Anhang 4-G

Zusätzliche Daten

Inebilizumab (UPLIZNA®)

Horizon Therapeutics GmbH

Modul 4A
Anhang 4-G

UPLIZNA als Monotherapie zur Behandlung von erwachsenen Patienten mit Neuromyelitis-optica-Spektrum-Erkrankungen (NMOSD), die Anti-Aquaporin-4-Immunglobulin-G(AQP4-IgG)-seropositiv sind

Stand: 15.07.2022

4 Anhang 4-G – Zusätzliche Daten

4.1 Kaplan-Meier-Kurven zu den Sensitivitätsanalysen des primären Endpunkts der Studie N-MOmentum der AQP4-IgG-seropositven Studienteilnehmer

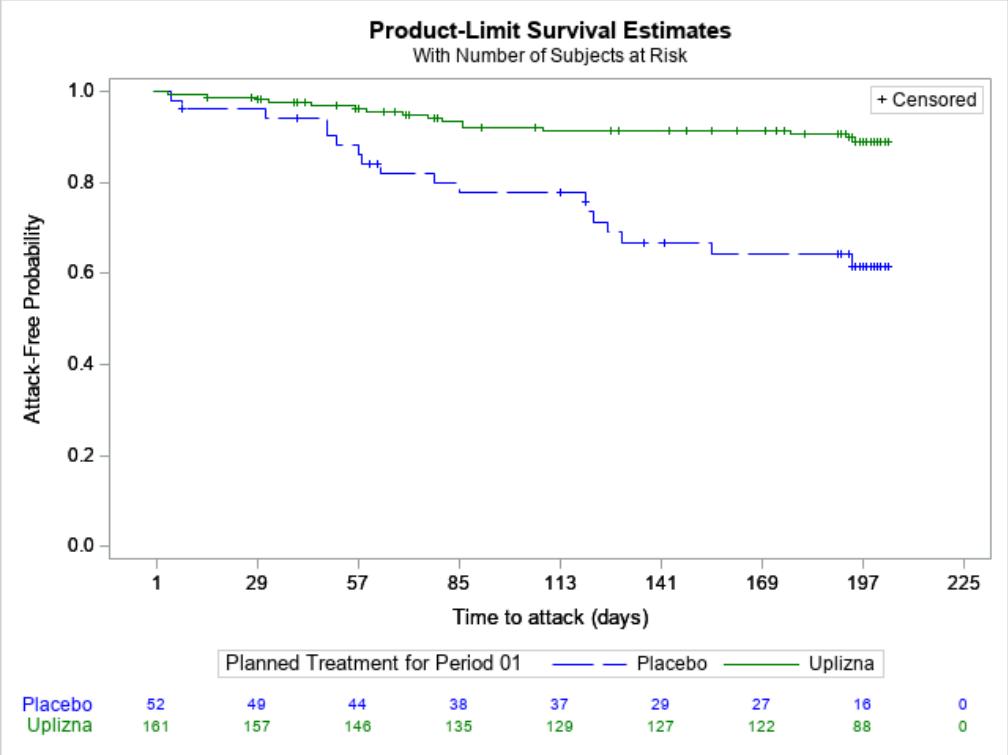

Abbildung 4-1: Sensitivitätsanalyse der Zeit bis zu einem durch das AC einstimmig bestätigten NMOSD-Schub (randomisiert-kontrollierte Phase) AQP4+-Population

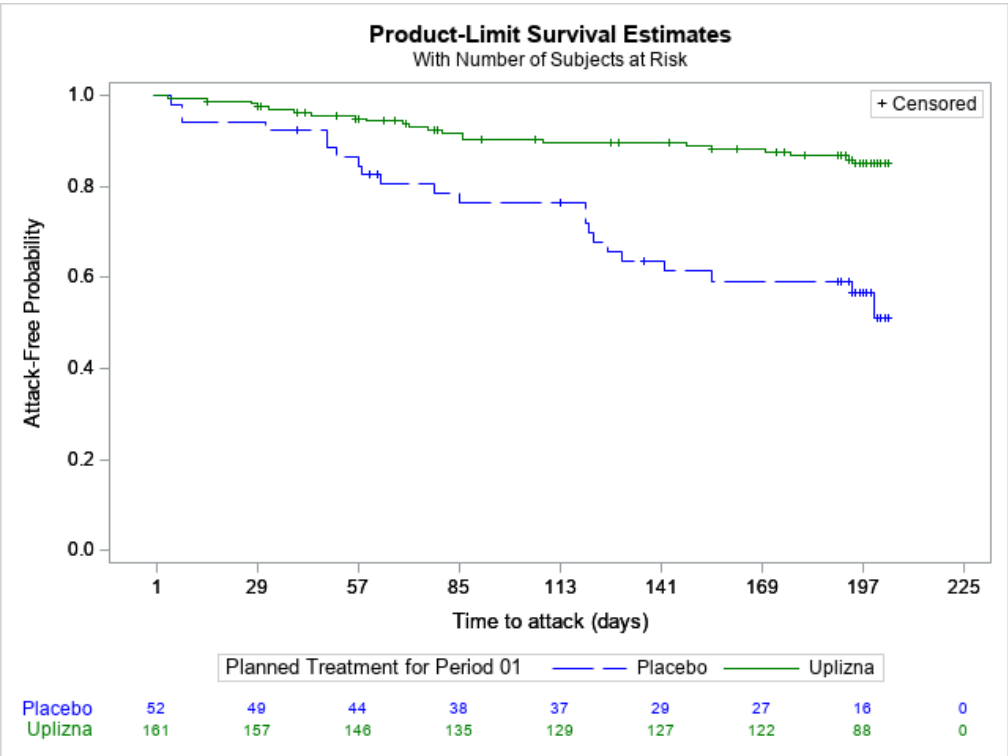

Abbildung 4-2: Sensitivitätsanalyse der Zeit bis einem AC-bestätigten NMOSD-Schub, einschließlich der Patienten, die den randomisiert-kontrollierte Phase vorzeitig abgebrochen haben, ohne einen NMOSD-Schub zu erleiden (randomisiert-kontrollierte Phase) AQP4+-Population

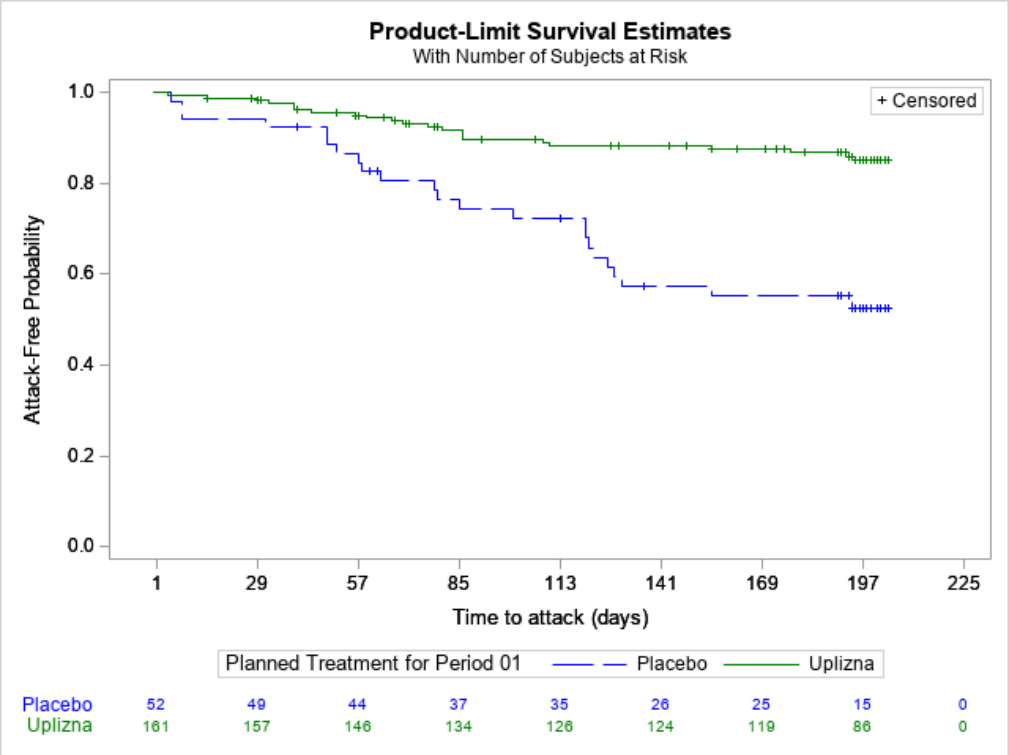

Abbildung 4-3: Sensitivitätsanalyse der Zeit bis einem AC-bestätigten NMOSD-Schub, einschließlich der Schübe aus der SFP bis zum Tag 204 bei Patienten, welche die randomisiert-kontrollierte Phase vorzeitig abgebrochen haben (randomisiert-kontrollierte Phase) AQP4+-Population

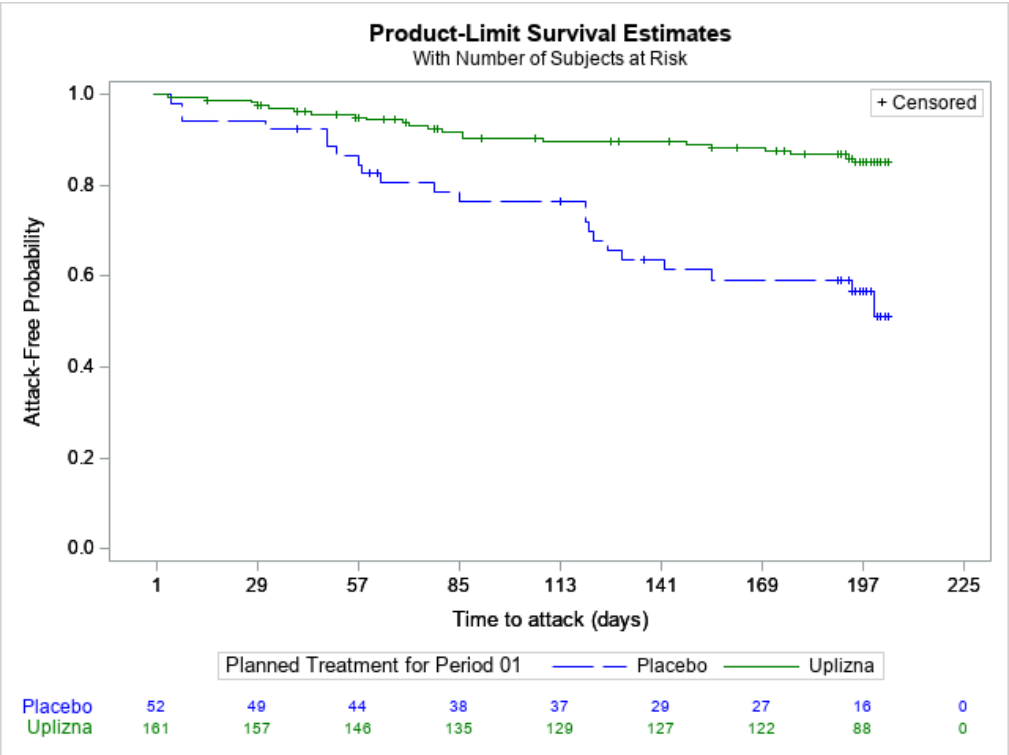

Abbildung 4-4: Sensitivitätsanalyse der Zeit bis einem AC-bestätigten NMOSD-Schub, basierend ausschließlich auf klinischen Kriterien (randomisiert-kontrollierte Phase) AQP4+-Population

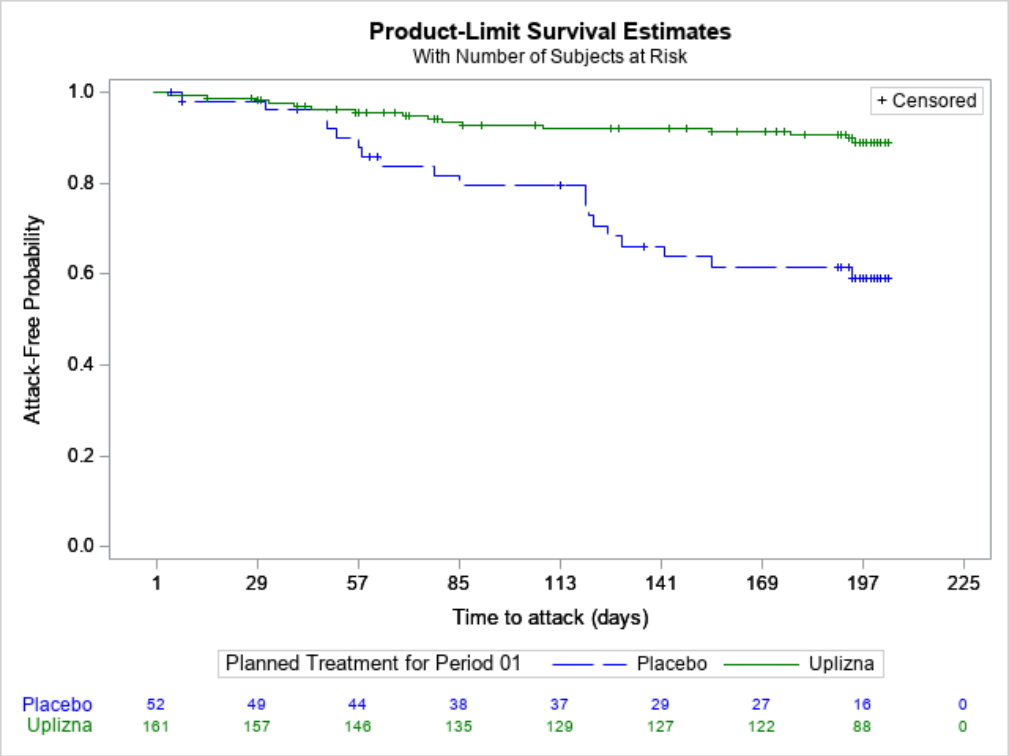

Abbildung 4-5: Sensitivitätsanalyse der Zeit bis zu entweder einem AC-bestätigten NMOSD-Schubs oder einer Rescue-Therapie (randomisiert-kontrollierte Phase) AQP4+-Population

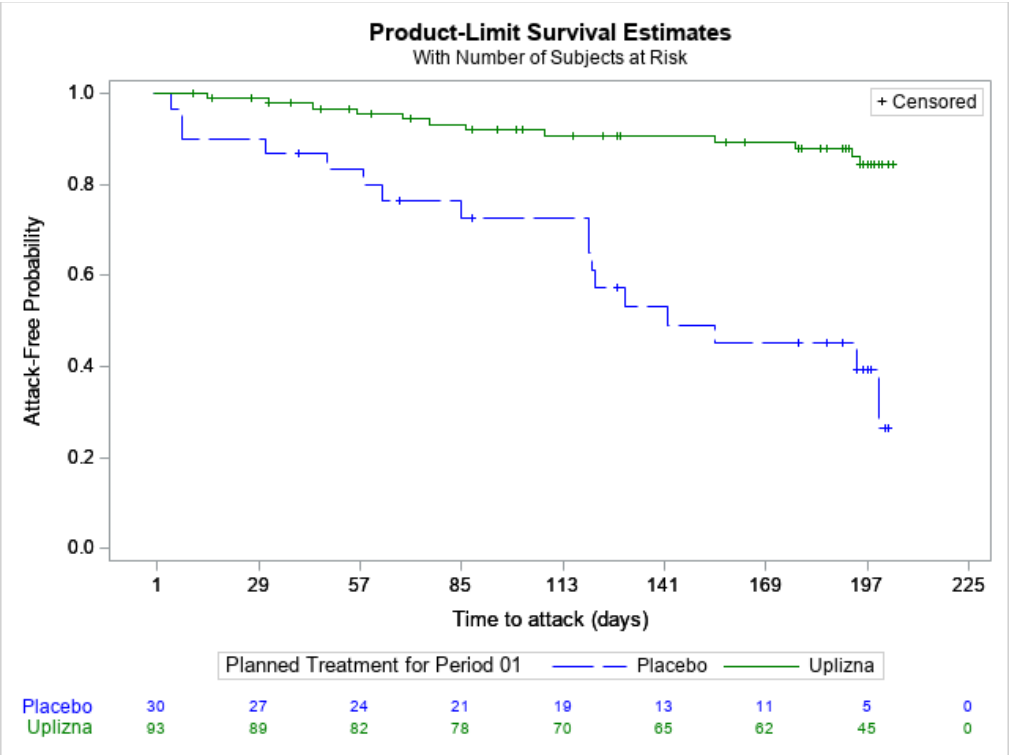

Abbildung 4-6: Sensitivitätsanalyse der Zeit bis zur Beurteilung der vom Patienten gemeldeten Symptome (randomisiert-kontrollierte Phase) AQP4+-Population

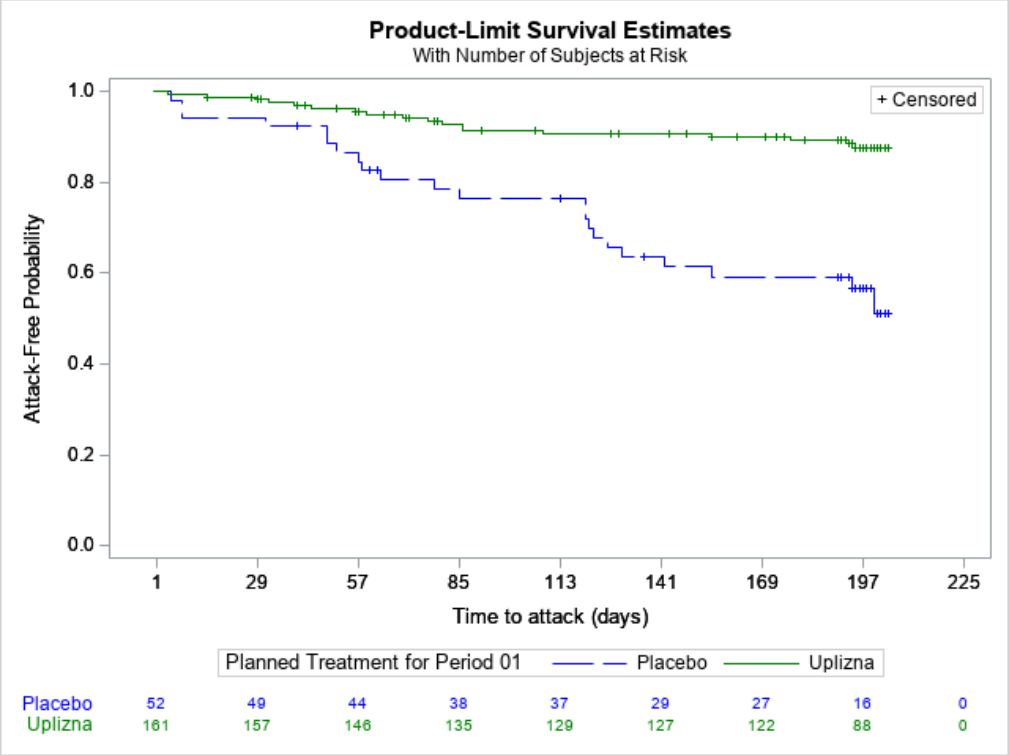

Abbildung 4-7: Sensitivitätsanalyse der Zeit bis einem AC-bestätigten NMOSD-Schub, Patienten mit AC-bestätigten Schüben vor oder an Tag 15 werden zum Zeitpunkt des Schubs zensiert (randomisiert-kontrollierte Phase) AQP4+-Population

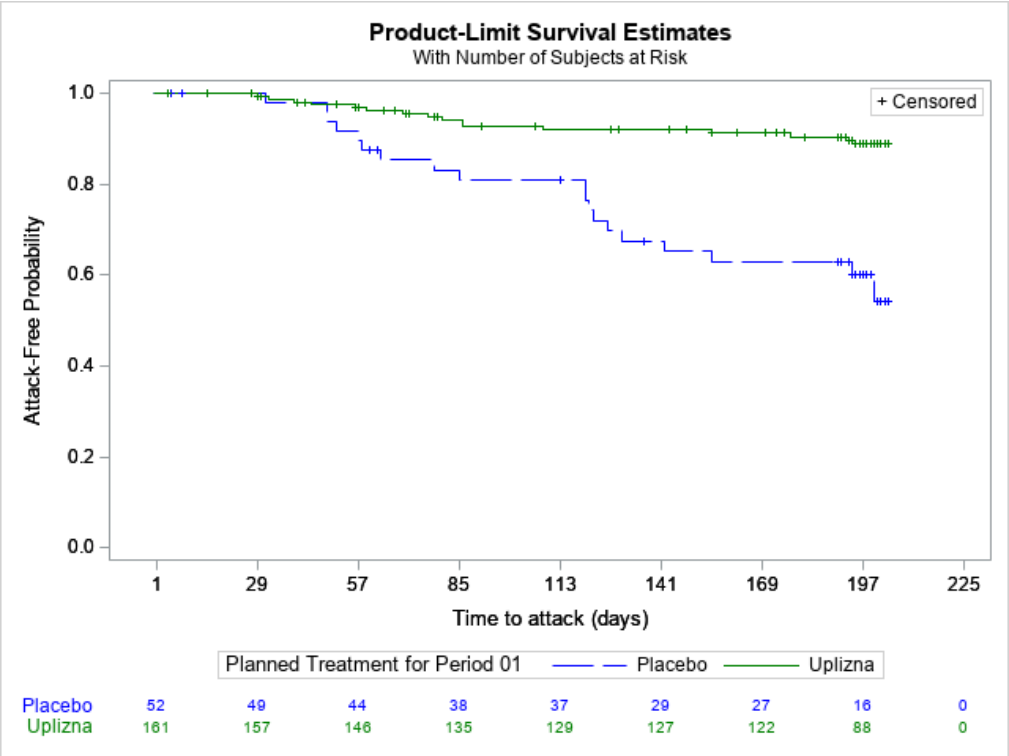

Abbildung 4-8: Sensitivitätsanalyse der Zeit bis einem AC-bestätigten NMOSD-Schub mit Daten bis einschließlich 27.01.2017 (randomisiert-kontrollierte Phase) AQP4+-Population

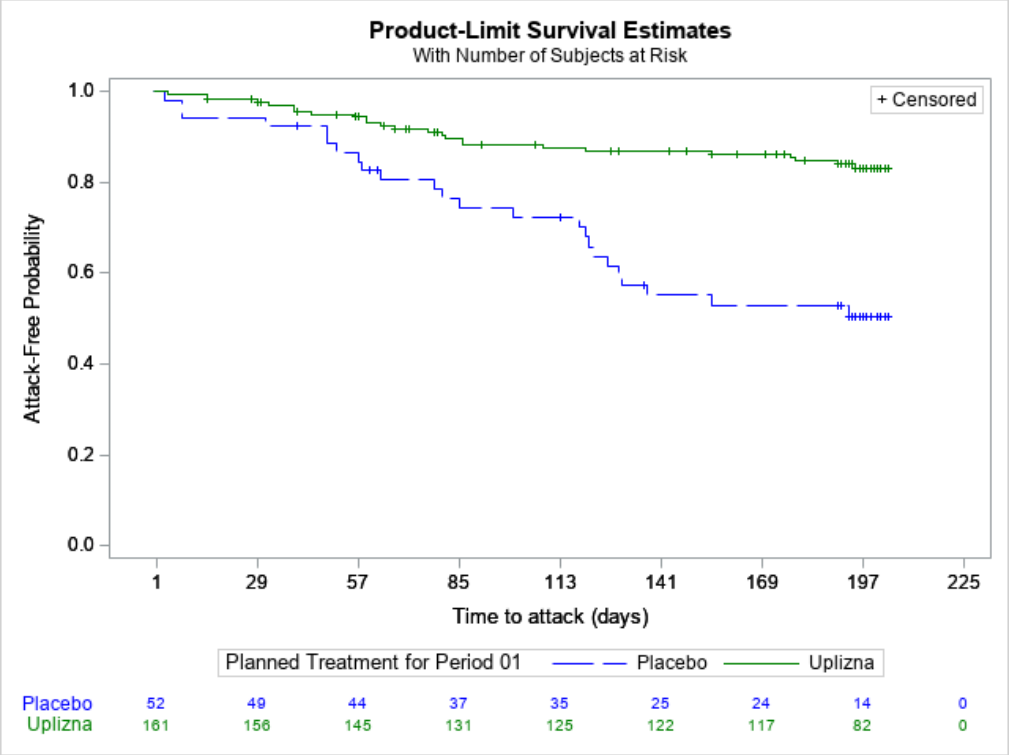

Abbildung 4-9: Sensitivitätsanalyse der Zeit bis einem Prüfarzt-bestätigten NMOSD-Schub (randomisiert-kontrollierte Phase) AQP4+-Population

4.2 Kaplan-Meier-Kurven zu den Time-to-event-Analysen des Endpunkts „Sicherheit und Verträglichkeit“

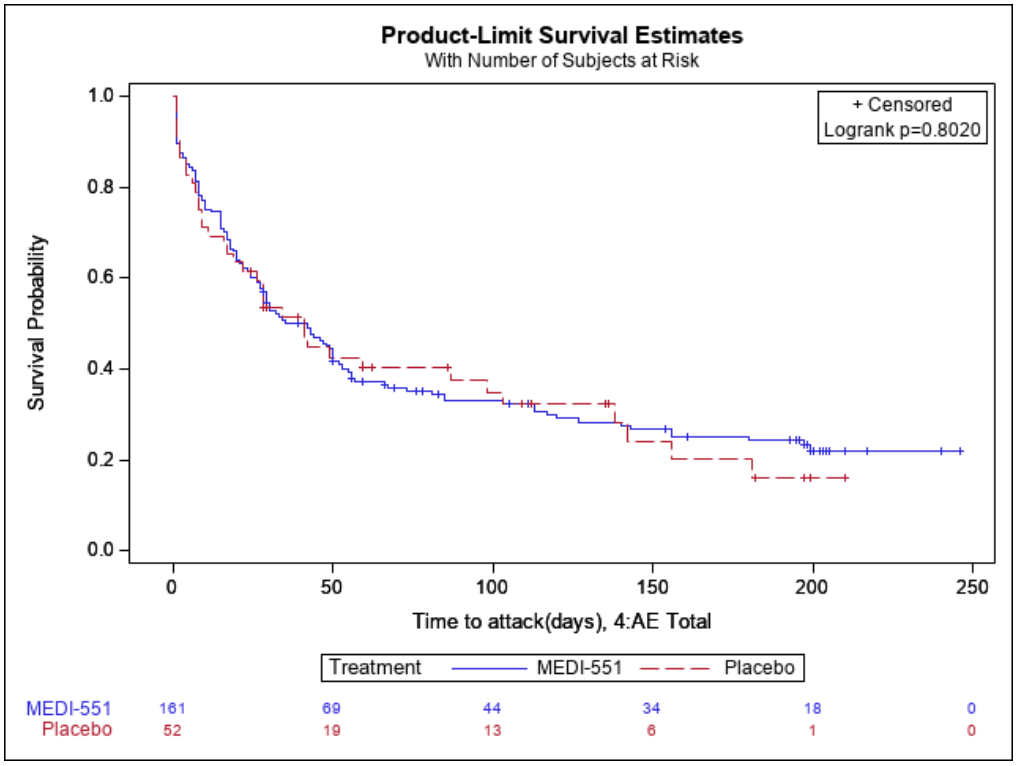

Abbildung 4-10: Zeit bis zum ersten Auftreten eines UEs (Gesamtrate) (randomisiert-kontrollierte Phase) AQP4+-Population

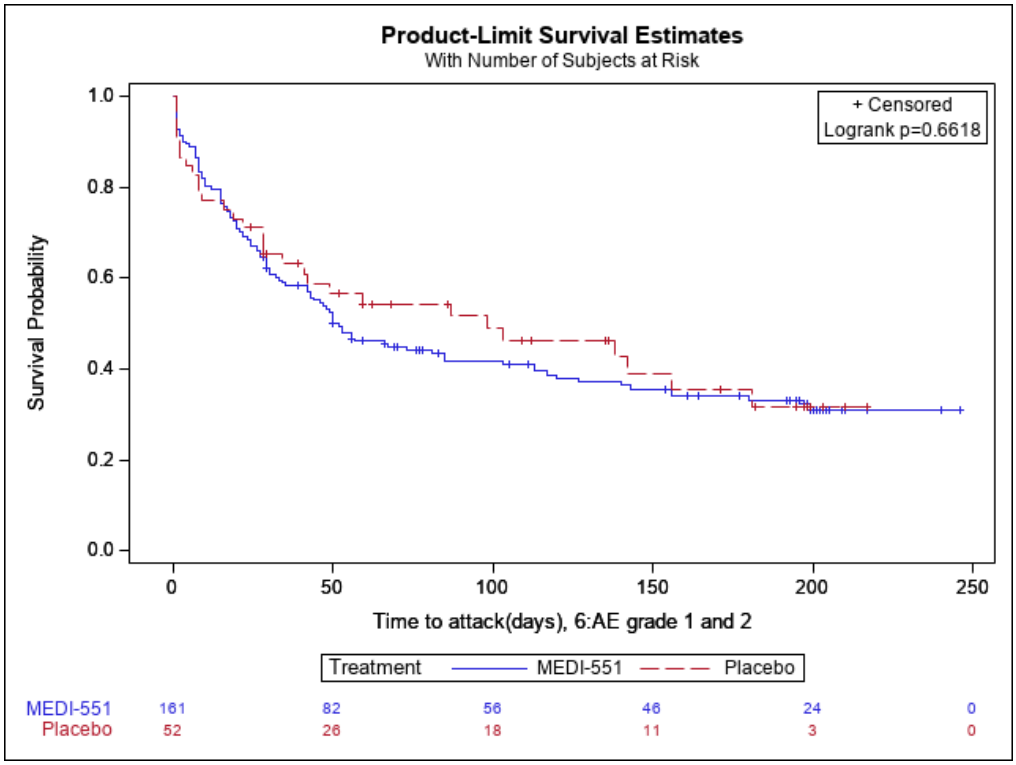

Abbildung 4-11: Zeit bis zum ersten Auftreten eines UEs Grad 1 & 2 (randomisiert-kontrollierte Phase) AQP4+-Population

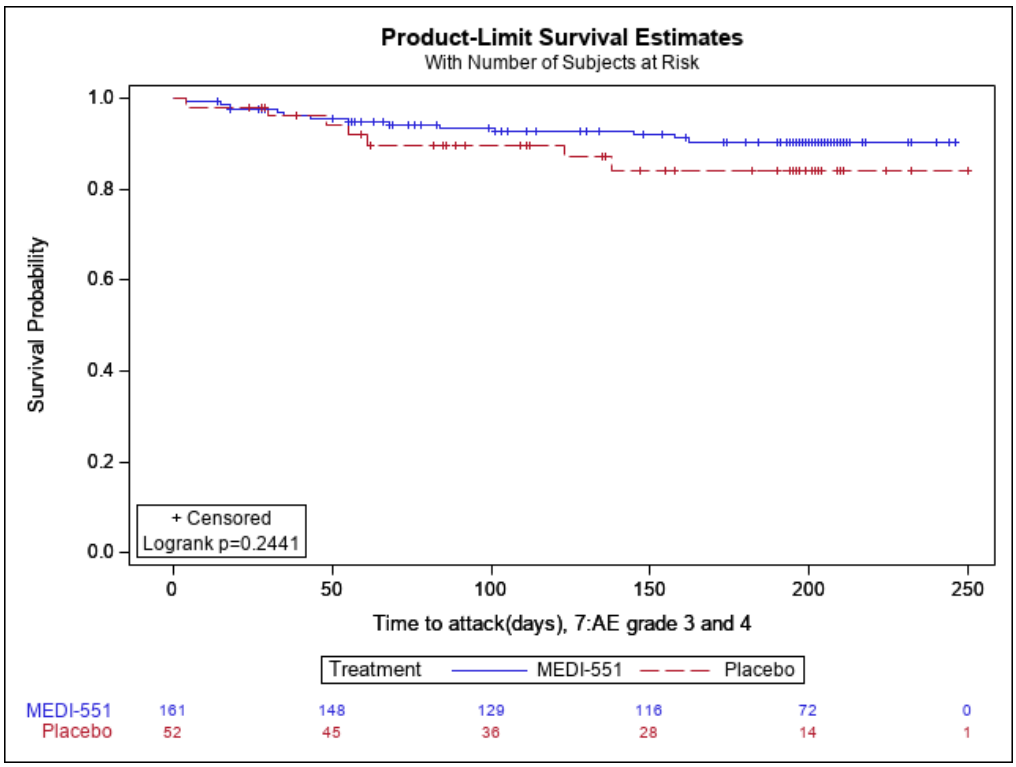

Abbildung 4-12: Zeit bis zum ersten Auftreten eines UEs Grad 3 & 4 (randomisiert-kontrollierte Phase) AQP4+-Population

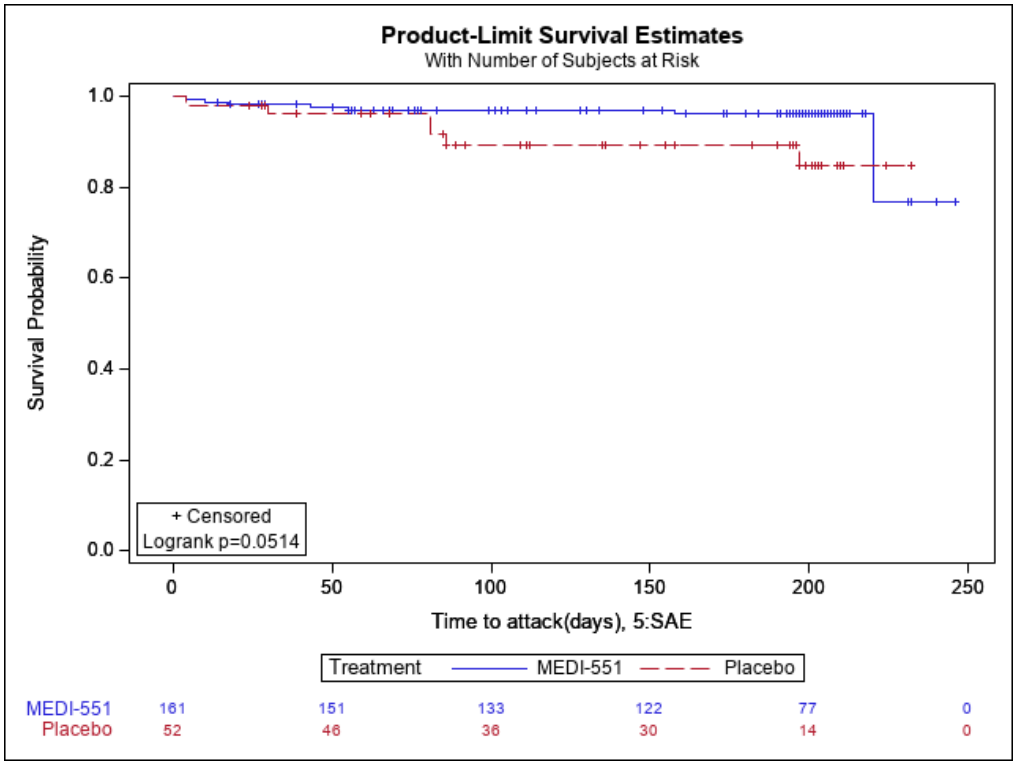

Abbildung 4-13: Zeit bis zum ersten Auftreten eines SUEs (randomisiert-kontrollierte Phase) AQP4+-Population

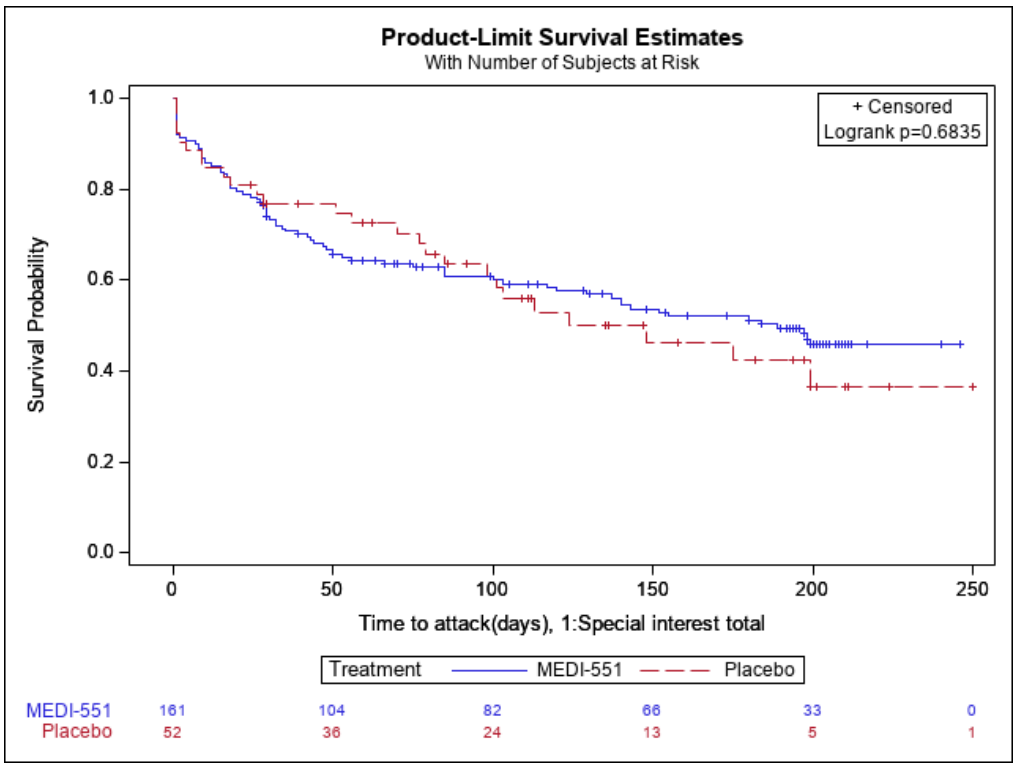

Abbildung 4-14: Zeit bis zum ersten Auftreten eines AESI (Gesamtrate) (randomisiert-kontrollierte Phase) AQP4+-Population

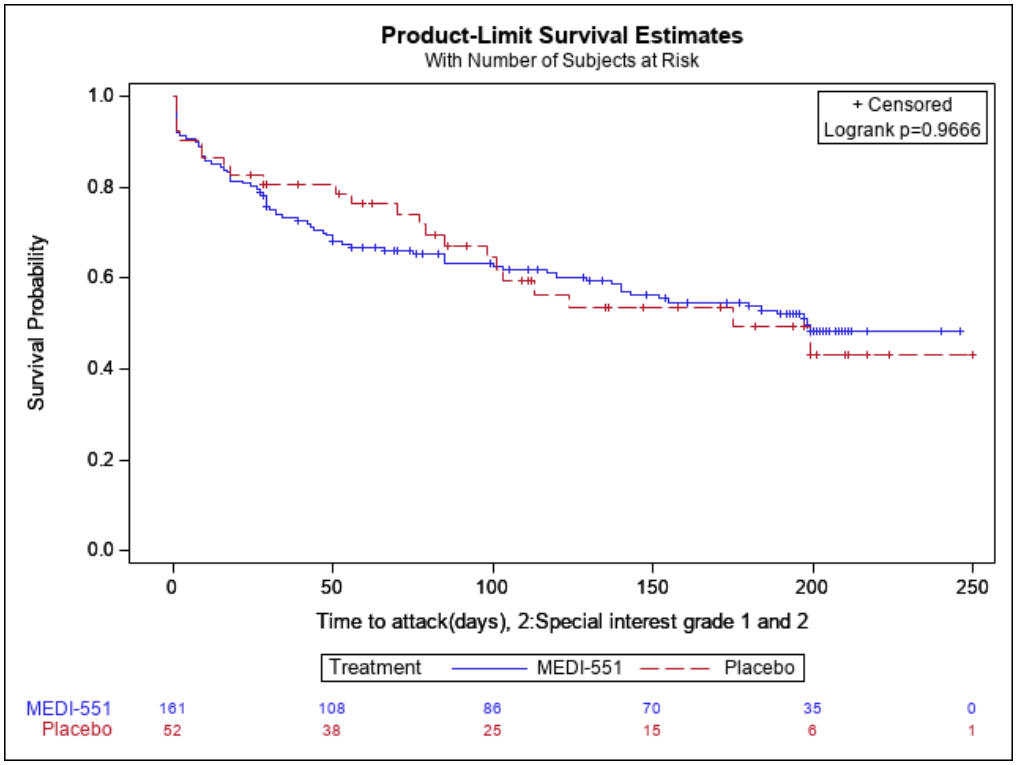

Abbildung 4-15: Zeit bis zum ersten Auftreten eines AESI Grad 1 & 2 (randomisiert-kontrollierte Phase) AQP4+-Population

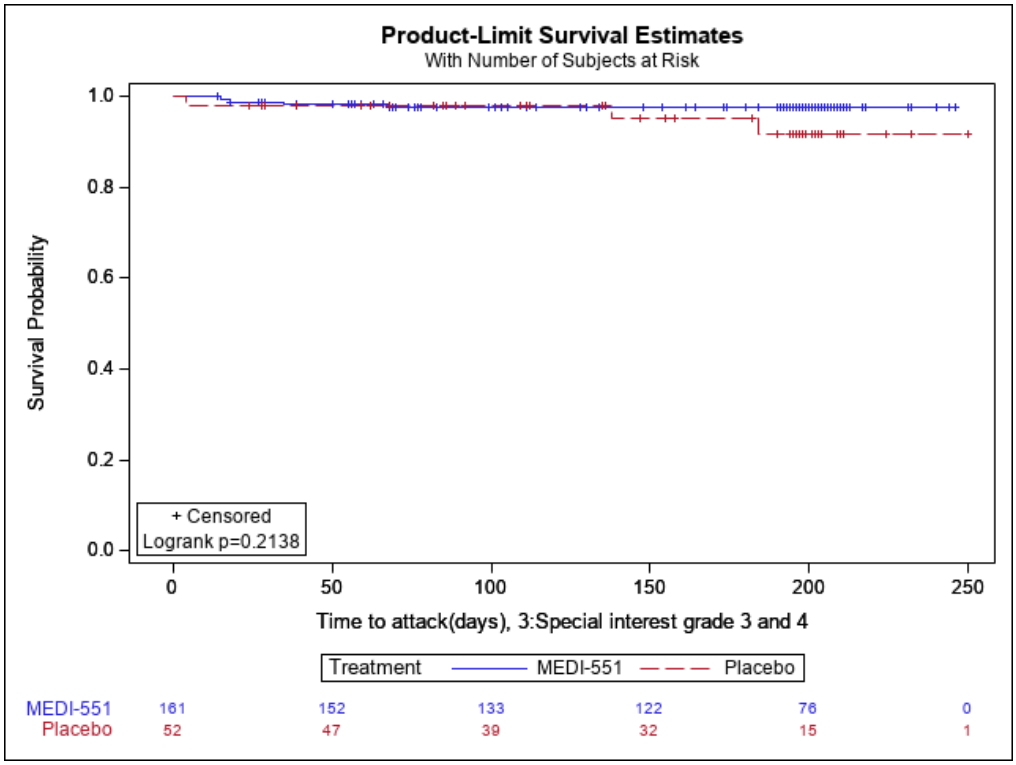

Abbildung 4-16: Zeit bis zum ersten Auftreten eines AESI Grad 3 & 4 (randomisiert-kontrollierte Phase) AQP4+-Population

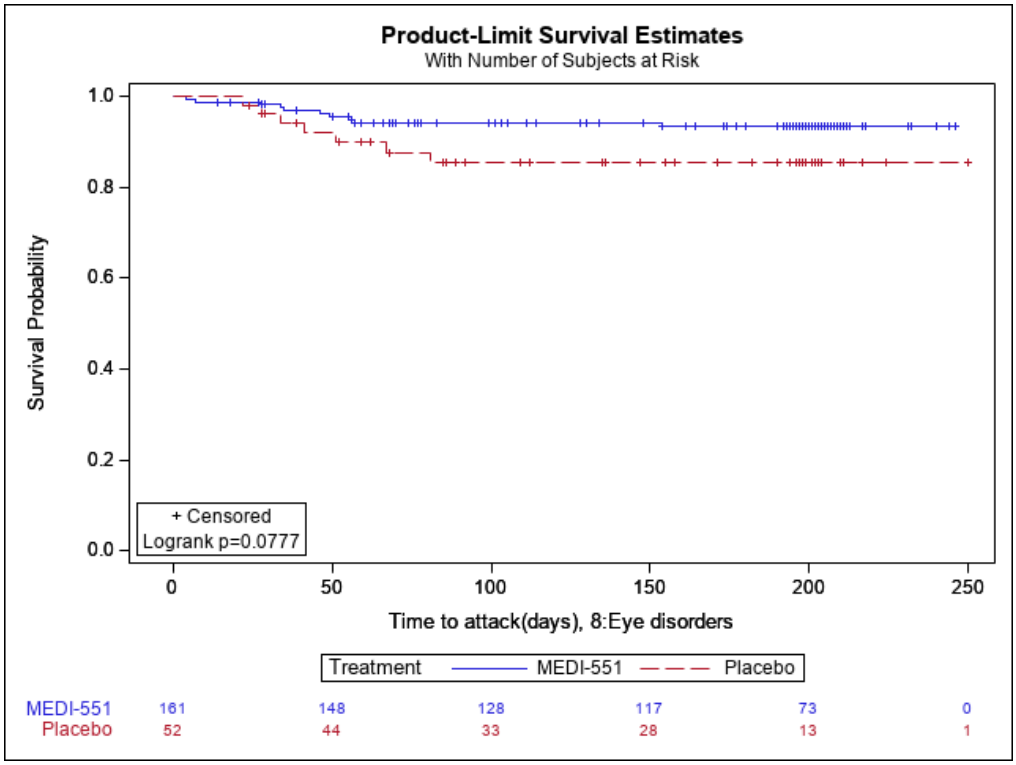

Abbildung 4-17: Zeit bis zum ersten Auftreten „Augenerkrankungen“ (randomisiert-kontrollierte Phase) AQP4+-Population

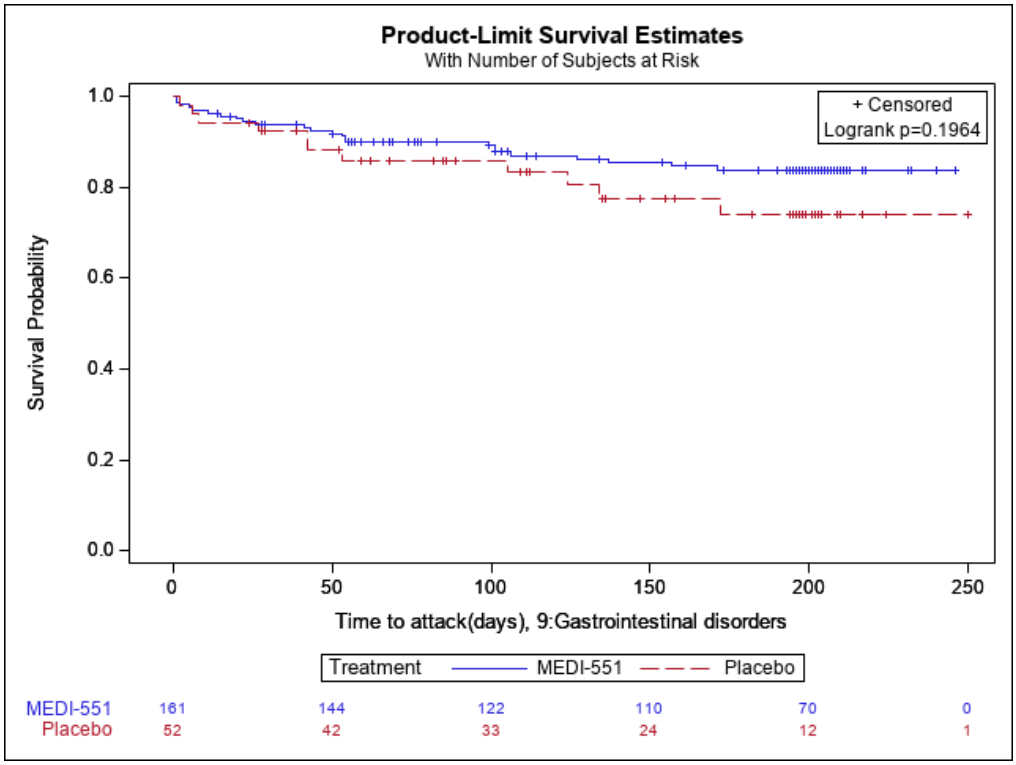

Abbildung 4-18: Zeit bis zum ersten Auftreten „Erkrankungen des Gastrointestinaltrakts“ (randomisiert-kontrollierte Phase) AQP4+-Population

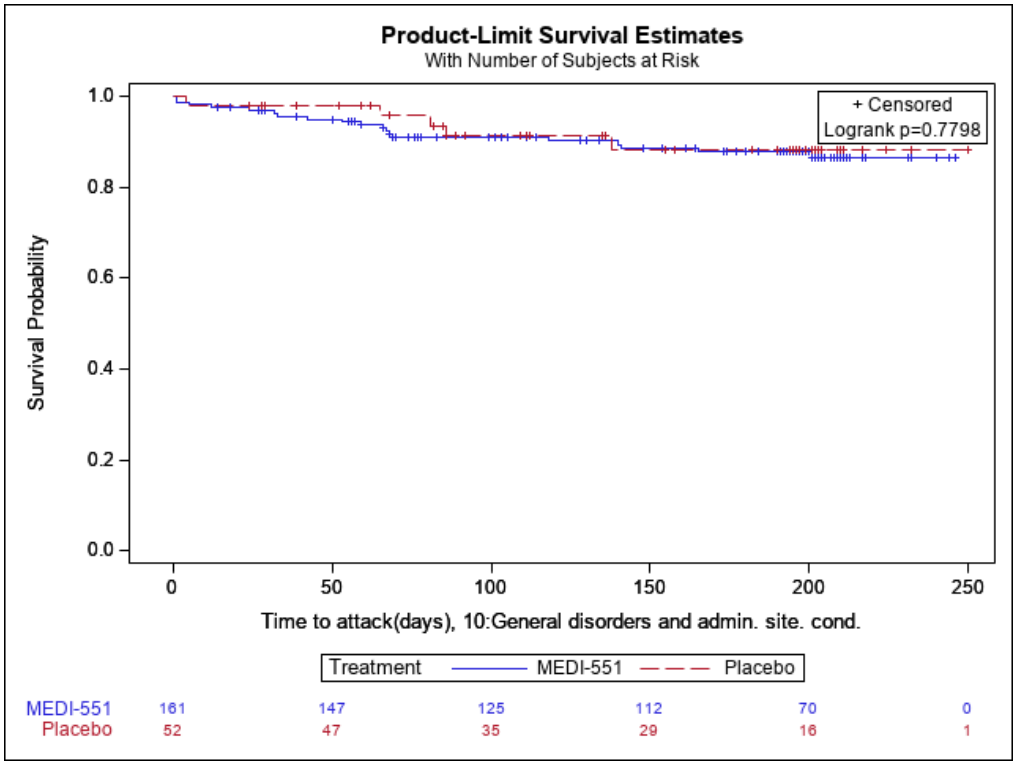

Abbildung 4-19: Zeit bis zum ersten Auftreten „Allgemeine Erkrankungen und Beschwerden am Verabreichungsort“ (randomisiert-kontrollierte Phase) AQP4+-Population

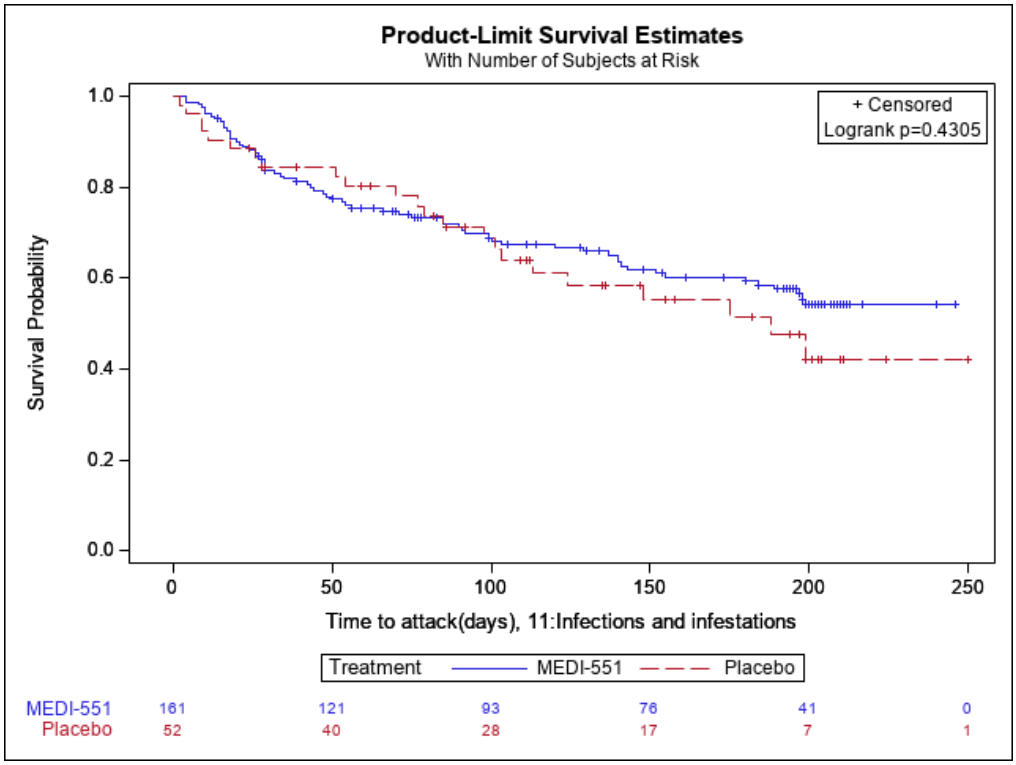

Abbildung 4-20: Zeit bis zum ersten Auftreten „Infektionen und parasitäre Erkrankungen“ (randomisiert-kontrollierte Phase) AQP4+-Population

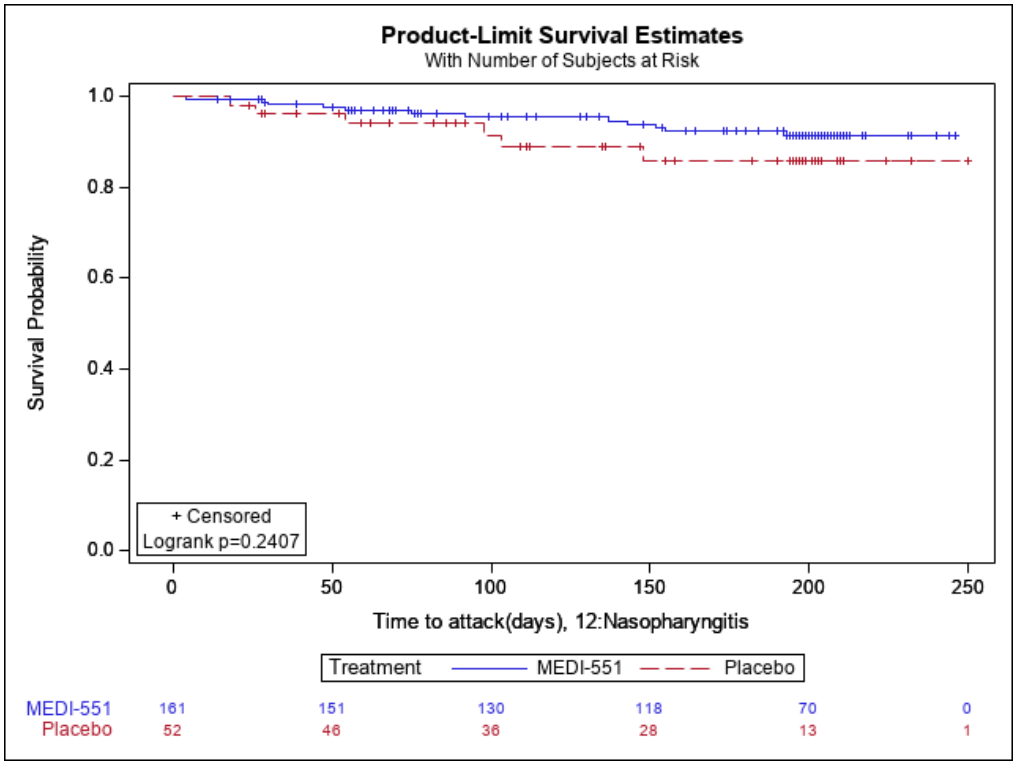

Abbildung 4-21: Zeit bis zum ersten Auftreten „Nasopharyngitis“ (randomisiert-kontrollierte Phase) AQP4+-Population

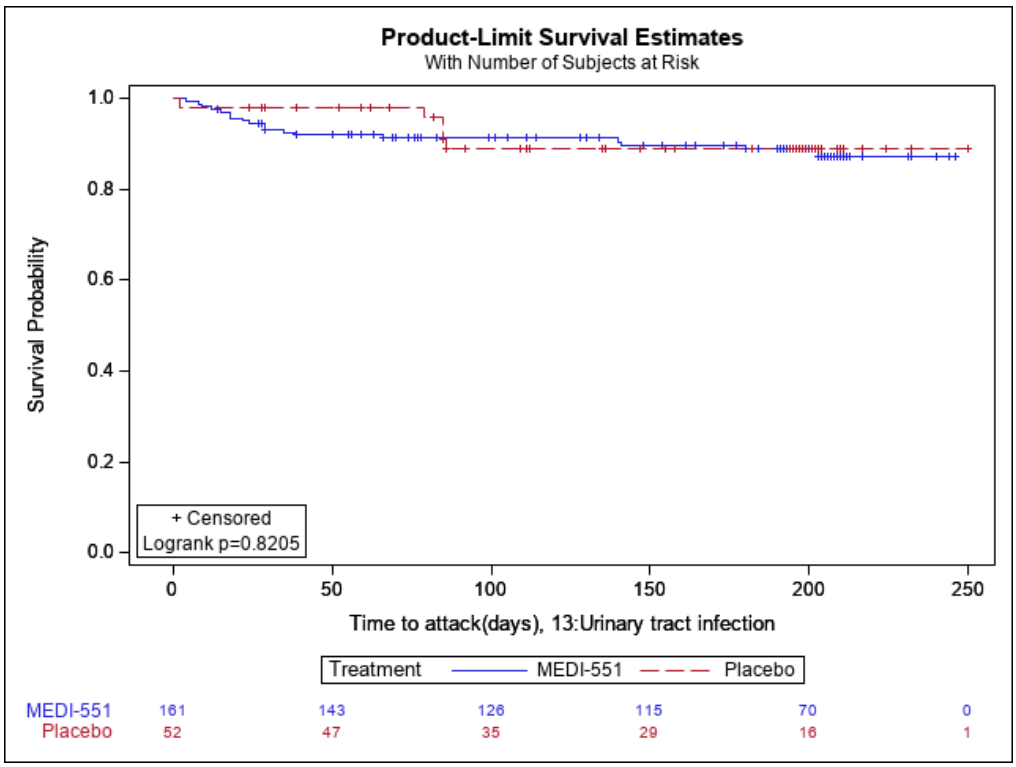

Abbildung 4-22: Zeit bis zum ersten Auftreten „Harnwegsinfektion“ (randomisiert-kontrollierte Phase) AQP4+-Population

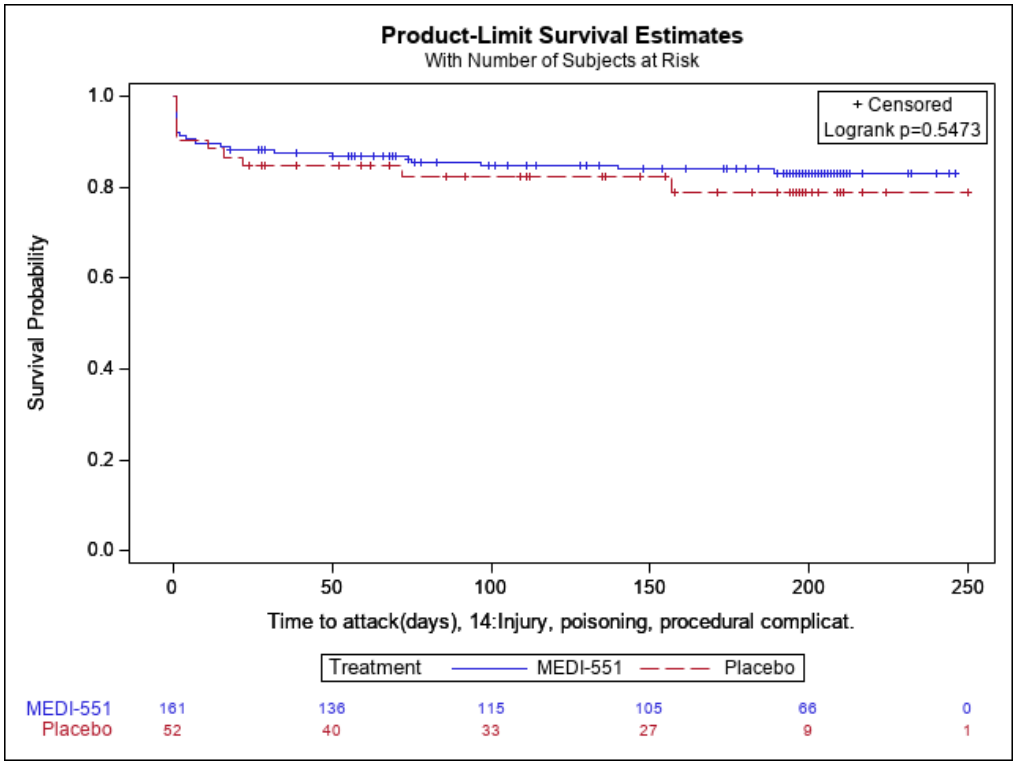

Abbildung 4-23: Zeit bis zum ersten Auftreten „Verletzung, Vergiftung und durch Eingriffe bedingte Komplikationen“ (randomisiert-kontrollierte Phase) AQP4+-Population

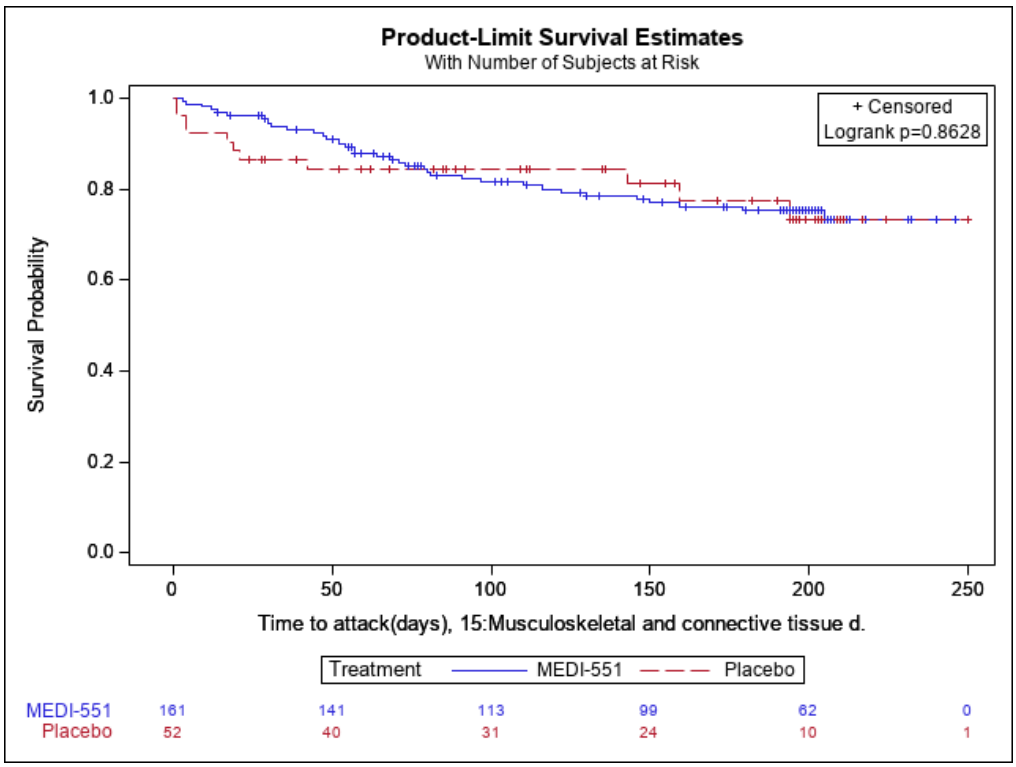

Abbildung 4-24: Zeit bis zum ersten Auftreten „Skelettmuskulatur-, Bindegewebs- und Knochenerkrankungen“ (randomisiert-kontrollierte Phase) AQP4+-Population

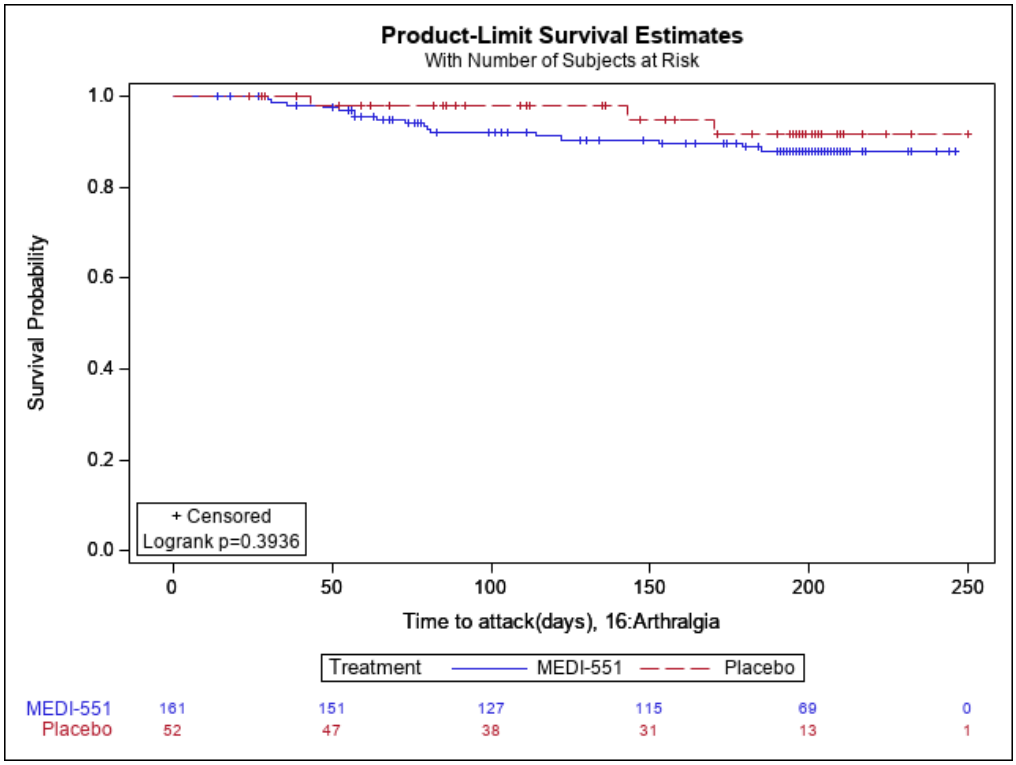

Abbildung 4-25: Zeit bis zum ersten Auftreten „Arthralgie“ (randomisiert-kontrollierte Phase) AQP4+-Population

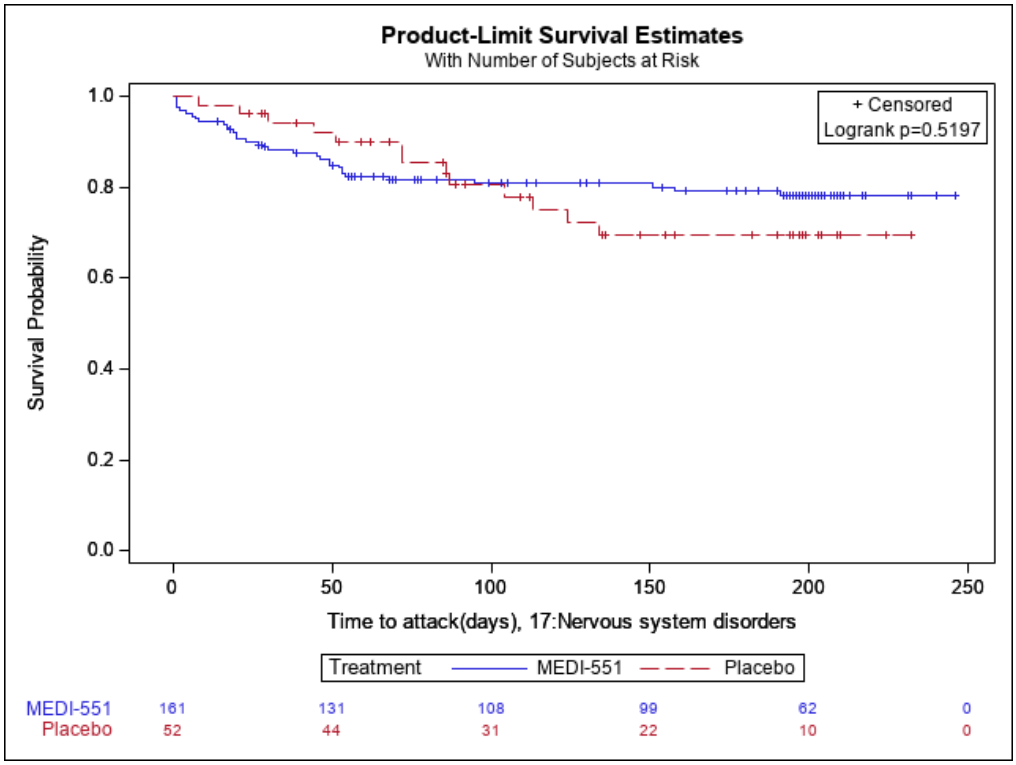

Abbildung 4-26: Zeit bis zum ersten Auftreten „Erkrankungen des Nervensystems“ (randomisiert-kontrollierte Phase) AQP4+-Population

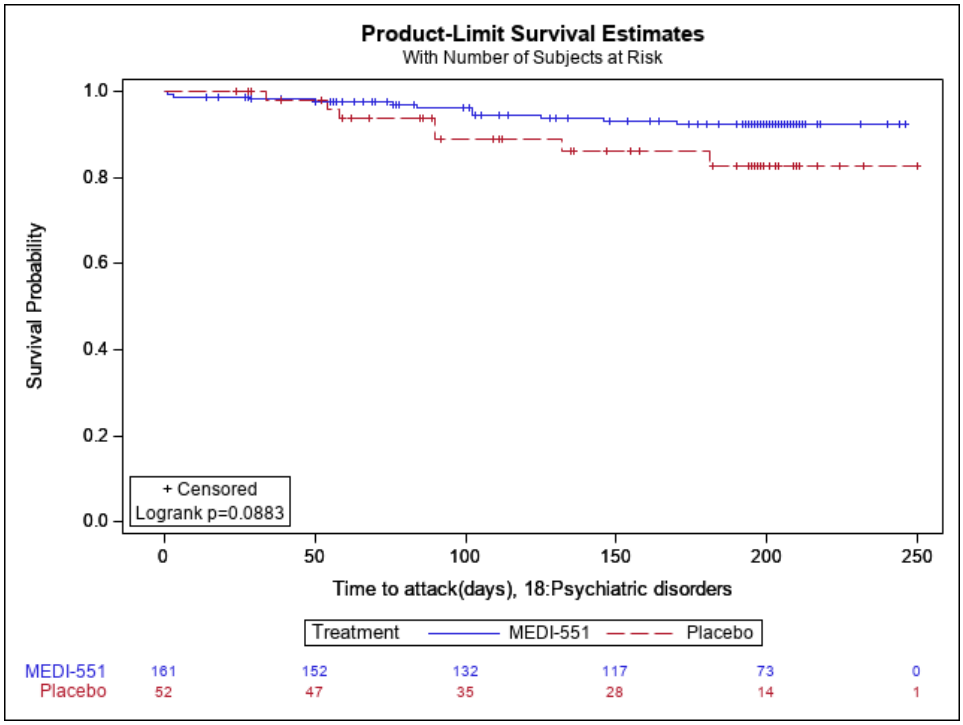

Abbildung 4-27: Zeit bis zum ersten Auftreten „Psychiatrische Erkrankungen“ (randomisiert-kontrollierte Phase) AQP4+-Population

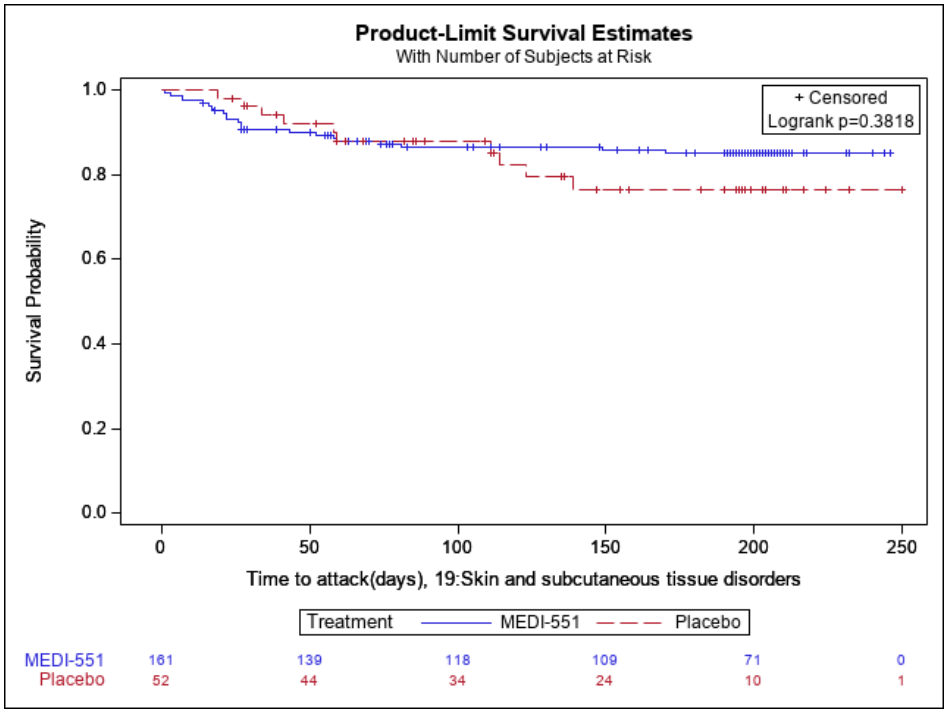

Abbildung 4-28: Zeit bis zum ersten Auftreten „Erkrankungen der Haut und des Unterhautzellgewebes“ (randomisiert-kontrollierte Phase) AQP4+-Population

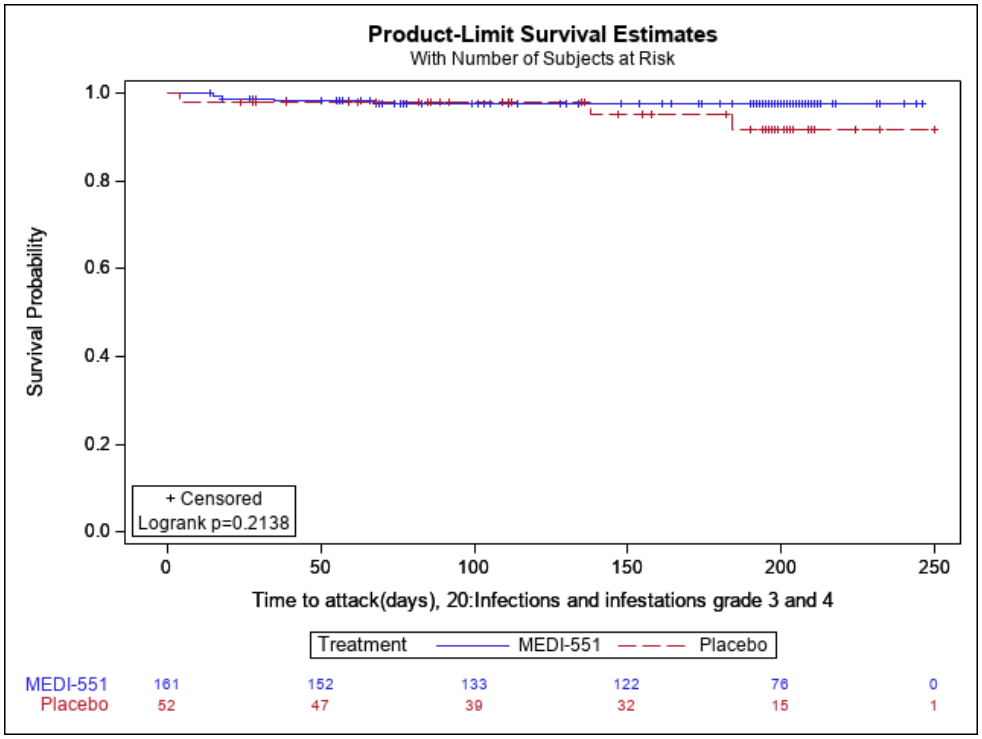

Abbildung 4-29: Zeit bis zum ersten Auftreten „Schwerwiegende Infektionen und parasitäre Erkrankungen“ (randomisiert-kontrollierte Phase) AQP4+-Population

4.3 Subgruppenanalysen

MedImmune
MEDI551-CD1155
CSR, DB lock 18Dec2020

Table 1.1

Subgroup Analysis of Time to Adjudication Committee (AC) - determined NMO Attacks (Randomized-controlled Period)
AQP4-IgG sero+ Subjects in the
Intent-to-treat Population

Subgroup			Placebo N = 52	MEDI551 N = 161
Age	< 65 years	Number of subjects with an attack	21/48 (43.8%)	16/155 (10.3%)
		Number of censored subjects	27/48 (56.3%)	139/155 (89.7%)
		Median time to attack[a]	200.000	NA
		95% CI[a]	(122.000, NA)	(NA, NA)
		Hazard ratio[b]		0.199
		95% CI[b]		(0.104 , 0.382)
		p-value[b]		<0.0001
	>= 65 years	Number of subjects with an attack	1/4 (25.0%)	2/6 (33.3%)
		Number of censored subjects	3/4 (75.0%)	4/6 (66.7%)
		Median time to attack[a]	NA	NA
		95% CI[a]	(126.000, NA)	(15.000, NA)
		Hazard ratio[b]		1.371
		95% CI[b]		(0.124 , 15.179)
		p-value[b]		0.7969
	Interaction with treatment	p-value[b]		0.1173

[a] Based on Kaplan-Meier method.
[b] Based on Cox regression method, with Placebo as the reference group.

Table 1.2

Subgroup Analysis of Time to Adjudication Committee (AC) - determined NMO Attacks (Randomized-controlled Period) AQP4-IgG seropositive in the Intent-to-treat Population

Subgroup			Placebo N = 52	MEDI551 N = 161
Age	< 45	Number of subjects with an attack	14/27 (51.9%)	9/84 (10.7%)
		Number of censored subjects	13/27 (48.1%)	75/84 (89.3%)
		Median time to attack[a]	142	NA
		95% CI[a]	(85, NA)	(NA, NA)
		Hazard ratio[b]		0.172
		95% CI[b]		(0.074 , 0.399)
		p-value[b]		<0.0001
	≥ 45	Number of subjects with an attack	8/25 (32.0%)	9/77 (11.7%)
		Number of censored subjects	17/25 (68.0%)	68/77 (88.3%)
		Median time to attack[a]	NA	NA
		95% CI[a]	(155, NA)	(NA, NA)
		Hazard ratio[b]		0.338
		95% CI[b]		(0.130 , 0.878)
		p-value[b]		0.0259
	Interaction with treatment	p-value[b]		0.2497

[a] Based on Kaplan-Meier method.
[b] Based on Cox regression method, with Placebo as the reference group.

Table 1.3

Subgroup Analysis of Time to Adjudication Committee (AC) - determined NMO Attacks (Randomized-controlled Period)
AQP4-IgG sero+ Subjects in the
Intent-to-treat Population

Subgroup			Placebo N = 52	MEDI551 N = 161
Sex	Male	Number of subjects with an attack	2/3 (66.7%)	2/10 (20.0%)
		Number of censored subjects	1/3 (33.3%)	8/10 (80.0%)
		Median time to attack[a]	48.000	NA
		95% CI[a]	(31.000, NA)	(86.000, NA)
		Hazard ratio[b]		0.160
		95% CI[b]		(0.022 , 1.195)
		p-value[b]		0.0741
	Female	Number of subjects with an attack	20/49 (40.8%)	16/151 (10.6%)
		Number of censored subjects	29/49 (59.2%)	135/151 (89.4%)
		Median time to attack[a]	NA	NA
		95% CI[a]	(130.000, NA)	(NA, NA)
		Hazard ratio[b]		0.225
		95% CI[b]		(0.116 , 0.435)
		p-value[b]		<0.0001
	Interaction with treatment	p-value[b]		0.8035

[a] Based on Kaplan-Meier method.
[b] Based on Cox regression method, with Placebo as the reference group.

Table 1.4

Subgroup Analysis of Time to Adjudication Committee (AC) - determined NMO Attacks (Randomized-controlled Period)
AQP4-IgG sero+ Subjects in the
Intent-to-treat Population

Subgroup			Placebo N = 52	MEDI551 N = 161
Baseline EDSS	< 5	Number of subjects with an attack	14/35 (40.0%)	10/120 (8.3%)
		Number of censored subjects	21/35 (60.0%)	110/120 (91.7%)
		Median time to attack[a]	NA	NA
		95% CI[a]	(142.000, NA)	(NA, NA)
		Hazard ratio[b]		0.178
		95% CI[b]		(0.079 , 0.402)
		p-value[b]		<0.0001
	≥ 5	Number of subjects with an attack	8/17 (47.1%)	8/41 (19.5%)
		Number of censored subjects	9/17 (52.9%)	33/41 (80.5%)
		Median time to attack[a]	NA	NA
		95% CI[a]	(85.000, NA)	(NA, NA)
		Hazard ratio[b]		0.367
		95% CI[b]		(0.137 , 0.981)
		p-value[b]		0.0456
	Interaction with treatment	p-value[b]		0.2573

[a] Based on Kaplan-Meier method.
[b] Based on Cox regression method, with Placebo as the reference group.

Table 1.5

Subgroup Analysis of Time to Adjudication Committee (AC) - determined NMO Attacks (Randomized-controlled Period)
AQP4-IgG sero+ Subjects in the
Intent-to-treat Population

Subgroup			Placebo N = 52	MEDI551 N = 161
No. of prior NMO/NMOSD relapses	< 2	Number of subjects with an attack	3/13 (23.1%)	1/24 (4.2%)
		Number of censored subjects	10/13 (76.9%)	23/24 (95.8%)
		Median time to attack[a]	NA	NA
		95% CI[a]	(122.000, NA)	(NA, NA)
		Hazard ratio[b]		0.160
		95% CI[b]		(0.017 , 1.542)
		p-value[b]		0.1130
	≥ 2	Number of subjects with an attack	19/39 (48.7%)	17/137 (12.4%)
		Number of censored subjects	20/39 (51.3%)	120/137 (87.6%)
		Median time to attack[a]	200.000	NA
		95% CI[a]	(120.000, NA)	(NA, NA)
		Hazard ratio[b]		0.212
		95% CI[b]		(0.110 , 0.408)
		p-value[b]		<0.0001
	Interaction with treatment	p-value[b]		0.8490

[a] Based on Kaplan-Meier method.
[b] Based on Cox regression method, with Placebo as the reference group.

Table 1.6

Subgroup Analysis of Time to Adjudication Committee (AC) - determined NMO Attacks (Randomized-controlled Period)
AQP4-IgG sero+ Subjects in the
Intent-to-treat Population

Subgroup			Placebo N = 52	MEDI551 N = 161
Disease duration category (year)	< 5	Number of subjects with an attack	15/42 (35.7%)	13/132 (9.8%)
		Number of censored subjects	27/42 (64.3%)	119/132 (90.2%)
		Median time to attack[a]	NA	NA
		95% CI[a]	(155.000, NA)	(NA, NA)
		Hazard ratio[b]		0.244
		95% CI[b]		(0.116 , 0.513)
		p-value[b]		0.0002
	≥ 5	Number of subjects with an attack	7/10 (70.0%)	5/29 (17.2%)
		Number of censored subjects	3/10 (30.0%)	24/29 (82.8%)
		Median time to attack[a]	128.000	NA
		95% CI[a]	(8.000, NA)	(NA, NA)
		Hazard ratio[b]		0.193
		95% CI[b]		(0.060 , 0.619)
		p-value[b]		0.0056
	Interaction with treatment	p-value[b]		0.7421

[a] Based on Kaplan-Meier method.
[b] Based on Cox regression method, with Placebo as the reference group.

Table 1.7

Subgroup Analysis of Time to Adjudication Committee (AC) - determined NMO Attacks (Randomized-controlled Period)
AQP4-IgG sero+ Subjects in the
Intent-to-treat Population

Subgroup			Placebo N = 52	MEDI551 N = 161
Region 1	US	Number of subjects with an attack	3/11 (27.3%)	2/27 (7.4%)
		Number of censored subjects	8/11 (72.7%)	25/27 (92.6%)
		Median time to attack[a]	NA	NA
		95% CI[a]	(63.000, NA)	(NA, NA)
		Hazard ratio[b]		0.226
		95% CI[b]		(0.038 , 1.360)
		p-value[b]		0.1045
	Non-US	Number of subjects with an attack	19/41 (46.3%)	16/134 (11.9%)
		Number of censored subjects	22/41 (53.7%)	118/134 (88.1%)
		Median time to attack[a]	200.000	NA
		95% CI[a]	(121.000, NA)	(NA, NA)
		Hazard ratio[b]		0.224
		95% CI[b]		(0.115 , 0.435)
		p-value[b]		<0.0001
	Interaction with treatment	p-value[b]		0.9911

[a] Based on Kaplan-Meier method.
[b] Based on Cox regression method, with Placebo as the reference group.

Table 1.8

Subgroup Analysis of Time to Adjudication Committee (AC) - determined NMO Attacks (Randomized-controlled Period)
AQP4-IgG sero+ Subjects in the
Intent-to-treat Population

Subgroup			Placebo N = 52	MEDI551 N = 161
Region 2	EU	Number of subjects with an attack	3/10 (30.0%)	5/40 (12.5%)
		Number of censored subjects	7/10 (70.0%)	35/40 (87.5%)
		Median time to attack[a]	NA	NA
		95% CI[a]	(31.000, NA)	(NA, NA)
		Hazard ratio[b]		0.361
		95% CI[b]		(0.086 , 1.516)
		p-value[b]		0.1640
	Non-EU	Number of subjects with an attack	19/42 (45.2%)	13/121 (10.7%)
		Number of censored subjects	23/42 (54.8%)	108/121 (89.3%)
		Median time to attack[a]	200.000	NA
		95% CI[a]	(122.000, NA)	(NA, NA)
		Hazard ratio[b]		0.205
		95% CI[b]		(0.101 , 0.416)
		p-value[b]		<0.0001
	Interaction with treatment	p-value[b]		0.5288

[a] Based on Kaplan-Meier method.
[b] Based on Cox regression method, with Placebo as the reference group.

Table 1.9

Subgroup Analysis of Time to Adjudication Committee (AC) - determined NMO Attacks (Randomized-controlled Period)
AQP4-IgG sero+ Subjects in the
Intent-to-treat Population

Subgroup			Placebo N = 52	MEDI551 N = 161
Race	American Indian or Alaskan Native	Number of subjects with an attack	2/5 (40.0%)	3/11 (27.3%)
		Number of censored subjects	3/5 (60.0%)	8/11 (72.7%)
		Median time to attack[a]	NA	NA
		95% CI[a]	(8.000, NA)	(80.000, NA)
		Hazard ratio[b]		0.532
		95% CI[b]		(0.088 , 3.213)
		p-value[b]		0.4919
	Asian	Number of subjects with an attack	5/8 (62.5%)	6/37 (16.2%)
		Number of censored subjects	3/8 (37.5%)	31/37 (83.8%)
		Median time to attack[a]	125.000	NA
		95% CI[a]	(8.000, NA)	(NA, NA)
		Hazard ratio[b]		0.198
		95% CI[b]		(0.060 , 0.653)
		p-value[b]		0.0078

[a] Based on Kaplan-Meier method.
[b] Based on Cox regression method, with Placebo as the reference group.

Table 1.9

Subgroup Analysis of Time to Adjudication Committee (AC) - determined NMO Attacks (Randomized-controlled Period)
AQP4-IgG sero+ Subjects in the
Intent-to-treat Population

Subgroup			Placebo N = 52	MEDI551 N = 161
Race	Black or African American	Number of subjects with an attack	1/5 (20.0%)	1/14 (7.1%)
		Number of censored subjects	4/5 (80.0%)	13/14 (92.9%)
		Median time to attack[a]	NA	NA
		95% CI[a]	(121.000, NA)	(NA, NA)
		Hazard ratio[b]		0.331
		95% CI[b]		(0.021 , 5.310)
		p-value[b]		0.4353
	White	Number of subjects with an attack	10/24 (41.7%)	8/86 (9.3%)
		Number of censored subjects	14/24 (58.3%)	78/86 (90.7%)
		Median time to attack[a]	NA	NA
		95% CI[a]	(120.000, NA)	(NA, NA)
		Hazard ratio[b]		0.189
		95% CI[b]		(0.074 , 0.480)
		p-value[b]		0.0005

[a] Based on Kaplan-Meier method.
[b] Based on Cox regression method, with Placebo as the reference group.

Table 1.9

Subgroup Analysis of Time to Adjudication Committee (AC) - determined NMO Attacks (Randomized-controlled Period)
AQP4-IgG sero+ Subjects in the
Intent-to-treat Population

Subgroup			Placebo N = 52	MEDI551 N = 161
Race	Other	Number of subjects with an attack	4/10 (40.0%)	0/13 (0%)
		Number of censored subjects	6/10 (60.0%)	13/13 (100%)
		Median time to attack[a]	200.000	NA
		95% CI[a]	(85.000, NA)	(NA, NA)
		Hazard ratio[b]		NA
		95% CI[b]		(NA , NA)
		p-value[b]		NA
	Interaction with treatment	p-value[b]		0.8950

[a] Based on Kaplan-Meier method.
[b] Based on Cox regression method, with Placebo as the reference group.

Table 1.10

Subgroup Analysis of Time to Adjudication Committee (AC) - determined NMO Attacks (Randomized-controlled Period)
AQP4-IgG sero+ Subjects in the
Intent-to-treat Population

Subgroup			Placebo N = 52	MEDI551 N = 161
Prior meds to prevent attack	Yes	Number of subjects with an attack	16/36 (44.4%)	13/109 (11.9%)
		Number of censored subjects	20/36 (55.6%)	96/109 (88.1%)
		Median time to attack[a]	200.000	NA
		95% CI[a]	(120.000, NA)	(NA, NA)
		Hazard ratio[b]		0.233
		95% CI[b]		(0.112 , 0.484)
		p-value[b]		0.0001
	No	Number of subjects with an attack	6/16 (37.5%)	5/52 (9.6%)
		Number of censored subjects	10/16 (62.5%)	47/52 (90.4%)
		Median time to attack[a]	NA	NA
		95% CI[a]	(122.000, NA)	(NA, NA)
		Hazard ratio[b]		0.219
		95% CI[b]		(0.067 , 0.720)
		p-value[b]		0.0124
	Interaction with treatment	p-value[b]		0.9353

[a] Based on Kaplan-Meier method.
[b] Based on Cox regression method, with Placebo as the reference group.

Table 1.11

Subgroup Analysis of Time to First AC-determined Attack (Randomized-controlled Period)
Intent-to-treat Population

			AQP4-IgG sero+ N = 213	
			Placebo N = 52	MEDI551 N = 161
Race	White	n	24	86
		Events	10	8
		Censored	14	78
		Median Time	.	.
		95% CI OF Median	(120.0, .)	(. , .)
		Hazard Ratio (HR)		0.189
		95% CI of HR		(0.074, 0.480)
		P-VALUE		0.0005
	Non-white	n	28	75
		Events	12	10
		Censored	16	65
		Median Time	200	.
		95% CI OF Median	(130.0, .)	(. , .)
		Hazard Ratio (HR)		0.275
		95% CI of HR		(0.118, 0.636)
		P-VALUE		0.0026
	Interaction with treatment	p-value[b]		0.5491

Table 2.1

Subgroup Analysis of Worsening from Baseline in EDSS at Last Visit Using a Logistic Regression Model (Randomized-controlled Period) AQP4-IgG sero+ Subjects in the Intent-to-treat Population

Subgroup			Placebo N = 52	MEDI551 N = 161
Age	< 65 years	Worsening from baseline in EDSS at last visit[a]	18/48 (37.5%)	22/155 (14.2%)
		Odds ratio		0.292
		95% CI		(0.139, 0.615)
		p-value		0.0012
	>= 65 years	Worsening from baseline in EDSS at last visit[a]	0/4 (0%)	2/6 (33.3%)
		Odds ratio		NA
		95% CI		(NA, NA)
		p-value		NA
	Interaction with treatment	p-value		0.9766

[a] Subjects with missing data are imputed as 'worsening'.

Table 2.2

Subgroup Analysis of Worsening from Baseline in EDSS at Last Visit Using a Logistic Regression Model (Randomized-controlled Period) Intent-to-treat Population

Subgroup			Placebo N = 56	MEDI551 N = 174
Age	< 45	Worsening from baseline in EDSS at last visit[a]	10/30 (33.3%)	14/91 (15.4%)
		Odds ratio		0.380
		95% CI		(0.146, 0.989)
		p-value		0.0474
	≥ 45	Worsening from baseline in EDSS at last visit[a]	9/26 (34.6%)	12/83 (14.5%)
		Odds ratio		0.325
		95% CI		(0.117, 0.900)
		p-value		0.0306
	Interaction with treatment	p-value		0.8546

EDSS = Expanded disability status scale.

[a] Subjects with missing data are imputed as 'worsening'.

Table 2.3

Subgroup Analysis of Worsening from Baseline in EDSS at Last Visit Using a Logistic Regression Model (Randomized-controlled Period) AQP4-IgG sero+ Subjects in the Intent-to-treat Population

Subgroup			Placebo N = 52	MEDI551 N = 161
Sex	Male	Worsening from baseline in EDSS at last visit[a]	3/3 (100.0%)	1/10 (10.0%)
		Odds ratio		NA
		95% CI		(NA, NA)
		p-value		NA
	Female	Worsening from baseline in EDSS at last visit[a]	15/49 (30.6%)	23/151 (15.2%)
		Odds ratio		0.424
		95% CI		(0.199, 0.904)
		p-value		0.0263
	Interaction with treatment	p-value		0.9489

[a] Subjects with missing data are imputed as 'worsening'.

Table 2.4

Subgroup Analysis of Worsening from Baseline in EDSS at Last Visit Using a Logistic Regression Model (Randomized-controlled Period) AQP4-IgG sero+ Subjects in the Intent-to-treat Population

Subgroup			Placebo N = 52	MEDI551 N = 161
Baseline EDSS	< 5	Worsening from baseline in EDSS at last visit[a]	10/35 (28.6%)	15/120 (12.5%)
		Odds ratio		0.348
		95% CI		(0.137, 0.886)
		p-value		0.0269
	≥ 5	Worsening from baseline in EDSS at last visit[a]	8/17 (47.1%)	9/41 (22.0%)
		Odds ratio		0.314
		95% CI		(0.094, 1.055)
		p-value		0.0610
	Interaction with treatment	p-value		0.9222

[a] Subjects with missing data are imputed as 'worsening'.

Table 2.5

Subgroup Analysis of Worsening from Baseline in EDSS at Last Visit Using a Logistic Regression Model (Randomized-controlled Period) AQP4-IgG sero+ Subjects in the Intent-to-treat Population

Subgroup			Placebo N = 52	MEDI551 N = 161
No. of prior NMO/NMOSD relapses	< 2	Worsening from baseline in EDSS at last visit[a]	3/13 (23.1%)	3/24 (12.5%)
		Odds ratio		0.503
		95% CI		(0.082, 3.081)
		p-value		0.4573
	≥ 2	Worsening from baseline in EDSS at last visit[a]	15/39 (38.5%)	21/137 (15.3%)
		Odds ratio		0.309
		95% CI		(0.138, 0.691)
		p-value		0.0042
	Interaction with treatment	p-value		0.6118

[a] Subjects with missing data are imputed as 'worsening'.

Table 2.6

Subgroup Analysis of Worsening from Baseline in EDSS at Last Visit Using a Logistic Regression Model (Randomized-controlled Period) AQP4-IgG sero+ Subjects in the Intent-to-treat Population

Subgroup			Placebo N = 52	MEDI551 N = 161
Disease duration category (year)	< 5	Worsening from baseline in EDSS at last visit[a]	14/42 (33.3%)	20/132 (15.2%)
		Odds ratio		0.399
		95% CI		(0.177, 0.901)
		p-value		0.0271
	≥ 5	Worsening from baseline in EDSS at last visit[a]	4/10 (40.0%)	4/29 (13.8%)
		Odds ratio		0.213
		95% CI		(0.038, 1.187)
		p-value		0.0776
	Interaction with treatment	p-value		0.6036

[a] Subjects with missing data are imputed as 'worsening'.

Table 2.7

Subgroup Analysis of Worsening from Baseline in EDSS at Last Visit Using a Logistic Regression Model (Randomized-controlled Period) AQP4-IgG sero+ Subjects in the Intent-to-treat Population

Subgroup			Placebo N = 52	MEDI551 N = 161
Region 1	US	Worsening from baseline in EDSS at last visit[a]	4/11 (36.4%)	4/27 (14.8%)
		Odds ratio		0.304
		95% CI		(0.052, 1.787)
		p-value		0.1878
	Non-US	Worsening from baseline in EDSS at last visit[a]	14/41 (34.1%)	20/134 (14.9%)
		Odds ratio		0.347
		95% CI		(0.155, 0.778)
		p-value		0.0102
	Interaction with treatment	p-value		0.9471

[a] Subjects with missing data are imputed as 'worsening'.

Table 2.8

Subgroup Analysis of Worsening from Baseline in EDSS at Last Visit Using a Logistic Regression Model (Randomized-controlled Period) AQP4-IgG sero+ Subjects in the Intent-to-treat Population

Subgroup			Placebo N = 52	MEDI551 N = 161
Region 2	EU	Worsening from baseline in EDSS at last visit[a]	3/10 (30.0%)	6/40 (15.0%)
		Odds ratio		0.438
		95% CI		(0.086, 2.222)
		p-value		0.3191
	Non-EU	Worsening from baseline in EDSS at last visit[a]	15/42 (35.7%)	18/121 (14.9%)
		Odds ratio		0.335
		95% CI		(0.149, 0.756)
		p-value		0.0084
	Interaction with treatment	p-value		0.7562

[a] Subjects with missing data are imputed as 'worsening'.

Table 2.9

Subgroup Analysis of Worsening from Baseline in EDSS at Last Visit Using a Logistic Regression Model (Randomized-controlled Period) AQP4-IgG sero+ Subjects in the Intent-to-treat Population

Subgroup			Placebo N = 52	MEDI551 N = 161
Race	American Indian or Alaskan Native	Worsening from baseline in EDSS at last visit[a]	1/5 (20.0%)	2/11 (18.2%)
		Odds ratio		1.182
		95% CI		(0.068, 20.400)
		p-value		0.9086
	Asian	Worsening from baseline in EDSS at last visit[a]	2/8 (25.0%)	6/37 (16.2%)
		Odds ratio		0.583
		95% CI		(0.094, 3.631)
		p-value		0.5635
	Black or African American	Worsening from baseline in EDSS at last visit[a]	1/5 (20.0%)	0/14 (0%)
		Odds ratio		NA
		95% CI		(NA, NA)
		p-value		NA

[a] Subjects with missing data are imputed as 'worsening'.

Table 2.9

Subgroup Analysis of Worsening from Baseline in EDSS at Last Visit Using a Logistic Regression Model (Randomized-controlled Period) AQP4-IgG sero+ Subjects in the Intent-to-treat Population

Subgroup			Placebo N = 52	MEDI551 N = 161
Race	White	Worsening from baseline in EDSS at last visit[a]	10/24 (41.7%)	14/86 (16.3%)
		Odds ratio		0.319
		95% CI		(0.115, 0.880)
		p-value		0.0273
	Other	Worsening from baseline in EDSS at last visit[a]	4/10 (40.0%)	2/13 (15.4%)
		Odds ratio		0.216
		95% CI		(0.025, 1.850)
		p-value		0.1619
	Interaction with treatment	p-value		0.9501

[a] Subjects with missing data are imputed as 'worsening'.

Table 2.10

Subgroup Analysis of Worsening from Baseline in EDSS at Last Visit Using a Logistic Regression Model (Randomized-controlled Period) AQP4-IgG sero+ Subjects in the Intent-to-treat Population

Subgroup			Placebo N = 52	MEDI551 N = 161
Prior meds to prevent attack	Yes	Worsening from baseline in EDSS at last visit[a]	13/36 (36.1%)	19/109 (17.4%)
		Odds ratio		0.404
		95% CI		(0.172, 0.949)
		p-value		0.0374
	No	Worsening from baseline in EDSS at last visit[a]	5/16 (31.3%)	5/52 (9.6%)
		Odds ratio		0.233
		95% CI		(0.057, 0.955)
		p-value		0.0430
	Interaction with treatment	p-value		0.5127

[a] Subjects with missing data are imputed as 'worsening'.

Table 2.11

Subgroup Analysis of Worsening from Baseline in EDSS at Last Visit Using a Logistic Regression Model (Randomized-controlled Period)
Intent-to-treat Population

			AQP4-IgG sero+ N = 213	
			Placebo N = 52	MEDI551 N = 161
Race	White	n	24	86
		Subjects with Worsening	10 (41.67%)	14 (16.28%)
		Odds Ratio		0.319
		95% CI of Odds Ratio		(0.115, 0.880)
		P-VALUE		0.0273
	Non-white	n	28	75
		Subjects with Worsening	8 (28.57%)	10 (13.33%)
		Odds Ratio		0.386
		95% CI of Odds Ratio		(0.134, 1.111)
		P-VALUE		0.0777
	Interaction with treatment	p-value[b]		0.7543

Table 3.1

Subgroup Analysis of the Cumulative Number of Active MRI Lesions
Using Negative Binomial Regression Model (Randomized-controlled Period)
AQP4-IgG sero+ Subjects in the
Intent-to-treat Population

Subgroup			Placebo N = 52	MEDI551 N = 161
Age	< 65 years	n	29	71
		Cumulative number of active MRI lesions, mean (SD)	2.34 (1.26)	1.66 (1.04)
		Rate Ratio[a]		0.537
		95% CI		(0.361, 0.799)
		p-value		0.0022
	>= 65 years	n	2	3
		Cumulative number of active MRI lesions, mean (SD)	1.00 (0.00)	1.67 (1.15)
		Rate Ratio[a]		1.667
		95% CI		(0.301, 9.244)
		p-value		0.5589
	Interaction with treatment	p-value		0.2468

[a] Rate reduction in cumulative number of active MRI lesions.

Table 3.2

Subgroup Analysis of the Cumulative Number of Active MRI Lesions Using Negative Binomial Regression Model (Randomized-controlled Period) AQP4-IgG sero+ Subjects in the Intent-to-treat Population

Subgroup			Placebo N = 52	MEDI551 N = 161
Sex	Male	n	1	5
		Cumulative number of active MRI lesions, mean (SD)	2.00 (NA)	2.00 (1.73)
		Rate Ratio[a]		1.500
		95% CI		(0.189, 11.899)
		p-value		0.7012
	Female	n	30	69
		Cumulative number of active MRI lesions, mean (SD)	2.27 (1.28)	1.64 (0.98)
		Rate Ratio[a]		0.539
		95% CI		(0.365, 0.798)
		p-value		0.0020
	Interaction with treatment	p-value		0.2725

[a] Rate reduction in cumulative number of active MRI lesions.

Table 3.3

Subgroup Analysis of the Cumulative Number of Active MRI Lesions Using Negative Binomial Regression Model (Randomized-controlled Period) AQP4-IgG sero+ Subjects in the Intent-to-treat Population

Subgroup			Placebo N = 52	MEDI551 N = 161
Baseline EDSS	< 5	n	21	56
		Cumulative number of active MRI lesions, mean (SD)	2.38 (1.36)	1.64 (1.07)
		Rate Ratio[a]		0.537
		95% CI		(0.338, 0.851)
		p-value		0.0082
	≥ 5	n	10	18
		Cumulative number of active MRI lesions, mean (SD)	2.00 (1.05)	1.72 (0.96)
		Rate Ratio[a]		0.643
		95% CI		(0.314, 1.315)
		p-value		0.2259
	Interaction with treatment	p-value		0.6804

[a] Rate reduction in cumulative number of active MRI lesions.

Table 3.4

Subgroup Analysis of the Cumulative Number of Active MRI Lesions Using Negative Binomial Regression Model (Randomized-controlled Period) AQP4-IgG sero+ Subjects in the Intent-to-treat Population

Subgroup			Placebo N = 52	MEDI551 N = 161
No. of prior NMO/NMOSD relapses	< 2	n	6	13
		Cumulative number of active MRI lesions, mean (SD)	2.17 (1.17)	1.46 (0.88)
		Rate Ratio[a]		0.792
		95% CI		(0.341, 1.839)
		p-value		0.5869
	≥ 2	n	25	61
		Cumulative number of active MRI lesions, mean (SD)	2.28 (1.31)	1.70 (1.07)
		Rate Ratio[a]		0.519
		95% CI		(0.336, 0.804)
		p-value		0.0033
	Interaction with treatment	p-value		0.4034

[a] Rate reduction in cumulative number of active MRI lesions.

Table 3.5

Subgroup Analysis of the Cumulative Number of Active MRI Lesions Using Negative Binomial Regression Model (Randomized-controlled Period) AQP4-IgG sero+ Subjects in the Intent-to-treat Population

Subgroup			Placebo N = 52	MEDI551 N = 161
Disease duration category (year)	< 5	n	24	60
		Cumulative number of active MRI lesions, mean (SD)	2.25 (1.15)	1.58 (1.01)
		Rate Ratio[a]		0.560
		95% CI		(0.364, 0.861)
		p-value		0.0083
	≥ 5	n	7	14
		Cumulative number of active MRI lesions, mean (SD)	2.29 (1.70)	2.00 (1.11)
		Rate Ratio[a]		0.603
		95% CI		(0.254, 1.434)
		p-value		0.2528
	Interaction with treatment	p-value		0.8764

[a] Rate reduction in cumulative number of active MRI lesions.

Table 3.6

Subgroup Analysis of the Cumulative Number of Active MRI Lesions Using Negative Binomial Regression Model (Randomized-controlled Period) AQP4-IgG sero+ Subjects in the Intent-to-treat Population

Subgroup			Placebo N = 52	MEDI551 N = 161
Region 1	US	n	5	14
		Cumulative number of active MRI lesions, mean (SD)	2.00 (1.00)	1.43 (0.65)
		Rate Ratio[a]		0.815
		95% CI		(0.356, 1.865)
		p-value		0.6279
	Non-US	n	26	60
		Cumulative number of active MRI lesions, mean (SD)	2.31 (1.32)	1.72 (1.11)
		Rate Ratio[a]		0.525
		95% CI		(0.340, 0.811)
		p-value		0.0037
	Interaction with treatment	p-value		0.4043

[a] Rate reduction in cumulative number of active MRI lesions.

Table 3.7

Subgroup Analysis of the Cumulative Number of Active MRI Lesions Using Negative Binomial Regression Model (Randomized-controlled Period) AQP4-IgG sero+ Subjects in the Intent-to-treat Population

Subgroup			Placebo N = 52	MEDI551 N = 161
Region 2	EU	n	6	18
		Cumulative number of active MRI lesions, mean (SD)	1.33 (0.52)	1.11 (0.32)
		Rate Ratio[a]		0.625
		95% CI		(0.275, 1.419)
		p-value		0.2612
	Non-EU	n	25	56
		Cumulative number of active MRI lesions, mean (SD)	2.48 (1.29)	1.84 (1.12)
		Rate Ratio[a]		0.577
		95% CI		(0.370, 0.899)
		p-value		0.0152
	Interaction with treatment	p-value		0.8818

[a] Rate reduction in cumulative number of active MRI lesions.

Table 3.8

Subgroup Analysis of the Cumulative Number of Active MRI Lesions Using Negative Binomial Regression Model (Randomized-controlled Period) AQP4-IgG sero+ Subjects in the Intent-to-treat Population

Subgroup			Placebo N = 52	MEDI551 N = 161
Prior meds to prevent attack	Yes	n	22	52
		Cumulative number of active MRI lesions, mean (SD)	2.18 (1.26)	1.75 (1.01)
		Rate Ratio[a]		0.626
		95% CI		(0.396, 0.990)
		p-value		0.0451
	No	n	9	22
		Cumulative number of active MRI lesions, mean (SD)	2.44 (1.33)	1.45 (1.10)
		Rate Ratio[a]		0.448
		95% CI		(0.219, 0.917)
		p-value		0.0279
	Interaction with treatment	p-value		0.4348

[a] Rate reduction in cumulative number of active MRI lesions.

Table 3.9

Subgroup Analysis of the Cumulative Number of Active MRI Lesions
Using Negative Binomial Regression Model (Randomized-controlled Period)
AQP4-IgG sero+ Subjects in the
Intent-to-treat Population

Subgroup			Placebo N = 52	MEDI551 N = 161
Race	American Indian or Alaskan Native	n	2	5
		Cumulative number of active MRI lesions, mean (SD)	1.50 (0.71)	2.40 (2.19)
		Rate Ratio[a]		1.818
		95% CI		(0.289, 11.450)
		p-value		0.5243
	Asian	n	6	20
		Cumulative number of active MRI lesions, mean (SD)	1.67 (0.82)	2.05 (1.10)
		Rate Ratio[a]		0.886
		95% CI		(0.382, 2.059)
		p-value		0.7793
	Black or African American	n	2	9
		Cumulative number of active MRI lesions, mean (SD)	2.50 (2.12)	1.56 (0.73)
		Rate Ratio[a]		1.000
		95% CI		(0.313, 3.197)
		p-value		>0.9999

[a] Rate reduction in cumulative number of active MRI lesions.

Table 3.9

Subgroup Analysis of the Cumulative Number of Active MRI Lesions
Using Negative Binomial Regression Model (Randomized-controlled Period)
AQP4-IgG sero+ Subjects in the
Intent-to-treat Population

Subgroup			Placebo N = 52	MEDI551 N = 161
Race	White	n	14	35
		Cumulative number of active MRI lesions, mean (SD)	2.14 (1.29)	1.34 (0.54)
		Rate Ratio[a]		0.437
		95% CI		(0.258, 0.740)
		p-value		0.0021
	Other	n	7	5
		Cumulative number of active MRI lesions, mean (SD)	3.14 (1.22)	1.80 (1.79)
		Rate Ratio[a]		0.315
		95% CI		(0.111, 0.895)
		p-value		0.0302
	Interaction with treatment	p-value		0.1603

[a] Rate reduction in cumulative number of active MRI lesions.

Table 3.10

Subgroup Analysis of the Cumulative Number of Active MRI Lesions Using Negative Binomial Regression Model (Randomized-controlled Period) Intent-to-treat Population

			AQP4-IgG sero+ N = 213	
			Placebo N = 52	**MEDI551 N = 161**
Race	White	n	14	35
		Mean	2.1	1.3
		SD	1.3	0.5
		Median	2	1
		(Min, Max)	(1.0, 5.0)	(1.0, 3.0)
		Rate Ratio		0.437
		95% CI		(0.258, 0.740)
		P-VALUE		0.0021
	Non-white	n	17	39
		Mean	2.4	1.9
		SD	1.3	1.3
		Median	2	2
		(Min, Max)	(1.0, 5.0)	(1.0, 6.0)
		Rate Ratio		0.709
		95% CI		(0.417, 1.208)
		P-VALUE		0.2059
	Interaction with treatment	p-value[b]		0.2136

Table 4.1

Subgroup Analysis of Number of NMO/NMOSD-related In-patient Hospitalizations
Using Negative Binomial regression Model (Randomized-controlled Period)
AQP4-IgG sero+ Subjects in the
Intent-to-treat Population

Subgroup			Placebo N = 52	MEDI551 N = 161
Age	< 65 years	n	7	9
		Cumulative number of NMO/NMOSD-related in-patient Hospitalizations, mean (SD)	1.43 (0.79)	1.00 (0.00)
		Rate Ratio[a]		0.279
		95% CI		(0.101, 0.766)
		p-value		0.0133
	≥ 65 years	n	0	0
		Cumulative number of NMO/NMOSD-related in-patient Hospitalizations, mean (SD)	NA	NA
		Rate Ratio[a]		NA
		95% CI		(NA, NA)
		p-value		NA

[a] Rate reduction in number of NMO/NMOSD-related In-patient Hospitalizations.

Table 4.2

Subgroup Analysis of Number of NMO/NMOSD-related In-patient Hospitalizations Using Negative Binomial Regression Model (Randomized-controlled Period) AQP4-IgG seropositive in the Intent-to-treat Population

Subgroup			Placebo N = 52	MEDI551 N = 161
Age	< 45	n	6	6
		Cumulative number of NMO/NMOSD-related in-patient Hospitalizations, mean (SD)	1.5 (0.8)	1.0 (0)
		Rate Ratio[a]		0.214
		95% CI		(0.068, 0.680)
		p-value		0.0089
	≥ 45	n	1	3
		Cumulative number of NMO/NMOSD-related in-patient Hospitalizations, mean (SD)	1	1.0 (0)
		Rate Ratio[a]		0.974
		95% CI		(0.101, 9.364)
		p-value		0.9818
	Interaction with treatment	p-value		0.2508

[a] Rate reduction in number of NMO/NMOSD-related In-patient hospitalizations. Rate ratio and it's 95% CI, and p-value are estimated from the negative binomial regression.

Table 4.3

Subgroup Analysis of Number of NMO/NMOSD-related In-patient Hospitalizations Using Negative Binomial regression Model (Randomized-controlled Period) AQP4-IgG sero+ Subjects in the Intent-to-treat Population

Subgroup			Placebo N = 52	MEDI551 N = 161
Sex	Male	n	0	0
		Cumulative number of NMO/NMOSD-related in-patient Hospitalizations, mean (SD)	NA	NA
		Rate Ratio[a]		NA
		95% CI		(NA, NA)
		p-value		NA
	Female	n	7	9
		Cumulative number of NMO/NMOSD-related in-patient Hospitalizations, mean (SD)	1.43 (0.79)	1.00 (0.00)
		Rate Ratio[a]		0.292
		95% CI		(0.106, 0.803)
		p-value		0.0171
	Interaction with treatment	p-value		NA

[a] Rate reduction in number of NMO/NMOSD-related In-patient Hospitalizations.

Table 4.4

Subgroup Analysis of Number of NMO/NMOSD-related In-patient Hospitalizations Using Negative Binomial regression Model (Randomized-controlled Period) AQP4-IgG sero+ Subjects in the Intent-to-treat Population

Subgroup			Placebo N = 52	MEDI551 N = 161
Baseline EDSS	< 5	n	4	5
		Cumulative number of NMO/NMOSD-related in-patient Hospitalizations, mean (SD)	1.75 (0.96)	1.00 (0.00)
		Rate Ratio[a]		0.208
		95% CI		(0.051, 0.860)
		p-value		0.0301
	≥ 5	n	3	4
		Cumulative number of NMO/NMOSD-related in-patient Hospitalizations, mean (SD)	1.00 (0.00)	1.00 (0.00)
		Rate Ratio[a]		0.553
		95% CI		(0.124, 2.470)
		p-value		0.4378
	Interaction with treatment	p-value		0.3684

[a] Rate reduction in number of NMO/NMOSD-related In-patient Hospitalizations.

Table 4.5

Subgroup Analysis of Number of NMO/NMOSD-related In-patient Hospitalizations Using Negative Binomial regression Model (Randomized-controlled Period) AQP4-IgG sero+ Subjects in the Intent-to-treat Population

Subgroup			Placebo N = 52	MEDI551 N = 161
No. of prior NMO/NMOSD relapses	< 2	n	1	0
		Cumulative number of NMO/NMOSD-related in-patient Hospitalizations, mean (SD)	1.00 (NA)	NA
		Rate Ratio[a]		NA
		95% CI		(NA, NA)
		p-value		NA
	≥ 2	n	6	9
		Cumulative number of NMO/NMOSD-related in-patient Hospitalizations, mean (SD)	1.50 (0.84)	1.00 (0.00)
		Rate Ratio[a]		0.285
		95% CI		(0.100, 0.814)
		p-value		0.0191
	Interaction with treatment	p-value		0.3739

[a] Rate reduction in number of NMO/NMOSD-related In-patient Hospitalizations.

Table 4.6

Subgroup Analysis of Number of NMO/NMOSD-related In-patient Hospitalizations Using Negative Binomial regression Model (Randomized-controlled Period) AQP4-IgG sero+ Subjects in the Intent-to-treat Population

Subgroup			Placebo N = 52	MEDI551 N = 161
Disease duration category (year)	< 5	n	5	6
		Cumulative number of NMO/NMOSD-related in-patient Hospitalizations, mean (SD)	1.60 (0.89)	1.00 (0.00)
		Rate Ratio[a]		0.239
		95% CI		(0.068, 0.841)
		p-value		0.0257
	≥ 5	n	2	3
		Cumulative number of NMO/NMOSD-related in-patient Hospitalizations, mean (SD)	1.00 (0.00)	1.00 (0.00)
		Rate Ratio[a]		0.517
		95% CI		(0.086, 3.096)
		p-value		0.4702
	Interaction with treatment	p-value		0.5236

[a] Rate reduction in number of NMO/NMOSD-related In-patient Hospitalizations.

Table 4.7

Subgroup Analysis of Number of NMO/NMOSD-related In-patient Hospitalizations
Using Negative Binomial regression Model (Randomized-controlled Period)
AQP4-IgG sero+ Subjects in the
Intent-to-treat Population

Subgroup			Placebo N = 52	MEDI551 N = 161
Region 1	US	n	1	0
		Cumulative number of NMO/NMOSD-related in-patient Hospitalizations, mean (SD)	1.00 (NA)	NA
		Rate Ratio[a]		NA
		95% CI		(NA, NA)
		p-value		NA
	Non-US	n	6	9
		Cumulative number of NMO/NMOSD-related in-patient Hospitalizations, mean (SD)	1.50 (0.84)	1.00 (0.00)
		Rate Ratio[a]		0.306
		95% CI		(0.107, 0.876)
		p-value		0.0274
	Interaction with treatment	p-value		0.3093

[a] Rate reduction in number of NMO/NMOSD-related In-patient Hospitalizations.

Table 4.8

Subgroup Analysis of Number of NMO/NMOSD-related In-patient Hospitalizations Using Negative Binomial regression Model (Randomized-controlled Period) AQP4-IgG sero+ Subjects in the Intent-to-treat Population

Subgroup			Placebo N = 52	MEDI551 N = 161
Region 2	EU	n	1	2
		Cumulative number of NMO/NMOSD-related in-patient Hospitalizations, mean (SD)	2.00 (NA)	1.00 (0.00)
		Rate Ratio[a]		0.250
		95% CI		(0.020, 3.057)
		p-value		0.2778
	Non-EU	n	6	7
		Cumulative number of NMO/NMOSD-related in-patient Hospitalizations, mean (SD)	1.33 (0.82)	1.00 (0.00)
		Rate Ratio[a]		0.304
		95% CI		(0.100, 0.925)
		p-value		0.0360
	Interaction with treatment	p-value		0.8784

[a] Rate reduction in number of NMO/NMOSD-related In-patient Hospitalizations.

Table 4.9

Subgroup Analysis of Number of NMO/NMOSD-related In-patient Hospitalizations Using Negative Binomial regression Model (Randomized-controlled Period) AQP4-IgG sero+ Subjects in the Intent-to-treat Population

Subgroup			Placebo N = 52	MEDI551 N = 161
Prior meds to prevent attack	Yes	n	5	5
		Cumulative number of NMO/NMOSD-related in-patient Hospitalizations, mean (SD)	1.60 (0.89)	1.00 (0.00)
		Rate Ratio[a]		0.206
		95% CI		(0.055, 0.772)
		p-value		0.0191
	No	n	2	4
		Cumulative number of NMO/NMOSD-related in-patient Hospitalizations, mean (SD)	1.00 (0.00)	1.00 (0.00)
		Rate Ratio[a]		0.615
		95% CI		(0.113, 3.360)
		p-value		0.5751
	Interaction with treatment	p-value		NA

[a] Rate reduction in number of NMO/NMOSD-related In-patient Hospitalizations.

Table 4.10

Subgroup Analysis of Number of NMO/NMOSD-related In-patient Hospitalizations
Using Negative Binomial regression Model (Randomized-controlled Period)
AQP4-IgG sero+ Subjects in the
Intent-to-treat Population

Subgroup			Placebo N = 52	MEDI551 N = 161
Race	American Indian or Alaskan Native	n	0	2
		Cumulative number of NMO/NMOSD-related in-patient Hospitalizations, mean (SD)	NA	1.00 (0.00)
		Rate Ratio[a]		NA
		95% CI		(NA, NA)
		p-value		NA
	Asian	n	1	1
		Cumulative number of NMO/NMOSD-related in-patient Hospitalizations, mean (SD)	1.00 (NA)	1.00 (NA)
		Rate Ratio[a]		0.216
		95% CI		(0.014, 3.457)
		p-value		0.2789
	Black or African American	n	1	0
		Cumulative number of NMO/NMOSD-related in-patient Hospitalizations, mean (SD)	1.00 (NA)	NA
		Rate Ratio[a]		NA
		95% CI		(NA, NA)
		p-value		NA

[a] Rate reduction in number of NMO/NMOSD-related In-patient Hospitalizations.

Table 4.10

Subgroup Analysis of Number of NMO/NMOSD-related In-patient Hospitalizations Using Negative Binomial regression Model (Randomized-controlled Period) AQP4-IgG sero+ Subjects in the Intent-to-treat Population

Subgroup			Placebo N = 52	MEDI551 N = 161
Race	White	n	2	6
		Cumulative number of NMO/NMOSD-related in-patient Hospitalizations, mean (SD)	1.50 (0.71)	1.00 (0.00)
		Rate Ratio[a]		0.558
		95% CI		(0.123, 2.535)
		p-value		0.4501
	Other	n	3	0
		Cumulative number of NMO/NMOSD-related in-patient Hospitalizations, mean (SD)	1.67 (1.15)	NA
		Rate Ratio[a]		NA
		95% CI		(NA, NA)
		p-value		NA
	Interaction with treatment	p-value		NA

[a] Rate reduction in number of NMO/NMOSD-related In-patient Hospitalizations.

Table 4.11

Subgroup Analysis of Number of NMO/NMOSD-related In-patient Hospitalization Using Negative Binomial Regression Model (Randomized-controlled Period) Intent-to-treat Population

			AQP4-IgG sero+ N = 213	
			Placebo N = 52	**MEDI551 N = 161**
Race	White	n	2	6
		Mean	1.5	1
		SD	0.7	0
		Median	1.5	1
		(Min, Max)	(1.0, 2.0)	(1.0, 1.0)
		Rate Ratio		0.558
		95% CI		(0.123, 2.535)
		P-VALUE		0.4501
	Non-white	n	5	3
		Mean	1.4	1
		SD	0.9	0
		Median	1	1
		(Min, Max)	(1.0, 3.0)	(1.0, 1.0)
		Rate Ratio		0.16
		95% CI		(0.036, 0.710)
		P-VALUE		0.0159
	Interaction with treatment	p-value[b]		0.2060

Table 5

Subgroup Analysis of Change from Baseline in Pain NRS at the Last Visit Using Analysis of Covariance Model (Randomized-controlled Period)
Pain score over for legs
Intent-to-treat Population

			AQP4-IgG sero+ N = 213	
			Placebo N = 52	**MEDI551 N = 161**
Sex	Male	n	3	10
		Observed mean (SE)	1.667 (1.202)	1.500 (0.778)
		LSMEAN (SE)[b]	2.975 (1.352)	1.107 (0.685)
		LSMEAN difference (SE)[b]		-1.868 (1.589)
		95% CI[b]		(-5.408, 1.673)
		p-value[b]		0.267
	Female	n	48	149
		Observed mean (SE)	1.042 (0.424)	0.201 (0.181)
		LSMEAN (SE)[b]	1.104 (0.328)	0.181 (0.186)
		LSMEAN difference (SE)[b]		-0.922 (0.377)
		95% CI[b]		(-1.665, -0.179)
		p-value[b]		0.0153
	Interaction with treatment	p-value[b]		0.8758
Age	< 45	n	26	83
		Observed mean (SE)	1.154 (0.436)	-0.048 (0.225)
		LSMEAN (SE)[b]	1.038 (0.396)	-0.012 (0.221)
		LSMEAN difference (SE)[b]		-1.049 (0.454)
		95% CI[b]		(-1.950, -0.149)
		p-value[b]		0.0228
	≥ 45	n	25	76
		Observed mean (SE)	1.000 (0.698)	0.645 (0.274)
		LSMEAN (SE)[b]	1.479 (0.504)	0.487 (0.285)
		LSMEAN difference (SE)[b]		-0.991 (0.585)
		95% CI[b]		(-2.152, 0.169)
		p-value[b]		0.0932
	Interaction with treatment	p-value[b]		0.8613

			AQP4-IgG sero+ N = 213	
			Placebo N = 52	**MEDI551 N = 161**
Baseline EDSS	< 5	n	34	119
		Observed mean (SE)	0.706 (0.492)	0.277 (0.202)
		LSMEAN (SE)[b]	0.844 (0.375)	0.238 (0.200)
		LSMEAN difference (SE)[b]		-0.606 (0.426)
		95% CI[b]		(-1.448, 0.235)
		p-value[b]		0.1565
	≥ 5	n	17	40
		Observed mean (SE)	1.824 (0.693)	0.300 (0.374)
		LSMEAN (SE)[b]	1.822 (0.580)	0.300 (0.378)
		LSMEAN difference (SE)[b]		-1.522 (0.693)
		95% CI[b]		(-2.911, -0.133)
		p-value[b]		0.0323
	Interaction with treatment	p-value[b]		0.2324
No of prior NMOSD relapses	< 2	n	12	24
		Observed mean (SE)	-0.333 (0.791)	0.750 (0.396)
		LSMEAN (SE)[b]	-0.083 (0.651)	0.625 (0.453)
		LSMEAN difference (SE)[b]		0.708 (0.810)
		95% CI[b]		(-0.940, 2.355)
		p-value[b]		0.3884
	≥ 2	n	39	135
		Observed mean (SE)	1.513 (0.451)	0.200 (0.197)
		LSMEAN (SE)[b]	1.572 (0.362)	0.183 (0.195)
		LSMEAN difference (SE)[b]		-1.389 (0.412)
		95% CI[b]		(-2.201, -0.576)
		p-value[b]		0.0009
	Interaction with treatment	p-value[b]		0.0265

			AQP4-IgG sero+ N = 213	
			Placebo N = 52	MEDI551 N = 161
Disease duration (years)	< 5	n	41	130
		Observed mean (SE)	1.122 (0.473)	0.277 (0.193)
		LSMEAN (SE)[b]	1.208 (0.359)	0.250 (0.201)
		LSMEAN difference (SE)[b]		-0.958 (0.412)
		95% CI[b]		(-1.770, -0.145)
		p-value[b]		0.0211
	≥ 5	n	10	29
		Observed mean (SE)	0.900 (0.737)	0.310 (0.452)
		LSMEAN (SE)[b]	1.078 (0.711)	0.249 (0.416)
		LSMEAN difference (SE)[b]		-0.829 (0.825)
		95% CI[b]		(-2.503, 0.844)
		p-value[b]		0.3217
	Interaction with treatment	p-value[b]		0.8638
Prior meds to prevent attack	Yes	n	36	108
		Observed mean (SE)	1.611 (0.485)	0.444 (0.213)
		LSMEAN (SE)[b]	1.672 (0.380)	0.424 (0.219)
		LSMEAN difference (SE)[b]		-1.248 (0.438)
		95% CI[b]		(-2.115, -0.382)
		p-value[b]		0.0051
	No	n	15	51
		Observed mean (SE)	-0.200 (0.634)	-0.059 (0.319)
		LSMEAN (SE)[b]	-0.002 (0.563)	-0.117 (0.304)
		LSMEAN difference (SE)[b]		-0.115 (0.642)
		95% CI[b]		(-1.397, 1.168)
		p-value[b]		0.8589
	Interaction with treatment	p-value[b]		0.1524