-Trial Relapse, excluding the time from 36 days after a missed or delayed dose due to COVID-19 related reasons until the day before the next dose.
For patients in the eculizumab group, the maximum length of study period will not exceed the maximum length of the ravulizumab study period; relapses occurring beyond that time will not be included in this analysis.
(1) Calculated as the total number of On-Trial relapses requiring hospitalization/treatment during the study period for all patients, divided by the total number of patient-years in the study period. P-value and confidence interval based on a Poisson regression with treatment group covariate and log of the time period as an offset variable.
95% CI could not be estimated when the ARR was 0.
For eculizumab arm, Americas: ARG and USA; Europe: CZE, DEU, DNK, ESP, HRV, ITA, RUS and TUR; Asia-Pacific: AUS, HKG, JPN, KOR, MYS, THA and TWN. For ravulizumab arm, Americas: CAN and USA; Europe: DEU, DNK, ESP, GBR, ITA and POL; Asia-Pacific: AUS, JPN and KOR.
Source: adsl, adce, adeff

Table RL-2.5
Summary of Adjudicated On-trial Relapse Treatment and Hospitalizations by Treatment Group by Region
Full Analysis Set

Region	Variable	Statistic	Eculizumab (N=96)	Ravulizumab (N=58)
Americas	Annualized relapse-related (1)			
	High-dose oral steroid rate	Rate	0.03	0.00
		95% CI	(0.00, 0.18)	(NA, NA)
		p-value		0.2720
	IV Methylprednisolone rate	Rate	0.00	0.00
		95% CI	(NA, NA)	(NA, NA)
		p-value		NA
	Plasma Exchange rate	Rate	0.00	0.00
		95% CI	(NA, NA)	(NA, NA)
		p-value		NA
	IVIg rate	Rate	0.00	0.00
		95% CI	(NA, NA)	(NA, NA)
	Number of relapse-related plasma exchange sessions			
		n	0	0
		Mean (SD)		
		Median		
		Q1, Q3		
		Min, Max		
		Total		

The eculizumab group data were collected as part of the PREVENT trial, Study ECU-NMO-301.
Summaries and analyses performed using a time period for patients in the ravulizumab arm that more closely matches the time period for patients in the eculizumab arm: the minimum of the end of primary treatment period date and the date of the Week 6 relapse evaluation visit for the first On-Trial Relapse, excluding the time from 36 days after a missed or delayed dose due to COVID-19 related reasons until the day before the next dose.
For patients in the eculizumab group, the maximum length of study period will not exceed the maximum length of the ravulizumab study period; relapses occurring beyond that time will not be included in this analysis.
(1) Calculated as the total number of On-Trial relapses requiring hospitalization/treatment during the study period for all patients, divided by the total number of patient-years in the study period. P-value and confidence interval based on a Poisson regression with treatment group covariate and log of the time period as an offset variable.
95% CI could not be estimated when the ARR was 0.
For eculizumab arm, Americas: ARG and USA; Europe: CZE, DEU, DNK, ESP, HRV, ITA, RUS and TUR; Asia-Pacific: AUS, HKG, JPN, KOR, MYS, THA and TWN. For ravulizumab arm, Americas: CAN and USA; Europe: DEU, DNK, ESP, GBR, ITA and POL; Asia-Pacific: AUS, JPN and KOR.
Source: adsl, adce, adeff

Table RL-2.5
Summary of Adjudicated On-trial Relapse Treatment and Hospitalizations by Treatment Group by Region
Full Analysis Set

Region	Variable	Statistic	Eculizumab (N=96)	Ravulizumab (N=58)
Europe		n	32	17
	Number of patients with an Adjudicated On-Trial relapse requiring hospitalization	n (%)	1 (3.1)	0 (0.0)
	Total number of Adjudicated On-Trial relapses requiring hospitalization	Sum	1	0
	Total number of patient-years in study period	Sum	51.53	19.70
	Annualized relapse-related hospitalization rate (1)	Rate	0.02	0.00
		95% CI	(0.00, 0.14)	(NA, NA)
		p-value		0.4210
	Number of patients with an Adjudicated On-Trial relapse requiring acute treatment with			
	High-dose oral steroids	n (%)	1 (3.1)	0 (0.0)
	IV Methylprednisolone	n (%)	1 (3.1)	0 (0.0)
	Plasma Exchange	n (%)	1 (3.1)	0 (0.0)
	IVIg	n (%)	0 (0.0)	0 (0.0)
	Total number of Adjudicated On-Trial relapses requiring acute treatment with			
	High-dose oral steroids	Sum	1	0
	IV Methylprednisolone	Sum	1	0
	Plasma Exchange	Sum	1	0
	IVIg	Sum	0	0

The eculizumab group data were collected as part of the PREVENT trial, Study ECU-NMO-301.
Summaries and analyses performed using a time period for patients in the ravulizumab arm that more closely matches the time period for patients in the eculizumab arm: the minimum of the end of primary treatment period date and the date of the Week 6 relapse evaluation visit for the first On-Trial Relapse, excluding the time from 36 days after a missed or delayed dose due to COVID-19 related reasons until the day before the next dose.
For patients in the eculizumab group, the maximum length of study period will not exceed the maximum length of the ravulizumab study period; relapses occurring beyond that time will not be included in this analysis.
(1) Calculated as the total number of On-Trial relapses requiring hospitalization/treatment during the study period for all patients, divided by the total number of patient-years in the study period. P-value and confidence interval based on a Poisson regression with treatment group covariate and log of the time period as an offset variable.
95% CI could not be estimated when the ARR was 0.
For eculizumab arm, Americas: ARG and USA; Europe: CZE, DEU, DNK, ESP, HRV, ITA, RUS and TUR; Asia-Pacific: AUS, HKG, JPN, KOR, MYS, THA and TWN. For ravulizumab arm, Americas: CAN and USA; Europe: DEU, DNK, ESP, GBR, ITA and POL; Asia-Pacific: AUS, JPN and KOR.
Source: adsl, adce, adeff

Table RL-2.5
Summary of Adjudicated On-trial Relapse Treatment and Hospitalizations by Treatment Group by Region
Full Analysis Set

Region	Variable	Statistic	Eculizumab (N=96)	Ravulizumab (N=58)
Europe	Annualized relapse-related (1)			
	High-dose oral steroid rate	Rate	0.02	0.00
		95% CI	(0.00, 0.14)	(NA, NA)
		p-value		0.4210
	IV Methylprednisolone rate	Rate	0.02	0.00
		95% CI	(0.00, 0.14)	(NA, NA)
		p-value		0.4210
	Plasma Exchange rate	Rate	0.02	0.00
		95% CI	(0.00, 0.14)	(NA, NA)
		p-value		0.4210
	IVIg rate	Rate	0.00	0.00
		95% CI	(NA, NA)	(NA, NA)
	Number of relapse-related plasma exchange sessions			
		n	1	0
		Mean (SD)	7.0 (NA)	
		Median	7.0	
		Q1, Q3	7, 7	
		Min, Max	7, 7	
		Total	7	

The eculizumab group data were collected as part of the PREVENT trial, Study ECU-NMO-301.

Summaries and analyses performed using a time period for patients in the ravulizumab arm that more closely matches the time period for patients in the eculizumab arm: the minimum of the end of primary treatment period date and the date of the Week 6 relapse evaluation visit for the first On-Trial Relapse, excluding the time from 36 days after a missed or delayed dose due to COVID-19 related reasons until the day before the next dose.

For patients in the eculizumab group, the maximum length of study period will not exceed the maximum length of the ravulizumab study period; relapses occurring beyond that time will not be included in this analysis.

(1) Calculated as the total number of On-Trial relapses requiring hospitalization/treatment during the study period for all patients, divided by the total number of patient-years in the study period. P-value and confidence interval based on a Poisson regression with treatment group covariate and log of the time period as an offset variable.

95% CI could not be estimated when the ARR was 0.

For eculizumab arm, Americas: ARG and USA; Europe: CZE, DEU, DNK, ESP, HRV, ITA, RUS and TUR; Asia-Pacific: AUS, HKG, JPN, KOR, MYS, THA and TWN. For ravulizumab arm, Americas: CAN and USA; Europe: DEU, DNK, ESP, GBR, ITA and POL; Asia-Pacific: AUS, JPN and KOR.

Source: adsl, adce, adeff

Table RL-2.6
Summary of Adjudicated On-trial Relapse Treatment and Hospitalizations by Treatment Group by Supportive IST use at baseline
Full Analysis Set

IST use at baseline	Variable	Statistic	Eculizumab (N=96)	Ravulizumab (N=58)
Yes		n	75	28
	Number of patients with an Adjudicated On-Trial relapse requiring hospitalization	n (%)	2 (2.7)	0 (0.0)
	Total number of Adjudicated On-Trial relapses requiring hospitalization	Sum	2	0
	Total number of patient-years in study period	Sum	111.90	39.06
	Annualized relapse-related hospitalization rate (1)	Rate	0.02	0.00
		95% CI	(0.00, 0.07)	(NA, NA)
		p-value		0.2738
	Number of patients with an Adjudicated On-Trial relapse requiring acute treatment with			
	High-dose oral steroids	n (%)	2 (2.7)	0 (0.0)
	IV Methylprednisolone	n (%)	2 (2.7)	0 (0.0)
	Plasma Exchange	n (%)	2 (2.7)	0 (0.0)
	IVIg	n (%)	0 (0.0)	0 (0.0)
	Total number of Adjudicated On-Trial relapses requiring acute treatment with			
	High-dose oral steroids	Sum	2	0
	IV Methylprednisolone	Sum	2	0
	Plasma Exchange	Sum	2	0
	IVIg	Sum	0	0

The eculizumab group data were collected as part of the PREVENT trial, Study ECU-NMO-301.
Summaries and analyses performed using a time period for patients in the ravulizumab arm that more closely matches the time period for patients in the eculizumab arm: the minimum of the end of primary treatment period date and the date of the Week 6 relapse evaluation visit for the first On-Trial Relapse, excluding the time from 36 days after a missed or delayed dose due to COVID-19 related reasons until the day before the next dose.
For patients in the eculizumab group, the maximum length of study period will not exceed the maximum length of the ravulizumab study period; relapses occurring beyond that time will not be included in this analysis.
(1) Calculated as the total number of On-Trial relapses requiring hospitalization/treatment during the study period for all patients, divided by the total number of patient-years in the study period. P-value and confidence interval based on a Poisson regression with treatment group covariate and log of the time period as an offset variable.
95% CI could not be estimated when the ARR was 0.
Source: adsl, adce, adeff

Table RL-2.6
Summary of Adjudicated On-trial Relapse Treatment and Hospitalizations by Treatment Group by Supportive IST use at baseline
Full Analysis Set

IST use at baseline	Variable	Statistic	Eculizumab (N=96)	Ravulizumab (N=58)
Yes	Annualized relapse-related (1)			
	High-dose oral steroid rate	Rate	0.02	0.00
		95% CI	(0.00, 0.07)	(NA, NA)
		p-value		0.2738
	IV Methylprednisolone rate	Rate	0.02	0.00
		95% CI	(0.00, 0.07)	(NA, NA)
		p-value		0.2738
	Plasma Exchange rate	Rate	0.02	0.00
		95% CI	(0.00, 0.07)	(NA, NA)
		p-value		0.2738
	IVIg rate	Rate	0.00	0.00
		95% CI	(NA, NA)	(NA, NA)
	Number of relapse-related plasma exchange sessions			
		n	2	0
		Mean (SD)	8.5 (2.12)	
		Median	8.5	
		Q1, Q3	7, 10	
		Min, Max	7, 10	
		Total	17	

The eculizumab group data were collected as part of the PREVENT trial, Study ECU-NMO-301.
Summaries and analyses performed using a time period for patients in the ravulizumab arm that more closely matches the time period for patients in the eculizumab arm: the minimum of the end of primary treatment period date and the date of the Week 6 relapse evaluation visit for the first On-Trial Relapse, excluding the time from 36 days after a missed or delayed dose due to COVID-19 related reasons until the day before the next dose.
For patients in the eculizumab group, the maximum length of study period will not exceed the maximum length of the ravulizumab study period; relapses occurring beyond that time will not be included in this analysis.
(1) Calculated as the total number of On-Trial relapses requiring hospitalization/treatment during the study period for all patients, divided by the total number of patient-years in the study period. P-value and confidence interval based on a Poisson regression with treatment group covariate and log of the time period as an offset variable.
95% CI could not be estimated when the ARR was 0.
Source: adsl, adce, adeff

Table RL-2.6
Summary of Adjudicated On-trial Relapse Treatment and Hospitalizations by Treatment Group by Supportive IST use at baseline
Full Analysis Set

IST use at baseline	Variable	Statistic	Eculizumab (N=96)	Ravulizumab (N=58)
No		n	21	30
	Number of patients with an Adjudicated On-Trial relapse requiring hospitalization	n (%)	0 (0.0)	0 (0.0)
	Total number of Adjudicated On-Trial relapses requiring hospitalization	Sum	0	0
	Total number of patient-years in study period	Sum	34.02	42.36
	Annualized relapse-related hospitalization rate (1)	Rate	0.00	0.00
		95% CI	(NA, NA)	(NA, NA)
		p-value		NA
	Number of patients with an Adjudicated On-Trial relapse requiring acute treatment with			
	High-dose oral steroids	n (%)	0 (0.0)	0 (0.0)
	IV Methylprednisolone	n (%)	0 (0.0)	0 (0.0)
	Plasma Exchange	n (%)	0 (0.0)	0 (0.0)
	IVIg	n (%)	0 (0.0)	0 (0.0)
	Total number of Adjudicated On-Trial relapses requiring acute treatment with			
	High-dose oral steroids	Sum	0	0
	IV Methylprednisolone	Sum	0	0
	Plasma Exchange	Sum	0	0
	IVIg	Sum	0	0

The eculizumab group data were collected as part of the PREVENT trial, Study ECU-NMO-301.
Summaries and analyses performed using a time period for patients in the ravulizumab arm that more closely matches the time period for patients in the eculizumab arm: the minimum of the end of primary treatment period date and the date of the Week 6 relapse evaluation visit for the first On-Trial Relapse, excluding the time from 36 days after a missed or delayed dose due to COVID-19 related reasons until the day before the next dose.
For patients in the eculizumab group, the maximum length of study period will not exceed the maximum length of the ravulizumab study period; relapses occurring beyond that time will not be included in this analysis.
(1) Calculated as the total number of On-Trial relapses requiring hospitalization/treatment during the study period for all patients, divided by the total number of patient-years in the study period. P-value and confidence interval based on a Poisson regression with treatment group covariate and log of the time period as an offset variable.
95% CI could not be estimated when the ARR was 0.
Source: adsl, adce, adeff

Table RL-2.6
Summary of Adjudicated On-trial Relapse Treatment and Hospitalizations by Treatment Group by Supportive IST use at baseline
Full Analysis Set

IST use at baseline	Variable	Statistic	Eculizumab (N=96)	Ravulizumab (N=58)
No	Annualized relapse-related (1)			
	High-dose oral steroid rate	Rate	0.00	0.00
		95% CI	(NA, NA)	(NA, NA)
		p-value		NA
	IV Methylprednisolone rate	Rate	0.00	0.00
		95% CI	(NA, NA)	(NA, NA)
		p-value		NA
	Plasma Exchange rate	Rate	0.00	0.00
		95% CI	(NA, NA)	(NA, NA)
		p-value		NA
	IVIg rate	Rate	0.00	0.00
		95% CI	(NA, NA)	(NA, NA)
	Number of relapse-related plasma exchange sessions			
		n	0	0
		Mean (SD)		
		Median		
		Q1, Q3		
		Min, Max		
		Total		

The eculizumab group data were collected as part of the PREVENT trial, Study ECU-NMO-301.
Summaries and analyses performed using a time period for patients in the ravulizumab arm that more closely matches the time period for patients in the eculizumab arm: the minimum of the end of primary treatment period date and the date of the Week 6 relapse evaluation visit for the first On-Trial Relapse, excluding the time from 36 days after a missed or delayed dose due to COVID-19 related reasons until the day before the next dose.
For patients in the eculizumab group, the maximum length of study period will not exceed the maximum length of the ravulizumab study period; relapses occurring beyond that time will not be included in this analysis.
(1) Calculated as the total number of On-Trial relapses requiring hospitalization/treatment during the study period for all patients, divided by the total number of patient-years in the study period. P-value and confidence interval based on a Poisson regression with treatment group covariate and log of the time period as an offset variable.
95% CI could not be estimated when the ARR was 0.
Source: adsl, adce, adeff

Table RL-2.7
Summary of Adjudicated On-trial Relapse Treatment and Hospitalizations by Treatment Group by Rituximab use in the prior year
Full Analysis Set

Rituximab use in the prior year	Variable	Statistic	Eculizumab (N=96)	Ravulizumab (N=58)
Yes		n	19	20
	Number of patients with an Adjudicated On-Trial relapse requiring hospitalization	n (%)	0 (0.0)	0 (0.0)
	Total number of Adjudicated On-Trial relapses requiring hospitalization	Sum	0	0
	Total number of patient-years in study period	Sum	27.47	27.85
	Annualized relapse-related hospitalization rate (1)	Rate	0.00	0.00
		95% CI	(NA, NA)	(NA, NA)
		p-value		NA
	Number of patients with an Adjudicated On-Trial relapse requiring acute treatment with			
	High-dose oral steroids	n (%)	1 (5.3)	0 (0.0)
	IV Methylprednisolone	n (%)	0 (0.0)	0 (0.0)
	Plasma Exchange	n (%)	0 (0.0)	0 (0.0)
	IVIg	n (%)	0 (0.0)	0 (0.0)
	Total number of Adjudicated On-Trial relapses requiring acute treatment with			
	High-dose oral steroids	Sum	1	0
	IV Methylprednisolone	Sum	0	0
	Plasma Exchange	Sum	0	0
	IVIg	Sum	0	0

The eculizumab group data were collected as part of the PREVENT trial, Study ECU-NMO-301.
Summaries and analyses performed using a time period for patients in the ravulizumab arm that more closely matches the time period for patients in the eculizumab arm: the minimum of the end of primary treatment period date and the date of the Week 6 relapse evaluation visit for the first On-Trial Relapse, excluding the time from 36 days after a missed or delayed dose due to COVID-19 related reasons until the day before the next dose.
For patients in the eculizumab group, the maximum length of study period will not exceed the maximum length of the ravulizumab study period; relapses occurring beyond that time will not be included in this analysis.
(1) Calculated as the total number of On-Trial relapses requiring hospitalization/treatment during the study period for all patients, divided by the total number of patient-years in the study period. P-value and confidence interval based on a Poisson regression with treatment group covariate and log of the time period as an offset variable.
95% CI could not be estimated when the ARR was 0.
Source: adsl, adce, adeff

Table RL-2.7
Summary of Adjudicated On-trial Relapse Treatment and Hospitalizations by Treatment Group by Rituximab use in the prior year
Full Analysis Set

Rituximab use in the prior year	Variable	Statistic	Eculizumab (N=96)	Ravulizumab (N=58)
Yes	Annualized relapse-related (1)			
	High-dose oral steroid rate	Rate	0.04	0.00
		95% CI	(0.01, 0.26)	(NA, NA)
		p-value		0.2367
	IV Methylprednisolone rate	Rate	0.00	0.00
		95% CI	(NA, NA)	(NA, NA)
		p-value		NA
	Plasma Exchange rate	Rate	0.00	0.00
		95% CI	(NA, NA)	(NA, NA)
		p-value		NA
	IVIg rate	Rate	0.00	0.00
		95% CI	(NA, NA)	(NA, NA)
	Number of relapse-related plasma exchange sessions			
		n	0	0
		Mean (SD)		
		Median		
		Q1, Q3		
		Min, Max		
		Total		

The eculizumab group data were collected as part of the PREVENT trial, Study ECU-NMO-301.
Summaries and analyses performed using a time period for patients in the ravulizumab arm that more closely matches the time period for patients in the eculizumab arm: the minimum of the end of primary treatment period date and the date of the Week 6 relapse evaluation visit for the first On-Trial Relapse, excluding the time from 36 days after a missed or delayed dose due to COVID-19 related reasons until the day before the next dose.
For patients in the eculizumab group, the maximum length of study period will not exceed the maximum length of the ravulizumab study period; relapses occurring beyond that time will not be included in this analysis.
(1) Calculated as the total number of On-Trial relapses requiring hospitalization/treatment during the study period for all patients, divided by the total number of patient-years in the study period. P-value and confidence interval based on a Poisson regression with treatment group covariate and log of the time period as an offset variable.
95% CI could not be estimated when the ARR was 0.
Source: adsl, adce, adeff

Table RL-2.7
Summary of Adjudicated On-trial Relapse Treatment and Hospitalizations by Treatment Group by Rituximab use in the prior year
Full Analysis Set

Rituximab use in the prior year	Variable	Statistic	Eculizumab (N=96)	Ravulizumab (N=58)
No		n	77	38
	Number of patients with an Adjudicated On-Trial relapse requiring hospitalization	n (%)	2 (2.6)	0 (0.0)
	Total number of Adjudicated On-Trial relapses requiring hospitalization	Sum	2	0
	Total number of patient-years in study period	Sum	118.45	53.57
	Annualized relapse-related hospitalization rate (1)	Rate	0.02	0.00
		95% CI	(0.00, 0.07)	(NA, NA)
		p-value		0.2218
	Number of patients with an Adjudicated On-Trial relapse requiring acute treatment with			
	High-dose oral steroids	n (%)	1 (1.3)	0 (0.0)
	IV Methylprednisolone	n (%)	2 (2.6)	0 (0.0)
	Plasma Exchange	n (%)	2 (2.6)	0 (0.0)
	IVIg	n (%)	0 (0.0)	0 (0.0)
	Total number of Adjudicated On-Trial relapses requiring acute treatment with			
	High-dose oral steroids	Sum	1	0
	IV Methylprednisolone	Sum	2	0
	Plasma Exchange	Sum	2	0
	IVIg	Sum	0	0

The eculizumab group data were collected as part of the PREVENT trial, Study ECU-NMO-301.
Summaries and analyses performed using a time period for patients in the ravulizumab arm that more closely matches the time period for patients in the eculizumab arm: the minimum of the end of primary treatment period date and the date of the Week 6 relapse evaluation visit for the first On-Trial Relapse, excluding the time from 36 days after a missed or delayed dose due to COVID-19 related reasons until the day before the next dose.
For patients in the eculizumab group, the maximum length of study period will not exceed the maximum length of the ravulizumab study period; relapses occurring beyond that time will not be included in this analysis.
(1) Calculated as the total number of On-Trial relapses requiring hospitalization/treatment during the study period for all patients, divided by the total number of patient-years in the study period. P-value and confidence interval based on a Poisson regression with treatment group covariate and log of the time period as an offset variable.
95% CI could not be estimated when the ARR was 0.
Source: adsl, adce, adeff

Table RL-2.7
Summary of Adjudicated On-trial Relapse Treatment and Hospitalizations by Treatment Group by Rituximab use in the prior year
Full Analysis Set

Rituximab use in the prior year	Variable	Statistic	Eculizumab (N=96)	Ravulizumab (N=58)
No	Annualized relapse-related (1)			
	High-dose oral steroid rate	Rate	0.01	0.00
		95% CI	(0.00, 0.06)	(NA, NA)
		p-value		0.3877
	IV Methylprednisolone rate	Rate	0.02	0.00
		95% CI	(0.00, 0.07)	(NA, NA)
		p-value		0.2218
	Plasma Exchange rate	Rate	0.02	0.00
		95% CI	(0.00, 0.07)	(NA, NA)
		p-value		0.2218
	IVIg rate	Rate	0.00	0.00
		95% CI	(NA, NA)	(NA, NA)
	Number of relapse-related plasma exchange sessions			
		n	2	0
		Mean (SD)	8.5 (2.12)	
		Median	8.5	
		Q1, Q3	7, 10	
		Min, Max	7, 10	
		Total	17	

The eculizumab group data were collected as part of the PREVENT trial, Study ECU-NMO-301.
Summaries and analyses performed using a time period for patients in the ravulizumab arm that more closely matches the time period for patients in the eculizumab arm: the minimum of the end of primary treatment period date and the date of the Week 6 relapse evaluation visit for the first On-Trial Relapse, excluding the time from 36 days after a missed or delayed dose due to COVID-19 related reasons until the day before the next dose.
For patients in the eculizumab group, the maximum length of study period will not exceed the maximum length of the ravulizumab study period; relapses occurring beyond that time will not be included in this analysis.
(1) Calculated as the total number of On-Trial relapses requiring hospitalization/treatment during the study period for all patients, divided by the total number of patient-years in the study period. P-value and confidence interval based on a Poisson regression with treatment group covariate and log of the time period as an offset variable.
95% CI could not be estimated when the ARR was 0.
Source: adsl, adce, adeff

Table RL-2.4
Summary of Adjudicated On-trial Relapse Treatment and Hospitalizations by Treatment Group by Disease severity via EDSS score
Full Analysis Set

EDSS score at baseline	Variable	Statistic	Eculizumab (N=96)	Ravulizumab (N=58)
< 5		n	66	49
	Number of patients with an Adjudicated On-Trial relapse requiring hospitalization	n (%)	1 (1.5)	0 (0.0)
	Total number of Adjudicated On-Trial relapses requiring hospitalization	Sum	1	0
	Total number of patient-years in study period	Sum	101.56	70.31
	Annualized relapse-related hospitalization rate (1)	Rate	0.01	0.00
		95% CI	(0.00, 0.07)	(NA, NA)
		p-value		0.3050
	Number of patients with an Adjudicated On-Trial relapse requiring acute treatment with			
	High-dose oral steroids	n (%)	0 (0.0)	0 (0.0)
	IV Methylprednisolone	n (%)	1 (1.5)	0 (0.0)
	Plasma Exchange	n (%)	1 (1.5)	0 (0.0)
	IVIg	n (%)	0 (0.0)	0 (0.0)
	Total number of Adjudicated On-Trial relapses requiring acute treatment with			
	High-dose oral steroids	Sum	0	0
	IV Methylprednisolone	Sum	1	0
	Plasma Exchange	Sum	1	0
	IVIg	Sum	0	0

The eculizumab group data were collected as part of the PREVENT trial, Study ECU-NMO-301.
Summaries and analyses performed using a time period for patients in the ravulizumab arm that more closely matches the time period for patients in the eculizumab arm: the minimum of the end of primary treatment period date and the date of the Week 6 relapse evaluation visit for the first On-Trial Relapse, excluding the time from 36 days after a missed or delayed dose due to COVID-19 related reasons until the day before the next dose.
For patients in the eculizumab group, the maximum length of study period will not exceed the maximum length of the ravulizumab study period; relapses occurring beyond that time will not be included in this analysis.
(1) Calculated as the total number of On-Trial relapses requiring hospitalization/treatment during the study period for all patients, divided by the total number of patient-years in the study period. P-value and confidence interval based on a Poisson regression with treatment group covariate and log of the time period as an offset variable.
95% CI could not be estimated when the ARR was 0.
Source: adsl, adce, adeff

Table RL-2.4
Summary of Adjudicated On-trial Relapse Treatment and Hospitalizations by Treatment Group by Disease severity via EDSS score
Full Analysis Set

EDSS score at baseline	Variable	Statistic	Eculizumab (N=96)	Ravulizumab (N=58)
< 5	Annualized relapse-related (1)			
	High-dose oral steroid rate	Rate	0.00	0.00
		95% CI	(NA, NA)	(NA, NA)
		p-value		NA
	IV Methylprednisolone rate	Rate	0.01	0.00
		95% CI	(0.00, 0.07)	(NA, NA)
		p-value		0.3050
	Plasma Exchange rate	Rate	0.01	0.00
		95% CI	(0.00, 0.07)	(NA, NA)
		p-value		0.3050
	IVIg rate	Rate	0.00	0.00
		95% CI	(NA, NA)	(NA, NA)
	Number of relapse-related plasma exchange sessions			
		n	1	0
		Mean (SD)	10.0 (NA)	
		Median	10.0	
		Q1, Q3	10, 10	
		Min, Max	10, 10	
		Total	10	

The eculizumab group data were collected as part of the PREVENT trial, Study ECU-NMO-301.
Summaries and analyses performed using a time period for patients in the ravulizumab arm that more closely matches the time period for patients in the eculizumab arm: the minimum of the end of primary treatment period date and the date of the Week 6 relapse evaluation visit for the first On-Trial Relapse, excluding the time from 36 days after a missed or delayed dose due to COVID-19 related reasons until the day before the next dose.
For patients in the eculizumab group, the maximum length of study period will not exceed the maximum length of the ravulizumab study period; relapses occurring beyond that time will not be included in this analysis.
(1) Calculated as the total number of On-Trial relapses requiring hospitalization/treatment during the study period for all patients, divided by the total number of patient-years in the study period. P-value and confidence interval based on a Poisson regression with treatment group covariate and log of the time period as an offset variable.
95% CI could not be estimated when the ARR was 0.
Source: adsl, adce, adeff

Table RL-2.4
Summary of Adjudicated On-trial Relapse Treatment and Hospitalizations by Treatment Group by Disease severity via EDSS score
Full Analysis Set

EDSS score at baseline	Variable	Statistic	Eculizumab (N=96)	Ravulizumab (N=58)
>= 5		n	30	9
	Number of patients with an Adjudicated On-Trial relapse requiring hospitalization	n (%)	1 (3.3)	0 (0.0)
	Total number of Adjudicated On-Trial relapses requiring hospitalization	Sum	1	0
	Total number of patient-years in study period	Sum	44.36	11.11
	Annualized relapse-related hospitalization rate (1)	Rate	0.02	0.00
		95% CI	(0.00, 0.16)	(NA, NA)
		p-value		0.5037
	Number of patients with an Adjudicated On-Trial relapse requiring acute treatment with			
	High-dose oral steroids	n (%)	2 (6.7)	0 (0.0)
	IV Methylprednisolone	n (%)	1 (3.3)	0 (0.0)
	Plasma Exchange	n (%)	1 (3.3)	0 (0.0)
	IVIg	n (%)	0 (0.0)	0 (0.0)
	Total number of Adjudicated On-Trial relapses requiring acute treatment with			
	High-dose oral steroids	Sum	2	0
	IV Methylprednisolone	Sum	1	0
	Plasma Exchange	Sum	1	0
	IVIg	Sum	0	0

The eculizumab group data were collected as part of the PREVENT trial, Study ECU-NMO-301.
Summaries and analyses performed using a time period for patients in the ravulizumab arm that more closely matches the time period for patients in the eculizumab arm: the minimum of the end of primary treatment period date and the date of the Week 6 relapse evaluation visit for the first On-Trial Relapse, excluding the time from 36 days after a missed or delayed dose due to COVID-19 related reasons until the day before the next dose.
For patients in the eculizumab group, the maximum length of study period will not exceed the maximum length of the ravulizumab study period; relapses occurring beyond that time will not be included in this analysis.
(1) Calculated as the total number of On-Trial relapses requiring hospitalization/treatment during the study period for all patients, divided by the total number of patient-years in the study period. P-value and confidence interval based on a Poisson regression with treatment group covariate and log of the time period as an offset variable.
95% CI could not be estimated when the ARR was 0.
Source: adsl, adce, adeff

Table RL-2.4
Summary of Adjudicated On-trial Relapse Treatment and Hospitalizations by Treatment Group by Disease severity via EDSS score
Full Analysis Set

EDSS score at baseline	Variable	Statistic	Eculizumab (N=96)	Ravulizumab (N=58)
>= 5	Annualized relapse-related (1)			
	High-dose oral steroid rate	Rate	0.05	0.00
		95% CI	(0.01, 0.18)	(NA, NA)
		p-value		0.3444
	IV Methylprednisolone rate	Rate	0.02	0.00
		95% CI	(0.00, 0.16)	(NA, NA)
		p-value		0.5037
	Plasma Exchange rate	Rate	0.02	0.00
		95% CI	(0.00, 0.16)	(NA, NA)
		p-value		0.5037
	IVIg rate	Rate	0.00	0.00
		95% CI	(NA, NA)	(NA, NA)
	Number of relapse-related plasma exchange sessions			
		n	1	0
		Mean (SD)	7.0 (NA)	
		Median	7.0	
		Q1, Q3	7, 7	
		Min, Max	7, 7	
		Total	7	

The eculizumab group data were collected as part of the PREVENT trial, Study ECU-NMO-301.
Summaries and analyses performed using a time period for patients in the ravulizumab arm that more closely matches the time period for patients in the eculizumab arm: the minimum of the end of primary treatment period date and the date of the Week 6 relapse evaluation visit for the first On-Trial Relapse, excluding the time from 36 days after a missed or delayed dose due to COVID-19 related reasons until the day before the next dose.
For patients in the eculizumab group, the maximum length of study period will not exceed the maximum length of the ravulizumab study period; relapses occurring beyond that time will not be included in this analysis.
(1) Calculated as the total number of On-Trial relapses requiring hospitalization/treatment during the study period for all patients, divided by the total number of patient-years in the study period. P-value and confidence interval based on a Poisson regression with treatment group covariate and log of the time period as an offset variable.
95% CI could not be estimated when the ARR was 0.
Source: adsl, adce, adeff

Table EDSS-2.2
Change from Baseline in EDSS Score to End of Study Period by Sex
Full Analysis Set

Sex		Statistic	Eculizumab (N=96)	Ravulizumab (N=58)	p-value (7)
Male	Change from Baseline to End of Study Period in EDSS Score	n	8	6	0.2682
		Mean (SD)	0.3 (0.70)	-0.1 (0.80)	
		Median	0.5	0.0	
		Q1, Q3	0.0, 0.5	-1.0, 0.5	
		Min, Max	-1, 2	-1, 1	
		Change from baseline			
		LS Means (SEM)	0.400 (0.269)	-0.201 (0.315)	
		95% CI for LS Means (1)	(-0.193, 0.994)	(-0.894, 0.493)	
		Difference in LS Means		-0.601	
		(95% CI) (1)		(-1.551, 0.349)	
		p-value (2)		0.1207	
		Standardized Mean Difference		-0.687	
		(95% CI) (3)		(-1.775, 0.402)	
		Responders (15% [1.5 points]), n(%)	0	0	
		Odds Ratio (4)		--	
		(95% CI)		--	
		p-value		--	
		Relative Risk (5)		--	
		(95% CI)		--	
		p-value		--	

The eculizumab group data were collected as part of the PREVENT trial, Study ECU-NMO-301.

End of Study Period is the 6-week assessment after the first On-Trial Relapse for patients who have an On-Trial Relapse or for patients with no On-Trial Relapse: the End of Primary Treatment Period visit for patients in Study ALXN1210-NMO-307 and the End of Study visit for patients in Study ECU-NMO-301.

For those patients who had a missed value at the EOPT Visit or the 6-week post-relapse visit, for patients who had a relapse, the end of study is the last value before the missed value.

(1) The LS means (95% CI) and the difference in LS means (95% CI) are from an ANCOVA model of change from baseline with treatment as factor and baseline value as covariate. (2) The p-value represents the significance of the treatment effect and was derived from an ANCOVA model of the ranked change from baseline, with treatment as a factor, and the ranks of the baseline value included as covariate.

(3) Standardized mean differences (95% CI) were computed using Cohen's D incorporating Hedge's correction on change from baseline. (4) Odds ratio statistics are from a logistic regression model adjusted for baseline value with Firth's adjustment; (5) Relative risk statistics are based on a generalized linear model of a binomial distribution with log link;

(6) Risk difference statistics are calculated from a generalized linear model, correcting for the baseline value. (7) P-value is for the interaction term of treatment:subgroup from a linear regression model of ranked change from baseline with the with ranked baseline value, treatment, subgroup, and treatment:subgroup interaction as covariates.

Odds ratio and relative risk are calculated as Ravulizumab/Eculizumab. LS mean difference and risk difference are calculated as Ravulizumab - Eculizumab.

Source: adsl, adedss

Table EDSS-2.2
Change from Baseline in EDSS Score to End of Study Period by Sex
Full Analysis Set

Sex	Statistic	Eculizumab (N=96)	Ravulizumab (N=58)	p-value (7)
	Risk Difference (6)		--	
	(95% CI)		--	
	p-value		--	
Baseline EDSS Score	n	8	6	
	Mean (SD)	3.8 (1.58)	2.7 (0.88)	
	Median	3.5	2.3	
	Q1, Q3	2.8, 5.0	2.0, 3.5	
	Min, Max	2, 6	2, 4	
End of Study Period EDSS Score	n	8	6	
	Mean (SD)	4.1 (1.52)	2.6 (0.86)	
	Median	3.5	2.5	
	Q1, Q3	3.0, 5.0	2.0, 3.0	
	Min, Max	3, 7	2, 4	

The eculizumab group data were collected as part of the PREVENT trial, Study ECU-NMO-301.

End of Study Period is the 6-week assessment after the first On-Trial Relapse for patients who have an On-Trial Relapse or for patients with no On-Trial Relapse: the End of Primary Treatment Period visit for patients in Study ALXN1210-NMO-307 and the End of Study visit for patients in Study ECU-NMO-301.

For those patients who had a missed value at the EOPT Visit or the 6-week post-relapse visit, for patients who had a relapse, the end of study is the last value before the missed value.

(1) The LS means (95% CI) and the difference in LS means (95% CI) are from an ANCOVA model of change from baseline with treatment as factor and baseline value as covariate. (2) The p-value represents the significance of the treatment effect and was derived from an ANCOVA model of the ranked change from baseline, with treatment as a factor, and the ranks of the baseline value included as covariate.

(3) Standardized mean differences (95% CI) were computed using Cohen's D incorporating Hedge's correction on change from baseline. (4) Odds ratio statistics are from a logistic regression model adjusted for baseline value with Firth's adjustment; (5) Relative risk statistics are based on a generalized linear model of a binomial distribution with log link;

(6) Risk difference statistics are calculated from a generalized linear model, correcting for the baseline value. (7) P-value is for the interaction term of treatment:subgroup from a linear regression model of ranked change from baseline with the with ranked baseline value, treatment, subgroup, and treatment:subgroup interaction as covariates.

Odds ratio and relative risk are calculated as Ravulizumab/Eculizumab. LS mean difference and risk difference are calculated as Ravulizumab - Eculizumab.

Source: adsl, adedss

Table EDSS-2.2
Change from Baseline in EDSS Score to End of Study Period by Sex
Full Analysis Set

Sex		Statistic	Eculizumab (N=96)	Ravulizumab (N=58)	p-value (7)
Female	Change from Baseline to End of Study Period in EDSS Score	n	88	52	
		Mean (SD)	-0.2 (0.81)	-0.3 (0.93)	
		Median	0.0	0.0	
		Q1, Q3	-0.5, 0.0	-0.5, 0.0	
		Min, Max	-4, 2	-3, 1	
		Change from baseline			
		LS Means (SEM)	-0.187 (0.090)	-0.385 (0.118)	
		95% CI for LS Means (1)	(-0.366, -0.009)	(-0.619, -0.151)	
		Difference in LS Means		-0.197	
		(95% CI) (1)		(-0.496, 0.101)	
		p-value (2)		0.3328	
		Standardized Mean Difference		-0.214	
		(95% CI) (3)		(-0.558, 0.130)	
		Responders (15% [1.5 points]), n(%)	7 (8.0)	8 (15.4)	
		Odds Ratio (4)		2.809	
		(95% CI)		(0.920, 8.576)	
		p-value		0.0697	
		Relative Risk (5)		1.934	
		(95% CI)		(0.744, 5.024)	
		p-value		0.1757	

The eculizumab group data were collected as part of the PREVENT trial, Study ECU-NMO-301.

End of Study Period is the 6-week assessment after the first On-Trial Relapse for patients who have an On-Trial Relapse or for patients with no On-Trial Relapse: the End of Primary Treatment Period visit for patients in Study ALXN1210-NMO-307 and the End of Study visit for patients in Study ECU-NMO-301.

For those patients who had a missed value at the EOPT Visit or the 6-week post-relapse visit, for patients who had a relapse, the end of study is the last value before the missed value.

(1) The LS means (95% CI) and the difference in LS means (95% CI) are from an ANCOVA model of change from baseline with treatment as factor and baseline value as covariate. (2) The p-value represents the significance of the treatment effect and was derived from an ANCOVA model of the ranked change from baseline, with treatment as a factor, and the ranks of the baseline value included as covariate.

(3) Standardized mean differences (95% CI) were computed using Cohen's D incorporating Hedge's correction on change from baseline. (4) Odds ratio statistics are from a logistic regression model adjusted for baseline value with Firth's adjustment; (5) Relative risk statistics are based on a generalized linear model of a binomial distribution with log link;

(6) Risk difference statistics are calculated from a generalized linear model, correcting for the baseline value. (7) P-value is for the interaction term of treatment:subgroup from a linear regression model of ranked change from baseline with the with ranked baseline value, treatment, subgroup, and treatment:subgroup interaction as covariates.

Odds ratio and relative risk are calculated as Ravulizumab/Eculizumab. LS mean difference and risk difference are calculated as Ravulizumab - Eculizumab.

Source: adsl, adedss

Table EDSS-2.2
Change from Baseline in EDSS Score to End of Study Period by Sex
Full Analysis Set

Sex	Statistic	Eculizumab (N=96)	Ravulizumab (N=58)	p-value (7)
	Risk Difference (6)		0.102	
	(95% CI)		(-0.007, 0.210)	
	p-value		0.0662	
Baseline EDSS Score	n	88	52	
	Mean (SD)	4.2 (1.66)	3.4 (1.64)	
	Median	4.0	3.5	
	Q1, Q3	3.0, 6.0	2.0, 4.5	
	Min, Max	1, 7	0, 7	
End of Study Period EDSS Score	n	88	52	
	Mean (SD)	4.0 (1.72)	3.0 (1.61)	
	Median	3.5	3.0	
	Q1, Q3	3.0, 5.8	2.0, 3.8	
	Min, Max	1, 8	0, 7	

The eculizumab group data were collected as part of the PREVENT trial, Study ECU-NMO-301.

End of Study Period is the 6-week assessment after the first On-Trial Relapse for patients who have an On-Trial Relapse or for patients with no On-Trial Relapse: the End of Primary Treatment Period visit for patients in Study ALXN1210-NMO-307 and the End of Study visit for patients in Study ECU-NMO-301.

For those patients who had a missed value at the EOPT Visit or the 6-week post-relapse visit, for patients who had a relapse, the end of study is the last value before the missed value.

(1) The LS means (95% CI) and the difference in LS means (95% CI) are from an ANCOVA model of change from baseline with treatment as factor and baseline value as covariate. (2) The p-value represents the significance of the treatment effect and was derived from an ANCOVA model of the ranked change from baseline, with treatment as a factor, and the ranks of the baseline value included as covariate.

(3) Standardized mean differences (95% CI) were computed using Cohen's D incorporating Hedge's correction on change from baseline. (4) Odds ratio statistics are from a logistic regression model adjusted for baseline value with Firth's adjustment; (5) Relative risk statistics are based on a generalized linear model of a binomial distribution with log link;

(6) Risk difference statistics are calculated from a generalized linear model, correcting for the baseline value. (7) P-value is for the interaction term of treatment:subgroup from a linear regression model of ranked change from baseline with the with ranked baseline value, treatment, subgroup, and treatment:subgroup interaction as covariates.

Odds ratio and relative risk are calculated as Ravulizumab/Eculizumab. LS mean difference and risk difference are calculated as Ravulizumab - Eculizumab.

Source: adsl, adedss

Table EDSS-2.3
Change from Baseline in EDSS Score to End of Study Period by Age Group
Full Analysis Set

Age Group		Statistic	Eculizumab (N=96)	Ravulizumab (N=58)	p-value (7)
< 45 years	Change from Baseline to End of Study Period in EDSS Score	n	47	25	0.9174
		Mean (SD)	-0.2 (0.76)	-0.4 (0.83)	
		Median	0.0	0.0	
		Q1, Q3	-0.5, 0.0	-0.5, 0.0	
		Min, Max	-3, 1	-3, 1	
		Change from baseline			
		LS Means (SEM)	-0.204 (0.111)	-0.437 (0.153)	
		95% CI for LS Means (1)	(-0.425, 0.018)	(-0.742, -0.132)	
		Difference in LS Means		-0.233	
		(95% CI) (1)		(-0.613, 0.146)	
		p-value (2)		0.2332	
		Standardized Mean Difference		-0.267	
		(95% CI) (3)		(-0.754, 0.220)	
		Responders (15% [1.5 points]), n(%)	3 (6.4)	2 (8.0)	
		Odds Ratio (4)		1.711	
		(95% CI)		(0.294, 9.974)	
		p-value		0.5503	
		Relative Risk (5)		1.253	
		(95% CI)		(0.224, 7.014)	
		p-value		0.7972	

The eculizumab group data were collected as part of the PREVENT trial, Study ECU-NMO-301.

End of Study Period is the 6-week assessment after the first On-Trial Relapse for patients who have an On-Trial Relapse or for patients with no On-Trial Relapse: the End of Primary Treatment Period visit for patients in Study ALXN1210-NMO-307 and the End of Study visit for patients in Study ECU-NMO-301.

For those patients who had a missed value at the EOPT Visit or the 6-week post-relapse visit, for patients who had a relapse, the end of study is the last value before the missed value.

(1) The LS means (95% CI) and the difference in LS means (95% CI) are from an ANCOVA model of change from baseline with treatment as factor and baseline value as covariate. (2) The p-value represents the significance of the treatment effect and was derived from an ANCOVA model of the ranked change from baseline, with treatment as a factor, and the ranks of the baseline value included as covariate.

(3) Standardized mean differences (95% CI) were computed using Cohen's D incorporating Hedge's correction on change from baseline. (4) Odds ratio statistics are from a logistic regression model adjusted for baseline value with Firth's adjustment; (5) Relative risk statistics are based on a generalized linear model of a binomial distribution with log link;

(6) Risk difference statistics are calculated from a generalized linear model, correcting for the baseline value. (7) P-value is for the interaction term of treatment:subgroup from a linear regression model of ranked change from baseline with the with ranked baseline value, treatment, subgroup, and treatment:subgroup interaction as covariates.

Odds ratio and relative risk are calculated as Ravulizumab/Eculizumab. LS mean difference and risk difference are calculated as Ravulizumab - Eculizumab.

Source: adsl, adedss

Table EDSS-2.3
Change from Baseline in EDSS Score to End of Study Period by Age Group
Full Analysis Set

Age Group	Statistic	Eculizumab (N=96)	Ravulizumab (N=58)	p-value (7)
	Risk Difference (6)		0.039	
	(95% CI)		(-0.088, 0.166)	
	p-value		0.5412	
Baseline EDSS Score	n	47	25	
	Mean (SD)	3.5 (1.40)	2.9 (1.69)	
	Median	3.5	2.5	
	Q1, Q3	2.0, 4.0	2.0, 4.0	
	Min, Max	1, 7	0, 6	
End of Study Period EDSS Score	n	47	25	
	Mean (SD)	3.2 (1.41)	2.5 (1.61)	
	Median	3.0	2.0	
	Q1, Q3	2.0, 4.0	1.5, 3.5	
	Min, Max	1, 7	0, 6	

The eculizumab group data were collected as part of the PREVENT trial, Study ECU-NMO-301.

End of Study Period is the 6-week assessment after the first On-Trial Relapse for patients who have an On-Trial Relapse or for patients with no On-Trial Relapse: the End of Primary Treatment Period visit for patients in Study ALXN1210-NMO-307 and the End of Study visit for patients in Study ECU-NMO-301.

For those patients who had a missed value at the EOPT Visit or the 6-week post-relapse visit, for patients who had a relapse, the end of study is the last value before the missed value.

(1) The LS means (95% CI) and the difference in LS means (95% CI) are from an ANCOVA model of change from baseline with treatment as factor and baseline value as covariate. (2) The p-value represents the significance of the treatment effect and was derived from an ANCOVA model of the ranked change from baseline, with treatment as a factor, and the ranks of the baseline value included as covariate.

(3) Standardized mean differences (95% CI) were computed using Cohen's D incorporating Hedge's correction on change from baseline. (4) Odds ratio statistics are from a logistic regression model adjusted for baseline value with Firth's adjustment; (5) Relative risk statistics are based on a generalized linear model of a binomial distribution with log link;

(6) Risk difference statistics are calculated from a generalized linear model, correcting for the baseline value. (7) P-value is for the interaction term of treatment:subgroup from a linear regression model of ranked change from baseline with the with ranked baseline value, treatment, subgroup, and treatment:subgroup interaction as covariates.

Odds ratio and relative risk are calculated as Ravulizumab/Eculizumab. LS mean difference and risk difference are calculated as Ravulizumab - Eculizumab.

Source: adsl, adedss

Table EDSS-2.3
Change from Baseline in EDSS Score to End of Study Period by Age Group
Full Analysis Set

Age Group		Statistic	Eculizumab (N=96)	Ravulizumab (N=58)	p-value (7)
>= 45 years	Change from Baseline to End of Study Period in EDSS Score	n	49	33	
		Mean (SD)	-0.1 (0.87)	-0.2 (0.98)	
		Median	0.0	0.0	
		Q1, Q3	0.0, 0.0	-0.5, 0.0	
		Min, Max	-4, 2	-3, 1	
		Change from baseline			
		LS Means (SEM)	-0.048 (0.130)	-0.353 (0.161)	
		95% CI for LS Means (1)	(-0.307, 0.211)	(-0.673, -0.033)	
		Difference in LS Means		-0.305	
		(95% CI) (1)		(-0.730, 0.119)	
		p-value (2)		0.2323	
		Standardized Mean Difference		-0.319	
		(95% CI) (3)		(-0.763, 0.125)	
		Responders (15% [1.5 points]), n(%)	4 (8.2)	6 (18.2)	
		Odds Ratio (4)		3.334	
		(95% CI)		(0.792, 14.026)	
		p-value		0.1005	
		Relative Risk (5)		2.227	
		(95% CI)		(0.681, 7.290)	
		p-value		0.1856	

The eculizumab group data were collected as part of the PREVENT trial, Study ECU-NMO-301.

End of Study Period is the 6-week assessment after the first On-Trial Relapse for patients who have an On-Trial Relapse or for patients with no On-Trial Relapse: the End of Primary Treatment Period visit for patients in Study ALXN1210-NMO-307 and the End of Study visit for patients in Study ECU-NMO-301.

For those patients who had a missed value at the EOPT Visit or the 6-week post-relapse visit, for patients who had a relapse, the end of study is the last value before the missed value.

(1) The LS means (95% CI) and the difference in LS means (95% CI) are from an ANCOVA model of change from baseline with treatment as factor and baseline value as covariate. (2) The p-value represents the significance of the treatment effect and was derived from an ANCOVA model of the ranked change from baseline, with treatment as a factor, and the ranks of the baseline value included as covariate.

(3) Standardized mean differences (95% CI) were computed using Cohen's D incorporating Hedge's correction on change from baseline. (4) Odds ratio statistics are from a logistic regression model adjusted for baseline value with Firth's adjustment; (5) Relative risk statistics are based on a generalized linear model of a binomial distribution with log link;

(6) Risk difference statistics are calculated from a generalized linear model, correcting for the baseline value. (7) P-value is for the interaction term of treatment:subgroup from a linear regression model of ranked change from baseline with the with ranked baseline value, treatment, subgroup, and treatment:subgroup interaction as covariates.

Odds ratio and relative risk are calculated as Ravulizumab/Eculizumab. LS mean difference and risk difference are calculated as Ravulizumab - Eculizumab.

Source: adsl, adedss

Table EDSS-2.3
Change from Baseline in EDSS Score to End of Study Period by Age Group
Full Analysis Set

Age Group	Statistic	Eculizumab (N=96)	Ravulizumab (N=58)	p-value (7)
	Risk Difference (6)		0.135	
	(95% CI)		(-0.021, 0.291)	
	p-value		0.0895	
Baseline EDSS Score	n	49	33	
	Mean (SD)	4.8 (1.62)	3.6 (1.45)	
	Median	4.5	3.5	
	Q1, Q3	3.5, 6.0	2.5, 4.0	
	Min, Max	2, 7	2, 7	
End of Study Period EDSS Score	n	49	33	
	Mean (SD)	4.7 (1.68)	3.4 (1.43)	
	Median	4.0	3.5	
	Q1, Q3	3.5, 6.5	2.5, 4.0	
	Min, Max	1, 8	1, 7	

The eculizumab group data were collected as part of the PREVENT trial, Study ECU-NMO-301.

End of Study Period is the 6-week assessment after the first On-Trial Relapse for patients who have an On-Trial Relapse or for patients with no On-Trial Relapse: the End of Primary Treatment Period visit for patients in Study ALXN1210-NMO-307 and the End of Study visit for patients in Study ECU-NMO-301.

For those patients who had a missed value at the EOPT Visit or the 6-week post-relapse visit, for patients who had a relapse, the end of study is the last value before the missed value.

(1) The LS means (95% CI) and the difference in LS means (95% CI) are from an ANCOVA model of change from baseline with treatment as factor and baseline value as covariate. (2) The p-value represents the significance of the treatment effect and was derived from an ANCOVA model of the ranked change from baseline, with treatment as a factor, and the ranks of the baseline value included as covariate.

(3) Standardized mean differences (95% CI) were computed using Cohen's D incorporating Hedge's correction on change from baseline. (4) Odds ratio statistics are from a logistic regression model adjusted for baseline value with Firth's adjustment; (5) Relative risk statistics are based on a generalized linear model of a binomial distribution with log link;

(6) Risk difference statistics are calculated from a generalized linear model, correcting for the baseline value. (7) P-value is for the interaction term of treatment:subgroup from a linear regression model of ranked change from baseline with the with ranked baseline value, treatment, subgroup, and treatment:subgroup interaction as covariates.

Odds ratio and relative risk are calculated as Ravulizumab/Eculizumab. LS mean difference and risk difference are calculated as Ravulizumab - Eculizumab.

Source: adsl, adedss

Table EDSS-2.5
Change from Baseline in EDSS Score to End of Study Period by Region
Full Analysis Set

Region		Statistic	Eculizumab (N=96)	Ravulizumab (N=58)	p-value (7)
Asia-Pacific	Change from Baseline to End of Study Period in EDSS Score	n	35	20	0.7211
		Mean (SD)	-0.2 (0.87)	-0.1 (0.79)	
		Median	0.0	0.0	
		Q1, Q3	-0.5, 0.5	0.0, 0.0	
		Min, Max	-4, 1	-3, 1	
		Change from baseline			
		LS Means (SEM)	-0.166 (0.144)	-0.210 (0.193)	
		95% CI for LS Means (1)	(-0.454, 0.123)	(-0.598, 0.178)	
		Difference in LS Means		-0.045	
		(95% CI) (1)		(-0.542, 0.452)	
		p-value (2)		0.8070	
		Standardized Mean Difference		-0.048	
		(95% CI) (3)		(-0.598, 0.501)	
		Responders (15% [1.5 points]), n(%)	3 (8.6)	2 (10.0)	
		Odds Ratio (4)		1.960	
		(95% CI)		(0.293, 13.108)	
		p-value		0.4875	
		Relative Risk (5)		1.167	
		(95% CI)		(0.213, 6.404)	
		p-value		0.8592	

The eculizumab group data were collected as part of the PREVENT trial, Study ECU-NMO-301.

End of Study Period is the 6-week assessment after the first On-Trial Relapse for patients who have an On-Trial Relapse or for patients with no On-Trial Relapse: the End of Primary Treatment Period visit for patients in Study ALXN1210-NMO-307 and the End of Study visit for patients in Study ECU-NMO-301.

For those patients who had a missed value at the EOPT Visit or the 6-week post-relapse visit, for patients who had a relapse, the end of study is the last value before the missed value.

(1) The LS means (95% CI) and the difference in LS means (95% CI) are from an ANCOVA model of change from baseline with treatment as factor and baseline value as covariate. (2) The p-value represents the significance of the treatment effect and was derived from an ANCOVA model of the ranked change from baseline, with treatment as a factor, and the ranks of the baseline value included as covariate.

(3) Standardized mean differences (95% CI) were computed using Cohen's D incorporating Hedge's correction on change from baseline. (4) Odds ratio statistics are from a logistic regression model adjusted for baseline value with Firth's adjustment; (5) Relative risk statistics are based on a generalized linear model of a binomial distribution with log link;

(6) Risk difference statistics are calculated from a generalized linear model, correcting for the baseline value. (7) P-value is for the interaction term of treatment:subgroup from a linear regression model of ranked change from baseline with the with ranked baseline value, treatment, subgroup, and treatment:subgroup interaction as covariates.

For eculizumab arm, Americas: ARG and USA; Europe: CZE, DEU, DNK, ESP, HRV, ITA, RUS and TUR; Asia-Pacific: AUS, HKG, JPN, KOR, MYS, THA and TWN. For ravulizumab arm, Americas: CAN and USA; Europe: DEU, DNK, ESP, GBR, ITA and POL; Asia-Pacific: AUS, JPN and KOR.

Odds ratio and relative risk are calculated as Ravulizumab/Eculizumab. LS mean difference and risk difference are calculated as Ravulizumab - Eculizumab.

Source: adsl, adedss

Table EDSS-2.5
Change from Baseline in EDSS Score to End of Study Period by Region
Full Analysis Set

Region	Statistic	Eculizumab (N=96)	Ravulizumab (N=58)	p-value (7)
	Risk Difference (6)		0.055	
	(95% CI)		(-0.119, 0.229)	
	p-value		0.5266	
Baseline EDSS Score	n	35	20	
	Mean (SD)	3.9 (1.62)	2.8 (1.57)	
	Median	3.5	3.0	
	Q1, Q3	3.0, 5.5	1.8, 3.8	
	Min, Max	1, 7	0, 6	
End of Study Period EDSS Score	n	35	20	
	Mean (SD)	3.7 (1.72)	2.6 (1.50)	
	Median	3.5	2.8	
	Q1, Q3	2.5, 4.5	1.8, 3.5	
	Min, Max	1, 7	0, 6	

The eculizumab group data were collected as part of the PREVENT trial, Study ECU-NMO-301.

End of Study Period is the 6-week assessment after the first On-Trial Relapse for patients who have an On-Trial Relapse or for patients with no On-Trial Relapse: the End of Primary Treatment Period visit for patients in Study ALXN1210-NMO-307 and the End of Study visit for patients in Study ECU-NMO-301.

For those patients who had a missed value at the EOPT Visit or the 6-week post-relapse visit, for patients who had a relapse, the end of study is the last value before the missed value.

(1) The LS means (95% CI) and the difference in LS means (95% CI) are from an ANCOVA model of change from baseline with treatment as factor and baseline value as covariate. (2) The p-value represents the significance of the treatment effect and was derived from an ANCOVA model of the ranked change from baseline, with treatment as a factor, and the ranks of the baseline value included as covariate.

(3) Standardized mean differences (95% CI) were computed using Cohen's D incorporating Hedge's correction on change from baseline. (4) Odds ratio statistics are from a logistic regression model adjusted for baseline value with Firth's adjustment; (5) Relative risk statistics are based on a generalized linear model of a binomial distribution with log link;

(6) Risk difference statistics are calculated from a generalized linear model, correcting for the baseline value. (7) P-value is for the interaction term of treatment:subgroup from a linear regression model of ranked change from baseline with the with ranked baseline value, treatment, subgroup, and treatment:subgroup interaction as covariates.

For eculizumab arm, Americas: ARG and USA; Europe: CZE, DEU, DNK, ESP, HRV, ITA, RUS and TUR; Asia-Pacific: AUS, HKG, JPN, KOR, MYS, THA and TWN. For ravulizumab arm, Americas: CAN and USA; Europe: DEU, DNK, ESP, GBR, ITA and POL; Asia-Pacific: AUS, JPN and KOR.

Odds ratio and relative risk are calculated as Ravulizumab/Eculizumab. LS mean difference and risk difference are calculated as Ravulizumab - Eculizumab.

Source: adsl, adedss

Table EDSS-2.5
Change from Baseline in EDSS Score to End of Study Period by Region
Full Analysis Set

Region		Statistic	Eculizumab (N=96)	Ravulizumab (N=58)	p-value (7)
Americas	Change from Baseline to End of Study Period in EDSS Score	n	29	21	0.5494
		Mean (SD)	-0.1 (0.81)	-0.5 (1.18)	
		Median	0.0	0.0	
		Q1, Q3	0.0, 0.0	-1.0, 0.0	
		Min, Max	-3, 2	-3, 1	
		Change from baseline			
		LS Means (SEM)	-0.004 (0.174)	-0.590 (0.205)	
		95% CI for LS Means (1)	(-0.354, 0.346)	(-1.003, -0.176)	
		Difference in LS Means		-0.586	
		(95% CI) (1)		(-1.137, -0.035)	
		p-value (2)		0.0928	
		Standardized Mean Difference		-0.605	
		(95% CI) (3)		(-1.179, -0.031)	
		Responders (15% [1.5 points]), n(%)	2 (6.9)	4 (19.0)	
		Odds Ratio (4)		4.960	
		(95% CI)		(0.758, 32.448)	
		p-value		0.0947	
		Relative Risk (5)		2.762	
		(95% CI)		(0.557, 13.704)	
		p-value		0.2138	

The eculizumab group data were collected as part of the PREVENT trial, Study ECU-NMO-301.

End of Study Period is the 6-week assessment after the first On-Trial Relapse for patients who have an On-Trial Relapse or for patients with no On-Trial Relapse: the End of Primary Treatment Period visit for patients in Study ALXN1210-NMO-307 and the End of Study visit for patients in Study ECU-NMO-301.

For those patients who had a missed value at the EOPT Visit or the 6-week post-relapse visit, for patients who had a relapse, the end of study is the last value before the missed value.

(1) The LS means (95% CI) and the difference in LS means (95% CI) are from an ANCOVA model of change from baseline with treatment as factor and baseline value as covariate. (2) The p-value represents the significance of the treatment effect and was derived from an ANCOVA model of the ranked change from baseline, with treatment as a factor, and the ranks of the baseline value included as covariate.

(3) Standardized mean differences (95% CI) were computed using Cohen's D incorporating Hedge's correction on change from baseline. (4) Odds ratio statistics are from a logistic regression model adjusted for baseline value with Firth's adjustment; (5) Relative risk statistics are based on a generalized linear model of a binomial distribution with log link;

(6) Risk difference statistics are calculated from a generalized linear model, correcting for the baseline value. (7) P-value is for the interaction term of treatment:subgroup from a linear regression model of ranked change from baseline with the with ranked baseline value, treatment, subgroup, and treatment:subgroup interaction as covariates.

For eculizumab arm, Americas: ARG and USA; Europe: CZE, DEU, DNK, ESP, HRV, ITA, RUS and TUR; Asia-Pacific: AUS, HKG, JPN, KOR, MYS, THA and TWN. For ravulizumab arm, Americas: CAN and USA; Europe: DEU, DNK, ESP, GBR, ITA and POL; Asia-Pacific: AUS, JPN and KOR.

Odds ratio and relative risk are calculated as Ravulizumab/Eculizumab. LS mean difference and risk difference are calculated as Ravulizumab - Eculizumab.

Source: adsl, adedss

Table EDSS-2.5
Change from Baseline in EDSS Score to End of Study Period by Region
Full Analysis Set

Region	Statistic	Eculizumab (N=96)	Ravulizumab (N=58)	p-value (7)
	Risk Difference (6)		0.175	
	(95% CI)		(-0.013, 0.362)	
	p-value		0.0675	
Baseline EDSS Score	n	29	21	
	Mean (SD)	4.4 (1.49)	3.6 (1.49)	
	Median	4.0	3.5	
	Q1, Q3	3.5, 6.0	2.5, 4.5	
	Min, Max	2, 7	2, 7	
End of Study Period EDSS Score	n	29	21	
	Mean (SD)	4.4 (1.42)	3.2 (1.49)	
	Median	4.0	3.5	
	Q1, Q3	3.0, 6.0	1.5, 4.0	
	Min, Max	2, 7	1, 6	

The eculizumab group data were collected as part of the PREVENT trial, Study ECU-NMO-301.

End of Study Period is the 6-week assessment after the first On-Trial Relapse for patients who have an On-Trial Relapse or for patients with no On-Trial Relapse: the End of Primary Treatment Period visit for patients in Study ALXN1210-NMO-307 and the End of Study visit for patients in Study ECU-NMO-301.

For those patients who had a missed value at the EOPT Visit or the 6-week post-relapse visit, for patients who had a relapse, the end of study is the last value before the missed value.

(1) The LS means (95% CI) and the difference in LS means (95% CI) are from an ANCOVA model of change from baseline with treatment as factor and baseline value as covariate. (2) The p-value represents the significance of the treatment effect and was derived from an ANCOVA model of the ranked change from baseline, with treatment as a factor, and the ranks of the baseline value included as covariate.

(3) Standardized mean differences (95% CI) were computed using Cohen's D incorporating Hedge's correction on change from baseline. (4) Odds ratio statistics are from a logistic regression model adjusted for baseline value with Firth's adjustment; (5) Relative risk statistics are based on a generalized linear model of a binomial distribution with log link;

(6) Risk difference statistics are calculated from a generalized linear model, correcting for the baseline value. (7) P-value is for the interaction term of treatment:subgroup from a linear regression model of ranked change from baseline with the with ranked baseline value, treatment, subgroup, and treatment:subgroup interaction as covariates.

For eculizumab arm, Americas: ARG and USA; Europe: CZE, DEU, DNK, ESP, HRV, ITA, RUS and TUR; Asia-Pacific: AUS, HKG, JPN, KOR, MYS, THA and TWN. For ravulizumab arm, Americas: CAN and USA; Europe: DEU, DNK, ESP, GBR, ITA and POL; Asia-Pacific: AUS, JPN and KOR.

Odds ratio and relative risk are calculated as Ravulizumab/Eculizumab. LS mean difference and risk difference are calculated as Ravulizumab - Eculizumab.

Source: adsl, adedss

Table EDSS-2.5
Change from Baseline in EDSS Score to End of Study Period by Region
Full Analysis Set

Region		Statistic	Eculizumab (N=96)	Ravulizumab (N=58)	p-value (7)
Europe	Change from Baseline to End of Study Period in EDSS Score	n	32	17	
		Mean (SD)	-0.2 (0.77)	-0.3 (0.64)	
		Median	0.0	0.0	
		Q1, Q3	-0.5, 0.0	-0.5, 0.0	
		Min, Max	-3, 1	-2, 1	
		Change from baseline LS Means (SEM)	-0.210 (0.130)	-0.310 (0.179)	
		95% CI for LS Means (1)	(-0.472, 0.052)	(-0.671, 0.051)	
		Difference in LS Means		-0.100	
		(95% CI) (1)		(-0.548, 0.349)	
		p-value (2)		0.5587	
		Standardized Mean Difference		-0.116	
		(95% CI) (3)		(-0.705, 0.473)	
		Responders (15% [1.5 points]), n(%)	2 (6.3)	2 (11.8)	
		Odds Ratio (4)		2.042	
		(95% CI)		(0.312, 13.363)	
		p-value		0.4564	
		Relative Risk (5)		1.882	
		(95% CI)		(0.290, 12.209)	
		p-value		0.5073	

The eculizumab group data were collected as part of the PREVENT trial, Study ECU-NMO-301.

End of Study Period is the 6-week assessment after the first On-Trial Relapse for patients who have an On-Trial Relapse or for patients with no On-Trial Relapse: the End of Primary Treatment Period visit for patients in Study ALXN1210-NMO-307 and the End of Study visit for patients in Study ECU-NMO-301.

For those patients who had a missed value at the EOPT Visit or the 6-week post-relapse visit, for patients who had a relapse, the end of study is the last value before the missed value.

(1) The LS means (95% CI) and the difference in LS means (95% CI) are from an ANCOVA model of change from baseline with treatment as factor and baseline value as covariate. (2) The p-value represents the significance of the treatment effect and was derived from an ANCOVA model of the ranked change from baseline, with treatment as a factor, and the ranks of the baseline value included as covariate.

(3) Standardized mean differences (95% CI) were computed using Cohen's D incorporating Hedge's correction on change from baseline. (4) Odds ratio statistics are from a logistic regression model adjusted for baseline value with Firth's adjustment; (5) Relative risk statistics are based on a generalized linear model of a binomial distribution with log link;

(6) Risk difference statistics are calculated from a generalized linear model, correcting for the baseline value. (7) P-value is for the interaction term of treatment:subgroup from a linear regression model of ranked change from baseline with the with ranked baseline value, treatment, subgroup, and treatment:subgroup interaction as covariates.

For eculizumab arm, Americas: ARG and USA; Europe: CZE, DEU, DNK, ESP, HRV, ITA, RUS and TUR; Asia-Pacific: AUS, HKG, JPN, KOR, MYS, THA and TWN. For ravulizumab arm, Americas: CAN and USA; Europe: DEU, DNK, ESP, GBR, ITA and POL; Asia-Pacific: AUS, JPN and KOR.

Odds ratio and relative risk are calculated as Ravulizumab/Eculizumab. LS mean difference and risk difference are calculated as Ravulizumab - Eculizumab.

Source: adsl, adedss

Table EDSS-2.5
Change from Baseline in EDSS Score to End of Study Period by Region
Full Analysis Set

Region	Statistic	Eculizumab (N=96)	Ravulizumab (N=58)	p-value (7)
	Risk Difference (6)		0.060	
	(95% CI)		(-0.112, 0.232)	
	p-value		0.4850	
Baseline EDSS Score	n	32	17	
	Mean (SD)	4.1 (1.81)	3.5 (1.62)	
	Median	3.5	3.5	
	Q1, Q3	2.8, 5.8	2.0, 4.0	
	Min, Max	2, 7	2, 7	
End of Study Period EDSS Score	n	32	17	
	Mean (SD)	3.9 (1.89)	3.2 (1.69)	
	Median	3.5	3.0	
	Q1, Q3	2.8, 5.3	2.0, 3.5	
	Min, Max	1, 8	2, 7	

The eculizumab group data were collected as part of the PREVENT trial, Study ECU-NMO-301.

End of Study Period is the 6-week assessment after the first On-Trial Relapse for patients who have an On-Trial Relapse or for patients with no On-Trial Relapse: the End of Primary Treatment Period visit for patients in Study ALXN1210-NMO-307 and the End of Study visit for patients in Study ECU-NMO-301.

For those patients who had a missed value at the EOPT Visit or the 6-week post-relapse visit, for patients who had a relapse, the end of study is the last value before the missed value.

(1) The LS means (95% CI) and the difference in LS means (95% CI) are from an ANCOVA model of change from baseline with treatment as factor and baseline value as covariate. (2) The p-value represents the significance of the treatment effect and was derived from an ANCOVA model of the ranked change from baseline, with treatment as a factor, and the ranks of the baseline value included as covariate.

(3) Standardized mean differences (95% CI) were computed using Cohen's D incorporating Hedge's correction on change from baseline. (4) Odds ratio statistics are from a logistic regression model adjusted for baseline value with Firth's adjustment; (5) Relative risk statistics are based on a generalized linear model of a binomial distribution with log link;

(6) Risk difference statistics are calculated from a generalized linear model, correcting for the baseline value. (7) P-value is for the interaction term of treatment:subgroup from a linear regression model of ranked change from baseline with the with ranked baseline value, treatment, subgroup, and treatment:subgroup interaction as covariates.

For eculizumab arm, Americas: ARG and USA; Europe: CZE, DEU, DNK, ESP, HRV, ITA, RUS and TUR; Asia-Pacific: AUS, HKG, JPN, KOR, MYS, THA and TWN. For ravulizumab arm, Americas: CAN and USA; Europe: DEU, DNK, ESP, GBR, ITA and POL; Asia-Pacific: AUS, JPN and KOR.

Odds ratio and relative risk are calculated as Ravulizumab/Eculizumab. LS mean difference and risk difference are calculated as Ravulizumab - Eculizumab.

Source: adsl, adedss

Table EDSS-2.6
Change from Baseline in EDSS Score to End of Study Period by Supportive IST use at baseline
Full Analysis Set

IST use at baseline		Statistic	Eculizumab (N=96)	Ravulizumab (N=58)	p-value (7)
Yes	Change from Baseline to End of Study Period in EDSS Score	n	75	28	0.8673
		Mean (SD)	-0.1 (0.82)	-0.1 (0.76)	
		Median	0.0	0.0	
		Q1, Q3	-0.5, 0.0	-0.5, 0.0	
		Min, Max	-4, 2	-3, 1	
		Change from baseline			
		LS Means (SEM)	-0.105 (0.091)	-0.201 (0.150)	
		95% CI for LS Means (1)	(-0.286, 0.076)	(-0.499, 0.097)	
		Difference in LS Means		-0.096	
		(95% CI) (1)		(-0.447, 0.255)	
		p-value (2)		0.4141	
		Standardized Mean Difference		-0.108	
		(95% CI) (3)		(-0.542, 0.326)	
		Responders (15% [1.5 points]), n(%)	5 (6.7)	2 (7.1)	
		Odds Ratio (4)		1.562	
		(95% CI)		(0.309, 7.890)	
		p-value		0.5894	
		Relative Risk (5)		1.071	
		(95% CI)		(0.220, 5.209)	
		p-value		0.9319	

The eculizumab group data were collected as part of the PREVENT trial, Study ECU-NMO-301.

End of Study Period is the 6-week assessment after the first On-Trial Relapse for patients who have an On-Trial Relapse or for patients with no On-Trial Relapse: the End of Primary Treatment Period visit for patients in Study ALXN1210-NMO-307 and the End of Study visit for patients in Study ECU-NMO-301.

For those patients who had a missed value at the EOPT Visit or the 6-week post-relapse visit, for patients who had a relapse, the end of study is the last value before the missed value.

(1) The LS means (95% CI) and the difference in LS means (95% CI) are from an ANCOVA model of change from baseline with treatment as factor and baseline value as covariate. (2) The p-value represents the significance of the treatment effect and was derived from an ANCOVA model of the ranked change from baseline, with treatment as a factor, and the ranks of the baseline value included as covariate.

(3) Standardized mean differences (95% CI) were computed using Cohen's D incorporating Hedge's correction on change from baseline. (4) Odds ratio statistics are from a logistic regression model adjusted for baseline value with Firth's adjustment; (5) Relative risk statistics are based on a generalized linear model of a binomial distribution with log link;

(6) Risk difference statistics are calculated from a generalized linear model, correcting for the baseline value. (7) P-value is for the interaction term of treatment:subgroup from a linear regression model of ranked change from baseline with the with ranked baseline value, treatment, subgroup, and treatment:subgroup interaction as covariates.

Odds ratio and relative risk are calculated as Ravulizumab/Eculizumab. LS mean difference and risk difference are calculated as Ravulizumab - Eculizumab.

Source: adsl, adedss

Table EDSS-2.6
Change from Baseline in EDSS Score to End of Study Period by Supportive IST use at baseline
Full Analysis Set

IST use at baseline	Statistic	Eculizumab (N=96)	Ravulizumab (N=58)	p-value (7)
	Risk Difference (6)		0.022	
	(95% CI)		(-0.091, 0.135)	
	p-value		0.7047	
Baseline EDSS Score	n	75	28	
	Mean (SD)	4.1 (1.70)	3.4 (1.56)	
	Median	4.0	3.3	
	Q1, Q3	3.0, 6.0	2.3, 4.3	
	Min, Max	1, 7	1, 7	
End of Study Period EDSS Score	n	75	28	
	Mean (SD)	4.0 (1.72)	3.3 (1.53)	
	Median	3.5	3.3	
	Q1, Q3	3.0, 6.0	2.0, 3.8	
	Min, Max	1, 7	1, 7	

The eculizumab group data were collected as part of the PREVENT trial, Study ECU-NMO-301.

End of Study Period is the 6-week assessment after the first On-Trial Relapse for patients who have an On-Trial Relapse or for patients with no On-Trial Relapse: the End of Primary Treatment Period visit for patients in Study ALXN1210-NMO-307 and the End of Study visit for patients in Study ECU-NMO-301.

For those patients who had a missed value at the EOPT Visit or the 6-week post-relapse visit, for patients who had a relapse, the end of study is the last value before the missed value.

(1) The LS means (95% CI) and the difference in LS means (95% CI) are from an ANCOVA model of change from baseline with treatment as factor and baseline value as covariate. (2) The p-value represents the significance of the treatment effect and was derived from an ANCOVA model of the ranked change from baseline, with treatment as a factor, and the ranks of the baseline value included as covariate.

(3) Standardized mean differences (95% CI) were computed using Cohen's D incorporating Hedge's correction on change from baseline. (4) Odds ratio statistics are from a logistic regression model adjusted for baseline value with Firth's adjustment; (5) Relative risk statistics are based on a generalized linear model of a binomial distribution with log link;

(6) Risk difference statistics are calculated from a generalized linear model, correcting for the baseline value. (7) P-value is for the interaction term of treatment:subgroup from a linear regression model of ranked change from baseline with the with ranked baseline value, treatment, subgroup, and treatment:subgroup interaction as covariates.

Odds ratio and relative risk are calculated as Ravulizumab/Eculizumab. LS mean difference and risk difference are calculated as Ravulizumab - Eculizumab.

Source: adsl, adedss

Table EDSS-2.6
Change from Baseline in EDSS Score to End of Study Period by Supportive IST use at baseline
Full Analysis Set

IST use at baseline		Statistic	Eculizumab (N=96)	Ravulizumab (N=58)	p-value (7)
No	Change from Baseline to End of Study Period in EDSS Score	n	21	30	
		Mean (SD)	-0.4 (0.79)	-0.5 (1.03)	
		Median	0.0	0.0	
		Q1, Q3	-0.5, 0.0	-1.0, 0.0	
		Min, Max	-3, 1	-3, 1	
		Change from baseline			
		LS Means (SEM)	-0.264 (0.205)	-0.515 (0.170)	
		95% CI for LS Means (1)	(-0.677, 0.149)	(-0.858, -0.173)	
		Difference in LS Means		-0.251	
		(95% CI) (1)		(-0.800, 0.297)	
		p-value (2)		0.7332	
		Standardized Mean Difference		-0.260	
		(95% CI) (3)		(-0.820, 0.300)	
		Responders (15% [1.5 points]), n(%)	2 (9.5)	6 (20.0)	
		Odds Ratio (4)		3.215	
		(95% CI)		(0.568, 18.211)	
		p-value		0.1868	
		Relative Risk (5)		2.100	
		(95% CI)		(0.469, 9.412)	
		p-value		0.3323	

The eculizumab group data were collected as part of the PREVENT trial, Study ECU-NMO-301.

End of Study Period is the 6-week assessment after the first On-Trial Relapse for patients who have an On-Trial Relapse or for patients with no On-Trial Relapse: the End of Primary Treatment Period visit for patients in Study ALXN1210-NMO-307 and the End of Study visit for patients in Study ECU-NMO-301.

For those patients who had a missed value at the EOPT Visit or the 6-week post-relapse visit, for patients who had a relapse, the end of study is the last value before the missed value.

(1) The LS means (95% CI) and the difference in LS means (95% CI) are from an ANCOVA model of change from baseline with treatment as factor and baseline value as covariate. (2) The p-value represents the significance of the treatment effect and was derived from an ANCOVA model of the ranked change from baseline, with treatment as a factor, and the ranks of the baseline value included as covariate.

(3) Standardized mean differences (95% CI) were computed using Cohen's D incorporating Hedge's correction on change from baseline. (4) Odds ratio statistics are from a logistic regression model adjusted for baseline value with Firth's adjustment; (5) Relative risk statistics are based on a generalized linear model of a binomial distribution with log link;

(6) Risk difference statistics are calculated from a generalized linear model, correcting for the baseline value. (7) P-value is for the interaction term of treatment:subgroup from a linear regression model of ranked change from baseline with the with ranked baseline value, treatment, subgroup, and treatment:subgroup interaction as covariates.

Odds ratio and relative risk are calculated as Ravulizumab/Eculizumab. LS mean difference and risk difference are calculated as Ravulizumab - Eculizumab.

Source: adsl, adedss

Table EDSS-2.6
Change from Baseline in EDSS Score to End of Study Period by Supportive IST use at baseline
Full Analysis Set

IST use at baseline	Statistic	Eculizumab (N=96)	Ravulizumab (N=58)	p-value (7)
	Risk Difference (6)		0.165	
	(95% CI)		(-0.049, 0.380)	
	p-value		0.1281	
Baseline EDSS Score	n	21	30	
	Mean (SD)	4.2 (1.50)	3.2 (1.62)	
	Median	4.0	3.3	
	Q1, Q3	3.5, 4.5	2.0, 4.0	
	Min, Max	2, 7	0, 7	
End of Study Period EDSS Score	n	21	30	
	Mean (SD)	3.8 (1.66)	2.8 (1.56)	
	Median	3.5	2.8	
	Q1, Q3	3.0, 4.5	1.5, 3.5	
	Min, Max	1, 8	0, 6	

The eculizumab group data were collected as part of the PREVENT trial, Study ECU-NMO-301.

End of Study Period is the 6-week assessment after the first On-Trial Relapse for patients who have an On-Trial Relapse or for patients with no On-Trial Relapse: the End of Primary Treatment Period visit for patients in Study ALXN1210-NMO-307 and the End of Study visit for patients in Study ECU-NMO-301.

For those patients who had a missed value at the EOPT Visit or the 6-week post-relapse visit, for patients who had a relapse, the end of study is the last value before the missed value.

(1) The LS means (95% CI) and the difference in LS means (95% CI) are from an ANCOVA model of change from baseline with treatment as factor and baseline value as covariate. (2) The p-value represents the significance of the treatment effect and was derived from an ANCOVA model of the ranked change from baseline, with treatment as a factor, and the ranks of the baseline value included as covariate.

(3) Standardized mean differences (95% CI) were computed using Cohen's D incorporating Hedge's correction on change from baseline. (4) Odds ratio statistics are from a logistic regression model adjusted for baseline value with Firth's adjustment; (5) Relative risk statistics are based on a generalized linear model of a binomial distribution with log link;

(6) Risk difference statistics are calculated from a generalized linear model, correcting for the baseline value. (7) P-value is for the interaction term of treatment:subgroup from a linear regression model of ranked change from baseline with the with ranked baseline value, treatment, subgroup, and treatment:subgroup interaction as covariates.

Odds ratio and relative risk are calculated as Ravulizumab/Eculizumab. LS mean difference and risk difference are calculated as Ravulizumab - Eculizumab.

Source: adsl, adedss

Table EDSS-2.7
Change from Baseline in EDSS Score to End of Study Period by Rituximab use in the prior year
Full Analysis Set

Rituximab use in the prior year		Statistic	Eculizumab (N=96)	Ravulizumab (N=58)	p-value (7)
Yes	Change from Baseline to End of Study Period in EDSS Score	n	19	20	0.2583
		Mean (SD)	-0.1 (0.74)	-0.7 (1.14)	
		Median	0.0	0.0	
		Q1, Q3	-0.5, 0.0	-1.5, 0.0	
		Min, Max	-2, 2	-3, 1	
		Change from baseline			
		LS Means (SEM)	0.030 (0.215)	-0.779 (0.209)	
		95% CI for LS Means (1)	(-0.406, 0.466)	(-1.203, -0.354)	
		Difference in LS Means		-0.809	
		(95% CI) (1)		(-1.427, -0.191)	
		p-value (2)		0.0964	
		Standardized Mean Difference		-0.836	
		(95% CI) (3)		(-1.491, -0.181)	
		Responders (15% [1.5 points]), n(%)	1 (5.3)	7 (35.0)	
		Odds Ratio (4)		7.906	
		(95% CI)		(1.093, 57.207)	
		p-value		0.0406	
		Relative Risk (5)		6.650	
		(95% CI)		(0.901, 49.088)	
		p-value		0.0632	

The eculizumab group data were collected as part of the PREVENT trial, Study ECU-NMO-301.

End of Study Period is the 6-week assessment after the first On-Trial Relapse for patients who have an On-Trial Relapse or for patients with no On-Trial Relapse: the End of Primary Treatment Period visit for patients in Study ALXN1210-NMO-307 and the End of Study visit for patients in Study ECU-NMO-301.

For those patients who had a missed value at the EOPT Visit or the 6-week post-relapse visit, for patients who had a relapse, the end of study is the last value before the missed value.

(1) The LS means (95% CI) and the difference in LS means (95% CI) are from an ANCOVA model of change from baseline with treatment as factor and baseline value as covariate. (2) The p-value represents the significance of the treatment effect and was derived from an ANCOVA model of the ranked change from baseline, with treatment as a factor, and the ranks of the baseline value included as covariate.

(3) Standardized mean differences (95% CI) were computed using Cohen's D incorporating Hedge's correction on change from baseline. (4) Odds ratio statistics are from a logistic regression model adjusted for baseline value with Firth's adjustment; (5) Relative risk statistics are based on a generalized linear model of a binomial distribution with log link;

(6) Risk difference statistics are calculated from a generalized linear model, correcting for the baseline value. (7) P-value is for the interaction term of treatment:subgroup from a linear regression model of ranked change from baseline with the with ranked baseline value, treatment, subgroup, and treatment:subgroup interaction as covariates.

Odds ratio and relative risk are calculated as Ravulizumab/Eculizumab. LS mean difference and risk difference are calculated as Ravulizumab - Eculizumab.

Source: adsl, adedss

Table EDSS-2.7
Change from Baseline in EDSS Score to End of Study Period by Rituximab use in the prior year
Full Analysis Set

Rituximab use in the prior year		Statistic	Eculizumab (N=96)	Ravulizumab (N=58)	p-value (7)
		Risk Difference (6)		0.323	
		(95% CI)		(0.064, 0.583)	
		p-value		0.0159	
	Baseline EDSS Score	n	19	20	
		Mean (SD)	4.6 (1.71)	3.7 (1.87)	
		Median	4.5	3.5	
		Q1, Q3	3.5, 6.5	2.3, 5.8	
		Min, Max	2, 7	0, 7	
	End of Study Period EDSS Score	n	19	20	
		Mean (SD)	4.5 (1.58)	3.0 (1.85)	
		Median	4.0	2.8	
		Q1, Q3	3.0, 6.0	1.5, 3.8	
		Min, Max	3, 7	0, 6	

The eculizumab group data were collected as part of the PREVENT trial, Study ECU-NMO-301.

End of Study Period is the 6-week assessment after the first On-Trial Relapse for patients who have an On-Trial Relapse or for patients with no On-Trial Relapse: the End of Primary Treatment Period visit for patients in Study ALXN1210-NMO-307 and the End of Study visit for patients in Study ECU-NMO-301.

For those patients who had a missed value at the EOPT Visit or the 6-week post-relapse visit, for patients who had a relapse, the end of study is the last value before the missed value.

(1) The LS means (95% CI) and the difference in LS means (95% CI) are from an ANCOVA model of change from baseline with treatment as factor and baseline value as covariate. (2) The p-value represents the significance of the treatment effect and was derived from an ANCOVA model of the ranked change from baseline, with treatment as a factor, and the ranks of the baseline value included as covariate.

(3) Standardized mean differences (95% CI) were computed using Cohen's D incorporating Hedge's correction on change from baseline. (4) Odds ratio statistics are from a logistic regression model adjusted for baseline value with Firth's adjustment; (5) Relative risk statistics are based on a generalized linear model of a binomial distribution with log link;

(6) Risk difference statistics are calculated from a generalized linear model, correcting for the baseline value. (7) P-value is for the interaction term of treatment:subgroup from a linear regression model of ranked change from baseline with the with ranked baseline value, treatment, subgroup, and treatment:subgroup interaction as covariates.

Odds ratio and relative risk are calculated as Ravulizumab/Eculizumab. LS mean difference and risk difference are calculated as Ravulizumab - Eculizumab.

Source: adsl, adedss

Table EDSS-2.7
Change from Baseline in EDSS Score to End of Study Period by Rituximab use in the prior year
Full Analysis Set

Rituximab use in the prior year		Statistic	Eculizumab (N=96)	Ravulizumab (N=58)	p-value (7)
No	Change from Baseline to End of Study Period in EDSS Score	n	77	38	
		Mean (SD)	-0.2 (0.83)	-0.1 (0.70)	
		Median	0.0	0.0	
		Q1, Q3	-0.5, 0.0	-0.5, 0.0	
		Min, Max	-4, 1	-3, 1	
		Change from baseline			
		LS Means (SEM)	-0.180 (0.090)	-0.148 (0.130)	
		95% CI for LS Means (1)	(-0.359, -0.001)	(-0.406, 0.110)	
		Difference in LS Means		0.032	
		(95% CI) (1)		(-0.288, 0.352)	
		p-value (2)		0.8254	
		Standardized Mean Difference		0.036	
		(95% CI) (3)		(-0.353, 0.425)	
		Responders (15% [1.5 points]), n(%)	6 (7.8)	1 (2.6)	
		Odds Ratio (4)		0.676	
		(95% CI)		(0.102, 4.485)	
		p-value		0.6854	
		Relative Risk (5)		0.338	
		(95% CI)		(0.042, 2.706)	
		p-value		0.3066	

The eculizumab group data were collected as part of the PREVENT trial, Study ECU-NMO-301.

End of Study Period is the 6-week assessment after the first On-Trial Relapse for patients who have an On-Trial Relapse or for patients with no On-Trial Relapse: the End of Primary Treatment Period visit for patients in Study ALXN1210-NMO-307 and the End of Study visit for patients in Study ECU-NMO-301.

For those patients who had a missed value at the EOPT Visit or the 6-week post-relapse visit, for patients who had a relapse, the end of study is the last value before the missed value.

(1) The LS means (95% CI) and the difference in LS means (95% CI) are from an ANCOVA model of change from baseline with treatment as factor and baseline value as covariate. (2) The p-value represents the significance of the treatment effect and was derived from an ANCOVA model of the ranked change from baseline, with treatment as a factor, and the ranks of the baseline value included as covariate.

(3) Standardized mean differences (95% CI) were computed using Cohen's D incorporating Hedge's correction on change from baseline. (4) Odds ratio statistics are from a logistic regression model adjusted for baseline value with Firth's adjustment; (5) Relative risk statistics are based on a generalized linear model of a binomial distribution with log link;

(6) Risk difference statistics are calculated from a generalized linear model, correcting for the baseline value. (7) P-value is for the interaction term of treatment:subgroup from a linear regression model of ranked change from baseline with the with ranked baseline value, treatment, subgroup, and treatment:subgroup interaction as covariates.

Odds ratio and relative risk are calculated as Ravulizumab/Eculizumab. LS mean difference and risk difference are calculated as Ravulizumab - Eculizumab.

Source: adsl, adedss

Table EDSS-2.7
Change from Baseline in EDSS Score to End of Study Period by Rituximab use in the prior year
Full Analysis Set

Rituximab use in the prior year		Statistic	Eculizumab (N=96)	Ravulizumab (N=58)	p-value (7)
		Risk Difference (6)		-0.025	
		(95% CI)		(-0.122, 0.072)	
		p-value		0.6114	
	Baseline EDSS Score	n	77	38	
		Mean (SD)	4.0 (1.62)	3.1 (1.39)	
		Median	3.5	3.0	
		Q1, Q3	3.0, 5.5	2.0, 4.0	
		Min, Max	1, 7	0, 7	
	End of Study Period EDSS Score	n	77	38	
		Mean (SD)	3.8 (1.71)	3.0 (1.40)	
		Median	3.5	3.0	
		Q1, Q3	3.0, 4.5	2.0, 3.5	
		Min, Max	1, 8	0, 7	

The eculizumab group data were collected as part of the PREVENT trial, Study ECU-NMO-301.

End of Study Period is the 6-week assessment after the first On-Trial Relapse for patients who have an On-Trial Relapse or for patients with no On-Trial Relapse: the End of Primary Treatment Period visit for patients in Study ALXN1210-NMO-307 and the End of Study visit for patients in Study ECU-NMO-301.

For those patients who had a missed value at the EOPT Visit or the 6-week post-relapse visit, for patients who had a relapse, the end of study is the last value before the missed value.

(1) The LS means (95% CI) and the difference in LS means (95% CI) are from an ANCOVA model of change from baseline with treatment as factor and baseline value as covariate. (2) The p-value represents the significance of the treatment effect and was derived from an ANCOVA model of the ranked change from baseline, with treatment as a factor, and the ranks of the baseline value included as covariate.

(3) Standardized mean differences (95% CI) were computed using Cohen's D incorporating Hedge's correction on change from baseline. (4) Odds ratio statistics are from a logistic regression model adjusted for baseline value with Firth's adjustment; (5) Relative risk statistics are based on a generalized linear model of a binomial distribution with log link;

(6) Risk difference statistics are calculated from a generalized linear model, correcting for the baseline value. (7) P-value is for the interaction term of treatment:subgroup from a linear regression model of ranked change from baseline with the with ranked baseline value, treatment, subgroup, and treatment:subgroup interaction as covariates.

Odds ratio and relative risk are calculated as Ravulizumab/Eculizumab. LS mean difference and risk difference are calculated as Ravulizumab - Eculizumab.

Source: adsl, adedss

Table EDSS-2.4
Change from Baseline in EDSS Score to End of Study Period by Disease severity via EDSS score at baseline
Full Analysis Set

EDSS score at baseline		Statistic	Eculizumab (N=96)	Ravulizumab (N=58)	p-value (7)
< 5	Change from Baseline to End of Study Period in EDSS Score	n	66	49	0.5333
		Mean (SD)	-0.1 (0.64)	-0.2 (0.81)	
		Median	0.0	0.0	
		Q1, Q3	-0.5, 0.0	-0.5, 0.0	
		Min, Max	-2, 2	-3, 1	
		Change from baseline LS Means (SEM)	-0.027 (0.086)	-0.290 (0.100)	
		95% CI for LS Means (1)	(-0.197, 0.143)	(-0.488, -0.093)	
		Difference in LS Means		-0.263	
		(95% CI) (1)		(-0.526, -0.001)	
		p-value (2)		0.1069	
		Standardized Mean Difference		-0.316	
		(95% CI) (3)		(-0.687, 0.056)	
		Responders (15% [1.5 points]), n(%)	2 (3.0)	6 (12.2)	
		Odds Ratio (4)		4.961	
		(95% CI)		(1.068, 23.042)	
		p-value		0.0409	
		Relative Risk (5)		4.041	
		(95% CI)		(0.852, 19.173)	
		p-value		0.0788	

The eculizumab group data were collected as part of the PREVENT trial, Study ECU-NMO-301.

End of Study Period is the 6-week assessment after the first On-Trial Relapse for patients who have an On-Trial Relapse or for patients with no On-Trial Relapse: the End of Primary Treatment Period visit for patients in Study ALXN1210-NMO-307 and the End of Study visit for patients in Study ECU-NMO-301.

For those patients who had a missed value at the EOPT Visit or the 6-week post-relapse visit, for patients who had a relapse, the end of study is the last value before the missed value.

(1) The LS means (95% CI) and the difference in LS means (95% CI) are from an ANCOVA model of change from baseline with treatment as factor and baseline value as covariate. (2) The p-value represents the significance of the treatment effect and was derived from an ANCOVA model of the ranked change from baseline, with treatment as a factor, and the ranks of the baseline value included as covariate.

(3) Standardized mean differences (95% CI) were computed using Cohen's D incorporating Hedge's correction on change from baseline. (4) Odds ratio statistics are from a logistic regression model adjusted for baseline value with Firth's adjustment; (5) Relative risk statistics are based on a generalized linear model of a binomial distribution with log link;

(6) Risk difference statistics are calculated from a generalized linear model, correcting for the baseline value. (7) P-value is for the interaction term of treatment:subgroup from a linear regression model of ranked change from baseline with the with ranked baseline value, treatment, subgroup, and treatment:subgroup interaction as covariates.

Odds ratio and relative risk are calculated as Ravulizumab/Eculizumab. LS mean difference and risk difference are calculated as Ravulizumab - Eculizumab.

Source: adsl, adedss

Table EDSS-2.4
Change from Baseline in EDSS Score to End of Study Period by Disease severity via EDSS score at baseline
Full Analysis Set

EDSS score at baseline	Statistic	Eculizumab (N=96)	Ravulizumab (N=58)	p-value (7)
	Risk Difference (6)		0.111	
	(95% CI)		(0.017, 0.206)	
	p-value		0.0216	
Baseline EDSS Score	n	66	49	
	Mean (SD)	3.2 (0.91)	2.8 (1.14)	
	Median	3.5	3.0	
	Q1, Q3	2.5, 4.0	2.0, 3.5	
	Min, Max	1, 5	0, 5	
End of Study Period EDSS Score	n	66	49	
	Mean (SD)	3.1 (1.01)	2.6 (1.12)	
	Median	3.5	2.5	
	Q1, Q3	3.0, 3.5	1.5, 3.5	
	Min, Max	1, 6	0, 5	

The eculizumab group data were collected as part of the PREVENT trial, Study ECU-NMO-301.

End of Study Period is the 6-week assessment after the first On-Trial Relapse for patients who have an On-Trial Relapse or for patients with no On-Trial Relapse: the End of Primary Treatment Period visit for patients in Study ALXN1210-NMO-307 and the End of Study visit for patients in Study ECU-NMO-301.

For those patients who had a missed value at the EOPT Visit or the 6-week post-relapse visit, for patients who had a relapse, the end of study is the last value before the missed value.

(1) The LS means (95% CI) and the difference in LS means (95% CI) are from an ANCOVA model of change from baseline with treatment as factor and baseline value as covariate. (2) The p-value represents the significance of the treatment effect and was derived from an ANCOVA model of the ranked change from baseline, with treatment as a factor, and the ranks of the baseline value included as covariate.

(3) Standardized mean differences (95% CI) were computed using Cohen's D incorporating Hedge's correction on change from baseline. (4) Odds ratio statistics are from a logistic regression model adjusted for baseline value with Firth's adjustment; (5) Relative risk statistics are based on a generalized linear model of a binomial distribution with log link;

(6) Risk difference statistics are calculated from a generalized linear model, correcting for the baseline value. (7) P-value is for the interaction term of treatment:subgroup from a linear regression model of ranked change from baseline with the with ranked baseline value, treatment, subgroup, and treatment:subgroup interaction as covariates.

Odds ratio and relative risk are calculated as Ravulizumab/Eculizumab. LS mean difference and risk difference are calculated as Ravulizumab - Eculizumab.

Source: adsl, adedss

Table EDSS-2.4
Change from Baseline in EDSS Score to End of Study Period by Disease severity via EDSS score at baseline
Full Analysis Set

EDSS score at baseline		Statistic	Eculizumab (N=96)	Ravulizumab (N=58)	p-value (7)
>= 5	Change from Baseline to End of Study Period in EDSS Score	n	30	9	
		Mean (SD)	-0.4 (1.07)	-0.6 (1.36)	
		Median	0.0	0.0	
		Q1, Q3	-0.5, 0.0	0.0, 0.0	
		Min, Max	-4, 1	-3, 1	
		Change from baseline			
		LS Means (SEM)	-0.465 (0.204)	-0.507 (0.375)	
		95% CI for LS Means (1)	(-0.878, -0.052)	(-1.267, 0.254)	
		Difference in LS Means		-0.042	
		(95% CI) (1)		(-0.913, 0.829)	
		p-value (2)		0.8324	
		Standardized Mean Difference		-0.040	
		(95% CI) (3)		(-0.785, 0.705)	
		Responders (15% [1.5 points]), n(%)	5 (16.7)	2 (22.2)	
		Odds Ratio (4)		1.108	
		(95% CI)		(0.165, 7.467)	
		p-value		0.9159	
		Relative Risk (5)		1.333	
		(95% CI)		(0.309, 5.746)	
		p-value		0.6995	

The eculizumab group data were collected as part of the PREVENT trial, Study ECU-NMO-301.

End of Study Period is the 6-week assessment after the first On-Trial Relapse for patients who have an On-Trial Relapse or for patients with no On-Trial Relapse: the End of Primary Treatment Period visit for patients in Study ALXN1210-NMO-307 and the End of Study visit for patients in Study ECU-NMO-301.

For those patients who had a missed value at the EOPT Visit or the 6-week post-relapse visit, for patients who had a relapse, the end of study is the last value before the missed value.

(1) The LS means (95% CI) and the difference in LS means (95% CI) are from an ANCOVA model of change from baseline with treatment as factor and baseline value as covariate. (2) The p-value represents the significance of the treatment effect and was derived from an ANCOVA model of the ranked change from baseline, with treatment as a factor, and the ranks of the baseline value included as covariate.

(3) Standardized mean differences (95% CI) were computed using Cohen's D incorporating Hedge's correction on change from baseline. (4) Odds ratio statistics are from a logistic regression model adjusted for baseline value with Firth's adjustment; (5) Relative risk statistics are based on a generalized linear model of a binomial distribution with log link;

(6) Risk difference statistics are calculated from a generalized linear model, correcting for the baseline value. (7) P-value is for the interaction term of treatment:subgroup from a linear regression model of ranked change from baseline with the with ranked baseline value, treatment, subgroup, and treatment:subgroup interaction as covariates.

Odds ratio and relative risk are calculated as Ravulizumab/Eculizumab. LS mean difference and risk difference are calculated as Ravulizumab - Eculizumab.

Source: adsl, adedss

Table EDSS-2.4
Change from Baseline in EDSS Score to End of Study Period by Disease severity via EDSS score at baseline
Full Analysis Set

EDSS score at baseline	Statistic	Eculizumab (N=96)	Ravulizumab (N=58)	p-value (7)
	Risk Difference (6)		-0.008	
	(95% CI)		(-0.297, 0.282)	
	p-value		0.9581	
Baseline EDSS Score	n	30	9	
	Mean (SD)	6.3 (0.60)	6.0 (0.56)	
	Median	6.0	6.0	
	Q1, Q3	6.0, 7.0	6.0, 6.0	
	Min, Max	5, 7	5, 7	
End of Study Period EDSS Score	n	30	9	
	Mean (SD)	5.8 (1.42)	5.4 (1.43)	
	Median	6.5	6.0	
	Q1, Q3	6.0, 6.5	5.5, 6.0	
	Min, Max	2, 8	3, 7	

The eculizumab group data were collected as part of the PREVENT trial, Study ECU-NMO-301.

End of Study Period is the 6-week assessment after the first On-Trial Relapse for patients who have an On-Trial Relapse or for patients with no On-Trial Relapse: the End of Primary Treatment Period visit for patients in Study ALXN1210-NMO-307 and the End of Study visit for patients in Study ECU-NMO-301.

For those patients who had a missed value at the EOPT Visit or the 6-week post-relapse visit, for patients who had a relapse, the end of study is the last value before the missed value.

(1) The LS means (95% CI) and the difference in LS means (95% CI) are from an ANCOVA model of change from baseline with treatment as factor and baseline value as covariate. (2) The p-value represents the significance of the treatment effect and was derived from an ANCOVA model of the ranked change from baseline, with treatment as a factor, and the ranks of the baseline value included as covariate.

(3) Standardized mean differences (95% CI) were computed using Cohen's D incorporating Hedge's correction on change from baseline. (4) Odds ratio statistics are from a logistic regression model adjusted for baseline value with Firth's adjustment; (5) Relative risk statistics are based on a generalized linear model of a binomial distribution with log link;

(6) Risk difference statistics are calculated from a generalized linear model, correcting for the baseline value. (7) P-value is for the interaction term of treatment:subgroup from a linear regression model of ranked change from baseline with the with ranked baseline value, treatment, subgroup, and treatment:subgroup interaction as covariates.

Odds ratio and relative risk are calculated as Ravulizumab/Eculizumab. LS mean difference and risk difference are calculated as Ravulizumab - Eculizumab.

Source: adsl, adedss

Table EDSS-1.2
Clinically Important Worsening from Baseline in EDSS Score to End of Study Period by Sex
Full Analysis Set

Sex		Statistic	Eculizumab (N=96)	Ravulizumab (N=58)	p-value (4)
Male	Clinically Important Worsening in EDSS Score from Baseline to End of Study Period				0.4674
		n	8	6	
		No Clinically Important Worsening	5 (62.5)	5 (83.3)	
		Clinically Important Worsening	3 (37.5)	1 (16.7)	
	Treatment Effect (Ravulizumab vs Eculizumab)				
		Odds Ratio (1)		0.575	
		(95% CI)		(0.042, 7.848)	
		p-value		0.6779	
		Relative Risk (2)		0.444	
		(95% CI)		(0.060, 3.285)	
		p-value		0.4269	
		Risk Difference (3)		-0.128	
		(95% CI)		(-0.757, 0.501)	
		p-value		0.6631	

The eculizumab group data were collected as part of the PREVENT trial, Study ECU-NMO-301.

End of Study Period is the 6-week assessment after the first On-Trial Relapse for patients who have an On-Trial Relapse or for patients with no On-Trial Relapse: the End of Primary Treatment Period visit for patients in Study ALXN1210-NMO-307 and the End of Study visit for patients in Study ECU-NMO-301.

For those patients who had a missed value at the EOPT Visit or the 6-week post-relapse visit, for patients who had a relapse, the end of study is the last value before the missed value.

Clinically important worsening is defined as an increase in EDSS score conditional on the baseline value: if the baseline EDSS is 0 and at least 2 points increase; if the baseline is 1-5, and at least 1 point increase; if the baseline is > 5 and at least 0.5 increase.

(1) Odds ratio statistics are from a logistic regression model adjusted for baseline value with Firth's adjustment; (2) Relative risk statistics are based on a generalized linear model of a binomial distribution with log link; (3) Risk difference statistics are calculated from a generalized linear model, correcting for the baseline value.

(4) P-value is for the interaction term of treatment:subgroup from a logistic regression model with the baseline value, treatment, subgroup, and treatment:subgroup interaction as covariates, with Firth's adjustment.

Odds ratio and relative risk are calculated as Ravulizumab/Eculizumab. Risk difference is calculated as Ravulizumab - Eculizumab.

Source: adsl, adedss

Table EDSS-1.2
Clinically Important Worsening from Baseline in EDSS Score to End of Study Period by Sex
Full Analysis Set

Sex		Statistic	Eculizumab (N=96)	Ravulizumab (N=58)	p-value (4)
Female	Clinically Important Worsening in EDSS Score from Baseline to End of Study Period				
		n	88	52	
		No Clinically Important Worsening	80 (90.9)	47 (90.4)	
		Clinically Important Worsening	8 (9.1)	5 (9.6)	
	Treatment Effect (Ravulizumab vs Eculizumab)				
		Odds Ratio (1)		0.875	
		(95% CI)		(0.271, 2.829)	
		p-value		0.8240	
		Relative Risk (2)		1.058	
		(95% CI)		(0.365, 3.063)	
		p-value		0.9177	
		Risk Difference (3)		-0.014	
		(95% CI)		(-0.117, 0.090)	
		p-value		0.7929	

The eculizumab group data were collected as part of the PREVENT trial, Study ECU-NMO-301.

End of Study Period is the 6-week assessment after the first On-Trial Relapse for patients who have an On-Trial Relapse or for patients with no On-Trial Relapse: the End of Primary Treatment Period visit for patients in Study ALXN1210-NMO-307 and the End of Study visit for patients in Study ECU-NMO-301.

For those patients who had a missed value at the EOPT Visit or the 6-week post-relapse visit, for patients who had a relapse, the end of study is the last value before the missed value.

Clinically important worsening is defined as an increase in EDSS score conditional on the baseline value: if the baseline EDSS is 0 and at least 2 points increase; if the baseline is 1-5, and at least 1 point increase; if the baseline is > 5 and at least 0.5 increase.

(1) Odds ratio statistics are from a logistic regression model adjusted for baseline value with Firth's adjustment; (2) Relative risk statistics are based on a generalized linear model of a binomial distribution with log link; (3) Risk difference statistics are calculated from a generalized linear model, correcting for the baseline value.

(4) P-value is for the interaction term of treatment:subgroup from a logistic regression model with the baseline value, treatment, subgroup, and treatment:subgroup interaction as covariates, with Firth's adjustment.

Odds ratio and relative risk are calculated as Ravulizumab/Eculizumab. Risk difference is calculated as Ravulizumab - Eculizumab.

Source: adsl, adedss

Table EDSS-1.3
Clinically Important Worsening from Baseline in EDSS Score to End of Study Period by Age Group
Full Analysis Set

Age Group		Statistic	Eculizumab (N=96)	Ravulizumab (N=58)	p-value (4)
< 45 years	Clinically Important Worsening in EDSS Score from Baseline to End of Study Period				0.7640
		n	47	25	
		No Clinically Important Worsening	43 (91.5)	23 (92.0)	
		Clinically Important Worsening	4 (8.5)	2 (8.0)	
	Treatment Effect (Ravulizumab vs Eculizumab)				
		Odds Ratio (1)		0.798	
		(95% CI)		(0.145, 4.401)	
		p-value		0.7956	
		Relative Risk (2)		0.940	
		(95% CI)		(0.185, 4.781)	
		p-value		0.9406	
		Risk Difference (3)		-0.022	
		(95% CI)		(-0.162, 0.118)	
		p-value		0.7513	

The eculizumab group data were collected as part of the PREVENT trial, Study ECU-NMO-301.
End of Study Period is the 6-week assessment after the first On-Trial Relapse for patients who have an On-Trial Relapse or for patients with no On-Trial Relapse: the End of Primary Treatment Period visit for patients in Study ALXN1210-NMO-307 and the End of Study visit for patients in Study ECU-NMO-301.
For those patients who had a missed value at the EOPT Visit or the 6-week post-relapse visit, for patients who had a relapse, the end of study is the last value before the missed value.
Clinically important worsening is defined as an increase in EDSS score conditional on the baseline value: if the baseline EDSS is 0 and at least 2 points increase; if the baseline is 1-5, and at least 1 point increase; if the baseline is > 5 and at least 0.5 increase.
(1) Odds ratio statistics are from a logistic regression model adjusted for baseline value with Firth's adjustment; (2) Relative risk statistics are based on a generalized linear model of a binomial distribution with log link; (3) Risk difference statistics are calculated from a generalized linear model, correcting for the baseline value.
(4) P-value is for the interaction term of treatment:subgroup from a logistic regression model with the baseline value, treatment, subgroup, and treatment:subgroup interaction as covariates, with Firth's adjustment.
Odds ratio and relative risk are calculated as Ravulizumab/Eculizumab. Risk difference is calculated as Ravulizumab - Eculizumab.
Source: adsl, adedss

Table EDSS-1.3
Clinically Important Worsening from Baseline in EDSS Score to End of Study Period by Age Group
Full Analysis Set

Age Group		Statistic	Eculizumab (N=96)	Ravulizumab (N=58)	p-value (4)
>= 45 years	Clinically Important Worsening in EDSS Score from Baseline to End of Study Period				
		n	49	33	
		No Clinically Important Worsening	42 (85.7)	29 (87.9)	
		Clinically Important Worsening	7 (14.3)	4 (12.1)	
	Treatment Effect (Ravulizumab vs Eculizumab)				
		Odds Ratio (1)		0.644	
		(95% CI)		(0.167, 2.490)	
		p-value		0.5236	
		Relative Risk (2)		0.848	
		(95% CI)		(0.270, 2.670)	
		p-value		0.7788	
		Risk Difference (3)		-0.058	
		(95% CI)		(-0.222, 0.107)	
		p-value		0.4875	

The eculizumab group data were collected as part of the PREVENT trial, Study ECU-NMO-301.

End of Study Period is the 6-week assessment after the first On-Trial Relapse for patients who have an On-Trial Relapse or for patients with no On-Trial Relapse: the End of Primary Treatment Period visit for patients in Study ALXN1210-NMO-307 and the End of Study visit for patients in Study ECU-NMO-301.

For those patients who had a missed value at the EOPT Visit or the 6-week post-relapse visit, for patients who had a relapse, the end of study is the last value before the missed value.

Clinically important worsening is defined as an increase in EDSS score conditional on the baseline value: if the baseline EDSS is 0 and at least 2 points increase; if the baseline is 1-5, and at least 1 point increase; if the baseline is > 5 and at least 0.5 increase.

(1) Odds ratio statistics are from a logistic regression model adjusted for baseline value with Firth's adjustment; (2) Relative risk statistics are based on a generalized linear model of a binomial distribution with log link; (3) Risk difference statistics are calculated from a generalized linear model, correcting for the baseline value.

(4) P-value is for the interaction term of treatment:subgroup from a logistic regression model with the baseline value, treatment, subgroup, and treatment:subgroup interaction as covariates, with Firth's adjustment.

Odds ratio and relative risk are calculated as Ravulizumab/Eculizumab. Risk difference is calculated as Ravulizumab - Eculizumab.

Source: adsl, adedss

Table EDSS-1.5
Clinically Important Worsening from Baseline in EDSS Score to End of Study Period by Region
Full Analysis Set

Region	Statistic	Eculizumab (N=96)	Ravulizumab (N=58)	p-value (4)
Asia-Pacific	Clinically Important Worsening in EDSS Score from Baseline to End of Study Period			0.9490
	n	35	20	
	No Clinically Important Worsening	31 (88.6)	18 (90.0)	
	Clinically Important Worsening	4 (11.4)	2 (10.0)	
	Treatment Effect (Ravulizumab vs Eculizumab)			
	Odds Ratio (1)		1.088	
	(95% CI)		(0.187, 6.317)	
	p-value		0.9253	
	Relative Risk (2)		0.875	
	(95% CI)		(0.176, 4.360)	
	p-value		0.8705	
	Risk Difference (3)		0.001	
	(95% CI)		(-0.191, 0.192)	
	p-value		0.9928	

The eculizumab group data were collected as part of the PREVENT trial, Study ECU-NMO-301.
End of Study Period is the 6-week assessment after the first On-Trial Relapse for patients who have an On-Trial Relapse or for patients with no On-Trial Relapse: the End of Primary Treatment Period visit for patients in Study ALXN1210-NMO-307 and the End of Study visit for patients in Study ECU-NMO-301.
For those patients who had a missed value at the EOPT Visit or the 6-week post-relapse visit, for patients who had a relapse, the end of study is the last value before the missed value.
Clinically important worsening is defined as an increase in EDSS score conditional on the baseline value: if the baseline EDSS is 0 and at least 2 points increase; if the baseline is 1-5, and at least 1 point increase; if the baseline is > 5 and at least 0.5 increase.
(1) Odds ratio statistics are from a logistic regression model adjusted for baseline value with Firth's adjustment; (2) Relative risk statistics are based on a generalized linear model of a binomial distribution with log link; (3) Risk difference statistics are calculated from a generalized linear model, correcting for the baseline value.
(4) P-value is for the interaction term of treatment:subgroup from a logistic regression model with the baseline value, treatment, subgroup, and treatment:subgroup interaction as covariates, with Firth's adjustment.
For eculizumab arm, Americas: ARG and USA; Europe: CZE, DEU, DNK, ESP, HRV, ITA, RUS and TUR; Asia-Pacific: AUS, HKG, JPN, KOR, MYS, THA and TWN. For ravulizumab arm, Americas: CAN and USA; Europe: DEU, DNK, ESP, GBR, ITA and POL; Asia-Pacific: AUS, JPN and KOR.
Odds ratio and relative risk are calculated as Ravulizumab/Eculizumab. Risk difference is calculated as Ravulizumab - Eculizumab.
Source: adsl, adedss

Table EDSS-1.5
Clinically Important Worsening from Baseline in EDSS Score to End of Study Period by Region
Full Analysis Set

Region		Statistic	Eculizumab (N=96)	Ravulizumab (N=58)	p-value (4)
Americas	Clinically Important Worsening in EDSS Score from Baseline to End of Study Period				0.5227
		n	29	21	
		No Clinically Important Worsening	26 (89.7)	18 (85.7)	
		Clinically Important Worsening	3 (10.3)	3 (14.3)	
	Treatment Effect (Ravulizumab vs Eculizumab)				
		Odds Ratio (1)		1.041	
		(95% CI)		(0.193, 5.631)	
		p-value		0.9624	
		Relative Risk (2)		1.381	
		(95% CI)		(0.309, 6.180)	
		p-value		0.6729	
		Risk Difference (3)		0.003	
		(95% CI)		(-0.192, 0.199)	
		p-value		0.9723	

The eculizumab group data were collected as part of the PREVENT trial, Study ECU-NMO-301.
End of Study Period is the 6-week assessment after the first On-Trial Relapse for patients who have an On-Trial Relapse or for patients with no On-Trial Relapse: the End of Primary Treatment Period visit for patients in Study ALXN1210-NMO-307 and the End of Study visit for patients in Study ECU-NMO-301.
For those patients who had a missed value at the EOPT Visit or the 6-week post-relapse visit, for patients who had a relapse, the end of study is the last value before the missed value.
Clinically important worsening is defined as an increase in EDSS score conditional on the baseline value: if the baseline EDSS is 0 and at least 2 points increase; if the baseline is 1-5, and at least 1 point increase; if the baseline is > 5 and at least 0.5 increase.
(1) Odds ratio statistics are from a logistic regression model adjusted for baseline value with Firth's adjustment; (2) Relative risk statistics are based on a generalized linear model of a binomial distribution with log link; (3) Risk difference statistics are calculated from a generalized linear model, correcting for the baseline value.
(4) P-value is for the interaction term of treatment:subgroup from a logistic regression model with the baseline value, treatment, subgroup, and treatment:subgroup interaction as covariates, with Firth's adjustment.
For eculizumab arm, Americas: ARG and USA; Europe: CZE, DEU, DNK, ESP, HRV, ITA, RUS and TUR; Asia-Pacific: AUS, HKG, JPN, KOR, MYS, THA and TWN. For ravulizumab arm, Americas: CAN and USA; Europe: DEU, DNK, ESP, GBR, ITA and POL; Asia-Pacific: AUS, JPN and KOR.
Odds ratio and relative risk are calculated as Ravulizumab/Eculizumab. Risk difference is calculated as Ravulizumab - Eculizumab.
Source: adsl, adedss

Table EDSS-1.5
Clinically Important Worsening from Baseline in EDSS Score to End of Study Period by Region
Full Analysis Set

Region		Statistic	Eculizumab (N=96)	Ravulizumab (N=58)	p-value (4)
Europe	Clinically Important Worsening in EDSS Score from Baseline to End of Study Period				
		n	32	17	
		No Clinically Important Worsening	28 (87.5)	16 (94.1)	
		Clinically Important Worsening	4 (12.5)	1 (5.9)	
	Treatment Effect (Ravulizumab vs Eculizumab)				
		Odds Ratio (1)		0.460	
		(95% CI)		(0.062, 3.406)	
		p-value		0.4475	
		Relative Risk (2)		0.471	
		(95% CI)		(0.057, 3.885)	
		p-value		0.4840	
		Risk Difference (3)		-0.087	
		(95% CI)		(-0.273, 0.098)	
		p-value		0.3484	

The eculizumab group data were collected as part of the PREVENT trial, Study ECU-NMO-301.
End of Study Period is the 6-week assessment after the first On-Trial Relapse for patients who have an On-Trial Relapse or for patients with no On-Trial Relapse: the End of Primary Treatment Period visit for patients in Study ALXN1210-NMO-307 and the End of Study visit for patients in Study ECU-NMO-301.
For those patients who had a missed value at the EOPT Visit or the 6-week post-relapse visit, for patients who had a relapse, the end of study is the last value before the missed value.
Clinically important worsening is defined as an increase in EDSS score conditional on the baseline value: if the baseline EDSS is 0 and at least 2 points increase; if the baseline is 1-5, and at least 1 point increase; if the baseline is > 5 and at least 0.5 increase.
(1) Odds ratio statistics are from a logistic regression model adjusted for baseline value with Firth's adjustment; (2) Relative risk statistics are based on a generalized linear model of a binomial distribution with log link; (3) Risk difference statistics are calculated from a generalized linear model, correcting for the baseline value.
(4) P-value is for the interaction term of treatment:subgroup from a logistic regression model with the baseline value, treatment, subgroup, and treatment:subgroup interaction as covariates, with Firth's adjustment.
For eculizumab arm, Americas: ARG and USA; Europe: CZE, DEU, DNK, ESP, HRV, ITA, RUS and TUR; Asia-Pacific: AUS, HKG, JPN, KOR, MYS, THA and TWN. For ravulizumab arm, Americas: CAN and USA; Europe: DEU, DNK, ESP, GBR, ITA and POL; Asia-Pacific: AUS, JPN and KOR.
Odds ratio and relative risk are calculated as Ravulizumab/Eculizumab. Risk difference is calculated as Ravulizumab - Eculizumab.
Source: adsl, adedss

Table EDSS-1.6
Clinically Important Worsening from Baseline in EDSS Score to End of Study Period by Supportive IST use at baseline
Full Analysis Set

IST use at baseline		Statistic	Eculizumab (N=96)	Ravulizumab (N=58)	p-value (4)
Yes	Clinically Important Worsening in EDSS Score from Baseline to End of Study Period				0.5965
		n	75	28	
		No Clinically Important Worsening	65 (86.7)	25 (89.3)	
		Clinically Important Worsening	10 (13.3)	3 (10.7)	
	Treatment Effect (Ravulizumab vs Eculizumab)				
		Odds Ratio (1)		0.703	
		(95% CI)		(0.185, 2.671)	
		p-value		0.6048	
		Relative Risk (2)		0.804	
		(95% CI)		(0.238, 2.708)	
		p-value		0.7243	
		Risk Difference (3)		-0.048	
		(95% CI)		(-0.197, 0.101)	
		p-value		0.5209	

The eculizumab group data were collected as part of the PREVENT trial, Study ECU-NMO-301.
End of Study Period is the 6-week assessment after the first On-Trial Relapse for patients who have an On-Trial Relapse or for patients with no On-Trial Relapse: the End of Primary Treatment Period visit for patients in Study ALXN1210-NMO-307 and the End of Study visit for patients in Study ECU-NMO-301.
For those patients who had a missed value at the EOPT Visit or the 6-week post-relapse visit, for patients who had a relapse, the end of study is the last value before the missed value.
Clinically important worsening is defined as an increase in EDSS score conditional on the baseline value: if the baseline EDSS is 0 and at least 2 points increase; if the baseline is 1-5, and at least 1 point increase; if the baseline is > 5 and at least 0.5 increase.
(1) Odds ratio statistics are from a logistic regression model adjusted for baseline value with Firth's adjustment; (2) Relative risk statistics are based on a generalized linear model of a binomial distribution with log link; (3) Risk difference statistics are calculated from a generalized linear model, correcting for the baseline value.
(4) P-value is for the interaction term of treatment:subgroup from a logistic regression model with the baseline value, treatment, subgroup, and treatment:subgroup interaction as covariates, with Firth's adjustment.
Odds ratio and relative risk are calculated as Ravulizumab/Eculizumab. Risk difference is calculated as Ravulizumab - Eculizumab.
Source: adsl, adedss

Table EDSS-1.6
Clinically Important Worsening from Baseline in EDSS Score to End of Study Period by Supportive IST use at baseline
Full Analysis Set

IST use at baseline		Statistic	Eculizumab (N=96)	Ravulizumab (N=58)	p-value (4)
No	Clinically Important Worsening in EDSS Score from Baseline to End of Study Period				
		n	21	30	
		No Clinically Important Worsening	20 (95.2)	27 (90.0)	
		Clinically Important Worsening	1 (4.8)	3 (10.0)	
	Treatment Effect (Ravulizumab vs Eculizumab)				
		Odds Ratio (1)		1.810	
		(95% CI)		(0.232, 14.105)	
		p-value		0.5711	
		Relative Risk (2)		2.100	
		(95% CI)		(0.234, 18.828)	
		p-value		0.5073	
		Risk Difference (3)		0.054	
		(95% CI)		(-0.111, 0.220)	
		p-value		0.5142	

The eculizumab group data were collected as part of the PREVENT trial, Study ECU-NMO-301.
End of Study Period is the 6-week assessment after the first On-Trial Relapse for patients who have an On-Trial Relapse or for patients with no On-Trial Relapse: the End of Primary Treatment Period visit for patients in Study ALXN1210-NMO-307 and the End of Study visit for patients in Study ECU-NMO-301.
For those patients who had a missed value at the EOPT Visit or the 6-week post-relapse visit, for patients who had a relapse, the end of study is the last value before the missed value.
Clinically important worsening is defined as an increase in EDSS score conditional on the baseline value: if the baseline EDSS is 0 and at least 2 points increase; if the baseline is 1-5, and at least 1 point increase; if the baseline is > 5 and at least 0.5 increase.
(1) Odds ratio statistics are from a logistic regression model adjusted for baseline value with Firth's adjustment; (2) Relative risk statistics are based on a generalized linear model of a binomial distribution with log link; (3) Risk difference statistics are calculated from a generalized linear model, correcting for the baseline value.
(4) P-value is for the interaction term of treatment:subgroup from a logistic regression model with the baseline value, treatment, subgroup, and treatment:subgroup interaction as covariates, with Firth's adjustment.
Odds ratio and relative risk are calculated as Ravulizumab/Eculizumab. Risk difference is calculated as Ravulizumab - Eculizumab.
Source: adsl, adedss

Table EDSS-1.7
Clinically Important Worsening from Baseline in EDSS Score to End of Study Period by Rituximab use in the prior year
Full Analysis Set

Rituximab use in the prior year		Statistic	Eculizumab (N=96)	Ravulizumab (N=58)	p-value (4)
Yes	Clinically Important Worsening in EDSS Score from Baseline to End of Study Period				0.2775
		n	19	20	
		No Clinically Important Worsening	16 (84.2)	19 (95.0)	
		Clinically Important Worsening	3 (15.8)	1 (5.0)	
	Treatment Effect (Ravulizumab vs Eculizumab)				
		Odds Ratio (1)		0.135	
		(95% CI)		(0.011, 1.721)	
		p-value		0.1230	
		Relative Risk (2)		0.317	
		(95% CI)		(0.036, 2.785)	
		p-value		0.3000	
		Risk Difference (3)		-0.167	
		(95% CI)		(-0.358, 0.025)	
		p-value		0.0864	

The eculizumab group data were collected as part of the PREVENT trial, Study ECU-NMO-301.
End of Study Period is the 6-week assessment after the first On-Trial Relapse for patients who have an On-Trial Relapse or for patients with no On-Trial Relapse: the End of Primary Treatment Period visit for patients in Study ALXN1210-NMO-307 and the End of Study visit for patients in Study ECU-NMO-301.
For those patients who had a missed value at the EOPT Visit or the 6-week post-relapse visit, for patients who had a relapse, the end of study is the last value before the missed value.
Clinically important worsening is defined as an increase in EDSS score conditional on the baseline value: if the baseline EDSS is 0 and at least 2 points increase; if the baseline is 1-5, and at least 1 point increase; if the baseline is > 5 and at least 0.5 increase.
(1) Odds ratio statistics are from a logistic regression model adjusted for baseline value with Firth's adjustment; (2) Relative risk statistics are based on a generalized linear model of a binomial distribution with log link; (3) Risk difference statistics are calculated from a generalized linear model, correcting for the baseline value.
(4) P-value is for the interaction term of treatment:subgroup from a logistic regression model with the baseline value, treatment, subgroup, and treatment:subgroup interaction as covariates, with Firth's adjustment.
Odds ratio and relative risk are calculated as Ravulizumab/Eculizumab. Risk difference is calculated as Ravulizumab - Eculizumab.
Source: adsl, adedss

Table EDSS-1.7
Clinically Important Worsening from Baseline in EDSS Score to End of Study Period by Rituximab use in the prior year
Full Analysis Set

Rituximab use in the prior year		Statistic	Eculizumab (N=96)	Ravulizumab (N=58)	p-value (4)
No	Clinically Important Worsening in EDSS Score from Baseline to End of Study Period				
		n	77	38	
		No Clinically Important Worsening	69 (89.6)	33 (86.8)	
		Clinically Important Worsening	8 (10.4)	5 (13.2)	
	Treatment Effect (Ravulizumab vs Eculizumab)				
		Odds Ratio (1)		1.325	
		(95% CI)		(0.399, 4.398)	
		p-value		0.6461	
		Relative Risk (2)		1.266	
		(95% CI)		(0.444, 3.610)	
		p-value		0.6585	
		Risk Difference (3)		0.027	
		(95% CI)		(-0.104, 0.158)	
		p-value		0.6869	

The eculizumab group data were collected as part of the PREVENT trial, Study ECU-NMO-301.
End of Study Period is the 6-week assessment after the first On-Trial Relapse for patients who have an On-Trial Relapse or for patients with no On-Trial Relapse: the End of Primary Treatment Period visit for patients in Study ALXN1210-NMO-307 and the End of Study visit for patients in Study ECU-NMO-301.
For those patients who had a missed value at the EOPT Visit or the 6-week post-relapse visit, for patients who had a relapse, the end of study is the last value before the missed value.
Clinically important worsening is defined as an increase in EDSS score conditional on the baseline value: if the baseline EDSS is 0 and at least 2 points increase; if the baseline is 1-5, and at least 1 point increase; if the baseline is > 5 and at least 0.5 increase.
(1) Odds ratio statistics are from a logistic regression model adjusted for baseline value with Firth's adjustment; (2) Relative risk statistics are based on a generalized linear model of a binomial distribution with log link; (3) Risk difference statistics are calculated from a generalized linear model, correcting for the baseline value.
(4) P-value is for the interaction term of treatment:subgroup from a logistic regression model with the baseline value, treatment, subgroup, and treatment:subgroup interaction as covariates, with Firth's adjustment.
Odds ratio and relative risk are calculated as Ravulizumab/Eculizumab. Risk difference is calculated as Ravulizumab - Eculizumab.
Source: adsl, adedss

Table EDSS-1.4
Clinically Important Worsening from Baseline in EDSS Score to End of Study Period by Disease severity via EDSS score at baseline
Full Analysis Set

EDSS score at baseline		Statistic	Eculizumab (N=96)	Ravulizumab (N=58)	p-value (4)
< 5	Clinically Important Worsening in EDSS Score from Baseline to End of Study Period				0.3592
		n	66	49	
		No Clinically Important Worsening	60 (90.9)	43 (87.8)	
		Clinically Important Worsening	6 (9.1)	6 (12.2)	
	Treatment Effect (Ravulizumab vs Eculizumab)				
		Odds Ratio (1)		0.952	
		(95% CI)		(0.274, 3.314)	
		p-value		0.9390	
		Relative Risk (2)		1.347	
		(95% CI)		(0.462, 3.925)	
		p-value		0.5852	
		Risk Difference (3)		0.000	
		(95% CI)		(-0.113, 0.114)	
		p-value		0.9937	

The eculizumab group data were collected as part of the PREVENT trial, Study ECU-NMO-301.
End of Study Period is the 6-week assessment after the first On-Trial Relapse for patients who have an On-Trial Relapse or for patients with no On-Trial Relapse: the End of Primary Treatment Period visit for patients in Study ALXN1210-NMO-307 and the End of Study visit for patients in Study ECU-NMO-301.
For those patients who had a missed value at the EOPT Visit or the 6-week post-relapse visit, for patients who had a relapse, the end of study is the last value before the missed value.
Clinically important worsening is defined as an increase in EDSS score conditional on the baseline value: if the baseline EDSS is 0 and at least 2 points increase; if the baseline is 1-5, and at least 1 point increase; if the baseline is > 5 and at least 0.5 increase.
(1) Odds ratio statistics are from a logistic regression model adjusted for baseline value with Firth's adjustment; (2) Relative risk statistics are based on a generalized linear model of a binomial distribution with log link; (3) Risk difference statistics are calculated from a generalized linear model, correcting for the baseline value.
(4) P-value is for the interaction term of treatment:subgroup from a logistic regression model with the baseline value, treatment, subgroup, and treatment:subgroup interaction as covariates, with Firth's adjustment.
Odds ratio and relative risk are calculated as Ravulizumab/Eculizumab. Risk difference is calculated as Ravulizumab - Eculizumab.
Source: adsl, adedss

Table EDSS-1.4
Clinically Important Worsening from Baseline in EDSS Score to End of Study Period by Disease severity via EDSS score at baseline
Full Analysis Set

EDSS score at baseline		Statistic	Eculizumab (N=96)	Ravulizumab (N=58)	p-value (4)
>= 5	Clinically Important Worsening in EDSS Score from Baseline to End of Study Period				
		n	30	9	
		No Clinically Important Worsening	25 (83.3)	9 (100.0)	
		Clinically Important Worsening	5 (16.7)	0 (0.0)	
	Treatment Effect (Ravulizumab vs Eculizumab)				
		Odds Ratio (1)		0.217	
		(95% CI)		(0.010, 4.772)	
		p-value		0.3325	
		Relative Risk (2)		0.000	
		(95% CI)		--	
		p-value		0.9999	
		Risk Difference (3)		-0.181	
		(95% CI)		(-0.446, 0.084)	
		p-value		0.1743	

The eculizumab group data were collected as part of the PREVENT trial, Study ECU-NMO-301.
End of Study Period is the 6-week assessment after the first On-Trial Relapse for patients who have an On-Trial Relapse or for patients with no On-Trial Relapse: the End of Primary Treatment Period visit for patients in Study ALXN1210-NMO-307 and the End of Study visit for patients in Study ECU-NMO-301.
For those patients who had a missed value at the EOPT Visit or the 6-week post-relapse visit, for patients who had a relapse, the end of study is the last value before the missed value.
Clinically important worsening is defined as an increase in EDSS score conditional on the baseline value: if the baseline EDSS is 0 and at least 2 points increase; if the baseline is 1-5, and at least 1 point increase; if the baseline is > 5 and at least 0.5 increase.
(1) Odds ratio statistics are from a logistic regression model adjusted for baseline value with Firth's adjustment; (2) Relative risk statistics are based on a generalized linear model of a binomial distribution with log link; (3) Risk difference statistics are calculated from a generalized linear model, correcting for the baseline value.
(4) P-value is for the interaction term of treatment:subgroup from a logistic regression model with the baseline value, treatment, subgroup, and treatment:subgroup interaction as covariates, with Firth's adjustment.
Odds ratio and relative risk are calculated as Ravulizumab/Eculizumab. Risk difference is calculated as Ravulizumab - Eculizumab.
Source: adsl, adedss

Table HAI-2.2
Change from Baseline in HAI Score to End of Study Period by Sex
Full Analysis Set

Sex		Statistic	Eculizumab (N=96)	Ravulizumab (N=58)	p-value (7)
Male	Change from Baseline to End of Study Period in HAI Score	n	8	6	0.2508
		Mean (SD)	0.5 (1.51)	-0.2 (0.98)	
		Median	0.5	0.0	
		Q1, Q3	-1.0, 1.5	0.0, 0.0	
		Min, Max	-1, 3	-2, 1	
		Change from baseline			
		LS Means (SEM)	0.412 (0.517)	-0.049 (0.610)	
		95% CI for LS Means (1)	(-0.725, 1.550)	(-1.391, 1.292)	
		Difference in LS Means		-0.462	
		(95% CI) (1)		(-2.345, 1.421)	
		p-value (2)		0.4661	
		Standardized Mean Difference		-0.380	
		(95% CI) (3)		(-1.448, 0.688)	
		Responders (15% [1.35 points]), n(%)	0	1 (16.7)	
		Odds Ratio (4)		17.734	
		(95% CI)		(0.137, 2292.374)	
		p-value		0.2464	
		Relative Risk (5)		--	
		(95% CI)		--	
		p-value		NA	

The eculizumab group data were collected as part of the PREVENT trial, Study ECU-NMO-301.

End of Study Period is the 6-week assessment after the first On-Trial Relapse for patients who have an On-Trial Relapse or for patients with no On-Trial Relapse: the End of Primary Treatment Period visit for patients in Study ALXN1210-NMO-307 and the End of Study visit for patients in Study ECU-NMO-301.

For those patients who had a missed value at the EOPT Visit or the 6-week post-relapse visit, for patients who had a relapse, the end of study is the last value before the missed value.

(1) The LS means (95% CI) and the difference in LS means (95% CI) are from an ANCOVA model of change from baseline with treatment as factor and baseline value as covariate. (2) The p-value represents the significance of the treatment effect and was derived from an ANCOVA model of the ranked change from baseline, with treatment as a factor, and the ranks of the baseline value included as covariate.

(3) Standardized mean differences (95% CI) were computed using Cohen's D incorporating Hedge's correction on change from baseline. (4) Odds ratio statistics are from a logistic regression model adjusted for baseline value with Firth's adjustment; (5) Relative risk statistics are based on a generalized linear model of a binomial distribution with log link;

(6) Risk difference statistics are calculated from a generalized linear model, correcting for the baseline value. (7) P-value is for the interaction term of treatment:subgroup from a linear regression model of ranked change from baseline with the with ranked baseline value, treatment, subgroup, and treatment:subgroup interaction as covariates.

Odds ratio and relative risk are calculated as Ravulizumab/Eculizumab. LS mean difference and risk difference are calculated as Ravulizumab - Eculizumab.

Source: adsl, adeff

Table HAI-2.2
Change from Baseline in HAI Score to End of Study Period by Sex
Full Analysis Set

Sex	Statistic	Eculizumab (N=96)	Ravulizumab (N=58)	p-value (7)
	Risk Difference (6)		0.269	
	(95% CI)		(-0.087, 0.625)	
	p-value		0.1244	
Baseline HAI Score	n	8	6	
	Mean (SD)	2.0 (1.31)	0.7 (1.03)	
	Median	1.5	0.0	
	Q1, Q3	1.0, 3.0	0.0, 2.0	
	Min, Max	1, 4	0, 2	
End of Study Period HAI Score	n	8	6	
	Mean (SD)	2.5 (2.39)	0.5 (0.84)	
	Median	1.5	0.0	
	Q1, Q3	1.0, 4.0	0.0, 1.0	
	Min, Max	0, 7	0, 2	

The eculizumab group data were collected as part of the PREVENT trial, Study ECU-NMO-301.

End of Study Period is the 6-week assessment after the first On-Trial Relapse for patients who have an On-Trial Relapse or for patients with no On-Trial Relapse: the End of Primary Treatment Period visit for patients in Study ALXN1210-NMO-307 and the End of Study visit for patients in Study ECU-NMO-301.

For those patients who had a missed value at the EOPT Visit or the 6-week post-relapse visit, for patients who had a relapse, the end of study is the last value before the missed value.

(1) The LS means (95% CI) and the difference in LS means (95% CI) are from an ANCOVA model of change from baseline with treatment as factor and baseline value as covariate. (2) The p-value represents the significance of the treatment effect and was derived from an ANCOVA model of the ranked change from baseline, with treatment as a factor, and the ranks of the baseline value included as covariate.

(3) Standardized mean differences (95% CI) were computed using Cohen's D incorporating Hedge's correction on change from baseline. (4) Odds ratio statistics are from a logistic regression model adjusted for baseline value with Firth's adjustment; (5) Relative risk statistics are based on a generalized linear model of a binomial distribution with log link;

(6) Risk difference statistics are calculated from a generalized linear model, correcting for the baseline value. (7) P-value is for the interaction term of treatment:subgroup from a linear regression model of ranked change from baseline with the with ranked baseline value, treatment, subgroup, and treatment:subgroup interaction as covariates.

Odds ratio and relative risk are calculated as Ravulizumab/Eculizumab. LS mean difference and risk difference are calculated as Ravulizumab - Eculizumab.

Source: adsl, adeff

Table HAI-2.2
Change from Baseline in HAI Score to End of Study Period by Sex
Full Analysis Set

Sex		Statistic	Eculizumab (N=96)	Ravulizumab (N=58)	p-value (7)
Female	Change from Baseline to End of Study Period in HAI Score	n	88	52	
		Mean (SD)	-0.5 (1.01)	-0.1 (0.60)	
		Median	0.0	0.0	
		Q1, Q3	-1.0, 0.0	0.0, 0.0	
		Min, Max	-5, 2	-1, 2	
		Change from baseline			
		LS Means (SEM)	-0.440 (0.094)	-0.179 (0.124)	
		95% CI for LS Means (1)	(-0.627, -0.253)	(-0.424, 0.067)	
		Difference in LS Means		0.261	
		(95% CI) (1)		(-0.053, 0.575)	
		p-value (2)		0.2301	
		Standardized Mean Difference		0.277	
		(95% CI) (3)		(-0.067, 0.621)	
		Responders (15% [1.35 points]), n(%)	6 (6.8)	0	
		Odds Ratio (4)		0.180	
		(95% CI)		(0.010, 3.355)	
		p-value		0.2508	
		Relative Risk (5)		0.000	
		(95% CI)		--	
		p-value		0.9999	

The eculizumab group data were collected as part of the PREVENT trial, Study ECU-NMO-301.

End of Study Period is the 6-week assessment after the first On-Trial Relapse for patients who have an On-Trial Relapse or for patients with no On-Trial Relapse: the End of Primary Treatment Period visit for patients in Study ALXN1210-NMO-307 and the End of Study visit for patients in Study ECU-NMO-301.

For those patients who had a missed value at the EOPT Visit or the 6-week post-relapse visit, for patients who had a relapse, the end of study is the last value before the missed value.

(1) The LS means (95% CI) and the difference in LS means (95% CI) are from an ANCOVA model of change from baseline with treatment as factor and baseline value as covariate. (2) The p-value represents the significance of the treatment effect and was derived from an ANCOVA model of the ranked change from baseline, with treatment as a factor, and the ranks of the baseline value included as covariate.

(3) Standardized mean differences (95% CI) were computed using Cohen's D incorporating Hedge's correction on change from baseline. (4) Odds ratio statistics are from a logistic regression model adjusted for baseline value with Firth's adjustment; (5) Relative risk statistics are based on a generalized linear model of a binomial distribution with log link;

(6) Risk difference statistics are calculated from a generalized linear model, correcting for the baseline value. (7) P-value is for the interaction term of treatment:subgroup from a linear regression model of ranked change from baseline with the with ranked baseline value, treatment, subgroup, and treatment:subgroup interaction as covariates.

Odds ratio and relative risk are calculated as Ravulizumab/Eculizumab. LS mean difference and risk difference are calculated as Ravulizumab - Eculizumab.

Source: adsl, adeff

Table HAI-2.2
Change from Baseline in HAI Score to End of Study Period by Sex
Full Analysis Set

Sex	Statistic	Eculizumab (N=96)	Ravulizumab (N=58)	p-value (7)
	Risk Difference (6)		-0.047	
	(95% CI)		(-0.119, 0.025)	
	p-value		0.1964	
Baseline HAI Score	n	88	52	
	Mean (SD)	2.4 (2.23)	1.2 (1.46)	
	Median	2.0	1.0	
	Q1, Q3	1.0, 3.0	0.0, 2.0	
	Min, Max	0, 8	0, 7	
End of Study Period HAI Score	n	88	52	
	Mean (SD)	1.9 (2.28)	1.1 (1.62)	
	Median	1.0	0.0	
	Q1, Q3	0.0, 3.0	0.0, 1.5	
	Min, Max	0, 9	0, 7	

The eculizumab group data were collected as part of the PREVENT trial, Study ECU-NMO-301.

End of Study Period is the 6-week assessment after the first On-Trial Relapse for patients who have an On-Trial Relapse or for patients with no On-Trial Relapse: the End of Primary Treatment Period visit for patients in Study ALXN1210-NMO-307 and the End of Study visit for patients in Study ECU-NMO-301.

For those patients who had a missed value at the EOPT Visit or the 6-week post-relapse visit, for patients who had a relapse, the end of study is the last value before the missed value.

(1) The LS means (95% CI) and the difference in LS means (95% CI) are from an ANCOVA model of change from baseline with treatment as factor and baseline value as covariate. (2) The p-value represents the significance of the treatment effect and was derived from an ANCOVA model of the ranked change from baseline, with treatment as a factor, and the ranks of the baseline value included as covariate.

(3) Standardized mean differences (95% CI) were computed using Cohen's D incorporating Hedge's correction on change from baseline. (4) Odds ratio statistics are from a logistic regression model adjusted for baseline value with Firth's adjustment; (5) Relative risk statistics are based on a generalized linear model of a binomial distribution with log link;

(6) Risk difference statistics are calculated from a generalized linear model, correcting for the baseline value. (7) P-value is for the interaction term of treatment:subgroup from a linear regression model of ranked change from baseline with the with ranked baseline value, treatment, subgroup, and treatment:subgroup interaction as covariates.

Odds ratio and relative risk are calculated as Ravulizumab/Eculizumab. LS mean difference and risk difference are calculated as Ravulizumab - Eculizumab.

Source: adsl, adeff

Table HAI-2.3
Change from Baseline in HAI Score to End of Study Period by Age Group
Full Analysis Set

Age Group		Statistic	Eculizumab (N=96)	Ravulizumab (N=58)	p-value (7)
< 45 years	Change from Baseline to End of Study Period in HAI Score	n	47	25	0.9435
		Mean (SD)	-0.4 (0.92)	-0.2 (0.58)	
		Median	0.0	0.0	
		Q1, Q3	-1.0, 0.0	-1.0, 0.0	
		Min, Max	-5, 1	-1, 1	
		Change from baseline			
		LS Means (SEM)	-0.363 (0.117)	-0.237 (0.161)	
		95% CI for LS Means (1)	(-0.597, -0.130)	(-0.559, 0.084)	
		Difference in LS Means		0.126	
		(95% CI) (1)		(-0.273, 0.524)	
		p-value (2)		0.7122	
		Standardized Mean Difference		0.140	
		(95% CI) (3)		(-0.345, 0.626)	
		Responders (15% [1.35 points]), n(%)	1 (2.1)	0	
		Odds Ratio (4)		0.758	
		(95% CI)		(0.025, 23.431)	
		p-value		0.8743	
		Relative Risk (5)		0.000	
		(95% CI)		--	
		p-value		1.0000	

The eculizumab group data were collected as part of the PREVENT trial, Study ECU-NMO-301.

End of Study Period is the 6-week assessment after the first On-Trial Relapse for patients who have an On-Trial Relapse or for patients with no On-Trial Relapse: the End of Primary Treatment Period visit for patients in Study ALXN1210-NMO-307 and the End of Study visit for patients in Study ECU-NMO-301.

For those patients who had a missed value at the EOPT Visit or the 6-week post-relapse visit, for patients who had a relapse, the end of study is the last value before the missed value.

(1) The LS means (95% CI) and the difference in LS means (95% CI) are from an ANCOVA model of change from baseline with treatment as factor and baseline value as covariate. (2) The p-value represents the significance of the treatment effect and was derived from an ANCOVA model of the ranked change from baseline, with treatment as a factor, and the ranks of the baseline value included as covariate.

(3) Standardized mean differences (95% CI) were computed using Cohen's D incorporating Hedge's correction on change from baseline. (4) Odds ratio statistics are from a logistic regression model adjusted for baseline value with Firth's adjustment; (5) Relative risk statistics are based on a generalized linear model of a binomial distribution with log link;

(6) Risk difference statistics are calculated from a generalized linear model, correcting for the baseline value. (7) P-value is for the interaction term of treatment:subgroup from a linear regression model of ranked change from baseline with the with ranked baseline value, treatment, subgroup, and treatment:subgroup interaction as covariates.

Odds ratio and relative risk are calculated as Ravulizumab/Eculizumab. LS mean difference and risk difference are calculated as Ravulizumab - Eculizumab.

Source: adsl, adeff

Table HAI-2.3
Change from Baseline in HAI Score to End of Study Period by Age Group
Full Analysis Set

Age Group	Statistic	Eculizumab (N=96)	Ravulizumab (N=58)	p-value (7)
	Risk Difference (6)		-0.010	
	(95% CI)		(-0.066, 0.046)	
	p-value		0.7215	
Baseline HAI Score	n	47	25	
	Mean (SD)	1.4 (1.29)	1.0 (1.29)	
	Median	1.0	1.0	
	Q1, Q3	1.0, 2.0	0.0, 1.0	
	Min, Max	0, 6	0, 5	
End of Study Period HAI Score	n	47	25	
	Mean (SD)	1.0 (1.33)	0.8 (1.38)	
	Median	1.0	0.0	
	Q1, Q3	0.0, 1.0	0.0, 1.0	
	Min, Max	0, 6	0, 5	

The eculizumab group data were collected as part of the PREVENT trial, Study ECU-NMO-301.

End of Study Period is the 6-week assessment after the first On-Trial Relapse for patients who have an On-Trial Relapse or for patients with no On-Trial Relapse: the End of Primary Treatment Period visit for patients in Study ALXN1210-NMO-307 and the End of Study visit for patients in Study ECU-NMO-301.

For those patients who had a missed value at the EOPT Visit or the 6-week post-relapse visit, for patients who had a relapse, the end of study is the last value before the missed value.

(1) The LS means (95% CI) and the difference in LS means (95% CI) are from an ANCOVA model of change from baseline with treatment as factor and baseline value as covariate. (2) The p-value represents the significance of the treatment effect and was derived from an ANCOVA model of the ranked change from baseline, with treatment as a factor, and the ranks of the baseline value included as covariate.

(3) Standardized mean differences (95% CI) were computed using Cohen's D incorporating Hedge's correction on change from baseline. (4) Odds ratio statistics are from a logistic regression model adjusted for baseline value with Firth's adjustment; (5) Relative risk statistics are based on a generalized linear model of a binomial distribution with log link;

(6) Risk difference statistics are calculated from a generalized linear model, correcting for the baseline value. (7) P-value is for the interaction term of treatment:subgroup from a linear regression model of ranked change from baseline with the with ranked baseline value, treatment, subgroup, and treatment:subgroup interaction as covariates.

Odds ratio and relative risk are calculated as Ravulizumab/Eculizumab. LS mean difference and risk difference are calculated as Ravulizumab - Eculizumab.

Source: adsl, adeff

Table HAI-2.3
Change from Baseline in HAI Score to End of Study Period by Age Group
Full Analysis Set

Age Group		Statistic	Eculizumab (N=96)	Ravulizumab (N=58)	p-value (7)
>= 45 years	Change from Baseline to End of Study Period in HAI Score	n	49	33	
		Mean (SD)	-0.4 (1.22)	-0.1 (0.68)	
		Median	0.0	0.0	
		Q1, Q3	-1.0, 0.0	0.0, 0.0	
		Min, Max	-5, 3	-2, 2	
		Change from baseline			
		LS Means (SEM)	-0.355 (0.156)	-0.139 (0.194)	
		95% CI for LS Means (1)	(-0.666, -0.045)	(-0.526, 0.247)	
		Difference in LS Means		0.216	
		(95% CI) (1)		(-0.305, 0.737)	
		p-value (2)		0.4799	
		Standardized Mean Difference		0.206	
		(95% CI) (3)		(-0.236, 0.649)	
		Responders (15% [1.35 points]), n(%)	5 (10.2)	1 (3.0)	
		Odds Ratio (4)		0.461	
		(95% CI)		(0.062, 3.439)	
		p-value		0.4502	
		Relative Risk (5)		0.297	
		(95% CI)		(0.036, 2.428)	
		p-value		0.2574	

The eculizumab group data were collected as part of the PREVENT trial, Study ECU-NMO-301.

End of Study Period is the 6-week assessment after the first On-Trial Relapse for patients who have an On-Trial Relapse or for patients with no On-Trial Relapse: the End of Primary Treatment Period visit for patients in Study ALXN1210-NMO-307 and the End of Study visit for patients in Study ECU-NMO-301.

For those patients who had a missed value at the EOPT Visit or the 6-week post-relapse visit, for patients who had a relapse, the end of study is the last value before the missed value.

(1) The LS means (95% CI) and the difference in LS means (95% CI) are from an ANCOVA model of change from baseline with treatment as factor and baseline value as covariate. (2) The p-value represents the significance of the treatment effect and was derived from an ANCOVA model of the ranked change from baseline, with treatment as a factor, and the ranks of the baseline value included as covariate.

(3) Standardized mean differences (95% CI) were computed using Cohen's D incorporating Hedge's correction on change from baseline. (4) Odds ratio statistics are from a logistic regression model adjusted for baseline value with Firth's adjustment; (5) Relative risk statistics are based on a generalized linear model of a binomial distribution with log link;

(6) Risk difference statistics are calculated from a generalized linear model, correcting for the baseline value. (7) P-value is for the interaction term of treatment:subgroup from a linear regression model of ranked change from baseline with the with ranked baseline value, treatment, subgroup, and treatment:subgroup interaction as covariates.

Odds ratio and relative risk are calculated as Ravulizumab/Eculizumab. LS mean difference and risk difference are calculated as Ravulizumab - Eculizumab.

Source: adsl, adeff

Table HAI-2.3
Change from Baseline in HAI Score to End of Study Period by Age Group
Full Analysis Set

Age Group	Statistic	Eculizumab (N=96)	Ravulizumab (N=58)	p-value (7)
	Risk Difference (6)		-0.054	
	(95% CI)		(-0.185, 0.077)	
	p-value		0.4147	
Baseline HAI Score	n	49	33	
	Mean (SD)	3.3 (2.39)	1.3 (1.53)	
	Median	3.0	1.0	
	Q1, Q3	1.0, 5.0	0.0, 2.0	
	Min, Max	0, 8	0, 7	
End of Study Period HAI Score	n	49	33	
	Mean (SD)	3.0 (2.57)	1.2 (1.69)	
	Median	2.0	1.0	
	Q1, Q3	1.0, 5.0	0.0, 2.0	
	Min, Max	0, 9	0, 7	

The eculizumab group data were collected as part of the PREVENT trial, Study ECU-NMO-301.

End of Study Period is the 6-week assessment after the first On-Trial Relapse for patients who have an On-Trial Relapse or for patients with no On-Trial Relapse: the End of Primary Treatment Period visit for patients in Study ALXN1210-NMO-307 and the End of Study visit for patients in Study ECU-NMO-301.

For those patients who had a missed value at the EOPT Visit or the 6-week post-relapse visit, for patients who had a relapse, the end of study is the last value before the missed value.

(1) The LS means (95% CI) and the difference in LS means (95% CI) are from an ANCOVA model of change from baseline with treatment as factor and baseline value as covariate. (2) The p-value represents the significance of the treatment effect and was derived from an ANCOVA model of the ranked change from baseline, with treatment as a factor, and the ranks of the baseline value included as covariate.

(3) Standardized mean differences (95% CI) were computed using Cohen's D incorporating Hedge's correction on change from baseline. (4) Odds ratio statistics are from a logistic regression model adjusted for baseline value with Firth's adjustment; (5) Relative risk statistics are based on a generalized linear model of a binomial distribution with log link;

(6) Risk difference statistics are calculated from a generalized linear model, correcting for the baseline value. (7) P-value is for the interaction term of treatment:subgroup from a linear regression model of ranked change from baseline with the with ranked baseline value, treatment, subgroup, and treatment:subgroup interaction as covariates.

Odds ratio and relative risk are calculated as Ravulizumab/Eculizumab. LS mean difference and risk difference are calculated as Ravulizumab - Eculizumab.

Source: adsl, adeff

Table HAI-2.5
Change from Baseline in HAI Score to End of Study Period by Region
Full Analysis Set

Region		Statistic	Eculizumab (N=96)	Ravulizumab (N=58)	p-value (7)
Asia-Pacific	Change from Baseline to End of Study Period in HAI Score	n	35	20	0.6972
		Mean (SD)	-0.3 (0.96)	0.0 (0.46)	
		Median	0.0	0.0	
		Q1, Q3	-1.0, 0.0	0.0, 0.0	
		Min, Max	-2, 3	-1, 1	
		Change from baseline			
		LS Means (SEM)	-0.298 (0.144)	-0.029 (0.195)	
		95% CI for LS Means (1)	(-0.587, -0.009)	(-0.420, 0.362)	
		Difference in LS Means		0.268	
		(95% CI) (1)		(-0.236, 0.773)	
		p-value (2)		0.3371	
		Standardized Mean Difference		0.290	
		(95% CI) (3)		(-0.262, 0.842)	
		Responders (15% [1.35 points]), n(%)	2 (5.7)	0	
		Odds Ratio (4)		0.553	
		(95% CI)		(0.020, 15.549)	
		p-value		0.7280	
		Relative Risk (5)		0.000	
		(95% CI)		--	
		p-value		0.9999	

The eculizumab group data were collected as part of the PREVENT trial, Study ECU-NMO-301.
End of Study Period is the 6-week assessment after the first On-Trial Relapse for patients who have an On-Trial Relapse or for patients with no On-Trial Relapse: the End of Primary Treatment Period visit for patients in Study ALXN1210-NMO-307 and the End of Study visit for patients in Study ECU-NMO-301.
For those patients who had a missed value at the EOPT Visit or the 6-week post-relapse visit, for patients who had a relapse, the end of study is the last value before the missed value.
(1) The LS means (95% CI) and the difference in LS means (95% CI) are from an ANCOVA model of change from baseline with treatment as factor and baseline value as covariate. (2) The p-value represents the significance of the treatment effect and was derived from an ANCOVA model of the ranked change from baseline, with treatment as a factor, and the ranks of the baseline value included as covariate.
(3) Standardized mean differences (95% CI) were computed using Cohen's D incorporating Hedge's correction on change from baseline. (4) Odds ratio statistics are from a logistic regression model adjusted for baseline value with Firth's adjustment; (5) Relative risk statistics are based on a generalized linear model of a binomial distribution with log link;
(6) Risk difference statistics are calculated from a generalized linear model, correcting for the baseline value. (7) P-value is for the interaction term of treatment:subgroup from a linear regression model of ranked change from baseline with the with ranked baseline value, treatment, subgroup, and treatment:subgroup interaction as covariates.
For eculizumab arm, Americas: ARG and USA; Europe: CZE, DEU, DNK, ESP, HRV, ITA, RUS and TUR; Asia-Pacific: AUS, HKG, JPN, KOR, MYS, THA and TWN. For ravulizumab arm, Americas: CAN and USA; Europe: DEU, DNK, ESP, GBR, ITA and POL; Asia-Pacific: AUS, JPN and KOR.
Odds ratio and relative risk are calculated as Ravulizumab/Eculizumab. LS mean difference and risk difference are calculated as Ravulizumab - Eculizumab.
Source: adsl, adeff

Table HAI-2.5
Change from Baseline in HAI Score to End of Study Period by Region
Full Analysis Set

Region	Statistic	Eculizumab (N=96)	Ravulizumab (N=58)	p-value (7)
	Risk Difference (6)		-0.026	
	(95% CI)		(-0.141, 0.088)	
	p-value		0.6471	
Baseline HAI Score	n	35	20	
	Mean (SD)	2.3 (2.17)	0.7 (1.04)	
	Median	1.0	0.0	
	Q1, Q3	1.0, 3.0	0.0, 1.0	
	Min, Max	0, 8	0, 4	
End of Study Period HAI Score	n	35	20	
	Mean (SD)	1.9 (2.35)	0.7 (0.99)	
	Median	1.0	0.0	
	Q1, Q3	0.0, 2.0	0.0, 1.0	
	Min, Max	0, 8	0, 4	

The eculizumab group data were collected as part of the PREVENT trial, Study ECU-NMO-301.

End of Study Period is the 6-week assessment after the first On-Trial Relapse for patients who have an On-Trial Relapse or for patients with no On-Trial Relapse: the End of Primary Treatment Period visit for patients in Study ALXN1210-NMO-307 and the End of Study visit for patients in Study ECU-NMO-301.

For those patients who had a missed value at the EOPT Visit or the 6-week post-relapse visit, for patients who had a relapse, the end of study is the last value before the missed value.

(1) The LS means (95% CI) and the difference in LS means (95% CI) are from an ANCOVA model of change from baseline with treatment as factor and baseline value as covariate. (2) The p-value represents the significance of the treatment effect and was derived from an ANCOVA model of the ranked change from baseline, with treatment as a factor, and the ranks of the baseline value included as covariate.

(3) Standardized mean differences (95% CI) were computed using Cohen's D incorporating Hedge's correction on change from baseline. (4) Odds ratio statistics are from a logistic regression model adjusted for baseline value with Firth's adjustment; (5) Relative risk statistics are based on a generalized linear model of a binomial distribution with log link;

(6) Risk difference statistics are calculated from a generalized linear model, correcting for the baseline value. (7) P-value is for the interaction term of treatment:subgroup from a linear regression model of ranked change from baseline with the with ranked baseline value, treatment, subgroup, and treatment:subgroup interaction as covariates.

For eculizumab arm, Americas: ARG and USA; Europe: CZE, DEU, DNK, ESP, HRV, ITA, RUS and TUR; Asia-Pacific: AUS, HKG, JPN, KOR, MYS, THA and TWN. For ravulizumab arm, Americas: CAN and USA; Europe: DEU, DNK, ESP, GBR, ITA and POL; Asia-Pacific: AUS, JPN and KOR.

Odds ratio and relative risk are calculated as Ravulizumab/Eculizumab. LS mean difference and risk difference are calculated as Ravulizumab - Eculizumab.

Source: adsl, adeff

Table HAI-2.5
Change from Baseline in HAI Score to End of Study Period by Region
Full Analysis Set

Region		Statistic	Eculizumab (N=96)	Ravulizumab (N=58)	p-value (7)
Americas	Change from Baseline to End of Study Period in HAI Score	n	29	21	0.0178
		Mean (SD)	-0.5 (1.55)	-0.5 (0.60)	
		Median	0.0	0.0	
		Q1, Q3	-1.0, 0.0	-1.0, 0.0	
		Min, Max	-5, 2	-2, 0	
		Change from baseline			
		LS Means (SEM)	-0.334 (0.218)	-0.730 (0.260)	
		95% CI for LS Means (1)	(-0.773, 0.106)	(-1.253, -0.207)	
		Difference in LS Means		-0.396	
		(95% CI) (1)		(-1.104, 0.313)	
		p-value (2)		0.1086	
		Standardized Mean Difference		-0.364	
		(95% CI) (3)		(-0.930, 0.202)	
		Responders (15% [1.35 points]), n(%)	3 (10.3)	1 (4.8)	
		Odds Ratio (4)		1.839	
		(95% CI)		(0.144, 23.496)	
		p-value		0.6391	
		Relative Risk (5)		0.460	
		(95% CI)		(0.051, 4.123)	
		p-value		0.4879	

The eculizumab group data were collected as part of the PREVENT trial, Study ECU-NMO-301.

End of Study Period is the 6-week assessment after the first On-Trial Relapse for patients who have an On-Trial Relapse or for patients with no On-Trial Relapse: the End of Primary Treatment Period visit for patients in Study ALXN1210-NMO-307 and the End of Study visit for patients in Study ECU-NMO-301.

For those patients who had a missed value at the EOPT Visit or the 6-week post-relapse visit, for patients who had a relapse, the end of study is the last value before the missed value.

(1) The LS means (95% CI) and the difference in LS means (95% CI) are from an ANCOVA model of change from baseline with treatment as factor and baseline value as covariate. (2) The p-value represents the significance of the treatment effect and was derived from an ANCOVA model of the ranked change from baseline, with treatment as a factor, and the ranks of the baseline value included as covariate.

(3) Standardized mean differences (95% CI) were computed using Cohen's D incorporating Hedge's correction on change from baseline. (4) Odds ratio statistics are from a logistic regression model adjusted for baseline value with Firth's adjustment; (5) Relative risk statistics are based on a generalized linear model of a binomial distribution with log link;

(6) Risk difference statistics are calculated from a generalized linear model, correcting for the baseline value. (7) P-value is for the interaction term of treatment:subgroup from a linear regression model of ranked change from baseline with the with ranked baseline value, treatment, subgroup, and treatment:subgroup interaction as covariates.

For eculizumab arm, Americas: ARG and USA; Europe: CZE, DEU, DNK, ESP, HRV, ITA, RUS and TUR; Asia-Pacific: AUS, HKG, JPN, KOR, MYS, THA and TWN. For ravulizumab arm, Americas: CAN and USA; Europe: DEU, DNK, ESP, GBR, ITA and POL; Asia-Pacific: AUS, JPN and KOR.

Odds ratio and relative risk are calculated as Ravulizumab/Eculizumab. LS mean difference and risk difference are calculated as Ravulizumab - Eculizumab.

Source: adsl, adeff

Table HAI-2.5
Change from Baseline in HAI Score to End of Study Period by Region
Full Analysis Set

Region	Statistic	Eculizumab (N=96)	Ravulizumab (N=58)	p-value (7)
	Risk Difference (6)		0.028	
	(95% CI)		(-0.133, 0.189)	
	p-value		0.7257	
Baseline HAI Score	n	29	21	
	Mean (SD)	2.4 (1.86)	1.1 (1.04)	
	Median	2.0	1.0	
	Q1, Q3	1.0, 4.0	0.0, 2.0	
	Min, Max	0, 6	0, 3	
End of Study Period HAI Score	n	29	21	
	Mean (SD)	1.9 (1.77)	0.6 (1.12)	
	Median	1.0	0.0	
	Q1, Q3	1.0, 3.0	0.0, 1.0	
	Min, Max	0, 6	0, 3	

The eculizumab group data were collected as part of the PREVENT trial, Study ECU-NMO-301.

End of Study Period is the 6-week assessment after the first On-Trial Relapse for patients who have an On-Trial Relapse or for patients with no On-Trial Relapse: the End of Primary Treatment Period visit for patients in Study ALXN1210-NMO-307 and the End of Study visit for patients in Study ECU-NMO-301.

For those patients who had a missed value at the EOPT Visit or the 6-week post-relapse visit, for patients who had a relapse, the end of study is the last value before the missed value.

(1) The LS means (95% CI) and the difference in LS means (95% CI) are from an ANCOVA model of change from baseline with treatment as factor and baseline value as covariate. (2) The p-value represents the significance of the treatment effect and was derived from an ANCOVA model of the ranked change from baseline, with treatment as a factor, and the ranks of the baseline value included as covariate.

(3) Standardized mean differences (95% CI) were computed using Cohen's D incorporating Hedge's correction on change from baseline. (4) Odds ratio statistics are from a logistic regression model adjusted for baseline value with Firth's adjustment; (5) Relative risk statistics are based on a generalized linear model of a binomial distribution with log link;

(6) Risk difference statistics are calculated from a generalized linear model, correcting for the baseline value. (7) P-value is for the interaction term of treatment:subgroup from a linear regression model of ranked change from baseline with the with ranked baseline value, treatment, subgroup, and treatment:subgroup interaction as covariates.

For eculizumab arm, Americas: ARG and USA; Europe: CZE, DEU, DNK, ESP, HRV, ITA, RUS and TUR; Asia-Pacific: AUS, HKG, JPN, KOR, MYS, THA and TWN. For ravulizumab arm, Americas: CAN and USA; Europe: DEU, DNK, ESP, GBR, ITA and POL; Asia-Pacific: AUS, JPN and KOR.

Odds ratio and relative risk are calculated as Ravulizumab/Eculizumab. LS mean difference and risk difference are calculated as Ravulizumab - Eculizumab.

Source: adsl, adeff

Table HAI-2.5
Change from Baseline in HAI Score to End of Study Period by Region
Full Analysis Set

Region		Statistic	Eculizumab (N=96)	Ravulizumab (N=58)	p-value (7)
Europe	Change from Baseline to End of Study Period in HAI Score	n	32	17	
		Mean (SD)	-0.3 (0.60)	0.1 (0.70)	
		Median	0.0	0.0	
		Q1, Q3	-1.0, 0.0	0.0, 0.0	
		Min, Max	-2, 1	-1, 2	
		Change from baseline			
		LS Means (SEM)	-0.355 (0.112)	0.139 (0.154)	
		95% CI for LS Means (1)	(-0.581, -0.129)	(-0.172, 0.450)	
		Difference in LS Means		0.494	
		(95% CI) (1)		(0.108, 0.880)	
		p-value (2)		0.0313	
		Standardized Mean Difference		0.619	
		(95% CI) (3)		(0.018, 1.220)	
		Responders (15% [1.35 points]), n(%)	1 (3.1)	0	
		Odds Ratio (4)		0.576	
		(95% CI)		(0.025, 13.173)	
		p-value		0.7300	
		Relative Risk (5)		0.000	
		(95% CI)		--	
		p-value		0.9999	

The eculizumab group data were collected as part of the PREVENT trial, Study ECU-NMO-301.
End of Study Period is the 6-week assessment after the first On-Trial Relapse for patients who have an On-Trial Relapse or for patients with no On-Trial Relapse: the End of Primary Treatment Period visit for patients in Study ALXN1210-NMO-307 and the End of Study visit for patients in Study ECU-NMO-301.
For those patients who had a missed value at the EOPT Visit or the 6-week post-relapse visit, for patients who had a relapse, the end of study is the last value before the missed value.
(1) The LS means (95% CI) and the difference in LS means (95% CI) are from an ANCOVA model of change from baseline with treatment as factor and baseline value as covariate. (2) The p-value represents the significance of the treatment effect and was derived from an ANCOVA model of the ranked change from baseline, with treatment as a factor, and the ranks of the baseline value included as covariate.
(3) Standardized mean differences (95% CI) were computed using Cohen's D incorporating Hedge's correction on change from baseline. (4) Odds ratio statistics are from a logistic regression model adjusted for baseline value with Firth's adjustment; (5) Relative risk statistics are based on a generalized linear model of a binomial distribution with log link;
(6) Risk difference statistics are calculated from a generalized linear model, correcting for the baseline value. (7) P-value is for the interaction term of treatment:subgroup from a linear regression model of ranked change from baseline with the with ranked baseline value, treatment, subgroup, and treatment:subgroup interaction as covariates.
For eculizumab arm, Americas: ARG and USA; Europe: CZE, DEU, DNK, ESP, HRV, ITA, RUS and TUR; Asia-Pacific: AUS, HKG, JPN, KOR, MYS, THA and TWN. For ravulizumab arm, Americas: CAN and USA; Europe: DEU, DNK, ESP, GBR, ITA and POL; Asia-Pacific: AUS, JPN and KOR.
Odds ratio and relative risk are calculated as Ravulizumab/Eculizumab. LS mean difference and risk difference are calculated as Ravulizumab - Eculizumab.
Source: adsl, adeff

Table HAI-2.5
Change from Baseline in HAI Score to End of Study Period by Region
Full Analysis Set

Region	Statistic	Eculizumab (N=96)	Ravulizumab (N=58)	p-value (7)
	Risk Difference (6)		-0.033	
	(95% CI)		(-0.121, 0.056)	
	p-value		0.4621	
Baseline HAI Score	n	32	17	
	Mean (SD)	2.5 (2.46)	1.8 (1.94)	
	Median	1.5	2.0	
	Q1, Q3	1.0, 3.0	0.0, 2.0	
	Min, Max	0, 8	0, 7	
End of Study Period HAI Score	n	32	17	
	Mean (SD)	2.2 (2.64)	1.9 (2.16)	
	Median	1.0	1.0	
	Q1, Q3	0.0, 2.5	0.0, 2.0	
	Min, Max	0, 9	0, 7	

The eculizumab group data were collected as part of the PREVENT trial, Study ECU-NMO-301.

End of Study Period is the 6-week assessment after the first On-Trial Relapse for patients who have an On-Trial Relapse or for patients with no On-Trial Relapse: the End of Primary Treatment Period visit for patients in Study ALXN1210-NMO-307 and the End of Study visit for patients in Study ECU-NMO-301.

For those patients who had a missed value at the EOPT Visit or the 6-week post-relapse visit, for patients who had a relapse, the end of study is the last value before the missed value.

(1) The LS means (95% CI) and the difference in LS means (95% CI) are from an ANCOVA model of change from baseline with treatment as factor and baseline value as covariate. (2) The p-value represents the significance of the treatment effect and was derived from an ANCOVA model of the ranked change from baseline, with treatment as a factor, and the ranks of the baseline value included as covariate.

(3) Standardized mean differences (95% CI) were computed using Cohen's D incorporating Hedge's correction on change from baseline. (4) Odds ratio statistics are from a logistic regression model adjusted for baseline value with Firth's adjustment; (5) Relative risk statistics are based on a generalized linear model of a binomial distribution with log link;

(6) Risk difference statistics are calculated from a generalized linear model, correcting for the baseline value. (7) P-value is for the interaction term of treatment:subgroup from a linear regression model of ranked change from baseline with the with ranked baseline value, treatment, subgroup, and treatment:subgroup interaction as covariates.

For eculizumab arm, Americas: ARG and USA; Europe: CZE, DEU, DNK, ESP, HRV, ITA, RUS and TUR; Asia-Pacific: AUS, HKG, JPN, KOR, MYS, THA and TWN. For ravulizumab arm, Americas: CAN and USA; Europe: DEU, DNK, ESP, GBR, ITA and POL; Asia-Pacific: AUS, JPN and KOR.

Odds ratio and relative risk are calculated as Ravulizumab/Eculizumab. LS mean difference and risk difference are calculated as Ravulizumab - Eculizumab.

Source: adsl, adeff

Table HAI-2.6
Change from Baseline in HAI Score to End of Study Period by Supportive IST use at baseline
Full Analysis Set

IST use at baseline		Statistic	Eculizumab (N=96)	Ravulizumab (N=58)	p-value (7)
Yes	Change from Baseline to End of Study Period in HAI Score	n	75	28	0.1336
		Mean (SD)	-0.4 (1.05)	0.0 (0.54)	
		Median	0.0	0.0	
		Q1, Q3	-1.0, 0.0	0.0, 0.0	
		Min, Max	-5, 3	-1, 2	
		Change from baseline			
		LS Means (SEM)	-0.369 (0.110)	-0.047 (0.183)	
		95% CI for LS Means (1)	(-0.587, -0.151)	(-0.410, 0.316)	
		Difference in LS Means		0.322	
		(95% CI) (1)		(-0.107, 0.752)	
		p-value (2)		0.0828	
		Standardized Mean Difference		0.330	
		(95% CI) (3)		(-0.107, 0.766)	
		Responders (15% [1.35 points]), n(%)	5 (6.7)	0	
		Odds Ratio (4)		0.329	
		(95% CI)		(0.017, 6.253)	
		p-value		0.4591	
		Relative Risk (5)		0.000	
		(95% CI)		--	
		p-value		0.9999	

The eculizumab group data were collected as part of the PREVENT trial, Study ECU-NMO-301.

End of Study Period is the 6-week assessment after the first On-Trial Relapse for patients who have an On-Trial Relapse or for patients with no On-Trial Relapse: the End of Primary Treatment Period visit for patients in Study ALXN1210-NMO-307 and the End of Study visit for patients in Study ECU-NMO-301.

For those patients who had a missed value at the EOPT Visit or the 6-week post-relapse visit, for patients who had a relapse, the end of study is the last value before the missed value.

(1) The LS means (95% CI) and the difference in LS means (95% CI) are from an ANCOVA model of change from baseline with treatment as factor and baseline value as covariate. (2) The p-value represents the significance of the treatment effect and was derived from an ANCOVA model of the ranked change from baseline, with treatment as a factor, and the ranks of the baseline value included as covariate.

(3) Standardized mean differences (95% CI) were computed using Cohen's D incorporating Hedge's correction on change from baseline. (4) Odds ratio statistics are from a logistic regression model adjusted for baseline value with Firth's adjustment; (5) Relative risk statistics are based on a generalized linear model of a binomial distribution with log link;

(6) Risk difference statistics are calculated from a generalized linear model, correcting for the baseline value. (7) P-value is for the interaction term of treatment:subgroup from a linear regression model of ranked change from baseline with the with ranked baseline value, treatment, subgroup, and treatment:subgroup interaction as covariates.

Odds ratio and relative risk are calculated as Ravulizumab/Eculizumab. LS mean difference and risk difference are calculated as Ravulizumab - Eculizumab.

Source: adsl, adeff

Table HAI-2.6
Change from Baseline in HAI Score to End of Study Period by Supportive IST use at baseline
Full Analysis Set

IST use at baseline	Statistic	Eculizumab (N=96)	Ravulizumab (N=58)	p-value (7)
	Risk Difference (6)		-0.045	
	(95% CI)		(-0.142, 0.053)	
	p-value		0.3646	
Baseline HAI Score	n	75	28	
	Mean (SD)	2.4 (2.06)	1.2 (1.66)	
	Median	2.0	1.0	
	Q1, Q3	1.0, 4.0	0.0, 2.0	
	Min, Max	0, 8	0, 7	
End of Study Period HAI Score	n	75	28	
	Mean (SD)	2.0 (2.17)	1.2 (1.81)	
	Median	1.0	1.0	
	Q1, Q3	0.0, 3.0	0.0, 1.0	
	Min, Max	0, 8	0, 7	

The eculizumab group data were collected as part of the PREVENT trial, Study ECU-NMO-301.

End of Study Period is the 6-week assessment after the first On-Trial Relapse for patients who have an On-Trial Relapse or for patients with no On-Trial Relapse: the End of Primary Treatment Period visit for patients in Study ALXN1210-NMO-307 and the End of Study visit for patients in Study ECU-NMO-301.

For those patients who had a missed value at the EOPT Visit or the 6-week post-relapse visit, for patients who had a relapse, the end of study is the last value before the missed value.

(1) The LS means (95% CI) and the difference in LS means (95% CI) are from an ANCOVA model of change from baseline with treatment as factor and baseline value as covariate. (2) The p-value represents the significance of the treatment effect and was derived from an ANCOVA model of the ranked change from baseline, with treatment as a factor, and the ranks of the baseline value included as covariate.

(3) Standardized mean differences (95% CI) were computed using Cohen's D incorporating Hedge's correction on change from baseline. (4) Odds ratio statistics are from a logistic regression model adjusted for baseline value with Firth's adjustment; (5) Relative risk statistics are based on a generalized linear model of a binomial distribution with log link;

(6) Risk difference statistics are calculated from a generalized linear model, correcting for the baseline value. (7) P-value is for the interaction term of treatment:subgroup from a linear regression model of ranked change from baseline with the with ranked baseline value, treatment, subgroup, and treatment:subgroup interaction as covariates.

Odds ratio and relative risk are calculated as Ravulizumab/Eculizumab. LS mean difference and risk difference are calculated as Ravulizumab - Eculizumab.

Source: adsl, adeff

Table HAI-2.6
Change from Baseline in HAI Score to End of Study Period by Supportive IST use at baseline
Full Analysis Set

IST use at baseline		Statistic	Eculizumab (N=96)	Ravulizumab (N=58)	p-value (7)
No	Change from Baseline to End of Study Period in HAI Score	n	21	30	
		Mean (SD)	-0.4 (1.20)	-0.3 (0.69)	
		Median	0.0	0.0	
		Q1, Q3	-1.0, 0.0	-1.0, 0.0	
		Min, Max	-5, 1	-2, 1	
		Change from baseline			
		LS Means (SEM)	-0.336 (0.210)	-0.298 (0.174)	
		95% CI for LS Means (1)	(-0.757, 0.086)	(-0.649, 0.052)	
		Difference in LS Means		0.037	
		(95% CI) (1)		(-0.523, 0.597)	
		p-value (2)		0.5547	
		Standardized Mean Difference		0.038	
		(95% CI) (3)		(-0.520, 0.596)	
		Responders (15% [1.35 points]), n(%)	1 (4.8)	1 (3.3)	
		Odds Ratio (4)		1.111	
		(95% CI)		(0.077, 16.021)	
		p-value		0.9384	
		Relative Risk (5)		0.700	
		(95% CI)		(0.046, 10.575)	
		p-value		0.7968	

The eculizumab group data were collected as part of the PREVENT trial, Study ECU-NMO-301.

End of Study Period is the 6-week assessment after the first On-Trial Relapse for patients who have an On-Trial Relapse or for patients with no On-Trial Relapse: the End of Primary Treatment Period visit for patients in Study ALXN1210-NMO-307 and the End of Study visit for patients in Study ECU-NMO-301.

For those patients who had a missed value at the EOPT Visit or the 6-week post-relapse visit, for patients who had a relapse, the end of study is the last value before the missed value.

(1) The LS means (95% CI) and the difference in LS means (95% CI) are from an ANCOVA model of change from baseline with treatment as factor and baseline value as covariate. (2) The p-value represents the significance of the treatment effect and was derived from an ANCOVA model of the ranked change from baseline, with treatment as a factor, and the ranks of the baseline value included as covariate.

(3) Standardized mean differences (95% CI) were computed using Cohen's D incorporating Hedge's correction on change from baseline. (4) Odds ratio statistics are from a logistic regression model adjusted for baseline value with Firth's adjustment; (5) Relative risk statistics are based on a generalized linear model of a binomial distribution with log link;

(6) Risk difference statistics are calculated from a generalized linear model, correcting for the baseline value. (7) P-value is for the interaction term of treatment:subgroup from a linear regression model of ranked change from baseline with the with ranked baseline value, treatment, subgroup, and treatment:subgroup interaction as covariates.

Odds ratio and relative risk are calculated as Ravulizumab/Eculizumab. LS mean difference and risk difference are calculated as Ravulizumab - Eculizumab.

Source: adsl, adeff

Table HAI-2.6
Change from Baseline in HAI Score to End of Study Period by Supportive IST use at baseline
Full Analysis Set

IST use at baseline	Statistic	Eculizumab (N=96)	Ravulizumab (N=58)	p-value (7)
	Risk Difference (6)		0.009	
	(95% CI)		(-0.108, 0.127)	
	p-value		0.8719	
Baseline HAI Score	n	21	30	
	Mean (SD)	2.3 (2.57)	1.1 (1.20)	
	Median	1.0	1.0	
	Q1, Q3	1.0, 3.0	0.0, 2.0	
	Min, Max	0, 8	0, 5	
End of Study Period HAI Score	n	21	30	
	Mean (SD)	1.9 (2.68)	0.9 (1.31)	
	Median	1.0	0.0	
	Q1, Q3	0.0, 2.0	0.0, 2.0	
	Min, Max	0, 9	0, 5	

The eculizumab group data were collected as part of the PREVENT trial, Study ECU-NMO-301.

End of Study Period is the 6-week assessment after the first On-Trial Relapse for patients who have an On-Trial Relapse or for patients with no On-Trial Relapse: the End of Primary Treatment Period visit for patients in Study ALXN1210-NMO-307 and the End of Study visit for patients in Study ECU-NMO-301.

For those patients who had a missed value at the EOPT Visit or the 6-week post-relapse visit, for patients who had a relapse, the end of study is the last value before the missed value.

(1) The LS means (95% CI) and the difference in LS means (95% CI) are from an ANCOVA model of change from baseline with treatment as factor and baseline value as covariate. (2) The p-value represents the significance of the treatment effect and was derived from an ANCOVA model of the ranked change from baseline, with treatment as a factor, and the ranks of the baseline value included as covariate.

(3) Standardized mean differences (95% CI) were computed using Cohen's D incorporating Hedge's correction on change from baseline. (4) Odds ratio statistics are from a logistic regression model adjusted for baseline value with Firth's adjustment; (5) Relative risk statistics are based on a generalized linear model of a binomial distribution with log link;

(6) Risk difference statistics are calculated from a generalized linear model, correcting for the baseline value. (7) P-value is for the interaction term of treatment:subgroup from a linear regression model of ranked change from baseline with the with ranked baseline value, treatment, subgroup, and treatment:subgroup interaction as covariates.

Odds ratio and relative risk are calculated as Ravulizumab/Eculizumab. LS mean difference and risk difference are calculated as Ravulizumab - Eculizumab.

Source: adsl, adeff

Table HAI-2.7
Change from Baseline in HAI Score to End of Study Period by Rituximab use in the prior year
Full Analysis Set

Rituximab use in the prior year		Statistic	Eculizumab (N=96)	Ravulizumab (N=58)	p-value (7)
Yes	Change from Baseline to End of Study Period in HAI Score	n	19	20	0.1211
		Mean (SD)	-0.3 (0.99)	-0.3 (0.80)	
		Median	0.0	0.0	
		Q1, Q3	-1.0, 0.0	-1.0, 0.0	
		Min, Max	-3, 2	-2, 2	
		Change from baseline			
		LS Means (SEM)	-0.277 (0.216)	-0.287 (0.210)	
		95% CI for LS Means (1)	(-0.715, 0.161)	(-0.713, 0.139)	
		Difference in LS Means		-0.010	
		(95% CI) (1)		(-0.639, 0.619)	
		p-value (2)		0.6784	
		Standardized Mean Difference		-0.010	
		(95% CI) (3)		(-0.638, 0.618)	
		Responders (15% [1.35 points]), n(%)	1 (5.3)	1 (5.0)	
		Odds Ratio (4)		1.032	
		(95% CI)		(0.086, 12.334)	
		p-value		0.9803	
		Relative Risk (5)		0.950	
		(95% CI)		(0.064, 14.132)	
		p-value		0.9703	

The eculizumab group data were collected as part of the PREVENT trial, Study ECU-NMO-301.

End of Study Period is the 6-week assessment after the first On-Trial Relapse for patients who have an On-Trial Relapse or for patients with no On-Trial Relapse: the End of Primary Treatment Period visit for patients in Study ALXN1210-NMO-307 and the End of Study visit for patients in Study ECU-NMO-301.

For those patients who had a missed value at the EOPT Visit or the 6-week post-relapse visit, for patients who had a relapse, the end of study is the last value before the missed value.

(1) The LS means (95% CI) and the difference in LS means (95% CI) are from an ANCOVA model of change from baseline with treatment as factor and baseline value as covariate. (2) The p-value represents the significance of the treatment effect and was derived from an ANCOVA model of the ranked change from baseline, with treatment as a factor, and the ranks of the baseline value included as covariate.

(3) Standardized mean differences (95% CI) were computed using Cohen's D incorporating Hedge's correction on change from baseline. (4) Odds ratio statistics are from a logistic regression model adjusted for baseline value with Firth's adjustment; (5) Relative risk statistics are based on a generalized linear model of a binomial distribution with log link;

(6) Risk difference statistics are calculated from a generalized linear model, correcting for the baseline value. (7) P-value is for the interaction term of treatment:subgroup from a linear regression model of ranked change from baseline with the with ranked baseline value, treatment, subgroup, and treatment:subgroup interaction as covariates.

Odds ratio and relative risk are calculated as Ravulizumab/Eculizumab. LS mean difference and risk difference are calculated as Ravulizumab - Eculizumab.

Source: adsl, adeff

Table HAI-2.7
Change from Baseline in HAI Score to End of Study Period by Rituximab use in the prior year
Full Analysis Set

Rituximab use in the prior year		Statistic	Eculizumab (N=96)	Ravulizumab (N=58)	p-value (7)
		Risk Difference (6)		0.005	
		(95% CI)		(-0.153, 0.164)	
		p-value		0.9485	
	Baseline HAI Score	n	19	20	
		Mean (SD)	2.8 (2.27)	1.5 (1.43)	
		Median	2.0	1.0	
		Q1, Q3	1.0, 4.0	0.0, 2.0	
		Min, Max	0, 7	0, 5	
	End of Study Period HAI Score	n	19	20	
		Mean (SD)	2.5 (2.41)	1.2 (1.81)	
		Median	2.0	0.0	
		Q1, Q3	1.0, 4.0	0.0, 2.0	
		Min, Max	0, 7	0, 6	

The eculizumab group data were collected as part of the PREVENT trial, Study ECU-NMO-301.

End of Study Period is the 6-week assessment after the first On-Trial Relapse for patients who have an On-Trial Relapse or for patients with no On-Trial Relapse: the End of Primary Treatment Period visit for patients in Study ALXN1210-NMO-307 and the End of Study visit for patients in Study ECU-NMO-301.

For those patients who had a missed value at the EOPT Visit or the 6-week post-relapse visit, for patients who had a relapse, the end of study is the last value before the missed value.

(1) The LS means (95% CI) and the difference in LS means (95% CI) are from an ANCOVA model of change from baseline with treatment as factor and baseline value as covariate. (2) The p-value represents the significance of the treatment effect and was derived from an ANCOVA model of the ranked change from baseline, with treatment as a factor, and the ranks of the baseline value included as covariate.

(3) Standardized mean differences (95% CI) were computed using Cohen's D incorporating Hedge's correction on change from baseline. (4) Odds ratio statistics are from a logistic regression model adjusted for baseline value with Firth's adjustment; (5) Relative risk statistics are based on a generalized linear model of a binomial distribution with log link;

(6) Risk difference statistics are calculated from a generalized linear model, correcting for the baseline value. (7) P-value is for the interaction term of treatment:subgroup from a linear regression model of ranked change from baseline with the with ranked baseline value, treatment, subgroup, and treatment:subgroup interaction as covariates.

Odds ratio and relative risk are calculated as Ravulizumab/Eculizumab. LS mean difference and risk difference are calculated as Ravulizumab - Eculizumab.

Source: adsl, adeff

Table HAI-2.7
Change from Baseline in HAI Score to End of Study Period by Rituximab use in the prior year
Full Analysis Set

Rituximab use in the prior year		Statistic	Eculizumab (N=96)	Ravulizumab (N=58)	p-value (7)
No	Change from Baseline to End of Study Period in HAI Score	n	77	38	
		Mean (SD)	-0.4 (1.10)	-0.1 (0.52)	
		Median	0.0	0.0	
		Q1, Q3	-1.0, 0.0	0.0, 0.0	
		Min, Max	-5, 3	-1, 1	
		Change from baseline			
		LS Means (SEM)	-0.382 (0.109)	-0.122 (0.158)	
		95% CI for LS Means (1)	(-0.598, -0.165)	(-0.435, 0.192)	
		Difference in LS Means		0.260	
		(95% CI) (1)		(-0.129, 0.648)	
		p-value (2)		0.1676	
		Standardized Mean Difference		0.265	
		(95% CI) (3)		(-0.125, 0.655)	
		Responders (15% [1.35 points]), n(%)	5 (6.5)	0	
		Odds Ratio (4)		0.287	
		(95% CI)		(0.015, 5.589)	
		p-value		0.4099	
		Relative Risk (5)		0.000	
		(95% CI)		--	
		p-value		0.9999	

The eculizumab group data were collected as part of the PREVENT trial, Study ECU-NMO-301.

End of Study Period is the 6-week assessment after the first On-Trial Relapse for patients who have an On-Trial Relapse or for patients with no On-Trial Relapse: the End of Primary Treatment Period visit for patients in Study ALXN1210-NMO-307 and the End of Study visit for patients in Study ECU-NMO-301.

For those patients who had a missed value at the EOPT Visit or the 6-week post-relapse visit, for patients who had a relapse, the end of study is the last value before the missed value.

(1) The LS means (95% CI) and the difference in LS means (95% CI) are from an ANCOVA model of change from baseline with treatment as factor and baseline value as covariate. (2) The p-value represents the significance of the treatment effect and was derived from an ANCOVA model of the ranked change from baseline, with treatment as a factor, and the ranks of the baseline value included as covariate.

(3) Standardized mean differences (95% CI) were computed using Cohen's D incorporating Hedge's correction on change from baseline. (4) Odds ratio statistics are from a logistic regression model adjusted for baseline value with Firth's adjustment; (5) Relative risk statistics are based on a generalized linear model of a binomial distribution with log link;

(6) Risk difference statistics are calculated from a generalized linear model, correcting for the baseline value. (7) P-value is for the interaction term of treatment:subgroup from a linear regression model of ranked change from baseline with the with ranked baseline value, treatment, subgroup, and treatment:subgroup interaction as covariates.

Odds ratio and relative risk are calculated as Ravulizumab/Eculizumab. LS mean difference and risk difference are calculated as Ravulizumab - Eculizumab.

Source: adsl, adeff

Table HAI-2.7
Change from Baseline in HAI Score to End of Study Period by Rituximab use in the prior year
Full Analysis Set

Rituximab use in the prior year		Statistic	Eculizumab (N=96)	Ravulizumab (N=58)	p-value (7)
		Risk Difference (6)		-0.036	
		(95% CI)		(-0.118, 0.046)	
		p-value		0.3872	
	Baseline HAI Score	n	77	38	
		Mean (SD)	2.3 (2.14)	1.0 (1.41)	
		Median	1.0	1.0	
		Q1, Q3	1.0, 3.0	0.0, 2.0	
		Min, Max	0, 8	0, 7	
	End of Study Period HAI Score	n	77	38	
		Mean (SD)	1.9 (2.24)	0.9 (1.43)	
		Median	1.0	0.5	
		Q1, Q3	0.0, 2.0	0.0, 1.0	
		Min, Max	0, 9	0, 7	

The eculizumab group data were collected as part of the PREVENT trial, Study ECU-NMO-301.

End of Study Period is the 6-week assessment after the first On-Trial Relapse for patients who have an On-Trial Relapse or for patients with no On-Trial Relapse: the End of Primary Treatment Period visit for patients in Study ALXN1210-NMO-307 and the End of Study visit for patients in Study ECU-NMO-301.

For those patients who had a missed value at the EOPT Visit or the 6-week post-relapse visit, for patients who had a relapse, the end of study is the last value before the missed value.

(1) The LS means (95% CI) and the difference in LS means (95% CI) are from an ANCOVA model of change from baseline with treatment as factor and baseline value as covariate. (2) The p-value represents the significance of the treatment effect and was derived from an ANCOVA model of the ranked change from baseline, with treatment as a factor, and the ranks of the baseline value included as covariate.

(3) Standardized mean differences (95% CI) were computed using Cohen's D incorporating Hedge's correction on change from baseline. (4) Odds ratio statistics are from a logistic regression model adjusted for baseline value with Firth's adjustment; (5) Relative risk statistics are based on a generalized linear model of a binomial distribution with log link;

(6) Risk difference statistics are calculated from a generalized linear model, correcting for the baseline value. (7) P-value is for the interaction term of treatment:subgroup from a linear regression model of ranked change from baseline with the with ranked baseline value, treatment, subgroup, and treatment:subgroup interaction as covariates.

Odds ratio and relative risk are calculated as Ravulizumab/Eculizumab. LS mean difference and risk difference are calculated as Ravulizumab - Eculizumab.

Source: adsl, adeff

Table HAI-2.4
Change from Baseline in HAI Score to End of Study Period by Disease severity via EDSS Score at baseline
Full Analysis Set

EDSS score at baseline		Statistic	Eculizumab (N=96)	Ravulizumab (N=58)	p-value (7)
< 5	Change from Baseline to End of Study Period in HAI Score	n	66	49	0.3581
		Mean (SD)	-0.3 (0.68)	-0.2 (0.60)	
		Median	0.0	0.0	
		Q1, Q3	-1.0, 0.0	0.0, 0.0	
		Min, Max	-2, 2	-2, 1	
		Change from baseline			
		LS Means (SEM)	-0.241 (0.074)	-0.287 (0.086)	
		95% CI for LS Means (1)	(-0.387, -0.095)	(-0.458, -0.117)	
		Difference in LS Means		-0.046	
		(95% CI) (1)		(-0.276, 0.184)	
		p-value (2)		0.9932	
		Standardized Mean Difference		-0.060	
		(95% CI) (3)		(-0.429, 0.310)	
		Responders (15% [1.35 points]), n(%)	1 (1.5)	1 (2.0)	
		Odds Ratio (4)		6.164	
		(95% CI)		(0.324, 117.265)	
		p-value		0.2262	
		Relative Risk (5)		1.347	
		(95% CI)		(0.086, 21.008)	
		p-value		0.8317	

The eculizumab group data were collected as part of the PREVENT trial, Study ECU-NMO-301.

End of Study Period is the 6-week assessment after the first On-Trial Relapse for patients who have an On-Trial Relapse or for patients with no On-Trial Relapse: the End of Primary Treatment Period visit for patients in Study ALXN1210-NMO-307 and the End of Study visit for patients in Study ECU-NMO-301.

For those patients who had a missed value at the EOPT Visit or the 6-week post-relapse visit, for patients who had a relapse, the end of study is the last value before the missed value.

(1) The LS means (95% CI) and the difference in LS means (95% CI) are from an ANCOVA model of change from baseline with treatment as factor and baseline value as covariate. (2) The p-value represents the significance of the treatment effect and was derived from an ANCOVA model of the ranked change from baseline, with treatment as a factor, and the ranks of the baseline value included as covariate.

(3) Standardized mean differences (95% CI) were computed using Cohen's D incorporating Hedge's correction on change from baseline. (4) Odds ratio statistics are from a logistic regression model adjusted for baseline value with Firth's adjustment; (5) Relative risk statistics are based on a generalized linear model of a binomial distribution with log link;

(6) Risk difference statistics are calculated from a generalized linear model, correcting for the baseline value. (7) P-value is for the interaction term of treatment:subgroup from a linear regression model of ranked change from baseline with the with ranked baseline value, treatment, subgroup, and treatment:subgroup interaction as covariates.

Odds ratio and relative risk are calculated as Ravulizumab/Eculizumab. LS mean difference and risk difference are calculated as Ravulizumab - Eculizumab.

Source: adsl, adeff

Table HAI-2.4
Change from Baseline in HAI Score to End of Study Period by Disease severity via EDSS Score at baseline
Full Analysis Set

EDSS score at baseline	Statistic	Eculizumab (N=96)	Ravulizumab (N=58)	p-value (7)
	Risk Difference (6)		0.027	
	(95% CI)		(-0.024, 0.077)	
	p-value		0.2976	
Baseline HAI Score	n	66	49	
	Mean (SD)	1.2 (0.85)	0.7 (0.77)	
	Median	1.0	1.0	
	Q1, Q3	1.0, 2.0	0.0, 1.0	
	Min, Max	0, 3	0, 2	
End of Study Period HAI Score	n	66	49	
	Mean (SD)	0.9 (0.81)	0.5 (0.77)	
	Median	1.0	0.0	
	Q1, Q3	0.0, 1.0	0.0, 1.0	
	Min, Max	0, 3	0, 3	

The eculizumab group data were collected as part of the PREVENT trial, Study ECU-NMO-301.

End of Study Period is the 6-week assessment after the first On-Trial Relapse for patients who have an On-Trial Relapse or for patients with no On-Trial Relapse: the End of Primary Treatment Period visit for patients in Study ALXN1210-NMO-307 and the End of Study visit for patients in Study ECU-NMO-301.

For those patients who had a missed value at the EOPT Visit or the 6-week post-relapse visit, for patients who had a relapse, the end of study is the last value before the missed value.

(1) The LS means (95% CI) and the difference in LS means (95% CI) are from an ANCOVA model of change from baseline with treatment as factor and baseline value as covariate. (2) The p-value represents the significance of the treatment effect and was derived from an ANCOVA model of the ranked change from baseline, with treatment as a factor, and the ranks of the baseline value included as covariate.

(3) Standardized mean differences (95% CI) were computed using Cohen's D incorporating Hedge's correction on change from baseline. (4) Odds ratio statistics are from a logistic regression model adjusted for baseline value with Firth's adjustment; (5) Relative risk statistics are based on a generalized linear model of a binomial distribution with log link;

(6) Risk difference statistics are calculated from a generalized linear model, correcting for the baseline value. (7) P-value is for the interaction term of treatment:subgroup from a linear regression model of ranked change from baseline with the with ranked baseline value, treatment, subgroup, and treatment:subgroup interaction as covariates.

Odds ratio and relative risk are calculated as Ravulizumab/Eculizumab. LS mean difference and risk difference are calculated as Ravulizumab - Eculizumab.

Source: adsl, adeff

Table HAI-2.4
Change from Baseline in HAI Score to End of Study Period by Disease severity via EDSS Score at baseline
Full Analysis Set

EDSS score at baseline		Statistic	Eculizumab (N=96)	Ravulizumab (N=58)	p-value (7)
>= 5	Change from Baseline to End of Study Period in HAI Score	n	30	9	
		Mean (SD)	-0.5 (1.66)	0.1 (0.78)	
		Median	0.0	0.0	
		Q1, Q3	-1.0, 0.0	0.0, 0.0	
		Min, Max	-5, 3	-1, 2	
		Change from baseline			
		LS Means (SEM)	-0.543 (0.282)	0.142 (0.526)	
		95% CI for LS Means (1)	(-1.114, 0.029)	(-0.924, 1.209)	
		Difference in LS Means		0.685	
		(95% CI) (1)		(-0.542, 1.912)	
		p-value (2)		0.2374	
		Standardized Mean Difference		0.550	
		(95% CI) (3)		(-0.205, 1.305)	
		Responders (15% [1.35 points]), n(%)	5 (16.7)	0	
		Odds Ratio (4)		0.187	
		(95% CI)		(0.008, 4.352)	
		p-value		0.2962	
		Relative Risk (5)		0.000	
		(95% CI)		--	
		p-value		0.9999	

The eculizumab group data were collected as part of the PREVENT trial, Study ECU-NMO-301.

End of Study Period is the 6-week assessment after the first On-Trial Relapse for patients who have an On-Trial Relapse or for patients with no On-Trial Relapse: the End of Primary Treatment Period visit for patients in Study ALXN1210-NMO-307 and the End of Study visit for patients in Study ECU-NMO-301.

For those patients who had a missed value at the EOPT Visit or the 6-week post-relapse visit, for patients who had a relapse, the end of study is the last value before the missed value.

(1) The LS means (95% CI) and the difference in LS means (95% CI) are from an ANCOVA model of change from baseline with treatment as factor and baseline value as covariate. (2) The p-value represents the significance of the treatment effect and was derived from an ANCOVA model of the ranked change from baseline, with treatment as a factor, and the ranks of the baseline value included as covariate.

(3) Standardized mean differences (95% CI) were computed using Cohen's D incorporating Hedge's correction on change from baseline. (4) Odds ratio statistics are from a logistic regression model adjusted for baseline value with Firth's adjustment; (5) Relative risk statistics are based on a generalized linear model of a binomial distribution with log link;

(6) Risk difference statistics are calculated from a generalized linear model, correcting for the baseline value. (7) P-value is for the interaction term of treatment:subgroup from a linear regression model of ranked change from baseline with the with ranked baseline value, treatment, subgroup, and treatment:subgroup interaction as covariates.

Odds ratio and relative risk are calculated as Ravulizumab/Eculizumab. LS mean difference and risk difference are calculated as Ravulizumab - Eculizumab.

Source: adsl, adeff

Table HAI-2.4
Change from Baseline in HAI Score to End of Study Period by Disease severity via EDSS Score at baseline
Full Analysis Set

EDSS score at baseline	Statistic	Eculizumab (N=96)	Ravulizumab (N=58)	p-value (7)
	Risk Difference (6)		-0.201	
	(95% CI)		(-0.471, 0.068)	
	p-value		0.1385	
Baseline HAI Score	n	30	9	
	Mean (SD)	4.9 (1.98)	3.7 (1.58)	
	Median	5.0	3.0	
	Q1, Q3	4.0, 6.0	3.0, 4.0	
	Min, Max	0, 8	2, 7	
End of Study Period HAI Score	n	30	9	
	Mean (SD)	4.4 (2.61)	3.8 (1.92)	
	Median	5.0	3.0	
	Q1, Q3	3.0, 7.0	3.0, 5.0	
	Min, Max	0, 9	1, 7	

The eculizumab group data were collected as part of the PREVENT trial, Study ECU-NMO-301.

End of Study Period is the 6-week assessment after the first On-Trial Relapse for patients who have an On-Trial Relapse or for patients with no On-Trial Relapse: the End of Primary Treatment Period visit for patients in Study ALXN1210-NMO-307 and the End of Study visit for patients in Study ECU-NMO-301.

For those patients who had a missed value at the EOPT Visit or the 6-week post-relapse visit, for patients who had a relapse, the end of study is the last value before the missed value.

(1) The LS means (95% CI) and the difference in LS means (95% CI) are from an ANCOVA model of change from baseline with treatment as factor and baseline value as covariate. (2) The p-value represents the significance of the treatment effect and was derived from an ANCOVA model of the ranked change from baseline, with treatment as a factor, and the ranks of the baseline value included as covariate.

(3) Standardized mean differences (95% CI) were computed using Cohen's D incorporating Hedge's correction on change from baseline. (4) Odds ratio statistics are from a logistic regression model adjusted for baseline value with Firth's adjustment; (5) Relative risk statistics are based on a generalized linear model of a binomial distribution with log link;

(6) Risk difference statistics are calculated from a generalized linear model, correcting for the baseline value. (7) P-value is for the interaction term of treatment:subgroup from a linear regression model of ranked change from baseline with the with ranked baseline value, treatment, subgroup, and treatment:subgroup interaction as covariates.

Odds ratio and relative risk are calculated as Ravulizumab/Eculizumab. LS mean difference and risk difference are calculated as Ravulizumab - Eculizumab.

Source: adsl, adeff

Table HAI-1.2
Clinically Important Worsening from Baseline in HAI Score to End of Study Period by Sex
Full Analysis Set

Sex		Statistic	Eculizumab (N=96)	Ravulizumab (N=58)	p-value (4)
Male	Clinically Important Worsening in HAI Score from Baseline to End of Study Period				0.1736
		n	8	6	
		No Clinically Important Worsening	4 (50.0)	6 (100.0)	
		Clinically Important Worsening	4 (50.0)	0 (0.0)	
	Treatment Effect (Ravulizumab vs Eculizumab)				
		Odds Ratio (1)		0.154	
		(95% CI)		(0.005, 5.055)	
		p-value		0.2939	
		Relative Risk (2)		0.000	
		(95% CI)		--	
		p-value		0.9999	
		Risk Difference (3)		-0.346	
		(95% CI)		(-0.900, 0.208)	
		p-value		0.1966	

The eculizumab group data were collected as part of the PREVENT trial, Study ECU-NMO-301.
End of Study Period is the 6-week assessment after the first On-Trial Relapse for patients who have an On-Trial Relapse or for patients with no On-Trial Relapse: the End of Primary Treatment Period visit for patients in Study ALXN1210-NMO-307 and the End of Study visit for patients in Study ECU-NMO-301.
For those patients who had a missed value at the EOPT Visit or the 6-week post-relapse visit, for patients who had a relapse, the end of study is the last value before the missed value.
Clinically important worsening is conditional on the baseline value: worsening if the baseline HAI is 0 and at least 2 points increase or if the baseline HAI is >0 and at least 1 point increase; improvement if the baseline value is at least 2 and at least 1 point decrease; and stable if baseline is 0 or 1 and a 0 or 1 point increase or decrease or baseline is at least 2 and not change.
(1) Odds ratio statistics are from a logistic regression model adjusted for baseline value with Firth's adjustment; (2) Relative risk statistics are based on a generalized linear model of a binomial distribution with log link; (3) Risk difference statistics are calculated from a generalized linear model, correcting for the baseline value.
(4) P-value is for the interaction term of treatment:subgroup from a logistic regression model with the baseline value, treatment, subgroup, and treatment:subgroup interaction as covariates, with Firth's adjustment.
Odds ratio and relative risk are calculated as Ravulizumab/Eculizumab. Risk difference is calculated as Ravulizumab - Eculizumab.
Source: adsl, adeff

Table HAI-1.2
Clinically Important Worsening from Baseline in HAI Score to End of Study Period by Sex
Full Analysis Set

Sex		Statistic	Eculizumab (N=96)	Ravulizumab (N=58)	p-value (4)
Female	Clinically Important Worsening in HAI Score from Baseline to End of Study Period				
		n	88	52	
		No Clinically Important Worsening	84 (95.5)	50 (96.2)	
		Clinically Important Worsening	4 (4.5)	2 (3.8)	
	Treatment Effect (Ravulizumab vs Eculizumab)				
		Odds Ratio (1)		1.542	
		(95% CI)		(0.274, 8.676)	
		p-value		0.6229	
		Relative Risk (2)		0.846	
		(95% CI)		(0.161, 4.461)	
		p-value		0.8439	
		Risk Difference (3)		0.015	
		(95% CI)		(-0.058, 0.088)	
		p-value		0.6841	

The eculizumab group data were collected as part of the PREVENT trial, Study ECU-NMO-301.
End of Study Period is the 6-week assessment after the first On-Trial Relapse for patients who have an On-Trial Relapse or for patients with no On-Trial Relapse: the End of Primary Treatment Period visit for patients in Study ALXN1210-NMO-307 and the End of Study visit for patients in Study ECU-NMO-301.
For those patients who had a missed value at the EOPT Visit or the 6-week post-relapse visit, for patients who had a relapse, the end of study is the last value before the missed value.
Clinically important worsening is conditional on the baseline value: worsening if the baseline HAI is 0 and at least 2 points increase or if the baseline HAI is >0 and at least 1 point increase; improvement if the baseline value is at least 2 and at least 1 point decrease; and stable if baseline is 0 or 1 and a 0 or 1 point increase or decrease or baseline is at least 2 and not change.
(1) Odds ratio statistics are from a logistic regression model adjusted for baseline value with Firth's adjustment; (2) Relative risk statistics are based on a generalized linear model of a binomial distribution with log link; (3) Risk difference statistics are calculated from a generalized linear model, correcting for the baseline value.
(4) P-value is for the interaction term of treatment:subgroup from a logistic regression model with the baseline value, treatment, subgroup, and treatment:subgroup interaction as covariates, with Firth's adjustment.
Odds ratio and relative risk are calculated as Ravulizumab/Eculizumab. Risk difference is calculated as Ravulizumab - Eculizumab.
Source: adsl, adeff

Table HAI-1.3
Clinically Important Worsening from Baseline in HAI Score to End of Study Period by Age Group
Full Analysis Set

Age Group		Statistic	Eculizumab (N=96)	Ravulizumab (N=58)	p-value (4)
< 45 years	Clinically Important Worsening in HAI Score from Baseline to End of Study Period				0.8394
		n	47	25	
		No Clinically Important Worsening	44 (93.6)	24 (96.0)	
		Clinically Important Worsening	3 (6.4)	1 (4.0)	
	Treatment Effect (Ravulizumab vs Eculizumab)				
		Odds Ratio (1)		0.905	
		(95% CI)		(0.121, 6.767)	
		p-value		0.9227	
		Relative Risk (2)		0.627	
		(95% CI)		(0.069, 5.716)	
		p-value		0.6786	
		Risk Difference (3)		-0.012	
		(95% CI)		(-0.126, 0.103)	
		p-value		0.8388	

The eculizumab group data were collected as part of the PREVENT trial, Study ECU-NMO-301.
End of Study Period is the 6-week assessment after the first On-Trial Relapse for patients who have an On-Trial Relapse or for patients with no On-Trial Relapse: the End of Primary Treatment Period visit for patients in Study ALXN1210-NMO-307 and the End of Study visit for patients in Study ECU-NMO-301.
For those patients who had a missed value at the EOPT Visit or the 6-week post-relapse visit, for patients who had a relapse, the end of study is the last value before the missed value.
Clinically important worsening is conditional on the baseline value: worsening if the baseline HAI is 0 and at least 2 points increase or if the baseline HAI is >0 and at least 1 point increase; improvement if the baseline value is at least 2 and at least 1 point decrease; and stable if baseline is 0 or 1 and a 0 or 1 point increase or decrease or baseline is at least 2 and not change.
(1) Odds ratio statistics are from a logistic regression model adjusted for baseline value with Firth's adjustment; (2) Relative risk statistics are based on a generalized linear model of a binomial distribution with log link; (3) Risk difference statistics are calculated from a generalized linear model, correcting for the baseline value.
(4) P-value is for the interaction term of treatment:subgroup from a logistic regression model with the baseline value, treatment, subgroup, and treatment:subgroup interaction as covariates, with Firth's adjustment.
Odds ratio and relative risk are calculated as Ravulizumab/Eculizumab. Risk difference is calculated as Ravulizumab - Eculizumab.
Source: adsl, adeff

Table HAI-1.3
Clinically Important Worsening from Baseline in HAI Score to End of Study Period by Age Group
Full Analysis Set

Age Group		Statistic	Eculizumab (N=96)	Ravulizumab (N=58)	p-value (4)
>= 45 years	Clinically Important Worsening in HAI Score from Baseline to End of Study Period				
		n	49	33	
		No Clinically Important Worsening	44 (89.8)	32 (97.0)	
		Clinically Important Worsening	5 (10.2)	1 (3.0)	
	Treatment Effect (Ravulizumab vs Eculizumab)				
		Odds Ratio (1)		0.532	
		(95% CI)		(0.070, 4.032)	
		p-value		0.5418	
		Relative Risk (2)		0.297	
		(95% CI)		(0.036, 2.428)	
		p-value		0.2574	
		Risk Difference (3)		-0.042	
		(95% CI)		(-0.173, 0.088)	
		p-value		0.5224	

The eculizumab group data were collected as part of the PREVENT trial, Study ECU-NMO-301.
End of Study Period is the 6-week assessment after the first On-Trial Relapse for patients who have an On-Trial Relapse or for patients with no On-Trial Relapse: the End of Primary Treatment Period visit for patients in Study ALXN1210-NMO-307 and the End of Study visit for patients in Study ECU-NMO-301.
For those patients who had a missed value at the EOPT Visit or the 6-week post-relapse visit, for patients who had a relapse, the end of study is the last value before the missed value.
Clinically important worsening is conditional on the baseline value: worsening if the baseline HAI is 0 and at least 2 points increase or if the baseline HAI is >0 and at least 1 point increase; improvement if the baseline value is at least 2 and at least 1 point decrease; and stable if baseline is 0 or 1 and a 0 or 1 point increase or decrease or baseline is at least 2 and not change.
(1) Odds ratio statistics are from a logistic regression model adjusted for baseline value with Firth's adjustment; (2) Relative risk statistics are based on a generalized linear model of a binomial distribution with log link; (3) Risk difference statistics are calculated from a generalized linear model, correcting for the baseline value.
(4) P-value is for the interaction term of treatment:subgroup from a logistic regression model with the baseline value, treatment, subgroup, and treatment:subgroup interaction as covariates, with Firth's adjustment.
Odds ratio and relative risk are calculated as Ravulizumab/Eculizumab. Risk difference is calculated as Ravulizumab - Eculizumab.
Source: adsl, adeff

Table HAI-1.5
Clinically Important Worsening from Baseline in HAI Score to End of Study Period by Region
Full Analysis Set

Region		Statistic	Eculizumab (N=96)	Ravulizumab (N=58)	p-value (4)
Asia-Pacific	Clinically Important Worsening in HAI Score from Baseline to End of Study Period				0.6121
		n	35	20	
		No Clinically Important Worsening	32 (91.4)	20 (100.0)	
		Clinically Important Worsening	3 (8.6)	0 (0.0)	
	Treatment Effect (Ravulizumab vs Eculizumab)				
		Odds Ratio (1)		0.322	
		(95% CI)		(0.013, 7.808)	
		p-value		0.4860	
		Relative Risk (2)		0.000	
		(95% CI)		--	
		p-value		0.9999	
		Risk Difference (3)		-0.057	
		(95% CI)		(-0.196, 0.082)	
		p-value		0.4134	

The eculizumab group data were collected as part of the PREVENT trial, Study ECU-NMO-301.
End of Study Period is the 6-week assessment after the first On-Trial Relapse for patients who have an On-Trial Relapse or for patients with no On-Trial Relapse: the End of Primary Treatment Period visit for patients in Study ALXN1210-NMO-307 and the End of Study visit for patients in Study ECU-NMO-301.
For those patients who had a missed value at the EOPT Visit or the 6-week post-relapse visit, for patients who had a relapse, the end of study is the last value before the missed value.
Clinically important worsening is conditional on the baseline value: worsening if the baseline HAI is 0 and at least 2 points increase or if the baseline HAI is >0 and at least 1 point increase; improvement if the baseline value is at least 2 and at least 1 point decrease; and stable if baseline is 0 or 1 and a 0 or 1 point increase or decrease or baseline is at least 2 and not change.
(1) Odds ratio statistics are from a logistic regression model adjusted for baseline value with Firth's adjustment; (2) Relative risk statistics are based on a generalized linear model of a binomial distribution with log link; (3) Risk difference statistics are calculated from a generalized linear model, correcting for the baseline value.
(4) P-value is for the interaction term of treatment:subgroup from a logistic regression model with the baseline value, treatment, subgroup, and treatment:subgroup interaction as covariates, with Firth's adjustment.
For eculizumab arm, Americas: ARG and USA; Europe: CZE, DEU, DNK, ESP, HRV, ITA, RUS and TUR; Asia-Pacific: AUS, HKG, JPN, KOR, MYS, THA and TWN. For ravulizumab arm, Americas: CAN and USA; Europe: DEU, DNK, ESP, GBR, ITA and POL; Asia-Pacific: AUS, JPN and KOR.
Odds ratio and relative risk are calculated as Ravulizumab/Eculizumab. Risk difference is calculated as Ravulizumab - Eculizumab.
Source: adsl, adeff

Table HAI-1.5
Clinically Important Worsening from Baseline in HAI Score to End of Study Period by Region
Full Analysis Set

Region		Statistic	Eculizumab (N=96)	Ravulizumab (N=58)	p-value (4)
Americas	Clinically Important Worsening in HAI Score from Baseline to End of Study Period				0.3010
		n	29	21	
		No Clinically Important Worsening	25 (86.2)	21 (100.0)	
		Clinically Important Worsening	4 (13.8)	0 (0.0)	
	Treatment Effect (Ravulizumab vs Eculizumab)				
		Odds Ratio (1)		0.113	
		(95% CI)		(0.005, 2.404)	
		p-value		0.1620	
		Relative Risk (2)		0.000	
		(95% CI)		--	
		p-value		0.9999	
		Risk Difference (3)		-0.154	
		(95% CI)		(-0.323, 0.014)	
		p-value		0.0714	

The eculizumab group data were collected as part of the PREVENT trial, Study ECU-NMO-301.
End of Study Period is the 6-week assessment after the first On-Trial Relapse for patients who have an On-Trial Relapse or for patients with no On-Trial Relapse: the End of Primary Treatment Period visit for patients in Study ALXN1210-NMO-307 and the End of Study visit for patients in Study ECU-NMO-301.
For those patients who had a missed value at the EOPT Visit or the 6-week post-relapse visit, for patients who had a relapse, the end of study is the last value before the missed value.
Clinically important worsening is conditional on the baseline value: worsening if the baseline HAI is 0 and at least 2 points increase or if the baseline HAI is >0 and at least 1 point increase; improvement if the baseline value is at least 2 and at least 1 point decrease; and stable if baseline is 0 or 1 and a 0 or 1 point increase or decrease or baseline is at least 2 and not change.
(1) Odds ratio statistics are from a logistic regression model adjusted for baseline value with Firth's adjustment; (2) Relative risk statistics are based on a generalized linear model of a binomial distribution with log link; (3) Risk difference statistics are calculated from a generalized linear model, correcting for the baseline value.
(4) P-value is for the interaction term of treatment:subgroup from a logistic regression model with the baseline value, treatment, subgroup, and treatment:subgroup interaction as covariates, with Firth's adjustment.
For eculizumab arm, Americas: ARG and USA; Europe: CZE, DEU, DNK, ESP, HRV, ITA, RUS and TUR; Asia-Pacific: AUS, HKG, JPN, KOR, MYS, THA and TWN. For ravulizumab arm, Americas: CAN and USA; Europe: DEU, DNK, ESP, GBR, ITA and POL; Asia-Pacific: AUS, JPN and KOR.
Odds ratio and relative risk are calculated as Ravulizumab/Eculizumab. Risk difference is calculated as Ravulizumab - Eculizumab.
Source: adsl, adeff

Table HAI-1.5
Clinically Important Worsening from Baseline in HAI Score to End of Study Period by Region
Full Analysis Set

Region		Statistic	Eculizumab (N=96)	Ravulizumab (N=58)	p-value (4)
Europe	Clinically Important Worsening in HAI Score from Baseline to End of Study Period				
		n	32	17	
		No Clinically Important Worsening	31 (96.9)	15 (88.2)	
		Clinically Important Worsening	1 (3.1)	2 (11.8)	
	Treatment Effect (Ravulizumab vs Eculizumab)				
		Odds Ratio (1)		5.833	
		(95% CI)		(0.493, 68.987)	
		p-value		0.1617	
		Relative Risk (2)		3.765	
		(95% CI)		(0.367, 38.588)	
		p-value		0.2642	
		Risk Difference (3)		0.108	
		(95% CI)		(-0.034, 0.250)	
		p-value		0.1330	

The eculizumab group data were collected as part of the PREVENT trial, Study ECU-NMO-301.
End of Study Period is the 6-week assessment after the first On-Trial Relapse for patients who have an On-Trial Relapse or for patients with no On-Trial Relapse: the End of Primary Treatment Period visit for patients in Study ALXN1210-NMO-307 and the End of Study visit for patients in Study ECU-NMO-301.
For those patients who had a missed value at the EOPT Visit or the 6-week post-relapse visit, for patients who had a relapse, the end of study is the last value before the missed value.
Clinically important worsening is conditional on the baseline value: worsening if the baseline HAI is 0 and at least 2 points increase or if the baseline HAI is >0 and at least 1 point increase; improvement if the baseline value is at least 2 and at least 1 point decrease; and stable if baseline is 0 or 1 and a 0 or 1 point increase or decrease or baseline is at least 2 and not change.
(1) Odds ratio statistics are from a logistic regression model adjusted for baseline value with Firth's adjustment; (2) Relative risk statistics are based on a generalized linear model of a binomial distribution with log link; (3) Risk difference statistics are calculated from a generalized linear model, correcting for the baseline value.
(4) P-value is for the interaction term of treatment:subgroup from a logistic regression model with the baseline value, treatment, subgroup, and treatment:subgroup interaction as covariates, with Firth's adjustment.
For eculizumab arm, Americas: ARG and USA; Europe: CZE, DEU, DNK, ESP, HRV, ITA, RUS and TUR; Asia-Pacific: AUS, HKG, JPN, KOR, MYS, THA and TWN. For ravulizumab arm, Americas: CAN and USA; Europe: DEU, DNK, ESP, GBR, ITA and POL; Asia-Pacific: AUS, JPN and KOR.
Odds ratio and relative risk are calculated as Ravulizumab/Eculizumab. Risk difference is calculated as Ravulizumab - Eculizumab.
Source: adsl, adeff

Table HAI-1.6

Clinically Important Worsening from Baseline in HAI Score to End of Study Period by Supportive IST use at baseline

Full Analysis Set

IST use at baseline		Statistic	Eculizumab (N=96)	Ravulizumab (N=58)	p-value (4)
Yes	Clinically Important Worsening in HAI Score from Baseline to End of Study Period				0.7890
		n	75	28	
		No Clinically Important Worsening	68 (90.7)	27 (96.4)	
		Clinically Important Worsening	7 (9.3)	1 (3.6)	
	Treatment Effect (Ravulizumab vs Eculizumab)				
		Odds Ratio (1)		0.588	
		(95% CI)		(0.092, 3.766)	
		p-value		0.5752	
		Relative Risk (2)		0.383	
		(95% CI)		(0.049, 2.972)	
		p-value		0.3584	
		Risk Difference (3)		-0.045	
		(95% CI)		(-0.168, 0.078)	
		p-value		0.4701	

The eculizumab group data were collected as part of the PREVENT trial, Study ECU-NMO-301.

End of Study Period is the 6-week assessment after the first On-Trial Relapse for patients who have an On-Trial Relapse or for patients with no On-Trial Relapse: the End of Primary Treatment Period visit for patients in Study ALXN1210-NMO-307 and the End of Study visit for patients in Study ECU-NMO-301.

For those patients who had a missed value at the EOPT Visit or the 6-week post-relapse visit, for patients who had a relapse, the end of study is the last value before the missed value.

Clinically important worsening is conditional on the baseline value: worsening if the baseline HAI is 0 and at least 2 points increase or if the baseline HAI is >0 and at least 1 point increase; improvement if the baseline value is at least 2 and at least 1 point decrease; and stable if baseline is 0 or 1 and a 0 or 1 point increase or decrease or baseline is at least 2 and not change.

(1) Odds ratio statistics are from a logistic regression model adjusted for baseline value with Firth's adjustment; (2) Relative risk statistics are based on a generalized linear model of a binomial distribution with log link; (3) Risk difference statistics are calculated from a generalized linear model, correcting for the baseline value.

(4) P-value is for the interaction term of treatment:subgroup from a logistic regression model with the baseline value, treatment, subgroup, and treatment:subgroup interaction as covariates, with Firth's adjustment.

Odds ratio and relative risk are calculated as Ravulizumab/Eculizumab. Risk difference is calculated as Ravulizumab - Eculizumab.

Source: adsl, adeff

Table HAI-1.6
Clinically Important Worsening from Baseline in HAI Score to End of Study Period by Supportive IST use at baseline
Full Analysis Set

IST use at baseline		Statistic	Eculizumab (N=96)	Ravulizumab (N=58)	p-value (4)
No	Clinically Important Worsening in HAI Score from Baseline to End of Study Period				
		n	21	30	
		No Clinically Important Worsening	20 (95.2)	29 (96.7)	
		Clinically Important Worsening	1 (4.8)	1 (3.3)	
	Treatment Effect (Ravulizumab vs Eculizumab)				
		Odds Ratio (1)		2.469	
		(95% CI)		(0.093, 65.211)	
		p-value		0.5884	
		Relative Risk (2)		0.700	
		(95% CI)		(0.046, 10.575)	
		p-value		0.7968	
		Risk Difference (3)		0.029	
		(95% CI)		(-0.082, 0.141)	
		p-value		0.5993	

The eculizumab group data were collected as part of the PREVENT trial, Study ECU-NMO-301.
End of Study Period is the 6-week assessment after the first On-Trial Relapse for patients who have an On-Trial Relapse or for patients with no On-Trial Relapse: the End of Primary Treatment Period visit for patients in Study ALXN1210-NMO-307 and the End of Study visit for patients in Study ECU-NMO-301.
For those patients who had a missed value at the EOPT Visit or the 6-week post-relapse visit, for patients who had a relapse, the end of study is the last value before the missed value.
Clinically important worsening is conditional on the baseline value: worsening if the baseline HAI is 0 and at least 2 points increase or if the baseline HAI is >0 and at least 1 point increase; improvement if the baseline value is at least 2 and at least 1 point decrease; and stable if baseline is 0 or 1 and a 0 or 1 point increase or decrease or baseline is at least 2 and not change.
(1) Odds ratio statistics are from a logistic regression model adjusted for baseline value with Firth's adjustment; (2) Relative risk statistics are based on a generalized linear model of a binomial distribution with log link; (3) Risk difference statistics are calculated from a generalized linear model, correcting for the baseline value.
(4) P-value is for the interaction term of treatment:subgroup from a logistic regression model with the baseline value, treatment, subgroup, and treatment:subgroup interaction as covariates, with Firth's adjustment.
Odds ratio and relative risk are calculated as Ravulizumab/Eculizumab. Risk difference is calculated as Ravulizumab - Eculizumab.
Source: adsl, adeff

Table HAI-1.7
Clinically Important Worsening from Baseline in HAI Score to End of Study Period by Rituximab use in the prior year
Full Analysis Set

Rituximab use in the prior year		Statistic	Eculizumab (N=96)	Ravulizumab (N=58)	p-value (4)
Yes	Clinically Important Worsening in HAI Score from Baseline to End of Study Period				0.5315
		n	19	20	
		No Clinically Important Worsening	18 (94.7)	19 (95.0)	
		Clinically Important Worsening	1 (5.3)	1 (5.0)	
	Treatment Effect (Ravulizumab vs Eculizumab)				
		Odds Ratio (1)		1.032	
		(95% CI)		(0.086, 12.334)	
		p-value		0.9803	
		Relative Risk (2)		0.950	
		(95% CI)		(0.064, 14.132)	
		p-value		0.9703	
		Risk Difference (3)		0.005	
		(95% CI)		(-0.153, 0.164)	
		p-value		0.9485	

The eculizumab group data were collected as part of the PREVENT trial, Study ECU-NMO-301.
End of Study Period is the 6-week assessment after the first On-Trial Relapse for patients who have an On-Trial Relapse or for patients with no On-Trial Relapse: the End of Primary Treatment Period visit for patients in Study ALXN1210-NMO-307 and the End of Study visit for patients in Study ECU-NMO-301.
For those patients who had a missed value at the EOPT Visit or the 6-week post-relapse visit, for patients who had a relapse, the end of study is the last value before the missed value.
Clinically important worsening is conditional on the baseline value: worsening if the baseline HAI is 0 and at least 2 points increase or if the baseline HAI is >0 and at least 1 point increase; improvement if the baseline value is at least 2 and at least 1 point decrease; and stable if baseline is 0 or 1 and a 0 or 1 point increase or decrease or baseline is at least 2 and not change.
(1) Odds ratio statistics are from a logistic regression model adjusted for baseline value with Firth's adjustment; (2) Relative risk statistics are based on a generalized linear model of a binomial distribution with log link; (3) Risk difference statistics are calculated from a generalized linear model, correcting for the baseline value.
(4) P-value is for the interaction term of treatment:subgroup from a logistic regression model with the baseline value, treatment, subgroup, and treatment:subgroup interaction as covariates, with Firth's adjustment.
Odds ratio and relative risk are calculated as Ravulizumab/Eculizumab. Risk difference is calculated as Ravulizumab - Eculizumab.
Source: adsl, adeff

Table HAI-1.7
Clinically Important Worsening from Baseline in HAI Score to End of Study Period by Rituximab use in the prior year
Full Analysis Set

Rituximab use in the prior year		Statistic	Eculizumab (N=96)	Ravulizumab (N=58)	p-value (4)
No	Clinically Important Worsening in HAI Score from Baseline to End of Study Period				
		n	77	38	
		No Clinically Important Worsening	70 (90.9)	37 (97.4)	
		Clinically Important Worsening	7 (9.1)	1 (2.6)	
	Treatment Effect (Ravulizumab vs Eculizumab)				
		Odds Ratio (1)		0.549	
		(95% CI)		(0.084, 3.574)	
		p-value		0.5301	
		Relative Risk (2)		0.289	
		(95% CI)		(0.037, 2.269)	
		p-value		0.2380	
		Risk Difference (3)		-0.034	
		(95% CI)		(-0.138, 0.069)	
		p-value		0.5137	

The eculizumab group data were collected as part of the PREVENT trial, Study ECU-NMO-301.
End of Study Period is the 6-week assessment after the first On-Trial Relapse for patients who have an On-Trial Relapse or for patients with no On-Trial Relapse: the End of Primary Treatment Period visit for patients in Study ALXN1210-NMO-307 and the End of Study visit for patients in Study ECU-NMO-301.
For those patients who had a missed value at the EOPT Visit or the 6-week post-relapse visit, for patients who had a relapse, the end of study is the last value before the missed value.
Clinically important worsening is conditional on the baseline value: worsening if the baseline HAI is 0 and at least 2 points increase or if the baseline HAI is >0 and at least 1 point increase; improvement if the baseline value is at least 2 and at least 1 point decrease; and stable if baseline is 0 or 1 and a 0 or 1 point increase or decrease or baseline is at least 2 and not change.
(1) Odds ratio statistics are from a logistic regression model adjusted for baseline value with Firth's adjustment; (2) Relative risk statistics are based on a generalized linear model of a binomial distribution with log link; (3) Risk difference statistics are calculated from a generalized linear model, correcting for the baseline value.
(4) P-value is for the interaction term of treatment:subgroup from a logistic regression model with the baseline value, treatment, subgroup, and treatment:subgroup interaction as covariates, with Firth's adjustment.
Odds ratio and relative risk are calculated as Ravulizumab/Eculizumab. Risk difference is calculated as Ravulizumab - Eculizumab.
Source: adsl, adeff

Table HAI-1.4
Clinically Important Worsening from Baseline in HAI Score to End of Study Period by Disease severity via HAI score at baseline
Full Analysis Set

EDSS score at baseline		Statistic	Eculizumab (N=96)	Ravulizumab (N=58)	p-value (4)
< 5	Clinically Important Worsening in HAI Score from Baseline to End of Study Period				0.8172
		n	66	49	
		No Clinically Important Worsening	63 (95.5)	48 (98.0)	
		Clinically Important Worsening	3 (4.5)	1 (2.0)	
	Treatment Effect (Ravulizumab vs Eculizumab)				
		Odds Ratio (1)		0.539	
		(95% CI)		(0.075, 3.868)	
		p-value		0.5392	
		Relative Risk (2)		0.449	
		(95% CI)		(0.048, 4.187)	
		p-value		0.4821	
		Risk Difference (3)		-0.027	
		(95% CI)		(-0.100, 0.045)	
		p-value		0.4574	

The eculizumab group data were collected as part of the PREVENT trial, Study ECU-NMO-301.
End of Study Period is the 6-week assessment after the first On-Trial Relapse for patients who have an On-Trial Relapse or for patients with no On-Trial Relapse: the End of Primary Treatment Period visit for patients in Study ALXN1210-NMO-307 and the End of Study visit for patients in Study ECU-NMO-301.
For those patients who had a missed value at the EOPT Visit or the 6-week post-relapse visit, for patients who had a relapse, the end of study is the last value before the missed value.
Clinically important worsening is conditional on the baseline value: worsening if the baseline HAI is 0 and at least 2 points increase or if the baseline HAI is >0 and at least 1 point increase; improvement if the baseline value is at least 2 and at least 1 point decrease; and stable if baseline is 0 or 1 and a 0 or 1 point increase or decrease or baseline is at least 2 and not change.
(1) Odds ratio statistics are from a logistic regression model adjusted for baseline value with Firth's adjustment; (2) Relative risk statistics are based on a generalized linear model of a binomial distribution with log link; (3) Risk difference statistics are calculated from a generalized linear model, correcting for the baseline value.
(4) P-value is for the interaction term of treatment:subgroup from a logistic regression model with the baseline value, treatment, subgroup, and treatment:subgroup interaction as covariates, with Firth's adjustment.
Odds ratio and relative risk are calculated as Ravulizumab/Eculizumab. Risk difference is calculated as Ravulizumab - Eculizumab.
Source: adsl, adeff

Table HAI-1.4
Clinically Important Worsening from Baseline in HAI Score to End of Study Period by Disease severity via HAI score at baseline
Full Analysis Set

EDSS score at baseline		Statistic	Eculizumab (N=96)	Ravulizumab (N=58)	p-value (4)
>= 5	Clinically Important Worsening in HAI Score from Baseline to End of Study Period				
		n	30	9	
		No Clinically Important Worsening	25 (83.3)	8 (88.9)	
		Clinically Important Worsening	5 (16.7)	1 (11.1)	
	Treatment Effect (Ravulizumab vs Eculizumab)				
		Odds Ratio (1)		0.777	
		(95% CI)		(0.095, 6.351)	
		p-value		0.8139	
		Relative Risk (2)		0.667	
		(95% CI)		(0.089, 4.994)	
		p-value		0.6931	
		Risk Difference (3)		-0.059	
		(95% CI)		(-0.359, 0.242)	
		p-value		0.6943	

The eculizumab group data were collected as part of the PREVENT trial, Study ECU-NMO-301.
End of Study Period is the 6-week assessment after the first On-Trial Relapse for patients who have an On-Trial Relapse or for patients with no On-Trial Relapse: the End of Primary Treatment Period visit for patients in Study ALXN1210-NMO-307 and the End of Study visit for patients in Study ECU-NMO-301.
For those patients who had a missed value at the EOPT Visit or the 6-week post-relapse visit, for patients who had a relapse, the end of study is the last value before the missed value.
Clinically important worsening is conditional on the baseline value: worsening if the baseline HAI is 0 and at least 2 points increase or if the baseline HAI is >0 and at least 1 point increase; improvement if the baseline value is at least 2 and at least 1 point decrease; and stable if baseline is 0 or 1 and a 0 or 1 point increase or decrease or baseline is at least 2 and not change.
(1) Odds ratio statistics are from a logistic regression model adjusted for baseline value with Firth's adjustment; (2) Relative risk statistics are based on a generalized linear model of a binomial distribution with log link; (3) Risk difference statistics are calculated from a generalized linear model, correcting for the baseline value.
(4) P-value is for the interaction term of treatment:subgroup from a logistic regression model with the baseline value, treatment, subgroup, and treatment:subgroup interaction as covariates, with Firth's adjustment.
Odds ratio and relative risk are calculated as Ravulizumab/Eculizumab. Risk difference is calculated as Ravulizumab - Eculizumab.
Source: adsl, adeff

Table VA-1.2
Change from Baseline in Visual Acuity to End of Study Period by Sex
Full Analysis Set

Sex		Statistic	Eculizumab (N=96)	Ravulizumab (N=58)	p-value (4)
Male	Change from Baseline to End of Study Period in Visual Acuity	n	7	5	0.0637
		Mean (SD)	-0.167 (0.2715)	0.036 (0.2612)	
		Median	0.000	0.130	
		Q1, Q3	-0.333, 0.000	0.000, 0.200	
		Min, Max	-0.67, 0.10	-0.40, 0.25	
		Change from baseline LS Means (SEM)	-0.175 (0.090)	0.048 (0.107)	
		95% CI for LS Means (1)	(-0.380, 0.030)	(-0.195, 0.290)	
		Difference in LS Means		0.223	
		(95% CI) (1)		(-0.095, 0.540)	
		p-value (2)		0.1450	
		Standardized Mean Difference		0.455	
		(95% CI) (3)		(-0.707, 1.617)	
	Baseline Visual Acuity	n	7	5	
		Mean (SD)	0.729 (0.4466)	0.780 (0.1789)	
		Median	0.800	0.800	
		Q1, Q3	0.200, 1.000	0.800, 0.800	
		Min, Max	0.10, 1.33	0.50, 1.00	
	End of Study Period Visual Acuity	n	7	5	
		Mean (SD)	0.562 (0.3106)	0.816 (0.3279)	
		Median	0.667	0.800	
		Q1, Q3	0.300, 0.800	0.630, 1.000	
		Min, Max	0.10, 1.00	0.40, 1.25	

The eculizumab group data were collected as part of the PREVENT trial, Study ECU-NMO-301. Visual acuity is analyzed according to the eye with the greater worsening, conditional on patients with adequate eyesight at baseline to perform the test.

End of Study Period is the 6-week assessment after the first On-Trial Relapse for patients who have an On-Trial Relapse or for patients with no On-Trial Relapse: the End of Primary Treatment Period visit for patients in Study ALXN1210-NMO-307 and the End of Study visit for patients in Study ECU-NMO-301.

For those patients who had a missed value at the EOPT Visit or the 6-week post-relapse visit, for patients who had a relapse, the end of study is the last value before the missed value.

(1) The LS means (95% CI) and the difference in LS means (95% CI) are from an ANCOVA model of change from baseline with treatment as factor and baseline value as covariate. (2) The p-value represents the significance of the treatment effect and was derived from an ANCOVA model of the ranked change from baseline, with treatment as a factor, and the ranks of the baseline value included as covariate.

(3) Standardized mean differences (95% CI) were computed using Cohen's D incorporating Hedge's correction on change from baseline. (4) P-value is for the interaction term of treatment:subgroup from a linear regression model of ranked change from baseline with the with ranked baseline value, treatment, subgroup, and treatment:subgroup interaction as covariates.

LS mean difference is calculated as Ravulizumab - Eculizumab.

Source: adsl, adeff

Table VA-1.2
Change from Baseline in Visual Acuity to End of Study Period by Sex
Full Analysis Set

Sex		Statistic	Eculizumab (N=96)	Ravulizumab (N=58)	p-value (4)
Female	Change from Baseline to End of Study Period in Visual Acuity	n	68	47	
		Mean (SD)	-0.028 (0.2596)	-0.110 (0.2603)	
		Median	0.000	0.000	
		Q1, Q3	-0.124, 0.000	-0.200, 0.000	
		Min, Max	-1.00, 0.60	-1.00, 0.50	
		Change from baseline			
		LS Means (SEM)	-0.038 (0.028)	-0.095 (0.034)	
		95% CI for LS Means (1)	(-0.094, 0.018)	(-0.163, -0.027)	
		Difference in LS Means		-0.057	
		(95% CI) (1)		(-0.145, 0.031)	
		p-value (2)		0.2675	
		Standardized Mean Difference		-0.118	
		(95% CI) (3)		(-0.490, 0.255)	
	Baseline Visual Acuity	n	68	47	
		Mean (SD)	0.739 (0.4859)	0.831 (0.3302)	
		Median	0.670	0.800	
		Q1, Q3	0.400, 1.000	0.667, 1.000	
		Min, Max	0.10, 3.00	0.10, 2.00	
	End of Study Period Visual Acuity	n	68	47	
		Mean (SD)	0.711 (0.4530)	0.722 (0.2749)	
		Median	0.667	0.800	
		Q1, Q3	0.365, 1.000	0.500, 1.000	
		Min, Max	0.00, 2.00	0.00, 1.25	

The eculizumab group data were collected as part of the PREVENT trial, Study ECU-NMO-301. Visual acuity is analyzed according to the eye with the greater worsening, conditional on patients with adequate eyesight at baseline to perform the test.

End of Study Period is the 6-week assessment after the first On-Trial Relapse for patients who have an On-Trial Relapse or for patients with no On-Trial Relapse: the End of Primary Treatment Period visit for patients in Study ALXN1210-NMO-307 and the End of Study visit for patients in Study ECU-NMO-301.

For those patients who had a missed value at the EOPT Visit or the 6-week post-relapse visit, for patients who had a relapse, the end of study is the last value before the missed value.

(1) The LS means (95% CI) and the difference in LS means (95% CI) are from an ANCOVA model of change from baseline with treatment as factor and baseline value as covariate. (2) The p-value represents the significance of the treatment effect and was derived from an ANCOVA model of the ranked change from baseline, with treatment as a factor, and the ranks of the baseline value included as covariate.

(3) Standardized mean differences (95% CI) were computed using Cohen's D incorporating Hedge's correction on change from baseline. (4) P-value is for the interaction term of treatment:subgroup from a linear regression model of ranked change from baseline with the with ranked baseline value, treatment, subgroup, and treatment:subgroup interaction as covariates.

LS mean difference is calculated as Ravulizumab - Eculizumab.

Source: adsl, adeff

Table VA-1.3
Change from Baseline in Visual Acuity to End of Study Period by Age Group
Full Analysis Set

Age Group		Statistic	Eculizumab (N=96)	Ravulizumab (N=58)	p-value (4)
< 45 years	Change from Baseline to End of Study Period in Visual Acuity	n	39	21	0.9963
		Mean (SD)	-0.036 (0.2957)	-0.053 (0.2503)	
		Median	0.000	0.000	
		Q1, Q3	-0.100, 0.000	-0.100, 0.000	
		Min, Max	-1.00, 0.53	-1.00, 0.31	
		Change from baseline			
		LS Means (SEM)	-0.034 (0.038)	-0.056 (0.052)	
		95% CI for LS Means (1)	(-0.110, 0.042)	(-0.159, 0.048)	
		Difference in LS Means		-0.021	
		(95% CI) (1)		(-0.150, 0.107)	
		p-value (2)		0.6732	
		Standardized Mean Difference		-0.044	
		(95% CI) (3)		(-0.574, 0.487)	
	Baseline Visual Acuity	n	39	21	
		Mean (SD)	0.816 (0.5435)	0.804 (0.4225)	
		Median	0.800	0.800	
		Q1, Q3	0.400, 1.000	0.630, 1.000	
		Min, Max	0.10, 3.00	0.10, 2.00	
	End of Study Period Visual Acuity	n	39	21	
		Mean (SD)	0.780 (0.4659)	0.750 (0.3222)	
		Median	0.800	0.800	
		Q1, Q3	0.400, 1.000	0.630, 1.000	
		Min, Max	0.00, 2.00	0.00, 1.00	

The eculizumab group data were collected as part of the PREVENT trial, Study ECU-NMO-301. Visual acuity is analyzed according to the eye with the greater worsening, conditional on patients with adequate eyesight at baseline to perform the test.

End of Study Period is the 6-week assessment after the first On-Trial Relapse for patients who have an On-Trial Relapse or for patients with no On-Trial Relapse: the End of Primary Treatment Period visit for patients in Study ALXN1210-NMO-307 and the End of Study visit for patients in Study ECU-NMO-301.

For those patients who had a missed value at the EOPT Visit or the 6-week post-relapse visit, for patients who had a relapse, the end of study is the last value before the missed value.

(1) The LS means (95% CI) and the difference in LS means (95% CI) are from an ANCOVA model of change from baseline with treatment as factor and baseline value as covariate. (2) The p-value represents the significance of the treatment effect and was derived from an ANCOVA model of the ranked change from baseline, with treatment as a factor, and the ranks of the baseline value included as covariate.

(3) Standardized mean differences (95% CI) were computed using Cohen's D incorporating Hedge's correction on change from baseline. (4) P-value is for the interaction term of treatment:subgroup from a linear regression model of ranked change from baseline with the with ranked baseline value, treatment, subgroup, and treatment:subgroup interaction as covariates.

LS mean difference is calculated as Ravulizumab - Eculizumab.

Source: adsl, adeff

Table VA-1.3
Change from Baseline in Visual Acuity to End of Study Period by Age Group
Full Analysis Set

Age Group		Statistic	Eculizumab (N=96)	Ravulizumab (N=58)	p-value (4)
>= 45 years	Change from Baseline to End of Study Period in Visual Acuity	n	36	31	
		Mean (SD)	-0.047 (0.2239)	-0.125 (0.2690)	
		Median	0.000	0.000	
		Q1, Q3	-0.200, 0.000	-0.370, 0.000	
		Min, Max	-0.51, 0.60	-0.68, 0.50	
		Change from baseline			
		LS Means (SEM)	-0.067 (0.040)	-0.100 (0.043)	
		95% CI for LS Means (1)	(-0.147, 0.013)	(-0.187, -0.014)	
		Difference in LS Means		-0.033	
		(95% CI) (1)		(-0.153, 0.087)	
		p-value (2)		0.9543	
		Standardized Mean Difference		-0.068	
		(95% CI) (3)		(-0.548, 0.413)	
	Baseline Visual Acuity	n	36	31	
		Mean (SD)	0.653 (0.3889)	0.842 (0.2286)	
		Median	0.667	0.800	
		Q1, Q3	0.400, 1.000	0.800, 1.000	
		Min, Max	0.10, 2.00	0.30, 1.25	
	End of Study Period Visual Acuity	n	36	31	
		Mean (SD)	0.607 (0.4022)	0.717 (0.2488)	
		Median	0.667	0.800	
		Q1, Q3	0.286, 0.800	0.500, 0.800	
		Min, Max	0.00, 2.00	0.12, 1.25	

The eculizumab group data were collected as part of the PREVENT trial, Study ECU-NMO-301. Visual acuity is analyzed according to the eye with the greater worsening, conditional on patients with adequate eyesight at baseline to perform the test.

End of Study Period is the 6-week assessment after the first On-Trial Relapse for patients who have an On-Trial Relapse or for patients with no On-Trial Relapse: the End of Primary Treatment Period visit for patients in Study ALXN1210-NMO-307 and the End of Study visit for patients in Study ECU-NMO-301.

For those patients who had a missed value at the EOPT Visit or the 6-week post-relapse visit, for patients who had a relapse, the end of study is the last value before the missed value.

(1) The LS means (95% CI) and the difference in LS means (95% CI) are from an ANCOVA model of change from baseline with treatment as factor and baseline value as covariate. (2) The p-value represents the significance of the treatment effect and was derived from an ANCOVA model of the ranked change from baseline, with treatment as a factor, and the ranks of the baseline value included as covariate.

(3) Standardized mean differences (95% CI) were computed using Cohen's D incorporating Hedge's correction on change from baseline. (4) P-value is for the interaction term of treatment:subgroup from a linear regression model of ranked change from baseline with the with ranked baseline value, treatment, subgroup, and treatment:subgroup interaction as covariates.

LS mean difference is calculated as Ravulizumab - Eculizumab.

Source: adsl, adeff

Table VA-1.5
Change from Baseline in Visual Acuity to End of Study Period by Region
Full Analysis Set

Region		Statistic	Eculizumab (N=96)	Ravulizumab (N=58)	p-value (4)
Asia-Pacific	Change from Baseline to End of Study Period in Visual Acuity	n	27	17	0.0856
		Mean (SD)	0.024 (0.3252)	-0.119 (0.3141)	
		Median	0.000	-0.170	
		Q1, Q3	-0.133, 0.333	-0.370, 0.000	
		Min, Max	-0.67, 0.60	-0.68, 0.50	
		Change from baseline			
		LS Means (SEM)	0.030 (0.054)	-0.128 (0.067)	
		95% CI for LS Means (1)	(-0.078, 0.138)	(-0.264, 0.009)	
		Difference in LS Means		-0.157	
		(95% CI) (1)		(-0.332, 0.017)	
		p-value (2)		0.0585	
		Standardized Mean Difference		-0.299	
		(95% CI) (3)		(-0.909, 0.311)	
	Baseline Visual Acuity	n	27	17	
		Mean (SD)	0.821 (0.4101)	0.789 (0.2523)	
		Median	0.800	0.800	
		Q1, Q3	0.400, 1.000	0.800, 1.000	
		Min, Max	0.20, 1.54	0.30, 1.20	
	End of Study Period Visual Acuity	n	27	17	
		Mean (SD)	0.845 (0.3843)	0.671 (0.2347)	
		Median	0.800	0.630	
		Q1, Q3	0.667, 1.000	0.630, 0.800	
		Min, Max	0.29, 2.00	0.12, 1.00	

The eculizumab group data were collected as part of the PREVENT trial, Study ECU-NMO-301. Visual acuity is analyzed according to the eye with the greater worsening, conditional on patients with adequate eyesight at baseline to perform the test.

End of Study Period is the 6-week assessment after the first On-Trial Relapse for patients who have an On-Trial Relapse or for patients with no On-Trial Relapse: the End of Primary Treatment Period visit for patients in Study ALXN1210-NMO-307 and the End of Study visit for patients in Study ECU-NMO-301.

For those patients who had a missed value at the EOPT Visit or the 6-week post-relapse visit, for patients who had a relapse, the end of study is the last value before the missed value.

(1) The LS means (95% CI) and the difference in LS means (95% CI) are from an ANCOVA model of change from baseline with treatment as factor and baseline value as covariate. (2) The p-value represents the significance of the treatment effect and was derived from an ANCOVA model of the ranked change from baseline, with treatment as a factor, and the ranks of the baseline value included as covariate.

(3) Standardized mean differences (95% CI) were computed using Cohen's D incorporating Hedge's correction on change from baseline. (4) P-value is for the interaction term of treatment:subgroup from a linear regression model of ranked change from baseline with the with ranked baseline value, treatment, subgroup, and treatment:subgroup interaction as covariates. LS mean difference is calculated as Ravulizumab - Eculizumab.

For eculizumab arm, Americas: ARG and USA; Europe: CZE, DEU, DNK, ESP, HRV, ITA, RUS and TUR; Asia-Pacific: AUS, HKG, JPN, KOR, MYS, THA and TWN. For ravulizumab arm, Americas: CAN and USA; Europe: DEU, DNK, ESP, GBR, ITA and POL; Asia-Pacific: AUS, JPN and KOR.

Source: adsl, adeff

Table VA-1.5
Change from Baseline in Visual Acuity to End of Study Period by Region
Full Analysis Set

Region		Statistic	Eculizumab (N=96)	Ravulizumab (N=58)	p-value (4)
Americas	Change from Baseline to End of Study Period in Visual Acuity	n	23	20	0.9168
		Mean (SD)	-0.061 (0.1826)	-0.108 (0.2751)	
		Median	0.000	0.000	
		Q1, Q3	-0.114, 0.000	-0.183, 0.000	
		Min, Max	-0.51, 0.20	-1.00, 0.25	
		Change from baseline			
		LS Means (SEM)	-0.101 (0.046)	-0.063 (0.050)	
		95% CI for LS Means (1)	(-0.194, -0.008)	(-0.163, 0.037)	
		Difference in LS Means		0.037	
		(95% CI) (1)		(-0.105, 0.180)	
		p-value (2)		0.9466	
		Standardized Mean Difference		0.080	
		(95% CI) (3)		(-0.520, 0.679)	
	Baseline Visual Acuity	n	23	20	
		Mean (SD)	0.570 (0.3436)	0.893 (0.4025)	
		Median	0.667	1.000	
		Q1, Q3	0.200, 0.800	0.800, 1.000	
		Min, Max	0.10, 1.00	0.10, 2.00	
	End of Study Period Visual Acuity	n	23	20	
		Mean (SD)	0.509 (0.3590)	0.785 (0.3277)	
		Median	0.571	0.800	
		Q1, Q3	0.100, 0.800	0.650, 1.000	
		Min, Max	0.00, 1.00	0.00, 1.25	

The eculizumab group data were collected as part of the PREVENT trial, Study ECU-NMO-301. Visual acuity is analyzed according to the eye with the greater worsening, conditional on patients with adequate eyesight at baseline to perform the test.

End of Study Period is the 6-week assessment after the first On-Trial Relapse for patients who have an On-Trial Relapse or for patients with no On-Trial Relapse: the End of Primary Treatment Period visit for patients in Study ALXN1210-NMO-307 and the End of Study visit for patients in Study ECU-NMO-301.

For those patients who had a missed value at the EOPT Visit or the 6-week post-relapse visit, for patients who had a relapse, the end of study is the last value before the missed value.

(1) The LS means (95% CI) and the difference in LS means (95% CI) are from an ANCOVA model of change from baseline with treatment as factor and baseline value as covariate. (2) The p-value represents the significance of the treatment effect and was derived from an ANCOVA model of the ranked change from baseline, with treatment as a factor, and the ranks of the baseline value included as covariate.

(3) Standardized mean differences (95% CI) were computed using Cohen's D incorporating Hedge's correction on change from baseline. (4) P-value is for the interaction term of treatment:subgroup from a linear regression model of ranked change from baseline with the with ranked baseline value, treatment, subgroup, and treatment:subgroup interaction as covariates. LS mean difference is calculated as Ravulizumab - Eculizumab.

For eculizumab arm, Americas: ARG and USA; Europe: CZE, DEU, DNK, ESP, HRV, ITA, RUS and TUR; Asia-Pacific: AUS, HKG, JPN, KOR, MYS, THA and TWN. For ravulizumab arm, Americas: CAN and USA; Europe: DEU, DNK, ESP, GBR, ITA and POL; Asia-Pacific: AUS, JPN and KOR.

Source: adsl, adeff

Table VA-1.5
Change from Baseline in Visual Acuity to End of Study Period by Region
Full Analysis Set

Region		Statistic	Eculizumab (N=96)	Ravulizumab (N=58)	p-value (4)
Europe	Change from Baseline to End of Study Period in Visual Acuity	n	25	15	
		Mean (SD)	-0.092 (0.2420)	-0.053 (0.1753)	
		Median	0.000	0.000	
		Q1, Q3	-0.170, 0.000	-0.130, 0.000	
		Min, Max	-1.00, 0.30	-0.53, 0.20	
		Change from baseline			
		LS Means (SEM)	-0.090 (0.038)	-0.056 (0.049)	
		95% CI for LS Means (1)	(-0.167, -0.014)	(-0.155, 0.043)	
		Difference in LS Means		0.034	
		(95% CI) (1)		(-0.091, 0.159)	
		p-value (2)		0.6185	
		Standardized Mean Difference		0.079	
		(95% CI) (3)		(-0.562, 0.719)	
	Baseline Visual Acuity	n	25	15	
		Mean (SD)	0.802 (0.6161)	0.779 (0.2553)	
		Median	0.670	0.800	
		Q1, Q3	0.400, 1.000	0.630, 1.000	
		Min, Max	0.10, 3.00	0.20, 1.20	
	End of Study Period Visual Acuity	n	25	15	
		Mean (SD)	0.710 (0.5159)	0.726 (0.2543)	
		Median	0.800	0.800	
		Q1, Q3	0.330, 1.000	0.500, 1.000	
		Min, Max	0.00, 2.00	0.20, 1.00	

The eculizumab group data were collected as part of the PREVENT trial, Study ECU-NMO-301. Visual acuity is analyzed according to the eye with the greater worsening, conditional on patients with adequate eyesight at baseline to perform the test.

End of Study Period is the 6-week assessment after the first On-Trial Relapse for patients who have an On-Trial Relapse or for patients with no On-Trial Relapse: the End of Primary Treatment Period visit for patients in Study ALXN1210-NMO-307 and the End of Study visit for patients in Study ECU-NMO-301.

For those patients who had a missed value at the EOPT Visit or the 6-week post-relapse visit, for patients who had a relapse, the end of study is the last value before the missed value.

(1) The LS means (95% CI) and the difference in LS means (95% CI) are from an ANCOVA model of change from baseline with treatment as factor and baseline value as covariate. (2) The p-value represents the significance of the treatment effect and was derived from an ANCOVA model of the ranked change from baseline, with treatment as a factor, and the ranks of the baseline value included as covariate.

(3) Standardized mean differences (95% CI) were computed using Cohen's D incorporating Hedge's correction on change from baseline. (4) P-value is for the interaction term of treatment:subgroup from a linear regression model of ranked change from baseline with the with ranked baseline value, treatment, subgroup, and treatment:subgroup interaction as covariates. LS mean difference is calculated as Ravulizumab - Eculizumab.

For eculizumab arm, Americas: ARG and USA; Europe: CZE, DEU, DNK, ESP, HRV, ITA, RUS and TUR; Asia-Pacific: AUS, HKG, JPN, KOR, MYS, THA and TWN. For ravulizumab arm, Americas: CAN and USA; Europe: DEU, DNK, ESP, GBR, ITA and POL; Asia-Pacific: AUS, JPN and KOR.

Source: adsl, adeff

Table VA-1.6
Change from Baseline in Visual Acuity to End of Study Period by Supportive IST use at baseline
Full Analysis Set

IST use at baseline		Statistic	Eculizumab (N=96)	Ravulizumab (N=58)	p-value (4)
Yes	Change from Baseline to End of Study Period in Visual Acuity	n	60	24	0.1203
		Mean (SD)	-0.041 (0.2841)	-0.169 (0.3196)	
		Median	0.000	-0.100	
		Q1, Q3	-0.142, 0.000	-0.370, 0.000	
		Min, Max	-1.00, 0.60	-1.00, 0.50	
		Change from baseline			
		LS Means (SEM)	-0.053 (0.032)	-0.140 (0.051)	
		95% CI for LS Means (1)	(-0.117, 0.011)	(-0.241, -0.039)	
		Difference in LS Means		-0.087	
		(95% CI) (1)		(-0.207, 0.033)	
		p-value (2)		0.1488	
		Standardized Mean Difference		-0.175	
		(95% CI) (3)		(-0.649, 0.300)	
	Baseline Visual Acuity	n	60	24	
		Mean (SD)	0.756 (0.4591)	0.865 (0.3782)	
		Median	0.775	0.800	
		Q1, Q3	0.400, 1.000	0.800, 1.000	
		Min, Max	0.10, 3.00	0.10, 2.00	
	End of Study Period Visual Acuity	n	60	24	
		Mean (SD)	0.714 (0.3946)	0.697 (0.2985)	
		Median	0.667	0.648	
		Q1, Q3	0.400, 1.000	0.565, 1.000	
		Min, Max	0.00, 2.00	0.00, 1.25	

The eculizumab group data were collected as part of the PREVENT trial, Study ECU-NMO-301. Visual acuity is analyzed according to the eye with the greater worsening, conditional on patients with adequate eyesight at baseline to perform the test.

End of Study Period is the 6-week assessment after the first On-Trial Relapse for patients who have an On-Trial Relapse or for patients with no On-Trial Relapse: the End of Primary Treatment Period visit for patients in Study ALXN1210-NMO-307 and the End of Study visit for patients in Study ECU-NMO-301.

For those patients who had a missed value at the EOPT Visit or the 6-week post-relapse visit, for patients who had a relapse, the end of study is the last value before the missed value.

(1) The LS means (95% CI) and the difference in LS means (95% CI) are from an ANCOVA model of change from baseline with treatment as factor and baseline value as covariate. (2) The p-value represents the significance of the treatment effect and was derived from an ANCOVA model of the ranked change from baseline, with treatment as a factor, and the ranks of the baseline value included as covariate.

(3) Standardized mean differences (95% CI) were computed using Cohen's D incorporating Hedge's correction on change from baseline. (4) P-value is for the interaction term of treatment:subgroup from a linear regression model of ranked change from baseline with the with ranked baseline value, treatment, subgroup, and treatment:subgroup interaction as covariates.

LS mean difference is calculated as Ravulizumab - Eculizumab.

Source: adsl, adeff

Table VA-1.6
Change from Baseline in Visual Acuity to End of Study Period by Supportive IST use at baseline
Full Analysis Set

IST use at baseline		Statistic	Eculizumab (N=96)	Ravulizumab (N=58)	p-value (4)
No	Change from Baseline to End of Study Period in Visual Acuity	n	15	28	
		Mean (SD)	-0.038 (0.1508)	-0.033 (0.1825)	
		Median	0.000	0.000	
		Q1, Q3	-0.186, 0.000	-0.148, 0.000	
		Min, Max	-0.27, 0.30	-0.50, 0.30	
		Change from baseline			
		LS Means (SEM)	-0.041 (0.045)	-0.031 (0.033)	
		95% CI for LS Means (1)	(-0.133, 0.050)	(-0.098, 0.035)	
		Difference in LS Means		0.010	
		(95% CI) (1)		(-0.104, 0.124)	
		p-value (2)		0.6372	
		Standardized Mean Difference		0.024	
		(95% CI) (3)		(-0.603, 0.651)	
	Baseline Visual Acuity	n	15	28	
		Mean (SD)	0.665 (0.5657)	0.793 (0.2580)	
		Median	0.630	0.800	
		Q1, Q3	0.100, 1.000	0.648, 1.000	
		Min, Max	0.10, 2.00	0.10, 1.25	
	End of Study Period Visual Acuity	n	15	28	
		Mean (SD)	0.627 (0.6091)	0.760 (0.2615)	
		Median	0.667	0.800	
		Q1, Q3	0.100, 1.000	0.565, 1.000	
		Min, Max	0.00, 2.00	0.10, 1.25	

The eculizumab group data were collected as part of the PREVENT trial, Study ECU-NMO-301. Visual acuity is analyzed according to the eye with the greater worsening, conditional on patients with adequate eyesight at baseline to perform the test.

End of Study Period is the 6-week assessment after the first On-Trial Relapse for patients who have an On-Trial Relapse or for patients with no On-Trial Relapse: the End of Primary Treatment Period visit for patients in Study ALXN1210-NMO-307 and the End of Study visit for patients in Study ECU-NMO-301.

For those patients who had a missed value at the EOPT Visit or the 6-week post-relapse visit, for patients who had a relapse, the end of study is the last value before the missed value.

(1) The LS means (95% CI) and the difference in LS means (95% CI) are from an ANCOVA model of change from baseline with treatment as factor and baseline value as covariate. (2) The p-value represents the significance of the treatment effect and was derived from an ANCOVA model of the ranked change from baseline, with treatment as a factor, and the ranks of the baseline value included as covariate.

(3) Standardized mean differences (95% CI) were computed using Cohen's D incorporating Hedge's correction on change from baseline. (4) P-value is for the interaction term of treatment:subgroup from a linear regression model of ranked change from baseline with the with ranked baseline value, treatment, subgroup, and treatment:subgroup interaction as covariates.

LS mean difference is calculated as Ravulizumab - Eculizumab.

Source: adsl, adeff

Table VA-1.7
Change from Baseline in Visual Acuity to End of Study Period by Rituximab use in the prior year
Full Analysis Set

Rituximab use in the prior year		Statistic	Eculizumab (N=96)	Ravulizumab (N=58)	p-value (4)
Yes	Change from Baseline to End of Study Period in Visual Acuity	n	17	20	0.0949
		Mean (SD)	-0.066 (0.2126)	-0.032 (0.1672)	
		Median	0.000	0.000	
		Q1, Q3	-0.150, 0.000	-0.100, 0.000	
		Min, Max	-0.51, 0.40	-0.50, 0.30	
		Change from baseline LS Means (SEM)	-0.085 (0.047)	-0.016 (0.043)	
		95% CI for LS Means (1)	(-0.181, 0.010)	(-0.103, 0.071)	
		Difference in LS Means (95% CI) (1)		0.069 (-0.064, 0.203)	
		p-value (2)		0.3600	
		Standardized Mean Difference (95% CI) (3)		0.158 (-0.490, 0.805)	
	Baseline Visual Acuity	n	17	20	
		Mean (SD)	0.566 (0.3577)	0.813 (0.3077)	
		Median	0.667	0.900	
		Q1, Q3	0.200, 0.800	0.650, 1.000	
		Min, Max	0.10, 1.00	0.10, 1.25	
	End of Study Period Visual Acuity	n	17	20	
		Mean (SD)	0.499 (0.3576)	0.780 (0.3201)	
		Median	0.571	0.800	
		Q1, Q3	0.100, 0.800	0.650, 1.000	
		Min, Max	0.00, 1.00	0.00, 1.25	

The eculizumab group data were collected as part of the PREVENT trial, Study ECU-NMO-301. Visual acuity is analyzed according to the eye with the greater worsening, conditional on patients with adequate eyesight at baseline to perform the test.

End of Study Period is the 6-week assessment after the first On-Trial Relapse for patients who have an On-Trial Relapse or for patients with no On-Trial Relapse: the End of Primary Treatment Period visit for patients in Study ALXN1210-NMO-307 and the End of Study visit for patients in Study ECU-NMO-301.

For those patients who had a missed value at the EOPT Visit or the 6-week post-relapse visit, for patients who had a relapse, the end of study is the last value before the missed value.

(1) The LS means (95% CI) and the difference in LS means (95% CI) are from an ANCOVA model of change from baseline with treatment as factor and baseline value as covariate. (2) The p-value represents the significance of the treatment effect and was derived from an ANCOVA model of the ranked change from baseline, with treatment as a factor, and the ranks of the baseline value included as covariate.

(3) Standardized mean differences (95% CI) were computed using Cohen's D incorporating Hedge's correction on change from baseline. (4) P-value is for the interaction term of treatment:subgroup from a linear regression model of ranked change from baseline with the with ranked baseline value, treatment, subgroup, and treatment:subgroup interaction as covariates.

LS mean difference is calculated as Ravulizumab - Eculizumab.

Source: adsl, adeff

Table VA-1.7
Change from Baseline in Visual Acuity to End of Study Period by Rituximab use in the prior year
Full Analysis Set

Rituximab use in the prior year		Statistic	Eculizumab (N=96)	Ravulizumab (N=58)	p-value (4)
No	Change from Baseline to End of Study Period in Visual Acuity	n	58	32	
		Mean (SD)	-0.033 (0.2760)	-0.135 (0.3019)	
		Median	0.000	-0.015	
		Q1, Q3	-0.133, 0.038	-0.300, 0.000	
		Min, Max	-1.00, 0.60	-1.00, 0.50	
		Change from baseline			
		LS Means (SEM)	-0.039 (0.033)	-0.126 (0.044)	
		95% CI for LS Means (1)	(-0.104, 0.026)	(-0.213, -0.038)	
		Difference in LS Means		-0.087	
		(95% CI) (1)		(-0.195, 0.022)	
		p-value (2)		0.2040	
		Standardized Mean Difference		-0.174	
		(95% CI) (3)		(-0.607, 0.258)	
	Baseline Visual Acuity	n	58	32	
		Mean (SD)	0.788 (0.5011)	0.835 (0.3287)	
		Median	0.735	0.800	
		Q1, Q3	0.400, 1.000	0.733, 1.000	
		Min, Max	0.10, 3.00	0.10, 2.00	
	End of Study Period Visual Acuity	n	58	32	
		Mean (SD)	0.755 (0.4505)	0.700 (0.2490)	
		Median	0.775	0.733	
		Q1, Q3	0.400, 1.000	0.565, 0.900	
		Min, Max	0.00, 2.00	0.10, 1.00	

The eculizumab group data were collected as part of the PREVENT trial, Study ECU-NMO-301. Visual acuity is analyzed according to the eye with the greater worsening, conditional on patients with adequate eyesight at baseline to perform the test.

End of Study Period is the 6-week assessment after the first On-Trial Relapse for patients who have an On-Trial Relapse or for patients with no On-Trial Relapse: the End of Primary Treatment Period visit for patients in Study ALXN1210-NMO-307 and the End of Study visit for patients in Study ECU-NMO-301.

For those patients who had a missed value at the EOPT Visit or the 6-week post-relapse visit, for patients who had a relapse, the end of study is the last value before the missed value.

(1) The LS means (95% CI) and the difference in LS means (95% CI) are from an ANCOVA model of change from baseline with treatment as factor and baseline value as covariate. (2) The p-value represents the significance of the treatment effect and was derived from an ANCOVA model of the ranked change from baseline, with treatment as a factor, and the ranks of the baseline value included as covariate.

(3) Standardized mean differences (95% CI) were computed using Cohen's D incorporating Hedge's correction on change from baseline. (4) P-value is for the interaction term of treatment:subgroup from a linear regression model of ranked change from baseline with the with ranked baseline value, treatment, subgroup, and treatment:subgroup interaction as covariates.

LS mean difference is calculated as Ravulizumab - Eculizumab.

Source: adsl, adeff

Table VA-1.4
Change from Baseline in Visual Acuity to End of Study Period by Disease severity via EDSS Score at baseline
Full Analysis Set

EDSS score at baseline		Statistic	Eculizumab (N=96)	Ravulizumab (N=58)	p-value (4)
< 5	Change from Baseline to End of Study Period in Visual Acuity	n	53	45	0.3315
		Mean (SD)	-0.044 (0.2602)	-0.085 (0.2727)	
		Median	0.000	0.000	
		Q1, Q3	-0.100, 0.000	-0.170, 0.000	
		Min, Max	-1.00, 0.53	-1.00, 0.50	
		Change from baseline			
		LS Means (SEM)	-0.047 (0.032)	-0.081 (0.035)	
		95% CI for LS Means (1)	(-0.111, 0.016)	(-0.150, -0.012)	
		Difference in LS Means		-0.034	
		(95% CI) (1)		(-0.127, 0.060)	
		p-value (2)		0.7504	
		Standardized Mean Difference		-0.070	
		(95% CI) (3)		(-0.467, 0.328)	
	Baseline Visual Acuity	n	53	45	
		Mean (SD)	0.822 (0.5122)	0.847 (0.3168)	
		Median	0.800	0.800	
		Q1, Q3	0.500, 1.000	0.800, 1.000	
		Min, Max	0.10, 3.00	0.10, 2.00	
	End of Study Period Visual Acuity	n	53	45	
		Mean (SD)	0.778 (0.4529)	0.762 (0.2756)	
		Median	0.800	0.800	
		Q1, Q3	0.500, 1.000	0.630, 1.000	
		Min, Max	0.00, 2.00	0.00, 1.25	

The eculizumab group data were collected as part of the PREVENT trial, Study ECU-NMO-301. Visual acuity is analyzed according to the eye with the greater worsening, conditional on patients with adequate eyesight at baseline to perform the test.

End of Study Period is the 6-week assessment after the first On-Trial Relapse for patients who have an On-Trial Relapse or for patients with no On-Trial Relapse: the End of Primary Treatment Period visit for patients in Study ALXN1210-NMO-307 and the End of Study visit for patients in Study ECU-NMO-301.

For those patients who had a missed value at the EOPT Visit or the 6-week post-relapse visit, for patients who had a relapse, the end of study is the last value before the missed value.

(1) The LS means (95% CI) and the difference in LS means (95% CI) are from an ANCOVA model of change from baseline with treatment as factor and baseline value as covariate. (2) The p-value represents the significance of the treatment effect and was derived from an ANCOVA model of the ranked change from baseline, with treatment as a factor, and the ranks of the baseline value included as covariate.

(3) Standardized mean differences (95% CI) were computed using Cohen's D incorporating Hedge's correction on change from baseline. (4) P-value is for the interaction term of treatment:subgroup from a linear regression model of ranked change from baseline with the with ranked baseline value, treatment, subgroup, and treatment:subgroup interaction as covariates.

LS mean difference is calculated as Ravulizumab - Eculizumab.

Source: adsl, adeff

Table VA-1.4
Change from Baseline in Visual Acuity to End of Study Period by Disease severity via EDSS Score at baseline
Full Analysis Set

EDSS score at baseline		Statistic	Eculizumab (N=96)	Ravulizumab (N=58)	p-value (4)
>= 5	Change from Baseline to End of Study Period in Visual Acuity	n	22	7	
		Mean (SD)	-0.034 (0.2724)	-0.167 (0.1700)	
		Median	0.000	-0.167	
		Q1, Q3	-0.186, 0.100	-0.200, 0.000	
		Min, Max	-0.51, 0.60	-0.50, 0.00	
		Change from baseline			
		LS Means (SEM)	-0.045 (0.052)	-0.132 (0.093)	
		95% CI for LS Means (1)	(-0.151, 0.061)	(-0.323, 0.059)	
		Difference in LS Means		-0.087	
		(95% CI) (1)		(-0.307, 0.134)	
		p-value (2)		0.4247	
		Standardized Mean Difference		-0.176	
		(95% CI) (3)		(-1.027, 0.676)	
	Baseline Visual Acuity	n	22	7	
		Mean (SD)	0.534 (0.3151)	0.695 (0.3165)	
		Median	0.450	0.667	
		Q1, Q3	0.286, 0.800	0.500, 1.000	
		Min, Max	0.10, 1.00	0.20, 1.00	
	End of Study Period Visual Acuity	n	22	7	
		Mean (SD)	0.500 (0.3520)	0.529 (0.2138)	
		Median	0.400	0.500	
		Q1, Q3	0.286, 0.800	0.400, 0.800	
		Min, Max	0.00, 1.00	0.20, 0.80	

The eculizumab group data were collected as part of the PREVENT trial, Study ECU-NMO-301. Visual acuity is analyzed according to the eye with the greater worsening, conditional on patients with adequate eyesight at baseline to perform the test.

End of Study Period is the 6-week assessment after the first On-Trial Relapse for patients who have an On-Trial Relapse or for patients with no On-Trial Relapse: the End of Primary Treatment Period visit for patients in Study ALXN1210-NMO-307 and the End of Study visit for patients in Study ECU-NMO-301.

For those patients who had a missed value at the EOPT Visit or the 6-week post-relapse visit, for patients who had a relapse, the end of study is the last value before the missed value.

(1) The LS means (95% CI) and the difference in LS means (95% CI) are from an ANCOVA model of change from baseline with treatment as factor and baseline value as covariate. (2) The p-value represents the significance of the treatment effect and was derived from an ANCOVA model of the ranked change from baseline, with treatment as a factor, and the ranks of the baseline value included as covariate.

(3) Standardized mean differences (95% CI) were computed using Cohen's D incorporating Hedge's correction on change from baseline. (4) P-value is for the interaction term of treatment:subgroup from a linear regression model of ranked change from baseline with the with ranked baseline value, treatment, subgroup, and treatment:subgroup interaction as covariates.

LS mean difference is calculated as Ravulizumab - Eculizumab.

Source: adsl, adeff

Table EQ-5D-1.2
Change from Baseline in EQ-5D VAS Score to End of Study Period by Sex
Full Analysis Set

Sex		Statistic	Eculizumab (N=96)	Ravulizumab (N=58)	p-value (7)
Male	Change from Baseline to End of Study Period in EQ-5D VAS Score	n	8	6	0.9542
		Mean (SD)	6.3 (23.84)	0.0 (8.10)	
		Median	3.5	0.0	
		Q1, Q3	-11.0, 29.0	-8.0, 8.0	
		Min, Max	-30, 37	-10, 10	
		Change from baseline			
		LS Means (SEM)	2.997 (7.315)	4.337 (8.685)	
		95% CI for LS Means (1)	(-13.103, 19.097)	(-14.778, 23.453)	
		Difference in LS Means		1.340	
		(95% CI) (1)		(-25.924, 28.605)	
		p-value (2)		0.6179	
		Standardized Mean Difference		0.293	
		(95% CI) (3)		(-0.771, 1.357)	
		Responders (15% [15 points]), n(%)	3 (37.5)	0	
		Odds Ratio (4)		0.206	
		(95% CI)		(0.005, 9.182)	
		p-value		0.4145	
		Relative Risk (5)		0.000	
		(95% CI)		--	
		p-value		0.9999	

The eculizumab group data were collected as part of the PREVENT trial, Study ECU-NMO-301.

End of Study Period is the 6-week assessment after the first On-Trial Relapse for patients who have an On-Trial Relapse or for patients with no On-Trial Relapse: the End of Primary Treatment Period visit for patients in Study ALXN1210-NMO-307 and the End of Study visit for patients in Study ECU-NMO-301.

For those patients who had a missed value at the EOPT Visit or the 6-week post-relapse visit, for patients who had a relapse, the end of study is the last value before the missed value.

(1) The LS means (95% CI) and the difference in LS means (95% CI) are from an ANCOVA model of change from baseline with treatment as factor and baseline value as covariate. (2) The p-value represents the significance of the treatment effect and was derived from an ANCOVA model of the ranked change from baseline, with treatment as a factor, and the ranks of the baseline value included as covariate.

(3) Standardized mean differences (95% CI) were computed using Cohen's D incorporating Hedge's correction on change from baseline. (4) Odds ratio statistics are from a logistic regression model adjusted for baseline value with Firth's adjustment; (5) Relative risk statistics are based on a generalized linear model of a binomial distribution with log link;

(6) Risk difference statistics are calculated from a generalized linear model, correcting for the baseline value. (7) P-value is for the interaction term of treatment:subgroup from a linear regression model of ranked change from baseline with the with ranked baseline value, treatment, subgroup, and treatment:subgroup interaction as covariates.

Odds ratio and relative risk are calculated as Ravulizumab/Eculizumab. LS mean difference and risk difference are calculated as Ravulizumab - Eculizumab.

Source: adsl, adeq5d

Table EQ-5D-1.2
Change from Baseline in EQ-5D VAS Score to End of Study Period by Sex
Full Analysis Set

Sex	Statistic	Eculizumab (N=96)	Ravulizumab (N=58)	p-value (7)
	Risk Difference (6)		-0.219	
	(95% CI)		(-0.789, 0.351)	
	p-value		0.4158	
Baseline EQ-5D VAS Score	n	8	6	
	Mean (SD)	60.9 (20.25)	81.3 (4.32)	
	Median	70.0	80.0	
	Q1, Q3	45.0, 75.0	80.0, 80.0	
	Min, Max	25, 82	78, 90	
End of Study Period EQ-5D VAS Score	n	8	6	
	Mean (SD)	67.1 (26.22)	81.3 (7.23)	
	Median	72.5	81.0	
	Q1, Q3	54.0, 86.0	78.0, 88.0	
	Min, Max	17, 95	70, 90	

The eculizumab group data were collected as part of the PREVENT trial, Study ECU-NMO-301.

End of Study Period is the 6-week assessment after the first On-Trial Relapse for patients who have an On-Trial Relapse or for patients with no On-Trial Relapse: the End of Primary Treatment Period visit for patients in Study ALXN1210-NMO-307 and the End of Study visit for patients in Study ECU-NMO-301.

For those patients who had a missed value at the EOPT Visit or the 6-week post-relapse visit, for patients who had a relapse, the end of study is the last value before the missed value.

(1) The LS means (95% CI) and the difference in LS means (95% CI) are from an ANCOVA model of change from baseline with treatment as factor and baseline value as covariate. (2) The p-value represents the significance of the treatment effect and was derived from an ANCOVA model of the ranked change from baseline, with treatment as a factor, and the ranks of the baseline value included as covariate.

(3) Standardized mean differences (95% CI) were computed using Cohen's D incorporating Hedge's correction on change from baseline. (4) Odds ratio statistics are from a logistic regression model adjusted for baseline value with Firth's adjustment; (5) Relative risk statistics are based on a generalized linear model of a binomial distribution with log link;

(6) Risk difference statistics are calculated from a generalized linear model, correcting for the baseline value. (7) P-value is for the interaction term of treatment:subgroup from a linear regression model of ranked change from baseline with the with ranked baseline value, treatment, subgroup, and treatment:subgroup interaction as covariates.

Odds ratio and relative risk are calculated as Ravulizumab/Eculizumab. LS mean difference and risk difference are calculated as Ravulizumab - Eculizumab.

Source: adsl, adeq5d

Table EQ-5D-1.2
Change from Baseline in EQ-5D VAS Score to End of Study Period by Sex
Full Analysis Set

Sex		Statistic	Eculizumab (N=96)	Ravulizumab (N=58)	p-value (7)
Female	Change from Baseline to End of Study Period in EQ-5D VAS Score	n	88	52	
		Mean (SD)	5.3 (18.14)	2.9 (14.62)	
		Median	0.0	1.5	
		Q1, Q3	-5.0, 13.0	-5.0, 10.0	
		Min, Max	-30, 60	-45, 40	
		Change from baseline			
		LS Means (SEM)	4.279 (1.711)	4.739 (2.241)	
		95% CI for LS Means (1)	(0.896, 7.663)	(0.308, 9.171)	
		Difference in LS Means		0.460	
		(95% CI) (1)		(-5.184, 6.104)	
		p-value (2)		0.8132	
		Standardized Mean Difference		0.115	
		(95% CI) (3)		(-0.228, 0.458)	
		Responders (15% [15 points]), n(%)	22 (25.0)	12 (23.1)	
		Odds Ratio (4)		1.635	
		(95% CI)		(0.649, 4.118)	
		p-value		0.2968	
		Relative Risk (5)		0.923	
		(95% CI)		(0.499, 1.706)	
		p-value		0.7984	

The eculizumab group data were collected as part of the PREVENT trial, Study ECU-NMO-301.

End of Study Period is the 6-week assessment after the first On-Trial Relapse for patients who have an On-Trial Relapse or for patients with no On-Trial Relapse: the End of Primary Treatment Period visit for patients in Study ALXN1210-NMO-307 and the End of Study visit for patients in Study ECU-NMO-301.

For those patients who had a missed value at the EOPT Visit or the 6-week post-relapse visit, for patients who had a relapse, the end of study is the last value before the missed value.

(1) The LS means (95% CI) and the difference in LS means (95% CI) are from an ANCOVA model of change from baseline with treatment as factor and baseline value as covariate. (2) The p-value represents the significance of the treatment effect and was derived from an ANCOVA model of the ranked change from baseline, with treatment as a factor, and the ranks of the baseline value included as covariate.

(3) Standardized mean differences (95% CI) were computed using Cohen's D incorporating Hedge's correction on change from baseline. (4) Odds ratio statistics are from a logistic regression model adjusted for baseline value with Firth's adjustment; (5) Relative risk statistics are based on a generalized linear model of a binomial distribution with log link;

(6) Risk difference statistics are calculated from a generalized linear model, correcting for the baseline value. (7) P-value is for the interaction term of treatment:subgroup from a linear regression model of ranked change from baseline with the with ranked baseline value, treatment, subgroup, and treatment:subgroup interaction as covariates.

Odds ratio and relative risk are calculated as Ravulizumab/Eculizumab. LS mean difference and risk difference are calculated as Ravulizumab - Eculizumab.

Source: adsl, adeq5d

Table EQ-5D-1.2
Change from Baseline in EQ-5D VAS Score to End of Study Period by Sex
Full Analysis Set

Sex	Statistic	Eculizumab (N=96)	Ravulizumab (N=58)	p-value (7)
	Risk Difference (6)		0.068	
	(95% CI)		(-0.071, 0.208)	
	p-value		0.3362	
Baseline EQ-5D VAS Score	n	88	52	
	Mean (SD)	63.9 (20.07)	72.7 (15.34)	
	Median	70.0	75.5	
	Q1, Q3	50.0, 80.0	70.0, 81.0	
	Min, Max	10, 100	30, 97	
End of Study Period EQ-5D VAS Score	n	88	52	
	Mean (SD)	69.2 (21.72)	75.6 (17.20)	
	Median	75.0	80.0	
	Q1, Q3	50.0, 90.0	70.0, 86.5	
	Min, Max	15, 100	13, 98	

The eculizumab group data were collected as part of the PREVENT trial, Study ECU-NMO-301.

End of Study Period is the 6-week assessment after the first On-Trial Relapse for patients who have an On-Trial Relapse or for patients with no On-Trial Relapse: the End of Primary Treatment Period visit for patients in Study ALXN1210-NMO-307 and the End of Study visit for patients in Study ECU-NMO-301.

For those patients who had a missed value at the EOPT Visit or the 6-week post-relapse visit, for patients who had a relapse, the end of study is the last value before the missed value.

(1) The LS means (95% CI) and the difference in LS means (95% CI) are from an ANCOVA model of change from baseline with treatment as factor and baseline value as covariate. (2) The p-value represents the significance of the treatment effect and was derived from an ANCOVA model of the ranked change from baseline, with treatment as a factor, and the ranks of the baseline value included as covariate.

(3) Standardized mean differences (95% CI) were computed using Cohen's D incorporating Hedge's correction on change from baseline. (4) Odds ratio statistics are from a logistic regression model adjusted for baseline value with Firth's adjustment; (5) Relative risk statistics are based on a generalized linear model of a binomial distribution with log link;

(6) Risk difference statistics are calculated from a generalized linear model, correcting for the baseline value. (7) P-value is for the interaction term of treatment:subgroup from a linear regression model of ranked change from baseline with the with ranked baseline value, treatment, subgroup, and treatment:subgroup interaction as covariates.

Odds ratio and relative risk are calculated as Ravulizumab/Eculizumab. LS mean difference and risk difference are calculated as Ravulizumab - Eculizumab.

Source: adsl, adeq5d

Table EQ-5D-1.3
Change from Baseline in EQ-5D VAS Score to End of Study Period by Age Group
Full Analysis Set

Age Group		Statistic	Eculizumab (N=96)	Ravulizumab (N=58)	p-value (7)
< 45 years	Change from Baseline to End of Study Period in EQ-5D VAS Score	n	47	25	0.8385
		Mean (SD)	6.1 (18.63)	3.5 (13.61)	
		Median	3.0	3.0	
		Q1, Q3	-2.0, 18.0	-4.0, 9.0	
		Min, Max	-30, 60	-20, 40	
		Change from baseline			
		LS Means (SEM)	5.030 (2.295)	5.504 (3.167)	
		95% CI for LS Means (1)	(0.452, 9.607)	(-0.813, 11.822)	
		Difference in LS Means		0.475	
		(95% CI) (1)		(-7.402, 8.352)	
		p-value (2)		0.9323	
		Standardized Mean Difference		0.120	
		(95% CI) (3)		(-0.366, 0.605)	
		Responders (15% [15 points]), n(%)	13 (27.7)	4 (16.0)	
		Odds Ratio (4)		0.777	
		(95% CI)		(0.203, 2.971)	
		p-value		0.7121	
		Relative Risk (5)		0.578	
		(95% CI)		(0.211, 1.589)	
		p-value		0.2882	

The eculizumab group data were collected as part of the PREVENT trial, Study ECU-NMO-301.

End of Study Period is the 6-week assessment after the first On-Trial Relapse for patients who have an On-Trial Relapse or for patients with no On-Trial Relapse: the End of Primary Treatment Period visit for patients in Study ALXN1210-NMO-307 and the End of Study visit for patients in Study ECU-NMO-301.

For those patients who had a missed value at the EOPT Visit or the 6-week post-relapse visit, for patients who had a relapse, the end of study is the last value before the missed value.

(1) The LS means (95% CI) and the difference in LS means (95% CI) are from an ANCOVA model of change from baseline with treatment as factor and baseline value as covariate. (2) The p-value represents the significance of the treatment effect and was derived from an ANCOVA model of the ranked change from baseline, with treatment as a factor, and the ranks of the baseline value included as covariate.

(3) Standardized mean differences (95% CI) were computed using Cohen's D incorporating Hedge's correction on change from baseline. (4) Odds ratio statistics are from a logistic regression model adjusted for baseline value with Firth's adjustment; (5) Relative risk statistics are based on a generalized linear model of a binomial distribution with log link;

(6) Risk difference statistics are calculated from a generalized linear model, correcting for the baseline value. (7) P-value is for the interaction term of treatment:subgroup from a linear regression model of ranked change from baseline with the with ranked baseline value, treatment, subgroup, and treatment:subgroup interaction as covariates.

Odds ratio and relative risk are calculated as Ravulizumab/Eculizumab. LS mean difference and risk difference are calculated as Ravulizumab - Eculizumab.

Source: adsl, adeq5d

Table EQ-5D-1.3
Change from Baseline in EQ-5D VAS Score to End of Study Period by Age Group
Full Analysis Set

Age Group	Statistic	Eculizumab (N=96)	Ravulizumab (N=58)	p-value (7)
	Risk Difference (6)		-0.039	
	(95% CI)		(-0.235, 0.158)	
	p-value		0.6973	
Baseline EQ-5D VAS Score	n	47	25	
	Mean (SD)	68.9 (16.48)	75.8 (14.48)	
	Median	70.0	79.0	
	Q1, Q3	60.0, 80.0	70.0, 85.0	
	Min, Max	30, 100	40, 94	
End of Study Period EQ-5D VAS Score	n	47	25	
	Mean (SD)	75.0 (18.77)	79.2 (15.61)	
	Median	80.0	82.0	
	Q1, Q3	60.0, 90.0	80.0, 90.0	
	Min, Max	25, 100	30, 95	

The eculizumab group data were collected as part of the PREVENT trial, Study ECU-NMO-301.

End of Study Period is the 6-week assessment after the first On-Trial Relapse for patients who have an On-Trial Relapse or for patients with no On-Trial Relapse: the End of Primary Treatment Period visit for patients in Study ALXN1210-NMO-307 and the End of Study visit for patients in Study ECU-NMO-301.

For those patients who had a missed value at the EOPT Visit or the 6-week post-relapse visit, for patients who had a relapse, the end of study is the last value before the missed value.

(1) The LS means (95% CI) and the difference in LS means (95% CI) are from an ANCOVA model of change from baseline with treatment as factor and baseline value as covariate. (2) The p-value represents the significance of the treatment effect and was derived from an ANCOVA model of the ranked change from baseline, with treatment as a factor, and the ranks of the baseline value included as covariate.

(3) Standardized mean differences (95% CI) were computed using Cohen's D incorporating Hedge's correction on change from baseline. (4) Odds ratio statistics are from a logistic regression model adjusted for baseline value with Firth's adjustment; (5) Relative risk statistics are based on a generalized linear model of a binomial distribution with log link;

(6) Risk difference statistics are calculated from a generalized linear model, correcting for the baseline value. (7) P-value is for the interaction term of treatment:subgroup from a linear regression model of ranked change from baseline with the with ranked baseline value, treatment, subgroup, and treatment:subgroup interaction as covariates.

Odds ratio and relative risk are calculated as Ravulizumab/Eculizumab. LS mean difference and risk difference are calculated as Ravulizumab - Eculizumab.

Source: adsl, adeq5d

Table EQ-5D-1.3
Change from Baseline in EQ-5D VAS Score to End of Study Period by Age Group
Full Analysis Set

Age Group		Statistic	Eculizumab (N=96)	Ravulizumab (N=58)	p-value (7)
>= 45 years	Change from Baseline to End of Study Period in EQ-5D VAS Score	n	49	33	
		Mean (SD)	4.8 (18.60)	2.0 (14.58)	
		Median	0.0	0.0	
		Q1, Q3	-10.0, 11.0	-5.0, 10.0	
		Min, Max	-30, 50	-45, 25	
		Change from baseline			
		LS Means (SEM)	3.151 (2.369)	4.382 (2.918)	
		95% CI for LS Means (1)	(-1.564, 7.865)	(-1.425, 10.190)	
		Difference in LS Means		1.232	
		(95% CI) (1)		(-6.445, 8.909)	
		p-value (2)		0.7152	
		Standardized Mean Difference		0.302	
		(95% CI) (3)		(-0.142, 0.746)	
		Responders (15% [15 points]), n(%)	12 (24.5)	8 (24.2)	
		Odds Ratio (4)		2.631	
		(95% CI)		(0.716, 9.675)	
		p-value		0.1453	
		Relative Risk (5)		0.990	
		(95% CI)		(0.455, 2.155)	
		p-value		0.9796	

The eculizumab group data were collected as part of the PREVENT trial, Study ECU-NMO-301.

End of Study Period is the 6-week assessment after the first On-Trial Relapse for patients who have an On-Trial Relapse or for patients with no On-Trial Relapse: the End of Primary Treatment Period visit for patients in Study ALXN1210-NMO-307 and the End of Study visit for patients in Study ECU-NMO-301.

For those patients who had a missed value at the EOPT Visit or the 6-week post-relapse visit, for patients who had a relapse, the end of study is the last value before the missed value.

(1) The LS means (95% CI) and the difference in LS means (95% CI) are from an ANCOVA model of change from baseline with treatment as factor and baseline value as covariate. (2) The p-value represents the significance of the treatment effect and was derived from an ANCOVA model of the ranked change from baseline, with treatment as a factor, and the ranks of the baseline value included as covariate.

(3) Standardized mean differences (95% CI) were computed using Cohen's D incorporating Hedge's correction on change from baseline. (4) Odds ratio statistics are from a logistic regression model adjusted for baseline value with Firth's adjustment; (5) Relative risk statistics are based on a generalized linear model of a binomial distribution with log link;

(6) Risk difference statistics are calculated from a generalized linear model, correcting for the baseline value. (7) P-value is for the interaction term of treatment:subgroup from a linear regression model of ranked change from baseline with the with ranked baseline value, treatment, subgroup, and treatment:subgroup interaction as covariates.

Odds ratio and relative risk are calculated as Ravulizumab/Eculizumab. LS mean difference and risk difference are calculated as Ravulizumab - Eculizumab.

Source: adsl, adeq5d

Table EQ-5D-1.3
Change from Baseline in EQ-5D VAS Score to End of Study Period by Age Group
Full Analysis Set

Age Group	Statistic	Eculizumab (N=96)	Ravulizumab (N=58)	p-value (7)
	Risk Difference (6)		0.133	
	(95% CI)		(-0.052, 0.318)	
	p-value		0.1563	
Baseline EQ-5D VAS Score	n	49	33	
	Mean (SD)	58.5 (21.85)	71.9 (15.06)	
	Median	50.0	75.0	
	Q1, Q3	50.0, 80.0	70.0, 80.0	
	Min, Max	10, 90	30, 97	
End of Study Period EQ-5D VAS Score	n	49	33	
	Mean (SD)	63.3 (23.43)	73.9 (17.03)	
	Median	70.0	80.0	
	Q1, Q3	40.0, 80.0	70.0, 85.0	
	Min, Max	15, 98	13, 98	

The eculizumab group data were collected as part of the PREVENT trial, Study ECU-NMO-301.

End of Study Period is the 6-week assessment after the first On-Trial Relapse for patients who have an On-Trial Relapse or for patients with no On-Trial Relapse: the End of Primary Treatment Period visit for patients in Study ALXN1210-NMO-307 and the End of Study visit for patients in Study ECU-NMO-301.

For those patients who had a missed value at the EOPT Visit or the 6-week post-relapse visit, for patients who had a relapse, the end of study is the last value before the missed value.

(1) The LS means (95% CI) and the difference in LS means (95% CI) are from an ANCOVA model of change from baseline with treatment as factor and baseline value as covariate. (2) The p-value represents the significance of the treatment effect and was derived from an ANCOVA model of the ranked change from baseline, with treatment as a factor, and the ranks of the baseline value included as covariate.

(3) Standardized mean differences (95% CI) were computed using Cohen's D incorporating Hedge's correction on change from baseline. (4) Odds ratio statistics are from a logistic regression model adjusted for baseline value with Firth's adjustment; (5) Relative risk statistics are based on a generalized linear model of a binomial distribution with log link;

(6) Risk difference statistics are calculated from a generalized linear model, correcting for the baseline value. (7) P-value is for the interaction term of treatment:subgroup from a linear regression model of ranked change from baseline with the with ranked baseline value, treatment, subgroup, and treatment:subgroup interaction as covariates.

Odds ratio and relative risk are calculated as Ravulizumab/Eculizumab. LS mean difference and risk difference are calculated as Ravulizumab - Eculizumab.

Source: adsl, adeq5d

Table EQ-5D-1.5
Change from Baseline in EQ-5D VAS Score to End of Study Period by Region
Full Analysis Set

Region		Statistic	Eculizumab (N=96)	Ravulizumab (N=58)	p-value (7)
Asia-Pacific	Change from Baseline to End of Study Period in EQ-5D VAS Score	n	35	20	0.8052
		Mean (SD)	8.9 (19.30)	1.7 (10.01)	
		Median	5.0	0.0	
		Q1, Q3	-5.0, 21.0	-6.5, 7.5	
		Min, Max	-22, 50	-12, 25	
		Change from baseline			
		LS Means (SEM)	6.878 (2.645)	5.113 (3.566)	
		95% CI for LS Means (1)	(1.571, 12.185)	(-2.043, 12.269)	
		Difference in LS Means		-1.765	
		(95% CI) (1)		(-10.957, 7.427)	
		p-value (2)		0.6901	
		Standardized Mean Difference		-0.445	
		(95% CI) (3)		(-1.000, 0.111)	
		Responders (15% [15 points]), n(%)	12 (34.3)	2 (10.0)	
		Odds Ratio (4)		0.451	
		(95% CI)		(0.088, 2.314)	
		p-value		0.3398	
		Relative Risk (5)		0.292	
		(95% CI)		(0.072, 1.174)	
		p-value		0.0829	

The eculizumab group data were collected as part of the PREVENT trial, Study ECU-NMO-301.
End of Study Period is the 6-week assessment after the first On-Trial Relapse for patients who have an On-Trial Relapse or for patients with no On-Trial Relapse: the End of Primary Treatment Period visit for patients in Study ALXN1210-NMO-307 and the End of Study visit for patients in Study ECU-NMO-301.
For those patients who had a missed value at the EOPT Visit or the 6-week post-relapse visit, for patients who had a relapse, the end of study is the last value before the missed value.
(1) The LS means (95% CI) and the difference in LS means (95% CI) are from an ANCOVA model of change from baseline with treatment as factor and baseline value as covariate. (2) The p-value represents the significance of the treatment effect and was derived from an ANCOVA model of the ranked change from baseline, with treatment as a factor, and the ranks of the baseline value included as covariate.
(3) Standardized mean differences (95% CI) were computed using Cohen's D incorporating Hedge's correction on change from baseline. (4) Odds ratio statistics are from a logistic regression model adjusted for baseline value with Firth's adjustment; (5) Relative risk statistics are based on a generalized linear model of a binomial distribution with log link;
(6) Risk difference statistics are calculated from a generalized linear model, correcting for the baseline value. (7) P-value is for the interaction term of treatment:subgroup from a linear regression model of ranked change from baseline with the with ranked baseline value, treatment, subgroup, and treatment:subgroup interaction as covariates.
For eculizumab arm, Americas: ARG and USA; Europe: CZE, DEU, DNK, ESP, HRV, ITA, RUS and TUR; Asia-Pacific: AUS, HKG, JPN, KOR, MYS, THA and TWN. For ravulizumab arm, Americas: CAN and USA; Europe: DEU, DNK, ESP, GBR, ITA and POL; Asia-Pacific: AUS, JPN and KOR.
Odds ratio and relative risk are calculated as Ravulizumab/Eculizumab. LS mean difference and risk difference are calculated as Ravulizumab - Eculizumab.
Source: adsl, adeq5d

Table EQ-5D-1.5
Change from Baseline in EQ-5D VAS Score to End of Study Period by Region
Full Analysis Set

Region	Statistic	Eculizumab (N=96)	Ravulizumab (N=58)	p-value (7)
	Risk Difference (6)		-0.122	
	(95% CI)		(-0.365, 0.121)	
	p-value		0.3193	
Baseline EQ-5D VAS Score	n	35	20	
	Mean (SD)	61.8 (22.38)	77.0 (11.26)	
	Median	70.0	80.0	
	Q1, Q3	50.0, 80.0	70.0, 83.0	
	Min, Max	10, 90	50, 94	
End of Study Period EQ-5D VAS Score	n	35	20	
	Mean (SD)	70.7 (22.63)	78.7 (11.80)	
	Median	75.0	80.0	
	Q1, Q3	55.0, 90.0	74.0, 87.5	
	Min, Max	17, 98	48, 94	

The eculizumab group data were collected as part of the PREVENT trial, Study ECU-NMO-301.

End of Study Period is the 6-week assessment after the first On-Trial Relapse for patients who have an On-Trial Relapse or for patients with no On-Trial Relapse: the End of Primary Treatment Period visit for patients in Study ALXN1210-NMO-307 and the End of Study visit for patients in Study ECU-NMO-301.

For those patients who had a missed value at the EOPT Visit or the 6-week post-relapse visit, for patients who had a relapse, the end of study is the last value before the missed value.

(1) The LS means (95% CI) and the difference in LS means (95% CI) are from an ANCOVA model of change from baseline with treatment as factor and baseline value as covariate. (2) The p-value represents the significance of the treatment effect and was derived from an ANCOVA model of the ranked change from baseline, with treatment as a factor, and the ranks of the baseline value included as covariate.

(3) Standardized mean differences (95% CI) were computed using Cohen's D incorporating Hedge's correction on change from baseline. (4) Odds ratio statistics are from a logistic regression model adjusted for baseline value with Firth's adjustment; (5) Relative risk statistics are based on a generalized linear model of a binomial distribution with log link;

(6) Risk difference statistics are calculated from a generalized linear model, correcting for the baseline value. (7) P-value is for the interaction term of treatment:subgroup from a linear regression model of ranked change from baseline with the with ranked baseline value, treatment, subgroup, and treatment:subgroup interaction as covariates.

For eculizumab arm, Americas: ARG and USA; Europe: CZE, DEU, DNK, ESP, HRV, ITA, RUS and TUR; Asia-Pacific: AUS, HKG, JPN, KOR, MYS, THA and TWN. For ravulizumab arm, Americas: CAN and USA; Europe: DEU, DNK, ESP, GBR, ITA and POL; Asia-Pacific: AUS, JPN and KOR.

Odds ratio and relative risk are calculated as Ravulizumab/Eculizumab. LS mean difference and risk difference are calculated as Ravulizumab - Eculizumab.

Source: adsl, adeq5d

Table EQ-5D-1.5
Change from Baseline in EQ-5D VAS Score to End of Study Period by Region
Full Analysis Set

Region		Statistic	Eculizumab (N=96)	Ravulizumab (N=58)	p-value (7)
Americas	Change from Baseline to End of Study Period in EQ-5D VAS Score	n	29	21	0.4550
		Mean (SD)	4.3 (18.81)	5.6 (18.62)	
		Median	5.0	6.0	
		Q1, Q3	-10.0, 15.0	-5.0, 20.0	
		Min, Max	-30, 40	-45, 40	
		Change from baseline			
		LS Means (SEM)	2.574 (3.202)	8.017 (3.781)	
		95% CI for LS Means (1)	(-3.867, 9.015)	(0.410, 15.623)	
		Difference in LS Means		5.443	
		(95% CI) (1)		(-4.674, 15.560)	
		p-value (2)		0.2170	
		Standardized Mean Difference		1.309	
		(95% CI) (3)		(0.692, 1.927)	
		Responders (15% [15 points]), n(%)	8 (27.6)	8 (38.1)	
		Odds Ratio (4)		5.877	
		(95% CI)		(0.995, 34.721)	
		p-value		0.0507	
		Relative Risk (5)		1.381	
		(95% CI)		(0.619, 3.083)	
		p-value		0.4309	

The eculizumab group data were collected as part of the PREVENT trial, Study ECU-NMO-301.

End of Study Period is the 6-week assessment after the first On-Trial Relapse for patients who have an On-Trial Relapse or for patients with no On-Trial Relapse: the End of Primary Treatment Period visit for patients in Study ALXN1210-NMO-307 and the End of Study visit for patients in Study ECU-NMO-301.

For those patients who had a missed value at the EOPT Visit or the 6-week post-relapse visit, for patients who had a relapse, the end of study is the last value before the missed value.

(1) The LS means (95% CI) and the difference in LS means (95% CI) are from an ANCOVA model of change from baseline with treatment as factor and baseline value as covariate. (2) The p-value represents the significance of the treatment effect and was derived from an ANCOVA model of the ranked change from baseline, with treatment as a factor, and the ranks of the baseline value included as covariate.

(3) Standardized mean differences (95% CI) were computed using Cohen's D incorporating Hedge's correction on change from baseline. (4) Odds ratio statistics are from a logistic regression model adjusted for baseline value with Firth's adjustment; (5) Relative risk statistics are based on a generalized linear model of a binomial distribution with log link;

(6) Risk difference statistics are calculated from a generalized linear model, correcting for the baseline value. (7) P-value is for the interaction term of treatment:subgroup from a linear regression model of ranked change from baseline with the with ranked baseline value, treatment, subgroup, and treatment:subgroup interaction as covariates.

For eculizumab arm, Americas: ARG and USA; Europe: CZE, DEU, DNK, ESP, HRV, ITA, RUS and TUR; Asia-Pacific: AUS, HKG, JPN, KOR, MYS, THA and TWN. For ravulizumab arm, Americas: CAN and USA; Europe: DEU, DNK, ESP, GBR, ITA and POL; Asia-Pacific: AUS, JPN and KOR.

Odds ratio and relative risk are calculated as Ravulizumab/Eculizumab. LS mean difference and risk difference are calculated as Ravulizumab - Eculizumab.

Source: adsl, adeq5d

Table EQ-5D-1.5
Change from Baseline in EQ-5D VAS Score to End of Study Period by Region
Full Analysis Set

Region	Statistic	Eculizumab (N=96)	Ravulizumab (N=58)	p-value (7)
	Risk Difference (6)		0.249	
	(95% CI)		(0.023, 0.476)	
	p-value		0.0315	
Baseline EQ-5D VAS Score	n	29	21	
	Mean (SD)	65.9 (17.39)	74.2 (15.10)	
	Median	70.0	75.0	
	Q1, Q3	50.0, 80.0	70.0, 85.0	
	Min, Max	25, 95	40, 97	
End of Study Period EQ-5D VAS Score	n	29	21	
	Mean (SD)	70.2 (21.07)	79.8 (14.92)	
	Median	70.0	82.0	
	Q1, Q3	57.0, 88.0	71.0, 90.0	
	Min, Max	25, 98	35, 98	

The eculizumab group data were collected as part of the PREVENT trial, Study ECU-NMO-301.

End of Study Period is the 6-week assessment after the first On-Trial Relapse for patients who have an On-Trial Relapse or for patients with no On-Trial Relapse: the End of Primary Treatment Period visit for patients in Study ALXN1210-NMO-307 and the End of Study visit for patients in Study ECU-NMO-301.

For those patients who had a missed value at the EOPT Visit or the 6-week post-relapse visit, for patients who had a relapse, the end of study is the last value before the missed value.

(1) The LS means (95% CI) and the difference in LS means (95% CI) are from an ANCOVA model of change from baseline with treatment as factor and baseline value as covariate. (2) The p-value represents the significance of the treatment effect and was derived from an ANCOVA model of the ranked change from baseline, with treatment as a factor, and the ranks of the baseline value included as covariate.

(3) Standardized mean differences (95% CI) were computed using Cohen's D incorporating Hedge's correction on change from baseline. (4) Odds ratio statistics are from a logistic regression model adjusted for baseline value with Firth's adjustment; (5) Relative risk statistics are based on a generalized linear model of a binomial distribution with log link;

(6) Risk difference statistics are calculated from a generalized linear model, correcting for the baseline value. (7) P-value is for the interaction term of treatment:subgroup from a linear regression model of ranked change from baseline with the with ranked baseline value, treatment, subgroup, and treatment:subgroup interaction as covariates.

For eculizumab arm, Americas: ARG and USA; Europe: CZE, DEU, DNK, ESP, HRV, ITA, RUS and TUR; Asia-Pacific: AUS, HKG, JPN, KOR, MYS, THA and TWN. For ravulizumab arm, Americas: CAN and USA; Europe: DEU, DNK, ESP, GBR, ITA and POL; Asia-Pacific: AUS, JPN and KOR.

Odds ratio and relative risk are calculated as Ravulizumab/Eculizumab. LS mean difference and risk difference are calculated as Ravulizumab - Eculizumab.

Source: adsl, adeq5d

Table EQ-5D-1.5
Change from Baseline in EQ-5D VAS Score to End of Study Period by Region
Full Analysis Set

Region		Statistic	Eculizumab (N=96)	Ravulizumab (N=58)	p-value (7)
Europe	Change from Baseline to End of Study Period in EQ-5D VAS Score	n	32	17	
		Mean (SD)	2.7 (17.36)	0.1 (11.54)	
		Median	0.0	0.0	
		Q1, Q3	-10.0, 10.0	-4.0, 9.0	
		Min, Max	-30, 60	-20, 20	
		Change from baseline			
		LS Means (SEM)	2.341 (2.740)	0.711 (3.770)	
		95% CI for LS Means (1)	(-3.174, 7.856)	(-6.877, 8.299)	
		Difference in LS Means		-1.630	
		(95% CI) (1)		(-11.049, 7.788)	
		p-value (2)		0.7132	
		Standardized Mean Difference		-0.414	
		(95% CI) (3)		(-1.008, 0.180)	
		Responders (15% [15 points]), n(%)	5 (15.6)	2 (11.8)	
		Odds Ratio (4)		1.096	
		(95% CI)		(0.181, 6.632)	
		p-value		0.9204	
		Relative Risk (5)		0.753	
		(95% CI)		(0.163, 3.480)	
		p-value		0.7163	

The eculizumab group data were collected as part of the PREVENT trial, Study ECU-NMO-301.

End of Study Period is the 6-week assessment after the first On-Trial Relapse for patients who have an On-Trial Relapse or for patients with no On-Trial Relapse: the End of Primary Treatment Period visit for patients in Study ALXN1210-NMO-307 and the End of Study visit for patients in Study ECU-NMO-301.

For those patients who had a missed value at the EOPT Visit or the 6-week post-relapse visit, for patients who had a relapse, the end of study is the last value before the missed value.

(1) The LS means (95% CI) and the difference in LS means (95% CI) are from an ANCOVA model of change from baseline with treatment as factor and baseline value as covariate. (2) The p-value represents the significance of the treatment effect and was derived from an ANCOVA model of the ranked change from baseline, with treatment as a factor, and the ranks of the baseline value included as covariate.

(3) Standardized mean differences (95% CI) were computed using Cohen's D incorporating Hedge's correction on change from baseline. (4) Odds ratio statistics are from a logistic regression model adjusted for baseline value with Firth's adjustment; (5) Relative risk statistics are based on a generalized linear model of a binomial distribution with log link;

(6) Risk difference statistics are calculated from a generalized linear model, correcting for the baseline value. (7) P-value is for the interaction term of treatment:subgroup from a linear regression model of ranked change from baseline with the with ranked baseline value, treatment, subgroup, and treatment:subgroup interaction as covariates.

For eculizumab arm, Americas: ARG and USA; Europe: CZE, DEU, DNK, ESP, HRV, ITA, RUS and TUR; Asia-Pacific: AUS, HKG, JPN, KOR, MYS, THA and TWN. For ravulizumab arm, Americas: CAN and USA; Europe: DEU, DNK, ESP, GBR, ITA and POL; Asia-Pacific: AUS, JPN and KOR.

Odds ratio and relative risk are calculated as Ravulizumab/Eculizumab. LS mean difference and risk difference are calculated as Ravulizumab - Eculizumab.

Source: adsl, adeq5d

Table EQ-5D-1.5
Change from Baseline in EQ-5D VAS Score to End of Study Period by Region
Full Analysis Set

Region	Statistic	Eculizumab (N=96)	Ravulizumab (N=58)	p-value (7)
	Risk Difference (6)		-0.002	
	(95% CI)		(-0.206, 0.202)	
	p-value		0.9852	
Baseline EQ-5D VAS Score	n	32	17	
	Mean (SD)	63.5 (19.86)	68.8 (17.50)	
	Median	62.5	77.0	
	Q1, Q3	50.0, 80.0	50.0, 80.0	
	Min, Max	30, 100	30, 90	
End of Study Period EQ-5D VAS Score	n	32	17	
	Mean (SD)	66.2 (22.45)	68.9 (21.13)	
	Median	72.5	72.0	
	Q1, Q3	50.0, 82.5	67.0, 81.0	
	Min, Max	15, 100	13, 95	

The eculizumab group data were collected as part of the PREVENT trial, Study ECU-NMO-301.

End of Study Period is the 6-week assessment after the first On-Trial Relapse for patients who have an On-Trial Relapse or for patients with no On-Trial Relapse: the End of Primary Treatment Period visit for patients in Study ALXN1210-NMO-307 and the End of Study visit for patients in Study ECU-NMO-301.

For those patients who had a missed value at the EOPT Visit or the 6-week post-relapse visit, for patients who had a relapse, the end of study is the last value before the missed value.

(1) The LS means (95% CI) and the difference in LS means (95% CI) are from an ANCOVA model of change from baseline with treatment as factor and baseline value as covariate. (2) The p-value represents the significance of the treatment effect and was derived from an ANCOVA model of the ranked change from baseline, with treatment as a factor, and the ranks of the baseline value included as covariate.

(3) Standardized mean differences (95% CI) were computed using Cohen's D incorporating Hedge's correction on change from baseline. (4) Odds ratio statistics are from a logistic regression model adjusted for baseline value with Firth's adjustment; (5) Relative risk statistics are based on a generalized linear model of a binomial distribution with log link;

(6) Risk difference statistics are calculated from a generalized linear model, correcting for the baseline value. (7) P-value is for the interaction term of treatment:subgroup from a linear regression model of ranked change from baseline with the with ranked baseline value, treatment, subgroup, and treatment:subgroup interaction as covariates.

For eculizumab arm, Americas: ARG and USA; Europe: CZE, DEU, DNK, ESP, HRV, ITA, RUS and TUR; Asia-Pacific: AUS, HKG, JPN, KOR, MYS, THA and TWN. For ravulizumab arm, Americas: CAN and USA; Europe: DEU, DNK, ESP, GBR, ITA and POL; Asia-Pacific: AUS, JPN and KOR.

Odds ratio and relative risk are calculated as Ravulizumab/Eculizumab. LS mean difference and risk difference are calculated as Ravulizumab - Eculizumab.

Source: adsl, adeq5d

Table EQ-5D-1.6
Change from Baseline in EQ-5D VAS Score to End of Study Period by Supportive IST use at baseline
Full Analysis Set

IST use at baseline		Statistic	Eculizumab (N=96)	Ravulizumab (N=58)	p-value (7)
Yes	Change from Baseline to End of Study Period in EQ-5D VAS Score	n	75	28	0.4996
		Mean (SD)	5.3 (17.44)	0.1 (11.73)	
		Median	1.0	0.0	
		Q1, Q3	-5.0, 15.0	-3.5, 6.0	
		Min, Max	-30, 50	-45, 25	
		Change from baseline			
		LS Means (SEM)	4.346 (1.809)	2.644 (3.028)	
		95% CI for LS Means (1)	(0.758, 7.935)	(-3.363, 8.652)	
		Difference in LS Means		-1.702	
		(95% CI) (1)		(-8.834, 5.431)	
		p-value (2)		0.5549	
		Standardized Mean Difference		-0.429	
		(95% CI) (3)		(-0.867, 0.009)	
		Responders (15% [15 points]), n(%)	19 (25.3)	1 (3.6)	
		Odds Ratio (4)		0.289	
		(95% CI)		(0.047, 1.786)	
		p-value		0.1818	
		Relative Risk (5)		0.141	
		(95% CI)		(0.020, 1.004)	
		p-value		0.0505	

The eculizumab group data were collected as part of the PREVENT trial, Study ECU-NMO-301.

End of Study Period is the 6-week assessment after the first On-Trial Relapse for patients who have an On-Trial Relapse or for patients with no On-Trial Relapse: the End of Primary Treatment Period visit for patients in Study ALXN1210-NMO-307 and the End of Study visit for patients in Study ECU-NMO-301.

For those patients who had a missed value at the EOPT Visit or the 6-week post-relapse visit, for patients who had a relapse, the end of study is the last value before the missed value.

(1) The LS means (95% CI) and the difference in LS means (95% CI) are from an ANCOVA model of change from baseline with treatment as factor and baseline value as covariate. (2) The p-value represents the significance of the treatment effect and was derived from an ANCOVA model of the ranked change from baseline, with treatment as a factor, and the ranks of the baseline value included as covariate.

(3) Standardized mean differences (95% CI) were computed using Cohen's D incorporating Hedge's correction on change from baseline. (4) Odds ratio statistics are from a logistic regression model adjusted for baseline value with Firth's adjustment; (5) Relative risk statistics are based on a generalized linear model of a binomial distribution with log link;

(6) Risk difference statistics are calculated from a generalized linear model, correcting for the baseline value. (7) P-value is for the interaction term of treatment:subgroup from a linear regression model of ranked change from baseline with the with ranked baseline value, treatment, subgroup, and treatment:subgroup interaction as covariates.

Odds ratio and relative risk are calculated as Ravulizumab/Eculizumab. LS mean difference and risk difference are calculated as Ravulizumab - Eculizumab.

Source: adsl, adeq5d

Table EQ-5D-1.6
Change from Baseline in EQ-5D VAS Score to End of Study Period by Supportive IST use at baseline
Full Analysis Set

IST use at baseline	Statistic	Eculizumab (N=96)	Ravulizumab (N=58)	p-value (7)
	Risk Difference (6)		-0.116	
	(95% CI)		(-0.283, 0.052)	
	p-value		0.1732	
Baseline EQ-5D VAS Score	n	75	28	
	Mean (SD)	64.0 (19.86)	77.0 (11.79)	
	Median	70.0	80.0	
	Q1, Q3	50.0, 80.0	71.5, 83.0	
	Min, Max	10, 100	41, 94	
End of Study Period EQ-5D VAS Score	n	75	28	
	Mean (SD)	69.3 (22.23)	77.1 (13.49)	
	Median	75.0	80.0	
	Q1, Q3	50.0, 90.0	70.0, 85.0	
	Min, Max	15, 98	35, 95	

The eculizumab group data were collected as part of the PREVENT trial, Study ECU-NMO-301.

End of Study Period is the 6-week assessment after the first On-Trial Relapse for patients who have an On-Trial Relapse or for patients with no On-Trial Relapse: the End of Primary Treatment Period visit for patients in Study ALXN1210-NMO-307 and the End of Study visit for patients in Study ECU-NMO-301.

For those patients who had a missed value at the EOPT Visit or the 6-week post-relapse visit, for patients who had a relapse, the end of study is the last value before the missed value.

(1) The LS means (95% CI) and the difference in LS means (95% CI) are from an ANCOVA model of change from baseline with treatment as factor and baseline value as covariate. (2) The p-value represents the significance of the treatment effect and was derived from an ANCOVA model of the ranked change from baseline, with treatment as a factor, and the ranks of the baseline value included as covariate.

(3) Standardized mean differences (95% CI) were computed using Cohen's D incorporating Hedge's correction on change from baseline. (4) Odds ratio statistics are from a logistic regression model adjusted for baseline value with Firth's adjustment; (5) Relative risk statistics are based on a generalized linear model of a binomial distribution with log link;

(6) Risk difference statistics are calculated from a generalized linear model, correcting for the baseline value. (7) P-value is for the interaction term of treatment:subgroup from a linear regression model of ranked change from baseline with the with ranked baseline value, treatment, subgroup, and treatment:subgroup interaction as covariates.

Odds ratio and relative risk are calculated as Ravulizumab/Eculizumab. LS mean difference and risk difference are calculated as Ravulizumab - Eculizumab.

Source: adsl, adeq5d

Table EQ-5D-1.6
Change from Baseline in EQ-5D VAS Score to End of Study Period by Supportive IST use at baseline
Full Analysis Set

IST use at baseline		Statistic	Eculizumab (N=96)	Ravulizumab (N=58)	p-value (7)
No	Change from Baseline to End of Study Period in EQ-5D VAS Score	n	21	30	
		Mean (SD)	5.9 (22.47)	5.0 (15.77)	
		Median	0.0	3.0	
		Q1, Q3	-10.0, 18.0	-9.0, 20.0	
		Min, Max	-30, 60	-20, 40	
		Change from baseline			
		LS Means (SEM)	3.832 (3.814)	6.418 (3.178)	
		95% CI for LS Means (1)	(-3.837, 11.501)	(0.028, 12.808)	
		Difference in LS Means		2.586	
		(95% CI) (1)		(-7.509, 12.681)	
		p-value (2)		0.4646	
		Standardized Mean Difference		0.619	
		(95% CI) (3)		(0.049, 1.190)	
		Responders (15% [15 points]), n(%)	6 (28.6)	11 (36.7)	
		Odds Ratio (4)		2.935	
		(95% CI)		(0.653, 13.193)	
		p-value		0.1603	
		Relative Risk (5)		1.283	
		(95% CI)		(0.563, 2.925)	
		p-value		0.5528	

The eculizumab group data were collected as part of the PREVENT trial, Study ECU-NMO-301.

End of Study Period is the 6-week assessment after the first On-Trial Relapse for patients who have an On-Trial Relapse or for patients with no On-Trial Relapse: the End of Primary Treatment Period visit for patients in Study ALXN1210-NMO-307 and the End of Study visit for patients in Study ECU-NMO-301.

For those patients who had a missed value at the EOPT Visit or the 6-week post-relapse visit, for patients who had a relapse, the end of study is the last value before the missed value.

(1) The LS means (95% CI) and the difference in LS means (95% CI) are from an ANCOVA model of change from baseline with treatment as factor and baseline value as covariate. (2) The p-value represents the significance of the treatment effect and was derived from an ANCOVA model of the ranked change from baseline, with treatment as a factor, and the ranks of the baseline value included as covariate.

(3) Standardized mean differences (95% CI) were computed using Cohen's D incorporating Hedge's correction on change from baseline. (4) Odds ratio statistics are from a logistic regression model adjusted for baseline value with Firth's adjustment; (5) Relative risk statistics are based on a generalized linear model of a binomial distribution with log link;

(6) Risk difference statistics are calculated from a generalized linear model, correcting for the baseline value. (7) P-value is for the interaction term of treatment:subgroup from a linear regression model of ranked change from baseline with the with ranked baseline value, treatment, subgroup, and treatment:subgroup interaction as covariates.

Odds ratio and relative risk are calculated as Ravulizumab/Eculizumab. LS mean difference and risk difference are calculated as Ravulizumab - Eculizumab.

Source: adsl, adeq5d

Table EQ-5D-1.6
Change from Baseline in EQ-5D VAS Score to End of Study Period by Supportive IST use at baseline
Full Analysis Set

IST use at baseline	Statistic	Eculizumab (N=96)	Ravulizumab (N=58)	p-value (7)
	Risk Difference (6)		0.182	
	(95% CI)		(-0.066, 0.430)	
	p-value		0.1470	
Baseline EQ-5D VAS Score	n	21	30	
	Mean (SD)	62.3 (20.94)	70.4 (16.74)	
	Median	67.0	75.0	
	Q1, Q3	50.0, 80.0	60.0, 80.0	
	Min, Max	30, 100	30, 97	
End of Study Period EQ-5D VAS Score	n	21	30	
	Mean (SD)	68.2 (21.53)	75.4 (19.10)	
	Median	75.0	80.5	
	Q1, Q3	60.0, 80.0	70.0, 88.0	
	Min, Max	25, 100	13, 98	

The eculizumab group data were collected as part of the PREVENT trial, Study ECU-NMO-301.

End of Study Period is the 6-week assessment after the first On-Trial Relapse for patients who have an On-Trial Relapse or for patients with no On-Trial Relapse: the End of Primary Treatment Period visit for patients in Study ALXN1210-NMO-307 and the End of Study visit for patients in Study ECU-NMO-301.

For those patients who had a missed value at the EOPT Visit or the 6-week post-relapse visit, for patients who had a relapse, the end of study is the last value before the missed value.

(1) The LS means (95% CI) and the difference in LS means (95% CI) are from an ANCOVA model of change from baseline with treatment as factor and baseline value as covariate. (2) The p-value represents the significance of the treatment effect and was derived from an ANCOVA model of the ranked change from baseline, with treatment as a factor, and the ranks of the baseline value included as covariate.

(3) Standardized mean differences (95% CI) were computed using Cohen's D incorporating Hedge's correction on change from baseline. (4) Odds ratio statistics are from a logistic regression model adjusted for baseline value with Firth's adjustment; (5) Relative risk statistics are based on a generalized linear model of a binomial distribution with log link;

(6) Risk difference statistics are calculated from a generalized linear model, correcting for the baseline value. (7) P-value is for the interaction term of treatment:subgroup from a linear regression model of ranked change from baseline with the with ranked baseline value, treatment, subgroup, and treatment:subgroup interaction as covariates.

Odds ratio and relative risk are calculated as Ravulizumab/Eculizumab. LS mean difference and risk difference are calculated as Ravulizumab - Eculizumab.

Source: adsl, adeq5d

Table EQ-5D-1.7
Change from Baseline in EQ-5D VAS Score to End of Study Period by Rituximab use in the prior year
Full Analysis Set

Rituximab use in the prior year		Statistic	Eculizumab (N=96)	Ravulizumab (N=58)	p-value (7)
Yes	Change from Baseline to End of Study Period in EQ-5D VAS Score	n	19	20	0.4903
		Mean (SD)	3.1 (17.27)	1.7 (16.80)	
		Median	0.0	2.5	
		Q1, Q3	-10.0, 10.0	-7.0, 16.0	
		Min, Max	-25, 40	-45, 25	
		Change from baseline			
		LS Means (SEM)	0.113 (3.625)	4.542 (3.528)	
		95% CI for LS Means (1)	(-7.239, 7.466)	(-2.612, 11.697)	
		Difference in LS Means		4.429	
		(95% CI) (1)		(-6.163, 15.021)	
		p-value (2)		0.2369	
		Standardized Mean Difference		1.115	
		(95% CI) (3)		(0.440, 1.789)	
		Responders (15% [15 points]), n(%)	4 (21.1)	6 (30.0)	
		Odds Ratio (4)		5.494	
		(95% CI)		(0.765, 39.474)	
		p-value		0.0904	
		Relative Risk (5)		1.425	
		(95% CI)		(0.475, 4.274)	
		p-value		0.5274	

The eculizumab group data were collected as part of the PREVENT trial, Study ECU-NMO-301.

End of Study Period is the 6-week assessment after the first On-Trial Relapse for patients who have an On-Trial Relapse or for patients with no On-Trial Relapse: the End of Primary Treatment Period visit for patients in Study ALXN1210-NMO-307 and the End of Study visit for patients in Study ECU-NMO-301.

For those patients who had a missed value at the EOPT Visit or the 6-week post-relapse visit, for patients who had a relapse, the end of study is the last value before the missed value.

(1) The LS means (95% CI) and the difference in LS means (95% CI) are from an ANCOVA model of change from baseline with treatment as factor and baseline value as covariate. (2) The p-value represents the significance of the treatment effect and was derived from an ANCOVA model of the ranked change from baseline, with treatment as a factor, and the ranks of the baseline value included as covariate.

(3) Standardized mean differences (95% CI) were computed using Cohen's D incorporating Hedge's correction on change from baseline. (4) Odds ratio statistics are from a logistic regression model adjusted for baseline value with Firth's adjustment; (5) Relative risk statistics are based on a generalized linear model of a binomial distribution with log link;

(6) Risk difference statistics are calculated from a generalized linear model, correcting for the baseline value. (7) P-value is for the interaction term of treatment:subgroup from a linear regression model of ranked change from baseline with the with ranked baseline value, treatment, subgroup, and treatment:subgroup interaction as covariates.

Odds ratio and relative risk are calculated as Ravulizumab/Eculizumab. LS mean difference and risk difference are calculated as Ravulizumab - Eculizumab.

Source: adsl, adeq5d

Table EQ-5D-1.7
Change from Baseline in EQ-5D VAS Score to End of Study Period by Rituximab use in the prior year
Full Analysis Set

Rituximab use in the prior year	Statistic	Eculizumab (N=96)	Ravulizumab (N=58)	p-value (7)
	Risk Difference (6)		0.271	
	(95% CI)		(0.010, 0.532)	
	p-value		0.0425	
Baseline EQ-5D VAS Score	n	19	20	
	Mean (SD)	59.5 (20.10)	72.7 (15.74)	
	Median	60.0	75.0	
	Q1, Q3	50.0, 80.0	65.0, 82.5	
	Min, Max	10, 82	41, 97	
End of Study Period EQ-5D VAS Score	n	19	20	
	Mean (SD)	62.6 (17.35)	74.4 (18.76)	
	Median	60.0	80.0	
	Q1, Q3	50.0, 75.0	69.0, 89.0	
	Min, Max	40, 90	30, 98	

The eculizumab group data were collected as part of the PREVENT trial, Study ECU-NMO-301.

End of Study Period is the 6-week assessment after the first On-Trial Relapse for patients who have an On-Trial Relapse or for patients with no On-Trial Relapse: the End of Primary Treatment Period visit for patients in Study ALXN1210-NMO-307 and the End of Study visit for patients in Study ECU-NMO-301.

For those patients who had a missed value at the EOPT Visit or the 6-week post-relapse visit, for patients who had a relapse, the end of study is the last value before the missed value.

(1) The LS means (95% CI) and the difference in LS means (95% CI) are from an ANCOVA model of change from baseline with treatment as factor and baseline value as covariate. (2) The p-value represents the significance of the treatment effect and was derived from an ANCOVA model of the ranked change from baseline, with treatment as a factor, and the ranks of the baseline value included as covariate.

(3) Standardized mean differences (95% CI) were computed using Cohen's D incorporating Hedge's correction on change from baseline. (4) Odds ratio statistics are from a logistic regression model adjusted for baseline value with Firth's adjustment; (5) Relative risk statistics are based on a generalized linear model of a binomial distribution with log link;

(6) Risk difference statistics are calculated from a generalized linear model, correcting for the baseline value. (7) P-value is for the interaction term of treatment:subgroup from a linear regression model of ranked change from baseline with the with ranked baseline value, treatment, subgroup, and treatment:subgroup interaction as covariates.

Odds ratio and relative risk are calculated as Ravulizumab/Eculizumab. LS mean difference and risk difference are calculated as Ravulizumab - Eculizumab.

Source: adsl, adeq5d

Table EQ-5D-1.7
Change from Baseline in EQ-5D VAS Score to End of Study Period by Rituximab use in the prior year
Full Analysis Set

Rituximab use in the prior year		Statistic	Eculizumab (N=96)	Ravulizumab (N=58)	p-value (7)
No	Change from Baseline to End of Study Period in EQ-5D VAS Score	n	77	38	
		Mean (SD)	6.0 (18.89)	3.1 (12.62)	
		Median	0.0	0.0	
		Q1, Q3	-5.0, 18.0	-4.0, 9.0	
		Min, Max	-30, 60	-17, 40	
		Change from baseline			
		LS Means (SEM)	5.049 (1.870)	5.032 (2.688)	
		95% CI for LS Means (1)	(1.344, 8.754)	(-0.294, 10.358)	
		Difference in LS Means		-0.018	
		(95% CI) (1)		(-6.588, 6.552)	
		p-value (2)		0.8249	
		Standardized Mean Difference		-0.004	
		(95% CI) (3)		(-0.393, 0.384)	
		Responders (15% [15 points]), n(%)	21 (27.3)	6 (15.8)	
		Odds Ratio (4)		0.844	
		(95% CI)		(0.285, 2.497)	
		p-value		0.7588	
		Relative Risk (5)		0.579	
		(95% CI)		(0.255, 1.314)	
		p-value		0.1914	

The eculizumab group data were collected as part of the PREVENT trial, Study ECU-NMO-301.

End of Study Period is the 6-week assessment after the first On-Trial Relapse for patients who have an On-Trial Relapse or for patients with no On-Trial Relapse: the End of Primary Treatment Period visit for patients in Study ALXN1210-NMO-307 and the End of Study visit for patients in Study ECU-NMO-301.

For those patients who had a missed value at the EOPT Visit or the 6-week post-relapse visit, for patients who had a relapse, the end of study is the last value before the missed value.

(1) The LS means (95% CI) and the difference in LS means (95% CI) are from an ANCOVA model of change from baseline with treatment as factor and baseline value as covariate. (2) The p-value represents the significance of the treatment effect and was derived from an ANCOVA model of the ranked change from baseline, with treatment as a factor, and the ranks of the baseline value included as covariate.

(3) Standardized mean differences (95% CI) were computed using Cohen's D incorporating Hedge's correction on change from baseline. (4) Odds ratio statistics are from a logistic regression model adjusted for baseline value with Firth's adjustment; (5) Relative risk statistics are based on a generalized linear model of a binomial distribution with log link;

(6) Risk difference statistics are calculated from a generalized linear model, correcting for the baseline value. (7) P-value is for the interaction term of treatment:subgroup from a linear regression model of ranked change from baseline with the with ranked baseline value, treatment, subgroup, and treatment:subgroup interaction as covariates.

Odds ratio and relative risk are calculated as Ravulizumab/Eculizumab. LS mean difference and risk difference are calculated as Ravulizumab - Eculizumab.

Source: adsl, adeq5d

Table EQ-5D-1.7
Change from Baseline in EQ-5D VAS Score to End of Study Period by Rituximab use in the prior year
Full Analysis Set

Rituximab use in the prior year	Statistic	Eculizumab (N=96)	Ravulizumab (N=58)	p-value (7)
	Risk Difference (6)		-0.031	
	(95% CI)		(-0.190, 0.128)	
	p-value		0.7017	
Baseline EQ-5D VAS Score	n	77	38	
	Mean (SD)	64.6 (19.97)	74.1 (14.49)	
	Median	70.0	78.5	
	Q1, Q3	50.0, 80.0	70.0, 81.0	
	Min, Max	10, 100	30, 91	
End of Study Period EQ-5D VAS Score	n	77	38	
	Mean (SD)	70.6 (22.79)	77.2 (15.36)	
	Median	77.0	80.0	
	Q1, Q3	57.0, 90.0	70.0, 85.0	
	Min, Max	15, 100	13, 95	

The eculizumab group data were collected as part of the PREVENT trial, Study ECU-NMO-301.

End of Study Period is the 6-week assessment after the first On-Trial Relapse for patients who have an On-Trial Relapse or for patients with no On-Trial Relapse: the End of Primary Treatment Period visit for patients in Study ALXN1210-NMO-307 and the End of Study visit for patients in Study ECU-NMO-301.

For those patients who had a missed value at the EOPT Visit or the 6-week post-relapse visit, for patients who had a relapse, the end of study is the last value before the missed value.

(1) The LS means (95% CI) and the difference in LS means (95% CI) are from an ANCOVA model of change from baseline with treatment as factor and baseline value as covariate. (2) The p-value represents the significance of the treatment effect and was derived from an ANCOVA model of the ranked change from baseline, with treatment as a factor, and the ranks of the baseline value included as covariate.

(3) Standardized mean differences (95% CI) were computed using Cohen's D incorporating Hedge's correction on change from baseline. (4) Odds ratio statistics are from a logistic regression model adjusted for baseline value with Firth's adjustment; (5) Relative risk statistics are based on a generalized linear model of a binomial distribution with log link;

(6) Risk difference statistics are calculated from a generalized linear model, correcting for the baseline value. (7) P-value is for the interaction term of treatment:subgroup from a linear regression model of ranked change from baseline with the with ranked baseline value, treatment, subgroup, and treatment:subgroup interaction as covariates.

Odds ratio and relative risk are calculated as Ravulizumab/Eculizumab. LS mean difference and risk difference are calculated as Ravulizumab - Eculizumab.

Source: adsl, adeq5d

Table EQ-5D-1.4
Change from Baseline in EQ-5D VAS Score to End of Study Period by Disease severity via EDSS Score at baseline
Full Analysis Set

EDSS score at baseline		Statistic	Eculizumab (N=96)	Ravulizumab (N=58)	p-value (7)
< 5	Change from Baseline to End of Study Period in EQ-5D VAS Score	n	66	49	0.4791
		Mean (SD)	6.6 (18.43)	2.6 (14.47)	
		Median	4.0	1.0	
		Q1, Q3	-1.0, 16.0	-8.0, 10.0	
		Min, Max	-30, 60	-45, 40	
		Change from baseline			
		LS Means (SEM)	5.075 (1.906)	4.715 (2.222)	
		95% CI for LS Means (1)	(1.298, 8.852)	(0.312, 9.118)	
		Difference in LS Means		-0.360	
		(95% CI) (1)		(-6.247, 5.527)	
		p-value (2)		0.7343	
		Standardized Mean Difference		-0.091	
		(95% CI) (3)		(-0.461, 0.278)	
		Responders (15% [15 points]), n(%)	18 (27.3)	10 (20.4)	
		Odds Ratio (4)		1.469	
		(95% CI)		(0.507, 4.253)	
		p-value		0.4785	
		Relative Risk (5)		0.748	
		(95% CI)		(0.380, 1.475)	
		p-value		0.4026	

The eculizumab group data were collected as part of the PREVENT trial, Study ECU-NMO-301.

End of Study Period is the 6-week assessment after the first On-Trial Relapse for patients who have an On-Trial Relapse or for patients with no On-Trial Relapse: the End of Primary Treatment Period visit for patients in Study ALXN1210-NMO-307 and the End of Study visit for patients in Study ECU-NMO-301.

For those patients who had a missed value at the EOPT Visit or the 6-week post-relapse visit, for patients who had a relapse, the end of study is the last value before the missed value.

(1) The LS means (95% CI) and the difference in LS means (95% CI) are from an ANCOVA model of change from baseline with treatment as factor and baseline value as covariate. (2) The p-value represents the significance of the treatment effect and was derived from an ANCOVA model of the ranked change from baseline, with treatment as a factor, and the ranks of the baseline value included as covariate.

(3) Standardized mean differences (95% CI) were computed using Cohen's D incorporating Hedge's correction on change from baseline. (4) Odds ratio statistics are from a logistic regression model adjusted for baseline value with Firth's adjustment; (5) Relative risk statistics are based on a generalized linear model of a binomial distribution with log link;

(6) Risk difference statistics are calculated from a generalized linear model, correcting for the baseline value. (7) P-value is for the interaction term of treatment:subgroup from a linear regression model of ranked change from baseline with the with ranked baseline value, treatment, subgroup, and treatment:subgroup interaction as covariates.

Odds ratio and relative risk are calculated as Ravulizumab/Eculizumab. LS mean difference and risk difference are calculated as Ravulizumab - Eculizumab.

Source: adsl, adeq5d

Table EQ-5D-1.4
Change from Baseline in EQ-5D VAS Score to End of Study Period by Disease severity via EDSS Score at baseline
Full Analysis Set

EDSS score at baseline	Statistic	Eculizumab (N=96)	Ravulizumab (N=58)	p-value (7)
	Risk Difference (6)		0.038	
	(95% CI)		(-0.107, 0.184)	
	p-value		0.6013	
Baseline EQ-5D VAS Score	n	66	49	
	Mean (SD)	66.9 (19.78)	75.6 (13.54)	
	Median	70.0	79.0	
	Q1, Q3	50.0, 80.0	70.0, 81.0	
	Min, Max	10, 100	30, 97	
End of Study Period EQ-5D VAS Score	n	66	49	
	Mean (SD)	73.5 (20.02)	78.2 (15.61)	
	Median	80.0	81.0	
	Q1, Q3	60.0, 90.0	71.0, 90.0	
	Min, Max	25, 100	13, 98	

The eculizumab group data were collected as part of the PREVENT trial, Study ECU-NMO-301.

End of Study Period is the 6-week assessment after the first On-Trial Relapse for patients who have an On-Trial Relapse or for patients with no On-Trial Relapse: the End of Primary Treatment Period visit for patients in Study ALXN1210-NMO-307 and the End of Study visit for patients in Study ECU-NMO-301.

For those patients who had a missed value at the EOPT Visit or the 6-week post-relapse visit, for patients who had a relapse, the end of study is the last value before the missed value.

(1) The LS means (95% CI) and the difference in LS means (95% CI) are from an ANCOVA model of change from baseline with treatment as factor and baseline value as covariate. (2) The p-value represents the significance of the treatment effect and was derived from an ANCOVA model of the ranked change from baseline, with treatment as a factor, and the ranks of the baseline value included as covariate.

(3) Standardized mean differences (95% CI) were computed using Cohen's D incorporating Hedge's correction on change from baseline. (4) Odds ratio statistics are from a logistic regression model adjusted for baseline value with Firth's adjustment; (5) Relative risk statistics are based on a generalized linear model of a binomial distribution with log link;

(6) Risk difference statistics are calculated from a generalized linear model, correcting for the baseline value. (7) P-value is for the interaction term of treatment:subgroup from a linear regression model of ranked change from baseline with the with ranked baseline value, treatment, subgroup, and treatment:subgroup interaction as covariates.

Odds ratio and relative risk are calculated as Ravulizumab/Eculizumab. LS mean difference and risk difference are calculated as Ravulizumab - Eculizumab.

Source: adsl, adeq5d

Table EQ-5D-1.4
Change from Baseline in EQ-5D VAS Score to End of Study Period by Disease severity via EDSS Score at baseline
Full Analysis Set

EDSS score at baseline		Statistic	Eculizumab (N=96)	Ravulizumab (N=58)	p-value (7)
>= 5	Change from Baseline to End of Study Period in EQ-5D VAS Score	n	30	9	
		Mean (SD)	2.7 (18.77)	2.8 (12.41)	
		Median	0.0	0.0	
		Q1, Q3	-10.0, 10.0	-5.0, 9.0	
		Min, Max	-25, 45	-20, 20	
		Change from baseline			
		LS Means (SEM)	2.406 (3.160)	3.868 (5.800)	
		95% CI for LS Means (1)	(-4.003, 8.816)	(-7.894, 15.631)	
		Difference in LS Means		1.462	
		(95% CI) (1)		(-11.979, 14.903)	
		p-value (2)		0.5331	
		Standardized Mean Difference		0.351	
		(95% CI) (3)		(-0.398, 1.100)	
		Responders (15% [15 points]), n(%)	7 (23.3)	2 (22.2)	
		Odds Ratio (4)		1.309	
		(95% CI)		(0.216, 7.942)	
		p-value		0.7700	
		Relative Risk (5)		0.952	
		(95% CI)		(0.239, 3.800)	
		p-value		0.9449	

The eculizumab group data were collected as part of the PREVENT trial, Study ECU-NMO-301.

End of Study Period is the 6-week assessment after the first On-Trial Relapse for patients who have an On-Trial Relapse or for patients with no On-Trial Relapse: the End of Primary Treatment Period visit for patients in Study ALXN1210-NMO-307 and the End of Study visit for patients in Study ECU-NMO-301.

For those patients who had a missed value at the EOPT Visit or the 6-week post-relapse visit, for patients who had a relapse, the end of study is the last value before the missed value.

(1) The LS means (95% CI) and the difference in LS means (95% CI) are from an ANCOVA model of change from baseline with treatment as factor and baseline value as covariate. (2) The p-value represents the significance of the treatment effect and was derived from an ANCOVA model of the ranked change from baseline, with treatment as a factor, and the ranks of the baseline value included as covariate.

(3) Standardized mean differences (95% CI) were computed using Cohen's D incorporating Hedge's correction on change from baseline. (4) Odds ratio statistics are from a logistic regression model adjusted for baseline value with Firth's adjustment; (5) Relative risk statistics are based on a generalized linear model of a binomial distribution with log link;

(6) Risk difference statistics are calculated from a generalized linear model, correcting for the baseline value. (7) P-value is for the interaction term of treatment:subgroup from a linear regression model of ranked change from baseline with the with ranked baseline value, treatment, subgroup, and treatment:subgroup interaction as covariates.

Odds ratio and relative risk are calculated as Ravulizumab/Eculizumab. LS mean difference and risk difference are calculated as Ravulizumab - Eculizumab.

Source: adsl, adeq5d

Table EQ-5D-1.4
Change from Baseline in EQ-5D VAS Score to End of Study Period by Disease severity via EDSS Score at baseline
Full Analysis Set

EDSS score at baseline	Statistic	Eculizumab (N=96)	Ravulizumab (N=58)	p-value (7)
	Risk Difference (6)		0.031	
	(95% CI)		(-0.294, 0.356)	
	p-value		0.8465	
Baseline EQ-5D VAS Score	n	30	9	
	Mean (SD)	56.5 (18.88)	62.4 (17.24)	
	Median	50.0	70.0	
	Q1, Q3	50.0, 70.0	50.0, 75.0	
	Min, Max	10, 80	40, 85	
End of Study Period EQ-5D VAS Score	n	30	9	
	Mean (SD)	59.2 (23.19)	65.2 (17.82)	
	Median	64.0	70.0	
	Q1, Q3	40.0, 75.0	59.0, 80.0	
	Min, Max	15, 95	30, 88	

The eculizumab group data were collected as part of the PREVENT trial, Study ECU-NMO-301.

End of Study Period is the 6-week assessment after the first On-Trial Relapse for patients who have an On-Trial Relapse or for patients with no On-Trial Relapse: the End of Primary Treatment Period visit for patients in Study ALXN1210-NMO-307 and the End of Study visit for patients in Study ECU-NMO-301.

For those patients who had a missed value at the EOPT Visit or the 6-week post-relapse visit, for patients who had a relapse, the end of study is the last value before the missed value.

(1) The LS means (95% CI) and the difference in LS means (95% CI) are from an ANCOVA model of change from baseline with treatment as factor and baseline value as covariate. (2) The p-value represents the significance of the treatment effect and was derived from an ANCOVA model of the ranked change from baseline, with treatment as a factor, and the ranks of the baseline value included as covariate.

(3) Standardized mean differences (95% CI) were computed using Cohen's D incorporating Hedge's correction on change from baseline. (4) Odds ratio statistics are from a logistic regression model adjusted for baseline value with Firth's adjustment; (5) Relative risk statistics are based on a generalized linear model of a binomial distribution with log link;

(6) Risk difference statistics are calculated from a generalized linear model, correcting for the baseline value. (7) P-value is for the interaction term of treatment:subgroup from a linear regression model of ranked change from baseline with the with ranked baseline value, treatment, subgroup, and treatment:subgroup interaction as covariates.

Odds ratio and relative risk are calculated as Ravulizumab/Eculizumab. LS mean difference and risk difference are calculated as Ravulizumab - Eculizumab.

Source: adsl, adeq5d

Table SF-36-2.2
Change from Baseline in SF-36 Physical Component Score to End of Study Period by Sex
Full Analysis Set

Sex		Statistic	Eculizumab (N=96)	Ravulizumab (N=58)	p-value (7)
Male	Change from Baseline to End of Study Period in SF-36 Physical Component Score	n	8	6	0.0753
		Mean (SD)	-2.9 (8.18)	1.9 (5.54)	
		Median	-2.5	1.7	
		Q1, Q3	-6.4, 2.4	-2.8, 7.2	
		Min, Max	-18, 8	-5, 9	
		Change from baseline			
		LS Means (SEM)	-5.718 (2.401)	5.610 (2.871)	
		95% CI for LS Means (1)	(-11.003, -0.432)	(-0.710, 11.930)	
		Difference in LS Means		11.328	
		(95% CI) (1)		(2.161, 20.495)	
		p-value (2)		0.0003	
		Standardized Mean Difference		4.314	
		(95% CI) (3)		(2.397, 6.231)	
		Responders (10% [10 points]), n(%)	0	0	
		Odds Ratio (4)		--	
		(95% CI)		--	
		p-value		--	
		Relative Risk (5)		--	
		(95% CI)		--	
		p-value		--	

The eculizumab group data were collected as part of the PREVENT trial, Study ECU-NMO-301.

End of Study Period is the 6-week assessment after the first On-Trial Relapse for patients who have an On-Trial Relapse or for patients with no On-Trial Relapse: the End of Primary Treatment Period visit for patients in Study ALXN1210-NMO-307 and the End of Study visit for patients in Study ECU-NMO-301.

For those patients who had a missed value at the EOPT Visit or the 6-week post-relapse visit, for patients who had a relapse, the end of study is the last value before the missed value.

(1) The LS means (95% CI) and the difference in LS means (95% CI) are from an ANCOVA model of change from baseline with treatment as factor and baseline value as covariate. (2) The p-value represents the significance of the treatment effect and was derived from an ANCOVA model of the ranked change from baseline, with treatment as a factor, and the ranks of the baseline value included as covariate.

(3) Standardized mean differences (95% CI) were computed using Cohen's D incorporating Hedge's correction on change from baseline. (4) Odds ratio statistics are from a logistic regression model adjusted for baseline value with Firth's adjustment; (5) Relative risk statistics are based on a generalized linear model of a binomial distribution with log link;

(6) Risk difference statistics are calculated from a generalized linear model, correcting for the baseline value. (7) P-value is for the interaction term of treatment:subgroup from a linear regression model of ranked change from baseline with the with ranked baseline value, treatment, subgroup, and treatment:subgroup interaction as covariates.

Odds ratio and relative risk are calculated as Ravulizumab/Eculizumab. LS mean difference and risk difference are calculated as Ravulizumab - Eculizumab.

Source: adsl, adsf36

Table SF-36-2.2
Change from Baseline in SF-36 Physical Component Score to End of Study Period by Sex
Full Analysis Set

Sex	Statistic	Eculizumab (N=96)	Ravulizumab (N=58)	p-value (7)
	Risk Difference (6)		--	
	(95% CI)		--	
	p-value		--	
Baseline SF-36 Physical Component Score	n	8	6	
	Mean (SD)	41.1 (5.76)	49.7 (5.56)	
	Median	41.2	47.4	
	Q1, Q3	39.7, 45.0	45.0, 56.4	
	Min, Max	29, 48	45, 57	
End of Study Period SF-36 Physical Component Score	n	8	6	
	Mean (SD)	38.2 (7.52)	51.6 (2.14)	
	Median	39.8	52.0	
	Q1, Q3	32.8, 43.0	49.8, 53.7	
	Min, Max	27, 48	48, 54	

The eculizumab group data were collected as part of the PREVENT trial, Study ECU-NMO-301.

End of Study Period is the 6-week assessment after the first On-Trial Relapse for patients who have an On-Trial Relapse or for patients with no On-Trial Relapse: the End of Primary Treatment Period visit for patients in Study ALXN1210-NMO-307 and the End of Study visit for patients in Study ECU-NMO-301.

For those patients who had a missed value at the EOPT Visit or the 6-week post-relapse visit, for patients who had a relapse, the end of study is the last value before the missed value.

(1) The LS means (95% CI) and the difference in LS means (95% CI) are from an ANCOVA model of change from baseline with treatment as factor and baseline value as covariate. (2) The p-value represents the significance of the treatment effect and was derived from an ANCOVA model of the ranked change from baseline, with treatment as a factor, and the ranks of the baseline value included as covariate.

(3) Standardized mean differences (95% CI) were computed using Cohen's D incorporating Hedge's correction on change from baseline. (4) Odds ratio statistics are from a logistic regression model adjusted for baseline value with Firth's adjustment; (5) Relative risk statistics are based on a generalized linear model of a binomial distribution with log link;

(6) Risk difference statistics are calculated from a generalized linear model, correcting for the baseline value. (7) P-value is for the interaction term of treatment:subgroup from a linear regression model of ranked change from baseline with the with ranked baseline value, treatment, subgroup, and treatment:subgroup interaction as covariates.

Odds ratio and relative risk are calculated as Ravulizumab/Eculizumab. LS mean difference and risk difference are calculated as Ravulizumab - Eculizumab.

Source: adsl, adsf36

Table SF-36-2.2
Change from Baseline in SF-36 Physical Component Score to End of Study Period by Sex
Full Analysis Set

Sex		Statistic	Eculizumab (N=96)	Ravulizumab (N=58)	p-value (7)
Female	Change from Baseline to End of Study Period in SF-36 Physical Component Score	n	88	52	
		Mean (SD)	3.9 (7.47)	2.4 (6.72)	
		Median	2.7	1.5	
		Q1, Q3	-0.1, 7.2	-1.2, 6.2	
		Min, Max	-20, 34	-17, 21	
		Change from baseline			
		LS Means (SEM)	3.643 (0.743)	2.845 (0.971)	
		95% CI for LS Means (1)	(2.173, 5.113)	(0.925, 4.765)	
		Difference in LS Means		-0.798	
		(95% CI) (1)		(-3.235, 1.638)	
		p-value (2)		0.5326	
		Standardized Mean Difference		-0.302	
		(95% CI) (3)		(-0.647, 0.043)	
		Responders (10% [10 points]), n(%)	13 (14.8)	7 (13.5)	
		Odds Ratio (4)		1.230	
		(95% CI)		(0.442, 3.425)	
		p-value		0.6919	
		Relative Risk (5)		0.911	
		(95% CI)		(0.389, 2.137)	
		p-value		0.8308	

The eculizumab group data were collected as part of the PREVENT trial, Study ECU-NMO-301.

End of Study Period is the 6-week assessment after the first On-Trial Relapse for patients who have an On-Trial Relapse or for patients with no On-Trial Relapse: the End of Primary Treatment Period visit for patients in Study ALXN1210-NMO-307 and the End of Study visit for patients in Study ECU-NMO-301.

For those patients who had a missed value at the EOPT Visit or the 6-week post-relapse visit, for patients who had a relapse, the end of study is the last value before the missed value.

(1) The LS means (95% CI) and the difference in LS means (95% CI) are from an ANCOVA model of change from baseline with treatment as factor and baseline value as covariate. (2) The p-value represents the significance of the treatment effect and was derived from an ANCOVA model of the ranked change from baseline, with treatment as a factor, and the ranks of the baseline value included as covariate.

(3) Standardized mean differences (95% CI) were computed using Cohen's D incorporating Hedge's correction on change from baseline. (4) Odds ratio statistics are from a logistic regression model adjusted for baseline value with Firth's adjustment; (5) Relative risk statistics are based on a generalized linear model of a binomial distribution with log link;

(6) Risk difference statistics are calculated from a generalized linear model, correcting for the baseline value. (7) P-value is for the interaction term of treatment:subgroup from a linear regression model of ranked change from baseline with the with ranked baseline value, treatment, subgroup, and treatment:subgroup interaction as covariates.

Odds ratio and relative risk are calculated as Ravulizumab/Eculizumab. LS mean difference and risk difference are calculated as Ravulizumab - Eculizumab.

Source: adsl, adsf36

Table SF-36-2.2
Change from Baseline in SF-36 Physical Component Score to End of Study Period by Sex
Full Analysis Set

Sex	Statistic	Eculizumab (N=96)	Ravulizumab (N=58)	p-value (7)
	Risk Difference (6)		0.023	
	(95% CI)		(-0.097, 0.142)	
	p-value		0.7082	
Baseline SF-36 Physical Component Score	n	88	52	
	Mean (SD)	38.4 (10.10)	42.1 (9.85)	
	Median	39.9	43.3	
	Q1, Q3	30.5, 45.5	34.1, 49.8	
	Min, Max	8, 57	22, 62	
End of Study Period SF-36 Physical Component Score	n	88	52	
	Mean (SD)	42.3 (10.79)	44.5 (10.10)	
	Median	44.0	46.1	
	Q1, Q3	35.6, 50.6	36.7, 52.2	
	Min, Max	16, 60	24, 66	

The eculizumab group data were collected as part of the PREVENT trial, Study ECU-NMO-301.

End of Study Period is the 6-week assessment after the first On-Trial Relapse for patients who have an On-Trial Relapse or for patients with no On-Trial Relapse: the End of Primary Treatment Period visit for patients in Study ALXN1210-NMO-307 and the End of Study visit for patients in Study ECU-NMO-301.

For those patients who had a missed value at the EOPT Visit or the 6-week post-relapse visit, for patients who had a relapse, the end of study is the last value before the missed value.

(1) The LS means (95% CI) and the difference in LS means (95% CI) are from an ANCOVA model of change from baseline with treatment as factor and baseline value as covariate. (2) The p-value represents the significance of the treatment effect and was derived from an ANCOVA model of the ranked change from baseline, with treatment as a factor, and the ranks of the baseline value included as covariate.

(3) Standardized mean differences (95% CI) were computed using Cohen's D incorporating Hedge's correction on change from baseline. (4) Odds ratio statistics are from a logistic regression model adjusted for baseline value with Firth's adjustment; (5) Relative risk statistics are based on a generalized linear model of a binomial distribution with log link;

(6) Risk difference statistics are calculated from a generalized linear model, correcting for the baseline value. (7) P-value is for the interaction term of treatment:subgroup from a linear regression model of ranked change from baseline with the with ranked baseline value, treatment, subgroup, and treatment:subgroup interaction as covariates.

Odds ratio and relative risk are calculated as Ravulizumab/Eculizumab. LS mean difference and risk difference are calculated as Ravulizumab - Eculizumab.

Source: adsl, adsf36

Table SF-36-2.3
Change from Baseline in SF-36 Physical Component Score to End of Study Period by Age Group
Full Analysis Set

Age Group		Statistic	Eculizumab (N=96)	Ravulizumab (N=58)	p-value (7)
< 45 years	Change from Baseline to End of Study Period in SF-36 Physical Component Score	n	47	25	0.0946
		Mean (SD)	3.6 (7.19)	1.3 (8.12)	
		Median	2.6	0.9	
		Q1, Q3	0.0, 8.7	-2.8, 5.5	
		Min, Max	-18, 22	-17, 21	
		Change from baseline LS Means (SEM)	3.060 (1.018)	2.316 (1.409)	
		95% CI for LS Means (1)	(1.028, 5.092)	(-0.495, 5.128)	
		Difference in LS Means		-0.743	
		(95% CI) (1)		(-4.259, 2.772)	
		p-value (2)		0.3616	
		Standardized Mean Difference		-0.281	
		(95% CI) (3)		(-0.768, 0.206)	
		Responders (10% [10 points]), n(%)	8 (17.0)	3 (12.0)	
		Odds Ratio (4)		1.013	
		(95% CI)		(0.223, 4.609)	
		p-value		0.9866	
		Relative Risk (5)		0.705	
		(95% CI)		(0.205, 2.424)	
		p-value		0.5791	

The eculizumab group data were collected as part of the PREVENT trial, Study ECU-NMO-301.

End of Study Period is the 6-week assessment after the first On-Trial Relapse for patients who have an On-Trial Relapse or for patients with no On-Trial Relapse: the End of Primary Treatment Period visit for patients in Study ALXN1210-NMO-307 and the End of Study visit for patients in Study ECU-NMO-301.

For those patients who had a missed value at the EOPT Visit or the 6-week post-relapse visit, for patients who had a relapse, the end of study is the last value before the missed value.

(1) The LS means (95% CI) and the difference in LS means (95% CI) are from an ANCOVA model of change from baseline with treatment as factor and baseline value as covariate. (2) The p-value represents the significance of the treatment effect and was derived from an ANCOVA model of the ranked change from baseline, with treatment as a factor, and the ranks of the baseline value included as covariate.

(3) Standardized mean differences (95% CI) were computed using Cohen's D incorporating Hedge's correction on change from baseline. (4) Odds ratio statistics are from a logistic regression model adjusted for baseline value with Firth's adjustment; (5) Relative risk statistics are based on a generalized linear model of a binomial distribution with log link;

(6) Risk difference statistics are calculated from a generalized linear model, correcting for the baseline value. (7) P-value is for the interaction term of treatment:subgroup from a linear regression model of ranked change from baseline with the with ranked baseline value, treatment, subgroup, and treatment:subgroup interaction as covariates.

Odds ratio and relative risk are calculated as Ravulizumab/Eculizumab. LS mean difference and risk difference are calculated as Ravulizumab - Eculizumab.

Source: adsl, adsf36

Table SF-36-2.3
Change from Baseline in SF-36 Physical Component Score to End of Study Period by Age Group
Full Analysis Set

Age Group	Statistic	Eculizumab (N=96)	Ravulizumab (N=58)	p-value (7)
	Risk Difference (6)		0.024	
	(95% CI)		(-0.147, 0.195)	
	p-value		0.7803	
Baseline SF-36 Physical Component Score	n	47	25	
	Mean (SD)	42.5 (7.87)	46.9 (9.64)	
	Median	44.5	49.5	
	Q1, Q3	35.4, 48.4	42.5, 54.4	
	Min, Max	25, 56	28, 62	
End of Study Period SF-36 Physical Component Score	n	47	25	
	Mean (SD)	46.1 (8.25)	48.2 (9.62)	
	Median	47.3	49.5	
	Q1, Q3	39.8, 52.4	42.5, 55.7	
	Min, Max	25, 60	26, 66	

The eculizumab group data were collected as part of the PREVENT trial, Study ECU-NMO-301.

End of Study Period is the 6-week assessment after the first On-Trial Relapse for patients who have an On-Trial Relapse or for patients with no On-Trial Relapse: the End of Primary Treatment Period visit for patients in Study ALXN1210-NMO-307 and the End of Study visit for patients in Study ECU-NMO-301.

For those patients who had a missed value at the EOPT Visit or the 6-week post-relapse visit, for patients who had a relapse, the end of study is the last value before the missed value.

(1) The LS means (95% CI) and the difference in LS means (95% CI) are from an ANCOVA model of change from baseline with treatment as factor and baseline value as covariate. (2) The p-value represents the significance of the treatment effect and was derived from an ANCOVA model of the ranked change from baseline, with treatment as a factor, and the ranks of the baseline value included as covariate.

(3) Standardized mean differences (95% CI) were computed using Cohen's D incorporating Hedge's correction on change from baseline. (4) Odds ratio statistics are from a logistic regression model adjusted for baseline value with Firth's adjustment; (5) Relative risk statistics are based on a generalized linear model of a binomial distribution with log link;

(6) Risk difference statistics are calculated from a generalized linear model, correcting for the baseline value. (7) P-value is for the interaction term of treatment:subgroup from a linear regression model of ranked change from baseline with the with ranked baseline value, treatment, subgroup, and treatment:subgroup interaction as covariates.

Odds ratio and relative risk are calculated as Ravulizumab/Eculizumab. LS mean difference and risk difference are calculated as Ravulizumab - Eculizumab.

Source: adsl, adsf36

Table SF-36-2.3
Change from Baseline in SF-36 Physical Component Score to End of Study Period by Age Group
Full Analysis Set

Age Group		Statistic	Eculizumab (N=96)	Ravulizumab (N=58)	p-value (7)
>= 45 years	Change from Baseline to End of Study Period in SF-36 Physical Component Score	n	49	33	
		Mean (SD)	3.1 (8.27)	3.1 (5.08)	
		Median	2.7	2.4	
		Q1, Q3	-1.3, 6.5	0.6, 6.4	
		Min, Max	-20, 34	-9, 13	
		Change from baseline			
		LS Means (SEM)	2.739 (1.013)	3.651 (1.242)	
		95% CI for LS Means (1)	(0.724, 4.755)	(1.179, 6.123)	
		Difference in LS Means		0.912	
		(95% CI) (1)		(-2.328, 4.151)	
		p-value (2)		0.3441	
		Standardized Mean Difference		0.342	
		(95% CI) (3)		(-0.102, 0.786)	
		Responders (10% [10 points]), n(%)	5 (10.2)	4 (12.1)	
		Odds Ratio (4)		2.070	
		(95% CI)		(0.473, 9.059)	
		p-value		0.3339	
		Relative Risk (5)		1.188	
		(95% CI)		(0.344, 4.099)	
		p-value		0.7853	

The eculizumab group data were collected as part of the PREVENT trial, Study ECU-NMO-301.

End of Study Period is the 6-week assessment after the first On-Trial Relapse for patients who have an On-Trial Relapse or for patients with no On-Trial Relapse: the End of Primary Treatment Period visit for patients in Study ALXN1210-NMO-307 and the End of Study visit for patients in Study ECU-NMO-301.

For those patients who had a missed value at the EOPT Visit or the 6-week post-relapse visit, for patients who had a relapse, the end of study is the last value before the missed value.

(1) The LS means (95% CI) and the difference in LS means (95% CI) are from an ANCOVA model of change from baseline with treatment as factor and baseline value as covariate. (2) The p-value represents the significance of the treatment effect and was derived from an ANCOVA model of the ranked change from baseline, with treatment as a factor, and the ranks of the baseline value included as covariate.

(3) Standardized mean differences (95% CI) were computed using Cohen's D incorporating Hedge's correction on change from baseline. (4) Odds ratio statistics are from a logistic regression model adjusted for baseline value with Firth's adjustment; (5) Relative risk statistics are based on a generalized linear model of a binomial distribution with log link;

(6) Risk difference statistics are calculated from a generalized linear model, correcting for the baseline value. (7) P-value is for the interaction term of treatment:subgroup from a linear regression model of ranked change from baseline with the with ranked baseline value, treatment, subgroup, and treatment:subgroup interaction as covariates.

Odds ratio and relative risk are calculated as Ravulizumab/Eculizumab. LS mean difference and risk difference are calculated as Ravulizumab - Eculizumab.

Source: adsl, adsf36

Table SF-36-2.3
Change from Baseline in SF-36 Physical Component Score to End of Study Period by Age Group
Full Analysis Set

Age Group	Statistic	Eculizumab (N=96)	Ravulizumab (N=58)	p-value (7)
	Risk Difference (6)		0.065	
	(95% CI)		(-0.077, 0.207)	
	p-value		0.3643	
Baseline SF-36 Physical Component Score	n	49	33	
	Mean (SD)	34.8 (10.10)	39.8 (8.78)	
	Median	36.4	42.0	
	Q1, Q3	26.8, 41.0	33.2, 46.9	
	Min, Max	8, 57	22, 53	
End of Study Period SF-36 Physical Component Score	n	49	33	
	Mean (SD)	37.9 (11.08)	42.9 (9.49)	
	Median	39.8	45.4	
	Q1, Q3	28.0, 45.5	36.3, 49.8	
	Min, Max	16, 58	24, 55	

The eculizumab group data were collected as part of the PREVENT trial, Study ECU-NMO-301.

End of Study Period is the 6-week assessment after the first On-Trial Relapse for patients who have an On-Trial Relapse or for patients with no On-Trial Relapse: the End of Primary Treatment Period visit for patients in Study ALXN1210-NMO-307 and the End of Study visit for patients in Study ECU-NMO-301.

For those patients who had a missed value at the EOPT Visit or the 6-week post-relapse visit, for patients who had a relapse, the end of study is the last value before the missed value.

(1) The LS means (95% CI) and the difference in LS means (95% CI) are from an ANCOVA model of change from baseline with treatment as factor and baseline value as covariate. (2) The p-value represents the significance of the treatment effect and was derived from an ANCOVA model of the ranked change from baseline, with treatment as a factor, and the ranks of the baseline value included as covariate.

(3) Standardized mean differences (95% CI) were computed using Cohen's D incorporating Hedge's correction on change from baseline. (4) Odds ratio statistics are from a logistic regression model adjusted for baseline value with Firth's adjustment; (5) Relative risk statistics are based on a generalized linear model of a binomial distribution with log link;

(6) Risk difference statistics are calculated from a generalized linear model, correcting for the baseline value. (7) P-value is for the interaction term of treatment:subgroup from a linear regression model of ranked change from baseline with the with ranked baseline value, treatment, subgroup, and treatment:subgroup interaction as covariates.

Odds ratio and relative risk are calculated as Ravulizumab/Eculizumab. LS mean difference and risk difference are calculated as Ravulizumab - Eculizumab.

Source: adsl, adsf36

Table SF-36-2.5
Change from Baseline in SF-36 Physical Component Score to End of Study Period by Region
Full Analysis Set

Region		Statistic	Eculizumab (N=96)	Ravulizumab (N=58)	p-value (7)
Asia-Pacific	Change from Baseline to End of Study Period in SF-36 Physical Component Score	n	35	20	0.3726
		Mean (SD)	2.1 (6.60)	1.2 (5.65)	
		Median	1.3	1.3	
		Q1, Q3	-1.3, 6.1	-0.3, 5.8	
		Min, Max	-20, 20	-17, 8	
		Change from baseline			
		LS Means (SEM)	1.938 (1.063)	1.589 (1.417)	
		95% CI for LS Means (1)	(-0.195, 4.071)	(-1.254, 4.431)	
		Difference in LS Means		-0.349	
		(95% CI) (1)		(-3.948, 3.249)	
		p-value (2)		0.9482	
		Standardized Mean Difference		-0.139	
		(95% CI) (3)		(-0.689, 0.411)	
		Responders (10% [10 points]), n(%)	3 (8.6)	0	
		Odds Ratio (4)		0.330	
		(95% CI)		(0.016, 6.853)	
		p-value		0.4734	
		Relative Risk (5)		0.000	
		(95% CI)		--	
		p-value		0.9999	

The eculizumab group data were collected as part of the PREVENT trial, Study ECU-NMO-301.

End of Study Period is the 6-week assessment after the first On-Trial Relapse for patients who have an On-Trial Relapse or for patients with no On-Trial Relapse: the End of Primary Treatment Period visit for patients in Study ALXN1210-NMO-307 and the End of Study visit for patients in Study ECU-NMO-301.

For those patients who had a missed value at the EOPT Visit or the 6-week post-relapse visit, for patients who had a relapse, the end of study is the last value before the missed value.

(1) The LS means (95% CI) and the difference in LS means (95% CI) are from an ANCOVA model of change from baseline with treatment as factor and baseline value as covariate. (2) The p-value represents the significance of the treatment effect and was derived from an ANCOVA model of the ranked change from baseline, with treatment as a factor, and the ranks of the baseline value included as covariate.

(3) Standardized mean differences (95% CI) were computed using Cohen's D incorporating Hedge's correction on change from baseline. (4) Odds ratio statistics are from a logistic regression model adjusted for baseline value with Firth's adjustment; (5) Relative risk statistics are based on a generalized linear model of a binomial distribution with log link;

(6) Risk difference statistics are calculated from a generalized linear model, correcting for the baseline value. (7) P-value is for the interaction term of treatment:subgroup from a linear regression model of ranked change from baseline with the with ranked baseline value, treatment, subgroup, and treatment:subgroup interaction as covariates.

For eculizumab arm, Americas: ARG and USA; Europe: CZE, DEU, DNK, ESP, HRV, ITA, RUS and TUR; Asia-Pacific: AUS, HKG, JPN, KOR, MYS, THA and TWN. For ravulizumab arm, Americas: CAN and USA; Europe: DEU, DNK, ESP, GBR, ITA and POL; Asia-Pacific: AUS, JPN and KOR.

Odds ratio and relative risk are calculated as Ravulizumab/Eculizumab. LS mean difference and risk difference are calculated as Ravulizumab - Eculizumab.

Source: adsl, adsf36

Table SF-36-2.5
Change from Baseline in SF-36 Physical Component Score to End of Study Period by Region
Full Analysis Set

Region	Statistic	Eculizumab (N=96)	Ravulizumab (N=58)	p-value (7)
	Risk Difference (6)		-0.062	
	(95% CI)		(-0.192, 0.068)	
	p-value		0.3406	
Baseline SF-36 Physical Component Score	n	35	20	
	Mean (SD)	41.5 (8.19)	45.4 (7.82)	
	Median	42.4	45.3	
	Q1, Q3	35.4, 46.8	41.6, 49.8	
	Min, Max	25, 57	29, 62	
End of Study Period SF-36 Physical Component Score	n	35	20	
	Mean (SD)	43.6 (10.22)	46.6 (7.20)	
	Median	45.5	47.9	
	Q1, Q3	38.6, 51.9	43.2, 50.9	
	Min, Max	20, 60	28, 59	

The eculizumab group data were collected as part of the PREVENT trial, Study ECU-NMO-301.

End of Study Period is the 6-week assessment after the first On-Trial Relapse for patients who have an On-Trial Relapse or for patients with no On-Trial Relapse: the End of Primary Treatment Period visit for patients in Study ALXN1210-NMO-307 and the End of Study visit for patients in Study ECU-NMO-301.

For those patients who had a missed value at the EOPT Visit or the 6-week post-relapse visit, for patients who had a relapse, the end of study is the last value before the missed value.

(1) The LS means (95% CI) and the difference in LS means (95% CI) are from an ANCOVA model of change from baseline with treatment as factor and baseline value as covariate. (2) The p-value represents the significance of the treatment effect and was derived from an ANCOVA model of the ranked change from baseline, with treatment as a factor, and the ranks of the baseline value included as covariate.

(3) Standardized mean differences (95% CI) were computed using Cohen's D incorporating Hedge's correction on change from baseline. (4) Odds ratio statistics are from a logistic regression model adjusted for baseline value with Firth's adjustment; (5) Relative risk statistics are based on a generalized linear model of a binomial distribution with log link;

(6) Risk difference statistics are calculated from a generalized linear model, correcting for the baseline value. (7) P-value is for the interaction term of treatment:subgroup from a linear regression model of ranked change from baseline with the with ranked baseline value, treatment, subgroup, and treatment:subgroup interaction as covariates.

For eculizumab arm, Americas: ARG and USA; Europe: CZE, DEU, DNK, ESP, HRV, ITA, RUS and TUR; Asia-Pacific: AUS, HKG, JPN, KOR, MYS, THA and TWN. For ravulizumab arm, Americas: CAN and USA; Europe: DEU, DNK, ESP, GBR, ITA and POL; Asia-Pacific: AUS, JPN and KOR.

Odds ratio and relative risk are calculated as Ravulizumab/Eculizumab. LS mean difference and risk difference are calculated as Ravulizumab - Eculizumab.

Source: adsl, adsf36

Table SF-36-2.5
Change from Baseline in SF-36 Physical Component Score to End of Study Period by Region
Full Analysis Set

Region		Statistic	Eculizumab (N=96)	Ravulizumab (N=58)	p-value (7)
Americas	Change from Baseline to End of Study Period in SF-36 Physical Component Score	n	29	21	0.1657
		Mean (SD)	2.7 (7.15)	4.3 (7.44)	
		Median	4.6	2.7	
		Q1, Q3	0.0, 6.0	0.7, 8.3	
		Min, Max	-18, 16	-9, 21	
		Change from baseline			
		LS Means (SEM)	2.225 (1.297)	5.011 (1.531)	
		95% CI for LS Means (1)	(-0.383, 4.834)	(1.932, 8.090)	
		Difference in LS Means		2.786	
		(95% CI) (1)		(-1.304, 6.876)	
		p-value (2)		0.3990	
		Standardized Mean Difference		1.053	
		(95% CI) (3)		(0.455, 1.652)	
		Responders (10% [10 points]), n(%)	3 (10.3)	4 (19.0)	
		Odds Ratio (4)		2.826	
		(95% CI)		(0.539, 14.809)	
		p-value		0.2191	
		Relative Risk (5)		1.841	
		(95% CI)		(0.460, 7.375)	
		p-value		0.3885	

The eculizumab group data were collected as part of the PREVENT trial, Study ECU-NMO-301.
End of Study Period is the 6-week assessment after the first On-Trial Relapse for patients who have an On-Trial Relapse or for patients with no On-Trial Relapse: the End of Primary Treatment Period visit for patients in Study ALXN1210-NMO-307 and the End of Study visit for patients in Study ECU-NMO-301.
For those patients who had a missed value at the EOPT Visit or the 6-week post-relapse visit, for patients who had a relapse, the end of study is the last value before the missed value.
(1) The LS means (95% CI) and the difference in LS means (95% CI) are from an ANCOVA model of change from baseline with treatment as factor and baseline value as covariate. (2) The p-value represents the significance of the treatment effect and was derived from an ANCOVA model of the ranked change from baseline, with treatment as a factor, and the ranks of the baseline value included as covariate.
(3) Standardized mean differences (95% CI) were computed using Cohen's D incorporating Hedge's correction on change from baseline. (4) Odds ratio statistics are from a logistic regression model adjusted for baseline value with Firth's adjustment; (5) Relative risk statistics are based on a generalized linear model of a binomial distribution with log link;
(6) Risk difference statistics are calculated from a generalized linear model, correcting for the baseline value. (7) P-value is for the interaction term of treatment:subgroup from a linear regression model of ranked change from baseline with the with ranked baseline value, treatment, subgroup, and treatment:subgroup interaction as covariates.
For eculizumab arm, Americas: ARG and USA; Europe: CZE, DEU, DNK, ESP, HRV, ITA, RUS and TUR; Asia-Pacific: AUS, HKG, JPN, KOR, MYS, THA and TWN. For ravulizumab arm, Americas: CAN and USA; Europe: DEU, DNK, ESP, GBR, ITA and POL; Asia-Pacific: AUS, JPN and KOR.
Odds ratio and relative risk are calculated as Ravulizumab/Eculizumab. LS mean difference and risk difference are calculated as Ravulizumab - Eculizumab.
Source: adsl, adsf36

Table SF-36-2.5
Change from Baseline in SF-36 Physical Component Score to End of Study Period by Region
Full Analysis Set

Region	Statistic	Eculizumab (N=96)	Ravulizumab (N=58)	p-value (7)
	Risk Difference (6)		0.137	
	(95% CI)		(-0.064, 0.338)	
	p-value		0.1761	
Baseline SF-36 Physical Component Score	n	29	21	
	Mean (SD)	36.2 (9.27)	41.0 (10.88)	
	Median	35.4	43.4	
	Q1, Q3	30.4, 44.9	32.7, 49.4	
	Min, Max	18, 50	22, 57	
End of Study Period SF-36 Physical Component Score	n	29	21	
	Mean (SD)	39.0 (8.80)	45.3 (11.70)	
	Median	39.8	46.3	
	Q1, Q3	32.3, 45.2	36.3, 55.1	
	Min, Max	19, 56	26, 66	

The eculizumab group data were collected as part of the PREVENT trial, Study ECU-NMO-301.

End of Study Period is the 6-week assessment after the first On-Trial Relapse for patients who have an On-Trial Relapse or for patients with no On-Trial Relapse: the End of Primary Treatment Period visit for patients in Study ALXN1210-NMO-307 and the End of Study visit for patients in Study ECU-NMO-301.

For those patients who had a missed value at the EOPT Visit or the 6-week post-relapse visit, for patients who had a relapse, the end of study is the last value before the missed value.

(1) The LS means (95% CI) and the difference in LS means (95% CI) are from an ANCOVA model of change from baseline with treatment as factor and baseline value as covariate. (2) The p-value represents the significance of the treatment effect and was derived from an ANCOVA model of the ranked change from baseline, with treatment as a factor, and the ranks of the baseline value included as covariate.

(3) Standardized mean differences (95% CI) were computed using Cohen's D incorporating Hedge's correction on change from baseline. (4) Odds ratio statistics are from a logistic regression model adjusted for baseline value with Firth's adjustment; (5) Relative risk statistics are based on a generalized linear model of a binomial distribution with log link;

(6) Risk difference statistics are calculated from a generalized linear model, correcting for the baseline value.
(7) P-value is for the interaction term of treatment:subgroup from a linear regression model of ranked change from baseline with the with ranked baseline value, treatment, subgroup, and treatment:subgroup interaction as covariates.

For eculizumab arm, Americas: ARG and USA; Europe: CZE, DEU, DNK, ESP, HRV, ITA, RUS and TUR; Asia-Pacific: AUS, HKG, JPN, KOR, MYS, THA and TWN. For ravulizumab arm, Americas: CAN and USA; Europe: DEU, DNK, ESP, GBR, ITA and POL; Asia-Pacific: AUS, JPN and KOR.

Odds ratio and relative risk are calculated as Ravulizumab/Eculizumab. LS mean difference and risk difference are calculated as Ravulizumab - Eculizumab.

Source: adsl, adsf36

Table SF-36-2.5
Change from Baseline in SF-36 Physical Component Score to End of Study Period by Region
Full Analysis Set

Region		Statistic	Eculizumab (N=96)	Ravulizumab (N=58)	p-value (7)
Europe	Change from Baseline to End of Study Period in SF-36 Physical Component Score	n	32	17	
		Mean (SD)	5.3 (9.12)	1.1 (6.17)	
		Median	2.6	1.1	
		Q1, Q3	-0.8, 9.1	-2.8, 2.9	
		Min, Max	-6, 34	-8, 13	
		Change from baseline			
		LS Means (SEM)	4.870 (1.410)	1.835 (1.947)	
		95% CI for LS Means (1)	(2.032, 7.708)	(-2.084, 5.755)	
		Difference in LS Means		-3.035	
		(95% CI) (1)		(-7.922, 1.852)	
		p-value (2)		0.2405	
		Standardized Mean Difference		-1.073	
		(95% CI) (3)		(-1.699, -0.448)	
		Responders (10% [10 points]), n(%)	7 (21.9)	3 (17.6)	
		Odds Ratio (4)		1.068	
		(95% CI)		(0.233, 4.889)	
		p-value		0.9328	
		Relative Risk (5)		0.807	
		(95% CI)		(0.239, 2.727)	
		p-value		0.7296	

The eculizumab group data were collected as part of the PREVENT trial, Study ECU-NMO-301.
End of Study Period is the 6-week assessment after the first On-Trial Relapse for patients who have an On-Trial Relapse or for patients with no On-Trial Relapse: the End of Primary Treatment Period visit for patients in Study ALXN1210-NMO-307 and the End of Study visit for patients in Study ECU-NMO-301.
For those patients who had a missed value at the EOPT Visit or the 6-week post-relapse visit, for patients who had a relapse, the end of study is the last value before the missed value.
(1) The LS means (95% CI) and the difference in LS means (95% CI) are from an ANCOVA model of change from baseline with treatment as factor and baseline value as covariate. (2) The p-value represents the significance of the treatment effect and was derived from an ANCOVA model of the ranked change from baseline, with treatment as a factor, and the ranks of the baseline value included as covariate.
(3) Standardized mean differences (95% CI) were computed using Cohen's D incorporating Hedge's correction on change from baseline. (4) Odds ratio statistics are from a logistic regression model adjusted for baseline value with Firth's adjustment; (5) Relative risk statistics are based on a generalized linear model of a binomial distribution with log link;
(6) Risk difference statistics are calculated from a generalized linear model, correcting for the baseline value. (7) P-value is for the interaction term of treatment:subgroup from a linear regression model of ranked change from baseline with the with ranked baseline value, treatment, subgroup, and treatment:subgroup interaction as covariates.
For eculizumab arm, Americas: ARG and USA; Europe: CZE, DEU, DNK, ESP, HRV, ITA, RUS and TUR; Asia-Pacific: AUS, HKG, JPN, KOR, MYS, THA and TWN. For ravulizumab arm, Americas: CAN and USA; Europe: DEU, DNK, ESP, GBR, ITA and POL; Asia-Pacific: AUS, JPN and KOR.
Odds ratio and relative risk are calculated as Ravulizumab/Eculizumab. LS mean difference and risk difference are calculated as Ravulizumab - Eculizumab.
Source: adsl, adsf36

Table SF-36-2.5
Change from Baseline in SF-36 Physical Component Score to End of Study Period by Region
Full Analysis Set

Region	Statistic	Eculizumab (N=96)	Ravulizumab (N=58)	p-value (7)
	Risk Difference (6)		0.003	
	(95% CI)		(-0.245, 0.251)	
	p-value		0.9785	
Baseline SF-36 Physical Component Score	n	32	17	
	Mean (SD)	37.5 (11.36)	42.3 (10.21)	
	Median	39.1	43.3	
	Q1, Q3	28.7, 45.7	33.2, 50.5	
	Min, Max	8, 56	27, 58	
End of Study Period SF-36 Physical Component Score	n	32	17	
	Mean (SD)	42.8 (12.10)	43.4 (10.24)	
	Median	45.1	45.9	
	Q1, Q3	35.6, 53.5	34.8, 51.6	
	Min, Max	16, 58	24, 57	

The eculizumab group data were collected as part of the PREVENT trial, Study ECU-NMO-301.

End of Study Period is the 6-week assessment after the first On-Trial Relapse for patients who have an On-Trial Relapse or for patients with no On-Trial Relapse: the End of Primary Treatment Period visit for patients in Study ALXN1210-NMO-307 and the End of Study visit for patients in Study ECU-NMO-301.

For those patients who had a missed value at the EOPT Visit or the 6-week post-relapse visit, for patients who had a relapse, the end of study is the last value before the missed value.

(1) The LS means (95% CI) and the difference in LS means (95% CI) are from an ANCOVA model of change from baseline with treatment as factor and baseline value as covariate. (2) The p-value represents the significance of the treatment effect and was derived from an ANCOVA model of the ranked change from baseline, with treatment as a factor, and the ranks of the baseline value included as covariate.

(3) Standardized mean differences (95% CI) were computed using Cohen's D incorporating Hedge's correction on change from baseline. (4) Odds ratio statistics are from a logistic regression model adjusted for baseline value with Firth's adjustment; (5) Relative risk statistics are based on a generalized linear model of a binomial distribution with log link;

(6) Risk difference statistics are calculated from a generalized linear model, correcting for the baseline value. (7) P-value is for the interaction term of treatment:subgroup from a linear regression model of ranked change from baseline with the with ranked baseline value, treatment, subgroup, and treatment:subgroup interaction as covariates.

For eculizumab arm, Americas: ARG and USA; Europe: CZE, DEU, DNK, ESP, HRV, ITA, RUS and TUR; Asia-Pacific: AUS, HKG, JPN, KOR, MYS, THA and TWN. For ravulizumab arm, Americas: CAN and USA; Europe: DEU, DNK, ESP, GBR, ITA and POL; Asia-Pacific: AUS, JPN and KOR.

Odds ratio and relative risk are calculated as Ravulizumab/Eculizumab. LS mean difference and risk difference are calculated as Ravulizumab - Eculizumab.

Source: adsl, adsf36

Table SF-36-2.6
Change from Baseline in SF-36 Physical Component Score to End of Study Period by Supportive IST use at baseline
Full Analysis Set

IST use at baseline		Statistic	Eculizumab (N=96)	Ravulizumab (N=58)	p-value (7)
Yes	Change from Baseline to End of Study Period in SF-36 Physical Component Score	n	75	28	0.9030
		Mean (SD)	2.5 (6.99)	1.3 (6.02)	
		Median	1.6	1.0	
		Q1, Q3	-1.2, 6.1	-1.2, 2.1	
		Min, Max	-20, 23	-17, 19	
		Change from baseline			
		LS Means (SEM)	2.206 (0.744)	2.072 (1.231)	
		95% CI for LS Means (1)	(0.730, 3.683)	(-0.370, 4.515)	
		Difference in LS Means		-0.134	
		(95% CI) (1)		(-3.014, 2.746)	
		p-value (2)		0.6833	
		Standardized Mean Difference		-0.053	
		(95% CI) (3)		(-0.487, 0.381)	
		Responders (10% [10 points]), n(%)	8 (10.7)	2 (7.1)	
		Odds Ratio (4)		1.096	
		(95% CI)		(0.227, 5.302)	
		p-value		0.9088	
		Relative Risk (5)		0.670	
		(95% CI)		(0.151, 2.964)	
		p-value		0.5972	

The eculizumab group data were collected as part of the PREVENT trial, Study ECU-NMO-301.

End of Study Period is the 6-week assessment after the first On-Trial Relapse for patients who have an On-Trial Relapse or for patients with no On-Trial Relapse: the End of Primary Treatment Period visit for patients in Study ALXN1210-NMO-307 and the End of Study visit for patients in Study ECU-NMO-301.

For those patients who had a missed value at the EOPT Visit or the 6-week post-relapse visit, for patients who had a relapse, the end of study is the last value before the missed value.

(1) The LS means (95% CI) and the difference in LS means (95% CI) are from an ANCOVA model of change from baseline with treatment as factor and baseline value as covariate. (2) The p-value represents the significance of the treatment effect and was derived from an ANCOVA model of the ranked change from baseline, with treatment as a factor, and the ranks of the baseline value included as covariate.

(3) Standardized mean differences (95% CI) were computed using Cohen's D incorporating Hedge's correction on change from baseline. (4) Odds ratio statistics are from a logistic regression model adjusted for baseline value with Firth's adjustment; (5) Relative risk statistics are based on a generalized linear model of a binomial distribution with log link;

(6) Risk difference statistics are calculated from a generalized linear model, correcting for the baseline value. (7) P-value is for the interaction term of treatment:subgroup from a linear regression model of ranked change from baseline with the with ranked baseline value, treatment, subgroup, and treatment:subgroup interaction as covariates.

Odds ratio and relative risk are calculated as Ravulizumab/Eculizumab. LS mean difference and risk difference are calculated as Ravulizumab - Eculizumab.

Source: adsl, adsf36

Table SF-36-2.6
Change from Baseline in SF-36 Physical Component Score to End of Study Period by Supportive IST use at baseline
Full Analysis Set

IST use at baseline	Statistic	Eculizumab (N=96)	Ravulizumab (N=58)	p-value (7)
	Risk Difference (6)		0.006	
	(95% CI)		(-0.123, 0.136)	
	p-value		0.9235	
Baseline SF-36 Physical Component Score	n	75	28	
	Mean (SD)	38.7 (10.08)	43.6 (10.41)	
	Median	40.3	45.3	
	Q1, Q3	30.6, 45.8	36.7, 50.4	
	Min, Max	8, 57	22, 62	
End of Study Period SF-36 Physical Component Score	n	75	28	
	Mean (SD)	41.2 (10.63)	44.9 (8.92)	
	Median	42.5	46.4	
	Q1, Q3	34.8, 48.1	38.8, 52.1	
	Min, Max	16, 60	24, 59	

The eculizumab group data were collected as part of the PREVENT trial, Study ECU-NMO-301.

End of Study Period is the 6-week assessment after the first On-Trial Relapse for patients who have an On-Trial Relapse or for patients with no On-Trial Relapse: the End of Primary Treatment Period visit for patients in Study ALXN1210-NMO-307 and the End of Study visit for patients in Study ECU-NMO-301.

For those patients who had a missed value at the EOPT Visit or the 6-week post-relapse visit, for patients who had a relapse, the end of study is the last value before the missed value.

(1) The LS means (95% CI) and the difference in LS means (95% CI) are from an ANCOVA model of change from baseline with treatment as factor and baseline value as covariate. (2) The p-value represents the significance of the treatment effect and was derived from an ANCOVA model of the ranked change from baseline, with treatment as a factor, and the ranks of the baseline value included as covariate.

(3) Standardized mean differences (95% CI) were computed using Cohen's D incorporating Hedge's correction on change from baseline. (4) Odds ratio statistics are from a logistic regression model adjusted for baseline value with Firth's adjustment; (5) Relative risk statistics are based on a generalized linear model of a binomial distribution with log link;

(6) Risk difference statistics are calculated from a generalized linear model, correcting for the baseline value. (7) P-value is for the interaction term of treatment:subgroup from a linear regression model of ranked change from baseline with the with ranked baseline value, treatment, subgroup, and treatment:subgroup interaction as covariates.

Odds ratio and relative risk are calculated as Ravulizumab/Eculizumab. LS mean difference and risk difference are calculated as Ravulizumab - Eculizumab.

Source: adsl, adsf36

Table SF-36-2.6
Change from Baseline in SF-36 Physical Component Score to End of Study Period by Supportive IST use at baseline
Full Analysis Set

IST use at baseline		Statistic	Eculizumab (N=96)	Ravulizumab (N=58)	p-value (7)
No	Change from Baseline to End of Study Period in SF-36 Physical Component Score	n	21	30	
		Mean (SD)	6.4 (9.50)	3.3 (7.00)	
		Median	4.6	3.7	
		Q1, Q3	1.5, 9.9	-2.8, 7.7	
		Min, Max	-6, 34	-9, 21	
		Change from baseline			
		LS Means (SEM)	5.883 (1.751)	3.646 (1.459)	
		95% CI for LS Means (1)	(2.363, 9.403)	(0.713, 6.579)	
		Difference in LS Means		-2.237	
		(95% CI) (1)		(-6.871, 2.398)	
		p-value (2)		0.5505	
		Standardized Mean Difference		-0.791	
		(95% CI) (3)		(-1.369, -0.212)	
		Responders (10% [10 points]), n(%)	5 (23.8)	5 (16.7)	
		Odds Ratio (4)		0.847	
		(95% CI)		(0.204, 3.525)	
		p-value		0.8199	
		Relative Risk (5)		0.700	
		(95% CI)		(0.231, 2.118)	
		p-value		0.5277	

The eculizumab group data were collected as part of the PREVENT trial, Study ECU-NMO-301.

End of Study Period is the 6-week assessment after the first On-Trial Relapse for patients who have an On-Trial Relapse or for patients with no On-Trial Relapse: the End of Primary Treatment Period visit for patients in Study ALXN1210-NMO-307 and the End of Study visit for patients in Study ECU-NMO-301.

For those patients who had a missed value at the EOPT Visit or the 6-week post-relapse visit, for patients who had a relapse, the end of study is the last value before the missed value.

(1) The LS means (95% CI) and the difference in LS means (95% CI) are from an ANCOVA model of change from baseline with treatment as factor and baseline value as covariate. (2) The p-value represents the significance of the treatment effect and was derived from an ANCOVA model of the ranked change from baseline, with treatment as a factor, and the ranks of the baseline value included as covariate.

(3) Standardized mean differences (95% CI) were computed using Cohen's D incorporating Hedge's correction on change from baseline. (4) Odds ratio statistics are from a logistic regression model adjusted for baseline value with Firth's adjustment; (5) Relative risk statistics are based on a generalized linear model of a binomial distribution with log link;

(6) Risk difference statistics are calculated from a generalized linear model, correcting for the baseline value. (7) P-value is for the interaction term of treatment:subgroup from a linear regression model of ranked change from baseline with the with ranked baseline value, treatment, subgroup, and treatment:subgroup interaction as covariates.

Odds ratio and relative risk are calculated as Ravulizumab/Eculizumab. LS mean difference and risk difference are calculated as Ravulizumab - Eculizumab.

Source: adsl, adsf36

Table SF-36-2.6
Change from Baseline in SF-36 Physical Component Score to End of Study Period by Supportive IST use at baseline
Full Analysis Set

IST use at baseline	Statistic	Eculizumab (N=96)	Ravulizumab (N=58)	p-value (7)
	Risk Difference (6)		-0.023	
	(95% CI)		(-0.253, 0.207)	
	p-value		0.8406	
Baseline SF-36 Physical Component Score	n	21	30	
	Mean (SD)	38.2 (9.08)	42.2 (9.20)	
	Median	38.5	43.3	
	Q1, Q3	31.9, 44.9	34.9, 49.4	
	Min, Max	24, 54	24, 58	
End of Study Period SF-36 Physical Component Score	n	21	30	
	Mean (SD)	44.6 (10.19)	45.5 (10.73)	
	Median	46.9	47.8	
	Q1, Q3	38.6, 53.7	38.8, 53.7	
	Min, Max	23, 58	26, 66	

The eculizumab group data were collected as part of the PREVENT trial, Study ECU-NMO-301.

End of Study Period is the 6-week assessment after the first On-Trial Relapse for patients who have an On-Trial Relapse or for patients with no On-Trial Relapse: the End of Primary Treatment Period visit for patients in Study ALXN1210-NMO-307 and the End of Study visit for patients in Study ECU-NMO-301.

For those patients who had a missed value at the EOPT Visit or the 6-week post-relapse visit, for patients who had a relapse, the end of study is the last value before the missed value.

(1) The LS means (95% CI) and the difference in LS means (95% CI) are from an ANCOVA model of change from baseline with treatment as factor and baseline value as covariate. (2) The p-value represents the significance of the treatment effect and was derived from an ANCOVA model of the ranked change from baseline, with treatment as a factor, and the ranks of the baseline value included as covariate.

(3) Standardized mean differences (95% CI) were computed using Cohen's D incorporating Hedge's correction on change from baseline. (4) Odds ratio statistics are from a logistic regression model adjusted for baseline value with Firth's adjustment; (5) Relative risk statistics are based on a generalized linear model of a binomial distribution with log link;

(6) Risk difference statistics are calculated from a generalized linear model, correcting for the baseline value. (7) P-value is for the interaction term of treatment:subgroup from a linear regression model of ranked change from baseline with the with ranked baseline value, treatment, subgroup, and treatment:subgroup interaction as covariates.

Odds ratio and relative risk are calculated as Ravulizumab/Eculizumab. LS mean difference and risk difference are calculated as Ravulizumab - Eculizumab.

Source: adsl, adsf36

Table SF-36-2.7
Change from Baseline in SF-36 Physical Component Score to End of Study Period by Rituximab use in the prior year
Full Analysis Set

Rituximab use in the prior year		Statistic	Eculizumab (N=96)	Ravulizumab (N=58)	p-value (7)
Yes	Change from Baseline to End of Study Period in SF-36 Physical Component Score	n	19	20	0.4580
		Mean (SD)	4.2 (8.68)	3.5 (8.68)	
		Median	2.8	5.0	
		Q1, Q3	0.0, 7.2	-2.0, 9.6	
		Min, Max	-8, 34	-17, 19	
		Change from baseline			
		LS Means (SEM)	3.820 (1.909)	3.815 (1.861)	
		95% CI for LS Means (1)	(-0.053, 7.693)	(0.042, 7.589)	
		Difference in LS Means		-0.005	
		(95% CI) (1)		(-5.434, 5.425)	
		p-value (2)		0.5916	
		Standardized Mean Difference		-0.002	
		(95% CI) (3)		(-0.630, 0.626)	
		Responders (10% [10 points]), n(%)	2 (10.5)	5 (25.0)	
		Odds Ratio (4)		3.218	
		(95% CI)		(0.543, 19.085)	
		p-value		0.1982	
		Relative Risk (5)		2.375	
		(95% CI)		(0.522, 10.803)	
		p-value		0.2631	

The eculizumab group data were collected as part of the PREVENT trial, Study ECU-NMO-301.

End of Study Period is the 6-week assessment after the first On-Trial Relapse for patients who have an On-Trial Relapse or for patients with no On-Trial Relapse: the End of Primary Treatment Period visit for patients in Study ALXN1210-NMO-307 and the End of Study visit for patients in Study ECU-NMO-301.

For those patients who had a missed value at the EOPT Visit or the 6-week post-relapse visit, for patients who had a relapse, the end of study is the last value before the missed value.

(1) The LS means (95% CI) and the difference in LS means (95% CI) are from an ANCOVA model of change from baseline with treatment as factor and baseline value as covariate. (2) The p-value represents the significance of the treatment effect and was derived from an ANCOVA model of the ranked change from baseline, with treatment as a factor, and the ranks of the baseline value included as covariate.

(3) Standardized mean differences (95% CI) were computed using Cohen's D incorporating Hedge's correction on change from baseline. (4) Odds ratio statistics are from a logistic regression model adjusted for baseline value with Firth's adjustment; (5) Relative risk statistics are based on a generalized linear model of a binomial distribution with log link;

(6) Risk difference statistics are calculated from a generalized linear model, correcting for the baseline value. (7) P-value is for the interaction term of treatment:subgroup from a linear regression model of ranked change from baseline with the with ranked baseline value, treatment, subgroup, and treatment:subgroup interaction as covariates.

Odds ratio and relative risk are calculated as Ravulizumab/Eculizumab. LS mean difference and risk difference are calculated as Ravulizumab - Eculizumab.

Source: adsl, adsf36

Table SF-36-2.7
Change from Baseline in SF-36 Physical Component Score to End of Study Period by Rituximab use in the prior year
Full Analysis Set

Rituximab use in the prior year		Statistic	Eculizumab (N=96)	Ravulizumab (N=58)	p-value (7)
		Risk Difference (6)		0.172	
		(95% CI)		(-0.075, 0.419)	
		p-value		0.1667	
	Baseline SF-36 Physical Component Score	n	19	20	
		Mean (SD)	35.7 (10.85)	38.4 (10.37)	
		Median	35.3	35.3	
		Q1, Q3	25.4, 44.9	31.3, 45.9	
		Min, Max	18, 56	22, 62	
	End of Study Period SF-36 Physical Component Score	n	19	20	
		Mean (SD)	39.9 (12.07)	41.8 (10.37)	
		Median	39.8	45.0	
		Q1, Q3	29.3, 53.4	32.4, 48.1	
		Min, Max	19, 58	26, 59	

The eculizumab group data were collected as part of the PREVENT trial, Study ECU-NMO-301.

End of Study Period is the 6-week assessment after the first On-Trial Relapse for patients who have an On-Trial Relapse or for patients with no On-Trial Relapse: the End of Primary Treatment Period visit for patients in Study ALXN1210-NMO-307 and the End of Study visit for patients in Study ECU-NMO-301.

For those patients who had a missed value at the EOPT Visit or the 6-week post-relapse visit, for patients who had a relapse, the end of study is the last value before the missed value.

(1) The LS means (95% CI) and the difference in LS means (95% CI) are from an ANCOVA model of change from baseline with treatment as factor and baseline value as covariate. (2) The p-value represents the significance of the treatment effect and was derived from an ANCOVA model of the ranked change from baseline, with treatment as a factor, and the ranks of the baseline value included as covariate.

(3) Standardized mean differences (95% CI) were computed using Cohen's D incorporating Hedge's correction on change from baseline. (4) Odds ratio statistics are from a logistic regression model adjusted for baseline value with Firth's adjustment; (5) Relative risk statistics are based on a generalized linear model of a binomial distribution with log link;

(6) Risk difference statistics are calculated from a generalized linear model, correcting for the baseline value. (7) P-value is for the interaction term of treatment:subgroup from a linear regression model of ranked change from baseline with the with ranked baseline value, treatment, subgroup, and treatment:subgroup interaction as covariates.

Odds ratio and relative risk are calculated as Ravulizumab/Eculizumab. LS mean difference and risk difference are calculated as Ravulizumab - Eculizumab.

Source: adsl, adsf36

Table SF-36-2.7
Change from Baseline in SF-36 Physical Component Score to End of Study Period by Rituximab use in the prior year
Full Analysis Set

Rituximab use in the prior year		Statistic	Eculizumab (N=96)	Ravulizumab (N=58)	p-value (7)
No	Change from Baseline to End of Study Period in SF-36 Physical Component Score	n	77	38	
		Mean (SD)	3.2 (7.52)	1.7 (5.16)	
		Median	2.6	1.4	
		Q1, Q3	-0.9, 6.5	-1.4, 4.4	
		Min, Max	-20, 23	-8, 21	
		Change from baseline			
		LS Means (SEM)	2.753 (0.765)	2.514 (1.106)	
		95% CI for LS Means (1)	(1.237, 4.270)	(0.322, 4.705)	
		Difference in LS Means		-0.240	
		(95% CI) (1)		(-2.957, 2.477)	
		p-value (2)		0.6427	
		Standardized Mean Difference		-0.092	
		(95% CI) (3)		(-0.481, 0.296)	
		Responders (10% [10 points]), n(%)	11 (14.3)	2 (5.3)	
		Odds Ratio (4)		0.615	
		(95% CI)		(0.138, 2.749)	
		p-value		0.5245	
		Relative Risk (5)		0.368	
		(95% CI)		(0.086, 1.580)	
		p-value		0.1788	

The eculizumab group data were collected as part of the PREVENT trial, Study ECU-NMO-301.

End of Study Period is the 6-week assessment after the first On-Trial Relapse for patients who have an On-Trial Relapse or for patients with no On-Trial Relapse: the End of Primary Treatment Period visit for patients in Study ALXN1210-NMO-307 and the End of Study visit for patients in Study ECU-NMO-301.

For those patients who had a missed value at the EOPT Visit or the 6-week post-relapse visit, for patients who had a relapse, the end of study is the last value before the missed value.

(1) The LS means (95% CI) and the difference in LS means (95% CI) are from an ANCOVA model of change from baseline with treatment as factor and baseline value as covariate. (2) The p-value represents the significance of the treatment effect and was derived from an ANCOVA model of the ranked change from baseline, with treatment as a factor, and the ranks of the baseline value included as covariate.

(3) Standardized mean differences (95% CI) were computed using Cohen's D incorporating Hedge's correction on change from baseline. (4) Odds ratio statistics are from a logistic regression model adjusted for baseline value with Firth's adjustment; (5) Relative risk statistics are based on a generalized linear model of a binomial distribution with log link;

(6) Risk difference statistics are calculated from a generalized linear model, correcting for the baseline value. (7) P-value is for the interaction term of treatment:subgroup from a linear regression model of ranked change from baseline with the with ranked baseline value, treatment, subgroup, and treatment:subgroup interaction as covariates.

Odds ratio and relative risk are calculated as Ravulizumab/Eculizumab. LS mean difference and risk difference are calculated as Ravulizumab - Eculizumab.

Source: adsl, adsf36

Table SF-36-2.7
Change from Baseline in SF-36 Physical Component Score to End of Study Period by Rituximab use in the prior year
Full Analysis Set

Rituximab use in the prior year		Statistic	Eculizumab (N=96)	Ravulizumab (N=58)	p-value (7)
		Risk Difference (6)		-0.039	
		(95% CI)		(-0.165, 0.088)	
		p-value		0.5431	
	Baseline SF-36 Physical Component Score	n	77	38	
		Mean (SD)	39.3 (9.50)	45.3 (8.61)	
		Median	40.3	45.8	
		Q1, Q3	32.3, 45.8	41.3, 50.5	
		Min, Max	8, 57	26, 58	
	End of Study Period SF-36 Physical Component Score	n	77	38	
		Mean (SD)	42.4 (10.21)	47.0 (9.16)	
		Median	43.7	49.4	
		Q1, Q3	37.2, 49.4	41.5, 53.7	
		Min, Max	16, 60	24, 66	

The eculizumab group data were collected as part of the PREVENT trial, Study ECU-NMO-301.

End of Study Period is the 6-week assessment after the first On-Trial Relapse for patients who have an On-Trial Relapse or for patients with no On-Trial Relapse: the End of Primary Treatment Period visit for patients in Study ALXN1210-NMO-307 and the End of Study visit for patients in Study ECU-NMO-301.

For those patients who had a missed value at the EOPT Visit or the 6-week post-relapse visit, for patients who had a relapse, the end of study is the last value before the missed value.

(1) The LS means (95% CI) and the difference in LS means (95% CI) are from an ANCOVA model of change from baseline with treatment as factor and baseline value as covariate. (2) The p-value represents the significance of the treatment effect and was derived from an ANCOVA model of the ranked change from baseline, with treatment as a factor, and the ranks of the baseline value included as covariate.

(3) Standardized mean differences (95% CI) were computed using Cohen's D incorporating Hedge's correction on change from baseline. (4) Odds ratio statistics are from a logistic regression model adjusted for baseline value with Firth's adjustment; (5) Relative risk statistics are based on a generalized linear model of a binomial distribution with log link;

(6) Risk difference statistics are calculated from a generalized linear model, correcting for the baseline value. (7) P-value is for the interaction term of treatment:subgroup from a linear regression model of ranked change from baseline with the with ranked baseline value, treatment, subgroup, and treatment:subgroup interaction as covariates.

Odds ratio and relative risk are calculated as Ravulizumab/Eculizumab. LS mean difference and risk difference are calculated as Ravulizumab - Eculizumab.

Source: adsl, adsf36

Table SF-36-2.4
Change from Baseline in SF-36 Physical Component Score to End of Study Period by Disease severity via EDSS Score at baseline
Full Analysis Set

EDSS score at baseline		Statistic	Eculizumab (N=96)	Ravulizumab (N=58)	p-value (7)
< 5	Change from Baseline to End of Study Period in SF-36 Physical Component Score	n	66	49	0.9570
		Mean (SD)	4.0 (7.42)	2.2 (6.69)	
		Median	2.7	1.5	
		Q1, Q3	-0.3, 7.3	-1.0, 6.1	
		Min, Max	-11, 34	-17, 21	
		Change from baseline			
		LS Means (SEM)	3.337 (0.785)	3.061 (0.914)	
		95% CI for LS Means (1)	(1.782, 4.892)	(1.250, 4.872)	
		Difference in LS Means		-0.276	
		(95% CI) (1)		(-2.689, 2.138)	
		p-value (2)		0.7832	
		Standardized Mean Difference		-0.109	
		(95% CI) (3)		(-0.479, 0.261)	
		Responders (10% [10 points]), n(%)	9 (13.6)	5 (10.2)	
		Odds Ratio (4)		1.228	
		(95% CI)		(0.355, 4.251)	
		p-value		0.7455	
		Relative Risk (5)		0.748	
		(95% CI)		(0.267, 2.094)	
		p-value		0.5807	

The eculizumab group data were collected as part of the PREVENT trial, Study ECU-NMO-301.

End of Study Period is the 6-week assessment after the first On-Trial Relapse for patients who have an On-Trial Relapse or for patients with no On-Trial Relapse: the End of Primary Treatment Period visit for patients in Study ALXN1210-NMO-307 and the End of Study visit for patients in Study ECU-NMO-301.

For those patients who had a missed value at the EOPT Visit or the 6-week post-relapse visit, for patients who had a relapse, the end of study is the last value before the missed value.

(1) The LS means (95% CI) and the difference in LS means (95% CI) are from an ANCOVA model of change from baseline with treatment as factor and baseline value as covariate. (2) The p-value represents the significance of the treatment effect and was derived from an ANCOVA model of the ranked change from baseline, with treatment as a factor, and the ranks of the baseline value included as covariate.

(3) Standardized mean differences (95% CI) were computed using Cohen's D incorporating Hedge's correction on change from baseline. (4) Odds ratio statistics are from a logistic regression model adjusted for baseline value with Firth's adjustment; (5) Relative risk statistics are based on a generalized linear model of a binomial distribution with log link;

(6) Risk difference statistics are calculated from a generalized linear model, correcting for the baseline value. (7) P-value is for the interaction term of treatment:subgroup from a linear regression model of ranked change from baseline with the with ranked baseline value, treatment, subgroup, and treatment:subgroup interaction as covariates.

Odds ratio and relative risk are calculated as Ravulizumab/Eculizumab. LS mean difference and risk difference are calculated as Ravulizumab - Eculizumab.

Source: adsl, adsf36

Table SF-36-2.4
Change from Baseline in SF-36 Physical Component Score to End of Study Period by Disease severity via EDSS Score at baseline
Full Analysis Set

EDSS score at baseline	Statistic	Eculizumab (N=96)	Ravulizumab (N=58)	p-value (7)
	Risk Difference (6)		0.020	
	(95% CI)		(-0.097, 0.137)	
	p-value		0.7389	
Baseline SF-36 Physical Component Score	n	66	49	
	Mean (SD)	41.6 (9.44)	45.5 (8.07)	
	Median	43.5	45.6	
	Q1, Q3	37.3, 48.3	41.3, 50.2	
	Min, Max	8, 57	28, 62	
End of Study Period SF-36 Physical Component Score	n	66	49	
	Mean (SD)	45.6 (8.64)	47.7 (8.02)	
	Median	46.4	48.4	
	Q1, Q3	40.7, 52.4	43.7, 53.7	
	Min, Max	16, 60	26, 66	

The eculizumab group data were collected as part of the PREVENT trial, Study ECU-NMO-301.

End of Study Period is the 6-week assessment after the first On-Trial Relapse for patients who have an On-Trial Relapse or for patients with no On-Trial Relapse: the End of Primary Treatment Period visit for patients in Study ALXN1210-NMO-307 and the End of Study visit for patients in Study ECU-NMO-301.

For those patients who had a missed value at the EOPT Visit or the 6-week post-relapse visit, for patients who had a relapse, the end of study is the last value before the missed value.

(1) The LS means (95% CI) and the difference in LS means (95% CI) are from an ANCOVA model of change from baseline with treatment as factor and baseline value as covariate. (2) The p-value represents the significance of the treatment effect and was derived from an ANCOVA model of the ranked change from baseline, with treatment as a factor, and the ranks of the baseline value included as covariate.

(3) Standardized mean differences (95% CI) were computed using Cohen's D incorporating Hedge's correction on change from baseline. (4) Odds ratio statistics are from a logistic regression model adjusted for baseline value with Firth's adjustment; (5) Relative risk statistics are based on a generalized linear model of a binomial distribution with log link;

(6) Risk difference statistics are calculated from a generalized linear model, correcting for the baseline value. (7) P-value is for the interaction term of treatment:subgroup from a linear regression model of ranked change from baseline with the with ranked baseline value, treatment, subgroup, and treatment:subgroup interaction as covariates.

Odds ratio and relative risk are calculated as Ravulizumab/Eculizumab. LS mean difference and risk difference are calculated as Ravulizumab - Eculizumab.

Source: adsl, adsf36

Table SF-36-2.4
Change from Baseline in SF-36 Physical Component Score to End of Study Period by Disease severity via EDSS Score at baseline
Full Analysis Set

EDSS score at baseline		Statistic	Eculizumab (N=96)	Ravulizumab (N=58)	p-value (7)
>= 5	Change from Baseline to End of Study Period in SF-36 Physical Component Score	n	30	9	
		Mean (SD)	2.0 (8.33)	2.8 (6.19)	
		Median	1.5	2.7	
		Q1, Q3	-1.3, 6.5	-2.8, 8.3	
		Min, Max	-20, 20	-6, 11	
		Change from baseline			
		LS Means (SEM)	2.156 (1.461)	2.386 (2.698)	
		95% CI for LS Means (1)	(-0.806, 5.119)	(-3.085, 7.857)	
		Difference in LS Means		0.230	
		(95% CI) (1)		(-6.038, 6.497)	
		p-value (2)		0.8642	
		Standardized Mean Difference		0.081	
		(95% CI) (3)		(-0.664, 0.826)	
		Responders (10% [10 points]), n(%)	4 (13.3)	2 (22.2)	
		Odds Ratio (4)		1.850	
		(95% CI)		(0.292, 11.718)	
		p-value		0.5138	
		Relative Risk (5)		1.667	
		(95% CI)		(0.363, 7.660)	
		p-value		0.5115	

The eculizumab group data were collected as part of the PREVENT trial, Study ECU-NMO-301.

End of Study Period is the 6-week assessment after the first On-Trial Relapse for patients who have an On-Trial Relapse or for patients with no On-Trial Relapse: the End of Primary Treatment Period visit for patients in Study ALXN1210-NMO-307 and the End of Study visit for patients in Study ECU-NMO-301.

For those patients who had a missed value at the EOPT Visit or the 6-week post-relapse visit, for patients who had a relapse, the end of study is the last value before the missed value.

(1) The LS means (95% CI) and the difference in LS means (95% CI) are from an ANCOVA model of change from baseline with treatment as factor and baseline value as covariate. (2) The p-value represents the significance of the treatment effect and was derived from an ANCOVA model of the ranked change from baseline, with treatment as a factor, and the ranks of the baseline value included as covariate.

(3) Standardized mean differences (95% CI) were computed using Cohen's D incorporating Hedge's correction on change from baseline. (4) Odds ratio statistics are from a logistic regression model adjusted for baseline value with Firth's adjustment; (5) Relative risk statistics are based on a generalized linear model of a binomial distribution with log link;

(6) Risk difference statistics are calculated from a generalized linear model, correcting for the baseline value. (7) P-value is for the interaction term of treatment:subgroup from a linear regression model of ranked change from baseline with the with ranked baseline value, treatment, subgroup, and treatment:subgroup interaction as covariates.

Odds ratio and relative risk are calculated as Ravulizumab/Eculizumab. LS mean difference and risk difference are calculated as Ravulizumab - Eculizumab.

Source: adsl, adsf36

Table SF-36-2.4
Change from Baseline in SF-36 Physical Component Score to End of Study Period by Disease severity via EDSS Score at baseline
Full Analysis Set

EDSS score at baseline	Statistic	Eculizumab (N=96)	Ravulizumab (N=58)	p-value (7)
	Risk Difference (6)		0.088	
	(95% CI)		(-0.206, 0.382)	
	p-value		0.5476	
Baseline SF-36 Physical Component Score	n	30	9	
	Mean (SD)	31.9 (6.97)	28.8 (4.39)	
	Median	30.5	29.5	
	Q1, Q3	26.8, 37.8	26.2, 31.7	
	Min, Max	18, 45	22, 35	
End of Study Period SF-36 Physical Component Score	n	30	9	
	Mean (SD)	33.9 (10.13)	31.5 (7.19)	
	Median	33.4	29.0	
	Q1, Q3	26.4, 40.7	26.5, 33.0	
	Min, Max	19, 55	24, 45	

The eculizumab group data were collected as part of the PREVENT trial, Study ECU-NMO-301.

End of Study Period is the 6-week assessment after the first On-Trial Relapse for patients who have an On-Trial Relapse or for patients with no On-Trial Relapse: the End of Primary Treatment Period visit for patients in Study ALXN1210-NMO-307 and the End of Study visit for patients in Study ECU-NMO-301.

For those patients who had a missed value at the EOPT Visit or the 6-week post-relapse visit, for patients who had a relapse, the end of study is the last value before the missed value.

(1) The LS means (95% CI) and the difference in LS means (95% CI) are from an ANCOVA model of change from baseline with treatment as factor and baseline value as covariate. (2) The p-value represents the significance of the treatment effect and was derived from an ANCOVA model of the ranked change from baseline, with treatment as a factor, and the ranks of the baseline value included as covariate.

(3) Standardized mean differences (95% CI) were computed using Cohen's D incorporating Hedge's correction on change from baseline. (4) Odds ratio statistics are from a logistic regression model adjusted for baseline value with Firth's adjustment; (5) Relative risk statistics are based on a generalized linear model of a binomial distribution with log link;

(6) Risk difference statistics are calculated from a generalized linear model, correcting for the baseline value. (7) P-value is for the interaction term of treatment:subgroup from a linear regression model of ranked change from baseline with the with ranked baseline value, treatment, subgroup, and treatment:subgroup interaction as covariates.

Odds ratio and relative risk are calculated as Ravulizumab/Eculizumab. LS mean difference and risk difference are calculated as Ravulizumab - Eculizumab.

Source: adsl, adsf36

Table SF-36-3.2
Change from Baseline in SF-36 Mental Component Score to End of Study Period by Sex
Full Analysis Set

Sex		Statistic	Eculizumab (N=96)	Ravulizumab (N=58)	p-value (7)
Male	Change from Baseline to End of Study Period in SF-36 Mental Component Score	n	8	6	0.2531
		Mean (SD)	1.2 (13.88)	-4.5 (5.53)	
		Median	5.8	-5.2	
		Q1, Q3	-3.5, 6.8	-9.8, 0.8	
		Min, Max	-28, 19	-10, 2	
		Change from baseline			
		LS Means (SEM)	-0.984 (3.837)	-1.581 (4.506)	
		95% CI for LS Means (1)	(-9.429, 7.461)	(-11.499, 8.337)	
		Difference in LS Means		-0.597	
		(95% CI) (1)		(-14.358, 13.164)	
		p-value (2)		0.2168	
		Standardized Mean Difference		-0.181	
		(95% CI) (3)		(-1.241, 0.880)	
		Responders (10% [10 points]), n(%)	1 (12.5)	0	
		Odds Ratio (4)		1.024	
		(95% CI)		(0.012, 87.065)	
		p-value		0.9916	
		Relative Risk (5)		0.000	
		(95% CI)		--	
		p-value		1.0000	

The eculizumab group data were collected as part of the PREVENT trial, Study ECU-NMO-301.

End of Study Period is the 6-week assessment after the first On-Trial Relapse for patients who have an On-Trial Relapse or for patients with no On-Trial Relapse: the End of Primary Treatment Period visit for patients in Study ALXN1210-NMO-307 and the End of Study visit for patients in Study ECU-NMO-301.

For those patients who had a missed value at the EOPT Visit or the 6-week post-relapse visit, for patients who had a relapse, the end of study is the last value before the missed value.

(1) The LS means (95% CI) and the difference in LS means (95% CI) are from an ANCOVA model of change from baseline with treatment as factor and baseline value as covariate. (2) The p-value represents the significance of the treatment effect and was derived from an ANCOVA model of the ranked change from baseline, with treatment as a factor, and the ranks of the baseline value included as covariate.

(3) Standardized mean differences (95% CI) were computed using Cohen's D incorporating Hedge's correction on change from baseline. (4) Odds ratio statistics are from a logistic regression model adjusted for baseline value with Firth's adjustment; (5) Relative risk statistics are based on a generalized linear model of a binomial distribution with log link;

(6) Risk difference statistics are calculated from a generalized linear model, correcting for the baseline value. (7) P-value is for the interaction term of treatment:subgroup from a linear regression model of ranked change from baseline with the with ranked baseline value, treatment, subgroup, and treatment:subgroup interaction as covariates.

Odds ratio and relative risk are calculated as Ravulizumab/Eculizumab. LS mean difference and risk difference are calculated as Ravulizumab - Eculizumab.

Source: adsl, adsf36

Table SF-36-3.2
Change from Baseline in SF-36 Mental Component Score to End of Study Period by Sex
Full Analysis Set

Sex	Statistic	Eculizumab (N=96)	Ravulizumab (N=58)	p-value (7)
	Risk Difference (6)		0.002	
	(95% CI)		(-0.329, 0.332)	
	p-value		0.9915	
Baseline SF-36 Mental Component Score	n	8	6	
	Mean (SD)	45.0 (11.49)	54.1 (5.24)	
	Median	49.6	54.4	
	Q1, Q3	32.4, 53.5	49.0, 56.9	
	Min, Max	30, 58	48, 62	
End of Study Period SF-36 Mental Component Score	n	8	6	
	Mean (SD)	46.2 (11.74)	49.6 (8.90)	
	Median	48.4	46.7	
	Q1, Q3	39.3, 55.2	44.4, 57.7	
	Min, Max	24, 59	39, 63	

The eculizumab group data were collected as part of the PREVENT trial, Study ECU-NMO-301.

End of Study Period is the 6-week assessment after the first On-Trial Relapse for patients who have an On-Trial Relapse or for patients with no On-Trial Relapse: the End of Primary Treatment Period visit for patients in Study ALXN1210-NMO-307 and the End of Study visit for patients in Study ECU-NMO-301.

For those patients who had a missed value at the EOPT Visit or the 6-week post-relapse visit, for patients who had a relapse, the end of study is the last value before the missed value.

(1) The LS means (95% CI) and the difference in LS means (95% CI) are from an ANCOVA model of change from baseline with treatment as factor and baseline value as covariate. (2) The p-value represents the significance of the treatment effect and was derived from an ANCOVA model of the ranked change from baseline, with treatment as a factor, and the ranks of the baseline value included as covariate.

(3) Standardized mean differences (95% CI) were computed using Cohen's D incorporating Hedge's correction on change from baseline. (4) Odds ratio statistics are from a logistic regression model adjusted for baseline value with Firth's adjustment; (5) Relative risk statistics are based on a generalized linear model of a binomial distribution with log link;

(6) Risk difference statistics are calculated from a generalized linear model, correcting for the baseline value. (7) P-value is for the interaction term of treatment:subgroup from a linear regression model of ranked change from baseline with the with ranked baseline value, treatment, subgroup, and treatment:subgroup interaction as covariates.

Odds ratio and relative risk are calculated as Ravulizumab/Eculizumab. LS mean difference and risk difference are calculated as Ravulizumab - Eculizumab.

Source: adsl, adsf36

Table SF-36-3.2
Change from Baseline in SF-36 Mental Component Score to End of Study Period by Sex
Full Analysis Set

Sex		Statistic	Eculizumab (N=96)	Ravulizumab (N=58)	p-value (7)
Female	Change from Baseline to End of Study Period in SF-36 Mental Component Score	n	88	52	
		Mean (SD)	0.4 (10.36)	1.4 (8.01)	
		Median	-0.5	1.0	
		Q1, Q3	-5.2, 7.3	-4.1, 5.4	
		Min, Max	-25, 29	-12, 23	
		Change from baseline			
		LS Means (SEM)	0.497 (0.907)	1.190 (1.181)	
		95% CI for LS Means (1)	(-1.297, 2.292)	(-1.145, 3.524)	
		Difference in LS Means		0.692	
		(95% CI) (1)		(-2.253, 3.637)	
		p-value (2)		0.9029	
		Standardized Mean Difference		0.237	
		(95% CI) (3)		(-0.107, 0.581)	
		Responders (10% [10 points]), n(%)	15 (17.0)	7 (13.5)	
		Odds Ratio (4)		0.730	
		(95% CI)		(0.269, 1.983)	
		p-value		0.5372	
		Relative Risk (5)		0.790	
		(95% CI)		(0.345, 1.809)	
		p-value		0.5768	

The eculizumab group data were collected as part of the PREVENT trial, Study ECU-NMO-301.

End of Study Period is the 6-week assessment after the first On-Trial Relapse for patients who have an On-Trial Relapse or for patients with no On-Trial Relapse: the End of Primary Treatment Period visit for patients in Study ALXN1210-NMO-307 and the End of Study visit for patients in Study ECU-NMO-301.

For those patients who had a missed value at the EOPT Visit or the 6-week post-relapse visit, for patients who had a relapse, the end of study is the last value before the missed value.

(1) The LS means (95% CI) and the difference in LS means (95% CI) are from an ANCOVA model of change from baseline with treatment as factor and baseline value as covariate. (2) The p-value represents the significance of the treatment effect and was derived from an ANCOVA model of the ranked change from baseline, with treatment as a factor, and the ranks of the baseline value included as covariate.

(3) Standardized mean differences (95% CI) were computed using Cohen's D incorporating Hedge's correction on change from baseline. (4) Odds ratio statistics are from a logistic regression model adjusted for baseline value with Firth's adjustment; (5) Relative risk statistics are based on a generalized linear model of a binomial distribution with log link;

(6) Risk difference statistics are calculated from a generalized linear model, correcting for the baseline value. (7) P-value is for the interaction term of treatment:subgroup from a linear regression model of ranked change from baseline with the with ranked baseline value, treatment, subgroup, and treatment:subgroup interaction as covariates.

Odds ratio and relative risk are calculated as Ravulizumab/Eculizumab. LS mean difference and risk difference are calculated as Ravulizumab - Eculizumab.

Source: adsl, adsf36

Table SF-36-3.2
Change from Baseline in SF-36 Mental Component Score to End of Study Period by Sex
Full Analysis Set

Sex	Statistic	Eculizumab (N=96)	Ravulizumab (N=58)	p-value (7)
	Risk Difference (6)		-0.044	
	(95% CI)		(-0.165, 0.077)	
	p-value		0.4748	
Baseline SF-36 Mental Component Score	n	88	52	
	Mean (SD)	47.2 (12.68)	46.3 (12.27)	
	Median	50.9	49.3	
	Q1, Q3	39.1, 57.3	39.2, 56.2	
	Min, Max	7, 65	18, 68	
End of Study Period SF-36 Mental Component Score	n	88	52	
	Mean (SD)	47.6 (12.30)	47.7 (10.74)	
	Median	49.5	51.1	
	Q1, Q3	39.8, 57.1	38.5, 55.5	
	Min, Max	8, 69	24, 72	

The eculizumab group data were collected as part of the PREVENT trial, Study ECU-NMO-301.

End of Study Period is the 6-week assessment after the first On-Trial Relapse for patients who have an On-Trial Relapse or for patients with no On-Trial Relapse: the End of Primary Treatment Period visit for patients in Study ALXN1210-NMO-307 and the End of Study visit for patients in Study ECU-NMO-301.

For those patients who had a missed value at the EOPT Visit or the 6-week post-relapse visit, for patients who had a relapse, the end of study is the last value before the missed value.

(1) The LS means (95% CI) and the difference in LS means (95% CI) are from an ANCOVA model of change from baseline with treatment as factor and baseline value as covariate. (2) The p-value represents the significance of the treatment effect and was derived from an ANCOVA model of the ranked change from baseline, with treatment as a factor, and the ranks of the baseline value included as covariate.

(3) Standardized mean differences (95% CI) were computed using Cohen's D incorporating Hedge's correction on change from baseline. (4) Odds ratio statistics are from a logistic regression model adjusted for baseline value with Firth's adjustment; (5) Relative risk statistics are based on a generalized linear model of a binomial distribution with log link;

(6) Risk difference statistics are calculated from a generalized linear model, correcting for the baseline value. (7) P-value is for the interaction term of treatment:subgroup from a linear regression model of ranked change from baseline with the with ranked baseline value, treatment, subgroup, and treatment:subgroup interaction as covariates.

Odds ratio and relative risk are calculated as Ravulizumab/Eculizumab. LS mean difference and risk difference are calculated as Ravulizumab - Eculizumab.

Source: adsl, adsf36

Table SF-36-3.3
Change from Baseline in SF-36 Mental Component Score to End of Study Period by Age Group
Full Analysis Set

Age Group		Statistic	Eculizumab (N=96)	Ravulizumab (N=58)	p-value (7)
< 45 years	Change from Baseline to End of Study Period in SF-36 Mental Component Score	n	47	25	0.8683
		Mean (SD)	0.8 (10.53)	0.9 (6.77)	
		Median	0.0	2.0	
		Q1, Q3	-5.8, 6.2	-4.4, 5.6	
		Min, Max	-20, 24	-10, 18	
		Change from baseline			
		LS Means (SEM)	0.972 (1.251)	0.458 (1.717)	
		95% CI for LS Means (1)	(-1.523, 3.468)	(-2.967, 3.882)	
		Difference in LS Means		-0.515	
		(95% CI) (1)		(-4.757, 3.728)	
		p-value (2)		0.7530	
		Standardized Mean Difference		-0.176	
		(95% CI) (3)		(-0.662, 0.310)	
		Responders (10% [10 points]), n(%)	8 (17.0)	2 (8.0)	
		Odds Ratio (4)		0.414	
		(95% CI)		(0.084, 2.034)	
		p-value		0.2775	
		Relative Risk (5)		0.470	
		(95% CI)		(0.108, 2.047)	
		p-value		0.3146	

The eculizumab group data were collected as part of the PREVENT trial, Study ECU-NMO-301.

End of Study Period is the 6-week assessment after the first On-Trial Relapse for patients who have an On-Trial Relapse or for patients with no On-Trial Relapse: the End of Primary Treatment Period visit for patients in Study ALXN1210-NMO-307 and the End of Study visit for patients in Study ECU-NMO-301.

For those patients who had a missed value at the EOPT Visit or the 6-week post-relapse visit, for patients who had a relapse, the end of study is the last value before the missed value.

(1) The LS means (95% CI) and the difference in LS means (95% CI) are from an ANCOVA model of change from baseline with treatment as factor and baseline value as covariate. (2) The p-value represents the significance of the treatment effect and was derived from an ANCOVA model of the ranked change from baseline, with treatment as a factor, and the ranks of the baseline value included as covariate.

(3) Standardized mean differences (95% CI) were computed using Cohen's D incorporating Hedge's correction on change from baseline. (4) Odds ratio statistics are from a logistic regression model adjusted for baseline value with Firth's adjustment; (5) Relative risk statistics are based on a generalized linear model of a binomial distribution with log link;

(6) Risk difference statistics are calculated from a generalized linear model, correcting for the baseline value. (7) P-value is for the interaction term of treatment:subgroup from a linear regression model of ranked change from baseline with the with ranked baseline value, treatment, subgroup, and treatment:subgroup interaction as covariates.

Odds ratio and relative risk are calculated as Ravulizumab/Eculizumab. LS mean difference and risk difference are calculated as Ravulizumab - Eculizumab.

Source: adsl, adsf36

Table SF-36-3.3
Change from Baseline in SF-36 Mental Component Score to End of Study Period by Age Group
Full Analysis Set

Age Group	Statistic	Eculizumab (N=96)	Ravulizumab (N=58)	p-value (7)
	Risk Difference (6)		-0.108	
	(95% CI)		(-0.272, 0.057)	
	p-value		0.1952	
Baseline SF-36 Mental Component Score	n	47	25	
	Mean (SD)	47.5 (12.28)	45.5 (11.98)	
	Median	51.3	49.0	
	Q1, Q3	38.8, 56.9	36.5, 54.6	
	Min, Max	11, 62	21, 64	
End of Study Period SF-36 Mental Component Score	n	47	25	
	Mean (SD)	48.2 (12.31)	46.4 (10.71)	
	Median	50.6	48.8	
	Q1, Q3	44.3, 57.2	38.3, 55.4	
	Min, Max	8, 63	24, 61	

The eculizumab group data were collected as part of the PREVENT trial, Study ECU-NMO-301.

End of Study Period is the 6-week assessment after the first On-Trial Relapse for patients who have an On-Trial Relapse or for patients with no On-Trial Relapse: the End of Primary Treatment Period visit for patients in Study ALXN1210-NMO-307 and the End of Study visit for patients in Study ECU-NMO-301.

For those patients who had a missed value at the EOPT Visit or the 6-week post-relapse visit, for patients who had a relapse, the end of study is the last value before the missed value.

(1) The LS means (95% CI) and the difference in LS means (95% CI) are from an ANCOVA model of change from baseline with treatment as factor and baseline value as covariate. (2) The p-value represents the significance of the treatment effect and was derived from an ANCOVA model of the ranked change from baseline, with treatment as a factor, and the ranks of the baseline value included as covariate.

(3) Standardized mean differences (95% CI) were computed using Cohen's D incorporating Hedge's correction on change from baseline. (4) Odds ratio statistics are from a logistic regression model adjusted for baseline value with Firth's adjustment; (5) Relative risk statistics are based on a generalized linear model of a binomial distribution with log link;

(6) Risk difference statistics are calculated from a generalized linear model, correcting for the baseline value. (7) P-value is for the interaction term of treatment:subgroup from a linear regression model of ranked change from baseline with the with ranked baseline value, treatment, subgroup, and treatment:subgroup interaction as covariates.

Odds ratio and relative risk are calculated as Ravulizumab/Eculizumab. LS mean difference and risk difference are calculated as Ravulizumab - Eculizumab.

Source: adsl, adsf36

Table SF-36-3.3
Change from Baseline in SF-36 Mental Component Score to End of Study Period by Age Group
Full Analysis Set

Age Group		Statistic	Eculizumab (N=96)	Ravulizumab (N=58)	p-value (7)
>= 45 years	Change from Baseline to End of Study Period in SF-36 Mental Component Score	n	49	33	
		Mean (SD)	0.2 (10.78)	0.7 (8.86)	
		Median	-0.2	-0.1	
		Q1, Q3	-5.1, 7.4	-5.7, 4.5	
		Min, Max	-28, 29	-12, 23	
		Change from baseline			
		LS Means (SEM)	-0.114 (1.252)	1.111 (1.527)	
		95% CI for LS Means (1)	(-2.607, 2.380)	(-1.928, 4.151)	
		Difference in LS Means		1.225	
		(95% CI) (1)		(-2.711, 5.160)	
		p-value (2)		0.9364	
		Standardized Mean Difference		0.414	
		(95% CI) (3)		(-0.032, 0.859)	
		Responders (10% [10 points]), n(%)	8 (16.3)	5 (15.2)	
		Odds Ratio (4)		1.072	
		(95% CI)		(0.304, 3.777)	
		p-value		0.9134	
		Relative Risk (5)		0.928	
		(95% CI)		(0.332, 2.590)	
		p-value		0.8866	

The eculizumab group data were collected as part of the PREVENT trial, Study ECU-NMO-301.

End of Study Period is the 6-week assessment after the first On-Trial Relapse for patients who have an On-Trial Relapse or for patients with no On-Trial Relapse: the End of Primary Treatment Period visit for patients in Study ALXN1210-NMO-307 and the End of Study visit for patients in Study ECU-NMO-301.

For those patients who had a missed value at the EOPT Visit or the 6-week post-relapse visit, for patients who had a relapse, the end of study is the last value before the missed value.

(1) The LS means (95% CI) and the difference in LS means (95% CI) are from an ANCOVA model of change from baseline with treatment as factor and baseline value as covariate. (2) The p-value represents the significance of the treatment effect and was derived from an ANCOVA model of the ranked change from baseline, with treatment as a factor, and the ranks of the baseline value included as covariate.

(3) Standardized mean differences (95% CI) were computed using Cohen's D incorporating Hedge's correction on change from baseline. (4) Odds ratio statistics are from a logistic regression model adjusted for baseline value with Firth's adjustment; (5) Relative risk statistics are based on a generalized linear model of a binomial distribution with log link;

(6) Risk difference statistics are calculated from a generalized linear model, correcting for the baseline value. (7) P-value is for the interaction term of treatment:subgroup from a linear regression model of ranked change from baseline with the with ranked baseline value, treatment, subgroup, and treatment:subgroup interaction as covariates.

Odds ratio and relative risk are calculated as Ravulizumab/Eculizumab. LS mean difference and risk difference are calculated as Ravulizumab - Eculizumab.

Source: adsl, adsf36

Table SF-36-3.3
Change from Baseline in SF-36 Mental Component Score to End of Study Period by Age Group
Full Analysis Set

Age Group	Statistic	Eculizumab (N=96)	Ravulizumab (N=58)	p-value (7)
	Risk Difference (6)		0.005	
	(95% CI)		(-0.152, 0.163)	
	p-value		0.9458	
Baseline SF-36 Mental Component Score	n	49	33	
	Mean (SD)	46.6 (12.91)	48.4 (11.97)	
	Median	50.6	50.6	
	Q1, Q3	38.3, 57.4	40.6, 56.9	
	Min, Max	7, 65	18, 68	
End of Study Period SF-36 Mental Component Score	n	49	33	
	Mean (SD)	46.8 (12.18)	49.1 (10.38)	
	Median	46.1	51.2	
	Q1, Q3	37.5, 56.5	44.4, 55.7	
	Min, Max	20, 69	29, 72	

The eculizumab group data were collected as part of the PREVENT trial, Study ECU-NMO-301.

End of Study Period is the 6-week assessment after the first On-Trial Relapse for patients who have an On-Trial Relapse or for patients with no On-Trial Relapse: the End of Primary Treatment Period visit for patients in Study ALXN1210-NMO-307 and the End of Study visit for patients in Study ECU-NMO-301.

For those patients who had a missed value at the EOPT Visit or the 6-week post-relapse visit, for patients who had a relapse, the end of study is the last value before the missed value.

(1) The LS means (95% CI) and the difference in LS means (95% CI) are from an ANCOVA model of change from baseline with treatment as factor and baseline value as covariate. (2) The p-value represents the significance of the treatment effect and was derived from an ANCOVA model of the ranked change from baseline, with treatment as a factor, and the ranks of the baseline value included as covariate.

(3) Standardized mean differences (95% CI) were computed using Cohen's D incorporating Hedge's correction on change from baseline. (4) Odds ratio statistics are from a logistic regression model adjusted for baseline value with Firth's adjustment; (5) Relative risk statistics are based on a generalized linear model of a binomial distribution with log link;

(6) Risk difference statistics are calculated from a generalized linear model, correcting for the baseline value. (7) P-value is for the interaction term of treatment:subgroup from a linear regression model of ranked change from baseline with the with ranked baseline value, treatment, subgroup, and treatment:subgroup interaction as covariates.

Odds ratio and relative risk are calculated as Ravulizumab/Eculizumab. LS mean difference and risk difference are calculated as Ravulizumab - Eculizumab.

Source: adsl, adsf36

Table SF-36-3.5
Change from Baseline in SF-36 Mental Component Score to End of Study Period by Region
Full Analysis Set

Region		Statistic	Eculizumab (N=96)	Ravulizumab (N=58)	p-value (7)
Asia-Pacific	Change from Baseline to End of Study Period in SF-36 Mental Component Score	n	35	20	0.3212
		Mean (SD)	-0.1 (11.01)	1.2 (9.45)	
		Median	-0.2	-2.0	
		Q1, Q3	-7.1, 6.2	-5.1, 5.6	
		Min, Max	-28, 29	-12, 23	
		Change from baseline			
		LS Means (SEM)	-0.348 (1.425)	1.722 (1.886)	
		95% CI for LS Means (1)	(-3.208, 2.511)	(-2.062, 5.507)	
		Difference in LS Means		2.071	
		(95% CI) (1)		(-2.676, 6.818)	
		p-value (2)		0.6035	
		Standardized Mean Difference		0.713	
		(95% CI) (3)		(0.148, 1.279)	
		Responders (10% [10 points]), n(%)	5 (14.3)	3 (15.0)	
		Odds Ratio (4)		1.272	
		(95% CI)		(0.226, 7.150)	
		p-value		0.7845	
		Relative Risk (5)		1.050	
		(95% CI)		(0.280, 3.937)	
		p-value		0.9423	

The eculizumab group data were collected as part of the PREVENT trial, Study ECU-NMO-301.
End of Study Period is the 6-week assessment after the first On-Trial Relapse for patients who have an On-Trial Relapse or for patients with no On-Trial Relapse: the End of Primary Treatment Period visit for patients in Study ALXN1210-NMO-307 and the End of Study visit for patients in Study ECU-NMO-301.
For those patients who had a missed value at the EOPT Visit or the 6-week post-relapse visit, for patients who had a relapse, the end of study is the last value before the missed value.
(1) The LS means (95% CI) and the difference in LS means (95% CI) are from an ANCOVA model of change from baseline with treatment as factor and baseline value as covariate. (2) The p-value represents the significance of the treatment effect and was derived from an ANCOVA model of the ranked change from baseline, with treatment as a factor, and the ranks of the baseline value included as covariate.
(3) Standardized mean differences (95% CI) were computed using Cohen's D incorporating Hedge's correction on change from baseline. (4) Odds ratio statistics are from a logistic regression model adjusted for baseline value with Firth's adjustment; (5) Relative risk statistics are based on a generalized linear model of a binomial distribution with log link;
(6) Risk difference statistics are calculated from a generalized linear model, correcting for the baseline value. (7) P-value is for the interaction term of treatment:subgroup from a linear regression model of ranked change from baseline with the with ranked baseline value, treatment, subgroup, and treatment:subgroup interaction as covariates.
For eculizumab arm, Americas: ARG and USA; Europe: CZE, DEU, DNK, ESP, HRV, ITA, RUS and TUR; Asia-Pacific: AUS, HKG, JPN, KOR, MYS, THA and TWN. For ravulizumab arm, Americas: CAN and USA; Europe: DEU, DNK, ESP, GBR, ITA and POL; Asia-Pacific: AUS, JPN and KOR.
Odds ratio and relative risk are calculated as Ravulizumab/Eculizumab. LS mean difference and risk difference are calculated as Ravulizumab - Eculizumab.
Source: adsl, adsf36

Table SF-36-3.5
Change from Baseline in SF-36 Mental Component Score to End of Study Period by Region
Full Analysis Set

Region	Statistic	Eculizumab (N=96)	Ravulizumab (N=58)	p-value (7)
	Risk Difference (6)		0.031	
	(95% CI)		(-0.144, 0.206)	
	p-value		0.7244	
Baseline SF-36 Mental Component Score	n	35	20	
	Mean (SD)	47.0 (12.74)	48.7 (12.73)	
	Median	51.1	53.2	
	Q1, Q3	39.4, 56.9	40.7, 58.1	
	Min, Max	7, 64	18, 61	
End of Study Period SF-36 Mental Component Score	n	35	20	
	Mean (SD)	47.0 (12.14)	49.9 (6.70)	
	Median	47.2	51.9	
	Q1, Q3	36.5, 56.8	46.7, 55.5	
	Min, Max	20, 69	32, 57	

The eculizumab group data were collected as part of the PREVENT trial, Study ECU-NMO-301.

End of Study Period is the 6-week assessment after the first On-Trial Relapse for patients who have an On-Trial Relapse or for patients with no On-Trial Relapse: the End of Primary Treatment Period visit for patients in Study ALXN1210-NMO-307 and the End of Study visit for patients in Study ECU-NMO-301.

For those patients who had a missed value at the EOPT Visit or the 6-week post-relapse visit, for patients who had a relapse, the end of study is the last value before the missed value.

(1) The LS means (95% CI) and the difference in LS means (95% CI) are from an ANCOVA model of change from baseline with treatment as factor and baseline value as covariate. (2) The p-value represents the significance of the treatment effect and was derived from an ANCOVA model of the ranked change from baseline, with treatment as a factor, and the ranks of the baseline value included as covariate.

(3) Standardized mean differences (95% CI) were computed using Cohen's D incorporating Hedge's correction on change from baseline. (4) Odds ratio statistics are from a logistic regression model adjusted for baseline value with Firth's adjustment; (5) Relative risk statistics are based on a generalized linear model of a binomial distribution with log link;

(6) Risk difference statistics are calculated from a generalized linear model, correcting for the baseline value. (7) P-value is for the interaction term of treatment:subgroup from a linear regression model of ranked change from baseline with the with ranked baseline value, treatment, subgroup, and treatment:subgroup interaction as covariates.

For eculizumab arm, Americas: ARG and USA; Europe: CZE, DEU, DNK, ESP, HRV, ITA, RUS and TUR; Asia-Pacific: AUS, HKG, JPN, KOR, MYS, THA and TWN. For ravulizumab arm, Americas: CAN and USA; Europe: DEU, DNK, ESP, GBR, ITA and POL; Asia-Pacific: AUS, JPN and KOR.

Odds ratio and relative risk are calculated as Ravulizumab/Eculizumab. LS mean difference and risk difference are calculated as Ravulizumab - Eculizumab.

Source: adsl, adsf36

Table SF-36-3.5
Change from Baseline in SF-36 Mental Component Score to End of Study Period by Region
Full Analysis Set

Region		Statistic	Eculizumab (N=96)	Ravulizumab (N=58)	p-value (7)
Americas	Change from Baseline to End of Study Period in SF-36 Mental Component Score	n	29	21	0.3986
		Mean (SD)	0.7 (10.35)	1.5 (7.73)	
		Median	0.0	2.0	
		Q1, Q3	-4.3, 6.0	-3.6, 5.6	
		Min, Max	-21, 21	-11, 18	
		Change from baseline			
		LS Means (SEM)	0.787 (1.679)	1.420 (1.973)	
		95% CI for LS Means (1)	(-2.591, 4.164)	(-2.549, 5.390)	
		Difference in LS Means		0.633	
		(95% CI) (1)		(-4.580, 5.847)	
		p-value (2)		0.8464	
		Standardized Mean Difference		0.211	
		(95% CI) (3)		(-0.353, 0.774)	
		Responders (10% [10 points]), n(%)	6 (20.7)	3 (14.3)	
		Odds Ratio (4)		0.663	
		(95% CI)		(0.148, 2.974)	
		p-value		0.5913	
		Relative Risk (5)		0.690	
		(95% CI)		(0.194, 2.451)	
		p-value		0.5667	

The eculizumab group data were collected as part of the PREVENT trial, Study ECU-NMO-301.

End of Study Period is the 6-week assessment after the first On-Trial Relapse for patients who have an On-Trial Relapse or for patients with no On-Trial Relapse: the End of Primary Treatment Period visit for patients in Study ALXN1210-NMO-307 and the End of Study visit for patients in Study ECU-NMO-301.

For those patients who had a missed value at the EOPT Visit or the 6-week post-relapse visit, for patients who had a relapse, the end of study is the last value before the missed value.

(1) The LS means (95% CI) and the difference in LS means (95% CI) are from an ANCOVA model of change from baseline with treatment as factor and baseline value as covariate. (2) The p-value represents the significance of the treatment effect and was derived from an ANCOVA model of the ranked change from baseline, with treatment as a factor, and the ranks of the baseline value included as covariate.

(3) Standardized mean differences (95% CI) were computed using Cohen's D incorporating Hedge's correction on change from baseline. (4) Odds ratio statistics are from a logistic regression model adjusted for baseline value with Firth's adjustment; (5) Relative risk statistics are based on a generalized linear model of a binomial distribution with log link;

(6) Risk difference statistics are calculated from a generalized linear model, correcting for the baseline value. (7) P-value is for the interaction term of treatment:subgroup from a linear regression model of ranked change from baseline with the with ranked baseline value, treatment, subgroup, and treatment:subgroup interaction as covariates.

For eculizumab arm, Americas: ARG and USA; Europe: CZE, DEU, DNK, ESP, HRV, ITA, RUS and TUR; Asia-Pacific: AUS, HKG, JPN, KOR, MYS, THA and TWN. For ravulizumab arm, Americas: CAN and USA; Europe: DEU, DNK, ESP, GBR, ITA and POL; Asia-Pacific: AUS, JPN and KOR.

Odds ratio and relative risk are calculated as Ravulizumab/Eculizumab. LS mean difference and risk difference are calculated as Ravulizumab - Eculizumab.

Source: adsl, adsf36

Table SF-36-3.5
Change from Baseline in SF-36 Mental Component Score to End of Study Period by Region
Full Analysis Set

Region	Statistic	Eculizumab (N=96)	Ravulizumab (N=58)	p-value (7)
	Risk Difference (6)		-0.072	
	(95% CI)		(-0.291, 0.148)	
	p-value		0.5151	
Baseline SF-36 Mental Component Score	n	29	21	
	Mean (SD)	47.6 (12.61)	46.7 (10.67)	
	Median	47.9	47.8	
	Q1, Q3	41.5, 57.2	39.6, 55.7	
	Min, Max	11, 65	21, 62	
End of Study Period SF-36 Mental Component Score	n	29	21	
	Mean (SD)	48.3 (13.43)	48.3 (11.78)	
	Median	51.5	52.8	
	Q1, Q3	43.7, 59.0	35.9, 57.7	
	Min, Max	8, 63	28, 63	

The eculizumab group data were collected as part of the PREVENT trial, Study ECU-NMO-301.

End of Study Period is the 6-week assessment after the first On-Trial Relapse for patients who have an On-Trial Relapse or for patients with no On-Trial Relapse: the End of Primary Treatment Period visit for patients in Study ALXN1210-NMO-307 and the End of Study visit for patients in Study ECU-NMO-301.

For those patients who had a missed value at the EOPT Visit or the 6-week post-relapse visit, for patients who had a relapse, the end of study is the last value before the missed value.

(1) The LS means (95% CI) and the difference in LS means (95% CI) are from an ANCOVA model of change from baseline with treatment as factor and baseline value as covariate. (2) The p-value represents the significance of the treatment effect and was derived from an ANCOVA model of the ranked change from baseline, with treatment as a factor, and the ranks of the baseline value included as covariate.

(3) Standardized mean differences (95% CI) were computed using Cohen's D incorporating Hedge's correction on change from baseline. (4) Odds ratio statistics are from a logistic regression model adjusted for baseline value with Firth's adjustment; (5) Relative risk statistics are based on a generalized linear model of a binomial distribution with log link;

(6) Risk difference statistics are calculated from a generalized linear model, correcting for the baseline value. (7) P-value is for the interaction term of treatment:subgroup from a linear regression model of ranked change from baseline with the with ranked baseline value, treatment, subgroup, and treatment:subgroup interaction as covariates.

For eculizumab arm, Americas: ARG and USA; Europe: CZE, DEU, DNK, ESP, HRV, ITA, RUS and TUR; Asia-Pacific: AUS, HKG, JPN, KOR, MYS, THA and TWN. For ravulizumab arm, Americas: CAN and USA; Europe: DEU, DNK, ESP, GBR, ITA and POL; Asia-Pacific: AUS, JPN and KOR.

Odds ratio and relative risk are calculated as Ravulizumab/Eculizumab. LS mean difference and risk difference are calculated as Ravulizumab - Eculizumab.

Source: adsl, adsf36

Table SF-36-3.5
Change from Baseline in SF-36 Mental Component Score to End of Study Period by Region
Full Analysis Set

Region		Statistic	Eculizumab (N=96)	Ravulizumab (N=58)	p-value (7)
Europe	Change from Baseline to End of Study Period in SF-36 Mental Component Score	n	32	17	
		Mean (SD)	0.8 (10.70)	-0.7 (6.45)	
		Median	0.8	-0.1	
		Q1, Q3	-5.2, 7.5	-5.1, 3.3	
		Min, Max	-25, 24	-10, 13	
		Change from baseline			
		LS Means (SEM)	0.861 (1.491)	-0.834 (2.046)	
		95% CI for LS Means (1)	(-2.141, 3.863)	(-4.953, 3.285)	
		Difference in LS Means		-1.695	
		(95% CI) (1)		(-6.793, 3.403)	
		p-value (2)		0.3248	
		Standardized Mean Difference		-0.584	
		(95% CI) (3)		(-1.183, 0.016)	
		Responders (10% [10 points]), n(%)	5 (15.6)	1 (5.9)	
		Odds Ratio (4)		0.436	
		(95% CI)		(0.063, 3.043)	
		p-value		0.4027	
		Relative Risk (5)		0.376	
		(95% CI)		(0.048, 2.968)	
		p-value		0.3538	

The eculizumab group data were collected as part of the PREVENT trial, Study ECU-NMO-301.
End of Study Period is the 6-week assessment after the first On-Trial Relapse for patients who have an On-Trial Relapse or for patients with no On-Trial Relapse: the End of Primary Treatment Period visit for patients in Study ALXN1210-NMO-307 and the End of Study visit for patients in Study ECU-NMO-301.
For those patients who had a missed value at the EOPT Visit or the 6-week post-relapse visit, for patients who had a relapse, the end of study is the last value before the missed value.
(1) The LS means (95% CI) and the difference in LS means (95% CI) are from an ANCOVA model of change from baseline with treatment as factor and baseline value as covariate. (2) The p-value represents the significance of the treatment effect and was derived from an ANCOVA model of the ranked change from baseline, with treatment as a factor, and the ranks of the baseline value included as covariate.
(3) Standardized mean differences (95% CI) were computed using Cohen's D incorporating Hedge's correction on change from baseline. (4) Odds ratio statistics are from a logistic regression model adjusted for baseline value with Firth's adjustment; (5) Relative risk statistics are based on a generalized linear model of a binomial distribution with log link;
(6) Risk difference statistics are calculated from a generalized linear model, correcting for the baseline value. (7) P-value is for the interaction term of treatment:subgroup from a linear regression model of ranked change from baseline with the with ranked baseline value, treatment, subgroup, and treatment:subgroup interaction as covariates.
For eculizumab arm, Americas: ARG and USA; Europe: CZE, DEU, DNK, ESP, HRV, ITA, RUS and TUR; Asia-Pacific: AUS, HKG, JPN, KOR, MYS, THA and TWN. For ravulizumab arm, Americas: CAN and USA; Europe: DEU, DNK, ESP, GBR, ITA and POL; Asia-Pacific: AUS, JPN and KOR.
Odds ratio and relative risk are calculated as Ravulizumab/Eculizumab. LS mean difference and risk difference are calculated as Ravulizumab - Eculizumab.
Source: adsl, adsf36

Table SF-36-3.5
Change from Baseline in SF-36 Mental Component Score to End of Study Period by Region
Full Analysis Set

Region	Statistic	Eculizumab (N=96)	Ravulizumab (N=58)	p-value (7)
	Risk Difference (6)		-0.101	
	(95% CI)		(-0.300, 0.099)	
	p-value		0.3150	
Baseline SF-36 Mental Component Score	n	32	17	
	Mean (SD)	46.5 (12.66)	45.8 (13.01)	
	Median	50.7	49.0	
	Q1, Q3	36.6, 58.4	38.3, 53.1	
	Min, Max	22, 62	21, 68	
End of Study Period SF-36 Mental Component Score	n	32	17	
	Mean (SD)	47.3 (11.43)	45.2 (12.40)	
	Median	49.5	45.8	
	Q1, Q3	35.2, 56.1	36.8, 51.6	
	Min, Max	23, 65	24, 72	

The eculizumab group data were collected as part of the PREVENT trial, Study ECU-NMO-301.

End of Study Period is the 6-week assessment after the first On-Trial Relapse for patients who have an On-Trial Relapse or for patients with no On-Trial Relapse: the End of Primary Treatment Period visit for patients in Study ALXN1210-NMO-307 and the End of Study visit for patients in Study ECU-NMO-301.

For those patients who had a missed value at the EOPT Visit or the 6-week post-relapse visit, for patients who had a relapse, the end of study is the last value before the missed value.

(1) The LS means (95% CI) and the difference in LS means (95% CI) are from an ANCOVA model of change from baseline with treatment as factor and baseline value as covariate. (2) The p-value represents the significance of the treatment effect and was derived from an ANCOVA model of the ranked change from baseline, with treatment as a factor, and the ranks of the baseline value included as covariate.

(3) Standardized mean differences (95% CI) were computed using Cohen's D incorporating Hedge's correction on change from baseline. (4) Odds ratio statistics are from a logistic regression model adjusted for baseline value with Firth's adjustment; (5) Relative risk statistics are based on a generalized linear model of a binomial distribution with log link;

(6) Risk difference statistics are calculated from a generalized linear model, correcting for the baseline value. (7) P-value is for the interaction term of treatment:subgroup from a linear regression model of ranked change from baseline with the with ranked baseline value, treatment, subgroup, and treatment:subgroup interaction as covariates.

For eculizumab arm, Americas: ARG and USA; Europe: CZE, DEU, DNK, ESP, HRV, ITA, RUS and TUR; Asia-Pacific: AUS, HKG, JPN, KOR, MYS, THA and TWN. For ravulizumab arm, Americas: CAN and USA; Europe: DEU, DNK, ESP, GBR, ITA and POL; Asia-Pacific: AUS, JPN and KOR.

Odds ratio and relative risk are calculated as Ravulizumab/Eculizumab. LS mean difference and risk difference are calculated as Ravulizumab - Eculizumab.

Source: adsl, adsf36

Table SF-36-3.6
Change from Baseline in SF-36 Mental Component Score to End of Study Period by Supportive IST use at baseline
Full Analysis Set

IST use at baseline		Statistic	Eculizumab (N=96)	Ravulizumab (N=58)	p-value (7)
Yes	Change from Baseline to End of Study Period in SF-36 Mental Component Score	n	75	28	0.9331
		Mean (SD)	0.4 (10.41)	0.3 (8.39)	
		Median	0.1	-0.9	
		Q1, Q3	-5.8, 6.2	-5.4, 3.3	
		Min, Max	-28, 29	-12, 23	
		Change from baseline			
		LS Means (SEM)	0.173 (0.993)	1.001 (1.627)	
		95% CI for LS Means (1)	(-1.796, 2.143)	(-2.227, 4.229)	
		Difference in LS Means		0.828	
		(95% CI) (1)		(-2.959, 4.614)	
		p-value (2)		0.8457	
		Standardized Mean Difference		0.282	
		(95% CI) (3)		(-0.154, 0.718)	
		Responders (10% [10 points]), n(%)	13 (17.3)	3 (10.7)	
		Odds Ratio (4)		0.689	
		(95% CI)		(0.175, 2.714)	
		p-value		0.5942	
		Relative Risk (5)		0.618	
		(95% CI)		(0.190, 2.008)	
		p-value		0.4235	

The eculizumab group data were collected as part of the PREVENT trial, Study ECU-NMO-301.

End of Study Period is the 6-week assessment after the first On-Trial Relapse for patients who have an On-Trial Relapse or for patients with no On-Trial Relapse: the End of Primary Treatment Period visit for patients in Study ALXN1210-NMO-307 and the End of Study visit for patients in Study ECU-NMO-301.

For those patients who had a missed value at the EOPT Visit or the 6-week post-relapse visit, for patients who had a relapse, the end of study is the last value before the missed value.

(1) The LS means (95% CI) and the difference in LS means (95% CI) are from an ANCOVA model of change from baseline with treatment as factor and baseline value as covariate. (2) The p-value represents the significance of the treatment effect and was derived from an ANCOVA model of the ranked change from baseline, with treatment as a factor, and the ranks of the baseline value included as covariate.

(3) Standardized mean differences (95% CI) were computed using Cohen's D incorporating Hedge's correction on change from baseline. (4) Odds ratio statistics are from a logistic regression model adjusted for baseline value with Firth's adjustment; (5) Relative risk statistics are based on a generalized linear model of a binomial distribution with log link;

(6) Risk difference statistics are calculated from a generalized linear model, correcting for the baseline value. (7) P-value is for the interaction term of treatment:subgroup from a linear regression model of ranked change from baseline with the with ranked baseline value, treatment, subgroup, and treatment:subgroup interaction as covariates.

Odds ratio and relative risk are calculated as Ravulizumab/Eculizumab. LS mean difference and risk difference are calculated as Ravulizumab - Eculizumab.

Source: adsl, adsf36

Table SF-36-3.6
Change from Baseline in SF-36 Mental Component Score to End of Study Period by Supportive IST use at baseline
Full Analysis Set

IST use at baseline	Statistic	Eculizumab (N=96)	Ravulizumab (N=58)	p-value (7)
	Risk Difference (6)		-0.042	
	(95% CI)		(-0.192, 0.108)	
	p-value		0.5796	
Baseline SF-36 Mental Component Score	n	75	28	
	Mean (SD)	47.5 (12.56)	49.7 (12.49)	
	Median	51.1	53.5	
	Q1, Q3	39.4, 57.4	41.0, 58.5	
	Min, Max	7, 65	18, 68	
End of Study Period SF-36 Mental Component Score	n	75	28	
	Mean (SD)	47.9 (12.15)	50.1 (8.93)	
	Median	49.2	52.1	
	Q1, Q3	39.8, 58.7	46.7, 55.4	
	Min, Max	8, 69	30, 72	

The eculizumab group data were collected as part of the PREVENT trial, Study ECU-NMO-301.

End of Study Period is the 6-week assessment after the first On-Trial Relapse for patients who have an On-Trial Relapse or for patients with no On-Trial Relapse: the End of Primary Treatment Period visit for patients in Study ALXN1210-NMO-307 and the End of Study visit for patients in Study ECU-NMO-301.

For those patients who had a missed value at the EOPT Visit or the 6-week post-relapse visit, for patients who had a relapse, the end of study is the last value before the missed value.

(1) The LS means (95% CI) and the difference in LS means (95% CI) are from an ANCOVA model of change from baseline with treatment as factor and baseline value as covariate. (2) The p-value represents the significance of the treatment effect and was derived from an ANCOVA model of the ranked change from baseline, with treatment as a factor, and the ranks of the baseline value included as covariate.

(3) Standardized mean differences (95% CI) were computed using Cohen's D incorporating Hedge's correction on change from baseline. (4) Odds ratio statistics are from a logistic regression model adjusted for baseline value with Firth's adjustment; (5) Relative risk statistics are based on a generalized linear model of a binomial distribution with log link;

(6) Risk difference statistics are calculated from a generalized linear model, correcting for the baseline value. (7) P-value is for the interaction term of treatment:subgroup from a linear regression model of ranked change from baseline with the with ranked baseline value, treatment, subgroup, and treatment:subgroup interaction as covariates.

Odds ratio and relative risk are calculated as Ravulizumab/Eculizumab. LS mean difference and risk difference are calculated as Ravulizumab - Eculizumab.

Source: adsl, adsf36

Table SF-36-3.6
Change from Baseline in SF-36 Mental Component Score to End of Study Period by Supportive IST use at baseline
Full Analysis Set

IST use at baseline		Statistic	Eculizumab (N=96)	Ravulizumab (N=58)	p-value (7)
No	Change from Baseline to End of Study Period in SF-36 Mental Component Score	n	21	30	
		Mean (SD)	0.6 (11.54)	1.2 (7.65)	
		Median	-0.9	1.4	
		Q1, Q3	-5.1, 7.6	-3.8, 5.6	
		Min, Max	-25, 24	-11, 18	
		Change from baseline			
		LS Means (SEM)	0.700 (1.926)	1.085 (1.612)	
		95% CI for LS Means (1)	(-3.173, 4.573)	(-2.155, 4.325)	
		Difference in LS Means		0.385	
		(95% CI) (1)		(-4.666, 5.436)	
		p-value (2)		0.9706	
		Standardized Mean Difference		0.130	
		(95% CI) (3)		(-0.429, 0.688)	
		Responders (10% [10 points]), n(%)	3 (14.3)	4 (13.3)	
		Odds Ratio (4)		0.885	
		(95% CI)		(0.184, 4.245)	
		p-value		0.8781	
		Relative Risk (5)		0.933	
		(95% CI)		(0.233, 3.744)	
		p-value		0.9225	

The eculizumab group data were collected as part of the PREVENT trial, Study ECU-NMO-301.

End of Study Period is the 6-week assessment after the first On-Trial Relapse for patients who have an On-Trial Relapse or for patients with no On-Trial Relapse: the End of Primary Treatment Period visit for patients in Study ALXN1210-NMO-307 and the End of Study visit for patients in Study ECU-NMO-301.

For those patients who had a missed value at the EOPT Visit or the 6-week post-relapse visit, for patients who had a relapse, the end of study is the last value before the missed value.

(1) The LS means (95% CI) and the difference in LS means (95% CI) are from an ANCOVA model of change from baseline with treatment as factor and baseline value as covariate. (2) The p-value represents the significance of the treatment effect and was derived from an ANCOVA model of the ranked change from baseline, with treatment as a factor, and the ranks of the baseline value included as covariate.

(3) Standardized mean differences (95% CI) were computed using Cohen's D incorporating Hedge's correction on change from baseline. (4) Odds ratio statistics are from a logistic regression model adjusted for baseline value with Firth's adjustment; (5) Relative risk statistics are based on a generalized linear model of a binomial distribution with log link;

(6) Risk difference statistics are calculated from a generalized linear model, correcting for the baseline value. (7) P-value is for the interaction term of treatment:subgroup from a linear regression model of ranked change from baseline with the with ranked baseline value, treatment, subgroup, and treatment:subgroup interaction as covariates.

Odds ratio and relative risk are calculated as Ravulizumab/Eculizumab. LS mean difference and risk difference are calculated as Ravulizumab - Eculizumab.

Source: adsl, adsf36

Table SF-36-3.6
Change from Baseline in SF-36 Mental Component Score to End of Study Period by Supportive IST use at baseline
Full Analysis Set

IST use at baseline	Statistic	Eculizumab (N=96)	Ravulizumab (N=58)	p-value (7)
	Risk Difference (6)		-0.014	
	(95% CI)		(-0.212, 0.184)	
	p-value		0.8858	
Baseline SF-36 Mental Component Score	n	21	30	
	Mean (SD)	45.4 (12.69)	44.7 (11.09)	
	Median	47.7	46.1	
	Q1, Q3	37.4, 56.0	38.3, 53.2	
	Min, Max	22, 62	21, 62	
End of Study Period SF-36 Mental Component Score	n	21	30	
	Mean (SD)	46.0 (12.54)	45.9 (11.58)	
	Median	49.6	46.9	
	Q1, Q3	42.1, 53.2	36.1, 56.4	
	Min, Max	13, 61	24, 63	

The eculizumab group data were collected as part of the PREVENT trial, Study ECU-NMO-301.

End of Study Period is the 6-week assessment after the first On-Trial Relapse for patients who have an On-Trial Relapse or for patients with no On-Trial Relapse: the End of Primary Treatment Period visit for patients in Study ALXN1210-NMO-307 and the End of Study visit for patients in Study ECU-NMO-301.

For those patients who had a missed value at the EOPT Visit or the 6-week post-relapse visit, for patients who had a relapse, the end of study is the last value before the missed value.

(1) The LS means (95% CI) and the difference in LS means (95% CI) are from an ANCOVA model of change from baseline with treatment as factor and baseline value as covariate. (2) The p-value represents the significance of the treatment effect and was derived from an ANCOVA model of the ranked change from baseline, with treatment as a factor, and the ranks of the baseline value included as covariate.

(3) Standardized mean differences (95% CI) were computed using Cohen's D incorporating Hedge's correction on change from baseline. (4) Odds ratio statistics are from a logistic regression model adjusted for baseline value with Firth's adjustment; (5) Relative risk statistics are based on a generalized linear model of a binomial distribution with log link;

(6) Risk difference statistics are calculated from a generalized linear model, correcting for the baseline value. (7) P-value is for the interaction term of treatment:subgroup from a linear regression model of ranked change from baseline with the with ranked baseline value, treatment, subgroup, and treatment:subgroup interaction as covariates.

Odds ratio and relative risk are calculated as Ravulizumab/Eculizumab. LS mean difference and risk difference are calculated as Ravulizumab - Eculizumab.

Source: adsl, adsf36

Table SF-36-3.7
Change from Baseline in SF-36 Mental Component Score to End of Study Period by Rituximab use in the prior year
Full Analysis Set

Rituximab use in the prior year		Statistic	Eculizumab (N=96)	Ravulizumab (N=58)	p-value (7)
Yes	Change from Baseline to End of Study Period in SF-36 Mental Component Score	n	19	20	0.2529
		Mean (SD)	-1.3 (9.46)	1.8 (7.24)	
		Median	-1.6	2.1	
		Q1, Q3	-5.8, 5.3	-3.1, 6.6	
		Min, Max	-21, 18	-11, 14	
		Change from baseline			
		LS Means (SEM)	-0.775 (1.829)	1.282 (1.782)	
		95% CI for LS Means (1)	(-4.484, 2.934)	(-2.332, 4.896)	
		Difference in LS Means		2.057	
		(95% CI) (1)		(-3.162, 7.276)	
		p-value (2)		0.3470	
		Standardized Mean Difference		0.729	
		(95% CI) (3)		(0.080, 1.377)	
		Responders (10% [10 points]), n(%)	2 (10.5)	3 (15.0)	
		Odds Ratio (4)		1.114	
		(95% CI)		(0.174, 7.142)	
		p-value		0.9091	
		Relative Risk (5)		1.425	
		(95% CI)		(0.267, 7.611)	
		p-value		0.6786	

The eculizumab group data were collected as part of the PREVENT trial, Study ECU-NMO-301.

End of Study Period is the 6-week assessment after the first On-Trial Relapse for patients who have an On-Trial Relapse or for patients with no On-Trial Relapse: the End of Primary Treatment Period visit for patients in Study ALXN1210-NMO-307 and the End of Study visit for patients in Study ECU-NMO-301.

For those patients who had a missed value at the EOPT Visit or the 6-week post-relapse visit, for patients who had a relapse, the end of study is the last value before the missed value.

(1) The LS means (95% CI) and the difference in LS means (95% CI) are from an ANCOVA model of change from baseline with treatment as factor and baseline value as covariate. (2) The p-value represents the significance of the treatment effect and was derived from an ANCOVA model of the ranked change from baseline, with treatment as a factor, and the ranks of the baseline value included as covariate.

(3) Standardized mean differences (95% CI) were computed using Cohen's D incorporating Hedge's correction on change from baseline. (4) Odds ratio statistics are from a logistic regression model adjusted for baseline value with Firth's adjustment; (5) Relative risk statistics are based on a generalized linear model of a binomial distribution with log link;

(6) Risk difference statistics are calculated from a generalized linear model, correcting for the baseline value. (7) P-value is for the interaction term of treatment:subgroup from a linear regression model of ranked change from baseline with the with ranked baseline value, treatment, subgroup, and treatment:subgroup interaction as covariates.

Odds ratio and relative risk are calculated as Ravulizumab/Eculizumab. LS mean difference and risk difference are calculated as Ravulizumab - Eculizumab.

Source: adsl, adsf36

Table SF-36-3.7
Change from Baseline in SF-36 Mental Component Score to End of Study Period by Rituximab use in the prior year
Full Analysis Set

Rituximab use in the prior year		Statistic	Eculizumab (N=96)	Ravulizumab (N=58)	p-value (7)
		Risk Difference (6)		0.017	
		(95% CI)		(-0.206, 0.239)	
		p-value		0.8797	
	Baseline SF-36 Mental Component Score	n	19	20	
		Mean (SD)	49.9 (9.70)	46.0 (12.31)	
		Median	51.3	48.6	
		Q1, Q3	42.2, 56.5	40.5, 55.2	
		Min, Max	28, 63	21, 62	
	End of Study Period SF-36 Mental Component Score	n	19	20	
		Mean (SD)	48.6 (9.74)	47.8 (12.40)	
		Median	47.9	51.1	
		Q1, Q3	41.8, 55.8	35.3, 57.5	
		Min, Max	30, 63	24, 63	

The eculizumab group data were collected as part of the PREVENT trial, Study ECU-NMO-301.

End of Study Period is the 6-week assessment after the first On-Trial Relapse for patients who have an On-Trial Relapse or for patients with no On-Trial Relapse: the End of Primary Treatment Period visit for patients in Study ALXN1210-NMO-307 and the End of Study visit for patients in Study ECU-NMO-301.

For those patients who had a missed value at the EOPT Visit or the 6-week post-relapse visit, for patients who had a relapse, the end of study is the last value before the missed value.

(1) The LS means (95% CI) and the difference in LS means (95% CI) are from an ANCOVA model of change from baseline with treatment as factor and baseline value as covariate. (2) The p-value represents the significance of the treatment effect and was derived from an ANCOVA model of the ranked change from baseline, with treatment as a factor, and the ranks of the baseline value included as covariate.

(3) Standardized mean differences (95% CI) were computed using Cohen's D incorporating Hedge's correction on change from baseline. (4) Odds ratio statistics are from a logistic regression model adjusted for baseline value with Firth's adjustment; (5) Relative risk statistics are based on a generalized linear model of a binomial distribution with log link;

(6) Risk difference statistics are calculated from a generalized linear model, correcting for the baseline value. (7) P-value is for the interaction term of treatment:subgroup from a linear regression model of ranked change from baseline with the with ranked baseline value, treatment, subgroup, and treatment:subgroup interaction as covariates.

Odds ratio and relative risk are calculated as Ravulizumab/Eculizumab. LS mean difference and risk difference are calculated as Ravulizumab - Eculizumab.

Source: adsl, adsf36

Table SF-36-3.7
Change from Baseline in SF-36 Mental Component Score to End of Study Period by Rituximab use in the prior year
Full Analysis Set

Rituximab use in the prior year		Statistic	Eculizumab (N=96)	Ravulizumab (N=58)	p-value (7)
No	Change from Baseline to End of Study Period in SF-36 Mental Component Score	n	77	38	
		Mean (SD)	0.9 (10.88)	0.2 (8.36)	
		Median	1.2	-0.5	
		Q1, Q3	-5.1, 7.6	-5.1, 3.8	
		Min, Max	-28, 29	-12, 23	
		Change from baseline			
		LS Means (SEM)	0.714 (1.014)	0.589 (1.445)	
		95% CI for LS Means (1)	(-1.296, 2.723)	(-2.273, 3.451)	
		Difference in LS Means		-0.125	
		(95% CI) (1)		(-3.624, 3.375)	
		p-value (2)		0.4367	
		Standardized Mean Difference		-0.042	
		(95% CI) (3)		(-0.430, 0.347)	
		Responders (10% [10 points]), n(%)	14 (18.2)	4 (10.5)	
		Odds Ratio (4)		0.613	
		(95% CI)		(0.184, 2.042)	
		p-value		0.4259	
		Relative Risk (5)		0.579	
		(95% CI)		(0.204, 1.640)	
		p-value		0.3035	

The eculizumab group data were collected as part of the PREVENT trial, Study ECU-NMO-301.

End of Study Period is the 6-week assessment after the first On-Trial Relapse for patients who have an On-Trial Relapse or for patients with no On-Trial Relapse: the End of Primary Treatment Period visit for patients in Study ALXN1210-NMO-307 and the End of Study visit for patients in Study ECU-NMO-301.

For those patients who had a missed value at the EOPT Visit or the 6-week post-relapse visit, for patients who had a relapse, the end of study is the last value before the missed value.

(1) The LS means (95% CI) and the difference in LS means (95% CI) are from an ANCOVA model of change from baseline with treatment as factor and baseline value as covariate. (2) The p-value represents the significance of the treatment effect and was derived from an ANCOVA model of the ranked change from baseline, with treatment as a factor, and the ranks of the baseline value included as covariate.

(3) Standardized mean differences (95% CI) were computed using Cohen's D incorporating Hedge's correction on change from baseline. (4) Odds ratio statistics are from a logistic regression model adjusted for baseline value with Firth's adjustment; (5) Relative risk statistics are based on a generalized linear model of a binomial distribution with log link;

(6) Risk difference statistics are calculated from a generalized linear model, correcting for the baseline value. (7) P-value is for the interaction term of treatment:subgroup from a linear regression model of ranked change from baseline with the with ranked baseline value, treatment, subgroup, and treatment:subgroup interaction as covariates.

Odds ratio and relative risk are calculated as Ravulizumab/Eculizumab. LS mean difference and risk difference are calculated as Ravulizumab - Eculizumab.

Source: adsl, adsf36

Table SF-36-3.7
Change from Baseline in SF-36 Mental Component Score to End of Study Period by Rituximab use in the prior year
Full Analysis Set

Rituximab use in the prior year		Statistic	Eculizumab (N=96)	Ravulizumab (N=58)	p-value (7)
		Risk Difference (6)		-0.063	
		(95% CI)		(-0.199, 0.073)	
		p-value		0.3597	
	Baseline SF-36 Mental Component Score	n	77	38	
		Mean (SD)	46.3 (13.11)	47.7 (11.89)	
		Median	50.7	50.1	
		Q1, Q3	37.8, 57.4	39.5, 56.9	
		Min, Max	7, 65	18, 68	
	End of Study Period SF-36 Mental Component Score	n	77	38	
		Mean (SD)	47.2 (12.77)	48.0 (9.55)	
		Median	49.5	49.3	
		Q1, Q3	37.5, 57.2	40.5, 55.2	
		Min, Max	8, 69	29, 72	

The eculizumab group data were collected as part of the PREVENT trial, Study ECU-NMO-301.

End of Study Period is the 6-week assessment after the first On-Trial Relapse for patients who have an On-Trial Relapse or for patients with no On-Trial Relapse: the End of Primary Treatment Period visit for patients in Study ALXN1210-NMO-307 and the End of Study visit for patients in Study ECU-NMO-301.

For those patients who had a missed value at the EOPT Visit or the 6-week post-relapse visit, for patients who had a relapse, the end of study is the last value before the missed value.

(1) The LS means (95% CI) and the difference in LS means (95% CI) are from an ANCOVA model of change from baseline with treatment as factor and baseline value as covariate. (2) The p-value represents the significance of the treatment effect and was derived from an ANCOVA model of the ranked change from baseline, with treatment as a factor, and the ranks of the baseline value included as covariate.

(3) Standardized mean differences (95% CI) were computed using Cohen's D incorporating Hedge's correction on change from baseline. (4) Odds ratio statistics are from a logistic regression model adjusted for baseline value with Firth's adjustment; (5) Relative risk statistics are based on a generalized linear model of a binomial distribution with log link;

(6) Risk difference statistics are calculated from a generalized linear model, correcting for the baseline value. (7) P-value is for the interaction term of treatment:subgroup from a linear regression model of ranked change from baseline with the with ranked baseline value, treatment, subgroup, and treatment:subgroup interaction as covariates.

Odds ratio and relative risk are calculated as Ravulizumab/Eculizumab. LS mean difference and risk difference are calculated as Ravulizumab - Eculizumab.

Source: adsl, adsf36

Table SF-36-3.4
Change from Baseline in SF-36 Mental Component Score to End of Study Period by Disease severity via EDSS Score at baseline
Full Analysis Set

EDSS score at baseline		Statistic	Eculizumab (N=96)	Ravulizumab (N=58)	p-value (7)
< 5	Change from Baseline to End of Study Period in SF-36 Mental Component Score	n	66	49	0.6432
		Mean (SD)	1.2 (9.90)	0.5 (7.91)	
		Median	-0.0	-0.1	
		Q1, Q3	-4.6, 7.3	-5.0, 4.0	
		Min, Max	-20, 29	-12, 23	
		Change from baseline			
		LS Means (SEM)	0.922 (0.977)	0.885 (1.135)	
		95% CI for LS Means (1)	(-1.015, 2.858)	(-1.363, 3.134)	
		Difference in LS Means		-0.037	
		(95% CI) (1)		(-3.007, 2.934)	
		p-value (2)		0.6566	
		Standardized Mean Difference		-0.013	
		(95% CI) (3)		(-0.383, 0.357)	
		Responders (10% [10 points]), n(%)	11 (16.7)	6 (12.2)	
		Odds Ratio (4)		0.857	
		(95% CI)		(0.274, 2.676)	
		p-value		0.7900	
		Relative Risk (5)		0.735	
		(95% CI)		(0.292, 1.850)	
		p-value		0.5129	

The eculizumab group data were collected as part of the PREVENT trial, Study ECU-NMO-301.
End of Study Period is the 6-week assessment after the first On-Trial Relapse for patients who have an On-Trial Relapse or for patients with no On-Trial Relapse: the End of Primary Treatment Period visit for patients in Study ALXN1210-NMO-307 and the End of Study visit for patients in Study ECU-NMO-301.
For those patients who had a missed value at the EOPT Visit or the 6-week post-relapse visit, for patients who had a relapse, the end of study is the last value before the missed value.
(1) The LS means (95% CI) and the difference in LS means (95% CI) are from an ANCOVA model of change from baseline with treatment as factor and baseline value as covariate. (2) The p-value represents the significance of the treatment effect and was derived from an ANCOVA model of the ranked change from baseline, with treatment as a factor, and the ranks of the baseline value included as covariate.
(3) Standardized mean differences (95% CI) were computed using Cohen's D incorporating Hedge's correction on change from baseline. (4) Odds ratio statistics are from a logistic regression model adjusted for baseline value with Firth's adjustment; (5) Relative risk statistics are based on a generalized linear model of a binomial distribution with log link;
(6) Risk difference statistics are calculated from a generalized linear model, correcting for the baseline value.
(7) P-value is for the interaction term of treatment:subgroup from a linear regression model of ranked change from baseline with the with ranked baseline value, treatment, subgroup, and treatment:subgroup interaction as covariates.
Odds ratio and relative risk are calculated as Ravulizumab/Eculizumab. LS mean difference and risk difference are calculated as Ravulizumab - Eculizumab.
Source: adsl, adsf36

Table SF-36-3.4
Change from Baseline in SF-36 Mental Component Score to End of Study Period by Disease severity via EDSS Score at baseline
Full Analysis Set

EDSS score at baseline	Statistic	Eculizumab (N=96)	Ravulizumab (N=58)	p-value (7)
	Risk Difference (6)		-0.026	
	(95% CI)		(-0.149, 0.098)	
	p-value		0.6819	
Baseline SF-36 Mental Component Score	n	66	49	
	Mean (SD)	46.6 (12.73)	48.2 (10.57)	
	Median	50.4	50.6	
	Q1, Q3	38.3, 56.1	40.6, 56.3	
	Min, Max	7, 65	18, 64	
End of Study Period SF-36 Mental Component Score	n	66	49	
	Mean (SD)	47.8 (12.00)	48.7 (8.86)	
	Median	50.0	51.2	
	Q1, Q3	42.1, 57.2	42.0, 55.5	
	Min, Max	8, 64	29, 63	

The eculizumab group data were collected as part of the PREVENT trial, Study ECU-NMO-301.

End of Study Period is the 6-week assessment after the first On-Trial Relapse for patients who have an On-Trial Relapse or for patients with no On-Trial Relapse: the End of Primary Treatment Period visit for patients in Study ALXN1210-NMO-307 and the End of Study visit for patients in Study ECU-NMO-301.

For those patients who had a missed value at the EOPT Visit or the 6-week post-relapse visit, for patients who had a relapse, the end of study is the last value before the missed value.

(1) The LS means (95% CI) and the difference in LS means (95% CI) are from an ANCOVA model of change from baseline with treatment as factor and baseline value as covariate. (2) The p-value represents the significance of the treatment effect and was derived from an ANCOVA model of the ranked change from baseline, with treatment as a factor, and the ranks of the baseline value included as covariate.

(3) Standardized mean differences (95% CI) were computed using Cohen's D incorporating Hedge's correction on change from baseline. (4) Odds ratio statistics are from a logistic regression model adjusted for baseline value with Firth's adjustment; (5) Relative risk statistics are based on a generalized linear model of a binomial distribution with log link;

(6) Risk difference statistics are calculated from a generalized linear model, correcting for the baseline value. (7) P-value is for the interaction term of treatment:subgroup from a linear regression model of ranked change from baseline with the with ranked baseline value, treatment, subgroup, and treatment:subgroup interaction as covariates.

Odds ratio and relative risk are calculated as Ravulizumab/Eculizumab. LS mean difference and risk difference are calculated as Ravulizumab - Eculizumab.

Source: adsl, adsf36

Table SF-36-3.4
Change from Baseline in SF-36 Mental Component Score to End of Study Period by Disease severity via EDSS Score at baseline
Full Analysis Set

EDSS score at baseline		Statistic	Eculizumab (N=96)	Ravulizumab (N=58)	p-value (7)
>= 5	Change from Baseline to End of Study Period in SF-36 Mental Component Score	n	30	9	
		Mean (SD)	-1.1 (12.05)	2.0 (8.61)	
		Median	-0.9	3.3	
		Q1, Q3	-7.1, 7.6	-2.4, 7.6	
		Min, Max	-28, 19	-11, 14	
		Change from baseline			
		LS Means (SEM)	-0.641 (1.945)	0.364 (3.589)	
		95% CI for LS Means (1)	(-4.584, 3.303)	(-6.915, 7.643)	
		Difference in LS Means		1.005	
		(95% CI) (1)		(-7.332, 9.342)	
		p-value (2)		0.7915	
		Standardized Mean Difference		0.308	
		(95% CI) (3)		(-0.441, 1.056)	
		Responders (10% [10 points]), n(%)	5 (16.7)	1 (11.1)	
		Odds Ratio (4)		0.697	
		(95% CI)		(0.085, 5.695)	
		p-value		0.7365	
		Relative Risk (5)		0.667	
		(95% CI)		(0.089, 4.994)	
		p-value		0.6931	

The eculizumab group data were collected as part of the PREVENT trial, Study ECU-NMO-301.

End of Study Period is the 6-week assessment after the first On-Trial Relapse for patients who have an On-Trial Relapse or for patients with no On-Trial Relapse: the End of Primary Treatment Period visit for patients in Study ALXN1210-NMO-307 and the End of Study visit for patients in Study ECU-NMO-301.

For those patients who had a missed value at the EOPT Visit or the 6-week post-relapse visit, for patients who had a relapse, the end of study is the last value before the missed value.

(1) The LS means (95% CI) and the difference in LS means (95% CI) are from an ANCOVA model of change from baseline with treatment as factor and baseline value as covariate. (2) The p-value represents the significance of the treatment effect and was derived from an ANCOVA model of the ranked change from baseline, with treatment as a factor, and the ranks of the baseline value included as covariate.

(3) Standardized mean differences (95% CI) were computed using Cohen's D incorporating Hedge's correction on change from baseline. (4) Odds ratio statistics are from a logistic regression model adjusted for baseline value with Firth's adjustment; (5) Relative risk statistics are based on a generalized linear model of a binomial distribution with log link;

(6) Risk difference statistics are calculated from a generalized linear model, correcting for the baseline value. (7) P-value is for the interaction term of treatment:subgroup from a linear regression model of ranked change from baseline with the with ranked baseline value, treatment, subgroup, and treatment:subgroup interaction as covariates.

Odds ratio and relative risk are calculated as Ravulizumab/Eculizumab. LS mean difference and risk difference are calculated as Ravulizumab - Eculizumab.

Source: adsl, adsf36

Table SF-36-3.4
Change from Baseline in SF-36 Mental Component Score to End of Study Period by Disease severity via EDSS Score at baseline
Full Analysis Set

EDSS score at baseline	Statistic	Eculizumab (N=96)	Ravulizumab (N=58)	p-value (7)
	Risk Difference (6)		-0.078	
	(95% CI)		(-0.370, 0.214)	
	p-value		0.5923	
Baseline SF-36 Mental Component Score	n	30	9	
	Mean (SD)	47.9 (12.30)	41.6 (17.51)	
	Median	51.7	39.6	
	Q1, Q3	39.4, 57.7	26.5, 54.3	
	Min, Max	22, 64	21, 68	
End of Study Period SF-36 Mental Component Score	n	30	9	
	Mean (SD)	46.8 (12.80)	43.6 (17.07)	
	Median	45.5	40.6	
	Q1, Q3	36.8, 56.5	29.5, 55.4	
	Min, Max	23, 69	24, 72	

The eculizumab group data were collected as part of the PREVENT trial, Study ECU-NMO-301.

End of Study Period is the 6-week assessment after the first On-Trial Relapse for patients who have an On-Trial Relapse or for patients with no On-Trial Relapse: the End of Primary Treatment Period visit for patients in Study ALXN1210-NMO-307 and the End of Study visit for patients in Study ECU-NMO-301.

For those patients who had a missed value at the EOPT Visit or the 6-week post-relapse visit, for patients who had a relapse, the end of study is the last value before the missed value.

(1) The LS means (95% CI) and the difference in LS means (95% CI) are from an ANCOVA model of change from baseline with treatment as factor and baseline value as covariate. (2) The p-value represents the significance of the treatment effect and was derived from an ANCOVA model of the ranked change from baseline, with treatment as a factor, and the ranks of the baseline value included as covariate.

(3) Standardized mean differences (95% CI) were computed using Cohen's D incorporating Hedge's correction on change from baseline. (4) Odds ratio statistics are from a logistic regression model adjusted for baseline value with Firth's adjustment; (5) Relative risk statistics are based on a generalized linear model of a binomial distribution with log link;

(6) Risk difference statistics are calculated from a generalized linear model, correcting for the baseline value. (7) P-value is for the interaction term of treatment:subgroup from a linear regression model of ranked change from baseline with the with ranked baseline value, treatment, subgroup, and treatment:subgroup interaction as covariates.

Odds ratio and relative risk are calculated as Ravulizumab/Eculizumab. LS mean difference and risk difference are calculated as Ravulizumab - Eculizumab.

Source: adsl, adsf36

Overview of All Treatment Emergent Adverse Events (TEAEs) by Treatment Group, Sex: Male

	Eculizumab (N=8) Patient-Years (PY)=13.8			Ravulizumab (N=6) Patient-Years (PY)=8.4			Treatment Effect	
Adverse Event category	Events n	Rate per 100 PY	Patients n (%)	Events n	Rate per 100 PY	Patients n (%)		Estimate (95% CI; p-value)
Treatment Emergent Adverse Events (TEAEs)								
							OR	0.544 (0.021, 13.922); 0.7130
Deaths	1	7.2	1 (12.5)	0	0.0	0 (0.0)	RR	1.011 (0.947, 1.060); 0.3173
							RD	0.010 (-0.052, 0.057); 0.3148
							OR	0.985 (0.289, 3.354); 0.9809
Any	81	585.7	7 (87.5)	15	178.0	4 (66.7)	RR	1.004 (0.894, 1.101); 0.9260
							RD	0.004 (-0.099, 0.087); 0.9260
							OR	0.985 (0.289, 3.354); 0.9809
Any without disease-related	81	585.7	7 (87.5)	15	178.0	4 (66.7)	RR	1.004 (0.894, 1.101); 0.9260
							RD	0.004 (-0.099, 0.087); 0.9260
							OR	0.752 (0.201, 2.823); 0.6733
Mild	67	484.5	7 (87.5)	6	71.2	3 (50.0)	RR	1.023 (0.919, 1.117); 0.5900
							RD	0.021 (-0.076, 0.101); 0.5904
							OR	1.049 (0.261, 4.217); 0.9461
Moderate	7	50.6	5 (62.5)	9	106.8	3 (50.0)	RR	1.000 (0.901, 1.084); 0.9922
							RD	0.000 (-0.095, 0.074); 0.9922
							OR	0.985 (0.289, 3.354); 0.9809
Non-Severe (Mild + Moderate)	74	535.1	7 (87.5)	15	178.0	4 (66.7)	RR	1.004 (0.894, 1.101); 0.9260
							RD	0.004 (-0.099, 0.087); 0.9260
							OR	0.228 (0.011, 4.611); 0.3354
Severe	7	50.6	3 (37.5)	0	0.0	0 (0.0)	RR	1.032 (0.967, 1.097); 0.0833
							RD	0.031 (-0.032, 0.088); 0.0784
							OR	0.228 (0.011, 4.611); 0.3354
Severe without disease-related	7	50.6	3 (37.5)	0	0.0	0 (0.0)	RR	1.032 (0.967, 1.097); 0.0833
							RD	0.031 (-0.032, 0.088); 0.0784
							OR	NA
TEAEs Leading to Withdrawal from Study Drug	0	0.0	0 (0.0)	0	0.0	0 (0.0)	RR	NA
							RD	NA
							OR	0.434 (0.068, 2.759); 0.3764
Treatment-related	20	144.6	5 (62.5)	4	47.5	1 (16.7)	RR	1.037 (0.954, 1.116); 0.2223
							RD	0.035 (-0.044, 0.102); 0.2198
							OR	0.985 (0.289, 3.354); 0.9809
Not treatment-related	61	441.1	7 (87.5)	11	130.5	4 (66.7)	RR	1.004 (0.894, 1.101); 0.9260
							RD	0.004 (-0.099, 0.087); 0.9260
Treatment Emergent Serious Adverse Events (TESAEs)								
							OR	0.697 (0.099, 4.925); 0.7173
Any	8	57.8	3 (37.5)	1	11.9	1 (16.7)	RR	1.014 (0.935, 1.081); 0.5699
							RD	0.014 (-0.063, 0.074); 0.5698
							OR	0.697 (0.099, 4.925); 0.7173
Any without disease-related	8	57.8	3 (37.5)	1	11.9	1 (16.7)	RR	1.014 (0.935, 1.081); 0.5699
							RD	0.014 (-0.063, 0.074); 0.5698
							OR	NA
Mild	0	0.0	0 (0.0)	0	0.0	0 (0.0)	RR	NA
							RD	NA
							OR	1.661 (0.166, 16.607); 0.6658
Moderate	1	7.2	1 (12.5)	1	11.9	1 (16.7)	RR	0.993 (0.917, 1.044); 0.7332
							RD	-0.007 (-0.082, 0.042); 0.7328
							OR	1.661 (0.166, 16.607); 0.6658
Non-Severe (Mild + Moderate)	1	7.2	1 (12.5)	1	11.9	1 (16.7)	RR	0.993 (0.917, 1.044); 0.7332
							RD	-0.007 (-0.082, 0.042); 0.7328
							OR	0.228 (0.011, 4.611); 0.3354
Severe	7	50.6	3 (37.5)	0	0.0	0 (0.0)	RR	1.032 (0.967, 1.097); 0.0833
							RD	0.031 (-0.032, 0.088); 0.0784
							OR	NA
TESAEs Leading to Withdrawal from Study Drug	0	0.0	0 (0.0)	0	0.0	0 (0.0)	RR	NA
							RD	NA
							OR	0.323 (0.015, 7.018); 0.4719
Treatment-related	2	14.5	2 (25.0)	0	0.0	0 (0.0)	RR	1.021 (0.957, 1.079); 0.1573

							RD	0.021 (-0.042, 0.073); 0.1530
							OR	0.986 (0.125, 7.779); 0.9893
Not treatment-related	6	43.4	2 (25.0)	1	11.9	1 (16.7)	RR	1.004 (0.926, 1.063); 0.8729
							RD	0.004 (-0.073, 0.058); 0.8730

AE: adverse event; CI: Confidence Interval; OR: Odds Ratio; PY: patient-years; RD: Risk Difference; RR: Risk Ratio; TEAE: treatment-emergent adverse event.
TEAEs are AEs with a start date on or after the date of the first dose of study drug.
Treatment emergent adverse events and follow-up were truncated at the maximum duration of follow-up in the ravulizumab arm.
Odds ratios were derived from a logistic regression model with treatment as the only covariate. Firth's correction was applied for odds ratios.

Overview of All Treatment Emergent Adverse Events (TEAEs) by Treatment Group, Sex: Female

	Eculizumab (N=88) Patient-Years (PY)=159			Ravulizumab (N=52) Patient-Years (PY)=75.6			Treatment Effect	
Adverse Event category	Events n	Rate per 100 PY	Patients n (%)	Events n	Rate per 100 PY	Patients n (%)		Estimate (95% CI; p-value)
Treatment Emergent Adverse Events (TEAEs)								
							OR	NA
Deaths	0	0.0	0 (0.0)	0	0.0	0 (0.0)	RR	NA
							RD	NA
							OR	0.991 (0.408, 2.408); 0.9838
Any	1049	659.8	81 (92.0)	313	413.8	49 (94.2)	RR	1.001 (0.852, 1.148); 0.9857
							RD	0.001 (-0.129, 0.115); 0.9857
							OR	0.991 (0.408, 2.408); 0.9838
Any without disease-related	1043	656.0	81 (92.0)	313	413.8	49 (94.2)	RR	1.001 (0.852, 1.148); 0.9857
							RD	0.001 (-0.129, 0.115); 0.9857
							OR	0.742 (0.332, 1.658); 0.4668
Mild	861	541.5	79 (89.8)	238	314.7	45 (86.5)	RR	0.943 (0.780, 1.105); 0.4884
							RD	-0.047 (-0.187, 0.079); 0.4838
							OR	0.636 (0.330, 1.225); 0.1761
Moderate	168	105.7	54 (61.4)	62	82.0	26 (50.0)	RR	0.797 (0.559, 1.098); 0.1850
							RD	-0.114 (-0.271, 0.049); 0.1669
							OR	0.991 (0.408, 2.408); 0.9838
Non-Severe (Mild + Moderate)	1029	647.2	81 (92.0)	300	396.6	49 (94.2)	RR	1.001 (0.852, 1.148); 0.9857
							RD	0.001 (-0.129, 0.115); 0.9857
							OR	1.297 (0.517, 3.256); 0.5794
Severe	17	10.7	12 (13.6)	13	17.2	9 (17.3)	RR	1.241 (0.562, 2.696); 0.5965
							RD	0.030 (-0.079, 0.157); 0.6048
							OR	1.581 (0.611, 4.093); 0.3454
Severe without disease-related	15	9.4	10 (11.4)	13	17.2	9 (17.3)	RR	1.490 (0.652, 3.363); 0.3521
							RD	0.051 (-0.055, 0.176); 0.3696
							OR	5.035 (0.198, 128.13); 0.3277
TEAEs Leading to Withdrawal from Study Drug	0	0.0	0 (0.0)	3	4.0	1 (1.9)	RR	0.983 (0.908, 1.023); 0.3173
							RD	-0.017 (-0.092, 0.022); 0.3131
							OR	0.936 (0.485, 1.806); 0.8441
Treatment-related	331	208.2	43 (48.9)	34	45.0	25 (48.1)	RR	0.962 (0.655, 1.378); 0.8386
							RD	-0.017 (-0.175, 0.145); 0.8378
							OR	0.947 (0.401, 2.233); 0.9006
Not treatment-related	718	451.6	80 (90.9)	279	368.9	48 (92.3)	RR	0.993 (0.838, 1.147); 0.9268
							RD	-0.006 (-0.139, 0.112); 0.9267
Treatment Emergent Serious Adverse Events (TESAEs)								
							OR	0.408 (0.167, 1.001); 0.0502
Any	39	24.5	25 (28.4)	7	9.3	7 (13.5)	RR	0.463 (0.214, 0.965); 0.0509
							RD	-0.140 (-0.257, -0.008); 0.0241
							OR	0.543 (0.218, 1.357); 0.1915
Any without disease-related	33	20.8	20 (22.7)	7	9.3	7 (13.5)	RR	0.579 (0.262, 1.239); 0.1792
							RD	-0.088 (-0.201, 0.041); 0.1412
							OR	0.119 (0.006, 2.205); 0.1530
Mild	6	3.8	6 (6.8)	0	0.0	0 (0.0)	RR	1.067 (0.998, 1.149); 0.0143
							RD	0.063 (-0.001, 0.130); 0.0114
							OR	0.194 (0.034, 1.114); 0.0659
Moderate	22	13.8	11 (12.5)	1	1.3	1 (1.9)	RR	1.110 (1.015, 1.223); 0.0102
							RD	0.097 (0.013, 0.180); 0.0080
							OR	0.118 (0.021, 0.659); 0.0148
Non-Severe (Mild + Moderate)	28	17.6	17 (19.3)	1	1.3	1 (1.9)	RR	1.194 (1.082, 1.342); 0.0004
							RD	0.160 (0.070, 0.252); 0.0002
							OR	1.140 (0.394, 3.299); 0.8086
Severe	11	6.9	9 (10.2)	6	7.9	6 (11.5)	RR	1.103 (0.424, 2.821); 0.8440
							RD	0.010 (-0.085, 0.124); 0.8457
							OR	5.035 (0.198, 128.13); 0.3277
TESAEs Leading to Withdrawal from Study Drug	0	0.0	0 (0.0)	1	1.3	1 (1.9)	RR	0.983 (0.908, 1.023); 0.3173
							RD	-0.017 (-0.092, 0.022); 0.3131
							OR	1.049 (0.261, 4.217); 0.9461
Treatment-related	6	3.8	5 (5.7)	3	4.0	3 (5.8)	RR	0.993 (0.267, 3.624); 0.9922

							RD	-0.000 (-0.074, 0.095); 0.9922
							OR	0.258 (0.088, 0.757); 0.0137
Not treatment-related	33	20.8	23 (26.1)	4	5.3	4 (7.7)	RR	1.224 (1.066, 1.414); 0.0027
							RD	0.171 (0.053, 0.278); 0.0019

AE: adverse event; CI: Confidence Interval; OR: Odds Ratio; PY: patient-years; RD: Risk Difference; RR: Risk Ratio; TEAE: treatment-emergent adverse event.
TEAEs are AEs with a start date on or after the date of the first dose of study drug.
Treatment emergent adverse events and follow-up were truncated at the maximum duration of follow-up in the ravulizumab arm.
Odds ratios were derived from a logistic regression model with treatment as the only covariate. Firth's correction was applied for odds ratios.

Overview of All Treatment Emergent Adverse Events (TEAEs) by Treatment Group, Age: < 45 years

Adverse Event category	Eculizumab (N=47) Patient-Years (PY)=79.8 Events n	Rate per 100 PY	Patients n (%)	Ravulizumab (N=25) Patient-Years (PY)=36.8 Events n	Rate per 100 PY	Patients n (%)	Treatment Effect	Estimate (95% CI; p-value)
Treatment Emergent Adverse Events (TEAEs)								
							OR	0.544 (0.021, 13.922); 0.7130
Deaths	1	1.3	1 (2.1)	0	0.0	0 (0.0)	RR	1.011 (0.947, 1.060); 0.3173
							RD	0.010 (-0.052, 0.057); 0.3148
							OR	0.950 (0.491, 1.838); 0.8783
Any	518	649.3	41 (87.2)	170	462.2	24 (96.0)	RR	0.969 (0.651, 1.407); 0.8718
							RD	-0.013 (-0.170, 0.148); 0.8713
							OR	0.950 (0.491, 1.838); 0.8783
Any without disease-related	517	648.0	41 (87.2)	170	462.2	24 (96.0)	RR	0.969 (0.651, 1.407); 0.8718
							RD	-0.013 (-0.170, 0.148); 0.8713
							OR	0.767 (0.392, 1.499); 0.4375
Mild	415	520.2	41 (87.2)	119	323.5	21 (84.0)	RR	0.848 (0.553, 1.262); 0.4329
							RD	-0.065 (-0.218, 0.096); 0.4211
							OR	0.888 (0.433, 1.824); 0.7471
Moderate	90	112.8	29 (61.7)	42	114.2	16 (64.0)	RR	0.913 (0.539, 1.506); 0.7302
							RD	-0.026 (-0.168, 0.126); 0.7270
							OR	0.950 (0.491, 1.838); 0.8783
Non-Severe (Mild + Moderate)	505	633.0	41 (87.2)	161	437.7	24 (96.0)	RR	0.969 (0.651, 1.407); 0.8718
							RD	-0.013 (-0.170, 0.148); 0.8713
							OR	1.724 (0.548, 5.428); 0.3520
Severe	12	15.0	6 (12.8)	9	24.5	6 (24.0)	RR	1.655 (0.582, 4.664); 0.3621
							RD	0.041 (-0.046, 0.152); 0.3837
							OR	1.724 (0.548, 5.428); 0.3520
Severe without disease-related	12	15.0	6 (12.8)	9	24.5	6 (24.0)	RR	1.655 (0.582, 4.664); 0.3621
							RD	0.041 (-0.046, 0.152); 0.3837
							OR	5.035 (0.198, 128.13); 0.3277
TEAEs Leading to Withdrawal from Study Drug	0	0.0	0 (0.0)	3	8.2	1 (4.0)	RR	0.983 (0.908, 1.023); 0.3173
							RD	-0.017 (-0.092, 0.022); 0.3131
							OR	1.019 (0.477, 2.176); 0.9603
Treatment-related	209	262.0	23 (48.9)	23	62.5	14 (56.0)	RR	1.007 (0.561, 1.769); 0.9798
							RD	0.002 (-0.132, 0.148); 0.9798
							OR	0.924 (0.475, 1.794); 0.8143
Not treatment-related	309	387.3	40 (85.1)	147	399.7	23 (92.0)	RR	0.952 (0.631, 1.398); 0.8065
							RD	-0.020 (-0.176, 0.141); 0.8053
Treatment Emergent Serious Adverse Events (TESAEs)								
							OR	0.947 (0.311, 2.879); 0.9234
Any	20	25.1	9 (19.1)	5	13.6	5 (20.0)	RR	0.920 (0.333, 2.481); 0.8748
							RD	-0.008 (-0.099, 0.103); 0.8735
							OR	1.070 (0.345, 3.324); 0.9064
Any without disease-related	19	23.8	8 (17.0)	5	13.6	5 (20.0)	RR	1.034 (0.367, 2.860); 0.9504
							RD	0.003 (-0.086, 0.112); 0.9506
							OR	0.323 (0.015, 7.018); 0.4719
Mild	2	2.5	2 (4.3)	0	0.0	0 (0.0)	RR	1.021 (0.957, 1.079); 0.1573
							RD	0.021 (-0.042, 0.073); 0.1530
							OR	0.142 (0.008, 2.684); 0.1931
Moderate	10	12.5	5 (10.6)	0	0.0	0 (0.0)	RR	1.055 (0.988, 1.132); 0.0254
							RD	0.052 (-0.012, 0.116); 0.0216
							OR	0.102 (0.006, 1.864); 0.1236
Non-Severe (Mild + Moderate)	12	15.0	7 (14.9)	0	0.0	0 (0.0)	RR	1.079 (1.009, 1.167); 0.0082
							RD	0.073 (0.009, 0.143); 0.0060
							OR	2.113 (0.576, 7.748); 0.2590
Severe	8	10.0	4 (8.5)	5	13.6	5 (20.0)	RR	2.069 (0.619, 6.886); 0.2632
							RD	0.045 (-0.033, 0.150); 0.2903
							OR	5.035 (0.198, 128.13); 0.3277
TESAEs Leading to Withdrawal from Study Drug	0	0.0	0 (0.0)	1	2.7	1 (4.0)	RR	0.983 (0.908, 1.023); 0.3173
							RD	-0.017 (-0.092, 0.022); 0.3131
							OR	1.182 (0.223, 6.267); 0.8443
Treatment-related	3	3.8	3 (6.4)	2	5.4	2 (8.0)	RR	1.103 (0.223, 5.381); 0.9127

							RD	0.003 (-0.060, 0.089); 0.9137
							OR	0.581 (0.161, 2.091); 0.4058
Not treatment-related	17	21.3	9 (19.1)	3	8.2	3 (12.0)	RR	1.046 (0.938, 1.152); 0.3129
							RD	0.042 (-0.057, 0.127); 0.3124

AE: adverse event; CI: Confidence Interval; OR: Odds Ratio; PY: patient-years; RD: Risk Difference; RR: Risk Ratio; TEAE: treatment-emergent adverse event.
TEAEs are AEs with a start date on or after the date of the first dose of study drug.
Treatment emergent adverse events and follow-up were truncated at the maximum duration of follow-up in the ravulizumab arm.
Odds ratios were derived from a logistic regression model with treatment as the only covariate. Firth's correction was applied for odds ratios.

Overview of All Treatment Emergent Adverse Events (TEAEs) by Treatment Group, Age: ≥ 45 years

Adverse Event category	Eculizumab (N=49) Patient-Years (PY)=93 Events n	Rate per 100 PY	Patients n (%)	Ravulizumab (N=33) Patient-Years (PY)=47.3 Events n	Rate per 100 PY	Patients n (%)	Treatment Effect	Estimate (95% CI; p-value)
Treatment Emergent Adverse Events (TEAEs)								
							OR	NA
Deaths	0	0.0	0 (0.0)	0	0.0	0 (0.0)	RR	NA
							RD	NA
							OR	1.042 (0.543, 2.000); 0.9013
Any	612	657.8	47 (95.9)	158	334.2	29 (87.9)	RR	0.980 (0.698, 1.341); 0.9006
							RD	-0.010 (-0.171, 0.151); 0.9003
							OR	1.042 (0.543, 2.000); 0.9013
Any without disease-related	607	652.4	47 (95.9)	158	334.2	29 (87.9)	RR	0.980 (0.698, 1.341); 0.9006
							RD	-0.010 (-0.171, 0.151); 0.9003
							OR	0.988 (0.514, 1.899); 0.9710
Mild	513	551.4	45 (91.8)	125	264.4	27 (81.8)	RR	1.006 (0.730, 1.353); 0.9689
							RD	0.003 (-0.158, 0.163); 0.9689
							OR	0.647 (0.306, 1.368); 0.2543
Moderate	85	91.4	30 (61.2)	29	61.3	13 (39.4)	RR	1.129 (0.917, 1.369); 0.2199
							RD	0.088 (-0.061, 0.224); 0.2220
							OR	1.042 (0.543, 2.000); 0.9013
Non-Severe (Mild + Moderate)	598	642.8	47 (95.9)	154	325.7	29 (87.9)	RR	0.980 (0.698, 1.341); 0.9006
							RD	-0.010 (-0.171, 0.151); 0.9003
							OR	0.581 (0.161, 2.091); 0.4058
Severe	12	12.9	9 (18.4)	4	8.5	3 (9.1)	RR	1.046 (0.938, 1.152); 0.3129
							RD	0.042 (-0.057, 0.127); 0.3124
							OR	0.752 (0.201, 2.823); 0.6733
Severe without disease-related	10	10.7	7 (14.3)	4	8.5	3 (9.1)	RR	1.023 (0.919, 1.117); 0.5900
							RD	0.021 (-0.076, 0.101); 0.5904
							OR	NA
TEAEs Leading to Withdrawal from Study Drug	0	0.0	0 (0.0)	0	0.0	0 (0.0)	RR	NA
							RD	NA
							OR	0.754 (0.347, 1.639); 0.4755
Treatment-related	142	152.6	25 (51.0)	15	31.7	12 (36.4)	RR	1.072 (0.883, 1.278); 0.4394
							RD	0.054 (-0.091, 0.184); 0.4415
							OR	1.042 (0.543, 2.000); 0.9013
Not treatment-related	470	505.2	47 (95.9)	143	302.4	29 (87.9)	RR	0.980 (0.698, 1.341); 0.9006
							RD	-0.010 (-0.171, 0.151); 0.9003
Treatment Emergent Serious Adverse Events (TESAEs)								
							OR	0.251 (0.076, 0.831); 0.0236
Any	27	29.0	19 (38.8)	3	6.3	3 (9.1)	RR	1.182 (1.045, 1.345); 0.0047
							RD	0.146 (0.037, 0.247); 0.0035
							OR	0.332 (0.098, 1.121); 0.0758
Any without disease-related	22	23.6	15 (30.6)	3	6.3	3 (9.1)	RR	1.124 (0.999, 1.262); 0.0292
							RD	0.105 (-0.001, 0.200); 0.0265
							OR	0.176 (0.009, 3.405); 0.2502
Mild	4	4.3	4 (8.2)	0	0.0	0 (0.0)	RR	1.043 (0.977, 1.114); 0.0455
							RD	0.042 (-0.022, 0.103); 0.0411
							OR	0.528 (0.120, 2.322); 0.3980
Moderate	13	14.0	7 (14.3)	2	4.2	2 (6.1)	RR	1.041 (0.945, 1.134); 0.2836
							RD	0.038 (-0.052, 0.115); 0.2824
							OR	0.329 (0.080, 1.360); 0.1247
Non-Severe (Mild + Moderate)	17	18.3	11 (22.4)	2	4.2	2 (6.1)	RR	1.090 (0.985, 1.205); 0.0507
							RD	0.080 (-0.014, 0.166); 0.0473
							OR	0.272 (0.046, 1.613); 0.1516
Severe	10	10.7	8 (16.3)	1	2.1	1 (3.0)	RR	1.072 (0.984, 1.168); 0.0489
							RD	0.066 (-0.015, 0.142); 0.0451
							OR	NA
TESAEs Leading to Withdrawal from Study Drug	0	0.0	0 (0.0)	0	0.0	0 (0.0)	RR	NA
							RD	NA
							OR	0.536 (0.081, 3.555); 0.5184
Treatment-related	5	5.4	4 (8.2)	1	2.1	1 (3.0)	RR	1.025 (0.945, 1.098); 0.3598

							RD	0.024 (-0.053, 0.088); 0.3587
							OR	0.216 (0.054, 0.862); 0.0300
Not treatment-related	22	23.6	16 (32.7)	2	4.2	2 (6.1)	RR	1.159 (1.039, 1.302); 0.0046
							RD	0.132 (0.033, 0.226); 0.0033

AE: adverse event; CI: Confidence Interval; OR: Odds Ratio; PY: patient-years; RD: Risk Difference; RR: Risk Ratio; TEAE: treatment-emergent adverse event.
TEAEs are AEs with a start date on or after the date of the first dose of study drug.
Treatment emergent adverse events and follow-up were truncated at the maximum duration of follow-up in the ravulizumab arm.
Odds ratios were derived from a logistic regression model with treatment as the only covariate. Firth's correction was applied for odds ratios.

Overview of All Treatment Emergent Adverse Events (TEAEs) by Treatment Group, Region: Asia-Pacific

Adverse Event category	Eculizumab (N=35) Patient-Years (PY)=63.1 Events n	Rate per 100 PY	Patients n (%)	Ravulizumab (N=20) Patient-Years (PY)=28.7 Events n	Rate per 100 PY	Patients n (%)	Treatment Effect	Estimate (95% CI; p-value)
Treatment Emergent Adverse Events (TEAEs)								
Deaths	0	0.0	0 (0.0)	0	0.0	0 (0.0)	OR	NA
							RR	NA
							RD	NA
Any	394	624.8	32 (91.4)	109	380.4	18 (90.0)	OR	0.907 (0.451, 1.822); 0.7830
							RR	0.931 (0.571, 1.478); 0.7689
							RD	-0.023 (-0.169, 0.133); 0.7667
Any without disease-related	391	620.1	32 (91.4)	109	380.4	18 (90.0)	OR	0.907 (0.451, 1.822); 0.7830
							RR	0.931 (0.571, 1.478); 0.7689
							RD	-0.023 (-0.169, 0.133); 0.7667
Mild	337	534.5	32 (91.4)	81	282.7	17 (85.0)	OR	0.837 (0.414, 1.694); 0.6206
							RR	0.879 (0.532, 1.412); 0.6067
							RD	-0.040 (-0.185, 0.115); 0.6001
Moderate	49	77.7	20 (57.1)	25	87.2	10 (50.0)	OR	0.808 (0.351, 1.857); 0.6154
							RR	0.828 (0.416, 1.603); 0.5885
							RD	-0.036 (-0.158, 0.101); 0.5784
Non-Severe (Mild + Moderate)	386	612.2	32 (91.4)	106	369.9	18 (90.0)	OR	0.907 (0.451, 1.822); 0.7830
							RR	0.931 (0.571, 1.478); 0.7689
							RD	-0.023 (-0.169, 0.133); 0.7667
Severe	8	12.7	5 (14.3)	3	10.5	3 (15.0)	OR	1.049 (0.261, 4.217); 0.9461
							RR	0.993 (0.267, 3.624); 0.9922
							RD	-0.000 (-0.074, 0.095); 0.9922
Severe without disease-related	7	11.1	4 (11.4)	3	10.5	3 (15.0)	OR	1.296 (0.305, 5.505); 0.7252
							RR	1.241 (0.317, 4.799); 0.7718
							RD	0.010 (-0.060, 0.104); 0.7771
TEAEs Leading to Withdrawal from Study Drug	0	0.0	0 (0.0)	0	0.0	0 (0.0)	OR	NA
							RR	NA
							RD	NA
Treatment-related	64	101.5	18 (51.4)	15	52.3	10 (50.0)	OR	0.919 (0.395, 2.136); 0.8438
							RR	0.920 (0.456, 1.811); 0.8146
							RD	-0.015 (-0.135, 0.120); 0.8125
Not treatment-related	330	523.3	32 (91.4)	94	328.0	18 (90.0)	OR	0.907 (0.451, 1.822); 0.7830
							RR	0.931 (0.571, 1.478); 0.7689
							RD	-0.023 (-0.169, 0.133); 0.7667
Treatment Emergent Serious Adverse Events (TESAEs)								
Any	17	27.0	12 (34.3)	4	14.0	4 (20.0)	OR	0.558 (0.179, 1.743); 0.3157
							RR	0.552 (0.193, 1.531); 0.2821
							RD	-0.056 (-0.150, 0.052); 0.2371
Any without disease-related	14	22.2	10 (28.6)	4	14.0	4 (20.0)	OR	0.680 (0.212, 2.178); 0.5163
							RR	0.662 (0.225, 1.890); 0.4676
							RD	-0.035 (-0.126, 0.071); 0.4401
Mild	1	1.6	1 (2.9)	0	0.0	0 (0.0)	OR	0.544 (0.021, 13.922); 0.7130
							RR	1.011 (0.947, 1.060); 0.3173
							RD	0.010 (-0.052, 0.057); 0.3148
Moderate	10	15.9	6 (17.1)	2	7.0	2 (10.0)	OR	0.616 (0.136, 2.782); 0.5289
							RR	1.030 (0.936, 1.117); 0.4159
							RD	0.028 (-0.061, 0.102); 0.4156
Non-Severe (Mild + Moderate)	11	17.4	7 (20.0)	2	7.0	2 (10.0)	OR	0.528 (0.120, 2.322); 0.3980
							RR	1.041 (0.945, 1.134); 0.2836
							RD	0.038 (-0.052, 0.115); 0.2824
Severe	6	9.5	5 (14.3)	2	7.0	2 (10.0)	OR	0.736 (0.157, 3.443); 0.6971
							RR	0.662 (0.150, 2.853); 0.6150
							RD	-0.018 (-0.088, 0.070); 0.5937
TESAEs Leading to Withdrawal from Study Drug	0	0.0	0 (0.0)	0	0.0	0 (0.0)	OR	NA
							RR	NA
							RD	NA
Treatment-related	4	6.3	3 (8.6)	1	3.5	1 (5.0)	OR	0.697 (0.099, 4.925); 0.7173
							RR	0.552 (0.079, 3.757); 0.6027

							RD	-0.014 (-0.074, 0.063); 0.5698
							OR	0.520 (0.147, 1.842); 0.3105
Not treatment-related	13	20.6	10 (28.6)	3	10.5	3 (15.0)	RR	1.059 (0.948, 1.169); 0.2200
							RD	0.052 (-0.048, 0.140); 0.2187

AE: adverse event; CI: Confidence Interval; OR: Odds Ratio; PY: patient-years; RD: Risk Difference; RR: Risk Ratio; TEAE: treatment-emergent adverse event.
TEAEs are AEs with a start date on or after the date of the first dose of study drug.
Treatment emergent adverse events and follow-up were truncated at the maximum duration of follow-up in the ravulizumab arm.
Odds ratios were derived from a logistic regression model with treatment as the only covariate. Firth's correction was applied for odds ratios.

Overview of All Treatment Emergent Adverse Events (TEAEs) by Treatment Group, Region: Americas

Adverse Event category	Eculizumab (N=29) Patient-Years (PY)=44.5 Events n	Rate per 100 PY	Patients n (%)	Ravulizumab (N=21) Patient-Years (PY)=35.7 Events n	Rate per 100 PY	Patients n (%)	Treatment Effect	Estimate (95% CI; p-value)
Treatment Emergent Adverse Events (TEAEs)								
							OR	0.544 (0.021, 13.922); 0.7130
Deaths	1	2.2	1 (3.4)	0	0.0	0 (0.0)	RR	1.011 (0.947, 1.060); 0.3173
							RD	0.010 (-0.052, 0.057); 0.3148
							OR	1.313 (0.647, 2.665); 0.4505
Any	378	849.8	26 (89.7)	108	302.9	19 (90.5)	RR	0.922 (0.727, 1.135); 0.4644
							RD	-0.057 (-0.210, 0.089); 0.4583
							OR	1.313 (0.647, 2.665); 0.4505
Any without disease-related	378	849.8	26 (89.7)	108	302.9	19 (90.5)	RR	0.922 (0.727, 1.135); 0.4644
							RD	-0.057 (-0.210, 0.089); 0.4583
							OR	1.182 (0.573, 2.438); 0.6502
Mild	298	669.9	25 (86.2)	78	218.7	17 (81.0)	RR	0.956 (0.764, 1.163); 0.6638
							RD	-0.033 (-0.184, 0.109); 0.6617
							OR	0.919 (0.395, 2.136); 0.8438
Moderate	65	146.1	18 (62.1)	26	72.9	10 (47.6)	RR	1.019 (0.858, 1.182); 0.8122
							RD	0.015 (-0.120, 0.135); 0.8125
							OR	1.313 (0.647, 2.665); 0.4505
Non-Severe (Mild + Moderate)	363	816.1	26 (89.7)	104	291.7	19 (90.5)	RR	0.922 (0.727, 1.135); 0.4644
							RD	-0.057 (-0.210, 0.089); 0.4583
							OR	0.461 (0.107, 1.984); 0.2983
Severe	14	31.5	8 (27.6)	4	11.2	2 (9.5)	RR	1.053 (0.955, 1.151); 0.1891
							RD	0.049 (-0.042, 0.128); 0.1869
							OR	0.461 (0.107, 1.984); 0.2983
Severe without disease-related	14	31.5	8 (27.6)	4	11.2	2 (9.5)	RR	1.053 (0.955, 1.151); 0.1891
							RD	0.049 (-0.042, 0.128); 0.1869
							OR	NA
TEAEs Leading to Withdrawal from Study Drug	0	0.0	0 (0.0)	0	0.0	0 (0.0)	RR	NA
							RD	NA
							OR	0.885 (0.355, 2.207); 0.7934
Treatment-related	181	406.9	15 (51.7)	13	36.5	8 (38.1)	RR	1.022 (0.875, 1.167); 0.7537
							RD	0.018 (-0.109, 0.129); 0.7542
							OR	1.281 (0.625, 2.623); 0.4990
Not treatment-related	197	442.9	25 (86.2)	95	266.4	18 (85.7)	RR	0.932 (0.741, 1.139); 0.5132
							RD	-0.050 (-0.202, 0.093); 0.5083
Treatment Emergent Serious Adverse Events (TESAEs)								
							OR	0.364 (0.087, 1.524); 0.1668
Any	24	54.0	10 (34.5)	2	5.6	2 (9.5)	RR	1.078 (0.974, 1.187); 0.0797
							RD	0.070 (-0.023, 0.154); 0.0764
							OR	0.364 (0.087, 1.524); 0.1668
Any without disease-related	24	54.0	10 (34.5)	2	5.6	2 (9.5)	RR	1.078 (0.974, 1.187); 0.0797
							RD	0.070 (-0.023, 0.154); 0.0764
							OR	0.323 (0.015, 7.018); 0.4719
Mild	2	4.5	2 (6.9)	0	0.0	0 (0.0)	RR	1.021 (0.957, 1.079); 0.1573
							RD	0.021 (-0.042, 0.073); 0.1530
							OR	0.176 (0.009, 3.405); 0.2502
Moderate	11	24.7	4 (13.8)	0	0.0	0 (0.0)	RR	1.043 (0.977, 1.114); 0.0455
							RD	0.042 (-0.022, 0.103); 0.0411
							OR	0.119 (0.006, 2.205); 0.1530
Non-Severe (Mild + Moderate)	13	29.2	6 (20.7)	0	0.0	0 (0.0)	RR	1.067 (0.998, 1.149); 0.0143
							RD	0.063 (-0.001, 0.130); 0.0114
							OR	0.616 (0.136, 2.782); 0.5289
Severe	11	24.7	6 (20.7)	2	5.6	2 (9.5)	RR	1.030 (0.936, 1.117); 0.4159
							RD	0.028 (-0.061, 0.102); 0.4156
							OR	NA
TESAEs Leading to Withdrawal from Study Drug	0	0.0	0 (0.0)	0	0.0	0 (0.0)	RR	NA
							RD	NA
							OR	0.176 (0.009, 3.405); 0.2502
Treatment-related	4	9.0	4 (13.8)	0	0.0	0 (0.0)	RR	1.043 (0.977, 1.114); 0.0455

							RD	0.042 (-0.022, 0.103); 0.0411
							OR	0.408 (0.096, 1.727); 0.2231
Not treatment-related	20	45.0	9 (31.0)	2	5.6	2 (9.5)	RR	1.065 (0.965, 1.169); 0.1237
							RD	0.059 (-0.033, 0.141); 0.1208

AE: adverse event; CI: Confidence Interval; OR: Odds Ratio; PY: patient-years; RD: Risk Difference; RR: Risk Ratio; TEAE: treatment-emergent adverse event.
TEAEs are AEs with a start date on or after the date of the first dose of study drug.
Treatment emergent adverse events and follow-up were truncated at the maximum duration of follow-up in the ravulizumab arm.
Odds ratios were derived from a logistic regression model with treatment as the only covariate. Firth's correction was applied for odds ratios.

Overview of All Treatment Emergent Adverse Events (TEAEs) by Treatment Group, Region: Europe

Adverse Event category	Eculizumab (N=32) Patient-Years (PY)=65.3 Events n	Rate per 100 PY	Patients n (%)	Ravulizumab (N=17) Patient-Years (PY)=19.7 Events n	Rate per 100 PY	Patients n (%)	Treatment Effect	Estimate (95% CI; p-value)
Treatment Emergent Adverse Events (TEAEs)								
Deaths	0	0.0	0 (0.0)	0	0.0	0 (0.0)	OR	NA
							RR	NA
							RD	NA
Any	358	548.4	30 (93.8)	111	562.1	16 (94.1)	OR	0.846 (0.413, 1.734); 0.6488
							RR	1.053 (0.841, 1.292); 0.6253
							RD	0.037 (-0.117, 0.179); 0.6269
Any without disease-related	355	543.8	30 (93.8)	111	562.1	16 (94.1)	OR	0.846 (0.413, 1.734); 0.6488
							RR	1.053 (0.841, 1.292); 0.6253
							RD	0.037 (-0.117, 0.179); 0.6269
Mild	293	448.8	29 (90.6)	85	430.4	14 (82.4)	OR	0.746 (0.356, 1.561); 0.4362
							RR	1.087 (0.879, 1.320); 0.4041
							RD	0.061 (-0.090, 0.198); 0.4067
Moderate	61	93.4	21 (65.6)	20	101.3	9 (52.9)	OR	0.674 (0.288, 1.576); 0.3627
							RR	1.081 (0.913, 1.261); 0.3158
							RD	0.064 (-0.071, 0.184); 0.3172
Non-Severe (Mild + Moderate)	354	542.3	30 (93.8)	105	531.7	16 (94.1)	OR	0.846 (0.413, 1.734); 0.6488
							RR	1.053 (0.841, 1.292); 0.6253
							RD	0.037 (-0.117, 0.179); 0.6269
Severe	2	3.1	2 (6.3)	6	30.4	4 (23.5)	OR	3.121 (0.635, 15.332); 0.1611
							RR	0.951 (0.851, 1.018); 0.1929
							RD	-0.048 (-0.146, 0.016); 0.1852
Severe without disease-related	1	1.5	1 (3.1)	6	30.4	4 (23.5)	OR	5.257 (0.795, 34.763); 0.0851
							RR	0.941 (0.843, 0.999); 0.1015
							RD	-0.059 (-0.155, -0.001); 0.0929
TEAEs Leading to Withdrawal from Study Drug	0	0.0	0 (0.0)	3	15.2	1 (5.9)	OR	5.035 (0.198, 128.13); 0.3277
							RR	0.983 (0.908, 1.023); 0.3173
							RD	-0.017 (-0.092, 0.022); 0.3131
Treatment-related	106	162.4	15 (46.9)	10	50.6	8 (47.1)	OR	0.885 (0.355, 2.207); 0.7934
							RR	1.022 (0.875, 1.167); 0.7537
							RD	0.018 (-0.109, 0.129); 0.7542
Not treatment-related	252	386.0	30 (93.8)	101	511.4	16 (94.1)	OR	0.846 (0.413, 1.734); 0.6488
							RR	1.053 (0.841, 1.292); 0.6253
							RD	0.037 (-0.117, 0.179); 0.6269
Treatment Emergent Serious Adverse Events (TESAEs)								
Any	6	9.2	6 (18.8)	2	10.1	2 (11.8)	OR	0.616 (0.136, 2.782); 0.5289
							RR	1.030 (0.936, 1.117); 0.4159
							RD	0.028 (-0.061, 0.102); 0.4156
Any without disease-related	3	4.6	3 (9.4)	2	10.1	2 (11.8)	OR	1.182 (0.223, 6.267); 0.8443
							RR	0.997 (0.908, 1.065); 0.9137
							RD	-0.003 (-0.089, 0.060); 0.9137
Mild	3	4.6	3 (9.4)	0	0.0	0 (0.0)	OR	0.228 (0.011, 4.611); 0.3354
							RR	1.032 (0.967, 1.097); 0.0833
							RD	0.031 (-0.032, 0.088); 0.0784
Moderate	2	3.1	2 (6.3)	0	0.0	0 (0.0)	OR	0.323 (0.015, 7.018); 0.4719
							RR	1.021 (0.957, 1.079); 0.1573
							RD	0.021 (-0.042, 0.073); 0.1530
Non-Severe (Mild + Moderate)	5	7.7	5 (15.6)	0	0.0	0 (0.0)	OR	0.142 (0.008, 2.684); 0.1931
							RR	1.055 (0.988, 1.132); 0.0254
							RD	0.052 (-0.012, 0.116); 0.0216
Severe	1	1.5	1 (3.1)	2	10.1	2 (11.8)	OR	2.817 (0.358, 22.193); 0.3254
							RR	0.976 (0.891, 1.029); 0.3607
							RD	-0.024 (-0.108, 0.027); 0.3566
TESAEs Leading to Withdrawal from Study Drug	0	0.0	0 (0.0)	1	5.1	1 (5.9)	OR	5.035 (0.198, 128.13); 0.3277
							RR	0.983 (0.908, 1.023); 0.3173
							RD	-0.017 (-0.092, 0.022); 0.3131
Treatment-related	0	0.0	0 (0.0)	2	10.1	2 (11.8)	OR	8.540 (0.396, 184.30); 0.1712
							RR	0.966 (0.882, 1.005); 0.1573

							RD	-0.034 (-0.118, 0.005); 0.1501
							OR	0.119 (0.006, 2.205); 0.1530
Not treatment-related	6	9.2	6 (18.8)	0	0.0	0 (0.0)	RR	1.067 (0.998, 1.149); 0.0143
							RD	0.063 (-0.001, 0.130); 0.0114

AE: adverse event; CI: Confidence Interval; OR: Odds Ratio; PY: patient-years; RD: Risk Difference; RR: Risk Ratio; TEAE: treatment-emergent adverse event.
TEAEs are AEs with a start date on or after the date of the first dose of study drug.
Treatment emergent adverse events and follow-up were truncated at the maximum duration of follow-up in the ravulizumab arm.
Odds ratios were derived from a logistic regression model with treatment as the only covariate. Firth's correction was applied for odds ratios.

Overview of All Treatment Emergent Adverse Events (TEAEs) by Treatment Group, Immunosuppressive Therapy (IST) Use: Yes

Adverse Event category	Eculizumab (N=75) Patient-Years (PY)=128.5 Events n	Rate per 100 PY	Patients n (%)	Ravulizumab (N=28) Patient-Years (PY)=40.1 Events n	Rate per 100 PY	Patients n (%)	Treatment Effect	Estimate (95% CI; p-value)
Treatment Emergent Adverse Events (TEAEs)								
							OR	0.544 (0.021, 13.922); 0.7130
Deaths	1	0.8	1 (1.3)	0	0.0	0 (0.0)	RR	1.011 (0.947, 1.060); 0.3173
							RD	0.010 (-0.052, 0.057); 0.3148
							OR	0.323 (0.163, 0.638); 0.0011
Any	895	696.7	69 (92.0)	149	371.6	26 (92.9)	RR	0.624 (0.446, 0.833); 0.0030
							RD	-0.270 (-0.420, -0.111); 0.0007
							OR	0.323 (0.163, 0.638); 0.0011
Any without disease-related	889	692.0	69 (92.0)	149	371.6	26 (92.9)	RR	0.624 (0.446, 0.833); 0.0030
							RD	-0.270 (-0.420, -0.111); 0.0007
							OR	0.269 (0.136, 0.535); 0.0002
Mild	748	582.3	67 (89.3)	105	261.9	22 (78.6)	RR	0.543 (0.373, 0.755); 0.0007
							RD	-0.319 (-0.464, -0.158); 0.0001
							OR	0.458 (0.229, 0.914); 0.0268
Moderate	124	96.5	46 (61.3)	38	94.8	17 (60.7)	RR	0.612 (0.383, 0.939); 0.0326
							RD	-0.186 (-0.332, -0.026); 0.0179
							OR	0.323 (0.163, 0.638); 0.0011
Non-Severe (Mild + Moderate)	872	678.8	69 (92.0)	143	356.6	26 (92.9)	RR	0.624 (0.446, 0.833); 0.0030
							RD	-0.270 (-0.420, -0.111); 0.0007
							OR	0.636 (0.221, 1.830); 0.4011
Severe	21	16.3	13 (17.3)	6	15.0	5 (17.9)	RR	0.637 (0.244, 1.611); 0.3657
							RD	-0.049 (-0.148, 0.065); 0.3324
							OR	0.764 (0.260, 2.251); 0.6256
Severe without disease-related	19	14.8	11 (14.7)	6	15.0	5 (17.9)	RR	0.752 (0.282, 1.956); 0.5792
							RD	-0.028 (-0.124, 0.084); 0.5636
							OR	NA
TEAEs Leading to Withdrawal from Study Drug	0	0.0	0 (0.0)	0	0.0	0 (0.0)	RR	NA
							RD	NA
							OR	0.541 (0.265, 1.105); 0.0918
Treatment-related	272	211.7	38 (50.7)	21	52.4	15 (53.6)	RR	0.653 (0.390, 1.055); 0.0959
							RD	-0.137 (-0.279, 0.019); 0.0715
							OR	0.317 (0.160, 0.625); 0.0009
Not treatment-related	623	485.0	68 (90.7)	128	319.2	25 (89.3)	RR	0.609 (0.431, 0.821); 0.0025
							RD	-0.277 (-0.426, -0.117); 0.0005
Treatment Emergent Serious Adverse Events (TESAEs)								
							OR	0.304 (0.112, 0.825); 0.0194
Any	40	31.1	24 (32.0)	5	12.5	5 (17.9)	RR	0.345 (0.141, 0.810); 0.0214
							RD	-0.164 (-0.275, -0.040); 0.0044
							OR	0.409 (0.148, 1.129); 0.0843
Any without disease-related	34	26.5	19 (25.3)	5	12.5	5 (17.9)	RR	0.436 (0.174, 1.048); 0.0797
							RD	-0.112 (-0.219, 0.008); 0.0418
							OR	0.176 (0.009, 3.405); 0.2502
Mild	4	3.1	4 (5.3)	0	0.0	0 (0.0)	RR	1.043 (0.977, 1.114); 0.0455
							RD	0.042 (-0.022, 0.103); 0.0411
							OR	0.329 (0.080, 1.360); 0.1247
Moderate	20	15.6	11 (14.7)	2	5.0	2 (7.1)	RR	1.090 (0.985, 1.205); 0.0507
							RD	0.080 (-0.014, 0.166); 0.0473
							OR	0.233 (0.058, 0.934); 0.0397
Non-Severe (Mild + Moderate)	24	18.7	15 (20.0)	2	5.0	2 (7.1)	RR	1.144 (1.027, 1.281); 0.0075
							RD	0.122 (0.024, 0.214); 0.0058
							OR	0.469 (0.134, 1.641); 0.2360
Severe	16	12.5	11 (14.7)	3	7.5	3 (10.7)	RR	0.451 (0.138, 1.423); 0.2066
							RD	-0.063 (-0.152, 0.038); 0.1495
							OR	NA
TESAEs Leading to Withdrawal from Study Drug	0	0.0	0 (0.0)	0	0.0	0 (0.0)	RR	NA
							RD	NA
							OR	0.528 (0.120, 2.322); 0.3980
Treatment-related	8	6.2	7 (9.3)	2	5.0	2 (7.1)	RR	0.473 (0.113, 1.918); 0.3397

							RD	-0.038 (-0.115, 0.052); 0.2824
							OR	0.221 (0.067, 0.729); 0.0131
Not treatment-related	32	24.9	21 (28.0)	3	7.5	3 (10.7)	RR	1.214 (1.069, 1.389); 0.0018
							RD	0.167 (0.056, 0.270); 0.0011

AE: adverse event; CI: Confidence Interval; IST: immunosuppressive therapy; OR: Odds Ratio; PY: patient-years; RD: Risk Difference; RR: Risk Ratio; TEAE: treatment-emergent a
TEAEs are AEs with a start date on or after the date of the first dose of study drug.
Treatment emergent adverse events and follow-up were truncated at the maximum duration of follow-up in the ravulizumab arm.
Odds ratios were derived from a logistic regression model with treatment as the only covariate. Firth's correction was applied for odds ratios.

Overview of All Treatment Emergent Adverse Events (TEAEs) by Treatment Group, Immunosuppressive Therapy (IST) Use: No

Adverse Event category	Eculizumab (N=21) Patient-Years (PY)=44.4 Events n	Rate per 100 PY	Patients n (%)	Ravulizumab (N=30) Patient-Years (PY)=44 Events n	Rate per 100 PY	Patients n (%)	Treatment Effect	Estimate (95% CI; p-value)
Treatment Emergent Adverse Events (TEAEs)								
							OR	NA
Deaths	0	0.0	0 (0.0)	0	0.0	0 (0.0)	RR	NA
							RD	NA
							OR	3.470 (1.693, 7.113); 0.0007
Any	235	529.8	19 (90.5)	179	407.1	27 (90.0)	RR	0.666 (0.501, 0.845); 0.0022
							RD	-0.268 (-0.415, -0.116); 0.0005
							OR	3.470 (1.693, 7.113); 0.0007
Any without disease-related	235	529.8	19 (90.5)	179	407.1	27 (90.0)	RR	0.666 (0.501, 0.845); 0.0022
							RD	-0.268 (-0.415, -0.116); 0.0005
							OR	3.241 (1.579, 6.651); 0.0013
Mild	180	405.8	19 (90.5)	139	316.1	26 (86.7)	RR	0.688 (0.521, 0.867); 0.0037
							RD	-0.250 (-0.398, -0.100); 0.0011
							OR	1.663 (0.707, 3.909); 0.2437
Moderate	51	115.0	13 (61.9)	33	75.1	12 (40.0)	RR	0.917 (0.767, 1.059); 0.2704
							RD	-0.071 (-0.206, 0.047); 0.2613
							OR	3.470 (1.693, 7.113); 0.0007
Non-Severe (Mild + Moderate)	231	520.8	19 (90.5)	172	391.2	27 (90.0)	RR	0.666 (0.501, 0.845); 0.0022
							RD	-0.268 (-0.415, -0.116); 0.0005
							OR	3.121 (0.635, 15.332); 0.1611
Severe	3	6.8	2 (9.5)	7	15.9	4 (13.3)	RR	0.951 (0.851, 1.018); 0.1929
							RD	-0.048 (-0.146, 0.016); 0.1852
							OR	3.121 (0.635, 15.332); 0.1611
Severe without disease-related	3	6.8	2 (9.5)	7	15.9	4 (13.3)	RR	0.951 (0.851, 1.018); 0.1929
							RD	-0.048 (-0.146, 0.016); 0.1852
							OR	5.035 (0.198, 128.13); 0.3277
TEAEs Leading to Withdrawal from Study Drug	0	0.0	0 (0.0)	3	6.8	1 (3.3)	RR	0.983 (0.908, 1.023); 0.3173
							RD	-0.017 (-0.092, 0.022); 0.3131
							OR	1.995 (0.799, 4.979); 0.1390
Treatment-related	79	178.1	10 (47.6)	17	38.7	11 (36.7)	RR	0.905 (0.764, 1.031); 0.1662
							RD	-0.085 (-0.216, 0.026); 0.1555
							OR	3.470 (1.693, 7.113); 0.0007
Not treatment-related	156	351.7	19 (90.5)	162	368.5	27 (90.0)	RR	0.666 (0.501, 0.845); 0.0022
							RD	-0.268 (-0.415, -0.116); 0.0005
Treatment Emergent Serious Adverse Events (TESAEs)								
							OR	1.296 (0.305, 5.505); 0.7252
Any	7	15.8	4 (19.0)	3	6.8	3 (10.0)	RR	0.990 (0.892, 1.067); 0.7775
							RD	-0.010 (-0.104, 0.060); 0.7771
							OR	1.296 (0.305, 5.505); 0.7252
Any without disease-related	7	15.8	4 (19.0)	3	6.8	3 (10.0)	RR	0.990 (0.892, 1.067); 0.7775
							RD	-0.010 (-0.104, 0.060); 0.7771
							OR	0.323 (0.015, 7.018); 0.4719
Mild	2	4.5	2 (9.5)	0	0.0	0 (0.0)	RR	1.021 (0.957, 1.079); 0.1573
							RD	0.021 (-0.042, 0.073); 0.1530
							OR	0.544 (0.021, 13.922); 0.7130
Moderate	3	6.8	1 (4.8)	0	0.0	0 (0.0)	RR	1.011 (0.947, 1.060); 0.3173
							RD	0.010 (-0.052, 0.057); 0.3148
							OR	0.228 (0.011, 4.611); 0.3354
Non-Severe (Mild + Moderate)	5	11.3	3 (14.3)	0	0.0	0 (0.0)	RR	1.032 (0.967, 1.097); 0.0833
							RD	0.031 (-0.032, 0.088); 0.0784
							OR	4.014 (0.569, 28.310); 0.1631
Severe	2	4.5	1 (4.8)	3	6.8	3 (10.0)	RR	0.958 (0.866, 1.014); 0.1882
							RD	-0.041 (-0.132, 0.013); 0.1809
							OR	5.035 (0.198, 128.13); 0.3277
TESAEs Leading to Withdrawal from Study Drug	0	0.0	0 (0.0)	1	2.3	1 (3.3)	RR	0.983 (0.908, 1.023); 0.3173
							RD	-0.017 (-0.092, 0.022); 0.3131
							OR	5.035 (0.198, 128.13); 0.3277
Treatment-related	0	0.0	0 (0.0)	1	2.3	1 (3.3)	RR	0.983 (0.908, 1.023); 0.3173

							RD	-0.017 (-0.092, 0.022); 0.3131
							OR	0.910 (0.185, 4.472); 0.9071
Not treatment-related	7	15.8	4 (19.0)	2	4.5	2 (6.7)	RR	1.007 (0.917, 1.082); 0.8193
							RD	0.007 (-0.080, 0.074); 0.8194

AE: adverse event; CI: Confidence Interval; IST: immunosuppressive therapy; OR: Odds Ratio; PY: patient-years; RD: Risk Difference; RR: Risk Ratio; TEAE: treatment-emergent a
TEAEs are AEs with a start date on or after the date of the first dose of study drug.
Treatment emergent adverse events and follow-up were truncated at the maximum duration of follow-up in the ravulizumab arm.
Odds ratios were derived from a logistic regression model with treatment as the only covariate. Firth's correction was applied for odds ratios.

Overview of All Treatment Emergent Adverse Events (TEAEs) by Treatment Group, Rituximab Use: Yes

Adverse Event category	Eculizumab (N=26) Patient-Years (PY)=38.4 Events n	Rate per 100 PY	Patients n (%)	Ravulizumab (N=20) Patient-Years (PY)=30.4 Events n	Rate per 100 PY	Patients n (%)	Treatment Effect	Estimate (95% CI; p-value)
Treatment Emergent Adverse Events (TEAEs)								
Deaths	0	0.0	0 (0.0)	0	0.0	0 (0.0)	OR	NA
							RR	NA
							RD	NA
Any	344	895.6	24 (92.3)	110	361.4	18 (90.0)	OR	1.352 (0.657, 2.779); 0.4128
							RR	1.241 (0.735, 2.061); 0.4123
							RD	0.060 (-0.082, 0.211); 0.4218
Any without disease-related	343	892.9	24 (92.3)	110	361.4	18 (90.0)	OR	1.352 (0.657, 2.779); 0.4128
							RR	1.241 (0.735, 2.061); 0.4123
							RD	0.060 (-0.082, 0.211); 0.4218
Mild	273	710.7	24 (92.3)	91	299.0	17 (85.0)	OR	1.248 (0.603, 2.583); 0.5511
							RR	1.172 (0.686, 1.967); 0.5556
							RD	0.043 (-0.098, 0.193); 0.5620
Moderate	62	161.4	18 (69.2)	16	52.6	8 (40.0)	OR	0.714 (0.293, 1.743); 0.4596
							RR	0.736 (0.342, 1.535); 0.4323
							RD	-0.050 (-0.164, 0.080); 0.4111
Non-Severe (Mild + Moderate)	335	872.1	24 (92.3)	107	351.5	18 (90.0)	OR	1.352 (0.657, 2.779); 0.4128
							RR	1.241 (0.735, 2.061); 0.4123
							RD	0.060 (-0.082, 0.211); 0.4218
Severe	7	18.2	5 (19.2)	3	9.9	2 (10.0)	OR	0.736 (0.157, 3.443); 0.6971
							RR	0.662 (0.150, 2.853); 0.6150
							RD	-0.018 (-0.088, 0.070); 0.5937
Severe without disease-related	7	18.2	5 (19.2)	3	9.9	2 (10.0)	OR	0.736 (0.157, 3.443); 0.6971
							RR	0.662 (0.150, 2.853); 0.6150
							RD	-0.018 (-0.088, 0.070); 0.5937
TEAEs Leading to Withdrawal from Study Drug	0	0.0	0 (0.0)	0	0.0	0 (0.0)	OR	NA
							RR	NA
							RD	NA
Treatment-related	153	398.3	16 (61.5)	9	29.6	8 (40.0)	OR	0.821 (0.332, 2.032); 0.6699
							RR	0.828 (0.379, 1.758); 0.6360
							RD	-0.029 (-0.141, 0.099); 0.6270
Not treatment-related	191	497.2	23 (88.5)	101	331.8	18 (90.0)	OR	1.428 (0.692, 2.950); 0.3351
							RR	1.295 (0.763, 2.166); 0.3327
							RD	0.071 (-0.071, 0.221); 0.3438
Treatment Emergent Serious Adverse Events (TESAEs)								
Any	15	39.1	8 (30.8)	2	6.6	2 (10.0)	OR	0.461 (0.107, 1.984); 0.2983
							RR	0.414 (0.101, 1.645); 0.2536
							RD	-0.049 (-0.128, 0.042); 0.1869
Any without disease-related	14	36.4	8 (30.8)	2	6.6	2 (10.0)	OR	0.461 (0.107, 1.984); 0.2983
							RR	0.414 (0.101, 1.645); 0.2536
							RD	-0.049 (-0.128, 0.042); 0.1869
Mild	2	5.2	2 (7.7)	0	0.0	0 (0.0)	OR	0.323 (0.015, 7.018); 0.4719
							RR	1.021 (0.957, 1.079); 0.1573
							RD	0.021 (-0.042, 0.073); 0.1530
Moderate	8	20.8	3 (11.5)	0	0.0	0 (0.0)	OR	0.228 (0.011, 4.611); 0.3354
							RR	1.032 (0.967, 1.097); 0.0833
							RD	0.031 (-0.032, 0.088); 0.0784
Non-Severe (Mild + Moderate)	10	26.0	5 (19.2)	0	0.0	0 (0.0)	OR	0.142 (0.008, 2.684); 0.1931
							RR	1.055 (0.988, 1.132); 0.0254
							RD	0.052 (-0.012, 0.116); 0.0216
Severe	5	13.0	4 (15.4)	2	6.6	2 (10.0)	OR	0.910 (0.185, 4.472); 0.9071
							RR	0.828 (0.180, 3.745); 0.8238
							RD	-0.007 (-0.074, 0.080); 0.8194
TESAEs Leading to Withdrawal from Study Drug	0	0.0	0 (0.0)	0	0.0	0 (0.0)	OR	NA
							RR	NA
							RD	NA
Treatment-related	2	5.2	2 (7.7)	1	3.3	1 (5.0)	OR	0.986 (0.125, 7.779); 0.9893
							RR	0.828 (0.109, 6.206); 0.8761

							RD	-0.004 (-0.058, 0.073); 0.8730
							OR	0.311 (0.052, 1.880); 0.2034
Not treatment-related	13	33.8	7 (26.9)	1	3.3	1 (5.0)	RR	1.060 (0.974, 1.150); 0.0816
							RD	0.056 (-0.025, 0.129); 0.0778

AE: adverse event; CI: Confidence Interval; OR: Odds Ratio; PY: patient-years; RD: Risk Difference; RR: Risk Ratio; TEAE: treatment-emergent adverse event.
TEAEs are AEs with a start date on or after the date of the first dose of study drug.
Treatment emergent adverse events and follow-up were truncated at the maximum duration of follow-up in the ravulizumab arm.
Odds ratios were derived from a logistic regression model with treatment as the only covariate. Firth's correction was applied for odds ratios.

Overview of All Treatment Emergent Adverse Events (TEAEs) by Treatment Group, Rituximab Use: No

Adverse Event category	Eculizumab (N=70) Patient-Years (PY)=134.4 Events n	Rate per 100 PY	Patients n (%)	Ravulizumab (N=38) Patient-Years (PY)=53.6 Events n	Rate per 100 PY	Patients n (%)	Treatment Effect	Estimate (95% CI; p-value)
Treatment Emergent Adverse Events (TEAEs)								
							OR	0.544 (0.021, 13.922); 0.7130
Deaths	1	0.7	1 (1.4)	0	0.0	0 (0.0)	RR	1.011 (0.947, 1.060); 0.3173
							RD	0.010 (-0.052, 0.057); 0.3148
							OR	0.761 (0.387, 1.496); 0.4285
Any	786	584.8	64 (91.4)	218	406.5	35 (92.1)	RR	1.190 (0.770, 1.806); 0.4234
							RD	0.063 (-0.091, 0.221); 0.4309
							OR	0.761 (0.387, 1.496); 0.4285
Any without disease-related	781	581.1	64 (91.4)	218	406.5	35 (92.1)	RR	1.190 (0.770, 1.806); 0.4234
							RD	0.063 (-0.091, 0.221); 0.4309
							OR	0.632 (0.326, 1.228); 0.1761
Mild	655	487.3	62 (88.6)	153	285.3	31 (81.6)	RR	1.314 (0.885, 1.925); 0.1651
							RD	0.111 (-0.048, 0.269); 0.1728
							OR	0.767 (0.392, 1.499); 0.4375
Moderate	113	84.1	41 (58.6)	55	102.6	21 (55.3)	RR	1.113 (0.847, 1.438); 0.4172
							RD	0.065 (-0.096, 0.218); 0.4211
							OR	0.761 (0.387, 1.496); 0.4285
Non-Severe (Mild + Moderate)	768	571.4	64 (91.4)	208	387.9	35 (92.1)	RR	1.190 (0.770, 1.806); 0.4234
							RD	0.063 (-0.091, 0.221); 0.4309
							OR	1.200 (0.439, 3.280); 0.7228
Severe	17	12.6	10 (14.3)	10	18.6	7 (18.4)	RR	0.982 (0.851, 1.100); 0.7556
							RD	-0.017 (-0.136, 0.083); 0.7549
							OR	1.516 (0.532, 4.322); 0.4363
Severe without disease-related	15	11.2	8 (11.4)	10	18.6	7 (18.4)	RR	0.959 (0.834, 1.068); 0.4698
							RD	-0.037 (-0.155, 0.058); 0.4660
							OR	5.035 (0.198, 128.13); 0.3277
TEAEs Leading to Withdrawal from Study Drug	0	0.0	0 (0.0)	3	5.6	1 (2.6)	RR	0.983 (0.908, 1.023); 0.3173
							RD	-0.017 (-0.092, 0.022); 0.3131
							OR	0.907 (0.451, 1.822); 0.7830
Treatment-related	198	147.3	32 (45.7)	29	54.1	18 (47.4)	RR	1.034 (0.813, 1.286); 0.7659
							RD	-0.017 (-0.092, 0.022); 0.3131
							OR	0.710 (0.362, 1.390); 0.3175
Not treatment-related	588	437.5	64 (91.4)	189	352.5	34 (89.5)	RR	1.241 (0.810, 1.871); 0.3095
							RD	-0.017 (-0.092, 0.022); 0.3131
Treatment Emergent Serious Adverse Events (TESAEs)								
							OR	0.462 (0.177, 1.203); 0.1138
Any	32	23.8	20 (28.6)	6	11.2	6 (15.8)	RR	1.132 (0.976, 1.304); 0.0705
							RD	0.105 (-0.020, 0.216); 0.0686
							OR	0.651 (0.243, 1.746); 0.3938
Any without disease-related	27	20.1	15 (21.4)	6	11.2	6 (15.8)	RR	1.063 (0.923, 1.205); 0.3322
							RD	0.053 (-0.067, 0.158); 0.3328
							OR	0.176 (0.009, 3.405); 0.2502
Mild	4	3.0	4 (5.7)	0	0.0	0 (0.0)	RR	1.043 (0.977, 1.114); 0.0455
							RD	0.042 (-0.022, 0.103); 0.0411
							OR	0.408 (0.096, 1.727); 0.2231
Moderate	15	11.2	9 (12.9)	2	3.7	2 (5.3)	RR	1.065 (0.965, 1.169); 0.1237
							RD	0.059 (-0.033, 0.141); 0.1208
							OR	0.274 (0.067, 1.112); 0.0701
Non-Severe (Mild + Moderate)	19	14.1	13 (18.6)	2	3.7	2 (5.3)	RR	1.117 (1.006, 1.242); 0.0198
							RD	0.101 (0.005, 0.190); 0.0172
							OR	0.860 (0.259, 2.855); 0.8050
Severe	13	9.7	8 (11.4)	4	7.5	4 (10.5)	RR	1.016 (0.904, 1.118); 0.7416
							RD	0.014 (-0.090, 0.100); 0.7419
							OR	5.035 (0.198, 128.13); 0.3277
TESAEs Leading to Withdrawal from Study Drug	0	0.0	0 (0.0)	1	1.9	1 (2.6)	RR	0.983 (0.908, 1.023); 0.3173
							RD	-0.017 (-0.092, 0.022); 0.3131
							OR	0.736 (0.157, 3.443); 0.6971
Treatment-related	6	4.5	5 (7.1)	2	3.7	2 (5.3)	RR	1.019 (0.926, 1.100); 0.5935

							RD	0.018 (-0.070, 0.088); 0.5937
							OR	0.350 (0.117, 1.047); 0.0605
Not treatment-related	26	19.3	18 (25.7)	4	7.5	4 (10.5)	RR	1.146 (1.006, 1.303); 0.0248
							RD	0.119 (0.005, 0.221); 0.0224

AE: adverse event; CI: Confidence Interval; OR: Odds Ratio; PY: patient-years; RD: Risk Difference; RR: Risk Ratio; TEAE: treatment-emergent adverse event.
TEAEs are AEs with a start date on or after the date of the first dose of study drug.
Treatment emergent adverse events and follow-up were truncated at the maximum duration of follow-up in the ravulizumab arm.
Odds ratios were derived from a logistic regression model with treatment as the only covariate. Firth's correction was applied for odds ratios.

Overview of All Treatment Emergent Adverse Events (TEAEs) by Treatment Group, Disease Severity via EDSS: < 5

	Eculizumab (N=66) Patient-Years (PY)=119.7			Ravulizumab (N=49) Patient-Years (PY)=70.4			Treatment Effect	
Adverse Event category	Events n	Rate per 100 PY	Patients n (%)	Events n	Rate per 100 PY	Patients n (%)		Estimate (95% CI; p-value)
Treatment Emergent Adverse Events (TEAEs)								
							OR	0.544 (0.021, 13.922); 0.7130
Deaths	1	0.8	1 (1.5)	0	0.0	0 (0.0)	RR	1.011 (0.947, 1.060); 0.3173
							RD	0.010 (-0.052, 0.057); 0.3148
							OR	2.033 (0.971, 4.257); 0.0597
Any	720	601.6	60 (90.9)	274	389.4	45 (91.8)	RR	1.241 (0.998, 1.532); 0.0413
							RD	0.151 (-0.002, 0.288); 0.0408
							OR	2.033 (0.971, 4.257); 0.0597
Any without disease-related	717	599.1	60 (90.9)	274	389.4	45 (91.8)	RR	1.241 (0.998, 1.532); 0.0413
							RD	0.151 (-0.002, 0.288); 0.0408
							OR	1.495 (0.744, 3.002); 0.2586
Mild	595	497.2	59 (89.4)	200	284.2	41 (83.7)	RR	1.150 (0.902, 1.444); 0.2315
							RD	0.092 (-0.065, 0.238); 0.2349
							OR	1.018 (0.527, 1.967); 0.9570
Moderate	107	89.4	41 (62.1)	63	89.5	25 (51.0)	RR	1.009 (0.684, 1.455); 0.9617
							RD	0.004 (-0.154, 0.165); 0.9617
							OR	2.033 (0.971, 4.257); 0.0597
Non-Severe (Mild + Moderate)	702	586.6	60 (90.9)	263	373.8	45 (91.8)	RR	1.241 (0.998, 1.532); 0.0413
							RD	0.151 (-0.002, 0.288); 0.0408
							OR	1.550 (0.573, 4.193); 0.3879
Severe	17	14.2	9 (13.6)	11	15.6	8 (16.3)	RR	1.471 (0.612, 3.494); 0.3977
							RD	0.044 (-0.057, 0.166); 0.4148
							OR	1.753 (0.633, 4.854); 0.2803
Severe without disease-related	16	13.4	8 (12.1)	11	15.6	8 (16.3)	RR	1.655 (0.671, 4.044); 0.2852
							RD	0.055 (-0.044, 0.175); 0.3061
							OR	5.035 (0.198, 128.13); 0.3277
TEAEs Leading to Withdrawal from Study Drug	0	0.0	0 (0.0)	3	4.3	1 (2.0)	RR	0.983 (0.908, 1.023); 0.3173
							RD	-0.017 (-0.092, 0.022); 0.3131
							OR	1.199 (0.613, 2.347); 0.5961
Treatment-related	205	171.3	34 (51.5)	33	46.9	23 (46.9)	RR	1.120 (0.730, 1.684); 0.5951
							RD	0.042 (-0.112, 0.201); 0.5993
							OR	1.934 (0.937, 3.995); 0.0746
Not treatment-related	515	430.3	59 (89.4)	241	342.5	44 (89.8)	RR	1.234 (0.985, 1.533); 0.0548
							RD	0.144 (-0.010, 0.284); 0.0548
Treatment Emergent Serious Adverse Events (TESAEs)								
							OR	0.901 (0.343, 2.364); 0.8319
Any	22	18.4	13 (19.7)	7	9.9	7 (14.3)	RR	0.891 (0.381, 2.033); 0.7928
							RD	-0.015 (-0.120, 0.107); 0.7897
							OR	1.200 (0.439, 3.280); 0.7228
Any without disease-related	19	15.9	10 (15.2)	7	9.9	7 (14.3)	RR	1.159 (0.475, 2.779); 0.7510
							RD	0.017 (-0.083, 0.136); 0.7549
							OR	0.323 (0.015, 7.018); 0.4719
Mild	2	1.7	2 (3.0)	0	0.0	0 (0.0)	RR	1.021 (0.957, 1.079); 0.1573
							RD	0.021 (-0.042, 0.073); 0.1530
							OR	0.736 (0.157, 3.443); 0.6971
Moderate	7	5.8	5 (7.6)	2	2.8	2 (4.1)	RR	1.019 (0.926, 1.100); 0.5935
							RD	0.018 (-0.070, 0.088); 0.5937
							OR	0.528 (0.120, 2.322); 0.3980
Non-Severe (Mild + Moderate)	9	7.5	7 (10.6)	2	2.8	2 (4.1)	RR	1.041 (0.945, 1.134); 0.2836
							RD	0.038 (-0.052, 0.115); 0.2824
							OR	1.227 (0.385, 3.911); 0.7298
Severe	13	10.9	7 (10.6)	5	7.1	5 (10.2)	RR	1.182 (0.408, 3.367); 0.7655
							RD	0.013 (-0.073, 0.121); 0.7698
							OR	5.035 (0.198, 128.13); 0.3277
TESAEs Leading to Withdrawal from Study Drug	0	0.0	0 (0.0)	1	1.4	1 (2.0)	RR	0.983 (0.908, 1.023); 0.3173
							RD	-0.017 (-0.092, 0.022); 0.3131
							OR	1.296 (0.305, 5.505); 0.7252
Treatment-related	5	4.2	4 (6.1)	3	4.3	3 (6.1)	RR	1.241 (0.317, 4.799); 0.7718

							RD	0.010 (-0.060, 0.104); 0.7771
							OR	0.614 (0.194, 1.939); 0.4057
Not treatment-related	17	14.2	11 (16.7)	4	5.7	4 (8.2)	RR	1.052 (0.932, 1.170); 0.3268
							RD	0.046 (-0.062, 0.138); 0.3268

AE: adverse event; CI: Confidence Interval; EDSS: Expanded Disability Status Scale; OR: Odds Ratio; PY: patient-years; RD: Risk Difference; RR: Risk Ratio; TEAE: treatment-emerg
TEAEs are AEs with a start date on or after the date of the first dose of study drug.
Treatment emergent adverse events and follow-up were truncated at the maximum duration of follow-up in the ravulizumab arm.
Odds ratios were derived from a logistic regression model with treatment as the only covariate. Firth's correction was applied for odds ratios.

Overview of All Treatment Emergent Adverse Events (TEAEs) by Treatment Group, Disease Severity via EDSS: ≥ 5

Adverse Event category	Eculizumab (N=30) Patient-Years (PY)=53.1 Events n	Rate per 100 PY	Patients n (%)	Ravulizumab (N=9) Patient-Years (PY)=13.7 Events n	Rate per 100 PY	Patients n (%)	Treatment Effect	Estimate (95% CI; p-value)
Treatment Emergent Adverse Events (TEAEs)								
							OR	NA
Deaths	0	0.0	0 (0.0)	0	0.0	0 (0.0)	RR	NA
							RD	NA
							OR	0.405 (0.172, 0.951); 0.0379
Any	410	771.6	28 (93.3)	54	394.2	8 (88.9)	RR	1.217 (1.022, 1.443); 0.0193
							RD	0.154 (0.017, 0.276); 0.0177
							OR	0.405 (0.172, 0.951); 0.0379
Any without disease-related	407	765.9	28 (93.3)	54	394.2	8 (88.9)	RR	1.217 (1.022, 1.443); 0.0193
							RD	0.154 (0.017, 0.276); 0.0177
							OR	0.368 (0.151, 0.897); 0.0279
Mild	333	626.7	27 (90.0)	44	321.2	7 (77.8)	RR	1.223 (1.036, 1.442); 0.0120
							RD	0.161 (0.027, 0.280); 0.0105
							OR	0.350 (0.117, 1.047); 0.0605
Moderate	68	128.0	18 (60.0)	8	58.4	4 (44.4)	RR	1.146 (1.006, 1.303); 0.0248
							RD	0.119 (0.005, 0.221); 0.0224
							OR	0.405 (0.172, 0.951); 0.0379
Non-Severe (Mild + Moderate)	401	754.6	28 (93.3)	52	379.6	8 (88.9)	RR	1.217 (1.022, 1.443); 0.0193
							RD	0.154 (0.017, 0.276); 0.0177
							OR	0.363 (0.059, 2.242); 0.2754
Severe	7	13.2	6 (20.0)	2	14.6	1 (11.1)	RR	1.048 (0.964, 1.133); 0.1354
							RD	0.045 (-0.034, 0.116); 0.1319
							OR	0.434 (0.068, 2.759); 0.3764
Severe without disease-related	6	11.3	5 (16.7)	2	14.6	1 (11.1)	RR	1.037 (0.954, 1.116); 0.2223
							RD	0.035 (-0.044, 0.102); 0.2198
							OR	NA
TEAEs Leading to Withdrawal from Study Drug	0	0.0	0 (0.0)	0	0.0	0 (0.0)	RR	NA
							RD	NA
							OR	0.359 (0.105, 1.222); 0.1011
Treatment-related	146	274.8	14 (46.7)	5	36.5	3 (33.3)	RR	1.110 (0.989, 1.243); 0.0450
							RD	0.094 (-0.010, 0.188); 0.0421
							OR	0.405 (0.172, 0.951); 0.0379
Not treatment-related	264	496.8	28 (93.3)	49	357.7	8 (88.9)	RR	1.217 (1.022, 1.443); 0.0193
							RD	0.154 (0.017, 0.276); 0.0177
Treatment Emergent Serious Adverse Events (TESAEs)								
							OR	0.137 (0.024, 0.769); 0.0239
Any	25	47.0	15 (50.0)	1	7.3	1 (11.1)	RR	1.165 (1.059, 1.301); 0.0012
							RD	0.139 (0.051, 0.228); 0.0007
							OR	0.161 (0.028, 0.914); 0.0392
Any without disease-related	22	41.4	13 (43.3)	1	7.3	1 (11.1)	RR	1.137 (1.036, 1.261); 0.0036
							RD	0.118 (0.032, 0.204); 0.0024
							OR	0.176 (0.009, 3.405); 0.2502
Mild	4	7.5	4 (13.3)	0	0.0	0 (0.0)	RR	1.043 (0.977, 1.114); 0.0455
							RD	0.042 (-0.022, 0.103); 0.0411
							OR	0.102 (0.006, 1.864); 0.1236
Moderate	16	30.1	7 (23.3)	0	0.0	0 (0.0)	RR	1.079 (1.009, 1.167); 0.0082
							RD	0.073 (0.009, 0.143); 0.0060
							OR	0.064 (0.004, 1.126); 0.0603
Non-Severe (Mild + Moderate)	20	37.6	11 (36.7)	0	0.0	0 (0.0)	RR	1.129 (1.056, 1.241); 0.0009
							RD	0.115 (0.049, 0.194); 0.0004
							OR	0.434 (0.068, 2.759); 0.3764
Severe	5	9.4	5 (16.7)	1	7.3	1 (11.1)	RR	1.037 (0.954, 1.116); 0.2223
							RD	0.035 (-0.044, 0.102); 0.2198
							OR	NA
TESAEs Leading to Withdrawal from Study Drug	0	0.0	0 (0.0)	0	0.0	0 (0.0)	RR	NA
							RD	NA
							OR	0.228 (0.011, 4.611); 0.3354
Treatment-related	3	5.6	3 (10.0)	0	0.0	0 (0.0)	RR	1.032 (0.967, 1.097); 0.0833

							RD	0.031 (-0.032, 0.088); 0.0784
							OR	0.148 (0.026, 0.836); 0.0305
Not treatment-related	22	41.4	14 (46.7)	1	7.3	1 (11.1)	RR	1.151 (1.047, 1.280); 0.0021
							RD	0.129 (0.042, 0.216); 0.0013

AE: adverse event; CI: Confidence Interval; EDSS: Expanded Disability Status Scale; OR: Odds Ratio; PY: patient-years; RD: Risk Difference; RR: Risk Ratio; TEAE: treatment-emerg
TEAEs are AEs with a start date on or after the date of the first dose of study drug.
Treatment emergent adverse events and follow-up were truncated at the maximum duration of follow-up in the ravulizumab arm.
Odds ratios were derived from a logistic regression model with treatment as the only covariate. Firth's correction was applied for odds ratios.

Treatment Emergent Adverse Events (TEAEs) by MedDRA System Organ Class/Preferred Term by Treatment Group, Sex: Female

System Organ Class / Preferred Term	Eculizumab (N=88) Patient-Years (PY)=159 Events n	Rate per 100 PY	Patients n (%)	Ravulizumab (N=52) Patient-Years (PY)=75.6 Events n	Rate per 100 PY	Patients n (%)	Treatment Effect	Estimate (95% CI; p-value)
Blood and lymphatic system disorders	36	23	19 (21.6)	4	5	4 (7.7)	OR	0.328 (0.110, 0.976); 0.0452
							RR	0.348 (0.127, 0.913); 0.0444
							RD	-0.129 (-0.233, -0.014); 0.0141
Eye disorders	43	27	17 (19.3)	9	12	6 (11.5)	OR	0.562 (0.213, 1.488); 0.2463
							RR	1.089 (0.943, 1.243); 0.1877
							RD	0.074 (-0.048, 0.181); 0.1872
Gastrointestinal disorders	120	75	38 (43.2)	32	42	22 (42.3)	OR	0.937 (0.480, 1.829); 0.8481
							RR	1.027 (0.781, 1.321); 0.8378
							RD	0.017 (-0.144, 0.171); 0.8382
Diarrhoea	22	14	15 (17.0)	3	4	3 (5.8)	OR	0.332 (0.098, 1.121); 0.0758
							RR	1.124 (0.999, 1.262); 0.0292
							RD	0.105 (-0.001, 0.200); 0.0265
Nausea	28	18	14 (15.9)	2	3	2 (3.8)	OR	0.252 (0.062, 1.016); 0.0527
							RR	1.130 (1.016, 1.262); 0.0123
							RD	0.111 (0.014, 0.202); 0.0101
General disorders and administration site conditions	83	52	24 (27.3)	36	48	17 (32.7)	OR	1.248 (0.603, 2.583); 0.5511
							RR	0.943 (0.754, 1.144); 0.5657
							RD	-0.043 (-0.193, 0.098); 0.5620
Infections and infestations	263	165	67 (76.1)	59	78	33 (63.5)	OR	0.574 (0.292, 1.130); 0.1084
							RR	0.815 (0.615, 1.042); 0.1233
							RD	-0.129 (-0.284, 0.026); 0.1077
COVID-19	0	0	0 (0.0)	13	17	13 (25.0)	OR	57.264 (3.280, 999.74); 0.0055
							RR	0.776 (0.653, 0.864); 0.0003
							RD	-0.224 (-0.347, -0.136); 0.0000
Nasopharyngitis	42	26	17 (19.3)	3	4	3 (5.8)	OR	0.286 (0.086, 0.958); 0.0424
							RR	1.152 (1.021, 1.303); 0.0120
							RD	0.125 (0.018, 0.224); 0.0099
Upper respiratory tract infection	45	28	28 (31.8)	3	4	3 (5.8)	OR	0.152 (0.047, 0.491); 0.0016
							RR	0.177 (0.058, 0.511); 0.0031
							RD	-0.240 (-0.348, -0.124); 0.0000
Urinary tract infection	40	25	11 (12.5)	6	8	5 (9.6)	OR	0.764 (0.260, 2.251); 0.6256
							RR	1.032 (0.907, 1.152); 0.5630
							RD	0.028 (-0.084, 0.124); 0.5636
Injury, poisoning and procedural complications	44	28	28 (31.8)	13	17	10 (19.2)	OR	0.520 (0.233, 1.162); 0.1110
							RR	0.591 (0.308, 1.094); 0.1098
							RD	-0.119 (-0.247, 0.023); 0.0791
Contusion	10	6	9 (10.2)	0	0	0 (0.0)	OR	0.079 (0.004, 1.412); 0.0844
							RR	1.103 (1.032, 1.203); 0.0027
							RD	0.094 (0.029, 0.169); 0.0016
Investigations	27	17	13 (14.8)	11	15	8 (15.4)	OR	1.041 (0.409, 2.647); 0.9327
							RR	0.997 (0.856, 1.132); 0.9649
							RD	-0.003 (-0.128, 0.105); 0.9649
Metabolism and nutrition disorders	12	8	11 (12.5)	5	7	5 (9.6)	OR	0.764 (0.260, 2.251); 0.6256
							RR	1.032 (0.907, 1.152); 0.5630
							RD	0.028 (-0.084, 0.124); 0.5636
Musculoskeletal and connective tissue disorders	69	43	37 (42.0)	30	40	21 (40.4)	OR	0.910 (0.463, 1.785); 0.7833
							RR	0.939 (0.606, 1.419); 0.7731
							RD	-0.023 (-0.176, 0.136); 0.7713
Arthralgia	10	6	9 (10.2)	6	8	6 (11.5)	OR	1.140 (0.394, 3.299); 0.8086
							RR	1.103 (0.424, 2.821); 0.8440
							RD	0.010 (-0.085, 0.124); 0.8457
Back pain	12	8	10 (11.4)	7	9	6 (11.5)	OR	1.020 (0.359, 2.898); 0.9699
							RR	1.001 (0.874, 1.117); 0.9887
							RD	0.001 (-0.115, 0.097); 0.9887
Pain in extremity	11	7	9 (10.2)	2	3	2 (3.8)	OR	0.408 (0.096, 1.727); 0.2231
							RR	1.065 (0.965, 1.169); 0.1237
							RD	0.059 (-0.033, 0.141); 0.1208
Nervous system disorders	174	109	42 (47.7)	43	57	17 (32.7)	OR	0.541 (0.270, 1.081); 0.0819
							RR	0.670 (0.416, 1.039); 0.0876
							RD	-0.144 (-0.291, 0.015); 0.0653
Dizziness	19	12	14 (15.9)	4	5	4 (7.7)	OR	0.470 (0.153, 1.440); 0.1862
							RR	0.473 (0.168, 1.284); 0.1671
							RD	-0.077 (-0.174, 0.033); 0.1170
Headache	80	50	19 (21.6)	24	32	14 (26.9)	OR	1.295 (0.594, 2.821); 0.5155
							RR	0.946 (0.776, 1.119); 0.5348

System Organ Class / Preferred Term	Eculizumab (N=88) Patient-Years (PY)=159 Events n	Rate per 100 PY	Patients n (%)	Ravulizumab (N=52) Patient-Years (PY)=75.6 Events n	Rate per 100 PY	Patients n (%)	Treatment Effect	Estimate (95% CI; p-value)
							RD	-0.043 (-0.187, 0.087); 0.5309
Psychiatric disorders	15	9	12 (13.6)	10	13	6 (11.5)	OR	0.837 (0.303, 2.312); 0.7313
							RR	1.025 (0.893, 1.151); 0.6799
							RD	0.022 (-0.096, 0.122); 0.6805
Renal and urinary disorders	20	13	15 (17.0)	10	13	5 (9.6)	OR	0.541 (0.191, 1.530); 0.2465
							RR	1.083 (0.947, 1.224); 0.1811
							RD	0.070 (-0.046, 0.172); 0.1802
Reproductive system and breast disorders	14	9	9 (10.2)	2	3	2 (3.8)	OR	0.408 (0.096, 1.727); 0.2231
							RR	1.065 (0.965, 1.169); 0.1237
							RD	0.059 (-0.033, 0.141); 0.1208
Respiratory, thoracic and mediastinal disorders	60	38	21 (23.9)	9	12	8 (15.4)	OR	0.591 (0.246, 1.421); 0.2398
							RR	1.103 (0.937, 1.283); 0.1913
							RD	0.081 (-0.051, 0.198); 0.1916
Cough	12	8	11 (12.5)	3	4	3 (5.8)	OR	0.469 (0.134, 1.641); 0.2360
							RR	1.071 (0.958, 1.187); 0.1516
							RD	0.063 (-0.038, 0.152); 0.1495
Skin and subcutaneous tissue disorders	31	19	22 (25.0)	16	21	12 (23.1)	OR	0.890 (0.405, 1.958); 0.7722
							RR	0.903 (0.481, 1.651); 0.7479
							RD	-0.022 (-0.151, 0.120); 0.7445
Vascular disorders	15	9	11 (12.5)	5	7	4 (7.7)	OR	0.614 (0.194, 1.939); 0.4057
							RR	1.052 (0.932, 1.170); 0.3268
							RD	0.046 (-0.062, 0.138); 0.3268

AE: Adverse Event; CI: Confidence Interval; OR: Odds Ratio; PY: person years; RD: Risk Difference; RR: Risk Ratio; TEAE: Treatment-emergent Adverse Event.
TEAEs are AEs with a start date on or after the date of the first dose of study drug.
Treatment-related adverse events and follow-up were truncated at the maximum duration of follow-up in the ravulizumab arm.
Odds ratios were derived from a logistic regression model with treatment as the only covariate. Firth's correction was applied for odds ratios.
Any TEAEs were examined for preferred terms and system organ classes reported in at least 10% of patients in one of the treatment arms within the subgroup.
Severe and serious TEAEs were examined for preferred terms and system organ classes reported in at least 5% of patients in one of the treatment arms within the subgroup.
Preferred terms and system organ classes for a given AE severity or type (i.e., leading for withdrawal) were only examined within each subgroup if they were also examined in

Treatment Emergent Adverse Events (TEAEs) by MedDRA System Organ Class/Preferred Term by Severity and Treatment Group, Sex: Female

System Organ Class / Preferred Term	Eculizumab (N=88) Patient-Years (PY)=159 Events n	Rate per 100 PY	Patients n (%)	Ravulizumab (N=52) Patient-Years (PY)=75.6 Events n	Rate per 100 PY	Patients n (%)	Treatment Effect	Estimate (95% CI; p-value)
Mild TEAEs								
Blood and lymphatic system disorders	29	18	15 (17.0)	3	4	3 (5.8)	OR	0.332 (0.098, 1.121); 0.0758
							RR	0.331 (0.105, 1.005); 0.0700
							RD	-0.105 (-0.200, 0.001); 0.0265
Eye disorders	27	17	17 (19.3)	5	7	4 (7.7)	OR	0.375 (0.125, 1.127); 0.0807
							RR	1.131 (0.994, 1.283); 0.0374
							RD	0.108 (-0.005, 0.210); 0.0348
Gastrointestinal disorders	101	64	33 (37.5)	27	36	19 (36.5)	OR	0.936 (0.469, 1.866); 0.8505
							RR	1.025 (0.800, 1.283); 0.8362
							RD	0.016 (-0.141, 0.165); 0.8367
Diarrhoea	19	12	14 (15.9)	3	4	3 (5.8)	OR	0.359 (0.105, 1.222); 0.1011
							RR	1.110 (0.989, 1.243); 0.0450
							RD	0.094 (-0.010, 0.188); 0.0421
Nausea	23	14	12 (13.6)	2	3	2 (3.8)	OR	0.299 (0.073, 1.225); 0.0934
							RR	1.103 (0.995, 1.224); 0.0319
							RD	0.091 (-0.004, 0.178); 0.0288
General disorders and administration site conditions	73	46	19 (21.6)	30	40	13 (25.0)	OR	1.179 (0.535, 2.599); 0.6828
							RR	0.967 (0.798, 1.139); 0.7021
							RD	-0.026 (-0.168, 0.102); 0.7006
Infections and infestations	211	133	56 (63.6)	38	50	22 (42.3)	OR	0.442 (0.227, 0.861); 0.0164
							RR	1.490 (1.085, 2.035); 0.0119
							RD	0.204 (0.041, 0.355); 0.0120
COVID-19	0	0	0 (0.0)	10	13	10 (19.2)	OR	41.779 (2.361, 739.20); 0.0109
							RR	0.828 (0.710, 0.904); 0.0016
							RD	-0.172 (-0.290, -0.096); 0.0005
Nasopharyngitis	35	22	13 (14.8)	2	3	2 (3.8)	OR	0.274 (0.067, 1.112); 0.0701
							RR	1.117 (1.006, 1.242); 0.0198
							RD	0.101 (0.005, 0.190); 0.0172
Upper respiratory tract infection	41	26	26 (29.5)	1	1	1 (1.9)	OR	0.069 (0.013, 0.378); 0.0020
							RR	1.348 (1.198, 1.558); 0.0000
							RD	0.254 (0.155, 0.354); 0.0000
Urinary tract infection	33	21	10 (11.4)	3	4	2 (3.8)	OR	0.364 (0.087, 1.524); 0.1668
							RR	1.078 (0.974, 1.187); 0.0797
							RD	0.070 (-0.023, 0.154); 0.0764
Injury, poisoning and procedural complications	31	19	22 (25.0)	7	9	5 (9.6)	OR	0.340 (0.125, 0.929); 0.0354
							RR	1.185 (1.026, 1.369); 0.0133
							RD	0.143 (0.021, 0.253); 0.0115
Investigations	20	13	12 (13.6)	11	15	8 (15.4)	OR	1.138 (0.442, 2.928); 0.7890
							RR	0.985 (0.847, 1.115); 0.8193
							RD	-0.013 (-0.137, 0.093); 0.8189
Metabolism and nutrition disorders	12	8	11 (12.5)	1	1	1 (1.9)	OR	0.194 (0.034, 1.114); 0.0659
							RR	1.110 (1.015, 1.223); 0.0102
							RD	0.097 (0.013, 0.180); 0.0080
Musculoskeletal and connective tissue disorders	53	33	30 (34.1)	22	29	15 (28.8)	OR	0.777 (0.376, 1.606); 0.4957
							RR	1.078 (0.866, 1.318); 0.4668
							RD	0.054 (-0.098, 0.194); 0.4693
Nervous system disorders	152	96	34 (38.6)	36	48	15 (28.8)	OR	0.645 (0.315, 1.324); 0.2325
							RR	0.730 (0.432, 1.195); 0.2294
							RD	-0.096 (-0.237, 0.059); 0.2052
Dizziness	17	11	13 (14.8)	3	4	3 (5.8)	OR	0.390 (0.114, 1.339); 0.1346
							RR	0.382 (0.119, 1.179); 0.1197
							RD	-0.084 (-0.176, 0.020); 0.0655
Headache	75	47	17 (19.3)	19	25	11 (21.2)	OR	1.100 (0.478, 2.528); 0.8227
							RR	0.985 (0.825, 1.144); 0.8459
							RD	-0.013 (-0.149, 0.109); 0.8456
Psychiatric disorders	13	8	11 (12.5)	5	7	5 (9.6)	OR	0.764 (0.260, 2.251); 0.6256
							RR	1.032 (0.907, 1.152); 0.5630
							RD	0.028 (-0.084, 0.124); 0.5636
Renal and urinary disorders	16	10	13 (14.8)	9	12	4 (7.7)	OR	0.511 (0.165, 1.579); 0.2433
							RR	1.077 (0.952, 1.206); 0.1698
							RD	0.066 (-0.043, 0.162); 0.1683
Reproductive system and breast disorders	14	9	9 (10.2)	2	3	2 (3.8)	OR	0.408 (0.096, 1.727); 0.2231
							RR	1.065 (0.965, 1.169); 0.1237
							RD	0.059 (-0.033, 0.141); 0.1208

Treatment Emergent Adverse Events (TEAEs) by MedDRA System Organ Class/Preferred Term by Severity and Treatment Group, Sex: Female

System Organ Class / Preferred Term	Eculizumab (N=88) Patient-Years (PY)=159 Events n	Rate per 100 PY	Patients n (%)	Ravulizumab (N=52) Patient-Years (PY)=75.6 Events n	Rate per 100 PY	Patients n (%)	Treatment Effect Estimate (95% CI; p-value)
Respiratory, thoracic and mediastinal disorders	58	36	19 (21.6)	8	11	7 (13.5)	OR 0.579 (0.231, 1.452); 0.2439 RR 1.096 (0.940, 1.263); 0.1908 RD 0.077 (-0.050, 0.190); 0.1907
Cough	11	7	10 (11.4)	3	4	3 (5.8)	OR 0.520 (0.147, 1.842); 0.3105 RR 1.059 (0.948, 1.169); 0.2200 RD 0.052 (-0.048, 0.140); 0.2187
Skin and subcutaneous tissue disorders	28	18	21 (23.9)	13	17	9 (17.3)	OR 0.674 (0.288, 1.576); 0.3627 RR 0.709 (0.348, 1.402); 0.3429 RD -0.064 (-0.184, 0.071); 0.3172
ModerateTEAEs							
Gastrointestinal disorders	17	11	13 (14.8)	5	7	4 (7.7)	OR 0.511 (0.165, 1.579); 0.2433 RR 1.077 (0.952, 1.206); 0.1698 RD 0.066 (-0.043, 0.162); 0.1683
Infections and infestations	48	30	26 (29.5)	16	21	14 (26.9)	OR 0.867 (0.410, 1.831); 0.7080 RR 0.891 (0.504, 1.536); 0.6881 RD -0.029 (-0.165, 0.119); 0.6834
Musculoskeletal and connective tissue disorders	14	9	11 (12.5)	6	8	5 (9.6)	OR 0.764 (0.260, 2.251); 0.6256 RR 0.752 (0.282, 1.956); 0.5792 RD -0.028 (-0.124, 0.084); 0.5636
Non-SevereTEAEs							
Blood and lymphatic system disorders	36	23	19 (21.6)	4	5	4 (7.7)	OR 0.328 (0.110, 0.976); 0.0452 RR 0.348 (0.127, 0.913); 0.0444 RD -0.129 (-0.233, -0.014); 0.0141
Eye disorders	42	26	17 (19.3)	9	12	6 (11.5)	OR 0.562 (0.213, 1.488); 0.2463 RR 1.089 (0.943, 1.243); 0.1877 RD 0.074 (-0.048, 0.181); 0.1872
Gastrointestinal disorders	118	74	37 (42.0)	32	42	22 (42.3)	OR 0.978 (0.500, 1.912); 0.9476 RR 1.010 (0.769, 1.295); 0.9397 RD 0.006 (-0.154, 0.160); 0.9397
Diarrhoea	22	14	15 (17.0)	3	4	3 (5.8)	OR 0.332 (0.098, 1.121); 0.0758 RR 1.124 (0.999, 1.262); 0.0292 RD 0.105 (-0.001, 0.200); 0.0265
Nausea	28	18	14 (15.9)	2	3	2 (3.8)	OR 0.252 (0.062, 1.016); 0.0527 RR 1.130 (1.016, 1.262); 0.0123 RD 0.111 (0.014, 0.202); 0.0101
General disorders and administration site conditions	81	51	24 (27.3)	35	46	17 (32.7)	OR 1.248 (0.603, 2.583); 0.5511 RR 0.943 (0.754, 1.144); 0.5657 RD -0.043 (-0.193, 0.098); 0.5620
Infections and infestations	259	163	66 (75.0)	54	71	32 (61.5)	OR 0.562 (0.287, 1.103); 0.0939 RR 0.803 (0.601, 1.034); 0.1080 RD -0.136 (-0.292, 0.021); 0.0922
COVID-19	0	0	0 (0.0)	13	17	13 (25.0)	OR 57.264 (3.280, 999.74); 0.0055 RR 0.776 (0.653, 0.864); 0.0003 RD -0.224 (-0.347, -0.136); 0.0000
Nasopharyngitis	42	26	17 (19.3)	3	4	3 (5.8)	OR 0.286 (0.086, 0.958); 0.0424 RR 1.152 (1.021, 1.303); 0.0120 RD 0.125 (0.018, 0.224); 0.0099
Upper respiratory tract infection	45	28	28 (31.8)	2	3	2 (3.8)	OR 0.106 (0.028, 0.411); 0.0011 RR 0.118 (0.032, 0.419); 0.0027 RD -0.257 (-0.362, -0.148); 0.0000
Urinary tract infection	40	25	11 (12.5)	6	8	5 (9.6)	OR 0.764 (0.260, 2.251); 0.6256 RR 1.032 (0.907, 1.152); 0.5630 RD 0.028 (-0.084, 0.124); 0.5636
Injury, poisoning and procedural complications	40	25	27 (30.7)	12	16	9 (17.3)	OR 0.485 (0.212, 1.111); 0.0872 RR 0.552 (0.278, 1.056); 0.0867 RD -0.126 (-0.251, 0.013); 0.0564
Contusion	10	6	9 (10.2)	0	0	0 (0.0)	OR 0.079 (0.004, 1.412); 0.0844 RR 1.103 (1.032, 1.203); 0.0027 RD 0.094 (0.029, 0.169); 0.0016
Investigations	27	17	13 (14.8)	11	15	8 (15.4)	OR 1.041 (0.409, 2.647); 0.9327 RR 0.997 (0.856, 1.132); 0.9649 RD -0.003 (-0.128, 0.105); 0.9649

Treatment Emergent Adverse Events (TEAEs) by MedDRA System Organ Class/Preferred Term by Severity and Treatment Group, Sex: Female

System Organ Class / Preferred Term	Eculizumab (N=88) Patient-Years (PY)=159 Events n	Rate per 100 PY	Patients n (%)	Ravulizumab (N=52) Patient-Years (PY)=75.6 Events n	Rate per 100 PY	Patients n (%)	Treatment Effect	Estimate (95% CI; p-value)
Metabolism and nutrition disorders	12	8	11 (12.5)	5	7	5 (9.6)	OR	0.764 (0.260, 2.251); 0.6256
							RR	1.032 (0.907, 1.152); 0.5630
							RD	0.028 (-0.084, 0.124); 0.5636
Musculoskeletal and connective tissue disorders	67	42	37 (42.0)	28	37	20 (38.5)	OR	0.845 (0.429, 1.666); 0.6265
							RR	0.895 (0.571, 1.364); 0.6165
							RD	-0.041 (-0.192, 0.119); 0.6109
Arthralgia	10	6	9 (10.2)	6	8	6 (11.5)	OR	1.140 (0.394, 3.299); 0.8086
							RR	1.103 (0.424, 2.821); 0.8440
							RD	0.010 (-0.085, 0.124); 0.8457
Back pain	11	7	10 (11.4)	6	8	5 (9.6)	OR	0.847 (0.283, 2.530); 0.7660
							RR	1.020 (0.898, 1.135); 0.7094
							RD	0.018 (-0.093, 0.111); 0.7099
Nervous system disorders	170	107	40 (45.5)	42	56	17 (32.7)	OR	0.588 (0.294, 1.178); 0.1341
							RR	0.703 (0.435, 1.098); 0.1377
							RD	-0.124 (-0.270, 0.035); 0.1138
Dizziness	19	12	14 (15.9)	3	4	3 (5.8)	OR	0.359 (0.105, 1.222); 0.1011
							RR	0.355 (0.111, 1.085); 0.0914
							RD	-0.094 (-0.188, 0.010); 0.0421
Headache	78	49	19 (21.6)	24	32	14 (26.9)	OR	1.295 (0.594, 2.821); 0.5155
							RR	0.946 (0.776, 1.119); 0.5348
							RD	-0.043 (-0.187, 0.087); 0.5309
Psychiatric disorders	15	9	12 (13.6)	9	12	6 (11.5)	OR	0.837 (0.303, 2.312); 0.7313
							RR	1.025 (0.893, 1.151); 0.6799
							RD	0.022 (-0.096, 0.122); 0.6805
Renal and urinary disorders	20	13	15 (17.0)	9	12	4 (7.7)	OR	0.434 (0.143, 1.321); 0.1416
							RR	1.103 (0.973, 1.243); 0.0821
							RD	0.087 (-0.024, 0.186); 0.0797
Reproductive system and breast disorders	14	9	9 (10.2)	2	3	2 (3.8)	OR	0.408 (0.096, 1.727); 0.2231
							RR	1.065 (0.965, 1.169); 0.1237
							RD	0.059 (-0.033, 0.141); 0.1208
Respiratory, thoracic and mediastinal disorders	60	38	21 (23.9)	9	12	8 (15.4)	OR	0.591 (0.246, 1.421); 0.2398
							RR	1.103 (0.937, 1.283); 0.1913
							RD	0.081 (-0.051, 0.198); 0.1916
Cough	12	8	11 (12.5)	3	4	3 (5.8)	OR	0.469 (0.134, 1.641); 0.2360
							RR	1.071 (0.958, 1.187); 0.1516
							RD	0.063 (-0.038, 0.152); 0.1495
Skin and subcutaneous tissue disorders	31	19	22 (25.0)	16	21	12 (23.1)	OR	0.890 (0.405, 1.958); 0.7722
							RR	0.903 (0.481, 1.651); 0.7479
							RD	-0.022 (-0.151, 0.120); 0.7445
Vascular disorders	15	9	11 (12.5)	5	7	4 (7.7)	OR	0.614 (0.194, 1.939); 0.4057
							RR	1.052 (0.932, 1.170); 0.3268
							RD	0.046 (-0.062, 0.138); 0.3268
Severe TEAEs								
Infections and infestations	3	2	3 (3.4)	5	7	5 (9.6)	OR	2.746 (0.684, 11.033); 0.1545
							RR	2.759 (0.749, 10.171); 0.1536
							RD	0.055 (-0.018, 0.159); 0.1791
Serious TEAEs								
Infections and infestations	9	6	7 (8.0)	5	7	5 (9.6)	OR	1.227 (0.385, 3.911); 0.7298
							RR	1.182 (0.408, 3.367); 0.7655
							RD	0.013 (-0.073, 0.121); 0.7698
Nervous system disorders	6	4	6 (6.8)	0	0	0 (0.0)	OR	0.119 (0.006, 2.205); 0.1530
							RR	1.067 (0.998, 1.149); 0.0143
							RD	0.063 (-0.001, 0.130); 0.0114
Neuromyelitis optica spectrum disorder	6	4	6 (6.8)	0	0	0 (0.0)	OR	0.119 (0.006, 2.205); 0.1530
							RR	1.067 (0.998, 1.149); 0.0143
							RD	0.063 (-0.001, 0.130); 0.0114
TEAEs leading to withdrawal from study drug								
Infections and infestations	0	0	0 (0.0)	3	4	1 (1.9)	OR	Not calculated
							RR	Not calculated
							RD	Not calculated
Bronchitis	0	0	0 (0.0)	1	1	1 (1.9)	OR	Not calculated
							RR	Not calculated
							RD	Not calculated
Encephalitis meningococcal	0	0	0 (0.0)	1	1	1 (1.9)	OR	Not calculated
							RR	Not calculated
							RD	Not calculated

Treatment Emergent Adverse Events (TEAEs) by MedDRA System Organ Class/Preferred Term by Severity and Treatment Group, Sex: Female

System Organ Class	Eculizumab (N=88) Patient-Years (PY)=159			Ravulizumab (N=52) Patient-Years (PY)=75.6			Treatment Effect	
Preferred Term	Events n	Rate per 100 PY	Patients n (%)	Events n	Rate per 100 PY	Patients n (%)	Estimate (95% CI; p-value)	
							OR	Not calculated
Stenotrophomonas infection	0	0	0 (0.0)	1	1	1 (1.9)	RR	Not calculated
							RD	Not calculated

AE: Adverse Event; CI: Confidence Interval; OR: Odds Ratio; PY: person years; RD: Risk Difference; RR: Risk Ratio; TEAE: Treatment-emergent Adverse Event.
TEAEs are AEs with a start date on or after the date of the first dose of study drug.
Treatment-related adverse events and follow-up were truncated at the maximum duration of follow-up in the ravulizumab arm.
Odds ratios were derived from a logistic regression model with treatment as the only covariate. Firth's correction was applied for odds ratios.
Mild, moderate and non-severe TEAEs were examined for preferred terms and system organ classes reported in at least 10% of patients in one of the treatment arms within the subgroup.
Severe and serious TEAEs were examined for preferred terms and system organ classes reported in at least 5% of patients in one of the treatment arms within the subgroup.
All TEAEs leading to withdrawal from study drug were examined.
TEAEs leading to withdrawal from study drug were examined descriptively (i.e., OR, RR, and RD not calculated).
Preferred terms and system organ classes for a given AE severity or type (i.e., leading for withdrawal) were only examined within each subgroup if they were also examined in the over

Treatment Emergent Adverse Events (TEAEs) by MedDRA System Organ Class/Preferred Term by Treatment Group, Sex: Male

System Organ Class	Eculizumab (N=8) Patient-Years (PY)=13.8			Ravulizumab (N=6) Patient-Years (PY)=8.4			Treatment Effect	
Preferred Term	Events n	Rate per 100 PY	Patients n (%)	Events n	Rate per 100 PY	Patients n (%)	Estimate (95% CI; p-value)	
Eye disorders	3	22	2 (25.0)	0	0	0 (0.0)	OR	0.323 (0.015, 7.018); 0.4719
							RR	1.021 (0.957, 1.079); 0.1573
							RD	0.021 (-0.042, 0.073); 0.1530
Gastrointestinal disorders	4	29	2 (25.0)	0	0	0 (0.0)	OR	0.323 (0.015, 7.018); 0.4719
							RR	1.021 (0.957, 1.079); 0.1573
							RD	0.021 (-0.042, 0.073); 0.1530
General disorders and administration site conditions	2	14	1 (12.5)	0	0	0 (0.0)	OR	0.544 (0.021, 13.922); 0.7130
							RR	1.011 (0.947, 1.060); 0.3173
							RD	0.010 (-0.052, 0.057); 0.3148
Infections and infestations	25	181	6 (75.0)	7	83	4 (66.7)	OR	1.150 (0.327, 4.041); 0.8280
							RR	0.993 (0.885, 1.084); 0.8761
							RD	-0.006 (-0.109, 0.074); 0.8760
COVID-19	0	0	0 (0.0)	1	12	1 (16.7)	OR	5.035 (0.198, 128.13); 0.3277
							RR	0.983 (0.908, 1.023); 0.3173
							RD	-0.017 (-0.092, 0.022); 0.3131
Nasopharyngitis	4	29	3 (37.5)	0	0	0 (0.0)	OR	0.228 (0.011, 4.611); 0.3354
							RR	1.032 (0.967, 1.097); 0.0833
							RD	0.031 (-0.032, 0.088); 0.0784
Pharyngitis	2	14	2 (25.0)	0	0	0 (0.0)	OR	0.323 (0.015, 7.018); 0.4719
							RR	1.021 (0.957, 1.079); 0.1573
							RD	0.021 (-0.042, 0.073); 0.1530
Upper respiratory tract infection	0	0	0 (0.0)	2	24	2 (33.3)	OR	8.540 (0.396, 184.30); 0.1712
							RR	0.966 (0.882, 1.005); 0.1573
							RD	-0.034 (-0.118, 0.005); 0.1501
Urinary tract infection	2	14	2 (25.0)	1	12	1 (16.7)	OR	0.986 (0.125, 7.779); 0.9893
							RR	1.004 (0.926, 1.063); 0.8729
							RD	0.004 (-0.073, 0.058); 0.8730
Injury, poisoning and procedural complications	6	43	3 (37.5)	5	59	2 (33.3)	OR	1.182 (0.223, 6.267); 0.8443
							RR	0.997 (0.908, 1.065); 0.9137
							RD	-0.003 (-0.089, 0.060); 0.9137
Contusion	1	7	1 (12.5)	0	0	0 (0.0)	OR	0.544 (0.021, 13.922); 0.7130
							RR	1.011 (0.947, 1.060); 0.3173
							RD	0.010 (-0.052, 0.057); 0.3148
Investigations	1	7	1 (12.5)	0	0	0 (0.0)	OR	0.544 (0.021, 13.922); 0.7130
							RR	1.011 (0.947, 1.060); 0.3173
							RD	0.010 (-0.052, 0.057); 0.3148
Musculoskeletal and connective tissue disorders	16	116	6 (75.0)	2	24	2 (33.3)	OR	0.616 (0.136, 2.782); 0.5289
							RR	1.030 (0.936, 1.117); 0.4159
							RD	0.028 (-0.061, 0.102); 0.4156
Arthralgia	1	7	1 (12.5)	0	0	0 (0.0)	OR	0.544 (0.021, 13.922); 0.7130
							RR	1.011 (0.947, 1.060); 0.3173
							RD	0.010 (-0.052, 0.057); 0.3148
Back pain	4	29	3 (37.5)	1	12	1 (16.7)	OR	0.697 (0.099, 4.925); 0.7173
							RR	1.014 (0.935, 1.081); 0.5699
							RD	0.014 (-0.063, 0.074); 0.5698
Pain in extremity	1	7	1 (12.5)	0	0	0 (0.0)	OR	0.544 (0.021, 13.922); 0.7130
							RR	1.011 (0.947, 1.060); 0.3173
							RD	0.010 (-0.052, 0.057); 0.3148
Nervous system disorders	4	29	3 (37.5)	0	0	0 (0.0)	OR	0.228 (0.011, 4.611); 0.3354
							RR	1.032 (0.967, 1.097); 0.0833
							RD	0.031 (-0.032, 0.088); 0.0784
Headache	2	14	2 (25.0)	0	0	0 (0.0)	OR	0.323 (0.015, 7.018); 0.4719
							RR	1.021 (0.957, 1.079); 0.1573
							RD	0.021 (-0.042, 0.073); 0.1530
Renal and urinary disorders	2	14	1 (12.5)	0	0	0 (0.0)	OR	0.544 (0.021, 13.922); 0.7130
							RR	1.011 (0.947, 1.060); 0.3173
							RD	0.010 (-0.052, 0.057); 0.3148
Reproductive system and breast disorders	1	7	1 (12.5)	0	0	0 (0.0)	OR	0.544 (0.021, 13.922); 0.7130
							RR	1.011 (0.947, 1.060); 0.3173
							RD	0.010 (-0.052, 0.057); 0.3148
Respiratory, thoracic and mediastinal disorders	3	22	2 (25.0)	1	12	1 (16.7)	OR	0.986 (0.125, 7.779); 0.9893
							RR	1.004 (0.926, 1.063); 0.8729
							RD	0.004 (-0.073, 0.058); 0.8730
Skin and subcutaneous tissue disorders	7	51	3 (37.5)	0	0	0 (0.0)	OR	0.228 (0.011, 4.611); 0.3354
							RR	1.032 (0.967, 1.097); 0.0833

System Organ Class Preferred Term	Eculizumab (N=8) Patient-Years (PY)=13.8 Events n	Rate per 100 PY	Patients n (%)	Ravulizumab (N=6) Patient-Years (PY)=8.4 Events n	Rate per 100 PY	Patients n (%)	Treatment Effect Estimate (95% CI; p-value)	
							RD	0.031 (-0.032, 0.088); 0.0784
							OR	0.323 (0.015, 7.018); 0.4719
Vascular disorders	2	14	2 (25.0)	0	0	0 (0.0)	RR	1.021 (0.957, 1.079); 0.1573
							RD	0.021 (-0.042, 0.073); 0.1530

AE: Adverse Event; CI: Confidence Interval; OR: Odds Ratio; PY: person years; RD: Risk Difference; RR: Risk Ratio; TEAE: Treatment-emergent Adverse Event.
TEAEs are AEs with a start date on or after the date of the first dose of study drug.
Treatment-related adverse events and follow-up were truncated at the maximum duration of follow-up in the ravulizumab arm.
Odds ratios were derived from a logistic regression model with treatment as the only covariate. Firth's correction was applied for odds ratios.
Any TEAEs were examined for preferred terms and system organ classes reported in at least 10% of patients in one of the treatment arms within the subgroup.
Severe and serious TEAEs were examined for preferred terms and system organ classes reported in at least 5% of patients in one of the treatment arms within the subgroup.
Preferred terms and system organ classes for a given AE severity or type (i.e., leading for withdrawal) were only examined within each subgroup if they were also examined in

Treatment Emergent Adverse Events (TEAEs) by MedDRA System Organ Class/Preferred Term by Severity and Treatment Group, Sex: Male

System Organ Class / Preferred Term	Eculizumab (N=8) Patient-Years (PY)=13.8 Events n	Rate per 100 PY	Patients n (%)	Ravulizumab (N=6) Patient-Years (PY)=8.4 Events n	Rate per 100 PY	Patients n (%)	Treatment Effect	Estimate (95% CI; p-value)
Mild TEAEs								
Eye disorders	3	22	2 (25.0)	0	0	0 (0.0)	OR	0.323 (0.015, 7.018); 0.4719
							RR	1.021 (0.957, 1.079); 0.1573
							RD	0.021 (-0.042, 0.073); 0.1530
Gastrointestinal disorders	3	22	2 (25.0)	0	0	0 (0.0)	OR	0.323 (0.015, 7.018); 0.4719
							RR	1.021 (0.957, 1.079); 0.1573
							RD	0.021 (-0.042, 0.073); 0.1530
General disorders and administration site conditions	2	14	1 (12.5)	0	0	0 (0.0)	OR	0.544 (0.021, 13.922); 0.7130
							RR	1.011 (0.947, 1.060); 0.3173
							RD	0.010 (-0.052, 0.057); 0.3148
Infections and infestations	20	145	6 (75.0)	5	59	3 (50.0)	OR	0.878 (0.227, 3.393); 0.8504
							RR	1.011 (0.910, 1.100); 0.7774
							RD	0.011 (-0.085, 0.088); 0.7776
COVID-19	0	0	0 (0.0)	1	12	1 (16.7)	OR	5.035 (0.198, 128.13); 0.3277
							RR	0.983 (0.908, 1.023); 0.3173
							RD	-0.017 (-0.092, 0.022); 0.3131
Nasopharyngitis	4	29	3 (37.5)	0	0	0 (0.0)	OR	0.228 (0.011, 4.611); 0.3354
							RR	1.032 (0.967, 1.097); 0.0833
							RD	0.031 (-0.032, 0.088); 0.0784
Upper respiratory tract infection	0	0	0 (0.0)	1	12	1 (16.7)	OR	5.035 (0.198, 128.13); 0.3277
							RR	0.983 (0.908, 1.023); 0.3173
							RD	-0.017 (-0.092, 0.022); 0.3131
Urinary tract infection	2	14	2 (25.0)	1	12	1 (16.7)	OR	0.986 (0.125, 7.779); 0.9893
							RR	1.004 (0.926, 1.063); 0.8729
							RD	0.004 (-0.073, 0.058); 0.8730
Injury, poisoning and procedural complications	6	43	3 (37.5)	0	0	0 (0.0)	OR	0.228 (0.011, 4.611); 0.3354
							RR	1.032 (0.967, 1.097); 0.0833
							RD	0.031 (-0.032, 0.088); 0.0784
Investigations	1	7	1 (12.5)	0	0	0 (0.0)	OR	0.544 (0.021, 13.922); 0.7130
							RR	1.011 (0.947, 1.060); 0.3173
							RD	0.010 (-0.052, 0.057); 0.3148
Musculoskeletal and connective tissue disorders	12	87	6 (75.0)	0	0	0 (0.0)	OR	0.119 (0.006, 2.205); 0.1530
							RR	1.067 (0.998, 1.149); 0.0143
							RD	0.063 (-0.001, 0.130); 0.0114
Nervous system disorders	4	29	3 (37.5)	0	0	0 (0.0)	OR	0.228 (0.011, 4.611); 0.3354
							RR	1.032 (0.967, 1.097); 0.0833
							RD	0.031 (-0.032, 0.088); 0.0784
Headache	2	14	2 (25.0)	0	0	0 (0.0)	OR	0.323 (0.015, 7.018); 0.4719
							RR	1.021 (0.957, 1.079); 0.1573
							RD	0.021 (-0.042, 0.073); 0.1530
Renal and urinary disorders	1	7	1 (12.5)	0	0	0 (0.0)	OR	0.544 (0.021, 13.922); 0.7130
							RR	1.011 (0.947, 1.060); 0.3173
							RD	0.010 (-0.052, 0.057); 0.3148
Reproductive system and breast disorders	1	7	1 (12.5)	0	0	0 (0.0)	OR	0.544 (0.021, 13.922); 0.7130
							RR	1.011 (0.947, 1.060); 0.3173
							RD	0.010 (-0.052, 0.057); 0.3148

Treatment Emergent Adverse Events (TEAEs) by MedDRA System Organ Class/Preferred Term by Severity and Treatment Group, Sex: Male

System Organ Class / Preferred Term	Eculizumab (N=8) Patient-Years (PY)=13.8 Events n	Rate per 100 PY	Patients n (%)	Ravulizumab (N=6) Patient-Years (PY)=8.4 Events n	Rate per 100 PY	Patients n (%)	Treatment Effect	Estimate (95% CI; p-value)
Respiratory, thoracic and mediastinal disorders	1	7	1 (12.5)	1	12	1 (16.7)	OR	1.661 (0.166, 16.607); 0.6658
							RR	0.993 (0.917, 1.044); 0.7332
							RD	-0.007 (-0.082, 0.042); 0.7328
Skin and subcutaneous tissue disorders	7	51	3 (37.5)	0	0	0 (0.0)	OR	0.228 (0.011, 4.611); 0.3354
							RR	1.032 (0.967, 1.097); 0.0833
							RD	0.031 (-0.032, 0.088); 0.0784
ModerateTEAEs								
Gastrointestinal disorders	1	7	1 (12.5)	0	0	0 (0.0)	OR	0.544 (0.021, 13.922); 0.7130
							RR	1.011 (0.947, 1.060); 0.3173
							RD	0.010 (-0.052, 0.057); 0.3148
Infections and infestations	1	7	1 (12.5)	2	24	2 (33.3)	OR	2.817 (0.358, 22.193); 0.3254
							RR	0.976 (0.891, 1.029); 0.3607
							RD	-0.024 (-0.108, 0.027); 0.3566
Injury, poisoning and procedural complications	0	0	0 (0.0)	5	59	2 (33.3)	OR	8.540 (0.396, 184.30); 0.1712
							RR	0.966 (0.882, 1.005); 0.1573
							RD	-0.034 (-0.118, 0.005); 0.1501
Musculoskeletal and connective tissue disorders	3	22	2 (25.0)	2	24	2 (33.3)	OR	1.673 (0.278, 10.081); 0.5744
							RR	0.986 (0.899, 1.047); 0.6276
							RD	-0.014 (-0.099, 0.044); 0.6265
Non-SevereTEAEs								
Eye disorders	3	22	2 (25.0)	0	0	0 (0.0)	OR	0.323 (0.015, 7.018); 0.4719
							RR	1.021 (0.957, 1.079); 0.1573
							RD	0.021 (-0.042, 0.073); 0.1530
Gastrointestinal disorders	4	29	2 (25.0)	0	0	0 (0.0)	OR	0.323 (0.015, 7.018); 0.4719
							RR	1.021 (0.957, 1.079); 0.1573
							RD	0.021 (-0.042, 0.073); 0.1530
General disorders and administration site conditions	2	14	1 (12.5)	0	0	0 (0.0)	OR	0.544 (0.021, 13.922); 0.7130
							RR	1.011 (0.947, 1.060); 0.3173
							RD	0.010 (-0.052, 0.057); 0.3148
Infections and infestations	21	152	6 (75.0)	7	83	4 (66.7)	OR	1.150 (0.327, 4.041); 0.8280
							RR	0.993 (0.885, 1.084); 0.8761
							RD	-0.006 (-0.109, 0.074); 0.8760
COVID-19	0	0	0 (0.0)	1	12	1 (16.7)	OR	5.035 (0.198, 128.13); 0.3277
							RR	0.983 (0.908, 1.023); 0.3173
							RD	-0.017 (-0.092, 0.022); 0.3131
Nasopharyngitis	4	29	3 (37.5)	0	0	0 (0.0)	OR	0.228 (0.011, 4.611); 0.3354
							RR	1.032 (0.967, 1.097); 0.0833
							RD	0.031 (-0.032, 0.088); 0.0784
Pharyngitis	2	14	2 (25.0)	0	0	0 (0.0)	OR	0.323 (0.015, 7.018); 0.4719
							RR	1.021 (0.957, 1.079); 0.1573
							RD	0.021 (-0.042, 0.073); 0.1530
Upper respiratory tract infection	0	0	0 (0.0)	2	24	2 (33.3)	OR	8.540 (0.396, 184.30); 0.1712
							RR	0.966 (0.882, 1.005); 0.1573
							RD	-0.034 (-0.118, 0.005); 0.1501
Urinary tract infection	2	14	2 (25.0)	1	12	1 (16.7)	OR	0.986 (0.125, 7.779); 0.9893
							RR	1.004 (0.926, 1.063); 0.8729
							RD	0.004 (-0.073, 0.058); 0.8730
Injury, poisoning and procedural complications	6	43	3 (37.5)	5	59	2 (33.3)	OR	1.182 (0.223, 6.267); 0.8443
							RR	0.997 (0.908, 1.065); 0.9137
							RD	-0.003 (-0.089, 0.060); 0.9137
Contusion	1	7	1 (12.5)	0	0	0 (0.0)	OR	0.544 (0.021, 13.922); 0.7130
							RR	1.011 (0.947, 1.060); 0.3173
							RD	0.010 (-0.052, 0.057); 0.3148
Investigations	1	7	1 (12.5)	0	0	0 (0.0)	OR	0.544 (0.021, 13.922); 0.7130
							RR	1.011 (0.947, 1.060); 0.3173
							RD	0.010 (-0.052, 0.057); 0.3148
Musculoskeletal and connective tissue disorders	15	108	6 (75.0)	2	24	2 (33.3)	OR	0.616 (0.136, 2.782); 0.5289
							RR	1.030 (0.936, 1.117); 0.4159
							RD	0.028 (-0.061, 0.102); 0.4156
Arthralgia	1	7	1 (12.5)	0	0	0 (0.0)	OR	0.544 (0.021, 13.922); 0.7130
							RR	1.011 (0.947, 1.060); 0.3173
							RD	0.010 (-0.052, 0.057); 0.3148
Back pain	4	29	3 (37.5)	1	12	1 (16.7)	OR	0.697 (0.099, 4.925); 0.7173
							RR	1.014 (0.935, 1.081); 0.5699
							RD	0.014 (-0.063, 0.074); 0.5698
Nervous system disorders	4	29	3 (37.5)	0	0	0 (0.0)	OR	0.228 (0.011, 4.611); 0.3354
							RR	1.032 (0.967, 1.097); 0.0833
							RD	0.031 (-0.032, 0.088); 0.0784

Treatment Emergent Adverse Events (TEAEs) by MedDRA System Organ Class/Preferred Term by Severity and Treatment Group, Sex: Male

System Organ Class / Preferred Term	Eculizumab (N=8) Patient-Years (PY)=13.8 Events n	Rate per 100 PY	Patients n (%)	Ravulizumab (N=6) Patient-Years (PY)=8.4 Events n	Rate per 100 PY	Patients n (%)	Treatment Effect	Estimate (95% CI; p-value)
Headache	2	14	2 (25.0)	0	0	0 (0.0)	OR	0.323 (0.015, 7.018); 0.4719
							RR	1.021 (0.957, 1.079); 0.1573
							RD	0.021 (-0.042, 0.073); 0.1530
Renal and urinary disorders	2	14	1 (12.5)	0	0	0 (0.0)	OR	0.544 (0.021, 13.922); 0.7130
							RR	1.011 (0.947, 1.060); 0.3173
							RD	0.010 (-0.052, 0.057); 0.3148
Reproductive system and breast disorders	1	7	1 (12.5)	0	0	0 (0.0)	OR	0.544 (0.021, 13.922); 0.7130
							RR	1.011 (0.947, 1.060); 0.3173
							RD	0.010 (-0.052, 0.057); 0.3148
Respiratory, thoracic and mediastinal disorders	2	14	2 (25.0)	1	12	1 (16.7)	OR	0.986 (0.125, 7.779); 0.9893
							RR	1.004 (0.926, 1.063); 0.8729
							RD	0.004 (-0.073, 0.058); 0.8730
Skin and subcutaneous tissue disorders	7	51	3 (37.5)	0	0	0 (0.0)	OR	0.228 (0.011, 4.611); 0.3354
							RR	1.032 (0.967, 1.097); 0.0833
							RD	0.031 (-0.032, 0.088); 0.0784
Vascular disorders	2	14	2 (25.0)	0	0	0 (0.0)	OR	0.323 (0.015, 7.018); 0.4719
							RR	1.021 (0.957, 1.079); 0.1573
							RD	0.021 (-0.042, 0.073); 0.1530
Severe TEAEs								
Infections and infestations	4	29	2 (25.0)	0	0	0 (0.0)	OR	0.323 (0.015, 7.018); 0.4719
							RR	1.021 (0.957, 1.079); 0.1573
							RD	0.021 (-0.042, 0.073); 0.1530
Serious TEAEs								
Infections and infestations	4	29	2 (25.0)	0	0	0 (0.0)	OR	0.323 (0.015, 7.018); 0.4719
							RR	1.021 (0.957, 1.079); 0.1573
							RD	0.021 (-0.042, 0.073); 0.1530
TEAEs leading to withdrawal from study drug								
None								

AE: Adverse Event; CI: Confidence Interval; OR: Odds Ratio; PY: person years; RD: Risk Difference; RR: Risk Ratio; TEAE: Treatment-emergent Adverse Event.
TEAEs are AEs with a start date on or after the date of the first dose of study drug.
Treatment-related adverse events and follow-up were truncated at the maximum duration of follow-up in the ravulizumab arm.
Odds ratios were derived from a logistic regression model with treatment as the only covariate. Firth's correction was applied for odds ratios.
Mild, moderate and non-severe TEAEs were examined for preferred terms and system organ classes reported in at least 10% of patients in one of the treatment arms within the subgroup.
Severe and serious TEAEs were examined for preferred terms and system organ classes reported in at least 5% of patients in one of the treatment arms within the subgroup.
All TEAEs leading to withdrawal from study drug were examined.
TEAEs leading to withdrawal from study drug were examined descriptively (i.e., OR, RR, and RD not calculated).
Preferred terms and system organ classes for a given AE severity or type (i.e., leading for withdrawal) were only examined within each subgroup if they were also examined in the over

Treatment Emergent Adverse Events (TEAEs) by MedDRA System Organ Class/Preferred Term by Treatment Group, Age: < 45 years

System Organ Class	Eculizumab (N=47) Patient-Years (PY)=79.8			Ravulizumab (N=25) Patient-Years (PY)=36.8			Treatment Effect	
Preferred Term	Events n	Rate per 100 PY	Patients n (%)	Events n	Rate per 100 PY	Patients n (%)	Estimate (95% CI; p-value)	
Blood and lymphatic system disorders	16	20	10 (21.3)	2	5	2 (8.0)	OR	0.364 (0.087, 1.524); 0.1668
							RR	0.331 (0.083, 1.278); 0.1439
							RD	-0.070 (-0.154, 0.023); 0.0764
Eye disorders	18	23	9 (19.1)	6	16	4 (16.0)	OR	0.760 (0.234, 2.476); 0.6493
							RR	1.027 (0.913, 1.135); 0.5782
							RD	0.025 (-0.080, 0.113); 0.5787
Gastrointestinal disorders	78	98	18 (38.3)	12	33	9 (36.0)	OR	0.814 (0.343, 1.936); 0.6420
							RR	1.040 (0.881, 1.203); 0.6011
							RD	0.032 (-0.100, 0.150); 0.6022
Diarrhoea	10	13	5 (10.6)	2	5	2 (8.0)	OR	0.736 (0.157, 3.443); 0.6971
							RR	1.019 (0.926, 1.100); 0.5935
							RD	0.018 (-0.070, 0.088); 0.5937
Nausea	20	25	9 (19.1)	1	3	1 (4.0)	OR	0.240 (0.041, 1.408); 0.1140
							RR	1.084 (0.994, 1.186); 0.0291
							RD	0.077 (-0.006, 0.155); 0.0258
General disorders and administration site conditions	29	36	10 (21.3)	23	63	11 (44.0)	OR	1.995 (0.799, 4.979); 0.1390
							RR	0.905 (0.764, 1.031); 0.1662
							RD	-0.085 (-0.216, 0.026); 0.1555
Infections and infestations	147	184	35 (74.5)	32	87	16 (64.0)	OR	0.673 (0.331, 1.365); 0.2721
							RR	0.757 (0.456, 1.216); 0.2681
							RD	-0.089 (-0.232, 0.067); 0.2464
COVID-19	0	0	0 (0.0)	7	19	7 (28.0)	OR	28.108 (1.549, 510.01); 0.0241
							RR	0.879 (0.771, 0.940); 0.0082
							RD	-0.121 (-0.229, -0.060); 0.0048
Nasopharyngitis	25	31	12 (25.5)	2	5	2 (8.0)	OR	0.299 (0.073, 1.225); 0.0934
							RR	1.103 (0.995, 1.224); 0.0319
							RD	0.091 (-0.004, 0.178); 0.0288
Pharyngitis	10	13	7 (14.9)	0	0	0 (0.0)	OR	0.102 (0.006, 1.864); 0.1236
							RR	1.079 (1.009, 1.167); 0.0082
							RD	0.073 (0.009, 0.143); 0.0060
Upper respiratory tract infection	26	33	17 (36.2)	3	8	3 (12.0)	OR	0.286 (0.086, 0.958); 0.0424
							RR	0.292 (0.093, 0.875); 0.0415
							RD	-0.125 (-0.224, -0.018); 0.0099
Urinary tract infection	13	16	5 (10.6)	1	3	1 (4.0)	OR	0.434 (0.068, 2.759); 0.3764
							RR	1.037 (0.954, 1.116); 0.2223
							RD	0.035 (-0.044, 0.102); 0.2198
Injury, poisoning and procedural complications	13	16	11 (23.4)	10	27	7 (28.0)	OR	1.083 (0.402, 2.913); 0.8750
							RR	1.053 (0.439, 2.478); 0.9089
							RD	0.006 (-0.096, 0.126); 0.9095
Musculoskeletal and connective tissue disorders	38	48	20 (42.6)	14	38	12 (48.0)	OR	1.003 (0.452, 2.228); 0.9938
							RR	0.993 (0.523, 1.843); 0.9830
							RD	-0.001 (-0.128, 0.139); 0.9830
Arthralgia	2	3	2 (4.3)	3	8	3 (12.0)	OR	2.384 (0.450, 12.631); 0.3073
							RR	2.483 (0.505, 12.192); 0.3110
							RD	0.031 (-0.030, 0.123); 0.3423
Back pain	8	10	8 (17.0)	2	5	2 (8.0)	OR	0.461 (0.107, 1.984); 0.2983
							RR	1.053 (0.955, 1.151); 0.1891
							RD	0.049 (-0.042, 0.128); 0.1869
Nervous system disorders	85	107	20 (42.6)	29	79	11 (44.0)	OR	0.903 (0.400, 2.038); 0.8068
							RR	0.910 (0.469, 1.723); 0.7802
							RD	-0.019 (-0.143, 0.120); 0.7775
Dizziness	4	5	3 (6.4)	4	11	4 (16.0)	OR	2.206 (0.520, 9.365); 0.2836
							RR	2.207 (0.566, 8.580); 0.2883
							RD	0.038 (-0.032, 0.137); 0.3173
Headache	66	83	13 (27.7)	14	38	9 (36.0)	OR	1.187 (0.479, 2.943); 0.7114
							RR	0.977 (0.833, 1.114); 0.7386
							RD	-0.020 (-0.148, 0.091); 0.7377
Psychiatric disorders	5	6	4 (8.5)	8	22	4 (16.0)	OR	1.698 (0.437, 6.602); 0.4450
							RR	0.972 (0.868, 1.051); 0.4872
							RD	-0.027 (-0.127, 0.046); 0.4842
Renal and urinary disorders	6	8	5 (10.6)	1	3	1 (4.0)	OR	0.434 (0.068, 2.759); 0.3764
							RR	1.037 (0.954, 1.116); 0.2223
							RD	0.035 (-0.044, 0.102); 0.2198
Reproductive system and breast disorders	9	11	5 (10.6)	2	5	2 (8.0)	OR	0.736 (0.157, 3.443); 0.6971
							RR	1.019 (0.926, 1.100); 0.5935

System Organ Class / Preferred Term	Eculizumab (N=47) Patient-Years (PY)=79.8 Events n	Rate per 100 PY	Patients n (%)	Ravulizumab (N=25) Patient-Years (PY)=36.8 Events n	Rate per 100 PY	Patients n (%)	Treatment Effect	Estimate (95% CI; p-value)
							RD	0.018 (-0.070, 0.088); 0.5937
							OR	0.829 (0.319, 2.153); 0.6995
Respiratory, thoracic and mediastinal disorders	27	34	14 (29.8)	7	19	7 (28.0)	RR	1.029 (0.889, 1.168); 0.6523
							RD	0.025 (-0.098, 0.132); 0.6530
							OR	0.616 (0.136, 2.782); 0.5289
Cough	7	9	6 (12.8)	2	5	2 (8.0)	RR	1.030 (0.936, 1.117); 0.4159
							RD	0.028 (-0.061, 0.102); 0.4156
							OR	1.297 (0.517, 3.256); 0.5794
Skin and subcutaneous tissue disorders	15	19	12 (25.5)	12	33	9 (36.0)	RR	1.241 (0.562, 2.696); 0.5965
							RD	0.030 (-0.079, 0.157); 0.6048

AE: Adverse Event; CI: Confidence Interval; OR: Odds Ratio; PY: person years; RD: Risk Difference; RR: Risk Ratio; TEAE: Treatment-emergent Adverse Event.
TEAEs are AEs with a start date on or after the date of the first dose of study drug.
Treatment-related adverse events and follow-up were truncated at the maximum duration of follow-up in the ravulizumab arm.
Odds ratios were derived from a logistic regression model with treatment as the only covariate. Firth's correction was applied for odds ratios.
Any TEAEs were examined for preferred terms and system organ classes reported in at least 10% of patients in one of the treatment arms within the subgroup.
Severe and serious TEAEs were examined for preferred terms and system organ classes reported in at least 5% of patients in one of the treatment arms within the subgroup.

Treatment Emergent Adverse Events (TEAEs) by MedDRA System Organ Class/Preferred Term by Severity and Treatment Group, Age: < 45 years

System Organ Class / Preferred Term	Eculizumab (N=47) Patient-Years (PY)=79.8 Events n	Rate per 100 PY	Patients n (%)	Ravulizumab (N=25) Patient-Years (PY)=36.8 Events n	Rate per 100 PY	Patients n (%)	Treatment Effect Estimate (95% CI; p-value)
Mild TEAEs							
Blood and lymphatic system disorders	10	13	6 (12.8)	2	5	2 (8.0)	OR 0.616 (0.136, 2.782); 0.5289 RR 0.552 (0.129, 2.297); 0.4569 RD -0.028 (-0.102, 0.061); 0.4156
Eye disorders	12	15	9 (19.1)	4	11	3 (12.0)	OR 0.581 (0.161, 2.091); 0.4058 RR 1.046 (0.938, 1.152); 0.3129 RD 0.042 (-0.057, 0.127); 0.3124
Gastrointestinal disorders	65	81	16 (34.0)	10	27	8 (32.0)	OR 0.821 (0.332, 2.032); 0.6699 RR 1.034 (0.885, 1.185); 0.6261 RD 0.029 (-0.099, 0.141); 0.6270
Diarrhoea	8	10	5 (10.6)	2	5	2 (8.0)	OR 0.736 (0.157, 3.443); 0.6971 RR 1.019 (0.926, 1.100); 0.5935 RD 0.018 (-0.070, 0.088); 0.5937
Nausea	16	20	7 (14.9)	1	3	1 (4.0)	OR 0.311 (0.052, 1.880); 0.2034 RR 1.060 (0.974, 1.150); 0.0816 RD 0.056 (-0.025, 0.129); 0.0778
General disorders and administration site conditions	24	30	7 (14.9)	19	52	9 (36.0)	OR 2.290 (0.821, 6.385); 0.1132 RR 0.911 (0.782, 1.020); 0.1411 RD -0.082 (-0.205, 0.017); 0.1308
Infections and infestations	117	147	32 (68.1)	20	54	12 (48.0)	OR 0.534 (0.250, 1.140); 0.1048 RR 1.190 (0.969, 1.446); 0.0779 RD 0.126 (-0.022, 0.261); 0.0779
COVID-19	0	0	0 (0.0)	6	16	6 (24.0)	OR 23.896 (1.299, 439.49); 0.0327 RR 0.897 (0.792, 0.952); 0.0144 RD -0.103 (-0.208, -0.048); 0.0097
Nasopharyngitis	20	25	10 (21.3)	1	3	1 (4.0)	OR 0.215 (0.037, 1.246); 0.0863 RR 1.097 (1.004, 1.204); 0.0173 RD 0.087 (0.004, 0.167); 0.0145
Upper respiratory tract infection	24	30	17 (36.2)	2	5	2 (8.0)	OR 0.201 (0.051, 0.799); 0.0226 RR 1.173 (1.050, 1.322); 0.0028 RD 0.143 (0.043, 0.238); 0.0018
Injury, poisoning and procedural complications	10	13	8 (17.0)	2	5	2 (8.0)	OR 0.461 (0.107, 1.984); 0.2983 RR 1.053 (0.955, 1.151); 0.1891 RD 0.049 (-0.042, 0.128); 0.1869
Musculoskeletal and connective tissue disorders	25	31	14 (29.8)	9	24	7 (28.0)	OR 0.829 (0.319, 2.153); 0.6995 RR 1.029 (0.889, 1.168); 0.6523 RD 0.025 (-0.098, 0.132); 0.6530
Nervous system disorders	74	93	17 (36.2)	22	60	9 (36.0)	OR 0.872 (0.364, 2.086); 0.7580 RR 0.876 (0.419, 1.788); 0.7262 RD -0.022 (-0.138, 0.110); 0.7215
Dizziness	2	3	2 (4.3)	3	8	3 (12.0)	OR 2.384 (0.450, 12.631); 0.3073 RR 2.483 (0.505, 12.192); 0.3110 RD 0.031 (-0.030, 0.123); 0.3423
Headache	61	76	11 (23.4)	9	24	6 (24.0)	OR 0.921 (0.329, 2.575); 0.8746 RR 1.013 (0.884, 1.134); 0.8287 RD 0.011 (-0.105, 0.110); 0.8289
Psychiatric disorders	4	5	3 (6.4)	3	8	3 (12.0)	OR 1.685 (0.365, 7.773); 0.5035 RR 0.979 (0.883, 1.050); 0.5499 RD -0.020 (-0.114, 0.046); 0.5479
Reproductive system and breast disorders	9	11	5 (10.6)	2	5	2 (8.0)	OR 0.736 (0.157, 3.443); 0.6971 RR 1.019 (0.926, 1.100); 0.5935 RD 0.018 (-0.070, 0.088); 0.5937

Treatment Emergent Adverse Events (TEAEs) by MedDRA System Organ Class/Preferred Term by Severity and Treatment Group, Age: < 45 years

System Organ Class / Preferred Term	Eculizumab (N=47) Patient-Years (PY)=79.8 Events n	Rate per 100 PY	Patients n (%)	Ravulizumab (N=25) Patient-Years (PY)=36.8 Events n	Rate per 100 PY	Patients n (%)	Treatment Effect Estimate (95% CI; p-value)
							OR 0.921 (0.329, 2.575); 0.8746
Respiratory, thoracic and mediastinal disorders	23	29	11 (23.4)	6	16	6 (24.0)	RR 1.013 (0.884, 1.134); 0.8287
							RD 0.011 (-0.105, 0.110); 0.8289
							OR 0.736 (0.157, 3.443); 0.6971
Cough	6	8	5 (10.6)	2	5	2 (8.0)	RR 1.019 (0.926, 1.100); 0.5935
							RD 0.018 (-0.070, 0.088); 0.5937
							OR 0.837 (0.303, 2.312); 0.7313
Skin and subcutaneous tissue disorders	14	18	12 (25.5)	9	24	6 (24.0)	RR 0.828 (0.334, 2.002); 0.6882
							RD -0.022 (-0.122, 0.096); 0.6805
ModerateTEAEs							
							OR 0.461 (0.107, 1.984); 0.2983
Gastrointestinal disorders	11	14	8 (17.0)	2	5	2 (8.0)	RR 1.053 (0.955, 1.151); 0.1891
							RD 0.049 (-0.042, 0.128); 0.1869
							OR 1.138 (0.442, 2.928); 0.7890
Infections and infestations	25	31	12 (25.5)	9	24	8 (32.0)	RR 1.103 (0.484, 2.466); 0.8169
							RD 0.013 (-0.093, 0.137); 0.8189
							OR 3.121 (0.635, 15.332); 0.1611
Injury, poisoning and procedural complications	2	3	2 (4.3)	7	19	4 (16.0)	RR 3.310 (0.725, 15.167); 0.1590
							RD 0.048 (-0.016, 0.146); 0.1852
							OR 0.760 (0.234, 2.476); 0.6493
Musculoskeletal and connective tissue disorders	12	15	9 (19.1)	4	11	4 (16.0)	RR 0.736 (0.247, 2.139); 0.5949
							RD -0.025 (-0.113, 0.080); 0.5787
Non-SevereTEAEs							
							OR 0.364 (0.087, 1.524); 0.1668
Blood and lymphatic system disorders	16	20	10 (21.3)	2	5	2 (8.0)	RR 0.331 (0.083, 1.278); 0.1439
							RD -0.070 (-0.154, 0.023); 0.0764
							OR 0.760 (0.234, 2.476); 0.6493
Eye disorders	18	23	9 (19.1)	6	16	4 (16.0)	RR 1.027 (0.913, 1.135); 0.5782
							RD 0.025 (-0.080, 0.113); 0.5787
							OR 0.872 (0.364, 2.086); 0.7580
Gastrointestinal disorders	76	95	17 (36.2)	12	33	9 (36.0)	RR 1.027 (0.871, 1.184); 0.7209
							RD 0.022 (-0.110, 0.138); 0.7215
							OR 0.736 (0.157, 3.443); 0.6971
Diarrhoea	10	13	5 (10.6)	2	5	2 (8.0)	RR 1.019 (0.926, 1.100); 0.5935
							RD 0.018 (-0.070, 0.088); 0.5937
							OR 0.240 (0.041, 1.408); 0.1140
Nausea	20	25	9 (19.1)	1	3	1 (4.0)	RR 1.084 (0.994, 1.186); 0.0291
							RD 0.077 (-0.006, 0.155); 0.0258
							OR 1.995 (0.799, 4.979); 0.1390
General disorders and administration site conditions	29	36	10 (21.3)	22	60	11 (44.0)	RR 0.905 (0.764, 1.031); 0.1662
							RD -0.085 (-0.216, 0.026); 0.1555
							OR 0.673 (0.331, 1.365); 0.2721
Infections and infestations	142	178	35 (74.5)	29	79	16 (64.0)	RR 0.757 (0.456, 1.216); 0.2681
							RD -0.089 (-0.232, 0.067); 0.2464
							OR 28.108 (1.549, 510.01); 0.0241
COVID-19	0	0	0 (0.0)	7	19	7 (28.0)	RR 0.879 (0.771, 0.940); 0.0082
							RD -0.121 (-0.229, -0.060); 0.0048
							OR 0.299 (0.073, 1.225); 0.0934
Nasopharyngitis	25	31	12 (25.5)	2	5	2 (8.0)	RR 1.103 (0.995, 1.224); 0.0319
							RD 0.091 (-0.004, 0.178); 0.0288
							OR 0.102 (0.006, 1.864); 0.1236
Pharyngitis	10	13	7 (14.9)	0	0	0 (0.0)	RR 1.079 (1.009, 1.167); 0.0082
							RD 0.073 (0.009, 0.143); 0.0060
							OR 0.286 (0.086, 0.958); 0.0424
Upper respiratory tract infection	26	33	17 (36.2)	3	8	3 (12.0)	RR 0.292 (0.093, 0.875); 0.0415
							RD -0.125 (-0.224, -0.018); 0.0099
							OR 0.434 (0.068, 2.759); 0.3764
Urinary tract infection	13	16	5 (10.6)	1	3	1 (4.0)	RR 1.037 (0.954, 1.116); 0.2223
							RD 0.035 (-0.044, 0.102); 0.2198
							OR 1.020 (0.359, 2.898); 0.9699
Injury, poisoning and procedural complications	12	15	10 (21.3)	9	24	6 (24.0)	RR 0.993 (0.389, 2.485); 0.9887
							RD -0.001 (-0.097, 0.115); 0.9887
							OR 0.903 (0.400, 2.038); 0.8068
Musculoskeletal and connective tissue disorders	37	46	20 (42.6)	13	35	11 (44.0)	RR 0.910 (0.469, 1.723); 0.7802
							RD -0.019 (-0.143, 0.120); 0.7775
							OR 2.384 (0.450, 12.631); 0.3073
Arthralgia	2	3	2 (4.3)	3	8	3 (12.0)	RR 2.483 (0.505, 12.192); 0.3110
							RD 0.031 (-0.030, 0.123); 0.3423

Treatment Emergent Adverse Events (TEAEs) by MedDRA System Organ Class/Preferred Term by Severity and Treatment Group, Age: < 45 years

System Organ Class / Preferred Term	Eculizumab (N=47) Patient-Years (PY)=79.8 Events n	Rate per 100 PY	Patients n (%)	Ravulizumab (N=25) Patient-Years (PY)=36.8 Events n	Rate per 100 PY	Patients n (%)	Treatment Effect	Estimate (95% CI; p-value)
							OR	0.272 (0.046, 1.613); 0.1516
Back pain	8	10	8 (17.0)	1	3	1 (4.0)	RR	1.072 (0.984, 1.168); 0.0489
							RD	0.066 (-0.015, 0.142); 0.0451
							OR	0.903 (0.400, 2.038); 0.8068
Nervous system disorders	83	104	20 (42.6)	28	76	11 (44.0)	RR	0.910 (0.469, 1.723); 0.7802
							RD	-0.019 (-0.143, 0.120); 0.7775
							OR	1.685 (0.365, 7.773); 0.5035
Dizziness	4	5	3 (6.4)	3	8	3 (12.0)	RR	1.655 (0.389, 6.985); 0.5285
							RD	0.020 (-0.046, 0.114); 0.5479
							OR	1.187 (0.479, 2.943); 0.7114
Headache	64	80	13 (27.7)	14	38	9 (36.0)	RR	0.977 (0.833, 1.114); 0.7386
							RD	-0.020 (-0.148, 0.091); 0.7377
							OR	1.698 (0.437, 6.602); 0.4450
Psychiatric disorders	5	6	4 (8.5)	7	19	4 (16.0)	RR	0.972 (0.868, 1.051); 0.4872
							RD	-0.027 (-0.127, 0.046); 0.4842
							OR	0.434 (0.068, 2.759); 0.3764
Renal and urinary disorders	6	8	5 (10.6)	1	3	1 (4.0)	RR	1.037 (0.954, 1.116); 0.2223
							RD	0.035 (-0.044, 0.102); 0.2198
							OR	0.736 (0.157, 3.443); 0.6971
Reproductive system and breast disorders	9	11	5 (10.6)	2	5	2 (8.0)	RR	1.019 (0.926, 1.100); 0.5935
							RD	0.018 (-0.070, 0.088); 0.5937
							OR	0.829 (0.319, 2.153); 0.6995
Respiratory, thoracic and mediastinal disorders	26	33	14 (29.8)	7	19	7 (28.0)	RR	1.029 (0.889, 1.168); 0.6523
							RD	0.025 (-0.098, 0.132); 0.6530
							OR	0.616 (0.136, 2.782); 0.5289
Cough	7	9	6 (12.8)	2	5	2 (8.0)	RR	1.030 (0.936, 1.117); 0.4159
							RD	0.028 (-0.061, 0.102); 0.4156
							OR	1.297 (0.517, 3.256); 0.5794
Skin and subcutaneous tissue disorders	15	19	12 (25.5)	12	33	9 (36.0)	RR	1.241 (0.562, 2.696); 0.5965
							RD	0.030 (-0.079, 0.157); 0.6048
Severe TEAEs								
							OR	1.685 (0.365, 7.773); 0.5035
Infections and infestations	5	6	3 (6.4)	3	8	3 (12.0)	RR	1.655 (0.389, 6.985); 0.5285
							RD	0.020 (-0.046, 0.114); 0.5479
Serious TEAEs								
							OR	1.296 (0.305, 5.505); 0.7252
Infections and infestations	7	9	4 (8.5)	3	8	3 (12.0)	RR	1.241 (0.317, 4.799); 0.7718
							RD	0.010 (-0.060, 0.104); 0.7771
TEAEs leading to withdrawal from study drug								
							OR	Not calculated
Infections and infestations	0	0	0 (0.0)	3	8	1 (4.0)	RR	Not calculated
							RD	Not calculated
							OR	Not calculated
Bronchitis	0	0	0 (0.0)	1	3	1 (4.0)	RR	Not calculated
							RD	Not calculated
							OR	Not calculated
Encephalitis meningococcal	0	0	0 (0.0)	1	3	1 (4.0)	RR	Not calculated
							RD	Not calculated

Treatment Emergent Adverse Events (TEAEs) by MedDRA System Organ Class/Preferred Term by Severity and Treatment Group, Age: < 45 years

System Organ Class	Eculizumab (N=47) Patient-Years (PY)=79.8			Ravulizumab (N=25) Patient-Years (PY)=36.8			Treatment Effect	
Preferred Term	Events n	Rate per 100 PY	Patients n (%)	Events n	Rate per 100 PY	Patients n (%)	Estimate (95% CI; p-value)	
							OR	Not calculated
Stenotrophomonas infection	0	0	0 (0.0)	1	3	1 (4.0)	RR	Not calculated
							RD	Not calculated

AE: Adverse Event; CI: Confidence Interval; OR: Odds Ratio; PY: person years; RD: Risk Difference; RR: Risk Ratio; TEAE: Treatment-emergent Adverse Event.
TEAEs are AEs with a start date on or after the date of the first dose of study drug.
Treatment-related adverse events and follow-up were truncated at the maximum duration of follow-up in the ravulizumab arm.
Odds ratios were derived from a logistic regression model with treatment as the only covariate. Firth's correction was applied for odds ratios.
Mild, moderate and non-severe TEAEs were examined for preferred terms and system organ classes reported in at least 10% of patients in one of the treatment arms within the subgroup.
Severe and serious TEAEs were examined for preferred terms and system organ classes reported in at least 5% of patients in one of the treatment arms within the subgroup.
All TEAEs leading to withdrawal from study drug were examined.
TEAEs leading to withdrawal from study drug were examined descriptively (i.e., OR, RR, and RD not calculated).

Treatment Emergent Adverse Events (TEAEs) by MedDRA System Organ Class/Preferred Term by Treatment Group, Age: ≥ 45 years

System Organ Class	Eculizumab (N=49) Patient-Years (PY)=93			Ravulizumab (N=33) Patient-Years (PY)=47.3			Treatment Effect	
Preferred Term	Events n	Rate per 100 PY	Patients n (%)	Events n	Rate per 100 PY	Patients n (%)	Estimate (95% CI; p-value)	
Blood and lymphatic system disorders	20	21	9 (18.4)	2	4	2 (6.1)	OR	0.408 (0.096, 1.727); 0.2231
							RR	1.065 (0.965, 1.169); 0.1237
							RD	0.059 (-0.033, 0.141); 0.1208
Eye disorders	28	30	10 (20.4)	3	6	2 (6.1)	OR	0.364 (0.087, 1.524); 0.1668
							RR	1.078 (0.974, 1.187); 0.0797
							RD	0.070 (-0.023, 0.154); 0.0764
Gastrointestinal disorders	46	49	22 (44.9)	20	42	13 (39.4)	OR	0.982 (0.453, 2.131); 0.9637
							RR	1.007 (0.828, 1.195); 0.9423
							RD	0.005 (-0.139, 0.136); 0.9424
Diarrhoea	12	13	10 (20.4)	1	2	1 (3.0)	OR	0.215 (0.037, 1.246); 0.0863
							RR	1.097 (1.004, 1.204); 0.0173
							RD	0.087 (0.004, 0.167); 0.0145
Nausea	8	9	5 (10.2)	1	2	1 (3.0)	OR	0.434 (0.068, 2.759); 0.3764
							RR	1.037 (0.954, 1.116); 0.2223
							RD	0.035 (-0.044, 0.102); 0.2198
General disorders and administration site conditions	56	60	15 (30.6)	13	27	6 (18.2)	OR	0.651 (0.243, 1.746); 0.3938
							RR	1.063 (0.923, 1.205); 0.3322
							RD	0.053 (-0.067, 0.158); 0.3328
Infections and infestations	141	152	38 (77.6)	34	72	21 (63.6)	OR	0.871 (0.444, 1.708); 0.6880
							RR	1.056 (0.807, 1.352); 0.6731
							RD	0.034 (-0.126, 0.186); 0.6747
COVID-19	0	0	0 (0.0)	7	15	7 (21.2)	OR	28.108 (1.549, 510.01); 0.0241
							RR	0.879 (0.771, 0.940); 0.0082
							RD	-0.121 (-0.229, -0.060); 0.0048
Nasopharyngitis	21	23	8 (16.3)	1	2	1 (3.0)	OR	0.272 (0.046, 1.613); 0.1516
							RR	1.072 (0.984, 1.168); 0.0489
							RD	0.066 (-0.015, 0.142); 0.0451
Upper respiratory tract infection	19	20	11 (22.4)	2	4	2 (6.1)	OR	0.329 (0.080, 1.360); 0.1247
							RR	1.090 (0.985, 1.205); 0.0507
							RD	0.080 (-0.014, 0.166); 0.0473
Urinary tract infection	29	31	8 (16.3)	6	13	5 (15.2)	OR	1.070 (0.345, 3.324); 0.9064
							RR	0.997 (0.880, 1.101); 0.9506
							RD	-0.003 (-0.112, 0.086); 0.9506
Injury, poisoning and procedural complications	37	40	20 (40.8)	8	17	5 (15.2)	OR	0.384 (0.139, 1.055); 0.0634
							RR	1.154 (1.002, 1.325); 0.0299
							RD	0.122 (0.002, 0.230); 0.0277
Contusion	9	10	8 (16.3)	0	0	0 (0.0)	OR	0.089 (0.005, 1.609); 0.1015
							RR	1.091 (1.021, 1.185); 0.0047
							RD	0.083 (0.019, 0.156); 0.0031
Investigations	19	20	10 (20.4)	10	21	7 (21.2)	OR	1.200 (0.439, 3.280); 0.7228
							RR	0.982 (0.851, 1.100); 0.7556
							RD	-0.017 (-0.136, 0.083); 0.7549
Metabolism and nutrition disorders	8	9	8 (16.3)	3	6	3 (9.1)	OR	0.657 (0.179, 2.407); 0.5255
							RR	1.034 (0.928, 1.134); 0.4352
							RD	0.032 (-0.067, 0.114); 0.4353
Musculoskeletal and connective tissue disorders	47	51	23 (46.9)	18	38	11 (33.3)	OR	0.757 (0.340, 1.685); 0.4956
							RR	1.066 (0.886, 1.259); 0.4572
							RD	0.050 (-0.091, 0.177); 0.4591
Arthralgia	9	10	8 (16.3)	3	6	3 (9.1)	OR	0.657 (0.179, 2.407); 0.5255
							RR	1.034 (0.928, 1.134); 0.4352
							RD	0.032 (-0.067, 0.114); 0.4353
Back pain	8	9	5 (10.2)	6	13	5 (15.2)	OR	1.711 (0.496, 5.897); 0.3952
							RR	0.964 (0.854, 1.052); 0.4343
							RD	-0.034 (-0.140, 0.047); 0.4304
Pain in extremity	9	10	7 (14.3)	0	0	0 (0.0)	OR	0.102 (0.006, 1.864); 0.1236
							RR	1.079 (1.009, 1.167); 0.0082
							RD	0.073 (0.009, 0.143); 0.0060
Nervous system disorders	93	100	25 (51.0)	14	30	6 (18.2)	OR	0.347 (0.136, 0.888); 0.0272
							RR	1.212 (1.036, 1.416); 0.0105
							RD	0.157 (0.029, 0.272); 0.0089
Dizziness	15	16	11 (22.4)	0	0	0 (0.0)	OR	0.064 (0.004, 1.126); 0.0603
							RR	1.129 (1.056, 1.241); 0.0009
							RD	0.115 (0.049, 0.194); 0.0004
Headache	16	17	8 (16.3)	10	21	5 (15.2)	OR	1.070 (0.345, 3.324); 0.9064
							RR	0.997 (0.880, 1.101); 0.9506

System Organ Class / Preferred Term	Eculizumab (N=49) Patient-Years (PY)=93 Events n	Rate per 100 PY	Patients n (%)	Ravulizumab (N=33) Patient-Years (PY)=47.3 Events n	Rate per 100 PY	Patients n (%)	Treatment Effect	Estimate (95% CI; p-value)
							RD	-0.003 (-0.112, 0.086); 0.9506
Psychiatric disorders	10	11	8 (16.3)	2	4	2 (6.1)	OR	0.461 (0.107, 1.984); 0.2983
							RR	1.053 (0.955, 1.151); 0.1891
							RD	0.049 (-0.042, 0.128); 0.1869
Renal and urinary disorders	16	17	11 (22.4)	9	19	4 (12.1)	OR	0.614 (0.194, 1.939); 0.4057
							RR	1.052 (0.932, 1.170); 0.3268
							RD	0.046 (-0.062, 0.138); 0.3268
Reproductive system and breast disorders	6	6	5 (10.2)	0	0	0 (0.0)	OR	0.142 (0.008, 2.684); 0.1931
							RR	1.055 (0.988, 1.132); 0.0254
							RD	0.052 (-0.012, 0.116); 0.0216
Respiratory, thoracic and mediastinal disorders	36	39	9 (18.4)	3	6	2 (6.1)	OR	0.408 (0.096, 1.727); 0.2231
							RR	1.065 (0.965, 1.169); 0.1237
							RD	0.059 (-0.033, 0.141); 0.1208
Cough	5	5	5 (10.2)	1	2	1 (3.0)	OR	0.434 (0.068, 2.759); 0.3764
							RR	1.037 (0.954, 1.116); 0.2223
							RD	0.035 (-0.044, 0.102); 0.2198
Skin and subcutaneous tissue disorders	23	25	13 (26.5)	4	8	3 (9.1)	OR	0.390 (0.114, 1.339); 0.1346
							RR	1.097 (0.978, 1.224); 0.0685
							RD	0.084 (-0.020, 0.176); 0.0655
Vascular disorders	13	14	9 (18.4)	4	8	3 (9.1)	OR	0.581 (0.161, 2.091); 0.4058
							RR	1.046 (0.938, 1.152); 0.3129
							RD	0.042 (-0.057, 0.127); 0.3124

AE: Adverse Event; CI: Confidence Interval; OR: Odds Ratio; PY: person years; RD: Risk Difference; RR: Risk Ratio; TEAE: Treatment-emergent Adverse Event.
TEAEs are AEs with a start date on or after the date of the first dose of study drug.
Treatment-related adverse events and follow-up were truncated at the maximum duration of follow-up in the ravulizumab arm.
Odds ratios were derived from a logistic regression model with treatment as the only covariate. Firth's correction was applied for odds ratios.
Any TEAEs were examined for preferred terms and system organ classes reported in at least 10% of patients in one of the treatment arms within the subgroup.
Severe and serious TEAEs were examined for preferred terms and system organ classes reported in at least 5% of patients in one of the treatment arms within the subgroup.

Treatment Emergent Adverse Events (TEAEs) by MedDRA System Organ Class/Preferred Term by Severity and Treatment Group, Age: ≥ 45 years

System Organ Class / Preferred Term	Eculizumab (N=49) Patient-Years (PY)=93 Events n	Rate per 100 PY	Patients n (%)	Ravulizumab (N=33) Patient-Years (PY)=47.3 Events n	Rate per 100 PY	Patients n (%)	Treatment Effect	Estimate (95% CI; p-value)
Mild TEAEs								
Blood and lymphatic system disorders	19	20	9 (18.4)	1	2	1 (3.0)	OR	0.240 (0.041, 1.408); 0.1140
							RR	1.084 (0.994, 1.186); 0.0291
							RD	0.077 (-0.006, 0.155); 0.0258
Eye disorders	18	19	10 (20.4)	1	2	1 (3.0)	OR	0.215 (0.037, 1.246); 0.0863
							RR	1.097 (1.004, 1.204); 0.0173
							RD	0.087 (0.004, 0.167); 0.0145
Gastrointestinal disorders	39	42	19 (38.8)	17	36	11 (33.3)	OR	0.962 (0.424, 2.183); 0.9266
							RR	1.010 (0.844, 1.181); 0.8997
							RD	0.008 (-0.130, 0.132); 0.8998
Diarrhoea	11	12	9 (18.4)	1	2	1 (3.0)	OR	0.240 (0.041, 1.408); 0.1140
							RR	1.084 (0.994, 1.186); 0.0291
							RD	0.077 (-0.006, 0.155); 0.0258
Nausea	7	8	5 (10.2)	1	2	1 (3.0)	OR	0.434 (0.068, 2.759); 0.3764
							RR	1.037 (0.954, 1.116); 0.2223
							RD	0.035 (-0.044, 0.102); 0.2198
General disorders and administration site conditions	51	55	13 (26.5)	11	23	4 (12.1)	OR	0.511 (0.165, 1.579); 0.2433
							RR	1.077 (0.952, 1.206); 0.1698
							RD	0.066 (-0.043, 0.162); 0.1683
Infections and infestations	114	123	30 (61.2)	23	49	13 (39.4)	OR	0.647 (0.306, 1.368); 0.2543
							RR	1.129 (0.917, 1.369); 0.2199
							RD	0.088 (-0.061, 0.224); 0.2220
COVID-19	0	0	0 (0.0)	5	11	5 (15.2)	OR	19.842 (1.059, 371.71); 0.0457
							RR	0.914 (0.813, 0.963); 0.0254
							RD	-0.086 (-0.187, -0.037); 0.0193
Nasopharyngitis	19	20	6 (12.2)	1	2	1 (3.0)	OR	0.363 (0.059, 2.242); 0.2754
							RR	1.048 (0.964, 1.133); 0.1354
							RD	0.045 (-0.034, 0.116); 0.1319
Upper respiratory tract infection	17	18	9 (18.4)	0	0	0 (0.0)	OR	0.079 (0.004, 1.412); 0.0844
							RR	1.103 (1.032, 1.203); 0.0027
							RD	0.094 (0.029, 0.169); 0.0016
Urinary tract infection	26	28	8 (16.3)	4	8	3 (9.1)	OR	0.657 (0.179, 2.407); 0.5255
							RR	1.034 (0.928, 1.134); 0.4352
							RD	0.032 (-0.067, 0.114); 0.4353
Injury, poisoning and procedural complications	27	29	17 (34.7)	5	11	3 (9.1)	OR	0.286 (0.086, 0.958); 0.0424
							RR	1.152 (1.021, 1.303); 0.0120
							RD	0.125 (0.018, 0.224); 0.0099
Investigations	14	15	9 (18.4)	10	21	7 (21.2)	OR	1.341 (0.481, 3.737); 0.5745
							RR	0.970 (0.843, 1.084); 0.6071
							RD	-0.027 (-0.145, 0.071); 0.6051
Metabolism and nutrition disorders	8	9	8 (16.3)	0	0	0 (0.0)	OR	0.089 (0.005, 1.609); 0.1015
							RR	1.091 (1.021, 1.185); 0.0047
							RD	0.083 (0.019, 0.156); 0.0031
Musculoskeletal and connective tissue disorders	40	43	22 (44.9)	13	27	8 (24.2)	OR	0.557 (0.233, 1.334); 0.1892
							RR	1.118 (0.948, 1.304); 0.1438
							RD	0.091 (-0.042, 0.210); 0.1435
Nervous system disorders	82	88	20 (40.8)	14	30	6 (18.2)	OR	0.462 (0.177, 1.203); 0.1138
							RR	1.132 (0.976, 1.304); 0.0705
							RD	0.105 (-0.020, 0.216); 0.0686
Dizziness	15	16	11 (22.4)	0	0	0 (0.0)	OR	0.064 (0.004, 1.126); 0.0603
							RR	1.129 (1.056, 1.241); 0.0009
							RD	0.115 (0.049, 0.194); 0.0004
Headache	16	17	8 (16.3)	10	21	5 (15.2)	OR	1.070 (0.345, 3.324); 0.9064
							RR	0.997 (0.880, 1.101); 0.9506
							RD	-0.003 (-0.112, 0.086); 0.9506
Psychiatric disorders	9	10	8 (16.3)	2	4	2 (6.1)	OR	0.461 (0.107, 1.984); 0.2983
							RR	1.053 (0.955, 1.151); 0.1891
							RD	0.049 (-0.042, 0.128); 0.1869
Renal and urinary disorders	12	13	10 (20.4)	8	17	3 (9.1)	OR	0.520 (0.147, 1.842); 0.3105
							RR	1.059 (0.948, 1.169); 0.2200
							RD	0.052 (-0.048, 0.140); 0.2187
Reproductive system and breast disorders	6	6	5 (10.2)	0	0	0 (0.0)	OR	0.142 (0.008, 2.684); 0.1931
							RR	1.055 (0.988, 1.132); 0.0254
							RD	0.052 (-0.012, 0.116); 0.0216

Treatment Emergent Adverse Events (TEAEs) by MedDRA System Organ Class/Preferred Term by Severity and Treatment Group, Age: ≥ 45 years

System Organ Class / Preferred Term	Eculizumab (N=49) Patient-Years (PY)=93 Events n	Rate per 100 PY	Patients n (%)	Ravulizumab (N=33) Patient-Years (PY)=47.3 Events n	Rate per 100 PY	Patients n (%)	Treatment Effect Estimate (95% CI; p-value)
							OR 0.408 (0.096, 1.727); 0.2231
Respiratory, thoracic and mediastinal disorders	36	39	9 (18.4)	3	6	2 (6.1)	RR 1.065 (0.965, 1.169); 0.1237
							RD 0.059 (-0.033, 0.141); 0.1208
							OR 0.434 (0.068, 2.759); 0.3764
Cough	5	5	5 (10.2)	1	2	1 (3.0)	RR 1.037 (0.954, 1.116); 0.2223
							RD 0.035 (-0.044, 0.102); 0.2198
							OR 0.426 (0.123, 1.477); 0.1786
Skin and subcutaneous tissue disorders	21	23	12 (24.5)	4	8	3 (9.1)	RR 1.084 (0.968, 1.205); 0.1027
							RD 0.073 (-0.029, 0.164); 0.1000
ModerateTEAEs							
							OR 0.616 (0.136, 2.782); 0.5289
Gastrointestinal disorders	7	8	6 (12.2)	3	6	2 (6.1)	RR 1.030 (0.936, 1.117); 0.4159
							RD 0.028 (-0.061, 0.102); 0.4156
							OR 0.885 (0.355, 2.207); 0.7934
Infections and infestations	24	26	15 (30.6)	9	19	8 (24.2)	RR 1.022 (0.875, 1.167); 0.7537
							RD 0.018 (-0.109, 0.129); 0.7542
							OR 1.049 (0.261, 4.217); 0.9461
Injury, poisoning and procedural complications	7	8	5 (10.2)	3	6	3 (9.1)	RR 1.000 (0.901, 1.084); 0.9922
							RD 0.000 (-0.095, 0.074); 0.9922
Non-SevereTEAEs							
							OR 0.408 (0.096, 1.727); 0.2231
Blood and lymphatic system disorders	20	21	9 (18.4)	2	4	2 (6.1)	RR 1.065 (0.965, 1.169); 0.1237
							RD 0.059 (-0.033, 0.141); 0.1208
							OR 0.364 (0.087, 1.524); 0.1668
Eye disorders	27	29	10 (20.4)	3	6	2 (6.1)	RR 1.078 (0.974, 1.187); 0.0797
							RD 0.070 (-0.023, 0.154); 0.0764
							OR 0.982 (0.453, 2.131); 0.9637
Gastrointestinal disorders	46	49	22 (44.9)	20	42	13 (39.4)	RR 1.007 (0.828, 1.195); 0.9423
							RD 0.005 (-0.139, 0.136); 0.9424
							OR 0.215 (0.037, 1.246); 0.0863
Diarrhoea	12	13	10 (20.4)	1	2	1 (3.0)	RR 1.097 (1.004, 1.204); 0.0173
							RD 0.087 (0.004, 0.167); 0.0145
							OR 0.434 (0.068, 2.759); 0.3764
Nausea	8	9	5 (10.2)	1	2	1 (3.0)	RR 1.037 (0.954, 1.116); 0.2223
							RD 0.035 (-0.044, 0.102); 0.2198
							OR 0.651 (0.243, 1.746); 0.3938
General disorders and administration site conditions	54	58	15 (30.6)	13	27	6 (18.2)	RR 1.063 (0.923, 1.205); 0.3322
							RD 0.053 (-0.067, 0.158); 0.3328
							OR 0.845 (0.429, 1.666); 0.6265
Infections and infestations	138	148	37 (75.5)	32	68	20 (60.6)	RR 1.066 (0.821, 1.355); 0.6087
							RD 0.041 (-0.119, 0.192); 0.6109
							OR 28.108 (1.549, 510.01); 0.0241
COVID-19	0	0	0 (0.0)	7	15	7 (21.2)	RR 0.879 (0.771, 0.940); 0.0082
							RD -0.121 (-0.229, -0.060); 0.0048
							OR 0.272 (0.046, 1.613); 0.1516
Nasopharyngitis	21	23	8 (16.3)	1	2	1 (3.0)	RR 1.072 (0.984, 1.168); 0.0489
							RD 0.066 (-0.015, 0.142); 0.0451
							OR 0.194 (0.034, 1.114); 0.0659
Upper respiratory tract infection	19	20	11 (22.4)	1	2	1 (3.0)	RR 1.110 (1.015, 1.223); 0.0102
							RD 0.097 (0.013, 0.180); 0.0080
							OR 1.070 (0.345, 3.324); 0.9064
Urinary tract infection	29	31	8 (16.3)	6	13	5 (15.2)	RR 0.997 (0.880, 1.101); 0.9506
							RD -0.003 (-0.112, 0.086); 0.9506
							OR 0.384 (0.139, 1.055); 0.0634
Injury, poisoning and procedural complications	34	37	20 (40.8)	8	17	5 (15.2)	RR 1.154 (1.002, 1.325); 0.0299
							RD 0.122 (0.002, 0.230); 0.0277
							OR 0.089 (0.005, 1.609); 0.1015
Contusion	9	10	8 (16.3)	0	0	0 (0.0)	RR 1.091 (1.021, 1.185); 0.0047
							RD 0.083 (0.019, 0.156); 0.0031
							OR 1.200 (0.439, 3.280); 0.7228
Investigations	19	20	10 (20.4)	10	21	7 (21.2)	RR 0.982 (0.851, 1.100); 0.7556
							RD -0.017 (-0.136, 0.083); 0.7549

Treatment Emergent Adverse Events (TEAEs) by MedDRA System Organ Class/Preferred Term by Severity and Treatment Group, Age: ≥ 45 years

System Organ Class / Preferred Term	Eculizumab (N=49) Patient-Years (PY)=93 Events n	Rate per 100 PY	Patients n (%)	Ravulizumab (N=33) Patient-Years (PY)=47.3 Events n	Rate per 100 PY	Patients n (%)	Treatment Effect	Estimate (95% CI; p-value)
Metabolism and nutrition disorders	8	9	8 (16.3)	3	6	3 (9.1)	OR	0.657 (0.179, 2.407); 0.5255
							RR	1.034 (0.928, 1.134); 0.4352
							RD	0.032 (-0.067, 0.114); 0.4353
Musculoskeletal and connective tissue disorders	45	48	23 (46.9)	17	36	11 (33.3)	OR	0.757 (0.340, 1.685); 0.4956
							RR	1.066 (0.886, 1.259); 0.4572
							RD	0.050 (-0.091, 0.177); 0.4591
Arthralgia	9	10	8 (16.3)	3	6	3 (9.1)	OR	0.657 (0.179, 2.407); 0.5255
							RR	1.034 (0.928, 1.134); 0.4352
							RD	0.032 (-0.067, 0.114); 0.4353
Back pain	7	8	5 (10.2)	6	13	5 (15.2)	OR	1.711 (0.496, 5.897); 0.3952
							RR	0.964 (0.854, 1.052); 0.4343
							RD	-0.034 (-0.140, 0.047); 0.4304
Nervous system disorders	91	98	23 (46.9)	14	30	6 (18.2)	OR	0.387 (0.150, 0.997); 0.0492
							RR	1.179 (1.011, 1.370); 0.0233
							RD	0.136 (0.009, 0.250); 0.0213
Dizziness	15	16	11 (22.4)	0	0	0 (0.0)	OR	0.064 (0.004, 1.126); 0.0603
							RR	1.129 (1.056, 1.241); 0.0009
							RD	0.115 (0.049, 0.194); 0.0004
Headache	16	17	8 (16.3)	10	21	5 (15.2)	OR	1.070 (0.345, 3.324); 0.9064
							RR	0.997 (0.880, 1.101); 0.9506
							RD	-0.003 (-0.112, 0.086); 0.9506
Psychiatric disorders	10	11	8 (16.3)	2	4	2 (6.1)	OR	0.461 (0.107, 1.984); 0.2983
							RR	1.053 (0.955, 1.151); 0.1891
							RD	0.049 (-0.042, 0.128); 0.1869
Renal and urinary disorders	16	17	11 (22.4)	8	17	3 (9.1)	OR	0.469 (0.134, 1.641); 0.2360
							RR	1.071 (0.958, 1.187); 0.1516
							RD	0.063 (-0.038, 0.152); 0.1495
Reproductive system and breast disorders	6	6	5 (10.2)	0	0	0 (0.0)	OR	0.142 (0.008, 2.684); 0.1931
							RR	1.055 (0.988, 1.132); 0.0254
							RD	0.052 (-0.012, 0.116); 0.0216
Respiratory, thoracic and mediastinal disorders	36	39	9 (18.4)	3	6	2 (6.1)	OR	0.408 (0.096, 1.727); 0.2231
							RR	1.065 (0.965, 1.169); 0.1237
							RD	0.059 (-0.033, 0.141); 0.1208
Cough	5	5	5 (10.2)	1	2	1 (3.0)	OR	0.434 (0.068, 2.759); 0.3764
							RR	1.037 (0.954, 1.116); 0.2223
							RD	0.035 (-0.044, 0.102); 0.2198
Skin and subcutaneous tissue disorders	23	25	13 (26.5)	4	8	3 (9.1)	OR	0.390 (0.114, 1.339); 0.1346
							RR	1.097 (0.978, 1.224); 0.0685
							RD	0.084 (-0.020, 0.176); 0.0655
Vascular disorders	13	14	9 (18.4)	4	8	3 (9.1)	OR	0.581 (0.161, 2.091); 0.4058
							RR	1.046 (0.938, 1.152); 0.3129
							RD	0.042 (-0.057, 0.127); 0.3124
Severe TEAEs								
Infections and infestations	2	2	2 (4.1)	2	4	2 (6.1)	OR	1.673 (0.278, 10.081); 0.5744
							RR	0.986 (0.899, 1.047); 0.6276
							RD	-0.014 (-0.099, 0.044); 0.6265
Serious TEAEs								
Infections and infestations	6	6	5 (10.2)	2	4	2 (6.1)	OR	0.736 (0.157, 3.443); 0.6971
							RR	1.019 (0.926, 1.100); 0.5935
							RD	0.018 (-0.070, 0.088); 0.5937
Nervous system disorders	5	5	5 (10.2)	0	0	0 (0.0)	OR	0.142 (0.008, 2.684); 0.1931
							RR	1.055 (0.988, 1.132); 0.0254
							RD	0.052 (-0.012, 0.116); 0.0216
Neuromyelitis optica spectrum disorder	5	5	5 (10.2)	0	0	0 (0.0)	OR	0.142 (0.008, 2.684); 0.1931
							RR	1.055 (0.988, 1.132); 0.0254
							RD	0.052 (-0.012, 0.116); 0.0216
TEAEs leading to withdrawal from study drug								
None								

AE: Adverse Event; CI: Confidence Interval; OR: Odds Ratio; PY: person years; RD: Risk Difference; RR: Risk Ratio; TEAE: Treatment-emergent Adverse Event.
TEAEs are AEs with a start date on or after the date of the first dose of study drug.
Treatment-related adverse events and follow-up were truncated at the maximum duration of follow-up in the ravulizumab arm.
Odds ratios were derived from a logistic regression model with treatment as the only covariate. Firth's correction was applied for odds ratios.
Mild, moderate and non-severe TEAEs were examined for preferred terms and system organ classes reported in at least 10% of patients in one of the treatment arms within the subgroup.
Severe and serious TEAEs were examined for preferred terms and system organ classes reported in at least 5% of patients in one of the treatment arms within the subgroup.
All TEAEs leading to withdrawal from study drug were examined.
TEAEs leading to withdrawal from study drug were examined descriptively (i.e., OR, RR, and RD not calculated).

Treatment Emergent Adverse Events (TEAEs) by MedDRA System Organ Class/Preferred Term by Treatment Group, Region: Americas

System Organ Class / Preferred Term	Eculizumab (N=29) Patient-Years (PY)=44.5 Events n	Rate per 100 PY	Patients n (%)	Ravulizumab (N=21) Patient-Years (PY)=35.7 Events n	Rate per 100 PY	Patients n (%)	Treatment Effect	Estimate (95% CI; p-value)
Eye disorders	25	56	6 (20.7)	5	14	3 (14.3)	OR	0.878 (0.227, 3.393); 0.8504
							RR	1.011 (0.910, 1.100); 0.7774
							RD	0.011 (-0.085, 0.088); 0.7776
Gastrointestinal disorders	58	130	12 (41.4)	8	22	6 (28.6)	OR	0.837 (0.303, 2.312); 0.7313
							RR	1.025 (0.893, 1.151); 0.6799
							RD	0.022 (-0.096, 0.122); 0.6805
Diarrhoea	10	22	6 (20.7)	1	3	1 (4.8)	OR	0.363 (0.059, 2.242); 0.2754
							RR	1.048 (0.964, 1.133); 0.1354
							RD	0.045 (-0.034, 0.116); 0.1319
Nausea	15	34	4 (13.8)	2	6	2 (9.5)	OR	0.910 (0.185, 4.472); 0.9071
							RR	1.007 (0.917, 1.082); 0.8193
							RD	0.007 (-0.080, 0.074); 0.8194
General disorders and administration site conditions	33	74	10 (34.5)	10	28	5 (23.8)	OR	0.847 (0.283, 2.530); 0.7660
							RR	1.020 (0.898, 1.135); 0.7094
							RD	0.018 (-0.093, 0.111); 0.7099
Infections and infestations	72	162	20 (69.0)	17	48	12 (57.1)	OR	1.003 (0.452, 2.228); 0.9938
							RR	1.002 (0.831, 1.178); 0.9830
							RD	0.001 (-0.139, 0.128); 0.9830
COVID-19	0	0	0 (0.0)	7	20	7 (33.3)	OR	28.108 (1.549, 510.01); 0.0241
							RR	0.879 (0.771, 0.940); 0.0082
							RD	-0.121 (-0.229, -0.060); 0.0048
Nasopharyngitis	11	25	4 (13.8)	0	0	0 (0.0)	OR	0.176 (0.009, 3.405); 0.2502
							RR	1.043 (0.977, 1.114); 0.0455
							RD	0.042 (-0.022, 0.103); 0.0411
Upper respiratory tract infection	5	11	3 (10.3)	0	0	0 (0.0)	OR	0.228 (0.011, 4.611); 0.3354
							RR	1.032 (0.967, 1.097); 0.0833
							RD	0.031 (-0.032, 0.088); 0.0784
Urinary tract infection	18	40	6 (20.7)	5	14	4 (19.0)	OR	1.150 (0.327, 4.041); 0.8280
							RR	0.993 (0.885, 1.084); 0.8761
							RD	-0.006 (-0.109, 0.074); 0.8760
Injury, poisoning and procedural complications	25	56	13 (44.8)	12	34	6 (28.6)	OR	0.766 (0.280, 2.092); 0.6026
							RR	1.037 (0.903, 1.169); 0.5463
							RD	0.032 (-0.086, 0.134); 0.5471
Contusion	5	11	4 (13.8)	0	0	0 (0.0)	OR	0.176 (0.009, 3.405); 0.2502
							RR	1.043 (0.977, 1.114); 0.0455
							RD	0.042 (-0.022, 0.103); 0.0411
Investigations	9	20	4 (13.8)	3	8	3 (14.3)	OR	1.296 (0.305, 5.505); 0.7252
							RR	0.990 (0.892, 1.067); 0.7775
							RD	-0.010 (-0.104, 0.060); 0.7771
Musculoskeletal and connective tissue disorders	34	76	17 (58.6)	5	14	4 (19.0)	OR	0.375 (0.125, 1.127); 0.0807
							RR	1.131 (0.994, 1.283); 0.0374
							RD	0.108 (-0.005, 0.210); 0.0348
Arthralgia	3	7	3 (10.3)	1	3	1 (4.8)	OR	0.697 (0.099, 4.925); 0.7173
							RR	1.014 (0.935, 1.081); 0.5699
							RD	0.014 (-0.063, 0.074); 0.5698
Back pain	6	13	5 (17.2)	1	3	1 (4.8)	OR	0.434 (0.068, 2.759); 0.3764
							RR	1.037 (0.954, 1.116); 0.2223
							RD	0.035 (-0.044, 0.102); 0.2198
Pain in extremity	7	16	5 (17.2)	1	3	1 (4.8)	OR	0.434 (0.068, 2.759); 0.3764
							RR	1.037 (0.954, 1.116); 0.2223
							RD	0.035 (-0.044, 0.102); 0.2198
Nervous system disorders	66	148	11 (37.9)	19	53	5 (23.8)	OR	0.764 (0.260, 2.251); 0.6256
							RR	1.032 (0.907, 1.152); 0.5630
							RD	0.028 (-0.084, 0.124); 0.5636
Headache	55	124	6 (20.7)	7	20	5 (23.8)	OR	1.431 (0.434, 4.719); 0.5560
							RR	0.975 (0.862, 1.068); 0.5950
							RD	-0.024 (-0.131, 0.060); 0.5931
Psychiatric disorders	5	11	4 (13.8)	7	20	3 (14.3)	OR	1.296 (0.305, 5.505); 0.7252
							RR	0.990 (0.892, 1.067); 0.7775
							RD	-0.010 (-0.104, 0.060); 0.7771
Renal and urinary disorders	5	11	3 (10.3)	1	3	1 (4.8)	OR	0.697 (0.099, 4.925); 0.7173
							RR	1.014 (0.935, 1.081); 0.5699
							RD	0.014 (-0.063, 0.074); 0.5698
Respiratory, thoracic and mediastinal disorders	18	40	5 (17.2)	5	14	5 (23.8)	OR	1.711 (0.496, 5.897); 0.3952
							RR	0.964 (0.854, 1.052); 0.4343

System Organ Class Preferred Term	Eculizumab (N=29) Patient-Years (PY)=44.5 Events n	Rate per 100 PY	Patients n (%)	Ravulizumab (N=21) Patient-Years (PY)=35.7 Events n	Rate per 100 PY	Patients n (%)	Treatment Effect Estimate (95% CI; p-value)
							RD -0.034 (-0.140, 0.047); 0.4304
Skin and subcutaneous tissue disorders	13	29	9 (31.0)	6	17	4 (19.0)	OR 0.760 (0.234, 2.476); 0.6493 RR 1.027 (0.913, 1.135); 0.5782 RD 0.025 (-0.080, 0.113); 0.5787
Vascular disorders	3	7	3 (10.3)	3	8	2 (9.5)	OR 1.182 (0.223, 6.267); 0.8443 RR 0.997 (0.908, 1.065); 0.9137 RD -0.003 (-0.089, 0.060); 0.9137

AE: Adverse Event; CI: Confidence Interval; OR: Odds Ratio; PY: person years; RD: Risk Difference; RR: Risk Ratio; TEAE: Treatment-emergent Adverse Event.
TEAEs are AEs with a start date on or after the date of the first dose of study drug.
Treatment-related adverse events and follow-up were truncated at the maximum duration of follow-up in the ravulizumab arm.
Odds ratios were derived from a logistic regression model with treatment as the only covariate. Firth's correction was applied for odds ratios.
Any TEAEs were examined for preferred terms and system organ classes reported in at least 10% of patients in one of the treatment arms within the subgroup.
Severe and serious TEAEs were examined for preferred terms and system organ classes reported in at least 5% of patients in one of the treatment arms within the subgroup.
Preferred terms and system organ classes for a given AE severity or type (i.e., leading for withdrawal) were only examined within each subgroup if they were also examined in

Treatment Emergent Adverse Events (TEAEs) by MedDRA System Organ Class/Preferred Term by Severity and Treatment Group, Region: Americas

System Organ Class / Preferred Term	Eculizumab (N=29) Patient-Years (PY)=44.5 Events n	Rate per 100 PY	Patients n (%)	Ravulizumab (N=21) Patient-Years (PY)=35.7 Events n	Rate per 100 PY	Patients n (%)	Treatment Effect	Estimate (95% CI; p-value)
Mild TEAEs								
Eye disorders	12	27	6 (20.7)	4	11	3 (14.3)	OR	0.878 (0.227, 3.393); 0.8504
							RR	1.011 (0.910, 1.100); 0.7774
							RD	0.011 (-0.085, 0.088); 0.7776
Gastrointestinal disorders	48	108	10 (34.5)	8	22	6 (28.6)	OR	1.020 (0.359, 2.898); 0.9699
							RR	1.001 (0.874, 1.117); 0.9887
							RD	0.001 (-0.115, 0.097); 0.9887
Diarrhoea	9	20	6 (20.7)	1	3	1 (4.8)	OR	0.363 (0.059, 2.242); 0.2754
							RR	1.048 (0.964, 1.133); 0.1354
							RD	0.045 (-0.034, 0.116); 0.1319
Nausea	13	29	4 (13.8)	2	6	2 (9.5)	OR	0.910 (0.185, 4.472); 0.9071
							RR	1.007 (0.917, 1.082); 0.8193
							RD	0.007 (-0.080, 0.074); 0.8194
General disorders and administration site conditions	28	63	8 (27.6)	7	20	3 (14.3)	OR	0.657 (0.179, 2.407); 0.5255
							RR	1.034 (0.928, 1.134); 0.4352
							RD	0.032 (-0.067, 0.114); 0.4353
Infections and infestations	50	112	16 (55.2)	12	34	8 (38.1)	OR	0.821 (0.332, 2.032); 0.6699
							RR	1.034 (0.885, 1.185); 0.6261
							RD	0.029 (-0.099, 0.141); 0.6270
COVID-19	0	0	0 (0.0)	5	14	5 (23.8)	OR	19.842 (1.059, 371.71); 0.0457
							RR	0.914 (0.813, 0.963); 0.0254
							RD	-0.086 (-0.187, -0.037); 0.0193
Nasopharyngitis	9	20	4 (13.8)	0	0	0 (0.0)	OR	0.176 (0.009, 3.405); 0.2502
							RR	1.043 (0.977, 1.114); 0.0455
							RD	0.042 (-0.022, 0.103); 0.0411
Urinary tract infection	14	31	5 (17.2)	4	11	3 (14.3)	OR	1.049 (0.261, 4.217); 0.9461
							RR	1.000 (0.901, 1.084); 0.9922
							RD	0.000 (-0.095, 0.074); 0.9922
Injury, poisoning and procedural complications	17	38	10 (34.5)	5	14	3 (14.3)	OR	0.520 (0.147, 1.842); 0.3105
							RR	1.059 (0.948, 1.169); 0.2200
							RD	0.052 (-0.048, 0.140); 0.2187
Investigations	7	16	4 (13.8)	3	8	3 (14.3)	OR	1.296 (0.305, 5.505); 0.7252
							RR	0.990 (0.892, 1.067); 0.7775
							RD	-0.010 (-0.104, 0.060); 0.7771
Musculoskeletal and connective tissue disorders	25	56	15 (51.7)	4	11	3 (14.3)	OR	0.332 (0.098, 1.121); 0.0758
							RR	1.124 (0.999, 1.262); 0.0292
							RD	0.105 (-0.001, 0.200); 0.0265
Nervous system disorders	63	142	10 (34.5)	16	45	5 (23.8)	OR	0.847 (0.283, 2.530); 0.7660
							RR	1.020 (0.898, 1.135); 0.7094
							RD	0.018 (-0.093, 0.111); 0.7099
Headache	54	121	6 (20.7)	5	14	4 (19.0)	OR	1.150 (0.327, 4.041); 0.8280
							RR	0.993 (0.885, 1.084); 0.8761
							RD	-0.006 (-0.109, 0.074); 0.8760
Psychiatric disorders	5	11	4 (13.8)	2	6	2 (9.5)	OR	0.910 (0.185, 4.472); 0.9071
							RR	1.007 (0.917, 1.082); 0.8193
							RD	0.007 (-0.080, 0.074); 0.8194

Treatment Emergent Adverse Events (TEAEs) by MedDRA System Organ Class/Preferred Term by Severity and Treatment Group, Region: Americas

System Organ Class / Preferred Term	Eculizumab (N=29) Patient-Years (PY)=44.5 Events n	Rate per 100 PY	Patients n (%)	Ravulizumab (N=21) Patient-Years (PY)=35.7 Events n	Rate per 100 PY	Patients n (%)	Treatment Effect Estimate (95% CI; p-value)
							OR 1.698 (0.437, 6.602); 0.4450
Respiratory, thoracic and mediastinal disorders	16	36	4 (13.8)	4	11	4 (19.0)	RR 0.972 (0.868, 1.051); 0.4872
							RD -0.027 (-0.127, 0.046); 0.4842
							OR 0.408 (0.096, 1.727); 0.2231
Skin and subcutaneous tissue disorders	13	29	9 (31.0)	4	11	2 (9.5)	RR 1.065 (0.965, 1.169); 0.1237
							RD 0.059 (-0.033, 0.141); 0.1208
ModerateTEAEs							
							OR 0.142 (0.008, 2.684); 0.1931
Gastrointestinal disorders	8	18	5 (17.2)	0	0	0 (0.0)	RR 1.055 (0.988, 1.132); 0.0254
							RD 0.052 (-0.012, 0.116); 0.0216
							OR 0.680 (0.212, 2.178); 0.5163
Infections and infestations	17	38	10 (34.5)	4	11	4 (19.0)	RR 1.039 (0.922, 1.152); 0.4397
							RD 0.035 (-0.071, 0.126); 0.4401
							OR 1.296 (0.305, 5.505); 0.7252
Injury, poisoning and procedural complications	4	9	4 (13.8)	6	17	3 (14.3)	RR 0.990 (0.892, 1.067); 0.7775
							RD -0.010 (-0.104, 0.060); 0.7771
							OR 0.119 (0.006, 2.205); 0.1530
Musculoskeletal and connective tissue disorders	7	16	6 (20.7)	0	0	0 (0.0)	RR 1.067 (0.998, 1.149); 0.0143
							RD 0.063 (-0.001, 0.130); 0.0114
Non-SevereTEAEs							
							OR 0.878 (0.227, 3.393); 0.8504
Eye disorders	25	56	6 (20.7)	5	14	3 (14.3)	RR 1.011 (0.910, 1.100); 0.7774
							RD 0.011 (-0.085, 0.088); 0.7776
							OR 0.921 (0.329, 2.575); 0.8746
Gastrointestinal disorders	56	126	11 (37.9)	8	22	6 (28.6)	RR 1.013 (0.884, 1.134); 0.8287
							RD 0.011 (-0.105, 0.110); 0.8289
							OR 0.363 (0.059, 2.242); 0.2754
Diarrhoea	10	22	6 (20.7)	1	3	1 (4.8)	RR 1.048 (0.964, 1.133); 0.1354
							RD 0.045 (-0.034, 0.116); 0.1319
							OR 0.910 (0.185, 4.472); 0.9071
Nausea	15	34	4 (13.8)	2	6	2 (9.5)	RR 1.007 (0.917, 1.082); 0.8193
							RD 0.007 (-0.080, 0.074); 0.8194
							OR 0.847 (0.283, 2.530); 0.7660
General disorders and administration site conditions	33	74	10 (34.5)	10	28	5 (23.8)	RR 1.020 (0.898, 1.135); 0.7094
							RD 0.018 (-0.093, 0.111); 0.7099
							OR 1.003 (0.452, 2.228); 0.9938
Infections and infestations	67	151	20 (69.0)	16	45	12 (57.1)	RR 1.002 (0.831, 1.178); 0.9830
							RD 0.001 (-0.139, 0.128); 0.9830
							OR 28.108 (1.549, 510.01); 0.0241
COVID-19	0	0	0 (0.0)	7	20	7 (33.3)	RR 0.879 (0.771, 0.940); 0.0082
							RD -0.121 (-0.229, -0.060); 0.0048
							OR 0.176 (0.009, 3.405); 0.2502
Nasopharyngitis	11	25	4 (13.8)	0	0	0 (0.0)	RR 1.043 (0.977, 1.114); 0.0455
							RD 0.042 (-0.022, 0.103); 0.0411
							OR 0.228 (0.011, 4.611); 0.3354
Upper respiratory tract infection	5	11	3 (10.3)	0	0	0 (0.0)	RR 1.032 (0.967, 1.097); 0.0833
							RD 0.031 (-0.032, 0.088); 0.0784
							OR 1.150 (0.327, 4.041); 0.8280
Urinary tract infection	18	40	6 (20.7)	5	14	4 (19.0)	RR 0.993 (0.885, 1.084); 0.8761
							RD -0.006 (-0.109, 0.074); 0.8760
							OR 0.695 (0.239, 2.021); 0.5040
Injury, poisoning and procedural complications	21	47	12 (41.4)	11	31	5 (23.8)	RR 1.044 (0.917, 1.169); 0.4370
							RD 0.039 (-0.074, 0.136); 0.4376
							OR 0.176 (0.009, 3.405); 0.2502
Contusion	5	11	4 (13.8)	0	0	0 (0.0)	RR 1.043 (0.977, 1.114); 0.0455
							RD 0.042 (-0.022, 0.103); 0.0411
							OR 1.296 (0.305, 5.505); 0.7252
Investigations	9	20	4 (13.8)	3	8	3 (14.3)	RR 0.990 (0.892, 1.067); 0.7775
							RD -0.010 (-0.104, 0.060); 0.7771
							OR 0.286 (0.086, 0.958); 0.0424
Musculoskeletal and connective tissue disorders	32	72	17 (58.6)	4	11	3 (14.3)	RR 1.152 (1.021, 1.303); 0.0120
							RD 0.125 (0.018, 0.224); 0.0099
							OR 0.697 (0.099, 4.925); 0.7173
Arthralgia	3	7	3 (10.3)	1	3	1 (4.8)	RR 1.014 (0.935, 1.081); 0.5699
							RD 0.014 (-0.063, 0.074); 0.5698
							OR 0.142 (0.008, 2.684); 0.1931
Back pain	6	13	5 (17.2)	0	0	0 (0.0)	RR 1.055 (0.988, 1.132); 0.0254
							RD 0.052 (-0.012, 0.116); 0.0216

Treatment Emergent Adverse Events (TEAEs) by MedDRA System Organ Class/Preferred Term by Severity and Treatment Group, Region: Americas

System Organ Class / Preferred Term	Eculizumab (N=29) Patient-Years (PY)=44.5 Events n	Rate per 100 PY	Patients n (%)	Ravulizumab (N=21) Patient-Years (PY)=35.7 Events n	Rate per 100 PY	Patients n (%)	Treatment Effect	Estimate (95% CI; p-value)
Nervous system disorders	66	148	11 (37.9)	19	53	5 (23.8)	OR	0.764 (0.260, 2.251); 0.6256
							RR	1.032 (0.907, 1.152); 0.5630
							RD	0.028 (-0.084, 0.124); 0.5636
Headache	55	124	6 (20.7)	7	20	5 (23.8)	OR	1.431 (0.434, 4.719); 0.5560
							RR	0.975 (0.862, 1.068); 0.5950
							RD	-0.024 (-0.131, 0.060); 0.5931
Psychiatric disorders	5	11	4 (13.8)	6	17	3 (14.3)	OR	1.296 (0.305, 5.505); 0.7252
							RR	0.990 (0.892, 1.067); 0.7775
							RD	-0.010 (-0.104, 0.060); 0.7771
Renal and urinary disorders	5	11	3 (10.3)	1	3	1 (4.8)	OR	0.697 (0.099, 4.925); 0.7173
							RR	1.014 (0.935, 1.081); 0.5699
							RD	0.014 (-0.063, 0.074); 0.5698
Respiratory, thoracic and mediastinal disorders	17	38	5 (17.2)	5	14	5 (23.8)	OR	1.711 (0.496, 5.897); 0.3952
							RR	0.964 (0.854, 1.052); 0.4343
							RD	-0.034 (-0.140, 0.047); 0.4304
Skin and subcutaneous tissue disorders	13	29	9 (31.0)	6	17	4 (19.0)	OR	0.760 (0.234, 2.476); 0.6493
							RR	1.027 (0.913, 1.135); 0.5782
							RD	0.025 (-0.080, 0.113); 0.5787
Vascular disorders	3	7	3 (10.3)	3	8	2 (9.5)	OR	1.182 (0.223, 6.267); 0.8443
							RR	0.997 (0.908, 1.065); 0.9137
							RD	-0.003 (-0.089, 0.060); 0.9137
Severe TEAEs								
Infections and infestations	5	11	3 (10.3)	1	3	1 (4.8)	OR	0.697 (0.099, 4.925); 0.7173
							RR	1.014 (0.935, 1.081); 0.5699
							RD	0.014 (-0.063, 0.074); 0.5698
Serious TEAEs								
Infections and infestations	7	16	4 (13.8)	1	3	1 (4.8)	OR	0.536 (0.081, 3.555); 0.5184
							RR	1.025 (0.945, 1.098); 0.3598
							RD	0.024 (-0.053, 0.088); 0.3587
TEAEs leading to withdrawal from study drug								
None								

AE: Adverse Event; CI: Confidence Interval; OR: Odds Ratio; PY: person years; RD: Risk Difference; RR: Risk Ratio; TEAE: Treatment-emergent Adverse Event.
TEAEs are AEs with a start date on or after the date of the first dose of study drug.
Treatment-related adverse events and follow-up were truncated at the maximum duration of follow-up in the ravulizumab arm.
Odds ratios were derived from a logistic regression model with treatment as the only covariate. Firth's correction was applied for odds ratios.
Mild, moderate and non-severe TEAEs were examined for preferred terms and system organ classes reported in at least 10% of patients in one of the treatment arms within the subgroup.
Severe and serious TEAEs were examined for preferred terms and system organ classes reported in at least 5% of patients in one of the treatment arms within the subgroup.
All TEAEs leading to withdrawal from study drug were examined.
TEAEs leading to withdrawal from study drug were examined descriptively (i.e., OR, RR, and RD not calculated).

Treatment Emergent Adverse Events (TEAEs) by MedDRA System Organ Class/Preferred Term by Treatment Group, Region: Asia-Pacific

System Organ Class	Eculizumab (N=35) Patient-Years (PY)=63.1			Ravulizumab (N=20) Patient-Years (PY)=28.7			Treatment Effect	
Preferred Term	Events n	Rate per 100 PY	Patients n (%)	Events n	Rate per 100 PY	Patients n (%)	Estimate (95% CI; p-value)	
Blood and lymphatic system disorders	18	29	10 (28.6)	1	3	1 (5.0)	OR	0.215 (0.037, 1.246); 0.0863
							RR	0.166 (0.027, 0.957); 0.0824
							RD	-0.087 (-0.167, -0.004); 0.0145
Eye disorders	13	21	8 (22.9)	3	10	2 (10.0)	OR	0.461 (0.107, 1.984); 0.2983
							RR	1.053 (0.955, 1.151); 0.1891
							RD	0.049 (-0.042, 0.128); 0.1869
Gastrointestinal disorders	46	73	18 (51.4)	14	49	8 (40.0)	OR	0.714 (0.293, 1.743); 0.4596
							RR	1.061 (0.905, 1.223); 0.4098
							RD	0.050 (-0.080, 0.164); 0.4111
Diarrhoea	8	13	6 (17.1)	1	3	1 (5.0)	OR	0.363 (0.059, 2.242); 0.2754
							RR	1.048 (0.964, 1.133); 0.1354
							RD	0.045 (-0.034, 0.116); 0.1319
Nausea	9	14	6 (17.1)	0	0	0 (0.0)	OR	0.119 (0.006, 2.205); 0.1530
							RR	1.067 (0.998, 1.149); 0.0143
							RD	0.063 (-0.001, 0.130); 0.0114
General disorders and administration site conditions	9	14	6 (17.1)	15	52	5 (25.0)	OR	1.431 (0.434, 4.719); 0.5560
							RR	0.975 (0.862, 1.068); 0.5950
							RD	-0.024 (-0.131, 0.060); 0.5931
Infections and infestations	117	186	28 (80.0)	22	77	13 (65.0)	OR	0.713 (0.336, 1.515); 0.3793
							RR	0.768 (0.430, 1.333); 0.3663
							RD	-0.068 (-0.202, 0.081); 0.3467
COVID-19	0	0	0 (0.0)	2	7	2 (10.0)	OR	8.540 (0.396, 184.30); 0.1712
							RR	0.966 (0.882, 1.005); 0.1573
							RD	-0.034 (-0.118, 0.005); 0.1501
Nasopharyngitis	20	32	8 (22.9)	0	0	0 (0.0)	OR	0.089 (0.005, 1.609); 0.1015
							RR	1.091 (1.021, 1.185); 0.0047
							RD	0.083 (0.019, 0.156); 0.0031
Upper respiratory tract infection	28	44	15 (42.9)	3	10	3 (15.0)	OR	0.332 (0.098, 1.121); 0.0758
							RR	0.331 (0.105, 1.005); 0.0700
							RD	-0.105 (-0.200, 0.001); 0.0265
Urinary tract infection	11	17	4 (11.4)	1	3	1 (5.0)	OR	0.536 (0.081, 3.555); 0.5184
							RR	1.025 (0.945, 1.098); 0.3598
							RD	0.024 (-0.053, 0.088); 0.3587
Injury, poisoning and procedural complications	19	30	12 (34.3)	4	14	4 (20.0)	OR	0.558 (0.179, 1.743); 0.3157
							RR	0.552 (0.193, 1.531); 0.2821
							RD	-0.056 (-0.150, 0.052); 0.2371
Contusion	6	10	6 (17.1)	0	0	0 (0.0)	OR	0.119 (0.006, 2.205); 0.1530
							RR	1.067 (0.998, 1.149); 0.0143
							RD	0.063 (-0.001, 0.130); 0.0114
Investigations	7	11	5 (14.3)	7	24	4 (20.0)	OR	1.373 (0.375, 5.037); 0.6322
							RR	0.982 (0.877, 1.068); 0.6761
							RD	-0.017 (-0.118, 0.060); 0.6750
Metabolism and nutrition disorders	8	13	7 (20.0)	3	10	3 (15.0)	OR	0.752 (0.201, 2.823); 0.6733
							RR	1.023 (0.919, 1.117); 0.5900
							RD	0.021 (-0.076, 0.101); 0.5904
Musculoskeletal and connective tissue disorders	30	48	13 (37.1)	11	38	9 (45.0)	OR	1.187 (0.479, 2.943); 0.7114
							RR	1.146 (0.526, 2.450); 0.7338
							RD	0.020 (-0.091, 0.148); 0.7377
Arthralgia	5	8	4 (11.4)	2	7	2 (10.0)	OR	0.910 (0.185, 4.472); 0.9071
							RR	0.828 (0.180, 3.745); 0.8238
							RD	-0.007 (-0.074, 0.080); 0.8194
Back pain	6	10	5 (14.3)	3	10	2 (10.0)	OR	0.736 (0.157, 3.443); 0.6971
							RR	1.019 (0.926, 1.100); 0.5935
							RD	0.018 (-0.070, 0.088); 0.5937
Nervous system disorders	47	75	18 (51.4)	6	21	4 (20.0)	OR	0.350 (0.117, 1.047); 0.0605
							RR	0.368 (0.134, 0.969); 0.0578
							RD	-0.119 (-0.221, -0.005); 0.0224
Dizziness	9	14	7 (20.0)	1	3	1 (5.0)	OR	0.311 (0.052, 1.880); 0.2034
							RR	0.236 (0.038, 1.415); 0.1721
							RD	-0.056 (-0.129, 0.025); 0.0778
Headache	18	29	10 (28.6)	4	14	3 (15.0)	OR	0.520 (0.147, 1.842); 0.3105
							RR	1.059 (0.948, 1.169); 0.2200
							RD	0.052 (-0.048, 0.140); 0.2187
Psychiatric disorders	6	10	4 (11.4)	1	3	1 (5.0)	OR	0.536 (0.081, 3.555); 0.5184
							RR	1.025 (0.945, 1.098); 0.3598

System Organ Class Preferred Term	Eculizumab (N=35) Patient-Years (PY)=63.1 Events n	Rate per 100 PY	Patients n (%)	Ravulizumab (N=20) Patient-Years (PY)=28.7 Events n	Rate per 100 PY	Patients n (%)	Treatment Effect Estimate (95% CI; p-value)	
							RD	0.024 (-0.053, 0.088); 0.3587
							OR	0.461 (0.107, 1.984); 0.2983
Renal and urinary disorders	12	19	8 (22.9)	3	10	2 (10.0)	RR	1.053 (0.955, 1.151); 0.1891
							RD	0.049 (-0.042, 0.128); 0.1869
							OR	0.176 (0.009, 3.405); 0.2502
Reproductive system and breast disorders	7	11	4 (11.4)	0	0	0 (0.0)	RR	1.043 (0.977, 1.114); 0.0455
							RD	0.042 (-0.022, 0.103); 0.0411
							OR	0.215 (0.037, 1.246); 0.0863
Respiratory, thoracic and mediastinal disorders	25	40	10 (28.6)	1	3	1 (5.0)	RR	1.097 (1.004, 1.204); 0.0173
							RD	0.087 (0.004, 0.167); 0.0145
							OR	0.142 (0.008, 2.684); 0.1931
Cough	5	8	5 (14.3)	0	0	0 (0.0)	RR	1.055 (0.988, 1.132); 0.0254
							RD	0.052 (-0.012, 0.116); 0.0216
							OR	1.477 (0.486, 4.492); 0.4916
Skin and subcutaneous tissue disorders	12	19	7 (20.0)	7	24	6 (30.0)	RR	1.419 (0.517, 3.841); 0.5100
							RD	0.031 (-0.059, 0.143); 0.5247
							OR	0.536 (0.081, 3.555); 0.5184
Vascular disorders	6	10	4 (11.4)	1	3	1 (5.0)	RR	1.025 (0.945, 1.098); 0.3598
							RD	0.024 (-0.053, 0.088); 0.3587

AE: Adverse Event; CI: Confidence Interval; OR: Odds Ratio; PY: person years; RD: Risk Difference; RR: Risk Ratio; TEAE: Treatment-emergent Adverse Event.
TEAEs are AEs with a start date on or after the date of the first dose of study drug.
Treatment-related adverse events and follow-up were truncated at the maximum duration of follow-up in the ravulizumab arm.
Odds ratios were derived from a logistic regression model with treatment as the only covariate. Firth's correction was applied for odds ratios.
Any TEAEs were examined for preferred terms and system organ classes reported in at least 10% of patients in one of the treatment arms within the subgroup.
Severe and serious TEAEs were examined for preferred terms and system organ classes reported in at least 5% of patients in one of the treatment arms within the subgroup.
Preferred terms and system organ classes for a given AE severity or type (i.e., leading for withdrawal) were only examined within each subgroup if they were also examined in

Treatment Emergent Adverse Events (TEAEs) by MedDRA System Organ Class/Preferred Term by Severity and Treatment Group, Region: Asia-Pacific

System Organ Class / Preferred Term	Eculizumab (N=35) Patient-Years (PY)=63.1 Events n	Rate per 100 PY	Patients n (%)	Ravulizumab (N=20) Patient-Years (PY)=28.7 Events n	Rate per 100 PY	Patients n (%)	Treatment Effect	Estimate (95% CI; p-value)
Mild TEAEs								
Blood and lymphatic system disorders	17	27	9 (25.7)	1	3	1 (5.0)	OR	0.240 (0.041, 1.408); 0.1140
							RR	0.184 (0.030, 1.073); 0.1038
							RD	-0.077 (-0.155, 0.006); 0.0258
Eye disorders	12	19	8 (22.9)	0	0	0 (0.0)	OR	0.089 (0.005, 1.609); 0.1015
							RR	1.091 (1.021, 1.185); 0.0047
							RD	0.083 (0.019, 0.156); 0.0031
Gastrointestinal disorders	39	62	16 (45.7)	11	38	6 (30.0)	OR	0.604 (0.227, 1.608); 0.3130
							RR	1.076 (0.933, 1.224); 0.2519
							RD	0.063 (-0.058, 0.170); 0.2520
Diarrhoea	6	10	5 (14.3)	1	3	1 (5.0)	OR	0.434 (0.068, 2.759); 0.3764
							RR	1.037 (0.954, 1.116); 0.2223
							RD	0.035 (-0.044, 0.102); 0.2198
Nausea	7	11	5 (14.3)	0	0	0 (0.0)	OR	0.142 (0.008, 2.684); 0.1931
							RR	1.055 (0.988, 1.132); 0.0254
							RD	0.052 (-0.012, 0.116); 0.0216
General disorders and administration site conditions	7	11	5 (14.3)	15	52	5 (25.0)	OR	1.711 (0.496, 5.897); 0.3952
							RR	0.964 (0.854, 1.052); 0.4343
							RD	-0.034 (-0.140, 0.047); 0.4304
Infections and infestations	103	163	26 (74.3)	12	42	8 (40.0)	OR	0.448 (0.190, 1.058); 0.0669
							RR	1.182 (0.996, 1.394); 0.0397
							RD	0.133 (-0.003, 0.254); 0.0381
COVID-19	0	0	0 (0.0)	2	7	2 (10.0)	OR	8.540 (0.396, 184.30); 0.1712
							RR	0.966 (0.882, 1.005); 0.1573
							RD	-0.034 (-0.118, 0.005); 0.1501
Nasopharyngitis	19	30	8 (22.9)	0	0	0 (0.0)	OR	0.089 (0.005, 1.609); 0.1015
							RR	1.091 (1.021, 1.185); 0.0047
							RD	0.083 (0.019, 0.156); 0.0031
Upper respiratory tract infection	28	44	15 (42.9)	0	0	0 (0.0)	OR	0.045 (0.003, 0.785); 0.0335
							RR	1.185 (1.106, 1.320); 0.0001
							RD	0.156 (0.090, 0.242); 0.0000
Urinary tract infection	11	17	4 (11.4)	0	0	0 (0.0)	OR	0.176 (0.009, 3.405); 0.2502
							RR	1.043 (0.977, 1.114); 0.0455
							RD	0.042 (-0.022, 0.103); 0.0411
Injury, poisoning and procedural complications	14	22	9 (25.7)	1	3	1 (5.0)	OR	0.240 (0.041, 1.408); 0.1140
							RR	1.084 (0.994, 1.186); 0.0291
							RD	0.077 (-0.006, 0.155); 0.0258
Investigations	6	10	5 (14.3)	7	24	4 (20.0)	OR	1.373 (0.375, 5.037); 0.6322
							RR	0.982 (0.877, 1.068); 0.6761
							RD	-0.017 (-0.118, 0.060); 0.6750
Metabolism and nutrition disorders	8	13	7 (20.0)	0	0	0 (0.0)	OR	0.102 (0.006, 1.864); 0.1236
							RR	1.079 (1.009, 1.167); 0.0082
							RD	0.073 (0.009, 0.143); 0.0060
Musculoskeletal and connective tissue disorders	25	40	11 (31.4)	8	28	6 (30.0)	OR	0.921 (0.329, 2.575); 0.8746
							RR	1.013 (0.884, 1.134); 0.8287
							RD	0.011 (-0.105, 0.110); 0.8289
Nervous system disorders	35	56	14 (40.0)	6	21	4 (20.0)	OR	0.470 (0.153, 1.440); 0.1862
							RR	0.473 (0.168, 1.284); 0.1671
							RD	-0.077 (-0.174, 0.033); 0.1170
Dizziness	8	13	6 (17.1)	1	3	1 (5.0)	OR	0.363 (0.059, 2.242); 0.2754
							RR	0.276 (0.044, 1.680); 0.2275
							RD	-0.045 (-0.116, 0.034); 0.1319
Headache	14	22	8 (22.9)	4	14	3 (15.0)	OR	0.657 (0.179, 2.407); 0.5255
							RR	1.034 (0.928, 1.134); 0.4352
							RD	0.032 (-0.067, 0.114); 0.4353
Psychiatric disorders	5	8	4 (11.4)	1	3	1 (5.0)	OR	0.536 (0.081, 3.555); 0.5184
							RR	1.025 (0.945, 1.098); 0.3598
							RD	0.024 (-0.053, 0.088); 0.3587
Renal and urinary disorders	10	16	8 (22.9)	3	10	2 (10.0)	OR	0.461 (0.107, 1.984); 0.2983
							RR	1.053 (0.955, 1.151); 0.1891
							RD	0.049 (-0.042, 0.128); 0.1869
Reproductive system and breast disorders	7	11	4 (11.4)	0	0	0 (0.0)	OR	0.176 (0.009, 3.405); 0.2502
							RR	1.043 (0.977, 1.114); 0.0455
							RD	0.042 (-0.022, 0.103); 0.0411

Treatment Emergent Adverse Events (TEAEs) by MedDRA System Organ Class/Preferred Term by Severity and Treatment Group, Region: Asia-Pacific

System Organ Class / Preferred Term	Eculizumab (N=35) Patient-Years (PY)=63.1 Events n	Rate per 100 PY	Patients n (%)	Ravulizumab (N=20) Patient-Years (PY)=28.7 Events n	Rate per 100 PY	Patients n (%)	Treatment Effect	Estimate (95% CI; p-value)
Respiratory, thoracic and mediastinal disorders	24	38	9 (25.7)	1	3	1 (5.0)	OR	0.240 (0.041, 1.408); 0.1140
							RR	1.084 (0.994, 1.186); 0.0291
							RD	0.077 (-0.006, 0.155); 0.0258
Cough	5	8	5 (14.3)	0	0	0 (0.0)	OR	0.142 (0.008, 2.684); 0.1931
							RR	1.055 (0.988, 1.132); 0.0254
							RD	0.052 (-0.012, 0.116); 0.0216
Skin and subcutaneous tissue disorders	12	19	7 (20.0)	6	21	5 (25.0)	OR	1.227 (0.385, 3.911); 0.7298
							RR	1.182 (0.408, 3.367); 0.7655
							RD	0.013 (-0.073, 0.121); 0.7698
ModerateTEAEs								
Gastrointestinal disorders	7	11	6 (17.1)	3	10	2 (10.0)	OR	0.616 (0.136, 2.782); 0.5289
							RR	1.030 (0.936, 1.117); 0.4159
							RD	0.028 (-0.061, 0.102); 0.4156
Infections and infestations	12	19	7 (20.0)	8	28	7 (35.0)	OR	1.738 (0.593, 5.097); 0.3140
							RR	1.655 (0.629, 4.313); 0.3212
							RD	0.048 (-0.045, 0.164); 0.3426
Injury, poisoning and procedural complications	5	8	3 (8.6)	3	10	3 (15.0)	OR	1.685 (0.365, 7.773); 0.5035
							RR	1.655 (0.389, 6.985); 0.5285
							RD	0.020 (-0.046, 0.114); 0.5479
Musculoskeletal and connective tissue disorders	4	6	3 (8.6)	3	10	3 (15.0)	OR	1.685 (0.365, 7.773); 0.5035
							RR	1.655 (0.389, 6.985); 0.5285
							RD	0.020 (-0.046, 0.114); 0.5479
Non-SevereTEAEs								
Blood and lymphatic system disorders	18	29	10 (28.6)	1	3	1 (5.0)	OR	0.215 (0.037, 1.246); 0.0863
							RR	0.166 (0.027, 0.957); 0.0824
							RD	-0.087 (-0.167, -0.004); 0.0145
Eye disorders	13	21	8 (22.9)	3	10	2 (10.0)	OR	0.461 (0.107, 1.984); 0.2983
							RR	1.053 (0.955, 1.151); 0.1891
							RD	0.049 (-0.042, 0.128); 0.1869
Gastrointestinal disorders	46	73	18 (51.4)	14	49	8 (40.0)	OR	0.714 (0.293, 1.743); 0.4596
							RR	1.061 (0.905, 1.223); 0.4098
							RD	0.050 (-0.080, 0.164); 0.4111
Diarrhoea	8	13	6 (17.1)	1	3	1 (5.0)	OR	0.363 (0.059, 2.242); 0.2754
							RR	1.048 (0.964, 1.133); 0.1354
							RD	0.045 (-0.034, 0.116); 0.1319
Nausea	9	14	6 (17.1)	0	0	0 (0.0)	OR	0.119 (0.006, 2.205); 0.1530
							RR	1.067 (0.998, 1.149); 0.0143
							RD	0.063 (-0.001, 0.130); 0.0114
General disorders and administration site conditions	8	13	6 (17.1)	15	52	5 (25.0)	OR	1.431 (0.434, 4.719); 0.5560
							RR	0.975 (0.862, 1.068); 0.5950
							RD	-0.024 (-0.131, 0.060); 0.5931
Infections and infestations	115	182	27 (77.1)	20	70	13 (65.0)	OR	0.750 (0.352, 1.598); 0.4557
							RR	0.797 (0.444, 1.389); 0.4397
							RD	-0.057 (-0.191, 0.090); 0.4240
COVID-19	0	0	0 (0.0)	2	7	2 (10.0)	OR	8.540 (0.396, 184.30); 0.1712
							RR	0.966 (0.882, 1.005); 0.1573
							RD	-0.034 (-0.118, 0.005); 0.1501
Nasopharyngitis	20	32	8 (22.9)	0	0	0 (0.0)	OR	0.089 (0.005, 1.609); 0.1015
							RR	1.091 (1.021, 1.185); 0.0047
							RD	0.083 (0.019, 0.156); 0.0031
Upper respiratory tract infection	28	44	15 (42.9)	2	7	2 (10.0)	OR	0.233 (0.058, 0.934); 0.0397
							RR	0.221 (0.057, 0.817); 0.0396
							RD	-0.122 (-0.214, -0.024); 0.0058
Urinary tract infection	11	17	4 (11.4)	1	3	1 (5.0)	OR	0.536 (0.081, 3.555); 0.5184
							RR	1.025 (0.945, 1.098); 0.3598
							RD	0.024 (-0.053, 0.088); 0.3587
Injury, poisoning and procedural complications	19	30	12 (34.3)	4	14	4 (20.0)	OR	0.558 (0.179, 1.743); 0.3157
							RR	0.552 (0.193, 1.531); 0.2821
							RD	-0.056 (-0.150, 0.052); 0.2371
Contusion	6	10	6 (17.1)	0	0	0 (0.0)	OR	0.119 (0.006, 2.205); 0.1530
							RR	1.067 (0.998, 1.149); 0.0143
							RD	0.063 (-0.001, 0.130); 0.0114
Investigations	7	11	5 (14.3)	7	24	4 (20.0)	OR	1.373 (0.375, 5.037); 0.6322
							RR	0.982 (0.877, 1.068); 0.6761
							RD	-0.017 (-0.118, 0.060); 0.6750

Treatment Emergent Adverse Events (TEAEs) by MedDRA System Organ Class/Preferred Term by Severity and Treatment Group, Region: Asia-Pacific

System Organ Class / Preferred Term	Eculizumab (N=35) Patient-Years (PY)=63.1 Events n	Rate per 100 PY	Patients n (%)	Ravulizumab (N=20) Patient-Years (PY)=28.7 Events n	Rate per 100 PY	Patients n (%)	Treatment Effect	Estimate (95% CI; p-value)
Metabolism and nutrition disorders	8	13	7 (20.0)	3	10	3 (15.0)	OR	0.752 (0.201, 2.823); 0.6733
							RR	1.023 (0.919, 1.117); 0.5900
							RD	0.021 (-0.076, 0.101); 0.5904
Musculoskeletal and connective tissue disorders	29	46	13 (37.1)	11	38	9 (45.0)	OR	1.187 (0.479, 2.943); 0.7114
							RR	1.146 (0.526, 2.450); 0.7338
							RD	0.020 (-0.091, 0.148); 0.7377
Arthralgia	5	8	4 (11.4)	2	7	2 (10.0)	OR	0.910 (0.185, 4.472); 0.9071
							RR	0.828 (0.180, 3.745); 0.8238
							RD	-0.007 (-0.074, 0.080); 0.8194
Back pain	5	8	5 (14.3)	3	10	2 (10.0)	OR	0.736 (0.157, 3.443); 0.6971
							RR	1.019 (0.926, 1.100); 0.5935
							RD	0.018 (-0.070, 0.088); 0.5937
Nervous system disorders	44	70	17 (48.6)	6	21	4 (20.0)	OR	0.375 (0.125, 1.127); 0.0807
							RR	0.389 (0.141, 1.033); 0.0753
							RD	-0.108 (-0.210, 0.005); 0.0348
Dizziness	9	14	7 (20.0)	1	3	1 (5.0)	OR	0.311 (0.052, 1.880); 0.2034
							RR	0.236 (0.038, 1.415); 0.1721
							RD	-0.056 (-0.129, 0.025); 0.0778
Headache	16	25	10 (28.6)	4	14	3 (15.0)	OR	0.520 (0.147, 1.842); 0.3105
							RR	1.059 (0.948, 1.169); 0.2200
							RD	0.052 (-0.048, 0.140); 0.2187
Psychiatric disorders	6	10	4 (11.4)	1	3	1 (5.0)	OR	0.536 (0.081, 3.555); 0.5184
							RR	1.025 (0.945, 1.098); 0.3598
							RD	0.024 (-0.053, 0.088); 0.3587
Renal and urinary disorders	12	19	8 (22.9)	3	10	2 (10.0)	OR	0.461 (0.107, 1.984); 0.2983
							RR	1.053 (0.955, 1.151); 0.1891
							RD	0.049 (-0.042, 0.128); 0.1869
Reproductive system and breast disorders	7	11	4 (11.4)	0	0	0 (0.0)	OR	0.176 (0.009, 3.405); 0.2502
							RR	1.043 (0.977, 1.114); 0.0455
							RD	0.042 (-0.022, 0.103); 0.0411
Respiratory, thoracic and mediastinal disorders	25	40	10 (28.6)	1	3	1 (5.0)	OR	0.215 (0.037, 1.246); 0.0863
							RR	1.097 (1.004, 1.204); 0.0173
							RD	0.087 (0.004, 0.167); 0.0145
Cough	5	8	5 (14.3)	0	0	0 (0.0)	OR	0.142 (0.008, 2.684); 0.1931
							RR	1.055 (0.988, 1.132); 0.0254
							RD	0.052 (-0.012, 0.116); 0.0216
Skin and subcutaneous tissue disorders	12	19	7 (20.0)	7	24	6 (30.0)	OR	1.477 (0.486, 4.492); 0.4916
							RR	1.419 (0.517, 3.841); 0.5100
							RD	0.031 (-0.059, 0.143); 0.5247
Vascular disorders	6	10	4 (11.4)	1	3	1 (5.0)	OR	0.536 (0.081, 3.555); 0.5184
							RR	1.025 (0.945, 1.098); 0.3598
							RD	0.024 (-0.053, 0.088); 0.3587
Severe TEAEs								
Infections and infestations	2	3	2 (5.7)	2	7	2 (10.0)	OR	1.673 (0.278, 10.081); 0.5744
							RR	1.655 (0.296, 9.209); 0.6093
							RD	0.014 (-0.044, 0.099); 0.6265
Serious TEAEs								
Infections and infestations	6	10	5 (14.3)	2	7	2 (10.0)	OR	0.736 (0.157, 3.443); 0.6971
							RR	0.662 (0.150, 2.853); 0.6150
							RD	-0.018 (-0.088, 0.070); 0.5937
Nervous system disorders	3	5	3 (8.6)	0	0	0 (0.0)	OR	0.228 (0.011, 4.611); 0.3354
							RR	1.032 (0.967, 1.097); 0.0833
							RD	0.031 (-0.032, 0.088); 0.0784
Neuromyelitis optica spectrum disorder	3	5	3 (8.6)	0	0	0 (0.0)	OR	0.228 (0.011, 4.611); 0.3354
							RR	1.032 (0.967, 1.097); 0.0833
							RD	0.031 (-0.032, 0.088); 0.0784
TEAEs leading to withdrawal from study drug								
None								

AE: Adverse Event; CI: Confidence Interval; OR: Odds Ratio; PY: person years; RD: Risk Difference; RR: Risk Ratio; TEAE: Treatment-emergent Adverse Event.
TEAEs are AEs with a start date on or after the date of the first dose of study drug.
Treatment-related adverse events and follow-up were truncated at the maximum duration of follow-up in the ravulizumab arm.
Odds ratios were derived from a logistic regression model with treatment as the only covariate. Firth's correction was applied for odds ratios.
Mild, moderate and non-severe TEAEs were examined for preferred terms and system organ classes reported in at least 10% of patients in one of the treatment arms within the subgroup.
Severe and serious TEAEs were examined for preferred terms and system organ classes reported in at least 5% of patients in one of the treatment arms within the subgroup.
All TEAEs leading to withdrawal from study drug were examined.
TEAEs leading to withdrawal from study drug were examined descriptively (i.e., OR, RR, and RD not calculated).

Treatment Emergent Adverse Events (TEAEs) by MedDRA System Organ Class/Preferred Term by Treatment Group, Region: Europe

System Organ Class / Preferred Term	Eculizumab (N=32) Patient-Years (PY)=65.3 Events n	Rate per 100 PY	Patients n (%)	Ravulizumab (N=17) Patient-Years (PY)=19.7 Events n	Rate per 100 PY	Patients n (%)	Treatment Effect Estimate (95% CI; p-value)
Blood and lymphatic system disorders	16	25	7 (21.9)	1	5	1 (5.9)	OR 0.311 (0.052, 1.880); 0.2034 RR 1.060 (0.974, 1.150); 0.0816 RD 0.056 (-0.025, 0.129); 0.0778
Eye disorders	8	12	5 (15.6)	1	5	1 (5.9)	OR 0.434 (0.068, 2.759); 0.3764 RR 1.037 (0.954, 1.116); 0.2223 RD 0.035 (-0.044, 0.102); 0.2198
Gastrointestinal disorders	20	31	10 (31.3)	10	51	8 (47.1)	OR 1.386 (0.523, 3.678); 0.5116 RR 0.962 (0.829, 1.083); 0.5420 RD -0.034 (-0.156, 0.069); 0.5391
Nausea	4	6	4 (12.5)	0	0	0 (0.0)	OR 0.176 (0.009, 3.405); 0.2502 RR 1.043 (0.977, 1.114); 0.0455 RD 0.042 (-0.022, 0.103); 0.0411
General disorders and administration site conditions	43	66	9 (28.1)	11	56	7 (41.2)	OR 1.341 (0.481, 3.737); 0.5745 RR 0.970 (0.843, 1.084); 0.6071 RD -0.027 (-0.145, 0.071); 0.6051
Infections and infestations	99	152	25 (78.1)	27	137	12 (70.6)	OR 0.754 (0.347, 1.639); 0.4755 RR 1.072 (0.883, 1.278); 0.4394 RD 0.054 (-0.091, 0.184); 0.4415
COVID-19	0	0	0 (0.0)	5	25	5 (29.4)	OR 19.842 (1.059, 371.71); 0.0457 RR 0.914 (0.813, 0.963); 0.0254 RD -0.086 (-0.187, -0.037); 0.0193
Nasopharyngitis	15	23	8 (25.0)	3	15	3 (17.6)	OR 0.657 (0.179, 2.407); 0.5255 RR 1.034 (0.928, 1.134); 0.4352 RD 0.032 (-0.067, 0.114); 0.4353
Pharyngitis	6	9	5 (15.6)	0	0	0 (0.0)	OR 0.142 (0.008, 2.684); 0.1931 RR 1.055 (0.988, 1.132); 0.0254 RD 0.052 (-0.012, 0.116); 0.0216
Upper respiratory tract infection	12	18	10 (31.3)	2	10	2 (11.8)	OR 0.364 (0.087, 1.524); 0.1668 RR 1.078 (0.974, 1.187); 0.0797 RD 0.070 (-0.023, 0.154); 0.0764
Injury, poisoning and procedural complications	6	9	6 (18.8)	2	10	2 (11.8)	OR 0.616 (0.136, 2.782); 0.5289 RR 1.030 (0.936, 1.117); 0.4159 RD 0.028 (-0.061, 0.102); 0.4156
Investigations	12	18	5 (15.6)	1	5	1 (5.9)	OR 0.434 (0.068, 2.759); 0.3764 RR 1.037 (0.954, 1.116); 0.2223 RD 0.035 (-0.044, 0.102); 0.2198
Metabolism and nutrition disorders	4	6	4 (12.5)	2	10	2 (11.8)	OR 0.910 (0.185, 4.472); 0.9071 RR 1.007 (0.917, 1.082); 0.8193 RD 0.007 (-0.080, 0.074); 0.8194
Musculoskeletal and connective tissue disorders	21	32	13 (40.6)	16	81	10 (58.8)	OR 1.339 (0.551, 3.251); 0.5190 RR 0.957 (0.811, 1.096); 0.5451 RD -0.037 (-0.168, 0.077); 0.5419
Arthralgia	3	5	3 (9.4)	3	15	3 (17.6)	OR 1.685 (0.365, 7.773); 0.5035 RR 0.979 (0.883, 1.050); 0.5499 RD -0.020 (-0.114, 0.046); 0.5479
Back pain	4	6	3 (9.4)	4	20	4 (23.5)	OR 2.206 (0.520, 9.365); 0.2836 RR 0.961 (0.860, 1.035); 0.3228 RD -0.038 (-0.137, 0.032); 0.3173
Nervous system disorders	65	100	16 (50.0)	18	91	8 (47.1)	OR 0.821 (0.332, 2.032); 0.6699 RR 1.034 (0.885, 1.185); 0.6261 RD 0.029 (-0.099, 0.141); 0.6270
Dizziness	7	11	5 (15.6)	2	10	2 (11.8)	OR 0.736 (0.157, 3.443); 0.6971 RR 1.019 (0.926, 1.100); 0.5935 RD 0.018 (-0.070, 0.088); 0.5937
Headache	9	14	5 (15.6)	13	66	6 (35.3)	OR 2.060 (0.625, 6.792); 0.2353 RR 0.946 (0.831, 1.037); 0.2710 RD -0.051 (-0.162, 0.033); 0.2639
Psychiatric disorders	4	6	4 (12.5)	2	10	2 (11.8)	OR 0.910 (0.185, 4.472); 0.9071 RR 1.007 (0.917, 1.082); 0.8193 RD 0.007 (-0.080, 0.074); 0.8194
Renal and urinary disorders	5	8	5 (15.6)	6	30	2 (11.8)	OR 0.736 (0.157, 3.443); 0.6971 RR 1.019 (0.926, 1.100); 0.5935 RD 0.018 (-0.070, 0.088); 0.5937
Reproductive system and breast disorders	5	8	4 (12.5)	0	0	0 (0.0)	OR 0.176 (0.009, 3.405); 0.2502 RR 1.043 (0.977, 1.114); 0.0455 RD 0.042 (-0.022, 0.103); 0.0411

System Organ Class Preferred Term	Eculizumab (N=32) Patient-Years (PY)=65.3 Events n	Rate per 100 PY	Patients n (%)	Ravulizumab (N=17) Patient-Years (PY)=19.7 Events n	Rate per 100 PY	Patients n (%)	Treatment Effect Estimate (95% CI; p-value)	
Respiratory, thoracic and mediastinal disorders	20	31	8 (25.0)	4	20	3 (17.6)	OR RR RD	0.657 (0.179, 2.407); 0.5255 1.034 (0.928, 1.134); 0.4352 0.032 (-0.067, 0.114); 0.4353
Cough	4	6	4 (12.5)	1	5	1 (5.9)	OR RR RD	0.536 (0.081, 3.555); 0.5184 1.025 (0.945, 1.098); 0.3598 0.024 (-0.053, 0.088); 0.3587
Skin and subcutaneous tissue disorders	13	20	9 (28.1)	3	15	2 (11.8)	OR RR RD	0.408 (0.096, 1.727); 0.2231 1.065 (0.965, 1.169); 0.1237 0.059 (-0.033, 0.141); 0.1208
Vascular disorders	8	12	6 (18.8)	1	5	1 (5.9)	OR RR RD	0.363 (0.059, 2.242); 0.2754 1.048 (0.964, 1.133); 0.1354 0.045 (-0.034, 0.116); 0.1319

AE: Adverse Event; CI: Confidence Interval; OR: Odds Ratio; PY: person years; RD: Risk Difference; RR: Risk Ratio; TEAE: Treatment-emergent Adverse Event.
TEAEs are AEs with a start date on or after the date of the first dose of study drug.
Treatment-related adverse events and follow-up were truncated at the maximum duration of follow-up in the ravulizumab arm.
Odds ratios were derived from a logistic regression model with treatment as the only covariate. Firth's correction was applied for odds ratios.
Any TEAEs were examined for preferred terms and system organ classes reported in at least 10% of patients in one of the treatment arms within the subgroup.
Severe and serious TEAEs were examined for preferred terms and system organ classes reported in at least 5% of patients in one of the treatment arms within the subgroup.
Preferred terms and system organ classes for a given AE severity or type (i.e., leading for withdrawal) were only examined within each subgroup if they were also examined in th

Treatment Emergent Adverse Events (TEAEs) by MedDRA System Organ Class/Preferred Term by Severity and Treatment Group, Region: Europe

System Organ Class / Preferred Term	Eculizumab (N=32) Patient-Years (PY)=65.3 Events n	Rate per 100 PY	Patients n (%)	Ravulizumab (N=17) Patient-Years (PY)=19.7 Events n	Rate per 100 PY	Patients n (%)	Treatment Effect	Estimate (95% CI; p-value)
Mild TEAEs								
Blood and lymphatic system disorders	11	17	5 (15.6)	1	5	1 (5.9)	OR	0.434 (0.068, 2.759); 0.3764
							RR	1.037 (0.954, 1.116); 0.2223
							RD	0.035 (-0.044, 0.102); 0.2198
Eye disorders	6	9	5 (15.6)	1	5	1 (5.9)	OR	0.434 (0.068, 2.759); 0.3764
							RR	1.037 (0.954, 1.116); 0.2223
							RD	0.035 (-0.044, 0.102); 0.2198
Gastrointestinal disorders	17	26	9 (28.1)	8	41	7 (41.2)	OR	1.341 (0.481, 3.737); 0.5745
							RR	0.970 (0.843, 1.084); 0.6071
							RD	-0.027 (-0.145, 0.071); 0.6051
General disorders and administration site conditions	40	61	7 (21.9)	8	41	5 (29.4)	OR	1.227 (0.385, 3.911); 0.7298
							RR	0.986 (0.871, 1.085); 0.7703
							RD	-0.013 (-0.121, 0.073); 0.7698
Infections and infestations	78	119	20 (62.5)	19	96	9 (52.9)	OR	0.716 (0.305, 1.683); 0.4438
							RR	1.067 (0.902, 1.241); 0.3978
							RD	0.053 (-0.081, 0.172); 0.3993
COVID-19	0	0	0 (0.0)	4	20	4 (23.5)	OR	15.936 (0.828, 306.58); 0.0665
							RR	0.931 (0.835, 0.973); 0.0455
							RD	-0.069 (-0.165, -0.027); 0.0382
Nasopharyngitis	11	17	4 (12.5)	2	10	2 (11.8)	OR	0.910 (0.185, 4.472); 0.9071
							RR	1.007 (0.917, 1.082); 0.8193
							RD	0.007 (-0.080, 0.074); 0.8194
Upper respiratory tract infection	10	15	9 (28.1)	2	10	2 (11.8)	OR	0.408 (0.096, 1.727); 0.2231
							RR	1.065 (0.965, 1.169); 0.1237
							RD	0.059 (-0.033, 0.141); 0.1208
Injury, poisoning and procedural complications	6	9	6 (18.8)	1	5	1 (5.9)	OR	0.363 (0.059, 2.242); 0.2754
							RR	1.048 (0.964, 1.133); 0.1354
							RD	0.045 (-0.034, 0.116); 0.1319
Investigations	8	12	4 (12.5)	1	5	1 (5.9)	OR	0.536 (0.081, 3.555); 0.5184
							RR	1.025 (0.945, 1.098); 0.3598
							RD	0.024 (-0.053, 0.088); 0.3587
Metabolism and nutrition disorders	4	6	4 (12.5)	1	5	1 (5.9)	OR	0.536 (0.081, 3.555); 0.5184
							RR	1.025 (0.945, 1.098); 0.3598
							RD	0.024 (-0.053, 0.088); 0.3587
Musculoskeletal and connective tissue disorders	15	23	10 (31.3)	10	51	6 (35.3)	OR	1.020 (0.359, 2.898); 0.9699
							RR	1.001 (0.874, 1.117); 0.9887
							RD	0.001 (-0.115, 0.097); 0.9887
Nervous system disorders	58	89	13 (40.6)	14	71	6 (35.3)	OR	0.766 (0.280, 2.092); 0.6026
							RR	1.037 (0.903, 1.169); 0.5463
							RD	0.032 (-0.086, 0.134); 0.5471
Dizziness	7	11	5 (15.6)	1	5	1 (5.9)	OR	0.434 (0.068, 2.759); 0.3764
							RR	1.037 (0.954, 1.116); 0.2223
							RD	0.035 (-0.044, 0.102); 0.2198
Headache	9	14	5 (15.6)	10	51	4 (23.5)	OR	1.373 (0.375, 5.037); 0.6322
							RR	0.982 (0.877, 1.068); 0.6761
							RD	-0.017 (-0.118, 0.060); 0.6750
Psychiatric disorders	3	5	3 (9.4)	2	10	2 (11.8)	OR	1.182 (0.223, 6.267); 0.8443
							RR	0.997 (0.908, 1.065); 0.9137
							RD	-0.003 (-0.089, 0.060); 0.9137
Renal and urinary disorders	4	6	4 (12.5)	5	25	1 (5.9)	OR	0.536 (0.081, 3.555); 0.5184
							RR	1.025 (0.945, 1.098); 0.3598
							RD	0.024 (-0.053, 0.088); 0.3587
Reproductive system and breast disorders	5	8	4 (12.5)	0	0	0 (0.0)	OR	0.176 (0.009, 3.405); 0.2502
							RR	1.043 (0.977, 1.114); 0.0455
							RD	0.042 (-0.022, 0.103); 0.0411

Treatment Emergent Adverse Events (TEAEs) by MedDRA System Organ Class/Preferred Term by Severity and Treatment Group, Region: Europe

System Organ Class / Preferred Term	Eculizumab (N=32) Patient-Years (PY)=65.3 Events n	Rate per 100 PY	Patients n (%)	Ravulizumab (N=17) Patient-Years (PY)=19.7 Events n	Rate per 100 PY	Patients n (%)	Treatment Effect	Estimate (95% CI; p-value)
Respiratory, thoracic and mediastinal disorders	19	29	7 (21.9)	4	20	3 (17.6)	OR	0.752 (0.201, 2.823); 0.6733
							RR	1.023 (0.919, 1.117); 0.5900
							RD	0.021 (-0.076, 0.101); 0.5904
Skin and subcutaneous tissue disorders	10	15	8 (25.0)	3	15	2 (11.8)	OR	0.461 (0.107, 1.984); 0.2983
							RR	1.053 (0.955, 1.151); 0.1891
							RD	0.049 (-0.042, 0.128); 0.1869
ModerateTEAEs								
Gastrointestinal disorders	3	5	3 (9.4)	2	10	2 (11.8)	OR	1.182 (0.223, 6.267); 0.8443
							RR	0.997 (0.908, 1.065); 0.9137
							RD	-0.003 (-0.089, 0.060); 0.9137
Infections and infestations	20	31	10 (31.3)	6	30	5 (29.4)	OR	0.847 (0.283, 2.530); 0.7660
							RR	1.020 (0.898, 1.135); 0.7094
							RD	0.018 (-0.093, 0.111); 0.7099
Musculoskeletal and connective tissue disorders	6	9	4 (12.5)	5	25	4 (23.5)	OR	1.698 (0.437, 6.602); 0.4450
							RR	0.972 (0.868, 1.051); 0.4872
							RD	-0.027 (-0.127, 0.046); 0.4842
Non-SevereTEAEs								
Blood and lymphatic system disorders	16	25	7 (21.9)	1	5	1 (5.9)	OR	0.311 (0.052, 1.880); 0.2034
							RR	1.060 (0.974, 1.150); 0.0816
							RD	0.056 (-0.025, 0.129); 0.0778
Eye disorders	7	11	5 (15.6)	1	5	1 (5.9)	OR	0.434 (0.068, 2.759); 0.3764
							RR	1.037 (0.954, 1.116); 0.2223
							RD	0.035 (-0.044, 0.102); 0.2198
Gastrointestinal disorders	20	31	10 (31.3)	10	51	8 (47.1)	OR	1.386 (0.523, 3.678); 0.5116
							RR	0.962 (0.829, 1.083); 0.5420
							RD	-0.034 (-0.156, 0.069); 0.5391
Nausea	4	6	4 (12.5)	0	0	0 (0.0)	OR	0.176 (0.009, 3.405); 0.2502
							RR	1.043 (0.977, 1.114); 0.0455
							RD	0.042 (-0.022, 0.103); 0.0411
General disorders and administration site conditions	42	64	9 (28.1)	10	51	7 (41.2)	OR	1.341 (0.481, 3.737); 0.5745
							RR	0.970 (0.843, 1.084); 0.6071
							RD	-0.027 (-0.145, 0.071); 0.6051
Infections and infestations	98	150	25 (78.1)	25	127	11 (64.7)	OR	0.679 (0.307, 1.500); 0.3381
							RR	1.096 (0.908, 1.301); 0.2978
							RD	0.071 (-0.072, 0.199); 0.2997
COVID-19	0	0	0 (0.0)	5	25	5 (29.4)	OR	19.842 (1.059, 371.71); 0.0457
							RR	0.914 (0.813, 0.963); 0.0254
							RD	-0.086 (-0.187, -0.037); 0.0193
Nasopharyngitis	15	23	8 (25.0)	3	15	3 (17.6)	OR	0.657 (0.179, 2.407); 0.5255
							RR	1.034 (0.928, 1.134); 0.4352
							RD	0.032 (-0.067, 0.114); 0.4353
Pharyngitis	6	9	5 (15.6)	0	0	0 (0.0)	OR	0.142 (0.008, 2.684); 0.1931
							RR	1.055 (0.988, 1.132); 0.0254
							RD	0.052 (-0.012, 0.116); 0.0216
Upper respiratory tract infection	12	18	10 (31.3)	2	10	2 (11.8)	OR	0.364 (0.087, 1.524); 0.1668
							RR	1.078 (0.974, 1.187); 0.0797
							RD	0.070 (-0.023, 0.154); 0.0764
Injury, poisoning and procedural complications	6	9	6 (18.8)	2	10	2 (11.8)	OR	0.616 (0.136, 2.782); 0.5289
							RR	1.030 (0.936, 1.117); 0.4159
							RD	0.028 (-0.061, 0.102); 0.4156
Investigations	12	18	5 (15.6)	1	5	1 (5.9)	OR	0.434 (0.068, 2.759); 0.3764
							RR	1.037 (0.954, 1.116); 0.2223
							RD	0.035 (-0.044, 0.102); 0.2198

Treatment Emergent Adverse Events (TEAEs) by MedDRA System Organ Class/Preferred Term by Severity and Treatment Group, Region: Europe

System Organ Class / Preferred Term	Eculizumab (N=32) Patient-Years (PY)=65.3 Events n	Rate per 100 PY	Patients n (%)	Ravulizumab (N=17) Patient-Years (PY)=19.7 Events n	Rate per 100 PY	Patients n (%)	Treatment Effect	Estimate (95% CI; p-value)
Metabolism and nutrition disorders	4	6	4 (12.5)	2	10	2 (11.8)	OR	0.910 (0.185, 4.472); 0.9071
							RR	1.007 (0.917, 1.082); 0.8193
							RD	0.007 (-0.080, 0.074); 0.8194
Musculoskeletal and connective tissue disorders	21	32	13 (40.6)	15	76	10 (58.8)	OR	1.339 (0.551, 3.251); 0.5190
							RR	0.957 (0.811, 1.096); 0.5451
							RD	-0.037 (-0.168, 0.077); 0.5419
Arthralgia	3	5	3 (9.4)	3	15	3 (17.6)	OR	1.685 (0.365, 7.773); 0.5035
							RR	0.979 (0.883, 1.050); 0.5499
							RD	-0.020 (-0.114, 0.046); 0.5479
Back pain	4	6	3 (9.4)	4	20	4 (23.5)	OR	2.206 (0.520, 9.365); 0.2836
							RR	0.961 (0.860, 1.035); 0.3228
							RD	-0.038 (-0.137, 0.032); 0.3173
Nervous system disorders	64	98	15 (46.9)	17	86	8 (47.1)	OR	0.885 (0.355, 2.207); 0.7934
							RR	1.022 (0.875, 1.167); 0.7537
							RD	0.018 (-0.109, 0.129); 0.7542
Dizziness	7	11	5 (15.6)	1	5	1 (5.9)	OR	0.434 (0.068, 2.759); 0.3764
							RR	1.037 (0.954, 1.116); 0.2223
							RD	0.035 (-0.044, 0.102); 0.2198
Headache	9	14	5 (15.6)	13	66	6 (35.3)	OR	2.060 (0.625, 6.792); 0.2353
							RR	0.946 (0.831, 1.037); 0.2710
							RD	-0.051 (-0.162, 0.033); 0.2639
Psychiatric disorders	4	6	4 (12.5)	2	10	2 (11.8)	OR	0.910 (0.185, 4.472); 0.9071
							RR	1.007 (0.917, 1.082); 0.8193
							RD	0.007 (-0.080, 0.074); 0.8194
Renal and urinary disorders	5	8	5 (15.6)	5	25	1 (5.9)	OR	0.434 (0.068, 2.759); 0.3764
							RR	1.037 (0.954, 1.116); 0.2223
							RD	0.035 (-0.044, 0.102); 0.2198
Reproductive system and breast disorders	5	8	4 (12.5)	0	0	0 (0.0)	OR	0.176 (0.009, 3.405); 0.2502
							RR	1.043 (0.977, 1.114); 0.0455
							RD	0.042 (-0.022, 0.103); 0.0411
Respiratory, thoracic and mediastinal disorders	20	31	8 (25.0)	4	20	3 (17.6)	OR	0.657 (0.179, 2.407); 0.5255
							RR	1.034 (0.928, 1.134); 0.4352
							RD	0.032 (-0.067, 0.114); 0.4353
Cough	4	6	4 (12.5)	1	5	1 (5.9)	OR	0.536 (0.081, 3.555); 0.5184
							RR	1.025 (0.945, 1.098); 0.3598
							RD	0.024 (-0.053, 0.088); 0.3587
Skin and subcutaneous tissue disorders	13	20	9 (28.1)	3	15	2 (11.8)	OR	0.408 (0.096, 1.727); 0.2231
							RR	1.065 (0.965, 1.169); 0.1237
							RD	0.059 (-0.033, 0.141); 0.1208
Vascular disorders	8	12	6 (18.8)	1	5	1 (5.9)	OR	0.363 (0.059, 2.242); 0.2754
							RR	1.048 (0.964, 1.133); 0.1354
							RD	0.045 (-0.034, 0.116); 0.1319
Severe TEAEs								
Infections and infestations	0	0	0 (0.0)	2	10	2 (11.8)	OR	8.540 (0.396, 184.30); 0.1712
							RR	0.966 (0.882, 1.005); 0.1573
							RD	-0.034 (-0.118, 0.005); 0.1501
Serious TEAEs								
Infections and infestations	0	0	0 (0.0)	2	10	2 (11.8)	OR	8.540 (0.396, 184.30); 0.1712
							RR	0.966 (0.882, 1.005); 0.1573
							RD	-0.034 (-0.118, 0.005); 0.1501
Nervous system disorders	3	5	3 (9.4)	0	0	0 (0.0)	OR	0.228 (0.011, 4.611); 0.3354
							RR	1.032 (0.967, 1.097); 0.0833
							RD	0.031 (-0.032, 0.088); 0.0784
Neuromyelitis optica spectrum disorder	3	5	3 (9.4)	0	0	0 (0.0)	OR	0.228 (0.011, 4.611); 0.3354
							RR	1.032 (0.967, 1.097); 0.0833
							RD	0.031 (-0.032, 0.088); 0.0784
TEAEs leading to withdrawal from study drug								
Infections and infestations	0	0	0 (0.0)	3	15	1 (5.9)	OR	Not calculated
							RR	Not calculated
							RD	Not calculated
Bronchitis	0	0	0 (0.0)	1	5	1 (5.9)	OR	Not calculated
							RR	Not calculated
							RD	Not calculated
Encephalitis meningococcal	0	0	0 (0.0)	1	5	1 (5.9)	OR	Not calculated
							RR	Not calculated
							RD	Not calculated

Treatment Emergent Adverse Events (TEAEs) by MedDRA System Organ Class/Preferred Term by Severity and Treatment Group, Region: Europe

System Organ Class	Eculizumab (N=32) Patient-Years (PY)=65.3			Ravulizumab (N=17) Patient-Years (PY)=19.7			Treatment Effect	
Preferred Term	Events n	Rate per 100 PY	Patients n (%)	Events n	Rate per 100 PY	Patients n (%)	Estimate (95% CI; p-value)	
Stenotrophomonas infection	0	0	0 (0.0)	1	5	1 (5.9)	OR	Not calculated
							RR	Not calculated
							RD	Not calculated

AE: Adverse Event; CI: Confidence Interval; OR: Odds Ratio; PY: person years; RD: Risk Difference; RR: Risk Ratio; TEAE: Treatment-emergent Adverse Event.
TEAEs are AEs with a start date on or after the date of the first dose of study drug.
Treatment-related adverse events and follow-up were truncated at the maximum duration of follow-up in the ravulizumab arm.
Odds ratios were derived from a logistic regression model with treatment as the only covariate. Firth's correction was applied for odds ratios.
Mild, moderate and non-severe TEAEs were examined for preferred terms and system organ classes reported in at least 10% of patients in one of the treatment arms within the subgroup.
Severe and serious TEAEs were examined for preferred terms and system organ classes reported in at least 5% of patients in one of the treatment arms within the subgroup.
All TEAEs leading to withdrawal from study drug were examined.
TEAEs leading to withdrawal from study drug were examined descriptively (i.e., OR, RR, and RD not calculated).

Treatment Emergent Adverse Events (TEAEs) by MedDRA System Organ Class/Preferred Term by Treatment Group, IST Use: Yes

System Organ Class	Eculizumab (N=75) Patient-Years (PY)=128.5			Ravulizumab (N=28) Patient-Years (PY)=40.1			Treatment Effect	
Preferred Term	Events n	Rate per 100 PY	Patients n (%)	Events n	Rate per 100 PY	Patients n (%)	Estimate (95% CI; p-value)	
Blood and lymphatic system disorders	27	21	16 (21.3)	2	5	2 (7.1)	OR	0.216 (0.054, 0.862); 0.0300
							RR	0.207 (0.054, 0.762); 0.0312
							RD	-0.132 (-0.226, -0.033); 0.0033
Eye disorders	39	30	17 (22.7)	4	10	3 (10.7)	OR	0.286 (0.086, 0.958); 0.0424
							RR	1.152 (1.021, 1.303); 0.0120
							RD	0.125 (0.018, 0.224); 0.0099
Gastrointestinal disorders	89	69	30 (40.0)	22	55	15 (53.6)	OR	0.777 (0.376, 1.606); 0.4957
							RR	1.078 (0.866, 1.318); 0.4668
							RD	0.054 (-0.098, 0.194); 0.4693
Diarrhoea	17	13	11 (14.7)	3	7	3 (10.7)	OR	0.469 (0.134, 1.641); 0.2360
							RR	1.071 (0.958, 1.187); 0.1516
							RD	0.063 (-0.038, 0.152); 0.1495
Nausea	24	19	12 (16.0)	2	5	2 (7.1)	OR	0.299 (0.073, 1.225); 0.0934
							RR	1.103 (0.995, 1.224); 0.0319
							RD	0.091 (-0.004, 0.178); 0.0288
General disorders and administration site conditions	75	58	21 (28.0)	16	40	8 (28.6)	OR	0.591 (0.246, 1.421); 0.2398
							RR	1.103 (0.937, 1.283); 0.1913
							RD	0.081 (-0.051, 0.198); 0.1916
Infections and infestations	215	167	56 (74.7)	26	65	17 (60.7)	OR	0.302 (0.151, 0.605); 0.0007
							RR	0.502 (0.319, 0.755); 0.0019
							RD	-0.290 (-0.433, -0.129); 0.0002
COVID-19	0	0	0 (0.0)	5	12	5 (17.9)	OR	19.842 (1.059, 371.71); 0.0457
							RR	0.914 (0.813, 0.963); 0.0254
							RD	-0.086 (-0.187, -0.037); 0.0193
Nasopharyngitis	27	21	13 (17.3)	0	0	0 (0.0)	OR	0.053 (0.003, 0.929); 0.0444
							RR	1.157 (1.080, 1.279); 0.0003
							RD	0.135 (0.070, 0.218); 0.0001
Pharyngitis	12	9	9 (12.0)	0	0	0 (0.0)	OR	0.079 (0.004, 1.412); 0.0844
							RR	1.103 (1.032, 1.203); 0.0027
							RD	0.094 (0.029, 0.169); 0.0016
Upper respiratory tract infection	32	25	21 (28.0)	3	7	3 (10.7)	OR	0.221 (0.067, 0.729); 0.0131
							RR	0.236 (0.077, 0.695); 0.0153
							RD	-0.167 (-0.270, -0.056); 0.0011
Urinary tract infection	33	26	11 (14.7)	2	5	2 (7.1)	OR	0.329 (0.080, 1.360); 0.1247
							RR	1.090 (0.985, 1.205); 0.0507
							RD	0.080 (-0.014, 0.166); 0.0473
Injury, poisoning and procedural complications	46	36	27 (36.0)	8	20	5 (17.9)	OR	0.260 (0.096, 0.699); 0.0076
							RR	0.307 (0.126, 0.712); 0.0098
							RD	-0.195 (-0.308, -0.069); 0.0009
Contusion	11	9	10 (13.3)	0	0	0 (0.0)	OR	0.070 (0.004, 1.255); 0.0710
							RR	1.116 (1.044, 1.222); 0.0016
							RD	0.104 (0.039, 0.182); 0.0008
Investigations	19	15	10 (13.3)	8	20	5 (17.9)	OR	0.847 (0.283, 2.530); 0.7660
							RR	1.020 (0.898, 1.135); 0.7094
							RD	0.018 (-0.093, 0.111); 0.7099
Metabolism and nutrition disorders	10	8	9 (12.0)	3	7	3 (10.7)	OR	0.581 (0.161, 2.091); 0.4058
							RR	1.046 (0.938, 1.152); 0.3129
							RD	0.042 (-0.057, 0.127); 0.3124
Musculoskeletal and connective tissue disorders	63	49	32 (42.7)	15	37	10 (35.7)	OR	0.430 (0.194, 0.952); 0.0373
							RR	0.517 (0.272, 0.943); 0.0405
							RD	-0.161 (-0.290, -0.016); 0.0199
Arthralgia	8	6	8 (10.7)	3	7	3 (10.7)	OR	0.657 (0.179, 2.407); 0.5255
							RR	0.621 (0.182, 2.056); 0.4674
							RD	-0.032 (-0.114, 0.067); 0.4353
Back pain	10	8	9 (12.0)	4	10	3 (10.7)	OR	0.581 (0.161, 2.091); 0.4058
							RR	1.046 (0.938, 1.152); 0.3129
							RD	0.042 (-0.057, 0.127); 0.3124
Pain in extremity	10	8	8 (10.7)	0	0	0 (0.0)	OR	0.089 (0.005, 1.609); 0.1015
							RR	1.091 (1.021, 1.185); 0.0047
							RD	0.083 (0.019, 0.156); 0.0031
Nervous system disorders	162	126	39 (52.0)	17	42	8 (28.6)	OR	0.245 (0.106, 0.567); 0.0010
							RR	0.340 (0.169, 0.649); 0.0021
							RD	-0.268 (-0.394, -0.125); 0.0001
Dizziness	16	12	12 (16.0)	1	2	1 (3.6)	OR	0.176 (0.031, 1.005); 0.0507
							RR	0.138 (0.023, 0.787); 0.0538

System Organ Class / Preferred Term	Eculizumab (N=75) Patient-Years (PY)=128.5 Events n	Rate per 100 PY	Patients n (%)	Ravulizumab (N=28) Patient-Years (PY)=40.1 Events n	Rate per 100 PY	Patients n (%)	Treatment Effect	Estimate (95% CI; p-value)
							RD	-0.108 (-0.192, -0.023); 0.0044
							OR	0.562 (0.213, 1.488); 0.2463
Headache	75	58	17 (22.7)	10	25	6 (21.4)	RR	1.089 (0.943, 1.243); 0.1877
							RD	0.074 (-0.048, 0.181); 0.1872
							OR	0.461 (0.107, 1.984); 0.2983
Psychiatric disorders	8	6	8 (10.7)	2	5	2 (7.1)	RR	1.053 (0.955, 1.151); 0.1891
							RD	0.049 (-0.042, 0.128); 0.1869
							OR	0.520 (0.147, 1.842); 0.3105
Renal and urinary disorders	15	12	10 (13.3)	4	10	3 (10.7)	RR	1.059 (0.948, 1.169); 0.2200
							RD	0.052 (-0.048, 0.140); 0.2187
							OR	0.165 (0.042, 0.649); 0.0099
Respiratory, thoracic and mediastinal disorders	58	45	20 (26.7)	2	5	2 (7.1)	RR	1.220 (1.086, 1.387); 0.0006
							RD	0.174 (0.071, 0.272); 0.0003
							OR	0.089 (0.005, 1.609); 0.1015
Cough	9	7	8 (10.7)	0	0	0 (0.0)	RR	1.091 (1.021, 1.185); 0.0047
							RD	0.083 (0.019, 0.156); 0.0031
							OR	0.765 (0.311, 1.878); 0.5583
Skin and subcutaneous tissue disorders	24	19	17 (22.7)	9	22	8 (28.6)	RR	0.779 (0.360, 1.639); 0.5272
							RD	-0.039 (-0.152, 0.090); 0.5122
							OR	0.329 (0.080, 1.360); 0.1247
Vascular disorders	14	11	11 (14.7)	3	7	2 (7.1)	RR	1.090 (0.985, 1.205); 0.0507
							RD	0.080 (-0.014, 0.166); 0.0473

AE: Adverse Event; CI: Confidence Interval; IST: Immunosuppressive Therapy; OR: Odds Ratio; PY: person years; RD: Risk Difference; RR: Risk Ratio; TEAE: Treatment-emergent
TEAEs are AEs with a start date on or after the date of the first dose of study drug.
Treatment-related adverse events and follow-up were truncated at the maximum duration of follow-up in the ravulizumab arm.
Odds ratios were derived from a logistic regression model with treatment as the only covariate. Firth's correction was applied for odds ratios.
Any TEAEs were examined for preferred terms and system organ classes reported in at least 10% of patients in one of the treatment arms within the subgroup.
Severe and serious TEAEs were examined for preferred terms and system organ classes reported in at least 5% of patients in one of the treatment arms within the subgroup.
Preferred terms and system organ classes for a given AE severity or type (i.e., leading for withdrawal) were only examined within each subgroup if they were also examined in

Treatment Emergent Adverse Events (TEAEs) by MedDRA System Organ Class/Preferred Term by Severity and Treatment Group, IST Use: Yes

System Organ Class	Eculizumab (N=75) Patient-Years (PY)=128.5			Ravulizumab (N=28) Patient-Years (PY)=40.1			Treatment Effect	
Preferred Term	Events n	Rate per 100 PY	Patients n (%)	Events n	Rate per 100 PY	Patients n (%)		Estimate (95% CI; p-value)
Mild TEAEs								
Blood and lymphatic system disorders	23	18	13 (17.3)	1	2	1 (3.6)	OR	0.161 (0.028, 0.914); 0.0392
							RR	0.127 (0.021, 0.722); 0.0442
							RD	-0.118 (-0.204, -0.032); 0.0024
Eye disorders	28	22	17 (22.7)	1	2	1 (3.6)	OR	0.118 (0.021, 0.659); 0.0148
							RR	1.194 (1.082, 1.342); 0.0004
							RD	0.160 (0.070, 0.252); 0.0002
Gastrointestinal disorders	75	58	27 (36.0)	18	45	12 (42.9)	OR	0.679 (0.314, 1.468); 0.3253
							RR	1.103 (0.906, 1.323); 0.2877
							RD	0.074 (-0.071, 0.206); 0.2899
Diarrhoea	14	11	10 (13.3)	3	7	3 (10.7)	OR	0.520 (0.147, 1.842); 0.3105
							RR	1.059 (0.948, 1.169); 0.2200
							RD	0.052 (-0.048, 0.140); 0.2187
Nausea	19	15	10 (13.3)	2	5	2 (7.1)	OR	0.364 (0.087, 1.524); 0.1668
							RR	1.078 (0.974, 1.187); 0.0797
							RD	0.070 (-0.023, 0.154); 0.0764
General disorders and administration site conditions	66	51	16 (21.3)	14	35	6 (21.4)	OR	0.604 (0.227, 1.608); 0.3130
							RR	1.076 (0.933, 1.224); 0.2519
							RD	0.063 (-0.058, 0.170); 0.2520
Infections and infestations	175	136	49 (65.3)	12	30	8 (28.6)	OR	0.161 (0.070, 0.372); 0.0000
							RR	1.761 (1.406, 2.239); 0.0000
							RD	0.372 (0.227, 0.496); 0.0000
COVID-19	0	0	0 (0.0)	3	7	3 (10.7)	OR	12.170 (0.607, 244.04); 0.1023
							RR	0.948 (0.858, 0.988); 0.0833
							RD	-0.052 (-0.142, -0.012); 0.0753
Nasopharyngitis	25	19	12 (16.0)	0	0	0 (0.0)	OR	0.058 (0.003, 1.019); 0.0516
							RR	1.143 (1.068, 1.260); 0.0005
							RD	0.125 (0.060, 0.206); 0.0002
Upper respiratory tract infection	30	23	20 (26.7)	0	0	0 (0.0)	OR	0.032 (0.002, 0.551); 0.0178
							RR	1.263 (1.161, 1.429); 0.0000
							RD	0.208 (0.139, 0.300); 0.0000
Urinary tract infection	26	20	10 (13.3)	0	0	0 (0.0)	OR	0.070 (0.004, 1.255); 0.0710
							RR	1.116 (1.044, 1.222); 0.0016
							RD	0.104 (0.039, 0.182); 0.0008
Injury, poisoning and procedural complications	34	26	22 (29.3)	4	10	2 (7.1)	OR	0.147 (0.037, 0.572); 0.0057
							RR	1.253 (1.111, 1.434); 0.0002
							RD	0.195 (0.090, 0.295); 0.0001
Investigations	15	12	10 (13.3)	8	20	5 (17.9)	OR	0.847 (0.283, 2.530); 0.7660
							RR	1.020 (0.898, 1.135); 0.7094
							RD	0.018 (-0.093, 0.111); 0.7099
Metabolism and nutrition disorders	10	8	9 (12.0)	0	0	0 (0.0)	OR	0.079 (0.004, 1.412); 0.0844
							RR	1.103 (1.032, 1.203); 0.0027
							RD	0.094 (0.029, 0.169); 0.0016
Musculoskeletal and connective tissue disorders	50	39	27 (36.0)	9	22	6 (21.4)	OR	0.313 (0.123, 0.796); 0.0148
							RR	1.247 (1.063, 1.466); 0.0045
							RD	0.178 (0.048, 0.294); 0.0035
Nervous system disorders	142	111	31 (41.3)	16	40	8 (28.6)	OR	0.350 (0.150, 0.817); 0.0153
							RR	0.427 (0.210, 0.834); 0.0181
							RD	-0.185 (-0.309, -0.046); 0.0049
Dizziness	15	12	11 (14.7)	1	2	1 (3.6)	OR	0.194 (0.034, 1.114); 0.0659
							RR	0.150 (0.025, 0.864); 0.0662
							RD	-0.097 (-0.180, -0.013); 0.0080
Headache	70	54	15 (20.0)	9	22	6 (21.4)	OR	0.651 (0.243, 1.746); 0.3938
							RR	1.063 (0.923, 1.205); 0.3322
							RD	0.053 (-0.067, 0.158); 0.3328
Renal and urinary disorders	12	9	9 (12.0)	3	7	2 (7.1)	OR	0.408 (0.096, 1.727); 0.2231
							RR	1.065 (0.965, 1.169); 0.1237
							RD	0.059 (-0.033, 0.141); 0.1208

Treatment Emergent Adverse Events (TEAEs) by MedDRA System Organ Class/Preferred Term by Severity and Treatment Group, IST Use: Yes

System Organ Class / Preferred Term	Eculizumab (N=75) Patient-Years (PY)=128.5 Events n	Rate per 100 PY	Patients n (%)	Ravulizumab (N=28) Patient-Years (PY)=40.1 Events n	Rate per 100 PY	Patients n (%)	Treatment Effect Estimate (95% CI; p-value)
							OR 0.201 (0.051, 0.799); 0.0226
Respiratory, thoracic and mediastinal disorders	54	42	17 (22.7)	2	5	2 (7.1)	RR 1.173 (1.050, 1.322); 0.0028
							RD 0.143 (0.043, 0.238); 0.0018
							OR 0.562 (0.213, 1.488); 0.2463
Skin and subcutaneous tissue disorders	23	18	17 (22.7)	7	17	6 (21.4)	RR 0.584 (0.246, 1.339); 0.2268
							RD -0.074 (-0.181, 0.048); 0.1872
ModerateTEAEs							
							OR 0.469 (0.134, 1.641); 0.2360
Gastrointestinal disorders	14	11	11 (14.7)	4	10	3 (10.7)	RR 1.071 (0.958, 1.187); 0.1516
							RD 0.063 (-0.038, 0.152); 0.1495
							OR 0.763 (0.323, 1.802); 0.5370
Infections and infestations	32	25	19 (25.3)	11	27	9 (32.1)	RR 0.784 (0.380, 1.572); 0.5095
							RD -0.043 (-0.161, 0.091); 0.4945
							OR 1.150 (0.327, 4.041); 0.8280
Injury, poisoning and procedural complications	8	6	6 (8.0)	4	10	4 (14.3)	RR 1.103 (0.343, 3.491); 0.8746
							RD 0.006 (-0.074, 0.109); 0.8760
							OR 0.760 (0.234, 2.476); 0.6493
Musculoskeletal and connective tissue disorders	11	9	9 (12.0)	5	12	4 (14.3)	RR 0.736 (0.247, 2.139); 0.5949
							RD -0.025 (-0.113, 0.080); 0.5787
Non-SevereTEAEs							
							OR 0.216 (0.054, 0.862); 0.0300
Blood and lymphatic system disorders	27	21	16 (21.3)	2	5	2 (7.1)	RR 0.207 (0.054, 0.762); 0.0312
							RD -0.132 (-0.226, -0.033); 0.0033
							OR 0.286 (0.086, 0.958); 0.0424
Eye disorders	38	30	17 (22.7)	4	10	3 (10.7)	RR 1.152 (1.021, 1.303); 0.0120
							RD 0.125 (0.018, 0.224); 0.0099
							OR 0.777 (0.376, 1.606); 0.4957
Gastrointestinal disorders	89	69	30 (40.0)	22	55	15 (53.6)	RR 1.078 (0.866, 1.318); 0.4668
							RD 0.054 (-0.098, 0.194); 0.4693
							OR 0.469 (0.134, 1.641); 0.2360
Diarrhoea	17	13	11 (14.7)	3	7	3 (10.7)	RR 1.071 (0.958, 1.187); 0.1516
							RD 0.063 (-0.038, 0.152); 0.1495
							OR 0.299 (0.073, 1.225); 0.0934
Nausea	24	19	12 (16.0)	2	5	2 (7.1)	RR 1.103 (0.995, 1.224); 0.0319
							RD 0.091 (-0.004, 0.178); 0.0288
							OR 0.591 (0.246, 1.421); 0.2398
General disorders and administration site conditions	74	58	21 (28.0)	16	40	8 (28.6)	RR 1.103 (0.937, 1.283); 0.1913
							RD 0.081 (-0.051, 0.198); 0.1916
							OR 0.290 (0.144, 0.586); 0.0005
Infections and infestations	207	161	55 (73.3)	23	57	16 (57.1)	RR 0.482 (0.301, 0.736); 0.0015
							RD -0.297 (-0.438, -0.137); 0.0001
							OR 19.842 (1.059, 371.71); 0.0457
COVID-19	0	0	0 (0.0)	5	12	5 (17.9)	RR 0.914 (0.813, 0.963); 0.0254
							RD -0.086 (-0.187, -0.037); 0.0193
							OR 0.053 (0.003, 0.929); 0.0444
Nasopharyngitis	27	21	13 (17.3)	0	0	0 (0.0)	RR 1.157 (1.080, 1.279); 0.0003
							RD 0.135 (0.070, 0.218); 0.0001
							OR 0.079 (0.004, 1.412); 0.0844
Pharyngitis	12	9	9 (12.0)	0	0	0 (0.0)	RR 1.103 (1.032, 1.203); 0.0027
							RD 0.094 (0.029, 0.169); 0.0016
							OR 0.155 (0.040, 0.609); 0.0075
Upper respiratory tract infection	32	25	21 (28.0)	2	5	2 (7.1)	RR 0.158 (0.042, 0.569); 0.0104
							RD -0.184 (-0.284, -0.081); 0.0001
							OR 0.329 (0.080, 1.360); 0.1247
Urinary tract infection	33	26	11 (14.7)	2	5	2 (7.1)	RR 1.090 (0.985, 1.205); 0.0507
							RD 0.080 (-0.014, 0.166); 0.0473
							OR 0.273 (0.101, 0.738); 0.0105
Injury, poisoning and procedural complications	42	33	26 (34.7)	8	20	5 (17.9)	RR 0.318 (0.131, 0.742); 0.0127
							RD -0.185 (-0.297, -0.060); 0.0016
							OR 0.070 (0.004, 1.255); 0.0710
Contusion	11	9	10 (13.3)	0	0	0 (0.0)	RR 1.116 (1.044, 1.222); 0.0016
							RD 0.104 (0.039, 0.182); 0.0008
							OR 0.847 (0.283, 2.530); 0.7660
Investigations	19	15	10 (13.3)	8	20	5 (17.9)	RR 1.020 (0.898, 1.135); 0.7094
							RD 0.018 (-0.093, 0.111); 0.7099

Treatment Emergent Adverse Events (TEAEs) by MedDRA System Organ Class/Preferred Term by Severity and Treatment Group, IST Use: Yes

System Organ Class / Preferred Term	Eculizumab (N=75) Patient-Years (PY)=128.5 Events n	Rate per 100 PY	Patients n (%)	Ravulizumab (N=28) Patient-Years (PY)=40.1 Events n	Rate per 100 PY	Patients n (%)	Treatment Effect	Estimate (95% CI; p-value)
Metabolism and nutrition disorders	10	8	9 (12.0)	3	7	3 (10.7)	OR	0.581 (0.161, 2.091); 0.4058
							RR	1.046 (0.938, 1.152); 0.3129
							RD	0.042 (-0.057, 0.127); 0.3124
Musculoskeletal and connective tissue disorders	61	47	32 (42.7)	14	35	10 (35.7)	OR	0.430 (0.194, 0.952); 0.0373
							RR	0.517 (0.272, 0.943); 0.0405
							RD	-0.161 (-0.290, -0.016); 0.0199
Arthralgia	8	6	8 (10.7)	3	7	3 (10.7)	OR	0.657 (0.179, 2.407); 0.5255
							RR	0.621 (0.182, 2.056); 0.4674
							RD	-0.032 (-0.114, 0.067); 0.4353
Back pain	10	8	9 (12.0)	4	10	3 (10.7)	OR	0.581 (0.161, 2.091); 0.4058
							RR	1.046 (0.938, 1.152); 0.3129
							RD	0.042 (-0.057, 0.127); 0.3124
Nervous system disorders	158	123	37 (49.3)	17	42	8 (28.6)	OR	0.267 (0.115, 0.619); 0.0021
							RR	0.358 (0.178, 0.687); 0.0036
							RD	-0.247 (-0.373, -0.105); 0.0002
Dizziness	16	12	12 (16.0)	1	2	1 (3.6)	OR	0.176 (0.031, 1.005); 0.0507
							RR	0.138 (0.023, 0.787); 0.0538
							RD	-0.108 (-0.192, -0.023); 0.0044
Headache	73	57	17 (22.7)	10	25	6 (21.4)	OR	0.562 (0.213, 1.488); 0.2463
							RR	1.089 (0.943, 1.243); 0.1877
							RD	0.074 (-0.048, 0.181); 0.1872
Psychiatric disorders	8	6	8 (10.7)	2	5	2 (7.1)	OR	0.461 (0.107, 1.984); 0.2983
							RR	1.053 (0.955, 1.151); 0.1891
							RD	0.049 (-0.042, 0.128); 0.1869
Renal and urinary disorders	15	12	10 (13.3)	3	7	2 (7.1)	OR	0.364 (0.087, 1.524); 0.1668
							RR	1.078 (0.974, 1.187); 0.0797
							RD	0.070 (-0.023, 0.154); 0.0764
Respiratory, thoracic and mediastinal disorders	57	44	20 (26.7)	2	5	2 (7.1)	OR	0.165 (0.042, 0.649); 0.0099
							RR	1.220 (1.086, 1.387); 0.0006
							RD	0.174 (0.071, 0.272); 0.0003
Cough	9	7	8 (10.7)	0	0	0 (0.0)	OR	0.089 (0.005, 1.609); 0.1015
							RR	1.091 (1.021, 1.185); 0.0047
							RD	0.083 (0.019, 0.156); 0.0031
Skin and subcutaneous tissue disorders	24	19	17 (22.7)	9	22	8 (28.6)	OR	0.765 (0.311, 1.878); 0.5583
							RR	0.779 (0.360, 1.639); 0.5272
							RD	-0.039 (-0.152, 0.090); 0.5122
Vascular disorders	14	11	11 (14.7)	3	7	2 (7.1)	OR	0.329 (0.080, 1.360); 0.1247
							RR	1.090 (0.985, 1.205); 0.0507
							RD	0.080 (-0.014, 0.166); 0.0473
Severe TEAEs								
Infections and infestations	7	5	5 (6.7)	3	7	3 (10.7)	OR	1.049 (0.261, 4.217); 0.9461
							RR	0.993 (0.267, 3.624); 0.9922
							RD	-0.000 (-0.074, 0.095); 0.9922
Serious TEAEs								
Infections and infestations	13	10	9 (12.0)	3	7	3 (10.7)	OR	0.581 (0.161, 2.091); 0.4058
							RR	0.552 (0.165, 1.792); 0.3570
							RD	-0.042 (-0.127, 0.057); 0.3124
Nervous system disorders	6	5	6 (8.0)	0	0	0 (0.0)	OR	0.119 (0.006, 2.205); 0.1530
							RR	1.067 (0.998, 1.149); 0.0143
							RD	0.063 (-0.001, 0.130); 0.0114
Neuromyelitis optica spectrum disorder	6	5	6 (8.0)	0	0	0 (0.0)	OR	0.119 (0.006, 2.205); 0.1530
							RR	1.067 (0.998, 1.149); 0.0143
							RD	0.063 (-0.001, 0.130); 0.0114
TEAEs leading to withdrawal from study drug								
None								

AE: Adverse Event; CI: Confidence Interval; IST: Immunosuppressive Therapy; OR: Odds Ratio; PY: person years; RD: Risk Difference; RR: Risk Ratio; TEAE: Treatment-emergent Adverse Event.

TEAEs are AEs with a start date on or after the date of the first dose of study drug.

Treatment-related adverse events and follow-up were truncated at the maximum duration of follow-up in the ravulizumab arm.

Odds ratios were derived from a logistic regression model with treatment as the only covariate. Firth's correction was applied for odds ratios.

Mild, moderate and non-severe TEAEs were examined for preferred terms and system organ classes reported in at least 10% of patients in one of the treatment arms within the subgroup.

Severe and serious TEAEs were examined for preferred terms and system organ classes reported in at least 5% of patients in one of the treatment arms within the subgroup.

All TEAEs leading to withdrawal from study drug were examined.

TEAEs leading to withdrawal from study drug were examined descriptively (i.e., OR, RR, and RD not calculated).

Treatment Emergent Adverse Events (TEAEs) by MedDRA System Organ Class/Preferred Term by Treatment Group, IST Use: No

System Organ Class / Preferred Term	Eculizumab (N=21) Patient-Years (PY)=44.4 Events n	Rate per 100 PY	Patients n (%)	Ravulizumab (N=30) Patient-Years (PY)=44 Events n	Rate per 100 PY	Patients n (%)	Treatment Effect Estimate (95% CI; p-value)
Blood and lymphatic system disorders	9	20	3 (14.3)	2	5	2 (6.7)	OR 1.182 (0.223, 6.267); 0.8443 RR 0.997 (0.908, 1.065); 0.9137 RD -0.003 (-0.089, 0.060); 0.9137
Eye disorders	7	16	2 (9.5)	5	11	3 (10.0)	OR 2.384 (0.450, 12.631); 0.3073 RR 0.968 (0.875, 1.032); 0.3470 RD -0.031 (-0.123, 0.030); 0.3423
Gastrointestinal disorders	35	79	10 (47.6)	10	23	7 (23.3)	OR 1.200 (0.439, 3.280); 0.7228 RR 0.982 (0.851, 1.100); 0.7556 RD -0.017 (-0.136, 0.083); 0.7549
Diarrhoea	5	11	4 (19.0)	0	0	0 (0.0)	OR 0.176 (0.009, 3.405); 0.2502 RR 1.043 (0.977, 1.114); 0.0455 RD 0.042 (-0.022, 0.103); 0.0411
General disorders and administration site conditions	10	23	4 (19.0)	20	45	9 (30.0)	OR 3.945 (1.211, 12.851); 0.0228 RR 0.882 (0.759, 0.976); 0.0361 RD -0.114 (-0.233, -0.022); 0.0282
Infections and infestations	73	165	17 (81.0)	40	91	20 (66.7)	OR 2.419 (1.142, 5.122); 0.0210 RR 0.796 (0.630, 0.964); 0.0321 RD -0.168 (-0.314, -0.027); 0.0226
COVID-19	0	0	0 (0.0)	9	20	9 (30.0)	OR 37.040 (2.080, 659.74); 0.0140 RR 0.845 (0.730, 0.916); 0.0027 RD -0.155 (-0.270, -0.084); 0.0011
Nasopharyngitis	19	43	7 (33.3)	3	7	3 (10.0)	OR 0.752 (0.201, 2.823); 0.6733 RR 1.023 (0.919, 1.117); 0.5900 RD 0.021 (-0.076, 0.101); 0.5904
Upper respiratory tract infection	13	29	7 (33.3)	2	5	2 (6.7)	OR 0.528 (0.120, 2.322); 0.3980 RR 1.041 (0.945, 1.134); 0.2836 RD 0.038 (-0.052, 0.115); 0.2824
Urinary tract infection	9	20	2 (9.5)	5	11	4 (13.3)	OR 3.121 (0.635, 15.332); 0.1611 RR 0.951 (0.851, 1.018); 0.1929 RD -0.048 (-0.146, 0.016); 0.1852
Injury, poisoning and procedural complications	4	9	4 (19.0)	10	23	7 (23.3)	OR 2.993 (0.879, 10.193); 0.0795 RR 0.918 (0.801, 1.006); 0.1051 RD -0.079 (-0.192, 0.005); 0.0954
Investigations	9	20	4 (19.0)	3	7	3 (10.0)	OR 1.296 (0.305, 5.505); 0.7252 RR 0.990 (0.892, 1.067); 0.7775 RD -0.010 (-0.104, 0.060); 0.7771
Musculoskeletal and connective tissue disorders	22	50	11 (52.4)	17	39	13 (43.3)	OR 2.206 (0.923, 5.269); 0.0750 RR 0.876 (0.730, 1.011); 0.0969 RD -0.110 (-0.244, 0.009); 0.0854
Arthralgia	3	7	2 (9.5)	3	7	3 (10.0)	OR 2.384 (0.450, 12.631); 0.3073 RR 0.968 (0.875, 1.032); 0.3470 RD -0.031 (-0.123, 0.030); 0.3423
Back pain	6	14	4 (19.0)	4	9	4 (13.3)	OR 1.698 (0.437, 6.602); 0.4450 RR 0.972 (0.868, 1.051); 0.4872 RD -0.027 (-0.127, 0.046); 0.4842
Nervous system disorders	16	36	6 (28.6)	26	59	9 (30.0)	OR 2.672 (0.923, 7.737); 0.0700 RR 0.901 (0.774, 1.005); 0.0939 RD -0.093 (-0.214, 0.004); 0.0837
Dizziness	3	7	2 (9.5)	3	7	3 (10.0)	OR 2.384 (0.450, 12.631); 0.3073 RR 0.968 (0.875, 1.032); 0.3470 RD -0.031 (-0.123, 0.030); 0.3423
Headache	7	16	4 (19.0)	14	32	8 (26.7)	OR 3.460 (1.041, 11.494); 0.0428 RR 0.900 (0.780, 0.991); 0.0618 RD -0.096 (-0.212, -0.009); 0.0526
Psychiatric disorders	7	16	4 (19.0)	8	18	4 (13.3)	OR 1.698 (0.437, 6.602); 0.4450 RR 0.972 (0.868, 1.051); 0.4872 RD -0.027 (-0.127, 0.046); 0.4842
Renal and urinary disorders	7	16	6 (28.6)	6	14	2 (6.7)	OR 0.616 (0.136, 2.782); 0.5289 RR 1.030 (0.936, 1.117); 0.4159 RD 0.028 (-0.061, 0.102); 0.4156
Reproductive system and breast disorders	6	14	3 (14.3)	2	5	2 (6.7)	OR 1.182 (0.223, 6.267); 0.8443 RR 0.997 (0.908, 1.065); 0.9137 RD -0.003 (-0.089, 0.060); 0.9137
Respiratory, thoracic and mediastinal disorders	5	11	3 (14.3)	8	18	7 (23.3)	OR 3.890 (1.037, 14.590); 0.0440 RR 0.908 (0.793, 0.990); 0.0624

System Organ Class	Eculizumab (N=21) Patient-Years (PY)=44.4			Ravulizumab (N=30) Patient-Years (PY)=44			Treatment Effect	
Preferred Term	Events n	Rate per 100 PY	Patients n (%)	Events n	Rate per 100 PY	Patients n (%)	Estimate (95% CI; p-value)	
							RD	-0.089 (-0.201, -0.009); 0.0535
							OR	1.685 (0.365, 7.773); 0.5035
Cough	3	7	3 (14.3)	3	7	3 (10.0)	RR	0.979 (0.883, 1.050); 0.5499
							RD	-0.020 (-0.114, 0.046); 0.5479
							OR	0.860 (0.259, 2.855); 0.8050
Skin and subcutaneous tissue disorders	14	32	8 (38.1)	7	16	4 (13.3)	RR	1.016 (0.904, 1.118); 0.7416
							RD	0.014 (-0.090, 0.100); 0.7419

AE: Adverse Event; CI: Confidence Interval; IST: Immunosuppressive Therapy; OR: Odds Ratio; PY: person years; RD: Risk Difference; RR: Risk Ratio; TEAE: Treatment-emergent
TEAEs are AEs with a start date on or after the date of the first dose of study drug.
Treatment-related adverse events and follow-up were truncated at the maximum duration of follow-up in the ravulizumab arm.
Odds ratios were derived from a logistic regression model with treatment as the only covariate. Firth's correction was applied for odds ratios.
Any TEAEs were examined for preferred terms and system organ classes reported in at least 10% of patients in one of the treatment arms within the subgroup.
Severe and serious TEAEs were examined for preferred terms and system organ classes reported in at least 5% of patients in one of the treatment arms within the subgroup.
Preferred terms and system organ classes for a given AE severity or type (i.e., leading for withdrawal) were only examined within each subgroup if they were also examined in

Treatment Emergent Adverse Events (TEAEs) by MedDRA System Organ Class/Preferred Term by Severity and Treatment Group, IST Use: No

System Organ Class / Preferred Term	Eculizumab (N=21) Patient-Years (PY)=44.4 Events n	Rate per 100 PY	Patients n (%)	Ravulizumab (N=30) Patient-Years (PY)=44 Events n	Rate per 100 PY	Patients n (%)	Treatment Effect	Estimate (95% CI; p-value)
Mild TEAEs								
Eye disorders	2	5	2 (9.5)	4	9	3 (10.0)	OR	2.384 (0.450, 12.631); 0.3073
							RR	0.968 (0.875, 1.032); 0.3470
							RD	-0.031 (-0.123, 0.030); 0.3423
Gastrointestinal disorders	29	65	8 (38.1)	9	20	7 (23.3)	OR	1.516 (0.532, 4.322); 0.4363
							RR	0.959 (0.834, 1.068); 0.4698
							RD	-0.037 (-0.155, 0.058); 0.4660
Diarrhoea	5	11	4 (19.0)	0	0	0 (0.0)	OR	0.176 (0.009, 3.405); 0.2502
							RR	1.043 (0.977, 1.114); 0.0455
							RD	0.042 (-0.022, 0.103); 0.0411
General disorders and administration site conditions	9	20	4 (19.0)	16	36	7 (23.3)	OR	2.993 (0.879, 10.193); 0.0795
							RR	0.918 (0.801, 1.006); 0.1051
							RD	-0.079 (-0.192, 0.005); 0.0954
Infections and infestations	56	126	13 (61.9)	31	71	17 (56.7)	OR	2.608 (1.164, 5.846); 0.0199
							RR	0.818 (0.663, 0.966); 0.0316
							RD	-0.158 (-0.299, -0.027); 0.0227
COVID-19	0	0	0 (0.0)	8	18	8 (26.7)	OR	32.487 (1.809, 583.38); 0.0182
							RR	0.862 (0.750, 0.929); 0.0047
							RD	-0.138 (-0.250, -0.071); 0.0023
Nasopharyngitis	14	32	4 (19.0)	2	5	2 (6.7)	OR	0.910 (0.185, 4.472); 0.9071
							RR	1.007 (0.917, 1.082); 0.8193
							RD	0.007 (-0.080, 0.074); 0.8194
Upper respiratory tract infection	11	25	6 (28.6)	2	5	2 (6.7)	OR	0.616 (0.136, 2.782); 0.5289
							RR	1.030 (0.936, 1.117); 0.4159
							RD	0.028 (-0.061, 0.102); 0.4156
Urinary tract infection	9	20	2 (9.5)	4	9	3 (10.0)	OR	2.384 (0.450, 12.631); 0.3073
							RR	0.968 (0.875, 1.032); 0.3470
							RD	-0.031 (-0.123, 0.030); 0.3423
Injury, poisoning and procedural complications	3	7	3 (14.3)	3	7	3 (10.0)	OR	1.685 (0.365, 7.773); 0.5035
							RR	0.979 (0.883, 1.050); 0.5499
							RD	-0.020 (-0.114, 0.046); 0.5479
Investigations	6	14	3 (14.3)	3	7	3 (10.0)	OR	1.685 (0.365, 7.773); 0.5035
							RR	0.979 (0.883, 1.050); 0.5499
							RD	-0.020 (-0.114, 0.046); 0.5479
Musculoskeletal and connective tissue disorders	15	34	9 (42.9)	13	30	9 (30.0)	OR	1.768 (0.669, 4.669); 0.2503
							RR	0.932 (0.799, 1.050); 0.2814
							RD	-0.061 (-0.186, 0.042); 0.2734
Nervous system disorders	14	32	6 (28.6)	20	45	7 (23.3)	OR	2.028 (0.667, 6.166); 0.2129
							RR	0.938 (0.817, 1.036); 0.2468
							RD	-0.058 (-0.173, 0.032); 0.2388
Headache	7	16	4 (19.0)	10	23	5 (16.7)	OR	2.113 (0.576, 7.748); 0.2590
							RR	0.954 (0.845, 1.036); 0.2966
							RD	-0.045 (-0.150, 0.033); 0.2903
Psychiatric disorders	6	14	4 (19.0)	3	7	3 (10.0)	OR	1.296 (0.305, 5.505); 0.7252
							RR	0.990 (0.892, 1.067); 0.7775
							RD	-0.010 (-0.104, 0.060); 0.7771
Renal and urinary disorders	5	11	5 (23.8)	6	14	2 (6.7)	OR	0.736 (0.157, 3.443); 0.6971
							RR	1.019 (0.926, 1.100); 0.5935
							RD	0.018 (-0.070, 0.088); 0.5937
Reproductive system and breast disorders	6	14	3 (14.3)	2	5	2 (6.7)	OR	1.182 (0.223, 6.267); 0.8443
							RR	0.997 (0.908, 1.065); 0.9137
							RD	-0.003 (-0.089, 0.060); 0.9137

Treatment Emergent Adverse Events (TEAEs) by MedDRA System Organ Class/Preferred Term by Severity and Treatment Group, IST Use: No

System Organ Class / Preferred Term	Eculizumab (N=21) Patient-Years (PY)=44.4 Events n	Rate per 100 PY	Patients n (%)	Ravulizumab (N=30) Patient-Years (PY)=44 Events n	Rate per 100 PY	Patients n (%)	Treatment Effect Estimate (95% CI; p-value)	
Respiratory, thoracic and mediastinal disorders	5	11	3 (14.3)	7	16	6 (20.0)	OR	3.307 (0.856, 12.775); 0.0828
							RR	0.925 (0.815, 1.005); 0.1083
							RD	-0.072 (-0.180, 0.005); 0.0989
Cough	3	7	3 (14.3)	3	7	3 (10.0)	OR	1.685 (0.365, 7.773); 0.5035
							RR	0.979 (0.883, 1.050); 0.5499
							RD	-0.020 (-0.114, 0.046); 0.5479
Skin and subcutaneous tissue disorders	12	27	7 (33.3)	6	14	3 (10.0)	OR	0.752 (0.201, 2.823); 0.6733
							RR	1.023 (0.919, 1.117); 0.5900
							RD	0.021 (-0.076, 0.101); 0.5904
ModerateTEAEs								
Gastrointestinal disorders	4	9	3 (14.3)	1	2	1 (3.3)	OR	0.697 (0.099, 4.925); 0.7173
							RR	1.014 (0.935, 1.081); 0.5699
							RD	0.014 (-0.063, 0.074); 0.5698
Infections and infestations	17	38	8 (38.1)	7	16	7 (23.3)	OR	1.516 (0.532, 4.322); 0.4363
							RR	0.959 (0.834, 1.068); 0.4698
							RD	-0.037 (-0.155, 0.058); 0.4660
Injury, poisoning and procedural complications	1	2	1 (4.8)	6	14	3 (10.0)	OR	4.014 (0.569, 28.310); 0.1631
							RR	0.958 (0.866, 1.014); 0.1882
							RD	-0.041 (-0.132, 0.013); 0.1809
Musculoskeletal and connective tissue disorders	6	14	4 (19.0)	3	7	3 (10.0)	OR	1.296 (0.305, 5.505); 0.7252
							RR	0.990 (0.892, 1.067); 0.7775
							RD	-0.010 (-0.104, 0.060); 0.7771
Non-SevereTEAEs								
Blood and lymphatic system disorders	9	20	3 (14.3)	2	5	2 (6.7)	OR	1.182 (0.223, 6.267); 0.8443
							RR	0.997 (0.908, 1.065); 0.9137
							RD	-0.003 (-0.089, 0.060); 0.9137
Eye disorders	7	16	2 (9.5)	5	11	3 (10.0)	OR	2.384 (0.450, 12.631); 0.3073
							RR	0.968 (0.875, 1.032); 0.3470
							RD	-0.031 (-0.123, 0.030); 0.3423
Gastrointestinal disorders	33	74	9 (42.9)	10	23	7 (23.3)	OR	1.341 (0.481, 3.737); 0.5745
							RR	0.970 (0.843, 1.084); 0.6071
							RD	-0.027 (-0.145, 0.071); 0.6051
Diarrhoea	5	11	4 (19.0)	0	0	0 (0.0)	OR	0.176 (0.009, 3.405); 0.2502
							RR	1.043 (0.977, 1.114); 0.0455
							RD	0.042 (-0.022, 0.103); 0.0411
General disorders and administration site conditions	9	20	4 (19.0)	19	43	9 (30.0)	OR	3.945 (1.211, 12.851); 0.0228
							RR	0.882 (0.759, 0.976); 0.0361
							RD	-0.114 (-0.233, -0.022); 0.0282
Infections and infestations	73	165	17 (81.0)	38	86	20 (66.7)	OR	2.419 (1.142, 5.122); 0.0210
							RR	0.796 (0.630, 0.964); 0.0321
							RD	-0.168 (-0.314, -0.027); 0.0226
COVID-19	0	0	0 (0.0)	9	20	9 (30.0)	OR	37.040 (2.080, 659.74); 0.0140
							RR	0.845 (0.730, 0.916); 0.0027
							RD	-0.155 (-0.270, -0.084); 0.0011
Nasopharyngitis	19	43	7 (33.3)	3	7	3 (10.0)	OR	0.752 (0.201, 2.823); 0.6733
							RR	1.023 (0.919, 1.117); 0.5900
							RD	0.021 (-0.076, 0.101); 0.5904
Upper respiratory tract infection	13	29	7 (33.3)	2	5	2 (6.7)	OR	0.528 (0.120, 2.322); 0.3980
							RR	1.041 (0.945, 1.134); 0.2836
							RD	0.038 (-0.052, 0.115); 0.2824
Urinary tract infection	9	20	2 (9.5)	5	11	4 (13.3)	OR	3.121 (0.635, 15.332); 0.1611
							RR	0.951 (0.851, 1.018); 0.1929
							RD	-0.048 (-0.146, 0.016); 0.1852
Injury, poisoning and procedural complications	4	9	4 (19.0)	9	20	6 (20.0)	OR	2.545 (0.724, 8.945); 0.1453
							RR	0.936 (0.823, 1.021); 0.1775
							RD	-0.062 (-0.171, 0.019); 0.1687
Investigations	9	20	4 (19.0)	3	7	3 (10.0)	OR	1.296 (0.305, 5.505); 0.7252
							RR	0.990 (0.892, 1.067); 0.7775
							RD	-0.010 (-0.104, 0.060); 0.7771
Musculoskeletal and connective tissue disorders	21	47	11 (52.4)	16	36	12 (40.0)	OR	1.999 (0.827, 4.833); 0.1243
							RR	0.896 (0.751, 1.028); 0.1498
							RD	-0.092 (-0.225, 0.023); 0.1386
Arthralgia	3	7	2 (9.5)	3	7	3 (10.0)	OR	2.384 (0.450, 12.631); 0.3073
							RR	0.968 (0.875, 1.032); 0.3470
							RD	-0.031 (-0.123, 0.030); 0.3423
Back pain	5	11	4 (19.0)	3	7	3 (10.0)	OR	1.296 (0.305, 5.505); 0.7252
							RR	0.990 (0.892, 1.067); 0.7775
							RD	-0.010 (-0.104, 0.060); 0.7771

Treatment Emergent Adverse Events (TEAEs) by MedDRA System Organ Class/Preferred Term by Severity and Treatment Group, IST Use: No

System Organ Class / Preferred Term	Eculizumab (N=21) Patient-Years (PY)=44.4 Events n	Rate per 100 PY	Patients n (%)	Ravulizumab (N=30) Patient-Years (PY)=44 Events n	Rate per 100 PY	Patients n (%)	Treatment Effect	Estimate (95% CI; p-value)
Nervous system disorders	16	36	6 (28.6)	25	57	9 (30.0)	OR	2.672 (0.923, 7.737); 0.0700
							RR	0.901 (0.774, 1.005); 0.0939
							RD	-0.093 (-0.214, 0.004); 0.0837
Headache	7	16	4 (19.0)	14	32	8 (26.7)	OR	3.460 (1.041, 11.494); 0.0428
							RR	0.900 (0.780, 0.991); 0.0618
							RD	-0.096 (-0.212, -0.009); 0.0526
Psychiatric disorders	7	16	4 (19.0)	7	16	4 (13.3)	OR	1.698 (0.437, 6.602); 0.4450
							RR	0.972 (0.868, 1.051); 0.4872
							RD	-0.027 (-0.127, 0.046); 0.4842
Renal and urinary disorders	7	16	6 (28.6)	6	14	2 (6.7)	OR	0.616 (0.136, 2.782); 0.5289
							RR	1.030 (0.936, 1.117); 0.4159
							RD	0.028 (-0.061, 0.102); 0.4156
Reproductive system and breast disorders	6	14	3 (14.3)	2	5	2 (6.7)	OR	1.182 (0.223, 6.267); 0.8443
							RR	0.997 (0.908, 1.065); 0.9137
							RD	-0.003 (-0.089, 0.060); 0.9137
Respiratory, thoracic and mediastinal disorders	5	11	3 (14.3)	8	18	7 (23.3)	OR	3.890 (1.037, 14.590); 0.0440
							RR	0.908 (0.793, 0.990); 0.0624
							RD	-0.089 (-0.201, -0.009); 0.0535
Cough	3	7	3 (14.3)	3	7	3 (10.0)	OR	1.685 (0.365, 7.773); 0.5035
							RR	0.979 (0.883, 1.050); 0.5499
							RD	-0.020 (-0.114, 0.046); 0.5479
Skin and subcutaneous tissue disorders	14	32	8 (38.1)	7	16	4 (13.3)	OR	0.860 (0.259, 2.855); 0.8050
							RR	1.016 (0.904, 1.118); 0.7416
							RD	0.014 (-0.090, 0.100); 0.7419
Severe TEAEs								
Infections and infestations	0	0	0 (0.0)	2	5	2 (6.7)	OR	8.540 (0.396, 184.30); 0.1712
							RR	0.966 (0.882, 1.005); 0.1573
							RD	-0.034 (-0.118, 0.005); 0.1501
Serious TEAEs								
Infections and infestations	0	0	0 (0.0)	2	5	2 (6.7)	OR	8.540 (0.396, 184.30); 0.1712
							RR	0.966 (0.882, 1.005); 0.1573
							RD	-0.034 (-0.118, 0.005); 0.1501
TEAEs leading to withdrawal from study drug								
Infections and infestations	0	0	0 (0.0)	3	7	1 (3.3)	OR	Not calculated
							RR	Not calculated
							RD	Not calculated
Bronchitis	0	0	0 (0.0)	1	2	1 (3.3)	OR	Not calculated
							RR	Not calculated
							RD	Not calculated
Encephalitis meningococcal	0	0	0 (0.0)	1	2	1 (3.3)	OR	Not calculated
							RR	Not calculated
							RD	Not calculated

Treatment Emergent Adverse Events (TEAEs) by MedDRA System Organ Class/Preferred Term by Severity and Treatment Group, IST Use: No

System Organ Class	Eculizumab (N=21) Patient-Years (PY)=44.4			Ravulizumab (N=30) Patient-Years (PY)=44			Treatment Effect	
Preferred Term	Events n	Rate per 100 PY	Patients n (%)	Events n	Rate per 100 PY	Patients n (%)	Estimate (95% CI; p-value)	
							OR	Not calculated
Stenotrophomonas infection	0	0	0 (0.0)	1	2	1 (3.3)	RR	Not calculated
							RD	Not calculated

AE: Adverse Event; CI: Confidence Interval; IST: Immunosuppressive Therapy; OR: Odds Ratio; PY: person years; RD: Risk Difference; RR: Risk Ratio; TEAE: Treatment-emergent Adverse Event.
TEAEs are AEs with a start date on or after the date of the first dose of study drug.
Treatment-related adverse events and follow-up were truncated at the maximum duration of follow-up in the ravulizumab arm.
Odds ratios were derived from a logistic regression model with treatment as the only covariate. Firth's correction was applied for odds ratios.
Mild, moderate and non-severe TEAEs were examined for preferred terms and system organ classes reported in at least 10% of patients in one of the treatment arms within the subgroup.
Severe and serious TEAEs were examined for preferred terms and system organ classes reported in at least 5% of patients in one of the treatment arms within the subgroup.
All TEAEs leading to withdrawal from study drug were examined.
TEAEs leading to withdrawal from study drug were examined descriptively (i.e., OR, RR, and RD not calculated).

Treatment Emergent Adverse Events (TEAEs) by MedDRA System Organ Class/Preferred Term by Treatment Group, Rituximab Use: Yes

System Organ Class / Preferred Term	Eculizumab (N=26) Patient-Years (PY)=38.4 Events n	Rate per 100 PY	Patients n (%)	Ravulizumab (N=20) Patient-Years (PY)=30.4 Events n	Rate per 100 PY	Patients n (%)	Treatment Effect	Estimate (95% CI; p-value)
Blood and lymphatic system disorders	8	21	5 (19.2)	4	13	4 (20.0)	OR	1.373 (0.375, 5.037); 0.6322
							RR	1.324 (0.395, 4.386); 0.6657
							RD	0.017 (-0.060, 0.118); 0.6750
Eye disorders	12	31	5 (19.2)	3	10	2 (10.0)	OR	0.736 (0.157, 3.443); 0.6971
							RR	1.019 (0.926, 1.100); 0.5935
							RD	0.018 (-0.070, 0.088); 0.5937
Gastrointestinal disorders	29	75	10 (38.5)	10	33	7 (35.0)	OR	1.200 (0.439, 3.280); 0.7228
							RR	0.982 (0.851, 1.100); 0.7556
							RD	-0.017 (-0.136, 0.083); 0.7549
Diarrhoea	3	8	3 (11.5)	1	3	1 (5.0)	OR	0.697 (0.099, 4.925); 0.7173
							RR	1.014 (0.935, 1.081); 0.5699
							RD	0.014 (-0.063, 0.074); 0.5698
General disorders and administration site conditions	50	130	11 (42.3)	12	39	6 (30.0)	OR	0.921 (0.329, 2.575); 0.8746
							RR	1.013 (0.884, 1.134); 0.8287
							RD	0.011 (-0.105, 0.110); 0.8289
Infections and infestations	74	193	19 (73.1)	21	69	11 (55.0)	OR	0.962 (0.424, 2.183); 0.9266
							RR	0.958 (0.490, 1.829); 0.9003
							RD	-0.008 (-0.132, 0.130); 0.8998
COVID-19	0	0	0 (0.0)	5	16	5 (25.0)	OR	19.842 (1.059, 371.71); 0.0457
							RR	0.914 (0.813, 0.963); 0.0254
							RD	-0.086 (-0.187, -0.037); 0.0193
Nasopharyngitis	16	42	5 (19.2)	1	3	1 (5.0)	OR	0.434 (0.068, 2.759); 0.3764
							RR	1.037 (0.954, 1.116); 0.2223
							RD	0.035 (-0.044, 0.102); 0.2198
Upper respiratory tract infection	8	21	5 (19.2)	1	3	1 (5.0)	OR	0.434 (0.068, 2.759); 0.3764
							RR	0.331 (0.052, 2.065); 0.3072
							RD	-0.035 (-0.102, 0.044); 0.2198
Urinary tract infection	14	36	5 (19.2)	5	16	4 (20.0)	OR	1.373 (0.375, 5.037); 0.6322
							RR	0.982 (0.877, 1.068); 0.6761
							RD	-0.017 (-0.118, 0.060); 0.6750
Injury, poisoning and procedural complications	23	60	11 (42.3)	7	23	4 (20.0)	OR	0.614 (0.194, 1.939); 0.4057
							RR	0.602 (0.208, 1.692); 0.3644
							RD	-0.046 (-0.138, 0.062); 0.3268
Contusion	4	10	3 (11.5)	0	0	0 (0.0)	OR	0.228 (0.011, 4.611); 0.3354
							RR	1.032 (0.967, 1.097); 0.0833
							RD	0.031 (-0.032, 0.088); 0.0784
Investigations	14	36	6 (23.1)	2	7	2 (10.0)	OR	0.616 (0.136, 2.782); 0.5289
							RR	1.030 (0.936, 1.117); 0.4159
							RD	0.028 (-0.061, 0.102); 0.4156
Metabolism and nutrition disorders	4	10	3 (11.5)	0	0	0 (0.0)	OR	0.228 (0.011, 4.611); 0.3354
							RR	1.032 (0.967, 1.097); 0.0833
							RD	0.031 (-0.032, 0.088); 0.0784
Musculoskeletal and connective tissue disorders	23	60	14 (53.8)	6	20	5 (25.0)	OR	0.585 (0.205, 1.668); 0.3159
							RR	0.591 (0.229, 1.480); 0.2870
							RD	-0.060 (-0.160, 0.055); 0.2473
Back pain	4	10	3 (11.5)	0	0	0 (0.0)	OR	0.228 (0.011, 4.611); 0.3354
							RR	1.032 (0.967, 1.097); 0.0833
							RD	0.031 (-0.032, 0.088); 0.0784
Pain in extremity	5	13	3 (11.5)	1	3	1 (5.0)	OR	0.697 (0.099, 4.925); 0.7173
							RR	1.014 (0.935, 1.081); 0.5699
							RD	0.014 (-0.063, 0.074); 0.5698
Nervous system disorders	58	151	12 (46.2)	19	62	5 (25.0)	OR	0.695 (0.239, 2.021); 0.5040
							RR	0.690 (0.261, 1.768); 0.4624
							RD	-0.039 (-0.136, 0.074); 0.4376
Dizziness	5	13	3 (11.5)	2	7	2 (10.0)	OR	1.182 (0.223, 6.267); 0.8443
							RR	1.103 (0.223, 5.381); 0.9127
							RD	0.003 (-0.060, 0.089); 0.9137
Headache	6	16	4 (15.4)	7	23	3 (15.0)	OR	1.296 (0.305, 5.505); 0.7252
							RR	0.990 (0.892, 1.067); 0.7775
							RD	-0.010 (-0.104, 0.060); 0.7771
Psychiatric disorders	4	10	3 (11.5)	6	20	4 (20.0)	OR	2.206 (0.520, 9.365); 0.2836
							RR	0.961 (0.860, 1.035); 0.3228
							RD	-0.038 (-0.137, 0.032); 0.3173
Renal and urinary disorders	7	18	5 (19.2)	5	16	1 (5.0)	OR	0.434 (0.068, 2.759); 0.3764
							RR	1.037 (0.954, 1.116); 0.2223

System Organ Class Preferred Term	Eculizumab (N=26) Patient-Years (PY)=38.4 Events n	Rate per 100 PY	Patients n (%)	Ravulizumab (N=20) Patient-Years (PY)=30.4 Events n	Rate per 100 PY	Patients n (%)	Treatment Effect Estimate (95% CI; p-value)	
							RD	0.035 (-0.044, 0.102); 0.2198
							OR	0.697 (0.099, 4.925); 0.7173
Reproductive system and breast disorders	4	10	3 (11.5)	1	3	1 (5.0)	RR	1.014 (0.935, 1.081); 0.5699
							RD	0.014 (-0.063, 0.074); 0.5698
							OR	1.182 (0.223, 6.267); 0.8443
Respiratory, thoracic and mediastinal disorders	3	8	3 (11.5)	2	7	2 (10.0)	RR	0.997 (0.908, 1.065); 0.9137
							RD	-0.003 (-0.089, 0.060); 0.9137
							OR	0.520 (0.147, 1.842); 0.3105
Skin and subcutaneous tissue disorders	17	44	10 (38.5)	3	10	3 (15.0)	RR	0.497 (0.150, 1.587); 0.2717
							RD	-0.052 (-0.140, 0.048); 0.2187
							OR	0.910 (0.185, 4.472); 0.9071
Vascular disorders	5	13	4 (15.4)	3	10	2 (10.0)	RR	1.007 (0.917, 1.082); 0.8193
							RD	0.007 (-0.080, 0.074); 0.8194

AE: Adverse Event; CI: Confidence Interval; IST: Immunosuppressive Therapy; OR: Odds Ratio; PY: person years; RD: Risk Difference; RR: Risk Ratio; TEAE: Treatment-emergent
TEAEs are AEs with a start date on or after the date of the first dose of study drug.
Treatment-related adverse events and follow-up were truncated at the maximum duration of follow-up in the ravulizumab arm.
Odds ratios were derived from a logistic regression model with treatment as the only covariate. Firth's correction was applied for odds ratios.
Any TEAEs were examined for preferred terms and system organ classes reported in at least 10% of patients in one of the treatment arms within the subgroup.
Severe and serious TEAEs were examined for preferred terms and system organ classes reported in at least 5% of patients in one of the treatment arms within the subgroup.
Preferred terms and system organ classes for a given AE severity or type (i.e., leading for withdrawal) were only examined within each subgroup if they were also examined in

Treatment Emergent Adverse Events (TEAEs) by MedDRA System Organ Class/Preferred Term by Severity and Treatment Group, Rituximab Use: Yes

System Organ Class / Preferred Term	Eculizumab (N=26) Patient-Years (PY)=38.4 Events n	Rate per 100 PY	Patients n (%)	Ravulizumab (N=20) Patient-Years (PY)=30.4 Events n	Rate per 100 PY	Patients n (%)	Treatment Effect Estimate (95% CI; p-value)
Mild TEAEs							
Blood and lymphatic system disorders	4	10	2 (7.7)	3	10	3 (15.0)	OR 2.384 (0.450, 12.631); 0.3073 RR 2.483 (0.505, 12.192); 0.3110 RD 0.031 (-0.030, 0.123); 0.3423
Eye disorders	7	18	5 (19.2)	3	10	2 (10.0)	OR 0.736 (0.157, 3.443); 0.6971 RR 1.019 (0.926, 1.100); 0.5935 RD 0.018 (-0.070, 0.088); 0.5937
Gastrointestinal disorders	22	57	8 (30.8)	10	33	7 (35.0)	OR 1.516 (0.532, 4.322); 0.4363 RR 0.959 (0.834, 1.068); 0.4698 RD -0.037 (-0.155, 0.058); 0.4660
Diarrhoea	3	8	3 (11.5)	1	3	1 (5.0)	OR 0.697 (0.099, 4.925); 0.7173 RR 1.014 (0.935, 1.081); 0.5699 RD 0.014 (-0.063, 0.074); 0.5698
General disorders and administration site conditions	45	117	8 (30.8)	10	33	4 (20.0)	OR 0.860 (0.259, 2.855); 0.8050 RR 1.016 (0.904, 1.118); 0.7416 RD 0.014 (-0.090, 0.100); 0.7419
Infections and infestations	53	138	15 (57.7)	15	49	8 (40.0)	OR 0.885 (0.355, 2.207); 0.7934 RR 1.022 (0.875, 1.167); 0.7537 RD 0.018 (-0.109, 0.129); 0.7542
COVID-19	0	0	0 (0.0)	4	13	4 (20.0)	OR 15.936 (0.828, 306.58); 0.0665 RR 0.931 (0.835, 0.973); 0.0455 RD -0.069 (-0.165, -0.027); 0.0382
Nasopharyngitis	13	34	4 (15.4)	1	3	1 (5.0)	OR 0.536 (0.081, 3.555); 0.5184 RR 1.025 (0.945, 1.098); 0.3598 RD 0.024 (-0.053, 0.088); 0.3587
Upper respiratory tract infection	6	16	4 (15.4)	0	0	0 (0.0)	OR 0.176 (0.009, 3.405); 0.2502 RR 1.043 (0.977, 1.114); 0.0455 RD 0.042 (-0.022, 0.103); 0.0411
Urinary tract infection	11	29	4 (15.4)	3	10	2 (10.0)	OR 0.910 (0.185, 4.472); 0.9071 RR 1.007 (0.917, 1.082); 0.8193 RD 0.007 (-0.080, 0.074); 0.8194
Injury, poisoning and procedural complications	18	47	11 (42.3)	3	10	1 (5.0)	OR 0.194 (0.034, 1.114); 0.0659 RR 1.110 (1.015, 1.223); 0.0102 RD 0.097 (0.013, 0.180); 0.0080
Investigations	12	31	6 (23.1)	2	7	2 (10.0)	OR 0.616 (0.136, 2.782); 0.5289 RR 1.030 (0.936, 1.117); 0.4159 RD 0.028 (-0.061, 0.102); 0.4156
Metabolism and nutrition disorders	4	10	3 (11.5)	0	0	0 (0.0)	OR 0.228 (0.011, 4.611); 0.3354 RR 1.032 (0.967, 1.097); 0.0833 RD 0.031 (-0.032, 0.088); 0.0784
Musculoskeletal and connective tissue disorders	17	44	11 (42.3)	5	16	4 (20.0)	OR 0.614 (0.194, 1.939); 0.4057 RR 1.052 (0.932, 1.170); 0.3268 RD 0.046 (-0.062, 0.138); 0.3268
Nervous system disorders	51	133	11 (42.3)	19	62	5 (25.0)	OR 0.764 (0.260, 2.251); 0.6256 RR 0.752 (0.282, 1.956); 0.5792 RD -0.028 (-0.124, 0.084); 0.5636
Dizziness	4	10	3 (11.5)	2	7	2 (10.0)	OR 1.182 (0.223, 6.267); 0.8443 RR 1.103 (0.223, 5.381); 0.9127 RD 0.003 (-0.060, 0.089); 0.9137
Headache	6	16	4 (15.4)	7	23	3 (15.0)	OR 1.296 (0.305, 5.505); 0.7252 RR 0.990 (0.892, 1.067); 0.7775 RD -0.010 (-0.104, 0.060); 0.7771
Psychiatric disorders	4	10	3 (11.5)	4	13	4 (20.0)	OR 2.206 (0.520, 9.365); 0.2836 RR 0.961 (0.860, 1.035); 0.3228 RD -0.038 (-0.137, 0.032); 0.3173
Renal and urinary disorders	4	10	3 (11.5)	5	16	1 (5.0)	OR 0.697 (0.099, 4.925); 0.7173 RR 1.014 (0.935, 1.081); 0.5699 RD 0.014 (-0.063, 0.074); 0.5698
Reproductive system and breast disorders	4	10	3 (11.5)	1	3	1 (5.0)	OR 0.697 (0.099, 4.925); 0.7173 RR 1.014 (0.935, 1.081); 0.5699 RD 0.014 (-0.063, 0.074); 0.5698

Treatment Emergent Adverse Events (TEAEs) by MedDRA System Organ Class/Preferred Term by Severity and Treatment Group, Rituximab Use: Yes

System Organ Class / Preferred Term	Eculizumab (N=26) Patient-Years (PY)=38.4 Events n	Rate per 100 PY	Patients n (%)	Ravulizumab (N=20) Patient-Years (PY)=30.4 Events n	Rate per 100 PY	Patients n (%)	Treatment Effect Estimate (95% CI; p-value)
Respiratory, thoracic and mediastinal disorders	3	8	3 (11.5)	1	3	1 (5.0)	OR 0.697 (0.099, 4.925); 0.7173 RR 1.014 (0.935, 1.081); 0.5699 RD 0.014 (-0.063, 0.074); 0.5698
Skin and subcutaneous tissue disorders	16	42	10 (38.5)	2	7	2 (10.0)	OR 0.364 (0.087, 1.524); 0.1668 RR 0.331 (0.083, 1.278); 0.1439 RD -0.070 (-0.154, 0.023); 0.0764
ModerateTEAEs							
Gastrointestinal disorders	5	13	3 (11.5)	0	0	0 (0.0)	OR 0.228 (0.011, 4.611); 0.3354 RR 1.032 (0.967, 1.097); 0.0833 RD 0.031 (-0.032, 0.088); 0.0784
Infections and infestations	19	49	10 (38.5)	5	16	4 (20.0)	OR 0.680 (0.212, 2.178); 0.5163 RR 0.662 (0.225, 1.890); 0.4676 RD -0.035 (-0.126, 0.071); 0.4401
Injury, poisoning and procedural complications	2	5	2 (7.7)	3	10	3 (15.0)	OR 2.384 (0.450, 12.631); 0.3073 RR 2.483 (0.505, 12.192); 0.3110 RD 0.031 (-0.030, 0.123); 0.3423
Musculoskeletal and connective tissue disorders	5	13	5 (19.2)	1	3	1 (5.0)	OR 0.434 (0.068, 2.759); 0.3764 RR 0.331 (0.052, 2.065); 0.3072 RD -0.035 (-0.102, 0.044); 0.2198
Non-SevereTEAEs							
Blood and lymphatic system disorders	8	21	5 (19.2)	4	13	4 (20.0)	OR 1.373 (0.375, 5.037); 0.6322 RR 1.324 (0.395, 4.386); 0.6657 RD 0.017 (-0.060, 0.118); 0.6750
Eye disorders	12	31	5 (19.2)	3	10	2 (10.0)	OR 0.736 (0.157, 3.443); 0.6971 RR 1.019 (0.926, 1.100); 0.5935 RD 0.018 (-0.070, 0.088); 0.5937
Gastrointestinal disorders	27	70	9 (34.6)	10	33	7 (35.0)	OR 1.341 (0.481, 3.737); 0.5745 RR 0.970 (0.843, 1.084); 0.6071 RD -0.027 (-0.145, 0.071); 0.6051
Diarrhoea	3	8	3 (11.5)	1	3	1 (5.0)	OR 0.697 (0.099, 4.925); 0.7173 RR 1.014 (0.935, 1.081); 0.5699 RD 0.014 (-0.063, 0.074); 0.5698
General disorders and administration site conditions	49	128	11 (42.3)	12	39	6 (30.0)	OR 0.921 (0.329, 2.575); 0.8746 RR 1.013 (0.884, 1.134); 0.8287 RD 0.011 (-0.105, 0.110); 0.8289
Infections and infestations	72	187	19 (73.1)	20	66	11 (55.0)	OR 0.962 (0.424, 2.183); 0.9266 RR 0.958 (0.490, 1.829); 0.9003 RD -0.008 (-0.132, 0.130); 0.8998
COVID-19	0	0	0 (0.0)	5	16	5 (25.0)	OR 19.842 (1.059, 371.71); 0.0457 RR 0.914 (0.813, 0.963); 0.0254 RD -0.086 (-0.187, -0.037); 0.0193
Nasopharyngitis	16	42	5 (19.2)	1	3	1 (5.0)	OR 0.434 (0.068, 2.759); 0.3764 RR 1.037 (0.954, 1.116); 0.2223 RD 0.035 (-0.044, 0.102); 0.2198
Upper respiratory tract infection	8	21	5 (19.2)	1	3	1 (5.0)	OR 0.434 (0.068, 2.759); 0.3764 RR 0.331 (0.052, 2.065); 0.3072 RD -0.035 (-0.102, 0.044); 0.2198
Urinary tract infection	14	36	5 (19.2)	5	16	4 (20.0)	OR 1.373 (0.375, 5.037); 0.6322 RR 0.982 (0.877, 1.068); 0.6761 RD -0.017 (-0.118, 0.060); 0.6750
Injury, poisoning and procedural complications	20	52	11 (42.3)	6	20	3 (15.0)	OR 0.469 (0.134, 1.641); 0.2360 RR 0.451 (0.138, 1.423); 0.2066 RD -0.063 (-0.152, 0.038); 0.1495
Contusion	4	10	3 (11.5)	0	0	0 (0.0)	OR 0.228 (0.011, 4.611); 0.3354 RR 1.032 (0.967, 1.097); 0.0833 RD 0.031 (-0.032, 0.088); 0.0784
Investigations	14	36	6 (23.1)	2	7	2 (10.0)	OR 0.616 (0.136, 2.782); 0.5289 RR 1.030 (0.936, 1.117); 0.4159 RD 0.028 (-0.061, 0.102); 0.4156

Treatment Emergent Adverse Events (TEAEs) by MedDRA System Organ Class/Preferred Term by Severity and Treatment Group, Rituximab Use: Yes

System Organ Class / Preferred Term	Eculizumab (N=26) Patient-Years (PY)=38.4 Events n	Rate per 100 PY	Patients n (%)	Ravulizumab (N=20) Patient-Years (PY)=30.4 Events n	Rate per 100 PY	Patients n (%)	Treatment Effect	Estimate (95% CI; p-value)
Metabolism and nutrition disorders	4	10	3 (11.5)	0	0	0 (0.0)	OR	0.228 (0.011, 4.611); 0.3354
							RR	1.032 (0.967, 1.097); 0.0833
							RD	0.031 (-0.032, 0.088); 0.0784
Musculoskeletal and connective tissue disorders	22	57	14 (53.8)	6	20	5 (25.0)	OR	0.585 (0.205, 1.668); 0.3159
							RR	0.591 (0.229, 1.480); 0.2870
							RD	-0.060 (-0.160, 0.055); 0.2473
Back pain	4	10	3 (11.5)	0	0	0 (0.0)	OR	0.228 (0.011, 4.611); 0.3354
							RR	1.032 (0.967, 1.097); 0.0833
							RD	0.031 (-0.032, 0.088); 0.0784
Nervous system disorders	58	151	12 (46.2)	19	62	5 (25.0)	OR	0.695 (0.239, 2.021); 0.5040
							RR	0.690 (0.261, 1.768); 0.4624
							RD	-0.039 (-0.136, 0.074); 0.4376
Dizziness	5	13	3 (11.5)	2	7	2 (10.0)	OR	1.182 (0.223, 6.267); 0.8443
							RR	1.103 (0.223, 5.381); 0.9127
							RD	0.003 (-0.060, 0.089); 0.9137
Headache	6	16	4 (15.4)	7	23	3 (15.0)	OR	1.296 (0.305, 5.505); 0.7252
							RR	0.990 (0.892, 1.067); 0.7775
							RD	-0.010 (-0.104, 0.060); 0.7771
Psychiatric disorders	4	10	3 (11.5)	5	16	4 (20.0)	OR	2.206 (0.520, 9.365); 0.2836
							RR	0.961 (0.860, 1.035); 0.3228
							RD	-0.038 (-0.137, 0.032); 0.3173
Renal and urinary disorders	7	18	5 (19.2)	5	16	1 (5.0)	OR	0.434 (0.068, 2.759); 0.3764
							RR	1.037 (0.954, 1.116); 0.2223
							RD	0.035 (-0.044, 0.102); 0.2198
Reproductive system and breast disorders	4	10	3 (11.5)	1	3	1 (5.0)	OR	0.697 (0.099, 4.925); 0.7173
							RR	1.014 (0.935, 1.081); 0.5699
							RD	0.014 (-0.063, 0.074); 0.5698
Respiratory, thoracic and mediastinal disorders	3	8	3 (11.5)	2	7	2 (10.0)	OR	1.182 (0.223, 6.267); 0.8443
							RR	0.997 (0.908, 1.065); 0.9137
							RD	-0.003 (-0.089, 0.060); 0.9137
Skin and subcutaneous tissue disorders	17	44	10 (38.5)	3	10	3 (15.0)	OR	0.520 (0.147, 1.842); 0.3105
							RR	0.497 (0.150, 1.587); 0.2717
							RD	-0.052 (-0.140, 0.048); 0.2187
Vascular disorders	5	13	4 (15.4)	3	10	2 (10.0)	OR	0.910 (0.185, 4.472); 0.9071
							RR	1.007 (0.917, 1.082); 0.8193
							RD	0.007 (-0.080, 0.074); 0.8194
Severe TEAEs								
Infections and infestations	2	5	2 (7.7)	1	3	1 (5.0)	OR	0.986 (0.125, 7.779); 0.9893
							RR	0.828 (0.109, 6.206); 0.8761
							RD	-0.004 (-0.058, 0.073); 0.8730
Serious TEAEs								
Infections and infestations	3	8	2 (7.7)	1	3	1 (5.0)	OR	0.986 (0.125, 7.779); 0.9893
							RR	0.828 (0.109, 6.206); 0.8761
							RD	-0.004 (-0.058, 0.073); 0.8730
TEAEs leading to withdrawal from study drug								
None								

AE: Adverse Event; CI: Confidence Interval; IST: Immunosuppressive Therapy; OR: Odds Ratio; PY: person years; RD: Risk Difference; RR: Risk Ratio; TEAE: Treatment-emergent Adverse
TEAEs are AEs with a start date on or after the date of the first dose of study drug.
Treatment-related adverse events and follow-up were truncated at the maximum duration of follow-up in the ravulizumab arm.
Odds ratios were derived from a logistic regression model with treatment as the only covariate. Firth's correction was applied for odds ratios.
Mild, moderate and non-severe TEAEs were examined for preferred terms and system organ classes reported in at least 10% of patients in one of the treatment arms within the subgroup.
Severe and serious TEAEs were examined for preferred terms and system organ classes reported in at least 5% of patients in one of the treatment arms within the subgroup.
All TEAEs leading to withdrawal from study drug were examined.
TEAEs leading to withdrawal from study drug were examined descriptively (i.e., OR, RR, and RD not calculated).
Preferred terms and system organ classes for a given AE severity or type (i.e., leading for withdrawal) were only examined within each subgroup if they were also examined in the over

Treatment Emergent Adverse Events (TEAEs) by MedDRA System Organ Class/Preferred Term by Treatment Group, Rituximab Use: No

System Organ Class	Eculizumab (N=70) Patient-Years (PY)=134.4			Ravulizumab (N=38) Patient-Years (PY)=53.6			Treatment Effect	
Preferred Term	Events n	Rate per 100 PY	Patients n (%)	Events n	Rate per 100 PY	Patients n (%)	Estimate (95% CI; p-value)	
Blood and lymphatic system disorders	28	21	14 (20.0)	0	0	0 (0.0)	OR	0.049 (0.003, 0.852); 0.0385
							RR	1.171 (1.093, 1.299); 0.0002
							RD	0.146 (0.080, 0.230); 0.0001
Eye disorders	34	25	14 (20.0)	6	11	4 (10.5)	OR	0.470 (0.153, 1.440); 0.1862
							RR	1.090 (0.962, 1.224); 0.1190
							RD	0.077 (-0.033, 0.174); 0.1170
Gastrointestinal disorders	95	71	30 (42.9)	22	41	15 (39.5)	OR	0.777 (0.376, 1.606); 0.4957
							RR	1.078 (0.866, 1.318); 0.4668
							RD	0.054 (-0.098, 0.194); 0.4693
Diarrhoea	19	14	12 (17.1)	2	4	2 (5.3)	OR	0.299 (0.073, 1.225); 0.0934
							RR	1.103 (0.995, 1.224); 0.0319
							RD	0.091 (-0.004, 0.178); 0.0288
Nausea	23	17	12 (17.1)	1	2	1 (2.6)	OR	0.176 (0.031, 1.005); 0.0507
							RR	1.123 (1.025, 1.242); 0.0061
							RD	0.108 (0.023, 0.192); 0.0044
General disorders and administration site conditions	35	26	14 (20.0)	24	45	11 (28.9)	OR	1.377 (0.584, 3.250); 0.4648
							RR	0.949 (0.798, 1.094); 0.4897
							RD	-0.044 (-0.178, 0.074); 0.4855
Infections and infestations	214	159	54 (77.1)	45	84	26 (68.4)	OR	0.636 (0.330, 1.225); 0.1761
							RR	1.261 (0.902, 1.739); 0.1611
							RD	0.114 (-0.049, 0.271); 0.1669
COVID-19	0	0	0 (0.0)	9	17	9 (23.7)	OR	37.040 (2.080, 659.74); 0.0140
							RR	0.845 (0.730, 0.916); 0.0027
							RD	-0.155 (-0.270, -0.084); 0.0011
Nasopharyngitis	30	22	15 (21.4)	2	4	2 (5.3)	OR	0.233 (0.058, 0.934); 0.0397
							RR	1.144 (1.027, 1.281); 0.0075
							RD	0.122 (0.024, 0.214); 0.0058
Pharyngitis	13	10	10 (14.3)	0	0	0 (0.0)	OR	0.070 (0.004, 1.255); 0.0710
							RR	1.116 (1.044, 1.222); 0.0016
							RD	0.104 (0.039, 0.182); 0.0008
Upper respiratory tract infection	37	28	23 (32.9)	4	7	4 (10.5)	OR	0.258 (0.088, 0.757); 0.0137
							RR	1.224 (1.066, 1.414); 0.0027
							RD	0.171 (0.053, 0.278); 0.0019
Urinary tract infection	28	21	8 (11.4)	2	4	2 (5.3)	OR	0.461 (0.107, 1.984); 0.2983
							RR	1.053 (0.955, 1.151); 0.1891
							RD	0.049 (-0.042, 0.128); 0.1869
Injury, poisoning and procedural complications	27	20	20 (28.6)	11	21	8 (21.1)	OR	0.628 (0.260, 1.517); 0.3011
							RR	1.089 (0.926, 1.262); 0.2506
							RD	0.070 (-0.061, 0.187); 0.2514
Contusion	7	5	7 (10.0)	0	0	0 (0.0)	OR	0.102 (0.006, 1.864); 0.1236
							RR	1.079 (1.009, 1.167); 0.0082
							RD	0.073 (0.009, 0.143); 0.0060
Investigations	14	10	8 (11.4)	9	17	6 (15.8)	OR	1.289 (0.436, 3.813); 0.6465
							RR	0.978 (0.857, 1.084); 0.6822
							RD	-0.020 (-0.134, 0.072); 0.6810
Metabolism and nutrition disorders	8	6	8 (11.4)	5	9	5 (13.2)	OR	1.070 (0.345, 3.324); 0.9064
							RR	0.997 (0.880, 1.101); 0.9506
							RD	-0.003 (-0.112, 0.086); 0.9506
Musculoskeletal and connective tissue disorders	62	46	29 (41.4)	26	48	18 (47.4)	OR	1.045 (0.517, 2.115); 0.9022
							RR	0.988 (0.781, 1.219); 0.9144
							RD	-0.008 (-0.163, 0.137); 0.9142
Arthralgia	9	7	8 (11.4)	5	9	5 (13.2)	OR	1.070 (0.345, 3.324); 0.9064
							RR	0.997 (0.880, 1.101); 0.9506
							RD	-0.003 (-0.112, 0.086); 0.9506
Back pain	12	9	10 (14.3)	8	15	7 (18.4)	OR	1.200 (0.439, 3.280); 0.7228
							RR	0.982 (0.851, 1.100); 0.7556
							RD	-0.017 (-0.136, 0.083); 0.7549
Pain in extremity	7	5	7 (10.0)	1	2	1 (2.6)	OR	0.311 (0.052, 1.880); 0.2034
							RR	1.060 (0.974, 1.150); 0.0816
							RD	0.056 (-0.025, 0.129); 0.0778
Nervous system disorders	120	89	33 (47.1)	24	45	12 (31.6)	OR	0.510 (0.239, 1.087); 0.0810
							RR	1.209 (0.982, 1.473); 0.0576
							RD	0.137 (-0.012, 0.271); 0.0572
Dizziness	14	10	11 (15.7)	2	4	2 (5.3)	OR	0.329 (0.080, 1.360); 0.1247
							RR	1.090 (0.985, 1.205); 0.0507

System Organ Class / Preferred Term	Eculizumab (N=70) Patient-Years (PY)=134.4 Events n	Rate per 100 PY	Patients n (%)	Ravulizumab (N=38) Patient-Years (PY)=53.6 Events n	Rate per 100 PY	Patients n (%)	Treatment Effect	Estimate (95% CI; p-value)
							RD	0.080 (-0.014, 0.166); 0.0473
Headache	76	57	17 (24.3)	17	32	11 (28.9)	OR	1.100 (0.478, 2.528); 0.8227
							RR	0.985 (0.825, 1.144); 0.8459
							RD	-0.013 (-0.149, 0.109); 0.8456
Psychiatric disorders	11	8	9 (12.9)	4	7	2 (5.3)	OR	0.408 (0.096, 1.727); 0.2231
							RR	1.065 (0.965, 1.169); 0.1237
							RD	0.059 (-0.033, 0.141); 0.1208
Renal and urinary disorders	15	11	11 (15.7)	5	9	4 (10.5)	OR	0.614 (0.194, 1.939); 0.4057
							RR	1.052 (0.932, 1.170); 0.3268
							RD	0.046 (-0.062, 0.138); 0.3268
Reproductive system and breast disorders	11	8	7 (10.0)	1	2	1 (2.6)	OR	0.311 (0.052, 1.880); 0.2034
							RR	1.060 (0.974, 1.150); 0.0816
							RD	0.056 (-0.025, 0.129); 0.0778
Respiratory, thoracic and mediastinal disorders	60	45	20 (28.6)	8	15	7 (18.4)	OR	0.543 (0.218, 1.357); 0.1915
							RR	1.111 (0.951, 1.283); 0.1418
							RD	0.088 (-0.041, 0.201); 0.1412
Cough	11	8	10 (14.3)	3	6	3 (7.9)	OR	0.520 (0.147, 1.842); 0.3105
							RR	1.059 (0.948, 1.169); 0.2200
							RD	0.052 (-0.048, 0.140); 0.2187
Skin and subcutaneous tissue disorders	21	16	15 (21.4)	13	24	9 (23.7)	OR	1.009 (0.415, 2.452); 0.9838
							RR	1.001 (0.852, 1.148); 0.9857
							RD	0.001 (-0.129, 0.115); 0.9857
Vascular disorders	12	9	9 (12.9)	2	4	2 (5.3)	OR	0.408 (0.096, 1.727); 0.2231
							RR	1.065 (0.965, 1.169); 0.1237
							RD	0.059 (-0.033, 0.141); 0.1208

AE: Adverse Event; CI: Confidence Interval; IST: Immunosuppressive Therapy; OR: Odds Ratio; PY: person years; RD: Risk Difference; RR: Risk Ratio; TEAE: Treatment-emergent
TEAEs are AEs with a start date on or after the date of the first dose of study drug.
Treatment-related adverse events and follow-up were truncated at the maximum duration of follow-up in the ravulizumab arm.
Odds ratios were derived from a logistic regression model with treatment as the only covariate. Firth's correction was applied for odds ratios.
Any TEAEs were examined for preferred terms and system organ classes reported in at least 10% of patients in one of the treatment arms within the subgroup.
Severe and serious TEAEs were examined for preferred terms and system organ classes reported in at least 5% of patients in one of the treatment arms within the subgroup.
Preferred terms and system organ classes for a given AE severity or type (i.e., leading for withdrawal) were only examined within each subgroup if they were also examined in

Treatment Emergent Adverse Events (TEAEs) by MedDRA System Organ Class/Preferred Term by Severity and Treatment Group, Rituximab Use: No

System Organ Class / Preferred Term	Eculizumab (N=70) Patient-Years (PY)=134.4 Events n	Rate per 100 PY	Patients n (%)	Ravulizumab (N=38) Patient-Years (PY)=53.6 Events n	Rate per 100 PY	Patients n (%)	Treatment Effect	Estimate (95% CI; p-value)
Mild TEAEs								
Blood and lymphatic system disorders	25	19	13 (18.6)	0	0	0 (0.0)	OR	0.053 (0.003, 0.929); 0.0444
							RR	1.157 (1.080, 1.279); 0.0003
							RD	0.135 (0.070, 0.218); 0.0001
Eye disorders	23	17	14 (20.0)	2	4	2 (5.3)	OR	0.252 (0.062, 1.016); 0.0527
							RR	1.130 (1.016, 1.262); 0.0123
							RD	0.111 (0.014, 0.202); 0.0101
Gastrointestinal disorders	82	61	27 (38.6)	17	32	12 (31.6)	OR	0.679 (0.314, 1.468); 0.3253
							RR	1.103 (0.906, 1.323); 0.2877
							RD	0.074 (-0.071, 0.206); 0.2899
Diarrhoea	16	12	11 (15.7)	2	4	2 (5.3)	OR	0.329 (0.080, 1.360); 0.1247
							RR	1.090 (0.985, 1.205); 0.0507
							RD	0.080 (-0.014, 0.166); 0.0473
Nausea	19	14	10 (14.3)	1	2	1 (2.6)	OR	0.215 (0.037, 1.246); 0.0863
							RR	1.097 (1.004, 1.204); 0.0173
							RD	0.087 (0.004, 0.167); 0.0145
General disorders and administration site conditions	30	22	12 (17.1)	20	37	9 (23.7)	OR	1.297 (0.517, 3.256); 0.5794
							RR	0.966 (0.824, 1.098); 0.6070
							RD	-0.030 (-0.157, 0.079); 0.6048
Infections and infestations	178	132	47 (67.1)	28	52	17 (44.7)	OR	0.439 (0.220, 0.877); 0.0197
							RR	1.385 (1.063, 1.795); 0.0129
							RD	0.196 (0.036, 0.342); 0.0124
COVID-19	0	0	0 (0.0)	7	13	7 (18.4)	OR	28.108 (1.549, 510.01); 0.0241
							RR	0.879 (0.771, 0.940); 0.0082
							RD	-0.121 (-0.229, -0.060); 0.0048
Nasopharyngitis	26	19	12 (17.1)	1	2	1 (2.6)	OR	0.176 (0.031, 1.005); 0.0507
							RR	1.123 (1.025, 1.242); 0.0061
							RD	0.108 (0.023, 0.192); 0.0044
Upper respiratory tract infection	35	26	22 (31.4)	2	4	2 (5.3)	OR	0.147 (0.037, 0.572); 0.0057
							RR	1.253 (1.111, 1.434); 0.0002
							RD	0.195 (0.090, 0.295); 0.0001
Urinary tract infection	24	18	8 (11.4)	1	2	1 (2.6)	OR	0.272 (0.046, 1.613); 0.1516
							RR	1.072 (0.984, 1.168); 0.0489
							RD	0.066 (-0.015, 0.142); 0.0451
Injury, poisoning and procedural complications	19	14	14 (20.0)	4	7	4 (10.5)	OR	0.470 (0.153, 1.440); 0.1862
							RR	1.090 (0.962, 1.224); 0.1190
							RD	0.077 (-0.033, 0.174); 0.1170
Investigations	9	7	7 (10.0)	9	17	6 (15.8)	OR	1.477 (0.486, 4.492); 0.4916
							RR	0.967 (0.848, 1.068); 0.5275
							RD	-0.031 (-0.143, 0.059); 0.5247
Metabolism and nutrition disorders	8	6	8 (11.4)	1	2	1 (2.6)	OR	0.272 (0.046, 1.613); 0.1516
							RR	1.072 (0.984, 1.168); 0.0489
							RD	0.066 (-0.015, 0.142); 0.0451
Musculoskeletal and connective tissue disorders	48	36	25 (35.7)	17	32	11 (28.9)	OR	0.679 (0.307, 1.500); 0.3381
							RR	1.096 (0.908, 1.301); 0.2978
							RD	0.071 (-0.072, 0.199); 0.2997
Nervous system disorders	105	78	26 (37.1)	17	32	10 (26.3)	OR	0.576 (0.256, 1.293); 0.1812
							RR	1.135 (0.945, 1.347); 0.1427
							RD	0.098 (-0.043, 0.225); 0.1431
Dizziness	13	10	10 (14.3)	1	2	1 (2.6)	OR	0.215 (0.037, 1.246); 0.0863
							RR	1.097 (1.004, 1.204); 0.0173
							RD	0.087 (0.004, 0.167); 0.0145
Headache	71	53	15 (21.4)	12	22	8 (21.1)	OR	0.885 (0.355, 2.207); 0.7934
							RR	1.022 (0.875, 1.167); 0.7537
							RD	0.018 (-0.109, 0.129); 0.7542
Psychiatric disorders	9	7	8 (11.4)	1	2	1 (2.6)	OR	0.272 (0.046, 1.613); 0.1516
							RR	1.072 (0.984, 1.168); 0.0489
							RD	0.066 (-0.015, 0.142); 0.0451
Renal and urinary disorders	13	10	11 (15.7)	4	7	3 (7.9)	OR	0.469 (0.134, 1.641); 0.2360
							RR	1.071 (0.958, 1.187); 0.1516
							RD	0.063 (-0.038, 0.152); 0.1495
Reproductive system and breast disorders	11	8	7 (10.0)	1	2	1 (2.6)	OR	0.311 (0.052, 1.880); 0.2034
							RR	1.060 (0.974, 1.150); 0.0816
							RD	0.056 (-0.025, 0.129); 0.0778

Treatment Emergent Adverse Events (TEAEs) by MedDRA System Organ Class/Preferred Term by Severity and Treatment Group, Rituximab Use: No

System Organ Class / Preferred Term	Eculizumab (N=70) Patient-Years (PY)=134.4 Events n	Rate per 100 PY	Patients n (%)	Ravulizumab (N=38) Patient-Years (PY)=53.6 Events n	Rate per 100 PY	Patients n (%)	Treatment Effect Estimate (95% CI; p-value)
Respiratory, thoracic and mediastinal disorders	56	42	17 (24.3)	8	15	7 (18.4)	OR 0.661 (0.261, 1.679); 0.3845
							RR 1.069 (0.919, 1.224); 0.3288
							RD 0.056 (-0.069, 0.167); 0.3297
Cough	10	7	9 (12.9)	3	6	3 (7.9)	OR 0.581 (0.161, 2.091); 0.4058
							RR 1.046 (0.938, 1.152); 0.3129
							RD 0.042 (-0.057, 0.127); 0.3124
Skin and subcutaneous tissue disorders	19	14	14 (20.0)	11	21	7 (18.4)	OR 0.829 (0.319, 2.153); 0.6995
							RR 1.029 (0.889, 1.168); 0.6523
							RD 0.025 (-0.098, 0.132); 0.6530
ModerateTEAEs							
Gastrointestinal disorders	13	10	11 (15.7)	5	9	4 (10.5)	OR 0.614 (0.194, 1.939); 0.4057
							RR 1.052 (0.932, 1.170); 0.3268
							RD 0.046 (-0.062, 0.138); 0.3268
Infections and infestations	30	22	17 (24.3)	13	24	12 (31.6)	OR 1.221 (0.539, 2.764); 0.6318
							RR 0.964 (0.802, 1.125); 0.6531
							RD -0.030 (-0.168, 0.094); 0.6511
Injury, poisoning and procedural complications	7	5	5 (7.1)	7	13	4 (10.5)	OR 1.373 (0.375, 5.037); 0.6322
							RR 0.982 (0.877, 1.068); 0.6761
							RD -0.017 (-0.118, 0.060); 0.6750
Musculoskeletal and connective tissue disorders	12	9	8 (11.4)	7	13	6 (15.8)	OR 1.289 (0.436, 3.813); 0.6465
							RR 0.978 (0.857, 1.084); 0.6822
							RD -0.020 (-0.134, 0.072); 0.6810
Non-SevereTEAEs							
Blood and lymphatic system disorders	28	21	14 (20.0)	0	0	0 (0.0)	OR 0.049 (0.003, 0.852); 0.0385
							RR 1.171 (1.093, 1.299); 0.0002
							RD 0.146 (0.080, 0.230); 0.0001
Eye disorders	33	25	14 (20.0)	6	11	4 (10.5)	OR 0.470 (0.153, 1.440); 0.1862
							RR 1.090 (0.962, 1.224); 0.1190
							RD 0.077 (-0.033, 0.174); 0.1170
Gastrointestinal disorders	95	71	30 (42.9)	22	41	15 (39.5)	OR 0.777 (0.376, 1.606); 0.4957
							RR 1.078 (0.866, 1.318); 0.4668
							RD 0.054 (-0.098, 0.194); 0.4693
Diarrhoea	19	14	12 (17.1)	2	4	2 (5.3)	OR 0.299 (0.073, 1.225); 0.0934
							RR 1.103 (0.995, 1.224); 0.0319
							RD 0.091 (-0.004, 0.178); 0.0288
Nausea	23	17	12 (17.1)	1	2	1 (2.6)	OR 0.176 (0.031, 1.005); 0.0507
							RR 1.123 (1.025, 1.242); 0.0061
							RD 0.108 (0.023, 0.192); 0.0044
General disorders and administration site conditions	34	25	14 (20.0)	23	43	11 (28.9)	OR 1.377 (0.584, 3.250); 0.4648
							RR 0.949 (0.798, 1.094); 0.4897
							RD -0.044 (-0.178, 0.074); 0.4855
Infections and infestations	208	155	53 (75.7)	41	76	25 (65.8)	OR 0.619 (0.321, 1.194); 0.1524
							RR 1.270 (0.917, 1.737); 0.1372
							RD 0.121 (-0.042, 0.277); 0.1422
COVID-19	0	0	0 (0.0)	9	17	9 (23.7)	OR 37.040 (2.080, 659.74); 0.0140
							RR 0.845 (0.730, 0.916); 0.0027
							RD -0.155 (-0.270, -0.084); 0.0011
Nasopharyngitis	30	22	15 (21.4)	2	4	2 (5.3)	OR 0.233 (0.058, 0.934); 0.0397
							RR 1.144 (1.027, 1.281); 0.0075
							RD 0.122 (0.024, 0.214); 0.0058
Pharyngitis	13	10	10 (14.3)	0	0	0 (0.0)	OR 0.070 (0.004, 1.255); 0.0710
							RR 1.116 (1.044, 1.222); 0.0016
							RD 0.104 (0.039, 0.182); 0.0008
Upper respiratory tract infection	37	28	23 (32.9)	3	6	3 (7.9)	OR 0.197 (0.060, 0.645); 0.0073
							RR 1.247 (1.094, 1.436); 0.0007
							RD 0.188 (0.076, 0.292); 0.0003
Urinary tract infection	28	21	8 (11.4)	2	4	2 (5.3)	OR 0.461 (0.107, 1.984); 0.2983
							RR 1.053 (0.955, 1.151); 0.1891
							RD 0.049 (-0.042, 0.128); 0.1869
Injury, poisoning and procedural complications	26	19	19 (27.1)	11	21	8 (21.1)	OR 0.669 (0.276, 1.623); 0.3741
							RR 1.075 (0.915, 1.242); 0.3232
							RD 0.060 (-0.071, 0.176); 0.3243
Contusion	7	5	7 (10.0)	0	0	0 (0.0)	OR 0.102 (0.006, 1.864); 0.1236
							RR 1.079 (1.009, 1.167); 0.0082
							RD 0.073 (0.009, 0.143); 0.0060
Investigations	14	10	8 (11.4)	9	17	6 (15.8)	OR 1.289 (0.436, 3.813); 0.6465
							RR 0.978 (0.857, 1.084); 0.6822
							RD -0.020 (-0.134, 0.072); 0.6810

Treatment Emergent Adverse Events (TEAEs) by MedDRA System Organ Class/Preferred Term by Severity and Treatment Group, Rituximab Use: No

System Organ Class / Preferred Term	Eculizumab (N=70) Patient-Years (PY)=134.4 Events n	Rate per 100 PY	Patients n (%)	Ravulizumab (N=38) Patient-Years (PY)=53.6 Events n	Rate per 100 PY	Patients n (%)	Treatment Effect	Estimate (95% CI; p-value)
Metabolism and nutrition disorders	8	6	8 (11.4)	5	9	5 (13.2)	OR	1.070 (0.345, 3.324); 0.9064
							RR	0.997 (0.880, 1.101); 0.9506
							RD	-0.003 (-0.112, 0.086); 0.9506
Musculoskeletal and connective tissue disorders	60	45	29 (41.4)	24	45	17 (44.7)	OR	0.965 (0.474, 1.966); 0.9216
							RR	1.013 (0.805, 1.244); 0.9057
							RD	0.009 (-0.145, 0.153); 0.9059
Arthralgia	9	7	8 (11.4)	5	9	5 (13.2)	OR	1.070 (0.345, 3.324); 0.9064
							RR	0.997 (0.880, 1.101); 0.9506
							RD	-0.003 (-0.112, 0.086); 0.9506
Back pain	11	8	10 (14.3)	7	13	6 (15.8)	OR	1.020 (0.359, 2.898); 0.9699
							RR	1.001 (0.874, 1.117); 0.9887
							RD	0.001 (-0.115, 0.097); 0.9887
Nervous system disorders	116	86	31 (44.3)	23	43	12 (31.6)	OR	0.559 (0.261, 1.196); 0.1340
							RR	1.171 (0.956, 1.420); 0.1040
							RD	0.116 (-0.032, 0.250); 0.1045
Dizziness	14	10	11 (15.7)	1	2	1 (2.6)	OR	0.194 (0.034, 1.114); 0.0659
							RR	1.110 (1.015, 1.223); 0.0102
							RD	0.097 (0.013, 0.180); 0.0080
Headache	74	55	17 (24.3)	17	32	11 (28.9)	OR	1.100 (0.478, 2.528); 0.8227
							RR	0.985 (0.825, 1.144); 0.8459
							RD	-0.013 (-0.149, 0.109); 0.8456
Psychiatric disorders	11	8	9 (12.9)	4	7	2 (5.3)	OR	0.408 (0.096, 1.727); 0.2231
							RR	1.065 (0.965, 1.169); 0.1237
							RD	0.059 (-0.033, 0.141); 0.1208
Renal and urinary disorders	15	11	11 (15.7)	4	7	3 (7.9)	OR	0.469 (0.134, 1.641); 0.2360
							RR	1.071 (0.958, 1.187); 0.1516
							RD	0.063 (-0.038, 0.152); 0.1495
Reproductive system and breast disorders	11	8	7 (10.0)	1	2	1 (2.6)	OR	0.311 (0.052, 1.880); 0.2034
							RR	1.060 (0.974, 1.150); 0.0816
							RD	0.056 (-0.025, 0.129); 0.0778
Respiratory, thoracic and mediastinal disorders	59	44	20 (28.6)	8	15	7 (18.4)	OR	0.543 (0.218, 1.357); 0.1915
							RR	1.111 (0.951, 1.283); 0.1418
							RD	0.088 (-0.041, 0.201); 0.1412
Cough	11	8	10 (14.3)	3	6	3 (7.9)	OR	0.520 (0.147, 1.842); 0.3105
							RR	1.059 (0.948, 1.169); 0.2200
							RD	0.052 (-0.048, 0.140); 0.2187
Skin and subcutaneous tissue disorders	21	16	15 (21.4)	13	24	9 (23.7)	OR	1.009 (0.415, 2.452); 0.9838
							RR	1.001 (0.852, 1.148); 0.9857
							RD	0.001 (-0.129, 0.115); 0.9857
Vascular disorders	12	9	9 (12.9)	2	4	2 (5.3)	OR	0.408 (0.096, 1.727); 0.2231
							RR	1.065 (0.965, 1.169); 0.1237
							RD	0.059 (-0.033, 0.141); 0.1208
Severe TEAEs								
Infections and infestations	5	4	3 (4.3)	4	7	4 (10.5)	OR	2.206 (0.520, 9.365); 0.2836
							RR	0.961 (0.860, 1.035); 0.3228
							RD	-0.038 (-0.137, 0.032); 0.3173
Serious TEAEs								
Infections and infestations	10	7	7 (10.0)	4	7	4 (10.5)	OR	0.985 (0.289, 3.354); 0.9809
							RR	1.004 (0.894, 1.101); 0.9260
							RD	0.004 (-0.099, 0.087); 0.9260
Nervous system disorders	5	4	5 (7.1)	0	0	0 (0.0)	OR	0.142 (0.008, 2.684); 0.1931
							RR	1.055 (0.988, 1.132); 0.0254
							RD	0.052 (-0.012, 0.116); 0.0216
Neuromyelitis optica spectrum disorder	5	4	5 (7.1)	0	0	0 (0.0)	OR	0.142 (0.008, 2.684); 0.1931
							RR	1.055 (0.988, 1.132); 0.0254
							RD	0.052 (-0.012, 0.116); 0.0216
TEAEs leading to withdrawal from study drug								
Infections and infestations	0	0	0 (0.0)	3	6	1 (2.6)	OR	Not calculated
							RR	Not calculated
							RD	Not calculated
Bronchitis	0	0	0 (0.0)	1	2	1 (2.6)	OR	Not calculated
							RR	Not calculated
							RD	Not calculated
Encephalitis meningococcal	0	0	0 (0.0)	1	2	1 (2.6)	OR	Not calculated
							RR	Not calculated
							RD	Not calculated

Treatment Emergent Adverse Events (TEAEs) by MedDRA System Organ Class/Preferred Term by Severity and Treatment Group, Rituximab Use: No

System Organ Class	Eculizumab (N=70) Patient-Years (PY)=134.4			Ravulizumab (N=38) Patient-Years (PY)=53.6			Treatment Effect	
Preferred Term	Events n	Rate per 100 PY	Patients n (%)	Events n	Rate per 100 PY	Patients n (%)	Estimate (95% CI; p-value)	
							OR	Not calculated
Stenotrophomonas infection	0	0	0 (0.0)	1	2	1 (2.6)	RR	Not calculated
							RD	Not calculated

AE: Adverse Event; CI: Confidence Interval; IST: Immunosuppressive Therapy; OR: Odds Ratio; PY: person years; RD: Risk Difference; RR: Risk Ratio; TEAE: Treatment-emergent Adverse
TEAEs are AEs with a start date on or after the date of the first dose of study drug.
Treatment-related adverse events and follow-up were truncated at the maximum duration of follow-up in the ravulizumab arm.
Odds ratios were derived from a logistic regression model with treatment as the only covariate. Firth's correction was applied for odds ratios.
Mild, moderate and non-severe TEAEs were examined for preferred terms and system organ classes reported in at least 10% of patients in one of the treatment arms within the subgroup.
Severe and serious TEAEs were examined for preferred terms and system organ classes reported in at least 5% of patients in one of the treatment arms within the subgroup.
All TEAEs leading to withdrawal from study drug were examined.
TEAEs leading to withdrawal from study drug were examined descriptively (i.e., OR, RR, and RD not calculated).
Preferred terms and system organ classes for a given AE severity or type (i.e., leading for withdrawal) were only examined within each subgroup if they were also examined in the over

Treatment Emergent Adverse Events (TEAEs) by MedDRA System Organ Class/Preferred Term by Treatment Group, EDSS: < 5

System Organ Class	Eculizumab (N=66) Patient-Years (PY)=119.7			Ravulizumab (N=49) Patient-Years (PY)=70.4			Treatment Effect	
Preferred Term	Events n	Rate per 100 PY	Patients n (%)	Events n	Rate per 100 PY	Patients n (%)	Estimate (95% CI; p-value)	
Blood and lymphatic system disorders	22	18	13 (19.7)	4	6	4 (8.2)	OR	0.511 (0.165, 1.579); 0.2433
							RR	0.509 (0.179, 1.397); 0.2174
							RD	-0.066 (-0.162, 0.043); 0.1683
Eye disorders	22	18	14 (21.2)	6	9	4 (8.2)	OR	0.470 (0.153, 1.440); 0.1862
							RR	1.090 (0.962, 1.224); 0.1190
							RD	0.077 (-0.033, 0.174); 0.1170
Gastrointestinal disorders	95	79	31 (47.0)	26	37	18 (36.7)	OR	0.950 (0.472, 1.913); 0.8855
							RR	1.019 (0.802, 1.263); 0.8705
							RD	0.013 (-0.143, 0.159); 0.8707
Diarrhoea	16	13	9 (13.6)	3	4	3 (6.1)	OR	0.581 (0.161, 2.091); 0.4058
							RR	1.046 (0.938, 1.152); 0.3129
							RD	0.042 (-0.057, 0.127); 0.3124
Nausea	23	19	12 (18.2)	2	3	2 (4.1)	OR	0.299 (0.073, 1.225); 0.0934
							RR	1.103 (0.995, 1.224); 0.0319
							RD	0.091 (-0.004, 0.178); 0.0288
General disorders and administration site conditions	29	24	12 (18.2)	26	37	13 (26.5)	OR	2.006 (0.853, 4.718); 0.1108
							RR	0.887 (0.738, 1.025); 0.1349
							RD	-0.099 (-0.235, 0.021); 0.1233
Infections and infestations	206	172	53 (80.3)	59	84	31 (63.3)	OR	0.931 (0.484, 1.792); 0.8313
							RR	0.968 (0.705, 1.295); 0.8325
							RD	-0.018 (-0.179, 0.142); 0.8318
COVID-19	0	0	0 (0.0)	12	17	12 (24.5)	OR	51.853 (2.961, 907.97); 0.0069
							RR	0.793 (0.672, 0.878); 0.0005
							RD	-0.207 (-0.328, -0.122); 0.0001
Nasopharyngitis	31	26	14 (21.2)	2	3	2 (4.1)	OR	0.252 (0.062, 1.016); 0.0527
							RR	1.130 (1.016, 1.262); 0.0123
							RD	0.111 (0.014, 0.202); 0.0101
Pharyngitis	10	8	7 (10.6)	0	0	0 (0.0)	OR	0.102 (0.006, 1.864); 0.1236
							RR	1.079 (1.009, 1.167); 0.0082
							RD	0.073 (0.009, 0.143); 0.0060
Upper respiratory tract infection	39	33	24 (36.4)	5	7	5 (10.2)	OR	0.304 (0.112, 0.825); 0.0194
							RR	0.345 (0.141, 0.810); 0.0214
							RD	-0.164 (-0.275, -0.040); 0.0044
Injury, poisoning and procedural complications	31	26	20 (30.3)	17	24	11 (22.4)	OR	0.903 (0.400, 2.038); 0.8068
							RR	0.910 (0.469, 1.723); 0.7802
							RD	-0.019 (-0.143, 0.120); 0.7775
Investigations	10	8	8 (12.1)	10	14	7 (14.3)	OR	1.516 (0.532, 4.322); 0.4363
							RR	0.959 (0.834, 1.068); 0.4698
							RD	-0.037 (-0.155, 0.058); 0.4660
Metabolism and nutrition disorders	8	7	7 (10.6)	5	7	5 (10.2)	OR	1.227 (0.385, 3.911); 0.7298
							RR	0.986 (0.871, 1.085); 0.7703
							RD	-0.013 (-0.121, 0.073); 0.7698
Musculoskeletal and connective tissue disorders	55	46	27 (40.9)	26	37	19 (38.8)	OR	1.248 (0.617, 2.524); 0.5384
							RR	1.165 (0.709, 1.878); 0.5403
							RD	0.046 (-0.100, 0.200); 0.5465
Arthralgia	8	7	7 (10.6)	5	7	5 (10.2)	OR	1.227 (0.385, 3.911); 0.7298
							RR	1.182 (0.408, 3.367); 0.7655
							RD	0.013 (-0.073, 0.121); 0.7698
Back pain	12	10	9 (13.6)	7	10	6 (12.2)	OR	1.140 (0.394, 3.299); 0.8086
							RR	0.989 (0.865, 1.101); 0.8460
							RD	-0.010 (-0.124, 0.085); 0.8457
Nervous system disorders	105	88	30 (45.5)	34	48	15 (30.6)	OR	0.777 (0.376, 1.606); 0.4957
							RR	0.828 (0.483, 1.377); 0.4817
							RD	-0.054 (-0.194, 0.098); 0.4693
Dizziness	11	9	9 (13.6)	3	4	3 (6.1)	OR	0.581 (0.161, 2.091); 0.4058
							RR	0.552 (0.165, 1.792); 0.3570
							RD	-0.042 (-0.127, 0.057); 0.3124
Headache	68	57	15 (22.7)	23	33	13 (26.5)	OR	1.560 (0.687, 3.544); 0.2881
							RR	0.920 (0.763, 1.072); 0.3129
							RD	-0.068 (-0.206, 0.056); 0.3045
Psychiatric disorders	12	10	9 (13.6)	5	7	3 (6.1)	OR	0.581 (0.161, 2.091); 0.4058
							RR	1.046 (0.938, 1.152); 0.3129
							RD	0.042 (-0.057, 0.127); 0.3124
Renal and urinary disorders	13	11	10 (15.2)	10	14	5 (10.2)	OR	0.847 (0.283, 2.530); 0.7660
							RR	1.020 (0.898, 1.135); 0.7094

System Organ Class Preferred Term	Eculizumab (N=66) Patient-Years (PY)=119.7 Events n	Rate per 100 PY	Patients n (%)	Ravulizumab (N=49) Patient-Years (PY)=70.4 Events n	Rate per 100 PY	Patients n (%)	Treatment Effect Estimate (95% CI; p-value)	
							RD	0.018 (-0.093, 0.111); 0.7099
							OR	0.364 (0.087, 1.524); 0.1668
Reproductive system and breast disorders	15	13	10 (15.2)	2	3	2 (4.1)	RR	1.078 (0.974, 1.187); 0.0797
							RD	0.070 (-0.023, 0.154); 0.0764
							OR	0.763 (0.323, 1.802); 0.5370
Respiratory, thoracic and mediastinal disorders	40	33	19 (28.8)	10	14	9 (18.4)	RR	1.053 (0.891, 1.222); 0.4930
							RD	0.043 (-0.091, 0.161); 0.4945
							OR	0.520 (0.147, 1.842); 0.3105
Cough	11	9	10 (15.2)	3	4	3 (6.1)	RR	1.059 (0.948, 1.169); 0.2200
							RD	0.052 (-0.048, 0.140); 0.2187
							OR	0.962 (0.424, 2.183); 0.9266
Skin and subcutaneous tissue disorders	26	22	19 (28.8)	15	21	11 (22.4)	RR	0.958 (0.490, 1.829); 0.9003
							RD	-0.008 (-0.132, 0.130); 0.8998
							OR	0.657 (0.179, 2.407); 0.5255
Vascular disorders	10	8	8 (12.1)	3	4	3 (6.1)	RR	1.034 (0.928, 1.134); 0.4352
							RD	0.032 (-0.067, 0.114); 0.4353

AE: Adverse Event; CI: Confidence Interval; EDSS: Expanded Disability Status Scale; OR: Odds Ratio; PY: person years; RD: Risk Difference; RR: Risk Ratio; TEAE: Treatment-eme
TEAEs are AEs with a start date on or after the date of the first dose of study drug.
Treatment-related adverse events and follow-up were truncated at the maximum duration of follow-up in the ravulizumab arm.
Odds ratios were derived from a logistic regression model with treatment as the only covariate. Firth's correction was applied for odds ratios.
Any TEAEs were examined for preferred terms and system organ classes reported in at least 10% of patients in one of the treatment arms within the subgroup.
Severe and serious TEAEs were examined for preferred terms and system organ classes reported in at least 5% of patients in one of the treatment arms within the subgroup.
Preferred terms and system organ classes for a given AE severity or type (i.e., leading for withdrawal) were only examined within each subgroup if they were also examined in

Treatment Emergent Adverse Events (TEAEs) by MedDRA System Organ Class/Preferred Term by Severity and Treatment Group, EDSS: < 5

System Organ Class / Preferred Term	Eculizumab (N=66) Patient-Years (PY)=119.7 Events n	Rate per 100 PY	Patients n (%)	Ravulizumab (N=49) Patient-Years (PY)=70.4 Events n	Rate per 100 PY	Patients n (%)	Treatment Effect	Estimate (95% CI; p-value)
Mild TEAEs								
Blood and lymphatic system disorders	17	14	10 (15.2)	3	4	3 (6.1)	OR	0.520 (0.147, 1.842); 0.3105
							RR	0.497 (0.150, 1.587); 0.2717
							RD	-0.052 (-0.140, 0.048); 0.2187
Eye disorders	19	16	14 (21.2)	2	3	2 (4.1)	OR	0.252 (0.062, 1.016); 0.0527
							RR	1.130 (1.016, 1.262); 0.0123
							RD	0.111 (0.014, 0.202); 0.0101
Gastrointestinal disorders	83	69	28 (42.4)	21	30	15 (30.6)	OR	0.856 (0.412, 1.779); 0.6779
							RR	1.047 (0.843, 1.272); 0.6533
							RD	0.033 (-0.118, 0.172); 0.6547
Diarrhoea	13	11	8 (12.1)	3	4	3 (6.1)	OR	0.657 (0.179, 2.407); 0.5255
							RR	1.034 (0.928, 1.134); 0.4352
							RD	0.032 (-0.067, 0.114); 0.4353
Nausea	19	16	10 (15.2)	2	3	2 (4.1)	OR	0.364 (0.087, 1.524); 0.1668
							RR	1.078 (0.974, 1.187); 0.0797
							RD	0.070 (-0.023, 0.154); 0.0764
General disorders and administration site conditions	22	18	9 (13.6)	21	30	10 (20.4)	OR	1.994 (0.770, 5.165); 0.1551
							RR	0.913 (0.777, 1.033); 0.1839
							RD	-0.079 (-0.205, 0.028); 0.1738
Infections and infestations	166	139	45 (68.2)	39	55	21 (42.9)	OR	0.649 (0.333, 1.266); 0.2047
							RR	1.201 (0.906, 1.569); 0.1840
							RD	0.107 (-0.056, 0.259); 0.1883
COVID-19	0	0	0 (0.0)	10	14	10 (20.4)	OR	41.779 (2.361, 739.20); 0.0109
							RR	0.828 (0.710, 0.904); 0.0016
							RD	-0.172 (-0.290, -0.096); 0.0005
Nasopharyngitis	27	23	11 (16.7)	1	1	1 (2.0)	OR	0.194 (0.034, 1.114); 0.0659
							RR	1.110 (1.015, 1.223); 0.0102
							RD	0.097 (0.013, 0.180); 0.0080
Upper respiratory tract infection	36	30	22 (33.3)	2	3	2 (4.1)	OR	0.147 (0.037, 0.572); 0.0057
							RR	1.253 (1.111, 1.434); 0.0002
							RD	0.195 (0.090, 0.295); 0.0001
Injury, poisoning and procedural complications	24	20	17 (25.8)	7	10	5 (10.2)	OR	0.467 (0.167, 1.304); 0.1461
							RR	1.110 (0.968, 1.263); 0.0921
							RD	0.091 (-0.027, 0.195); 0.0902
Investigations	7	6	7 (10.6)	10	14	7 (14.3)	OR	1.738 (0.593, 5.097); 0.3140
							RR	0.948 (0.826, 1.052); 0.3486
							RD	-0.048 (-0.164, 0.045); 0.3426
Metabolism and nutrition disorders	8	7	7 (10.6)	1	1	1 (2.0)	OR	0.311 (0.052, 1.880); 0.2034
							RR	1.060 (0.974, 1.150); 0.0816
							RD	0.056 (-0.025, 0.129); 0.0778
Musculoskeletal and connective tissue disorders	43	36	22 (33.3)	18	26	12 (24.5)	OR	0.890 (0.405, 1.958); 0.7722
							RR	1.029 (0.851, 1.217); 0.7438
							RD	0.022 (-0.120, 0.151); 0.7445
Nervous system disorders	91	76	25 (37.9)	27	38	13 (26.5)	OR	0.832 (0.388, 1.784); 0.6364
							RR	0.861 (0.475, 1.516); 0.6156
							RD	-0.036 (-0.169, 0.110); 0.6081
Dizziness	10	8	8 (12.1)	2	3	2 (4.1)	OR	0.461 (0.107, 1.984); 0.2983
							RR	0.414 (0.101, 1.645); 0.2536
							RD	-0.049 (-0.128, 0.042); 0.1869
Headache	63	53	13 (19.7)	18	26	10 (20.4)	OR	1.339 (0.551, 3.251); 0.5190
							RR	0.957 (0.811, 1.096); 0.5451
							RD	-0.037 (-0.168, 0.077); 0.5419
Psychiatric disorders	10	8	8 (12.1)	2	3	2 (4.1)	OR	0.461 (0.107, 1.984); 0.2983
							RR	1.053 (0.955, 1.151); 0.1891
							RD	0.049 (-0.042, 0.128); 0.1869
Renal and urinary disorders	12	10	10 (15.2)	9	13	4 (8.2)	OR	0.680 (0.212, 2.178); 0.5163
							RR	1.039 (0.922, 1.152); 0.4397
							RD	0.035 (-0.071, 0.126); 0.4401
Reproductive system and breast disorders	15	13	10 (15.2)	2	3	2 (4.1)	OR	0.364 (0.087, 1.524); 0.1668
							RR	1.078 (0.974, 1.187); 0.0797
							RD	0.070 (-0.023, 0.154); 0.0764

Treatment Emergent Adverse Events (TEAEs) by MedDRA System Organ Class/Preferred Term by Severity and Treatment Group, EDSS: < 5

System Organ Class / Preferred Term	Eculizumab (N=66) Patient-Years (PY)=119.7 Events n	Rate per 100 PY	Patients n (%)	Ravulizumab (N=49) Patient-Years (PY)=70.4 Events n	Rate per 100 PY	Patients n (%)	Treatment Effect Estimate (95% CI; p-value)
							OR 0.821 (0.332, 2.032); 0.6699
Respiratory, thoracic and mediastinal disorders	36	30	16 (24.2)	9	13	8 (16.3)	RR 1.034 (0.885, 1.185); 0.6261
							RD 0.029 (-0.099, 0.141); 0.6270
							OR 0.581 (0.161, 2.091); 0.4058
Cough	10	8	9 (13.6)	3	4	3 (6.1)	RR 1.046 (0.938, 1.152); 0.3129
							RD 0.042 (-0.057, 0.127); 0.3124
							OR 0.714 (0.293, 1.743); 0.4596
Skin and subcutaneous tissue disorders	23	19	18 (27.3)	12	17	8 (16.3)	RR 0.736 (0.342, 1.535); 0.4323
							RD -0.050 (-0.164, 0.080); 0.4111
ModerateTEAEs							
							OR 0.760 (0.234, 2.476); 0.6493
Gastrointestinal disorders	11	9	9 (13.6)	5	7	4 (8.2)	RR 1.027 (0.913, 1.135); 0.5782
							RD 0.025 (-0.080, 0.113); 0.5787
							OR 1.295 (0.594, 2.821); 0.5155
Infections and infestations	34	28	19 (28.8)	15	21	14 (28.6)	RR 1.220 (0.661, 2.210); 0.5226
							RD 0.043 (-0.087, 0.187); 0.5309
							OR 2.993 (0.879, 10.193); 0.0795
Injury, poisoning and procedural complications	4	3	4 (6.1)	10	14	7 (14.3)	RR 2.897 (0.938, 8.960); 0.0784
							RD 0.079 (-0.005, 0.192); 0.0954
							OR 1.289 (0.436, 3.813); 0.6465
Musculoskeletal and connective tissue disorders	11	9	8 (12.1)	6	9	6 (12.2)	RR 1.241 (0.466, 3.256); 0.6739
							RD 0.020 (-0.072, 0.134); 0.6810
Non-SevereTEAEs							
							OR 0.511 (0.165, 1.579); 0.2433
Blood and lymphatic system disorders	22	18	13 (19.7)	4	6	4 (8.2)	RR 0.509 (0.179, 1.397); 0.2174
							RD -0.066 (-0.162, 0.043); 0.1683
							OR 0.470 (0.153, 1.440); 0.1862
Eye disorders	21	18	14 (21.2)	6	9	4 (8.2)	RR 1.090 (0.962, 1.224); 0.1190
							RD 0.077 (-0.033, 0.174); 0.1170
							OR 0.996 (0.493, 2.010); 0.9908
Gastrointestinal disorders	94	79	30 (45.5)	26	37	18 (36.7)	RR 1.003 (0.791, 1.241); 0.9777
							RD 0.002 (-0.153, 0.148); 0.9777
							OR 0.581 (0.161, 2.091); 0.4058
Diarrhoea	16	13	9 (13.6)	3	4	3 (6.1)	RR 1.046 (0.938, 1.152); 0.3129
							RD 0.042 (-0.057, 0.127); 0.3124
							OR 0.299 (0.073, 1.225); 0.0934
Nausea	23	19	12 (18.2)	2	3	2 (4.1)	RR 1.103 (0.995, 1.224); 0.0319
							RD 0.091 (-0.004, 0.178); 0.0288
							OR 2.006 (0.853, 4.718); 0.1108
General disorders and administration site conditions	28	23	12 (18.2)	25	36	13 (26.5)	RR 0.887 (0.738, 1.025); 0.1349
							RD -0.099 (-0.235, 0.021); 0.1233
							OR 0.907 (0.472, 1.743); 0.7698
Infections and infestations	200	167	52 (78.8)	54	77	30 (61.2)	RR 0.955 (0.689, 1.288); 0.7700
							RD -0.024 (-0.185, 0.136); 0.7686
							OR 51.853 (2.961, 907.97); 0.0069
COVID-19	0	0	0 (0.0)	12	17	12 (24.5)	RR 0.793 (0.672, 0.878); 0.0005
							RD -0.207 (-0.328, -0.122); 0.0001
							OR 0.252 (0.062, 1.016); 0.0527
Nasopharyngitis	31	26	14 (21.2)	2	3	2 (4.1)	RR 1.130 (1.016, 1.262); 0.0123
							RD 0.111 (0.014, 0.202); 0.0101
							OR 0.102 (0.006, 1.864); 0.1236
Pharyngitis	10	8	7 (10.6)	0	0	0 (0.0)	RR 1.079 (1.009, 1.167); 0.0082
							RD 0.073 (0.009, 0.143); 0.0060
							OR 0.244 (0.084, 0.715); 0.0101
Upper respiratory tract infection	39	33	24 (36.4)	4	6	4 (8.2)	RR 0.276 (0.103, 0.707); 0.0122
							RD -0.181 (-0.289, -0.062); 0.0011
							OR 0.962 (0.424, 2.183); 0.9266
Injury, poisoning and procedural complications	28	23	19 (28.8)	17	24	11 (22.4)	RR 0.958 (0.490, 1.829); 0.9003
							RD -0.008 (-0.132, 0.130); 0.8998
							OR 1.516 (0.532, 4.322); 0.4363
Investigations	10	8	8 (12.1)	10	14	7 (14.3)	RR 0.959 (0.834, 1.068); 0.4698
							RD -0.037 (-0.155, 0.058); 0.4660

Treatment Emergent Adverse Events (TEAEs) by MedDRA System Organ Class/Preferred Term by Severity and Treatment Group, EDSS: < 5

System Organ Class / Preferred Term	Eculizumab (N=66) Patient-Years (PY)=119.7 Events n	Rate per 100 PY	Patients n (%)	Ravulizumab (N=49) Patient-Years (PY)=70.4 Events n	Rate per 100 PY	Patients n (%)	Treatment Effect	Estimate (95% CI; p-value)
Metabolism and nutrition disorders	8	7	7 (10.6)	5	7	5 (10.2)	OR	1.227 (0.385, 3.911); 0.7298
							RR	0.986 (0.871, 1.085); 0.7703
							RD	-0.013 (-0.121, 0.073); 0.7698
Musculoskeletal and connective tissue disorders	54	45	27 (40.9)	24	34	18 (36.7)	OR	1.154 (0.567, 2.349); 0.6921
							RR	1.103 (0.664, 1.797); 0.6993
							RD	0.029 (-0.115, 0.182); 0.7023
Arthralgia	8	7	7 (10.6)	5	7	5 (10.2)	OR	1.227 (0.385, 3.911); 0.7298
							RR	1.182 (0.408, 3.367); 0.7655
							RD	0.013 (-0.073, 0.121); 0.7698
Back pain	11	9	9 (13.6)	6	9	5 (10.2)	OR	0.947 (0.311, 2.879); 0.9234
							RR	1.008 (0.889, 1.118); 0.8734
							RD	0.008 (-0.103, 0.099); 0.8735
Nervous system disorders	102	85	29 (43.9)	33	47	15 (30.6)	OR	0.815 (0.393, 1.690); 0.5829
							RR	0.856 (0.498, 1.431); 0.5666
							RD	-0.043 (-0.183, 0.108); 0.5579
Dizziness	11	9	9 (13.6)	2	3	2 (4.1)	OR	0.408 (0.096, 1.727); 0.2231
							RR	0.368 (0.091, 1.439); 0.1904
							RD	-0.059 (-0.141, 0.033); 0.1208
Headache	66	55	15 (22.7)	23	33	13 (26.5)	OR	1.560 (0.687, 3.544); 0.2881
							RR	0.920 (0.763, 1.072); 0.3129
							RD	-0.068 (-0.206, 0.056); 0.3045
Psychiatric disorders	12	10	9 (13.6)	5	7	3 (6.1)	OR	0.581 (0.161, 2.091); 0.4058
							RR	1.046 (0.938, 1.152); 0.3129
							RD	0.042 (-0.057, 0.127); 0.3124
Renal and urinary disorders	13	11	10 (15.2)	9	13	4 (8.2)	OR	0.680 (0.212, 2.178); 0.5163
							RR	1.039 (0.922, 1.152); 0.4397
							RD	0.035 (-0.071, 0.126); 0.4401
Reproductive system and breast disorders	15	13	10 (15.2)	2	3	2 (4.1)	OR	0.364 (0.087, 1.524); 0.1668
							RR	1.078 (0.974, 1.187); 0.0797
							RD	0.070 (-0.023, 0.154); 0.0764
Respiratory, thoracic and mediastinal disorders	39	33	19 (28.8)	10	14	9 (18.4)	OR	0.763 (0.323, 1.802); 0.5370
							RR	1.053 (0.891, 1.222); 0.4930
							RD	0.043 (-0.091, 0.161); 0.4945
Cough	11	9	10 (15.2)	3	4	3 (6.1)	OR	0.520 (0.147, 1.842); 0.3105
							RR	1.059 (0.948, 1.169); 0.2200
							RD	0.052 (-0.048, 0.140); 0.2187
Skin and subcutaneous tissue disorders	26	22	19 (28.8)	15	21	11 (22.4)	OR	0.962 (0.424, 2.183); 0.9266
							RR	0.958 (0.490, 1.829); 0.9003
							RD	-0.008 (-0.132, 0.130); 0.8998
Vascular disorders	10	8	8 (12.1)	3	4	3 (6.1)	OR	0.657 (0.179, 2.407); 0.5255
							RR	1.034 (0.928, 1.134); 0.4352
							RD	0.032 (-0.067, 0.114); 0.4353
Severe TEAEs								
Infections and infestations	6	5	4 (6.1)	5	7	5 (10.2)	OR	2.113 (0.576, 7.748); 0.2590
							RR	2.069 (0.619, 6.886); 0.2632
							RD	0.045 (-0.033, 0.150); 0.2903
Serious TEAEs								
Infections and infestations	9	8	6 (9.1)	5	7	5 (10.2)	OR	1.431 (0.434, 4.719); 0.5560
							RR	1.379 (0.460, 4.079); 0.5807
							RD	0.024 (-0.060, 0.131); 0.5931
TEAEs leading to withdrawal from study drug								
Infections and infestations	0	0	0 (0.0)	3	4	1 (2.0)	OR	Not calculated
							RR	Not calculated
							RD	Not calculated
Bronchitis	0	0	0 (0.0)	1	1	1 (2.0)	OR	Not calculated
							RR	Not calculated
							RD	Not calculated
Encephalitis meningococcal	0	0	0 (0.0)	1	1	1 (2.0)	OR	Not calculated
							RR	Not calculated
							RD	Not calculated

Treatment Emergent Adverse Events (TEAEs) by MedDRA System Organ Class/Preferred Term by Severity and Treatment Group, EDSS: < 5

System Organ Class	Eculizumab (N=66) Patient-Years (PY)=119.7			Ravulizumab (N=49) Patient-Years (PY)=70.4			Treatment Effect	
Preferred Term	Events n	Rate per 100 PY	Patients n (%)	Events n	Rate per 100 PY	Patients n (%)	Estimate (95% CI; p-value)	
Stenotrophomonas infection	0	0	0 (0.0)	1	1	1 (2.0)	OR	Not calculated
							RR	Not calculated
							RD	Not calculated

AE: Adverse Event; CI: Confidence Interval; EDSS: Expanded Disability Status Scale; OR: Odds Ratio; PY: person years; RD: Risk Difference; RR: Risk Ratio; TEAE: Treatment-emergent Adverse Event.

TEAEs are AEs with a start date on or after the date of the first dose of study drug.

Treatment-related adverse events and follow-up were truncated at the maximum duration of follow-up in the ravulizumab arm.

Odds ratios were derived from a logistic regression model with treatment as the only covariate. Firth's correction was applied for odds ratios.

Mild, moderate and non-severe TEAEs were examined for preferred terms and system organ classes reported in at least 10% of patients in one of the treatment arms within the subgroup.

Severe and serious TEAEs were examined for preferred terms and system organ classes reported in at least 5% of patients in one of the treatment arms within the subgroup.

All TEAEs leading to withdrawal from study drug were examined.

TEAEs leading to withdrawal from study drug were examined descriptively (i.e., OR, RR, and RD not calculated).

Treatment Emergent Adverse Events (TEAEs) by MedDRA System Organ Class/Preferred Term by Treatment Group, EDSS: ≥ 5

System Organ Class	Eculizumab (N=30) Patient-Years (PY)=53.1			Ravulizumab (N=9) Patient-Years (PY)=13.7			Treatment Effect	
Preferred Term	Events n	Rate per 100 PY	Patients n (%)	Events n	Rate per 100 PY	Patients n (%)	Estimate (95% CI; p-value)	
Blood and lymphatic system disorders	14	26	6 (20.0)	0	0	0 (0.0)	OR	0.119 (0.006, 2.205); 0.1530
							RR	1.067 (0.998, 1.149); 0.0143
							RD	0.063 (-0.001, 0.130); 0.0114
Eye disorders	24	45	5 (16.7)	3	22	2 (22.2)	OR	0.736 (0.157, 3.443); 0.6971
							RR	1.019 (0.926, 1.100); 0.5935
							RD	0.018 (-0.070, 0.088); 0.5937
Gastrointestinal disorders	29	55	9 (30.0)	6	44	4 (44.4)	OR	0.760 (0.234, 2.476); 0.6493
							RR	1.027 (0.913, 1.135); 0.5782
							RD	0.025 (-0.080, 0.113); 0.5787
Diarrhoea	6	11	6 (20.0)	0	0	0 (0.0)	OR	0.119 (0.006, 2.205); 0.1530
							RR	1.067 (0.998, 1.149); 0.0143
							RD	0.063 (-0.001, 0.130); 0.0114
General disorders and administration site conditions	56	105	13 (43.3)	10	73	4 (44.4)	OR	0.511 (0.165, 1.579); 0.2433
							RR	1.077 (0.952, 1.206); 0.1698
							RD	0.066 (-0.043, 0.162); 0.1683
Infections and infestations	82	154	20 (66.7)	7	51	6 (66.7)	OR	0.462 (0.177, 1.203); 0.1138
							RR	1.132 (0.976, 1.304); 0.0705
							RD	0.105 (-0.020, 0.216); 0.0686
COVID-19	0	0	0 (0.0)	2	15	2 (22.2)	OR	8.540 (0.396, 184.30); 0.1712
							RR	0.966 (0.882, 1.005); 0.1573
							RD	-0.034 (-0.118, 0.005); 0.1501
Nasopharyngitis	15	28	6 (20.0)	1	7	1 (11.1)	OR	0.363 (0.059, 2.242); 0.2754
							RR	1.048 (0.964, 1.133); 0.1354
							RD	0.045 (-0.034, 0.116); 0.1319
Pharyngitis	3	6	3 (10.0)	0	0	0 (0.0)	OR	0.228 (0.011, 4.611); 0.3354
							RR	1.032 (0.967, 1.097); 0.0833
							RD	0.031 (-0.032, 0.088); 0.0784
Upper respiratory tract infection	6	11	4 (13.3)	0	0	0 (0.0)	OR	0.176 (0.009, 3.405); 0.2502
							RR	1.043 (0.977, 1.114); 0.0455
							RD	0.042 (-0.022, 0.103); 0.0411
Urinary tract infection	21	40	7 (23.3)	3	22	3 (33.3)	OR	0.752 (0.201, 2.823); 0.6733
							RR	1.023 (0.919, 1.117); 0.5900
							RD	0.021 (-0.076, 0.101); 0.5904
Injury, poisoning and procedural complications	19	36	11 (36.7)	1	7	1 (11.1)	OR	0.194 (0.034, 1.114); 0.0659
							RR	1.110 (1.015, 1.223); 0.0102
							RD	0.097 (0.013, 0.180); 0.0080
Contusion	5	9	4 (13.3)	0	0	0 (0.0)	OR	0.176 (0.009, 3.405); 0.2502
							RR	1.043 (0.977, 1.114); 0.0455
							RD	0.042 (-0.022, 0.103); 0.0411
Investigations	18	34	6 (20.0)	1	7	1 (11.1)	OR	0.363 (0.059, 2.242); 0.2754
							RR	1.048 (0.964, 1.133); 0.1354
							RD	0.045 (-0.034, 0.116); 0.1319
Metabolism and nutrition disorders	4	8	4 (13.3)	0	0	0 (0.0)	OR	0.176 (0.009, 3.405); 0.2502
							RR	1.043 (0.977, 1.114); 0.0455
							RD	0.042 (-0.022, 0.103); 0.0411
Musculoskeletal and connective tissue disorders	30	56	16 (53.3)	6	44	4 (44.4)	OR	0.403 (0.133, 1.218); 0.1071
							RR	1.117 (0.983, 1.263); 0.0558
							RD	0.098 (-0.014, 0.198); 0.0532
Arthralgia	3	6	3 (10.0)	1	7	1 (11.1)	OR	0.697 (0.099, 4.925); 0.7173
							RR	1.014 (0.935, 1.081); 0.5699
							RD	0.014 (-0.063, 0.074); 0.5698
Back pain	4	8	4 (13.3)	1	7	1 (11.1)	OR	0.536 (0.081, 3.555); 0.5184
							RR	1.025 (0.945, 1.098); 0.3598
							RD	0.024 (-0.053, 0.088); 0.3587
Pain in extremity	6	11	4 (13.3)	0	0	0 (0.0)	OR	0.176 (0.009, 3.405); 0.2502
							RR	1.043 (0.977, 1.114); 0.0455
							RD	0.042 (-0.022, 0.103); 0.0411
Nervous system disorders	73	137	15 (50.0)	9	66	2 (22.2)	OR	0.233 (0.058, 0.934); 0.0397
							RR	1.144 (1.027, 1.281); 0.0075
							RD	0.122 (0.024, 0.214); 0.0058
Dizziness	8	15	5 (16.7)	1	7	1 (11.1)	OR	0.434 (0.068, 2.759); 0.3764
							RR	1.037 (0.954, 1.116); 0.2223
							RD	0.035 (-0.044, 0.102); 0.2198
Headache	14	26	6 (20.0)	1	7	1 (11.1)	OR	0.363 (0.059, 2.242); 0.2754
							RR	1.048 (0.964, 1.133); 0.1354

System Organ Class Preferred Term	Eculizumab (N=30) Patient-Years (PY)=53.1 Events n	Rate per 100 PY	Patients n (%)	Ravulizumab (N=9) Patient-Years (PY)=13.7 Events n	Rate per 100 PY	Patients n (%)	Treatment Effect Estimate (95% CI; p-value)	
							RD	0.045 (-0.034, 0.116); 0.1319
							OR	1.685 (0.365, 7.773); 0.5035
Psychiatric disorders	3	6	3 (10.0)	5	37	3 (33.3)	RR	0.979 (0.883, 1.050); 0.5499
							RD	-0.020 (-0.114, 0.046); 0.5479
							OR	0.119 (0.006, 2.205); 0.1530
Renal and urinary disorders	9	17	6 (20.0)	0	0	0 (0.0)	RR	1.067 (0.998, 1.149); 0.0143
							RD	0.063 (-0.001, 0.130); 0.0114
							OR	0.176 (0.009, 3.405); 0.2502
Respiratory, thoracic and mediastinal disorders	23	43	4 (13.3)	0	0	0 (0.0)	RR	1.043 (0.977, 1.114); 0.0455
							RD	0.042 (-0.022, 0.103); 0.0411
							OR	0.363 (0.059, 2.242); 0.2754
Skin and subcutaneous tissue disorders	12	23	6 (20.0)	1	7	1 (11.1)	RR	1.048 (0.964, 1.133); 0.1354
							RD	0.045 (-0.034, 0.116); 0.1319
							OR	0.434 (0.068, 2.759); 0.3764
Vascular disorders	7	13	5 (16.7)	2	15	1 (11.1)	RR	1.037 (0.954, 1.116); 0.2223
							RD	0.035 (-0.044, 0.102); 0.2198

AE: Adverse Event; CI: Confidence Interval; EDSS: Expanded Disability Status Scale; OR: Odds Ratio; PY: person years; RD: Risk Difference; RR: Risk Ratio; TEAE: Treatment-eme
TEAEs are AEs with a start date on or after the date of the first dose of study drug.
Treatment-related adverse events and follow-up were truncated at the maximum duration of follow-up in the ravulizumab arm.
Odds ratios were derived from a logistic regression model with treatment as the only covariate. Firth's correction was applied for odds ratios.
Any TEAEs were examined for preferred terms and system organ classes reported in at least 10% of patients in one of the treatment arms within the subgroup.
Severe and serious TEAEs were examined for preferred terms and system organ classes reported in at least 5% of patients in one of the treatment arms within the subgroup.
Preferred terms and system organ classes for a given AE severity or type (i.e., leading for withdrawal) were only examined within each subgroup if they were also examined in

Treatment Emergent Adverse Events (TEAEs) by MedDRA System Organ Class/Preferred Term by Severity and Treatment Group, EDSS: ≥ 5

System Organ Class	Eculizumab (N=30) Patient-Years (PY)=53.1			Ravulizumab (N=9) Patient-Years (PY)=13.7			Treatment Effect	
Preferred Term	Events n	Rate per 100 PY	Patients n (%)	Events n	Rate per 100 PY	Patients n (%)		Estimate (95% CI; p-value)
Mild TEAEs								
Blood and lymphatic system disorders	12	23	5 (16.7)	0	0	0 (0.0)	OR	0.142 (0.008, 2.684); 0.1931
							RR	1.055 (0.988, 1.132); 0.0254
							RD	0.052 (-0.012, 0.116); 0.0216
Eye disorders	11	21	5 (16.7)	3	22	2 (22.2)	OR	0.736 (0.157, 3.443); 0.6971
							RR	1.019 (0.926, 1.100); 0.5935
							RD	0.018 (-0.070, 0.088); 0.5937
Gastrointestinal disorders	21	40	7 (23.3)	6	44	4 (44.4)	OR	0.985 (0.289, 3.354); 0.9809
							RR	1.004 (0.894, 1.101); 0.9260
							RD	0.004 (-0.099, 0.087); 0.9260
Diarrhoea	6	11	6 (20.0)	0	0	0 (0.0)	OR	0.119 (0.006, 2.205); 0.1530
							RR	1.067 (0.998, 1.149); 0.0143
							RD	0.063 (-0.001, 0.130); 0.0114
General disorders and administration site conditions	53	100	11 (36.7)	9	66	3 (33.3)	OR	0.469 (0.134, 1.641); 0.2360
							RR	1.071 (0.958, 1.187); 0.1516
							RD	0.063 (-0.038, 0.152); 0.1495
Infections and infestations	65	122	17 (56.7)	4	29	4 (44.4)	OR	0.375 (0.125, 1.127); 0.0807
							RR	1.131 (0.994, 1.283); 0.0374
							RD	0.108 (-0.005, 0.210); 0.0348
COVID-19	0	0	0 (0.0)	1	7	1 (11.1)	OR	5.035 (0.198, 128.13); 0.3277
							RR	0.983 (0.908, 1.023); 0.3173
							RD	-0.017 (-0.092, 0.022); 0.3131
Nasopharyngitis	12	23	5 (16.7)	1	7	1 (11.1)	OR	0.434 (0.068, 2.759); 0.3764
							RR	1.037 (0.954, 1.116); 0.2223
							RD	0.035 (-0.044, 0.102); 0.2198
Upper respiratory tract infection	5	9	4 (13.3)	0	0	0 (0.0)	OR	0.176 (0.009, 3.405); 0.2502
							RR	1.043 (0.977, 1.114); 0.0455
							RD	0.042 (-0.022, 0.103); 0.0411
Urinary tract infection	17	32	6 (20.0)	1	7	1 (11.1)	OR	0.363 (0.059, 2.242); 0.2754
							RR	1.048 (0.964, 1.133); 0.1354
							RD	0.045 (-0.034, 0.116); 0.1319
Injury, poisoning and procedural complications	13	24	8 (26.7)	0	0	0 (0.0)	OR	0.089 (0.005, 1.609); 0.1015
							RR	1.091 (1.021, 1.185); 0.0047
							RD	0.083 (0.019, 0.156); 0.0031
Investigations	14	26	6 (20.0)	1	7	1 (11.1)	OR	0.363 (0.059, 2.242); 0.2754
							RR	1.048 (0.964, 1.133); 0.1354
							RD	0.045 (-0.034, 0.116); 0.1319
Metabolism and nutrition disorders	4	8	4 (13.3)	0	0	0 (0.0)	OR	0.176 (0.009, 3.405); 0.2502
							RR	1.043 (0.977, 1.114); 0.0455
							RD	0.042 (-0.022, 0.103); 0.0411
Musculoskeletal and connective tissue disorders	22	41	14 (46.7)	4	29	3 (33.3)	OR	0.359 (0.105, 1.222); 0.1011
							RR	1.110 (0.989, 1.243); 0.0450
							RD	0.094 (-0.010, 0.188); 0.0421
Nervous system disorders	65	122	12 (40.0)	9	66	2 (22.2)	OR	0.299 (0.073, 1.225); 0.0934
							RR	1.103 (0.995, 1.224); 0.0319
							RD	0.091 (-0.004, 0.178); 0.0288
Dizziness	7	13	5 (16.7)	1	7	1 (11.1)	OR	0.434 (0.068, 2.759); 0.3764
							RR	1.037 (0.954, 1.116); 0.2223
							RD	0.035 (-0.044, 0.102); 0.2198
Headache	14	26	6 (20.0)	1	7	1 (11.1)	OR	0.363 (0.059, 2.242); 0.2754
							RR	1.048 (0.964, 1.133); 0.1354
							RD	0.045 (-0.034, 0.116); 0.1319
Psychiatric disorders	3	6	3 (10.0)	3	22	3 (33.3)	OR	1.685 (0.365, 7.773); 0.5035
							RR	0.979 (0.883, 1.050); 0.5499
							RD	-0.020 (-0.114, 0.046); 0.5479
Renal and urinary disorders	5	9	4 (13.3)	0	0	0 (0.0)	OR	0.176 (0.009, 3.405); 0.2502
							RR	1.043 (0.977, 1.114); 0.0455
							RD	0.042 (-0.022, 0.103); 0.0411

Treatment Emergent Adverse Events (TEAEs) by MedDRA System Organ Class/Preferred Term by Severity and Treatment Group, EDSS: ≥ 5

System Organ Class / Preferred Term	Eculizumab (N=30) Patient-Years (PY)=53.1 Events n	Rate per 100 PY	Patients n (%)	Ravulizumab (N=9) Patient-Years (PY)=13.7 Events n	Rate per 100 PY	Patients n (%)	Treatment Effect	Estimate (95% CI; p-value)
Respiratory, thoracic and mediastinal disorders	23	43	4 (13.3)	0	0	0 (0.0)	OR	0.176 (0.009, 3.405); 0.2502
							RR	1.043 (0.977, 1.114); 0.0455
							RD	0.042 (-0.022, 0.103); 0.0411
Skin and subcutaneous tissue disorders	12	23	6 (20.0)	1	7	1 (11.1)	OR	0.363 (0.059, 2.242); 0.2754
							RR	1.048 (0.964, 1.133); 0.1354
							RD	0.045 (-0.034, 0.116); 0.1319
ModerateTEAEs								
Gastrointestinal disorders	7	13	5 (16.7)	0	0	0 (0.0)	OR	0.142 (0.008, 2.684); 0.1931
							RR	1.055 (0.988, 1.132); 0.0254
							RD	0.052 (-0.012, 0.116); 0.0216
Infections and infestations	15	28	8 (26.7)	3	22	2 (22.2)	OR	0.461 (0.107, 1.984); 0.2983
							RR	1.053 (0.955, 1.151); 0.1891
							RD	0.049 (-0.042, 0.128); 0.1869
Injury, poisoning and procedural complications	5	9	3 (10.0)	0	0	0 (0.0)	OR	0.228 (0.011, 4.611); 0.3354
							RR	1.032 (0.967, 1.097); 0.0833
							RD	0.031 (-0.032, 0.088); 0.0784
Musculoskeletal and connective tissue disorders	6	11	5 (16.7)	2	15	1 (11.1)	OR	0.434 (0.068, 2.759); 0.3764
							RR	1.037 (0.954, 1.116); 0.2223
							RD	0.035 (-0.044, 0.102); 0.2198
Non-SevereTEAEs								
Blood and lymphatic system disorders	14	26	6 (20.0)	0	0	0 (0.0)	OR	0.119 (0.006, 2.205); 0.1530
							RR	1.067 (0.998, 1.149); 0.0143
							RD	0.063 (-0.001, 0.130); 0.0114
Eye disorders	24	45	5 (16.7)	3	22	2 (22.2)	OR	0.736 (0.157, 3.443); 0.6971
							RR	1.019 (0.926, 1.100); 0.5935
							RD	0.018 (-0.070, 0.088); 0.5937
Gastrointestinal disorders	28	53	9 (30.0)	6	44	4 (44.4)	OR	0.760 (0.234, 2.476); 0.6493
							RR	1.027 (0.913, 1.135); 0.5782
							RD	0.025 (-0.080, 0.113); 0.5787
Diarrhoea	6	11	6 (20.0)	0	0	0 (0.0)	OR	0.119 (0.006, 2.205); 0.1530
							RR	1.067 (0.998, 1.149); 0.0143
							RD	0.063 (-0.001, 0.130); 0.0114
General disorders and administration site conditions	55	104	13 (43.3)	10	73	4 (44.4)	OR	0.511 (0.165, 1.579); 0.2433
							RR	1.077 (0.952, 1.206); 0.1698
							RD	0.066 (-0.043, 0.162); 0.1683
Infections and infestations	80	151	20 (66.7)	7	51	6 (66.7)	OR	0.462 (0.177, 1.203); 0.1138
							RR	1.132 (0.976, 1.304); 0.0705
							RD	0.105 (-0.020, 0.216); 0.0686
COVID-19	0	0	0 (0.0)	2	15	2 (22.2)	OR	8.540 (0.396, 184.30); 0.1712
							RR	0.966 (0.882, 1.005); 0.1573
							RD	-0.034 (-0.118, 0.005); 0.1501
Nasopharyngitis	15	28	6 (20.0)	1	7	1 (11.1)	OR	0.363 (0.059, 2.242); 0.2754
							RR	1.048 (0.964, 1.133); 0.1354
							RD	0.045 (-0.034, 0.116); 0.1319
Pharyngitis	3	6	3 (10.0)	0	0	0 (0.0)	OR	0.228 (0.011, 4.611); 0.3354
							RR	1.032 (0.967, 1.097); 0.0833
							RD	0.031 (-0.032, 0.088); 0.0784
Upper respiratory tract infection	6	11	4 (13.3)	0	0	0 (0.0)	OR	0.176 (0.009, 3.405); 0.2502
							RR	1.043 (0.977, 1.114); 0.0455
							RD	0.042 (-0.022, 0.103); 0.0411
Urinary tract infection	21	40	7 (23.3)	3	22	3 (33.3)	OR	0.752 (0.201, 2.823); 0.6733
							RR	1.023 (0.919, 1.117); 0.5900
							RD	0.021 (-0.076, 0.101); 0.5904
Injury, poisoning and procedural complications	18	34	11 (36.7)	0	0	0 (0.0)	OR	0.064 (0.004, 1.126); 0.0603
							RR	1.129 (1.056, 1.241); 0.0009
							RD	0.115 (0.049, 0.194); 0.0004
Contusion	5	9	4 (13.3)	0	0	0 (0.0)	OR	0.176 (0.009, 3.405); 0.2502
							RR	1.043 (0.977, 1.114); 0.0455
							RD	0.042 (-0.022, 0.103); 0.0411
Investigations	18	34	6 (20.0)	1	7	1 (11.1)	OR	0.363 (0.059, 2.242); 0.2754
							RR	1.048 (0.964, 1.133); 0.1354
							RD	0.045 (-0.034, 0.116); 0.1319

Treatment Emergent Adverse Events (TEAEs) by MedDRA System Organ Class/Preferred Term by Severity and Treatment Group, EDSS: ≥ 5

System Organ Class / Preferred Term	Eculizumab (N=30) Patient-Years (PY)=53.1 Events n	Rate per 100 PY	Patients n (%)	Ravulizumab (N=9) Patient-Years (PY)=13.7 Events n	Rate per 100 PY	Patients n (%)	Treatment Effect Estimate (95% CI; p-value)
Metabolism and nutrition disorders	4	8	4 (13.3)	0	0	0 (0.0)	OR 0.176 (0.009, 3.405); 0.2502 RR 1.043 (0.977, 1.114); 0.0455 RD 0.042 (-0.022, 0.103); 0.0411
Musculoskeletal and connective tissue disorders	28	53	16 (53.3)	6	44	4 (44.4)	OR 0.403 (0.133, 1.218); 0.1071 RR 1.117 (0.983, 1.263); 0.0558 RD 0.098 (-0.014, 0.198); 0.0532
Arthralgia	3	6	3 (10.0)	1	7	1 (11.1)	OR 0.697 (0.099, 4.925); 0.7173 RR 1.014 (0.935, 1.081); 0.5699 RD 0.014 (-0.063, 0.074); 0.5698
Back pain	4	8	4 (13.3)	1	7	1 (11.1)	OR 0.536 (0.081, 3.555); 0.5184 RR 1.025 (0.945, 1.098); 0.3598 RD 0.024 (-0.053, 0.088); 0.3587
Nervous system disorders	72	135	14 (46.7)	9	66	2 (22.2)	OR 0.252 (0.062, 1.016); 0.0527 RR 1.130 (1.016, 1.262); 0.0123 RD 0.111 (0.014, 0.202); 0.0101
Dizziness	8	15	5 (16.7)	1	7	1 (11.1)	OR 0.434 (0.068, 2.759); 0.3764 RR 1.037 (0.954, 1.116); 0.2223 RD 0.035 (-0.044, 0.102); 0.2198
Headache	14	26	6 (20.0)	1	7	1 (11.1)	OR 0.363 (0.059, 2.242); 0.2754 RR 1.048 (0.964, 1.133); 0.1354 RD 0.045 (-0.034, 0.116); 0.1319
Psychiatric disorders	3	6	3 (10.0)	4	29	3 (33.3)	OR 1.685 (0.365, 7.773); 0.5035 RR 0.979 (0.883, 1.050); 0.5499 RD -0.020 (-0.114, 0.046); 0.5479
Renal and urinary disorders	9	17	6 (20.0)	0	0	0 (0.0)	OR 0.119 (0.006, 2.205); 0.1530 RR 1.067 (0.998, 1.149); 0.0143 RD 0.063 (-0.001, 0.130); 0.0114
Respiratory, thoracic and mediastinal disorders	23	43	4 (13.3)	0	0	0 (0.0)	OR 0.176 (0.009, 3.405); 0.2502 RR 1.043 (0.977, 1.114); 0.0455 RD 0.042 (-0.022, 0.103); 0.0411
Skin and subcutaneous tissue disorders	12	23	6 (20.0)	1	7	1 (11.1)	OR 0.363 (0.059, 2.242); 0.2754 RR 1.048 (0.964, 1.133); 0.1354 RD 0.045 (-0.034, 0.116); 0.1319
Vascular disorders	7	13	5 (16.7)	2	15	1 (11.1)	OR 0.434 (0.068, 2.759); 0.3764 RR 1.037 (0.954, 1.116); 0.2223 RD 0.035 (-0.044, 0.102); 0.2198
Severe TEAEs							
None							
Serious TEAEs							
Infections and infestations	4	8	3 (10.0)	0	0	0 (0.0)	OR 0.228 (0.011, 4.611); 0.3354 RR 1.032 (0.967, 1.097); 0.0833 RD 0.031 (-0.032, 0.088); 0.0784
Nervous system disorders	3	6	3 (10.0)	0	0	0 (0.0)	OR 0.228 (0.011, 4.611); 0.3354 RR 1.032 (0.967, 1.097); 0.0833 RD 0.031 (-0.032, 0.088); 0.0784
Neuromyelitis optica spectrum disorder	3	6	3 (10.0)	0	0	0 (0.0)	OR 0.228 (0.011, 4.611); 0.3354 RR 1.032 (0.967, 1.097); 0.0833 RD 0.031 (-0.032, 0.088); 0.0784
TEAEs leading to withdrawal from study drug							
None							

AE: Adverse Event; CI: Confidence Interval; EDSS: Expanded Disability Status Scale; OR: Odds Ratio; PY: person years; RD: Risk Difference; RR: Risk Ratio; TEAE: Treatment-emergent Adverse Event.

TEAEs are AEs with a start date on or after the date of the first dose of study drug.

Treatment-related adverse events and follow-up were truncated at the maximum duration of follow-up in the ravulizumab arm.

Odds ratios were derived from a logistic regression model with treatment as the only covariate. Firth's correction was applied for odds ratios.

Mild, moderate and non-severe TEAEs were examined for preferred terms and system organ classes reported in at least 10% of patients in one of the treatment arms within the subgroup.

Severe and serious TEAEs were examined for preferred terms and system organ classes reported in at least 5% of patients in one of the treatment arms within the subgroup.

All TEAEs leading to withdrawal from study drug were examined.

TEAEs leading to withdrawal from study drug were examined descriptively (i.e., OR, RR, and RD not calculated).