SIPONIMOD/Mayzent®

CBAF312A2304 (EXPAND) AMNOG Analysis

Modul 4A, Anhang 2 Subpopulation B

Patient Disposition Tables

1. Patient Disposition and Baseline Characteristics

Table 1.1 Patient Disposition and Compliance (RAN, FAS)

	Treatment groups		
Disposition/Reason	**BAF312 (N=128) n (%)**	**Placebo (N=61) n (%)**	**Total (N=189) n (%)**
Randomized (RAN)	**128**	**61**	**189**
Full Analysis Set (FAS)	**127 (99,2)**	**61 (100,0)**	**188 (99,5)**
Reasons for exclusion			
Subject was randomized but did not receive any study drug	1 (0,8)	0 (0,0)	1 (0,5)
Study Discontinuation (RAN)	**24 (18,8)**	**16 (26,2)**	**40 (21,2)**
Reasons for study discontinuation			
Subject/guardian decision	**13 (10,2)**	**10 (16,4)**	**23 (12,2)**
Adverse event	**5 (3,9)**	**3 (4,9)**	**8 (4,2)**
Physician decision	**3 (2,3)**	**0 (0,0)**	**3 (1,6)**
Lost to follow-up	**1 (0,8)**	**1 (1,6)**	**2 (1,1)**
Death	**1 (0,8)**	**0 (0,0)**	**1 (0,5)**
Progressive disease	**1 (0,8)**	**0 (0,0)**	**1 (0,5)**
Lack of efficacy	**0 (0,0)**	**1 (1,6)**	**1 (0,5)**
Protocol deviation	**0 (0,0)**	**1 (1,6)**	**1 (0,5)**
Received study drug	**127 (99,2)**	**61 (100,0)**	**188 (99,5)**
Did not receive study drug	**1 (0,8)**	**0 (0,0)**	**1 (0,5)**
Completed Treatment Epoch on double-blind study drug	**83 (64,8)**	**36 (59,0)**	**119 (63,0)**
Prematurely discontinued double-blind study drug during Treatment Epoch[1]	**45 (35,2)**	**25 (41,0)**	**70 (37,0)**
Continued on open-label siponimod treatment	14 (10,9)	9 (14,8)	23 (12,2)
Continued on abbreviated visit schedule	7 (5,5)	2 (3,3)	9 (4,8)
Discontinued Treatment Epoch directly from study drug	24 (18,8)	14 (23,0)	38 (20,1)
Primary reason for premature discontinuation from double-blind study drug			
Disease progression	16 (12,5)	8 (13,1)	24 (12,7)
Subject/guardian decision	16 (12,5)	8 (13,1)	24 (12,7)
Adverse event	9 (7,0)	4 (6,6)	13 (6,9)
Physician decision	2 (1,6)	0 (0,0)	2 (1,1)
Lack of efficacy	1 (0,8)	4 (6,6)	5 (2,6)
As per protocol	1 (0,8)	0 (0,0)	1 (0,5)
Dosing error	0 (0,0)	1 (1,6)	1 (0,5)
Subject with at least one protocol deviation	**74 (57,8)**	**38 (62,3)**	**112 (59,3)**
Key procedures not performed as per protocol	45 (35,2)	23 (37,7)	68 (36,0)
Other GCP deviation	35 (27,3)	17 (27,9)	52 (27,5)

	Treatment groups		
Disposition/Reason	**BAF312 (N=128) n (%)**	**Placebo (N=61) n (%)**	**Total (N=189) n (%)**
Prohibited concomitant medication	10 (7,8)	3 (4,9)	13 (6,9)
Selection criteria not met	11 (8,6)	3 (4,9)	14 (7,4)
Treatment deviation	4 (3,1)	5 (8,2)	9 (4,8)

[1] This includes patients that did not receive study drug.

Percentages refer to the number of randomized patients.

Analysis population: A2304 RAN subpopulation "ACTIVE MS WITHOUT RELAPSES"

Table 1.2 Length of Study Participation (FAS)

	Treatment groups		
Study participation (FAS)	**BAF312 (N=127)**	**Placebo (N=61)**	**Total (N=188)**
Mean ± SD (in days)	650,0 ± 249,59	612,4 ± 245,88	637,8 ± 248,36
Median (in days)	654,0	605,0	642,0
Minimum, Maximum (in days)	7; 1101	48; 1078	7; 1101
Patients ≥ 365 days in study, n (%)	111 (87,4)	53 (86,9)	164 (87,2)
Patients < 365 days in study, n (%)	16 (12,6)	8 (13,1)	24 (12,8)
Patients ≥ 730 days in study, n (%)	54 (42,5)	22 (36,1)	76 (40,4)
Patients < 730 days in study, n (%)	73 (57,5)	39 (63,9)	112 (59,6)
Analysis population: A2304 FAS subpopulation "ACTIVE MS WITHOUT RELAPSES"			

Table 1.3 Characterization of Study Population, Demographic Characteristics (FAS)

	Treatment Groups		
Patient characteristics	**BAF312 (N=127)**	**Placebo (N=61)**	**Total (N=188)**
Age (years)			
Mean ± SD	47,1 ± 7,03	48,4 ± 8,68	47,6 ± 7,61
Median	47,0	50,0	48,0
Range	25 to 61	24 to 60	24 to 61
Age group (years), n (%)			
18-30	3 (2,4)	2 (3,3)	5 (2,7)
31-40	15 (11,8)	11 (18,0)	26 (13,8)
41-55	95 (74,8)	33 (54,1)	128 (68,1)
>55	14 (11,0)	15 (24,6)	29 (15,4)
Sex, n (%)			
Female	76 (59,8)	37 (60,7)	113 (60,1)
Male	51 (40,2)	24 (39,3)	75 (39,9)
Weight (kg)			
Mean ± SD	70,5 ± 15,83	68,0 ± 12,41	69,7 ± 14,82
Median	69,0	67,4	68,0
Range	42,6 to 142,1	47,2 to 97,2	42,6 to 142,1
Height (cm)			
Mean ± SD	169,0 ± 9,69	168,7 ± 9,60	168,9 ± 9,64
Median	168,0	168,0	168,0
Range	142,2 to 193,0	152,0 to 195,0	142,2 to 195,0
BMI (kg/m^2)			
Mean ± SD	24,6 ± 4,75	23,9 ± 3,34	24,4 ± 4,35
Median	24,2	23,9	24,0
Range	16,4 to 52,2	17,3 to 31,6	16,4 to 52,2
Race, n (%)			
Asian	1 (0,8)	0 (0,0)	1 (0,5)
Black or African American	0 (0,0)	1 (1,6)	1 (0,5)
Other	0 (0,0)	2 (3,3)	2 (1,1)
Unknown	0 (0,0)	1 (1,6)	1 (0,5)
White	126 (99,2)	57 (93,4)	183 (97,3)
Ethnicity, n (%)			
Hispanic or Latino	8 (6,3)	1 (1,6)	9 (4,8)
Not Hispanic or Latino	90 (70,9)	47 (77,0)	137 (72,9)
Not Reported	18 (14,2)	7 (11,5)	25 (13,3)
Unknown	11 (8,7)	6 (9,8)	17 (9,0)
Analysis population: A2304 FAS subpopulation "ACTIVE MS WITHOUT RELAPSES"			

Table 1.4 MS Disease History (FAS)

	Treatment Groups		
	BAF312 (N=127)	**Placebo (N=61)**	**Total (N=188)**
Duration of MS since first diagnosis (years)			
Mean ± SD	13,2 ± 6,76	12,0 ± 6,73	12,8 ± 6,75
Median	12,4	10,5	11,9
Range	0,5 to 32,9	0,4 to 33,2	0,4 to 33,2
Duration of MS since first symptom (years)			
Mean ± SD	17,1 ± 7,53	15,8 ± 7,86	16,7 ± 7,64
Median	16,2	15,3	16,0
Range	3,2 to 41,3	2,3 to 33,5	2,3 to 41,3
Time since conversion to SPMS (years)			
Mean ± SD	4,4 ± 3,78	4,0 ± 2,95	4,3 ± 3,53
Median	3,3	3,2	3,2
Range	0,6 to 20,0	0,5 to 12,8	0,5 to 20,0
Number of relapses in the last 24 months prior to screening			
Mean ± SD	0,0 ± 0,00	0,0 ± 0,00	0,0 ± 0,00
Median	0,0	0,0	0,0
Range	0 to 0	0 to 0	0 to 0
Number of relapses in the last 24 months prior to screening (categories), n (%)			
0	127 (100,0)	61 (100,0)	188 (100,0)
1	0 (0,0)	0 (0,0)	0 (0,0)
2-3	0 (0,0)	0 (0,0)	0 (0,0)
4-5	0 (0,0)	0 (0,0)	0 (0,0)
>5	0 (0,0)	0 (0,0)	0 (0,0)
Number of relapses in the last 12 months prior to screening			
Mean ± SD	0,0 ± 0,00	0,0 ± 0,00	0,0 ± 0,00
Median	0,0	0,0	0,0
Range	0 to 0	0 to 0	0 to 0
Number of relapses in the last 12 months prior to screening (categories), n (%)			
0	127 (100,0)	61 (100,0)	188 (100,0)
1	0 (0,0)	0 (0,0)	0 (0,0)
2-3	0 (0,0)	0 (0,0)	0 (0,0)
4-5	0 (0,0)	0 (0,0)	0 (0,0)
Analysis population: A2304 FAS subpopulation "ACTIVE MS WITHOUT RELAPSES"			

Table 1.5 Clinical MS Baseline Characteristics (FAS)

	Treatment Groups		
	BAF312 (N=127)	**Placebo (N=61)**	**Total (N=188)**
EDSS			
Mean ± SD	5,6 ± 1,08	5,5 ± 1,08	5,6 ± 1,08
Median	6,0	6,0	6,0
Range	2,5 to 6,5	3,0 to 6,5	2,5 to 6,5
EDSS categories, n (%)			
<3.0	1 (0,8)	0 (0,0)	1 (0,5)
3.0-4.5	29 (22,8)	16 (26,2)	45 (23,9)
5.0-5.5	15 (11,8)	9 (14,8)	24 (12,8)
6.0-6.5	82 (64,6)	36 (59,0)	118 (62,8)
>6.5	0 (0,0)	0 (0,0)	0 (0,0)
Number of Gd-enhancing T1 lesions			
Mean ± SD	3,0 ± 3,18	3,1 ± 8,36	3,0 ± 5,41
Median	2,0	1,0	2,0
Range	1 to 18	1 to 65	1 to 65
Number of Gd-enhancing T1 lesions (categories), n (%)			
0	0 (0,0)	0 (0,0)	0 (0,0)
≥ 1	127 (100,0)	61 (100,0)	188 (100,0)
Volume of T2 lesions (mm^3)			
Mean ± SD	21552,1 ± 16818,91	22260,6 ± 19500,54	21782,0 ± 17683,99
Median	17826,0	15771,0	17319,0
Range	918,0 to 81591,0	918,0 to 103560,0	918,0 to 103560,0
Normalized brain volume (cc)			
Mean ± SD	1414,8 ± 91,92	1423,2 ± 92,92	1417,5 ± 92,08
Median	1411,5	1417,5	1411,6
Range	1171,4 to 1644,1	1230,2 to 1678,7	1171,4 to 1678,7
Analysis population: A2304 FAS subpopulation "ACTIVE MS WITHOUT RELAPSES"			

Safety Tables

11. Adverse Events: Binary Analysis

Table 11.0: List of excluded disease-specific Preferred Terms

Preferred Terms (grouped by System Organ Class)
EAR AND LABYRINTH DISORDERS
VERTIGO
VERTIGO POSITIONAL
EYE DISORDERS
DIPLOPIA
LOSS OF VISUAL CONTRAST SENSITIVITY
VISION BLURRED
VISUAL ACUITY REDUCED
VISUAL IMPAIRMENT
GASTROINTESTINAL DISORDERS
ABDOMINAL PAIN
ABDOMINAL PAIN LOWER
ABDOMINAL PAIN UPPER
ANAL INCONTINENCE
ANAL PARAESTHESIA
BOWEL MOVEMENT IRREGULARITY
CONSTIPATION
DIARRHOEA
FAECES SOFT
GASTROINTESTINAL PAIN
IRRITABLE BOWEL SYNDROME
SMALL INTESTINAL OBSTRUCTION
GENERAL DISORDERS AND ADMINISTRATION SITE CONDITIONS
ABASIA
ASTHENIA
FATIGUE
FEELING COLD
FEELING DRUNK
FEELING HOT
FEELING OF BODY TEMPERATURE CHANGE
GAIT DISTURBANCE
OEDEMA PERIPHERAL
PAIN
PERIPHERAL SWELLING

Preferred Terms (grouped by System Organ Class)
INJURY, POISONING AND PROCEDURAL COMPLICATIONS
FALL
INVESTIGATIONS
COLUMBIA SUICIDE SEVERITY RATING SCALE
COLUMBIA SUICIDE SEVERITY RATING SCALE ABNORMAL
VITAMIN D DECREASED
WALKING DISTANCE TEST ABNORMAL
METABOLISM AND NUTRITION DISORDERS
VITAMIN D DEFICIENCY
MUSCULOSKELETAL AND CONNECTIVE TISSUE DISORDERS
ARTHRALGIA
BACK PAIN
BONE PAIN
FLANK PAIN
GROIN PAIN
JOINT SWELLING
MOBILITY DECREASED
MUSCLE SPASMS
MUSCLE TIGHTNESS
MUSCULAR WEAKNESS
MUSCULOSKELETAL PAIN
MUSCULOSKELETAL STIFFNESS
MYALGIA
NECK PAIN
PAIN IN EXTREMITY
SPINAL PAIN
NERVOUS SYSTEM DISORDERS
ALLODYNIA
APHASIA
ATAXIA
BALANCE DISORDER
BURNING SENSATION
CENTRAL NERVOUS SYSTEM LESION
CLUMSINESS
COGNITIVE DISORDER
COORDINATION ABNORMAL
DEPRESSED LEVEL OF CONSCIOUSNESS
DISTURBANCE IN ATTENTION
DIZZINESS

Preferred Terms (grouped by System Organ Class)
DIZZINESS POSTURAL
DROOLING
DYSAESTHESIA
DYSARTHRIA
DYSGEUSIA
DYSKINESIA
DYSTONIA
EPILEPSY
FACIAL NEURALGIA
FACIAL PARALYSIS
FACIAL SPASM
FINE MOTOR DELAY
FINE MOTOR SKILL DYSFUNCTION
FREEZING PHENOMENON
GAIT SPASTIC
GENERALISED TONIC-CLONIC SEIZURE
HEAD TITUBATION
HEMIPARESIS
HEMIPLEGIA
HYPOAESTHESIA
INTENTION TREMOR
LOSS OF PROPRIOCEPTION
MEMORY IMPAIRMENT
MENTAL IMPAIRMENT
MONOPARESIS
MOTOR DYSFUNCTION
MOVEMENT DISORDER
MULTIPLE SCLEROSIS
MULTIPLE SCLEROSIS RELAPSE
MUSCLE CONTRACTIONS INVOLUNTARY
MUSCLE SPASTICITY
MYOCLONIC EPILEPSY
NEURALGIA
NEUROMUSCULAR PAIN
OCCIPITAL NEURALGIA
OPTIC NEURITIS
PARAESTHESIA
PARAPARESIS
PARTIAL SEIZURES

Preferred Terms (grouped by System Organ Class)
POOR QUALITY SLEEP
SCIATICA
SEIZURE
SENSORY DISTURBANCE
SENSORY LOSS
SLOW SPEECH
SOMNOLENCE
SPEECH DISORDER
TARDIVE DYSKINESIA
TRANSIENT GLOBAL AMNESIA
TREMOR
TRIGEMINAL NEURALGIA
UHTHOFF'S PHENOMENON
VISUAL FIELD DEFECT
VITH NERVE PARALYSIS
PSYCHIATRIC DISORDERS
ABNORMAL DREAMS
ADJUSTMENT DISORDER
ADJUSTMENT DISORDER WITH DEPRESSED MOOD
AFFECT LABILITY
AGGRESSION
AGITATION
ANGER
ANXIETY
ANXIETY DISORDER
ANXIETY DISORDER DUE TO A GENERAL MEDICAL CONDITION
CONFUSIONAL STATE
DEPRESSED MOOD
DEPRESSION
DEPRESSION SUICIDAL
DEPRESSIVE SYMPTOM
DEREALISATION
DISORIENTATION
EMOTIONAL DISTRESS
EUPHORIC MOOD
FRUSTRATION TOLERANCE DECREASED
GENERALISED ANXIETY DISORDER
HALLUCINATION
HALLUCINATION, AUDITORY

Preferred Terms (grouped by System Organ Class)
INITIAL INSOMNIA
INSOMNIA
IRRITABILITY
LOSS OF LIBIDO
MAJOR DEPRESSION
MANIA
MENTAL STATUS CHANGES
MOOD ALTERED
NERVOUSNESS
NIGHTMARE
PANIC ATTACK
PSYCHOTIC DISORDER
RESTLESSNESS
SLEEP ATTACKS
SLEEP DISORDER
SUICIDAL BEHAVIOUR
SUICIDAL IDEATION
SUICIDE ATTEMPT
TEARFULNESS
TIC
RENAL AND URINARY DISORDERS
BLADDER DISCOMFORT
BLADDER DIVERTICULUM
BLADDER DYSFUNCTION
CALCULUS BLADDER
DYSURIA
HYPERTONIC BLADDER
MICTURITION URGENCY
NEUROGENIC BLADDER
NOCTURIA
POLLAKIURIA
URGE INCONTINENCE
URINARY HESITATION
URINARY INCONTINENCE
URINARY RETENTION
REPRODUCTIVE SYSTEM AND BREAST DISORDERS
ERECTILE DYSFUNCTION
SEXUAL DYSFUNCTION

Preferred Terms (grouped by System Organ Class)
SKIN AND SUBCUTANEOUS TISSUE DISORDERS
SKIN BURNING SENSATION
SOCIAL CIRCUMSTANCES
IMMOBILE
WALKING DISABILITY

11.1 Entire Population

Table 11.1.1: Adverse Events, Binary Analysis (SAF)

	Treatment groups		Comparison		
	BAF312 (N=127)	**Placebo (N=61)**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
N'	127	61			
Any AE n (%)	114 (89,8)	47 (77,0)	2,61 [1,14; 5,98] 0,020 *	1,17 [1,00; 1,35] 0,045 *	0,13 [0,01; 0,25] 0,035 *
Any AE, disease specific events excluded[1] n (%)	108 (85,0)	46 (75,4)	1,85 [0,87; 3,96] 0,108	1,13 [0,96; 1,32] 0,143	0,10 [-0,03; 0,22] 0,130
Any SAE n (%)	16 (12,6)	11 (18,0)	0,66 [0,28; 1,51] 0,320	0,70 [0,35; 1,41] 0,318	-0,05 [-0,17; 0,06] 0,343
Any SAE, disease specific events excluded[1] n (%)	12 (9,4)	8 (13,1)	0,69 [0,27; 1,79] 0,445	0,72 [0,31; 1,67] 0,445	-0,04 [-0,14; 0,06] 0,467
Any severe AE[2] n (%)	11 (8,7)	10 (16,4)	0,48 [0,19; 1,21] 0,115	0,53 [0,24; 1,18] 0,118	-0,08 [-0,18; 0,03] 0,149
Any severe AE[2], disease specific events excluded[1] n (%)	9 (7,1)	8 (13,1)	0,51 [0,18; 1,38] 0,177	0,54 [0,22; 1,33] 0,181	-0,06 [-0,16; 0,04] 0,217
Any AE leading to study discontinuation n (%)	2 (1,6)	3 (4,9)	0,31 [0,05; 1,90] 0,182	0,32 [0,05; 1,87] 0,205	-0,03 [-0,09; 0,02] 0,262
Any AE leading to study drug discontinuation n (%)	6 (4,7)	4 (6,6)	0,71 [0,19; 2,60] 0,600	0,72 [0,21; 2,46] 0,601	-0,02 [-0,09; 0,05] 0,619

N': Number of patients in the analysis
CI: Confidence Interval
OR: Odds Ratio
RR: Relative Risk
RD: Risk Difference
*: $p < 0,05$

Applied estimator for OR: unadjusted OR
Applied test for OR: Pearson Chi-Square test

[1] The following disease-specific Preferred Terms were excluded: see Table 11.0
[2] Definition of 'severe': CTCAE grade ≥ 3

Analysis population: A2304 SAF subpopulation "ACTIVE MS WITHOUT RELAPSES"

Table 11.1.2: Any Adverse Event by Severity, Binary Analysis (SAF)

	Treatment groups		Comparison		
	BAF312 (N=127)	**Placebo (N=61)**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
N'	127	61			
Grade 1 n (%)	108 (85,0)	40 (65,6)	2,98 [1,45; 6,12] 0,002 *	1,30 [1,07; 1,58] 0,009 *	0,19 [0,06; 0,33] 0,005 *
Grade 2 n (%)	60 (47,2)	28 (45,9)	1,06 [0,57; 1,95] 0,863	1,03 [0,74; 1,43] 0,863	0,01 [-0,14; 0,17] 0,863
Grade 3 n (%)	10 (7,9)	10 (16,4)	0,44 [0,17; 1,11] 0,076	0,48 [0,21; 1,09] 0,080	-0,09 [-0,19; 0,02] 0,109
Grade 4 n (%)	3 (2,4)	0 (0,0)	3,46 [0,18; 68,00] 0,226	3,39 [0,18; 64,63] 0,417	0,02 [-0,00; 0,05] 0,080
Severe (Grade ≥ 3) n (%)	11 (8,7)	10 (16,4)	0,48 [0,19; 1,21] 0,115	0,53 [0,24; 1,18] 0,118	-0,08 [-0,18; 0,03] 0,149
Not severe (Grade < 3) n (%)	113 (89,0)	47 (77,0)	2,40 [1,06; 5,43] 0,032 *	1,15 [0,99; 1,34] 0,060	0,12 [0,00; 0,24] 0,049 *

N': Number of patients in the analysis
CI: Confidence Interval
OR: Odds Ratio
RR: Relative Risk
RD: Risk Difference
*: p < 0,05

Applied estimator for OR: unadjusted OR
Applied test for OR: Pearson Chi-Square test

Analysis population: A2304 SAF subpopulation "ACTIVE MS WITHOUT RELAPSES"

Table 11.1.3: Any AE by SOC and PT, Binary Analysis (SAF)

	Treatment groups		Comparison		
	BAF312 (N=127)	**Placebo (N=61)**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
N'	127	61			
BLOOD AND LYMPHATIC SYSTEM DISORDERS, n (%)	10 (7,9)	1 (1,6)	5,13 [0,64; 41,01] 0,088	4,80 [0,63; 36,68] 0,130	0,06 [0,01; 0,12] 0,031 *
CARDIAC DISORDERS, n (%)	15 (11,8)	5 (8,2)	1,50 [0,52; 4,34] 0,452	1,44 [0,55; 3,78] 0,458	0,04 [-0,05; 0,12] 0,425
EYE DISORDERS, n (%)	19 (15,0)	3 (4,9)	3,40 [0,97; 11,98] 0,045 *	3,04 [0,94; 9,89] 0,064	0,10 [0,02; 0,18] 0,017 *
GASTROINTESTINAL DISORDERS, n (%)	27 (21,3)	9 (14,8)	1,56 [0,68; 3,56] 0,289	1,44 [0,72; 2,87] 0,299	0,07 [-0,05; 0,18] 0,263
GENERAL DISORDERS AND ADMINISTRATION SITE CONDITIONS, n (%)	31 (24,4)	6 (9,8)	2,96 [1,16; 7,54] 0,019 *	2,48 [1,09; 5,63] 0,030 *	0,15 [0,04; 0,25] 0,007 *
FATIGUE, n (%)	15 (11,8)	0 (0,0)	16,95 [1,00; 288,11] 0,005 *	15,02 [0,91; 246,87] 0,058	0,12 [0,06; 0,17] <0,001 *
INFECTIONS AND INFESTATIONS, n (%)	65 (51,2)	26 (42,6)	1,41 [0,76; 2,61] 0,272	1,20 [0,86; 1,68] 0,287	0,09 [-0,07; 0,24] 0,268
NASOPHARYNGITIS, n (%)	18 (14,2)	7 (11,5)	1,27 [0,50; 3,24] 0,610	1,24 [0,55; 2,80] 0,613	0,03 [-0,07; 0,13] 0,598
UPPER RESPIRATORY TRACT INFECTION, n (%)	10 (7,9)	5 (8,2)	0,96 [0,31; 2,93] 0,939	0,96 [0,34; 2,69] 0,939	-0,00 [-0,09; 0,08] 0,939
URINARY TRACT INFECTION, n (%)	21 (16,5)	8 (13,1)	1,31 [0,55; 3,16] 0,543	1,26 [0,59; 2,68] 0,547	0,03 [-0,07; 0,14] 0,529
INJURY, POISONING AND PROCEDURAL COMPLICATIONS, n (%)	31 (24,4)	16 (26,2)	0,91 [0,45; 1,83] 0,787	0,93 [0,55; 1,57] 0,786	-0,02 [-0,15; 0,12] 0,789
FALL, n (%)	23 (18,1)	11 (18,0)	1,01 [0,45; 2,22] 0,990	1,00 [0,52; 1,92] 0,990	0,00 [-0,12; 0,12] 0,990
INVESTIGATIONS, n (%)	41 (32,3)	9 (14,8)	2,75 [1,24; 6,13] 0,011 *	2,19 [1,14; 4,21] 0,019 *	0,18 [0,05; 0,30] 0,004 *

	Treatment groups		Comparison		
	BAF312 (N=127)	**Placebo (N=61)**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
ALANINE AMINOTRANSFERASE INCREASED, n (%)	11 (8,7)	2 (3,3)	2,80 [0,60; 13,03] 0,173	2,64 [0,60; 11,55] 0,197	0,05 [-0,01; 0,12] 0,111
METABOLISM AND NUTRITION DISORDERS, n (%)	12 (9,4)	3 (4,9)	2,02 [0,55; 7,43] 0,283	1,92 [0,56; 6,56] 0,297	0,05 [-0,03; 0,12] 0,233
MUSCULOSKELETAL AND CONNECTIVE TISSUE DISORDERS, n (%)	33 (26,0)	14 (23,0)	1,18 [0,58; 2,41] 0,653	1,13 [0,66; 1,95] 0,656	0,03 [-0,10; 0,16] 0,648
ARTHRALGIA, n (%)	7 (5,5)	8 (13,1)	0,39 [0,13; 1,12] 0,072	0,42 [0,16; 1,11] 0,079	-0,08 [-0,17; 0,02] 0,111
NEOPLASMS BENIGN, MALIGNANT AND UNSPECIFIED (INCL CYSTS AND POLYPS), n (%)	15 (11,8)	1 (1,6)	8,04 [1,04; 62,32] 0,019 *	7,20 [0,97; 53,29] 0,053	0,10 [0,04; 0,17] 0,002 *
NERVOUS SYSTEM DISORDERS, n (%)	45 (35,4)	21 (34,4)	1,05 [0,55; 1,98] 0,892	1,03 [0,68; 1,56] 0,893	0,01 [-0,14; 0,16] 0,892
HEADACHE, n (%)	14 (11,0)	8 (13,1)	0,82 [0,32; 2,08] 0,676	0,84 [0,37; 1,90] 0,675	-0,02 [-0,12; 0,08] 0,684
PSYCHIATRIC DISORDERS, n (%)	16 (12,6)	13 (21,3)	0,53 [0,24; 1,19] 0,121	0,59 [0,30; 1,15] 0,121	-0,09 [-0,20; 0,03] 0,147
DEPRESSION, n (%)	8 (6,3)	8 (13,1)	0,45 [0,16; 1,25] 0,117	0,48 [0,19; 1,22] 0,123	-0,07 [-0,16; 0,03] 0,158
RENAL AND URINARY DISORDERS, n (%)	13 (10,2)	6 (9,8)	1,05 [0,38; 2,90] 0,932	1,04 [0,42; 2,61] 0,932	0,00 [-0,09; 0,10] 0,932
RESPIRATORY, THORACIC AND MEDIASTINAL DISORDERS, n (%)	22 (17,3)	11 (18,0)	0,95 [0,43; 2,12] 0,905	0,96 [0,50; 1,85] 0,905	-0,01 [-0,12; 0,11] 0,905
SKIN AND SUBCUTANEOUS TISSUE DISORDERS, n (%)	19 (15,0)	8 (13,1)	1,17 [0,48; 2,84] 0,735	1,14 [0,53; 2,46] 0,737	0,02 [-0,09; 0,12] 0,730
VASCULAR DISORDERS, n (%)	20 (15,7)	5 (8,2)	2,09 [0,75; 5,88] 0,153	1,92 [0,76; 4,88] 0,169	0,08 [-0,02; 0,17] 0,114

	Treatment groups		Comparison		
	BAF312 (N=127)	**Placebo (N=61)**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
HYPERTENSION, n (%)	14 (11,0)	5 (8,2)	1,39 [0,48; 4,05] 0,547	1,34 [0,51; 3,56] 0,551	0,03 [-0,06; 0,12] 0,528

N': Number of patients in the analysis
CI: Confidence Interval
OR: Odds Ratio
RR: Relative Risk
RD: Risk Difference
*: p < 0,05

Applied estimator for OR: unadjusted OR
Applied test for OR: Pearson Chi-Square test

Only SOCs/PTs with prevalence of ≥ 10 patients and ≥ 1% or ≥ 10% in at least one treatment arm are displayed.

Analysis population: A2304 SAF subpopulation "ACTIVE MS WITHOUT RELAPSES"

Table 11.1.4: Any SAE by SOC and PT, Binary Analysis (SAF)

There are no data meeting the display criteria for this table.

Table 11.1.5: Any AE by SOC, PT and Severity, Binary Analysis (SAF)

	Treatment groups		Comparison		
	BAF312 (N=127)	Placebo (N=61)	OR [95% CI] p-value	RR [95% CI] p-value	RD [95% CI] p-value
N'	127	61			
BLOOD AND LYMPHATIC SYSTEM DISORDERS					
not severe[1]	10 (7,9)	1 (1,6)	5,13 [0,64; 41,01] 0,088	4,80 [0,63; 36,68] 0,130	0,06 [0,01; 0,12] 0,031 *
severe[1]	0 (0,0)	0 (0,0)	-	-	-
CARDIAC DISORDERS					
not severe[1]	15 (11,8)	4 (6,6)	1,91 [0,61; 6,02] 0,263	1,80 [0,62; 5,20] 0,276	0,05 [-0,03; 0,14] 0,219
severe[1]	0 (0,0)	1 (1,6)	0,16 [0,01; 3,94] 0,148	0,16 [0,01; 3,91] 0,262	-0,02 [-0,05; 0,02] 0,313
BRADYCARDIA					
not severe[1]	7 (5,5)	1 (1,6)	3,50 [0,42; 29,10] 0,218	3,36 [0,42; 26,72] 0,252	0,04 [-0,01; 0,09] 0,136
severe[1]	0 (0,0)	0 (0,0)	-	-	-
EYE DISORDERS					
not severe[1]	19 (15,0)	3 (4,9)	3,40 [0,97; 11,98] 0,045 *	3,04 [0,94; 9,89] 0,064	0,10 [0,02; 0,18] 0,017 *
severe[1]	1 (0,8)	1 (1,6)	0,48 [0,03; 7,74] 0,594	0,48 [0,03; 7,55] 0,602	-0,01 [-0,04; 0,03] 0,637
GASTROINTESTINAL DISORDERS					
not severe[1]	27 (21,3)	8 (13,1)	1,79 [0,76; 4,21] 0,179	1,62 [0,78; 3,36] 0,193	0,08 [-0,03; 0,19] 0,149
severe[1]	0 (0,0)	1 (1,6)	0,16 [0,01; 3,94] 0,148	0,16 [0,01; 3,91] 0,262	-0,02 [-0,05; 0,02] 0,313
NAUSEA					
not severe[1]	4 (3,1)	4 (6,6)	0,46 [0,11; 1,92] 0,278	0,48 [0,12; 1,86] 0,288	-0,03 [-0,10; 0,04] 0,334
severe[1]	0 (0,0)	0 (0,0)	-	-	-

	Treatment groups		Comparison		
	BAF312 (N=127)	Placebo (N=61)	OR [95% CI] p-value	RR [95% CI] p-value	RD [95% CI] p-value
GENERAL DISORDERS AND ADMINISTRATION SITE CONDITIONS					
not severe[1]	30 (23,6)	6 (9,8)	2,84 [1,11; 7,24] 0,025 *	2,40 [1,06; 5,46] 0,037 *	0,14 [0,03; 0,24] 0,010 *
severe[1]	1 (0,8)	0 (0,0)	1,46 [0,06; 36,32] 0,487	1,45 [0,06; 35,16] 0,818	0,01 [-0,01; 0,02] 0,315
FATIGUE					
not severe[1]	15 (11,8)	0 (0,0)	16,95 [1,00; 288,11] 0,005 *	15,02 [0,91; 246,87] 0,058	0,12 [0,06; 0,17] <0,001 *
severe[1]	0 (0,0)	0 (0,0)	-	-	-
INFECTIONS AND INFESTATIONS					
not severe[1]	64 (50,4)	26 (42,6)	1,37 [0,74; 2,53] 0,318	1,18 [0,84; 1,66] 0,332	0,08 [-0,07; 0,23] 0,315
severe[1]	4 (3,1)	2 (3,3)	0,96 [0,17; 5,39] 0,962	0,96 [0,18; 5,10] 0,962	-0,00 [-0,06; 0,05] 0,963
INFLUENZA					
not severe[1]	7 (5,5)	4 (6,6)	0,83 [0,23; 2,95] 0,775	0,84 [0,26; 2,76] 0,775	-0,01 [-0,08; 0,06] 0,781
severe[1]	0 (0,0)	1 (1,6)	0,16 [0,01; 3,94] 0,148	0,16 [0,01; 3,91] 0,262	-0,02 [-0,05; 0,02] 0,313
NASOPHARYNGITIS					
not severe[1]	18 (14,2)	7 (11,5)	1,27 [0,50; 3,24] 0,610	1,24 [0,55; 2,80] 0,613	0,03 [-0,07; 0,13] 0,598
severe[1]	0 (0,0)	0 (0,0)	-	-	-
UPPER RESPIRATORY TRACT INFECTION					
not severe[1]	10 (7,9)	5 (8,2)	0,96 [0,31; 2,93] 0,939	0,96 [0,34; 2,69] 0,939	-0,00 [-0,09; 0,08] 0,939
severe[1]	0 (0,0)	0 (0,0)	-	-	-
URINARY TRACT INFECTION					
not severe[1]	20 (15,7)	8 (13,1)	1,24 [0,51; 3,00] 0,635	1,20 [0,56; 2,57] 0,637	0,03 [-0,08; 0,13] 0,626
severe[1]	2 (1,6)	0 (0,0)	2,45 [0,12; 51,82] 0,324	2,42 [0,12; 49,69] 0,566	0,02 [-0,01; 0,04] 0,154

	Treatment groups		Comparison		
	BAF312 (N=127)	Placebo (N=61)	OR [95% CI] p-value	RR [95% CI] p-value	RD [95% CI] p-value
INJURY, POISONING AND PROCEDURAL COMPLICATIONS					
not severe[1]	30 (23,6)	16 (26,2)	0,87 [0,43; 1,76] 0,697	0,90 [0,53; 1,52] 0,696	-0,03 [-0,16; 0,11] 0,700
severe[1]	1 (0,8)	1 (1,6)	0,48 [0,03; 7,74] 0,594	0,48 [0,03; 7,55] 0,602	-0,01 [-0,04; 0,03] 0,637
CONTUSION					
not severe[1]	6 (4,7)	5 (8,2)	0,56 [0,16; 1,90] 0,342	0,58 [0,18; 1,81] 0,346	-0,03 [-0,11; 0,04] 0,384
severe[1]	0 (0,0)	0 (0,0)	-	-	-
FALL					
not severe[1]	23 (18,1)	11 (18,0)	1,01 [0,45; 2,22] 0,990	1,00 [0,52; 1,92] 0,990	0,00 [-0,12; 0,12] 0,990
severe[1]	0 (0,0)	0 (0,0)	-	-	-
INVESTIGATIONS					
not severe[1]	40 (31,5)	8 (13,1)	3,05 [1,33; 7,00] 0,007 *	2,40 [1,20; 4,81] 0,013 *	0,18 [0,07; 0,30] 0,002 *
severe[1]	1 (0,8)	2 (3,3)	0,23 [0,02; 2,63] 0,202	0,24 [0,02; 2,60] 0,240	-0,02 [-0,07; 0,02] 0,301
ALANINE AMINOTRANSFERASE INCREASED					
not severe[1]	10 (7,9)	1 (1,6)	5,13 [0,64; 41,01] 0,088	4,80 [0,63; 36,68] 0,130	0,06 [0,01; 0,12] 0,031 *
severe[1]	1 (0,8)	1 (1,6)	0,48 [0,03; 7,74] 0,594	0,48 [0,03; 7,55] 0,602	-0,01 [-0,04; 0,03] 0,637
GAMMA-GLUTAMYLTRANSFERASE INCREASED					
not severe[1]	9 (7,1)	1 (1,6)	4,58 [0,57; 36,97] 0,119	4,32 [0,56; 33,36] 0,160	0,05 [-0,00; 0,11] 0,052
severe[1]	0 (0,0)	0 (0,0)	-	-	-
WEIGHT DECREASED					
not severe[1]	7 (5,5)	1 (1,6)	3,50 [0,42; 29,10] 0,218	3,36 [0,42; 26,72] 0,252	0,04 [-0,01; 0,09] 0,136
severe[1]	0 (0,0)	0 (0,0)	-	-	-

	Treatment groups		Comparison		
	BAF312 (N=127)	Placebo (N=61)	OR [95% CI] p-value	RR [95% CI] p-value	RD [95% CI] p-value
WEIGHT INCREASED					
not severe[1]	2 (1,6)	4 (6,6)	0,23 [0,04; 1,28] 0,069	0,24 [0,05; 1,28] 0,094	-0,05 [-0,12; 0,02] 0,138
severe[1]	0 (0,0)	0 (0,0)	-	-	-
METABOLISM AND NUTRITION DISORDERS					
not severe[1]	12 (9,4)	3 (4,9)	2,02 [0,55; 7,43] 0,283	1,92 [0,56; 6,56] 0,297	0,05 [-0,03; 0,12] 0,233
severe[1]	0 (0,0)	0 (0,0)	-	-	-
MUSCULOSKELETAL AND CONNECTIVE TISSUE DISORDERS					
not severe[1]	33 (26,0)	13 (21,3)	1,30 [0,62; 2,69] 0,485	1,22 [0,69; 2,14] 0,491	0,05 [-0,08; 0,17] 0,474
severe[1]	1 (0,8)	1 (1,6)	0,48 [0,03; 7,74] 0,594	0,48 [0,03; 7,55] 0,602	-0,01 [-0,04; 0,03] 0,637
ARTHRALGIA					
not severe[1]	7 (5,5)	7 (11,5)	0,45 [0,15; 1,35] 0,145	0,48 [0,18; 1,31] 0,152	-0,06 [-0,15; 0,03] 0,191
severe[1]	0 (0,0)	1 (1,6)	0,16 [0,01; 3,94] 0,148	0,16 [0,01; 3,91] 0,262	-0,02 [-0,05; 0,02] 0,313
NEOPLASMS BENIGN, MALIGNANT AND UNSPECIFIED (INCL CYSTS AND POLYPS)					
not severe[1]	15 (11,8)	0 (0,0)	16,95 [1,00; 288,11] 0,005 *	15,02 [0,91; 246,87] 0,058	0,12 [0,06; 0,17] <0,001 *
severe[1]	0 (0,0)	1 (1,6)	0,16 [0,01; 3,94] 0,148	0,16 [0,01; 3,91] 0,262	-0,02 [-0,05; 0,02] 0,313
MELANOCYTIC NAEVUS					
not severe[1]	8 (6,3)	0 (0,0)	8,75 [0,50; 154,11] 0,045 *	8,23 [0,48; 140,37] 0,145	0,06 [0,02; 0,11] 0,003 *
severe[1]	0 (0,0)	0 (0,0)	-	-	-
NERVOUS SYSTEM DISORDERS					
not severe[1]	45 (35,4)	20 (32,8)	1,13 [0,59; 2,15] 0,721	1,08 [0,70; 1,66] 0,723	0,03 [-0,12; 0,17] 0,719
severe[1]	1 (0,8)	1 (1,6)	0,48 [0,03; 7,74] 0,594	0,48 [0,03; 7,55] 0,602	-0,01 [-0,04; 0,03] 0,637

	Treatment groups		Comparison		
	BAF312 (N=127)	Placebo (N=61)	OR [95% CI] p-value	RR [95% CI] p-value	RD [95% CI] p-value
DIZZINESS					
not severe[1]	8 (6,3)	3 (4,9)	1,30 [0,33; 5,08] 0,706	1,28 [0,35; 4,66] 0,707	0,01 [-0,05; 0,08] 0,694
severe[1]	0 (0,0)	0 (0,0)	-	-	-
HEADACHE					
not severe[1]	14 (11,0)	8 (13,1)	0,82 [0,32; 2,08] 0,676	0,84 [0,37; 1,90] 0,675	-0,02 [-0,12; 0,08] 0,684
severe[1]	1 (0,8)	0 (0,0)	1,46 [0,06; 36,32] 0,487	1,45 [0,06; 35,16] 0,818	0,01 [-0,01; 0,02] 0,315
MUSCLE SPASTICITY					
not severe[1]	8 (6,3)	4 (6,6)	0,96 [0,28; 3,31] 0,946	0,96 [0,30; 3,07] 0,946	-0,00 [-0,08; 0,07] 0,946
severe[1]	0 (0,0)	0 (0,0)	-	-	-
PSYCHIATRIC DISORDERS					
not severe[1]	16 (12,6)	10 (16,4)	0,74 [0,31; 1,73] 0,480	0,77 [0,37; 1,59] 0,479	-0,04 [-0,15; 0,07] 0,496
severe[1]	2 (1,6)	3 (4,9)	0,31 [0,05; 1,90] 0,182	0,32 [0,05; 1,87] 0,205	-0,03 [-0,09; 0,02] 0,262
DEPRESSION					
not severe[1]	7 (5,5)	7 (11,5)	0,45 [0,15; 1,35] 0,145	0,48 [0,18; 1,31] 0,152	-0,06 [-0,15; 0,03] 0,191
severe[1]	1 (0,8)	1 (1,6)	0,48 [0,03; 7,74] 0,594	0,48 [0,03; 7,55] 0,602	-0,01 [-0,04; 0,03] 0,637
RENAL AND URINARY DISORDERS					
not severe[1]	13 (10,2)	6 (9,8)	1,05 [0,38; 2,90] 0,932	1,04 [0,42; 2,61] 0,932	0,00 [-0,09; 0,10] 0,932
severe[1]	1 (0,8)	0 (0,0)	1,46 [0,06; 36,32] 0,487	1,45 [0,06; 35,16] 0,818	0,01 [-0,01; 0,02] 0,315
REPRODUCTIVE SYSTEM AND BREAST DISORDERS					
not severe[1]	7 (5,5)	3 (4,9)	1,13 [0,28; 4,52] 0,865	1,12 [0,30; 4,19] 0,865	0,01 [-0,06; 0,07] 0,863
severe[1]	0 (0,0)	1 (1,6)	0,16 [0,01; 3,94] 0,148	0,16 [0,01; 3,91] 0,262	-0,02 [-0,05; 0,02] 0,313

	Treatment groups		Comparison		
	BAF312 (N=127)	Placebo (N=61)	OR [95% CI] p-value	RR [95% CI] p-value	RD [95% CI] p-value
RESPIRATORY, THORACIC AND MEDIASTINAL DISORDERS					
not severe[1]	22 (17,3)	11 (18,0)	0,95 [0,43; 2,12] 0,905	0,96 [0,50; 1,85] 0,905	-0,01 [-0,12; 0,11] 0,905
severe[1]	0 (0,0)	0 (0,0)	-	-	-
COUGH					
not severe[1]	7 (5,5)	1 (1,6)	3,50 [0,42; 29,10] 0,218	3,36 [0,42; 26,72] 0,252	0,04 [-0,01; 0,09] 0,136
severe[1]	0 (0,0)	0 (0,0)	-	-	-
SKIN AND SUBCUTANEOUS TISSUE DISORDERS					
not severe[1]	19 (15,0)	8 (13,1)	1,17 [0,48; 2,84] 0,735	1,14 [0,53; 2,46] 0,737	0,02 [-0,09; 0,12] 0,730
severe[1]	1 (0,8)	0 (0,0)	1,46 [0,06; 36,32] 0,487	1,45 [0,06; 35,16] 0,818	0,01 [-0,01; 0,02] 0,315
VASCULAR DISORDERS					
not severe[1]	20 (15,7)	5 (8,2)	2,09 [0,75; 5,88] 0,153	1,92 [0,76; 4,88] 0,169	0,08 [-0,02; 0,17] 0,114
severe[1]	1 (0,8)	0 (0,0)	1,46 [0,06; 36,32] 0,487	1,45 [0,06; 35,16] 0,818	0,01 [-0,01; 0,02] 0,315
HYPERTENSION					
not severe[1]	14 (11,0)	5 (8,2)	1,39 [0,48; 4,05] 0,547	1,34 [0,51; 3,56] 0,551	0,03 [-0,06; 0,12] 0,528
severe[1]	0 (0,0)	0 (0,0)	-	-	-

N': Number of patients in the analysis
CI: Confidence Interval
OR: Odds Ratio
RR: Relative Risk
RD: Risk Difference
*: $p < 0,05$

Applied estimator for OR: unadjusted OR
Applied test for OR: Pearson Chi-Square test

[1] Definition of 'severe': CTCAE grade ≥ 3, 'not severe': CTCAE grade < 3

Only SOCs/PTs with prevalence of ≥ 10 patients and ≥ 1% or ≥ 5% in at least one treatment arm are displayed.

Analysis population: A2304 SAF subpopulation "ACTIVE MS WITHOUT RELAPSES"

Table 11.1.6: Any AE leading to Study Discontinuation by SOC and PT, Frequencies (SAF)

	Treatment groups	
	BAF312 (N=127)	**Placebo (N=61)**
N'	127	61
GENERAL DISORDERS AND ADMINISTRATION SITE CONDITIONS, n (%)	1 (0,8)	0 (0,0)
OEDEMA PERIPHERAL, n (%)	1 (0,8)	0 (0,0)
NERVOUS SYSTEM DISORDERS, n (%)	1 (0,8)	1 (1,6)
CENTRAL NERVOUS SYSTEM LESION, n (%)	0 (0,0)	1 (1,6)
MUSCLE SPASTICITY, n (%)	1 (0,8)	0 (0,0)
PSYCHIATRIC DISORDERS, n (%)	0 (0,0)	2 (3,3)
SUICIDAL IDEATION, n (%)	0 (0,0)	1 (1,6)
SUICIDE ATTEMPT, n (%)	0 (0,0)	1 (1,6)
SOCIAL CIRCUMSTANCES, n (%)	0 (0,0)	1 (1,6)
WALKING DISABILITY, n (%)	0 (0,0)	1 (1,6)

N': Number of patients in the analysis
Analysis population: A2304 SAF subpopulation "ACTIVE MS WITHOUT RELAPSES"

Table 11.1.7: Any AE leading to Study Drug Discontinuation by SOC and PT, Frequencies (SAF)

	Treatment groups	
	BAF312 (N=127)	**Placebo (N=61)**
N'	127	61
EYE DISORDERS, n (%)	0 (0,0)	1 (1,6)
MACULAR OEDEMA, n (%)	0 (0,0)	1 (1,6)
GENERAL DISORDERS AND ADMINISTRATION SITE CONDITIONS, n (%)	1 (0,8)	0 (0,0)
OEDEMA PERIPHERAL, n (%)	1 (0,8)	0 (0,0)
INVESTIGATIONS, n (%)	1 (0,8)	0 (0,0)
ALANINE AMINOTRANSFERASE INCREASED, n (%)	1 (0,8)	0 (0,0)
ASPARTATE AMINOTRANSFERASE INCREASED, n (%)	1 (0,8)	0 (0,0)
NERVOUS SYSTEM DISORDERS, n (%)	1 (0,8)	1 (1,6)
CENTRAL NERVOUS SYSTEM LESION, n (%)	0 (0,0)	1 (1,6)
MUSCLE SPASTICITY, n (%)	1 (0,8)	0 (0,0)
PSYCHIATRIC DISORDERS, n (%)	1 (0,8)	2 (3,3)
SUICIDAL IDEATION, n (%)	0 (0,0)	1 (1,6)
SUICIDE ATTEMPT, n (%)	1 (0,8)	1 (1,6)
SKIN AND SUBCUTANEOUS TISSUE DISORDERS, n (%)	1 (0,8)	0 (0,0)
ECZEMA, n (%)	1 (0,8)	0 (0,0)
SOCIAL CIRCUMSTANCES, n (%)	0 (0,0)	1 (1,6)
WALKING DISABILITY, n (%)	0 (0,0)	1 (1,6)
VASCULAR DISORDERS, n (%)	1 (0,8)	0 (0,0)
DEEP VEIN THROMBOSIS, n (%)	1 (0,8)	0 (0,0)

N': Number of patients in the analysis
Analysis population: A2304 SAF subpopulation "ACTIVE MS WITHOUT RELAPSES"

Table 11.1.8: Adverse Events of Special Interest by Severity, Binary Analysis (SAF)

	Treatment groups		Comparison		
	BAF312 (N=127)	**Placebo (N=61)**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
N'	127	61			
Infections and infestations, n (%)	65 (51,2)	26 (42,6)	1,41 [0,76; 2,61] 0,272	1,20 [0,86; 1,68] 0,287	0,09 [-0,07; 0,24] 0,268
not severe	64 (50,4)	26 (42,6)	1,37 [0,74; 2,53] 0,318	1,18 [0,84; 1,66] 0,332	0,08 [-0,07; 0,23] 0,315
severe	4 (3,1)	2 (3,3)	0,96 [0,17; 5,39] 0,962	0,96 [0,18; 5,10] 0,962	-0,00 [-0,06; 0,05] 0,963
serious	5 (3,9)	2 (3,3)	1,21 [0,23; 6,42] 0,823	1,20 [0,24; 6,01] 0,824	0,01 [-0,05; 0,06] 0,818
Herpes simplex virus infections, n (%)	4 (3,1)	1 (1,6)	1,95 [0,21; 17,84] 0,547	1,92 [0,22; 16,83] 0,555	0,02 [-0,03; 0,06] 0,501
not severe	4 (3,1)	1 (1,6)	1,95 [0,21; 17,84] 0,547	1,92 [0,22; 16,83] 0,555	0,02 [-0,03; 0,06] 0,501
severe	0 (0,0)	0 (0,0)	-	-	-
serious	0 (0,0)	0 (0,0)	-	-	-
Varicella-zoster virus infections, n (%)	1 (0,8)	0 (0,0)	1,46 [0,06; 36,32] 0,487	1,45 [0,06; 35,16] 0,818	0,01 [-0,01; 0,02] 0,315
not severe	0 (0,0)	0 (0,0)	-	-	-
severe	1 (0,8)	0 (0,0)	1,46 [0,06; 36,32] 0,487	1,45 [0,06; 35,16] 0,818	0,01 [-0,01; 0,02] 0,315
serious	0 (0,0)	0 (0,0)	-	-	-
Lymphopenia, n (%)	2 (1,6)	0 (0,0)	2,45 [0,12; 51,82] 0,324	2,42 [0,12; 49,69] 0,566	0,02 [-0,01; 0,04] 0,154
not severe	2 (1,6)	0 (0,0)	2,45 [0,12; 51,82] 0,324	2,42 [0,12; 49,69] 0,566	0,02 [-0,01; 0,04] 0,154
severe	0 (0,0)	0 (0,0)	-	-	-
serious	0 (0,0)	0 (0,0)	-	-	-

	Treatment groups		Comparison		
	BAF312 (N=127)	**Placebo (N=61)**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Macular edema, n (%)	2 (1,6)	1 (1,6)	0,96 [0,09; 10,80] 0,974	0,96 [0,09; 10,39] 0,974	-0,00 [-0,04; 0,04] 0,974
not severe	1 (0,8)	0 (0,0)	1,46 [0,06; 36,32] 0,487	1,45 [0,06; 35,16] 0,818	0,01 [-0,01; 0,02] 0,315
severe	1 (0,8)	1 (1,6)	0,48 [0,03; 7,74] 0,594	0,48 [0,03; 7,55] 0,602	-0,01 [-0,04; 0,03] 0,637
serious	0 (0,0)	0 (0,0)	-	-	-
Abnormal hepatic enzymes, n (%)	19 (15,0)	4 (6,6)	2,51 [0,81; 7,72] 0,100	2,28 [0,81; 6,42] 0,118	0,08 [-0,00; 0,17] 0,061
not severe	18 (14,2)	2 (3,3)	4,87 [1,09; 21,72] 0,023 *	4,32 [1,04; 18,04] 0,045 *	0,11 [0,03; 0,18] 0,005 *
severe	1 (0,8)	2 (3,3)	0,23 [0,02; 2,63] 0,202	0,24 [0,02; 2,60] 0,240	-0,02 [-0,07; 0,02] 0,301
serious	2 (1,6)	2 (3,3)	0,47 [0,06; 3,43] 0,448	0,48 [0,07; 3,33] 0,458	-0,02 [-0,07; 0,03] 0,501
Malignancies, n (%)	0 (0,0)	1 (1,6)	0,16 [0,01; 3,94] 0,148	0,16 [0,01; 3,91] 0,262	-0,02 [-0,05; 0,02] 0,313
not severe	0 (0,0)	0 (0,0)	-	-	-
severe	0 (0,0)	1 (1,6)	0,16 [0,01; 3,94] 0,148	0,16 [0,01; 3,91] 0,262	-0,02 [-0,05; 0,02] 0,313
serious	0 (0,0)	1 (1,6)	0,16 [0,01; 3,94] 0,148	0,16 [0,01; 3,91] 0,262	-0,02 [-0,05; 0,02] 0,313
Hypertension, n (%)	17 (13,4)	5 (8,2)	1,73 [0,61; 4,94] 0,300	1,63 [0,63; 4,22] 0,311	0,05 [-0,04; 0,14] 0,263
not severe	17 (13,4)	5 (8,2)	1,73 [0,61; 4,94] 0,300	1,63 [0,63; 4,22] 0,311	0,05 [-0,04; 0,14] 0,263
severe	0 (0,0)	0 (0,0)	-	-	-
serious	0 (0,0)	0 (0,0)	-	-	-
Seizures, n (%)	0 (0,0)	0 (0,0)	-	-	-
not severe	0 (0,0)	0 (0,0)	-	-	-
severe	0 (0,0)	0 (0,0)	-	-	-
serious	0 (0,0)	0 (0,0)	-	-	-

	Treatment groups		Comparison		
	BAF312 (N=127)	**Placebo (N=61)**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Thromboembolic events, n (%)	5 (3,9)	1 (1,6)	2,46 [0,28; 21,52] 0,401	2,40 [0,29; 20,11] 0,419	0,02 [-0,02; 0,07] 0,332
not severe	5 (3,9)	0 (0,0)	5,52 [0,30; 101,50] 0,116	5,33 [0,30; 94,83] 0,255	0,04 [0,01; 0,07] 0,023 *
severe	0 (0,0)	1 (1,6)	0,16 [0,01; 3,94] 0,148	0,16 [0,01; 3,91] 0,262	-0,02 [-0,05; 0,02] 0,313
serious	1 (0,8)	1 (1,6)	0,48 [0,03; 7,74] 0,594	0,48 [0,03; 7,55] 0,602	-0,01 [-0,04; 0,03] 0,637
Respiratory disorders, n (%)	22 (17,3)	11 (18,0)	0,95 [0,43; 2,12] 0,905	0,96 [0,50; 1,85] 0,905	-0,01 [-0,12; 0,11] 0,905
not severe	22 (17,3)	11 (18,0)	0,95 [0,43; 2,12] 0,905	0,96 [0,50; 1,85] 0,905	-0,01 [-0,12; 0,11] 0,905
severe	0 (0,0)	0 (0,0)	-	-	-
serious	0 (0,0)	0 (0,0)	-	-	-
Peripheral edema/swelling, n (%)	6 (4,7)	1 (1,6)	2,98 [0,35; 25,28] 0,296	2,88 [0,35; 23,41] 0,322	0,03 [-0,02; 0,08] 0,215
not severe	6 (4,7)	1 (1,6)	2,98 [0,35; 25,28] 0,296	2,88 [0,35; 23,41] 0,322	0,03 [-0,02; 0,08] 0,215
severe	0 (0,0)	0 (0,0)	-	-	-
serious	0 (0,0)	0 (0,0)	-	-	-

N': Number of patients in the analysis
CI: Confidence Interval
OR: Odds Ratio
RR: Relative Risk
RD: Risk Difference
*: p < 0,05

Applied estimator for OR: unadjusted OR
Applied test for OR: Pearson Chi-Square test

Analysis population: A2304 SAF subpopulation "ACTIVE MS WITHOUT RELAPSES"

	Treatment groups		Comparison		
	BAF312 (N=127)	**Placebo (N=61)**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
N'	127	61			
Asthma/bronchospasm, n (%)	1 (0,8)	0 (0,0)	1,46 [0,06; 36,32] 0,487	1,45 [0,06; 35,16] 0,818	0,01 [-0,01; 0,02] 0,315
not severe	1 (0,8)	0 (0,0)	1,46 [0,06; 36,32] 0,487	1,45 [0,06; 35,16] 0,818	0,01 [-0,01; 0,02] 0,315
severe	0 (0,0)	0 (0,0)	-	-	-
serious	0 (0,0)	0 (0,0)	-	-	-
Pregnancy and neonatal topics, n (%)	1 (0,8)	0 (0,0)	1,46 [0,06; 36,32] 0,487	1,45 [0,06; 35,16] 0,818	0,01 [-0,01; 0,02] 0,315
not severe	1 (0,8)	0 (0,0)	1,46 [0,06; 36,32] 0,487	1,45 [0,06; 35,16] 0,818	0,01 [-0,01; 0,02] 0,315
severe	0 (0,0)	0 (0,0)	-	-	-
serious	0 (0,0)	0 (0,0)	-	-	-
Bradyarrhythmias and bradycardia, n (%)	11 (8,7)	1 (1,6)	5,69 [0,72; 45,12] 0,065	5,28 [0,70; 40,00] 0,107	0,07 [0,01; 0,13] 0,018 *
not severe	11 (8,7)	1 (1,6)	5,69 [0,72; 45,12] 0,065	5,28 [0,70; 40,00] 0,107	0,07 [0,01; 0,13] 0,018 *
severe	0 (0,0)	0 (0,0)	-	-	-
serious	0 (0,0)	0 (0,0)	-	-	-

N': Number of patients in the analysis
CI: Confidence Interval
OR: Odds Ratio
RR: Relative Risk
RD: Risk Difference
*: $p < 0,05$

Applied estimator for OR: unadjusted OR
Applied test for OR: Pearson Chi-Square test

Analysis population: A2304 SAF subpopulation "ACTIVE MS WITHOUT RELAPSES"

11.2 Subgroup: Age

Table 11.2.1: Adverse Events, Binary Analysis (SAF) by Age

	Treatment groups		Comparison		
	BAF312 (N=127)	Placebo (N=61)	OR [95% CI] p-value	RR [95% CI] p-value	RD [95% CI] p-value
N'	127	61			
N' Age = 18-40 years	18	13			
N' Age = 41-55 years	95	33			
N' Age = >55 years	14	15			
Any AE					
Interaction test:	p=0,155				
Age = 18-40 years	14 (77,8)	11 (84,6)	0,64 [0,10; 4,14] 0,634	0,92 [0,66; 1,29] 0,626	-0,07 [-0,34; 0,21] 0,625
Age = 41-55 years	89 (93,7)	25 (75,8)	4,75 [1,51; 14,96] 0,004 *	1,24 [1,01; 1,51] 0,037 *	0,18 [0,03; 0,33] 0,023 *
Age = >55 years	11 (78,6)	11 (73,3)	1,33 [0,24; 7,40] 0,742	1,07 [0,71; 1,61] 0,741	0,05 [-0,26; 0,36] 0,741
Any AE, disease specific events excluded[1]					
Interaction test:	p=0,491				
Age = 18-40 years	13 (72,2)	10 (76,9)	0,78 [0,15; 4,07] 0,768	0,94 [0,62; 1,42] 0,765	-0,05 [-0,36; 0,26] 0,765
Age = 41-55 years	84 (88,4)	25 (75,8)	2,44 [0,89; 6,74] 0,078	1,17 [0,95; 1,43] 0,142	0,13 [-0,03; 0,29] 0,120
Age = >55 years	11 (78,6)	11 (73,3)	1,33 [0,24; 7,40] 0,742	1,07 [0,71; 1,61] 0,741	0,05 [-0,26; 0,36] 0,741
Any SAE					
Interaction test:	p=0,851				
Age = 18-40 years	1 (5,6)	2 (15,4)	0,32 [0,03; 4,01] 0,361	0,36 [0,04; 3,57] 0,384	-0,10 [-0,32; 0,12] 0,387
Age = 41-55 years	13 (13,7)	6 (18,2)	0,71 [0,25; 2,06] 0,531	0,75 [0,31; 1,82] 0,528	-0,04 [-0,19; 0,10] 0,553
Age = >55 years	2 (14,3)	3 (20,0)	0,67 [0,09; 4,73] 0,684	0,71 [0,14; 3,66] 0,687	-0,06 [-0,33; 0,22] 0,682

	Treatment groups		Comparison		
	BAF312 (N=127)	**Placebo (N=61)**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Any SAE, disease specific events excluded[1]					
Interaction test:	p=0,716				
Age = 18-40 years	1 (5,6)	2 (15,4)	0,32 [0,03; 4,01] 0,361	0,36 [0,04; 3,57] 0,384	-0,10 [-0,32; 0,12] 0,387
Age = 41-55 years	9 (9,5)	3 (9,1)	1,05 [0,27; 4,12] 0,948	1,04 [0,30; 3,62] 0,948	0,00 [-0,11; 0,12] 0,948
Age = >55 years	2 (14,3)	3 (20,0)	0,67 [0,09; 4,73] 0,684	0,71 [0,14; 3,66] 0,687	-0,06 [-0,33; 0,22] 0,682
Any severe AE[2]					
Interaction test:	N.E.				
Age = 18-40 years	1 (5,6)	1 (7,7)	0,71 [0,04; 12,43] 0,811	0,72 [0,05; 10,52] 0,812	-0,02 [-0,20; 0,16] 0,815
Age = 41-55 years	10 (10,5)	6 (18,2)	0,53 [0,18; 1,59] 0,252	0,58 [0,23; 1,47] 0,250	-0,08 [-0,22; 0,07] 0,302
Age = >55 years	0 (0,0)	3 (20,0)	0,12 [0,01; 2,62] 0,077	0,15 [0,01; 2,71] 0,200	-0,20 [-0,40; 0,00] 0,053
Any severe AE[2], disease specific events excluded[1]					
Interaction test:	N.E.				
Age = 18-40 years	1 (5,6)	1 (7,7)	0,71 [0,04; 12,43] 0,811	0,72 [0,05; 10,52] 0,812	-0,02 [-0,20; 0,16] 0,815
Age = 41-55 years	8 (8,4)	4 (12,1)	0,67 [0,19; 2,38] 0,530	0,69 [0,22; 2,16] 0,529	-0,04 [-0,16; 0,09] 0,560
Age = >55 years	0 (0,0)	3 (20,0)	0,12 [0,01; 2,62] 0,077	0,15 [0,01; 2,71] 0,200	-0,20 [-0,40; 0,00] 0,053
Any AE leading to study discontinuation					
Interaction test:	N.E.				
Age = 18-40 years	0 (0,0)	0 (0,0)	-	-	-
Age = 41-55 years	2 (2,1)	3 (9,1)	0,22 [0,03; 1,35] 0,074	0,23 [0,04; 1,33] 0,100	-0,07 [-0,17; 0,03] 0,181
Age = >55 years	0 (0,0)	0 (0,0)	-	-	-

	Treatment groups		Comparison		
	BAF312 (N=127)	**Placebo (N=61)**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Any AE leading to study drug discontinuation					
Interaction test:	N.E.				
Age = 18-40 years	0 (0,0)	0 (0,0)	-	-	-
Age = 41-55 years	6 (6,3)	3 (9,1)	0,67 [0,16; 2,86] 0,591	0,69 [0,18; 2,62] 0,591	-0,03 [-0,14; 0,08] 0,620
Age = >55 years	0 (0,0)	1 (6,7)	0,33 [0,01; 8,88] 0,326	0,36 [0,02; 8,07] 0,516	-0,07 [-0,19; 0,06] 0,301

N': Number of patients in the analysis
CI: Confidence Interval
OR: Odds Ratio
RR: Relative Risk
RD: Risk Difference
N.E.: not estimable
*: p < 0,05

Applied model for interaction test:
Any AE: logit(proportion) = treatment + age + treatment * age
Any AE, disease specific events excluded[1]: logit(proportion) = treatment + age + treatment * age
Any SAE: logit(proportion) = treatment + age + treatment * age
Any SAE, disease specific events excluded[1]: logit(proportion) = treatment + age + treatment * age
Any severe AE[2]: logit(proportion) = treatment + age + treatment * age
Any severe AE[2], disease specific events excluded[1]: logit(proportion) = treatment + age + treatment * age
Any AE leading to study discontinuation: logit(proportion) = treatment + age + treatment * age
Any AE leading to study drug discontinuation: logit(proportion) = treatment + age + treatment * age

Applied estimator for OR: unadjusted OR
Applied test for OR: Pearson Chi-Square test

[1] The following disease-specific Preferred Terms were excluded: see Table 11.0
[2] Definition of 'severe': CTCAE grade ≥ 3

Analysis population: A2304 SAF subpopulation "ACTIVE MS WITHOUT RELAPSES"

Table 11.2.2: Adverse Events by SOC and PT, Binary Analysis (SAF) by Age

	Treatment groups		Comparison		
	BAF312 (N=127)	**Placebo (N=61)**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
N'	127	61			
N' Age = 18-40 years	18	13			
N' Age = 41-55 years	95	33			
N' Age = >55 years	14	15			
GENERAL DISORDERS AND ADMINISTRATION SITE CONDITIONS					
Interaction test:	N.E.				
Age = 18-40 years	4 (22,2)	3 (23,1)	0,95 [0,17; 5,23] 0,955	0,96 [0,26; 3,59] 0,955	-0,01 [-0,31; 0,29] 0,955
Age = 41-55 years	27 (28,4)	2 (6,1)	6,15 [1,38; 27,52] 0,008 *	4,69 [1,18; 18,65] 0,028 *	0,22 [0,10; 0,35] <0,001 *
Age = >55 years	0 (0,0)	1 (6,7)	0,33 [0,01; 8,88] 0,326	0,36 [0,02; 8,07] 0,516	-0,07 [-0,19; 0,06] 0,301
INVESTIGATIONS					
Interaction test:	p=0,638				
Age = 18-40 years	5 (27,8)	1 (7,7)	4,62 [0,47; 45,39] 0,162	3,61 [0,48; 27,36] 0,214	0,20 [-0,05; 0,45] 0,119
Age = 41-55 years	31 (32,6)	4 (12,1)	3,51 [1,13; 10,87] 0,023 *	2,69 [1,03; 7,05] 0,044 *	0,21 [0,06; 0,35] 0,006 *
Age = >55 years	5 (35,7)	4 (26,7)	1,53 [0,31; 7,44] 0,599	1,34 [0,45; 4,00] 0,601	0,09 [-0,25; 0,43] 0,598

N': Number of patients in the analysis
CI: Confidence Interval
OR: Odds Ratio
RR: Relative Risk
RD: Risk Difference
N.E.: not estimable
*: p < 0,05

Applied model for interaction test: logit(proportion) = treatment + age + treatment * age

Applied estimator for OR: unadjusted OR
Applied test for OR: Pearson Chi-Square test

SOCs/PTs are only displayed in this subgroup analysis, if the p-value for RR in the entire population is significant (p<0.05).

Analysis population: A2304 SAF subpopulation "ACTIVE MS WITHOUT RELAPSES"

Table 11.2.3: Serious Adverse Events by SOC and PT, Binary Analysis (SAF) by Age

There are no data meeting the display criteria for this table.

Table 11.2.4: Severe Adverse Events by SOC and PT, Binary Analysis (SAF) by Age

There are no data meeting the display criteria for this table.

Table 11.2.5: Adverse Events of Special Interest, Binary Analysis (SAF) by Age

	Treatment groups		Comparison		
	BAF312 (N=127)	**Placebo (N=61)**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
N'	127	61			
N' Age = 18-40 years	18	13			
N' Age = 41-55 years	95	33			
N' Age = >55 years	14	15			
Infections and infestations					
Interaction test:	p=0,156				
Age = 18-40 years	4 (22,2)	4 (30,8)	0,64 [0,13; 3,25] 0,592	0,72 [0,22; 2,37] 0,591	-0,09 [-0,40; 0,23] 0,596
Age = 41-55 years	55 (57,9)	13 (39,4)	2,12 [0,94; 4,75] 0,067	1,47 [0,93; 2,32] 0,098	0,19 [-0,01; 0,38] 0,062
Age = >55 years	6 (42,9)	9 (60,0)	0,50 [0,11; 2,19] 0,356	0,71 [0,34; 1,49] 0,368	-0,17 [-0,53; 0,19] 0,349
Herpes simplex virus infections					
Interaction test:	N.E.				
Age = 18-40 years	0 (0,0)	0 (0,0)	-	-	-
Age = 41-55 years	4 (4,2)	1 (3,0)	1,41 [0,15; 13,06] 0,763	1,39 [0,16; 11,99] 0,765	0,01 [-0,06; 0,08] 0,745
Age = >55 years	0 (0,0)	0 (0,0)	-	-	-
Varicella-zoster virus infections					
Interaction test:	N.E.				
Age = 18-40 years	0 (0,0)	0 (0,0)	-	-	-
Age = 41-55 years	1 (1,1)	0 (0,0)	1,06 [0,04; 26,74] 0,554	1,06 [0,04; 25,46] 0,970	0,01 [-0,01; 0,03] 0,315
Age = >55 years	0 (0,0)	0 (0,0)	-	-	-
Lymphopenia					
Interaction test:	N.E.				
Age = 18-40 years	1 (5,6)	0 (0,0)	2,31 [0,09; 61,41] 0,388	2,21 [0,10; 50,32] 0,619	0,06 [-0,05; 0,16] 0,303
Age = 41-55 years	1 (1,1)	0 (0,0)	1,06 [0,04; 26,74] 0,554	1,06 [0,04; 25,46] 0,970	0,01 [-0,01; 0,03] 0,315
Age = >55 years	0 (0,0)	0 (0,0)	-	-	-

	Treatment groups		Comparison		
	BAF312 (N=127)	**Placebo (N=61)**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Macular edema					
Interaction test:	N.E.				
Age = 18-40 years	0 (0,0)	0 (0,0)	-	-	-
Age = 41-55 years	2 (2,1)	0 (0,0)	1,79 [0,08; 38,28] 0,401	1,77 [0,09; 35,96] 0,710	0,02 [-0,01; 0,05] 0,153
Age = >55 years	0 (0,0)	1 (6,7)	0,33 [0,01; 8,88] 0,326	0,36 [0,02; 8,07] 0,516	-0,07 [-0,19; 0,06] 0,301
Abnormal hepatic enzymes					
Interaction test:	p=0,994				
Age = 18-40 years	3 (16,7)	1 (7,7)	2,40 [0,22; 26,12] 0,462	2,17 [0,25; 18,56] 0,480	0,09 [-0,14; 0,31] 0,434
Age = 41-55 years	14 (14,7)	2 (6,1)	2,68 [0,58; 12,48] 0,194	2,43 [0,58; 10,14] 0,223	0,09 [-0,02; 0,19] 0,116
Age = >55 years	2 (14,3)	1 (6,7)	2,33 [0,19; 29,04] 0,501	2,14 [0,22; 21,10] 0,514	0,08 [-0,15; 0,30] 0,502
Malignancies					
Interaction test:	N.E.				
Age = 18-40 years	0 (0,0)	0 (0,0)	-	-	-
Age = 41-55 years	0 (0,0)	0 (0,0)	-	-	-
Age = >55 years	0 (0,0)	1 (6,7)	0,33 [0,01; 8,88] 0,326	0,36 [0,02; 8,07] 0,516	-0,07 [-0,19; 0,06] 0,301
Hypertension					
Interaction test:	N.E.				
Age = 18-40 years	0 (0,0)	0 (0,0)	-	-	-
Age = 41-55 years	16 (16,8)	5 (15,2)	1,13 [0,38; 3,38] 0,821	1,11 [0,44; 2,80] 0,822	0,02 [-0,13; 0,16] 0,818
Age = >55 years	1 (7,1)	0 (0,0)	3,44 [0,13; 91,79] 0,292	3,20 [0,14; 72,62] 0,465	0,07 [-0,06; 0,21] 0,299
Seizures					
Interaction test:	N.E.				
Age = 18-40 years	0 (0,0)	0 (0,0)	-	-	-
Age = 41-55 years	0 (0,0)	0 (0,0)	-	-	-
Age = >55 years	0 (0,0)	0 (0,0)	-	-	-

	Treatment groups		Comparison		
	BAF312 (N=127)	**Placebo (N=61)**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Thromboembolic events					
Interaction test:	N.E.				
Age = 18-40 years	0 (0,0)	0 (0,0)	-	-	-
Age = 41-55 years	4 (4,2)	1 (3,0)	1,41 [0,15; 13,06] 0,763	1,39 [0,16; 11,99] 0,765	0,01 [-0,06; 0,08] 0,745
Age = >55 years	1 (7,1)	0 (0,0)	3,44 [0,13; 91,79] 0,292	3,20 [0,14; 72,62] 0,465	0,07 [-0,06; 0,21] 0,299
Respiratory disorders					
Interaction test:	N.E.				
Age = 18-40 years	1 (5,6)	1 (7,7)	0,71 [0,04; 12,43] 0,811	0,72 [0,05; 10,52] 0,812	-0,02 [-0,20; 0,16] 0,815
Age = 41-55 years	21 (22,1)	6 (18,2)	1,28 [0,47; 3,50] 0,634	1,22 [0,54; 2,75] 0,639	0,04 [-0,12; 0,20] 0,622
Age = >55 years	0 (0,0)	4 (26,7)	0,09 [0,00; 1,81] 0,037 *	0,12 [0,01; 2,02] 0,140	-0,27 [-0,49; -0,04] 0,020 *
Peripheral edema/swelling					
Interaction test:	N.E.				
Age = 18-40 years	0 (0,0)	1 (7,7)	0,23 [0,01; 5,99] 0,232	0,25 [0,01; 5,59] 0,379	-0,08 [-0,22; 0,07] 0,298
Age = 41-55 years	6 (6,3)	0 (0,0)	4,87 [0,27; 88,76] 0,139	4,60 [0,27; 79,57] 0,294	0,06 [0,01; 0,11] 0,011 *
Age = >55 years	0 (0,0)	0 (0,0)	-	-	-

N': Number of patients in the analysis
CI: Confidence Interval
OR: Odds Ratio
RR: Relative Risk
RD: Risk Difference
N.E.: not estimable
*: p < 0,05

Applied model for interaction test: logit(proportion) = treatment + age + treatment * age

Applied estimator for OR: unadjusted OR
Applied test for OR: Pearson Chi-Square test

Analysis population: A2304 SAF subpopulation "ACTIVE MS WITHOUT RELAPSES"

	Treatment groups		Comparison		
	BAF312 (N=127)	**Placebo (N=61)**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
N'	127	61			
N' Age = 18-40 years	18	13			
N' Age = 41-55 years	95	33			
N' Age = >55 years	14	15			
Asthma/bronchospasm					
Interaction test:	N.E.				
Age = 18-40 years	0 (0,0)	0 (0,0)	-	-	-
Age = 41-55 years	1 (1,1)	0 (0,0)	1,06 [0,04; 26,74] 0,554	1,06 [0,04; 25,46] 0,970	0,01 [-0,01; 0,03] 0,315
Age = >55 years	0 (0,0)	0 (0,0)	-	-	-
Pregnancy and neonatal topics					
Interaction test:	N.E.				
Age = 18-40 years	0 (0,0)	0 (0,0)	-	-	-
Age = 41-55 years	1 (1,1)	0 (0,0)	1,06 [0,04; 26,74] 0,554	1,06 [0,04; 25,46] 0,970	0,01 [-0,01; 0,03] 0,315
Age = >55 years	0 (0,0)	0 (0,0)	-	-	-
Bradyarrhythmias and bradycardia					
Interaction test:	N.E.				
Age = 18-40 years	4 (22,2)	1 (7,7)	3,43 [0,34; 34,99] 0,278	2,89 [0,36; 22,94] 0,316	0,15 [-0,10; 0,39] 0,236
Age = 41-55 years	6 (6,3)	0 (0,0)	4,87 [0,27; 88,76] 0,139	4,60 [0,27; 79,57] 0,294	0,06 [0,01; 0,11] 0,011 *
Age = >55 years	1 (7,1)	0 (0,0)	3,44 [0,13; 91,79] 0,292	3,20 [0,14; 72,62] 0,465	0,07 [-0,06; 0,21] 0,299

N': Number of patients in the analysis
CI: Confidence Interval
OR: Odds Ratio
RR: Relative Risk
RD: Risk Difference
N.E.: not estimable
*: p < 0,05

Applied model for interaction test: logit(proportion) = treatment + age + treatment * age

Applied estimator for OR: unadjusted OR
Applied test for OR: Pearson Chi-Square test

Analysis population: A2304 SAF subpopulation "ACTIVE MS WITHOUT RELAPSES"

11.3 Subgroup: Gender

Table 11.3.1: Adverse Events, Binary Analysis (SAF) by Gender

	Treatment groups		Comparison		
	BAF312 (N=127)	Placebo (N=61)	OR [95% CI] p-value	RR [95% CI] p-value	RD [95% CI] p-value
N'	127	61			
N' Gender = Male	51	24			
N' Gender = Female	76	37			
Any AE					
Interaction test:	p=0,028 *				
Gender = Male	43 (84,3)	21 (87,5)	0,77 [0,18; 3,20] 0,716	0,96 [0,80; 1,17] 0,705	-0,03 [-0,20; 0,13] 0,706
Gender = Female	71 (93,4)	26 (70,3)	6,01 [1,90; 18,95] 0,001 *	1,33 [1,07; 1,65] 0,010 *	0,23 [0,07; 0,39] 0,004 *
Any AE, disease specific events excluded[1]					
Interaction test:	p=0,103				
Gender = Male	41 (80,4)	20 (83,3)	0,82 [0,23; 2,94] 0,760	0,96 [0,77; 1,21] 0,754	-0,03 [-0,21; 0,16] 0,755
Gender = Female	67 (88,2)	26 (70,3)	3,15 [1,17; 8,48] 0,019 *	1,25 [1,00; 1,57] 0,048 *	0,18 [0,01; 0,34] 0,033 *
Any SAE					
Interaction test:	p=0,088				
Gender = Male	4 (7,8)	6 (25,0)	0,26 [0,06; 1,01] 0,041 *	0,31 [0,10; 1,01] 0,052	-0,17 [-0,36; 0,02] 0,074
Gender = Female	12 (15,8)	5 (13,5)	1,20 [0,39; 3,70] 0,751	1,17 [0,44; 3,07] 0,752	0,02 [-0,11; 0,16] 0,745
Any SAE, disease specific events excluded[1]					
Interaction test:	p=0,162				
Gender = Male	4 (7,8)	5 (20,8)	0,32 [0,08; 1,34] 0,106	0,38 [0,11; 1,28] 0,117	-0,13 [-0,31; 0,05] 0,154
Gender = Female	8 (10,5)	3 (8,1)	1,33 [0,33; 5,35] 0,684	1,30 [0,37; 4,61] 0,686	0,02 [-0,09; 0,14] 0,672

	Treatment groups		Comparison		
	BAF312 (N=127)	**Placebo (N=61)**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Any severe AE[2]					
Interaction test:	N.E.				
Gender = Male	0 (0,0)	5 (20,8)	0,03 [0,00; 0,65] 0,001 *	0,04 [0,00; 0,76] 0,032 *	-0,21 [-0,37; -0,05] 0,012 *
Gender = Female	11 (14,5)	5 (13,5)	1,08 [0,35; 3,38] 0,891	1,07 [0,40; 2,86] 0,891	0,01 [-0,13; 0,15] 0,890
Any severe AE[2], disease specific events excluded[1]					
Interaction test:	N.E.				
Gender = Male	0 (0,0)	4 (16,7)	0,04 [0,00; 0,86] 0,003 *	0,05 [0,00; 0,95] 0,046 *	-0,17 [-0,32; -0,02] 0,028 *
Gender = Female	9 (11,8)	4 (10,8)	1,11 [0,32; 3,87] 0,872	1,10 [0,36; 3,32] 0,872	0,01 [-0,11; 0,13] 0,870
Any AE leading to study discontinuation					
Interaction test:	p=0,721				
Gender = Male	1 (2,0)	1 (4,2)	0,46 [0,03; 7,68] 0,580	0,47 [0,03; 7,21] 0,588	-0,02 [-0,11; 0,07] 0,625
Gender = Female	1 (1,3)	2 (5,4)	0,23 [0,02; 2,66] 0,204	0,24 [0,02; 2,60] 0,242	-0,04 [-0,12; 0,04] 0,299

	Treatment groups		Comparison		
	BAF312 (N=127)	**Placebo (N=61)**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Any AE leading to study drug discontinuation					
Interaction test:	p=0,257				
Gender = Male	1 (2,0)	2 (8,3)	0,22 [0,02; 2,56] 0,189	0,24 [0,02; 2,47] 0,228	-0,06 [-0,18; 0,05] 0,285
Gender = Female	5 (6,6)	2 (5,4)	1,23 [0,23; 6,67] 0,808	1,22 [0,25; 5,98] 0,809	0,01 [-0,08; 0,10] 0,802

N': Number of patients in the analysis
CI: Confidence Interval
OR: Odds Ratio
RR: Relative Risk
RD: Risk Difference
N.E.: not estimable
*: p < 0,05

Applied model for interaction test:
Any AE: logit(proportion) = treatment + gender + treatment * gender
Any AE, disease specific events excluded[1]: logit(proportion) = treatment + gender + treatment * gender
Any SAE: logit(proportion) = treatment + gender + treatment * gender
Any SAE, disease specific events excluded[1]: logit(proportion) = treatment + gender + treatment * gender
Any severe AE[2]: logit(proportion) = treatment + gender + treatment * gender
Any severe AE[2], disease specific events excluded[1]: logit(proportion) = treatment + gender + treatment * gender
Any AE leading to study discontinuation: logit(proportion) = treatment + gender + treatment * gender
Any AE leading to study drug discontinuation: logit(proportion) = treatment + gender + treatment * gender

Applied estimator for OR: unadjusted OR
Applied test for OR: Pearson Chi-Square test

[1] The following disease-specific Preferred Terms were excluded: see Table 11.0
[2] Definition of 'severe': CTCAE grade ≥ 3

Analysis population: A2304 SAF subpopulation "ACTIVE MS WITHOUT RELAPSES"

Table 11.3.2: Adverse Events by SOC and PT, Binary Analysis (SAF) by Gender

	Treatment groups		Comparison		
	BAF312 (N=127)	**Placebo (N=61)**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
N'	127	61			
N' Gender = Male	51	24			
N' Gender = Female	76	37			
GENERAL DISORDERS AND ADMINISTRATION SITE CONDITIONS					
Interaction test:	p=0,092				
Gender = Male	10 (19,6)	4 (16,7)	1,22 [0,34; 4,37] 0,760	1,18 [0,41; 3,37] 0,762	0,03 [-0,16; 0,21] 0,755
Gender = Female	21 (27,6)	2 (5,4)	6,68 [1,47; 30,28] 0,006 *	5,11 [1,27; 20,65] 0,022 *	0,22 [0,10; 0,35] <0,001 *
INVESTIGATIONS					
Interaction test:	p=0,653				
Gender = Male	17 (33,3)	3 (12,5)	3,50 [0,91; 13,40] 0,057	2,67 [0,86; 8,23] 0,088	0,21 [0,02; 0,39] 0,027 *
Gender = Female	24 (31,6)	6 (16,2)	2,38 [0,88; 6,48] 0,083	1,95 [0,87; 4,35] 0,104	0,15 [-0,00; 0,31] 0,057

N': Number of patients in the analysis
CI: Confidence Interval
OR: Odds Ratio
RR: Relative Risk
RD: Risk Difference
*: p < 0,05

Applied model for interaction test: logit(proportion) = treatment + gender + treatment * gender

Applied estimator for OR: unadjusted OR
Applied test for OR: Pearson Chi-Square test

SOCs/PTs are only displayed in this subgroup analysis, if the p-value for RR in the entire population is significant (p<0.05).

Analysis population: A2304 SAF subpopulation "ACTIVE MS WITHOUT RELAPSES"

Table 11.3.3: Serious Adverse Events by SOC and PT, Binary Analysis (SAF) by Gender

There are no data meeting the display criteria for this table.

Table 11.3.4: Severe Adverse Events by SOC and PT, Binary Analysis (SAF) by Gender

There are no data meeting the display criteria for this table.

Table 11.3.5: Adverse Events of Special Interest, Binary Analysis (SAF) by Gender

	Treatment groups		Comparison		
	BAF312 (N=127)	**Placebo (N=61)**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
N'	127	61			
N' Gender = Male	51	24			
N' Gender = Female	76	37			
Infections and infestations					
Interaction test:	p=0,510				
Gender = Male	20 (39,2)	6 (25,0)	1,94 [0,66; 5,71] 0,228	1,57 [0,72; 3,40] 0,253	0,14 [-0,08; 0,36] 0,203
Gender = Female	45 (59,2)	20 (54,1)	1,23 [0,56; 2,72] 0,603	1,10 [0,77; 1,56] 0,611	0,05 [-0,14; 0,25] 0,604
Herpes simplex virus infections					
Interaction test:	N.E.				
Gender = Male	0 (0,0)	0 (0,0)	-	-	-
Gender = Female	4 (5,3)	1 (2,7)	2,00 [0,22; 18,55] 0,535	1,95 [0,23; 16,82] 0,545	0,03 [-0,05; 0,10] 0,489
Varicella-zoster virus infections					
Interaction test:	N.E.				
Gender = Male	0 (0,0)	0 (0,0)	-	-	-
Gender = Female	1 (1,3)	0 (0,0)	1,49 [0,06; 37,46] 0,483	1,48 [0,06; 35,49] 0,809	0,01 [-0,01; 0,04] 0,314
Lymphopenia					
Interaction test:	N.E.				
Gender = Male	0 (0,0)	0 (0,0)	-	-	-
Gender = Female	2 (2,6)	0 (0,0)	2,52 [0,12; 53,76] 0,319	2,47 [0,12; 50,13] 0,557	0,03 [-0,01; 0,06] 0,152
Macular edema					
Interaction test:	N.E.				
Gender = Male	0 (0,0)	1 (4,2)	0,15 [0,01; 3,87] 0,142	0,16 [0,01; 3,80] 0,257	-0,04 [-0,12; 0,04] 0,307
Gender = Female	2 (2,6)	0 (0,0)	2,52 [0,12; 53,76] 0,319	2,47 [0,12; 50,13] 0,557	0,03 [-0,01; 0,06] 0,152

	Treatment groups		Comparison		
	BAF312 (N=127)	**Placebo (N=61)**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Abnormal hepatic enzymes					
Interaction test:	p=0,316				
Gender = Male	9 (17,6)	3 (12,5)	1,50 [0,37; 6,13] 0,571	1,41 [0,42; 4,75] 0,577	0,05 [-0,12; 0,22] 0,550
Gender = Female	10 (13,2)	1 (2,7)	5,45 [0,67; 44,34] 0,078	4,87 [0,65; 36,62] 0,124	0,10 [0,01; 0,20] 0,026 *
Malignancies					
Interaction test:	N.E.				
Gender = Male	0 (0,0)	1 (4,2)	0,15 [0,01; 3,87] 0,142	0,16 [0,01; 3,80] 0,257	-0,04 [-0,12; 0,04] 0,307
Gender = Female	0 (0,0)	0 (0,0)	-	-	-
Hypertension					
Interaction test:	p=0,050 *				
Gender = Male	5 (9,8)	4 (16,7)	0,54 [0,13; 2,24] 0,394	0,59 [0,17; 2,00] 0,395	-0,07 [-0,24; 0,10] 0,429
Gender = Female	12 (15,8)	1 (2,7)	6,75 [0,84; 54,05] 0,041 *	5,84 [0,79; 43,25] 0,084	0,13 [0,03; 0,23] 0,008 *
Seizures					
Interaction test:	N.E.				
Gender = Male	0 (0,0)	0 (0,0)	-	-	-
Gender = Female	0 (0,0)	0 (0,0)	-	-	-
Thromboembolic events					
Interaction test:	N.E.				
Gender = Male	2 (3,9)	1 (4,2)	0,94 [0,08; 10,89] 0,960	0,94 [0,09; 9,88] 0,960	-0,00 [-0,10; 0,09] 0,960
Gender = Female	3 (3,9)	0 (0,0)	3,57 [0,18; 70,96] 0,221	3,45 [0,18; 65,19] 0,408	0,04 [-0,00; 0,08] 0,077
Respiratory disorders					
Interaction test:	p=0,175				
Gender = Male	9 (17,6)	2 (8,3)	2,36 [0,47; 11,87] 0,288	2,12 [0,50; 9,06] 0,312	0,09 [-0,06; 0,25] 0,230
Gender = Female	13 (17,1)	9 (24,3)	0,64 [0,25; 1,68] 0,363	0,70 [0,33; 1,49] 0,360	-0,07 [-0,23; 0,09] 0,383

	Treatment groups		Comparison		
	BAF312 (N=127)	**Placebo (N=61)**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Peripheral edema/swelling					
Interaction test:	N.E.				
Gender = Male	0 (0,0)	1 (4,2)	0,15 [0,01; 3,87] 0,142	0,16 [0,01; 3,80] 0,257	-0,04 [-0,12; 0,04] 0,307
Gender = Female	6 (7,9)	0 (0,0)	6,91 [0,38; 126,12] 0,079	6,42 [0,37; 110,92] 0,201	0,08 [0,02; 0,14] 0,011 *

N': Number of patients in the analysis
CI: Confidence Interval
OR: Odds Ratio
RR: Relative Risk
RD: Risk Difference
N.E.: not estimable
*: p < 0,05

Applied model for interaction test: logit(proportion) = treatment + gender + treatment * gender

Applied estimator for OR: unadjusted OR
Applied test for OR: Pearson Chi-Square test

Analysis population: A2304 SAF subpopulation "ACTIVE MS WITHOUT RELAPSES"

	Treatment groups		Comparison		
	BAF312 (N=127)	**Placebo (N=61)**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
N'	127	61			
N' Gender = Male	51	24			
N' Gender = Female	76	37			
Asthma/bronchospasm					
Interaction test:	N.E.				
Gender = Male	0 (0,0)	0 (0,0)	-	-	-
Gender = Female	1 (1,3)	0 (0,0)	1,49 [0,06; 37,46] 0,483	1,48 [0,06; 35,49] 0,809	0,01 [-0,01; 0,04] 0,314
Pregnancy and neonatal topics					
Interaction test:	N.E.				
Gender = Male	1 (2,0)	0 (0,0)	1,46 [0,06; 37,04] 0,490	1,44 [0,06; 34,16] 0,821	0,02 [-0,02; 0,06] 0,313
Gender = Female	0 (0,0)	0 (0,0)	-	-	-
Bradyarrhythmias and bradycardia					
Interaction test:	N.E.				
Gender = Male	7 (13,7)	1 (4,2)	3,66 [0,42; 31,57] 0,211	3,29 [0,43; 25,29] 0,252	0,10 [-0,03; 0,22] 0,130
Gender = Female	4 (5,3)	0 (0,0)	4,66 [0,24; 88,78] 0,155	4,44 [0,25; 80,38] 0,313	0,05 [0,00; 0,10] 0,040 *

N': Number of patients in the analysis
CI: Confidence Interval
OR: Odds Ratio
RR: Relative Risk
RD: Risk Difference
N.E.: not estimable
*: p < 0,05

Applied model for interaction test: logit(proportion) = treatment + gender + treatment * gender

Applied estimator for OR: unadjusted OR
Applied test for OR: Pearson Chi-Square test

Analysis population: A2304 SAF subpopulation "ACTIVE MS WITHOUT RELAPSES"

11.4 Subgroup: Previous MS DMT

Table 11.4.1: Adverse Events, Binary Analysis (SAF) by Previous MS DMT

	Treatment groups		Comparison		
	BAF312 (N=127)	**Placebo (N=61)**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
N'	127	61			
N' Previous MS DMT = No	20	17			
N' Previous MS DMT = Yes	107	44			
Any AE					
Interaction test:	p=0,705				
Previous MS DMT = No	18 (90,0)	14 (82,4)	1,93 [0,28; 13,16] 0,498	1,09 [0,84; 1,42] 0,510	0,08 [-0,15; 0,30] 0,503
Previous MS DMT = Yes	96 (89,7)	33 (75,0)	2,91 [1,15; 7,33] 0,020 *	1,20 [1,00; 1,44] 0,054	0,15 [0,01; 0,29] 0,040 *
Any AE, disease specific events excluded[1]					
Interaction test:	p=0,978				
Previous MS DMT = No	18 (90,0)	14 (82,4)	1,93 [0,28; 13,16] 0,498	1,09 [0,84; 1,42] 0,510	0,08 [-0,15; 0,30] 0,503
Previous MS DMT = Yes	90 (84,1)	32 (72,7)	1,99 [0,86; 4,61] 0,107	1,16 [0,95; 1,41] 0,152	0,11 [-0,03; 0,26] 0,133
Any SAE					
Interaction test:	p=0,096				
Previous MS DMT = No	5 (25,0)	2 (11,8)	2,50 [0,42; 14,96] 0,306	2,13 [0,47; 9,59] 0,327	0,13 [-0,11; 0,38] 0,287
Previous MS DMT = Yes	11 (10,3)	9 (20,5)	0,45 [0,17; 1,17] 0,094	0,50 [0,22; 1,13] 0,095	-0,10 [-0,23; 0,03] 0,132
Any SAE, disease specific events excluded[1]					
Interaction test:	p=0,111				
Previous MS DMT = No	5 (25,0)	2 (11,8)	2,50 [0,42; 14,96] 0,306	2,13 [0,47; 9,59] 0,327	0,13 [-0,11; 0,38] 0,287
Previous MS DMT = Yes	7 (6,5)	6 (13,6)	0,44 [0,14; 1,40] 0,158	0,48 [0,17; 1,35] 0,163	-0,07 [-0,18; 0,04] 0,213

	Treatment groups		Comparison		
	BAF312 (N=127)	**Placebo (N=61)**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Any severe AE[2]					
Interaction test:	p=0,906				
Previous MS DMT = No	1 (5,0)	2 (11,8)	0,39 [0,03; 4,78] 0,452	0,43 [0,04; 4,29] 0,468	-0,07 [-0,25; 0,11] 0,463
Previous MS DMT = Yes	10 (9,3)	8 (18,2)	0,46 [0,17; 1,27] 0,128	0,51 [0,22; 1,22] 0,130	-0,09 [-0,21; 0,04] 0,171
Any severe AE[2], disease specific events excluded[1]					
Interaction test:	p=0,852				
Previous MS DMT = No	1 (5,0)	2 (11,8)	0,39 [0,03; 4,78] 0,452	0,43 [0,04; 4,29] 0,468	-0,07 [-0,25; 0,11] 0,463
Previous MS DMT = Yes	8 (7,5)	6 (13,6)	0,51 [0,17; 1,57] 0,236	0,55 [0,20; 1,49] 0,238	-0,06 [-0,17; 0,05] 0,285
Any AE leading to study discontinuation					
Interaction test:	N.E.				
Previous MS DMT = No	0 (0,0)	0 (0,0)	-	-	-
Previous MS DMT = Yes	2 (1,9)	3 (6,8)	0,26 [0,04; 1,62] 0,122	0,27 [0,05; 1,58] 0,148	-0,05 [-0,13; 0,03] 0,218

	Treatment groups		Comparison		
	BAF312 (N=127)	**Placebo (N=61)**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Any AE leading to study drug discontinuation					
Interaction test:	N.E.				
Previous MS DMT = No	2 (10,0)	0 (0,0)	4,73 [0,21; 105,61] 0,180	4,29 [0,22; 83,57] 0,337	0,10 [-0,03; 0,23] 0,136
Previous MS DMT = Yes	4 (3,7)	4 (9,1)	0,39 [0,09; 1,63] 0,182	0,41 [0,11; 1,57] 0,194	-0,05 [-0,15; 0,04] 0,255

N': Number of patients in the analysis
CI: Confidence Interval
OR: Odds Ratio
RR: Relative Risk
RD: Risk Difference
N.E.: not estimable
*: p < 0,05

Applied model for interaction test:
Any AE: logit(proportion) = treatment + previous MS DMT + treatment * previous MS DMT
Any AE, disease specific events excluded[1]: logit(proportion) = treatment + previous MS DMT + treatment * previous MS DMT
Any SAE: logit(proportion) = treatment + previous MS DMT + treatment * previous MS DMT
Any SAE, disease specific events excluded[1]: logit(proportion) = treatment + previous MS DMT + treatment * previous MS DMT
Any severe AE[2]: logit(proportion) = treatment + previous MS DMT + treatment * previous MS DMT
Any severe AE[2], disease specific events excluded[1]: logit(proportion) = treatment + previous MS DMT + treatment * previous MS DMT
Any AE leading to study discontinuation: logit(proportion) = treatment + previous MS DMT + treatment * previous MS DMT
Any AE leading to study drug discontinuation: logit(proportion) = treatment + previous MS DMT + treatment * previous MS DMT

Applied estimator for OR: unadjusted OR
Applied test for OR: Pearson Chi-Square test

[1] The following disease-specific Preferred Terms were excluded: see Table 11.0
[2] Definition of 'severe': CTCAE grade ≥ 3

Analysis population: A2304 SAF subpopulation "ACTIVE MS WITHOUT RELAPSES"

Table 11.4.2: Adverse Events by SOC and PT, Binary Analysis (SAF) by Previous MS DMT

	Treatment groups		Comparison		
	BAF312 (N=127)	**Placebo (N=61)**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
N'	127	61			
N' Previous MS DMT = No	20	17			
N' Previous MS DMT = Yes	107	44			
GENERAL DISORDERS AND ADMINISTRATION SITE CONDITIONS					
Interaction test:	p=0,011 *				
Previous MS DMT = No	2 (10,0)	4 (23,5)	0,36 [0,06; 2,28] 0,266	0,43 [0,09; 2,04] 0,285	-0,14 [-0,38; 0,11] 0,271
Previous MS DMT = Yes	29 (27,1)	2 (4,5)	7,81 [1,78; 34,34] 0,002 *	5,96 [1,49; 23,92] 0,012 *	0,23 [0,12; 0,33] <0,001 *
INVESTIGATIONS					
Interaction test:	p=0,802				
Previous MS DMT = No	9 (45,0)	4 (23,5)	2,66 [0,64; 11,06] 0,173	1,91 [0,71; 5,12] 0,197	0,21 [-0,08; 0,51] 0,156
Previous MS DMT = Yes	32 (29,9)	5 (11,4)	3,33 [1,20; 9,22] 0,016 *	2,63 [1,10; 6,31] 0,030 *	0,19 [0,06; 0,31] 0,004 *

N': Number of patients in the analysis
CI: Confidence Interval
OR: Odds Ratio
RR: Relative Risk
RD: Risk Difference
*: p < 0,05

Applied model for interaction test: logit(proportion) = treatment + previous MS DMT + treatment * previous MS DMT

Applied estimator for OR: unadjusted OR
Applied test for OR: Pearson Chi-Square test

SOCs/PTs are only displayed in this subgroup analysis, if the p-value for RR in the entire population is significant (p<0.05).

Analysis population: A2304 SAF subpopulation "ACTIVE MS WITHOUT RELAPSES"

Table 11.4.3: Serious Adverse Events by SOC and PT, Binary Analysis (SAF) by Previous MS DMT

There are no data meeting the display criteria for this table.

Table 11.4.4: Severe Adverse Events by SOC and PT, Binary Analysis (SAF) by Previous MS DMT

There are no data meeting the display criteria for this table.

Table 11.4.5: Adverse Events of Special Interest, Binary Analysis (SAF) by Previous MS DMT

	Treatment groups		Comparison		
	BAF312 (N=127)	**Placebo (N=61)**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
N'	127	61			
N' Previous MS DMT = No	20	17			
N' Previous MS DMT = Yes	107	44			
Infections and infestations					
Interaction test:	p=0,551				
Previous MS DMT = No	8 (40,0)	7 (41,2)	0,95 [0,26; 3,55] 0,942	0,97 [0,44; 2,12] 0,942	-0,01 [-0,33; 0,31] 0,942
Previous MS DMT = Yes	57 (53,3)	19 (43,2)	1,50 [0,74; 3,04] 0,260	1,23 [0,84; 1,81] 0,282	0,10 [-0,07; 0,28] 0,256
Herpes simplex virus infections					
Interaction test:	N.E.				
Previous MS DMT = No	0 (0,0)	1 (5,9)	0,27 [0,01; 7,03] 0,272	0,29 [0,01; 6,59] 0,434	-0,06 [-0,17; 0,05] 0,303
Previous MS DMT = Yes	4 (3,7)	0 (0,0)	3,87 [0,20; 73,40] 0,194	3,75 [0,21; 68,22] 0,372	0,04 [0,00; 0,07] 0,042 *
Varicella-zoster virus infections					
Interaction test:	N.E.				
Previous MS DMT = No	0 (0,0)	0 (0,0)	-	-	-
Previous MS DMT = Yes	1 (0,9)	0 (0,0)	1,25 [0,05; 31,36] 0,520	1,25 [0,05; 30,11] 0,891	0,01 [-0,01; 0,03] 0,315
Lymphopenia					
Interaction test:	N.E.				
Previous MS DMT = No	0 (0,0)	0 (0,0)	-	-	-
Previous MS DMT = Yes	2 (1,9)	0 (0,0)	2,11 [0,10; 44,82] 0,361	2,08 [0,10; 42,54] 0,633	0,02 [-0,01; 0,04] 0,153
Macular edema					
Interaction test:	N.E.				
Previous MS DMT = No	0 (0,0)	0 (0,0)	-	-	-
Previous MS DMT = Yes	2 (1,9)	1 (2,3)	0,82 [0,07; 9,27] 0,872	0,82 [0,08; 8,84] 0,872	-0,00 [-0,06; 0,05] 0,877

	Treatment groups		Comparison		
	BAF312 (N=127)	**Placebo (N=61)**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Abnormal hepatic enzymes					
Interaction test:	p=0,329				
Previous MS DMT = No	6 (30,0)	1 (5,9)	6,86 [0,73; 64,10] 0,062	5,10 [0,68; 38,29] 0,113	0,24 [0,01; 0,47] 0,040 *
Previous MS DMT = Yes	13 (12,1)	3 (6,8)	1,89 [0,51; 6,99] 0,333	1,78 [0,53; 5,95] 0,348	0,05 [-0,04; 0,15] 0,281
Malignancies					
Interaction test:	N.E.				
Previous MS DMT = No	0 (0,0)	0 (0,0)	-	-	-
Previous MS DMT = Yes	0 (0,0)	1 (2,3)	0,13 [0,01; 3,38] 0,118	0,14 [0,01; 3,35] 0,224	-0,02 [-0,07; 0,02] 0,312
Hypertension					
Interaction test:	p=0,709				
Previous MS DMT = No	3 (15,0)	2 (11,8)	1,32 [0,19; 9,02] 0,774	1,28 [0,24; 6,76] 0,775	0,03 [-0,19; 0,25] 0,772
Previous MS DMT = Yes	14 (13,1)	3 (6,8)	2,06 [0,56; 7,55] 0,268	1,92 [0,58; 6,35] 0,286	0,06 [-0,04; 0,16] 0,211
Seizures					
Interaction test:	N.E.				
Previous MS DMT = No	0 (0,0)	0 (0,0)	-	-	-
Previous MS DMT = Yes	0 (0,0)	0 (0,0)	-	-	-
Thromboembolic events					
Interaction test:	N.E.				
Previous MS DMT = No	1 (5,0)	1 (5,9)	0,84 [0,05; 14,57] 0,906	0,85 [0,06; 12,59] 0,906	-0,01 [-0,16; 0,14] 0,906
Previous MS DMT = Yes	4 (3,7)	0 (0,0)	3,87 [0,20; 73,40] 0,194	3,75 [0,21; 68,22] 0,372	0,04 [0,00; 0,07] 0,042 *
Respiratory disorders					
Interaction test:	p=0,038 *				
Previous MS DMT = No	2 (10,0)	6 (35,3)	0,20 [0,03; 1,19] 0,063	0,28 [0,07; 1,22] 0,091	-0,25 [-0,52; 0,01] 0,059
Previous MS DMT = Yes	20 (18,7)	5 (11,4)	1,79 [0,63; 5,13] 0,271	1,64 [0,66; 4,11] 0,286	0,07 [-0,05; 0,19] 0,229

	Treatment groups		Comparison		
	BAF312 (N=127)	**Placebo (N=61)**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Peripheral edema/swelling					
Interaction test:	N.E.				
Previous MS DMT = No	0 (0,0)	0 (0,0)	-	-	-
Previous MS DMT = Yes	6 (5,6)	1 (2,3)	2,55 [0,30; 21,86] 0,376	2,47 [0,31; 19,90] 0,397	0,03 [-0,03; 0,10] 0,292

N': Number of patients in the analysis
CI: Confidence Interval
OR: Odds Ratio
RR: Relative Risk
RD: Risk Difference
N.E.: not estimable
*: p < 0,05

Applied model for interaction test: logit(proportion) = treatment + previous MS DMT + treatment * previous MS DMT

Applied estimator for OR: unadjusted OR
Applied test for OR: Pearson Chi-Square test

Analysis population: A2304 SAF subpopulation "ACTIVE MS WITHOUT RELAPSES"

	Treatment groups		Comparison		
	BAF312 (N=127)	**Placebo (N=61)**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
N'	127	61			
N' Previous MS DMT = No	20	17			
N' Previous MS DMT = Yes	107	44			
Asthma/bronchospasm					
Interaction test:	N.E.				
Previous MS DMT = No	0 (0,0)	0 (0,0)	-	-	-
Previous MS DMT = Yes	1 (0,9)	0 (0,0)	1,25 [0,05; 31,36] 0,520	1,25 [0,05; 30,11] 0,891	0,01 [-0,01; 0,03] 0,315
Pregnancy and neonatal topics					
Interaction test:	N.E.				
Previous MS DMT = No	0 (0,0)	0 (0,0)	-	-	-
Previous MS DMT = Yes	1 (0,9)	0 (0,0)	1,25 [0,05; 31,36] 0,520	1,25 [0,05; 30,11] 0,891	0,01 [-0,01; 0,03] 0,315
Bradyarrhythmias and bradycardia					
Interaction test:	N.E.				
Previous MS DMT = No	3 (15,0)	0 (0,0)	7,00 [0,34; 145,81] 0,096	6,00 [0,33; 108,56] 0,225	0,15 [-0,01; 0,31] 0,060
Previous MS DMT = Yes	8 (7,5)	1 (2,3)	3,47 [0,42; 28,64] 0,220	3,29 [0,42; 25,53] 0,255	0,05 [-0,01; 0,12] 0,125

N': Number of patients in the analysis
CI: Confidence Interval
OR: Odds Ratio
RR: Relative Risk
RD: Risk Difference
N.E.: not estimable
*: p < 0,05

Applied model for interaction test: logit(proportion) = treatment + previous MS DMT + treatment * previous MS DMT

Applied estimator for OR: unadjusted OR
Applied test for OR: Pearson Chi-Square test

Analysis population: A2304 SAF subpopulation "ACTIVE MS WITHOUT RELAPSES"

11.5 Subgroup: Previous IFN-beta-1b Treatment

Table 11.5.1: Adverse Events, Binary Analysis (SAF) by Previous IFN-beta-1b Treatment

	Treatment groups		Comparison		
	BAF312 (N=127)	Placebo (N=61)	OR [95% CI] p-value	RR [95% CI] p-value	RD [95% CI] p-value
N'	127	61			
N' Previous IFN-beta-1b Treatment = No	82	48			
N' Previous IFN-beta-1b Treatment = Yes	45	13			
Any AE					
Interaction test:	p=0,681				
Previous IFN-beta-1b Treatment = No	74 (90,2)	38 (79,2)	2,43 [0,89; 6,67] 0,078	1,14 [0,97; 1,34] 0,112	0,11 [-0,02; 0,24] 0,099
Previous IFN-beta-1b Treatment = Yes	40 (88,9)	9 (69,2)	3,56 [0,79; 15,94] 0,085	1,28 [0,88; 1,87] 0,194	0,20 [-0,07; 0,46] 0,149
Any AE, disease specific events excluded[1]					
Interaction test:	p=0,528				
Previous IFN-beta-1b Treatment = No	71 (86,6)	38 (79,2)	1,70 [0,66; 4,36] 0,267	1,09 [0,92; 1,29] 0,297	0,07 [-0,06; 0,21] 0,287
Previous IFN-beta-1b Treatment = Yes	37 (82,2)	8 (61,5)	2,89 [0,75; 11,19] 0,115	1,34 [0,85; 2,10] 0,208	0,21 [-0,08; 0,49] 0,158
Any SAE					
Interaction test:	p=0,738				
Previous IFN-beta-1b Treatment = No	10 (12,2)	9 (18,8)	0,60 [0,23; 1,61] 0,307	0,65 [0,28; 1,49] 0,308	-0,07 [-0,20; 0,07] 0,327
Previous IFN-beta-1b Treatment = Yes	6 (13,3)	2 (15,4)	0,85 [0,15; 4,79] 0,850	0,87 [0,20; 3,79] 0,849	-0,02 [-0,24; 0,20] 0,855
Any SAE, disease specific events excluded[1]					
Interaction test:	p=0,753				
Previous IFN-beta-1b Treatment = No	8 (9,8)	6 (12,5)	0,76 [0,25; 2,33] 0,626	0,78 [0,29; 2,11] 0,626	-0,03 [-0,14; 0,09] 0,636
Previous IFN-beta-1b Treatment = Yes	4 (8,9)	2 (15,4)	0,54 [0,09; 3,32] 0,498	0,58 [0,12; 2,81] 0,497	-0,06 [-0,28; 0,15] 0,550

	Treatment groups		Comparison		
	BAF312 (N=127)	**Placebo (N=61)**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Any severe AE[2]					
Interaction test:	p=0,246				
Previous IFN-beta-1b Treatment = No	6 (7,3)	9 (18,8)	0,34 [0,11; 1,03] 0,049 *	0,39 [0,15; 1,03] 0,057	-0,11 [-0,24; 0,01] 0,071
Previous IFN-beta-1b Treatment = Yes	5 (11,1)	1 (7,7)	1,50 [0,16; 14,12] 0,721	1,44 [0,18; 11,29] 0,726	0,03 [-0,14; 0,21] 0,696
Any severe AE[2], disease specific events excluded[1]					
Interaction test:	p=0,223				
Previous IFN-beta-1b Treatment = No	4 (4,9)	7 (14,6)	0,30 [0,08; 1,09] 0,055	0,33 [0,10; 1,08] 0,068	-0,10 [-0,21; 0,01] 0,084
Previous IFN-beta-1b Treatment = Yes	5 (11,1)	1 (7,7)	1,50 [0,16; 14,12] 0,721	1,44 [0,18; 11,29] 0,726	0,03 [-0,14; 0,21] 0,696
Any AE leading to study discontinuation					
Interaction test:	N.E.				
Previous IFN-beta-1b Treatment = No	2 (2,4)	3 (6,3)	0,38 [0,06; 2,33] 0,276	0,39 [0,07; 2,25] 0,293	-0,04 [-0,11; 0,04] 0,327
Previous IFN-beta-1b Treatment = Yes	0 (0,0)	0 (0,0)	-	-	-

	Treatment groups		Comparison		
	BAF312 (N=127)	**Placebo (N=61)**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Any AE leading to study drug discontinuation					
Interaction test:	N.E.				
Previous IFN-beta-1b Treatment = No	5 (6,1)	4 (8,3)	0,71 [0,18; 2,80] 0,628	0,73 [0,21; 2,59] 0,629	-0,02 [-0,12; 0,07] 0,640
Previous IFN-beta-1b Treatment = Yes	1 (2,2)	0 (0,0)	0,91 [0,04; 23,66] 0,588	0,91 [0,04; 21,18] 0,955	0,02 [-0,02; 0,07] 0,312

N': Number of patients in the analysis
CI: Confidence Interval
OR: Odds Ratio
RR: Relative Risk
RD: Risk Difference
N.E.: not estimable
*: p < 0,05

Applied model for interaction test:
Any AE: logit(proportion) = treatment + previous IFN-beta-1b treatment + treatment * previous IFN-beta-1b treatment
Any AE, disease specific events excluded[1]: logit(proportion) = treatment + previous IFN-beta-1b treatment + treatment * previous IFN-beta-1b treatment
Any SAE: logit(proportion) = treatment + previous IFN-beta-1b treatment + treatment * previous IFN-beta-1b treatment
Any SAE, disease specific events excluded[1]: logit(proportion) = treatment + previous IFN-beta-1b treatment + treatment * previous IFN-beta-1b treatment
Any severe AE[2]: logit(proportion) = treatment + previous IFN-beta-1b treatment + treatment * previous IFN-beta-1b treatment
Any severe AE[2], disease specific events excluded[1]: logit(proportion) = treatment + previous IFN-beta-1b treatment + treatment * previous IFN-beta-1b treatment
Any AE leading to study discontinuation: logit(proportion) = treatment + previous IFN-beta-1b treatment + treatment * previous IFN-beta-1b treatment
Any AE leading to study drug discontinuation: logit(proportion) = treatment + previous IFN-beta-1b treatment + treatment * previous IFN-beta-1b treatment

Applied estimator for OR: unadjusted OR
Applied test for OR: Pearson Chi-Square test

[1] The following disease-specific Preferred Terms were excluded: see Table 11.0
[2] Definition of 'severe': CTCAE grade ≥ 3

Analysis population: A2304 SAF subpopulation "ACTIVE MS WITHOUT RELAPSES"

Table 11.5.2: Adverse Events by SOC and PT, Binary Analysis (SAF) by Previous IFN-beta-1b Treatment

	Treatment groups		Comparison		
	BAF312 (N=127)	Placebo (N=61)	OR [95% CI] p-value	RR [95% CI] p-value	RD [95% CI] p-value
N'	127	61			
N' Previous IFN-beta-1b Treatment = No	82	48			
N' Previous IFN-beta-1b Treatment = Yes	45	13			
GENERAL DISORDERS AND ADMINISTRATION SITE CONDITIONS					
Interaction test:	p=0,566				
Previous IFN-beta-1b Treatment = No	18 (22,0)	5 (10,4)	2,42 [0,84; 7,01] 0,096	2,11 [0,84; 5,31] 0,114	0,12 [-0,01; 0,24] 0,069
Previous IFN-beta-1b Treatment = Yes	13 (28,9)	1 (7,7)	4,88 [0,57; 41,41] 0,116	3,76 [0,54; 26,08] 0,181	0,21 [0,02; 0,41] 0,034 *
INVESTIGATIONS					
Interaction test:	p=0,802				
Previous IFN-beta-1b Treatment = No	30 (36,6)	8 (16,7)	2,88 [1,19; 6,97] 0,016 *	2,20 [1,10; 4,39] 0,026 *	0,20 [0,05; 0,35] 0,008 *
Previous IFN-beta-1b Treatment = Yes	11 (24,4)	1 (7,7)	3,88 [0,45; 33,34] 0,189	3,18 [0,45; 22,38] 0,246	0,17 [-0,02; 0,36] 0,087

N': Number of patients in the analysis
CI: Confidence Interval
OR: Odds Ratio
RR: Relative Risk
RD: Risk Difference
*: p < 0,05

Applied model for interaction test: logit(proportion) = treatment + previous IFN-beta-1b treatment + treatment * previous IFN-beta-1b treatment

Applied estimator for OR: unadjusted OR
Applied test for OR: Pearson Chi-Square test

SOCs/PTs are only displayed in this subgroup analysis, if the p-value for RR in the entire population is significant (p<0.05).

Analysis population: A2304 SAF subpopulation "ACTIVE MS WITHOUT RELAPSES"

Table 11.5.3: Serious Adverse Events by SOC and PT, Binary Analysis (SAF) by Previous IFN-beta-1b Treatment

There are no data meeting the display criteria for this table.

Table 11.5.4: Severe Adverse Events by SOC and PT, Binary Analysis (SAF) by Previous IFN-beta-1b Treatment

There are no data meeting the display criteria for this table.

Table 11.5.5: Adverse Events of Special Interest, Binary Analysis (SAF) by Previous IFN-beta-1b Treatment

	Treatment groups		Comparison		
	BAF312 (N=127)	Placebo (N=61)	OR [95% CI] p-value	RR [95% CI] p-value	RD [95% CI] p-value
N'	127	61			
N' Previous IFN-beta-1b Treatment = No	82	48			
N' Previous IFN-beta-1b Treatment = Yes	45	13			
Infections and infestations					
Interaction test:	p=0,299				
Previous IFN-beta-1b Treatment = No	38 (46,3)	21 (43,8)	1,11 [0,54; 2,27] 0,775	1,06 [0,71; 1,57] 0,776	0,03 [-0,15; 0,20] 0,774
Previous IFN-beta-1b Treatment = Yes	27 (60,0)	5 (38,5)	2,40 [0,68; 8,52] 0,169	1,56 [0,75; 3,23] 0,231	0,22 [-0,09; 0,52] 0,160
Herpes simplex virus infections					
Interaction test:	N.E.				
Previous IFN-beta-1b Treatment = No	0 (0,0)	1 (2,1)	0,19 [0,01; 4,81] 0,189	0,20 [0,01; 4,74] 0,317	-0,02 [-0,06; 0,02] 0,312
Previous IFN-beta-1b Treatment = Yes	4 (8,9)	0 (0,0)	2,93 [0,15; 57,96] 0,265	2,74 [0,16; 47,82] 0,490	0,09 [0,01; 0,17] 0,036 *
Varicella-zoster virus infections					
Interaction test:	N.E.				
Previous IFN-beta-1b Treatment = No	0 (0,0)	0 (0,0)	-	-	-
Previous IFN-beta-1b Treatment = Yes	1 (2,2)	0 (0,0)	0,91 [0,04; 23,66] 0,588	0,91 [0,04; 21,18] 0,955	0,02 [-0,02; 0,07] 0,312
Lymphopenia					
Interaction test:	N.E.				
Previous IFN-beta-1b Treatment = No	1 (1,2)	0 (0,0)	1,79 [0,07; 44,69] 0,442	1,77 [0,07; 42,63] 0,725	0,01 [-0,01; 0,04] 0,314
Previous IFN-beta-1b Treatment = Yes	1 (2,2)	0 (0,0)	0,91 [0,04; 23,66] 0,588	0,91 [0,04; 21,18] 0,955	0,02 [-0,02; 0,07] 0,312

	Treatment groups		Comparison		
	BAF312 (N=127)	**Placebo (N=61)**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Macular edema					
Interaction test:	N.E.				
Previous IFN-beta-1b Treatment = No	0 (0,0)	1 (2,1)	0,19 [0,01; 4,81] 0,189	0,20 [0,01; 4,74] 0,317	-0,02 [-0,06; 0,02] 0,312
Previous IFN-beta-1b Treatment = Yes	2 (4,4)	0 (0,0)	1,55 [0,07; 34,35] 0,439	1,52 [0,08; 29,87] 0,782	0,04 [-0,02; 0,10] 0,148
Abnormal hepatic enzymes					
Interaction test:	p=0,746				
Previous IFN-beta-1b Treatment = No	13 (15,9)	3 (6,3)	2,83 [0,76; 10,48] 0,108	2,54 [0,76; 8,45] 0,130	0,10 [-0,01; 0,20] 0,072
Previous IFN-beta-1b Treatment = Yes	6 (13,3)	1 (7,7)	1,85 [0,20; 16,89] 0,582	1,73 [0,23; 13,13] 0,594	0,06 [-0,12; 0,23] 0,529
Malignancies					
Interaction test:	N.E.				
Previous IFN-beta-1b Treatment = No	0 (0,0)	1 (2,1)	0,19 [0,01; 4,81] 0,189	0,20 [0,01; 4,74] 0,317	-0,02 [-0,06; 0,02] 0,312
Previous IFN-beta-1b Treatment = Yes	0 (0,0)	0 (0,0)	-	-	-
Hypertension					
Interaction test:	N.E.				
Previous IFN-beta-1b Treatment = No	13 (15,9)	5 (10,4)	1,62 [0,54; 4,86] 0,386	1,52 [0,58; 4,01] 0,395	0,05 [-0,06; 0,17] 0,363
Previous IFN-beta-1b Treatment = Yes	4 (8,9)	0 (0,0)	2,93 [0,15; 57,96] 0,265	2,74 [0,16; 47,82] 0,490	0,09 [0,01; 0,17] 0,036 *
Seizures					
Interaction test:	N.E.				
Previous IFN-beta-1b Treatment = No	0 (0,0)	0 (0,0)	-	-	-
Previous IFN-beta-1b Treatment = Yes	0 (0,0)	0 (0,0)	-	-	-

	Treatment groups		Comparison		
	BAF312 (N=127)	**Placebo (N=61)**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Thromboembolic events					
Interaction test:	N.E.				
Previous IFN-beta-1b Treatment = No	2 (2,4)	1 (2,1)	1,18 [0,10; 13,31] 0,896	1,17 [0,11; 12,57] 0,896	0,00 [-0,05; 0,06] 0,894
Previous IFN-beta-1b Treatment = Yes	3 (6,7)	0 (0,0)	2,22 [0,11; 45,83] 0,339	2,13 [0,12; 38,80] 0,610	0,07 [-0,01; 0,14] 0,073
Respiratory disorders					
Interaction test:	p=0,694				
Previous IFN-beta-1b Treatment = No	14 (17,1)	8 (16,7)	1,03 [0,40; 2,67] 0,952	1,02 [0,46; 2,26] 0,952	0,00 [-0,13; 0,14] 0,952
Previous IFN-beta-1b Treatment = Yes	8 (17,8)	3 (23,1)	0,72 [0,16; 3,23] 0,668	0,77 [0,24; 2,49] 0,663	-0,05 [-0,31; 0,20] 0,684
Peripheral edema/swelling					
Interaction test:	N.E.				
Previous IFN-beta-1b Treatment = No	3 (3,7)	0 (0,0)	4,27 [0,22; 84,47] 0,180	4,13 [0,22; 78,33] 0,345	0,04 [-0,00; 0,08] 0,078
Previous IFN-beta-1b Treatment = Yes	3 (6,7)	1 (7,7)	0,86 [0,08; 9,01] 0,898	0,87 [0,10; 7,65] 0,898	-0,01 [-0,17; 0,15] 0,901

N': Number of patients in the analysis
CI: Confidence Interval
OR: Odds Ratio
RR: Relative Risk
RD: Risk Difference
N.E.: not estimable
*: p < 0,05

Applied model for interaction test: logit(proportion) = treatment + previous IFN-beta-1b treatment + treatment * previous IFN-beta-1b treatment

Applied estimator for OR: unadjusted OR
Applied test for OR: Pearson Chi-Square test

Analysis population: A2304 SAF subpopulation "ACTIVE MS WITHOUT RELAPSES"

	Treatment groups		Comparison		
	BAF312 (N=127)	**Placebo (N=61)**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
N'	127	61			
N' Previous IFN-beta-1b Treatment = No	82	48			
N' Previous IFN-beta-1b Treatment = Yes	45	13			
Asthma/bronchospasm					
Interaction test:	N.E.				
Previous IFN-beta-1b Treatment = No	0 (0,0)	0 (0,0)	-	-	-
Previous IFN-beta-1b Treatment = Yes	1 (2,2)	0 (0,0)	0,91 [0,04; 23,66] 0,588	0,91 [0,04; 21,18] 0,955	0,02 [-0,02; 0,07] 0,312
Pregnancy and neonatal topics					
Interaction test:	N.E.				
Previous IFN-beta-1b Treatment = No	1 (1,2)	0 (0,0)	1,79 [0,07; 44,69] 0,442	1,77 [0,07; 42,63] 0,725	0,01 [-0,01; 0,04] 0,314
Previous IFN-beta-1b Treatment = Yes	0 (0,0)	0 (0,0)	-	-	-
Bradyarrhythmias and bradycardia					
Interaction test:	N.E.				
Previous IFN-beta-1b Treatment = No	7 (8,5)	1 (2,1)	4,39 [0,52; 36,79] 0,140	4,10 [0,52; 32,30] 0,181	0,06 [-0,01; 0,14] 0,082
Previous IFN-beta-1b Treatment = Yes	4 (8,9)	0 (0,0)	2,93 [0,15; 57,96] 0,265	2,74 [0,16; 47,82] 0,490	0,09 [0,01; 0,17] 0,036 *

N': Number of patients in the analysis
CI: Confidence Interval
OR: Odds Ratio
RR: Relative Risk
RD: Risk Difference
N.E.: not estimable
*: p < 0,05

Applied model for interaction test: logit(proportion) = treatment + previous IFN-beta-1b treatment + treatment * previous IFN-beta-1b treatment

Applied estimator for OR: unadjusted OR
Applied test for OR: Pearson Chi-Square test

Analysis population: A2304 SAF subpopulation "ACTIVE MS WITHOUT RELAPSES"

11.6 Subgroup: Rapid Evolvement

Table 11.6.1: Adverse Events, Binary Analysis (SAF) by Rapid Evolvement

	Treatment groups		Comparison		
	BAF312 (N=127)	**Placebo (N=61)**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
N'	127	61			
N' Rapid Evolvement = No	95	47			
N' Rapid Evolvement = Yes	32	14			
Any AE					
Interaction test:	p=0,605				
Rapid Evolvement = No	84 (88,4)	36 (76,6)	2,33 [0,93; 5,87] 0,067	1,15 [0,97; 1,37] 0,106	0,12 [-0,02; 0,26] 0,091
Rapid Evolvement = Yes	30 (93,8)	11 (78,6)	4,09 [0,60; 27,85] 0,128	1,19 [0,89; 1,59] 0,229	0,15 [-0,08; 0,38] 0,197
Any AE, disease specific events excluded[1]					
Interaction test:	p=0,654				
Rapid Evolvement = No	79 (83,2)	35 (74,5)	1,69 [0,73; 3,95] 0,221	1,12 [0,92; 1,35] 0,256	0,09 [-0,06; 0,23] 0,242
Rapid Evolvement = Yes	29 (90,6)	11 (78,6)	2,64 [0,46; 15,09] 0,264	1,15 [0,86; 1,55] 0,344	0,12 [-0,12; 0,36] 0,320
Any SAE					
Interaction test:	p=0,257				
Rapid Evolvement = No	14 (14,7)	8 (17,0)	0,84 [0,33; 2,18] 0,723	0,87 [0,39; 1,92] 0,722	-0,02 [-0,15; 0,11] 0,728
Rapid Evolvement = Yes	2 (6,3)	3 (21,4)	0,24 [0,04; 1,66] 0,128	0,29 [0,05; 1,56] 0,149	-0,15 [-0,38; 0,08] 0,197
Any SAE, disease specific events excluded[1]					
Interaction test:	p=0,268				
Rapid Evolvement = No	11 (11,6)	6 (12,8)	0,89 [0,31; 2,59] 0,838	0,91 [0,36; 2,30] 0,837	-0,01 [-0,13; 0,10] 0,840
Rapid Evolvement = Yes	1 (3,1)	2 (14,3)	0,19 [0,02; 2,34] 0,158	0,22 [0,02; 2,22] 0,199	-0,11 [-0,30; 0,08] 0,257

	Treatment groups		Comparison		
	BAF312 (N=127)	**Placebo (N=61)**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Any severe AE[2]					
Interaction test:	p=0,428				
Rapid Evolvement = No	10 (10,5)	8 (17,0)	0,57 [0,21; 1,57] 0,274	0,62 [0,26; 1,46] 0,274	-0,06 [-0,19; 0,06] 0,304
Rapid Evolvement = Yes	1 (3,1)	2 (14,3)	0,19 [0,02; 2,34] 0,158	0,22 [0,02; 2,22] 0,199	-0,11 [-0,30; 0,08] 0,257
Any severe AE[2], disease specific events excluded[1]					
Interaction test:	p=0,885				
Rapid Evolvement = No	8 (8,4)	7 (14,9)	0,53 [0,18; 1,55] 0,238	0,57 [0,22; 1,47] 0,241	-0,06 [-0,18; 0,05] 0,275
Rapid Evolvement = Yes	1 (3,1)	1 (7,1)	0,42 [0,02; 7,22] 0,539	0,44 [0,03; 6,51] 0,548	-0,04 [-0,19; 0,11] 0,594
Any AE leading to study discontinuation					
Interaction test:	p=0,769				
Rapid Evolvement = No	1 (1,1)	2 (4,3)	0,24 [0,02; 2,71] 0,212	0,25 [0,02; 2,66] 0,249	-0,03 [-0,09; 0,03] 0,305
Rapid Evolvement = Yes	1 (3,1)	1 (7,1)	0,42 [0,02; 7,22] 0,539	0,44 [0,03; 6,51] 0,548	-0,04 [-0,19; 0,11] 0,594

	Treatment groups		Comparison		
	BAF312 (N=127)	**Placebo (N=61)**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Any AE leading to study drug discontinuation					
Interaction test:	p=0,843				
Rapid Evolvement = No	4 (4,2)	3 (6,4)	0,64 [0,14; 3,01] 0,574	0,66 [0,15; 2,83] 0,575	-0,02 [-0,10; 0,06] 0,598
Rapid Evolvement = Yes	2 (6,3)	1 (7,1)	0,87 [0,07; 10,42] 0,910	0,88 [0,09; 8,88] 0,910	-0,01 [-0,17; 0,15] 0,912

N': Number of patients in the analysis
CI: Confidence Interval
OR: Odds Ratio
RR: Relative Risk
RD: Risk Difference
*: p < 0,05

Applied model for interaction test:
Any AE: logit(proportion) = treatment + rapid evolvement + treatment * rapid evolvement
Any AE, disease specific events excluded[1]: logit(proportion) = treatment + rapid evolvement + treatment * rapid evolvement
Any SAE: logit(proportion) = treatment + rapid evolvement + treatment * rapid evolvement
Any SAE, disease specific events excluded[1]: logit(proportion) = treatment + rapid evolvement + treatment * rapid evolvement
Any severe AE[2]: logit(proportion) = treatment + rapid evolvement + treatment * rapid evolvement
Any severe AE[2], disease specific events excluded[1]: logit(proportion) = treatment + rapid evolvement + treatment * rapid evolvement
Any AE leading to study discontinuation: logit(proportion) = treatment + rapid evolvement + treatment * rapid evolvement
Any AE leading to study drug discontinuation: logit(proportion) = treatment + rapid evolvement + treatment * rapid evolvement

Applied estimator for OR: unadjusted OR
Applied test for OR: Pearson Chi-Square test

[1] The following disease-specific Preferred Terms were excluded: see Table 11.0
[2] Definition of 'severe': CTCAE grade ≥ 3

Analysis population: A2304 SAF subpopulation "ACTIVE MS WITHOUT RELAPSES"

Table 11.6.2: Adverse Events by SOC and PT, Binary Analysis (SAF) by Rapid Evolvement

	Treatment groups		Comparison		
	BAF312 (N=127)	Placebo (N=61)	OR [95% CI] p-value	RR [95% CI] p-value	RD [95% CI] p-value
N'	127	61			
N' Rapid Evolvement = No	95	47			
N' Rapid Evolvement = Yes	32	14			
GENERAL DISORDERS AND ADMINISTRATION SITE CONDITIONS					
Interaction test:	p=1,000				
Rapid Evolvement = No	25 (26,3)	5 (10,6)	3,00 [1,07; 8,43] 0,031 *	2,47 [1,01; 6,05] 0,047 *	0,16 [0,03; 0,28] 0,014 *
Rapid Evolvement = Yes	6 (18,8)	1 (7,1)	3,00 [0,33; 27,60] 0,313	2,63 [0,35; 19,82] 0,349	0,12 [-0,07; 0,31] 0,234
INVESTIGATIONS					
Interaction test:	p=0,809				
Rapid Evolvement = No	34 (35,8)	8 (17,0)	2,72 [1,14; 6,48] 0,021 *	2,10 [1,06; 4,18] 0,034 *	0,19 [0,04; 0,33] 0,011 *
Rapid Evolvement = Yes	7 (21,9)	1 (7,1)	3,64 [0,40; 32,85] 0,225	3,06 [0,41; 22,61] 0,272	0,15 [-0,05; 0,34] 0,142

N': Number of patients in the analysis
CI: Confidence Interval
OR: Odds Ratio
RR: Relative Risk
RD: Risk Difference
*: p < 0,05

Applied model for interaction test: logit(proportion) = treatment + rapid evolvement + treatment * rapid evolvement

Applied estimator for OR: unadjusted OR
Applied test for OR: Pearson Chi-Square test

SOCs/PTs are only displayed in this subgroup analysis, if the p-value for RR in the entire population is significant (p<0.05).

Analysis population: A2304 SAF subpopulation "ACTIVE MS WITHOUT RELAPSES"

Table 11.6.3: Serious Adverse Events by SOC and PT, Binary Analysis (SAF) by Rapid Evolvement

There are no data meeting the display criteria for this table.

Table 11.6.4: Severe Adverse Events by SOC and PT, Binary Analysis (SAF) by Rapid Evolvement

There are no data meeting the display criteria for this table.

Table 11.6.5: Adverse Events of Special Interest, Binary Analysis (SAF) by Rapid Evolvement

	Treatment groups		Comparison		
	BAF312 (N=127)	Placebo (N=61)	OR [95% CI] p-value	RR [95% CI] p-value	RD [95% CI] p-value
N'	127	61			
N' Rapid Evolvement = No	95	47			
N' Rapid Evolvement = Yes	32	14			
Infections and infestations					
Interaction test:	p=0,191				
Rapid Evolvement = No	45 (47,4)	21 (44,7)	1,11 [0,55; 2,25] 0,763	1,06 [0,72; 1,55] 0,765	0,03 [-0,15; 0,20] 0,762
Rapid Evolvement = Yes	20 (62,5)	5 (35,7)	3,00 [0,81; 11,08] 0,093	1,75 [0,82; 3,71] 0,145	0,27 [-0,03; 0,57] 0,082
Herpes simplex virus infections					
Interaction test:	N.E.				
Rapid Evolvement = No	4 (4,2)	0 (0,0)	4,67 [0,25; 88,62] 0,154	4,50 [0,25; 81,88] 0,310	0,04 [0,00; 0,08] 0,041 *
Rapid Evolvement = Yes	0 (0,0)	1 (7,1)	0,14 [0,01; 3,62] 0,126	0,15 [0,01; 3,51] 0,239	-0,07 [-0,21; 0,06] 0,299
Varicella-zoster virus infections					
Interaction test:	N.E.				
Rapid Evolvement = No	1 (1,1)	0 (0,0)	1,51 [0,06; 37,72] 0,480	1,50 [0,06; 36,14] 0,803	0,01 [-0,01; 0,03] 0,315
Rapid Evolvement = Yes	0 (0,0)	0 (0,0)	-	-	-
Lymphopenia					
Interaction test:	N.E.				
Rapid Evolvement = No	2 (2,1)	0 (0,0)	2,54 [0,12; 53,98] 0,316	2,50 [0,12; 51,05] 0,552	0,02 [-0,01; 0,05] 0,153
Rapid Evolvement = Yes	0 (0,0)	0 (0,0)	-	-	-
Macular edema					
Interaction test:	N.E.				
Rapid Evolvement = No	1 (1,1)	1 (2,1)	0,49 [0,03; 8,00] 0,609	0,49 [0,03; 7,74] 0,616	-0,01 [-0,06; 0,04] 0,647
Rapid Evolvement = Yes	1 (3,1)	0 (0,0)	1,38 [0,05; 35,99] 0,504	1,36 [0,06; 31,56] 0,847	0,03 [-0,03; 0,09] 0,310

	Treatment groups		Comparison		
	BAF312 (N=127)	**Placebo (N=61)**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Abnormal hepatic enzymes					
Interaction test:	p=0,846				
Rapid Evolvement = No	13 (13,7)	3 (6,4)	2,33 [0,63; 8,60] 0,195	2,14 [0,64; 7,16] 0,215	0,07 [-0,03; 0,17] 0,145
Rapid Evolvement = Yes	6 (18,8)	1 (7,1)	3,00 [0,33; 27,60] 0,313	2,63 [0,35; 19,82] 0,349	0,12 [-0,07; 0,31] 0,234
Malignancies					
Interaction test:	N.E.				
Rapid Evolvement = No	0 (0,0)	1 (2,1)	0,16 [0,01; 4,06] 0,154	0,17 [0,01; 4,02] 0,270	-0,02 [-0,06; 0,02] 0,312
Rapid Evolvement = Yes	0 (0,0)	0 (0,0)	-	-	-
Hypertension					
Interaction test:	p=0,810				
Rapid Evolvement = No	14 (14,7)	4 (8,5)	1,86 [0,58; 5,99] 0,294	1,73 [0,60; 4,97] 0,308	0,06 [-0,04; 0,17] 0,254
Rapid Evolvement = Yes	3 (9,4)	1 (7,1)	1,34 [0,13; 14,18] 0,805	1,31 [0,15; 11,54] 0,806	0,02 [-0,15; 0,19] 0,795
Seizures					
Interaction test:	N.E.				
Rapid Evolvement = No	0 (0,0)	0 (0,0)	-	-	-
Rapid Evolvement = Yes	0 (0,0)	0 (0,0)	-	-	-
Thromboembolic events					
Interaction test:	N.E.				
Rapid Evolvement = No	3 (3,2)	1 (2,1)	1,50 [0,15; 14,82] 0,727	1,48 [0,16; 13,89] 0,729	0,01 [-0,04; 0,06] 0,710
Rapid Evolvement = Yes	2 (6,3)	0 (0,0)	2,38 [0,11; 52,77] 0,339	2,27 [0,12; 44,49] 0,589	0,06 [-0,02; 0,15] 0,144
Respiratory disorders					
Interaction test:	p=0,448				
Rapid Evolvement = No	15 (15,8)	9 (19,1)	0,79 [0,32; 1,97] 0,615	0,82 [0,39; 1,74] 0,614	-0,03 [-0,17; 0,10] 0,624
Rapid Evolvement = Yes	7 (21,9)	2 (14,3)	1,68 [0,30; 9,34] 0,550	1,53 [0,36; 6,47] 0,562	0,08 [-0,16; 0,31] 0,523

	Treatment groups		Comparison		
	BAF312 (N=127)	**Placebo (N=61)**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Peripheral edema/swelling					
Interaction test:	N.E.				
Rapid Evolvement = No	5 (5,3)	1 (2,1)	2,56 [0,29; 22,52] 0,382	2,47 [0,30; 20,58] 0,402	0,03 [-0,03; 0,09] 0,314
Rapid Evolvement = Yes	1 (3,1)	0 (0,0)	1,38 [0,05; 35,99] 0,504	1,36 [0,06; 31,56] 0,847	0,03 [-0,03; 0,09] 0,310

N': Number of patients in the analysis
CI: Confidence Interval
OR: Odds Ratio
RR: Relative Risk
RD: Risk Difference
N.E.: not estimable
*: p < 0,05

Applied model for interaction test: logit(proportion) = treatment + rapid evolvement + treatment * rapid evolvement

Applied estimator for OR: unadjusted OR
Applied test for OR: Pearson Chi-Square test

Analysis population: A2304 SAF subpopulation "ACTIVE MS WITHOUT RELAPSES"

	Treatment groups		Comparison		
	BAF312 (N=127)	**Placebo (N=61)**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
N'	127	61			
N' Rapid Evolvement = No	95	47			
N' Rapid Evolvement = Yes	32	14			
Asthma/bronchospasm					
Interaction test:	N.E.				
Rapid Evolvement = No	0 (0,0)	0 (0,0)	-	-	-
Rapid Evolvement = Yes	1 (3,1)	0 (0,0)	1,38 [0,05; 35,99] 0,504	1,36 [0,06; 31,56] 0,847	0,03 [-0,03; 0,09] 0,310
Pregnancy and neonatal topics					
Interaction test:	N.E.				
Rapid Evolvement = No	0 (0,0)	0 (0,0)	-	-	-
Rapid Evolvement = Yes	1 (3,1)	0 (0,0)	1,38 [0,05; 35,99] 0,504	1,36 [0,06; 31,56] 0,847	0,03 [-0,03; 0,09] 0,310
Bradyarrhythmias and bradycardia					
Interaction test:	N.E.				
Rapid Evolvement = No	10 (10,5)	1 (2,1)	5,41 [0,67; 43,61] 0,078	4,95 [0,65; 37,51] 0,122	0,08 [0,01; 0,16] 0,027 *
Rapid Evolvement = Yes	1 (3,1)	0 (0,0)	1,38 [0,05; 35,99] 0,504	1,36 [0,06; 31,56] 0,847	0,03 [-0,03; 0,09] 0,310

N': Number of patients in the analysis
CI: Confidence Interval
OR: Odds Ratio
RR: Relative Risk
RD: Risk Difference
N.E.: not estimable
*: p < 0,05

Applied model for interaction test: logit(proportion) = treatment + rapid evolvement + treatment * rapid evolvement

Applied estimator for OR: unadjusted OR
Applied test for OR: Pearson Chi-Square test

Analysis population: A2304 SAF subpopulation "ACTIVE MS WITHOUT RELAPSES"

11.7 Subgroup: Disease Course

Table 11.7.1: Adverse Events, Binary Analysis (SAF) by Disease Course

	Treatment groups		Comparison		
	BAF312 (N=127)	**Placebo (N=61)**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
N'	127	61			
N' Moderate or Severe Disease Course = No	18	11			
N' Moderate or Severe Disease Course = Yes	109	50			
Any AE					
Interaction test:	p=0,873				
Moderate or Severe Disease Course = No	16 (88,9)	8 (72,7)	3,00 [0,41; 21,73] 0,264	1,22 [0,82; 1,82] 0,322	0,16 [-0,14; 0,46] 0,292
Moderate or Severe Disease Course = Yes	98 (89,9)	39 (78,0)	2,51 [1,01; 6,27] 0,043 *	1,15 [0,98; 1,35] 0,082	0,12 [-0,01; 0,25] 0,068
Any AE, disease specific events excluded[1]					
Interaction test:	p=0,607				
Moderate or Severe Disease Course = No	16 (88,9)	8 (72,7)	3,00 [0,41; 21,73] 0,264	1,22 [0,82; 1,82] 0,322	0,16 [-0,14; 0,46] 0,292
Moderate or Severe Disease Course = Yes	92 (84,4)	38 (76,0)	1,71 [0,75; 3,92] 0,203	1,11 [0,93; 1,32] 0,241	0,08 [-0,05; 0,22] 0,228
Any SAE					
Interaction test:	N.E.				
Moderate or Severe Disease Course = No	3 (16,7)	0 (0,0)	5,19 [0,24; 110,74] 0,153	4,42 [0,25; 78,26] 0,311	0,17 [-0,01; 0,34] 0,058
Moderate or Severe Disease Course = Yes	13 (11,9)	11 (22,0)	0,48 [0,20; 1,16] 0,099	0,54 [0,26; 1,12] 0,100	-0,10 [-0,23; 0,03] 0,129
Any SAE, disease specific events excluded[1]					
Interaction test:	N.E.				
Moderate or Severe Disease Course = No	2 (11,1)	0 (0,0)	3,48 [0,15; 79,58] 0,252	3,16 [0,17; 60,28] 0,445	0,11 [-0,03; 0,26] 0,134
Moderate or Severe Disease Course = Yes	10 (9,2)	8 (16,0)	0,53 [0,20; 1,44] 0,207	0,57 [0,24; 1,36] 0,209	-0,07 [-0,18; 0,05] 0,245

	Treatment groups		Comparison		
	BAF312 (N=127)	**Placebo (N=61)**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Any severe AE[2]					
Interaction test:	p=0,874				
Moderate or Severe Disease Course = No	1 (5,6)	1 (9,1)	0,59 [0,03; 10,48] 0,715	0,61 [0,04; 8,81] 0,718	-0,04 [-0,24; 0,16] 0,729
Moderate or Severe Disease Course = Yes	10 (9,2)	9 (18,0)	0,46 [0,17; 1,22] 0,111	0,51 [0,22; 1,18] 0,114	-0,09 [-0,21; 0,03] 0,148
Any severe AE[2], disease specific events excluded[1]					
Interaction test:	p=0,904				
Moderate or Severe Disease Course = No	1 (5,6)	1 (9,1)	0,59 [0,03; 10,48] 0,715	0,61 [0,04; 8,81] 0,718	-0,04 [-0,24; 0,16] 0,729
Moderate or Severe Disease Course = Yes	8 (7,3)	7 (14,0)	0,49 [0,17; 1,43] 0,182	0,52 [0,20; 1,37] 0,186	-0,07 [-0,17; 0,04] 0,226
Any AE leading to study discontinuation					
Interaction test:	N.E.				
Moderate or Severe Disease Course = No	0 (0,0)	0 (0,0)	-	-	-
Moderate or Severe Disease Course = Yes	2 (1,8)	3 (6,0)	0,29 [0,05; 1,81] 0,162	0,31 [0,05; 1,77] 0,186	-0,04 [-0,11; 0,03] 0,247

	Treatment groups		Comparison		
	BAF312 (N=127)	**Placebo (N=61)**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Any AE leading to study drug discontinuation					
Interaction test:	N.E.				
Moderate or Severe Disease Course = No	0 (0,0)	0 (0,0)	-	-	-
Moderate or Severe Disease Course = Yes	6 (5,5)	4 (8,0)	0,67 [0,18; 2,49] 0,547	0,69 [0,20; 2,33] 0,548	-0,02 [-0,11; 0,06] 0,572

N': Number of patients in the analysis
CI: Confidence Interval
OR: Odds Ratio
RR: Relative Risk
RD: Risk Difference
N.E.: not estimable
*: p < 0,05

Applied model for interaction test:
Any AE: logit(proportion) = treatment + disease course + treatment * disease course
Any AE, disease specific events excluded[1]: logit(proportion) = treatment + disease course + treatment * disease course
Any SAE: logit(proportion) = treatment + disease course + treatment * disease course
Any SAE, disease specific events excluded[1]: logit(proportion) = treatment + disease course + treatment * disease course
Any severe AE[2]: logit(proportion) = treatment + disease course + treatment * disease course
Any severe AE[2], disease specific events excluded[1]: logit(proportion) = treatment + disease course + treatment * disease course
Any AE leading to study discontinuation: logit(proportion) = treatment + disease course + treatment * disease course
Any AE leading to study drug discontinuation: logit(proportion) = treatment + disease course + treatment * disease course

Applied estimator for OR: unadjusted OR
Applied test for OR: Pearson Chi-Square test

[1] The following disease-specific Preferred Terms were excluded: see Table 11.0
[2] Definition of 'severe': CTCAE grade ≥ 3

Analysis population: A2304 SAF subpopulation "ACTIVE MS WITHOUT RELAPSES"

Table 11.7.2: Adverse Events by SOC and PT, Binary Analysis (SAF) by Disease Course

	Treatment groups		Comparison		
	BAF312 (N=127)	**Placebo (N=61)**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
N'	127	61			
N' Moderate or Severe Disease Course = No	18	11			
N' Moderate or Severe Disease Course = Yes	109	50			
GENERAL DISORDERS AND ADMINISTRATION SITE CONDITIONS					
Interaction test:	N.E.				
Moderate or Severe Disease Course = No	1 (5,6)	0 (0,0)	1,97 [0,07; 52,70] 0,426	1,89 [0,08; 42,82] 0,688	0,06 [-0,05; 0,16] 0,303
Moderate or Severe Disease Course = Yes	30 (27,5)	6 (12,0)	2,78 [1,08; 7,21] 0,030 *	2,29 [1,02; 5,16] 0,045 *	0,16 [0,03; 0,28] 0,013 *
INVESTIGATIONS					
Interaction test:	p=0,400				
Moderate or Severe Disease Course = No	4 (22,2)	2 (18,2)	1,29 [0,19; 8,53] 0,794	1,22 [0,27; 5,60] 0,796	0,04 [-0,26; 0,34] 0,790
Moderate or Severe Disease Course = Yes	37 (33,9)	7 (14,0)	3,16 [1,29; 7,70] 0,009 *	2,42 [1,16; 5,06] 0,018 *	0,20 [0,07; 0,33] 0,003 *

N': Number of patients in the analysis
CI: Confidence Interval
OR: Odds Ratio
RR: Relative Risk
RD: Risk Difference
N.E.: not estimable
*: p < 0,05

Applied model for interaction test: logit(proportion) = treatment + disease course + treatment * disease course

Applied estimator for OR: unadjusted OR
Applied test for OR: Pearson Chi-Square test

SOCs/PTs are only displayed in this subgroup analysis, if the p-value for RR in the entire population is significant (p<0.05).

Analysis population: A2304 SAF subpopulation "ACTIVE MS WITHOUT RELAPSES"

Table 11.7.3: Serious Adverse Events by SOC and PT, Binary Analysis (SAF) by Disease Course

There are no data meeting the display criteria for this table.

Table 11.7.4: Severe Adverse Events by SOC and PT, Binary Analysis (SAF) by Disease Course

There are no data meeting the display criteria for this table.

Table 11.7.5: Adverse Events of Special Interest, Binary Analysis (SAF) by Disease Course

	Treatment groups		Comparison		
	BAF312 (N=127)	Placebo (N=61)	OR [95% CI] p-value	RR [95% CI] p-value	RD [95% CI] p-value
N'	127	61			
N' Moderate or Severe Disease Course = No	18	11			
N' Moderate or Severe Disease Course = Yes	109	50			
Infections and infestations					
Interaction test:	p=0,285				
Moderate or Severe Disease Course = No	8 (44,4)	6 (54,5)	0,67 [0,15; 3,01] 0,597	0,81 [0,39; 1,72] 0,591	-0,10 [-0,47; 0,27] 0,596
Moderate or Severe Disease Course = Yes	57 (52,3)	20 (40,0)	1,64 [0,83; 3,24] 0,150	1,31 [0,89; 1,92] 0,171	0,12 [-0,04; 0,29] 0,144
Herpes simplex virus infections					
Interaction test:	N.E.				
Moderate or Severe Disease Course = No	0 (0,0)	1 (9,1)	0,19 [0,01; 5,07] 0,193	0,21 [0,01; 4,76] 0,327	-0,09 [-0,26; 0,08] 0,294
Moderate or Severe Disease Course = Yes	4 (3,7)	0 (0,0)	4,31 [0,23; 81,57] 0,170	4,17 [0,23; 76,05] 0,335	0,04 [0,00; 0,07] 0,042 *
Varicella-zoster virus infections					
Interaction test:	N.E.				
Moderate or Severe Disease Course = No	1 (5,6)	0 (0,0)	1,97 [0,07; 52,70] 0,426	1,89 [0,08; 42,82] 0,688	0,06 [-0,05; 0,16] 0,303
Moderate or Severe Disease Course = Yes	0 (0,0)	0 (0,0)	-	-	-
Lymphopenia					
Interaction test:	N.E.				
Moderate or Severe Disease Course = No	0 (0,0)	0 (0,0)	-	-	-
Moderate or Severe Disease Course = Yes	2 (1,8)	0 (0,0)	2,35 [0,11; 49,83] 0,335	2,32 [0,11; 47,41] 0,585	0,02 [-0,01; 0,04] 0,153

	Treatment groups		Comparison		
	BAF312 (N=127)	**Placebo (N=61)**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Macular edema					
Interaction test:	N.E.				
Moderate or Severe Disease Course = No	0 (0,0)	0 (0,0)	-	-	-
Moderate or Severe Disease Course = Yes	2 (1,8)	1 (2,0)	0,92 [0,08; 10,34] 0,943	0,92 [0,09; 9,88] 0,943	-0,00 [-0,05; 0,04] 0,944
Abnormal hepatic enzymes					
Interaction test:	p=0,229				
Moderate or Severe Disease Course = No	3 (16,7)	2 (18,2)	0,90 [0,13; 6,46] 0,917	0,92 [0,18; 4,65] 0,916	-0,02 [-0,30; 0,27] 0,917
Moderate or Severe Disease Course = Yes	16 (14,7)	2 (4,0)	4,13 [0,91; 18,70] 0,048 *	3,67 [0,88; 15,36] 0,075	0,11 [0,02; 0,19] 0,015 *
Malignancies					
Interaction test:	N.E.				
Moderate or Severe Disease Course = No	0 (0,0)	0 (0,0)	-	-	-
Moderate or Severe Disease Course = Yes	0 (0,0)	1 (2,0)	0,15 [0,01; 3,76] 0,139	0,15 [0,01; 3,73] 0,250	-0,02 [-0,06; 0,02] 0,312
Hypertension					
Interaction test:	N.E.				
Moderate or Severe Disease Course = No	0 (0,0)	0 (0,0)	-	-	-
Moderate or Severe Disease Course = Yes	17 (15,6)	5 (10,0)	1,66 [0,58; 4,80] 0,343	1,56 [0,61; 3,99] 0,354	0,06 [-0,05; 0,16] 0,308
Seizures					
Interaction test:	N.E.				
Moderate or Severe Disease Course = No	0 (0,0)	0 (0,0)	-	-	-
Moderate or Severe Disease Course = Yes	0 (0,0)	0 (0,0)	-	-	-
Thromboembolic events					
Interaction test:	N.E.				
Moderate or Severe Disease Course = No	1 (5,6)	0 (0,0)	1,97 [0,07; 52,70] 0,426	1,89 [0,08; 42,82] 0,688	0,06 [-0,05; 0,16] 0,303
Moderate or Severe Disease Course = Yes	4 (3,7)	1 (2,0)	1,87 [0,20; 17,14] 0,575	1,83 [0,21; 16,00] 0,583	0,02 [-0,04; 0,07] 0,533

	Treatment groups		Comparison		
	BAF312 (N=127)	**Placebo (N=61)**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Respiratory disorders					
Interaction test:	p=0,808				
Moderate or Severe Disease Course = No	2 (11,1)	1 (9,1)	1,25 [0,10; 15,65] 0,862	1,22 [0,12; 11,95] 0,863	0,02 [-0,20; 0,24] 0,859
Moderate or Severe Disease Course = Yes	20 (18,3)	10 (20,0)	0,90 [0,39; 2,09] 0,805	0,92 [0,46; 1,81] 0,804	-0,02 [-0,15; 0,12] 0,807
Peripheral edema/swelling					
Interaction test:	N.E.				
Moderate or Severe Disease Course = No	0 (0,0)	0 (0,0)	-	-	-
Moderate or Severe Disease Course = Yes	6 (5,5)	1 (2,0)	2,85 [0,33; 24,36] 0,317	2,75 [0,34; 22,26] 0,342	0,04 [-0,02; 0,09] 0,235

N': Number of patients in the analysis
CI: Confidence Interval
OR: Odds Ratio
RR: Relative Risk
RD: Risk Difference
N.E.: not estimable
*: p < 0,05

Applied model for interaction test: logit(proportion) = treatment + disease course + treatment * disease course

Applied estimator for OR: unadjusted OR
Applied test for OR: Pearson Chi-Square test

Analysis population: A2304 SAF subpopulation "ACTIVE MS WITHOUT RELAPSES"

	Treatment groups		Comparison		
	BAF312 (N=127)	**Placebo (N=61)**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
N'	127	61			
N' Moderate or Severe Disease Course = No	18	11			
N' Moderate or Severe Disease Course = Yes	109	50			
Asthma/bronchospasm					
Interaction test:	N.E.				
Moderate or Severe Disease Course = No	0 (0,0)	0 (0,0)	-	-	-
Moderate or Severe Disease Course = Yes	1 (0,9)	0 (0,0)	1,40 [0,06; 34,88] 0,497	1,39 [0,06; 33,56] 0,839	0,01 [-0,01; 0,03] 0,315
Pregnancy and neonatal topics					
Interaction test:	N.E.				
Moderate or Severe Disease Course = No	0 (0,0)	0 (0,0)	-	-	-
Moderate or Severe Disease Course = Yes	1 (0,9)	0 (0,0)	1,40 [0,06; 34,88] 0,497	1,39 [0,06; 33,56] 0,839	0,01 [-0,01; 0,03] 0,315
Bradyarrhythmias and bradycardia					
Interaction test:	N.E.				
Moderate or Severe Disease Course = No	0 (0,0)	1 (9,1)	0,19 [0,01; 5,07] 0,193	0,21 [0,01; 4,76] 0,327	-0,09 [-0,26; 0,08] 0,294
Moderate or Severe Disease Course = Yes	11 (10,1)	0 (0,0)	11,79 [0,68; 204,20] 0,020 *	10,66 [0,64; 177,46] 0,099	0,10 [0,04; 0,16] <0,001 *

N': Number of patients in the analysis
CI: Confidence Interval
OR: Odds Ratio
RR: Relative Risk
RD: Risk Difference
N.E.: not estimable
*: p < 0,05

Applied model for interaction test: logit(proportion) = treatment + disease course + treatment * disease course

Applied estimator for OR: unadjusted OR
Applied test for OR: Pearson Chi-Square test

Analysis population: A2304 SAF subpopulation "ACTIVE MS WITHOUT RELAPSES"

11.8 Subgroup: Region

Table 11.8.1: Adverse Events, Binary Analysis (SAF) by Region

	Treatment groups		Comparison		
	BAF312 (N=127)	**Placebo (N=61)**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
N'	127	61			
N' Region = Europe	106	52			
N' Region = Other	21	9			
Any AE					
Interaction test:	p=0,138				
Region = Europe	97 (91,5)	39 (75,0)	3,59 [1,42; 9,08] 0,005 *	1,22 [1,03; 1,44] 0,020 *	0,17 [0,04; 0,29] 0,012 *
Region = Other	17 (81,0)	8 (88,9)	0,53 [0,05; 5,55] 0,593	0,91 [0,67; 1,24] 0,555	-0,08 [-0,34; 0,19] 0,558
Any AE, disease specific events excluded[1]					
Interaction test:	p=0,243				
Region = Europe	93 (87,7)	39 (75,0)	2,38 [1,01; 5,61] 0,042 *	1,17 [0,98; 1,39] 0,074	0,13 [-0,01; 0,26] 0,061
Region = Other	15 (71,4)	7 (77,8)	0,71 [0,11; 4,47] 0,719	0,92 [0,59; 1,43] 0,706	-0,06 [-0,40; 0,27] 0,709
Any SAE					
Interaction test:	p=0,115				
Region = Europe	10 (9,4)	10 (19,2)	0,44 [0,17; 1,13] 0,082	0,49 [0,22; 1,10] 0,085	-0,10 [-0,22; 0,02] 0,112
Region = Other	6 (28,6)	1 (11,1)	3,20 [0,33; 31,42] 0,300	2,57 [0,36; 18,40] 0,347	0,17 [-0,11; 0,46] 0,225
Any SAE, disease specific events excluded[1]					
Interaction test:	p=0,192				
Region = Europe	7 (6,6)	7 (13,5)	0,45 [0,15; 1,37] 0,154	0,49 [0,18; 1,33] 0,160	-0,07 [-0,17; 0,04] 0,197
Region = Other	5 (23,8)	1 (11,1)	2,50 [0,25; 25,15] 0,426	2,14 [0,29; 15,83] 0,455	0,13 [-0,15; 0,40] 0,365

	Treatment groups		Comparison		
	BAF312 (N=127)	**Placebo (N=61)**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Any severe AE[2]					
Interaction test:	p=0,190				
Region = Europe	7 (6,6)	9 (17,3)	0,34 [0,12; 0,97] 0,036 *	0,38 [0,15; 0,97] 0,042 *	-0,11 [-0,22; 0,01] 0,064
Region = Other	4 (19,0)	1 (11,1)	1,88 [0,18; 19,68] 0,593	1,71 [0,22; 13,28] 0,606	0,08 [-0,19; 0,34] 0,558
Any severe AE[2], disease specific events excluded[1]					
Interaction test:	p=0,363				
Region = Europe	6 (5,7)	7 (13,5)	0,39 [0,12; 1,21] 0,094	0,42 [0,15; 1,19] 0,102	-0,08 [-0,18; 0,02] 0,136
Region = Other	3 (14,3)	1 (11,1)	1,33 [0,12; 14,87] 0,815	1,29 [0,15; 10,76] 0,817	0,03 [-0,22; 0,29] 0,807
Any AE leading to study discontinuation					
Interaction test:	N.E.				
Region = Europe	1 (0,9)	3 (5,8)	0,16 [0,02; 1,53] 0,070	0,16 [0,02; 1,53] 0,113	-0,05 [-0,11; 0,02] 0,152
Region = Other	1 (4,8)	0 (0,0)	1,39 [0,05; 37,38] 0,506	1,36 [0,06; 30,64] 0,845	0,05 [-0,04; 0,14] 0,306

	Treatment groups		Comparison		
	BAF312 (N=127)	**Placebo (N=61)**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Any AE leading to study drug discontinuation					
Interaction test:	N.E.				
Region = Europe	4 (3,8)	4 (7,7)	0,47 [0,11; 1,96] 0,291	0,49 [0,13; 1,88] 0,300	-0,04 [-0,12; 0,04] 0,343
Region = Other	2 (9,5)	0 (0,0)	2,44 [0,11; 55,93] 0,338	2,27 [0,12; 43,12] 0,585	0,10 [-0,03; 0,22] 0,137

N': Number of patients in the analysis
CI: Confidence Interval
OR: Odds Ratio
RR: Relative Risk
RD: Risk Difference
N.E.: not estimable
*: $p < 0,05$

Applied model for interaction test:
Any AE: logit(proportion) = treatment + region + treatment * region
Any AE, disease specific events excluded[1]: logit(proportion) = treatment + region + treatment * region
Any SAE: logit(proportion) = treatment + region + treatment * region
Any SAE, disease specific events excluded[1]: logit(proportion) = treatment + region + treatment * region
Any severe AE[2]: logit(proportion) = treatment + region + treatment * region
Any severe AE[2], disease specific events excluded[1]: logit(proportion) = treatment + region + treatment * region
Any AE leading to study discontinuation: logit(proportion) = treatment + region + treatment * region
Any AE leading to study drug discontinuation: logit(proportion) = treatment + region + treatment * region

Applied estimator for OR: unadjusted OR
Applied test for OR: Pearson Chi-Square test

[1] The following disease-specific Preferred Terms were excluded: see Table 11.0
[2] Definition of 'severe': CTCAE grade ≥ 3

Analysis population: A2304 SAF subpopulation "ACTIVE MS WITHOUT RELAPSES"

Table 11.8.2: Adverse Events by SOC and PT, Binary Analysis (SAF) by Region

	Treatment groups		Comparison		
	BAF312 (N=127)	**Placebo (N=61)**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
N'	127	61			
N' Region = Europe	106	52			
N' Region = Other	21	9			
GENERAL DISORDERS AND ADMINISTRATION SITE CONDITIONS					
Interaction test:	p=0,012 *				
Region = Europe	28 (26,4)	3 (5,8)	5,86 [1,69; 20,32] 0,002 *	4,58 [1,46; 14,37] 0,009 *	0,21 [0,10; 0,31] <0,001 *
Region = Other	3 (14,3)	3 (33,3)	0,33 [0,05; 2,12] 0,232	0,43 [0,11; 1,73] 0,234	-0,19 [-0,53; 0,15] 0,276
INVESTIGATIONS					
Interaction test:	N.E.				
Region = Europe	35 (33,0)	9 (17,3)	2,36 [1,03; 5,37] 0,038 *	1,91 [0,99; 3,67] 0,053	0,16 [0,02; 0,29] 0,024 *
Region = Other	6 (28,6)	0 (0,0)	7,97 [0,40; 158,07] 0,073	5,91 [0,37; 95,02] 0,210	0,29 [0,09; 0,48] 0,004 *

N': Number of patients in the analysis
CI: Confidence Interval
OR: Odds Ratio
RR: Relative Risk
RD: Risk Difference
N.E.: not estimable
*: p < 0,05

Applied model for interaction test: logit(proportion) = treatment + region + treatment * region

Applied estimator for OR: unadjusted OR
Applied test for OR: Pearson Chi-Square test

SOCs/PTs are only displayed in this subgroup analysis, if the p-value for RR in the entire population is significant (p<0.05).

Analysis population: A2304 SAF subpopulation "ACTIVE MS WITHOUT RELAPSES"

Table 11.8.3: Serious Adverse Events by SOC and PT, Binary Analysis (SAF) by Region

There are no data meeting the display criteria for this table.

Table 11.8.4: Severe Adverse Events by SOC and PT, Binary Analysis (SAF) by Region

There are no data meeting the display criteria for this table.

Table 11.8.5: Adverse Events of Special Interest, Binary Analysis (SAF) by Region

	Treatment groups		Comparison		
	BAF312 (N=127)	**Placebo (N=61)**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
N'	127	61			
N' Region = Europe	106	52			
N' Region = Other	21	9			
Infections and infestations					
Interaction test:	p=0,524				
Region = Europe	54 (50,9)	21 (40,4)	1,53 [0,78; 3,00] 0,212	1,26 [0,86; 1,84] 0,230	0,11 [-0,06; 0,27] 0,207
Region = Other	11 (52,4)	5 (55,6)	0,88 [0,18; 4,23] 0,873	0,94 [0,46; 1,92] 0,871	-0,03 [-0,42; 0,36] 0,873
Herpes simplex virus infections					
Interaction test:	N.E.				
Region = Europe	3 (2,8)	1 (1,9)	1,49 [0,15; 14,64] 0,733	1,47 [0,16; 13,81] 0,735	0,01 [-0,04; 0,06] 0,716
Region = Other	1 (4,8)	0 (0,0)	1,39 [0,05; 37,38] 0,506	1,36 [0,06; 30,64] 0,845	0,05 [-0,04; 0,14] 0,306
Varicella-zoster virus infections					
Interaction test:	N.E.				
Region = Europe	1 (0,9)	0 (0,0)	1,49 [0,06; 37,28] 0,482	1,49 [0,06; 35,86] 0,807	0,01 [-0,01; 0,03] 0,315
Region = Other	0 (0,0)	0 (0,0)	-	-	-
Lymphopenia					
Interaction test:	N.E.				
Region = Europe	2 (1,9)	0 (0,0)	2,51 [0,12; 53,28] 0,319	2,48 [0,12; 50,67] 0,556	0,02 [-0,01; 0,04] 0,153
Region = Other	0 (0,0)	0 (0,0)	-	-	-
Macular edema					
Interaction test:	N.E.				
Region = Europe	2 (1,9)	1 (1,9)	0,98 [0,09; 11,07] 0,987	0,98 [0,09; 10,57] 0,987	-0,00 [-0,05; 0,05] 0,988
Region = Other	0 (0,0)	0 (0,0)	-	-	-

	Treatment groups		Comparison		
	BAF312 (N=127)	**Placebo (N=61)**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Abnormal hepatic enzymes					
Interaction test:	N.E.				
Region = Europe	17 (16,0)	4 (7,7)	2,29 [0,73; 7,20] 0,147	2,08 [0,74; 5,88] 0,165	0,08 [-0,02; 0,18] 0,104
Region = Other	2 (9,5)	0 (0,0)	2,44 [0,11; 55,93] 0,338	2,27 [0,12; 43,12] 0,585	0,10 [-0,03; 0,22] 0,137
Malignancies					
Interaction test:	N.E.				
Region = Europe	0 (0,0)	1 (1,9)	0,16 [0,01; 4,03] 0,152	0,17 [0,01; 3,98] 0,267	-0,02 [-0,06; 0,02] 0,313
Region = Other	0 (0,0)	0 (0,0)	-	-	-
Hypertension					
Interaction test:	N.E.				
Region = Europe	15 (14,2)	5 (9,6)	1,55 [0,53; 4,52] 0,420	1,47 [0,57; 3,83] 0,428	0,05 [-0,06; 0,15] 0,393
Region = Other	2 (9,5)	0 (0,0)	2,44 [0,11; 55,93] 0,338	2,27 [0,12; 43,12] 0,585	0,10 [-0,03; 0,22] 0,137
Seizures					
Interaction test:	N.E.				
Region = Europe	0 (0,0)	0 (0,0)	-	-	-
Region = Other	0 (0,0)	0 (0,0)	-	-	-
Thromboembolic events					
Interaction test:	N.E.				
Region = Europe	3 (2,8)	1 (1,9)	1,49 [0,15; 14,64] 0,733	1,47 [0,16; 13,81] 0,735	0,01 [-0,04; 0,06] 0,716
Region = Other	2 (9,5)	0 (0,0)	2,44 [0,11; 55,93] 0,338	2,27 [0,12; 43,12] 0,585	0,10 [-0,03; 0,22] 0,137
Respiratory disorders					
Interaction test:	p=0,538				
Region = Europe	18 (17,0)	10 (19,2)	0,86 [0,37; 2,02] 0,728	0,88 [0,44; 1,77] 0,727	-0,02 [-0,15; 0,11] 0,732
Region = Other	4 (19,0)	1 (11,1)	1,88 [0,18; 19,68] 0,593	1,71 [0,22; 13,28] 0,606	0,08 [-0,19; 0,34] 0,558

	Treatment groups		Comparison		
	BAF312 (N=127)	**Placebo (N=61)**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Peripheral edema/swelling					
Interaction test:	N.E.				
Region = Europe	6 (5,7)	0 (0,0)	6,79 [0,38; 122,90] 0,080	6,44 [0,37; 112,16] 0,201	0,06 [0,01; 0,10] 0,012 *
Region = Other	0 (0,0)	1 (11,1)	0,13 [0,00; 3,56] 0,120	0,15 [0,01; 3,40] 0,235	-0,11 [-0,32; 0,09] 0,289

N': Number of patients in the analysis
CI: Confidence Interval
OR: Odds Ratio
RR: Relative Risk
RD: Risk Difference
N.E.: not estimable
*: p < 0,05

Applied model for interaction test: logit(proportion) = treatment + region + treatment * region

Applied estimator for OR: unadjusted OR
Applied test for OR: Pearson Chi-Square test

Analysis population: A2304 SAF subpopulation "ACTIVE MS WITHOUT RELAPSES"

	Treatment groups		Comparison		
	BAF312 (N=127)	**Placebo (N=61)**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
N'	127	61			
N' Region = Europe	106	52			
N' Region = Other	21	9			
Asthma/bronchospasm					
Interaction test:	N.E.				
Region = Europe	1 (0,9)	0 (0,0)	1,49 [0,06; 37,28] 0,482	1,49 [0,06; 35,86] 0,807	0,01 [-0,01; 0,03] 0,315
Region = Other	0 (0,0)	0 (0,0)	-	-	-
Pregnancy and neonatal topics					
Interaction test:	N.E.				
Region = Europe	1 (0,9)	0 (0,0)	1,49 [0,06; 37,28] 0,482	1,49 [0,06; 35,86] 0,807	0,01 [-0,01; 0,03] 0,315
Region = Other	0 (0,0)	0 (0,0)	-	-	-
Bradyarrhythmias and bradycardia					
Interaction test:	N.E.				
Region = Europe	9 (8,5)	1 (1,9)	4,73 [0,58; 38,40] 0,111	4,42 [0,57; 33,93] 0,153	0,07 [0,00; 0,13] 0,047 *
Region = Other	2 (9,5)	0 (0,0)	2,44 [0,11; 55,93] 0,338	2,27 [0,12; 43,12] 0,585	0,10 [-0,03; 0,22] 0,137

N': Number of patients in the analysis
CI: Confidence Interval
OR: Odds Ratio
RR: Relative Risk
RD: Risk Difference
N.E.: not estimable
*: p < 0,05

Applied model for interaction test: logit(proportion) = treatment + region + treatment * region

Applied estimator for OR: unadjusted OR
Applied test for OR: Pearson Chi-Square test

Analysis population: A2304 SAF subpopulation "ACTIVE MS WITHOUT RELAPSES"

12. Adverse Events: Time-to-Event Analysis

12.1 Entire Population

Table 12.1.1: Time to First Adverse Event (SAF)

	Treatment groups		Comparison	
	BAF312 (N=127)	Placebo (N=61)	HR [95% CI]	p-value
N'	127	61		
Any AE				
Number of patients with event	114	47		
Median (in weeks)	3,6 [2,4; 8,4]	9,7 [4,3; 22,4]		
% of event-free patients+	7,50 [1,99; 13,02]	21,47 [10,90; 32,04]		
			1,48 [1,05; 2,08]	0,024 *
Any AE, disease specific events excluded[1]				
Number of patients with event	108	46		
Median (in weeks)	11,0 [6,4; 13,7]	13,1 [7,3; 25,0]		
% of event-free patients+	10,03 [3,69; 16,38]	17,26 [4,17; 30,36]		
			1,31 [0,93; 1,86]	0,122
Any SAE				
Number of patients with event	16	11		
Median (in weeks)	-	-		
% of event-free patients+	84,56 [77,19; 91,93]	78,99 [66,75; 91,22]		
			0,64 [0,30; 1,38]	0,253
Any SAE, disease specific events excluded[1]				
Number of patients with event	12	8		
Median (in weeks)	-	-		
% of event-free patients+	89,00 [82,90; 95,10]	83,60 [71,81; 95,38]		
			0,67 [0,27; 1,64]	0,382
Any severe AE[2]				
Number of patients with event	11	10		
Median (in weeks)	-	-		
% of event-free patients+	89,27 [83,06; 95,48]	80,61 [68,74; 92,49]		
			0,48 [0,20; 1,13]	0,093
Any severe AE[2], disease specific events excluded[1]				
Number of patients with event	9	8		
Median (in weeks)	-	-		
% of event-free patients+	90,89 [85,00; 96,77]	83,58 [72,00; 95,15]		
			0,48 [0,19; 1,25]	0,134

	Treatment groups		Comparison	
	BAF312 (N=127)	**Placebo (N=61)**	**HR [95% CI]**	**p-value**
Any AE leading to study discontinuation				
Number of patients with event	2	3		
Median (in weeks)	-	-		
% of event-free patients+	98,41 [96,23; 100,00]	94,66 [88,76; 100,00]		
			0,32 [0,05; 1,90]	0,208
Any AE leading to study drug discontinuation				
Number of patients with event	6	4		
Median (in weeks)	-	-		
% of event-free patients+	94,34 [89,78; 98,91]	91,16 [82,34; 99,98]		
			0,67 [0,19; 2,39]	0,539

N': Number of patients in the analysis
CI: Confidence Interval
HR: Hazard Ratio
*: p < 0,05

+ K-M estimate (%) of outcome-free patients, Greenwood formula is used for CIs of KM estimates

Applied model for HR: log(hazard ratio) = treatment
If it was not possible to fit the minimal model, the HR is not given.

1 The following disease-specific Preferred Terms were excluded: see Table 11.0
2 Definition of 'severe': CTCAE grade ≥ 3

Analysis population: A2304 SAF subpopulation "ACTIVE MS WITHOUT RELAPSES"

Table 12.1.2: Time to First AE by Severity (SAF)

	Treatment groups		Comparison	
	BAF312 (N=127)	**Placebo (N=61)**	**HR [95% CI]**	**p-value**
N'	127	61		
Grade 1				
Number of patients with event	108	40		
Median (in weeks)	5,9 [3,6; 10,7]	23,9 [11,3; 47,3]		
% of event-free patients+	13,10 [6,97; 19,23]	32,00 [19,88; 44,12]		
			1,77 [1,23; 2,54]	0,002 *
Grade 2				
Number of patients with event	60	28		
Median (in weeks)	91,6 [54,3; .]	94,6 [62,6; .]		
% of event-free patients+	46,59 [36,50; 56,67]	44,99 [28,18; 61,80]		
			0,98 [0,63; 1,53]	0,927
Grade 3				
Number of patients with event	10	10		
Median (in weeks)	-	-		
% of event-free patients+	90,05 [83,98; 96,13]	80,61 [68,74; 92,49]		
			0,44 [0,18; 1,05]	0,064
Grade 4				
Number of patients with event	3	0		
Median (in weeks)	-	-		
% of event-free patients+	96,98 [93,51; 100,00]	100,00 [100,00; 100,00]		
			-	-
Severe (Grade ≥ 3)				
Number of patients with event	11	10		
Median (in weeks)	-	-		
% of event-free patients+	89,27 [83,06; 95,48]	80,61 [68,74; 92,49]		
			0,48 [0,20; 1,13]	0,093

	Treatment groups		Comparison	
	BAF312 (N=127)	**Placebo (N=61)**	**HR [95% CI]**	**p-value**
Not severe (Grade < 3)				
Number of patients with event	113	47		
Median (in weeks)	3,6 [2,4; 8,4]	9,9 [4,3; 22,6]		
% of event-free patients+	9,12 [3,47; 14,77]	21,43 [10,87; 32,00]		
			1,48 [1,05; 2,08]	0,025 *

N': Number of patients in the analysis
CI: Confidence Interval
HR: Hazard Ratio
*: p < 0,05

+ K-M estimate (%) of outcome-free patients, Greenwood formula is used for CIs of KM estimates

Applied model for HR: log(hazard ratio) = treatment
If it was not possible to fit the minimal model, the HR is not given.

Analysis population: A2304 SAF subpopulation "ACTIVE MS WITHOUT RELAPSES"

Table 12.1.3: Time to First Adverse Event by SOC and PT (SAF)

	Treatment groups		Comparison	
	BAF312 (N=127)	Placebo (N=61)	HR [95% CI]	p-value
N'	127	61		
BLOOD AND LYMPHATIC SYSTEM DISORDERS				
Number of patients with event	10	1		
Median (in weeks)	-	-		
% of event-free patients+	89,59 [82,95; 96,22]	97,62 [93,01; 100,00]		
			4,61 [0,59; 36,00]	0,145
CARDIAC DISORDERS				
Number of patients with event	15	5		
Median (in weeks)	-	-		
% of event-free patients+	87,14 [80,88; 93,40]	91,14 [83,69; 98,59]		
			1,45 [0,53; 3,99]	0,471
EYE DISORDERS				
Number of patients with event	19	3		
Median (in weeks)	-	-		
% of event-free patients+	78,39 [68,20; 88,58]	93,15 [85,15; 100,00]		
			2,94 [0,87; 9,94]	0,083
GASTROINTESTINAL DISORDERS				
Number of patients with event	27	9		
Median (in weeks)	-	-		
% of event-free patients+	74,32 [64,87; 83,77]	79,39 [65,32; 93,47]		
			1,44 [0,68; 3,07]	0,342
GENERAL DISORDERS AND ADMINISTRATION SITE CONDITIONS				
Number of patients with event	31	6		
Median (in weeks)	-	-		
% of event-free patients+	70,78 [60,92; 80,64]	85,99 [74,80; 97,18]		
			2,62 [1,09; 6,28]	0,031 *
FATIGUE				
Number of patients with event	15	0		
Median (in weeks)	-	-		
% of event-free patients+	86,07 [79,05; 93,10]	100,00 [100,00; 100,00]		
			-	-

	Treatment groups		Comparison	
	BAF312 (N=127)	**Placebo (N=61)**	**HR [95% CI]**	**p-value**
INFECTIONS AND INFESTATIONS				
Number of patients with event	65	26		
Median (in weeks)	75,6 [59,4; 100,1]	95,4 [58,0; .]		
% of event-free patients+	36,78 [25,87; 47,68]	43,06 [24,87; 61,25]		
			1,25 [0,79; 1,97]	0,336
NASOPHARYNGITIS				
Number of patients with event	18	7		
Median (in weeks)	-	-		
% of event-free patients+	78,48 [65,40; 91,57]	87,37 [78,54; 96,19]		
			1,19 [0,50; 2,84]	0,700
UPPER RESPIRATORY TRACT INFECTION				
Number of patients with event	10	5		
Median (in weeks)	-	-		
% of event-free patients+	90,04 [84,05; 96,03]	88,48 [78,48; 98,47]		
			0,86 [0,29; 2,53]	0,788
URINARY TRACT INFECTION				
Number of patients with event	21	8		
Median (in weeks)	-	-		
% of event-free patients+	73,48 [59,77; 87,20]	80,93 [67,40; 94,47]		
			1,19 [0,53; 2,69]	0,679
INJURY, POISONING AND PROCEDURAL COMPLICATIONS				
Number of patients with event	31	16		
Median (in weeks)	-	-		
% of event-free patients+	68,54 [58,49; 78,58]	56,73 [37,63; 75,82]		
			0,85 [0,46; 1,56]	0,603
FALL				
Number of patients with event	23	11		
Median (in weeks)	-	-		
% of event-free patients+	77,69 [68,95; 86,44]	71,63 [55,07; 88,19]		
			0,96 [0,47; 1,97]	0,911
INVESTIGATIONS				
Number of patients with event	41	9		
Median (in weeks)	-	-		
% of event-free patients+	51,65 [32,64; 70,66]	81,08 [68,28; 93,88]		
			2,44 [1,18; 5,02]	0,016 *

	Treatment groups		Comparison	
	BAF312 (N=127)	Placebo (N=61)	HR [95% CI]	p-value
ALANINE AMINOTRANSFERASE INCREASED				
Number of patients with event	11	2		
Median (in weeks)	-	-		
% of event-free patients+	90,41 [84,90; 95,91]	96,54 [91,82; 100,00]		
			2,63 [0,58; 11,85]	0,209
METABOLISM AND NUTRITION DISORDERS				
Number of patients with event	12	3		
Median (in weeks)	-	-		
% of event-free patients+	82,41 [69,51; 95,30]	93,72 [86,66; 100,00]		
			1,81 [0,51; 6,41]	0,359
MUSCULOSKELETAL AND CONNECTIVE TISSUE DISORDERS				
Number of patients with event	33	14		
Median (in weeks)	-	-		
% of event-free patients+	65,49 [52,29; 78,70]	68,42 [51,95; 84,89]		
			1,12 [0,60; 2,09]	0,728
ARTHRALGIA				
Number of patients with event	7	8		
Median (in weeks)	-	-		
% of event-free patients+	94,10 [89,83; 98,37]	79,58 [64,25; 94,92]		
			0,40 [0,14; 1,10]	0,075
NEOPLASMS BENIGN, MALIGNANT AND UNSPECIFIED (INCL CYSTS AND POLYPS)				
Number of patients with event	15	1		
Median (in weeks)	-	-		
% of event-free patients+	81,83 [71,05; 92,61]	95,45 [86,75; 100,00]		
			6,92 [0,91; 52,42]	0,061
NERVOUS SYSTEM DISORDERS				
Number of patients with event	45	21		
Median (in weeks)	-	-		
% of event-free patients+	63,34 [54,73; 71,94]	60,09 [45,75; 74,44]		
			1,01 [0,60; 1,70]	0,957
HEADACHE				
Number of patients with event	14	8		
Median (in weeks)	-	-		
% of event-free patients+	88,28 [82,48; 94,09]	77,35 [58,71; 95,99]		
			0,81 [0,34; 1,93]	0,629

	Treatment groups		Comparison	
	BAF312 (N=127)	**Placebo (N=61)**	**HR [95% CI]**	**p-value**
PSYCHIATRIC DISORDERS				
Number of patients with event	16	13		
Median (in weeks)	-	-		
% of event-free patients+	84,39 [76,73; 92,05]	73,21 [58,60; 87,82]		
			0,56 [0,27; 1,16]	0,120
DEPRESSION				
Number of patients with event	8	8		
Median (in weeks)	-	-		
% of event-free patients+	91,35 [85,03; 97,66]	85,06 [75,35; 94,77]		
			0,44 [0,17; 1,18]	0,103
RENAL AND URINARY DISORDERS				
Number of patients with event	13	6		
Median (in weeks)	-	-		
% of event-free patients+	87,91 [81,50; 94,33]	83,16 [68,73; 97,58]		
			1,01 [0,38; 2,65]	0,987
RESPIRATORY, THORACIC AND MEDIASTINAL DISORDERS				
Number of patients with event	22	11		
Median (in weeks)	-	-		
% of event-free patients+	78,34 [69,90; 86,79]	72,78 [56,85; 88,72]		
			0,89 [0,43; 1,84]	0,754
SKIN AND SUBCUTANEOUS TISSUE DISORDERS				
Number of patients with event	19	8		
Median (in weeks)	-	-		
% of event-free patients+	81,25 [72,92; 89,57]	66,44 [35,19; 97,69]		
			1,09 [0,48; 2,49]	0,841
VASCULAR DISORDERS				
Number of patients with event	20	5		
Median (in weeks)	-	-		
% of event-free patients+	76,30 [62,77; 89,83]	91,71 [84,75; 98,67]		
			1,91 [0,72; 5,10]	0,194

	Treatment groups		Comparison	
	BAF312 (N=127)	**Placebo (N=61)**	**HR [95% CI]**	**p-value**
HYPERTENSION				
Number of patients with event	14	5		
Median (in weeks)	-	-		
% of event-free patients+	86,23 [78,37; 94,09]	91,71 [84,75; 98,67]		
			1,31 [0,47; 3,64]	0,606

N': Number of patients in the analysis
CI: Confidence Interval
HR: Hazard Ratio
*: p < 0,05

+ K-M estimate (%) of outcome-free patients, Greenwood formula is used for CIs of KM estimates

Applied model for HR: log(hazard ratio) = treatment
If it was not possible to fit the minimal model, the HR is not given.

Only SOCs/PTs with prevalence of ≥ 10 patients and ≥ 1% or ≥ 10% in at least one treatment arm are displayed.

Analysis population: A2304 SAF subpopulation "ACTIVE MS WITHOUT RELAPSES"

Table 12.1.4: Time to First SAE by SOC and PT (SAF)

There are no data meeting the display criteria for this table.

Table 12.1.5: Time to First Adverse Event by SOC, PT and Severity (SAF)

	Treatment groups		Comparison	
	BAF312 (N=127)	**Placebo (N=61)**	**HR [95% CI]**	**p-value**
N'	127	61		
BLOOD AND LYMPHATIC SYSTEM DISORDERS				
not severe[1]				
Number of patients with event	10	1		
Median (in weeks)	-	-		
% of event-free patients+	89,59 [82,95; 96,22]	97,62 [93,01; 100,00]		
			4,61 [0,59; 36,00]	0,145
severe[1]				
Number of patients with event	0	0		
Median (in weeks)	-	-		
% of event-free patients+	100,00 [100,00; 100,00]	100,00 [100,00; 100,00]		
			-	-
CARDIAC DISORDERS				
not severe[1]				
Number of patients with event	15	4		
Median (in weeks)	-	-		
% of event-free patients+	87,14 [80,88; 93,40]	92,97 [86,30; 99,65]		
			1,81 [0,60; 5,47]	0,290
severe[1]				
Number of patients with event	0	1		
Median (in weeks)	-	-		
% of event-free patients+	100,00 [100,00; 100,00]	98,15 [94,55; 100,00]		
			-	-
BRADYCARDIA				
not severe[1]				
Number of patients with event	7	1		
Median (in weeks)	-	-		
% of event-free patients+	94,46 [90,47; 98,45]	98,36 [95,17; 100,00]		
			3,38 [0,42; 27,48]	0,254

	Treatment groups		Comparison	
	BAF312 (N=127)	**Placebo (N=61)**	**HR [95% CI]**	**p-value**
severe[1]				
Number of patients with event	0	0		
Median (in weeks)	-	-		
% of event-free patients+	100,00 [100,00; 100,00]	100,00 [100,00; 100,00]		
			-	-
EYE DISORDERS				
not severe[1]				
Number of patients with event	19	3		
Median (in weeks)	-	-		
% of event-free patients+	78,35 [68,15; 88,55]	93,07 [85,02; 100,00]		
			2,94 [0,87; 9,94]	0,083
severe[1]				
Number of patients with event	1	1		
Median (in weeks)	-	-		
% of event-free patients+	99,09 [97,32; 100,00]	98,36 [95,17; 100,00]		
			0,48 [0,03; 7,68]	0,604
GASTROINTESTINAL DISORDERS				
not severe[1]				
Number of patients with event	27	8		
Median (in weeks)	-	-		
% of event-free patients+	74,32 [64,87; 83,77]	81,60 [67,82; 95,38]		
			1,63 [0,74; 3,58]	0,227
severe[1]				
Number of patients with event	0	1		
Median (in weeks)	-	-		
% of event-free patients+	100,00 [100,00; 100,00]	97,62 [93,01; 100,00]		
			-	-
NAUSEA				
not severe[1]				
Number of patients with event	4	4		
Median (in weeks)	-	-		
% of event-free patients+	95,26 [89,97; 100,00]	87,88 [74,51; 100,00]		
			0,43 [0,11; 1,72]	0,231

	Treatment groups		Comparison	
	BAF312 (N=127)	**Placebo (N=61)**	**HR [95% CI]**	**p-value**
severe[1]				
Number of patients with event	0	0		
Median (in weeks)	-	-		
% of event-free patients+	100,00 [100,00; 100,00]	100,00 [100,00; 100,00]		
			-	-
GENERAL DISORDERS AND ADMINISTRATION SITE CONDITIONS				
not severe[1]				
Number of patients with event	30	6		
Median (in weeks)	-	-		
% of event-free patients+	71,50 [61,65; 81,36]	85,99 [74,80; 97,18]		
			2,52 [1,05; 6,06]	0,039 *
severe[1]				
Number of patients with event	1	0		
Median (in weeks)	-	-		
% of event-free patients+	99,18 [97,58; 100,00]	100,00 [100,00; 100,00]		
			-	-
FATIGUE				
not severe[1]				
Number of patients with event	15	0		
Median (in weeks)	-	-		
% of event-free patients+	86,07 [79,05; 93,10]	100,00 [100,00; 100,00]		
			-	-
severe[1]				
Number of patients with event	0	0		
Median (in weeks)	-	-		
% of event-free patients+	100,00 [100,00; 100,00]	100,00 [100,00; 100,00]		
			-	-
INFECTIONS AND INFESTATIONS				
not severe[1]				
Number of patients with event	64	26		
Median (in weeks)	77,0 [63,0; 118,1]	95,4 [58,0; .]		
% of event-free patients+	32,12 [17,45; 46,79]	43,06 [24,87; 61,25]		
			1,21 [0,76; 1,90]	0,423

	Treatment groups		Comparison	
	BAF312 (N=127)	**Placebo (N=61)**	**HR [95% CI]**	**p-value**
severe[1]				
Number of patients with event	4	2		
Median (in weeks)	-	-		
% of event-free patients+	96,11 [92,27; 99,94]	88,50 [69,99; 100,00]		
			0,88 [0,16; 4,80]	0,879
INFLUENZA				
not severe[1]				
Number of patients with event	7	4		
Median (in weeks)	-	-		
% of event-free patients+	91,51 [85,08; 97,94]	86,95 [73,26; 100,00]		
			0,71 [0,21; 2,42]	0,580
severe[1]				
Number of patients with event	0	1		
Median (in weeks)	-	-		
% of event-free patients+	100,00 [100,00; 100,00]	90,91 [73,92; 100,00]		
			-	-
NASOPHARYNGITIS				
not severe[1]				
Number of patients with event	18	7		
Median (in weeks)	-	-		
% of event-free patients+	78,48 [65,40; 91,57]	87,37 [78,54; 96,19]		
			1,19 [0,50; 2,84]	0,700
severe[1]				
Number of patients with event	0	0		
Median (in weeks)	-	-		
% of event-free patients+	100,00 [100,00; 100,00]	100,00 [100,00; 100,00]		
			-	-
UPPER RESPIRATORY TRACT INFECTION				
not severe[1]				
Number of patients with event	10	5		
Median (in weeks)	-	-		
% of event-free patients+	90,04 [84,05; 96,03]	88,48 [78,48; 98,47]		
			0,86 [0,29; 2,53]	0,788

	Treatment groups		Comparison	
	BAF312 (N=127)	**Placebo (N=61)**	**HR [95% CI]**	**p-value**
severe[1]				
Number of patients with event	0	0		
Median (in weeks)	-	-		
% of event-free patients+	100,00 [100,00; 100,00]	100,00 [100,00; 100,00]		
			-	-
URINARY TRACT INFECTION				
not severe[1]				
Number of patients with event	20	8		
Median (in weeks)	-	-		
% of event-free patients+	74,72 [61,52; 87,91]	80,93 [67,40; 94,47]		
			1,11 [0,49; 2,53]	0,798
severe[1]				
Number of patients with event	2	0		
Median (in weeks)	-	-		
% of event-free patients+	98,35 [96,09; 100,00]	100,00 [100,00; 100,00]		
			-	-
INJURY, POISONING AND PROCEDURAL COMPLICATIONS				
not severe[1]				
Number of patients with event	30	16		
Median (in weeks)	-	-		
% of event-free patients+	69,87 [60,01; 79,73]	56,65 [37,57; 75,74]		
			0,83 [0,45; 1,52]	0,546
severe[1]				
Number of patients with event	1	1		
Median (in weeks)	-	-		
% of event-free patients+	98,73 [96,27; 100,00]	98,36 [95,17; 100,00]		
			0,44 [0,03; 7,07]	0,563
CONTUSION				
not severe[1]				
Number of patients with event	6	5		
Median (in weeks)	-	-		
% of event-free patients+	94,66 [90,41; 98,92]	88,59 [78,48; 98,70]		
			0,55 [0,17; 1,82]	0,330

	Treatment groups		Comparison	
	BAF312 (N=127)	**Placebo (N=61)**	**HR [95% CI]**	**p-value**
severe[1]				
Number of patients with event	0	0		
Median (in weeks)	-	-		
% of event-free patients+	100,00 [100,00; 100,00]	100,00 [100,00; 100,00]		
			-	-
FALL				
not severe[1]				
Number of patients with event	23	11		
Median (in weeks)	-	-		
% of event-free patients+	77,69 [68,95; 86,44]	71,63 [55,07; 88,19]		
			0,96 [0,47; 1,97]	0,911
severe[1]				
Number of patients with event	0	0		
Median (in weeks)	-	-		
% of event-free patients+	100,00 [100,00; 100,00]	100,00 [100,00; 100,00]		
			-	-
INVESTIGATIONS				
not severe[1]				
Number of patients with event	40	8		
Median (in weeks)	-	-		
% of event-free patients+	52,09 [32,94; 71,24]	82,69 [70,04; 95,35]		
			2,69 [1,26; 5,75]	0,011 *
severe[1]				
Number of patients with event	1	2		
Median (in weeks)	-	-		
% of event-free patients+	99,21 [97,68; 100,00]	96,48 [91,67; 100,00]		
			0,24 [0,02; 2,66]	0,245
ALANINE AMINOTRANSFERASE INCREASED				
not severe[1]				
Number of patients with event	10	1		
Median (in weeks)	-	-		
% of event-free patients+	91,14 [85,78; 96,50]	98,36 [95,17; 100,00]		
			4,74 [0,61; 37,04]	0,138

	Treatment groups		Comparison	
	BAF312 (N=127)	**Placebo (N=61)**	**HR [95% CI]**	**p-value**
severe[1]				
Number of patients with event	1	1		
Median (in weeks)	-	-		
% of event-free patients+	99,21 [97,68; 100,00]	98,15 [94,55; 100,00]		
			0,48 [0,03; 7,73]	0,607
GAMMA-GLUTAMYLTRANSFERASE INCREASED				
not severe[1]				
Number of patients with event	9	1		
Median (in weeks)	-	-		
% of event-free patients+	92,21 [87,28; 97,15]	98,36 [95,17; 100,00]		
			4,33 [0,55; 34,16]	0,165
severe[1]				
Number of patients with event	0	0		
Median (in weeks)	-	-		
% of event-free patients+	100,00 [100,00; 100,00]	100,00 [100,00; 100,00]		
			-	-
WEIGHT DECREASED				
not severe[1]				
Number of patients with event	7	1		
Median (in weeks)	-	-		
% of event-free patients+	94,08 [89,82; 98,34]	98,25 [94,84; 100,00]		
			3,32 [0,41; 26,96]	0,262
severe[1]				
Number of patients with event	0	0		
Median (in weeks)	-	-		
% of event-free patients+	100,00 [100,00; 100,00]	100,00 [100,00; 100,00]		
			-	-
WEIGHT INCREASED				
not severe[1]				
Number of patients with event	2	4		
Median (in weeks)	-	-		
% of event-free patients+	95,52 [88,48; 100,00]	88,94 [76,92; 100,00]		
			0,21 [0,04; 1,18]	0,076

	Treatment groups		Comparison	
	BAF312 (N=127)	**Placebo (N=61)**	**HR [95% CI]**	**p-value**
severe[1]				
Number of patients with event	0	0		
Median (in weeks)	-	-		
% of event-free patients+	100,00 [100,00; 100,00]	100,00 [100,00; 100,00]		
			-	-
METABOLISM AND NUTRITION DISORDERS				
not severe[1]				
Number of patients with event	12	3		
Median (in weeks)	-	-		
% of event-free patients+	82,41 [69,51; 95,30]	93,72 [86,66; 100,00]		
			1,81 [0,51; 6,41]	0,359
severe[1]				
Number of patients with event	0	0		
Median (in weeks)	-	-		
% of event-free patients+	100,00 [100,00; 100,00]	100,00 [100,00; 100,00]		
			-	-
MUSCULOSKELETAL AND CONNECTIVE TISSUE DISORDERS				
not severe[1]				
Number of patients with event	33	13		
Median (in weeks)	-	-		
% of event-free patients+	65,49 [52,29; 78,70]	74,64 [61,96; 87,32]		
			1,21 [0,64; 2,30]	0,561
severe[1]				
Number of patients with event	1	1		
Median (in weeks)	-	-		
% of event-free patients+	98,48 [95,54; 100,00]	94,12 [82,93; 100,00]		
			0,39 [0,02; 6,19]	0,502
ARTHRALGIA				
not severe[1]				
Number of patients with event	7	7		
Median (in weeks)	-	-		
% of event-free patients+	94,10 [89,83; 98,37]	86,22 [76,58; 95,86]		
			0,47 [0,16; 1,33]	0,153

	Treatment groups		Comparison	
	BAF312 (N=127)	**Placebo (N=61)**	**HR [95% CI]**	**p-value**
severe[1]				
Number of patients with event	0	1		
Median (in weeks)	-	-		
% of event-free patients+	100,00 [100,00; 100,00]	94,12 [82,93; 100,00]		
			-	-
NEOPLASMS BENIGN, MALIGNANT AND UNSPECIFIED (INCL CYSTS AND POLYPS)				
not severe[1]				
Number of patients with event	15	0		
Median (in weeks)	-	-		
% of event-free patients+	81,83 [71,05; 92,61]	100,00 [100,00; 100,00]		
			-	-
severe[1]				
Number of patients with event	0	1		
Median (in weeks)	-	-		
% of event-free patients+	100,00 [100,00; 100,00]	95,45 [86,75; 100,00]		
			-	-
MELANOCYTIC NAEVUS				
not severe[1]				
Number of patients with event	8	0		
Median (in weeks)	-	-		
% of event-free patients+	87,54 [76,75; 98,33]	100,00 [100,00; 100,00]		
			-	-
severe[1]				
Number of patients with event	0	0		
Median (in weeks)	-	-		
% of event-free patients+	100,00 [100,00; 100,00]	100,00 [100,00; 100,00]		
			-	-
NERVOUS SYSTEM DISORDERS				
not severe[1]				
Number of patients with event	45	20		
Median (in weeks)	-	-		
% of event-free patients+	63,34 [54,73; 71,94]	61,92 [47,59; 76,24]		
			1,07 [0,63; 1,80]	0,813

	Treatment groups		Comparison	
	BAF312 (N=127)	**Placebo (N=61)**	**HR [95% CI]**	**p-value**
severe[1]				
Number of patients with event	1	1		
Median (in weeks)	-	-		
% of event-free patients+	97,62 [93,01; 100,00]	97,96 [94,00; 100,00]		
			0,43 [0,03; 6,89]	0,552
DIZZINESS				
not severe[1]				
Number of patients with event	8	3		
Median (in weeks)	-	-		
% of event-free patients+	93,63 [89,35; 97,90]	91,03 [79,42; 100,00]		
			1,26 [0,33; 4,74]	0,735
severe[1]				
Number of patients with event	0	0		
Median (in weeks)	-	-		
% of event-free patients+	100,00 [100,00; 100,00]	100,00 [100,00; 100,00]		
			-	-
HEADACHE				
not severe[1]				
Number of patients with event	14	8		
Median (in weeks)	-	-		
% of event-free patients+	88,28 [82,48; 94,09]	77,35 [58,71; 95,99]		
			0,81 [0,34; 1,93]	0,629
severe[1]				
Number of patients with event	1	0		
Median (in weeks)	-	-		
% of event-free patients+	97,62 [93,01; 100,00]	100,00 [100,00; 100,00]		
			-	-
MUSCLE SPASTICITY				
not severe[1]				
Number of patients with event	8	4		
Median (in weeks)	-	-		
% of event-free patients+	92,57 [87,36; 97,79]	93,32 [86,99; 99,65]		
			0,91 [0,28; 3,04]	0,884

	Treatment groups		Comparison	
	BAF312 (N=127)	**Placebo (N=61)**	**HR [95% CI]**	**p-value**
severe[1]				
Number of patients with event	0	0		
Median (in weeks)	-	-		
% of event-free patients+	100,00 [100,00; 100,00]	100,00 [100,00; 100,00]		
			-	-
PSYCHIATRIC DISORDERS				
not severe[1]				
Number of patients with event	16	10		
Median (in weeks)	-	-		
% of event-free patients+	84,16 [76,42; 91,90]	77,61 [63,02; 92,20]		
			0,72 [0,33; 1,59]	0,415
severe[1]				
Number of patients with event	2	3		
Median (in weeks)	-	-		
% of event-free patients+	98,35 [96,07; 100,00]	94,88 [89,23; 100,00]		
			0,32 [0,05; 1,91]	0,211
DEPRESSION				
not severe[1]				
Number of patients with event	7	7		
Median (in weeks)	-	-		
% of event-free patients+	92,20 [86,10; 98,30]	86,91 [77,71; 96,11]		
			0,44 [0,15; 1,25]	0,122
severe[1]				
Number of patients with event	1	1		
Median (in weeks)	-	-		
% of event-free patients+	99,19 [97,60; 100,00]	98,18 [94,65; 100,00]		
			0,49 [0,03; 7,76]	0,609
RENAL AND URINARY DISORDERS				
not severe[1]				
Number of patients with event	13	6		
Median (in weeks)	-	-		
% of event-free patients+	87,91 [81,50; 94,33]	83,16 [68,73; 97,58]		
			1,01 [0,38; 2,65]	0,987

	Treatment groups		Comparison	
	BAF312 (N=127)	**Placebo (N=61)**	**HR [95% CI]**	**p-value**
severe[1]				
Number of patients with event	1	0		
Median (in weeks)	-	-		
% of event-free patients+	98,65 [96,02; 100,00]	100,00 [100,00; 100,00]		
			-	-
REPRODUCTIVE SYSTEM AND BREAST DISORDERS				
not severe[1]				
Number of patients with event	7	3		
Median (in weeks)	-	-		
% of event-free patients+	93,84 [89,35; 98,33]	91,74 [81,75; 100,00]		
			1,08 [0,28; 4,19]	0,910
severe[1]				
Number of patients with event	0	1		
Median (in weeks)	-	-		
% of event-free patients+	100,00 [100,00; 100,00]	98,33 [95,09; 100,00]		
			-	-
RESPIRATORY, THORACIC AND MEDIASTINAL DISORDERS				
not severe[1]				
Number of patients with event	22	11		
Median (in weeks)	-	-		
% of event-free patients+	78,34 [69,90; 86,79]	72,78 [56,85; 88,72]		
			0,89 [0,43; 1,84]	0,754
severe[1]				
Number of patients with event	0	0		
Median (in weeks)	-	-		
% of event-free patients+	100,00 [100,00; 100,00]	100,00 [100,00; 100,00]		
			-	-
COUGH				
not severe[1]				
Number of patients with event	7	1		
Median (in weeks)	-	-		
% of event-free patients+	92,09 [86,13; 98,05]	96,88 [90,85; 100,00]		
			3,13 [0,38; 25,42]	0,287

	Treatment groups		Comparison	
	BAF312 (N=127)	**Placebo (N=61)**	**HR [95% CI]**	**p-value**
severe[1]				
Number of patients with event	0	0		
Median (in weeks)	-	-		
% of event-free patients+	100,00 [100,00; 100,00]	100,00 [100,00; 100,00]		
			-	-
SKIN AND SUBCUTANEOUS TISSUE DISORDERS				
not severe[1]				
Number of patients with event	19	8		
Median (in weeks)	-	-		
% of event-free patients+	81,25 [72,92; 89,57]	66,44 [35,19; 97,69]		
			1,09 [0,48; 2,49]	0,841
severe[1]				
Number of patients with event	1	0		
Median (in weeks)	-	-		
% of event-free patients+	99,16 [97,52; 100,00]	100,00 [100,00; 100,00]		
			-	-
VASCULAR DISORDERS				
not severe[1]				
Number of patients with event	20	5		
Median (in weeks)	-	-		
% of event-free patients+	76,30 [62,77; 89,83]	91,71 [84,75; 98,67]		
			1,91 [0,72; 5,10]	0,194
severe[1]				
Number of patients with event	1	0		
Median (in weeks)	-	-		
% of event-free patients+	98,48 [95,54; 100,00]	100,00 [100,00; 100,00]		
			-	-
HYPERTENSION				
not severe[1]				
Number of patients with event	14	5		
Median (in weeks)	-	-		
% of event-free patients+	86,23 [78,37; 94,09]	91,71 [84,75; 98,67]		
			1,31 [0,47; 3,64]	0,606

	Treatment groups		Comparison	
	BAF312 (N=127)	**Placebo (N=61)**	**HR [95% CI]**	**p-value**
severe[1]				
Number of patients with event	0	0		
Median (in weeks)	-	-		
% of event-free patients[+]	100,00 [100,00; 100,00]	100,00 [100,00; 100,00]		
			-	-

N': Number of patients in the analysis
CI: Confidence Interval
HR: Hazard Ratio
*: p < 0,05

[+] K-M estimate (%) of outcome-free patients, Greenwood formula is used for CIs of KM estimates

Applied model for HR: log(hazard ratio) = treatment
If it was not possible to fit the minimal model, the HR is not given.

[1] Definition of 'severe': CTCAE grade ≥ 3, 'not severe': CTCAE grade < 3

Only SOCs/PTs with prevalence of ≥ 10 patients and ≥ 1% or ≥ 5% in at least one treatment arm are displayed.

Analysis population: A2304 SAF subpopulation "ACTIVE MS WITHOUT RELAPSES"

Table 12.1.6: Time to First Adverse Event of Special Interest by Severity (SAF)

	Treatment groups		Comparison	
	BAF312 (N=127)	**Placebo (N=61)**	**HR [95% CI]**	**p-value**
N'	127	61		
Infections and infestations				
Number of patients with event	65	26		
Median (in weeks)	75,6 [59,4; 100,1]	95,4 [58,0; .]		
% of event-free patients+	36,78 [25,87; 47,68]	43,06 [24,87; 61,25]		
			1,25 [0,79; 1,97]	0,336
not severe				
Number of patients with event	64	26		
Median (in weeks)	77,0 [63,0; 118,1]	95,4 [58,0; .]		
% of event-free patients+	32,12 [17,45; 46,79]	43,06 [24,87; 61,25]		
			1,21 [0,76; 1,90]	0,423
severe				
Number of patients with event	4	2		
Median (in weeks)	-	-		
% of event-free patients+	96,11 [92,27; 99,94]	88,50 [69,99; 100,00]		
			0,88 [0,16; 4,80]	0,879
serious				
Number of patients with event	5	2		
Median (in weeks)	-	-		
% of event-free patients+	95,41 [91,37; 99,45]	88,50 [69,99; 100,00]		
			1,13 [0,22; 5,85]	0,882
Herpes simplex virus infections				
Number of patients with event	4	1		
Median (in weeks)	-	-		
% of event-free patients+	96,20 [92,41; 99,98]	98,36 [95,17; 100,00]		
			1,84 [0,21; 16,51]	0,585
not severe				
Number of patients with event	4	1		
Median (in weeks)	-	-		
% of event-free patients+	96,20 [92,41; 99,98]	98,36 [95,17; 100,00]		
			1,84 [0,21; 16,51]	0,585

	Treatment groups		Comparison	
	BAF312 (N=127)	**Placebo (N=61)**	**HR [95% CI]**	**p-value**
severe				
Number of patients with event	0	0		
Median (in weeks)	-	-		
% of event-free patients+	100,00 [100,00; 100,00]	100,00 [100,00; 100,00]		
			-	-
serious				
Number of patients with event	0	0		
Median (in weeks)	-	-		
% of event-free patients+	100,00 [100,00; 100,00]	100,00 [100,00; 100,00]		
			-	-
Varicella-zoster virus infections				
Number of patients with event	1	0		
Median (in weeks)	-	-		
% of event-free patients+	99,08 [97,29; 100,00]	100,00 [100,00; 100,00]		
			-	-
not severe				
Number of patients with event	0	0		
Median (in weeks)	-	-		
% of event-free patients+	100,00 [100,00; 100,00]	100,00 [100,00; 100,00]		
			-	-
severe				
Number of patients with event	1	0		
Median (in weeks)	-	-		
% of event-free patients+	99,08 [97,29; 100,00]	100,00 [100,00; 100,00]		
			-	-
serious				
Number of patients with event	0	0		
Median (in weeks)	-	-		
% of event-free patients+	100,00 [100,00; 100,00]	100,00 [100,00; 100,00]		
			-	-

	Treatment groups		Comparison	
	BAF312 (N=127)	**Placebo (N=61)**	**HR [95% CI]**	**p-value**
Lymphopenia				
Number of patients with event	2	0		
Median (in weeks)	-	-		
% of event-free patients+	98,30 [95,97; 100,00]	100,00 [100,00; 100,00]		
			-	-
not severe				
Number of patients with event	2	0		
Median (in weeks)	-	-		
% of event-free patients+	98,30 [95,97; 100,00]	100,00 [100,00; 100,00]		
			-	-
severe				
Number of patients with event	0	0		
Median (in weeks)	-	-		
% of event-free patients+	100,00 [100,00; 100,00]	100,00 [100,00; 100,00]		
			-	-
serious				
Number of patients with event	0	0		
Median (in weeks)	-	-		
% of event-free patients+	100,00 [100,00; 100,00]	100,00 [100,00; 100,00]		
			-	-
Macular edema				
Number of patients with event	2	1		
Median (in weeks)	-	-		
% of event-free patients+	98,27 [95,89; 100,00]	96,30 [89,17; 100,00]		
			0,89 [0,08; 9,82]	0,922
not severe				
Number of patients with event	1	0		
Median (in weeks)	-	-		
% of event-free patients+	99,18 [97,58; 100,00]	100,00 [100,00; 100,00]		
			-	-

	Treatment groups		Comparison	
	BAF312 (N=127)	**Placebo (N=61)**	**HR [95% CI]**	**p-value**
severe				
Number of patients with event	1	1		
Median (in weeks)	-	-		
% of event-free patients+	99,09 [97,32; 100,00]	96,30 [89,17; 100,00]		
			0,43 [0,03; 6,83]	0,546
serious				
Number of patients with event	0	0		
Median (in weeks)	-	-		
% of event-free patients+	100,00 [100,00; 100,00]	100,00 [100,00; 100,00]		
			-	-
Abnormal hepatic enzymes				
Number of patients with event	19	4		
Median (in weeks)	-	-		
% of event-free patients+	83,60 [76,70; 90,49]	93,26 [86,87; 99,65]		
			2,33 [0,79; 6,85]	0,124
not severe				
Number of patients with event	18	2		
Median (in weeks)	-	-		
% of event-free patients+	84,28 [77,46; 91,10]	96,72 [92,25; 100,00]		
			4,43 [1,03; 19,08]	0,046 *
severe				
Number of patients with event	1	2		
Median (in weeks)	-	-		
% of event-free patients+	99,21 [97,68; 100,00]	96,48 [91,67; 100,00]		
			0,24 [0,02; 2,66]	0,245
serious				
Number of patients with event	2	2		
Median (in weeks)	-	-		
% of event-free patients+	98,39 [96,18; 100,00]	96,69 [92,19; 100,00]		
			0,47 [0,07; 3,35]	0,452

	Treatment groups		Comparison	
	BAF312 (N=127)	**Placebo (N=61)**	**HR [95% CI]**	**p-value**
Malignancies				
Number of patients with event	0	1		
Median (in weeks)	-	-		
% of event-free patients+	100,00 [100,00; 100,00]	95,45 [86,75; 100,00]		
			-	-
not severe				
Number of patients with event	0	0		
Median (in weeks)	-	-		
% of event-free patients+	100,00 [100,00; 100,00]	100,00 [100,00; 100,00]		
			-	-
severe				
Number of patients with event	0	1		
Median (in weeks)	-	-		
% of event-free patients+	100,00 [100,00; 100,00]	95,45 [86,75; 100,00]		
			-	-
serious				
Number of patients with event	0	1		
Median (in weeks)	-	-		
% of event-free patients+	100,00 [100,00; 100,00]	95,45 [86,75; 100,00]		
			-	-
Hypertension				
Number of patients with event	17	5		
Median (in weeks)	-	-		
% of event-free patients+	82,22 [73,09; 91,35]	91,71 [84,75; 98,67]		
			1,60 [0,59; 4,34]	0,356
not severe				
Number of patients with event	17	5		
Median (in weeks)	-	-		
% of event-free patients+	82,22 [73,09; 91,35]	91,71 [84,75; 98,67]		
			1,60 [0,59; 4,34]	0,356

	Treatment groups		Comparison	
	BAF312 (N=127)	**Placebo (N=61)**	**HR [95% CI]**	**p-value**
severe				
Number of patients with event	0	0		
Median (in weeks)	-	-		
% of event-free patients+	100,00 [100,00; 100,00]	100,00 [100,00; 100,00]		
			-	-
serious				
Number of patients with event	0	0		
Median (in weeks)	-	-		
% of event-free patients+	100,00 [100,00; 100,00]	100,00 [100,00; 100,00]		
			-	-
Seizures				
Number of patients with event	0	0		
Median (in weeks)	-	-		
% of event-free patients+	100,00 [100,00; 100,00]	100,00 [100,00; 100,00]		
			-	-
not severe				
Number of patients with event	0	0		
Median (in weeks)	-	-		
% of event-free patients+	100,00 [100,00; 100,00]	100,00 [100,00; 100,00]		
			-	-
severe				
Number of patients with event	0	0		
Median (in weeks)	-	-		
% of event-free patients+	100,00 [100,00; 100,00]	100,00 [100,00; 100,00]		
			-	-
serious				
Number of patients with event	0	0		
Median (in weeks)	-	-		
% of event-free patients+	100,00 [100,00; 100,00]	100,00 [100,00; 100,00]		
			-	-

	Treatment groups		Comparison	
	BAF312 (N=127)	**Placebo (N=61)**	**HR [95% CI]**	**p-value**
Thromboembolic events				
Number of patients with event	5	1		
Median (in weeks)	-	-		
% of event-free patients+	91,31 [80,65; 100,00]	98,15 [94,55; 100,00]		
			2,34 [0,27; 20,07]	0,437
not severe				
Number of patients with event	5	0		
Median (in weeks)	-	-		
% of event-free patients+	91,31 [80,65; 100,00]	100,00 [100,00; 100,00]		
			-	-
severe				
Number of patients with event	0	1		
Median (in weeks)	-	-		
% of event-free patients+	100,00 [100,00; 100,00]	98,15 [94,55; 100,00]		
			-	-
serious				
Number of patients with event	1	1		
Median (in weeks)	-	-		
% of event-free patients+	99,08 [97,29; 100,00]	98,15 [94,55; 100,00]		
			0,47 [0,03; 7,48]	0,591
Respiratory disorders				
Number of patients with event	22	11		
Median (in weeks)	-	-		
% of event-free patients+	78,34 [69,90; 86,79]	72,78 [56,85; 88,72]		
			0,89 [0,43; 1,84]	0,754
not severe				
Number of patients with event	22	11		
Median (in weeks)	-	-		
% of event-free patients+	78,34 [69,90; 86,79]	72,78 [56,85; 88,72]		
			0,89 [0,43; 1,84]	0,754

	Treatment groups		Comparison	
	BAF312 (N=127)	**Placebo (N=61)**	**HR [95% CI]**	**p-value**
severe				
Number of patients with event	0	0		
Median (in weeks)	-	-		
% of event-free patients+	100,00 [100,00; 100,00]	100,00 [100,00; 100,00]		
			-	-
serious				
Number of patients with event	0	0		
Median (in weeks)	-	-		
% of event-free patients+	100,00 [100,00; 100,00]	100,00 [100,00; 100,00]		
			-	-
Peripheral edema/swelling				
Number of patients with event	6	1		
Median (in weeks)	-	-		
% of event-free patients+	92,67 [85,47; 99,86]	98,18 [94,65; 100,00]		
			2,82 [0,34; 23,43]	0,338
not severe				
Number of patients with event	6	1		
Median (in weeks)	-	-		
% of event-free patients+	92,67 [85,47; 99,86]	98,18 [94,65; 100,00]		
			2,82 [0,34; 23,43]	0,338
severe				
Number of patients with event	0	0		
Median (in weeks)	-	-		
% of event-free patients+	100,00 [100,00; 100,00]	100,00 [100,00; 100,00]		
			-	-

	Treatment groups		Comparison	
	BAF312 (N=127)	**Placebo (N=61)**	**HR [95% CI]**	**p-value**
serious				
Number of patients with event	0	0		
Median (in weeks)	-	-		
% of event-free patients+	100,00 [100,00; 100,00]	100,00 [100,00; 100,00]		
			-	-

N': Number of patients in the analysis
CI: Confidence Interval
HR: Hazard Ratio
*: p < 0,05

+ K-M estimate (%) of outcome-free patients, Greenwood formula is used for CIs of KM estimates

Applied model for HR: log(hazard ratio) = treatment
If it was not possible to fit the minimal model, the HR is not given.

Analysis population: A2304 SAF subpopulation "ACTIVE MS WITHOUT RELAPSES"

	Treatment groups		Comparison	
	BAF312 (N=127)	**Placebo (N=61)**	**HR [95% CI]**	**p-value**
N'	127	61		
Asthma/bronchospasm				
Number of patients with event	1	0		
Median (in weeks)	-	-		
% of event-free patients+	99,19 [97,60; 100,00]	100,00 [100,00; 100,00]		
			-	-
not severe				
Number of patients with event	1	0		
Median (in weeks)	-	-		
% of event-free patients+	99,19 [97,60; 100,00]	100,00 [100,00; 100,00]		
			-	-
severe				
Number of patients with event	0	0		
Median (in weeks)	-	-		
% of event-free patients+	100,00 [100,00; 100,00]	100,00 [100,00; 100,00]		
			-	-
serious				
Number of patients with event	0	0		
Median (in weeks)	-	-		
% of event-free patients+	100,00 [100,00; 100,00]	100,00 [100,00; 100,00]		
			-	-
Pregnancy and neonatal topics				
Number of patients with event	1	0		
Median (in weeks)	-	-		
% of event-free patients+	99,21 [97,68; 100,00]	100,00 [100,00; 100,00]		
			-	-
not severe				
Number of patients with event	1	0		
Median (in weeks)	-	-		
% of event-free patients+	99,21 [97,68; 100,00]	100,00 [100,00; 100,00]		
			-	-

	Treatment groups		Comparison	
	BAF312 (N=127)	**Placebo (N=61)**	**HR [95% CI]**	**p-value**
severe				
Number of patients with event	0	0		
Median (in weeks)	-	-		
% of event-free patients+	100,00 [100,00; 100,00]	100,00 [100,00; 100,00]		
			-	-
serious				
Number of patients with event	0	0		
Median (in weeks)	-	-		
% of event-free patients+	100,00 [100,00; 100,00]	100,00 [100,00; 100,00]		
			-	-
Bradyarrhythmias and bradycardia				
Number of patients with event	11	1		
Median (in weeks)	-	-		
% of event-free patients+	91,31 [86,40; 96,22]	98,36 [95,17; 100,00]		
			5,35 [0,69; 41,42]	0,108
not severe				
Number of patients with event	11	1		
Median (in weeks)	-	-		
% of event-free patients+	91,31 [86,40; 96,22]	98,36 [95,17; 100,00]		
			5,35 [0,69; 41,42]	0,108
severe				
Number of patients with event	0	0		
Median (in weeks)	-	-		
% of event-free patients+	100,00 [100,00; 100,00]	100,00 [100,00; 100,00]		
			-	-

	Treatment groups		Comparison	
	BAF312 (N=127)	**Placebo (N=61)**	**HR [95% CI]**	**p-value**
serious				
Number of patients with event	0	0		
Median (in weeks)	-	-		
% of event-free patients+	100,00 [100,00; 100,00]	100,00 [100,00; 100,00]		
			-	-

N': Number of patients in the analysis
CI: Confidence Interval
HR: Hazard Ratio
*: p < 0,05

+ K-M estimate (%) of outcome-free patients, Greenwood formula is used for CIs of KM estimates

Applied model for HR: log(hazard ratio) = treatment
If it was not possible to fit the minimal model, the HR is not given.

Analysis population: A2304 SAF subpopulation "ACTIVE MS WITHOUT RELAPSES"

12.2 Subgroup: Age

Table 12.2.1: Time to First Adverse Event (SAF) by Age

	Treatment groups		Comparison	
	BAF312 (N=127)	**Placebo (N=61)**	**HR [95% CI]**	**p-value**
N'	127	61		
N' Age = 18-40 years	18	13		
N' Age = 41-55 years	95	33		
N' Age = >55 years	14	15		
Any AE				
Interaction test:	p=0,738			
Age = 18-40 years				
Number of patients with event	14	11		
Median (in weeks)	5,6 [1,6; 13,1]	9,9 [2,9; 28,6]		
% of event-free patients+	22,22 [3,02; 41,43]	15,38 [0,00; 35,00]		
			1,09 [0,49; 2,40]	0,831
Age = 41-55 years				
Number of patients with event	89	25		
Median (in weeks)	3,6 [2,0; 8,3]	6,7 [2,6; 18,6]		
% of event-free patients+	4,37 [0,00; 9,34]	23,33 [8,62; 38,04]		
			1,53 [0,98; 2,39]	0,059
Age = >55 years				
Number of patients with event	11	11		
Median (in weeks)	13,0 [2,9; 28,9]	22,4 [5,9; 52,4]		
% of event-free patients+	15,87 [0,00; 35,97]	23,33 [0,80; 45,87]		
			1,26 [0,55; 2,91]	0,589
Any AE, disease specific events excluded[1]				
Interaction test:	p=0,848			
Age = 18-40 years				
Number of patients with event	13	10		
Median (in weeks)	11,9 [2,0; 45,4]	11,3 [2,9; 91,0]		
% of event-free patients+	27,78 [7,09; 48,47]	0,00 [0,00; 0,00]		
			1,00 [0,44; 2,28]	0,999
Age = 41-55 years				
Number of patients with event	84	25		
Median (in weeks)	10,3 [5,0; 13,7]	11,9 [4,4; 23,6]		
% of event-free patients+	7,03 [0,83; 13,24]	19,70 [3,70; 35,69]		
			1,29 [0,83; 2,02]	0,260

	Treatment groups		Comparison	
	BAF312 (N=127)	**Placebo (N=61)**	**HR [95% CI]**	**p-value**
Age = >55 years				
Number of patients with event	11	11		
Median (in weeks)	15,3 [5,9; 43,4]	30,0 [7,0; 52,4]		
% of event-free patients+	15,71 [0,00; 35,66]	22,50 [0,33; 44,67]		
			1,34 [0,58; 3,11]	0,488
Any SAE				
Interaction test:	p=0,852			
Age = 18-40 years				
Number of patients with event	1	2		
Median (in weeks)	-	-		
% of event-free patients+	94,12 [82,93; 100,00]	84,62 [65,00; 100,00]		
			0,35 [0,03; 3,82]	0,387
Age = 41-55 years				
Number of patients with event	13	6		
Median (in weeks)	-	-		
% of event-free patients+	83,32 [74,66; 91,98]	81,24 [67,66; 94,82]		
			0,65 [0,25; 1,71]	0,382
Age = >55 years				
Number of patients with event	2	3		
Median (in weeks)	-	-		
% of event-free patients+	85,12 [66,05; 100,00]	72,22 [42,67; 100,00]		
			0,81 [0,14; 4,88]	0,822
Any SAE, disease specific events excluded[1]				
Interaction test:	p=0,771			
Age = 18-40 years				
Number of patients with event	1	2		
Median (in weeks)	-	-		
% of event-free patients+	94,12 [82,93; 100,00]	84,62 [65,00; 100,00]		
			0,34 [0,03; 3,80]	0,384
Age = 41-55 years				
Number of patients with event	9	3		
Median (in weeks)	-	-		
% of event-free patients+	88,88 [81,81; 95,95]	90,14 [79,51; 100,00]		
			0,94 [0,25; 3,47]	0,922

	Treatment groups		Comparison	
	BAF312 (N=127)	**Placebo (N=61)**	**HR [95% CI]**	**p-value**
Age = >55 years				
Number of patients with event	2	3		
Median (in weeks)	-	-		
% of event-free patients+	85,12 [66,05; 100,00]	72,22 [42,67; 100,00]		
			0,81 [0,13; 4,84]	0,815
Any severe AE[2]				
Interaction test:	p=0,964			
Age = 18-40 years				
Number of patients with event	1	1		
Median (in weeks)	-	-		
% of event-free patients+	94,12 [82,93; 100,00]	92,31 [77,82; 100,00]		
			0,73 [0,05; 11,67]	0,824
Age = 41-55 years				
Number of patients with event	10	6		
Median (in weeks)	-	-		
% of event-free patients+	87,30 [79,74; 94,86]	81,24 [67,66; 94,82]		
			0,49 [0,18; 1,34]	0,164
Age = >55 years				
Number of patients with event	0	3		
Median (in weeks)	-	-		
% of event-free patients+	100,00 [100,00; 100,00]	73,85 [46,78; 100,00]		
			-	-
Any severe AE[2], disease specific events excluded[1]				
Interaction test:	p=0,985			
Age = 18-40 years				
Number of patients with event	1	1		
Median (in weeks)	-	-		
% of event-free patients+	94,12 [82,93; 100,00]	92,31 [77,82; 100,00]		
			0,74 [0,05; 11,84]	0,831
Age = 41-55 years				
Number of patients with event	8	4		
Median (in weeks)	-	-		
% of event-free patients+	89,43 [82,32; 96,55]	87,09 [75,21; 98,96]		
			0,56 [0,17; 1,88]	0,353

	Treatment groups		Comparison	
	BAF312 (N=127)	**Placebo (N=61)**	**HR [95% CI]**	**p-value**
Age = >55 years				
Number of patients with event	0	3		
Median (in weeks)	-	-		
% of event-free patients+	100,00 [100,00; 100,00]	73,85 [46,78; 100,00]		
			-	-
Any AE leading to study discontinuation				
Interaction test:	p=1,000			
Age = 18-40 years				
Number of patients with event	0	0		
Median (in weeks)	-	-		
% of event-free patients+	100,00 [100,00; 100,00]	100,00 [100,00; 100,00]		
			-	-
Age = 41-55 years				
Number of patients with event	2	3		
Median (in weeks)	-	-		
% of event-free patients+	97,88 [94,98; 100,00]	89,99 [79,17; 100,00]		
			0,22 [0,04; 1,34]	0,101
Age = >55 years				
Number of patients with event	0	0		
Median (in weeks)	-	-		
% of event-free patients+	100,00 [100,00; 100,00]	100,00 [100,00; 100,00]		
			-	-
Any AE leading to study drug discontinuation				
Interaction test:	p=1,000			
Age = 18-40 years				
Number of patients with event	0	0		
Median (in weeks)	-	-		
% of event-free patients+	100,00 [100,00; 100,00]	100,00 [100,00; 100,00]		
			-	-

	Treatment groups		Comparison	
	BAF312 (N=127)	**Placebo (N=61)**	**HR [95% CI]**	**p-value**
Age = 41-55 years				
Number of patients with event	6	3		
Median (in weeks)	-	-		
% of event-free patients+	92,67 [86,85; 98,48]	89,99 [79,17; 100,00]		
			0,61 [0,15; 2,44]	0,484
Age = >55 years				
Number of patients with event	0	1		
Median (in weeks)	-	-		
% of event-free patients+	100,00 [100,00; 100,00]	87,50 [64,58; 100,00]		
			-	-

N': Number of patients in the analysis
CI: Confidence Interval
HR: Hazard Ratio
*: p < 0,05

+ K-M estimate (%) of outcome-free patients, Greenwood formula is used for CIs of KM estimates

Applied model for HR: log(hazard ratio) = treatment + age + age * treatment
If it was not possible to fit the minimal model, the HR is not given.

[1] The following disease-specific Preferred Terms were excluded: see Table 11.0
[2] Definition of 'severe': CTCAE grade ≥ 3

Analysis population: A2304 SAF subpopulation "ACTIVE MS WITHOUT RELAPSES"

Table 12.2.2: Time to First Adverse Event by SOC and PT (SAF) by Age

	Treatment groups		Comparison	
	BAF312 (N=127)	**Placebo (N=61)**	**HR [95% CI]**	**p-value**
N'	127	61		
N' Age = 18-40 years	18	13		
N' Age = 41-55 years	95	33		
N' Age = >55 years	14	15		
GENERAL DISORDERS AND ADMINISTRATION SITE CONDITIONS				
Interaction test:	p=0,308			
Age = 18-40 years				
Number of patients with event	4	3		
Median (in weeks)	-	-		
% of event-free patients+	77,38 [57,84; 96,92]	75,52 [51,38; 99,67]		
			0,97 [0,22; 4,33]	0,967
Age = 41-55 years				
Number of patients with event	27	2		
Median (in weeks)	-	-		
% of event-free patients+	66,16 [54,37; 77,95]	89,33 [74,18; 100,00]		
			4,92 [1,17; 20,70]	0,030 *
Age = >55 years				
Number of patients with event	0	1		
Median (in weeks)	-	-		
% of event-free patients+	100,00 [100,00; 100,00]	88,89 [68,36; 100,00]		
			-	-
INVESTIGATIONS				
Interaction test:	p=0,650			
Age = 18-40 years				
Number of patients with event	5	1		
Median (in weeks)	-	-		
% of event-free patients+	68,21 [44,45; 91,97]	92,31 [77,82; 100,00]		
			4,29 [0,50; 36,82]	0,184
Age = 41-55 years				
Number of patients with event	31	4		
Median (in weeks)	130,0 [118,6; .]	-		
% of event-free patients+	49,43 [27,72; 71,13]	86,67 [74,38; 98,95]		
			2,92 [1,03; 8,27]	0,044 *

	Treatment groups		Comparison	
	BAF312 (N=127)	**Placebo (N=61)**	**HR [95% CI]**	**p-value**
Age = >55 years				
Number of patients with event	5	4		
Median (in weeks)	-	-		
% of event-free patients+	59,83 [32,37; 87,29]	63,18 [30,71; 95,65]		
			1,53 [0,41; 5,70]	0,528

N': Number of patients in the analysis
CI: Confidence Interval
HR: Hazard Ratio
*: p < 0,05

+ K-M estimate (%) of outcome-free patients, Greenwood formula is used for CIs of KM estimates

Applied model for HR: log(hazard ratio) = treatment + age + age * treatment
If it was not possible to fit the minimal model, the HR is not given.

SOCs/PTs are only displayed in this subgroup analysis, if the p-value for HR in the entire population is significant (p<0.05).

Analysis population: A2304 SAF subpopulation "ACTIVE MS WITHOUT RELAPSES"

Table 12.2.3: Time to First Serious Adverse Event by SOC and PT (SAF) by Age

There are no data meeting the display criteria for this table.

Table 12.2.4: Time to First Severe Adverse Event by SOC and PT (SAF) by Age

There are no data meeting the display criteria for this table.

Table 12.2.5: Time to First Adverse Event of Special Interest (SAF) by Age

	Treatment groups		Comparison	
	BAF312 (N=127)	**Placebo (N=61)**	**HR [95% CI]**	**p-value**
N'	127	61		
N' Age = 18-40 years	18	13		
N' Age = 41-55 years	95	33		
N' Age = >55 years	14	15		
Infections and infestations				
Interaction test:	p=0,425			
Age = 18-40 years				
Number of patients with event	4	4		
Median (in weeks)	-	-		
% of event-free patients+	75,66 [54,68; 96,64]	62,94 [32,74; 93,14]		
			0,69 [0,17; 2,77]	0,604
Age = 41-55 years				
Number of patients with event	55	13		
Median (in weeks)	68,1 [50,4; 80,9]	95,4 [51,0; .]		
% of event-free patients+	30,42 [18,37; 42,47]	43,32 [15,05; 71,58]		
			1,49 [0,81; 2,72]	0,199
Age = >55 years				
Number of patients with event	6	9		
Median (in weeks)	100,1 [49,0; .]	77,6 [45,6; .]		
% of event-free patients+	40,38 [3,37; 77,40]	33,50 [7,73; 59,28]		
			0,79 [0,28; 2,22]	0,651
Herpes simplex virus infections				
Interaction test:	p=1,000			
Age = 18-40 years				
Number of patients with event	0	0		
Median (in weeks)	-	-		
% of event-free patients+	100,00 [100,00; 100,00]	100,00 [100,00; 100,00]		
			-	-
Age = 41-55 years				
Number of patients with event	4	1		
Median (in weeks)	-	-		
% of event-free patients+	95,06 [90,22; 99,90]	96,97 [91,12; 100,00]		
			1,26 [0,14; 11,30]	0,839

	Treatment groups		Comparison	
	BAF312 (N=127)	**Placebo (N=61)**	**HR [95% CI]**	**p-value**
Age = >55 years				
Number of patients with event	0	0		
Median (in weeks)	-	-		
% of event-free patients+	100,00 [100,00; 100,00]	100,00 [100,00; 100,00]		
			-	-
Varicella-zoster virus infections				
Interaction test:	p=1,000			
Age = 18-40 years				
Number of patients with event	0	0		
Median (in weeks)	-	-		
% of event-free patients+	100,00 [100,00; 100,00]	100,00 [100,00; 100,00]		
			-	-
Age = 41-55 years				
Number of patients with event	1	0		
Median (in weeks)	-	-		
% of event-free patients+	98,78 [96,40; 100,00]	100,00 [100,00; 100,00]		
			-	-
Age = >55 years				
Number of patients with event	0	0		
Median (in weeks)	-	-		
% of event-free patients+	100,00 [100,00; 100,00]	100,00 [100,00; 100,00]		
			-	-
Lymphopenia				
Interaction test:	p=1,000			
Age = 18-40 years				
Number of patients with event	1	0		
Median (in weeks)	-	-		
% of event-free patients+	94,12 [82,93; 100,00]	100,00 [100,00; 100,00]		
			-	-
Age = 41-55 years				
Number of patients with event	1	0		
Median (in weeks)	-	-		
% of event-free patients+	98,84 [96,57; 100,00]	100,00 [100,00; 100,00]		
			-	-

	Treatment groups		Comparison	
	BAF312 (N=127)	**Placebo (N=61)**	**HR [95% CI]**	**p-value**
Age = >55 years				
Number of patients with event	0	0		
Median (in weeks)	-	-		
% of event-free patients+	100,00 [100,00; 100,00]	100,00 [100,00; 100,00]		
			-	-
Macular edema				
Interaction test:	p=1,000			
Age = 18-40 years				
Number of patients with event	0	0		
Median (in weeks)	-	-		
% of event-free patients+	100,00 [100,00; 100,00]	100,00 [100,00; 100,00]		
			-	-
Age = 41-55 years				
Number of patients with event	2	0		
Median (in weeks)	-	-		
% of event-free patients+	97,68 [94,50; 100,00]	100,00 [100,00; 100,00]		
			-	-
Age = >55 years				
Number of patients with event	0	1		
Median (in weeks)	-	-		
% of event-free patients+	100,00 [100,00; 100,00]	87,50 [64,58; 100,00]		
			-	-
Abnormal hepatic enzymes				
Interaction test:	p=0,999			
Age = 18-40 years				
Number of patients with event	3	1		
Median (in weeks)	-	-		
% of event-free patients+	79,69 [58,42; 100,00]	92,31 [77,82; 100,00]		
			2,26 [0,24; 21,76]	0,480
Age = 41-55 years				
Number of patients with event	14	2		
Median (in weeks)	-	-		
% of event-free patients+	84,11 [76,34; 91,88]	93,84 [85,57; 100,00]		
			2,38 [0,54; 10,47]	0,252

	Treatment groups		Comparison	
	BAF312 (N=127)	**Placebo (N=61)**	**HR [95% CI]**	**p-value**
Age = >55 years				
Number of patients with event	2	1		
Median (in weeks)	-	-		
% of event-free patients+	84,62 [65,00; 100,00]	92,86 [79,37; 100,00]		
			2,45 [0,22; 27,03]	0,465
Malignancies				
Interaction test:	p=1,000			
Age = 18-40 years				
Number of patients with event	0	0		
Median (in weeks)	-	-		
% of event-free patients+	100,00 [100,00; 100,00]	100,00 [100,00; 100,00]		
			-	-
Age = 41-55 years				
Number of patients with event	0	0		
Median (in weeks)	-	-		
% of event-free patients+	100,00 [100,00; 100,00]	100,00 [100,00; 100,00]		
			-	-
Age = >55 years				
Number of patients with event	0	1		
Median (in weeks)	-	-		
% of event-free patients+	100,00 [100,00; 100,00]	85,71 [59,79; 100,00]		
			-	-
Hypertension				
Interaction test:	p=1,000			
Age = 18-40 years				
Number of patients with event	0	0		
Median (in weeks)	-	-		
% of event-free patients+	100,00 [100,00; 100,00]	100,00 [100,00; 100,00]		
			-	-
Age = 41-55 years				
Number of patients with event	16	5		
Median (in weeks)	-	-		
% of event-free patients+	78,25 [67,20; 89,29]	84,62 [72,21; 97,04]		
			1,02 [0,37; 2,79]	0,970

	Treatment groups		Comparison	
	BAF312 (N=127)	**Placebo (N=61)**	**HR [95% CI]**	**p-value**
Age = >55 years				
Number of patients with event	1	0		
Median (in weeks)	-	-		
% of event-free patients+	90,00 [71,41; 100,00]	100,00 [100,00; 100,00]		
			-	-
Seizures				
Interaction test:	N.E.			
Age = 18-40 years				
Number of patients with event	0	0		
Median (in weeks)	-	-		
% of event-free patients+	100,00 [100,00; 100,00]	100,00 [100,00; 100,00]		
			-	-
Age = 41-55 years				
Number of patients with event	0	0		
Median (in weeks)	-	-		
% of event-free patients+	100,00 [100,00; 100,00]	100,00 [100,00; 100,00]		
			-	-
Age = >55 years				
Number of patients with event	0	0		
Median (in weeks)	-	-		
% of event-free patients+	100,00 [100,00; 100,00]	100,00 [100,00; 100,00]		
			-	-
Thromboembolic events				
Interaction test:	p=1,000			
Age = 18-40 years				
Number of patients with event	0	0		
Median (in weeks)	-	-		
% of event-free patients+	100,00 [100,00; 100,00]	100,00 [100,00; 100,00]		
			-	-
Age = 41-55 years				
Number of patients with event	4	1		
Median (in weeks)	-	-		
% of event-free patients+	90,70 [78,73; 100,00]	96,43 [89,55; 100,00]		
			1,30 [0,14; 11,65]	0,815

	Treatment groups		Comparison	
	BAF312 (N=127)	**Placebo (N=61)**	**HR [95% CI]**	**p-value**
Age = >55 years				
Number of patients with event	1	0		
Median (in weeks)	-	-		
% of event-free patients+	91,67 [76,03; 100,00]	100,00 [100,00; 100,00]		
			-	-
Respiratory disorders				
Interaction test:	p=0,953			
Age = 18-40 years				
Number of patients with event	1	1		
Median (in weeks)	-	-		
% of event-free patients+	93,75 [81,89; 100,00]	92,31 [77,82; 100,00]		
			0,67 [0,04; 10,66]	0,774
Age = 41-55 years				
Number of patients with event	21	6		
Median (in weeks)	-	-		
% of event-free patients+	72,89 [62,50; 83,29]	70,53 [45,71; 95,35]		
			1,06 [0,43; 2,62]	0,906
Age = >55 years				
Number of patients with event	0	4		
Median (in weeks)	-	-		
% of event-free patients+	100,00 [100,00; 100,00]	63,82 [33,59; 94,04]		
			-	-
Peripheral edema/swelling				
Interaction test:	p=1,000			
Age = 18-40 years				
Number of patients with event	0	1		
Median (in weeks)	-	-		
% of event-free patients+	100,00 [100,00; 100,00]	91,67 [76,03; 100,00]		
			-	-
Age = 41-55 years				
Number of patients with event	6	0		
Median (in weeks)	-	-		
% of event-free patients+	90,52 [81,49; 99,54]	100,00 [100,00; 100,00]		
			-	-

	Treatment groups		Comparison	
	BAF312 (N=127)	**Placebo (N=61)**	**HR [95% CI]**	**p-value**
Age = >55 years				
Number of patients with event	0	0		
Median (in weeks)	-	-		
% of event-free patients+	100,00 [100,00; 100,00]	100,00 [100,00; 100,00]		
			-	-

N': Number of patients in the analysis
CI: Confidence Interval
HR: Hazard Ratio
N.E.: not estimable
*: p < 0,05

+ K-M estimate (%) of outcome-free patients, Greenwood formula is used for CIs of KM estimates

Applied model for HR: log(hazard ratio) = treatment + age + age * treatment
If it was not possible to fit the minimal model, the HR is not given.

Analysis population: A2304 SAF subpopulation "ACTIVE MS WITHOUT RELAPSES"

	Treatment groups		Comparison	
	BAF312 (N=127)	**Placebo (N=61)**	**HR [95% CI]**	**p-value**
N'	127	61		
N' Age = 18-40 years	18	13		
N' Age = 41-55 years	95	33		
N' Age = >55 years	14	15		
Asthma/bronchospasm				
Interaction test:	p=1,000			
Age = 18-40 years				
Number of patients with event	0	0		
Median (in weeks)	-	-		
% of event-free patients+	100,00 [100,00; 100,00]	100,00 [100,00; 100,00]		
			-	-
Age = 41-55 years				
Number of patients with event	1	0		
Median (in weeks)	-	-		
% of event-free patients+	98,91 [96,79; 100,00]	100,00 [100,00; 100,00]		
			-	-
Age = >55 years				
Number of patients with event	0	0		
Median (in weeks)	-	-		
% of event-free patients+	100,00 [100,00; 100,00]	100,00 [100,00; 100,00]		
			-	-
Pregnancy and neonatal topics				
Interaction test:	p=1,000			
Age = 18-40 years				
Number of patients with event	0	0		
Median (in weeks)	-	-		
% of event-free patients+	100,00 [100,00; 100,00]	100,00 [100,00; 100,00]		
			-	-
Age = 41-55 years				
Number of patients with event	1	0		
Median (in weeks)	-	-		
% of event-free patients+	98,95 [96,90; 100,00]	100,00 [100,00; 100,00]		
			-	-

	Treatment groups		Comparison	
	BAF312 (N=127)	**Placebo (N=61)**	**HR [95% CI]**	**p-value**
Age = >55 years				
Number of patients with event	0	0		
Median (in weeks)	-	-		
% of event-free patients+	100,00 [100,00; 100,00]	100,00 [100,00; 100,00]		
			-	-
Bradyarrhythmias and bradycardia				
Interaction test:	p=1,000			
Age = 18-40 years				
Number of patients with event	4	1		
Median (in weeks)	-	-		
% of event-free patients+	77,78 [58,57; 96,98]	92,31 [77,82; 100,00]		
			2,94 [0,33; 26,29]	0,335
Age = 41-55 years				
Number of patients with event	6	0		
Median (in weeks)	-	-		
% of event-free patients+	93,68 [88,79; 98,58]	100,00 [100,00; 100,00]		
			-	-
Age = >55 years				
Number of patients with event	1	0		
Median (in weeks)	-	-		
% of event-free patients+	92,86 [79,37; 100,00]	100,00 [100,00; 100,00]		
			-	-

N': Number of patients in the analysis
CI: Confidence Interval
HR: Hazard Ratio
*: p < 0,05

+ K-M estimate (%) of outcome-free patients, Greenwood formula is used for CIs of KM estimates

Applied model for HR: log(hazard ratio) = treatment + age + age * treatment
If it was not possible to fit the minimal model, the HR is not given.

Analysis population: A2304 SAF subpopulation "ACTIVE MS WITHOUT RELAPSES"

12.3 Subgroup: Gender

Table 12.3.1: Time to First Adverse Event (SAF) by Gender

	Treatment groups		Comparison	
	BAF312 (N=127)	Placebo (N=61)	HR [95% CI]	p-value
N'	127	61		
N' Gender = Male	51	24		
N' Gender = Female	76	37		
Any AE				
Interaction test:	p=0,028 *			
Gender = Male				
Number of patients with event	43	21		
Median (in weeks)	4,1 [2,0; 10,7]	4,4 [1,1; 18,7]		
% of event-free patients+	14,94 [4,88; 25,00]	5,71 [0,00; 16,38]		
			0,91 [0,54; 1,54]	0,737
Gender = Female				
Number of patients with event	71	26		
Median (in weeks)	3,6 [2,0; 10,0]	12,9 [5,9; 35,1]		
% of event-free patients+	4,06 [0,00; 9,10]	29,73 [15,00; 44,46]		
			2,00 [1,27; 3,14]	0,003 *
Any AE, disease specific events excluded[1]				
Interaction test:	p=0,033 *			
Gender = Male				
Number of patients with event	41	20		
Median (in weeks)	12,9 [4,1; 15,3]	6,8 [2,4; 23,6]		
% of event-free patients+	16,30 [5,44; 27,16]	0,00 [0,00; 0,00]		
			0,81 [0,48; 1,39]	0,451
Gender = Female				
Number of patients with event	67	26		
Median (in weeks)	10,3 [5,9; 16,7]	22,4 [9,9; 50,9]		
% of event-free patients+	7,15 [0,32; 13,98]	24,32 [6,51; 42,14]		
			1,75 [1,11; 2,77]	0,016 *
Any SAE				
Interaction test:	p=0,072			
Gender = Male				
Number of patients with event	4	6		
Median (in weeks)	-	-		
% of event-free patients+	92,04 [84,55; 99,52]	62,75 [32,12; 93,37]		
			0,25 [0,07; 0,91]	0,035 *

	Treatment groups		Comparison	
	BAF312 (N=127)	**Placebo (N=61)**	**HR [95% CI]**	**p-value**
Gender = Female				
Number of patients with event	12	5		
Median (in weeks)	-	-		
% of event-free patients+	79,85 [69,00; 90,69]	86,40 [75,32; 97,49]		
			1,15 [0,40; 3,26]	0,795
Any SAE, disease specific events excluded[1]				
Interaction test:	p=0,140			
Gender = Male				
Number of patients with event	4	5		
Median (in weeks)	-	-		
% of event-free patients+	92,04 [84,55; 99,52]	65,73 [34,22; 97,25]		
			0,31 [0,08; 1,18]	0,086
Gender = Female				
Number of patients with event	8	3		
Median (in weeks)	-	-		
% of event-free patients+	87,31 [78,77; 95,84]	91,89 [83,10; 100,00]		
			1,29 [0,34; 4,86]	0,709
Any severe AE[2]				
Interaction test:	p=0,990			
Gender = Male				
Number of patients with event	0	5		
Median (in weeks)	-	-		
% of event-free patients+	100,00 [100,00; 100,00]	65,88 [34,35; 97,41]		
			-	-
Gender = Female				
Number of patients with event	11	5		
Median (in weeks)	-	-		
% of event-free patients+	82,33 [72,56; 92,10]	86,32 [75,18; 97,47]		
			1,06 [0,37; 3,06]	0,909

	Treatment groups		Comparison	
	BAF312 (N=127)	**Placebo (N=61)**	**HR [95% CI]**	**p-value**
Any severe AE[2], disease specific events excluded[1]				
Interaction test:	p=0,991			
Gender = Male				
Number of patients with event	0	4		
Median (in weeks)	-	-		
% of event-free patients+	100,00 [100,00; 100,00]	68,88 [36,46; 100,00]		
			-	-
Gender = Female				
Number of patients with event	9	4		
Median (in weeks)	-	-		
% of event-free patients+	85,03 [75,74; 94,32]	89,02 [78,86; 99,18]		
			1,07 [0,33; 3,48]	0,908
Any AE leading to study discontinuation				
Interaction test:	p=0,762			
Gender = Male				
Number of patients with event	1	1		
Median (in weeks)	-	-		
% of event-free patients+	98,04 [94,23; 100,00]	95,83 [87,84; 100,00]		
			0,44 [0,03; 7,05]	0,562
Gender = Female				
Number of patients with event	1	2		
Median (in weeks)	-	-		
% of event-free patients+	98,65 [96,02; 100,00]	94,18 [86,35; 100,00]		
			0,25 [0,02; 2,75]	0,257
Any AE leading to study drug discontinuation				
Interaction test:	p=0,232			
Gender = Male				
Number of patients with event	1	2		
Median (in weeks)	-	-		
% of event-free patients+	98,04 [94,23; 100,00]	83,85 [60,80; 100,00]		
			0,20 [0,02; 2,24]	0,193

	Treatment groups		Comparison	
	BAF312 (N=127)	**Placebo (N=61)**	**HR [95% CI]**	**p-value**
Gender = Female				
Number of patients with event	5	2		
Median (in weeks)	-	-		
% of event-free patients[+]	92,00 [85,06; 98,93]	94,18 [86,35; 100,00]		
			1,19 [0,23; 6,15]	0,833

N': Number of patients in the analysis
CI: Confidence Interval
HR: Hazard Ratio
*: p < 0,05

[+] K-M estimate (%) of outcome-free patients, Greenwood formula is used for CIs of KM estimates

Applied model for HR: log(hazard ratio) = treatment + gender + gender * treatment
If it was not possible to fit the minimal model, the HR is not given.

[1] The following disease-specific Preferred Terms were excluded: see Table 11.0
[2] Definition of 'severe': CTCAE grade ≥ 3

Analysis population: A2304 SAF subpopulation "ACTIVE MS WITHOUT RELAPSES"

Table 12.3.2: Time to First Adverse Event by SOC and PT (SAF) by Gender

	Treatment groups		Comparison	
	BAF312 (N=127)	**Placebo (N=61)**	**HR [95% CI]**	**p-value**
N'	127	61		
N' Gender = Male	51	24		
N' Gender = Female	76	37		
GENERAL DISORDERS AND ADMINISTRATION SITE CONDITIONS				
Interaction test:	p=0,072			
Gender = Male				
Number of patients with event	10	4		
Median (in weeks)	-	-		
% of event-free patients+	77,51 [64,23; 90,78]	75,60 [52,12; 99,07]		
			1,07 [0,34; 3,43]	0,904
Gender = Female				
Number of patients with event	21	2		
Median (in weeks)	-	-		
% of event-free patients+	65,81 [51,42; 80,20]	92,03 [80,96; 100,00]		
			5,90 [1,38; 25,17]	0,016 *
INVESTIGATIONS				
Interaction test:	p=0,869			
Gender = Male				
Number of patients with event	17	3		
Median (in weeks)	-	-		
% of event-free patients+	61,46 [45,88; 77,05]	87,30 [73,86; 100,00]		
			2,64 [0,77; 9,02]	0,121
Gender = Female				
Number of patients with event	24	6		
Median (in weeks)	-	-		
% of event-free patients+	50,01 [27,25; 72,77]	79,10 [62,68; 95,53]		
			2,33 [0,95; 5,70]	0,065

N': Number of patients in the analysis
CI: Confidence Interval
HR: Hazard Ratio
*: p < 0,05

+ K-M estimate (%) of outcome-free patients, Greenwood formula is used for CIs of KM estimates

Applied model for HR: log(hazard ratio) = treatment + gender + gender * treatment
If it was not possible to fit the minimal model, the HR is not given.

SOCs/PTs are only displayed in this subgroup analysis, if the p-value for HR in the entire population is significant (p<0.05).

Analysis population: A2304 SAF subpopulation "ACTIVE MS WITHOUT RELAPSES"

Table 12.3.3: Time to First Serious Adverse Event by SOC and PT (SAF) by Gender

There are no data meeting the display criteria for this table.

Table 12.3.4: Time to First Severe Adverse Event by SOC and PT (SAF) by Gender

There are no data meeting the display criteria for this table.

Table 12.3.5: Time to First Adverse Event of Special Interest (SAF) by Gender

	Treatment groups		Comparison	
	BAF312 (N=127)	**Placebo (N=61)**	**HR [95% CI]**	**p-value**
N'	127	61		
N' Gender = Male	51	24		
N' Gender = Female	76	37		
Infections and infestations				
Interaction test:	p=0,752			
Gender = Male				
Number of patients with event	20	6		
Median (in weeks)	-	-		
% of event-free patients+	50,23 [32,05; 68,41]	66,66 [44,04; 89,29]		
			1,47 [0,59; 3,65]	0,412
Gender = Female				
Number of patients with event	45	20		
Median (in weeks)	63,0 [46,9; 79,0]	77,6 [49,4; .]		
% of event-free patients+	27,88 [15,24; 40,51]	30,76 [8,42; 53,09]		
			1,24 [0,73; 2,09]	0,431
Herpes simplex virus infections				
Interaction test:	p=1,000			
Gender = Male				
Number of patients with event	0	0		
Median (in weeks)	-	-		
% of event-free patients+	100,00 [100,00; 100,00]	100,00 [100,00; 100,00]		
			-	-
Gender = Female				
Number of patients with event	4	1		
Median (in weeks)	-	-		
% of event-free patients+	93,72 [87,60; 99,85]	97,30 [92,07; 100,00]		
			1,93 [0,21; 17,25]	0,558
Varicella-zoster virus infections				
Interaction test:	p=0,999			
Gender = Male				
Number of patients with event	0	0		
Median (in weeks)	-	-		
% of event-free patients+	100,00 [100,00; 100,00]	100,00 [100,00; 100,00]		
			-	-

	Treatment groups		Comparison	
	BAF312 (N=127)	**Placebo (N=61)**	**HR [95% CI]**	**p-value**
Gender = Female				
Number of patients with event	1	0		
Median (in weeks)	-	-		
% of event-free patients+	98,41 [95,33; 100,00]	100,00 [100,00; 100,00]		
			-	-
Lymphopenia				
Interaction test:	p=0,999			
Gender = Male				
Number of patients with event	0	0		
Median (in weeks)	-	-		
% of event-free patients+	100,00 [100,00; 100,00]	100,00 [100,00; 100,00]		
			-	-
Gender = Female				
Number of patients with event	2	0		
Median (in weeks)	-	-		
% of event-free patients+	97,07 [93,08; 100,00]	100,00 [100,00; 100,00]		
			-	-
Macular edema				
Interaction test:	p=0,996			
Gender = Male				
Number of patients with event	0	1		
Median (in weeks)	-	-		
% of event-free patients+	100,00 [100,00; 100,00]	87,50 [64,58; 100,00]		
			-	-
Gender = Female				
Number of patients with event	2	0		
Median (in weeks)	-	-		
% of event-free patients+	97,02 [92,94; 100,00]	100,00 [100,00; 100,00]		
			-	-

	Treatment groups		Comparison	
	BAF312 (N=127)	**Placebo (N=61)**	**HR [95% CI]**	**p-value**
Abnormal hepatic enzymes				
Interaction test:	p=0,259			
Gender = Male				
Number of patients with event	9	3		
Median (in weeks)	-	-		
% of event-free patients+	78,79 [65,85; 91,74]	87,30 [73,86; 100,00]		
			1,30 [0,35; 4,81]	0,692
Gender = Female				
Number of patients with event	10	1		
Median (in weeks)	-	-		
% of event-free patients+	86,50 [78,71; 94,29]	97,14 [91,62; 100,00]		
			5,29 [0,68; 41,34]	0,112
Malignancies				
Interaction test:	p=0,999			
Gender = Male				
Number of patients with event	0	1		
Median (in weeks)	-	-		
% of event-free patients+	100,00 [100,00; 100,00]	83,33 [53,51; 100,00]		
			-	-
Gender = Female				
Number of patients with event	0	0		
Median (in weeks)	-	-		
% of event-free patients+	100,00 [100,00; 100,00]	100,00 [100,00; 100,00]		
			-	-
Hypertension				
Interaction test:	p=0,042 *			
Gender = Male				
Number of patients with event	5	4		
Median (in weeks)	-	-		
% of event-free patients+	84,71 [69,60; 99,81]	82,89 [67,59; 98,20]		
			0,50 [0,13; 1,87]	0,303

	Treatment groups		Comparison	
	BAF312 (N=127)	**Placebo (N=61)**	**HR [95% CI]**	**p-value**
Gender = Female				
Number of patients with event	12	1		
Median (in weeks)	-	-		
% of event-free patients+	80,38 [69,01; 91,75]	97,30 [92,07; 100,00]		
			6,24 [0,81; 47,99]	0,079
Seizures				
Interaction test:	N.E.			
Gender = Male				
Number of patients with event	0	0		
Median (in weeks)	-	-		
% of event-free patients+	100,00 [100,00; 100,00]	100,00 [100,00; 100,00]		
			-	-
Gender = Female				
Number of patients with event	0	0		
Median (in weeks)	-	-		
% of event-free patients+	100,00 [100,00; 100,00]	100,00 [100,00; 100,00]		
			-	-
Thromboembolic events				
Interaction test:	p=0,995			
Gender = Male				
Number of patients with event	2	1		
Median (in weeks)	-	-		
% of event-free patients+	95,95 [90,46; 100,00]	94,74 [84,70; 100,00]		
			0,72 [0,06; 8,13]	0,788
Gender = Female				
Number of patients with event	3	0		
Median (in weeks)	-	-		
% of event-free patients+	89,08 [73,48; 100,00]	100,00 [100,00; 100,00]		
			-	-

	Treatment groups		Comparison	
	BAF312 (N=127)	**Placebo (N=61)**	**HR [95% CI]**	**p-value**
Respiratory disorders				
Interaction test:	p=0,279			
Gender = Male				
Number of patients with event	9	2		
Median (in weeks)	-	-		
% of event-free patients+	77,36 [63,73; 91,00]	89,28 [74,91; 100,00]		
			1,81 [0,39; 8,40]	0,447
Gender = Female				
Number of patients with event	13	9		
Median (in weeks)	-	-		
% of event-free patients+	78,69 [67,64; 89,74]	66,19 [46,01; 86,38]		
			0,69 [0,29; 1,61]	0,390
Peripheral edema/swelling				
Interaction test:	p=0,994			
Gender = Male				
Number of patients with event	0	1		
Median (in weeks)	-	-		
% of event-free patients+	100,00 [100,00; 100,00]	95,00 [85,45; 100,00]		
			-	-
Gender = Female				
Number of patients with event	6	0		
Median (in weeks)	-	-		
% of event-free patients+	87,00 [74,06; 99,93]	100,00 [100,00; 100,00]		
			-	-

N': Number of patients in the analysis
CI: Confidence Interval
HR: Hazard Ratio
N.E.: not estimable
*: p < 0,05

+ K-M estimate (%) of outcome-free patients, Greenwood formula is used for CIs of KM estimates

Applied model for HR: log(hazard ratio) = treatment + gender + gender * treatment
If it was not possible to fit the minimal model, the HR is not given.

Analysis population: A2304 SAF subpopulation "ACTIVE MS WITHOUT RELAPSES"

	Treatment groups		Comparison	
	BAF312 (N=127)	**Placebo (N=61)**	**HR [95% CI]**	**p-value**
N'	127	61		
N' Gender = Male	51	24		
N' Gender = Female	76	37		
Asthma/bronchospasm				
Interaction test:	p=0,999			
Gender = Male				
Number of patients with event	0	0		
Median (in weeks)	-	-		
% of event-free patients+	100,00 [100,00; 100,00]	100,00 [100,00; 100,00]		
			-	-
Gender = Female				
Number of patients with event	1	0		
Median (in weeks)	-	-		
% of event-free patients+	98,63 [95,96; 100,00]	100,00 [100,00; 100,00]		
			-	-
Pregnancy and neonatal topics				
Interaction test:	p=0,999			
Gender = Male				
Number of patients with event	1	0		
Median (in weeks)	-	-		
% of event-free patients+	98,04 [94,23; 100,00]	100,00 [100,00; 100,00]		
			-	-
Gender = Female				
Number of patients with event	0	0		
Median (in weeks)	-	-		
% of event-free patients+	100,00 [100,00; 100,00]	100,00 [100,00; 100,00]		
			-	-

	Treatment groups		Comparison	
	BAF312 (N=127)	**Placebo (N=61)**	**HR [95% CI]**	**p-value**
Bradyarrhythmias and bradycardia				
Interaction test:	p=0,992			
Gender = Male				
Number of patients with event	7	1		
Median (in weeks)	-	-		
% of event-free patients+	86,27 [76,83; 95,72]	95,83 [87,84; 100,00]		
			3,35 [0,41; 27,20]	0,259
Gender = Female				
Number of patients with event	4	0		
Median (in weeks)	-	-		
% of event-free patients+	94,68 [89,61; 99,75]	100,00 [100,00; 100,00]		
			-	-

N': Number of patients in the analysis
CI: Confidence Interval
HR: Hazard Ratio
*: p < 0,05

+ K-M estimate (%) of outcome-free patients, Greenwood formula is used for CIs of KM estimates

Applied model for HR: log(hazard ratio) = treatment + gender + gender * treatment
If it was not possible to fit the minimal model, the HR is not given.

Analysis population: A2304 SAF subpopulation "ACTIVE MS WITHOUT RELAPSES"

12.4 Subgroup: Previous MS DMT

Table 12.4.1: Time to First Adverse Event (SAF) by Previous MS DMT

	Treatment groups		Comparison	
	BAF312 (N=127)	**Placebo (N=61)**	**HR [95% CI]**	**p-value**
N'	127	61		
N' Previous MS DMT = No	20	17		
N' Previous MS DMT = Yes	107	44		
Any AE				
Interaction test:	p=0,753			
Previous MS DMT = No				
Number of patients with event	18	14		
Median (in weeks)	2,1 [0,4; 26,1]	7,3 [1,1; 35,1]		
% of event-free patients+	7,50 [0,00; 20,51]	17,65 [0,00; 35,77]		
			1,35 [0,67; 2,72]	0,400
Previous MS DMT = Yes				
Number of patients with event	96	33		
Median (in weeks)	4,1 [2,7; 9,0]	9,8 [4,3; 25,0]		
% of event-free patients+	8,07 [2,19; 13,95]	23,10 [10,22; 35,98]		
			1,54 [1,03; 2,28]	0,034 *
Any AE, disease specific events excluded[1]				
Interaction test:	p=0,915			
Previous MS DMT = No				
Number of patients with event	18	14		
Median (in weeks)	9,8 [0,7; 27,0]	11,9 [1,1; 52,4]		
% of event-free patients+	7,50 [0,00; 20,51]	11,76 [0,00; 30,93]		
			1,29 [0,64; 2,60]	0,472
Previous MS DMT = Yes				
Number of patients with event	90	32		
Median (in weeks)	11,7 [6,4; 15,3]	15,9 [7,0; 28,6]		
% of event-free patients+	11,15 [4,31; 18,00]	20,67 [5,12; 36,23]		
			1,35 [0,90; 2,02]	0,145

	Treatment groups		Comparison	
	BAF312 (N=127)	**Placebo (N=61)**	**HR [95% CI]**	**p-value**
Any SAE				
Interaction test:	p=0,093			
Previous MS DMT = No				
Number of patients with event	5	2		
Median (in weeks)	-	-		
% of event-free patients+	72,00 [50,32; 93,68]	88,24 [72,92; 100,00]		
			2,17 [0,42; 11,21]	0,353
Previous MS DMT = Yes				
Number of patients with event	11	9		
Median (in weeks)	-	-		
% of event-free patients+	87,24 [79,77; 94,71]	75,79 [60,43; 91,14]		
			0,44 [0,18; 1,06]	0,068
Any SAE, disease specific events excluded[1]				
Interaction test:	p=0,108			
Previous MS DMT = No				
Number of patients with event	5	2		
Median (in weeks)	-	-		
% of event-free patients+	72,00 [50,32; 93,68]	88,24 [72,92; 100,00]		
			2,17 [0,42; 11,21]	0,354
Previous MS DMT = Yes				
Number of patients with event	7	6		
Median (in weeks)	-	-		
% of event-free patients+	92,56 [87,12; 98,01]	82,20 [67,37; 97,03]		
			0,43 [0,14; 1,29]	0,131
Any severe AE[2]				
Interaction test:	p=0,890			
Previous MS DMT = No				
Number of patients with event	1	2		
Median (in weeks)	-	-		
% of event-free patients+	92,31 [77,82; 100,00]	88,24 [72,92; 100,00]		
			0,38 [0,03; 4,22]	0,433

	Treatment groups		Comparison	
	BAF312 (N=127)	**Placebo (N=61)**	**HR [95% CI]**	**p-value**
Previous MS DMT = Yes				
Number of patients with event	10	8		
Median (in weeks)	-	-		
% of event-free patients+	88,87 [82,19; 95,56]	78,06 [63,26; 92,87]		
			0,46 [0,18; 1,16]	0,101
Any severe AE[2], disease specific events excluded[1]				
Interaction test:	p=0,857			
Previous MS DMT = No				
Number of patients with event	1	2		
Median (in weeks)	-	-		
% of event-free patients+	92,31 [77,82; 100,00]	88,24 [72,92; 100,00]		
			0,38 [0,03; 4,17]	0,426
Previous MS DMT = Yes				
Number of patients with event	8	6		
Median (in weeks)	-	-		
% of event-free patients+	90,80 [84,55; 97,05]	82,18 [67,73; 96,62]		
			0,48 [0,17; 1,39]	0,175
Any AE leading to study discontinuation				
Interaction test:	p=1,000			
Previous MS DMT = No				
Number of patients with event	0	0		
Median (in weeks)	-	-		
% of event-free patients+	100,00 [100,00; 100,00]	100,00 [100,00; 100,00]		
			-	-
Previous MS DMT = Yes				
Number of patients with event	2	3		
Median (in weeks)	-	-		
% of event-free patients+	98,11 [95,52; 100,00]	92,40 [84,07; 100,00]		
			0,27 [0,04; 1,60]	0,149

	Treatment groups		Comparison	
	BAF312 (N=127)	**Placebo (N=61)**	**HR [95% CI]**	**p-value**
Any AE leading to study drug discontinuation				
Interaction test:	p=0,994			
Previous MS DMT = No				
Number of patients with event	2	0		
Median (in weeks)	-	-		
% of event-free patients+	86,27 [68,34; 100,00]	100,00 [100,00; 100,00]		
			-	-
Previous MS DMT = Yes				
Number of patients with event	4	4		
Median (in weeks)	-	-		
% of event-free patients+	96,20 [92,54; 99,85]	87,53 [75,35; 99,71]		
			0,37 [0,09; 1,50]	0,165

N': Number of patients in the analysis
CI: Confidence Interval
HR: Hazard Ratio
*: p < 0,05

+ K-M estimate (%) of outcome-free patients, Greenwood formula is used for CIs of KM estimates

Applied model for HR: log(hazard ratio) = treatment + previous MS DMT + previous MS DMT * treatment
If it was not possible to fit the minimal model, the HR is not given.

[1] The following disease-specific Preferred Terms were excluded: see Table 11.0
[2] Definition of 'severe': CTCAE grade ≥ 3

Analysis population: A2304 SAF subpopulation "ACTIVE MS WITHOUT RELAPSES"

Table 12.4.2: Time to First Adverse Event by SOC and PT (SAF) by Previous MS DMT

	Treatment groups		Comparison	
	BAF312 (N=127)	**Placebo (N=61)**	**HR [95% CI]**	**p-value**
N'	127	61		
N' Previous MS DMT = No	20	17		
N' Previous MS DMT = Yes	107	44		
GENERAL DISORDERS AND ADMINISTRATION SITE CONDITIONS				
Interaction test:	p=0,014 *			
Previous MS DMT = No				
Number of patients with event	2	4		
Median (in weeks)	-	-		
% of event-free patients+	90,00 [76,85; 100,00]	67,23 [39,11; 95,35]		
			0,40 [0,07; 2,16]	0,285
Previous MS DMT = Yes				
Number of patients with event	29	2		
Median (in weeks)	-	-		
% of event-free patients+	66,79 [55,26; 78,31]	94,74 [87,64; 100,00]		
			6,44 [1,54; 26,99]	0,011 *
INVESTIGATIONS				
Interaction test:	p=0,657			
Previous MS DMT = No				
Number of patients with event	9	4		
Median (in weeks)	-	-		
% of event-free patients+	52,14 [28,75; 75,52]	61,76 [24,27; 99,26]		
			2,10 [0,65; 6,83]	0,217
Previous MS DMT = Yes				
Number of patients with event	32	5		
Median (in weeks)	-	-		
% of event-free patients+	51,75 [29,69; 73,80]	87,56 [77,28; 97,85]		
			2,96 [1,15; 7,61]	0,024 *

N': Number of patients in the analysis
CI: Confidence Interval
HR: Hazard Ratio
*: p < 0,05

+ K-M estimate (%) of outcome-free patients, Greenwood formula is used for CIs of KM estimates

Applied model for HR: log(hazard ratio) = treatment + previous MS DMT + previous MS DMT * treatment
If it was not possible to fit the minimal model, the HR is not given.

SOCs/PTs are only displayed in this subgroup analysis, if the p-value for HR in the entire population is significant (p<0.05).

Analysis population: A2304 SAF subpopulation "ACTIVE MS WITHOUT RELAPSES"

Table 12.4.3: Time to First Serious Adverse Event by SOC and PT (SAF) by Previous MS DMT

There are no data meeting the display criteria for this table.

Table 12.4.4: Time to First Severe Adverse Event by SOC and PT (SAF) by Previous MS DMT

There are no data meeting the display criteria for this table.

Table 12.4.5: Time to First Adverse Event of Special Interest (SAF) by Previous MS DMT

	Treatment groups		Comparison	
	BAF312 (N=127)	**Placebo (N=61)**	**HR [95% CI]**	**p-value**
N'	127	61		
N' Previous MS DMT = No	20	17		
N' Previous MS DMT = Yes	107	44		
Infections and infestations				
Interaction test:	p=0,570			
Previous MS DMT = No				
Number of patients with event	8	7		
Median (in weeks)	-	88,6 [57,0; .]		
% of event-free patients+	56,25 [32,49; 80,01]	48,78 [19,40; 78,16]		
			0,92 [0,33; 2,53]	0,865
Previous MS DMT = Yes				
Number of patients with event	57	19		
Median (in weeks)	71,9 [52,4; 90,3]	64,3 [51,0; .]		
% of event-free patients+	32,06 [19,93; 44,19]	41,57 [20,90; 62,24]		
			1,27 [0,76; 2,14]	0,360
Herpes simplex virus infections				
Interaction test:	p=0,995			
Previous MS DMT = No				
Number of patients with event	0	1		
Median (in weeks)	-	-		
% of event-free patients+	100,00 [100,00; 100,00]	94,12 [82,93; 100,00]		
			-	-
Previous MS DMT = Yes				
Number of patients with event	4	0		
Median (in weeks)	-	-		
% of event-free patients+	95,40 [90,81; 99,99]	100,00 [100,00; 100,00]		
			-	-

	Treatment groups		Comparison	
	BAF312 (N=127)	**Placebo (N=61)**	**HR [95% CI]**	**p-value**
Varicella-zoster virus infections				
Interaction test:	p=0,999			
Previous MS DMT = No				
Number of patients with event	0	0		
Median (in weeks)	-	-		
% of event-free patients+	100,00 [100,00; 100,00]	100,00 [100,00; 100,00]		
			-	-
Previous MS DMT = Yes				
Number of patients with event	1	0		
Median (in weeks)	-	-		
% of event-free patients+	98,89 [96,72; 100,00]	100,00 [100,00; 100,00]		
			-	-
Lymphopenia				
Interaction test:	p=0,999			
Previous MS DMT = No				
Number of patients with event	0	0		
Median (in weeks)	-	-		
% of event-free patients+	100,00 [100,00; 100,00]	100,00 [100,00; 100,00]		
			-	-
Previous MS DMT = Yes				
Number of patients with event	2	0		
Median (in weeks)	-	-		
% of event-free patients+	97,96 [95,15; 100,00]	100,00 [100,00; 100,00]		
			-	-
Macular edema				
Interaction test:	p=1,000			
Previous MS DMT = No				
Number of patients with event	0	0		
Median (in weeks)	-	-		
% of event-free patients+	100,00 [100,00; 100,00]	100,00 [100,00; 100,00]		
			-	-

	Treatment groups		Comparison	
	BAF312 (N=127)	**Placebo (N=61)**	**HR [95% CI]**	**p-value**
Previous MS DMT = Yes				
Number of patients with event	2	1		
Median (in weeks)	-	-		
% of event-free patients+	97,92 [95,06; 100,00]	94,74 [84,70; 100,00]		
			0,76 [0,07; 8,38]	0,821
Abnormal hepatic enzymes				
Interaction test:	p=0,370			
Previous MS DMT = No				
Number of patients with event	6	1		
Median (in weeks)	-	-		
% of event-free patients+	68,18 [46,73; 89,63]	94,12 [82,93; 100,00]		
			5,47 [0,66; 45,41]	0,116
Previous MS DMT = Yes				
Number of patients with event	13	3		
Median (in weeks)	-	-		
% of event-free patients+	86,93 [80,23; 93,64]	92,87 [85,08; 100,00]		
			1,77 [0,51; 6,23]	0,371
Malignancies				
Interaction test:	p=0,999			
Previous MS DMT = No				
Number of patients with event	0	0		
Median (in weeks)	-	-		
% of event-free patients+	100,00 [100,00; 100,00]	100,00 [100,00; 100,00]		
			-	-
Previous MS DMT = Yes				
Number of patients with event	0	1		
Median (in weeks)	-	-		
% of event-free patients+	100,00 [100,00; 100,00]	93,75 [81,89; 100,00]		
			-	-

	Treatment groups		Comparison	
	BAF312 (N=127)	**Placebo (N=61)**	**HR [95% CI]**	**p-value**
Hypertension				
Interaction test:	p=0,722			
Previous MS DMT = No				
Number of patients with event	3	2		
Median (in weeks)	-	-		
% of event-free patients+	72,00 [38,74; 100,00]	88,24 [72,92; 100,00]		
			1,26 [0,21; 7,52]	0,804
Previous MS DMT = Yes				
Number of patients with event	14	3		
Median (in weeks)	-	-		
% of event-free patients+	84,18 [75,70; 92,66]	93,18 [85,73; 100,00]		
			1,87 [0,54; 6,49]	0,327
Seizures				
Interaction test:	N.E.			
Previous MS DMT = No				
Number of patients with event	0	0		
Median (in weeks)	-	-		
% of event-free patients+	100,00 [100,00; 100,00]	100,00 [100,00; 100,00]		
			-	-
Previous MS DMT = Yes				
Number of patients with event	0	0		
Median (in weeks)	-	-		
% of event-free patients+	100,00 [100,00; 100,00]	100,00 [100,00; 100,00]		
			-	-
Thromboembolic events				
Interaction test:	p=0,995			
Previous MS DMT = No				
Number of patients with event	1	1		
Median (in weeks)	-	-		
% of event-free patients+	95,00 [85,45; 100,00]	94,12 [82,93; 100,00]		
			0,83 [0,05; 13,38]	0,899

	Treatment groups		Comparison	
	BAF312 (N=127)	**Placebo (N=61)**	**HR [95% CI]**	**p-value**
Previous MS DMT = Yes				
Number of patients with event	4	0		
Median (in weeks)	-	-		
% of event-free patients+	90,93 [79,00; 100,00]	100,00 [100,00; 100,00]		
			-	-
Respiratory disorders				
Interaction test:	p=0,046 *			
Previous MS DMT = No				
Number of patients with event	2	6		
Median (in weeks)	-	90,4 [73,6; .]		
% of event-free patients+	90,00 [76,85; 100,00]	45,61 [5,95; 85,27]		
			0,23 [0,05; 1,14]	0,072
Previous MS DMT = Yes				
Number of patients with event	20	5		
Median (in weeks)	-	-		
% of event-free patients+	75,63 [65,72; 85,54]	84,14 [69,45; 98,83]		
			1,56 [0,58; 4,15]	0,375
Peripheral edema/swelling				
Interaction test:	p=1,000			
Previous MS DMT = No				
Number of patients with event	0	0		
Median (in weeks)	-	-		
% of event-free patients+	100,00 [100,00; 100,00]	100,00 [100,00; 100,00]		
			-	-

	Treatment groups		Comparison	
	BAF312 (N=127)	**Placebo (N=61)**	**HR [95% CI]**	**p-value**
Previous MS DMT = Yes				
Number of patients with event	6	1		
Median (in weeks)	-	-		
% of event-free patients+	91,06 [82,21; 99,92]	97,37 [92,28; 100,00]		
			2,46 [0,30; 20,44]	0,405

N': Number of patients in the analysis
CI: Confidence Interval
HR: Hazard Ratio
N.E.: not estimable
*: p < 0,05

+ K-M estimate (%) of outcome-free patients, Greenwood formula is used for CIs of KM estimates

Applied model for HR: log(hazard ratio) = treatment + previous MS DMT + previous MS DMT * treatment
If it was not possible to fit the minimal model, the HR is not given.

Analysis population: A2304 SAF subpopulation "ACTIVE MS WITHOUT RELAPSES"

	Treatment groups		Comparison	
	BAF312 (N=127)	**Placebo (N=61)**	**HR [95% CI]**	**p-value**
N'	127	61		
N' Previous MS DMT = No	20	17		
N' Previous MS DMT = Yes	107	44		
Asthma/bronchospasm				
Interaction test:	p=0,999			
Previous MS DMT = No				
Number of patients with event	0	0		
Median (in weeks)	-	-		
% of event-free patients+	100,00 [100,00; 100,00]	100,00 [100,00; 100,00]		
			-	-
Previous MS DMT = Yes				
Number of patients with event	1	0		
Median (in weeks)	-	-		
% of event-free patients+	99,03 [97,14; 100,00]	100,00 [100,00; 100,00]		
			-	-
Pregnancy and neonatal topics				
Interaction test:	p=0,999			
Previous MS DMT = No				
Number of patients with event	0	0		
Median (in weeks)	-	-		
% of event-free patients+	100,00 [100,00; 100,00]	100,00 [100,00; 100,00]		
			-	-
Previous MS DMT = Yes				
Number of patients with event	1	0		
Median (in weeks)	-	-		
% of event-free patients+	99,07 [97,24; 100,00]	100,00 [100,00; 100,00]		
			-	-

	Treatment groups		Comparison	
	BAF312 (N=127)	**Placebo (N=61)**	**HR [95% CI]**	**p-value**
Bradyarrhythmias and bradycardia				
Interaction test:	p=0,994			
Previous MS DMT = No				
Number of patients with event	3	0		
Median (in weeks)	-	-		
% of event-free patients+	85,00 [69,35; 100,00]	100,00 [100,00; 100,00]		
			-	-
Previous MS DMT = Yes				
Number of patients with event	8	1		
Median (in weeks)	-	-		
% of event-free patients+	92,48 [87,47; 97,49]	97,73 [93,32; 100,00]		
			3,32 [0,42; 26,54]	0,258

N': Number of patients in the analysis
CI: Confidence Interval
HR: Hazard Ratio
*: p < 0,05

+ K-M estimate (%) of outcome-free patients, Greenwood formula is used for CIs of KM estimates

Applied model for HR: log(hazard ratio) = treatment + previous MS DMT + previous MS DMT * treatment
If it was not possible to fit the minimal model, the HR is not given.

Analysis population: A2304 SAF subpopulation "ACTIVE MS WITHOUT RELAPSES"

12.5 Subgroup: Previous IFN-beta-1b Treatment

Table 12.5.1: Time to First Adverse Event (SAF) by Previous IFN-beta-1b Treatment

	Treatment groups		Comparison	
	BAF312 (N=127)	**Placebo (N=61)**	**HR [95% CI]**	**p-value**
N'	127	61		
N' Previous IFN-beta-1b Treatment = No	82	48		
N' Previous IFN-beta-1b Treatment = Yes	45	13		
Any AE				
Interaction test:	p=0,536			
Previous IFN-beta-1b Treatment = No				
Number of patients with event	74	38		
Median (in weeks)	3,6 [2,0; 8,4]	8,5 [4,3; 22,4]		
% of event-free patients+	6,90 [0,56; 13,24]	18,77 [7,31; 30,22]		
			1,40 [0,95; 2,08]	0,090
Previous IFN-beta-1b Treatment = Yes				
Number of patients with event	40	9		
Median (in weeks)	5,9 [2,4; 10,7]	12,9 [1,1; -]		
% of event-free patients+	10,67 [1,45; 19,89]	30,77 [5,68; 55,86]		
			1,82 [0,88; 3,77]	0,106
Any AE, disease specific events excluded[1]				
Interaction test:	p=0,354			
Previous IFN-beta-1b Treatment = No				
Number of patients with event	71	38		
Median (in weeks)	12,4 [4,6; 16,7]	15,2 [6,9; 25,0]		
% of event-free patients+	9,51 [2,28; 16,74]	12,77 [0,00; 25,88]		
			1,21 [0,81; 1,79]	0,347
Previous IFN-beta-1b Treatment = Yes				
Number of patients with event	37	8		
Median (in weeks)	10,7 [5,9; 16,7]	13,1 [2,9; -]		
% of event-free patients+	11,24 [0,00; 23,10]	36,92 [9,87; 63,98]		
			1,81 [0,84; 3,90]	0,127

	Treatment groups		Comparison	
	BAF312 (N=127)	**Placebo (N=61)**	**HR [95% CI]**	**p-value**
Any SAE				
Interaction test:	p=0,811			
Previous IFN-beta-1b Treatment = No				
Number of patients with event	10	9		
Median (in weeks)	-	-		
% of event-free patients+	86,11 [77,85; 94,37]	77,77 [63,66; 91,88]		
			0,60 [0,25; 1,49]	0,273
Previous IFN-beta-1b Treatment = Yes				
Number of patients with event	6	2		
Median (in weeks)	-	-		
% of event-free patients+	81,79 [67,82; 95,77]	84,62 [65,00; 100,00]		
			0,76 [0,15; 3,75]	0,733
Any SAE, disease specific events excluded[1]				
Interaction test:	p=0,717			
Previous IFN-beta-1b Treatment = No				
Number of patients with event	8	6		
Median (in weeks)	-	-		
% of event-free patients+	88,68 [81,01; 96,34]	83,59 [70,06; 97,12]		
			0,74 [0,26; 2,13]	0,573
Previous IFN-beta-1b Treatment = Yes				
Number of patients with event	4	2		
Median (in weeks)	-	-		
% of event-free patients+	88,99 [78,23; 99,75]	84,62 [65,00; 100,00]		
			0,51 [0,09; 2,78]	0,436
Any severe AE[2]				
Interaction test:	p=0,289			
Previous IFN-beta-1b Treatment = No				
Number of patients with event	6	9		
Median (in weeks)	-	-		
% of event-free patients+	90,72 [83,37; 98,07]	77,93 [64,13; 91,74]		
			0,36 [0,13; 1,00]	0,050 *

	Treatment groups		Comparison	
	BAF312 (N=127)	**Placebo (N=61)**	**HR [95% CI]**	**p-value**
Previous IFN-beta-1b Treatment = Yes				
Number of patients with event	5	1		
Median (in weeks)	-	-		
% of event-free patients+	86,49 [74,98; 98,00]	92,31 [77,82; 100,00]		
			1,29 [0,15; 11,07]	0,816
Any severe AE[2], disease specific events excluded[1]				
Interaction test:	p=0,256			
Previous IFN-beta-1b Treatment = No				
Number of patients with event	4	7		
Median (in weeks)	-	-		
% of event-free patients+	93,27 [86,66; 99,87]	81,65 [68,19; 95,11]		
			0,30 [0,09; 1,02]	0,055
Previous IFN-beta-1b Treatment = Yes				
Number of patients with event	5	1		
Median (in weeks)	-	-		
% of event-free patients+	86,49 [74,98; 98,00]	92,31 [77,82; 100,00]		
			1,26 [0,15; 10,79]	0,834
Any AE leading to study discontinuation				
Interaction test:	p=1,000			
Previous IFN-beta-1b Treatment = No				
Number of patients with event	2	3		
Median (in weeks)	-	-		
% of event-free patients+	97,55 [94,19; 100,00]	93,24 [85,82; 100,00]		
			0,39 [0,06; 2,31]	0,297
Previous IFN-beta-1b Treatment = Yes				
Number of patients with event	0	0		
Median (in weeks)	-	-		
% of event-free patients+	100,00 [100,00; 100,00]	100,00 [100,00; 100,00]		
			-	-

	Treatment groups		Comparison	
	BAF312 (N=127)	**Placebo (N=61)**	**HR [95% CI]**	**p-value**
Any AE leading to study drug discontinuation				
Interaction test:	p=0,993			
Previous IFN-beta-1b Treatment = No				
Number of patients with event	5	4		
Median (in weeks)	-	-		
% of event-free patients+	92,55 [86,05; 99,06]	89,00 [78,23; 99,77]		
			0,68 [0,18; 2,55]	0,573
Previous IFN-beta-1b Treatment = Yes				
Number of patients with event	1	0		
Median (in weeks)	-	-		
% of event-free patients+	97,78 [93,47; 100,00]	100,00 [100,00; 100,00]		
			-	-

N': Number of patients in the analysis
CI: Confidence Interval
HR: Hazard Ratio
*: p < 0,05

+ K-M estimate (%) of outcome-free patients, Greenwood formula is used for CIs of KM estimates

Applied model for HR: log(hazard ratio) = treatment + previous IFN-beta-1b treatment + previous IFN-beta-1b treatment * treatment
If it was not possible to fit the minimal model, the HR is not given.

[1] The following disease-specific Preferred Terms were excluded: see Table 11.0
[2] Definition of 'severe': CTCAE grade ≥ 3

Analysis population: A2304 SAF subpopulation "ACTIVE MS WITHOUT RELAPSES"

Table 12.5.2: Time to First Adverse Event by SOC and PT (SAF) by Previous IFN-beta-1b Treatment

	Treatment groups		Comparison	
	BAF312 (N=127)	**Placebo (N=61)**	**HR [95% CI]**	**p-value**
N'	127	61		
N' Previous IFN-beta-1b Treatment = No	82	48		
N' Previous IFN-beta-1b Treatment = Yes	45	13		
GENERAL DISORDERS AND ADMINISTRATION SITE CONDITIONS				
Interaction test:	p=0,558			
Previous IFN-beta-1b Treatment = No				
Number of patients with event	18	5		
Median (in weeks)	-	-		
% of event-free patients+	74,57 [63,73; 85,41]	84,70 [71,47; 97,94]		
			2,15 [0,80; 5,80]	0,130
Previous IFN-beta-1b Treatment = Yes				
Number of patients with event	13	1		
Median (in weeks)	-	-		
% of event-free patients+	64,53 [45,52; 83,53]	91,67 [76,03; 100,00]		
			4,23 [0,55; 32,34]	0,165
INVESTIGATIONS				
Interaction test:	p=0,731			
Previous IFN-beta-1b Treatment = No				
Number of patients with event	30	8		
Median (in weeks)	130,0 [130,0; .]	-		
% of event-free patients+	49,26 [25,88; 72,64]	78,31 [63,19; 93,43]		
			2,45 [1,12; 5,35]	0,025 *

	Treatment groups		Comparison	
	BAF312 (N=127)	**Placebo (N=61)**	**HR [95% CI]**	**p-value**
Previous IFN-beta-1b Treatment = Yes				
Number of patients with event	11	1		
Median (in weeks)	-	-		
% of event-free patients+	56,80 [27,87; 85,74]	92,31 [77,82; 100,00]		
			3,60 [0,46; 27,89]	0,220

N': Number of patients in the analysis
CI: Confidence Interval
HR: Hazard Ratio
*: p < 0,05

+ K-M estimate (%) of outcome-free patients, Greenwood formula is used for CIs of KM estimates

Applied model for HR: log(hazard ratio) = treatment + previous IFN-beta-1b treatment + previous IFN-beta-1b treatment * treatment
If it was not possible to fit the minimal model, the HR is not given.

SOCs/PTs are only displayed in this subgroup analysis, if the p-value for HR in the entire population is significant (p<0.05).

Analysis population: A2304 SAF subpopulation "ACTIVE MS WITHOUT RELAPSES"

Table 12.5.3: Time to First Serious Adverse Event by SOC and PT (SAF) by Previous IFN-beta-1b Treatment

There are no data meeting the display criteria for this table.

Table 12.5.4: Time to First Severe Adverse Event by SOC and PT (SAF) by Previous IFN-beta-1b Treatment

There are no data meeting the display criteria for this table.

Table 12.5.5: Time to First Adverse Event of Special Interest (SAF) by Previous IFN-beta-1b Treatment

	Treatment groups		Comparison	
	BAF312 (N=127)	**Placebo (N=61)**	**HR [95% CI]**	**p-value**
N'	127	61		
N' Previous IFN-beta-1b Treatment = No	82	48		
N' Previous IFN-beta-1b Treatment = Yes	45	13		
Infections and infestations				
Interaction test:	p=0,541			
Previous IFN-beta-1b Treatment = No				
Number of patients with event	38	21		
Median (in weeks)	80,9 [63,7; .]	95,4 [58,0; .]		
% of event-free patients+	42,88 [29,04; 56,71]	43,15 [24,10; 62,20]		
			1,08 [0,63; 1,84]	0,775
Previous IFN-beta-1b Treatment = Yes				
Number of patients with event	27	5		
Median (in weeks)	63,0 [34,3; 90,3]	-		
% of event-free patients+	24,79 [7,64; 41,94]	54,95 [24,44; 85,45]		
			1,52 [0,58; 3,95]	0,390
Herpes simplex virus infections				
Interaction test:	p=0,996			
Previous IFN-beta-1b Treatment = No				
Number of patients with event	0	1		
Median (in weeks)	-	-		
% of event-free patients+	100,00 [100,00; 100,00]	97,92 [93,88; 100,00]		
			-	-
Previous IFN-beta-1b Treatment = Yes				
Number of patients with event	4	0		
Median (in weeks)	-	-		
% of event-free patients+	88,69 [77,59; 99,79]	100,00 [100,00; 100,00]		
			-	-

	Treatment groups		Comparison	
	BAF312 (N=127)	**Placebo (N=61)**	**HR [95% CI]**	**p-value**
Varicella-zoster virus infections				
Interaction test:	p=1,000			
Previous IFN-beta-1b Treatment = No				
Number of patients with event	0	0		
Median (in weeks)	-	-		
% of event-free patients+	100,00 [100,00; 100,00]	100,00 [100,00; 100,00]		
			-	-
Previous IFN-beta-1b Treatment = Yes				
Number of patients with event	1	0		
Median (in weeks)	-	-		
% of event-free patients+	97,44 [92,48; 100,00]	100,00 [100,00; 100,00]		
			-	-
Lymphopenia				
Interaction test:	p=1,000			
Previous IFN-beta-1b Treatment = No				
Number of patients with event	1	0		
Median (in weeks)	-	-		
% of event-free patients+	98,72 [96,22; 100,00]	100,00 [100,00; 100,00]		
			-	-
Previous IFN-beta-1b Treatment = Yes				
Number of patients with event	1	0		
Median (in weeks)	-	-		
% of event-free patients+	97,50 [92,66; 100,00]	100,00 [100,00; 100,00]		
			-	-
Macular edema				
Interaction test:	p=0,997			
Previous IFN-beta-1b Treatment = No				
Number of patients with event	0	1		
Median (in weeks)	-	-		
% of event-free patients+	100,00 [100,00; 100,00]	95,45 [86,75; 100,00]		
			-	-

	Treatment groups		Comparison	
	BAF312 (N=127)	**Placebo (N=61)**	**HR [95% CI]**	**p-value**
Previous IFN-beta-1b Treatment = Yes				
Number of patients with event	2	0		
Median (in weeks)	-	-		
% of event-free patients+	95,10 [88,47; 100,00]	100,00 [100,00; 100,00]		
			-	-
Abnormal hepatic enzymes				
Interaction test:	p=0,762			
Previous IFN-beta-1b Treatment = No				
Number of patients with event	13	3		
Median (in weeks)	-	-		
% of event-free patients+	82,60 [73,85; 91,35]	93,45 [86,27; 100,00]		
			2,58 [0,73; 9,05]	0,139
Previous IFN-beta-1b Treatment = Yes				
Number of patients with event	6	1		
Median (in weeks)	-	-		
% of event-free patients+	85,72 [75,00; 96,44]	92,31 [77,82; 100,00]		
			1,76 [0,21; 14,63]	0,600
Malignancies				
Interaction test:	p=1,000			
Previous IFN-beta-1b Treatment = No				
Number of patients with event	0	1		
Median (in weeks)	-	-		
% of event-free patients+	100,00 [100,00; 100,00]	94,44 [83,86; 100,00]		
			-	-
Previous IFN-beta-1b Treatment = Yes				
Number of patients with event	0	0		
Median (in weeks)	-	-		
% of event-free patients+	100,00 [100,00; 100,00]	100,00 [100,00; 100,00]		
			-	-

	Treatment groups		Comparison	
	BAF312 (N=127)	**Placebo (N=61)**	**HR [95% CI]**	**p-value**
Hypertension				
Interaction test:	p=0,992			
Previous IFN-beta-1b Treatment = No				
Number of patients with event	13	5		
Median (in weeks)	-	-		
% of event-free patients+	79,98 [68,24; 91,71]	89,43 [80,66; 98,20]		
			1,50 [0,53; 4,21]	0,440
Previous IFN-beta-1b Treatment = Yes				
Number of patients with event	4	0		
Median (in weeks)	-	-		
% of event-free patients+	86,73 [72,95; 100,00]	100,00 [100,00; 100,00]		
			-	-
Seizures				
Interaction test:	N.E.			
Previous IFN-beta-1b Treatment = No				
Number of patients with event	0	0		
Median (in weeks)	-	-		
% of event-free patients+	100,00 [100,00; 100,00]	100,00 [100,00; 100,00]		
			-	-
Previous IFN-beta-1b Treatment = Yes				
Number of patients with event	0	0		
Median (in weeks)	-	-		
% of event-free patients+	100,00 [100,00; 100,00]	100,00 [100,00; 100,00]		
			-	-
Thromboembolic events				
Interaction test:	p=0,994			
Previous IFN-beta-1b Treatment = No				
Number of patients with event	2	1		
Median (in weeks)	-	-		
% of event-free patients+	97,45 [93,96; 100,00]	97,62 [93,01; 100,00]		
			1,09 [0,10; 12,02]	0,946

	Treatment groups		Comparison	
	BAF312 (N=127)	**Placebo (N=61)**	**HR [95% CI]**	**p-value**
Previous IFN-beta-1b Treatment = Yes				
Number of patients with event	3	0		
Median (in weeks)	-	-		
% of event-free patients+	76,22 [42,42; 100,00]	100,00 [100,00; 100,00]		
			-	-
Respiratory disorders				
Interaction test:	p=0,691			
Previous IFN-beta-1b Treatment = No				
Number of patients with event	14	8		
Median (in weeks)	-	-		
% of event-free patients+	79,85 [70,15; 89,54]	76,29 [60,26; 92,32]		
			0,96 [0,40; 2,29]	0,924
Previous IFN-beta-1b Treatment = Yes				
Number of patients with event	8	3		
Median (in weeks)	-	-		
% of event-free patients+	75,79 [60,29; 91,28]	63,46 [24,66; 100,00]		
			0,69 [0,18; 2,62]	0,591
Peripheral edema/swelling				
Interaction test:	p=0,995			
Previous IFN-beta-1b Treatment = No				
Number of patients with event	3	0		
Median (in weeks)	-	-		
% of event-free patients+	96,30 [92,18; 100,00]	100,00 [100,00; 100,00]		
			-	-

	Treatment groups		Comparison	
	BAF312 (N=127)	**Placebo (N=61)**	**HR [95% CI]**	**p-value**
Previous IFN-beta-1b Treatment = Yes				
Number of patients with event	3	1		
Median (in weeks)	-	-		
% of event-free patients+	86,77 [69,62; 100,00]	91,67 [76,03; 100,00]		
			0,83 [0,09; 8,04]	0,875

N': Number of patients in the analysis
CI: Confidence Interval
HR: Hazard Ratio
N.E.: not estimable
*: p < 0,05

+ K-M estimate (%) of outcome-free patients, Greenwood formula is used for CIs of KM estimates

Applied model for HR: log(hazard ratio) = treatment + previous IFN-beta-1b treatment + previous IFN-beta-1b treatment * treatment
If it was not possible to fit the minimal model, the HR is not given.

Analysis population: A2304 SAF subpopulation "ACTIVE MS WITHOUT RELAPSES"

	Treatment groups		Comparison	
	BAF312 (N=127)	**Placebo (N=61)**	**HR [95% CI]**	**p-value**
N'	127	61		
N' Previous IFN-beta-1b Treatment = No	82	48		
N' Previous IFN-beta-1b Treatment = Yes	45	13		
Asthma/bronchospasm				
Interaction test:	p=0,999			
Previous IFN-beta-1b Treatment = No				
Number of patients with event	0	0		
Median (in weeks)	-	-		
% of event-free patients+	100,00 [100,00; 100,00]	100,00 [100,00; 100,00]		
			-	-
Previous IFN-beta-1b Treatment = Yes				
Number of patients with event	1	0		
Median (in weeks)	-	-		
% of event-free patients+	97,67 [93,17; 100,00]	100,00 [100,00; 100,00]		
			-	-
Pregnancy and neonatal topics				
Interaction test:	p=0,999			
Previous IFN-beta-1b Treatment = No				
Number of patients with event	1	0		
Median (in weeks)	-	-		
% of event-free patients+	98,78 [96,40; 100,00]	100,00 [100,00; 100,00]		
			-	-
Previous IFN-beta-1b Treatment = Yes				
Number of patients with event	0	0		
Median (in weeks)	-	-		
% of event-free patients+	100,00 [100,00; 100,00]	100,00 [100,00; 100,00]		
			-	-

	Treatment groups		Comparison	
	BAF312 (N=127)	**Placebo (N=61)**	**HR [95% CI]**	**p-value**
Bradyarrhythmias and bradycardia				
Interaction test:	p=0,995			
Previous IFN-beta-1b Treatment = No				
Number of patients with event	7	1		
Median (in weeks)	-	-		
% of event-free patients+	91,43 [85,36; 97,50]	97,92 [93,88; 100,00]		
			4,13 [0,51; 33,60]	0,184
Previous IFN-beta-1b Treatment = Yes				
Number of patients with event	4	0		
Median (in weeks)	-	-		
% of event-free patients+	91,11 [82,80; 99,43]	100,00 [100,00; 100,00]		
			-	-

N': Number of patients in the analysis
CI: Confidence Interval
HR: Hazard Ratio
*: p < 0,05

+ K-M estimate (%) of outcome-free patients, Greenwood formula is used for CIs of KM estimates

Applied model for HR: log(hazard ratio) = treatment + previous IFN-beta-1b treatment + previous IFN-beta-1b treatment * treatment
If it was not possible to fit the minimal model, the HR is not given.

Analysis population: A2304 SAF subpopulation "ACTIVE MS WITHOUT RELAPSES"

12.6 Subgroup: Rapid Evolvement

Table 12.6.1: Time to First Adverse Event (SAF) by Rapid Evolvement

	Treatment groups		Comparison	
	BAF312 (N=127)	**Placebo (N=61)**	**HR [95% CI]**	**p-value**
N'	127	61		
N' Rapid Evolvement = No	95	47		
N' Rapid Evolvement = Yes	32	14		
Any AE				
Interaction test:	p=0,907			
Rapid Evolvement = No				
Number of patients with event	84	36		
Median (in weeks)	3,6 [2,0; 8,3]	9,9 [4,3; 22,4]		
% of event-free patients+	8,55 [1,64; 15,47]	21,56 [9,40; 33,72]		
			1,46 [0,99; 2,17]	0,056
Rapid Evolvement = Yes				
Number of patients with event	30	11		
Median (in weeks)	7,1 [2,4; 10,7]	8,5 [2,9; 52,4]		
% of event-free patients+	6,25 [0,00; 14,64]	21,43 [0,00; 42,92]		
			1,54 [0,77; 3,07]	0,225
Any AE, disease specific events excluded[1]				
Interaction test:	p=0,439			
Rapid Evolvement = No				
Number of patients with event	79	35		
Median (in weeks)	12,4 [5,9; 19,9]	12,9 [6,9; 25,0]		
% of event-free patients+	12,61 [4,86; 20,37]	23,42 [10,84; 36,00]		
			1,21 [0,81; 1,81]	0,343
Rapid Evolvement = Yes				
Number of patients with event	29	11		
Median (in weeks)	9,3 [5,0; 13,0]	23,4 [2,9; 91,0]		
% of event-free patients+	6,70 [0,00; 15,64]	0,00 [0,00; 0,00]		
			1,67 [0,83; 3,35]	0,152
Any SAE				
Interaction test:	p=0,228			
Rapid Evolvement = No				
Number of patients with event	14	8		
Median (in weeks)	-	-		
% of event-free patients+	82,45 [73,65; 91,24]	79,57 [65,60; 93,55]		
			0,82 [0,34; 1,95]	0,651

	Treatment groups		Comparison	
	BAF312 (N=127)	**Placebo (N=61)**	**HR [95% CI]**	**p-value**
Rapid Evolvement = Yes				
Number of patients with event	2	3		
Median (in weeks)	-	-		
% of event-free patients+	91,18 [78,95; 100,00]	78,57 [57,08; 100,00]		
			0,24 [0,04; 1,44]	0,119
Any SAE, disease specific events excluded[1]				
Interaction test:	p=0,247			
Rapid Evolvement = No				
Number of patients with event	11	6		
Median (in weeks)	-	-		
% of event-free patients+	86,13 [78,09; 94,16]	83,43 [69,84; 97,01]		
			0,87 [0,32; 2,35]	0,779
Rapid Evolvement = Yes				
Number of patients with event	1	2		
Median (in weeks)	-	-		
% of event-free patients+	96,88 [90,85; 100,00]	85,71 [67,38; 100,00]		
			0,19 [0,02; 2,06]	0,171
Any severe AE[2]				
Interaction test:	p=0,381			
Rapid Evolvement = No				
Number of patients with event	10	8		
Median (in weeks)	-	-		
% of event-free patients+	86,53 [78,36; 94,69]	79,73 [66,08; 93,39]		
			0,58 [0,23; 1,46]	0,248
Rapid Evolvement = Yes				
Number of patients with event	1	2		
Median (in weeks)	-	-		
% of event-free patients+	96,67 [90,24; 100,00]	85,71 [67,38; 100,00]		
			0,18 [0,02; 2,02]	0,166

	Treatment groups		Comparison	
	BAF312 (N=127)	**Placebo (N=61)**	**HR [95% CI]**	**p-value**
Any severe AE[2], disease specific events excluded[1]				
Interaction test:	p=0,797			
Rapid Evolvement = No				
Number of patients with event	8	7		
Median (in weeks)	-	-		
% of event-free patients+	88,69 [80,94; 96,44]	81,49 [67,97; 95,01]		
			0,52 [0,19; 1,44]	0,209
Rapid Evolvement = Yes				
Number of patients with event	1	1		
Median (in weeks)	-	-		
% of event-free patients+	96,67 [90,24; 100,00]	92,86 [79,37; 100,00]		
			0,35 [0,02; 5,68]	0,464
Any AE leading to study discontinuation				
Interaction test:	p=0,786			
Rapid Evolvement = No				
Number of patients with event	1	2		
Median (in weeks)	-	-		
% of event-free patients+	98,92 [96,83; 100,00]	95,49 [89,36; 100,00]		
			0,25 [0,02; 2,74]	0,255
Rapid Evolvement = Yes				
Number of patients with event	1	1		
Median (in weeks)	-	-		
% of event-free patients+	96,88 [90,85; 100,00]	92,86 [79,37; 100,00]		
			0,41 [0,03; 6,63]	0,532
Any AE leading to study drug discontinuation				
Interaction test:	p=0,930			
Rapid Evolvement = No				
Number of patients with event	4	3		
Median (in weeks)	-	-		
% of event-free patients+	94,67 [89,28; 100,00]	90,94 [80,46; 100,00]		
			0,64 [0,14; 2,85]	0,557

	Treatment groups		Comparison	
	BAF312 (N=127)	**Placebo (N=61)**	**HR [95% CI]**	**p-value**
Rapid Evolvement = Yes				
Number of patients with event	2	1		
Median (in weeks)	-	-		
% of event-free patients[+]	93,42 [84,58; 100,00]	92,86 [79,37; 100,00]		
			0,73 [0,07; 8,04]	0,793

N': Number of patients in the analysis
CI: Confidence Interval
HR: Hazard Ratio
*: p < 0,05

[+] K-M estimate (%) of outcome-free patients, Greenwood formula is used for CIs of KM estimates

Applied model for HR: log(hazard ratio) = treatment + rapid evolvement + rapid evolvement * treatment
If it was not possible to fit the minimal model, the HR is not given.

[1] The following disease-specific Preferred Terms were excluded: see Table 11.0
[2] Definition of 'severe': CTCAE grade ≥ 3

Analysis population: A2304 SAF subpopulation "ACTIVE MS WITHOUT RELAPSES"

Table 12.6.2: Time to First Adverse Event by SOC and PT (SAF) by Rapid Evolvement

	Treatment groups		Comparison	
	BAF312 (N=127)	**Placebo (N=61)**	**HR [95% CI]**	**p-value**
N'	127	61		
N' Rapid Evolvement = No	95	47		
N' Rapid Evolvement = Yes	32	14		
GENERAL DISORDERS AND ADMINISTRATION SITE CONDITIONS				
Interaction test:	p=0,968			
Rapid Evolvement = No				
Number of patients with event	25	5		
Median (in weeks)	-	-		
% of event-free patients+	71,54 [61,84; 81,24]	86,65 [75,10; 98,20]		
			2,68 [1,03; 7,01]	0,044 *
Rapid Evolvement = Yes				
Number of patients with event	6	1		
Median (in weeks)	-	-		
% of event-free patients+	67,83 [42,01; 93,66]	83,33 [53,51; 100,00]		
			2,56 [0,31; 21,25]	0,384
INVESTIGATIONS				
Interaction test:	p=0,817			
Rapid Evolvement = No				
Number of patients with event	34	8		
Median (in weeks)	130,0 [105,3; .]	-		
% of event-free patients+	43,69 [17,11; 70,26]	78,23 [63,11; 93,36]		
			2,42 [1,12; 5,24]	0,025 *
Rapid Evolvement = Yes				
Number of patients with event	7	1		
Median (in weeks)	-	-		
% of event-free patients+	69,24 [45,17; 93,32]	92,86 [79,37; 100,00]		
			3,15 [0,39; 25,66]	0,283

N': Number of patients in the analysis
CI: Confidence Interval
HR: Hazard Ratio
*: p < 0,05

+ K-M estimate (%) of outcome-free patients, Greenwood formula is used for CIs of KM estimates

Applied model for HR: log(hazard ratio) = treatment + rapid evolvement + rapid evolvement * treatment
If it was not possible to fit the minimal model, the HR is not given.

SOCs/PTs are only displayed in this subgroup analysis, if the p-value for HR in the entire population is significant (p<0.05).

Analysis population: A2304 SAF subpopulation "ACTIVE MS WITHOUT RELAPSES"

Table 12.6.3: Time to First Serious Adverse Event by SOC and PT (SAF) by Rapid Evolvement

There are no data meeting the display criteria for this table.

Table 12.6.4: Time to First Severe Adverse Event by SOC and PT (SAF) by Rapid Evolvement

There are no data meeting the display criteria for this table.

Table 12.6.5: Time to First Adverse Event of Special Interest (SAF) by Rapid Evolvement

	Treatment groups		Comparison	
	BAF312 (N=127)	**Placebo (N=61)**	**HR [95% CI]**	**p-value**
N'	127	61		
N' Rapid Evolvement = No	95	47		
N' Rapid Evolvement = Yes	32	14		
Infections and infestations				
Interaction test:	p=0,378			
Rapid Evolvement = No				
Number of patients with event	45	21		
Median (in weeks)	79,0 [57,0; .]	88,6 [51,1; .]		
% of event-free patients+	40,38 [26,97; 53,80]	46,49 [29,85; 63,14]		
			1,10 [0,66; 1,86]	0,706
Rapid Evolvement = Yes				
Number of patients with event	20	5		
Median (in weeks)	68,1 [46,9; 90,3]	95,4 [57,0; .]		
% of event-free patients+	28,72 [10,90; 46,55]	33,67 [0,00; 82,32]		
			1,82 [0,68; 4,85]	0,232
Herpes simplex virus infections				
Interaction test:	p=0,995			
Rapid Evolvement = No				
Number of patients with event	4	0		
Median (in weeks)	-	-		
% of event-free patients+	94,86 [89,76; 99,97]	100,00 [100,00; 100,00]		
			-	-
Rapid Evolvement = Yes				
Number of patients with event	0	1		
Median (in weeks)	-	-		
% of event-free patients+	100,00 [100,00; 100,00]	92,86 [79,37; 100,00]		
			-	-

	Treatment groups		Comparison	
	BAF312 (N=127)	**Placebo (N=61)**	**HR [95% CI]**	**p-value**
Varicella-zoster virus infections				
Interaction test:	p=0,999			
Rapid Evolvement = No				
Number of patients with event	1	0		
Median (in weeks)	-	-		
% of event-free patients+	98,73 [96,27; 100,00]	100,00 [100,00; 100,00]		
			-	-
Rapid Evolvement = Yes				
Number of patients with event	0	0		
Median (in weeks)	-	-		
% of event-free patients+	100,00 [100,00; 100,00]	100,00 [100,00; 100,00]		
			-	-
Lymphopenia				
Interaction test:	p=0,999			
Rapid Evolvement = No				
Number of patients with event	2	0		
Median (in weeks)	-	-		
% of event-free patients+	97,72 [94,60; 100,00]	100,00 [100,00; 100,00]		
			-	-
Rapid Evolvement = Yes				
Number of patients with event	0	0		
Median (in weeks)	-	-		
% of event-free patients+	100,00 [100,00; 100,00]	100,00 [100,00; 100,00]		
			-	-
Macular edema				
Interaction test:	p=0,997			
Rapid Evolvement = No				
Number of patients with event	1	1		
Median (in weeks)	-	-		
% of event-free patients+	98,90 [96,76; 100,00]	95,24 [86,13; 100,00]		
			0,47 [0,03; 7,56]	0,595

	Treatment groups		Comparison	
	BAF312 (N=127)	**Placebo (N=61)**	**HR [95% CI]**	**p-value**
Rapid Evolvement = Yes				
Number of patients with event	1	0		
Median (in weeks)	-	-		
% of event-free patients+	96,67 [90,24; 100,00]	100,00 [100,00; 100,00]		
			-	-
Abnormal hepatic enzymes				
Interaction test:	p=0,861			
Rapid Evolvement = No				
Number of patients with event	13	3		
Median (in weeks)	-	-		
% of event-free patients+	84,32 [76,23; 92,40]	93,36 [86,10; 100,00]		
			2,18 [0,62; 7,64]	0,224
Rapid Evolvement = Yes				
Number of patients with event	6	1		
Median (in weeks)	-	-		
% of event-free patients+	80,79 [66,94; 94,63]	92,86 [79,37; 100,00]		
			2,72 [0,33; 22,58]	0,355
Malignancies				
Interaction test:	p=1,000			
Rapid Evolvement = No				
Number of patients with event	0	1		
Median (in weeks)	-	-		
% of event-free patients+	100,00 [100,00; 100,00]	94,74 [84,70; 100,00]		
			-	-
Rapid Evolvement = Yes				
Number of patients with event	0	0		
Median (in weeks)	-	-		
% of event-free patients+	100,00 [100,00; 100,00]	100,00 [100,00; 100,00]		
			-	-

	Treatment groups		Comparison	
	BAF312 (N=127)	**Placebo (N=61)**	**HR [95% CI]**	**p-value**
Hypertension				
Interaction test:	p=0,752			
Rapid Evolvement = No				
Number of patients with event	14	4		
Median (in weeks)	-	-		
% of event-free patients+	79,07 [67,23; 90,90]	91,33 [83,21; 99,46]		
			1,75 [0,58; 5,31]	0,325
Rapid Evolvement = Yes				
Number of patients with event	3	1		
Median (in weeks)	-	-		
% of event-free patients+	90,63 [80,53; 100,00]	92,86 [79,37; 100,00]		
			1,16 [0,12; 11,21]	0,895
Seizures				
Interaction test:	N.E.			
Rapid Evolvement = No				
Number of patients with event	0	0		
Median (in weeks)	-	-		
% of event-free patients+	100,00 [100,00; 100,00]	100,00 [100,00; 100,00]		
			-	-
Rapid Evolvement = Yes				
Number of patients with event	0	0		
Median (in weeks)	-	-		
% of event-free patients+	100,00 [100,00; 100,00]	100,00 [100,00; 100,00]		
			-	-
Thromboembolic events				
Interaction test:	p=0,996			
Rapid Evolvement = No				
Number of patients with event	3	1		
Median (in weeks)	-	-		
% of event-free patients+	91,27 [78,61; 100,00]	97,62 [93,01; 100,00]		
			1,41 [0,15; 13,60]	0,767

	Treatment groups		Comparison	
	BAF312 (N=127)	**Placebo (N=61)**	**HR [95% CI]**	**p-value**
Rapid Evolvement = Yes				
Number of patients with event	2	0		
Median (in weeks)	-	-		
% of event-free patients+	93,53 [84,86; 100,00]	100,00 [100,00; 100,00]		
			-	-
Respiratory disorders				
Interaction test:	p=0,690			
Rapid Evolvement = No				
Number of patients with event	15	9		
Median (in weeks)	-	-		
% of event-free patients+	79,79 [70,15; 89,43]	71,01 [53,08; 88,94]		
			0,81 [0,35; 1,85]	0,614
Rapid Evolvement = Yes				
Number of patients with event	7	2		
Median (in weeks)	-	-		
% of event-free patients+	74,53 [57,67; 91,38]	85,71 [67,38; 100,00]		
			1,16 [0,24; 5,60]	0,852
Peripheral edema/swelling				
Interaction test:	p=0,996			
Rapid Evolvement = No				
Number of patients with event	5	1		
Median (in weeks)	-	-		
% of event-free patients+	94,62 [90,03; 99,21]	97,67 [93,17; 100,00]		
			2,44 [0,28; 20,88]	0,416

	Treatment groups		Comparison	
	BAF312 (N=127)	**Placebo (N=61)**	**HR [95% CI]**	**p-value**
Rapid Evolvement = Yes				
Number of patients with event	1	0		
Median (in weeks)	-	-		
% of event-free patients+	87,50 [64,58; 100,00]	100,00 [100,00; 100,00]		
			-	-

N': Number of patients in the analysis
CI: Confidence Interval
HR: Hazard Ratio
N.E.: not estimable
*: p < 0,05

+ K-M estimate (%) of outcome-free patients, Greenwood formula is used for CIs of KM estimates

Applied model for HR: log(hazard ratio) = treatment + rapid evolvement + rapid evolvement * treatment
If it was not possible to fit the minimal model, the HR is not given.

Analysis population: A2304 SAF subpopulation "ACTIVE MS WITHOUT RELAPSES"

	Treatment groups		Comparison	
	BAF312 (N=127)	**Placebo (N=61)**	**HR [95% CI]**	**p-value**
N'	127	61		
N' Rapid Evolvement = No	95	47		
N' Rapid Evolvement = Yes	32	14		
Asthma/bronchospasm				
Interaction test:	p=0,999			
Rapid Evolvement = No				
Number of patients with event	0	0		
Median (in weeks)	-	-		
% of event-free patients+	100,00 [100,00; 100,00]	100,00 [100,00; 100,00]		
			-	-
Rapid Evolvement = Yes				
Number of patients with event	1	0		
Median (in weeks)	-	-		
% of event-free patients+	96,77 [90,55; 100,00]	100,00 [100,00; 100,00]		
			-	-
Pregnancy and neonatal topics				
Interaction test:	p=0,999			
Rapid Evolvement = No				
Number of patients with event	0	0		
Median (in weeks)	-	-		
% of event-free patients+	100,00 [100,00; 100,00]	100,00 [100,00; 100,00]		
			-	-
Rapid Evolvement = Yes				
Number of patients with event	1	0		
Median (in weeks)	-	-		
% of event-free patients+	96,88 [90,85; 100,00]	100,00 [100,00; 100,00]		
			-	-

	Treatment groups		Comparison	
	BAF312 (N=127)	**Placebo (N=61)**	**HR [95% CI]**	**p-value**
Bradyarrhythmias and bradycardia				
Interaction test:	p=0,995			
Rapid Evolvement = No				
Number of patients with event	10	1		
Median (in weeks)	-	-		
% of event-free patients+	89,47 [83,30; 95,64]	97,87 [93,75; 100,00]		
			5,02 [0,64; 39,26]	0,124
Rapid Evolvement = Yes				
Number of patients with event	1	0		
Median (in weeks)	-	-		
% of event-free patients+	96,77 [90,55; 100,00]	100,00 [100,00; 100,00]		
			-	-

N': Number of patients in the analysis
CI: Confidence Interval
HR: Hazard Ratio
*: p < 0,05

+ K-M estimate (%) of outcome-free patients, Greenwood formula is used for CIs of KM estimates

Applied model for HR: log(hazard ratio) = treatment + rapid evolvement + rapid evolvement * treatment
If it was not possible to fit the minimal model, the HR is not given.

Analysis population: A2304 SAF subpopulation "ACTIVE MS WITHOUT RELAPSES"

12.7 Subgroup: Disease Course

Table 12.7.1: Time to First Adverse Event (SAF) by Disease Course

	Treatment groups		Comparison	
	BAF312 (N=127)	**Placebo (N=61)**	**HR [95% CI]**	**p-value**
N'	127	61		
N' Moderate or Severe Disease Course = No	18	11		
N' Moderate or Severe Disease Course = Yes	109	50		
Any AE				
Interaction test:	p=0,716			
Moderate or Severe Disease Course = No				
Number of patients with event	16	8		
Median (in weeks)	5,9 [2,3; 23,0]	7,3 [4,3; -]		
% of event-free patients+	6,17 [0,00; 17,86]	27,27 [0,95; 53,59]		
			1,70 [0,73; 3,99]	0,221
Moderate or Severe Disease Course = Yes				
Number of patients with event	98	39		
Median (in weeks)	3,6 [2,0; 8,4]	9,8 [4,0; 23,6]		
% of event-free patients+	7,76 [1,78; 13,75]	20,01 [8,55; 31,48]		
			1,43 [0,99; 2,08]	0,059
Any AE, disease specific events excluded[1]				
Interaction test:	p=0,339			
Moderate or Severe Disease Course = No				
Number of patients with event	16	8		
Median (in weeks)	12,9 [4,1; 27,0]	30,0 [7,3; -]		
% of event-free patients+	6,06 [0,00; 17,56]	27,27 [0,95; 53,59]		
			1,91 [0,81; 4,47]	0,138
Moderate or Severe Disease Course = Yes				
Number of patients with event	92	38		
Median (in weeks)	10,7 [6,1; 15,1]	12,4 [4,4; 24,9]		
% of event-free patients+	10,76 [3,72; 17,79]	14,64 [0,03; 29,26]		
			1,21 [0,83; 1,77]	0,324

	Treatment groups		Comparison	
	BAF312 (N=127)	**Placebo (N=61)**	**HR [95% CI]**	**p-value**
Any SAE				
Interaction test:	p=0,987			
Moderate or Severe Disease Course = No				
Number of patients with event	3	0		
Median (in weeks)	-	-		
% of event-free patients+	77,47 [53,33; 100,00]	100,00 [100,00; 100,00]		
			-	-
Moderate or Severe Disease Course = Yes				
Number of patients with event	13	11		
Median (in weeks)	-	-		
% of event-free patients+	85,47 [77,79; 93,15]	74,81 [60,68; 88,95]		
			0,47 [0,21; 1,06]	0,069
Any SAE, disease specific events excluded[1]				
Interaction test:	p=0,989			
Moderate or Severe Disease Course = No				
Number of patients with event	2	0		
Median (in weeks)	-	-		
% of event-free patients+	88,54 [73,58; 100,00]	100,00 [100,00; 100,00]		
			-	-
Moderate or Severe Disease Course = Yes				
Number of patients with event	10	8		
Median (in weeks)	-	-		
% of event-free patients+	89,26 [82,77; 95,76]	80,32 [66,59; 94,04]		
			0,52 [0,20; 1,31]	0,163
Any severe AE[2]				
Interaction test:	p=0,855			
Moderate or Severe Disease Course = No				
Number of patients with event	1	1		
Median (in weeks)	-	-		
% of event-free patients+	93,75 [81,89; 100,00]	90,00 [71,41; 100,00]		
			0,60 [0,04; 9,59]	0,718

	Treatment groups		Comparison	
	BAF312 (N=127)	**Placebo (N=61)**	**HR [95% CI]**	**p-value**
Moderate or Severe Disease Course = Yes				
Number of patients with event	10	9		
Median (in weeks)	-	-		
% of event-free patients+	88,82 [82,08; 95,56]	78,83 [65,34; 92,32]		
			0,46 [0,19; 1,13]	0,089
Any severe AE[2], disease specific events excluded[1]				
Interaction test:	p=0,866			
Moderate or Severe Disease Course = No				
Number of patients with event	1	1		
Median (in weeks)	-	-		
% of event-free patients+	93,75 [81,89; 100,00]	88,89 [68,36; 100,00]		
			0,60 [0,04; 9,53]	0,714
Moderate or Severe Disease Course = Yes				
Number of patients with event	8	7		
Median (in weeks)	-	-		
% of event-free patients+	90,70 [84,36; 97,03]	82,47 [69,34; 95,60]		
			0,46 [0,17; 1,28]	0,137
Any AE leading to study discontinuation				
Interaction test:	p=1,000			
Moderate or Severe Disease Course = No				
Number of patients with event	0	0		
Median (in weeks)	-	-		
% of event-free patients+	100,00 [100,00; 100,00]	100,00 [100,00; 100,00]		
			-	-
Moderate or Severe Disease Course = Yes				
Number of patients with event	2	3		
Median (in weeks)	-	-		
% of event-free patients+	98,16 [95,63; 100,00]	93,58 [86,52; 100,00]		
			0,30 [0,05; 1,81]	0,191

	Treatment groups		Comparison	
	BAF312 (N=127)	**Placebo (N=61)**	**HR [95% CI]**	**p-value**
Any AE leading to study drug discontinuation				
Interaction test:	p=1,000			
Moderate or Severe Disease Course = No				
Number of patients with event	0	0		
Median (in weeks)	-	-		
% of event-free patients+	100,00 [100,00; 100,00]	100,00 [100,00; 100,00]		
			-	-
Moderate or Severe Disease Course = Yes				
Number of patients with event	6	4		
Median (in weeks)	-	-		
% of event-free patients+	93,59 [88,47; 98,71]	89,51 [79,19; 99,82]		
			0,63 [0,18; 2,25]	0,481

N': Number of patients in the analysis
CI: Confidence Interval
HR: Hazard Ratio
*: p < 0,05

+ K-M estimate (%) of outcome-free patients, Greenwood formula is used for CIs of KM estimates

Applied model for HR: log(hazard ratio) = treatment + disease course + disease course * treatment
If it was not possible to fit the minimal model, the HR is not given.

[1] The following disease-specific Preferred Terms were excluded: see Table 11.0
[2] Definition of 'severe': CTCAE grade ≥ 3

Analysis population: A2304 SAF subpopulation "ACTIVE MS WITHOUT RELAPSES"

Table 12.7.2: Time to First Adverse Event by SOC and PT (SAF) by Disease Course

	Treatment groups		Comparison	
	BAF312 (N=127)	**Placebo (N=61)**	**HR [95% CI]**	**p-value**
N'	127	61		
N' Moderate or Severe Disease Course = No	18	11		
N' Moderate or Severe Disease Course = Yes	109	50		
GENERAL DISORDERS AND ADMINISTRATION SITE CONDITIONS				
Interaction test:	p=0,988			
Moderate or Severe Disease Course = No				
Number of patients with event	1	0		
Median (in weeks)	-	-		
% of event-free patients+	94,44 [83,86; 100,00]	100,00 [100,00; 100,00]		
			-	-
Moderate or Severe Disease Course = Yes				
Number of patients with event	30	6		
Median (in weeks)	-	-		
% of event-free patients+	67,32 [56,40; 78,25]	83,35 [70,34; 96,36]		
			2,44 [1,01; 5,86]	0,046 *
INVESTIGATIONS				
Interaction test:	p=0,473			
Moderate or Severe Disease Course = No				
Number of patients with event	4	2		
Median (in weeks)	-	-		
% of event-free patients+	76,74 [56,73; 96,74]	80,81 [56,80; 100,00]		
			1,36 [0,25; 7,42]	0,724

	Treatment groups		Comparison	
	BAF312 (N=127)	**Placebo (N=61)**	**HR [95% CI]**	**p-value**
Moderate or Severe Disease Course = Yes				
Number of patients with event	37	7		
Median (in weeks)	130,0 [118,6; .]	-		
% of event-free patients+	47,87 [26,88; 68,86]	81,11 [66,39; 95,84]		
			2,70 [1,20; 6,06]	0,016 *

N': Number of patients in the analysis
CI: Confidence Interval
HR: Hazard Ratio
*: p < 0,05

+ K-M estimate (%) of outcome-free patients, Greenwood formula is used for CIs of KM estimates

Applied model for HR: log(hazard ratio) = treatment + disease course + disease course * treatment
If it was not possible to fit the minimal model, the HR is not given.

SOCs/PTs are only displayed in this subgroup analysis, if the p-value for HR in the entire population is significant (p<0.05).

Analysis population: A2304 SAF subpopulation "ACTIVE MS WITHOUT RELAPSES"

Table 12.7.3: Time to First Serious Adverse Event by SOC and PT (SAF) by Disease Course

There are no data meeting the display criteria for this table.

Table 12.7.4: Time to First Severe Adverse Event by SOC and PT (SAF) by Disease Course

There are no data meeting the display criteria for this table.

Table 12.7.5: Time to First Adverse Event of Special Interest (SAF) by Disease Course

	Treatment groups		Comparison	
	BAF312 (N=127)	**Placebo (N=61)**	**HR [95% CI]**	**p-value**
N'	127	61		
N' Moderate or Severe Disease Course = No	18	11		
N' Moderate or Severe Disease Course = Yes	109	50		
Infections and infestations				
Interaction test:	p=0,346			
Moderate or Severe Disease Course = No				
Number of patients with event	8	6		
Median (in weeks)	59,4 [27,0; .]	57,0 [30,0; .]		
% of event-free patients+	47,06 [19,21; 74,91]	35,35 [3,79; 66,92]		
			0,79 [0,27; 2,27]	0,659
Moderate or Severe Disease Course = Yes				
Number of patients with event	57	20		
Median (in weeks)	76,7 [60,3; 100,1]	95,4 [64,3; .]		
% of event-free patients+	35,26 [23,33; 47,20]	44,86 [23,85; 65,87]		
			1,39 [0,83; 2,31]	0,210
Herpes simplex virus infections				
Interaction test:	p=0,995			
Moderate or Severe Disease Course = No				
Number of patients with event	0	1		
Median (in weeks)	-	-		
% of event-free patients+	100,00 [100,00; 100,00]	90,91 [73,92; 100,00]		
			-	-
Moderate or Severe Disease Course = Yes				
Number of patients with event	4	0		
Median (in weeks)	-	-		
% of event-free patients+	95,68 [91,43; 99,93]	100,00 [100,00; 100,00]		
			-	-

	Treatment groups		Comparison	
	BAF312 (N=127)	**Placebo (N=61)**	**HR [95% CI]**	**p-value**
Varicella-zoster virus infections				
Interaction test:	p=1,000			
Moderate or Severe Disease Course = No				
Number of patients with event	1	0		
Median (in weeks)	-	-		
% of event-free patients+	93,75 [81,89; 100,00]	100,00 [100,00; 100,00]		
			-	-
Moderate or Severe Disease Course = Yes				
Number of patients with event	0	0		
Median (in weeks)	-	-		
% of event-free patients+	100,00 [100,00; 100,00]	100,00 [100,00; 100,00]		
			-	-
Lymphopenia				
Interaction test:	p=0,999			
Moderate or Severe Disease Course = No				
Number of patients with event	0	0		
Median (in weeks)	-	-		
% of event-free patients+	100,00 [100,00; 100,00]	100,00 [100,00; 100,00]		
			-	-
Moderate or Severe Disease Course = Yes				
Number of patients with event	2	0		
Median (in weeks)	-	-		
% of event-free patients+	98,02 [95,30; 100,00]	100,00 [100,00; 100,00]		
			-	-
Macular edema				
Interaction test:	p=1,000			
Moderate or Severe Disease Course = No				
Number of patients with event	0	0		
Median (in weeks)	-	-		
% of event-free patients+	100,00 [100,00; 100,00]	100,00 [100,00; 100,00]		
			-	-

	Treatment groups		Comparison	
	BAF312 (N=127)	**Placebo (N=61)**	**HR [95% CI]**	**p-value**
Moderate or Severe Disease Course = Yes				
Number of patients with event	2	1		
Median (in weeks)	-	-		
% of event-free patients+	97,98 [95,21; 100,00]	95,65 [87,32; 100,00]		
			0,85 [0,08; 9,39]	0,893
Abnormal hepatic enzymes				
Interaction test:	p=0,268			
Moderate or Severe Disease Course = No				
Number of patients with event	3	2		
Median (in weeks)	-	-		
% of event-free patients+	82,64 [64,75; 100,00]	80,81 [56,80; 100,00]		
			1,00 [0,17; 6,01]	0,997
Moderate or Severe Disease Course = Yes				
Number of patients with event	16	2		
Median (in weeks)	-	-		
% of event-free patients+	83,97 [76,63; 91,30]	95,96 [90,47; 100,00]		
			3,72 [0,85; 16,16]	0,080
Malignancies				
Interaction test:	p=1,000			
Moderate or Severe Disease Course = No				
Number of patients with event	0	0		
Median (in weeks)	-	-		
% of event-free patients+	100,00 [100,00; 100,00]	100,00 [100,00; 100,00]		
			-	-
Moderate or Severe Disease Course = Yes				
Number of patients with event	0	1		
Median (in weeks)	-	-		
% of event-free patients+	100,00 [100,00; 100,00]	94,74 [84,70; 100,00]		
			-	-

	Treatment groups		Comparison	
	BAF312 (N=127)	**Placebo (N=61)**	**HR [95% CI]**	**p-value**
Hypertension				
Interaction test:	p=1,000			
Moderate or Severe Disease Course = No				
Number of patients with event	0	0		
Median (in weeks)	-	-		
% of event-free patients+	100,00 [100,00; 100,00]	100,00 [100,00; 100,00]		
			-	-
Moderate or Severe Disease Course = Yes				
Number of patients with event	17	5		
Median (in weeks)	-	-		
% of event-free patients+	79,34 [68,88; 89,81]	89,91 [81,52; 98,30]		
			1,53 [0,56; 4,15]	0,404
Seizures				
Interaction test:	N.E.			
Moderate or Severe Disease Course = No				
Number of patients with event	0	0		
Median (in weeks)	-	-		
% of event-free patients+	100,00 [100,00; 100,00]	100,00 [100,00; 100,00]		
			-	-
Moderate or Severe Disease Course = Yes				
Number of patients with event	0	0		
Median (in weeks)	-	-		
% of event-free patients+	100,00 [100,00; 100,00]	100,00 [100,00; 100,00]		
			-	-
Thromboembolic events				
Interaction test:	p=0,994			
Moderate or Severe Disease Course = No				
Number of patients with event	1	0		
Median (in weeks)	-	-		
% of event-free patients+	94,12 [82,93; 100,00]	100,00 [100,00; 100,00]		
			-	-

	Treatment groups		Comparison	
	BAF312 (N=127)	**Placebo (N=61)**	**HR [95% CI]**	**p-value**
Moderate or Severe Disease Course = Yes				
Number of patients with event	4	1		
Median (in weeks)	-	-		
% of event-free patients+	91,09 [79,19; 100,00]	97,78 [93,47; 100,00]		
			1,75 [0,20; 15,74]	0,616
Respiratory disorders				
Interaction test:	p=0,807			
Moderate or Severe Disease Course = No				
Number of patients with event	2	1		
Median (in weeks)	-	-		
% of event-free patients+	73,33 [38,85; 100,00]	90,91 [73,92; 100,00]		
			1,16 [0,11; 12,84]	0,902
Moderate or Severe Disease Course = Yes				
Number of patients with event	20	10		
Median (in weeks)	-	-		
% of event-free patients+	78,15 [69,35; 86,95]	70,12 [52,45; 87,80]		
			0,85 [0,40; 1,82]	0,674
Peripheral edema/swelling				
Interaction test:	p=1,000			
Moderate or Severe Disease Course = No				
Number of patients with event	0	0		
Median (in weeks)	-	-		
% of event-free patients+	100,00 [100,00; 100,00]	100,00 [100,00; 100,00]		
			-	-

	Treatment groups		Comparison	
	BAF312 (N=127)	**Placebo (N=61)**	**HR [95% CI]**	**p-value**
Moderate or Severe Disease Course = Yes				
Number of patients with event	6	1		
Median (in weeks)	-	-		
% of event-free patients+	91,51 [83,24; 99,78]	97,78 [93,47; 100,00]		
			2,69 [0,32; 22,37]	0,360

N': Number of patients in the analysis
CI: Confidence Interval
HR: Hazard Ratio
N.E.: not estimable
*: p < 0,05

+ K-M estimate (%) of outcome-free patients, Greenwood formula is used for CIs of KM estimates

Applied model for HR: log(hazard ratio) = treatment + disease course + disease course * treatment
If it was not possible to fit the minimal model, the HR is not given.

Analysis population: A2304 SAF subpopulation "ACTIVE MS WITHOUT RELAPSES"

	Treatment groups		Comparison	
	BAF312 (N=127)	**Placebo (N=61)**	**HR [95% CI]**	**p-value**
N'	127	61		
N' Moderate or Severe Disease Course = No	18	11		
N' Moderate or Severe Disease Course = Yes	109	50		
Asthma/bronchospasm				
Interaction test:	p=0,999			
Moderate or Severe Disease Course = No				
Number of patients with event	0	0		
Median (in weeks)	-	-		
% of event-free patients+	100,00 [100,00; 100,00]	100,00 [100,00; 100,00]		
			-	-
Moderate or Severe Disease Course = Yes				
Number of patients with event	1	0		
Median (in weeks)	-	-		
% of event-free patients+	99,06 [97,22; 100,00]	100,00 [100,00; 100,00]		
			-	-
Pregnancy and neonatal topics				
Interaction test:	p=0,999			
Moderate or Severe Disease Course = No				
Number of patients with event	0	0		
Median (in weeks)	-	-		
% of event-free patients+	100,00 [100,00; 100,00]	100,00 [100,00; 100,00]		
			-	-
Moderate or Severe Disease Course = Yes				
Number of patients with event	1	0		
Median (in weeks)	-	-		
% of event-free patients+	99,08 [97,29; 100,00]	100,00 [100,00; 100,00]		
			-	-

	Treatment groups		Comparison	
	BAF312 (N=127)	**Placebo (N=61)**	**HR [95% CI]**	**p-value**
Bradyarrhythmias and bradycardia				
Interaction test:	p=0,993			
Moderate or Severe Disease Course = No				
Number of patients with event	0	1		
Median (in weeks)	-	-		
% of event-free patients+	100,00 [100,00; 100,00]	90,91 [73,92; 100,00]		
			-	-
Moderate or Severe Disease Course = Yes				
Number of patients with event	11	0		
Median (in weeks)	-	-		
% of event-free patients+	89,88 [84,21; 95,55]	100,00 [100,00; 100,00]		
			-	-

N': Number of patients in the analysis
CI: Confidence Interval
HR: Hazard Ratio
*: p < 0,05

+ K-M estimate (%) of outcome-free patients, Greenwood formula is used for CIs of KM estimates

Applied model for HR: log(hazard ratio) = treatment + disease course + disease course * treatment
If it was not possible to fit the minimal model, the HR is not given.

Analysis population: A2304 SAF subpopulation "ACTIVE MS WITHOUT RELAPSES"

12.8 Subgroup: Region

Table 12.8.1: Time to First Adverse Event (SAF) by Region

	Treatment groups		Comparison	
	BAF312 (N=127)	**Placebo (N=61)**	**HR [95% CI]**	**p-value**
N'	127	61		
N' Region = Europe	106	52		
N' Region = Other	21	9		
Any AE				
Interaction test:	p=0,955			
Region = Europe				
Number of patients with event	97	39		
Median (in weeks)	3,6 [2,1; 9,7]	6,9 [4,1; 18,7]		
% of event-free patients+	6,92 [1,41; 12,42]	24,43 [12,62; 36,25]		
			1,49 [1,02; 2,16]	0,037 *
Region = Other				
Number of patients with event	17	8		
Median (in weeks)	4,3 [1,7; 11,0]	25,0 [9,9; 34,9]		
% of event-free patients+	15,87 [0,00; 32,18]	0,00 [0,00; 0,00]		
			1,45 [0,62; 3,36]	0,389
Any AE, disease specific events excluded[1]				
Interaction test:	p=0,973			
Region = Europe				
Number of patients with event	93	39		
Median (in weeks)	10,0 [4,6; 13,0]	10,8 [4,4; 22,4]		
% of event-free patients+	9,04 [2,71; 15,38]	24,36 [12,55; 36,17]		
			1,31 [0,90; 1,91]	0,157
Region = Other				
Number of patients with event	15	7		
Median (in weeks)	16,7 [11,0; 49,0]	50,9 [25,0; 79,0]		
% of event-free patients+	17,44 [0,00; 36,96]	0,00 [0,00; 0,00]		
			1,29 [0,52; 3,16]	0,580
Any SAE				
Interaction test:	p=0,071			
Region = Europe				
Number of patients with event	10	10		
Median (in weeks)	-	-		
% of event-free patients+	88,42 [81,33; 95,50]	76,97 [62,72; 91,21]		
			0,42 [0,17; 1,01]	0,051

	Treatment groups		Comparison	
	BAF312 (N=127)	**Placebo (N=61)**	**HR [95% CI]**	**p-value**
Region = Other				
Number of patients with event	6	1		
Median (in weeks)	-	-		
% of event-free patients+	59,44 [29,08; 89,80]	88,89 [68,36; 100,00]		
			3,47 [0,42; 28,98]	0,251
Any SAE, disease specific events excluded[1]				
Interaction test:	p=0,136			
Region = Europe				
Number of patients with event	7	7		
Median (in weeks)	-	-		
% of event-free patients+	92,47 [86,94; 98,00]	82,28 [68,38; 96,17]		
			0,43 [0,15; 1,23]	0,117
Region = Other				
Number of patients with event	5	1		
Median (in weeks)	-	-		
% of event-free patients+	66,34 [38,31; 94,38]	88,89 [68,36; 100,00]		
			2,67 [0,31; 22,96]	0,371
Any severe AE[2]				
Interaction test:	p=0,122			
Region = Europe				
Number of patients with event	7	9		
Median (in weeks)	-	-		
% of event-free patients+	91,97 [86,13; 97,82]	78,95 [65,21; 92,69]		
			0,33 [0,12; 0,88]	0,026 *
Region = Other				
Number of patients with event	4	1		
Median (in weeks)	-	-		
% of event-free patients+	67,72 [35,39; 100,00]	88,89 [68,36; 100,00]		
			2,19 [0,24; 19,71]	0,484

	Treatment groups		Comparison	
	BAF312 (N=127)	**Placebo (N=61)**	**HR [95% CI]**	**p-value**
Any severe AE[2], disease specific events excluded[1]				
Interaction test:	p=0,245			
Region = Europe				
Number of patients with event	6	7		
Median (in weeks)	-	-		
% of event-free patients+	92,91 [87,30; 98,52]	82,35 [68,85; 95,85]		
			0,35 [0,12; 1,06]	0,063
Region = Other				
Number of patients with event	3	1		
Median (in weeks)	-	-		
% of event-free patients+	74,96 [45,95; 100,00]	88,89 [68,36; 100,00]		
			1,58 [0,16; 15,31]	0,692
Any AE leading to study discontinuation				
Interaction test:	p=0,995			
Region = Europe				
Number of patients with event	1	3		
Median (in weeks)	-	-		
% of event-free patients+	99,05 [97,19; 100,00]	93,79 [86,95; 100,00]		
			0,16 [0,02; 1,53]	0,111
Region = Other				
Number of patients with event	1	0		
Median (in weeks)	-	-		
% of event-free patients+	95,24 [86,13; 100,00]	100,00 [100,00; 100,00]		
			-	-
Any AE leading to study drug discontinuation				
Interaction test:	p=0,993			
Region = Europe				
Number of patients with event	4	4		
Median (in weeks)	-	-		
% of event-free patients+	95,35 [90,77; 99,93]	89,32 [78,58; 100,00]		
			0,43 [0,11; 1,71]	0,230

	Treatment groups		Comparison	
	BAF312 (N=127)	**Placebo (N=61)**	**HR [95% CI]**	**p-value**
Region = Other				
Number of patients with event	2	0		
Median (in weeks)	-	-		
% of event-free patients[+]	90,48 [77,92; 100,00]	100,00 [100,00; 100,00]		
			-	-

N': Number of patients in the analysis
CI: Confidence Interval
HR: Hazard Ratio
*: p < 0,05

[+] K-M estimate (%) of outcome-free patients, Greenwood formula is used for CIs of KM estimates

Applied model for HR: log(hazard ratio) = treatment + region + region * treatment
If it was not possible to fit the minimal model, the HR is not given.

[1] The following disease-specific Preferred Terms were excluded: see Table 11.0
[2] Definition of 'severe': CTCAE grade ≥ 3

Analysis population: A2304 SAF subpopulation "ACTIVE MS WITHOUT RELAPSES"

Table 12.8.2: Time to First Adverse Event by SOC and PT (SAF) by Region

	Treatment groups		Comparison	
	BAF312 (N=127)	**Placebo (N=61)**	**HR [95% CI]**	**p-value**
N'	127	61		
N' Region = Europe	106	52		
N' Region = Other	21	9		
GENERAL DISORDERS AND ADMINISTRATION SITE CONDITIONS				
Interaction test:	p=0,031 *			
Region = Europe				
Number of patients with event	28	3		
Median (in weeks)	-	-		
% of event-free patients+	68,70 [57,76; 79,65]	91,71 [81,92; 100,00]		
			4,71 [1,43; 15,52]	0,011 *
Region = Other				
Number of patients with event	3	3		
Median (in weeks)	-	-		
% of event-free patients+	84,59 [68,45; 100,00]	60,00 [24,40; 95,60]		
			0,52 [0,10; 2,58]	0,424
INVESTIGATIONS				
Interaction test:	p=0,989			
Region = Europe				
Number of patients with event	35	9		
Median (in weeks)	130,0 [118,6; .]	-		
% of event-free patients+	48,99 [24,93; 73,04]	76,80 [60,63; 92,97]		
			1,98 [0,95; 4,12]	0,067

	Treatment groups		Comparison	
	BAF312 (N=127)	**Placebo (N=61)**	**HR [95% CI]**	**p-value**
Region = Other				
Number of patients with event	6	0		
Median (in weeks)	105,3 [105,3; .]	-		
% of event-free patients+	49,59 [7,83; 91,35]	100,00 [100,00; 100,00]		
			-	-

N': Number of patients in the analysis
CI: Confidence Interval
HR: Hazard Ratio
*: p < 0,05

+ K-M estimate (%) of outcome-free patients, Greenwood formula is used for CIs of KM estimates

Applied model for HR: log(hazard ratio) = treatment + region + region * treatment
If it was not possible to fit the minimal model, the HR is not given.

SOCs/PTs are only displayed in this subgroup analysis, if the p-value for HR in the entire population is significant (p<0.05).

Analysis population: A2304 SAF subpopulation "ACTIVE MS WITHOUT RELAPSES"

Table 12.8.3: Time to First Serious Adverse Event by SOC and PT (SAF) by Region

There are no data meeting the display criteria for this table.

Table 12.8.4: Time to First Severe Adverse Event by SOC and PT (SAF) by Region

There are no data meeting the display criteria for this table.

Table 12.8.5: Time to First Adverse Event of Special Interest (SAF) by Region

	Treatment groups		Comparison	
	BAF312 (N=127)	**Placebo (N=61)**	**HR [95% CI]**	**p-value**
N'	127	61		
N' Region = Europe	106	52		
N' Region = Other	21	9		
Infections and infestations				
Interaction test:	p=0,810			
Region = Europe				
Number of patients with event	54	21		
Median (in weeks)	76,7 [60,3; .]	95,4 [63,0; .]		
% of event-free patients+	38,66 [26,85; 50,47]	43,81 [23,07; 64,55]		
			1,28 [0,77; 2,13]	0,332
Region = Other				
Number of patients with event	11	5		
Median (in weeks)	50,0 [16,7; .]	50,9 [25,0; .]		
% of event-free patients+	24,42 [0,00; 51,19]	33,86 [0,00; 69,46]		
			1,11 [0,39; 3,20]	0,845
Herpes simplex virus infections				
Interaction test:	p=0,995			
Region = Europe				
Number of patients with event	3	1		
Median (in weeks)	-	-		
% of event-free patients+	97,13 [93,93; 100,00]	98,08 [94,34; 100,00]		
			1,35 [0,14; 12,99]	0,798
Region = Other				
Number of patients with event	1	0		
Median (in weeks)	-	-		
% of event-free patients+	83,33 [53,51; 100,00]	100,00 [100,00; 100,00]		
			-	-
Varicella-zoster virus infections				
Interaction test:	p=0,999			
Region = Europe				
Number of patients with event	1	0		
Median (in weeks)	-	-		
% of event-free patients+	98,95 [96,90; 100,00]	100,00 [100,00; 100,00]		
			-	-

	Treatment groups		Comparison	
	BAF312 (N=127)	**Placebo (N=61)**	**HR [95% CI]**	**p-value**
Region = Other				
Number of patients with event	0	0		
Median (in weeks)	-	-		
% of event-free patients+	100,00 [100,00; 100,00]	100,00 [100,00; 100,00]		
			-	-
Lymphopenia				
Interaction test:	p=0,999			
Region = Europe				
Number of patients with event	2	0		
Median (in weeks)	-	-		
% of event-free patients+	98,01 [95,27; 100,00]	100,00 [100,00; 100,00]		
			-	-
Region = Other				
Number of patients with event	0	0		
Median (in weeks)	-	-		
% of event-free patients+	100,00 [100,00; 100,00]	100,00 [100,00; 100,00]		
			-	-
Macular edema				
Interaction test:	p=1,000			
Region = Europe				
Number of patients with event	2	1		
Median (in weeks)	-	-		
% of event-free patients+	97,98 [95,22; 100,00]	95,24 [86,13; 100,00]		
			0,84 [0,08; 9,38]	0,889
Region = Other				
Number of patients with event	0	0		
Median (in weeks)	-	-		
% of event-free patients+	100,00 [100,00; 100,00]	100,00 [100,00; 100,00]		
			-	-

	Treatment groups		Comparison	
	BAF312 (N=127)	**Placebo (N=61)**	**HR [95% CI]**	**p-value**
Abnormal hepatic enzymes				
Interaction test:	p=0,990			
Region = Europe				
Number of patients with event	17	4		
Median (in weeks)	-	-		
% of event-free patients+	82,69 [75,08; 90,31]	92,10 [84,66; 99,54]		
			2,07 [0,70; 6,16]	0,190
Region = Other				
Number of patients with event	2	0		
Median (in weeks)	-	-		
% of event-free patients+	90,23 [77,35; 100,00]	100,00 [100,00; 100,00]		
			-	-
Malignancies				
Interaction test:	p=1,000			
Region = Europe				
Number of patients with event	0	1		
Median (in weeks)	-	-		
% of event-free patients+	100,00 [100,00; 100,00]	94,12 [82,93; 100,00]		
			-	-
Region = Other				
Number of patients with event	0	0		
Median (in weeks)	-	-		
% of event-free patients+	100,00 [100,00; 100,00]	100,00 [100,00; 100,00]		
			-	-
Hypertension				
Interaction test:	p=0,989			
Region = Europe				
Number of patients with event	15	5		
Median (in weeks)	-	-		
% of event-free patients+	83,07 [74,03; 92,10]	90,30 [82,22; 98,38]		
			1,38 [0,50; 3,81]	0,535

	Treatment groups		Comparison	
	BAF312 (N=127)	**Placebo (N=61)**	**HR [95% CI]**	**p-value**
Region = Other				
Number of patients with event	2	0		
Median (in weeks)	-	-		
% of event-free patients+	70,83 [29,98; 100,00]	100,00 [100,00; 100,00]		
			-	-
Seizures				
Interaction test:	N.E.			
Region = Europe				
Number of patients with event	0	0		
Median (in weeks)	-	-		
% of event-free patients+	100,00 [100,00; 100,00]	100,00 [100,00; 100,00]		
			-	-
Region = Other				
Number of patients with event	0	0		
Median (in weeks)	-	-		
% of event-free patients+	100,00 [100,00; 100,00]	100,00 [100,00; 100,00]		
			-	-
Thromboembolic events				
Interaction test:	p=0,994			
Region = Europe				
Number of patients with event	3	1		
Median (in weeks)	-	-		
% of event-free patients+	97,11 [93,89; 100,00]	97,83 [93,61; 100,00]		
			1,30 [0,13; 12,63]	0,823
Region = Other				
Number of patients with event	2	0		
Median (in weeks)	-	-		
% of event-free patients+	70,59 [29,78; 100,00]	100,00 [100,00; 100,00]		
			-	-

	Treatment groups		Comparison	
	BAF312 (N=127)	**Placebo (N=61)**	**HR [95% CI]**	**p-value**
Respiratory disorders				
Interaction test:	p=0,387			
Region = Europe				
Number of patients with event	18	10		
Median (in weeks)	-	-		
% of event-free patients+	80,64 [72,42; 88,85]	68,81 [49,56; 88,06]		
			0,77 [0,36; 1,68]	0,518
Region = Other				
Number of patients with event	4	1		
Median (in weeks)	-	-		
% of event-free patients+	50,68 [6,86; 94,50]	87,50 [64,58; 100,00]		
			2,17 [0,24; 19,48]	0,490
Peripheral edema/swelling				
Interaction test:	p=0,994			
Region = Europe				
Number of patients with event	6	0		
Median (in weeks)	-	-		
% of event-free patients+	91,42 [83,12; 99,72]	100,00 [100,00; 100,00]		
			-	-
Region = Other				
Number of patients with event	0	1		
Median (in weeks)	-	-		
% of event-free patients+	100,00 [100,00; 100,00]	87,50 [64,58; 100,00]		
			-	-

N': Number of patients in the analysis
CI: Confidence Interval
HR: Hazard Ratio
N.E.: not estimable
*: p < 0,05

+ K-M estimate (%) of outcome-free patients, Greenwood formula is used for CIs of KM estimates

Applied model for HR: log(hazard ratio) = treatment + region + region * treatment
If it was not possible to fit the minimal model, the HR is not given.

Analysis population: A2304 SAF subpopulation "ACTIVE MS WITHOUT RELAPSES"

	Treatment groups		Comparison	
	BAF312 (N=127)	**Placebo (N=61)**	**HR [95% CI]**	**p-value**
N'	127	61		
N' Region = Europe	106	52		
N' Region = Other	21	9		
Asthma/bronchospasm				
Interaction test:	p=0,999			
Region = Europe				
Number of patients with event	1	0		
Median (in weeks)	-	-		
% of event-free patients+	99,05 [97,19; 100,00]	100,00 [100,00; 100,00]		
			-	-
Region = Other				
Number of patients with event	0	0		
Median (in weeks)	-	-		
% of event-free patients+	100,00 [100,00; 100,00]	100,00 [100,00; 100,00]		
			-	-
Pregnancy and neonatal topics				
Interaction test:	p=0,999			
Region = Europe				
Number of patients with event	1	0		
Median (in weeks)	-	-		
% of event-free patients+	99,06 [97,22; 100,00]	100,00 [100,00; 100,00]		
			-	-
Region = Other				
Number of patients with event	0	0		
Median (in weeks)	-	-		
% of event-free patients+	100,00 [100,00; 100,00]	100,00 [100,00; 100,00]		
			-	-

	Treatment groups		Comparison	
	BAF312 (N=127)	**Placebo (N=61)**	**HR [95% CI]**	**p-value**
Bradyarrhythmias and bradycardia				
Interaction test:	p=0,993			
Region = Europe				
Number of patients with event	9	1		
Median (in weeks)	-	-		
% of event-free patients+	91,50 [86,19; 96,81]	98,08 [94,34; 100,00]		
			4,45 [0,56; 35,15]	0,157
Region = Other				
Number of patients with event	2	0		
Median (in weeks)	-	-		
% of event-free patients+	90,48 [77,92; 100,00]	100,00 [100,00; 100,00]		
			-	-

N': Number of patients in the analysis
CI: Confidence Interval
HR: Hazard Ratio
*: p < 0,05

+ K-M estimate (%) of outcome-free patients, Greenwood formula is used for CIs of KM estimates

Applied model for HR: log(hazard ratio) = treatment + region + region * treatment
If it was not possible to fit the minimal model, the HR is not given.

Analysis population: A2304 SAF subpopulation "ACTIVE MS WITHOUT RELAPSES"

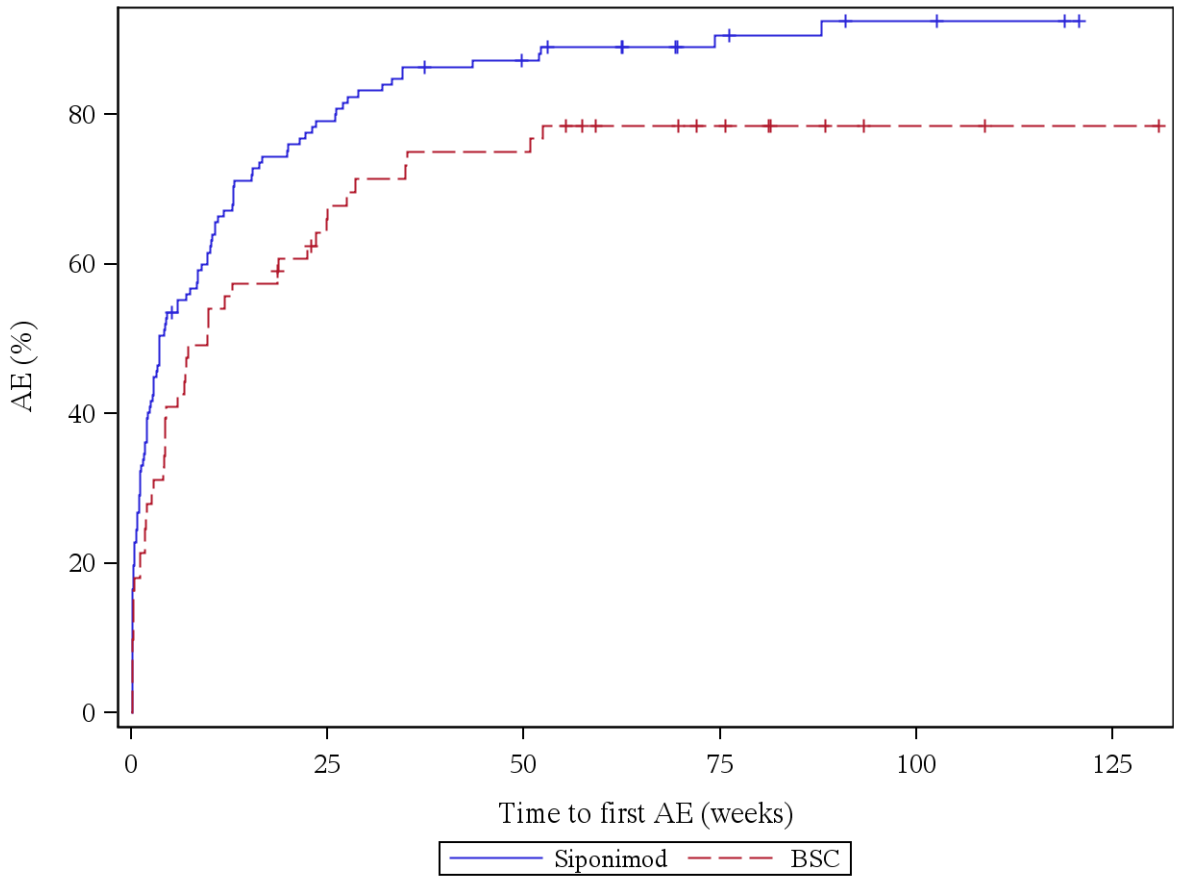
Safety Figures

12. Adverse Events: Time-to-Event Analysis

12.1 Entire Population

12.1.1: Time to First Adverse Event (SAF)

Figure 12.1.1.1: Any AE

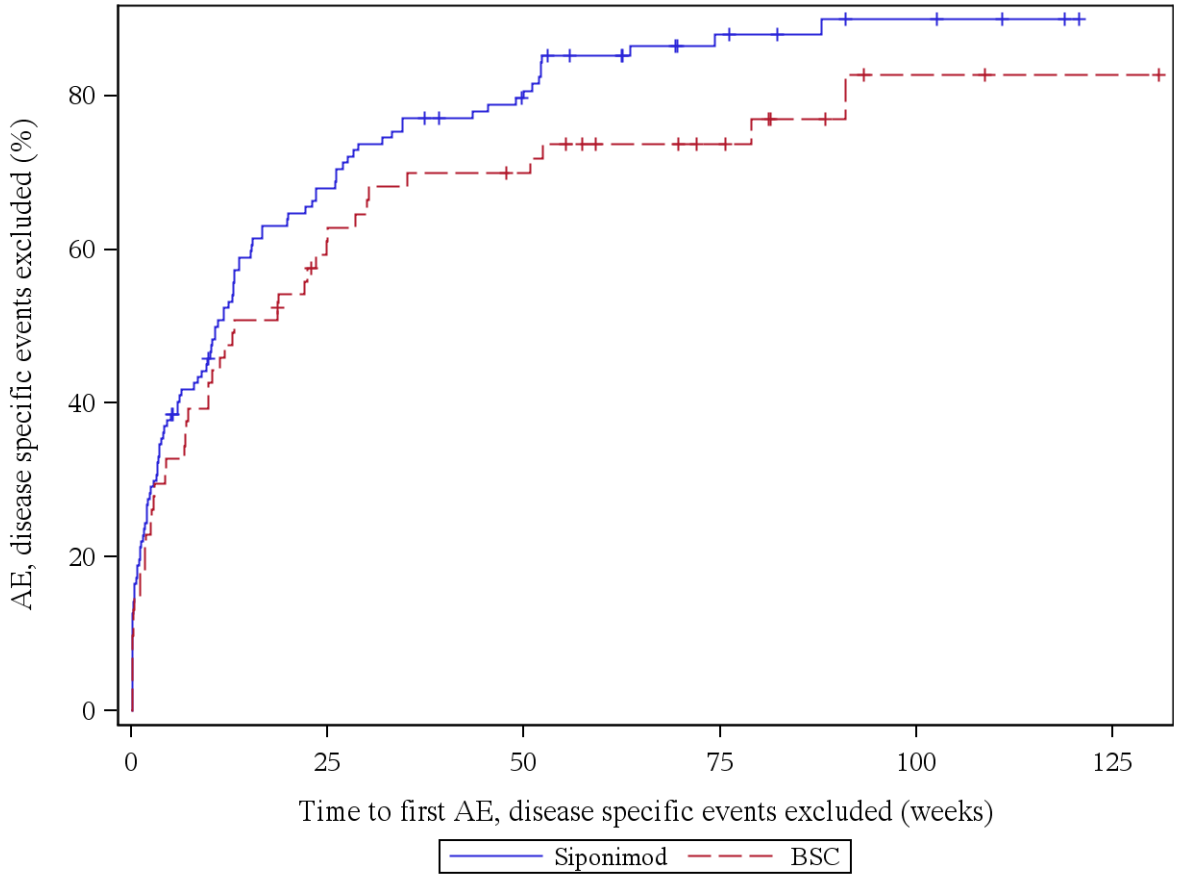


Patients at risk (Siponimod/BSC): Week 0: 127/61, Week 4: 63/41, Week 12: 41/27, Week 24: 26/20, Week 36: 17/14, Week 48: 15/14, Week 60: 11/9, Week 72: 7/7, Week 84: 5/4, Week 96: 3/2, Week 108: 2/2, Week 120: 1/1, Week 132: 0/0

Log rank test: p-value = 0,021 *
*: p < 0,05

Analysis population: A2304 SAF subpopulation "ACTIVE MS WITHOUT RELAPSES"

Figure 12.1.1.2: Any AE, disease specific events excluded

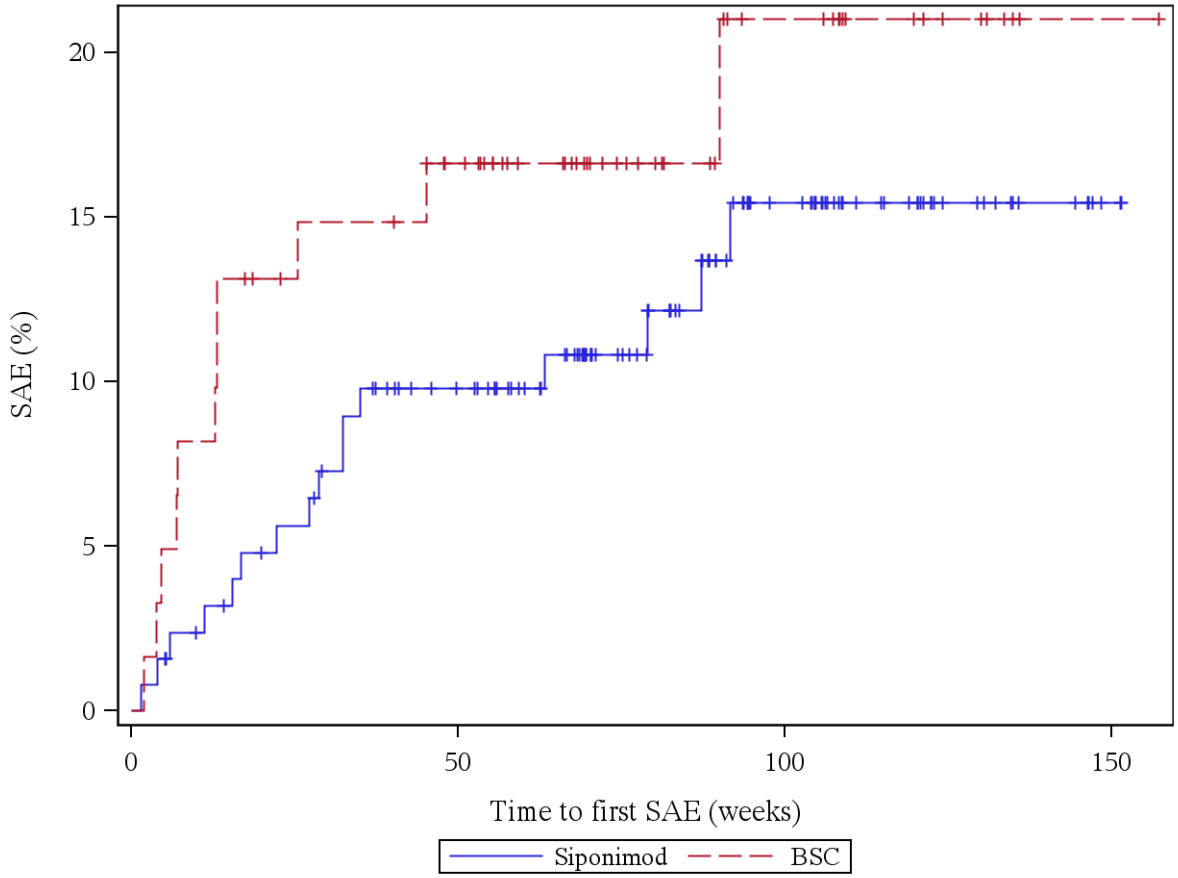


Patients at risk (Siponimod/BSC): Week 0: 127/61, Week 4: 81/43, Week 12: 58/32, Week 24: 39/23, Week 36: 28/17, Week 48: 24/16, Week 60: 14/11, Week 72: 9/9, Week 84: 6/5, Week 96: 4/2, Week 108: 3/2, Week 120: 1/1, Week 132: 0/0

Log rank test: p-value = 0,117
*: p < 0,05

Analysis population: A2304 SAF subpopulation "ACTIVE MS WITHOUT RELAPSES"

Figure 12.1.1.3: Any SAE

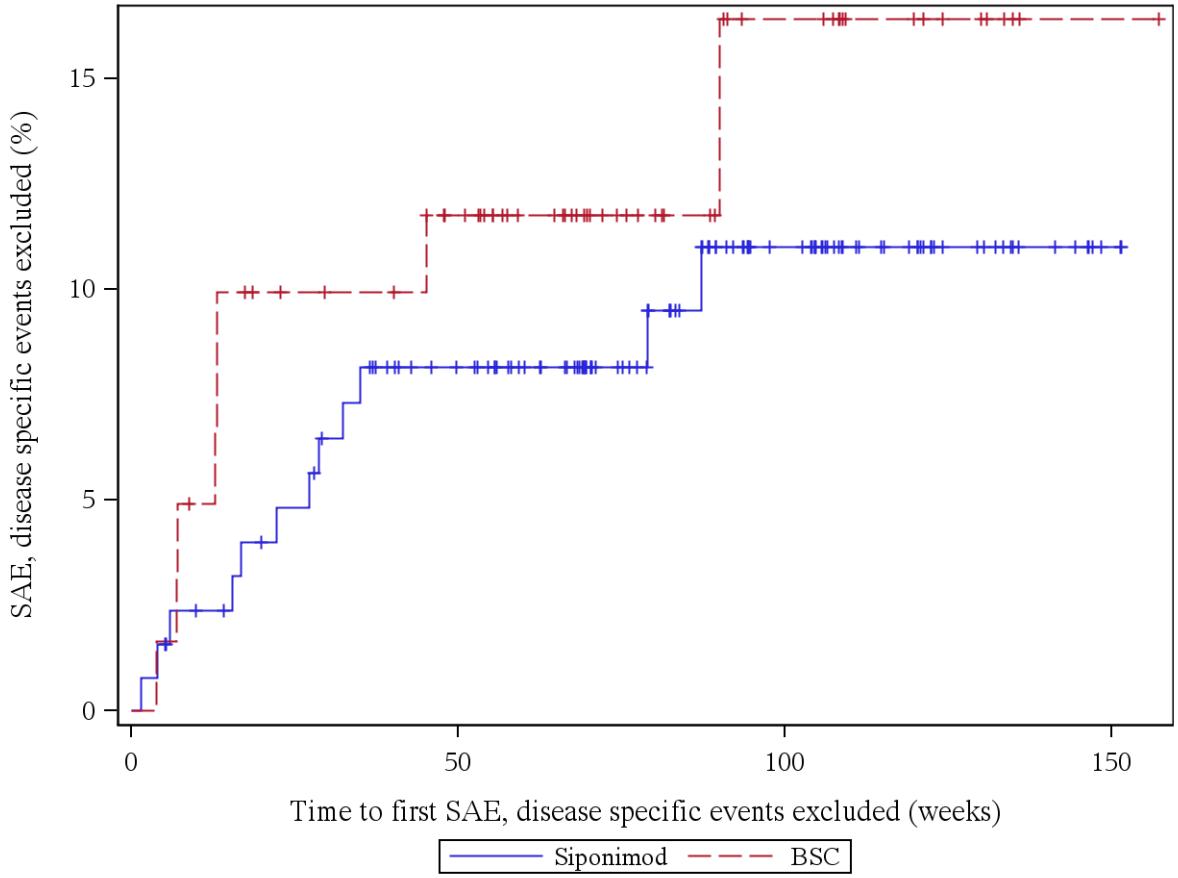


Patients at risk (Siponimod/BSC): Week 0: 127/61, Week 4: 125/59, Week 12: 120/56, Week 24: 115/50, Week 36: 108/49, Week 48: 101/44, Week 60: 91/35, Week 72: 71/27, Week 84: 58/21, Week 96: 40/15, Week 108: 28/13, Week 120: 21/8, Week 132: 11/4, Week 144: 7/1, Week 156: 0/1

Log rank test: p-value = 0,249
*: p < 0,05

Analysis population: A2304 SAF subpopulation "ACTIVE MS WITHOUT RELAPSES"

Figure 12.1.1.4: Any SAE, disease specific events excluded

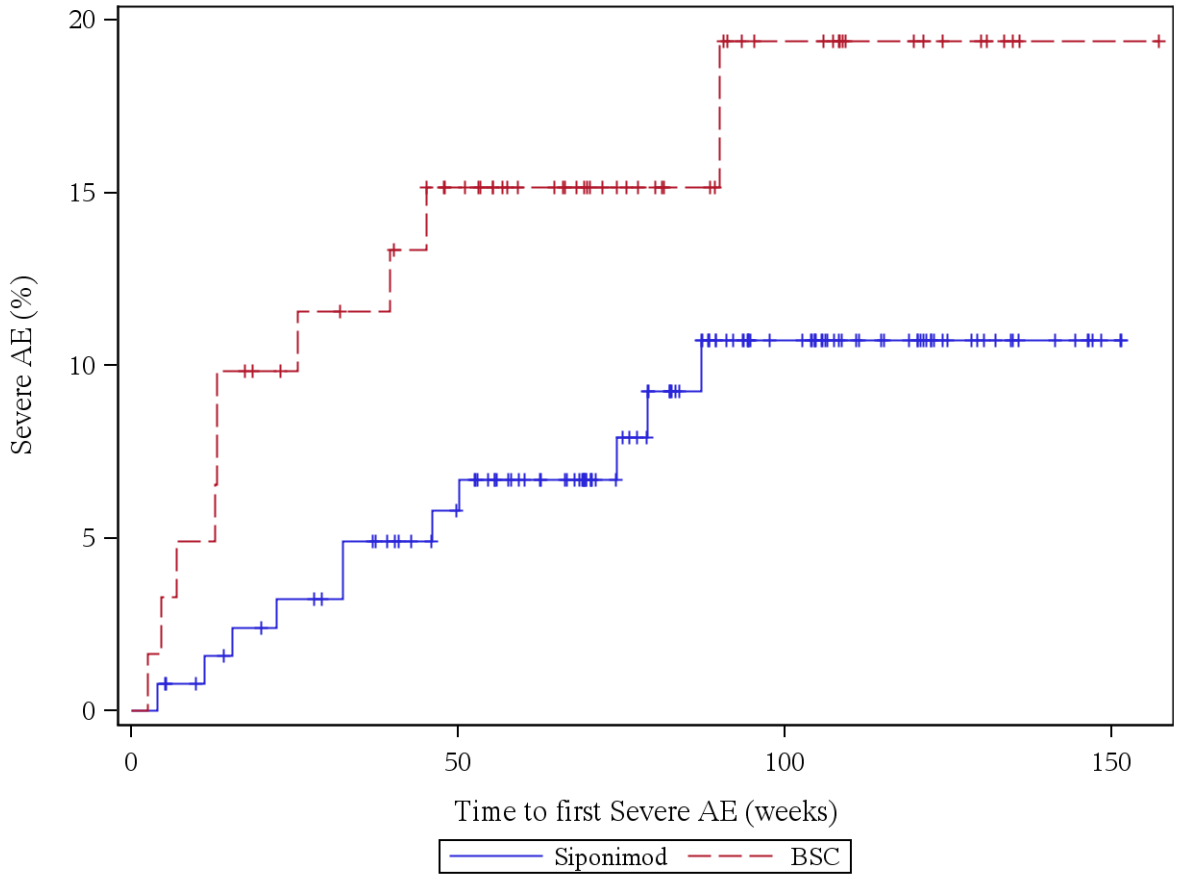


Patients at risk (Siponimod/BSC): Week 0: 127/61, Week 4: 125/60, Week 12: 121/57, Week 24: 116/51, Week 36: 110/50, Week 48: 102/45, Week 60: 92/36, Week 72: 73/27, Week 84: 60/21, Week 96: 43/15, Week 108: 31/13, Week 120: 23/8, Week 132: 13/4, Week 144: 7/1, Week 156: 0/1

Log rank test: p-value = 0,379
*: p < 0,05

Analysis population: A2304 SAF subpopulation "ACTIVE MS WITHOUT RELAPSES"

Figure 12.1.1.5: Any severe AE

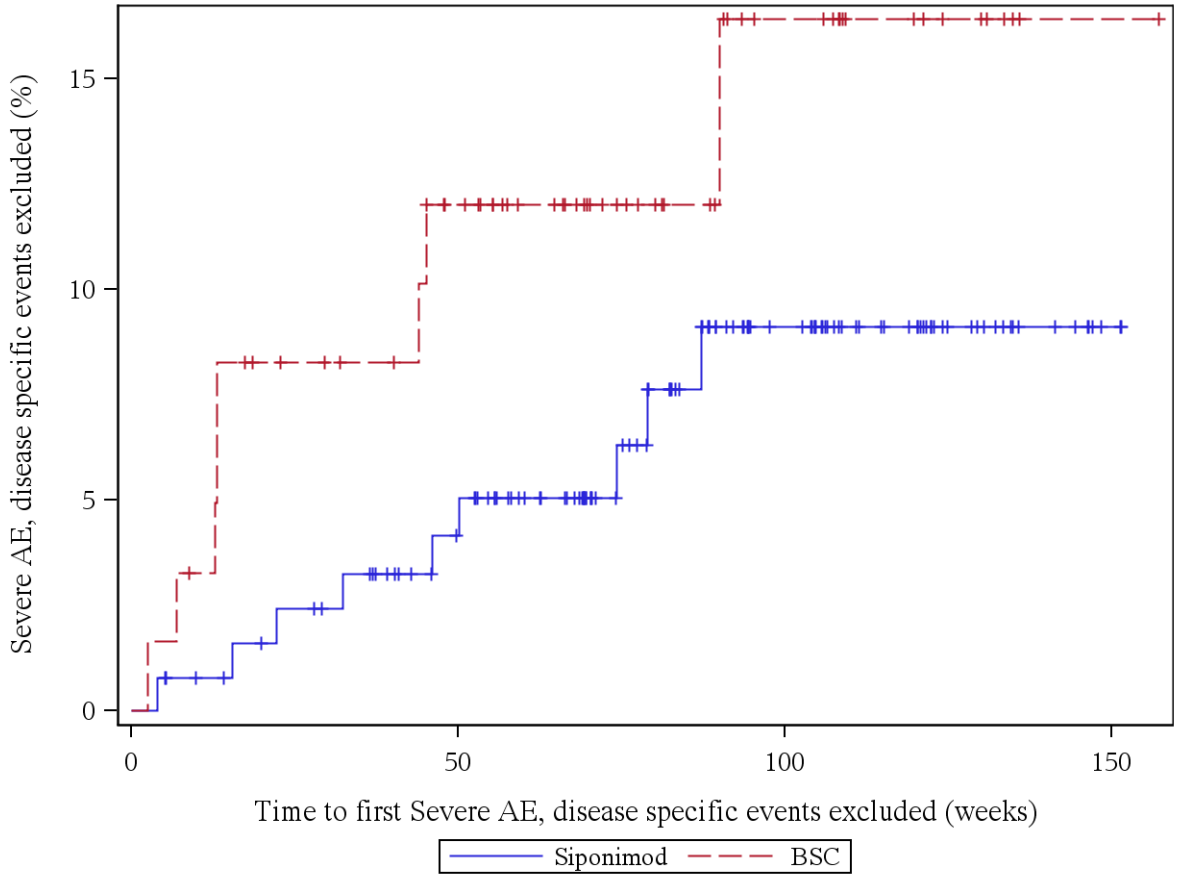


Patients at risk (Siponimod/BSC): Week 0: 127/61, Week 4: 126/60, Week 12: 122/58, Week 24: 118/52, Week 36: 114/50, Week 48: 106/44, Week 60: 94/36, Week 72: 76/28, Week 84: 61/22, Week 96: 44/15, Week 108: 32/13, Week 120: 25/8, Week 132: 12/4, Week 144: 7/1, Week 156: 0/1

Log rank test: p-value = 0,086
*: p < 0,05

Analysis population: A2304 SAF subpopulation "ACTIVE MS WITHOUT RELAPSES"

Figure 12.1.1.6: Any severe AE, disease specific events excluded

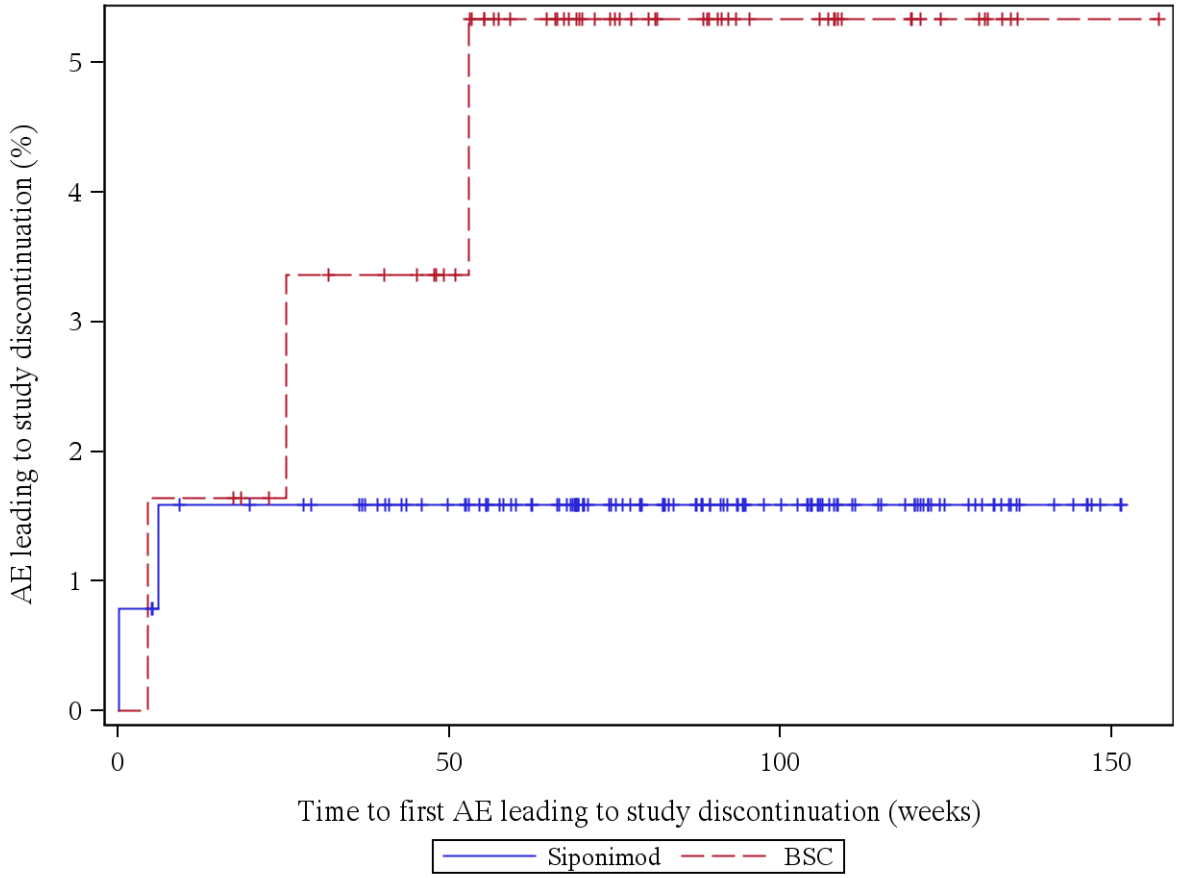


Patients at risk (Siponimod/BSC): Week 0: 127/61, Week 4: 126/60, Week 12: 123/58, Week 24: 119/52, Week 36: 116/50, Week 48: 107/44, Week 60: 95/36, Week 72: 77/28, Week 84: 62/22, Week 96: 45/15, Week 108: 33/13, Week 120: 26/8, Week 132: 13/4, Week 144: 7/1, Week 156: 0/1

Log rank test: p-value = 0,126
*: p < 0,05

Analysis population: A2304 SAF subpopulation "ACTIVE MS WITHOUT RELAPSES"

Figure 12.1.1.7: Any AE leading to study discontinuation

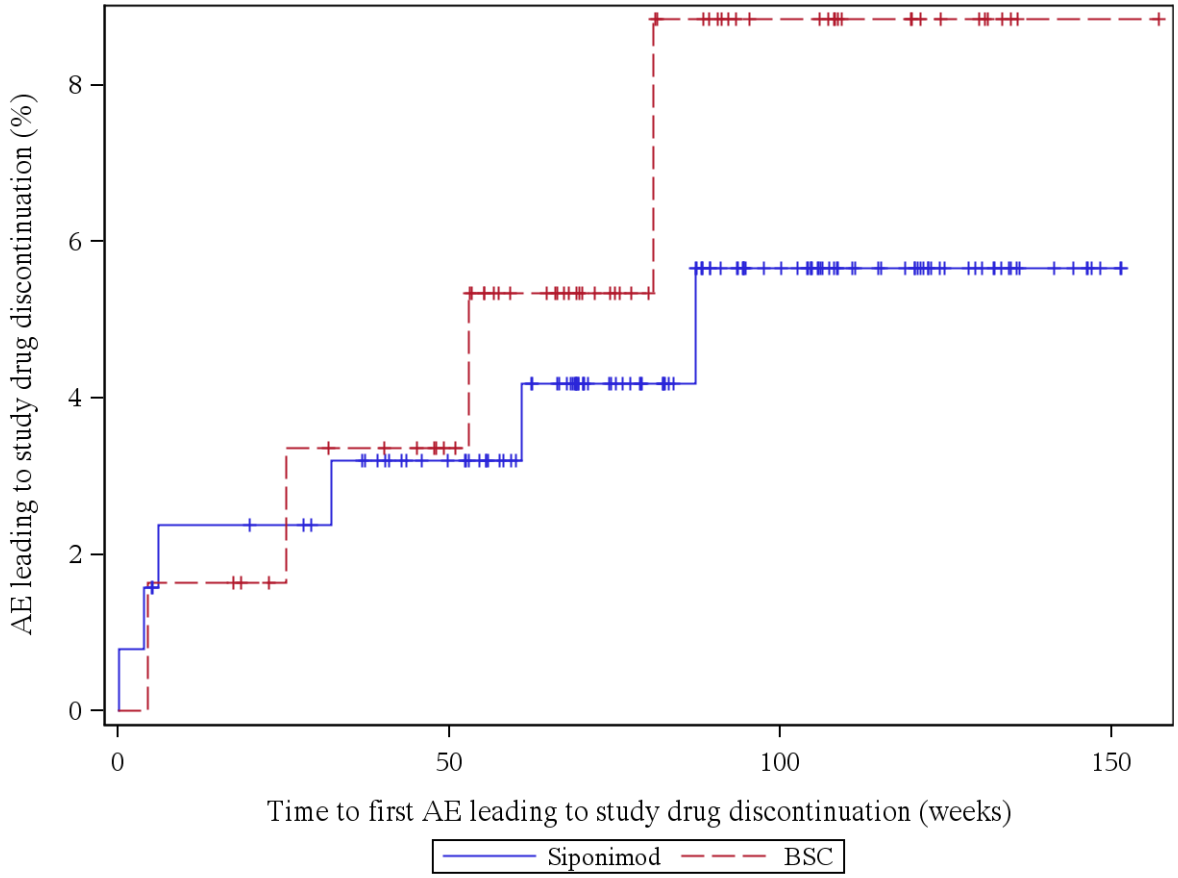


Patients at risk (Siponimod/BSC): Week 0: 127/61, Week 4: 126/61, Week 12: 122/60, Week 24: 121/57, Week 36: 119/55, Week 48: 110/51, Week 60: 99/41, Week 72: 80/32, Week 84: 66/25, Week 96: 49/17, Week 108: 36/15, Week 120: 28/9, Week 132: 15/4, Week 144: 7/1, Week 156: 0/1

Log rank test: p-value = 0,184
*: p < 0,05

Analysis population: A2304 SAF subpopulation "ACTIVE MS WITHOUT RELAPSES"

Figure 12.1.1.8: Any AE leading to study drug discontinuation



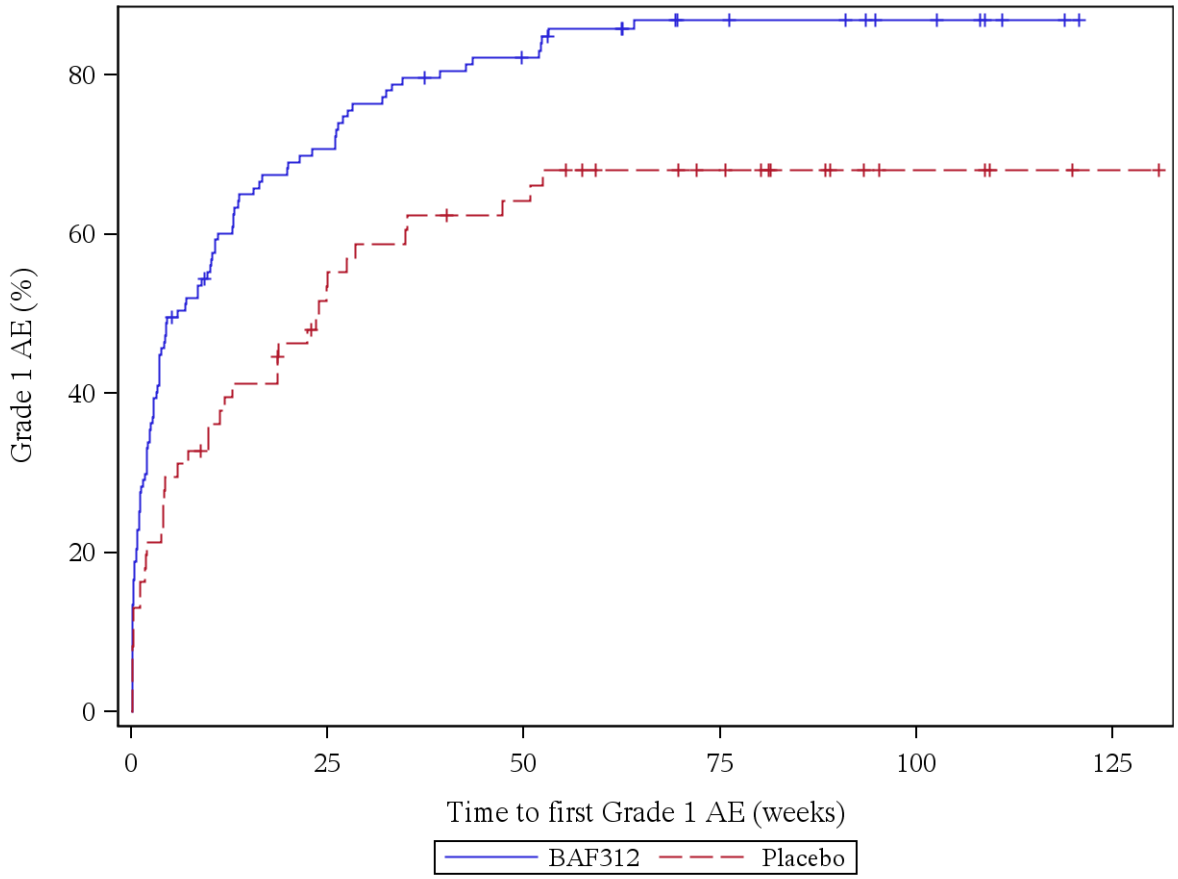
Patients at risk (Siponimod/BSC): Week 0: 127/61, Week 4: 125/61, Week 12: 122/60, Week 24: 121/57, Week 36: 118/55, Week 48: 110/51, Week 60: 99/41, Week 72: 79/32, Week 84: 65/24, Week 96: 49/17, Week 108: 36/15, Week 120: 28/9, Week 132: 15/4, Week 144: 7/1, Week 156: 0/1

Log rank test: p-value = 0,536
*: p < 0,05

Analysis population: A2304 SAF subpopulation "ACTIVE MS WITHOUT RELAPSES"

12.1.2: Time to First Adverse Event by Severity (SAF)

Figure 12.1.2.1: Grade 1

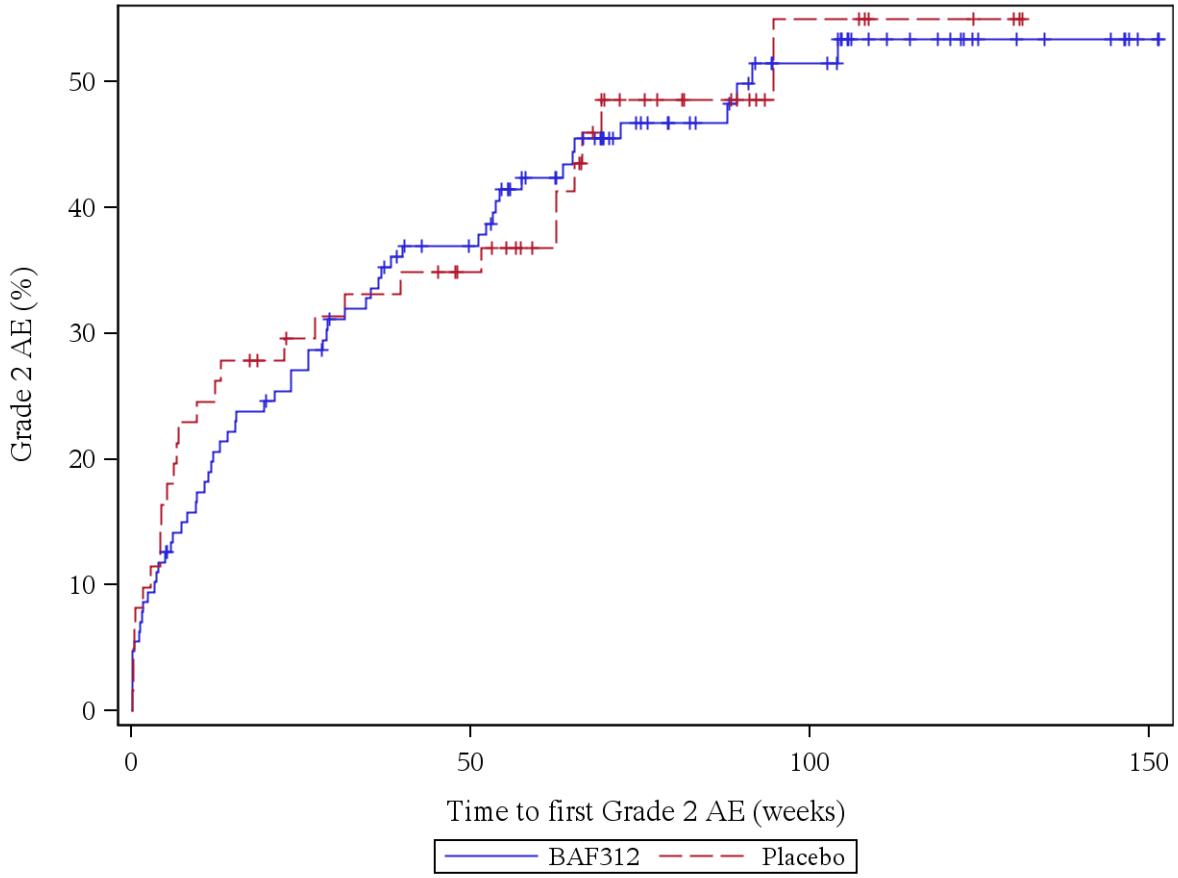


Patients at risk (BAF312/Placebo): Week 0: 127/61, Week 4: 69/45, Week 12: 49/36, Week 24: 36/27, Week 36: 25/21, Week 48: 21/19, Week 60: 15/14, Week 72: 10/12, Week 84: 9/8, Week 96: 6/4, Week 108: 5/4, Week 120: 1/1, Week 132: 0/0

Log rank test: p-value = 0,002 *
*: p < 0,05

Analysis population: A2304 SAF subpopulation "ACTIVE MS WITHOUT RELAPSES"

Figure 12.1.2.2: Grade 2

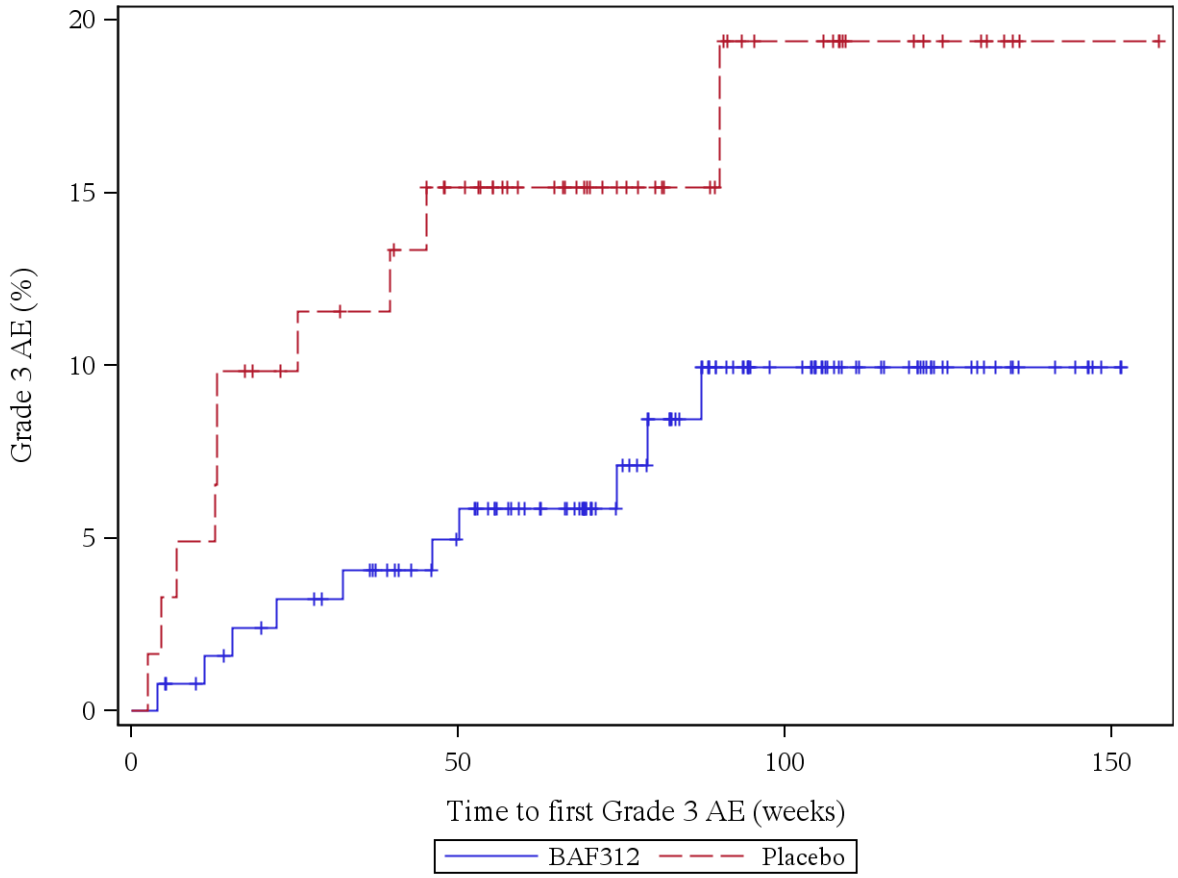


Patients at risk (BAF312/Placebo): Week 0: 127/61, Week 4: 112/54, Week 12: 99/46, Week 24: 90/40, Week 36: 80/38, Week 48: 72/34, Week 60: 58/28, Week 72: 43/17, Week 84: 35/13, Week 96: 27/7, Week 108: 18/6, Week 120: 14/4, Week 132: 8/0, Week 144: 7/0, Week 156: 0/0

Log rank test: p-value = 0,927
*: p < 0,05

Analysis population: A2304 SAF subpopulation "ACTIVE MS WITHOUT RELAPSES"

Figure 12.1.2.3: Grade 3

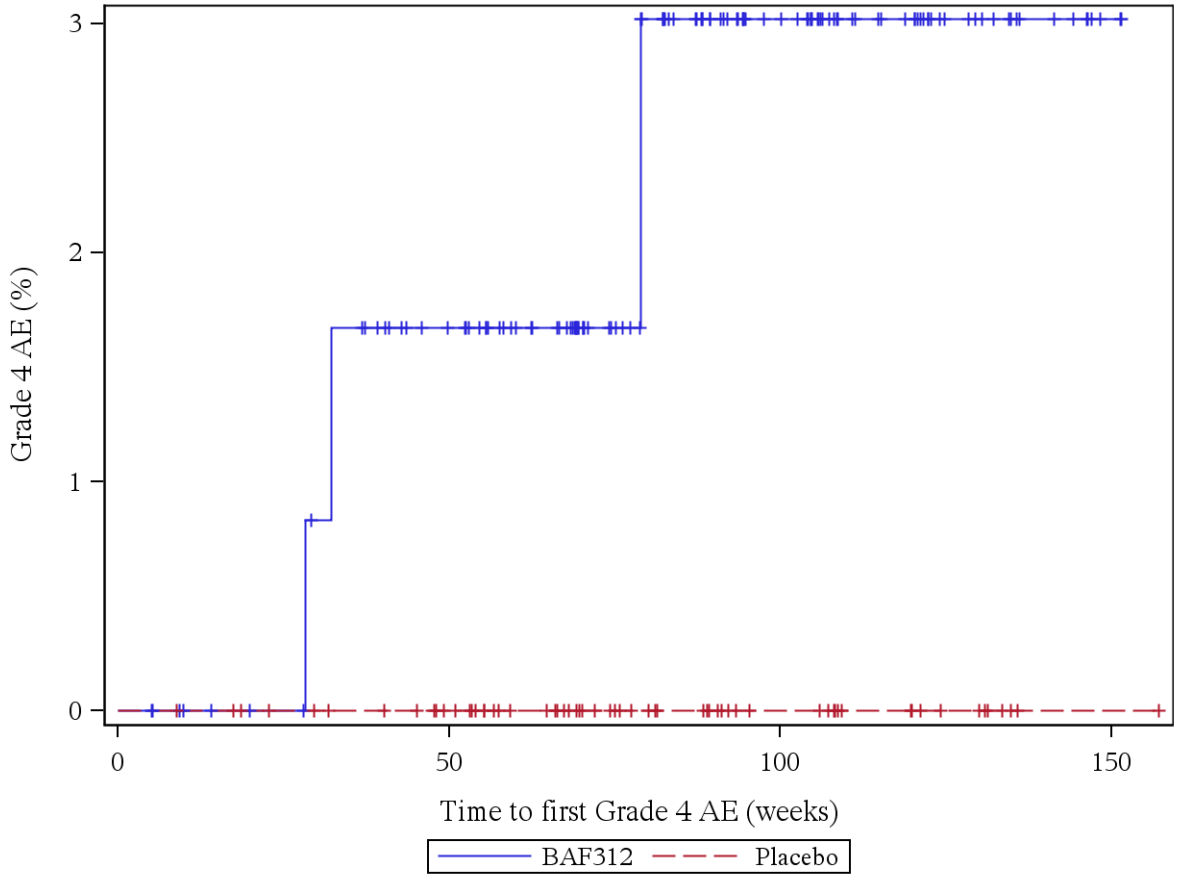


Patients at risk (BAF312/Placebo): Week 0: 127/61, Week 4: 126/60, Week 12: 122/58, Week 24: 118/52, Week 36: 115/50, Week 48: 106/44, Week 60: 94/36, Week 72: 76/28, Week 84: 61/22, Week 96: 44/15, Week 108: 32/13, Week 120: 25/8, Week 132: 12/4, Week 144: 7/1, Week 156: 0/1

Log rank test: p-value = 0,057
*: p < 0,05

Analysis population: A2304 SAF subpopulation "ACTIVE MS WITHOUT RELAPSES"

Figure 12.1.2.4: Grade 4

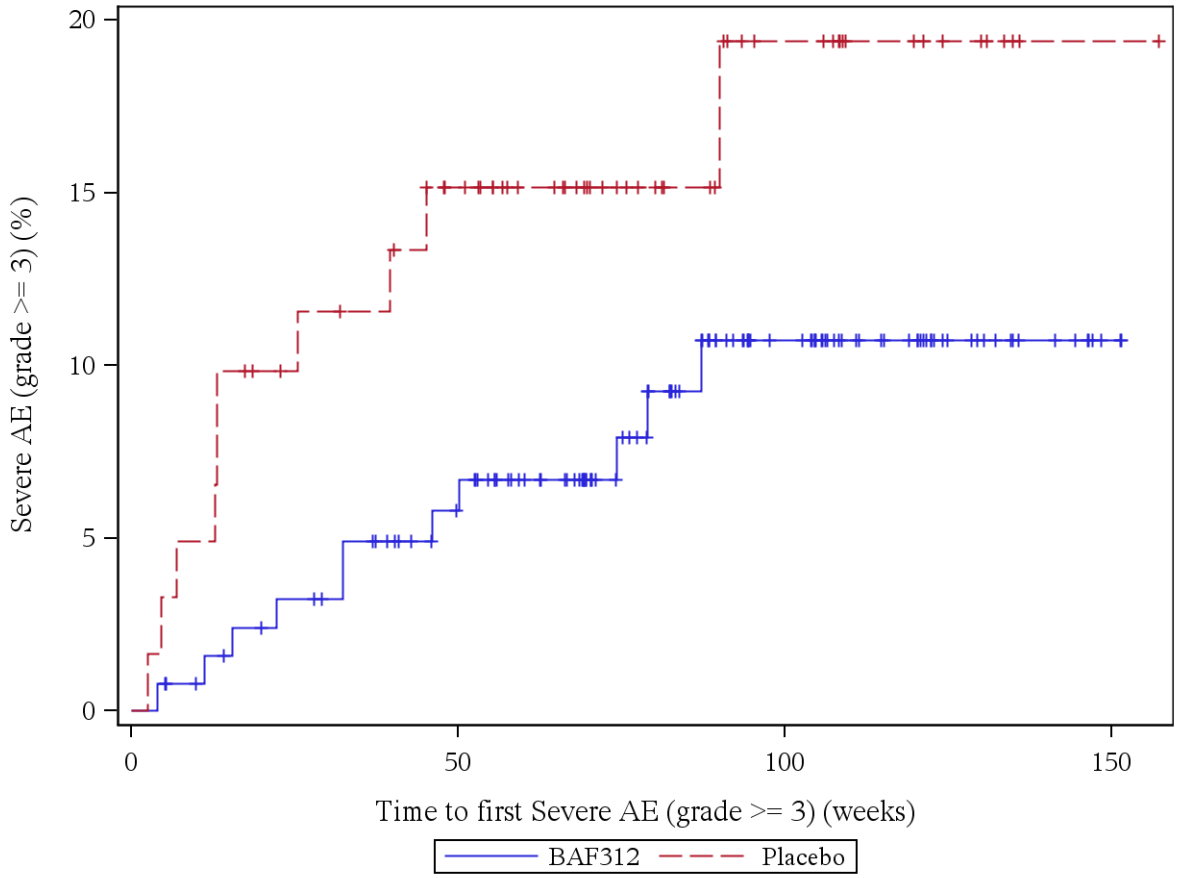


Patients at risk (BAF312/Placebo): Week 0: 127/61, Week 4: 127/61, Week 12: 123/60, Week 24: 121/57, Week 36: 117/55, Week 48: 109/51, Week 60: 98/41, Week 72: 79/32, Week 84: 64/25, Week 96: 47/17, Week 108: 34/15, Week 120: 26/9, Week 132: 13/4, Week 144: 7/1, Week 156: 0/1

Log rank test: p-value = -
*: p < 0,05

Analysis population: A2304 SAF subpopulation "ACTIVE MS WITHOUT RELAPSES"

Figure 12.1.2.5: Severe (Grade ≥ 3)

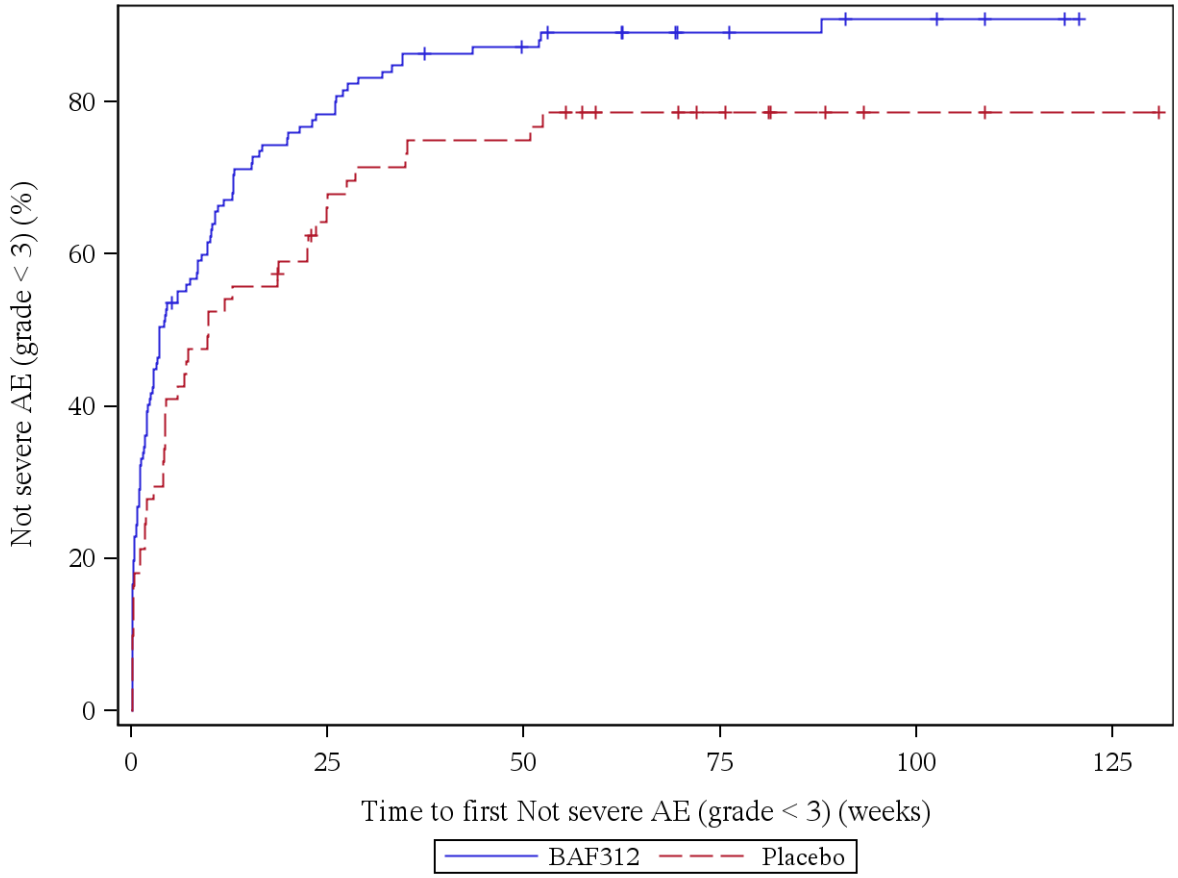


Patients at risk (BAF312/Placebo): Week 0: 127/61, Week 4: 126/60, Week 12: 122/58, Week 24: 118/52, Week 36: 114/50, Week 48: 106/44, Week 60: 94/36, Week 72: 76/28, Week 84: 61/22, Week 96: 44/15, Week 108: 32/13, Week 120: 25/8, Week 132: 12/4, Week 144: 7/1, Week 156: 0/1

Log rank test: p-value = 0,086
*: p < 0,05

Analysis population: A2304 SAF subpopulation "ACTIVE MS WITHOUT RELAPSES"

Figure 12.1.2.6: Not severe (Grade < 3)



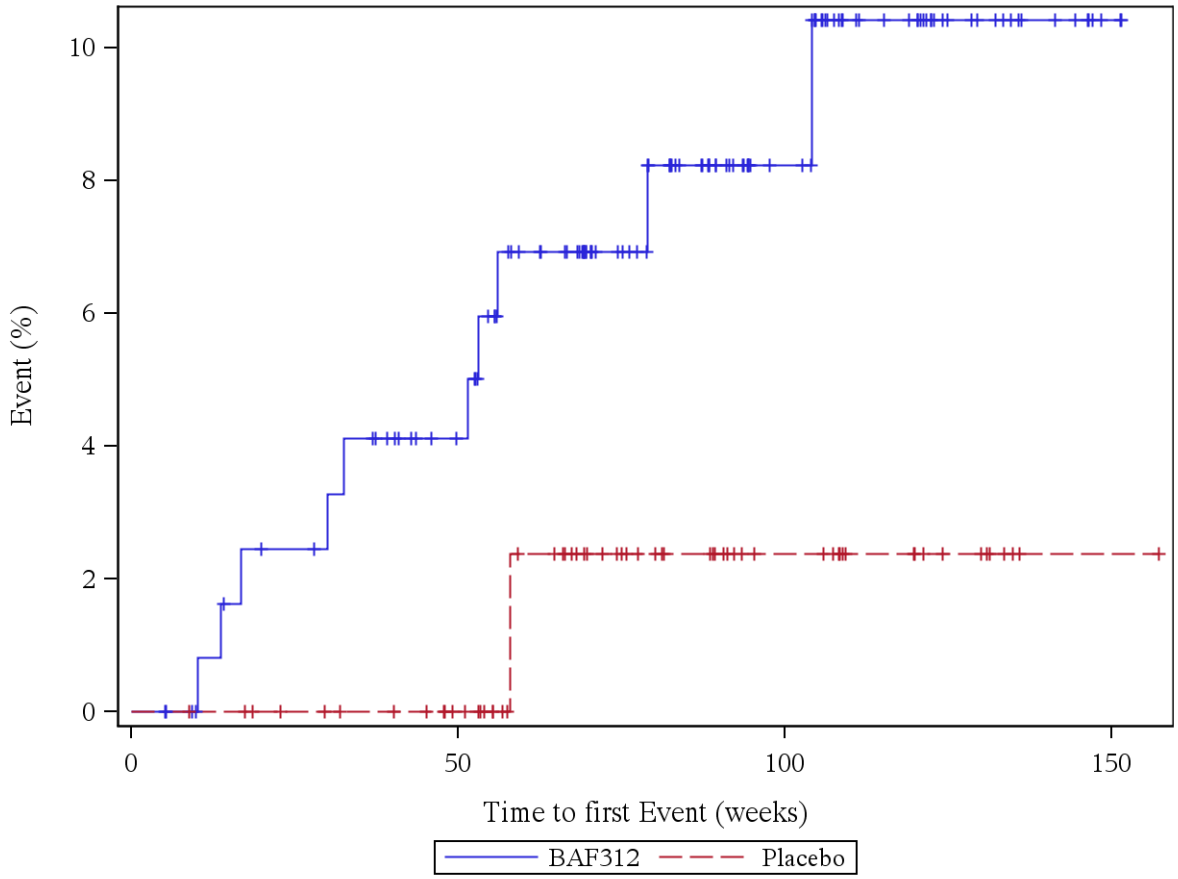
Patients at risk (BAF312/Placebo): Week 0: 127/61, Week 4: 63/41, Week 12: 41/28, Week 24: 27/20, Week 36: 17/14, Week 48: 15/14, Week 60: 11/9, Week 72: 7/7, Week 84: 6/4, Week 96: 4/2, Week 108: 3/2, Week 120: 1/1, Week 132: 0/0

Log rank test: p-value = 0,022 *
*: p < 0,05

Analysis population: A2304 SAF subpopulation "ACTIVE MS WITHOUT RELAPSES"

12.1.3: Time to First Adverse Event by SOC and PT (SAF)

Figure 12.1.3.1: BLOOD AND LYMPHATIC SYSTEM DISORDERS (SOC)

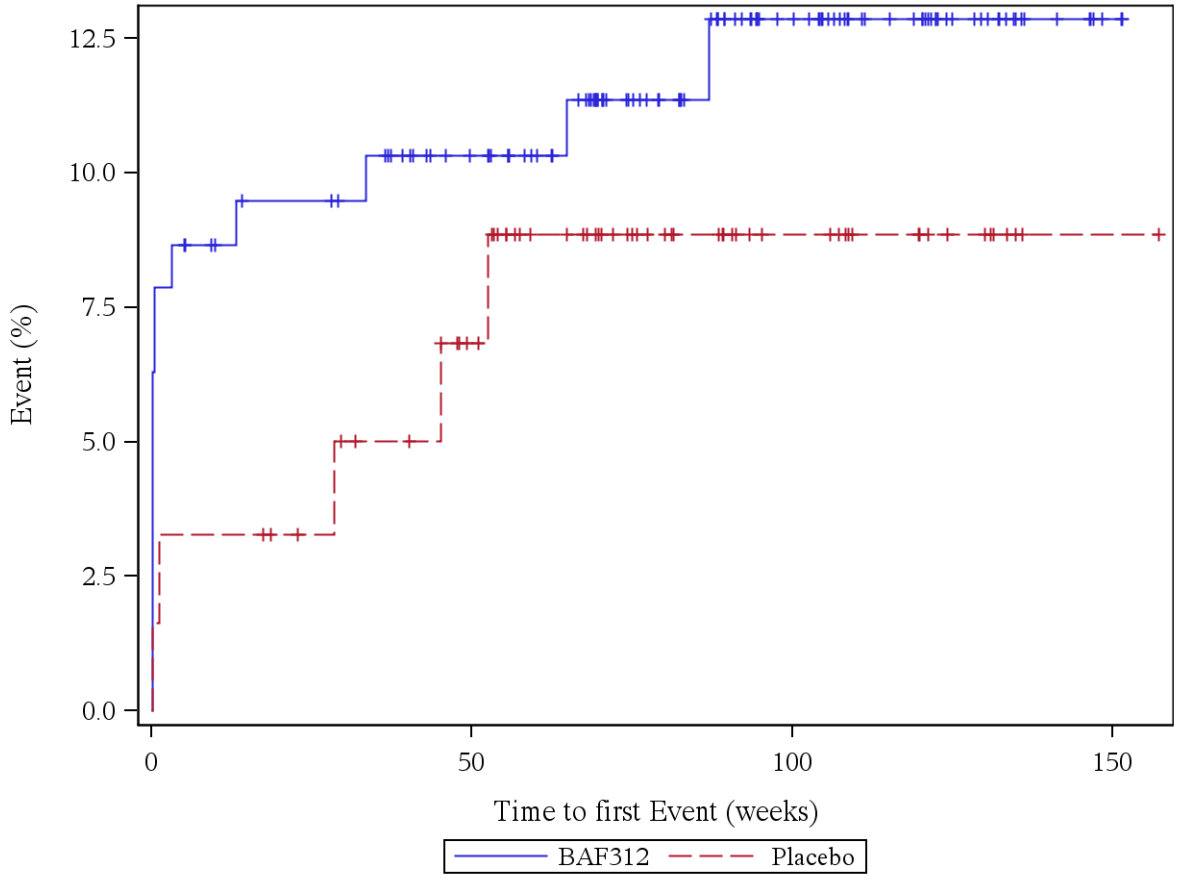


Patients at risk (BAF312/Placebo): Week 0: 127/61, Week 4: 127/61, Week 12: 122/60, Week 24: 118/57, Week 36: 115/55, Week 48: 107/51, Week 60: 93/40, Week 72: 76/32, Week 84: 62/25, Week 96: 45/17, Week 108: 32/15, Week 120: 25/9, Week 132: 13/4, Week 144: 7/1, Week 156: 0/1

Log rank test: p-value = 0,109
*: p < 0,05

Analysis population: A2304 SAF subpopulation "ACTIVE MS WITHOUT RELAPSES"

Figure 12.1.3.2: CARDIAC DISORDERS (SOC)

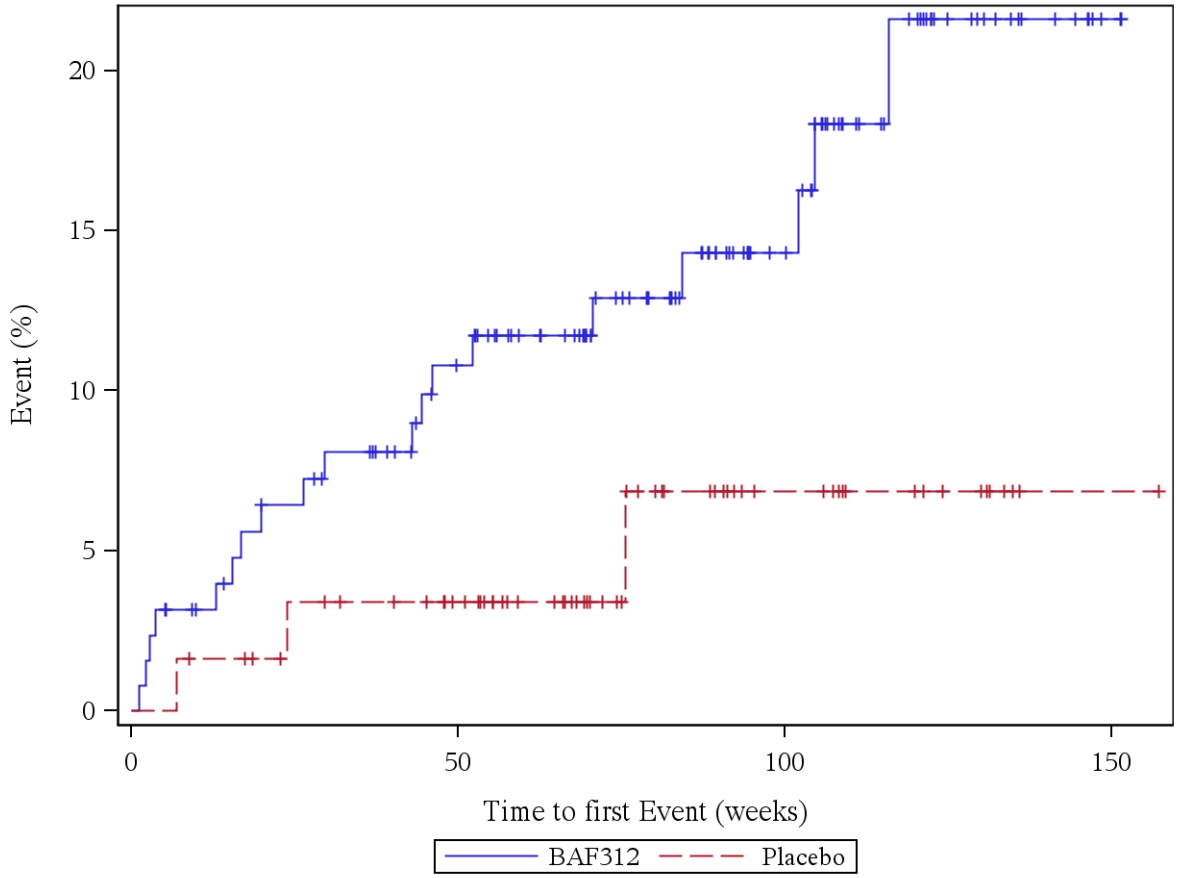


Patients at risk (BAF312/Placebo): Week 0: 127/61, Week 4: 116/59, Week 12: 112/59, Week 24: 110/56, Week 36: 107/53, Week 48: 98/48, Week 60: 89/37, Week 72: 71/30, Week 84: 59/23, Week 96: 44/16, Week 108: 34/14, Week 120: 27/9, Week 132: 14/4, Week 144: 6/1, Week 156: 0/1

Log rank test: p-value = 0,464
*: p < 0,05

Analysis population: A2304 SAF subpopulation "ACTIVE MS WITHOUT RELAPSES"

Figure 12.1.3.3: EYE DISORDERS (SOC)

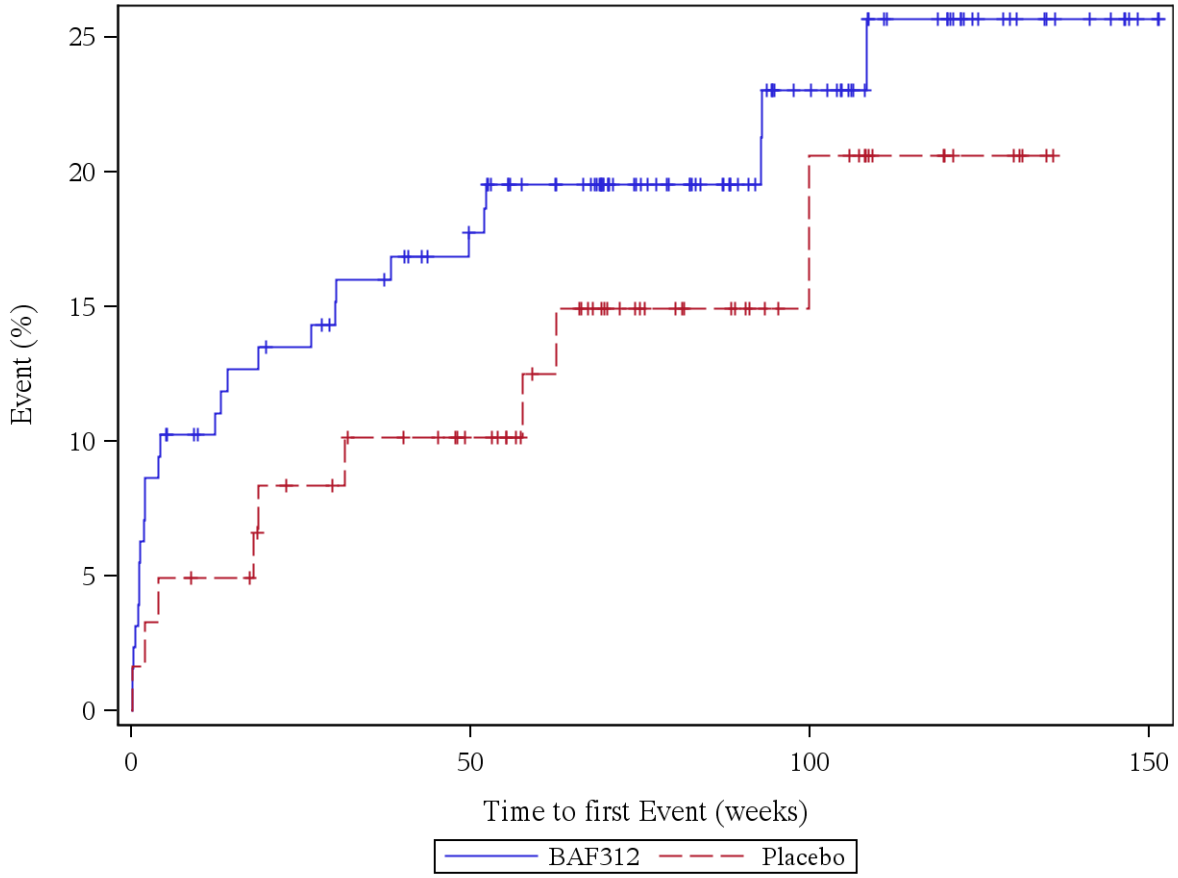


Patients at risk (BAF312/Placebo): Week 0: 127/61, Week 4: 123/61, Week 12: 119/59, Week 24: 113/55, Week 36: 109/53, Week 48: 98/49, Week 60: 87/39, Week 72: 73/30, Week 84: 62/22, Week 96: 46/15, Week 108: 32/13, Week 120: 23/9, Week 132: 12/4, Week 144: 7/1, Week 156: 0/1

Log rank test: p-value = 0,069
*: p < 0,05

Analysis population: A2304 SAF subpopulation "ACTIVE MS WITHOUT RELAPSES"

Figure 12.1.3.4: GASTROINTESTINAL DISORDERS (SOC)

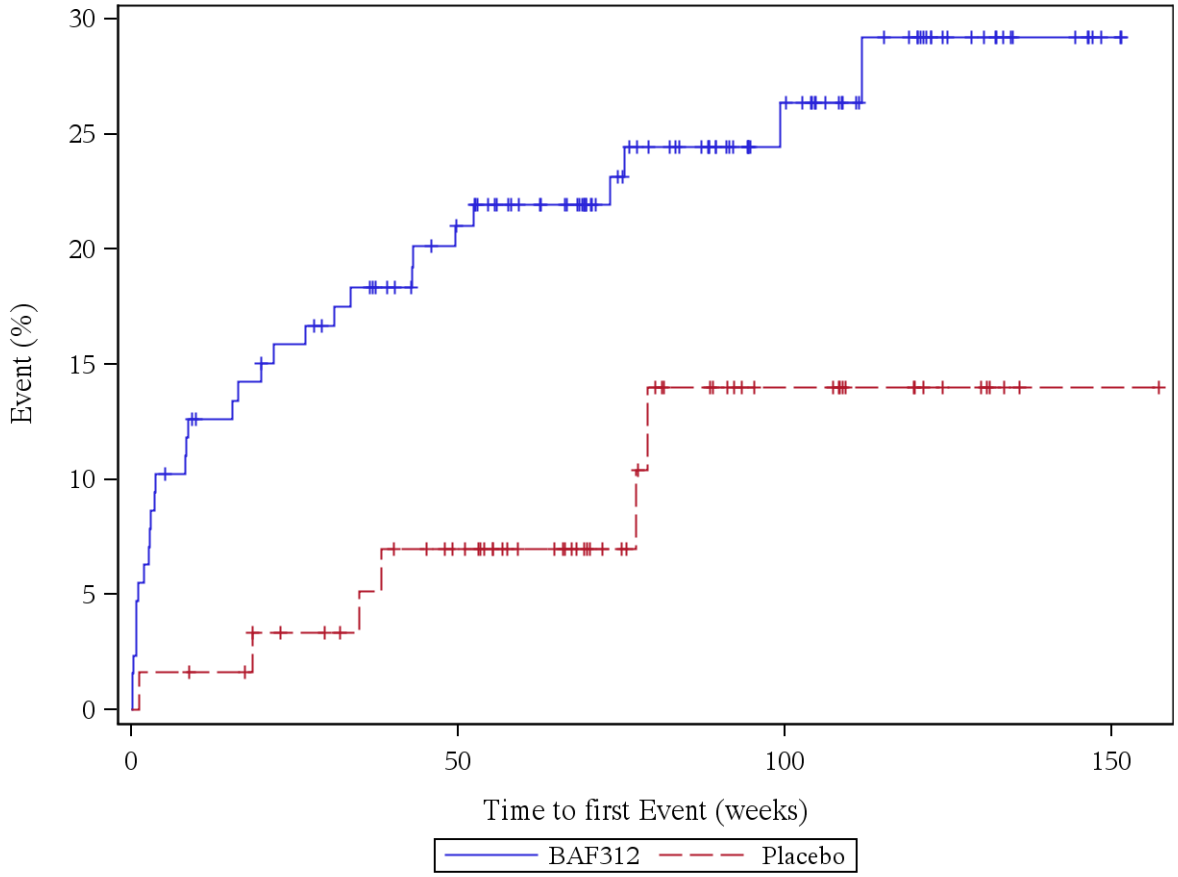


Patients at risk (BAF312/Placebo): Week 0: 127/61, Week 4: 115/58, Week 12: 110/57, Week 24: 105/52, Week 36: 100/49, Week 48: 94/45, Week 60: 83/36, Week 72: 66/27, Week 84: 54/21, Week 96: 39/15, Week 108: 30/12, Week 120: 23/6, Week 132: 11/2, Week 144: 7/0, Week 156: 0/0

Log rank test: p-value = 0,338
*: p < 0,05

Analysis population: A2304 SAF subpopulation "ACTIVE MS WITHOUT RELAPSES"

Figure 12.1.3.5: GENERAL DISORDERS AND ADMINISTRATION SITE CONDITIONS (SOC)

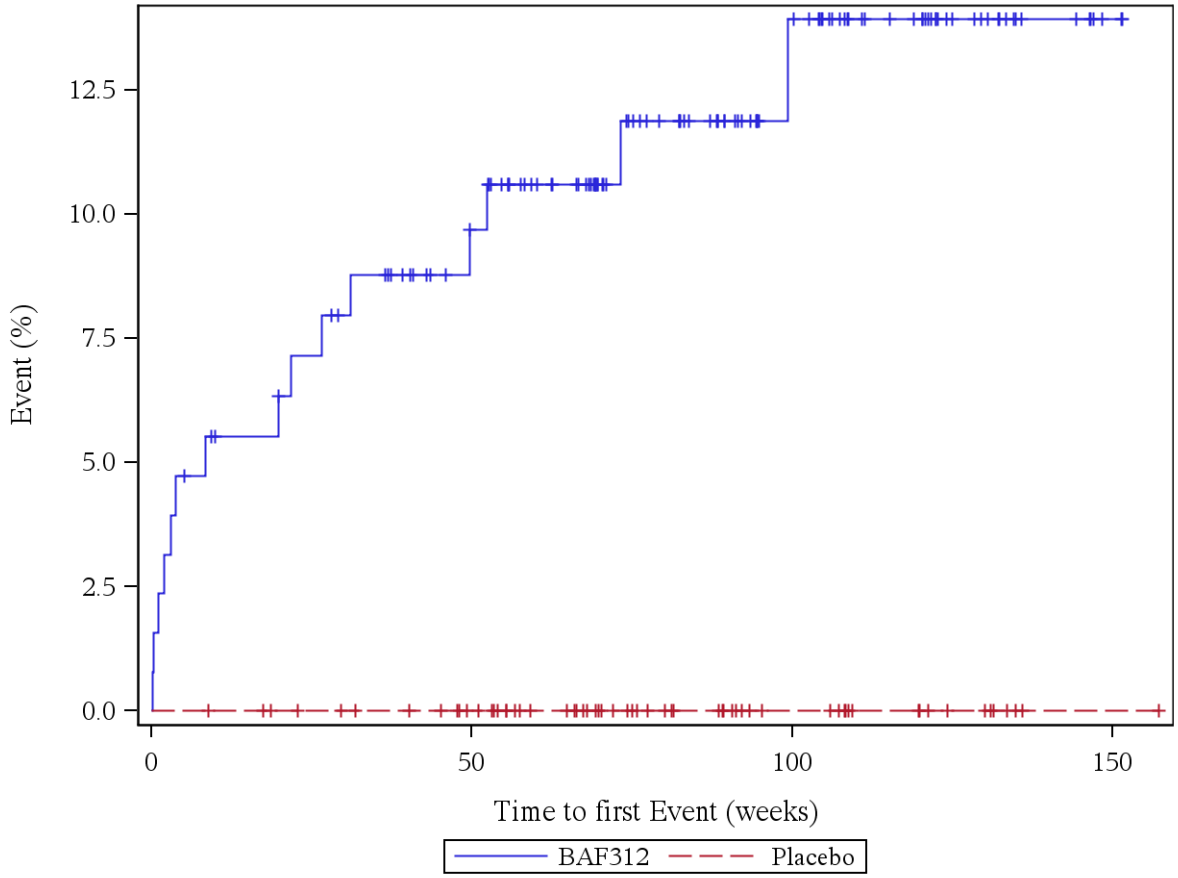


Patients at risk (BAF312/Placebo): Week 0: 127/61, Week 4: 114/60, Week 12: 108/59, Week 24: 103/55, Week 36: 98/52, Week 48: 89/48, Week 60: 77/38, Week 72: 63/29, Week 84: 53/21, Week 96: 39/15, Week 108: 31/14, Week 120: 23/8, Week 132: 12/3, Week 144: 7/1, Week 156: 0/1

Log rank test: p-value = 0,025 *
*: p < 0,05

Analysis population: A2304 SAF subpopulation "ACTIVE MS WITHOUT RELAPSES"

Figure 12.1.3.6: FATIGUE (PT)

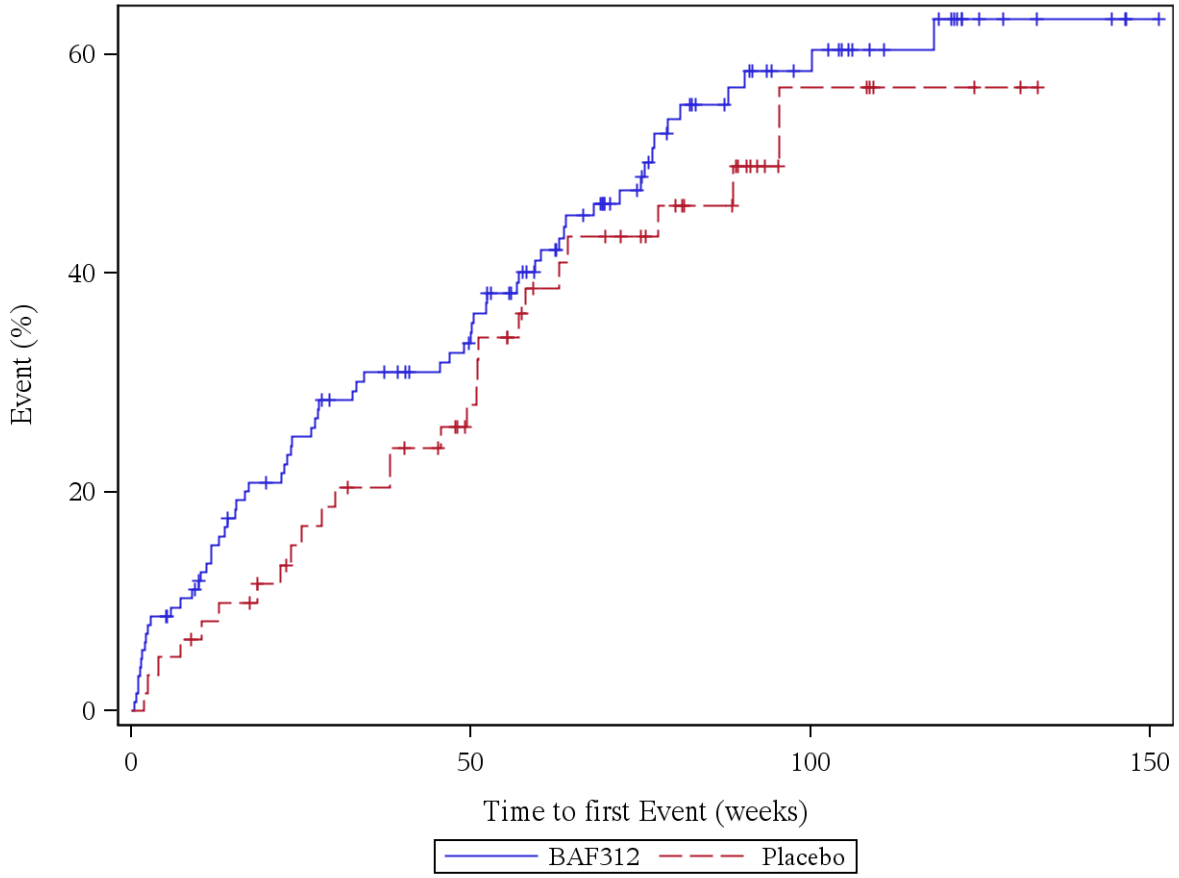


Patients at risk (BAF312/Placebo): Week 0: 127/61, Week 4: 121/61, Week 12: 117/60, Week 24: 114/57, Week 36: 110/55, Week 48: 101/51, Week 60: 88/41, Week 72: 70/32, Week 84: 58/25, Week 96: 43/17, Week 108: 33/15, Week 120: 26/9, Week 132: 13/4, Week 144: 7/1, Week 156: 0/1

Log rank test: p-value = -
*: p < 0,05

Analysis population: A2304 SAF subpopulation "ACTIVE MS WITHOUT RELAPSES"

Figure 12.1.3.7: INFECTIONS AND INFESTATIONS (SOC)

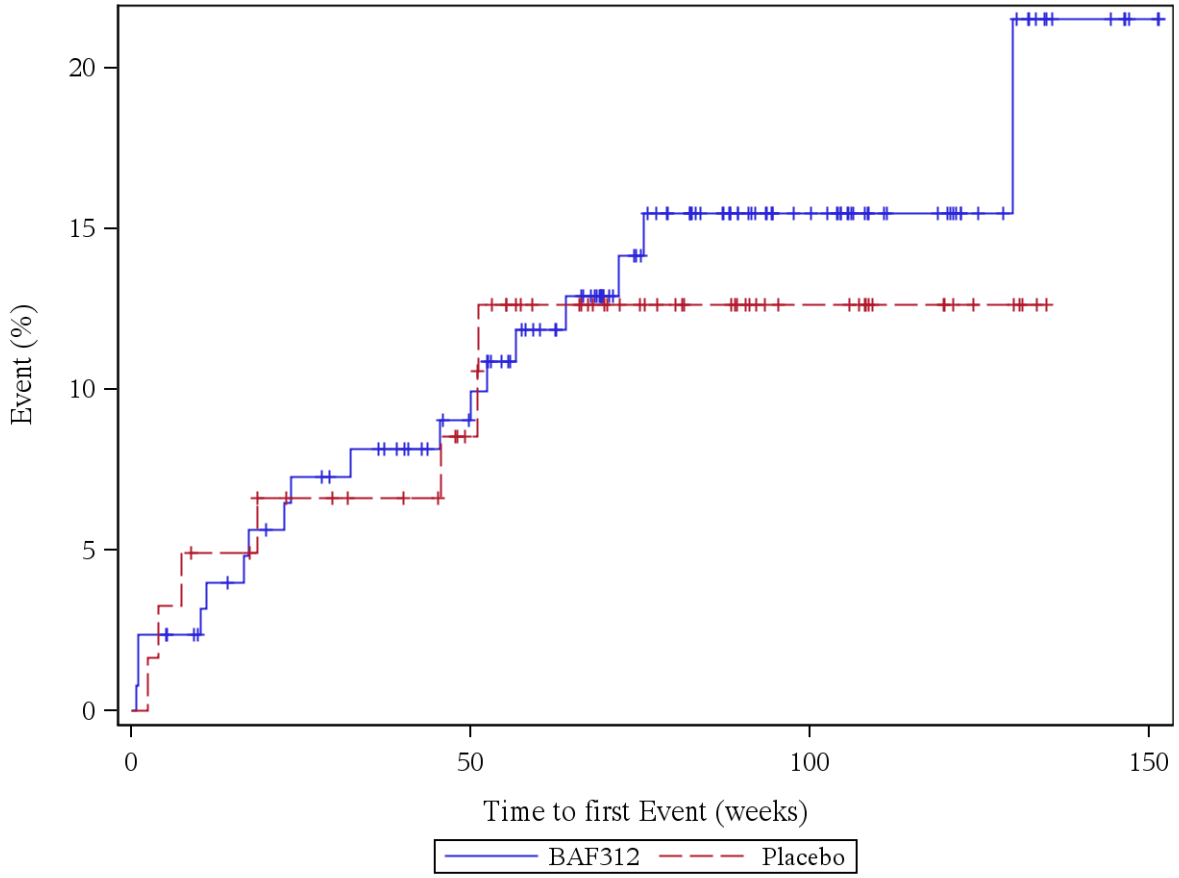


Patients at risk (BAF312/Placebo): Week 0: 127/61, Week 4: 116/58, Week 12: 104/55, Week 24: 90/48, Week 36: 81/44, Week 48: 75/37, Week 60: 58/26, Week 72: 43/22, Week 84: 30/16, Week 96: 23/6, Week 108: 16/6, Week 120: 12/3, Week 132: 5/1, Week 144: 4/0, Week 156: 0/0

Log rank test: p-value = 0,334
*: p < 0,05

Analysis population: A2304 SAF subpopulation "ACTIVE MS WITHOUT RELAPSES"

Figure 12.1.3.8: NASOPHARYNGITIS (PT)

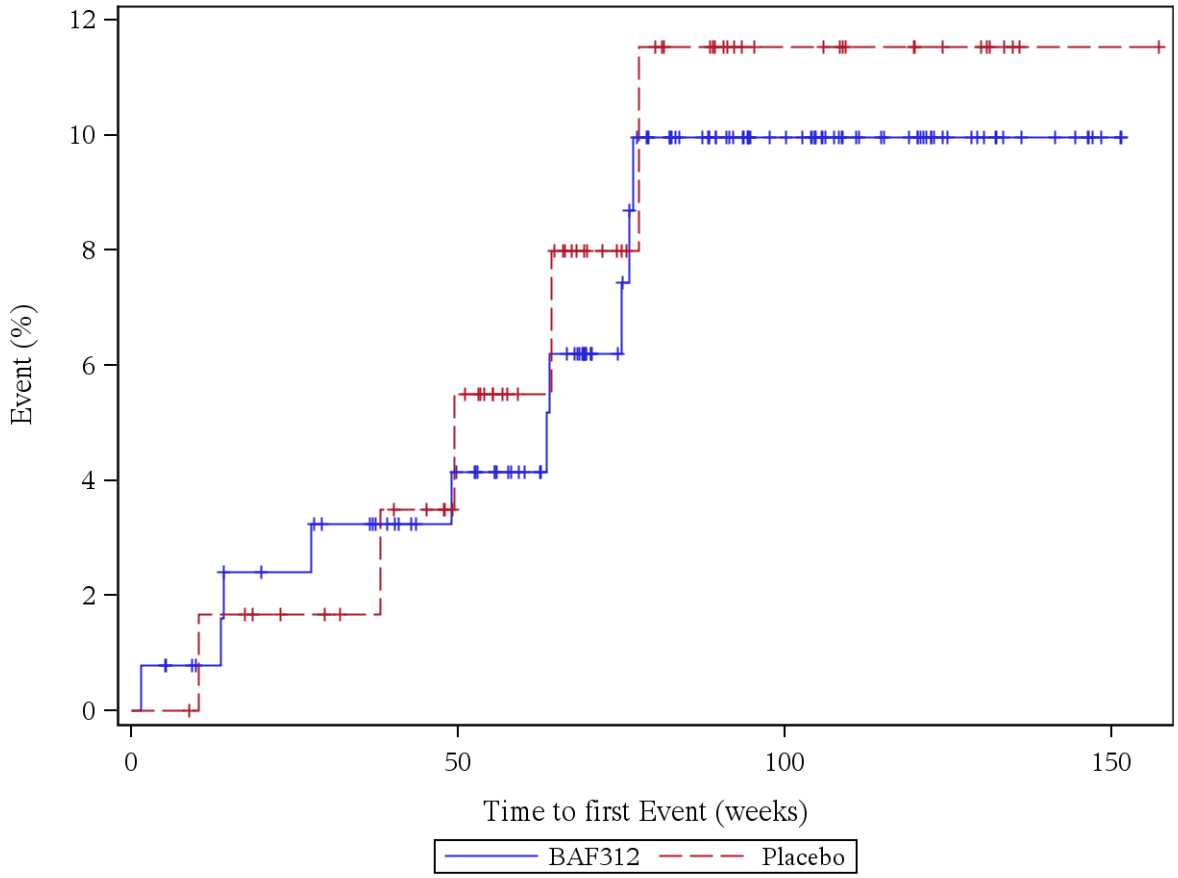


Patients at risk (BAF312/Placebo): Week 0: 127/61, Week 4: 124/59, Week 12: 118/57, Week 24: 112/53, Week 36: 109/51, Week 48: 100/46, Week 60: 87/36, Week 72: 68/29, Week 84: 54/23, Week 96: 39/15, Week 108: 28/13, Week 120: 22/7, Week 132: 12/2, Week 144: 6/0, Week 156: 0/0

Log rank test: p-value = 0,699
*: p < 0,05

Analysis population: A2304 SAF subpopulation "ACTIVE MS WITHOUT RELAPSES"

Figure 12.1.3.9: UPPER RESPIRATORY TRACT INFECTION (PT)

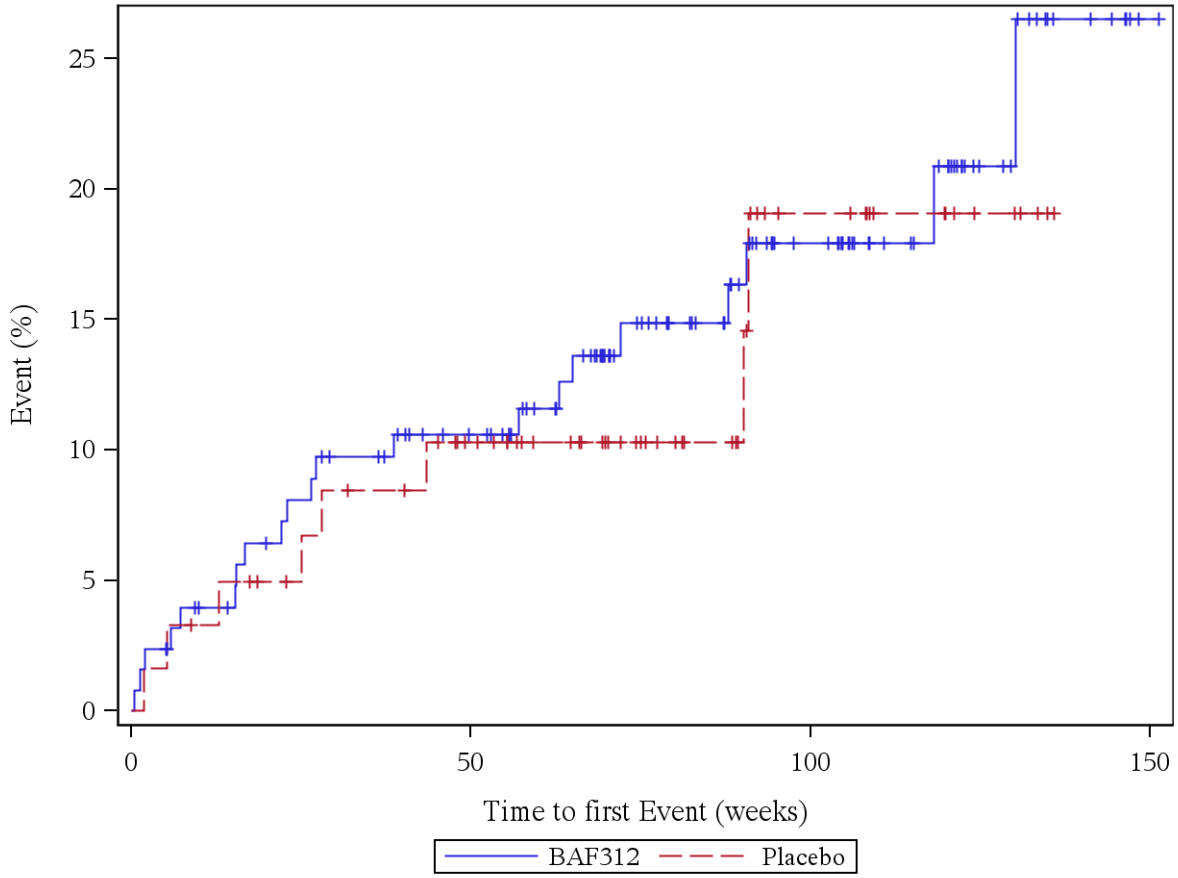


Patients at risk (BAF312/Placebo): Week 0: 127/61, Week 4: 126/61, Week 12: 122/59, Week 24: 118/56, Week 36: 115/54, Week 48: 107/49, Week 60: 96/38, Week 72: 77/29, Week 84: 61/22, Week 96: 45/14, Week 108: 33/13, Week 120: 25/8, Week 132: 12/4, Week 144: 7/1, Week 156: 0/1

Log rank test: p-value = 0,788
*: p < 0,05

Analysis population: A2304 SAF subpopulation "ACTIVE MS WITHOUT RELAPSES"

Figure 12.1.3.10: URINARY TRACT INFECTION (PT)

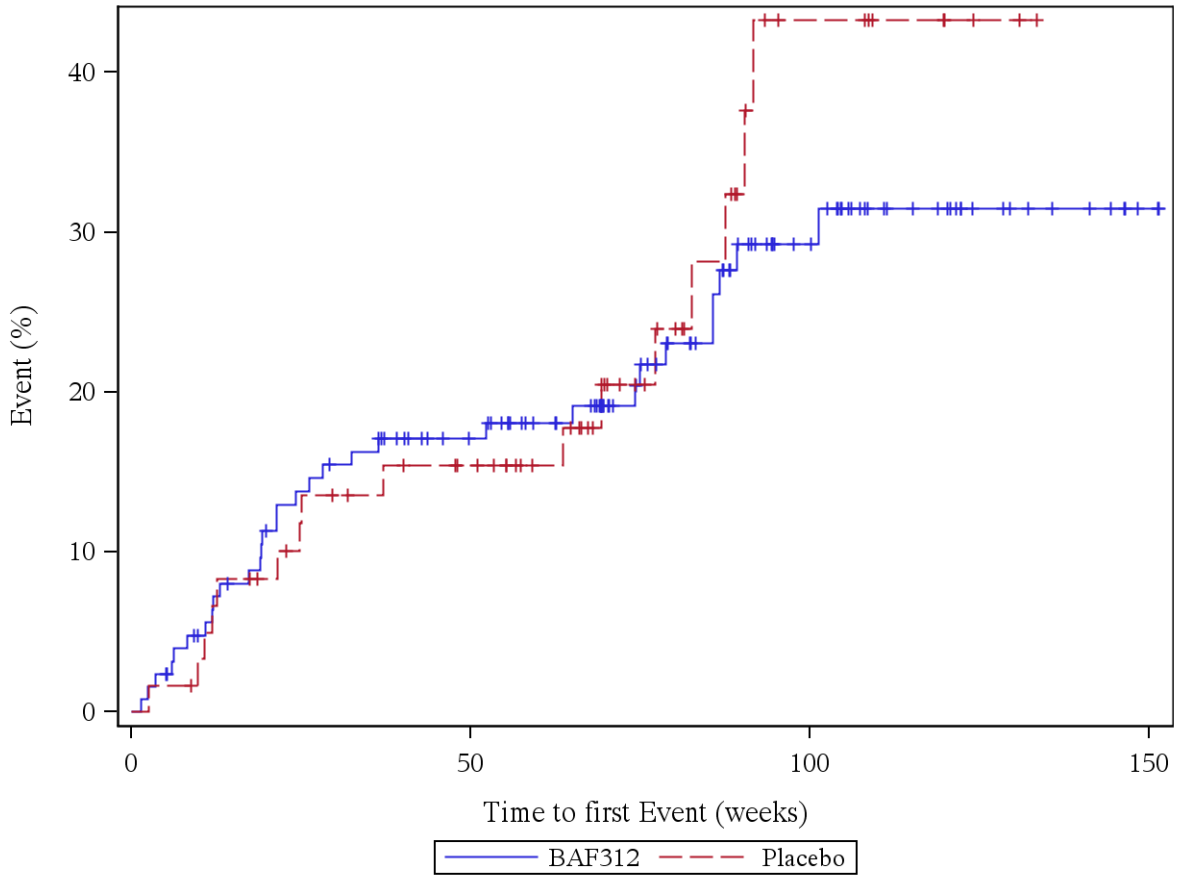


Patients at risk (BAF312/Placebo): Week 0: 127/61, Week 4: 124/60, Week 12: 118/58, Week 24: 111/54, Week 36: 107/51, Week 48: 99/46, Week 60: 88/38, Week 72: 69/31, Week 84: 59/24, Week 96: 44/14, Week 108: 33/13, Week 120: 26/7, Week 132: 12/3, Week 144: 6/0, Week 156: 0/0

Log rank test: p-value = 0,678
*: p < 0,05

Analysis population: A2304 SAF subpopulation "ACTIVE MS WITHOUT RELAPSES"

Figure 12.1.3.11: INJURY, POISONING AND PROCEDURAL COMPLICATIONS (SOC)

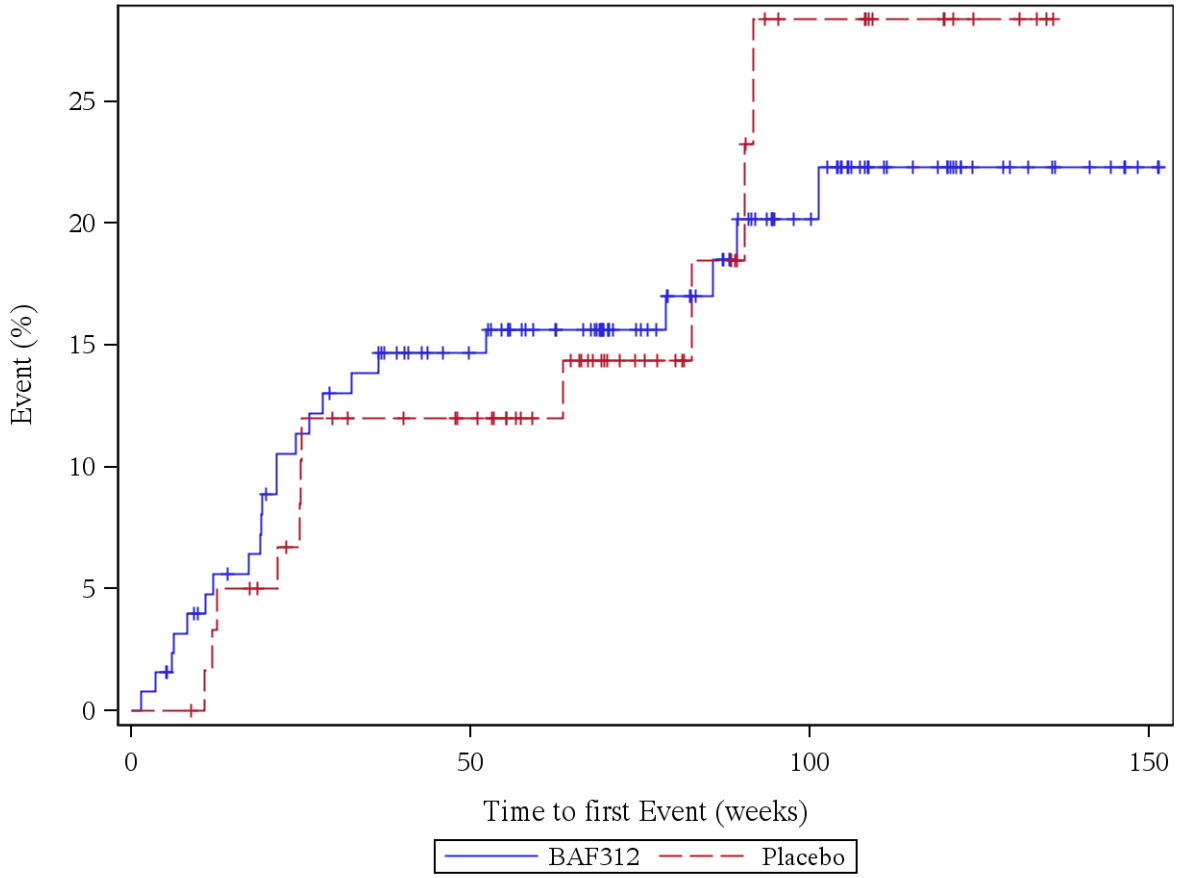


Patients at risk (BAF312/Placebo): Week 0: 127/61, Week 4: 124/60, Week 12: 114/56, Week 24: 105/51, Week 36: 100/47, Week 48: 90/43, Week 60: 79/36, Week 72: 63/25, Week 84: 51/17, Week 96: 34/8, Week 108: 23/8, Week 120: 17/3, Week 132: 9/1, Week 144: 6/0, Week 156: 0/0

Log rank test: p-value = 0,602
*: p < 0,05

Analysis population: A2304 SAF subpopulation "ACTIVE MS WITHOUT RELAPSES"

Figure 12.1.3.12: FALL (PT)

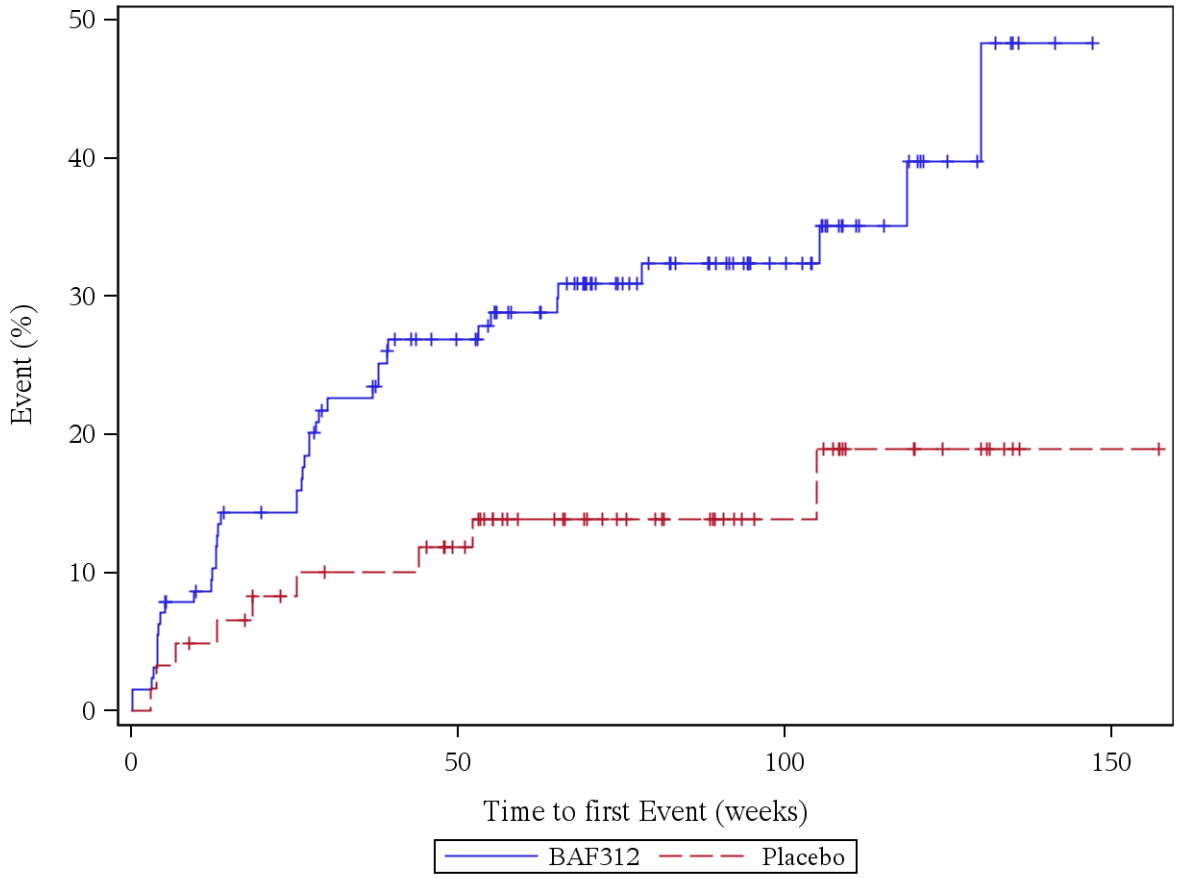


Patients at risk (BAF312/Placebo): Week 0: 127/61, Week 4: 125/61, Week 12: 116/58, Week 24: 108/53, Week 36: 103/48, Week 48: 93/45, Week 60: 82/37, Week 72: 65/27, Week 84: 55/20, Week 96: 39/12, Week 108: 27/12, Week 120: 20/6, Week 132: 10/3, Week 144: 6/0, Week 156: 0/0

Log rank test: p-value = 0,912
*: p < 0,05

Analysis population: A2304 SAF subpopulation "ACTIVE MS WITHOUT RELAPSES"

Figure 12.1.3.13: INVESTIGATIONS (SOC)

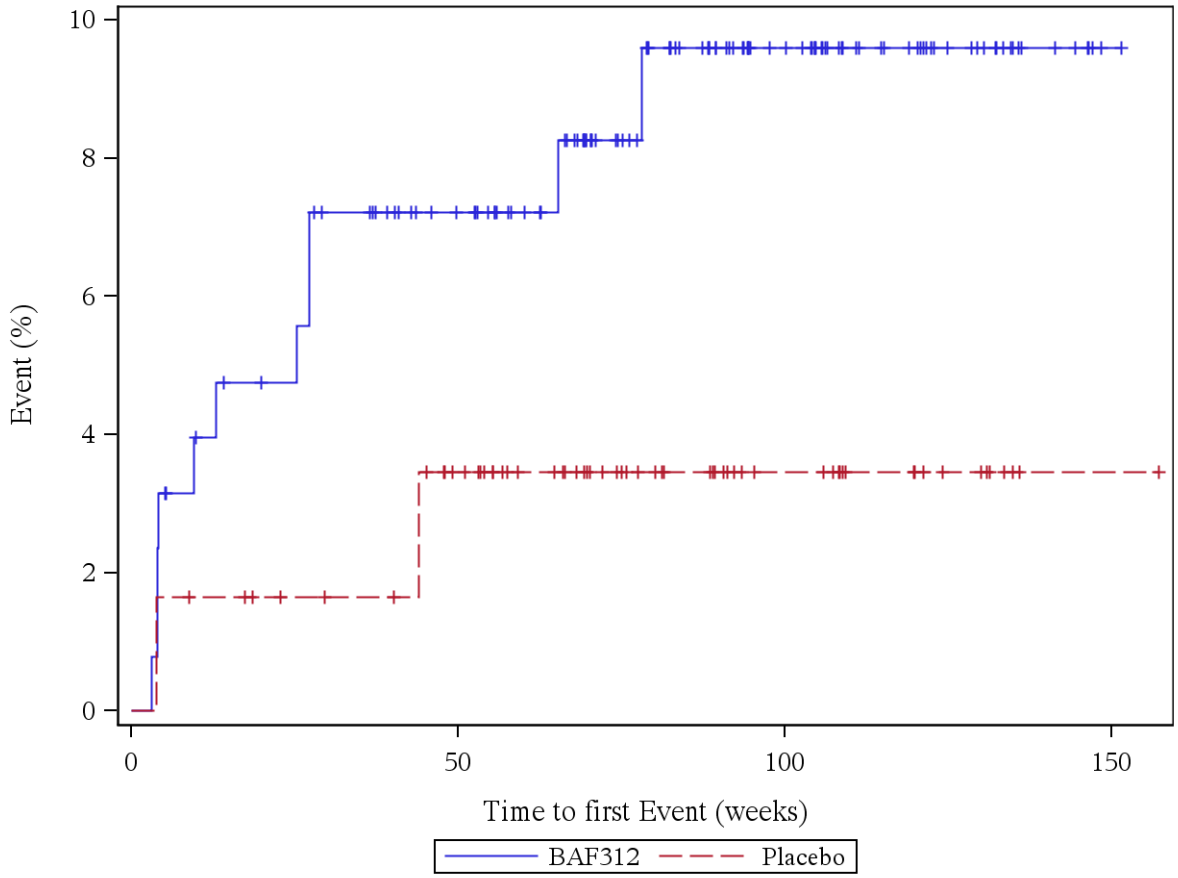


Patients at risk (BAF312/Placebo): Week 0: 127/61, Week 4: 120/59, Week 12: 113/57, Week 24: 104/52, Week 36: 92/50, Week 48: 80/46, Week 60: 69/35, Week 72: 52/29, Week 84: 42/24, Week 96: 30/17, Week 108: 20/14, Week 120: 12/8, Week 132: 6/4, Week 144: 1/1, Week 156: 0/1

Log rank test: p-value = 0,012 *
*: p < 0,05

Analysis population: A2304 SAF subpopulation "ACTIVE MS WITHOUT RELAPSES"

Figure 12.1.3.14: ALANINE AMINOTRANSFERASE INCREASED (PT)

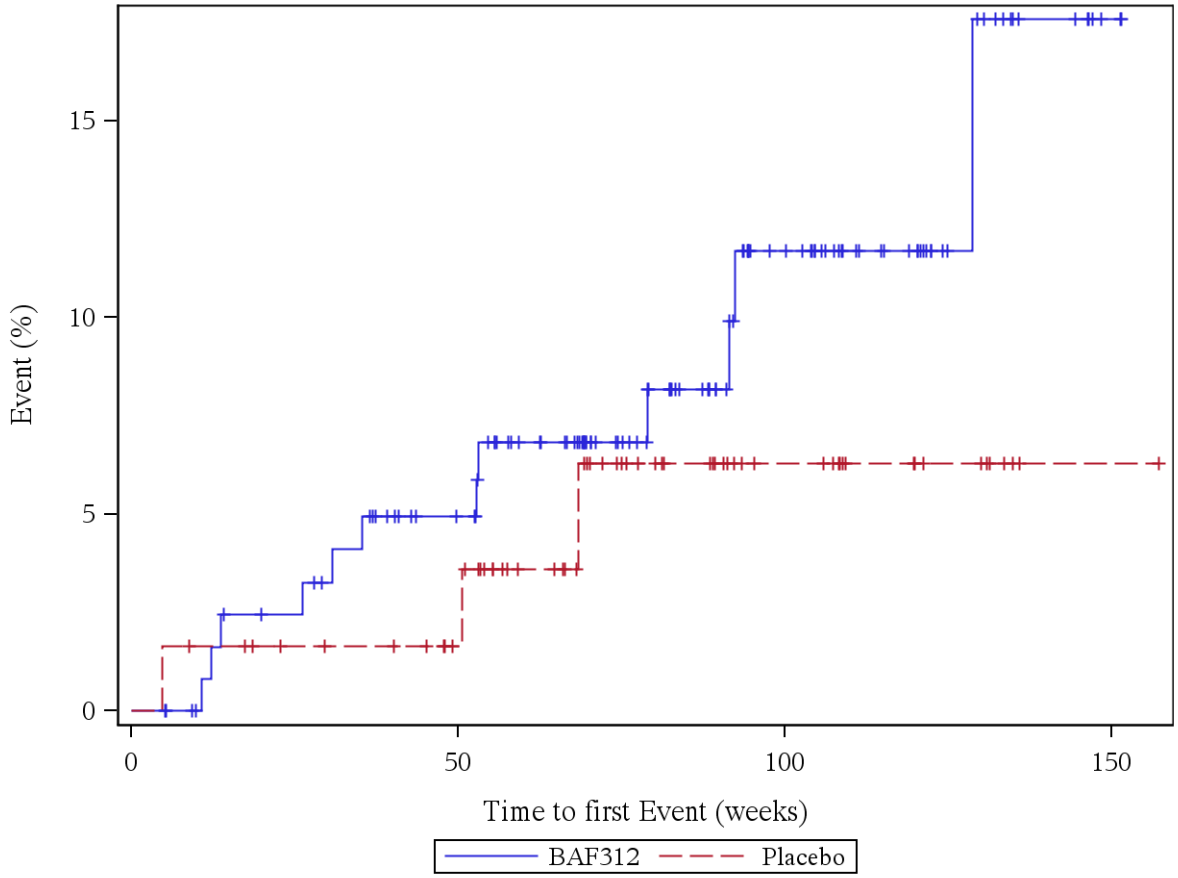


Patients at risk (BAF312/Placebo): Week 0: 127/61, Week 4: 124/60, Week 12: 119/59, Week 24: 116/56, Week 36: 111/55, Week 48: 102/50, Week 60: 92/40, Week 72: 74/32, Week 84: 60/25, Week 96: 44/17, Week 108: 32/15, Week 120: 24/9, Week 132: 14/4, Week 144: 6/1, Week 156: 0/1

Log rank test: p-value = 0,192
*: p < 0,05

Analysis population: A2304 SAF subpopulation "ACTIVE MS WITHOUT RELAPSES"

Figure 12.1.3.15: METABOLISM AND NUTRITION DISORDERS (SOC)

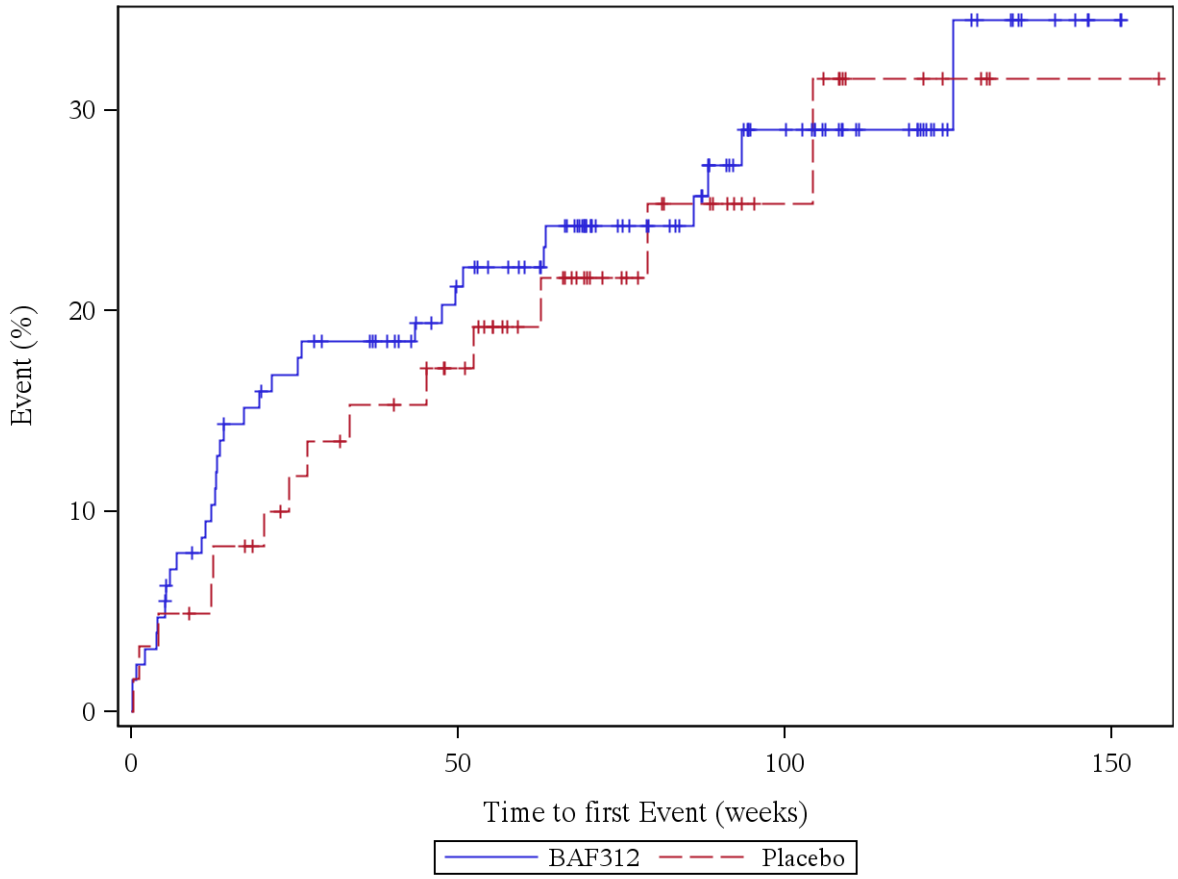


Patients at risk (BAF312/Placebo): Week 0: 127/61, Week 4: 127/61, Week 12: 122/59, Week 24: 118/56, Week 36: 113/55, Week 48: 105/51, Week 60: 92/40, Week 72: 75/31, Week 84: 60/24, Week 96: 42/16, Week 108: 32/14, Week 120: 24/8, Week 132: 12/4, Week 144: 7/1, Week 156: 0/1

Log rank test: p-value = 0,352
*: p < 0,05

Analysis population: A2304 SAF subpopulation "ACTIVE MS WITHOUT RELAPSES"

Figure 12.1.3.16: MUSCULOSKELETAL AND CONNECTIVE TISSUE DISORDERS (SOC)

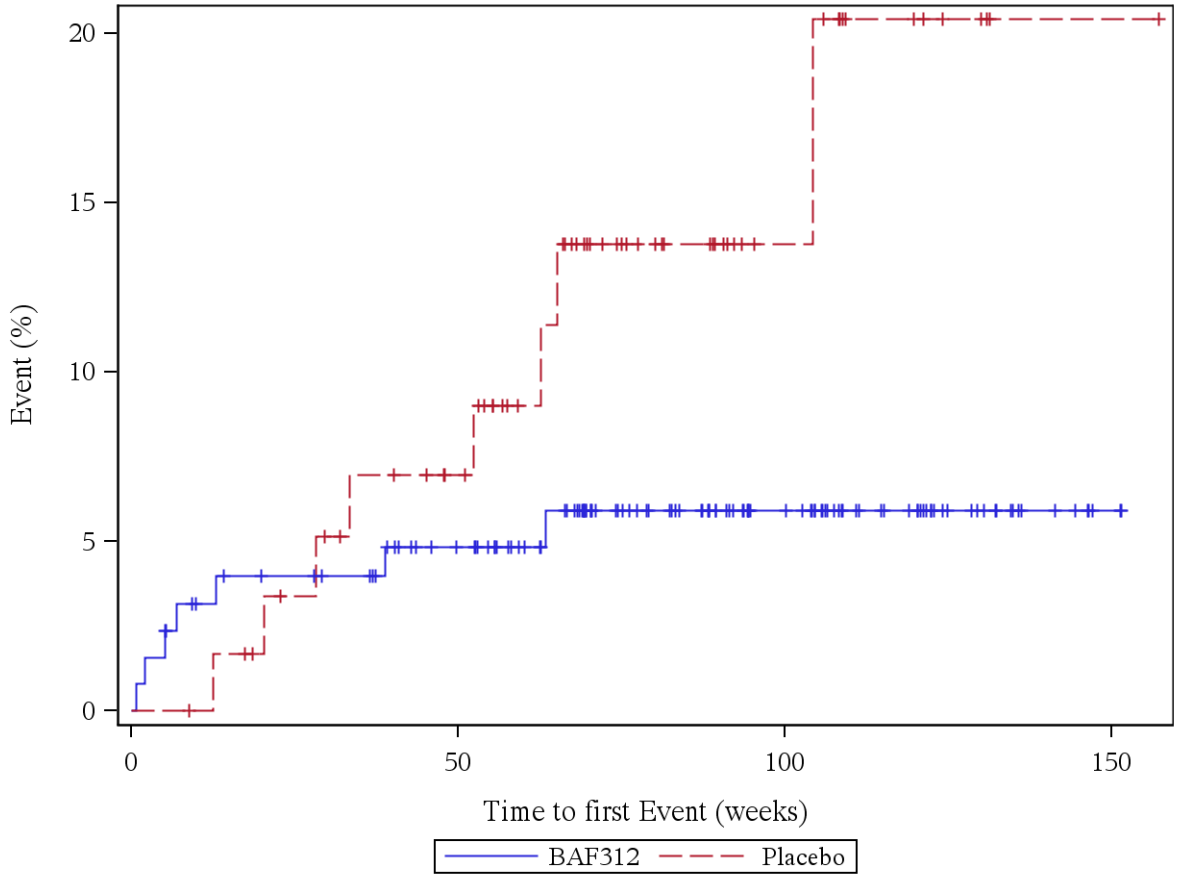


Patients at risk (BAF312/Placebo): Week 0: 127/61, Week 4: 121/59, Week 12: 112/57, Week 24: 101/51, Week 36: 97/47, Week 48: 86/42, Week 60: 78/33, Week 72: 59/24, Week 84: 51/18, Week 96: 35/12, Week 108: 28/10, Week 120: 22/6, Week 132: 10/1, Week 144: 5/1, Week 156: 0/1

Log rank test: p-value = 0,727
*: p < 0,05

Analysis population: A2304 SAF subpopulation "ACTIVE MS WITHOUT RELAPSES"

Figure 12.1.3.17: ARTHRALGIA (PT)

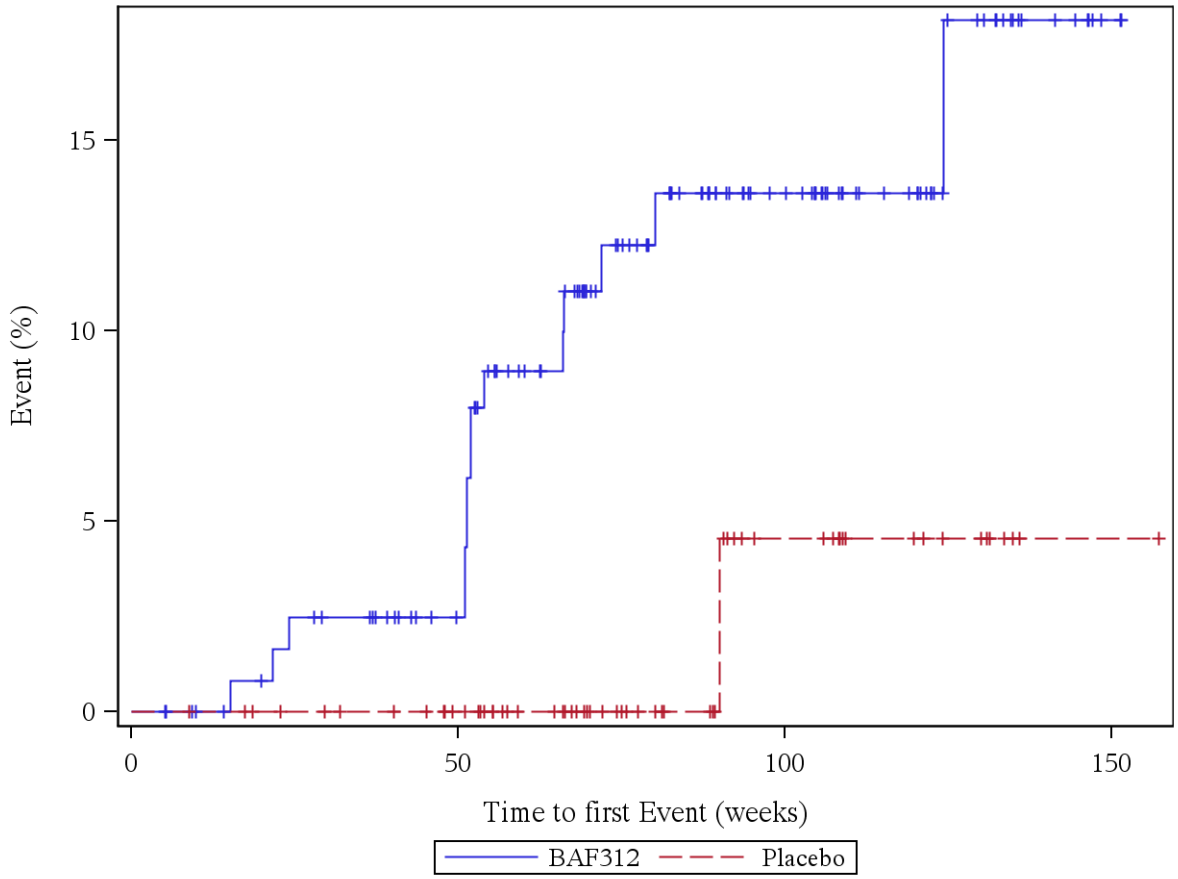


Patients at risk (BAF312/Placebo): Week 0: 127/61, Week 4: 125/61, Week 12: 119/60, Week 24: 116/55, Week 36: 114/51, Week 48: 104/47, Week 60: 93/38, Week 72: 73/28, Week 84: 62/21, Week 96: 45/13, Week 108: 34/11, Week 120: 26/6, Week 132: 13/1, Week 144: 6/1, Week 156: 0/1

Log rank test: p-value = 0,065
*: p < 0,05

Analysis population: A2304 SAF subpopulation "ACTIVE MS WITHOUT RELAPSES"

Figure 12.1.3.18: NEOPLASMS BENIGN, MALIGNANT AND UNSPECIFIED (INCL CYSTS AND POLYPS) (SOC)

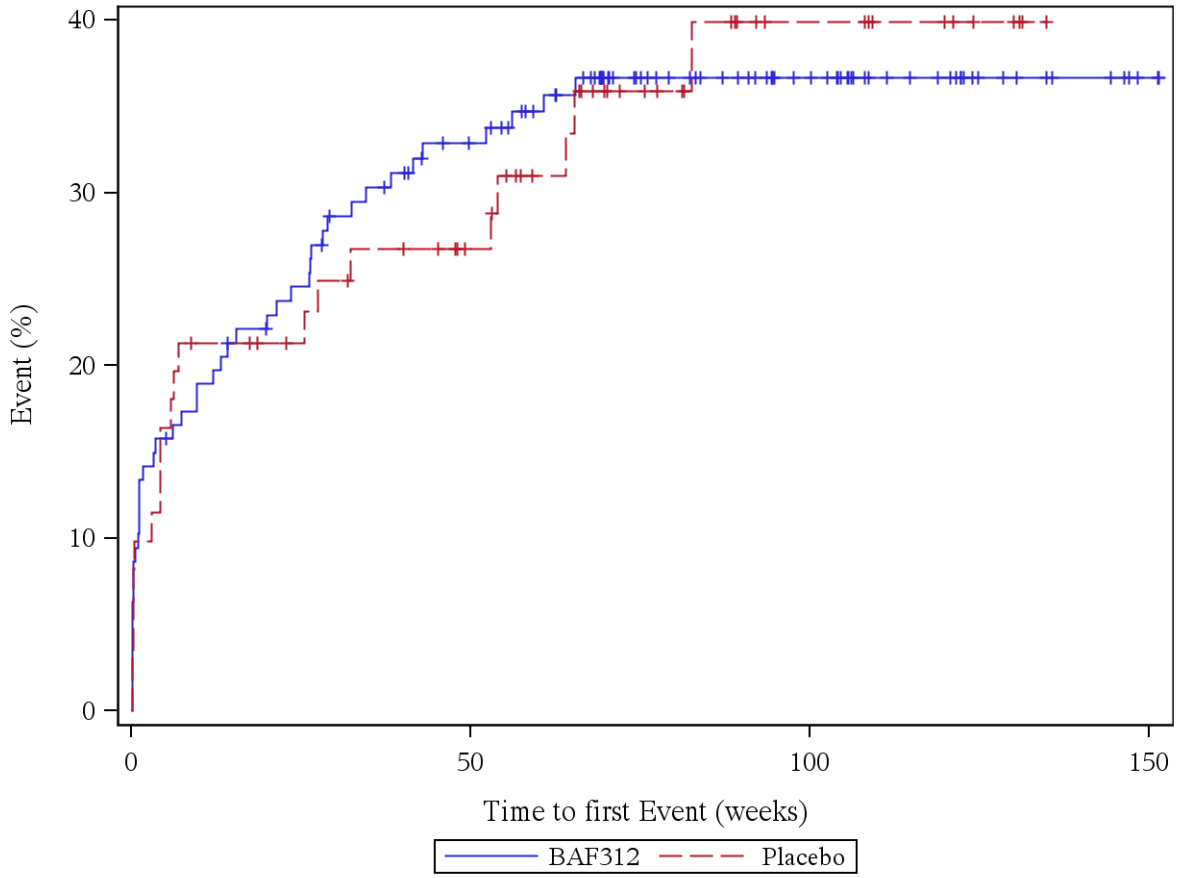


Patients at risk (BAF312/Placebo): Week 0: 127/61, Week 4: 127/61, Week 12: 123/60, Week 24: 119/57, Week 36: 116/55, Week 48: 107/51, Week 60: 90/41, Week 72: 72/32, Week 84: 58/25, Week 96: 45/16, Week 108: 34/14, Week 120: 27/9, Week 132: 15/4, Week 144: 7/1, Week 156: 0/1

Log rank test: p-value = 0,029 *
*: p < 0,05

Analysis population: A2304 SAF subpopulation "ACTIVE MS WITHOUT RELAPSES"

Figure 12.1.3.19: NERVOUS SYSTEM DISORDERS (SOC)

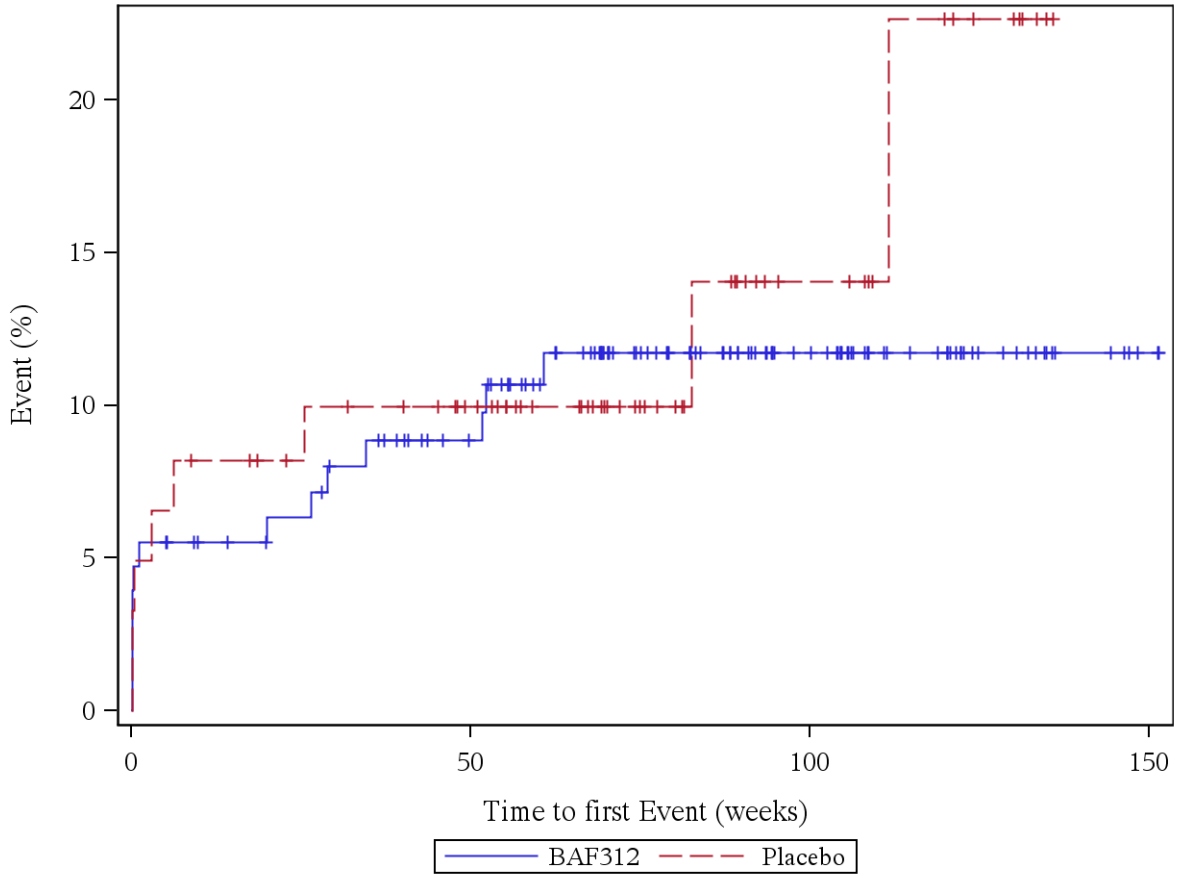


Patients at risk (BAF312/Placebo): Week 0: 127/61, Week 4: 107/54, Week 12: 101/47, Week 24: 93/44, Week 36: 84/40, Week 48: 76/36, Week 60: 67/28, Week 72: 50/20, Week 84: 41/15, Week 96: 32/10, Week 108: 22/10, Week 120: 17/6, Week 132: 8/1, Week 144: 6/0, Week 156: 0/0

Log rank test: p-value = 0,957
*: p < 0,05

Analysis population: A2304 SAF subpopulation "ACTIVE MS WITHOUT RELAPSES"

Figure 12.1.3.20: HEADACHE (PT)

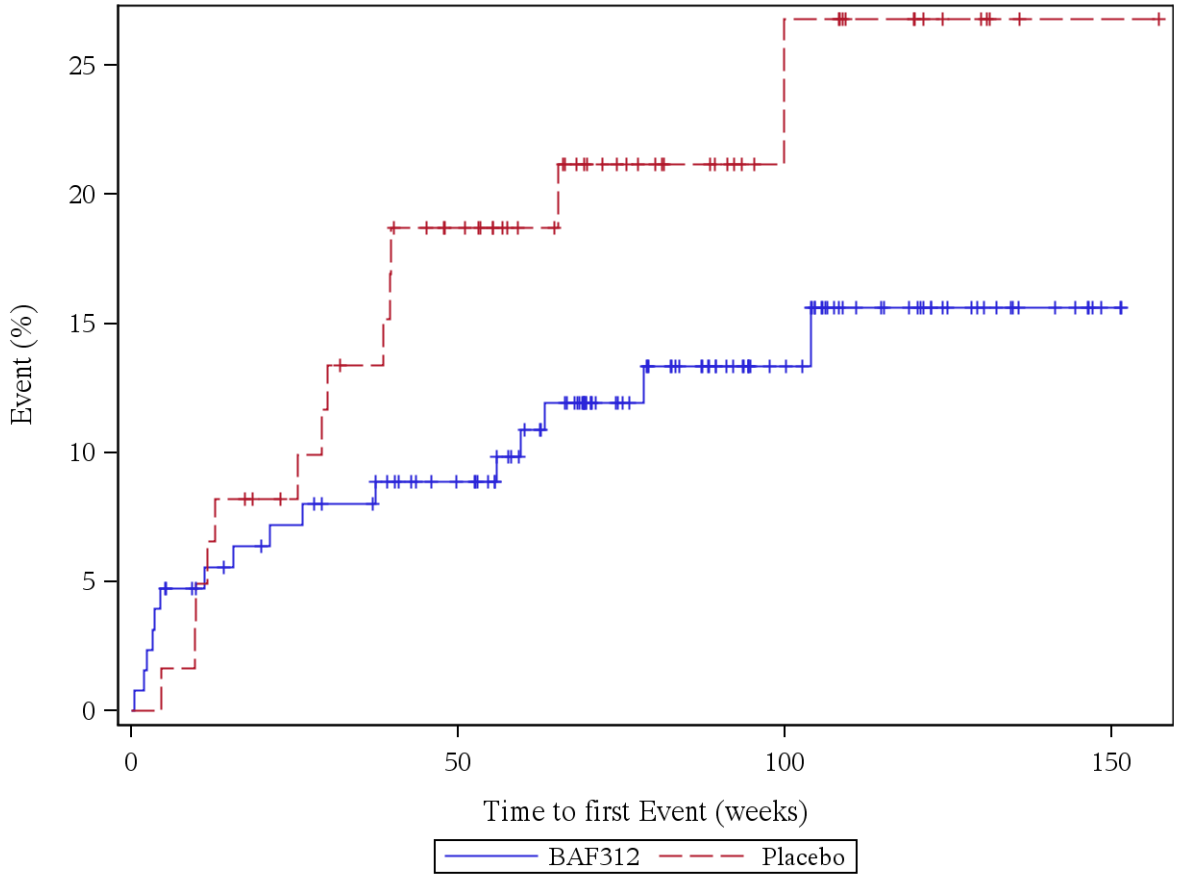


Patients at risk (BAF312/Placebo): Week 0: 127/61, Week 4: 120/57, Week 12: 116/55, Week 24: 113/52, Week 36: 108/50, Week 48: 100/46, Week 60: 88/37, Week 72: 70/29, Week 84: 57/21, Week 96: 42/14, Week 108: 30/13, Week 120: 23/8, Week 132: 12/3, Week 144: 6/0, Week 156: 0/0

Log rank test: p-value = 0,627
*: p < 0,05

Analysis population: A2304 SAF subpopulation "ACTIVE MS WITHOUT RELAPSES"

Figure 12.1.3.21: PSYCHIATRIC DISORDERS (SOC)

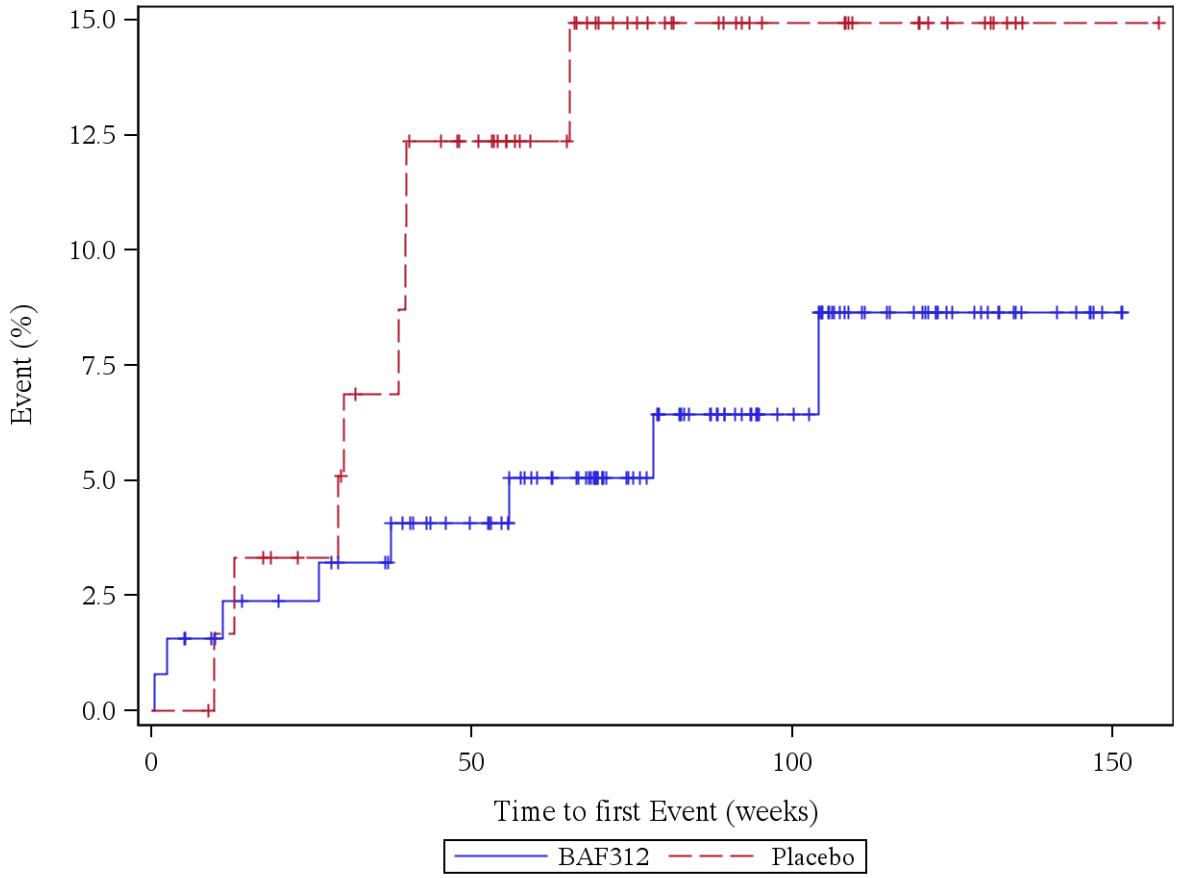


Patients at risk (BAF312/Placebo): Week 0: 127/61, Week 4: 122/61, Week 12: 116/57, Week 24: 112/53, Week 36: 109/49, Week 48: 100/42, Week 60: 87/34, Week 72: 67/26, Week 84: 55/20, Week 96: 41/14, Week 108: 28/13, Week 120: 22/7, Week 132: 12/2, Week 144: 7/1, Week 156: 0/1

Log rank test: p-value = 0,115
*: p < 0,05

Analysis population: A2304 SAF subpopulation "ACTIVE MS WITHOUT RELAPSES"

Figure 12.1.3.22: DEPRESSION (PT)

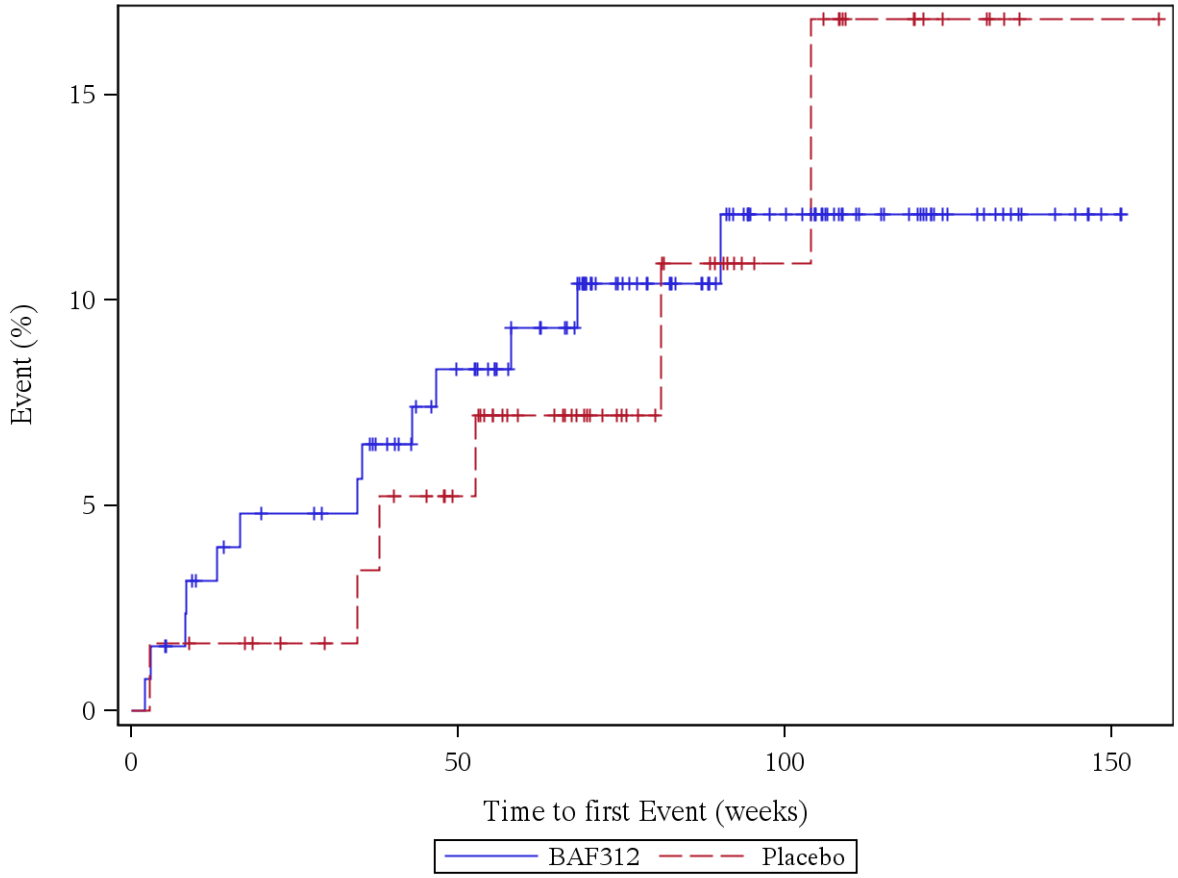


Patients at risk (BAF312/Placebo): Week 0: 127/61, Week 4: 125/61, Week 12: 120/59, Week 24: 118/55, Week 36: 115/51, Week 48: 105/44, Week 60: 93/35, Week 72: 74/27, Week 84: 60/21, Week 96: 45/15, Week 108: 31/15, Week 120: 24/9, Week 132: 13/4, Week 144: 7/1, Week 156: 0/1

Log rank test: p-value = 0,094
*: p < 0,05

Analysis population: A2304 SAF subpopulation "ACTIVE MS WITHOUT RELAPSES"

Figure 12.1.3.23: RENAL AND URINARY DISORDERS (SOC)

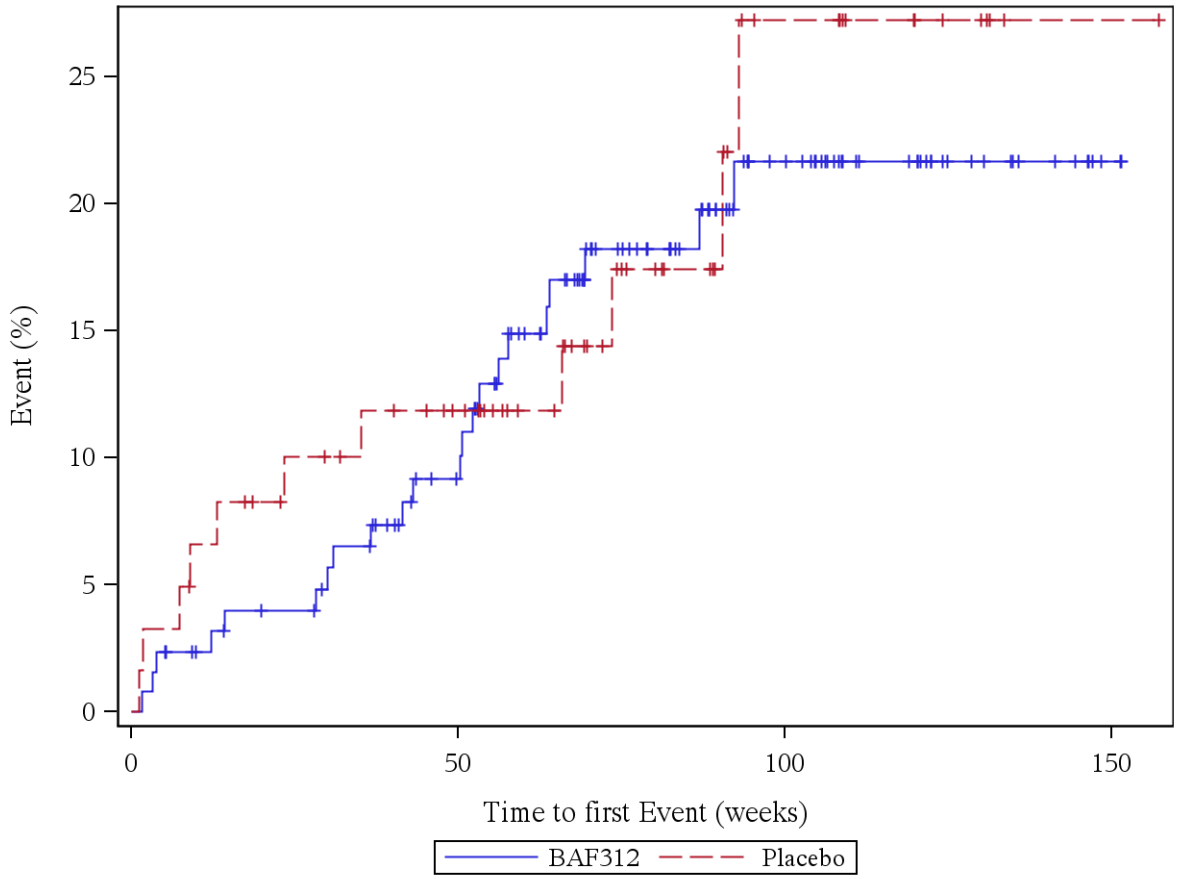


Patients at risk (BAF312/Placebo): Week 0: 127/61, Week 4: 125/60, Week 12: 119/59, Week 24: 115/56, Week 36: 111/54, Week 48: 100/49, Week 60: 89/39, Week 72: 70/30, Week 84: 59/22, Week 96: 43/15, Week 108: 31/13, Week 120: 23/7, Week 132: 12/3, Week 144: 6/1, Week 156: 0/1

Log rank test: p-value = 0,987
*: p < 0,05

Analysis population: A2304 SAF subpopulation "ACTIVE MS WITHOUT RELAPSES"

Figure 12.1.3.24: RESPIRATORY, THORACIC AND MEDIASTINAL DISORDERS (SOC)

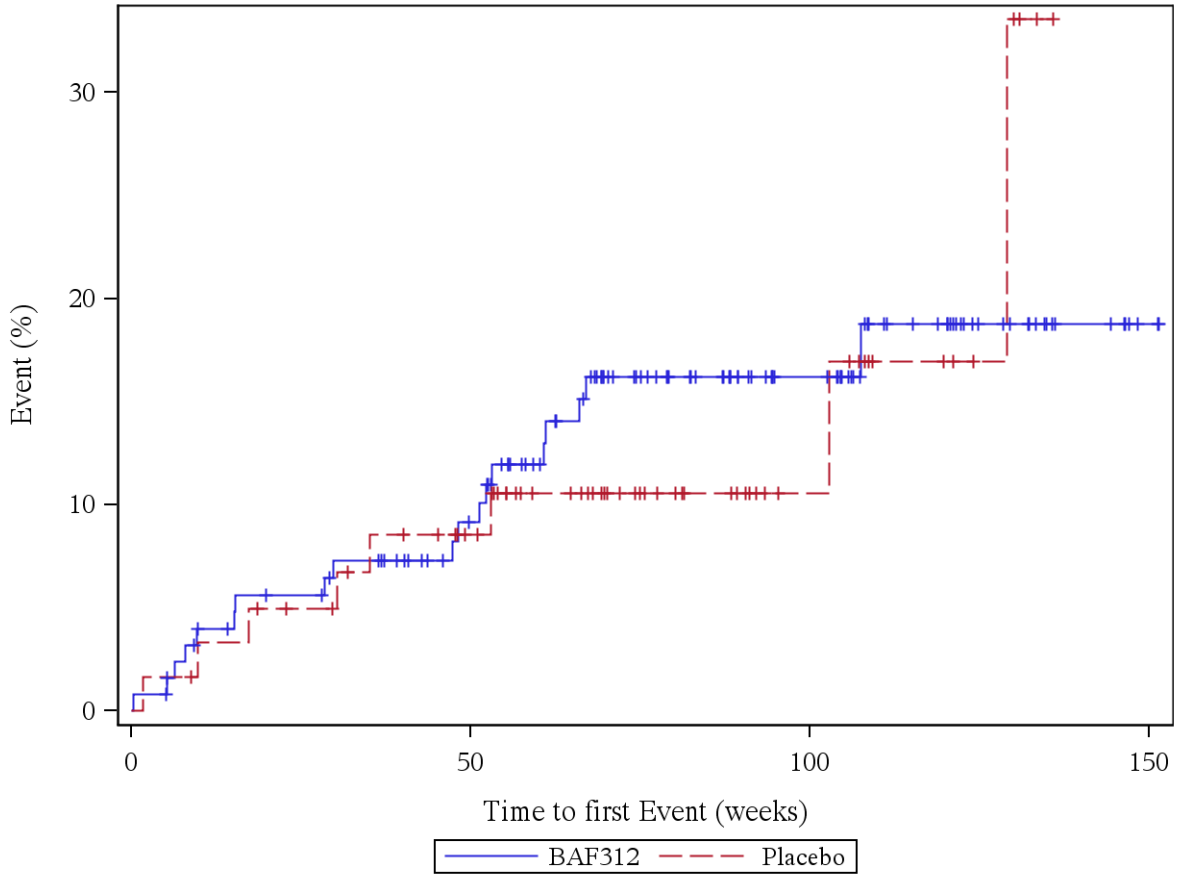


Patients at risk (BAF312/Placebo): Week 0: 127/61, Week 4: 124/59, Week 12: 120/56, Week 24: 116/51, Week 36: 111/48, Week 48: 99/45, Week 60: 83/36, Week 72: 64/28, Week 84: 53/21, Week 96: 37/12, Week 108: 27/12, Week 120: 21/6, Week 132: 11/2, Week 144: 7/1, Week 156: 0/1

Log rank test: p-value = 0,754
*: p < 0,05

Analysis population: A2304 SAF subpopulation "ACTIVE MS WITHOUT RELAPSES"

Figure 12.1.3.25: SKIN AND SUBCUTANEOUS TISSUE DISORDERS (SOC)

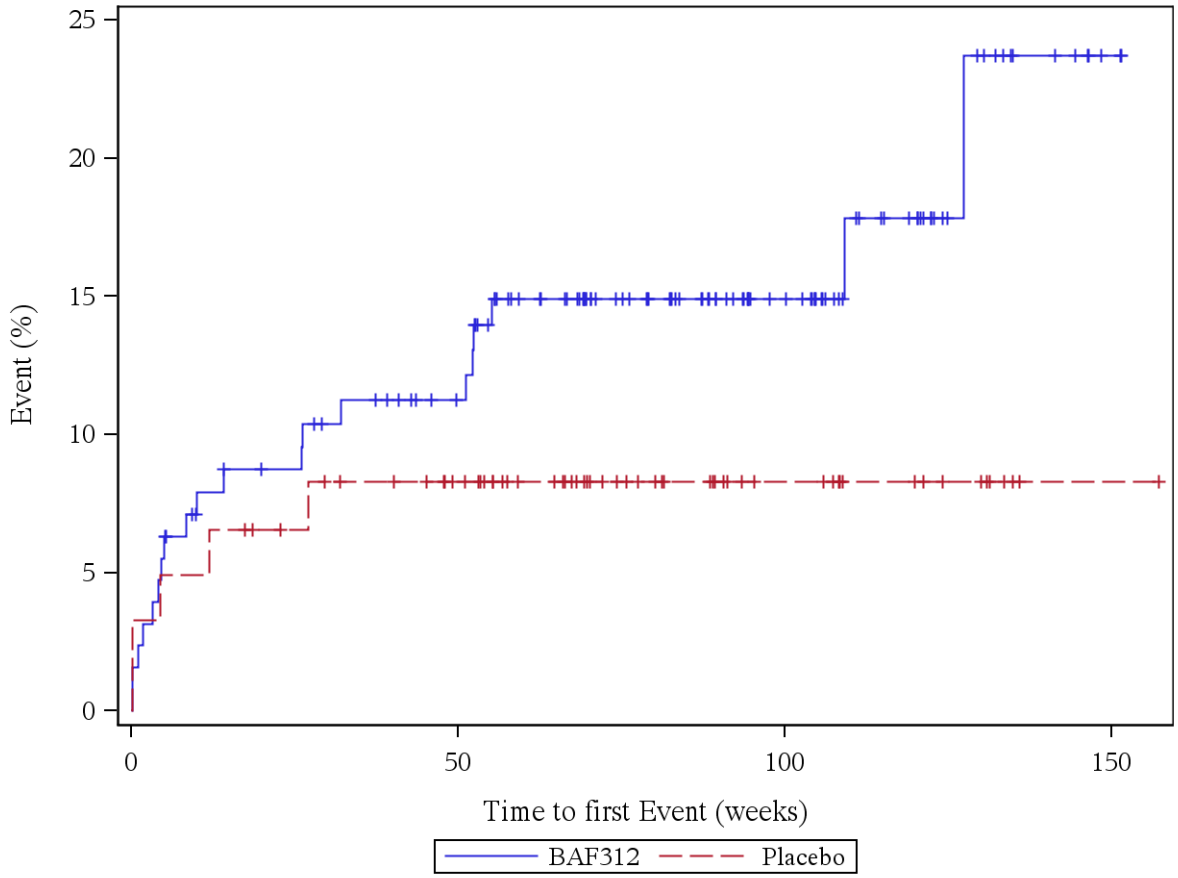


Patients at risk (BAF312/Placebo): Week 0: 127/61, Week 4: 126/60, Week 12: 118/58, Week 24: 114/55, Week 36: 110/51, Week 48: 100/47, Week 60: 85/36, Week 72: 68/28, Week 84: 57/21, Week 96: 43/14, Week 108: 32/11, Week 120: 25/7, Week 132: 14/2, Week 144: 7/0, Week 156: 0/0

Log rank test: p-value = 0,841
*: p < 0,05

Analysis population: A2304 SAF subpopulation "ACTIVE MS WITHOUT RELAPSES"

Figure 12.1.3.26: VASCULAR DISORDERS (SOC)

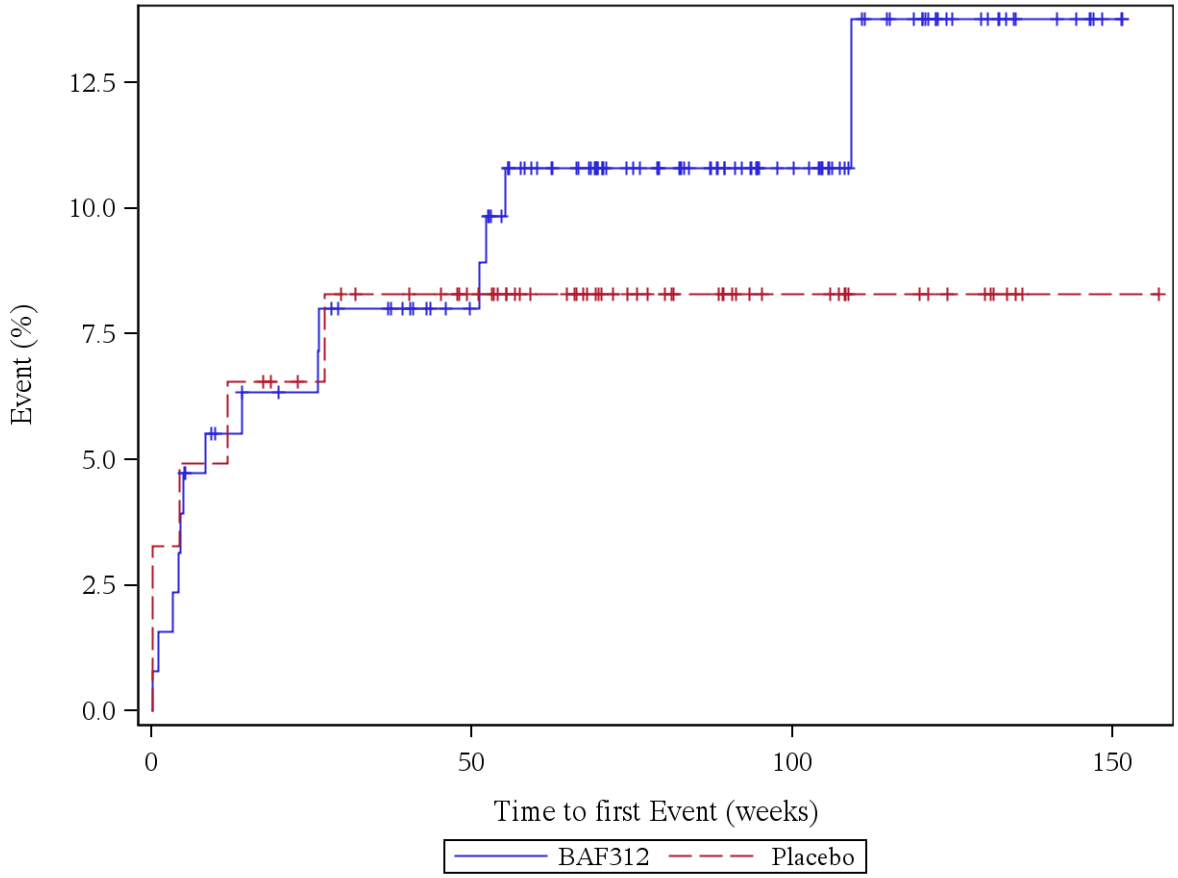


Patients at risk (BAF312/Placebo): Week 0: 127/61, Week 4: 122/59, Week 12: 113/57, Week 24: 110/54, Week 36: 105/51, Week 48: 99/47, Week 60: 84/37, Week 72: 69/28, Week 84: 58/22, Week 96: 43/15, Week 108: 31/13, Week 120: 23/9, Week 132: 11/4, Week 144: 6/1, Week 156: 0/1

Log rank test: p-value = 0,186
*: p < 0,05

Analysis population: A2304 SAF subpopulation "ACTIVE MS WITHOUT RELAPSES"

Figure 12.1.3.27: HYPERTENSION (PT)



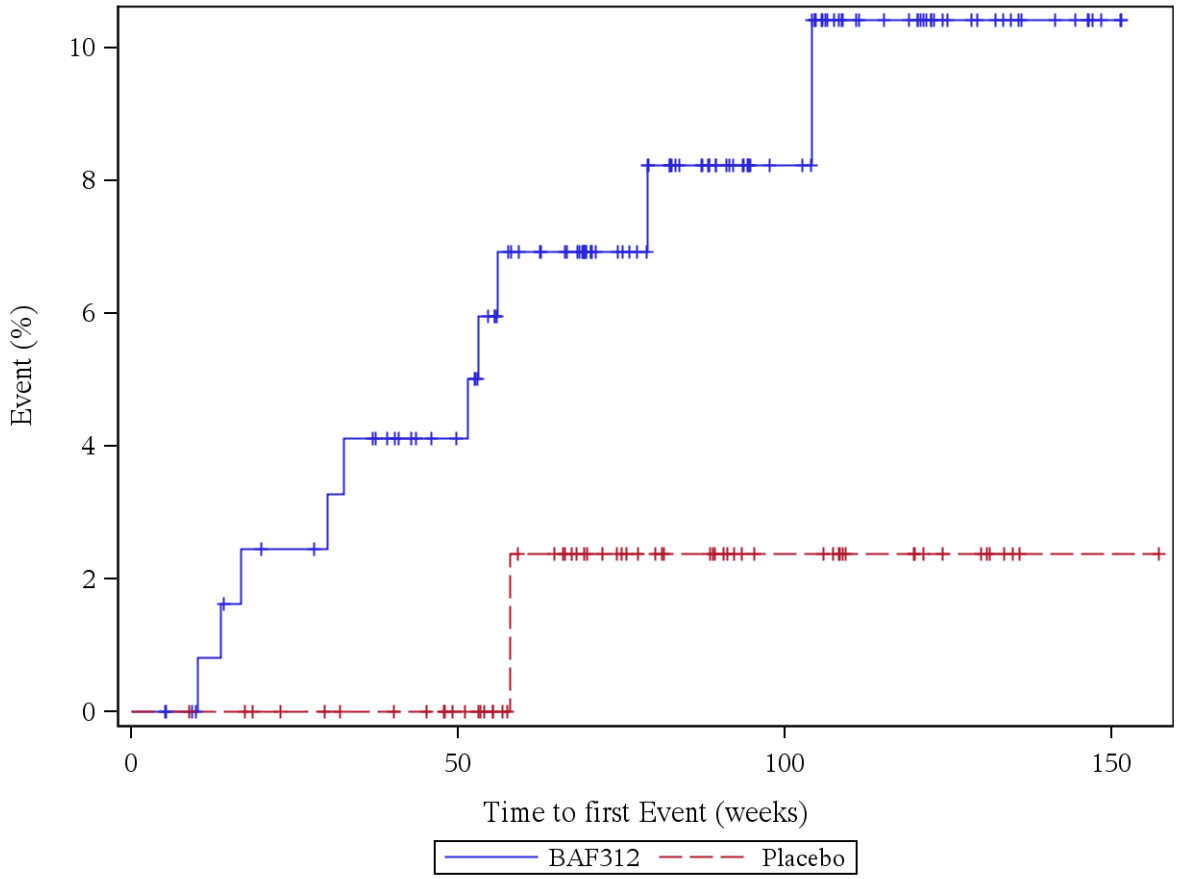
Patients at risk (BAF312/Placebo): Week 0: 127/61, Week 4: 124/59, Week 12: 116/57, Week 24: 113/54, Week 36: 109/51, Week 48: 101/47, Week 60: 87/37, Week 72: 70/28, Week 84: 59/22, Week 96: 44/15, Week 108: 32/13, Week 120: 24/9, Week 132: 13/4, Week 144: 7/1, Week 156: 0/1

Log rank test: p-value = 0,604
*: p < 0,05

Analysis population: A2304 SAF subpopulation "ACTIVE MS WITHOUT RELAPSES"

12.1.5: Time to First Adverse Event by SOC, PT and Severity (SAF)

Figure 12.1.5.1: BLOOD AND LYMPHATIC SYSTEM DISORDERS (SOC, not severe)

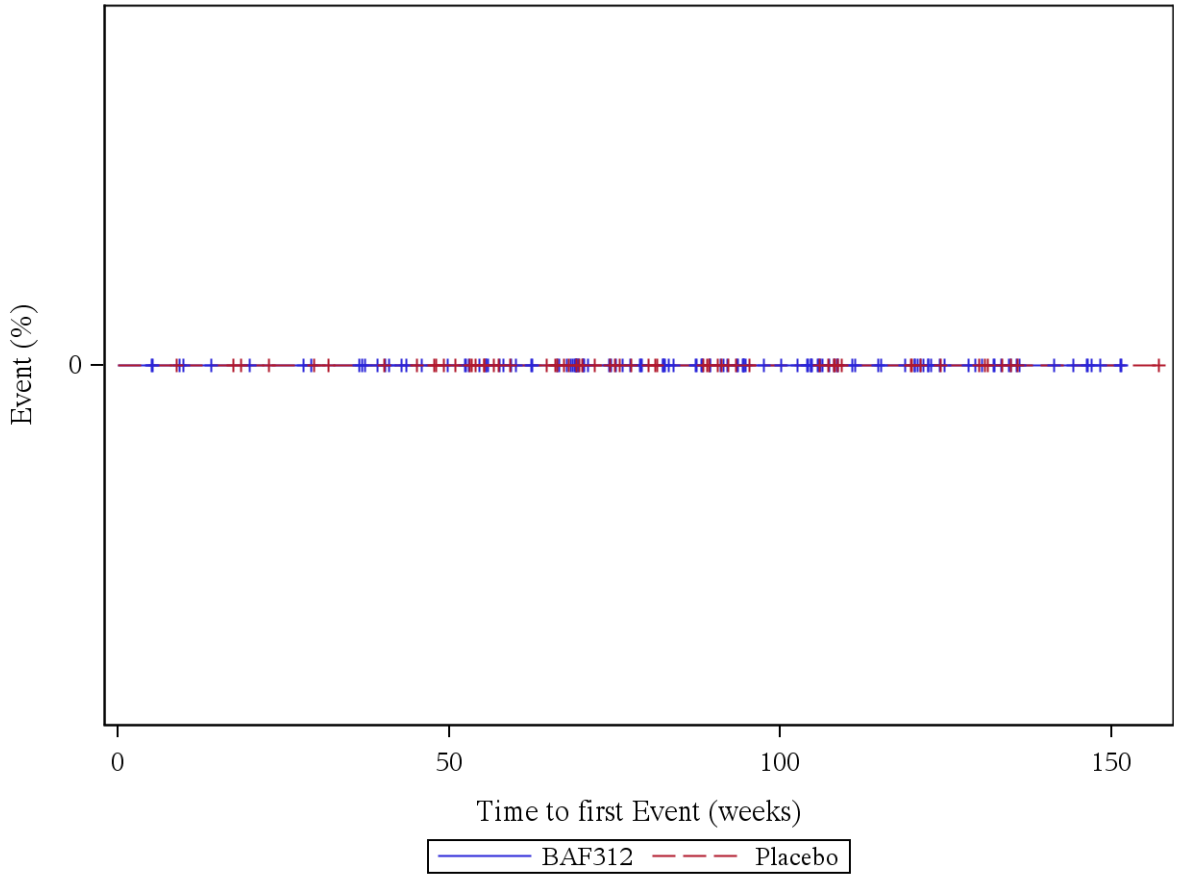


Patients at risk (BAF312/Placebo): Week 0: 127/61, Week 4: 127/61, Week 12: 122/60, Week 24: 118/57, Week 36: 115/55, Week 48: 107/51, Week 60: 93/40, Week 72: 76/32, Week 84: 62/25, Week 96: 45/17, Week 108: 32/15, Week 120: 25/9, Week 132: 13/4, Week 144: 7/1, Week 156: 0/1

Log rank test: p-value = 0,109
*: p < 0,05

Analysis population: A2304 SAF subpopulation "ACTIVE MS WITHOUT RELAPSES"

Figure 12.1.5.2: BLOOD AND LYMPHATIC SYSTEM DISORDERS (SOC, severe)

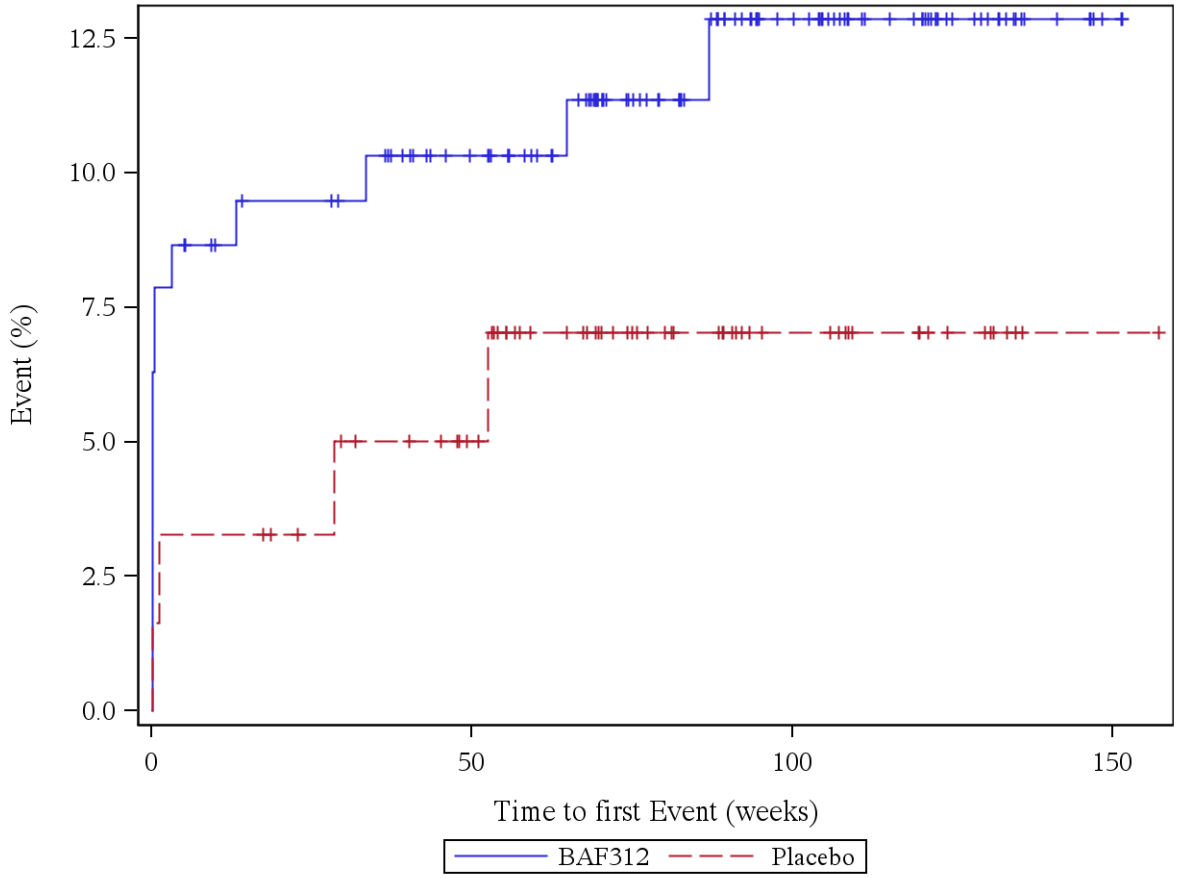


Patients at risk (BAF312/Placebo): Week 0: 127/61, Week 4: 127/61, Week 12: 123/60, Week 24: 121/57, Week 36: 119/55, Week 48: 110/51, Week 60: 99/41, Week 72: 80/32, Week 84: 66/25, Week 96: 49/17, Week 108: 36/15, Week 120: 28/9, Week 132: 15/4, Week 144: 7/1, Week 156: 0/1

Log rank test: p-value = -
*: p < 0,05

Analysis population: A2304 SAF subpopulation "ACTIVE MS WITHOUT RELAPSES"

Figure 12.1.5.3: CARDIAC DISORDERS (SOC, not severe)

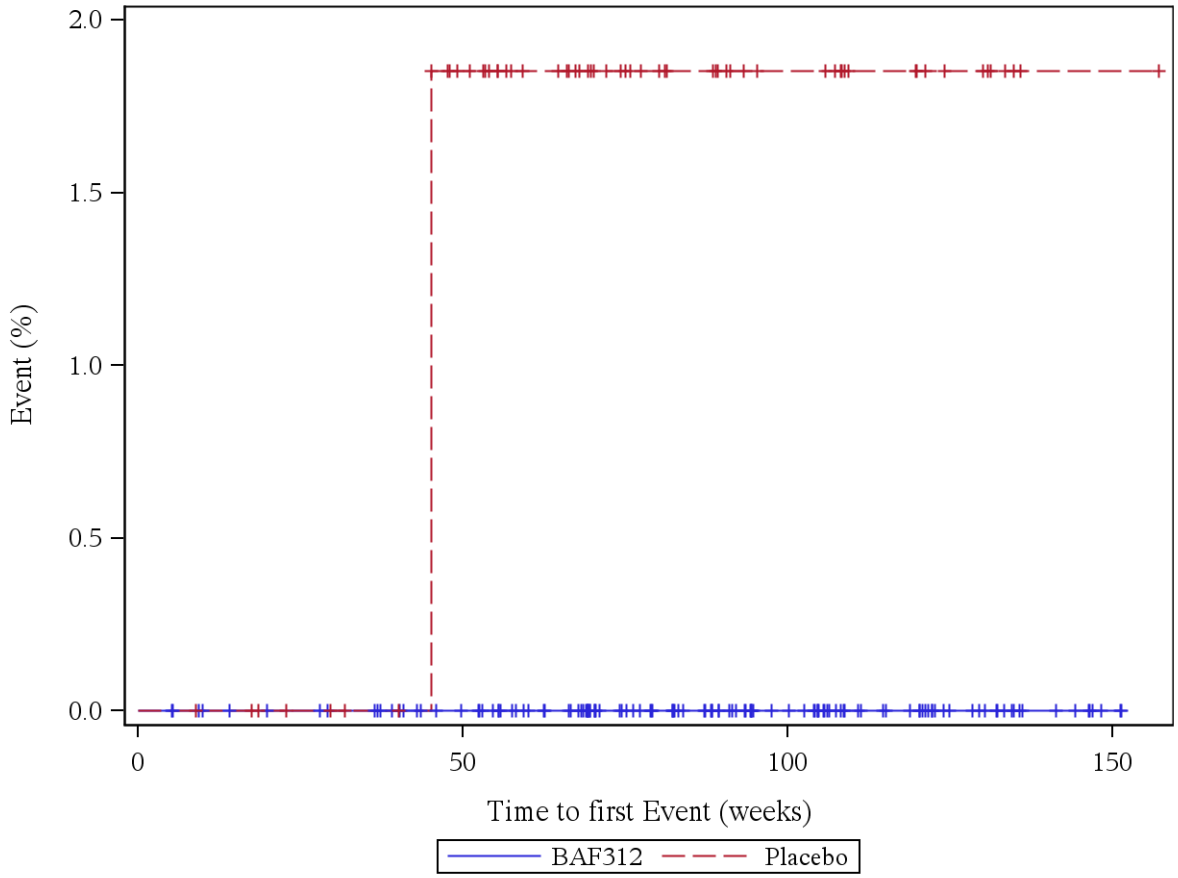


Patients at risk (BAF312/Placebo): Week 0: 127/61, Week 4: 116/59, Week 12: 112/59, Week 24: 110/56, Week 36: 107/53, Week 48: 98/49, Week 60: 89/38, Week 72: 71/31, Week 84: 59/24, Week 96: 44/16, Week 108: 34/14, Week 120: 27/9, Week 132: 14/4, Week 144: 6/1, Week 156: 0/1

Log rank test: p-value = 0,278
*: p < 0,05

Analysis population: A2304 SAF subpopulation "ACTIVE MS WITHOUT RELAPSES"

Figure 12.1.5.4: CARDIAC DISORDERS (SOC, severe)

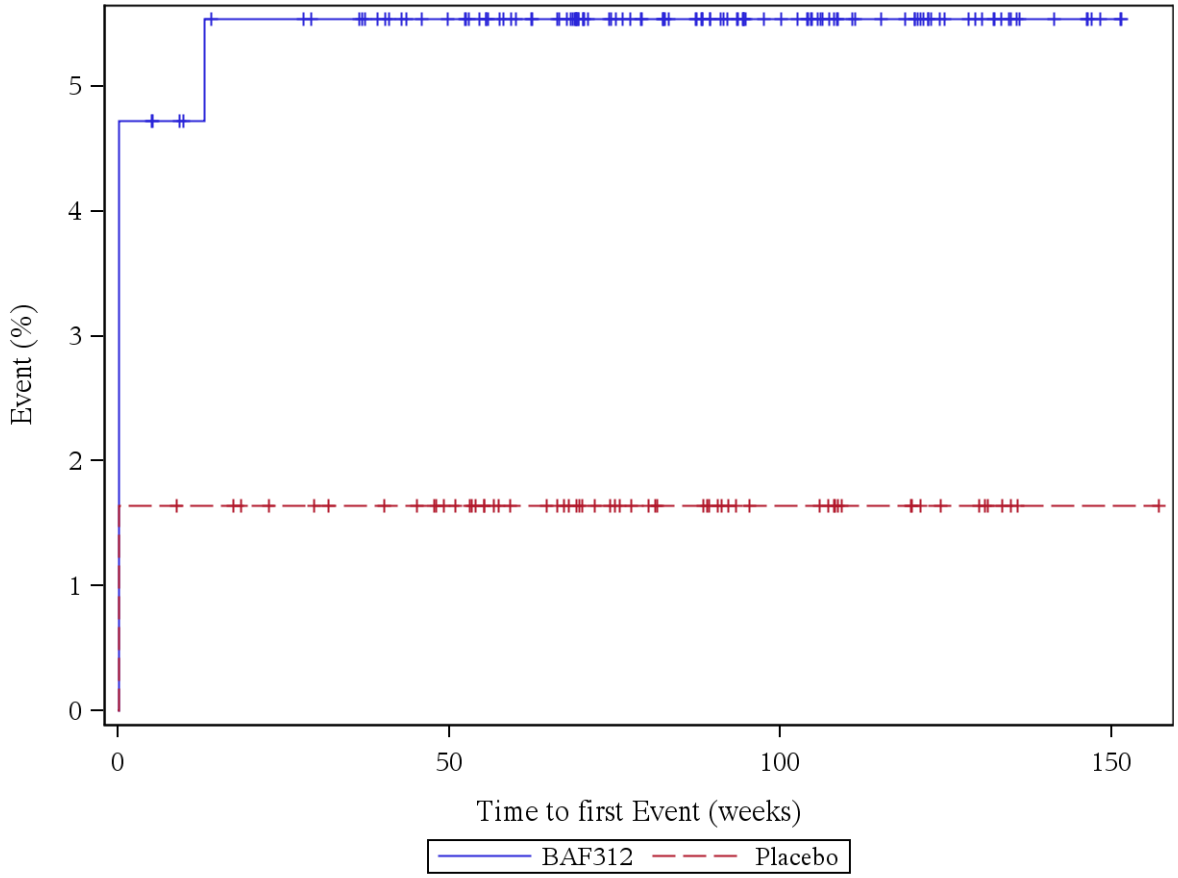


Patients at risk (BAF312/Placebo): Week 0: 127/61, Week 4: 127/61, Week 12: 123/60, Week 24: 121/57, Week 36: 119/55, Week 48: 110/50, Week 60: 99/40, Week 72: 80/31, Week 84: 66/24, Week 96: 49/17, Week 108: 36/15, Week 120: 28/9, Week 132: 15/4, Week 144: 7/1, Week 156: 0/1

Log rank test: p-value = -
*: p < 0,05

Analysis population: A2304 SAF subpopulation "ACTIVE MS WITHOUT RELAPSES"

Figure 12.1.5.5: BRADYCARDIA (PT, not severe)

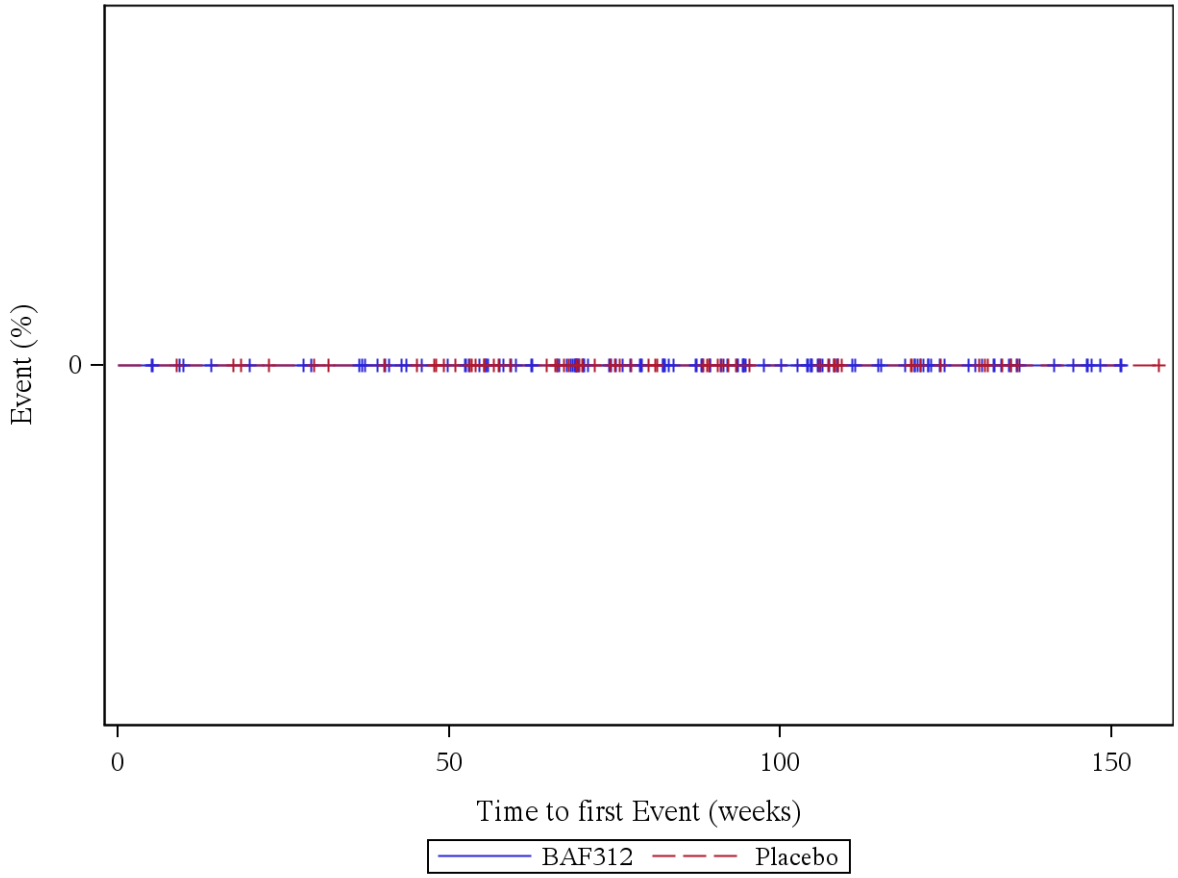


Patients at risk (BAF312/Placebo): Week 0: 127/61, Week 4: 121/60, Week 12: 117/59, Week 24: 115/56, Week 36: 113/54, Week 48: 104/50, Week 60: 93/40, Week 72: 74/32, Week 84: 62/25, Week 96: 45/17, Week 108: 34/15, Week 120: 27/9, Week 132: 14/4, Week 144: 6/1, Week 156: 0/1

Log rank test: p-value = 0,219
*: p < 0,05

Analysis population: A2304 SAF subpopulation "ACTIVE MS WITHOUT RELAPSES"

Figure 12.1.5.6: BRADYCARDIA (PT, severe)

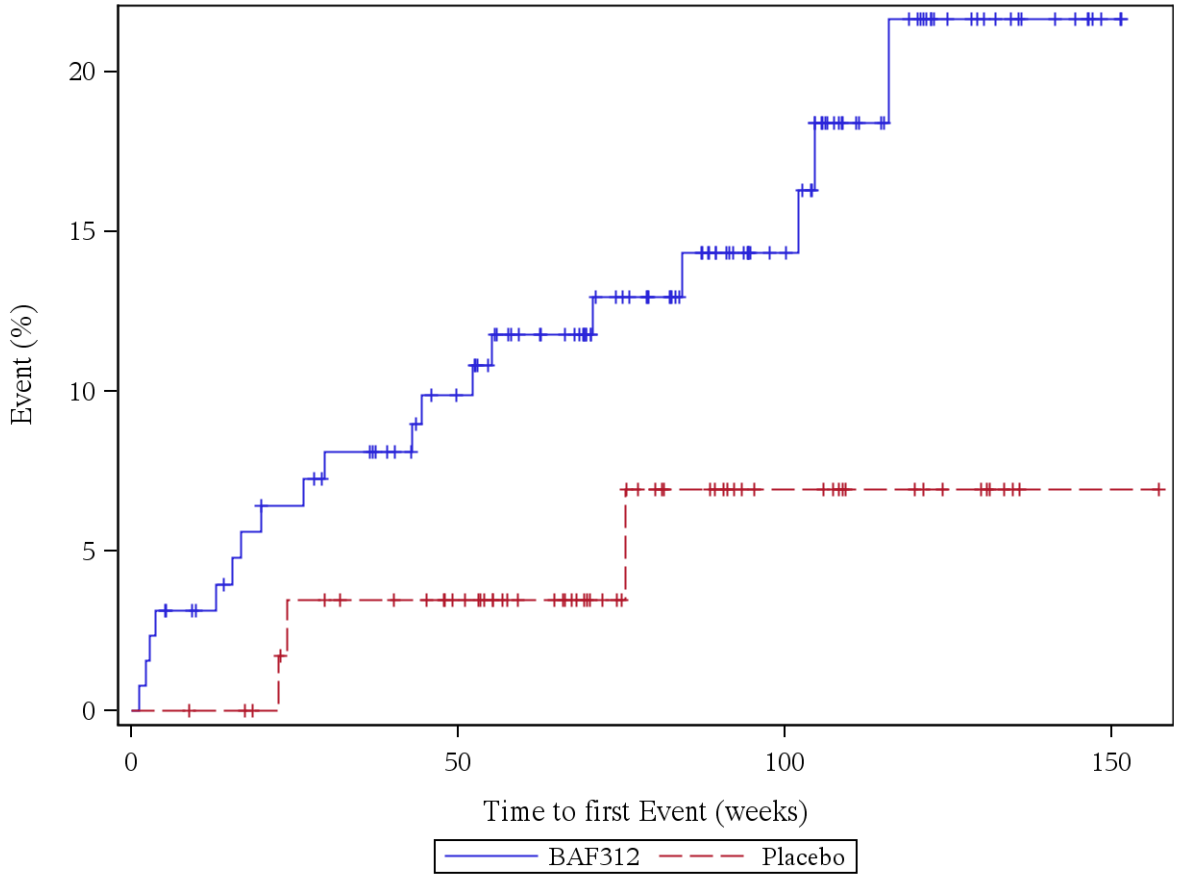


Patients at risk (BAF312/Placebo): Week 0: 127/61, Week 4: 127/61, Week 12: 123/60, Week 24: 121/57, Week 36: 119/55, Week 48: 110/51, Week 60: 99/41, Week 72: 80/32, Week 84: 66/25, Week 96: 49/17, Week 108: 36/15, Week 120: 28/9, Week 132: 15/4, Week 144: 7/1, Week 156: 0/1

Log rank test: p-value = -
*: p < 0,05

Analysis population: A2304 SAF subpopulation "ACTIVE MS WITHOUT RELAPSES"

Figure 12.1.5.7: EYE DISORDERS (SOC, not severe)

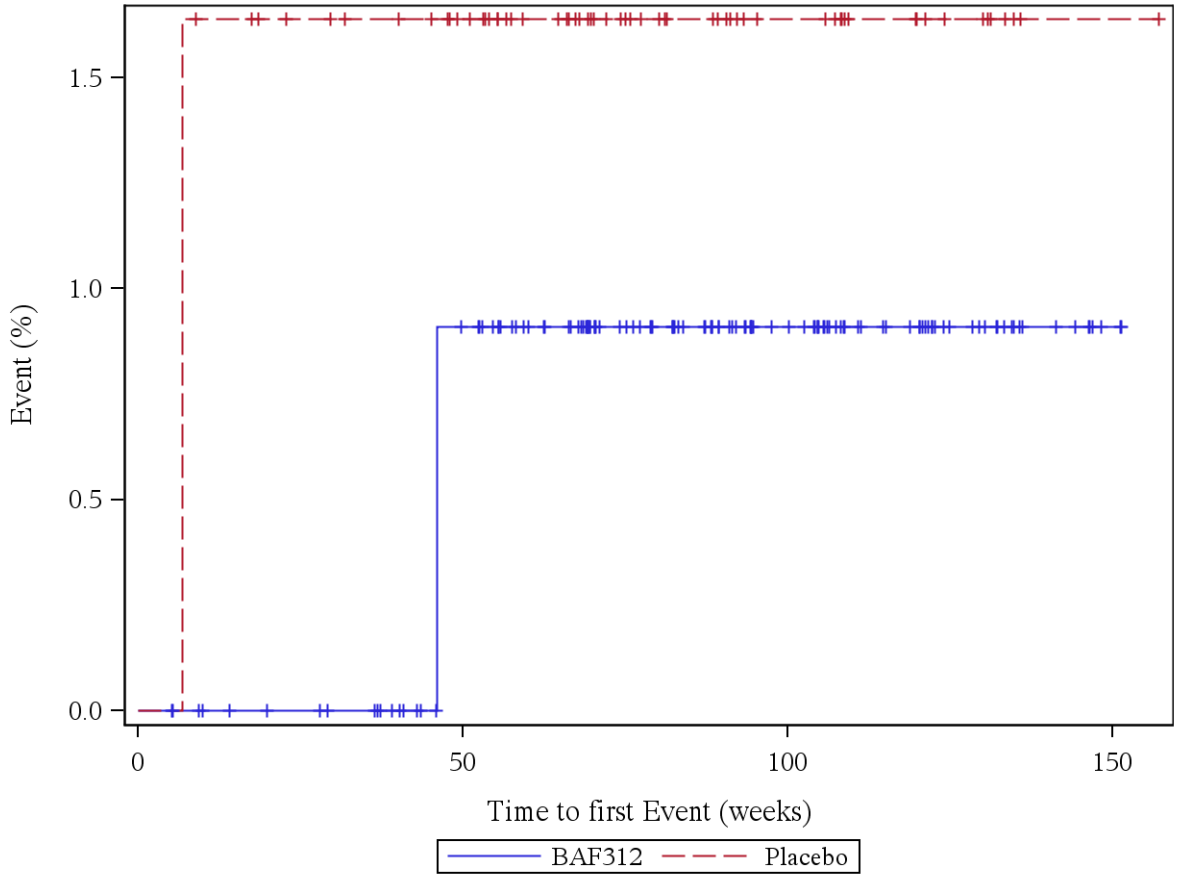


Patients at risk (BAF312/Placebo): Week 0: 127/61, Week 4: 123/61, Week 12: 119/60, Week 24: 113/55, Week 36: 109/53, Week 48: 99/49, Week 60: 87/39, Week 72: 73/30, Week 84: 62/22, Week 96: 46/15, Week 108: 32/13, Week 120: 23/9, Week 132: 12/4, Week 144: 7/1, Week 156: 0/1

Log rank test: p-value = 0,069
*: p < 0,05

Analysis population: A2304 SAF subpopulation "ACTIVE MS WITHOUT RELAPSES"

Figure 12.1.5.8: EYE DISORDERS (SOC, severe)

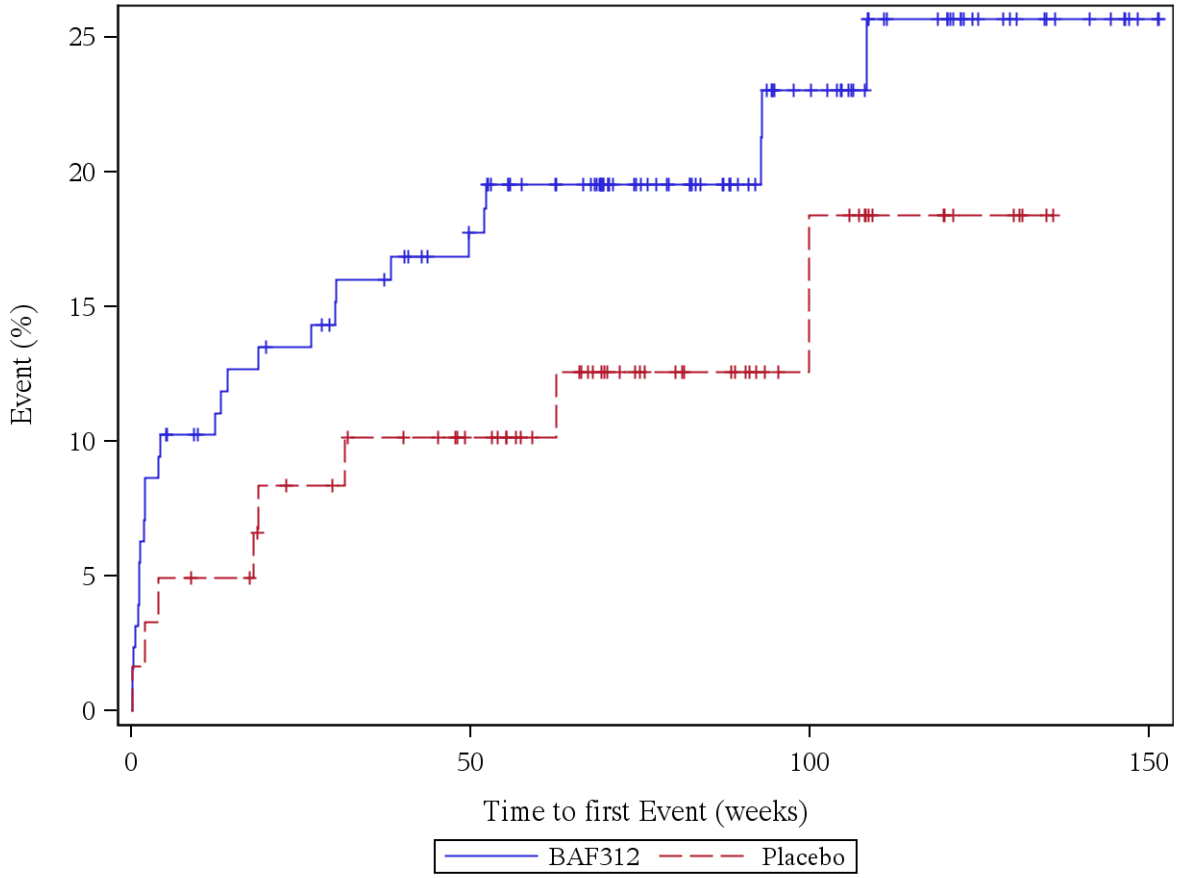


Patients at risk (BAF312/Placebo): Week 0: 127/61, Week 4: 127/61, Week 12: 123/59, Week 24: 121/56, Week 36: 119/54, Week 48: 109/50, Week 60: 98/40, Week 72: 79/31, Week 84: 66/24, Week 96: 49/17, Week 108: 36/15, Week 120: 28/9, Week 132: 15/4, Week 144: 7/1, Week 156: 0/1

Log rank test: p-value = 0,596
*: p < 0,05

Analysis population: A2304 SAF subpopulation "ACTIVE MS WITHOUT RELAPSES"

Figure 12.1.5.9: GASTROINTESTINAL DISORDERS (SOC, not severe)

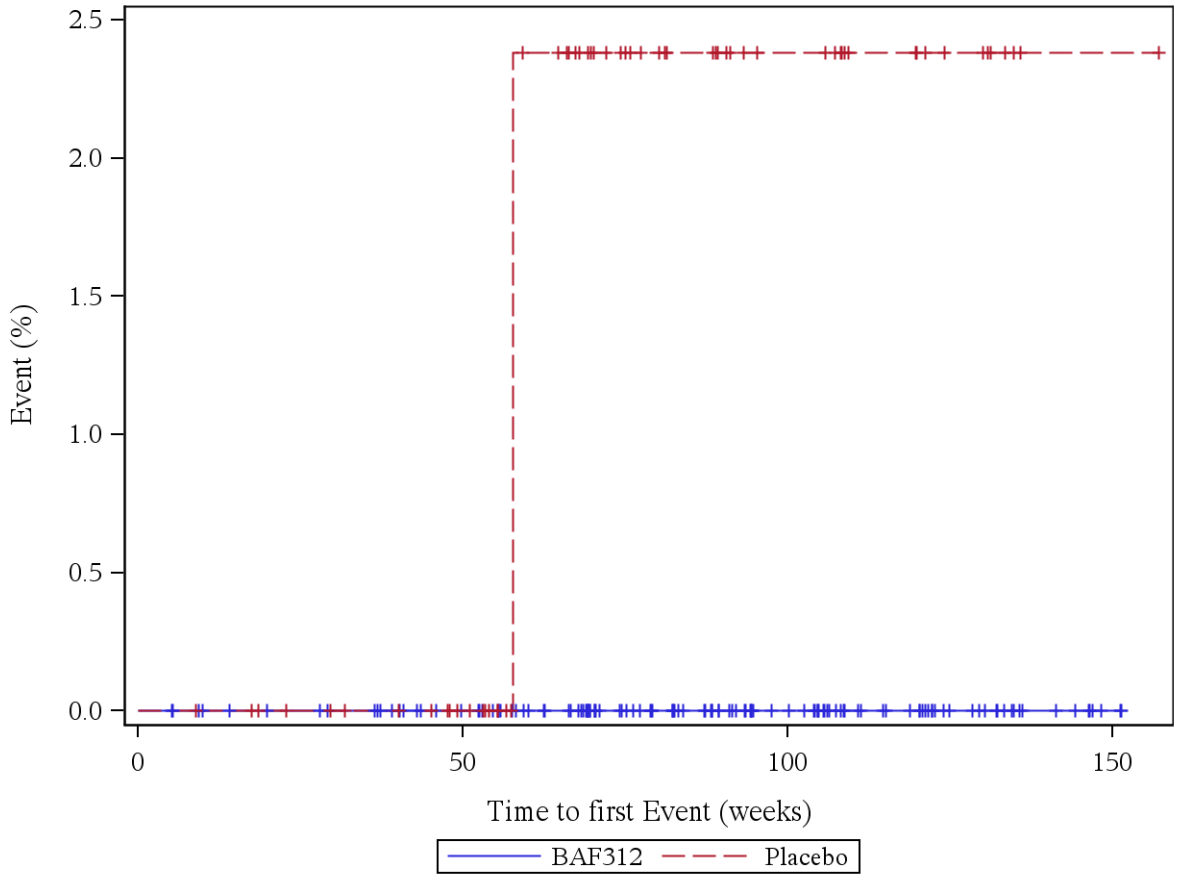


Patients at risk (BAF312/Placebo): Week 0: 127/61, Week 4: 115/58, Week 12: 110/57, Week 24: 105/52, Week 36: 100/49, Week 48: 94/45, Week 60: 83/37, Week 72: 66/28, Week 84: 54/22, Week 96: 39/15, Week 108: 30/12, Week 120: 23/6, Week 132: 11/2, Week 144: 7/0, Week 156: 0/0

Log rank test: p-value = 0,222
*: p < 0,05

Analysis population: A2304 SAF subpopulation "ACTIVE MS WITHOUT RELAPSES"

Figure 12.1.5.10: GASTROINTESTINAL DISORDERS (SOC, severe)

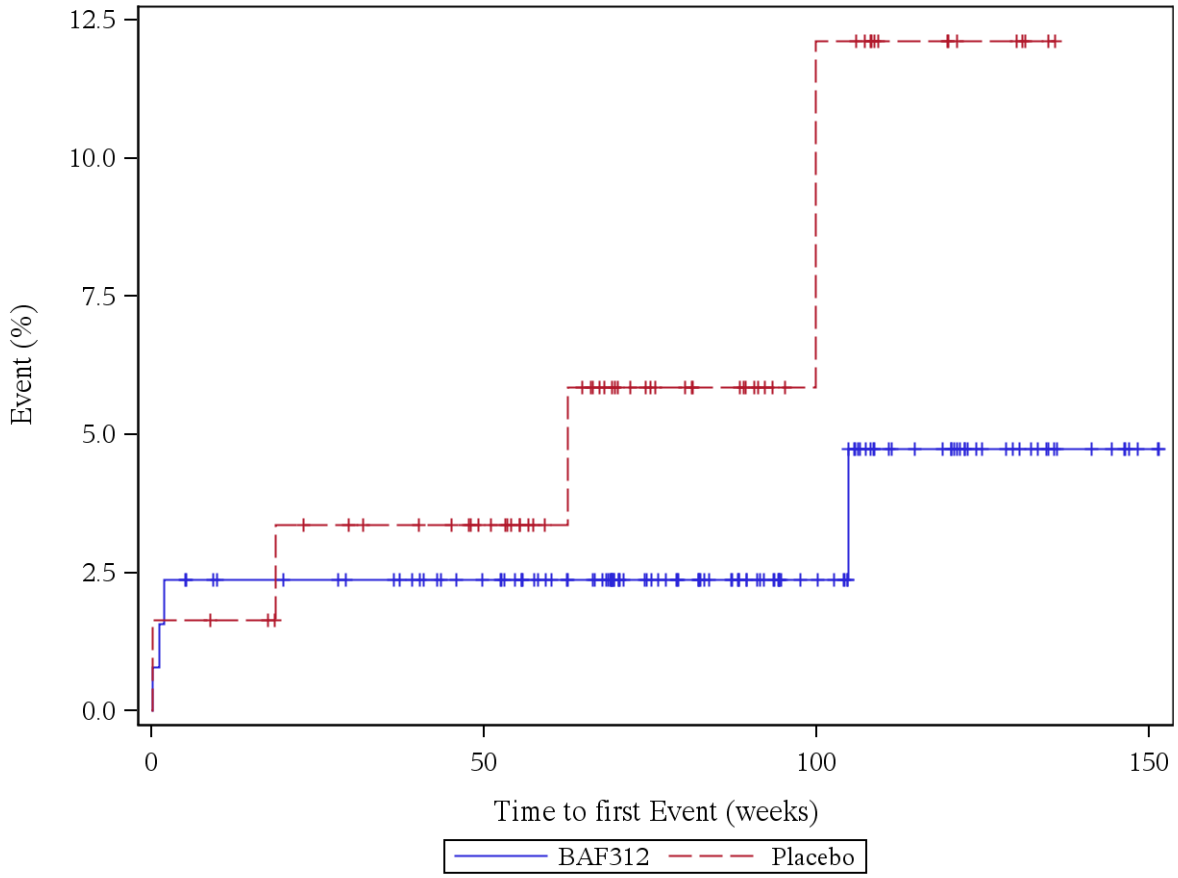


Patients at risk (BAF312/Placebo): Week 0: 127/61, Week 4: 127/61, Week 12: 123/60, Week 24: 121/57, Week 36: 119/55, Week 48: 110/51, Week 60: 99/40, Week 72: 80/31, Week 84: 66/24, Week 96: 49/17, Week 108: 36/15, Week 120: 28/9, Week 132: 15/4, Week 144: 7/1, Week 156: 0/1

Log rank test: p-value = -
*: p < 0,05

Analysis population: A2304 SAF subpopulation "ACTIVE MS WITHOUT RELAPSES"

Figure 12.1.5.11: NAUSEA (PT, not severe)

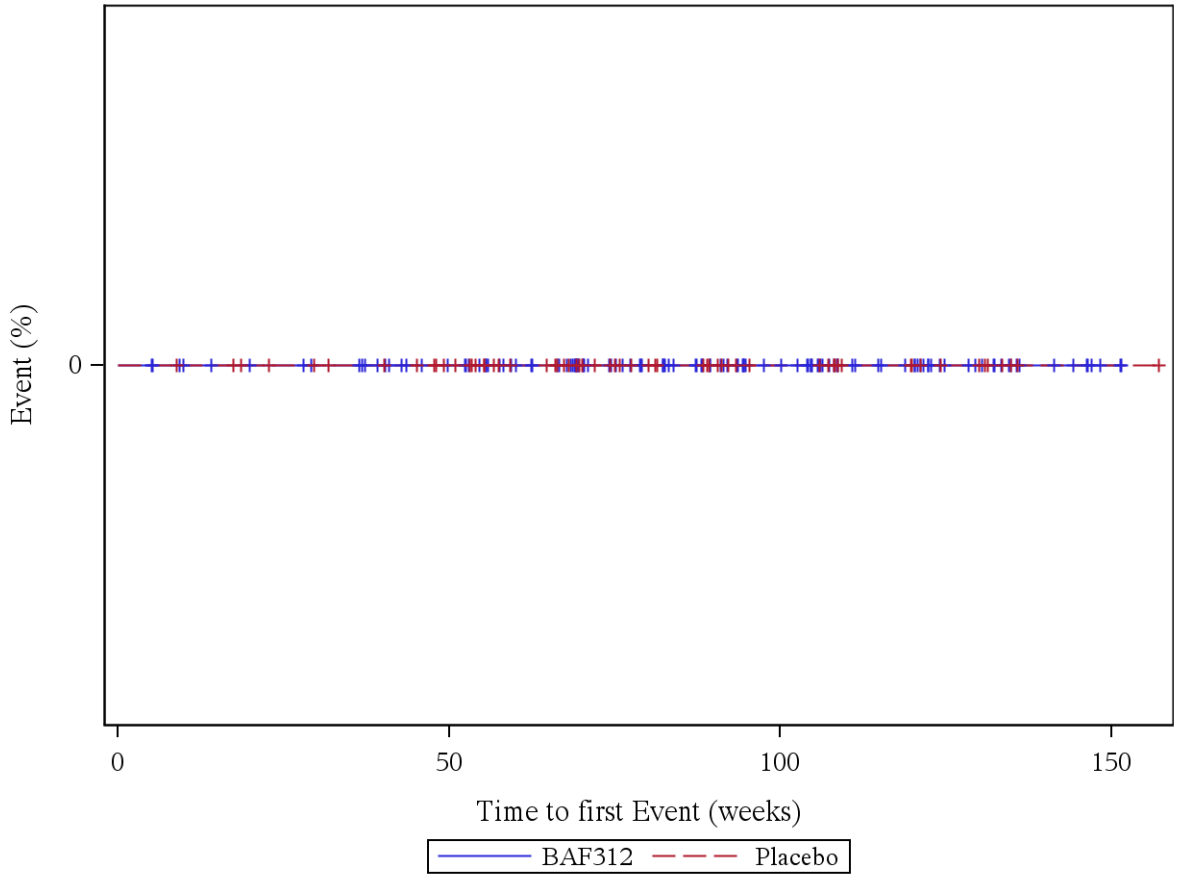


Patients at risk (BAF312/Placebo): Week 0: 127/61, Week 4: 124/60, Week 12: 120/59, Week 24: 119/55, Week 36: 117/53, Week 48: 109/49, Week 60: 98/39, Week 72: 79/29, Week 84: 65/23, Week 96: 48/15, Week 108: 34/12, Week 120: 27/6, Week 132: 14/2, Week 144: 7/0, Week 156: 0/0

Log rank test: p-value = 0,217
*: p < 0,05

Analysis population: A2304 SAF subpopulation "ACTIVE MS WITHOUT RELAPSES"

Figure 12.1.5.12: NAUSEA (PT, severe)

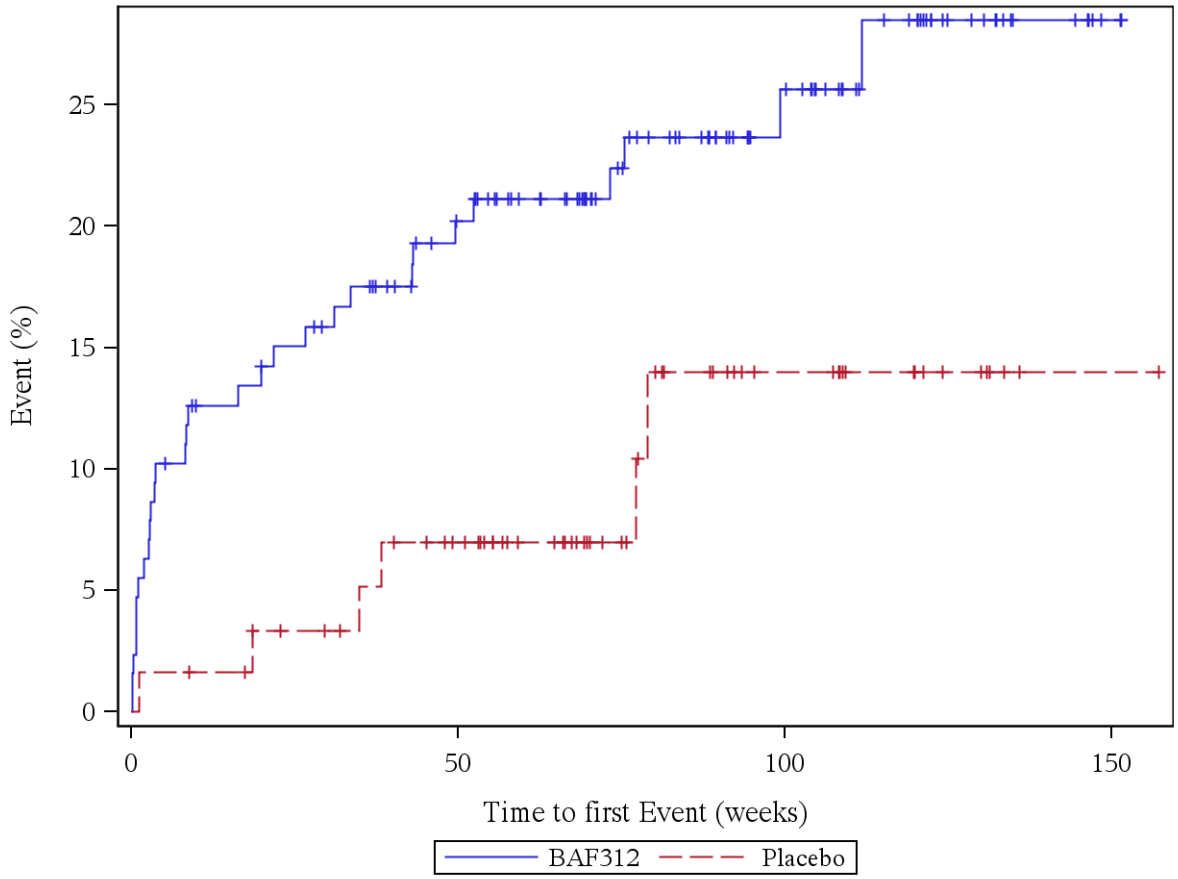


Patients at risk (BAF312/Placebo): Week 0: 127/61, Week 4: 127/61, Week 12: 123/60, Week 24: 121/57, Week 36: 119/55, Week 48: 110/51, Week 60: 99/41, Week 72: 80/32, Week 84: 66/25, Week 96: 49/17, Week 108: 36/15, Week 120: 28/9, Week 132: 15/4, Week 144: 7/1, Week 156: 0/1

Log rank test: p-value = -
*: p < 0,05

Analysis population: A2304 SAF subpopulation "ACTIVE MS WITHOUT RELAPSES"

Figure 12.1.5.13: GENERAL DISORDERS AND ADMINISTRATION SITE CONDITIONS (SOC, not severe)

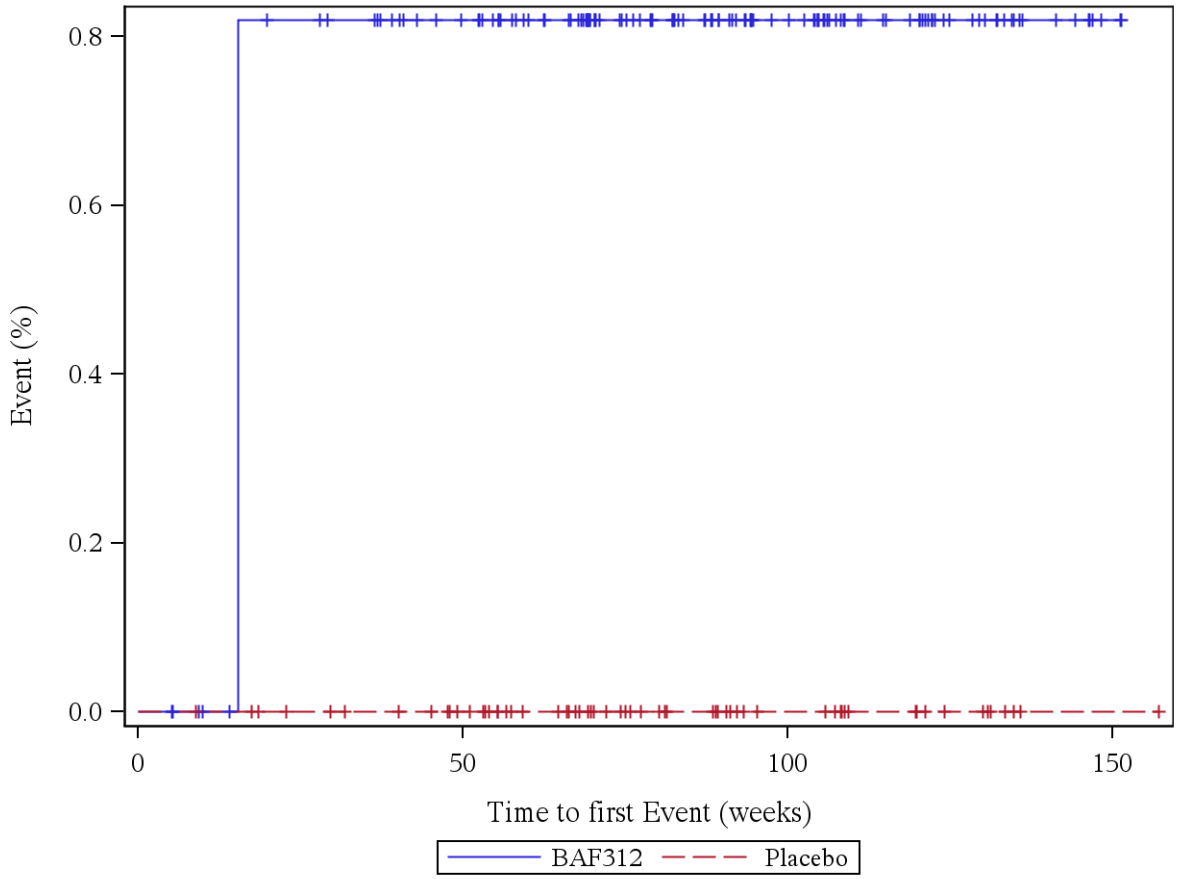


Patients at risk (BAF312/Placebo): Week 0: 127/61, Week 4: 114/60, Week 12: 108/59, Week 24: 104/55, Week 36: 99/52, Week 48: 89/48, Week 60: 77/38, Week 72: 63/29, Week 84: 53/21, Week 96: 39/15, Week 108: 31/14, Week 120: 23/8, Week 132: 12/3, Week 144: 7/1, Week 156: 0/1

Log rank test: p-value = 0,032 *
*: p < 0,05

Analysis population: A2304 SAF subpopulation "ACTIVE MS WITHOUT RELAPSES"

Figure 12.1.5.14: GENERAL DISORDERS AND ADMINISTRATION SITE CONDITIONS (SOC, severe)

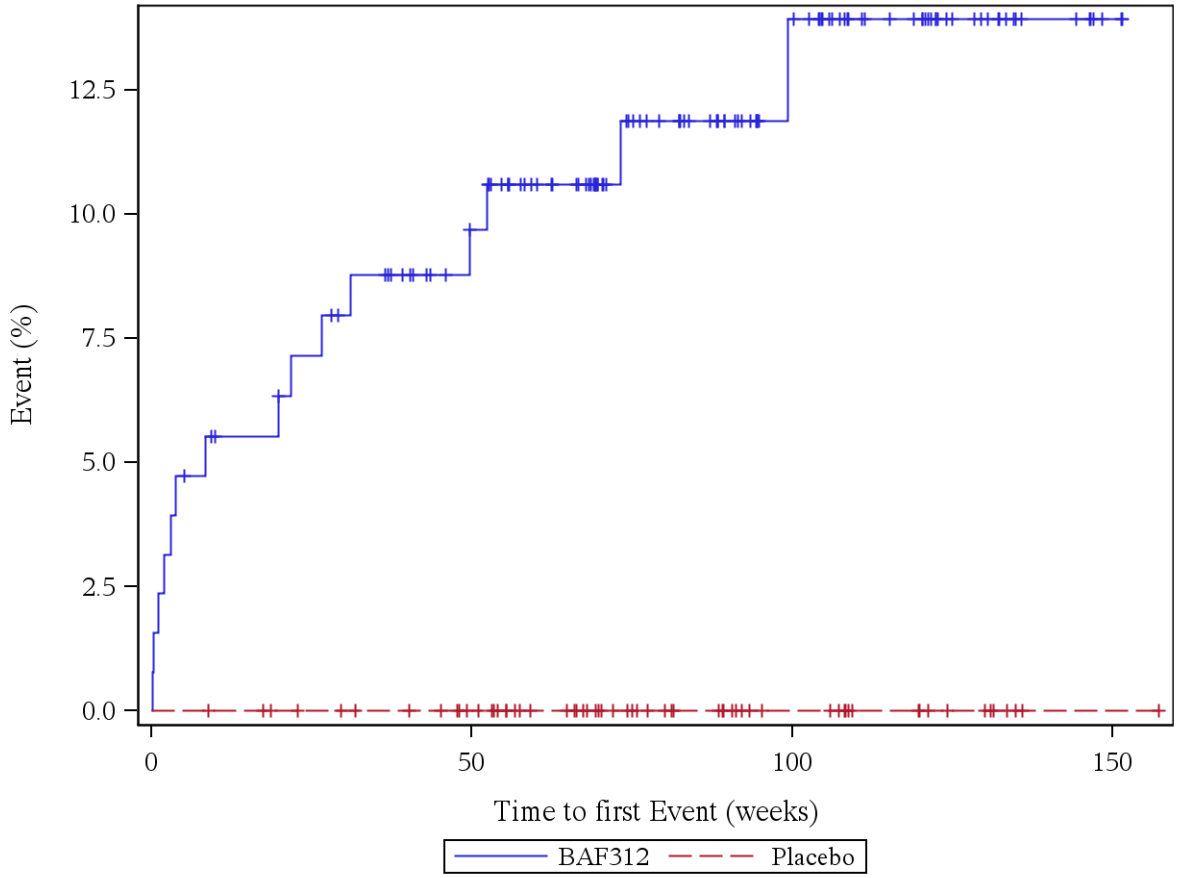


Patients at risk (BAF312/Placebo): Week 0: 127/61, Week 4: 127/61, Week 12: 123/60, Week 24: 120/57, Week 36: 118/55, Week 48: 110/51, Week 60: 99/41, Week 72: 80/32, Week 84: 66/25, Week 96: 49/17, Week 108: 36/15, Week 120: 28/9, Week 132: 15/4, Week 144: 7/1, Week 156: 0/1

Log rank test: p-value = -
*: p < 0,05

Analysis population: A2304 SAF subpopulation "ACTIVE MS WITHOUT RELAPSES"

Figure 12.1.5.15: FATIGUE (PT, not severe)

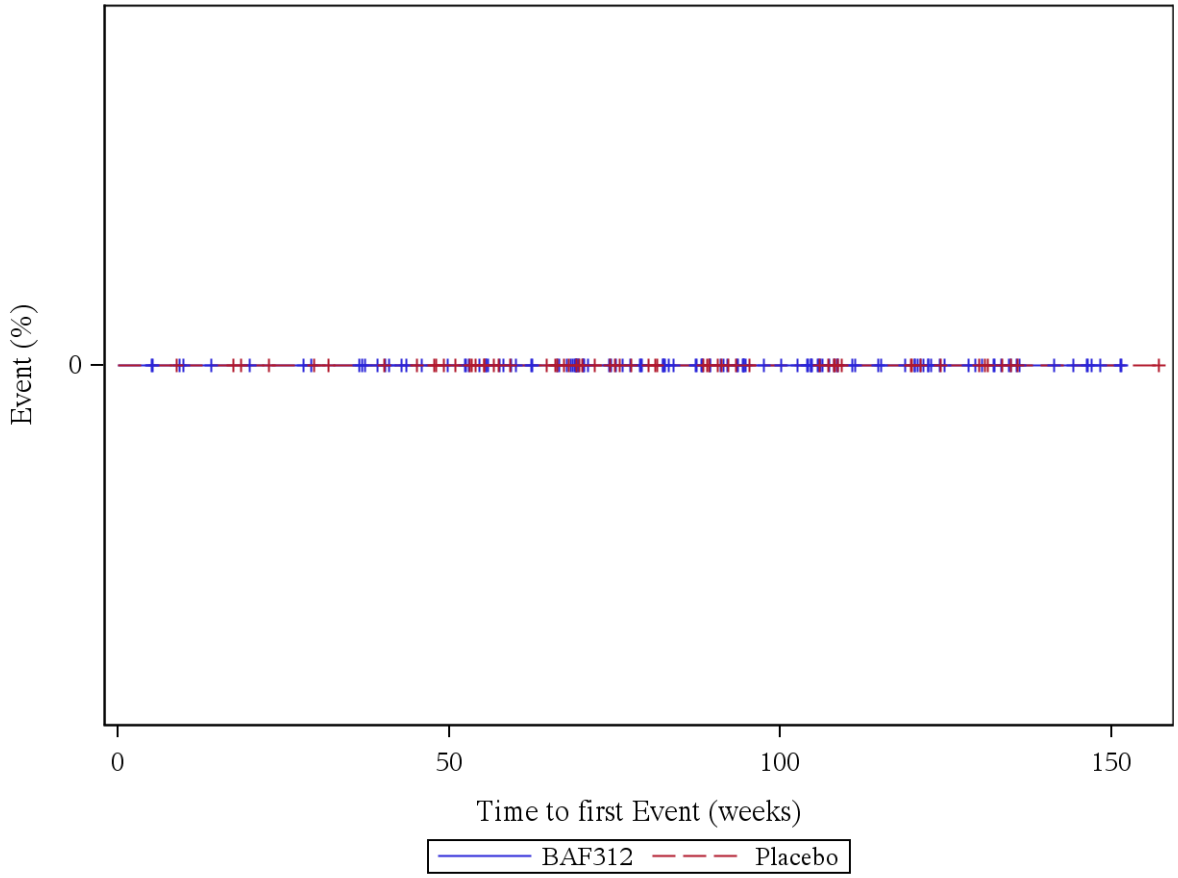


Patients at risk (BAF312/Placebo): Week 0: 127/61, Week 4: 121/61, Week 12: 117/60, Week 24: 114/57, Week 36: 110/55, Week 48: 101/51, Week 60: 88/41, Week 72: 70/32, Week 84: 58/25, Week 96: 43/17, Week 108: 33/15, Week 120: 26/9, Week 132: 13/4, Week 144: 7/1, Week 156: 0/1

Log rank test: p-value = -
*: p < 0,05

Analysis population: A2304 SAF subpopulation "ACTIVE MS WITHOUT RELAPSES"

Figure 12.1.5.16: FATIGUE (PT, severe)

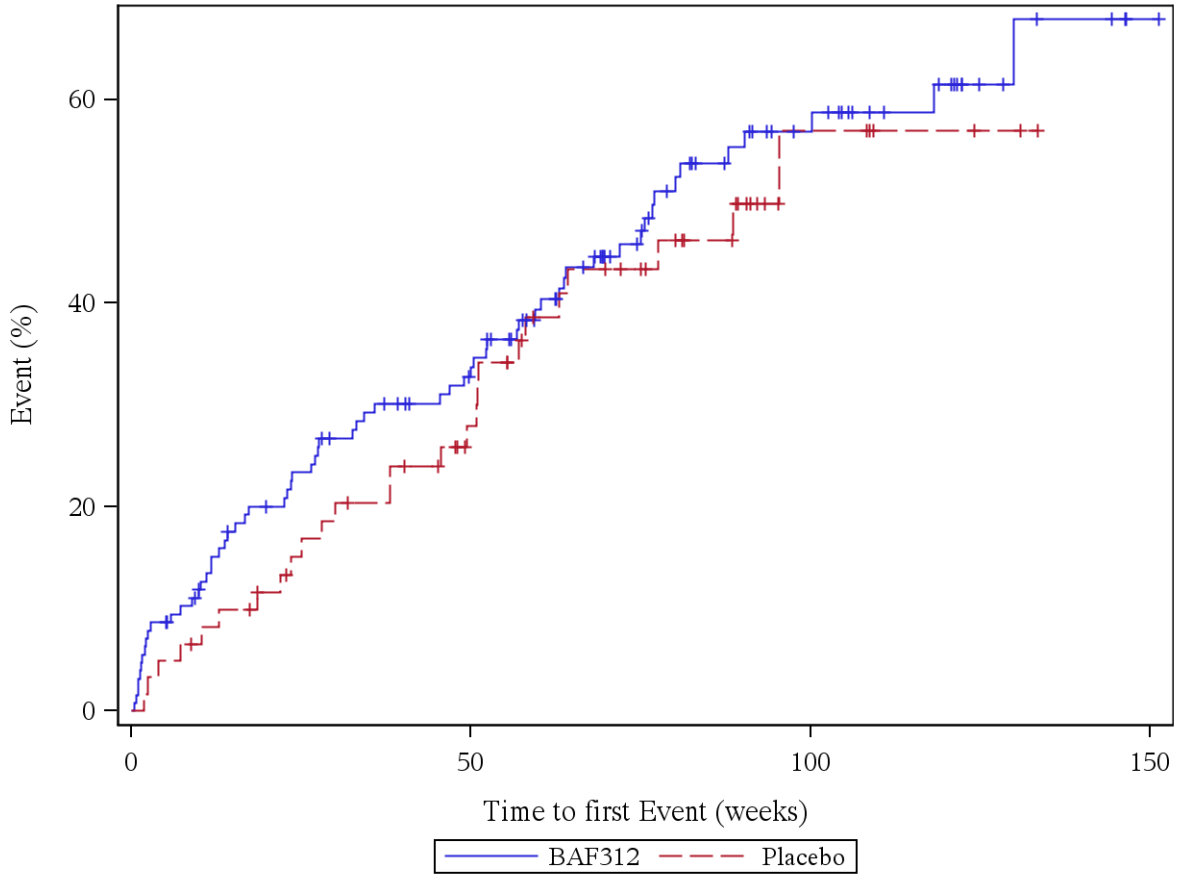


Patients at risk (BAF312/Placebo): Week 0: 127/61, Week 4: 127/61, Week 12: 123/60, Week 24: 121/57, Week 36: 119/55, Week 48: 110/51, Week 60: 99/41, Week 72: 80/32, Week 84: 66/25, Week 96: 49/17, Week 108: 36/15, Week 120: 28/9, Week 132: 15/4, Week 144: 7/1, Week 156: 0/1

Log rank test: p-value = -
*: p < 0,05

Analysis population: A2304 SAF subpopulation "ACTIVE MS WITHOUT RELAPSES"

Figure 12.1.5.17: INFECTIONS AND INFESTATIONS (SOC, not severe)

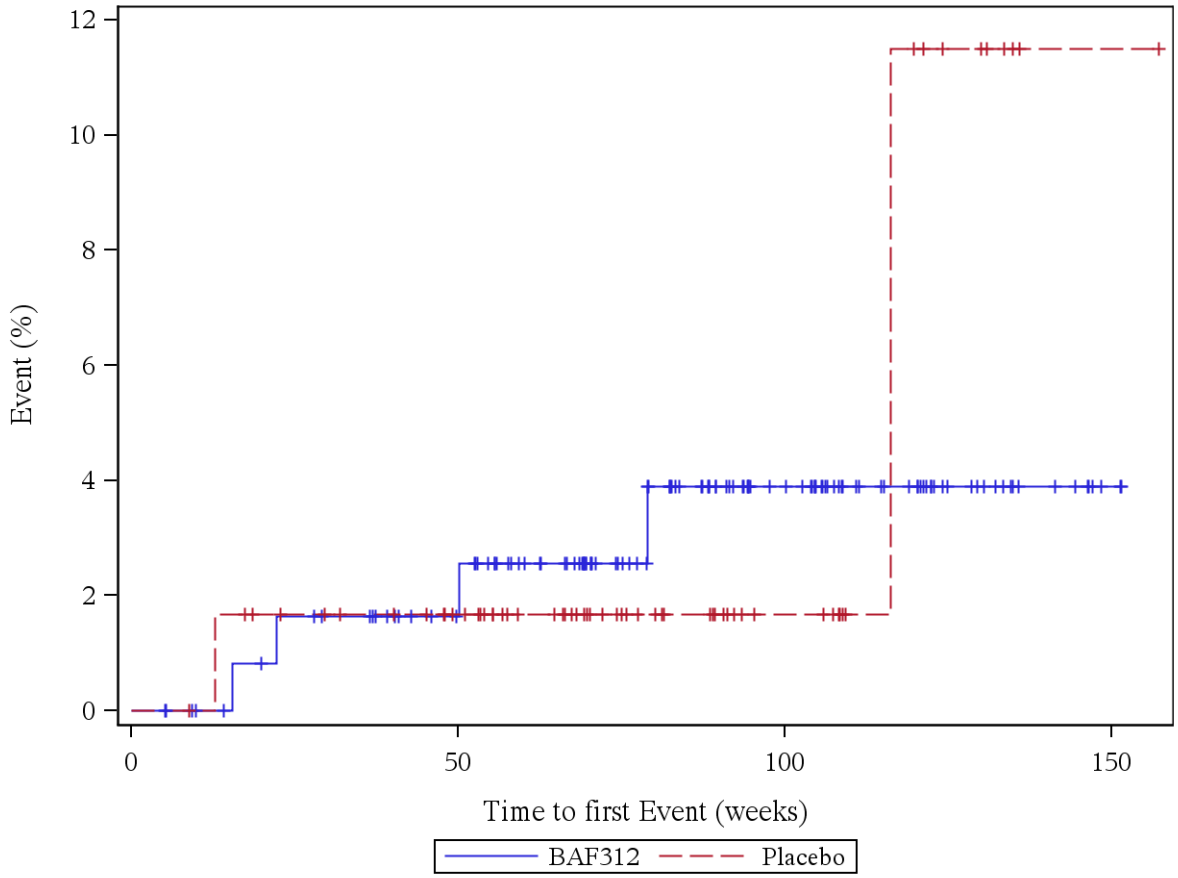


Patients at risk (BAF312/Placebo): Week 0: 127/61, Week 4: 116/58, Week 12: 104/55, Week 24: 92/48, Week 36: 82/44, Week 48: 76/37, Week 60: 60/26, Week 72: 44/22, Week 84: 31/16, Week 96: 24/6, Week 108: 17/6, Week 120: 13/3, Week 132: 5/1, Week 144: 4/0, Week 156: 0/0

Log rank test: p-value = 0,422
*: p < 0,05

Analysis population: A2304 SAF subpopulation "ACTIVE MS WITHOUT RELAPSES"

Figure 12.1.5.18: INFECTIONS AND INFESTATIONS (SOC, severe)

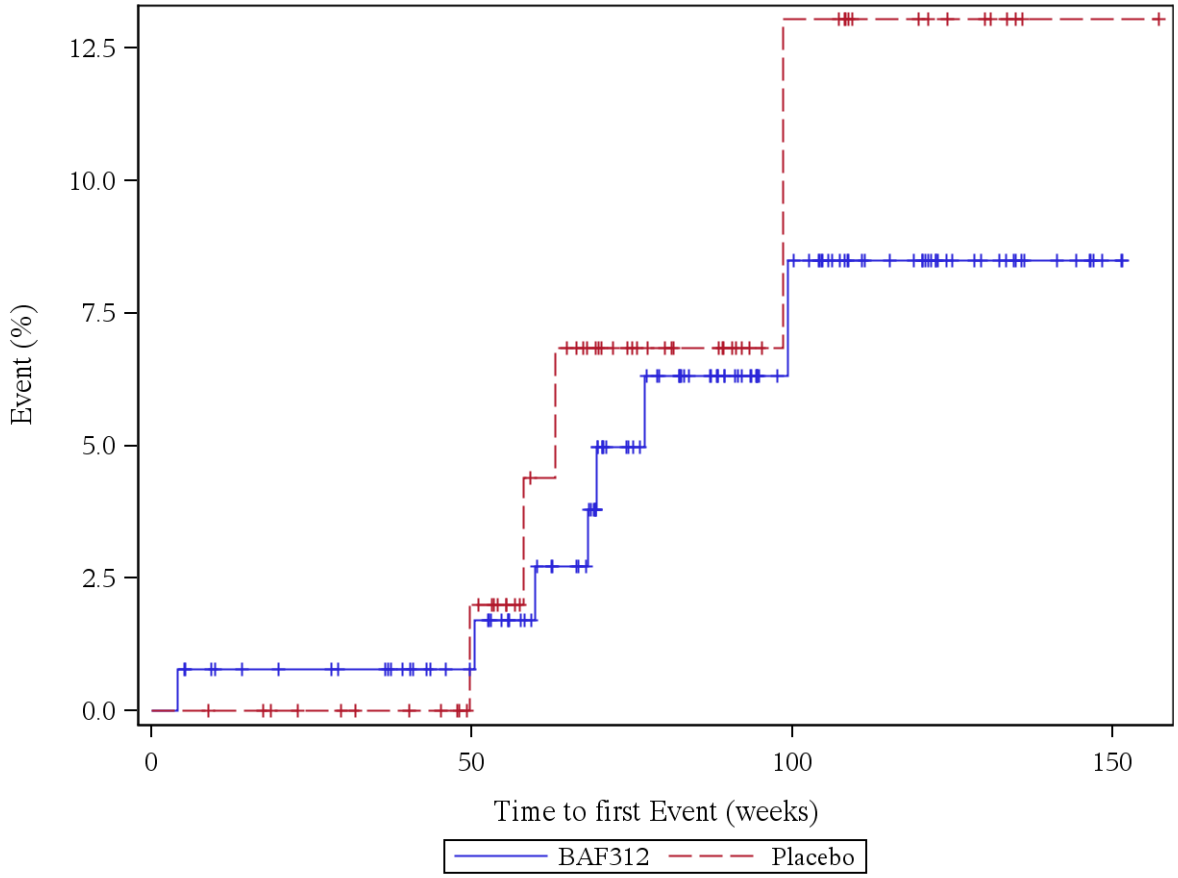


Patients at risk (BAF312/Placebo): Week 0: 127/61, Week 4: 127/61, Week 12: 123/60, Week 24: 119/56, Week 36: 117/54, Week 48: 109/50, Week 60: 97/40, Week 72: 79/31, Week 84: 64/24, Week 96: 47/16, Week 108: 34/14, Week 120: 26/8, Week 132: 13/4, Week 144: 7/1, Week 156: 0/1

Log rank test: p-value = 0,879
*: p < 0,05

Analysis population: A2304 SAF subpopulation "ACTIVE MS WITHOUT RELAPSES"

Figure 12.1.5.19: INFLUENZA (PT, not severe)

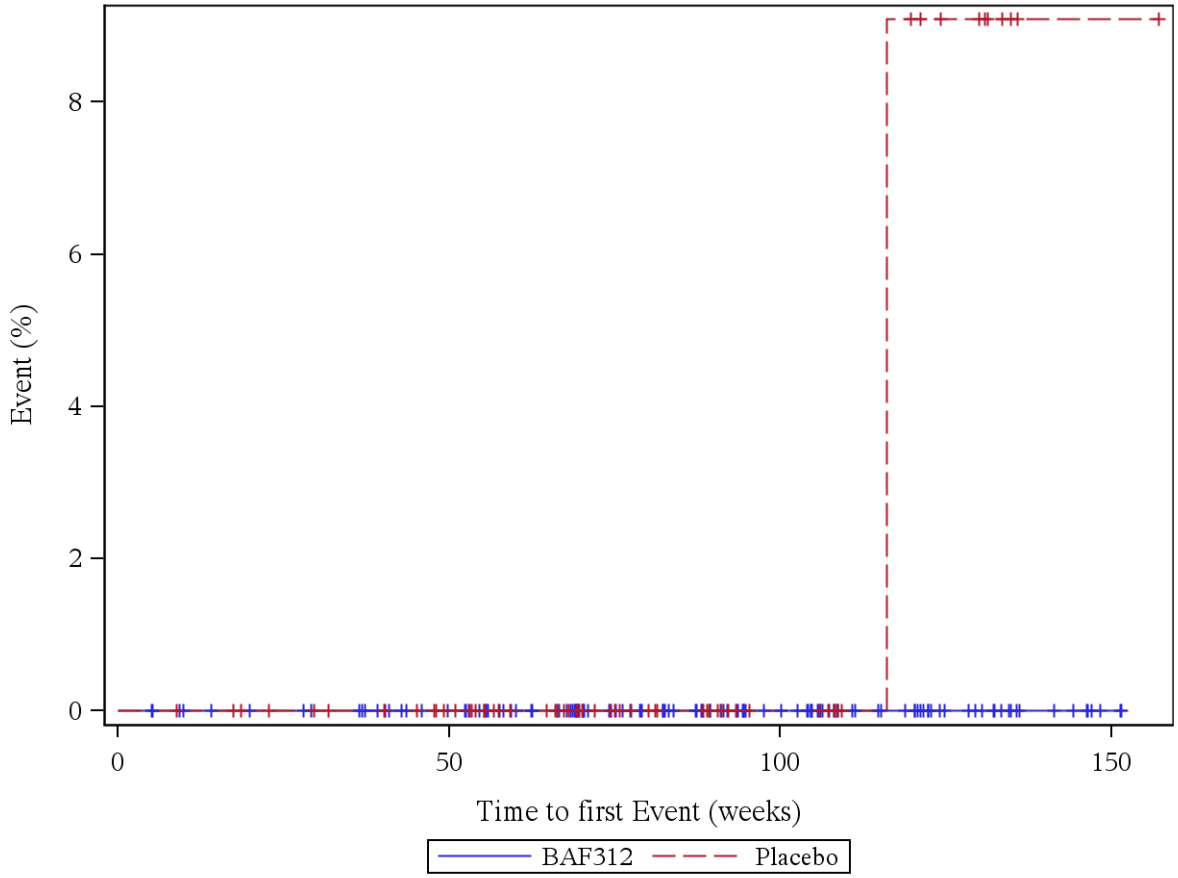


Patients at risk (BAF312/Placebo): Week 0: 127/61, Week 4: 126/61, Week 12: 122/60, Week 24: 120/57, Week 36: 118/55, Week 48: 109/51, Week 60: 96/39, Week 72: 75/30, Week 84: 61/23, Week 96: 44/15, Week 108: 33/13, Week 120: 26/8, Week 132: 14/4, Week 144: 7/1, Week 156: 0/1

Log rank test: p-value = 0,579
*: p < 0,05

Analysis population: A2304 SAF subpopulation "ACTIVE MS WITHOUT RELAPSES"

Figure 12.1.5.20: INFLUENZA (PT, severe)

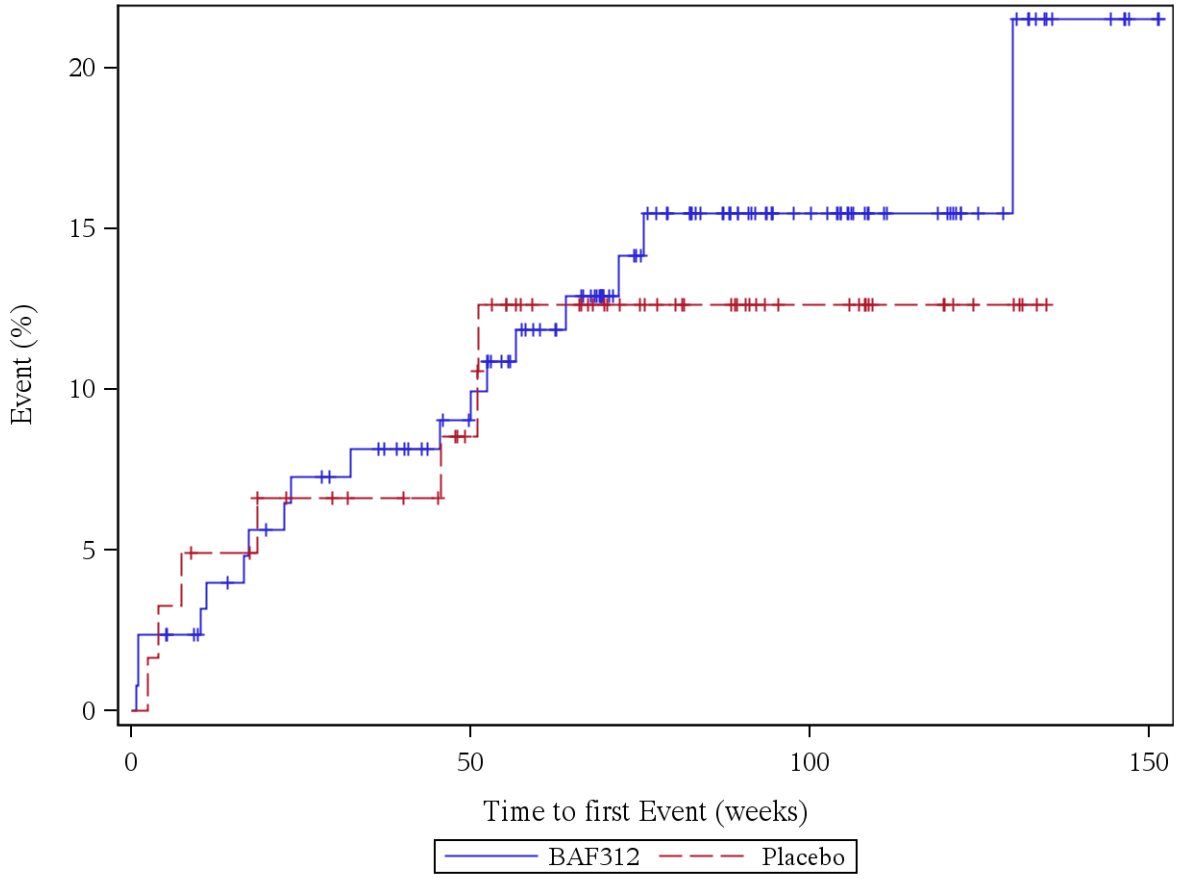


Patients at risk (BAF312/Placebo): Week 0: 127/61, Week 4: 127/61, Week 12: 123/60, Week 24: 121/57, Week 36: 119/55, Week 48: 110/51, Week 60: 99/41, Week 72: 80/32, Week 84: 66/25, Week 96: 49/17, Week 108: 36/15, Week 120: 28/9, Week 132: 15/4, Week 144: 7/1, Week 156: 0/1

Log rank test: p-value = -
*: p < 0,05

Analysis population: A2304 SAF subpopulation "ACTIVE MS WITHOUT RELAPSES"

Figure 12.1.5.21: NASOPHARYNGITIS (PT, not severe)

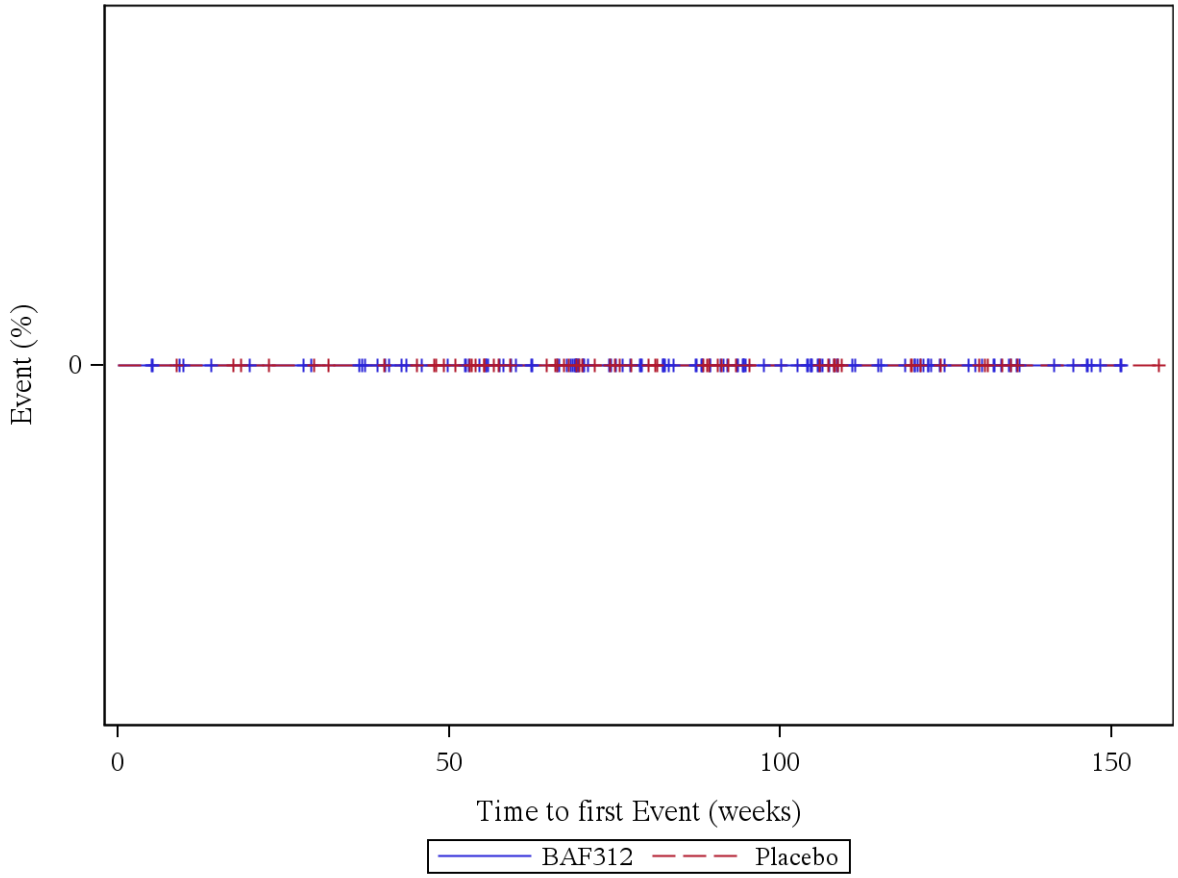


Patients at risk (BAF312/Placebo): Week 0: 127/61, Week 4: 124/59, Week 12: 118/57, Week 24: 112/53, Week 36: 109/51, Week 48: 100/46, Week 60: 87/36, Week 72: 68/29, Week 84: 54/23, Week 96: 39/15, Week 108: 28/13, Week 120: 22/7, Week 132: 12/2, Week 144: 6/0, Week 156: 0/0

Log rank test: p-value = 0,699
*: p < 0,05

Analysis population: A2304 SAF subpopulation "ACTIVE MS WITHOUT RELAPSES"

Figure 12.1.5.22: NASOPHARYNGITIS (PT, severe)

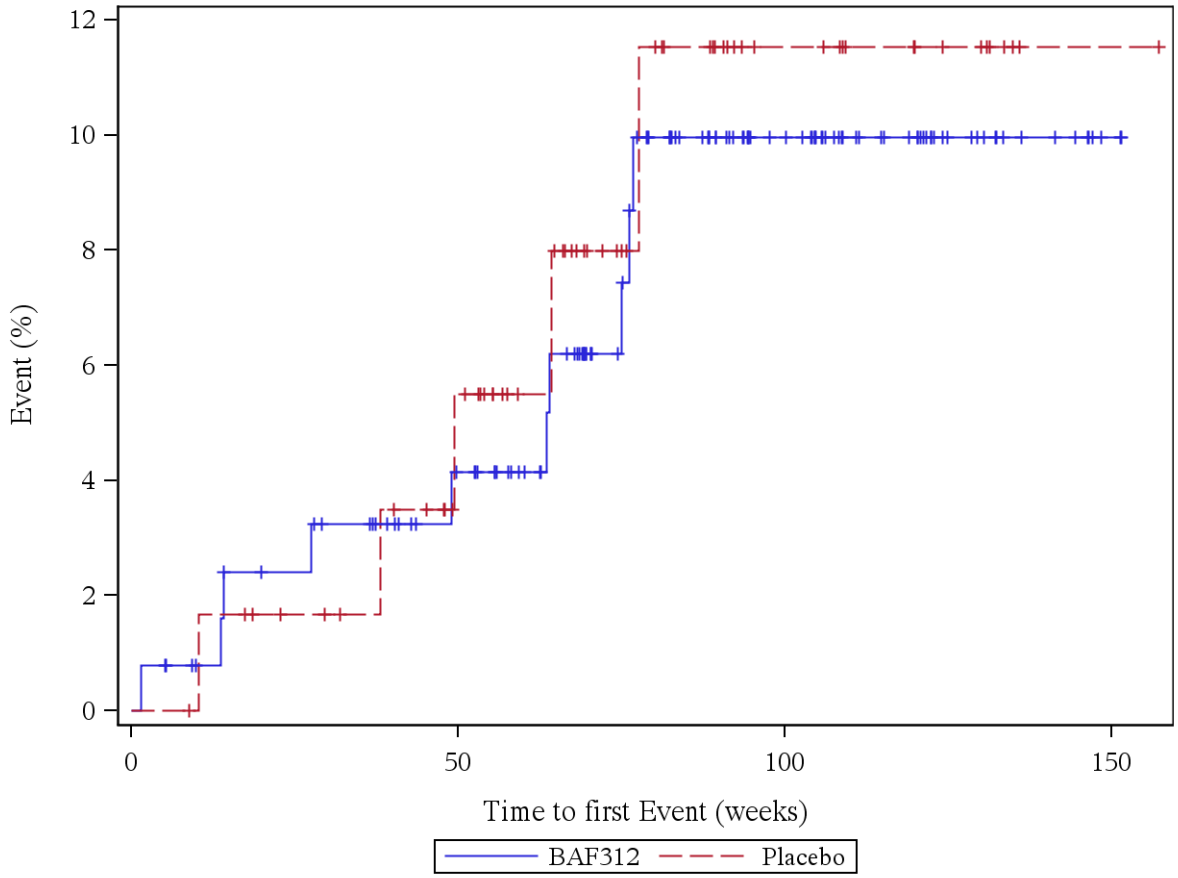


Patients at risk (BAF312/Placebo): Week 0: 127/61, Week 4: 127/61, Week 12: 123/60, Week 24: 121/57, Week 36: 119/55, Week 48: 110/51, Week 60: 99/41, Week 72: 80/32, Week 84: 66/25, Week 96: 49/17, Week 108: 36/15, Week 120: 28/9, Week 132: 15/4, Week 144: 7/1, Week 156: 0/1

Log rank test: p-value = -
*: p < 0,05

Analysis population: A2304 SAF subpopulation "ACTIVE MS WITHOUT RELAPSES"

Figure 12.1.5.23: UPPER RESPIRATORY TRACT INFECTION (PT, not severe)

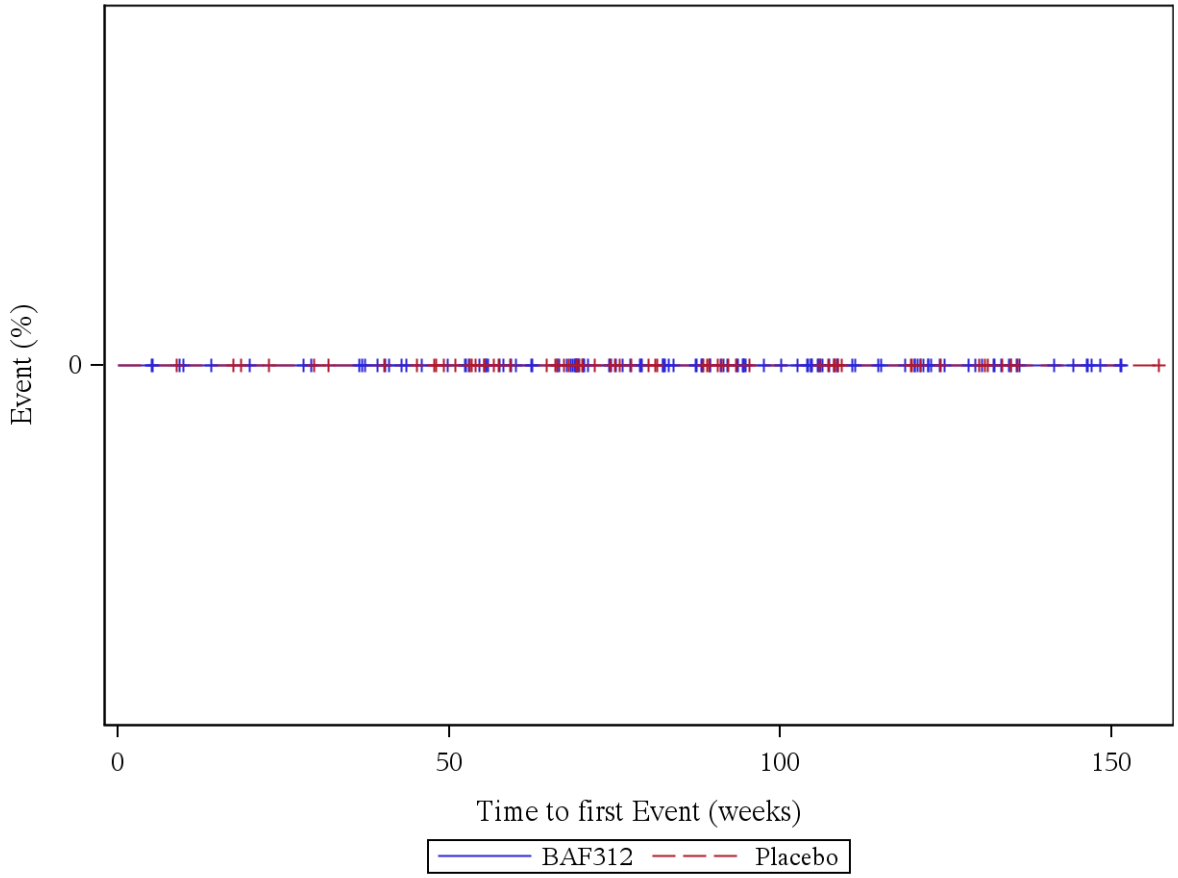


Patients at risk (BAF312/Placebo): Week 0: 127/61, Week 4: 126/61, Week 12: 122/59, Week 24: 118/56, Week 36: 115/54, Week 48: 107/49, Week 60: 96/38, Week 72: 77/29, Week 84: 61/22, Week 96: 45/14, Week 108: 33/13, Week 120: 25/8, Week 132: 12/4, Week 144: 7/1, Week 156: 0/1

Log rank test: p-value = 0,788
*: p < 0,05

Analysis population: A2304 SAF subpopulation "ACTIVE MS WITHOUT RELAPSES"

Figure 12.1.5.24: UPPER RESPIRATORY TRACT INFECTION (PT, severe)

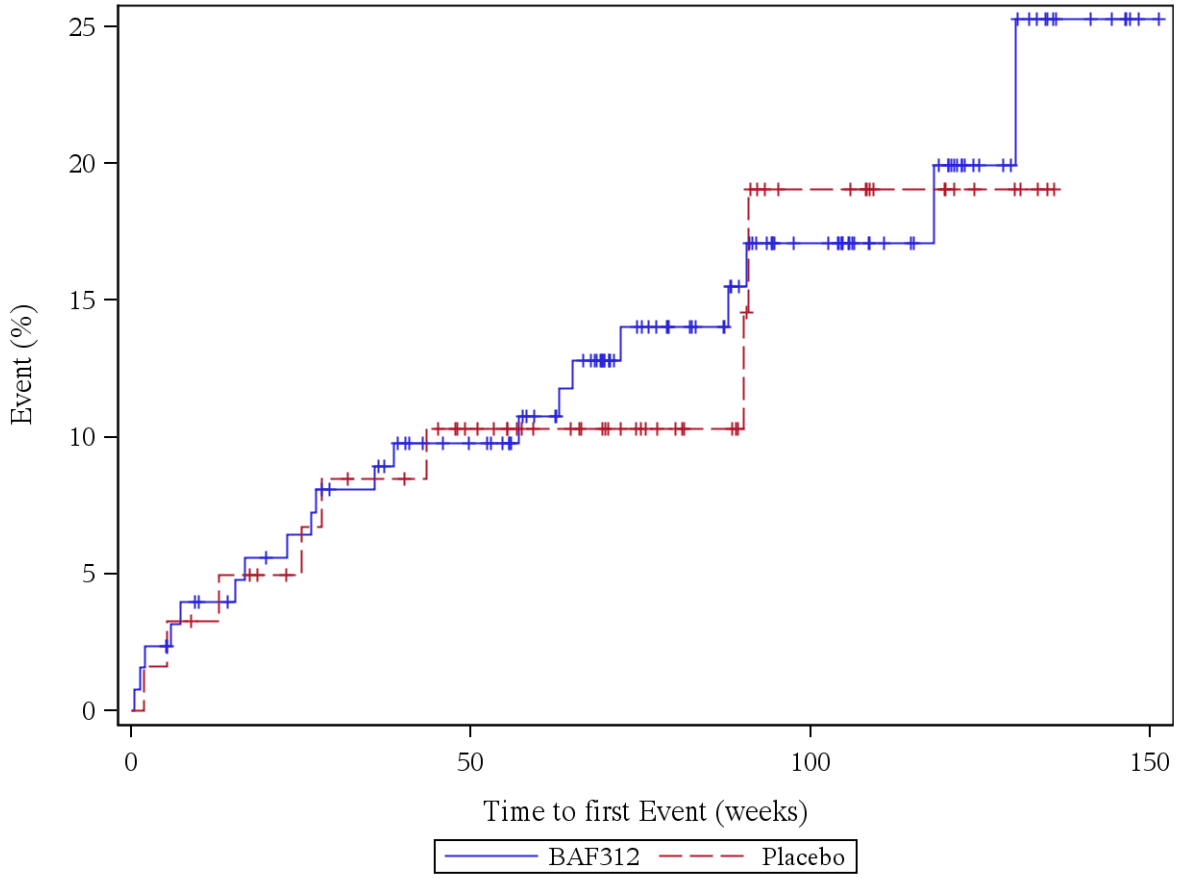


Patients at risk (BAF312/Placebo): Week 0: 127/61, Week 4: 127/61, Week 12: 123/60, Week 24: 121/57, Week 36: 119/55, Week 48: 110/51, Week 60: 99/41, Week 72: 80/32, Week 84: 66/25, Week 96: 49/17, Week 108: 36/15, Week 120: 28/9, Week 132: 15/4, Week 144: 7/1, Week 156: 0/1

Log rank test: p-value = -
*: p < 0,05

Analysis population: A2304 SAF subpopulation "ACTIVE MS WITHOUT RELAPSES"

Figure 12.1.5.25: URINARY TRACT INFECTION (PT, not severe)

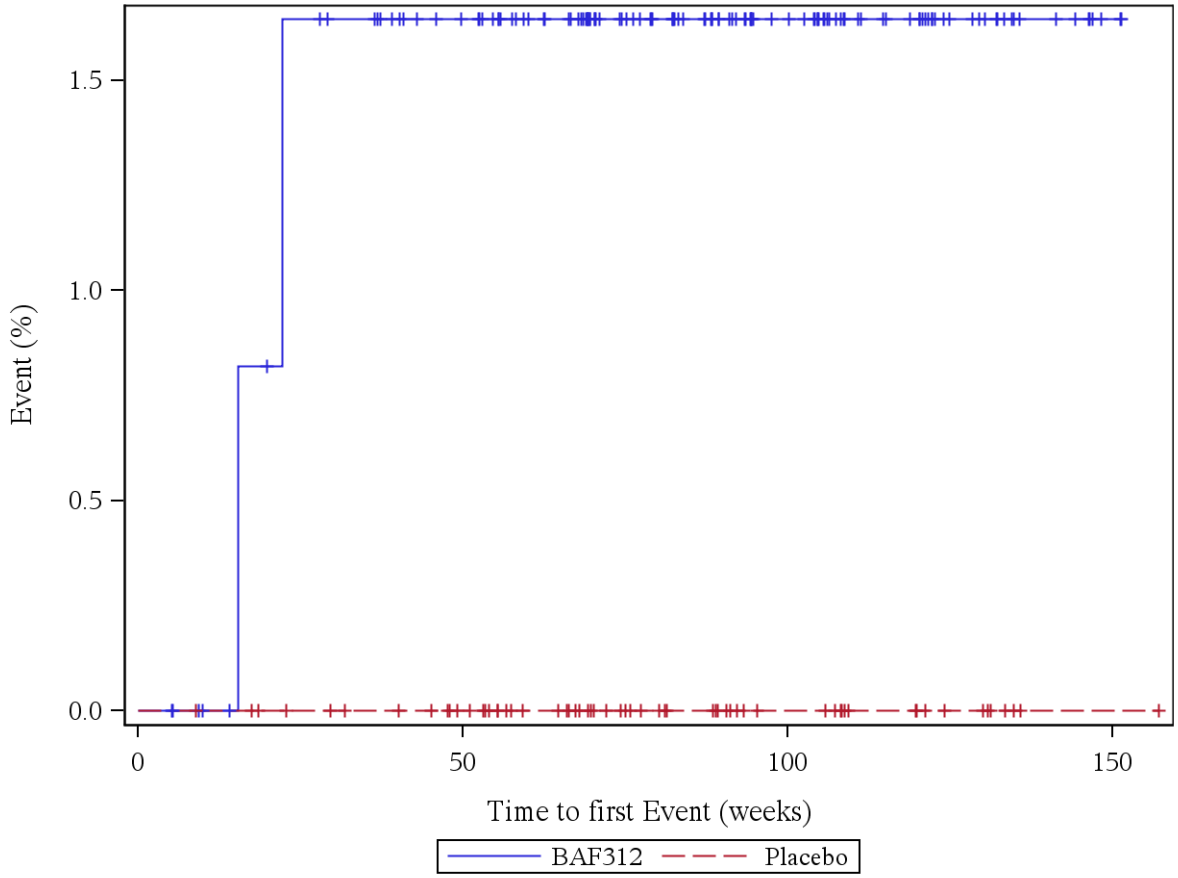


Patients at risk (BAF312/Placebo): Week 0: 127/61, Week 4: 124/60, Week 12: 118/58, Week 24: 113/54, Week 36: 108/51, Week 48: 100/46, Week 60: 89/38, Week 72: 70/31, Week 84: 60/24, Week 96: 45/14, Week 108: 34/13, Week 120: 27/7, Week 132: 13/3, Week 144: 6/0, Week 156: 0/0

Log rank test: p-value = 0,798
*: p < 0,05

Analysis population: A2304 SAF subpopulation "ACTIVE MS WITHOUT RELAPSES"

Figure 12.1.5.26: URINARY TRACT INFECTION (PT, severe)

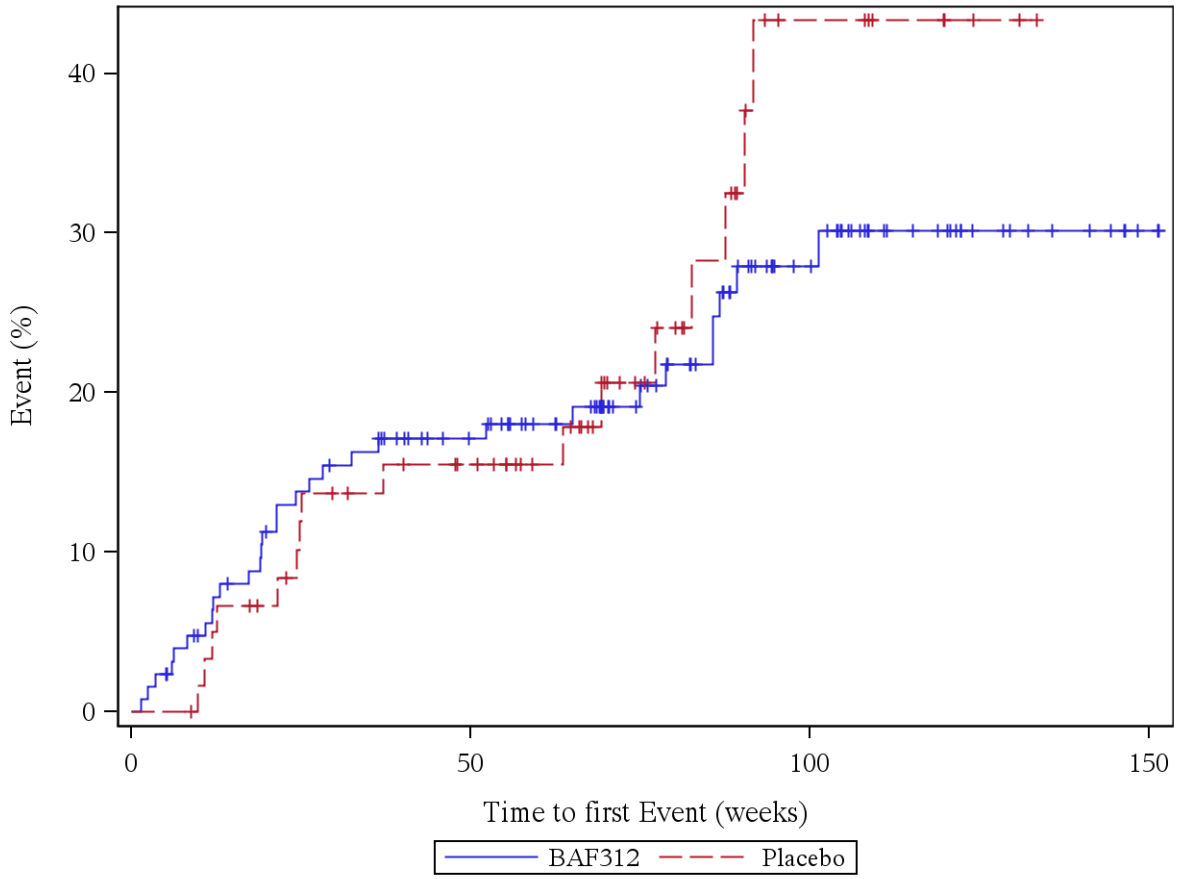


Patients at risk (BAF312/Placebo): Week 0: 127/61, Week 4: 127/61, Week 12: 123/60, Week 24: 119/57, Week 36: 117/55, Week 48: 109/51, Week 60: 98/41, Week 72: 79/32, Week 84: 65/25, Week 96: 48/17, Week 108: 35/15, Week 120: 27/9, Week 132: 14/4, Week 144: 7/1, Week 156: 0/1

Log rank test: p-value = -
*: p < 0,05

Analysis population: A2304 SAF subpopulation "ACTIVE MS WITHOUT RELAPSES"

Figure 12.1.5.27: INJURY, POISONING AND PROCEDURAL COMPLICATIONS (SOC, not severe)

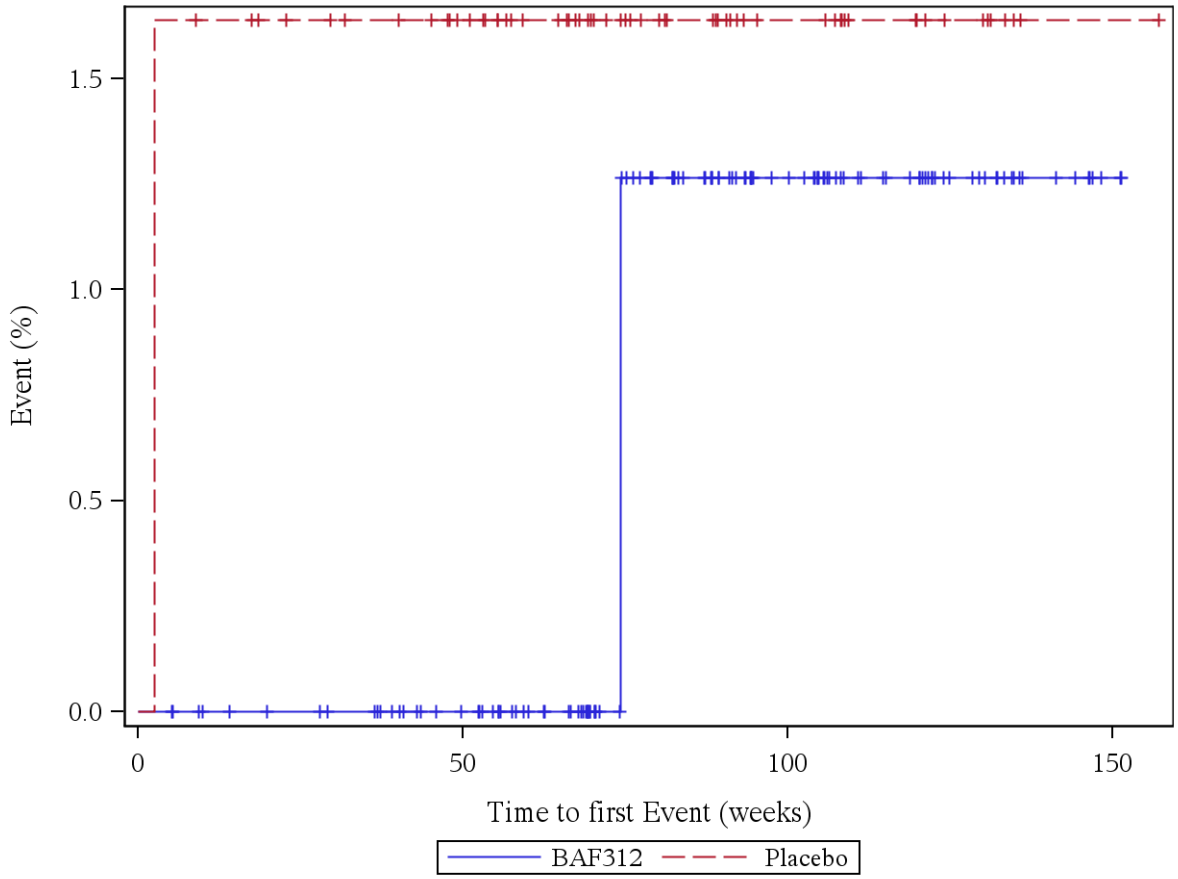


Patients at risk (BAF312/Placebo): Week 0: 127/61, Week 4: 124/61, Week 12: 114/57, Week 24: 105/52, Week 36: 100/47, Week 48: 90/43, Week 60: 79/36, Week 72: 63/25, Week 84: 52/17, Week 96: 35/8, Week 108: 24/8, Week 120: 17/3, Week 132: 9/1, Week 144: 6/0, Week 156: 0/0

Log rank test: p-value = 0,545
*: p < 0,05

Analysis population: A2304 SAF subpopulation "ACTIVE MS WITHOUT RELAPSES"

Figure 12.1.5.28: INJURY, POISONING AND PROCEDURAL COMPLICATIONS (SOC, severe)

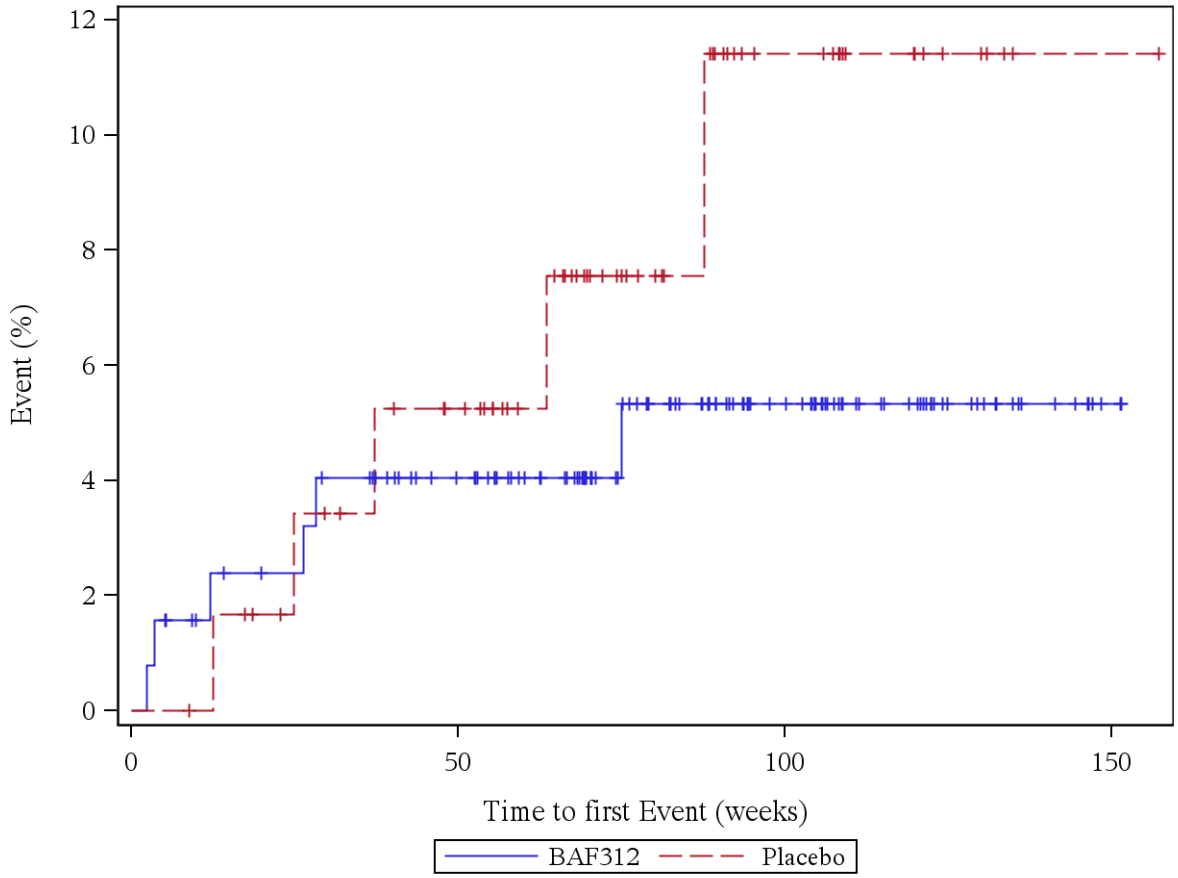


Patients at risk (BAF312/Placebo): Week 0: 127/61, Week 4: 127/60, Week 12: 123/59, Week 24: 121/56, Week 36: 119/54, Week 48: 110/50, Week 60: 99/41, Week 72: 80/32, Week 84: 65/25, Week 96: 48/17, Week 108: 35/15, Week 120: 28/9, Week 132: 15/4, Week 144: 7/1, Week 156: 0/1

Log rank test: p-value = 0,552
*: p < 0,05

Analysis population: A2304 SAF subpopulation "ACTIVE MS WITHOUT RELAPSES"

Figure 12.1.5.29: CONTUSION (PT, not severe)

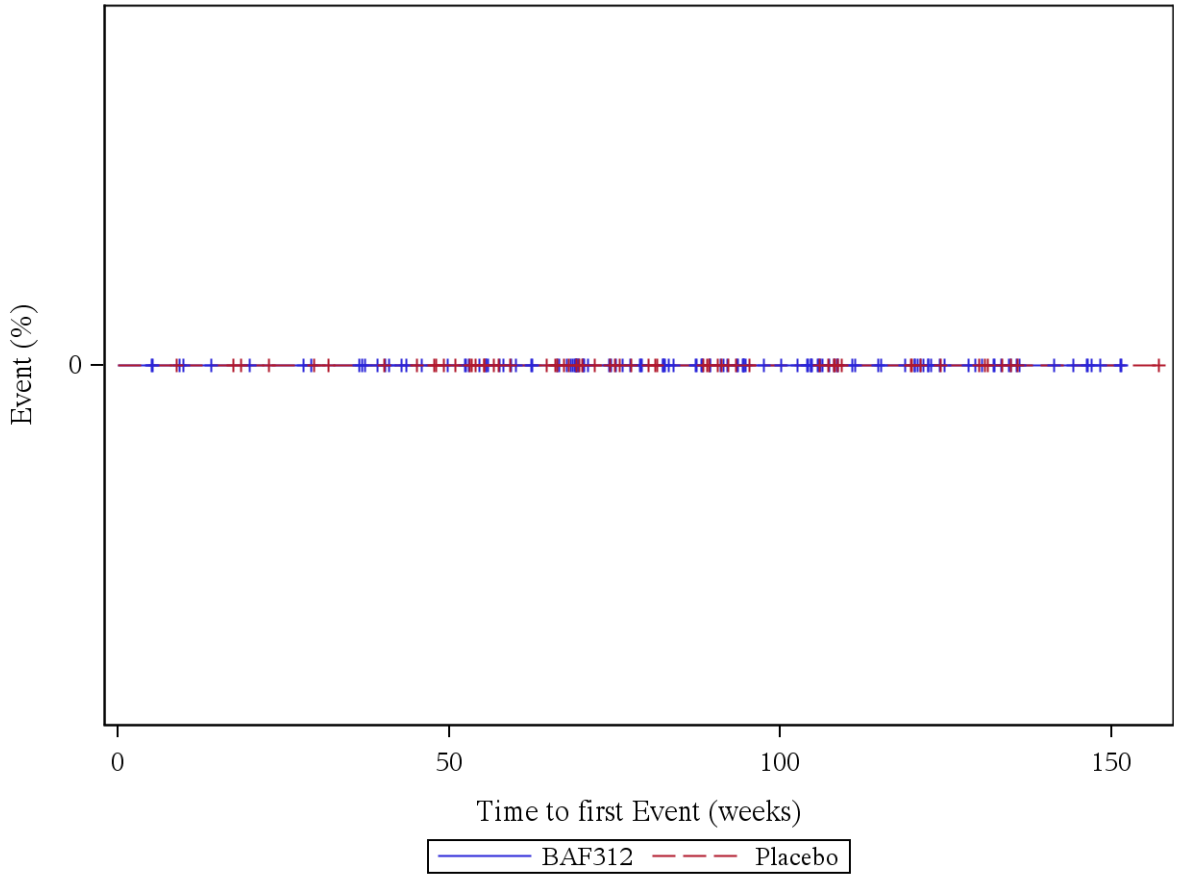


Patients at risk (BAF312/Placebo): Week 0: 127/61, Week 4: 125/61, Week 12: 120/60, Week 24: 118/56, Week 36: 115/53, Week 48: 106/49, Week 60: 95/41, Week 72: 76/31, Week 84: 62/24, Week 96: 46/15, Week 108: 33/13, Week 120: 25/7, Week 132: 13/3, Week 144: 7/1, Week 156: 0/1

Log rank test: p-value = 0,323
*: p < 0,05

Analysis population: A2304 SAF subpopulation "ACTIVE MS WITHOUT RELAPSES"

Figure 12.1.5.30: CONTUSION (PT, severe)

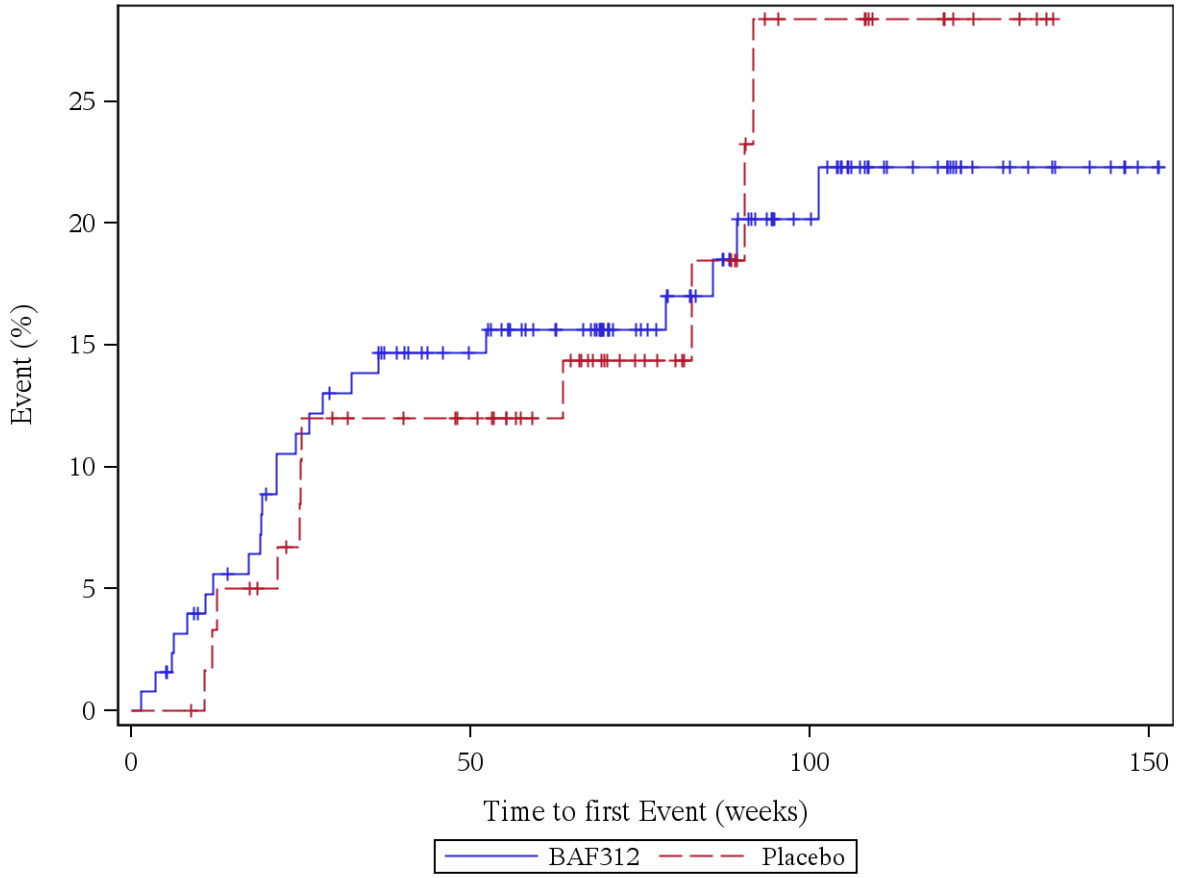


Patients at risk (BAF312/Placebo): Week 0: 127/61, Week 4: 127/61, Week 12: 123/60, Week 24: 121/57, Week 36: 119/55, Week 48: 110/51, Week 60: 99/41, Week 72: 80/32, Week 84: 66/25, Week 96: 49/17, Week 108: 36/15, Week 120: 28/9, Week 132: 15/4, Week 144: 7/1, Week 156: 0/1

Log rank test: p-value = -
*: p < 0,05

Analysis population: A2304 SAF subpopulation "ACTIVE MS WITHOUT RELAPSES"

Figure 12.1.5.31: FALL (PT, not severe)

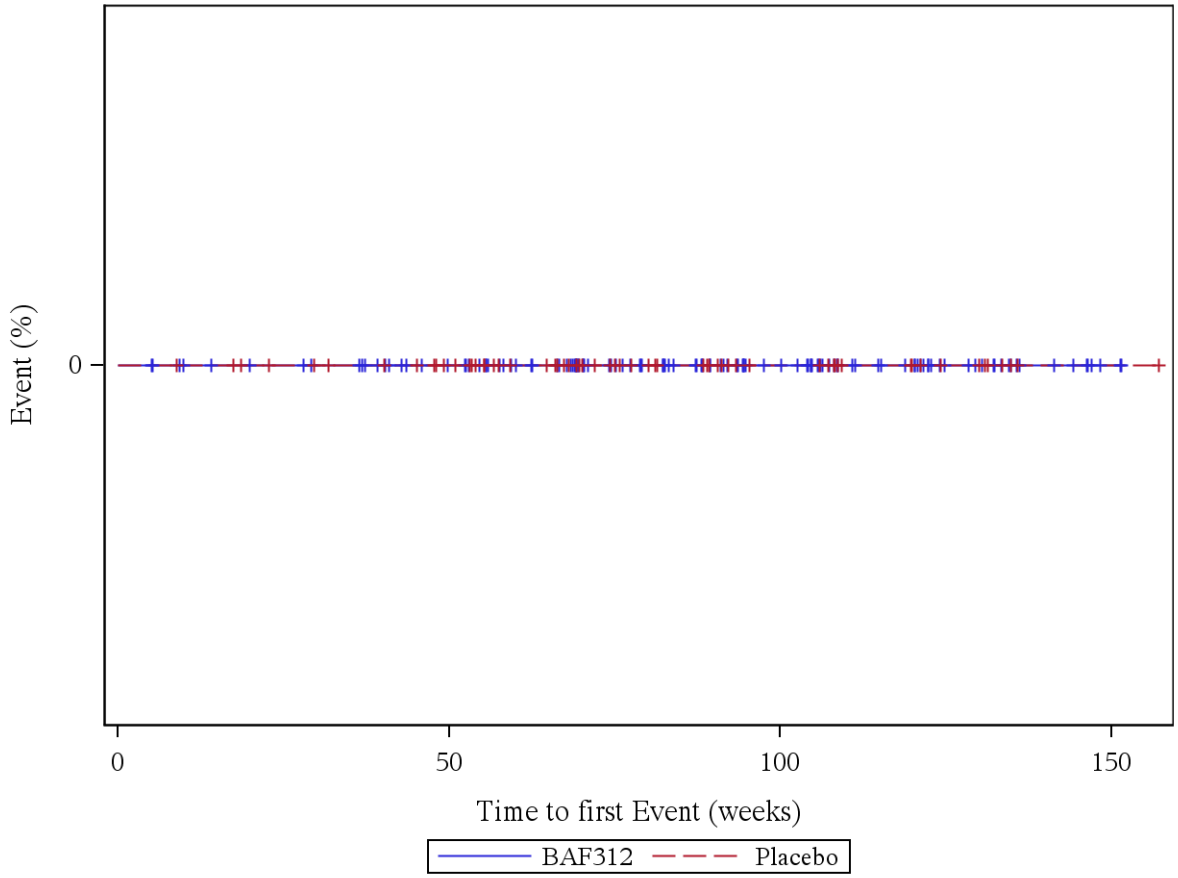


Patients at risk (BAF312/Placebo): Week 0: 127/61, Week 4: 125/61, Week 12: 116/58, Week 24: 108/53, Week 36: 103/48, Week 48: 93/45, Week 60: 82/37, Week 72: 65/27, Week 84: 55/20, Week 96: 39/12, Week 108: 27/12, Week 120: 20/6, Week 132: 10/3, Week 144: 6/0, Week 156: 0/0

Log rank test: p-value = 0,912
*: p < 0,05

Analysis population: A2304 SAF subpopulation "ACTIVE MS WITHOUT RELAPSES"

Figure 12.1.5.32: FALL (PT, severe)

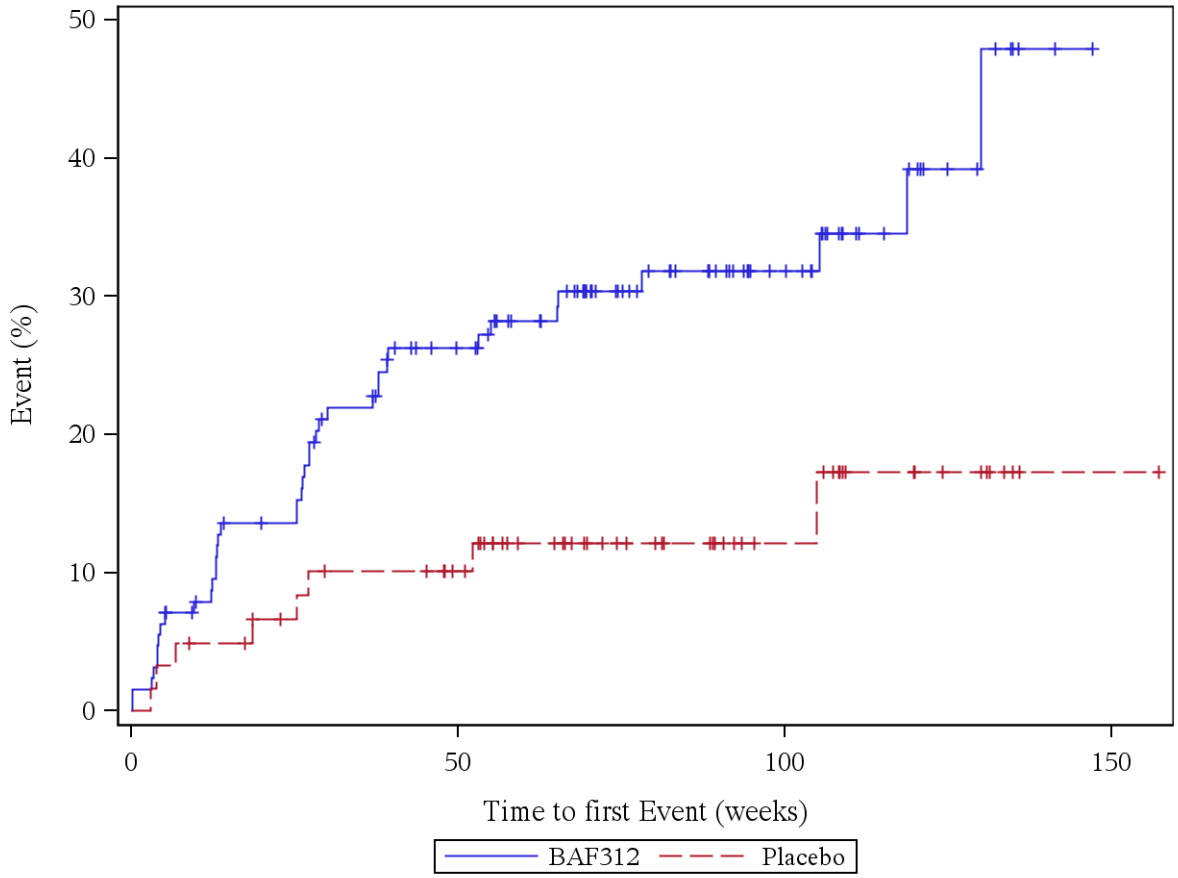


Patients at risk (BAF312/Placebo): Week 0: 127/61, Week 4: 127/61, Week 12: 123/60, Week 24: 121/57, Week 36: 119/55, Week 48: 110/51, Week 60: 99/41, Week 72: 80/32, Week 84: 66/25, Week 96: 49/17, Week 108: 36/15, Week 120: 28/9, Week 132: 15/4, Week 144: 7/1, Week 156: 0/1

Log rank test: p-value = -
*: p < 0,05

Analysis population: A2304 SAF subpopulation "ACTIVE MS WITHOUT RELAPSES"

Figure 12.1.5.33: INVESTIGATIONS (SOC, not severe)

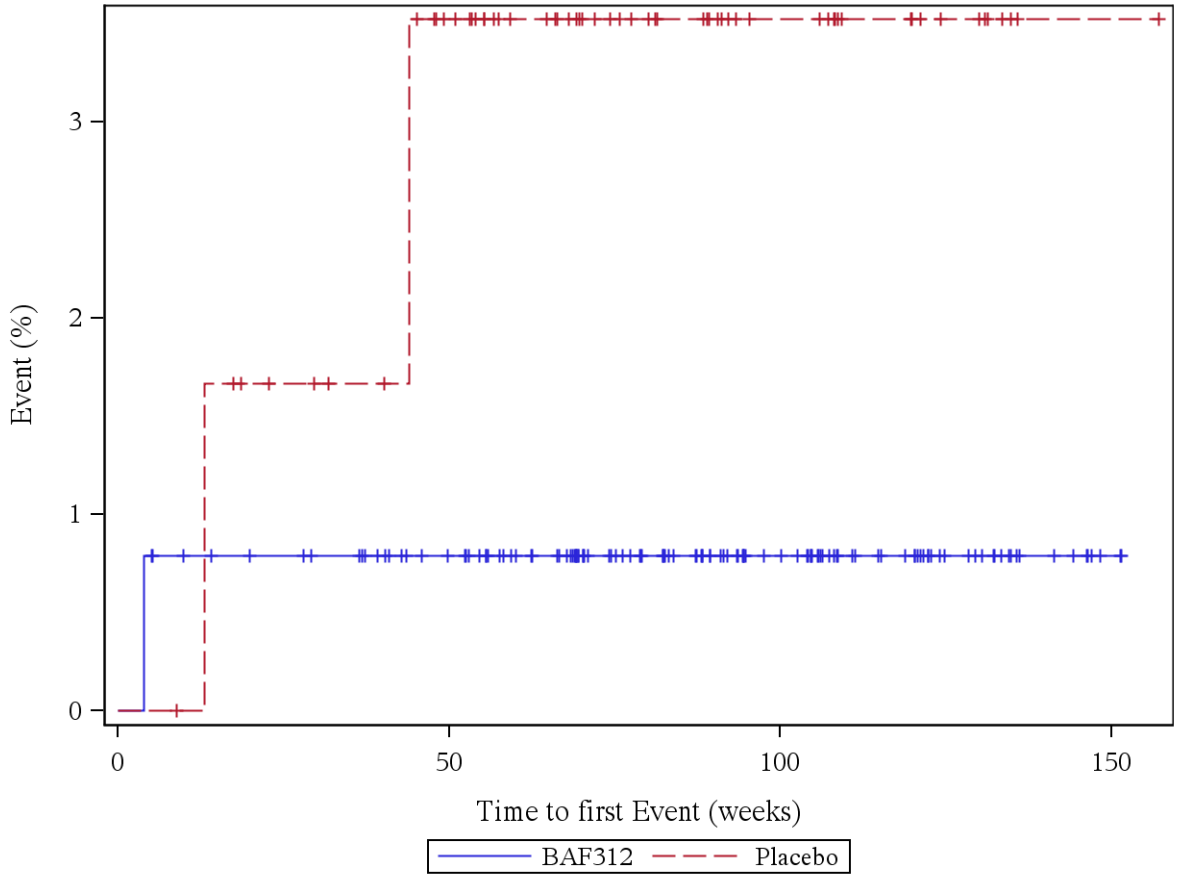


Patients at risk (BAF312/Placebo): Week 0: 127/61, Week 4: 121/59, Week 12: 113/57, Week 24: 104/53, Week 36: 92/50, Week 48: 80/47, Week 60: 69/36, Week 72: 52/29, Week 84: 42/24, Week 96: 30/17, Week 108: 20/14, Week 120: 12/8, Week 132: 6/4, Week 144: 1/1, Week 156: 0/1

Log rank test: p-value = 0,008 *
*: p < 0,05

Analysis population: A2304 SAF subpopulation "ACTIVE MS WITHOUT RELAPSES"

Figure 12.1.5.34: INVESTIGATIONS (SOC, severe)

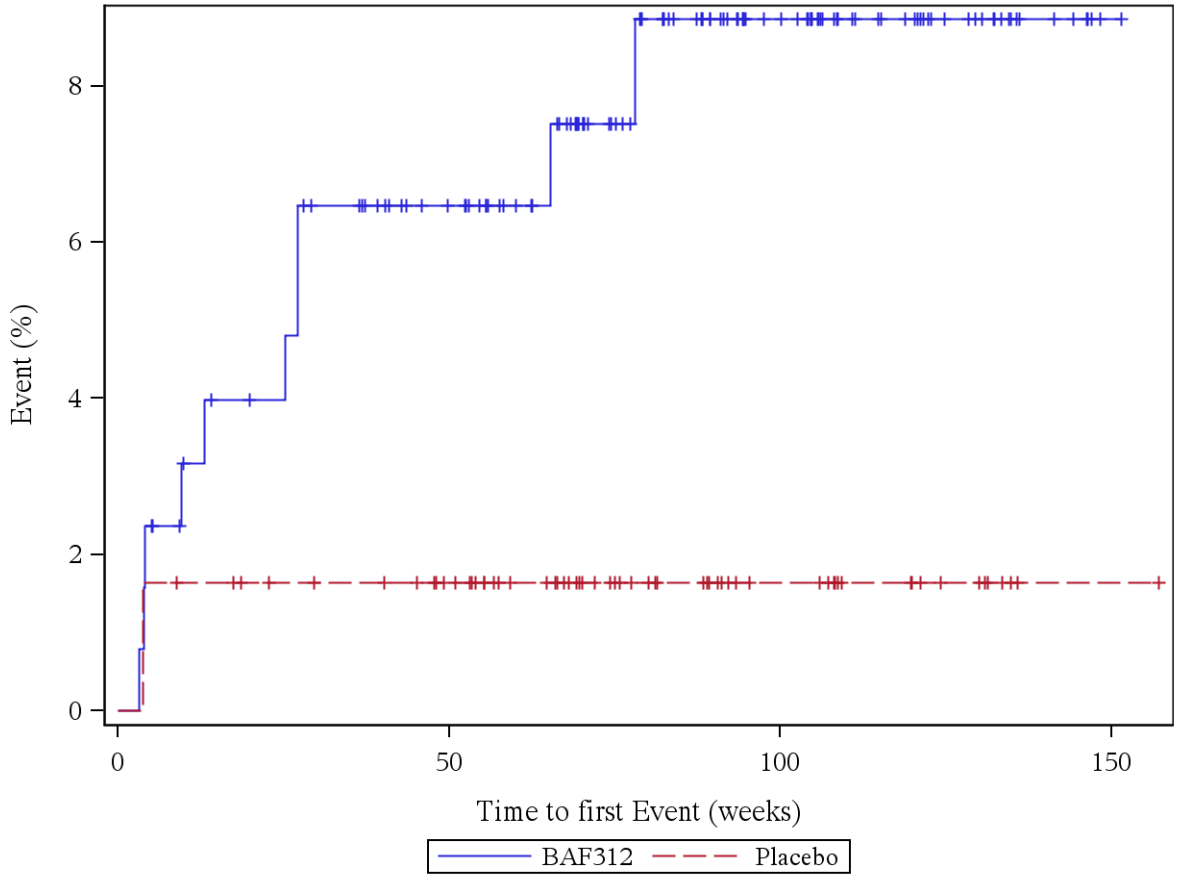


Patients at risk (BAF312/Placebo): Week 0: 127/61, Week 4: 126/61, Week 12: 123/60, Week 24: 121/56, Week 36: 119/54, Week 48: 110/49, Week 60: 99/39, Week 72: 80/31, Week 84: 66/25, Week 96: 49/17, Week 108: 36/15, Week 120: 28/9, Week 132: 15/4, Week 144: 7/1, Week 156: 0/1

Log rank test: p-value = 0,207
*: p < 0,05

Analysis population: A2304 SAF subpopulation "ACTIVE MS WITHOUT RELAPSES"

Figure 12.1.5.35: ALANINE AMINOTRANSFERASE INCREASED (PT, not severe)

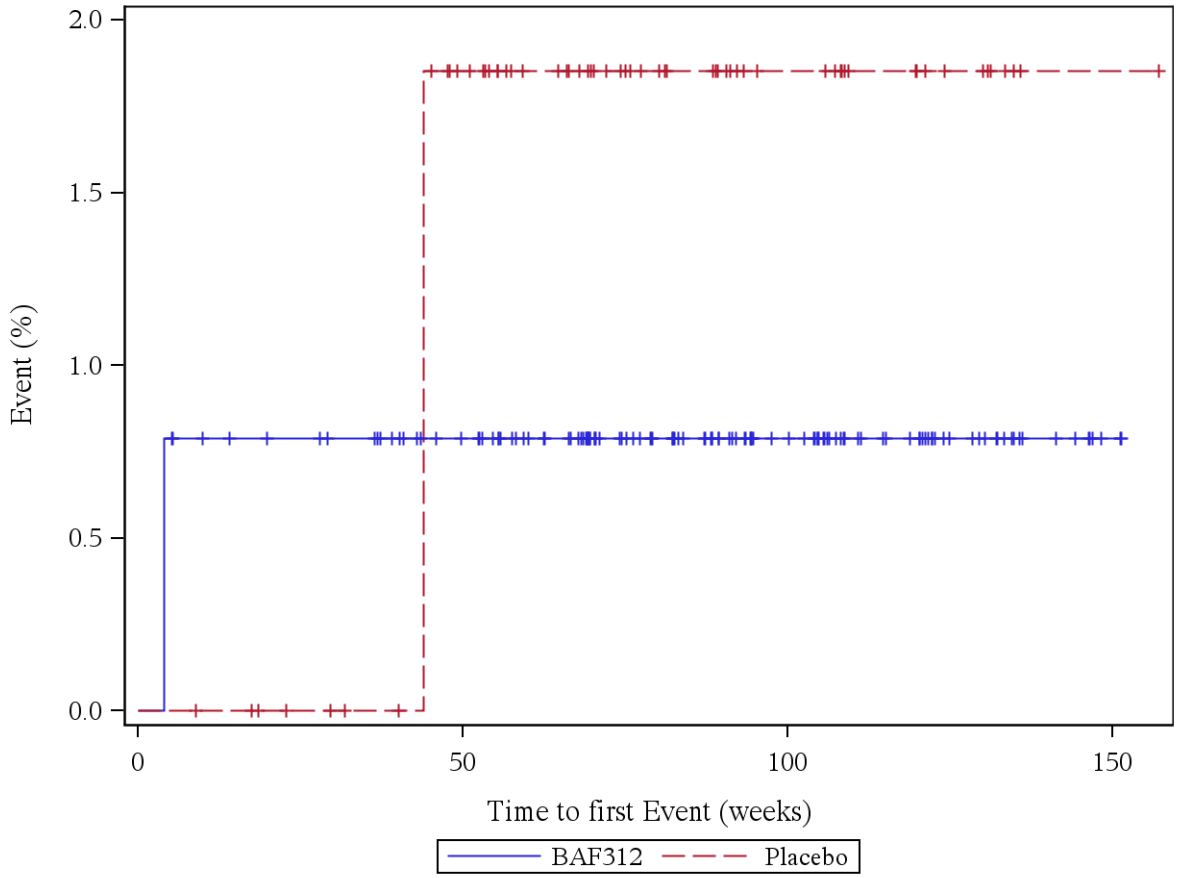


Patients at risk (BAF312/Placebo): Week 0: 127/61, Week 4: 125/60, Week 12: 119/59, Week 24: 116/56, Week 36: 111/55, Week 48: 102/51, Week 60: 92/41, Week 72: 74/32, Week 84: 60/25, Week 96: 44/17, Week 108: 32/15, Week 120: 24/9, Week 132: 14/4, Week 144: 6/1, Week 156: 0/1

Log rank test: p-value = 0,101
*: p < 0,05

Analysis population: A2304 SAF subpopulation "ACTIVE MS WITHOUT RELAPSES"

Figure 12.1.5.36: ALANINE AMINOTRANSFERASE INCREASED (PT, severe)

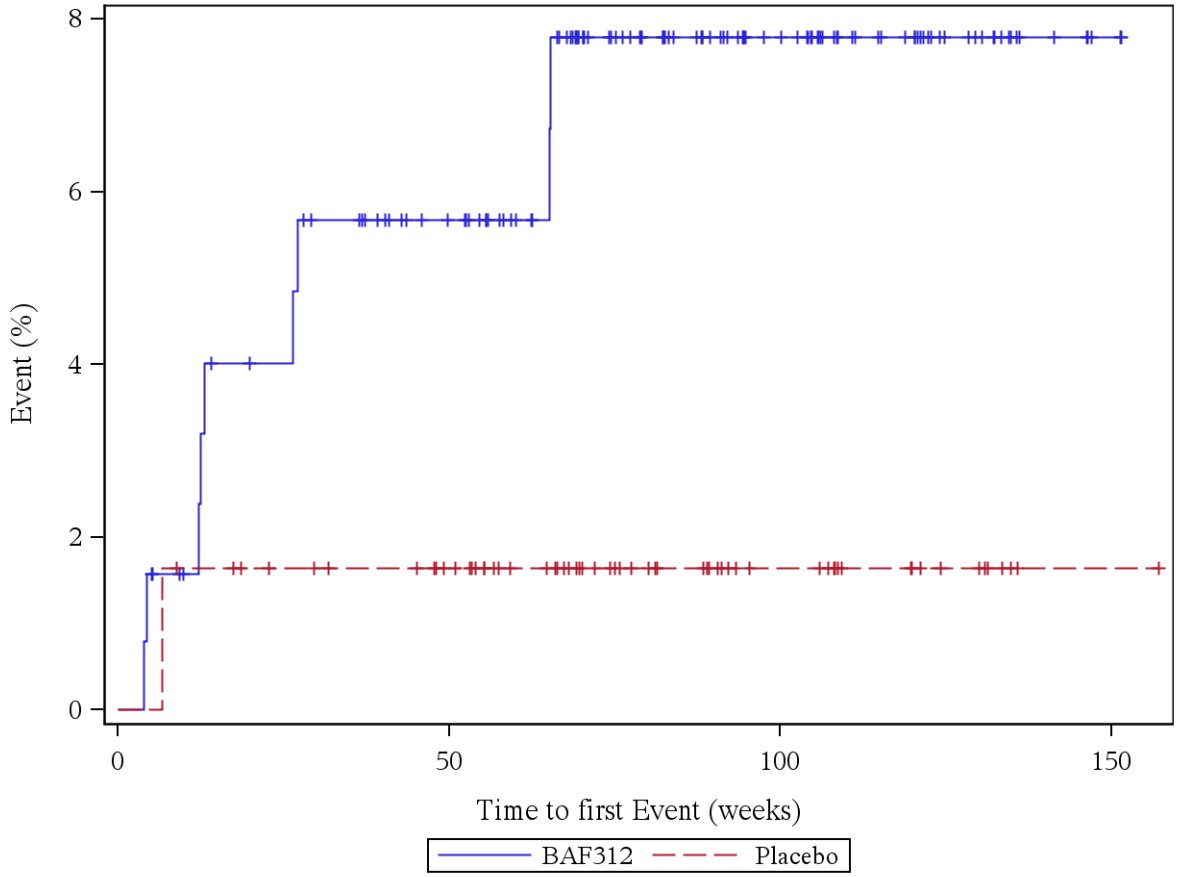


Patients at risk (BAF312/Placebo): Week 0: 127/61, Week 4: 126/61, Week 12: 123/60, Week 24: 121/57, Week 36: 119/55, Week 48: 110/50, Week 60: 99/40, Week 72: 80/32, Week 84: 66/25, Week 96: 49/17, Week 108: 36/15, Week 120: 28/9, Week 132: 15/4, Week 144: 7/1, Week 156: 0/1

Log rank test: p-value = 0,599
*: p < 0,05

Analysis population: A2304 SAF subpopulation "ACTIVE MS WITHOUT RELAPSES"

Figure 12.1.5.37: GAMMA-GLUTAMYLTRANSFERASE INCREASED (PT, not severe)

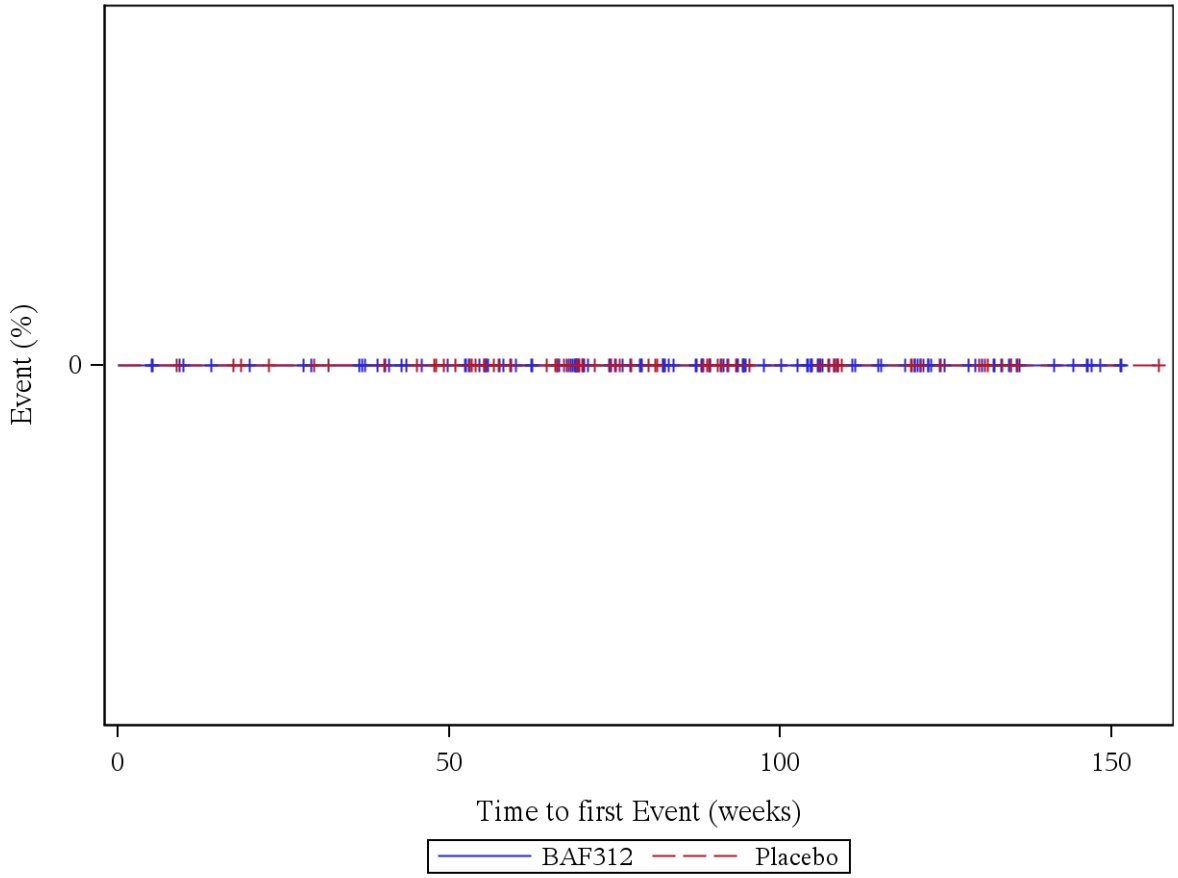


Patients at risk (BAF312/Placebo): Week 0: 127/61, Week 4: 126/61, Week 12: 121/59, Week 24: 116/56, Week 36: 112/54, Week 48: 103/51, Week 60: 92/41, Week 72: 72/32, Week 84: 58/25, Week 96: 44/17, Week 108: 33/15, Week 120: 25/9, Week 132: 13/4, Week 144: 5/1, Week 156: 0/1

Log rank test: p-value = 0,129
*: p < 0,05

Analysis population: A2304 SAF subpopulation "ACTIVE MS WITHOUT RELAPSES"

Figure 12.1.5.38: GAMMA-GLUTAMYLTRANSFERASE INCREASED (PT, severe)

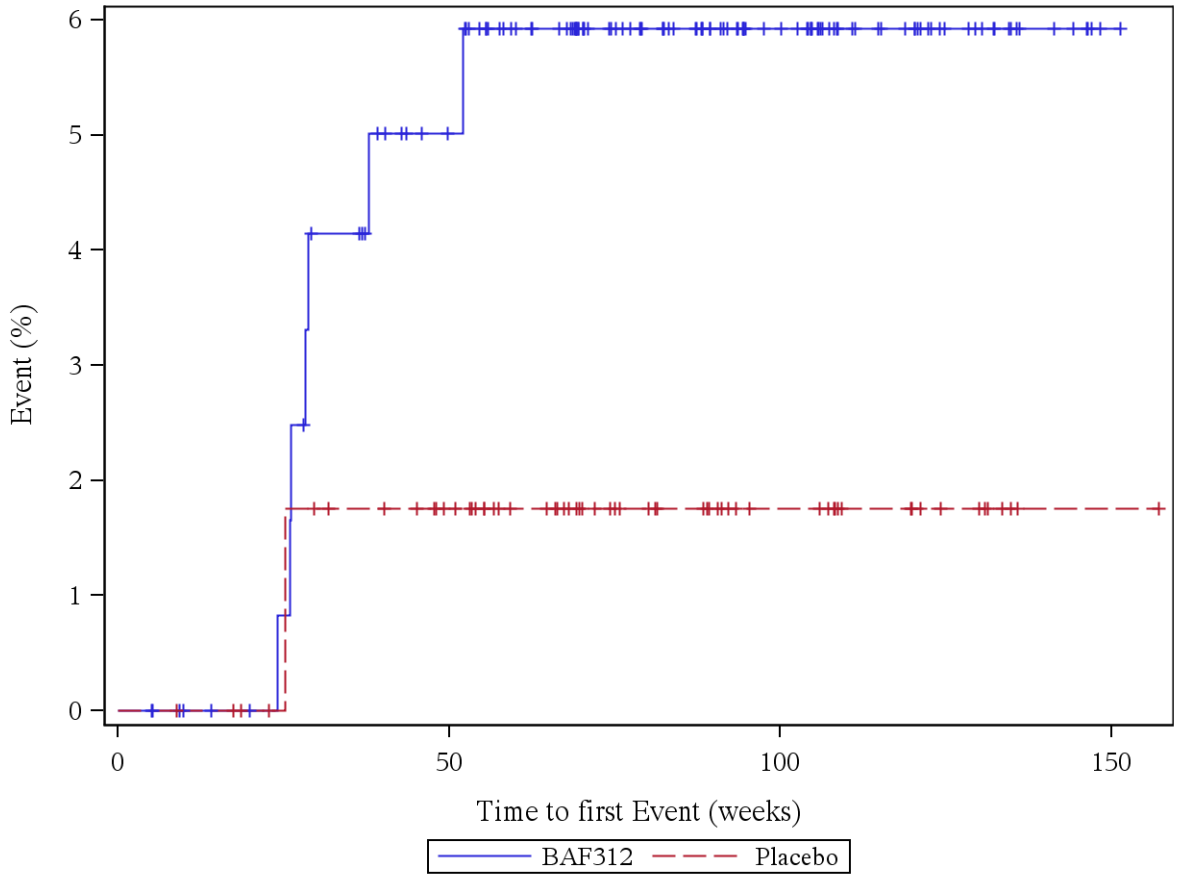


Patients at risk (BAF312/Placebo): Week 0: 127/61, Week 4: 127/61, Week 12: 123/60, Week 24: 121/57, Week 36: 119/55, Week 48: 110/51, Week 60: 99/41, Week 72: 80/32, Week 84: 66/25, Week 96: 49/17, Week 108: 36/15, Week 120: 28/9, Week 132: 15/4, Week 144: 7/1, Week 156: 0/1

Log rank test: p-value = -
*: p < 0,05

Analysis population: A2304 SAF subpopulation "ACTIVE MS WITHOUT RELAPSES"

Figure 12.1.5.39: WEIGHT DECREASED (PT, not severe)

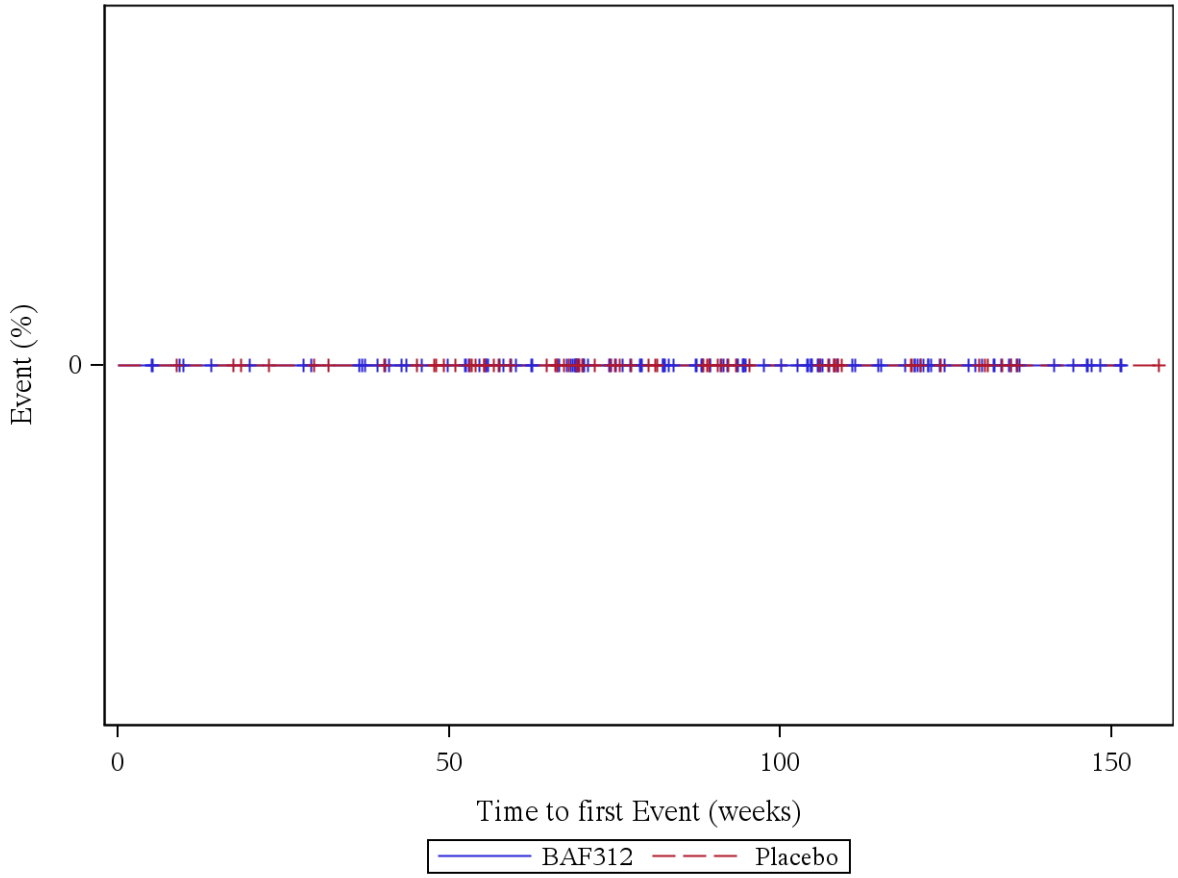


Patients at risk (BAF312/Placebo): Week 0: 127/61, Week 4: 127/61, Week 12: 123/60, Week 24: 121/57, Week 36: 114/54, Week 48: 105/50, Week 60: 93/40, Week 72: 75/31, Week 84: 62/25, Week 96: 45/17, Week 108: 32/15, Week 120: 24/9, Week 132: 13/4, Week 144: 6/1, Week 156: 0/1

Log rank test: p-value = 0,234
*: p < 0,05

Analysis population: A2304 SAF subpopulation "ACTIVE MS WITHOUT RELAPSES"

Figure 12.1.5.40: WEIGHT DECREASED (PT, severe)

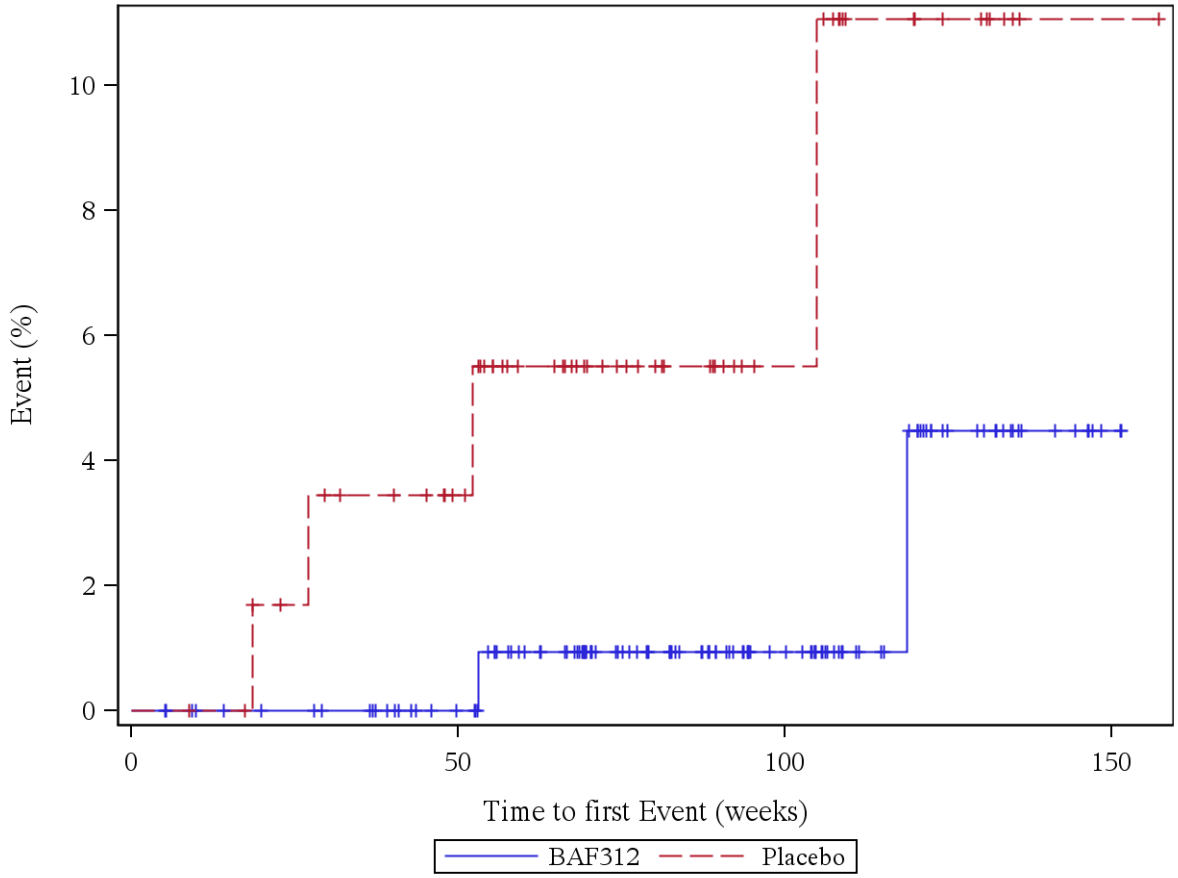


Patients at risk (BAF312/Placebo): Week 0: 127/61, Week 4: 127/61, Week 12: 123/60, Week 24: 121/57, Week 36: 119/55, Week 48: 110/51, Week 60: 99/41, Week 72: 80/32, Week 84: 66/25, Week 96: 49/17, Week 108: 36/15, Week 120: 28/9, Week 132: 15/4, Week 144: 7/1, Week 156: 0/1

Log rank test: p-value = -
*: p < 0,05

Analysis population: A2304 SAF subpopulation "ACTIVE MS WITHOUT RELAPSES"

Figure 12.1.5.41: WEIGHT INCREASED (PT, not severe)

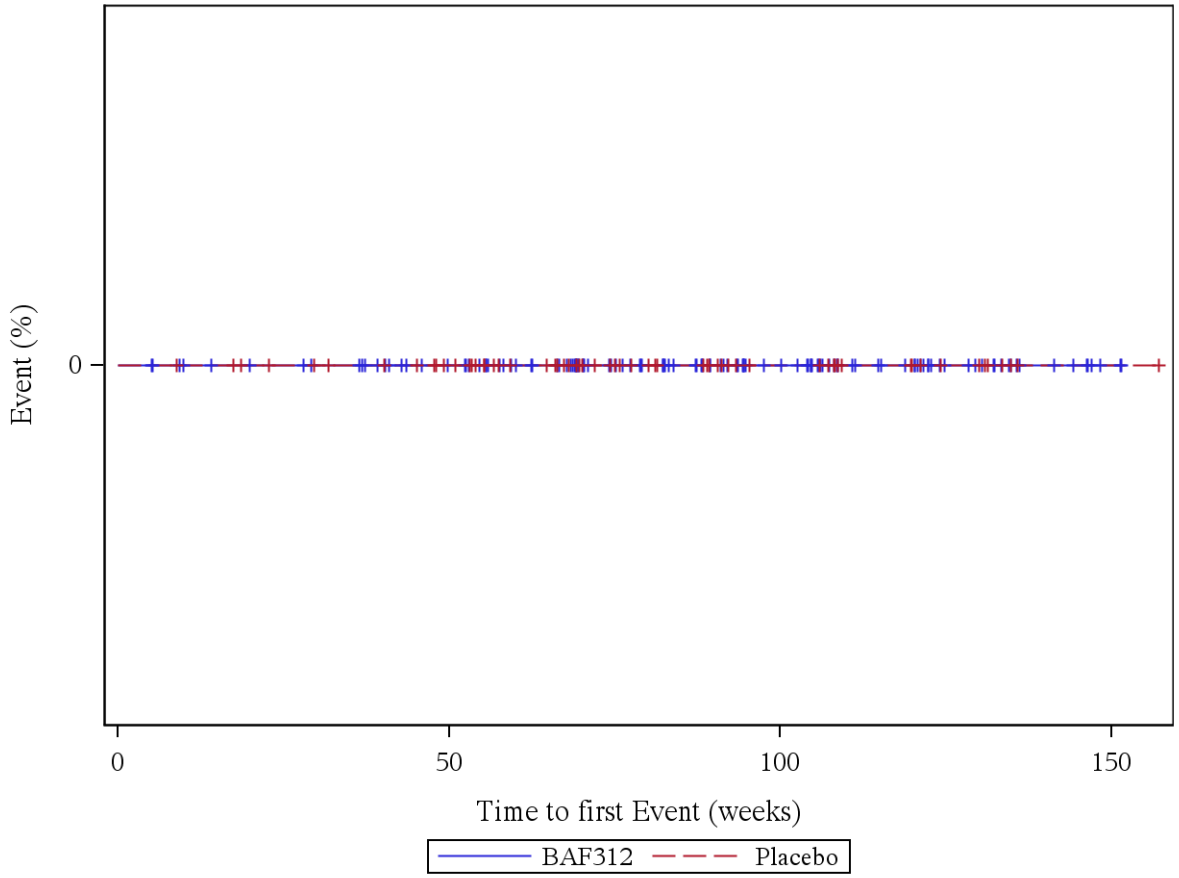


Patients at risk (BAF312/Placebo): Week 0: 127/61, Week 4: 127/61, Week 12: 123/60, Week 24: 121/56, Week 36: 119/53, Week 48: 110/49, Week 60: 98/38, Week 72: 79/30, Week 84: 65/24, Week 96: 48/17, Week 108: 35/14, Week 120: 26/8, Week 132: 15/4, Week 144: 7/1, Week 156: 0/1

Log rank test: p-value = 0,051
*: p < 0,05

Analysis population: A2304 SAF subpopulation "ACTIVE MS WITHOUT RELAPSES"

Figure 12.1.5.42: WEIGHT INCREASED (PT, severe)

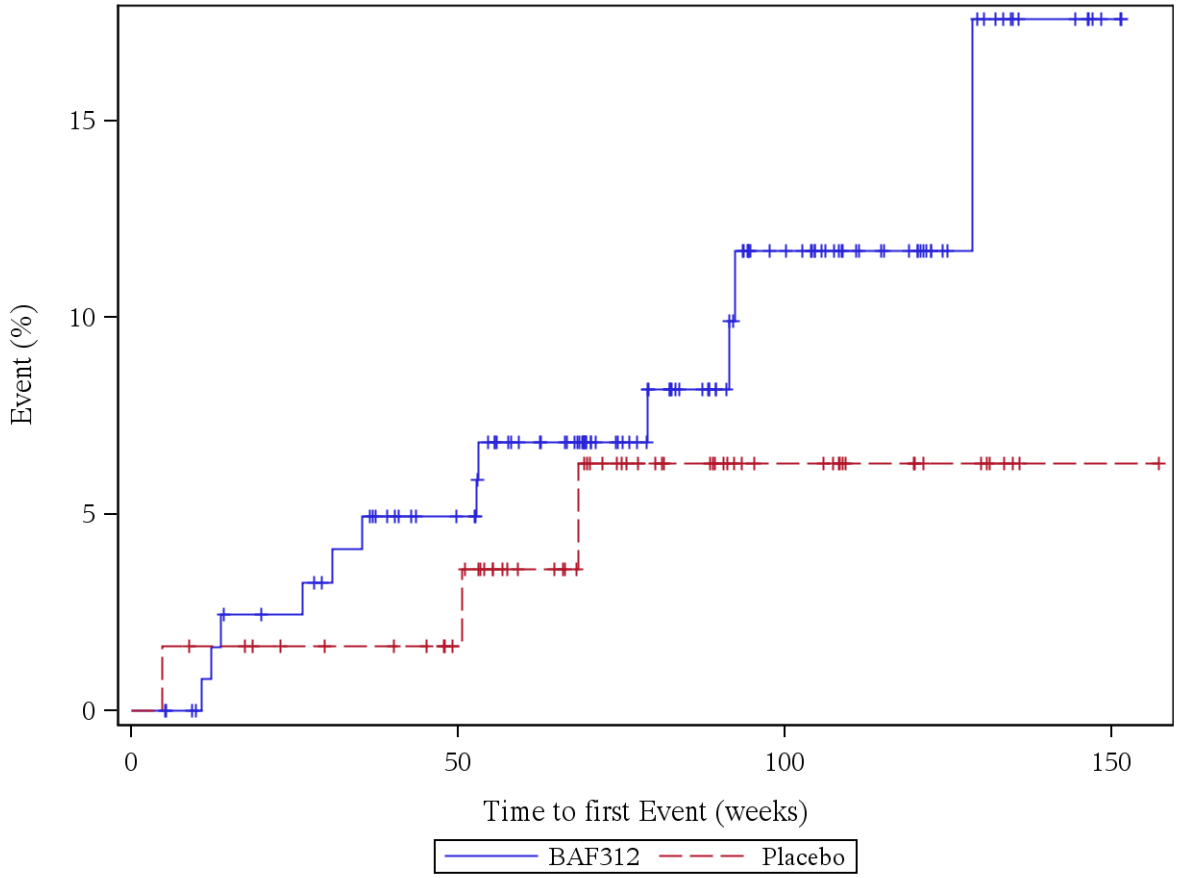


Patients at risk (BAF312/Placebo): Week 0: 127/61, Week 4: 127/61, Week 12: 123/60, Week 24: 121/57, Week 36: 119/55, Week 48: 110/51, Week 60: 99/41, Week 72: 80/32, Week 84: 66/25, Week 96: 49/17, Week 108: 36/15, Week 120: 28/9, Week 132: 15/4, Week 144: 7/1, Week 156: 0/1

Log rank test: p-value = -
*: p < 0,05

Analysis population: A2304 SAF subpopulation "ACTIVE MS WITHOUT RELAPSES"

Figure 12.1.5.43: METABOLISM AND NUTRITION DISORDERS (SOC, not severe)

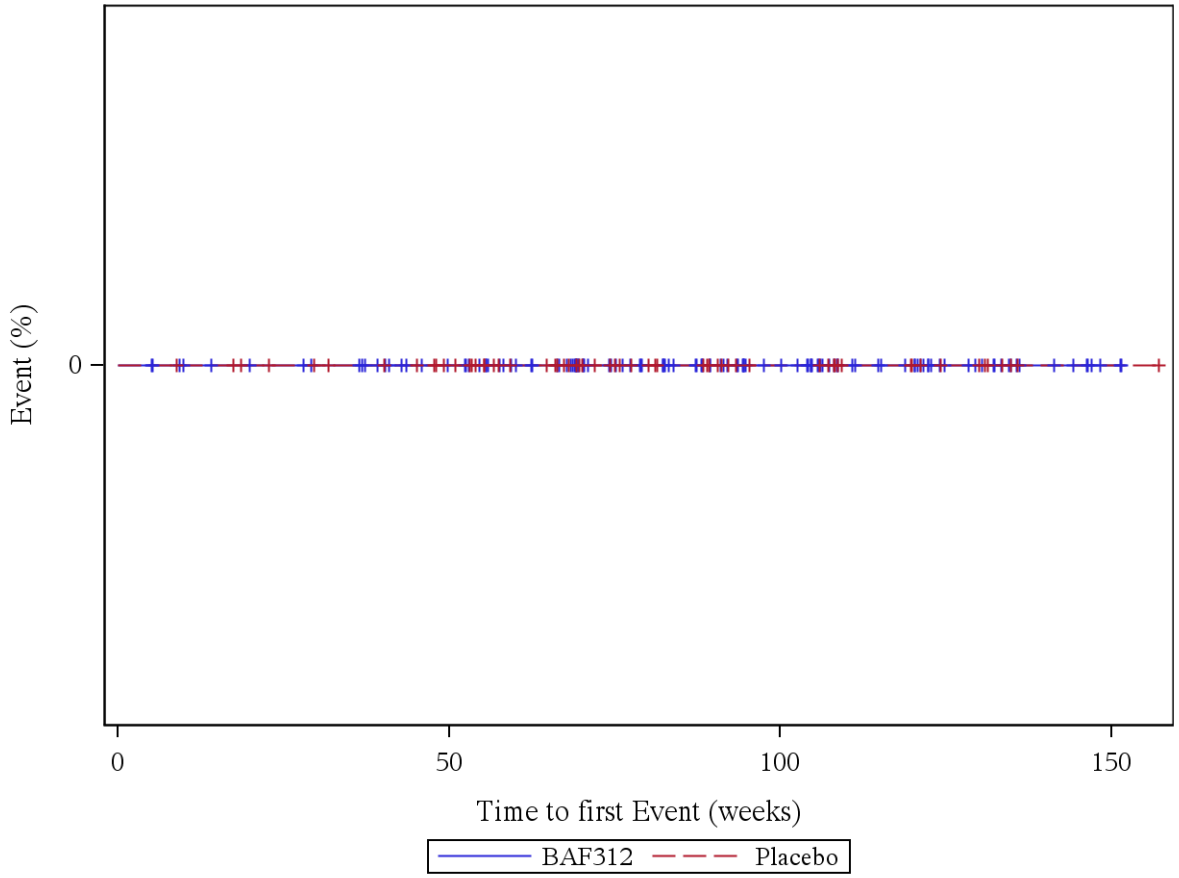


Patients at risk (BAF312/Placebo): Week 0: 127/61, Week 4: 127/61, Week 12: 122/59, Week 24: 118/56, Week 36: 113/55, Week 48: 105/51, Week 60: 92/40, Week 72: 75/31, Week 84: 60/24, Week 96: 42/16, Week 108: 32/14, Week 120: 24/8, Week 132: 12/4, Week 144: 7/1, Week 156: 0/1

Log rank test: p-value = 0,352
*: p < 0,05

Analysis population: A2304 SAF subpopulation "ACTIVE MS WITHOUT RELAPSES"

Figure 12.1.5.44: METABOLISM AND NUTRITION DISORDERS (SOC, severe)

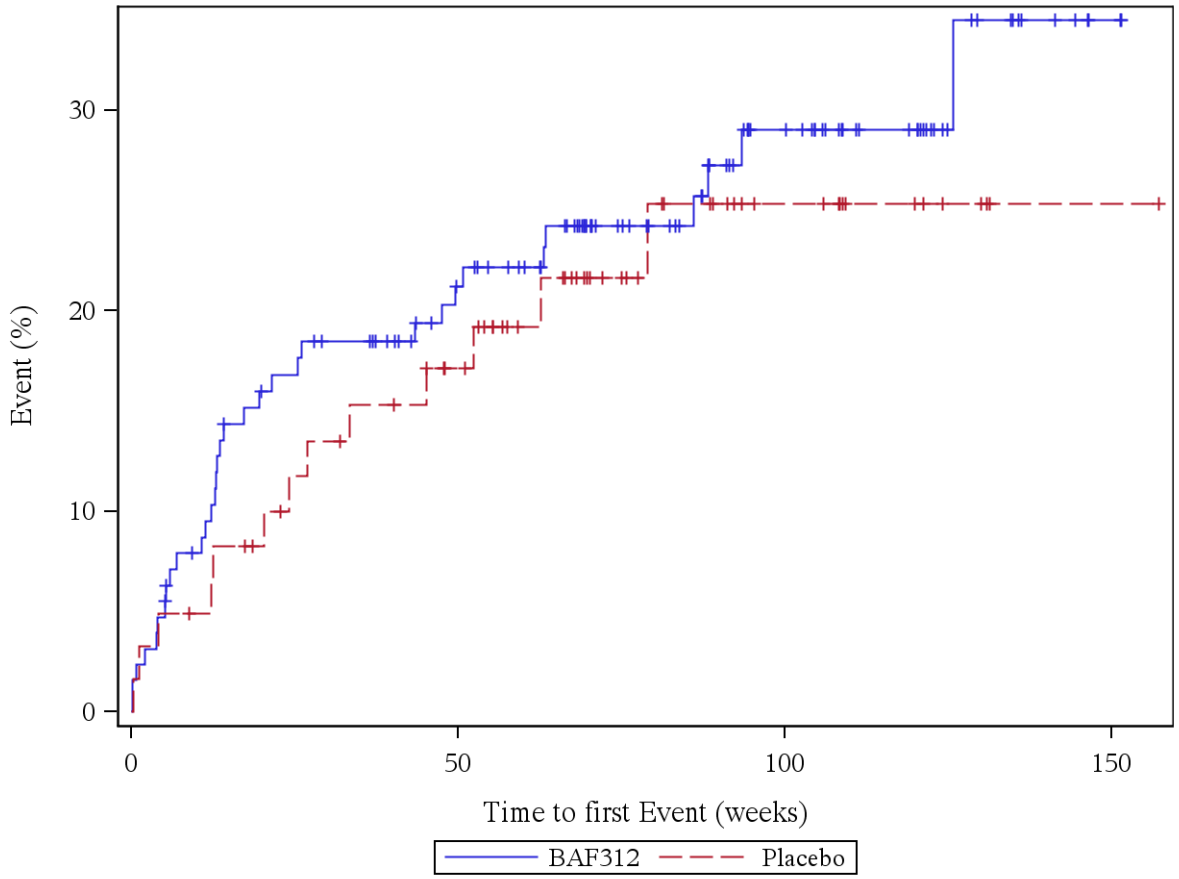


Patients at risk (BAF312/Placebo): Week 0: 127/61, Week 4: 127/61, Week 12: 123/60, Week 24: 121/57, Week 36: 119/55, Week 48: 110/51, Week 60: 99/41, Week 72: 80/32, Week 84: 66/25, Week 96: 49/17, Week 108: 36/15, Week 120: 28/9, Week 132: 15/4, Week 144: 7/1, Week 156: 0/1

Log rank test: p-value = -
*: p < 0,05

Analysis population: A2304 SAF subpopulation "ACTIVE MS WITHOUT RELAPSES"

Figure 12.1.5.45: MUSCULOSKELETAL AND CONNECTIVE TISSUE DISORDERS (SOC, not severe)

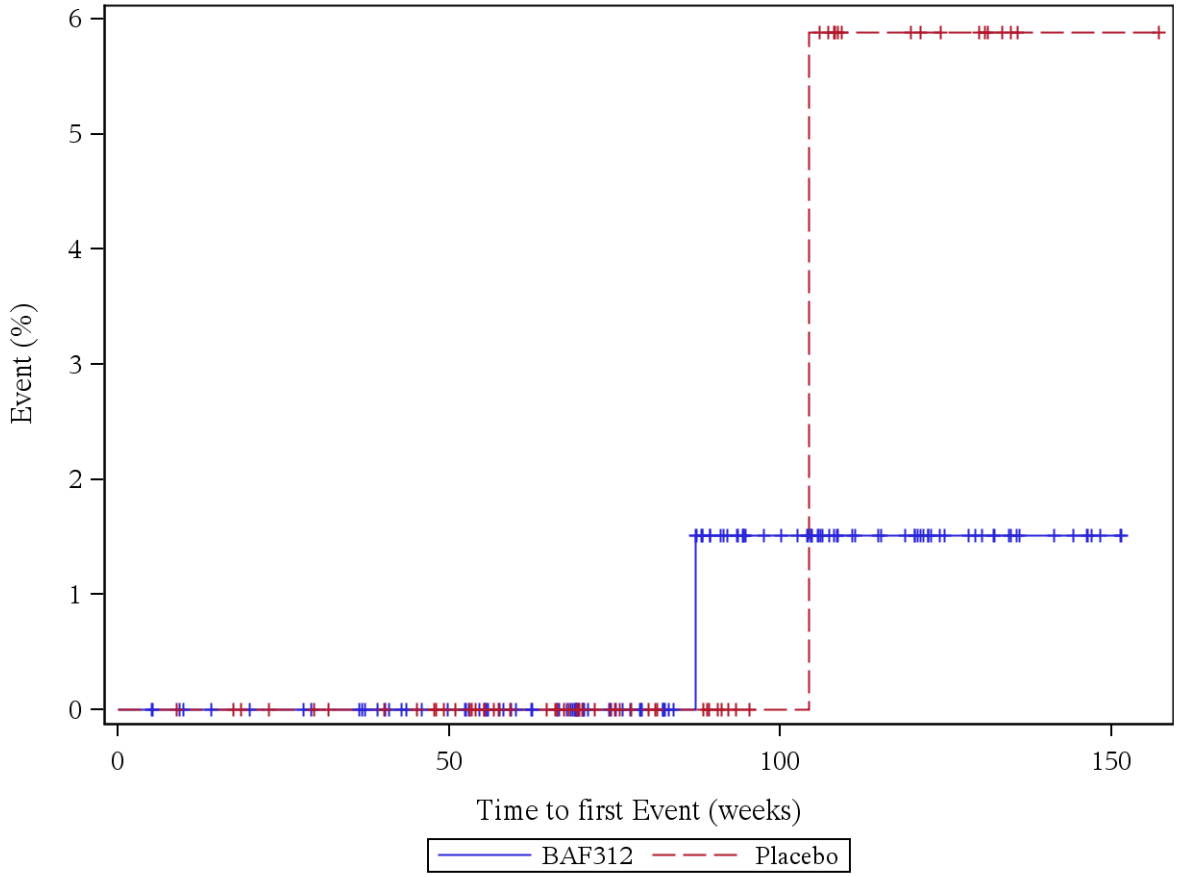


Patients at risk (BAF312/Placebo): Week 0: 127/61, Week 4: 121/59, Week 12: 112/57, Week 24: 101/51, Week 36: 97/47, Week 48: 86/42, Week 60: 78/33, Week 72: 59/24, Week 84: 51/18, Week 96: 35/12, Week 108: 28/11, Week 120: 22/6, Week 132: 10/1, Week 144: 5/1, Week 156: 0/1

Log rank test: p-value = 0,561
*: p < 0,05

Analysis population: A2304 SAF subpopulation "ACTIVE MS WITHOUT RELAPSES"

Figure 12.1.5.46: MUSCULOSKELETAL AND CONNECTIVE TISSUE DISORDERS (SOC, severe)

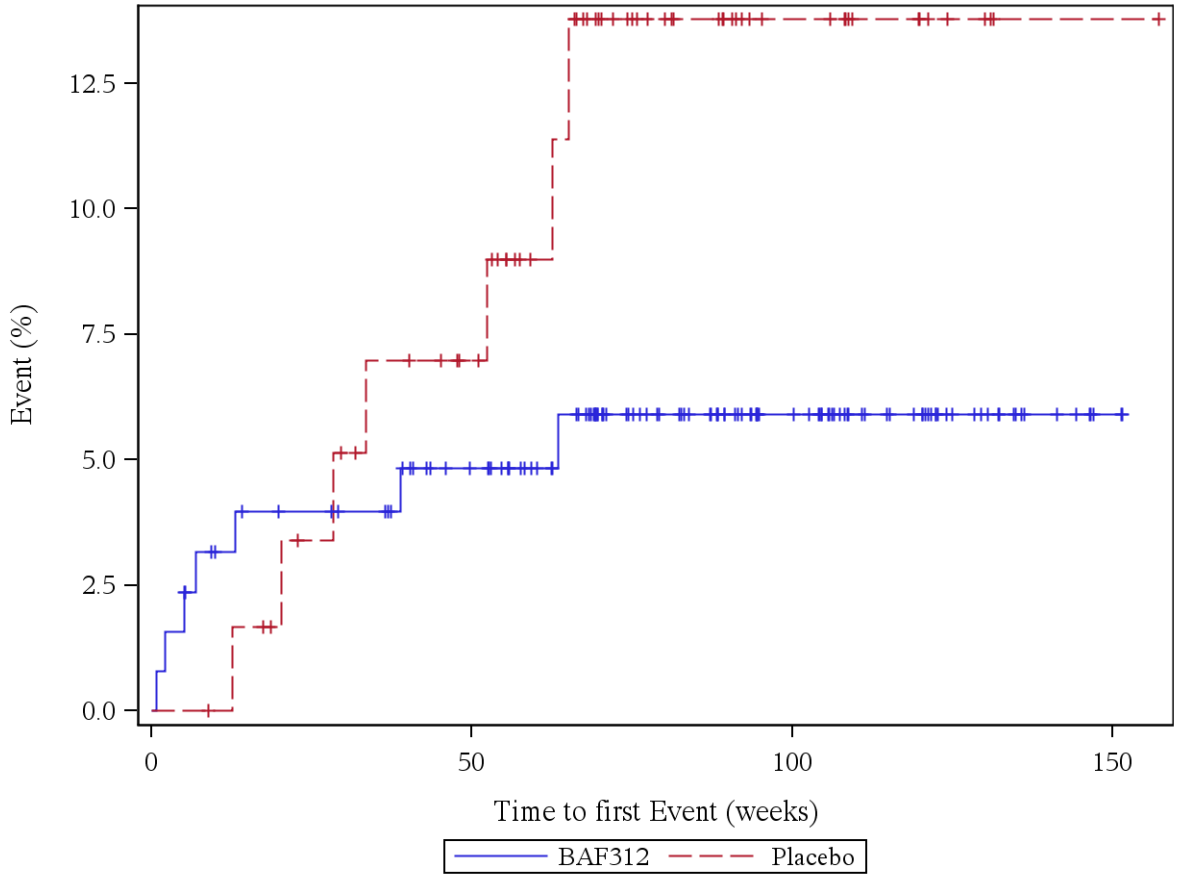


Patients at risk (BAF312/Placebo): Week 0: 127/61, Week 4: 127/61, Week 12: 123/60, Week 24: 121/57, Week 36: 119/55, Week 48: 110/51, Week 60: 99/41, Week 72: 80/32, Week 84: 66/25, Week 96: 48/17, Week 108: 35/14, Week 120: 27/9, Week 132: 14/4, Week 144: 7/1, Week 156: 0/1

Log rank test: p-value = 0,486
*: p < 0,05

Analysis population: A2304 SAF subpopulation "ACTIVE MS WITHOUT RELAPSES"

Figure 12.1.5.47: ARTHRALGIA (PT, not severe)

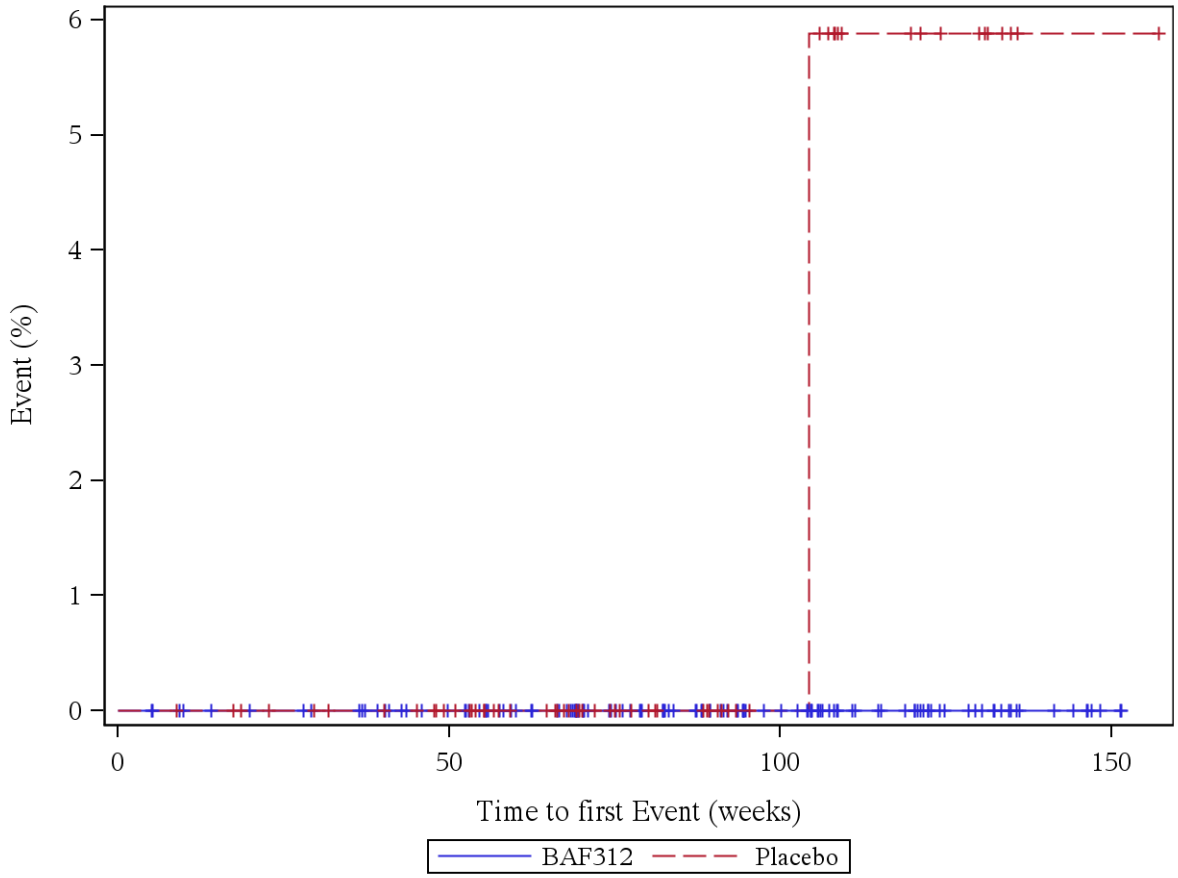


Patients at risk (BAF312/Placebo): Week 0: 127/61, Week 4: 125/61, Week 12: 119/60, Week 24: 116/55, Week 36: 114/51, Week 48: 104/47, Week 60: 93/38, Week 72: 73/28, Week 84: 62/21, Week 96: 45/13, Week 108: 34/12, Week 120: 26/6, Week 132: 13/1, Week 144: 6/1, Week 156: 0/1

Log rank test: p-value = 0,143
*: p < 0,05

Analysis population: A2304 SAF subpopulation "ACTIVE MS WITHOUT RELAPSES"

Figure 12.1.5.48: ARTHRALGIA (PT, severe)

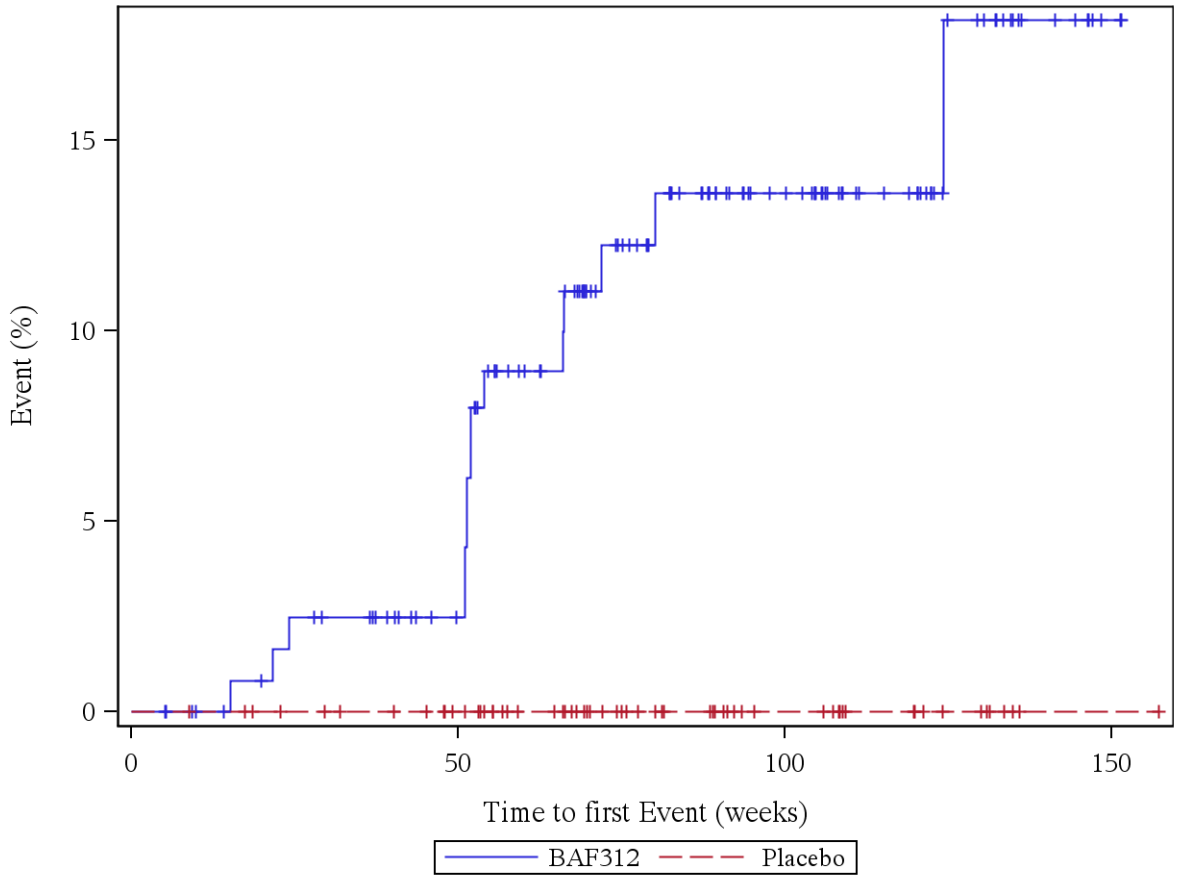


Patients at risk (BAF312/Placebo): Week 0: 127/61, Week 4: 127/61, Week 12: 123/60, Week 24: 121/57, Week 36: 119/55, Week 48: 110/51, Week 60: 99/41, Week 72: 80/32, Week 84: 66/25, Week 96: 49/17, Week 108: 36/14, Week 120: 28/9, Week 132: 15/4, Week 144: 7/1, Week 156: 0/1

Log rank test: p-value = -
*: p < 0,05

Analysis population: A2304 SAF subpopulation "ACTIVE MS WITHOUT RELAPSES"

Figure 12.1.5.49: NEOPLASMS BENIGN, MALIGNANT AND UNSPECIFIED (INCL CYSTS AND POLYPS) (SOC, not severe)

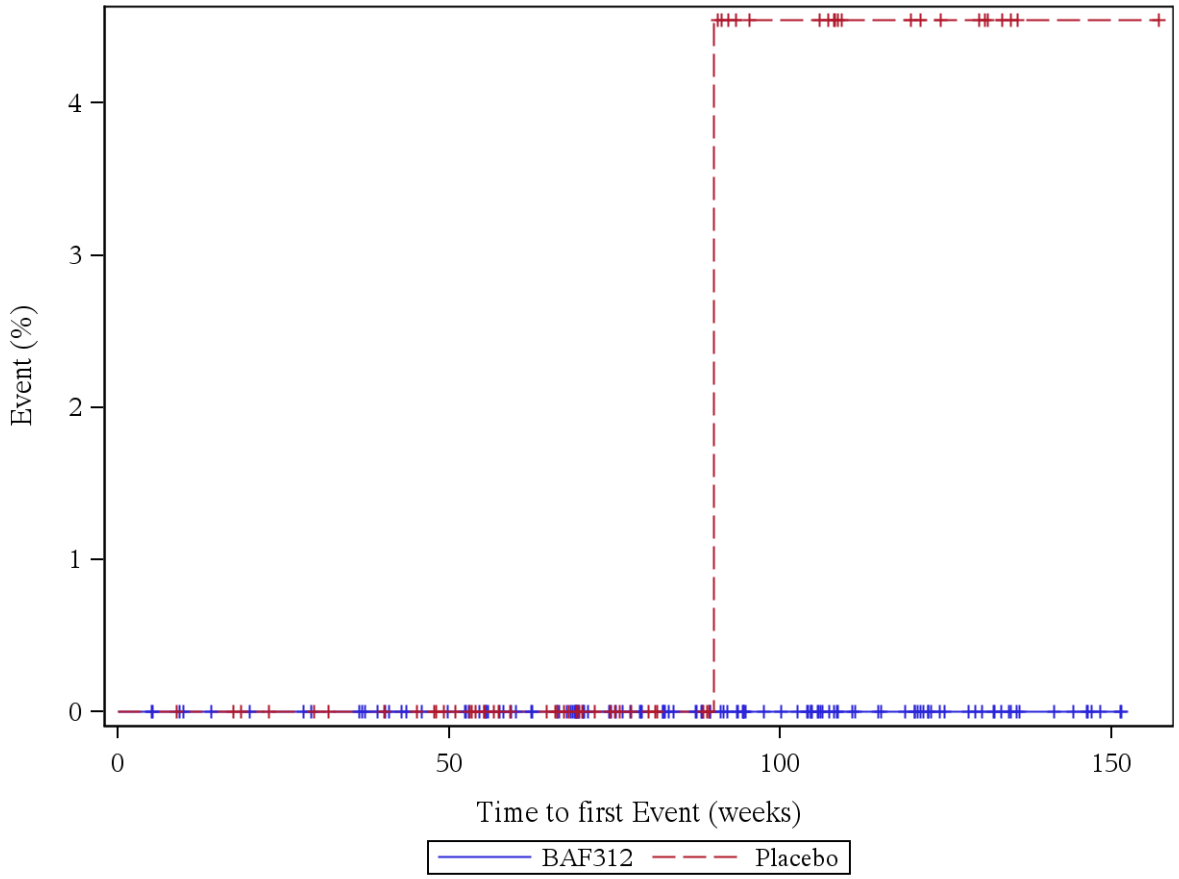


Patients at risk (BAF312/Placebo): Week 0: 127/61, Week 4: 127/61, Week 12: 123/60, Week 24: 119/57, Week 36: 116/55, Week 48: 107/51, Week 60: 90/41, Week 72: 72/32, Week 84: 58/25, Week 96: 45/17, Week 108: 34/15, Week 120: 27/9, Week 132: 15/4, Week 144: 7/1, Week 156: 0/1

Log rank test: p-value = -
*: p < 0,05

Analysis population: A2304 SAF subpopulation "ACTIVE MS WITHOUT RELAPSES"

Figure 12.1.5.50: NEOPLASMS BENIGN, MALIGNANT AND UNSPECIFIED (INCL CYSTS AND POLYPS) (SOC, severe)

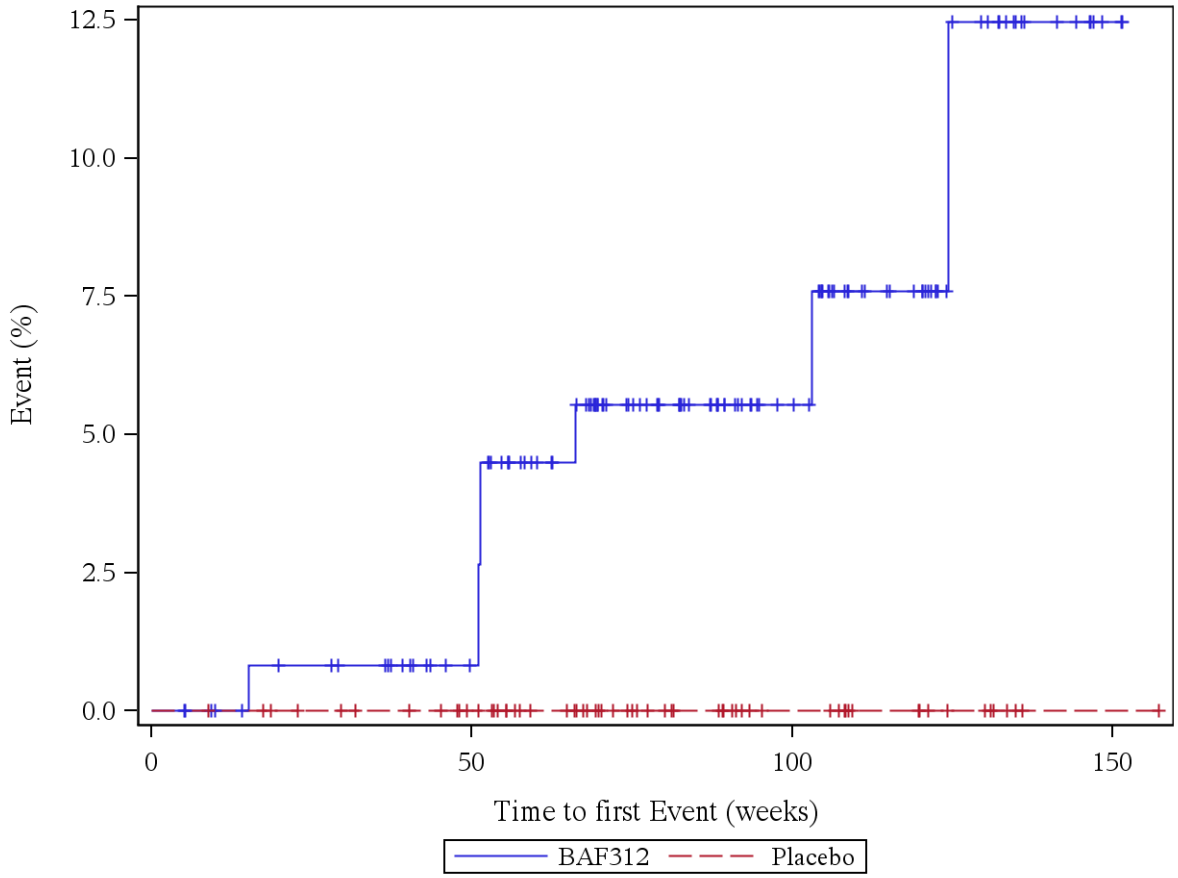


Patients at risk (BAF312/Placebo): Week 0: 127/61, Week 4: 127/61, Week 12: 123/60, Week 24: 121/57, Week 36: 119/55, Week 48: 110/51, Week 60: 99/41, Week 72: 80/32, Week 84: 66/25, Week 96: 49/16, Week 108: 36/14, Week 120: 28/9, Week 132: 15/4, Week 144: 7/1, Week 156: 0/1

Log rank test: p-value = -
*: p < 0,05

Analysis population: A2304 SAF subpopulation "ACTIVE MS WITHOUT RELAPSES"

Figure 12.1.5.51: MELANOCYTIC NAEVUS (PT, not severe)

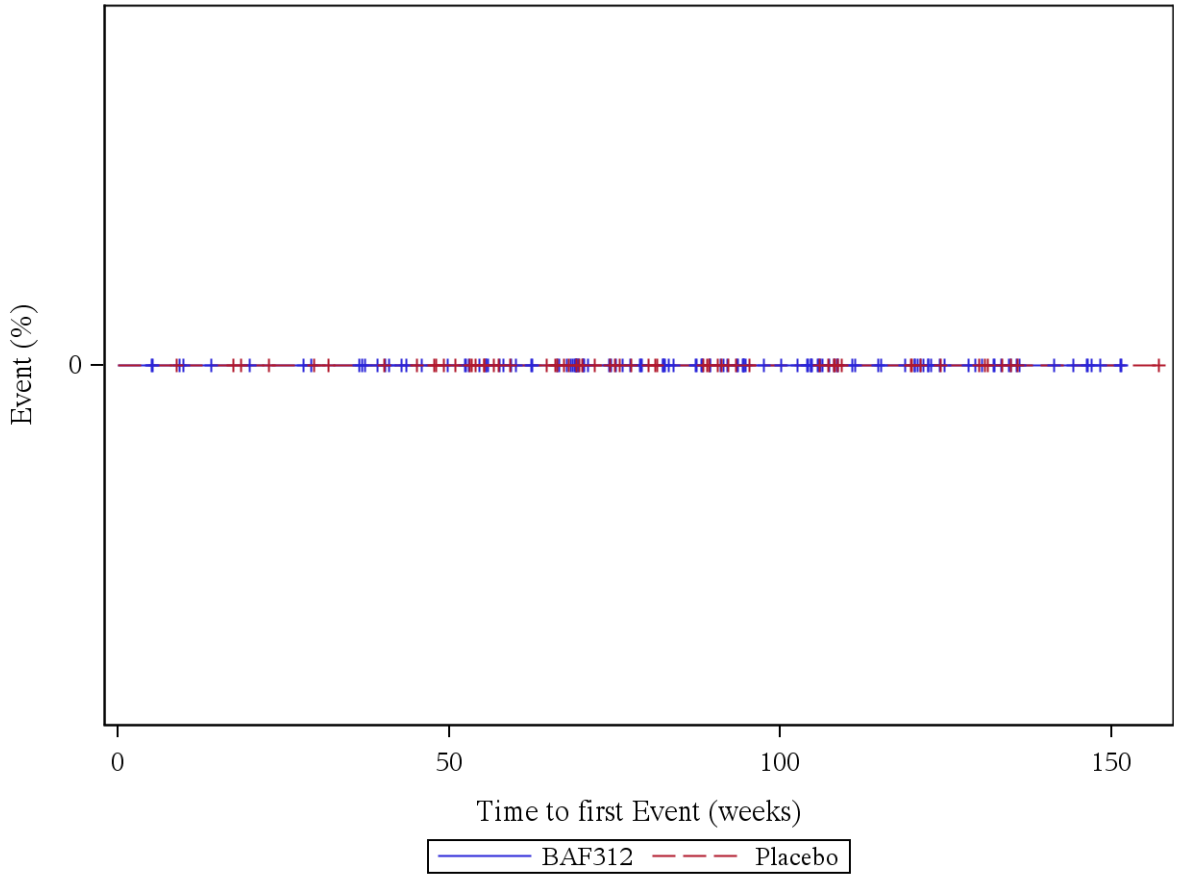


Patients at risk (BAF312/Placebo): Week 0: 127/61, Week 4: 127/61, Week 12: 123/60, Week 24: 120/57, Week 36: 118/55, Week 48: 109/51, Week 60: 94/41, Week 72: 77/32, Week 84: 63/25, Week 96: 49/17, Week 108: 36/15, Week 120: 28/9, Week 132: 15/4, Week 144: 7/1, Week 156: 0/1

Log rank test: p-value = -
*: p < 0,05

Analysis population: A2304 SAF subpopulation "ACTIVE MS WITHOUT RELAPSES"

Figure 12.1.5.52: MELANOCYTIC NAEVUS (PT, severe)

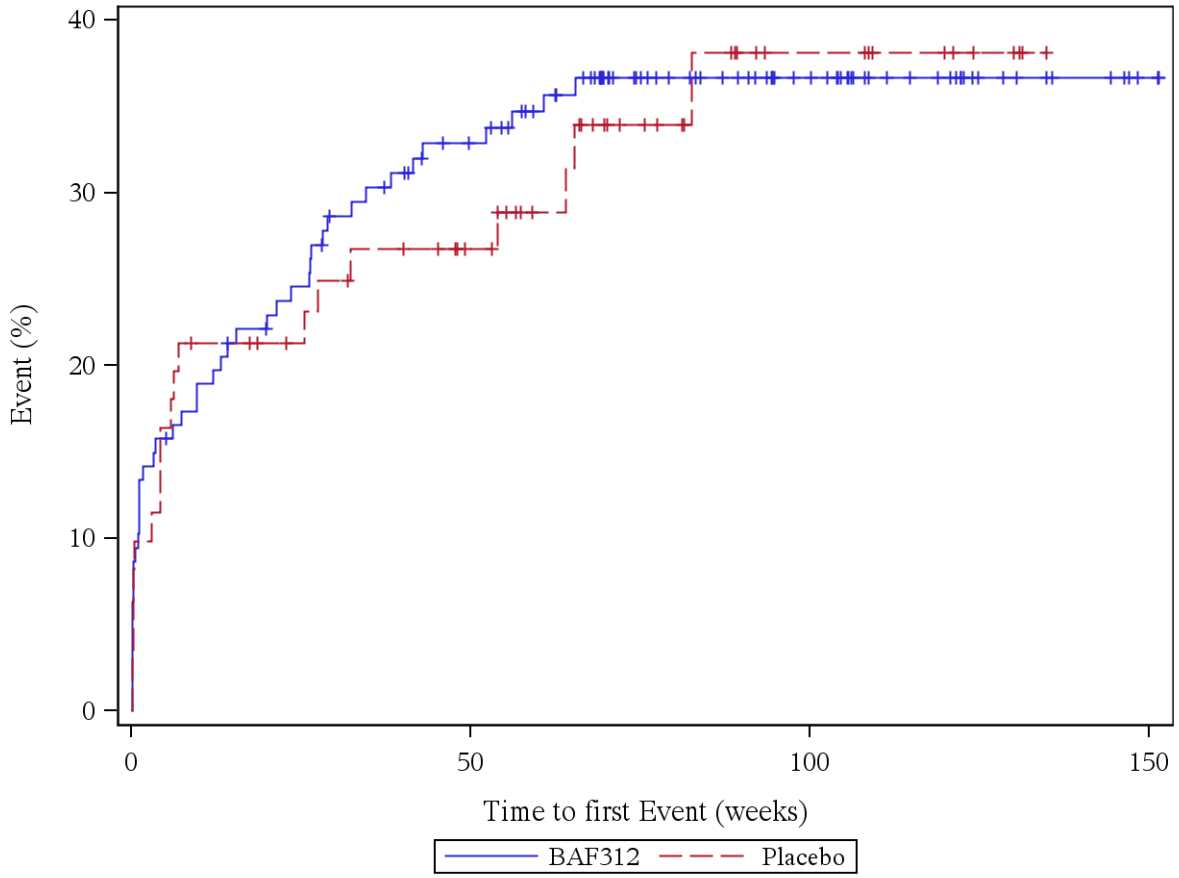


Patients at risk (BAF312/Placebo): Week 0: 127/61, Week 4: 127/61, Week 12: 123/60, Week 24: 121/57, Week 36: 119/55, Week 48: 110/51, Week 60: 99/41, Week 72: 80/32, Week 84: 66/25, Week 96: 49/17, Week 108: 36/15, Week 120: 28/9, Week 132: 15/4, Week 144: 7/1, Week 156: 0/1

Log rank test: p-value = -
*: p < 0,05

Analysis population: A2304 SAF subpopulation "ACTIVE MS WITHOUT RELAPSES"

Figure 12.1.5.53: NERVOUS SYSTEM DISORDERS (SOC, not severe)

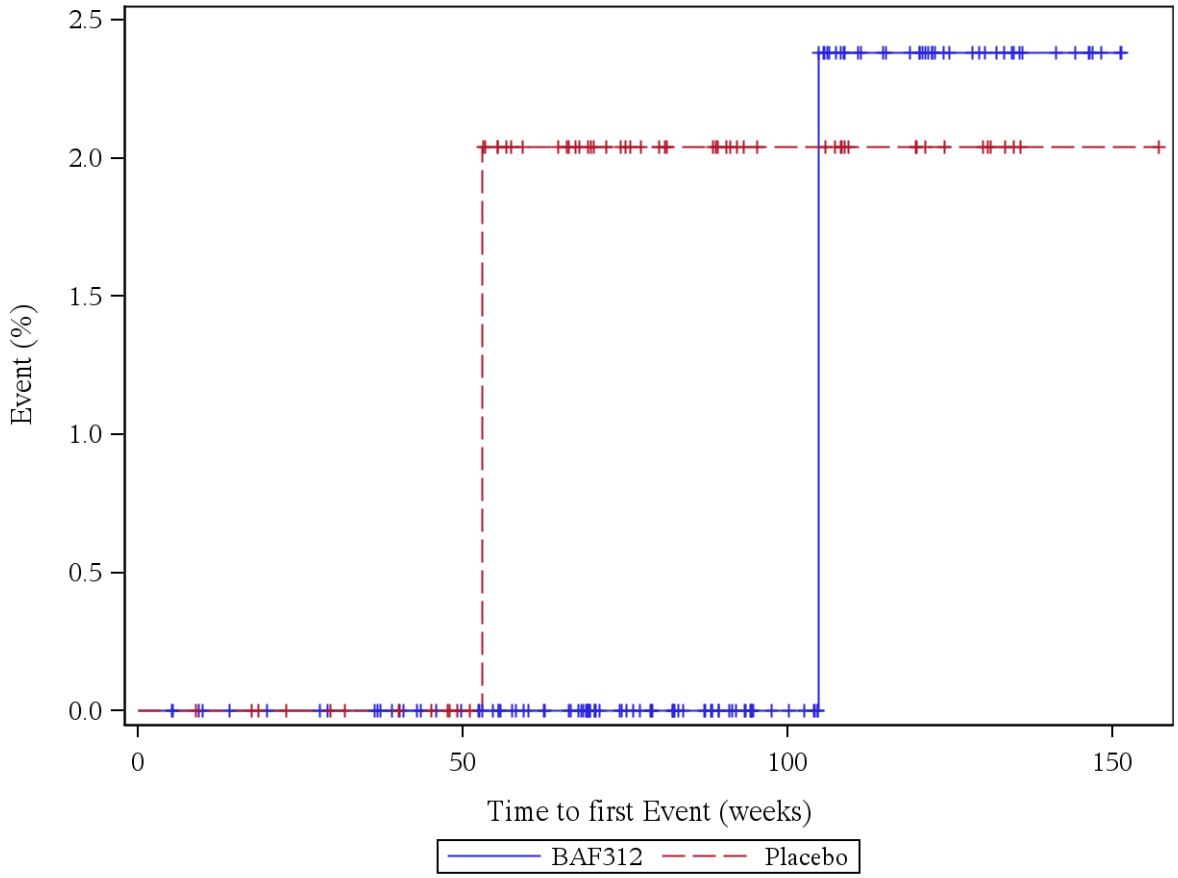


Patients at risk (BAF312/Placebo): Week 0: 127/61, Week 4: 107/54, Week 12: 101/47, Week 24: 93/44, Week 36: 84/40, Week 48: 76/36, Week 60: 67/28, Week 72: 50/20, Week 84: 41/15, Week 96: 32/10, Week 108: 22/10, Week 120: 17/6, Week 132: 8/1, Week 144: 6/0, Week 156: 0/0

Log rank test: p-value = 0,812
*: p < 0,05

Analysis population: A2304 SAF subpopulation "ACTIVE MS WITHOUT RELAPSES"

Figure 12.1.5.54: NERVOUS SYSTEM DISORDERS (SOC, severe)

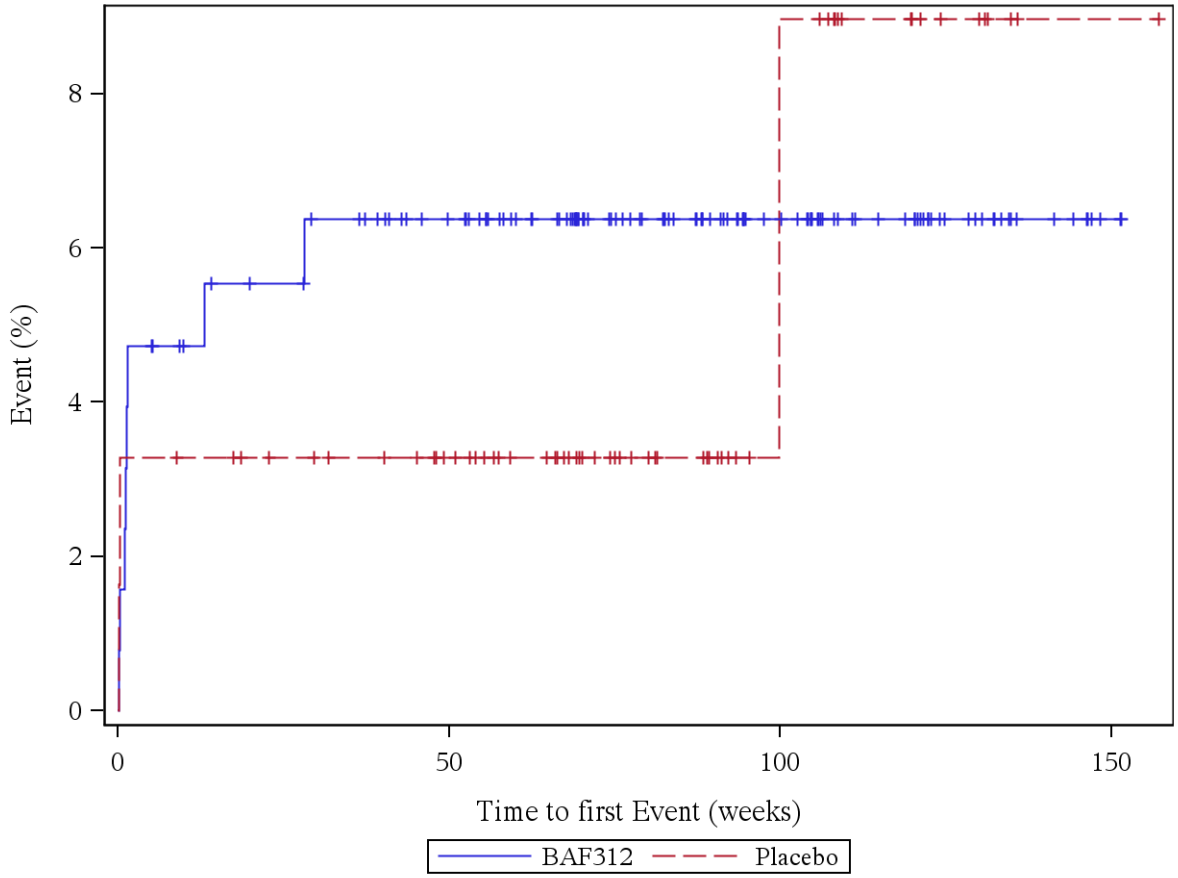


Patients at risk (BAF312/Placebo): Week 0: 127/61, Week 4: 127/61, Week 12: 123/60, Week 24: 121/57, Week 36: 119/55, Week 48: 110/51, Week 60: 99/41, Week 72: 80/32, Week 84: 66/25, Week 96: 49/17, Week 108: 35/15, Week 120: 27/9, Week 132: 14/4, Week 144: 7/1, Week 156: 0/1

Log rank test: p-value = 0,540
*: p < 0,05

Analysis population: A2304 SAF subpopulation "ACTIVE MS WITHOUT RELAPSES"

Figure 12.1.5.55: DIZZINESS (PT, not severe)

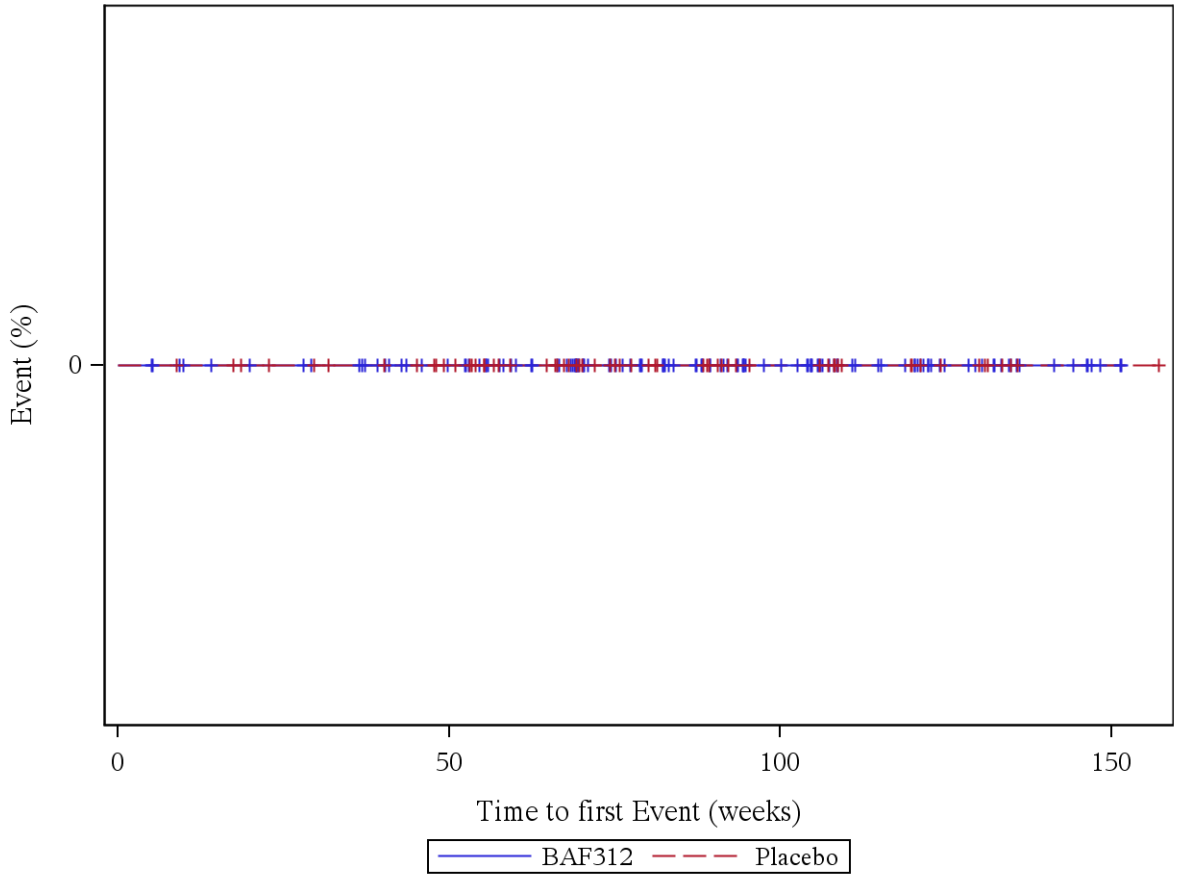


Patients at risk (BAF312/Placebo): Week 0: 127/61, Week 4: 121/59, Week 12: 117/58, Week 24: 114/55, Week 36: 111/53, Week 48: 103/49, Week 60: 92/41, Week 72: 73/32, Week 84: 61/25, Week 96: 45/17, Week 108: 33/14, Week 120: 27/8, Week 132: 14/3, Week 144: 7/1, Week 156: 0/1

Log rank test: p-value = 0,734
*: p < 0,05

Analysis population: A2304 SAF subpopulation "ACTIVE MS WITHOUT RELAPSES"

Figure 12.1.5.56: DIZZINESS (PT, severe)

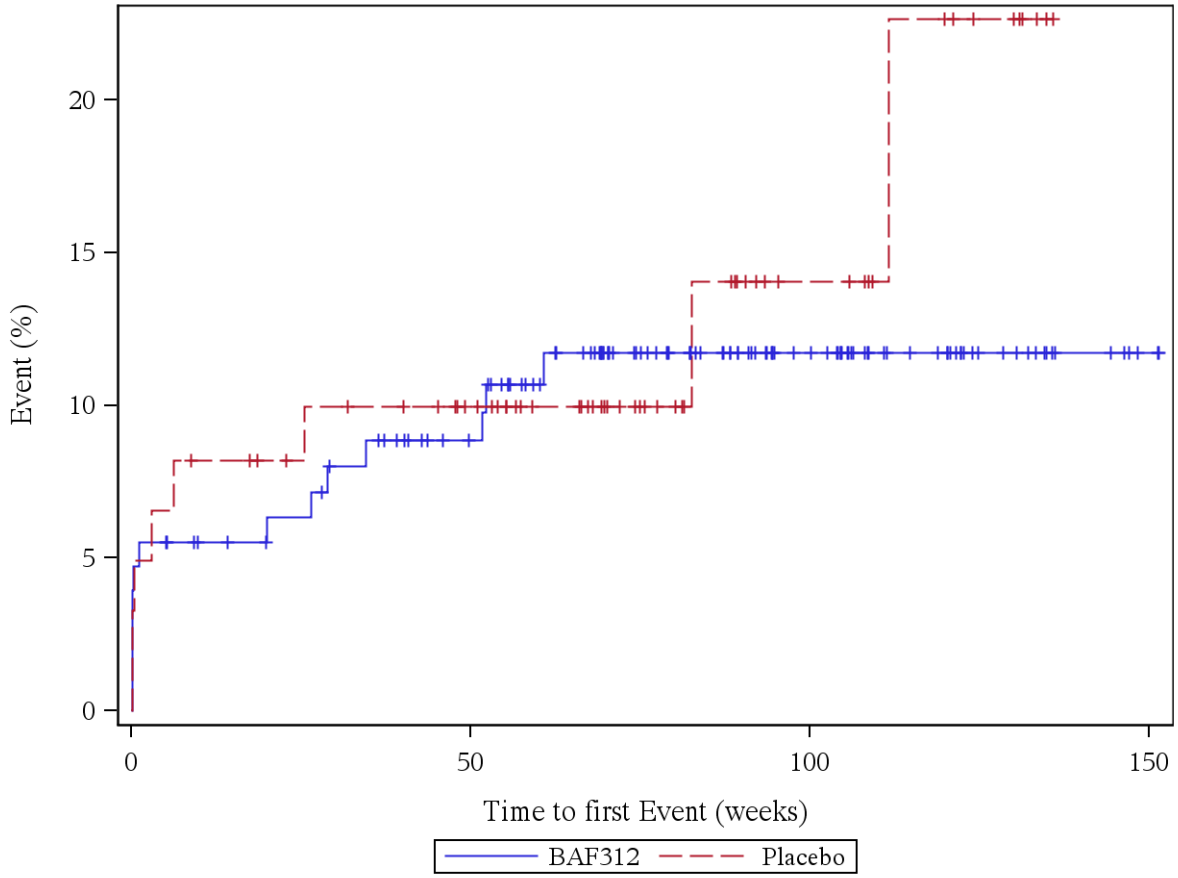


Patients at risk (BAF312/Placebo): Week 0: 127/61, Week 4: 127/61, Week 12: 123/60, Week 24: 121/57, Week 36: 119/55, Week 48: 110/51, Week 60: 99/41, Week 72: 80/32, Week 84: 66/25, Week 96: 49/17, Week 108: 36/15, Week 120: 28/9, Week 132: 15/4, Week 144: 7/1, Week 156: 0/1

Log rank test: p-value = -
*: p < 0,05

Analysis population: A2304 SAF subpopulation "ACTIVE MS WITHOUT RELAPSES"

Figure 12.1.5.57: HEADACHE (PT, not severe)

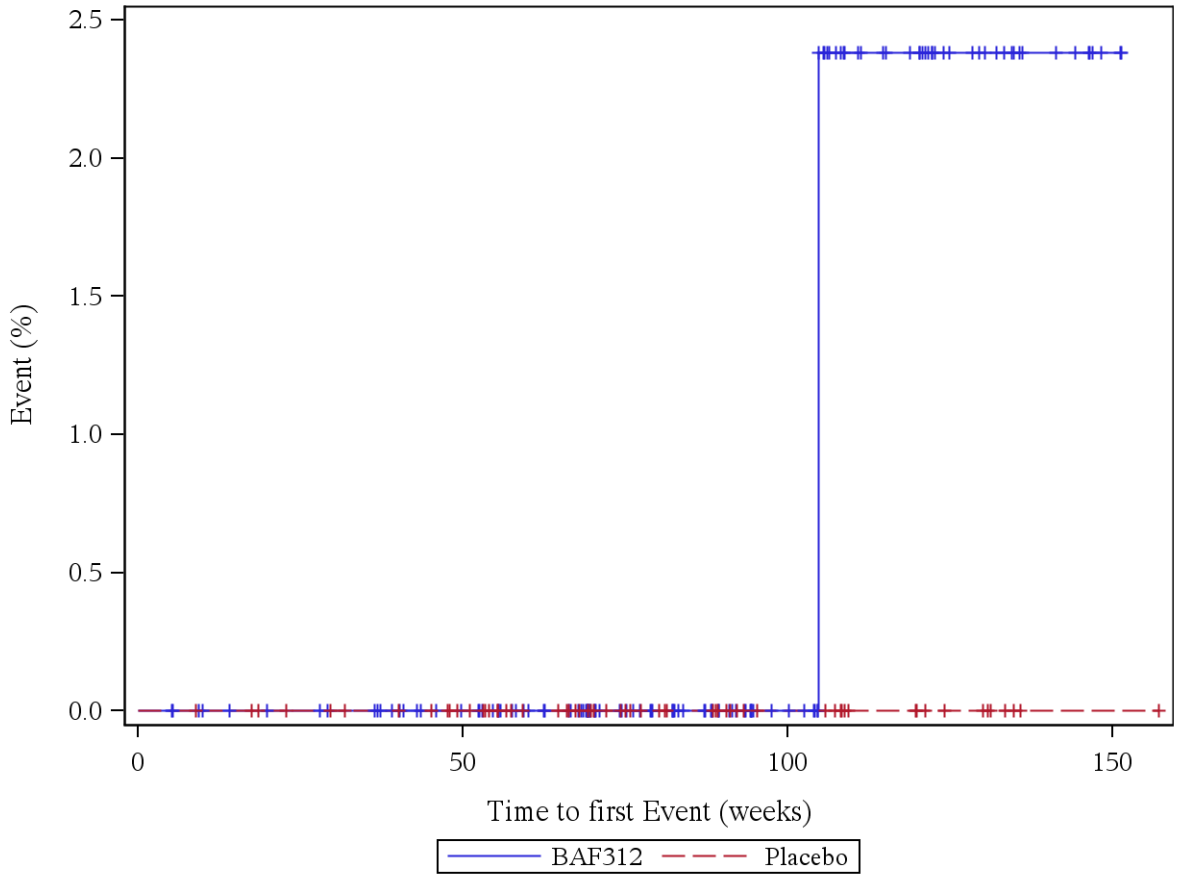


Patients at risk (BAF312/Placebo): Week 0: 127/61, Week 4: 120/57, Week 12: 116/55, Week 24: 113/52, Week 36: 108/50, Week 48: 100/46, Week 60: 88/37, Week 72: 70/29, Week 84: 57/21, Week 96: 42/14, Week 108: 30/13, Week 120: 23/8, Week 132: 12/3, Week 144: 6/0, Week 156: 0/0

Log rank test: p-value = 0,627
*: p < 0,05

Analysis population: A2304 SAF subpopulation "ACTIVE MS WITHOUT RELAPSES"

Figure 12.1.5.58: HEADACHE (PT, severe)

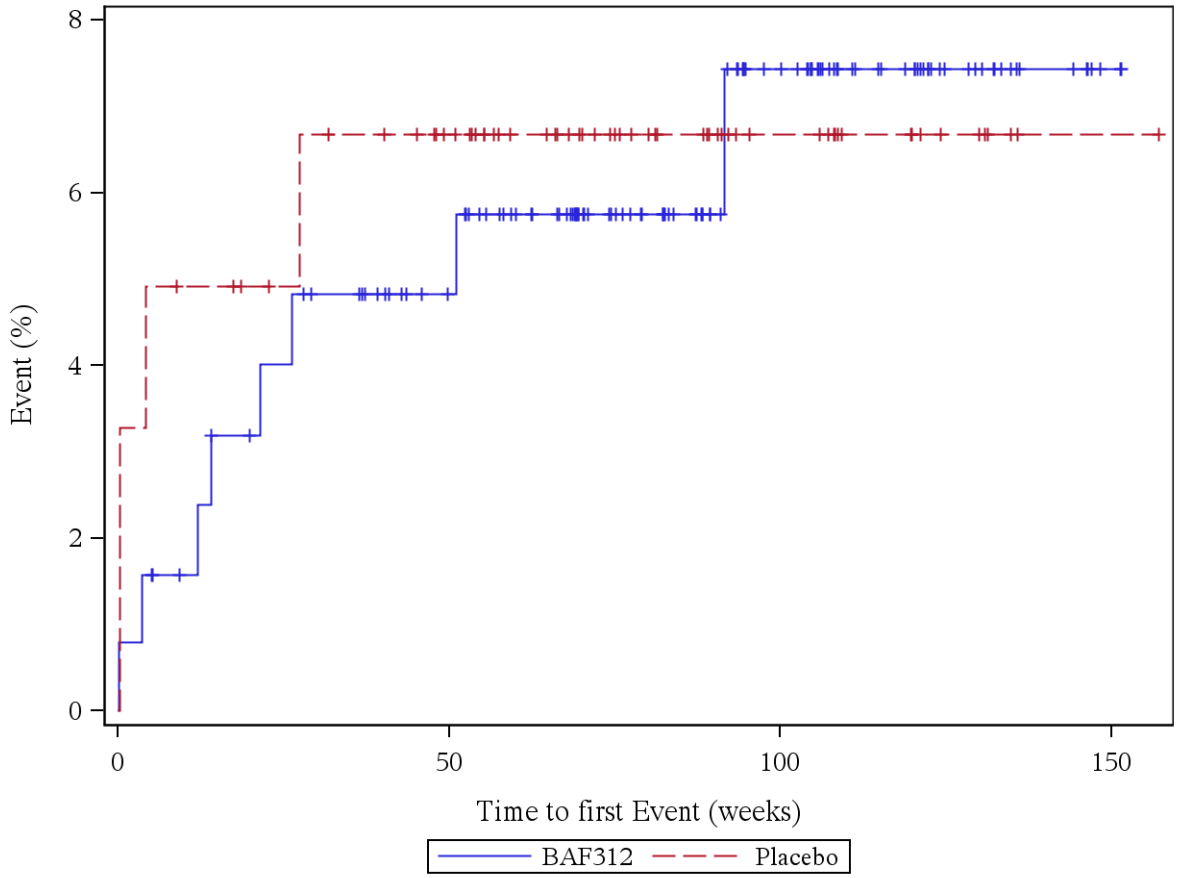


Patients at risk (BAF312/Placebo): Week 0: 127/61, Week 4: 127/61, Week 12: 123/60, Week 24: 121/57, Week 36: 119/55, Week 48: 110/51, Week 60: 99/41, Week 72: 80/32, Week 84: 66/25, Week 96: 49/17, Week 108: 35/15, Week 120: 27/9, Week 132: 14/4, Week 144: 7/1, Week 156: 0/1

Log rank test: p-value = -
*: p < 0,05

Analysis population: A2304 SAF subpopulation "ACTIVE MS WITHOUT RELAPSES"

Figure 12.1.5.59: MUSCLE SPASTICITY (PT, not severe)

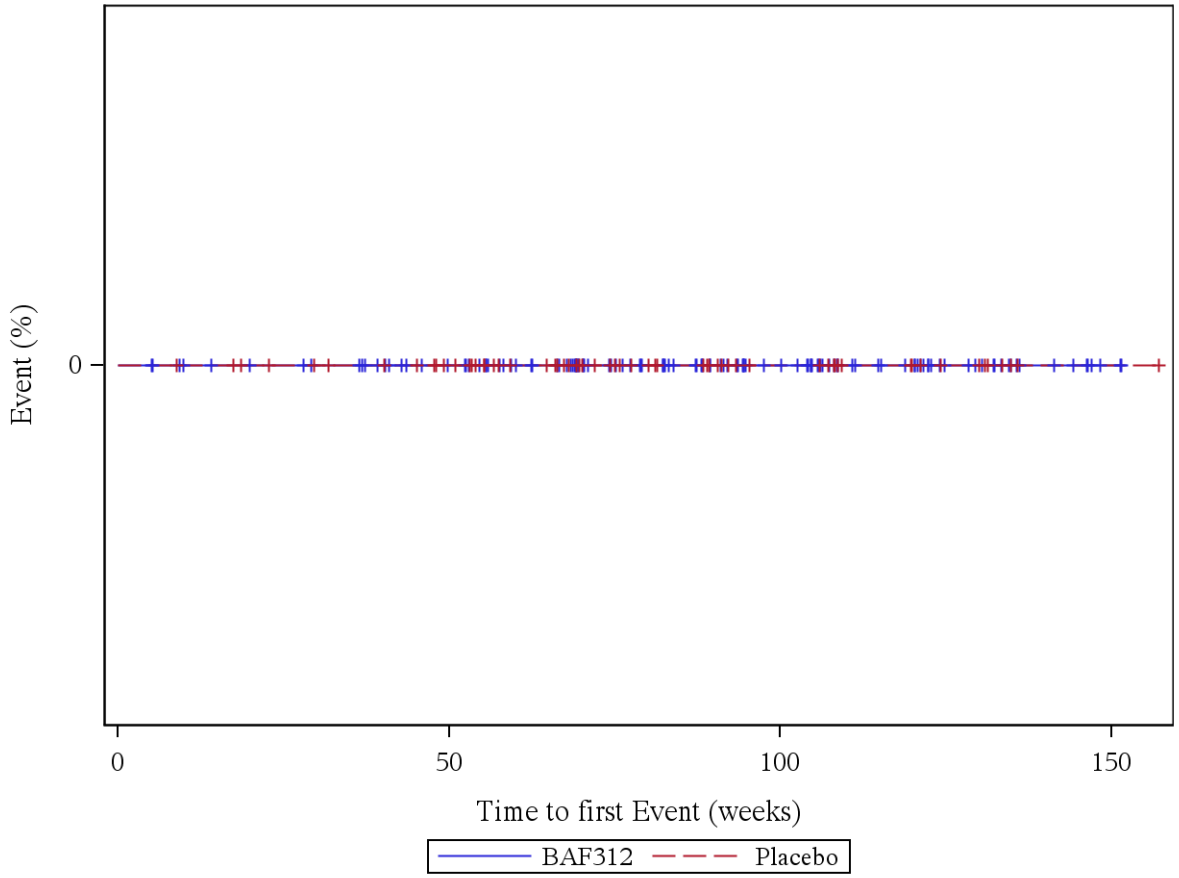


Patients at risk (BAF312/Placebo): Week 0: 127/61, Week 4: 125/59, Week 12: 121/57, Week 24: 117/54, Week 36: 114/52, Week 48: 105/48, Week 60: 95/38, Week 72: 77/31, Week 84: 64/24, Week 96: 47/16, Week 108: 34/14, Week 120: 26/8, Week 132: 13/3, Week 144: 7/1, Week 156: 0/1

Log rank test: p-value = 0,884
*: p < 0,05

Analysis population: A2304 SAF subpopulation "ACTIVE MS WITHOUT RELAPSES"

Figure 12.1.5.60: MUSCLE SPASTICITY (PT, severe)

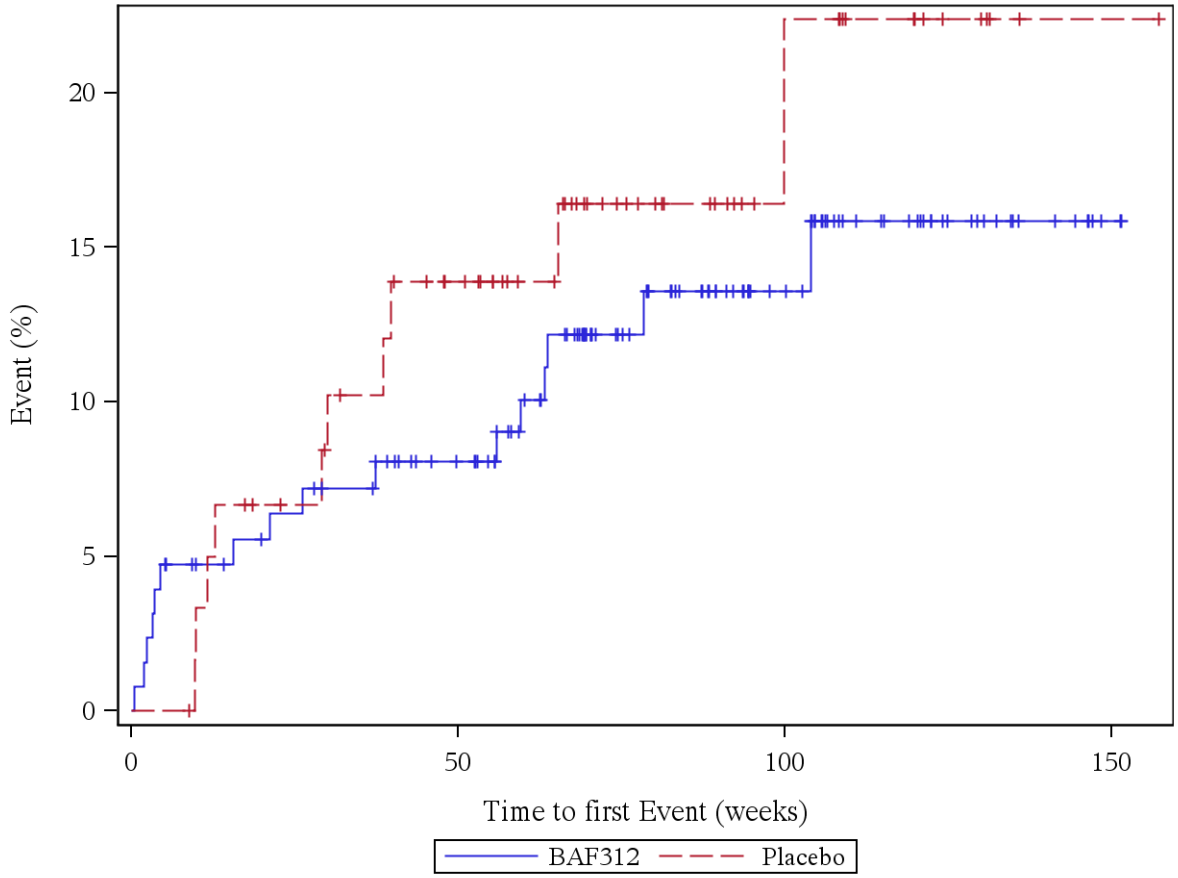


Patients at risk (BAF312/Placebo): Week 0: 127/61, Week 4: 127/61, Week 12: 123/60, Week 24: 121/57, Week 36: 119/55, Week 48: 110/51, Week 60: 99/41, Week 72: 80/32, Week 84: 66/25, Week 96: 49/17, Week 108: 36/15, Week 120: 28/9, Week 132: 15/4, Week 144: 7/1, Week 156: 0/1

Log rank test: p-value = -
*: p < 0,05

Analysis population: A2304 SAF subpopulation "ACTIVE MS WITHOUT RELAPSES"

Figure 12.1.5.61: PSYCHIATRIC DISORDERS (SOC, not severe)

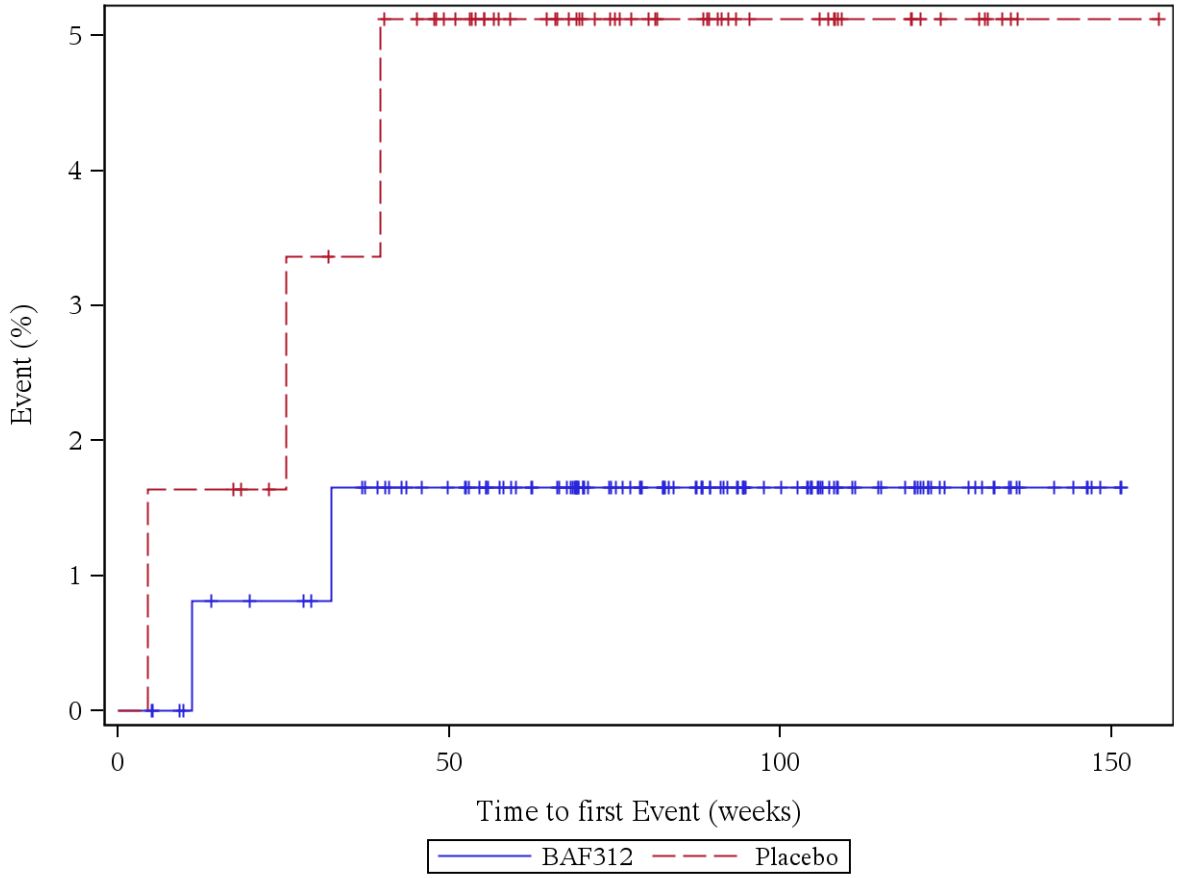


Patients at risk (BAF312/Placebo): Week 0: 127/61, Week 4: 122/61, Week 12: 117/57, Week 24: 113/53, Week 36: 110/49, Week 48: 101/43, Week 60: 88/35, Week 72: 67/26, Week 84: 55/20, Week 96: 41/14, Week 108: 28/13, Week 120: 22/7, Week 132: 12/2, Week 144: 7/1, Week 156: 0/1

Log rank test: p-value = 0,413
*: p < 0,05

Analysis population: A2304 SAF subpopulation "ACTIVE MS WITHOUT RELAPSES"

Figure 12.1.5.62: PSYCHIATRIC DISORDERS (SOC, severe)

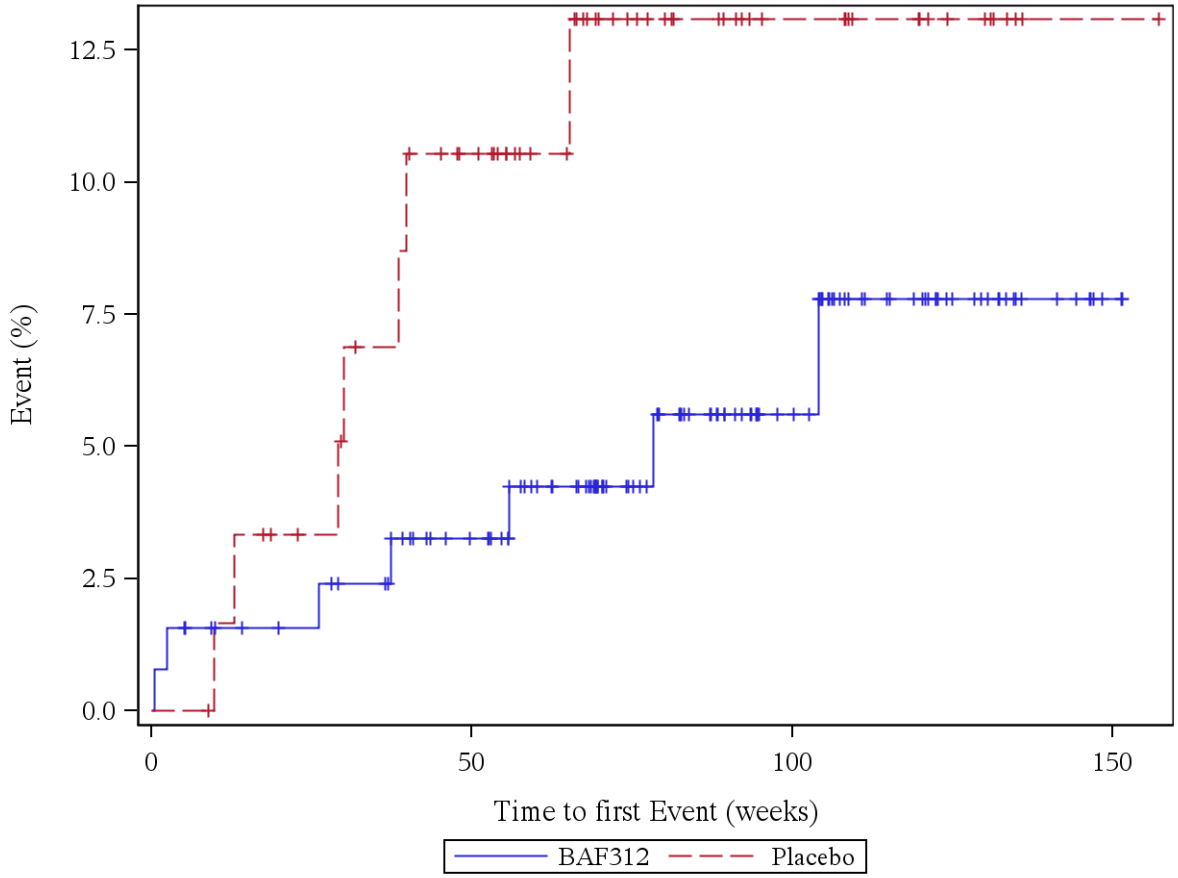


Patients at risk (BAF312/Placebo): Week 0: 127/61, Week 4: 127/61, Week 12: 122/60, Week 24: 120/57, Week 36: 117/55, Week 48: 109/50, Week 60: 98/40, Week 72: 79/32, Week 84: 65/25, Week 96: 48/17, Week 108: 35/15, Week 120: 27/9, Week 132: 14/4, Week 144: 7/1, Week 156: 0/1

Log rank test: p-value = 0,186
*: p < 0,05

Analysis population: A2304 SAF subpopulation "ACTIVE MS WITHOUT RELAPSES"

Figure 12.1.5.63: DEPRESSION (PT, not severe)

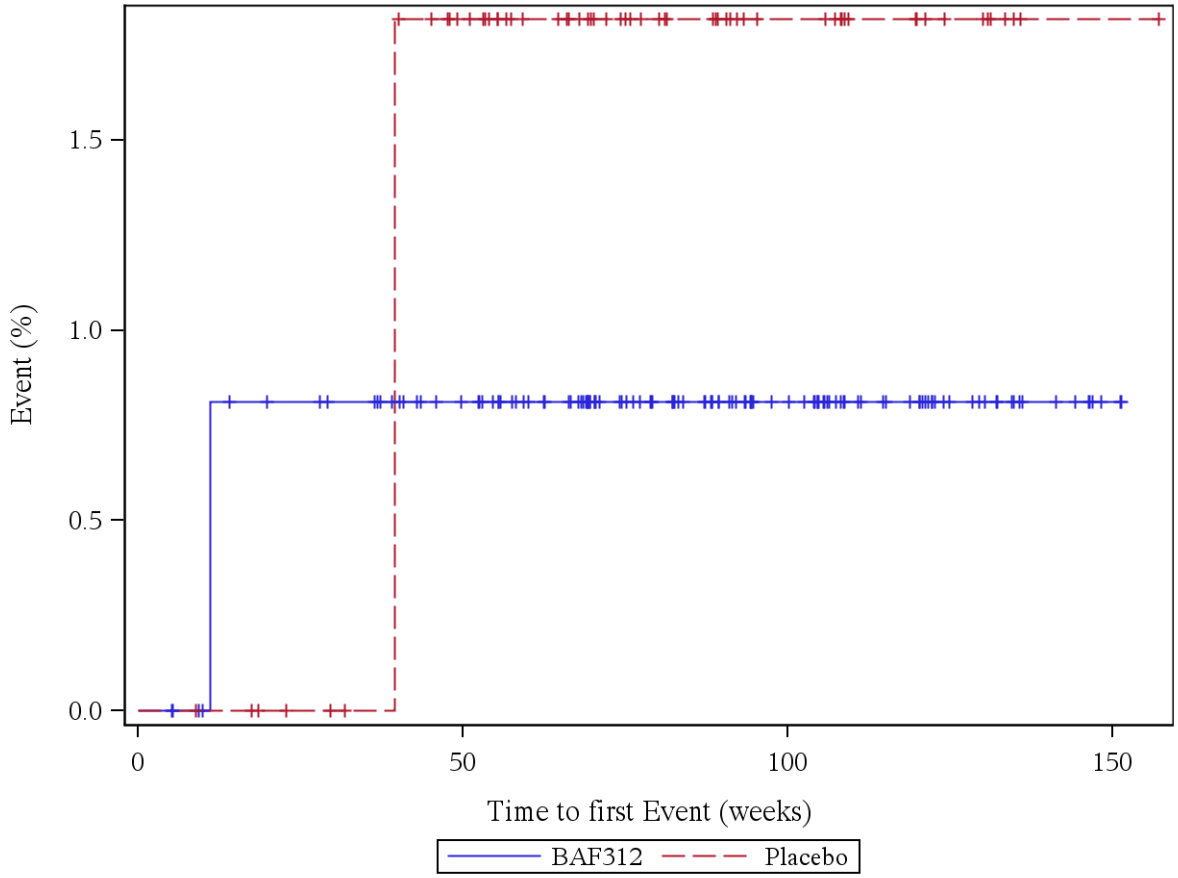


Patients at risk (BAF312/Placebo): Week 0: 127/61, Week 4: 125/61, Week 12: 121/59, Week 24: 119/55, Week 36: 116/51, Week 48: 106/45, Week 60: 94/36, Week 72: 75/27, Week 84: 61/21, Week 96: 46/15, Week 108: 32/15, Week 120: 25/9, Week 132: 14/4, Week 144: 7/1, Week 156: 0/1

Log rank test: p-value = 0,112
*: p < 0,05

Analysis population: A2304 SAF subpopulation "ACTIVE MS WITHOUT RELAPSES"

Figure 12.1.5.64: DEPRESSION (PT, severe)

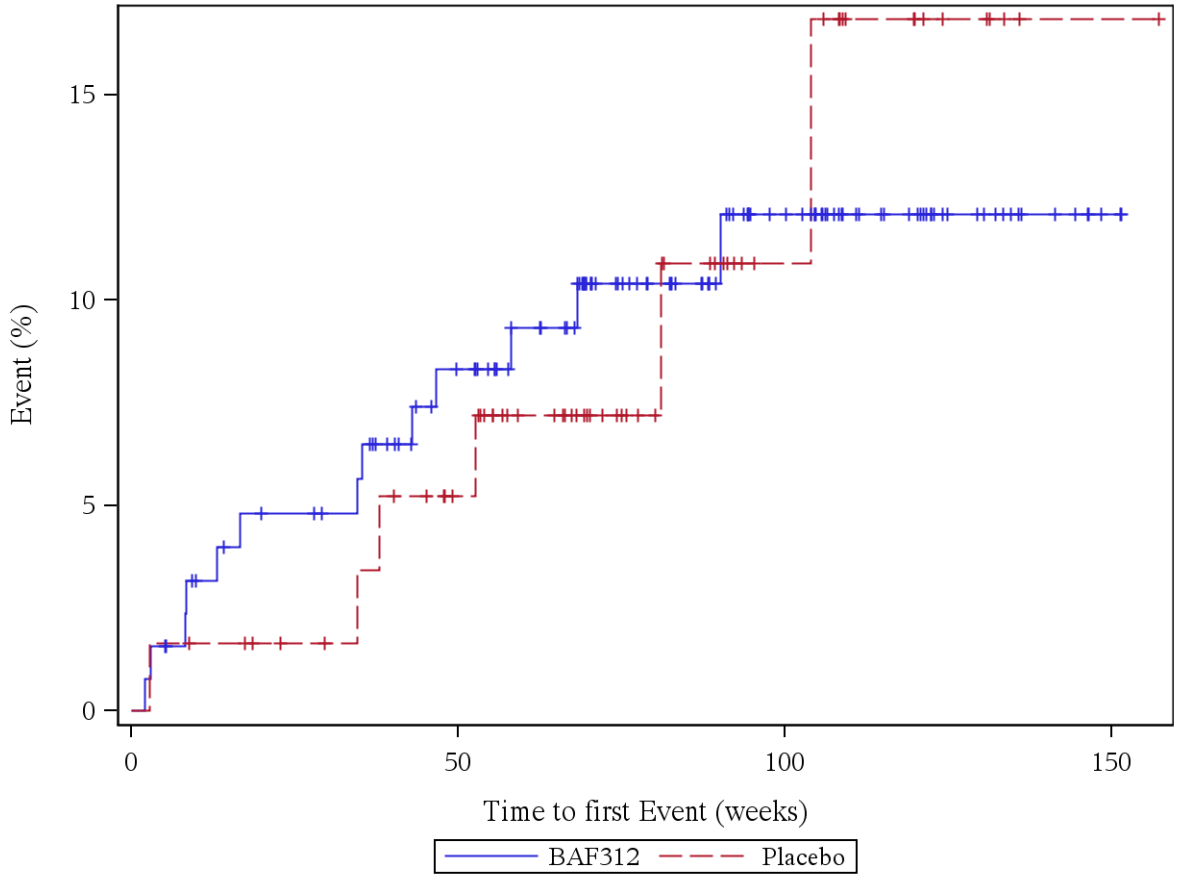


Patients at risk (BAF312/Placebo): Week 0: 127/61, Week 4: 127/61, Week 12: 122/60, Week 24: 120/57, Week 36: 118/55, Week 48: 109/50, Week 60: 98/40, Week 72: 79/32, Week 84: 65/25, Week 96: 48/17, Week 108: 35/15, Week 120: 27/9, Week 132: 14/4, Week 144: 7/1, Week 156: 0/1

Log rank test: p-value = 0,601
*: p < 0,05

Analysis population: A2304 SAF subpopulation "ACTIVE MS WITHOUT RELAPSES"

Figure 12.1.5.65: RENAL AND URINARY DISORDERS (SOC, not severe)

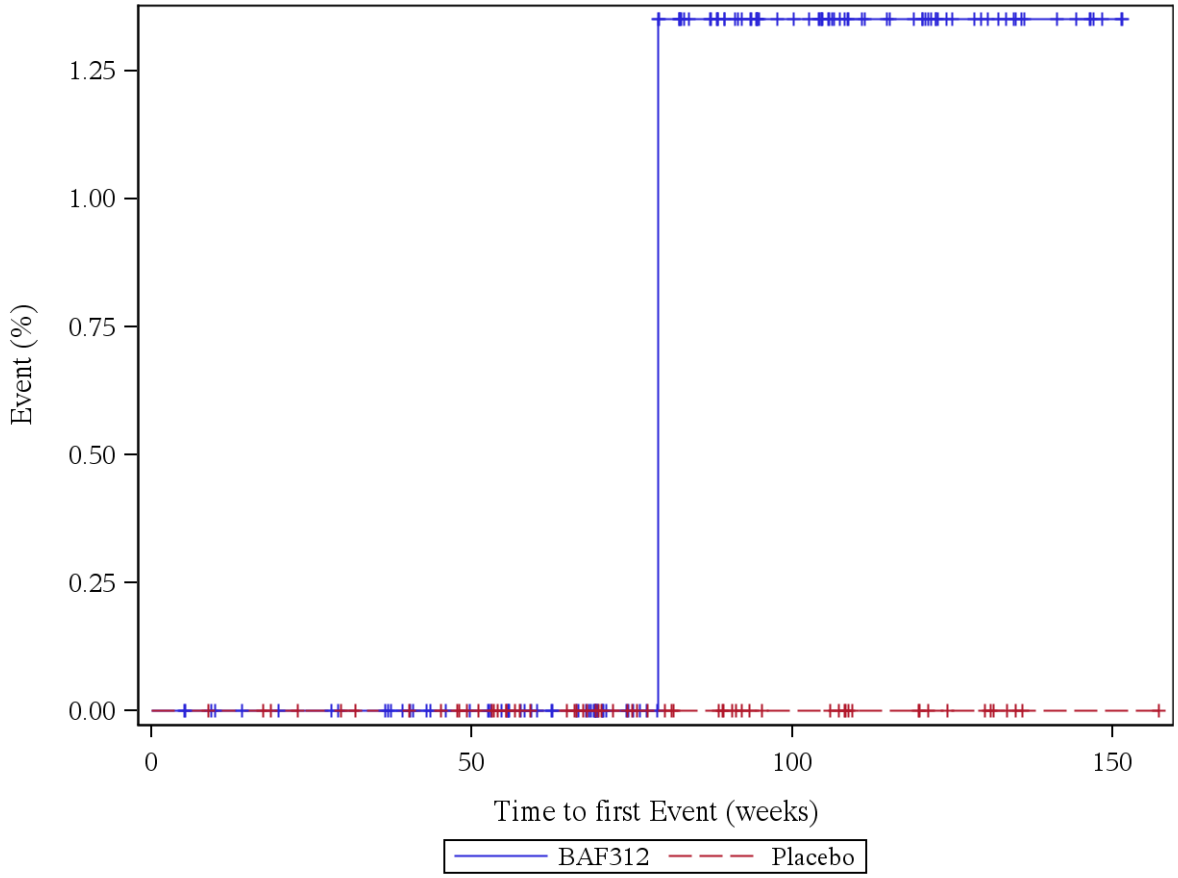


Patients at risk (BAF312/Placebo): Week 0: 127/61, Week 4: 125/60, Week 12: 119/59, Week 24: 115/56, Week 36: 111/54, Week 48: 100/49, Week 60: 89/39, Week 72: 70/30, Week 84: 59/22, Week 96: 43/15, Week 108: 31/13, Week 120: 23/7, Week 132: 12/3, Week 144: 6/1, Week 156: 0/1

Log rank test: p-value = 0,987
*: p < 0,05

Analysis population: A2304 SAF subpopulation "ACTIVE MS WITHOUT RELAPSES"

Figure 12.1.5.66: RENAL AND URINARY DISORDERS (SOC, severe)

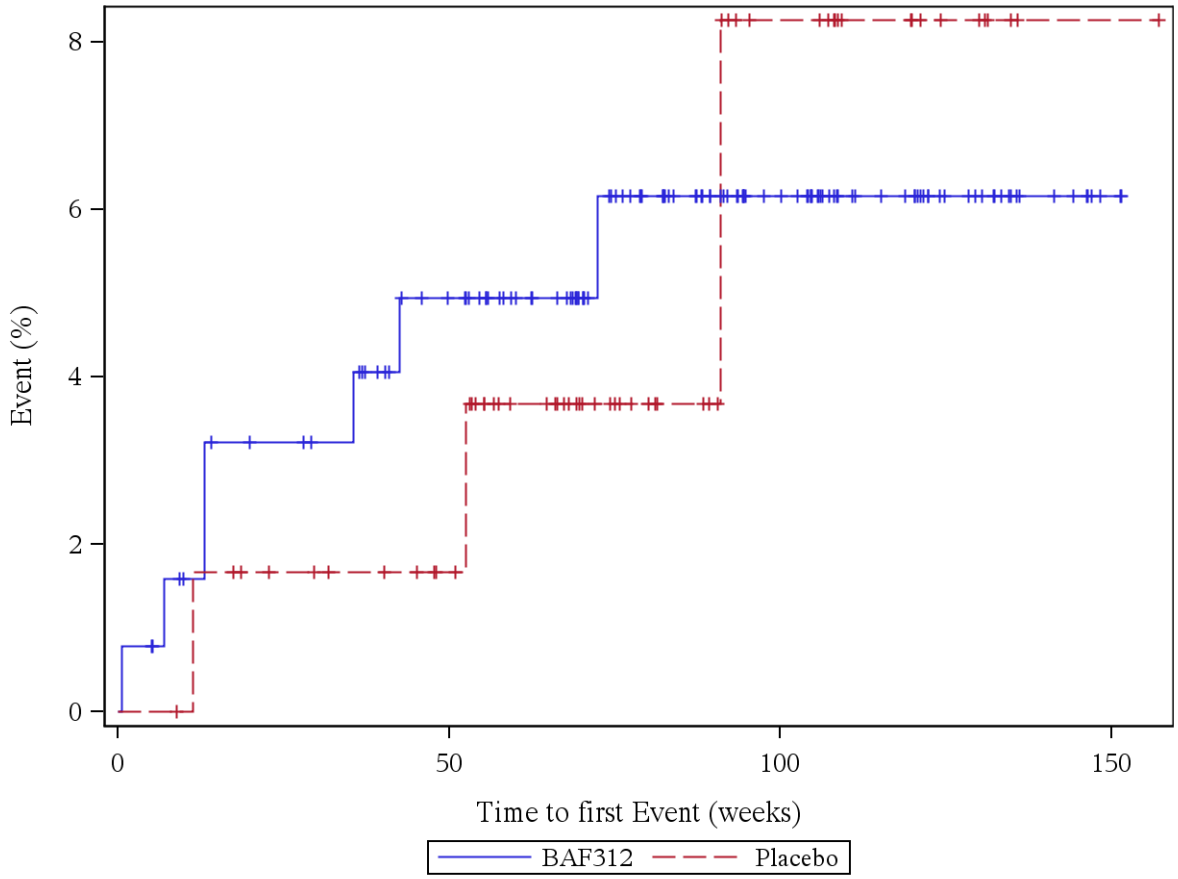


Patients at risk (BAF312/Placebo): Week 0: 127/61, Week 4: 127/61, Week 12: 123/60, Week 24: 121/57, Week 36: 119/55, Week 48: 110/51, Week 60: 99/41, Week 72: 80/32, Week 84: 65/25, Week 96: 48/17, Week 108: 35/15, Week 120: 27/9, Week 132: 14/4, Week 144: 7/1, Week 156: 0/1

Log rank test: p-value = -
*: p < 0,05

Analysis population: A2304 SAF subpopulation "ACTIVE MS WITHOUT RELAPSES"

Figure 12.1.5.67: REPRODUCTIVE SYSTEM AND BREAST DISORDERS (SOC, not severe)

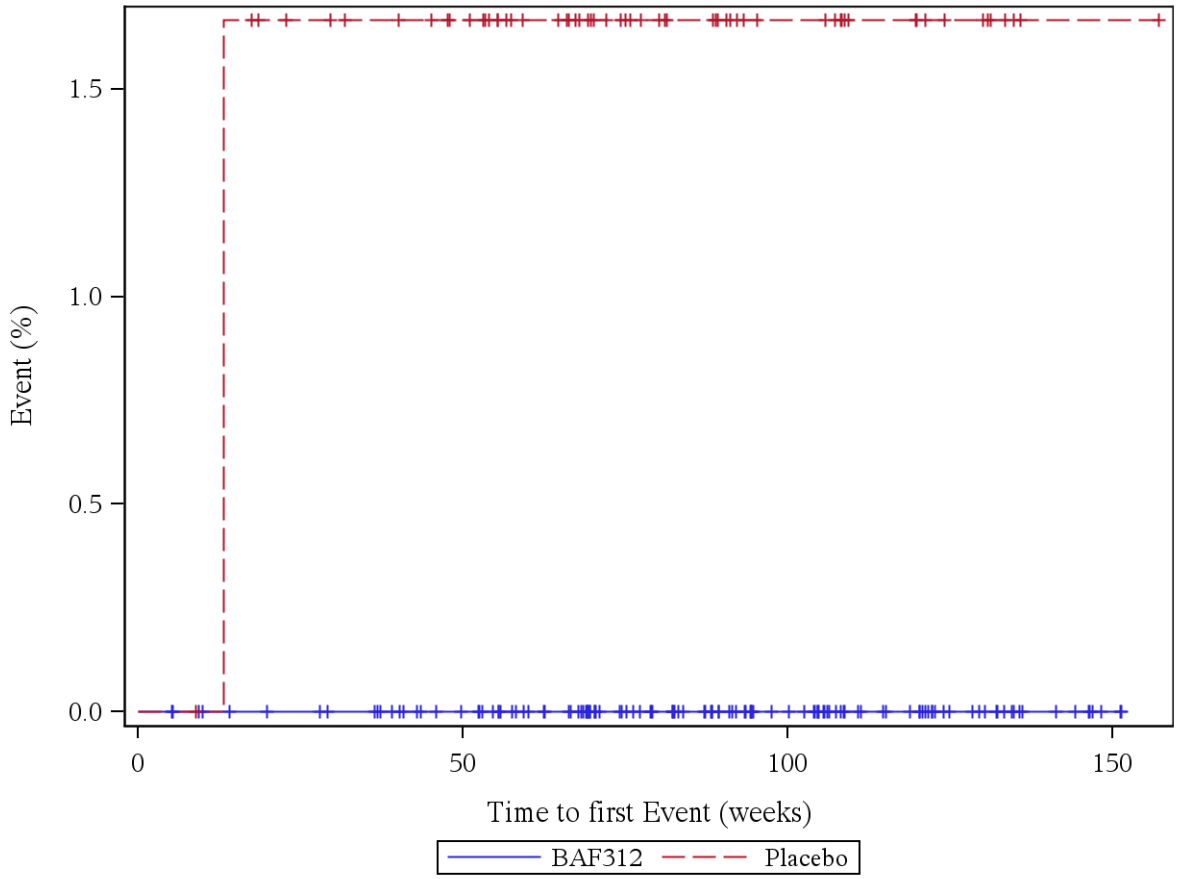


Patients at risk (BAF312/Placebo): Week 0: 127/61, Week 4: 126/61, Week 12: 121/59, Week 24: 117/56, Week 36: 114/54, Week 48: 105/50, Week 60: 94/40, Week 72: 78/31, Week 84: 63/24, Week 96: 47/16, Week 108: 34/14, Week 120: 27/8, Week 132: 15/3, Week 144: 7/1, Week 156: 0/1

Log rank test: p-value = 0,910
*: p < 0,05

Analysis population: A2304 SAF subpopulation "ACTIVE MS WITHOUT RELAPSES"

Figure 12.1.5.68: REPRODUCTIVE SYSTEM AND BREAST DISORDERS (SOC, severe)

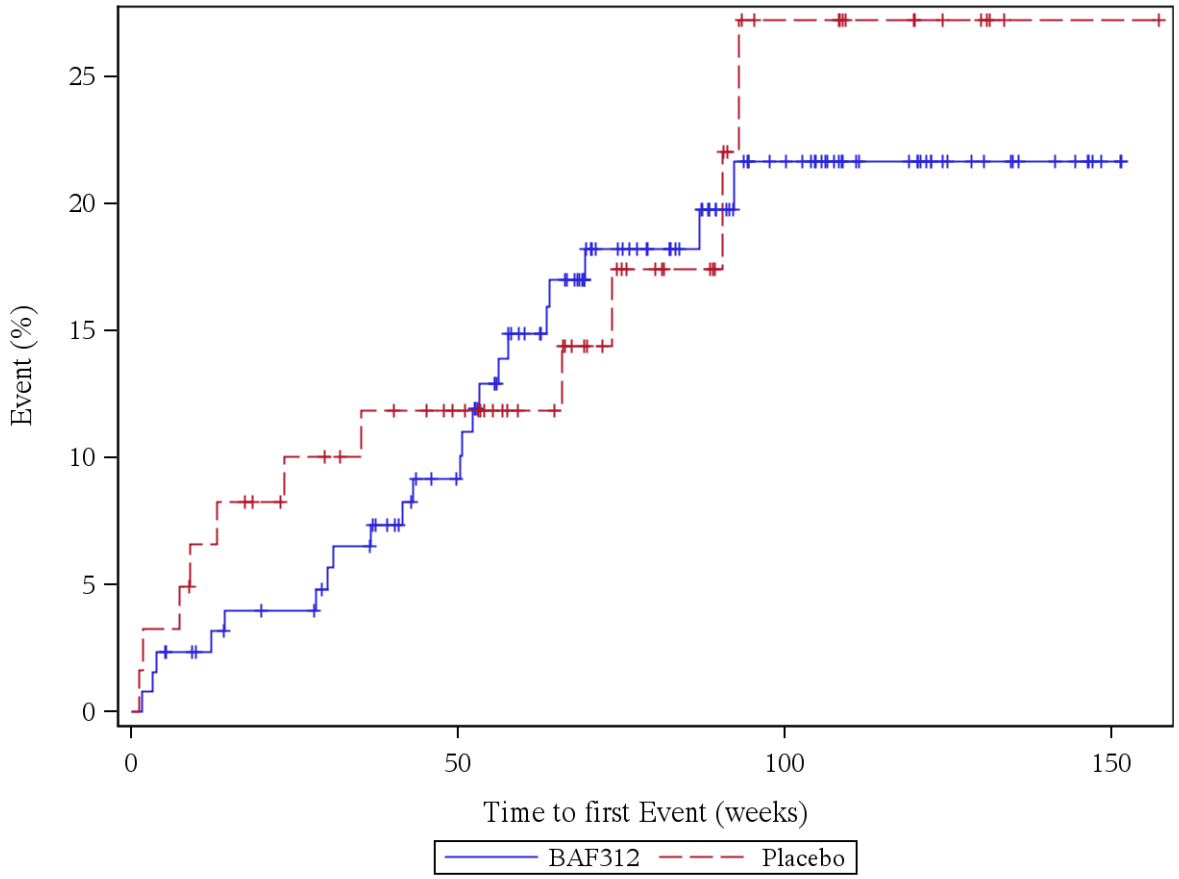


Patients at risk (BAF312/Placebo): Week 0: 127/61, Week 4: 127/61, Week 12: 123/60, Week 24: 121/56, Week 36: 119/54, Week 48: 110/50, Week 60: 99/41, Week 72: 80/32, Week 84: 66/25, Week 96: 49/17, Week 108: 36/15, Week 120: 28/9, Week 132: 15/4, Week 144: 7/1, Week 156: 0/1

Log rank test: p-value = -
*: p < 0,05

Analysis population: A2304 SAF subpopulation "ACTIVE MS WITHOUT RELAPSES"

Figure 12.1.5.69: RESPIRATORY, THORACIC AND MEDIASTINAL DISORDERS (SOC, not severe)

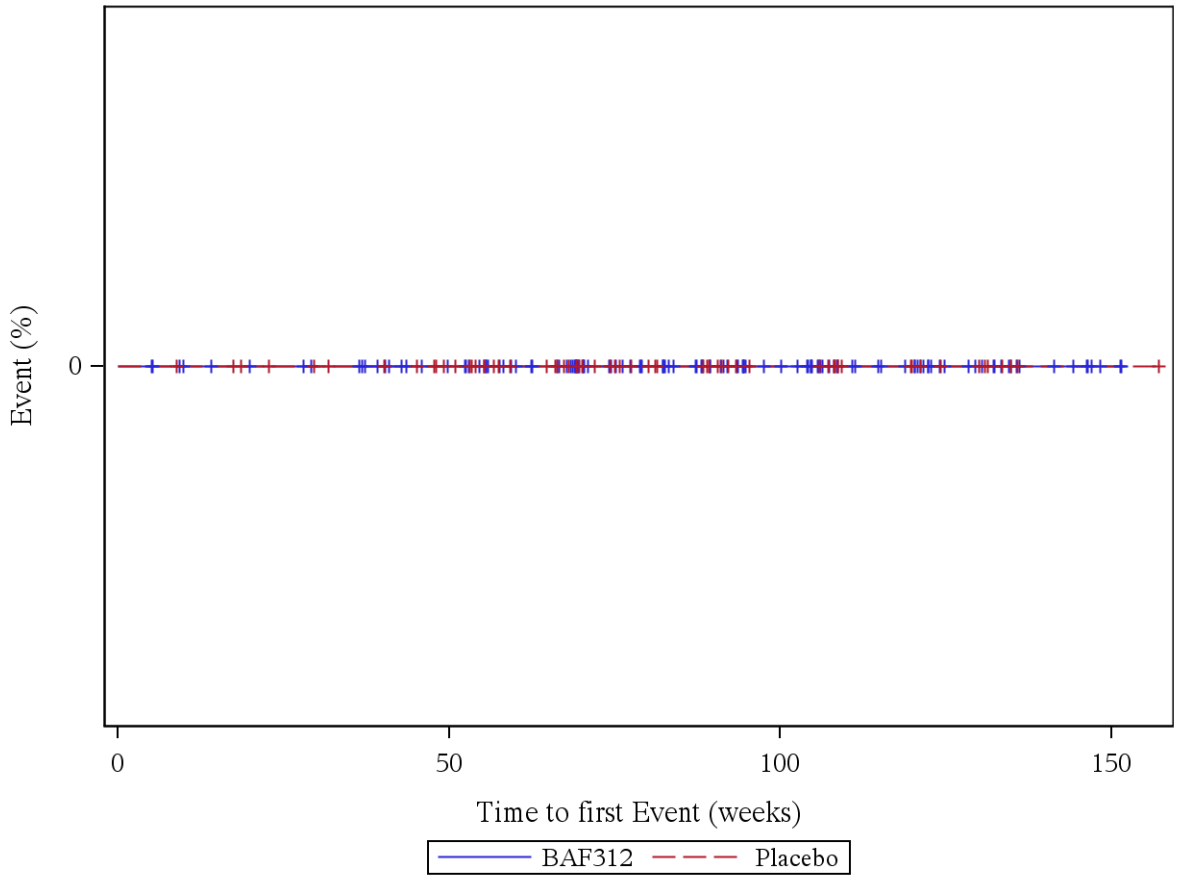


Patients at risk (BAF312/Placebo): Week 0: 127/61, Week 4: 124/59, Week 12: 120/56, Week 24: 116/51, Week 36: 111/48, Week 48: 99/45, Week 60: 83/36, Week 72: 64/28, Week 84: 53/21, Week 96: 37/12, Week 108: 27/12, Week 120: 21/6, Week 132: 11/2, Week 144: 7/1, Week 156: 0/1

Log rank test: p-value = 0,754
*: p < 0,05

Analysis population: A2304 SAF subpopulation "ACTIVE MS WITHOUT RELAPSES"

Figure 12.1.5.70: RESPIRATORY, THORACIC AND MEDIASTINAL DISORDERS (SOC, severe)

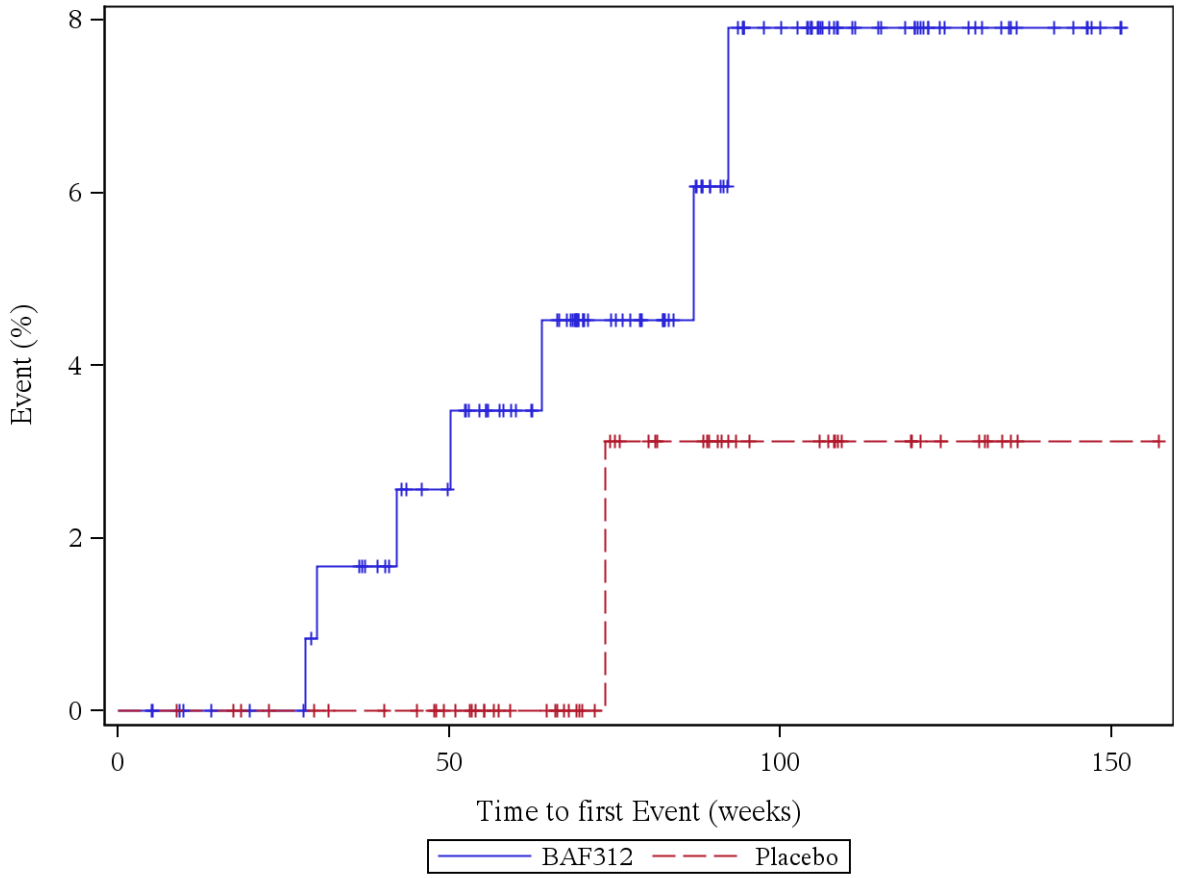


Patients at risk (BAF312/Placebo): Week 0: 127/61, Week 4: 127/61, Week 12: 123/60, Week 24: 121/57, Week 36: 119/55, Week 48: 110/51, Week 60: 99/41, Week 72: 80/32, Week 84: 66/25, Week 96: 49/17, Week 108: 36/15, Week 120: 28/9, Week 132: 15/4, Week 144: 7/1, Week 156: 0/1

Log rank test: p-value = -
*: p < 0,05

Analysis population: A2304 SAF subpopulation "ACTIVE MS WITHOUT RELAPSES"

Figure 12.1.5.71: COUGH (PT, not severe)

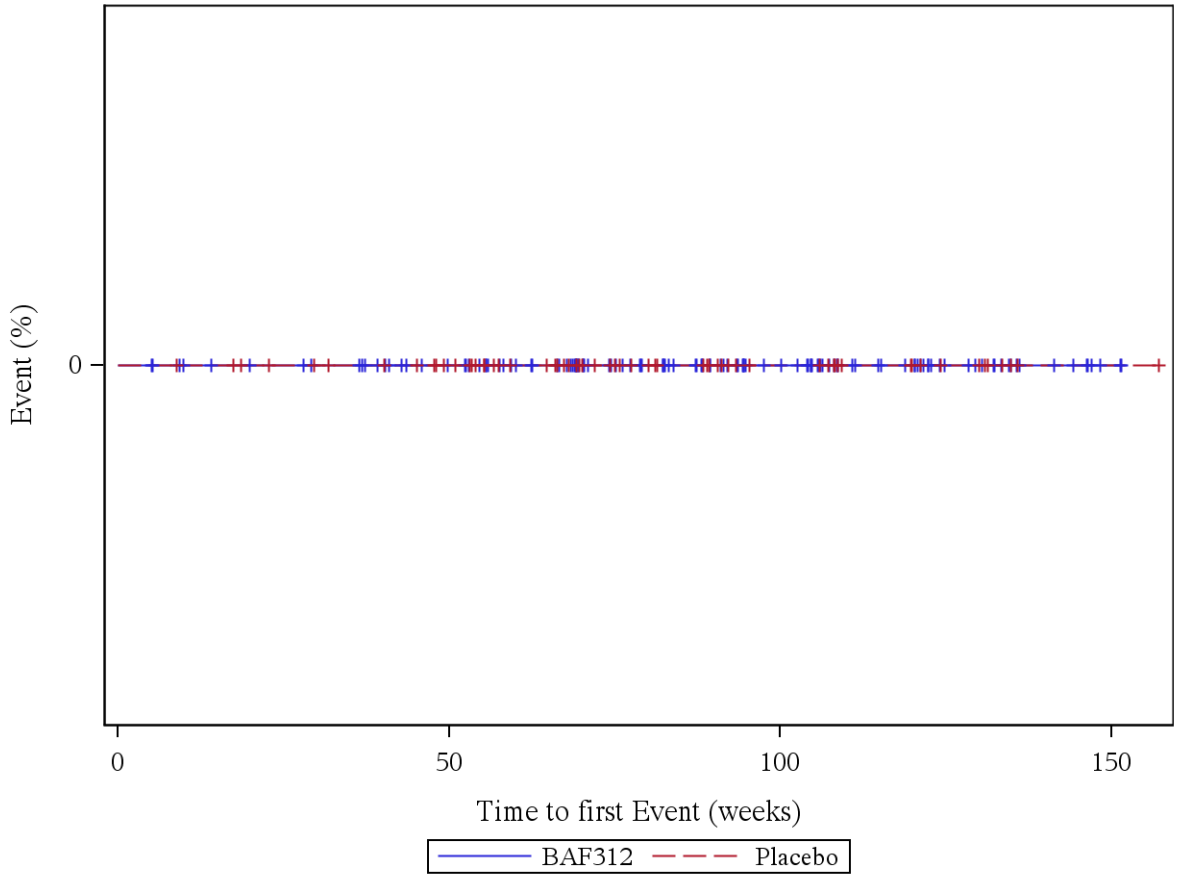


Patients at risk (BAF312/Placebo): Week 0: 127/61, Week 4: 127/61, Week 12: 123/60, Week 24: 121/57, Week 36: 117/55, Week 48: 107/51, Week 60: 95/41, Week 72: 75/32, Week 84: 62/25, Week 96: 45/17, Week 108: 32/15, Week 120: 24/9, Week 132: 12/4, Week 144: 7/1, Week 156: 0/1

Log rank test: p-value = 0,261
*: p < 0,05

Analysis population: A2304 SAF subpopulation "ACTIVE MS WITHOUT RELAPSES"

Figure 12.1.5.72: COUGH (PT, severe)

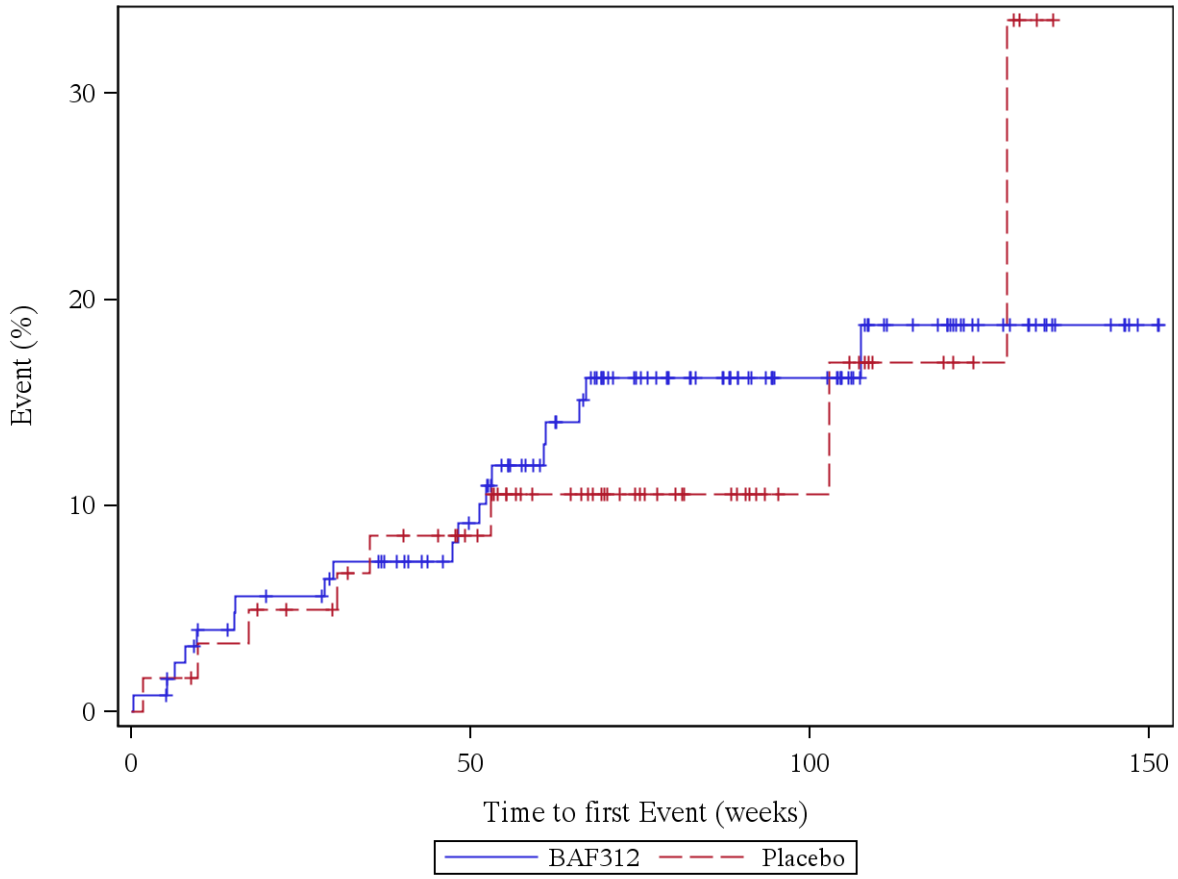


Patients at risk (BAF312/Placebo): Week 0: 127/61, Week 4: 127/61, Week 12: 123/60, Week 24: 121/57, Week 36: 119/55, Week 48: 110/51, Week 60: 99/41, Week 72: 80/32, Week 84: 66/25, Week 96: 49/17, Week 108: 36/15, Week 120: 28/9, Week 132: 15/4, Week 144: 7/1, Week 156: 0/1

Log rank test: p-value = -
*: p < 0,05

Analysis population: A2304 SAF subpopulation "ACTIVE MS WITHOUT RELAPSES"

Figure 12.1.5.73: SKIN AND SUBCUTANEOUS TISSUE DISORDERS (SOC, not severe)

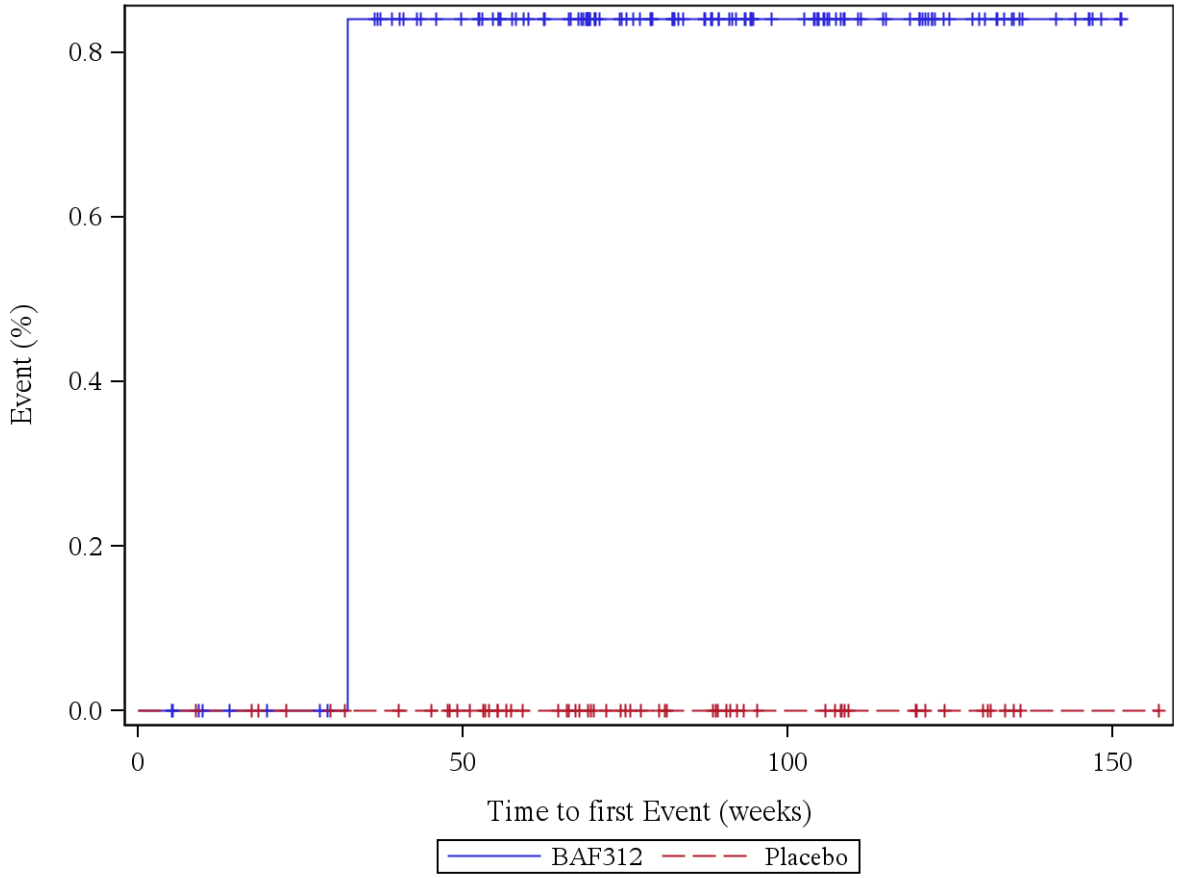


Patients at risk (BAF312/Placebo): Week 0: 127/61, Week 4: 126/60, Week 12: 118/58, Week 24: 114/55, Week 36: 110/51, Week 48: 100/47, Week 60: 85/36, Week 72: 68/28, Week 84: 57/21, Week 96: 43/14, Week 108: 32/11, Week 120: 25/7, Week 132: 14/2, Week 144: 7/0, Week 156: 0/0

Log rank test: p-value = 0,841
*: p < 0,05

Analysis population: A2304 SAF subpopulation "ACTIVE MS WITHOUT RELAPSES"

Figure 12.1.5.74: SKIN AND SUBCUTANEOUS TISSUE DISORDERS (SOC, severe)

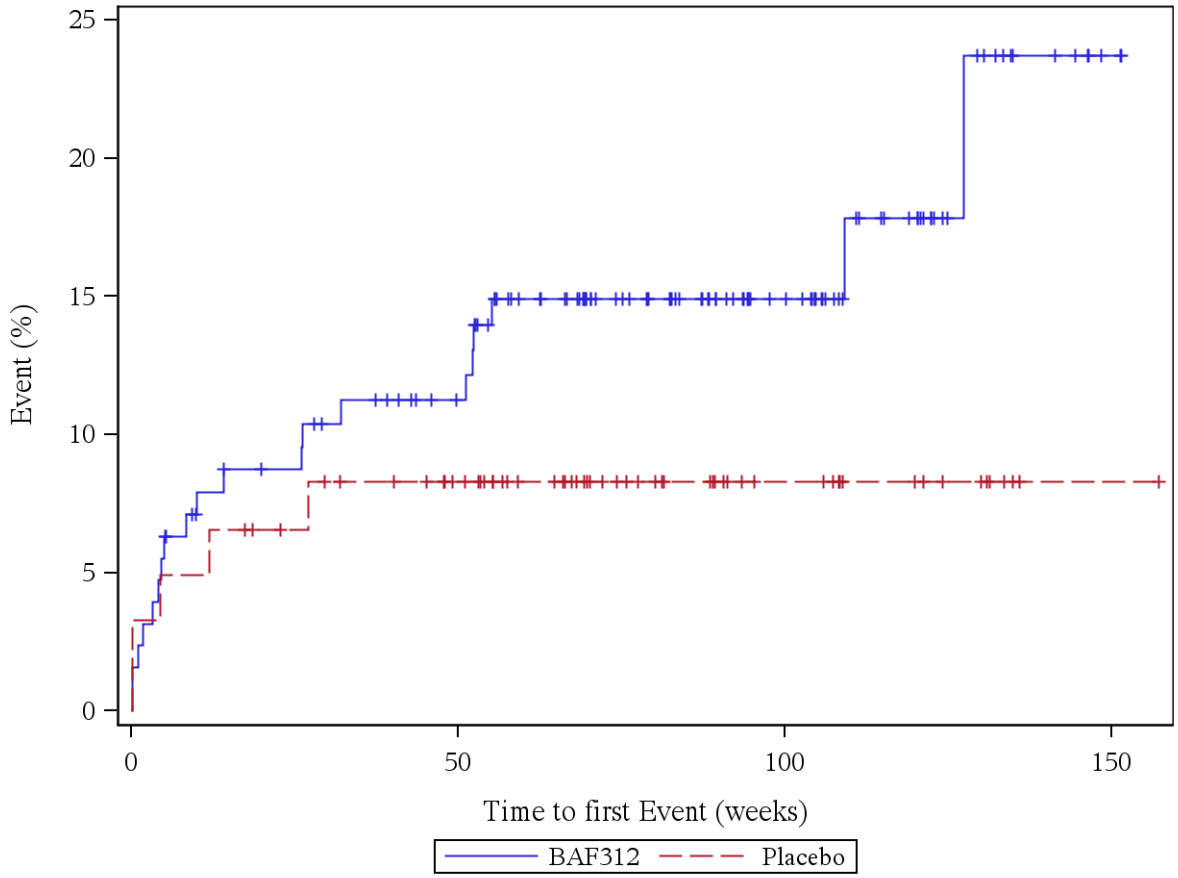


Patients at risk (BAF312/Placebo): Week 0: 127/61, Week 4: 127/61, Week 12: 123/60, Week 24: 121/57, Week 36: 118/55, Week 48: 109/51, Week 60: 98/41, Week 72: 79/32, Week 84: 65/25, Week 96: 48/17, Week 108: 36/15, Week 120: 28/9, Week 132: 15/4, Week 144: 7/1, Week 156: 0/1

Log rank test: p-value = -
*: p < 0,05

Analysis population: A2304 SAF subpopulation "ACTIVE MS WITHOUT RELAPSES"

Figure 12.1.5.75: VASCULAR DISORDERS (SOC, not severe)

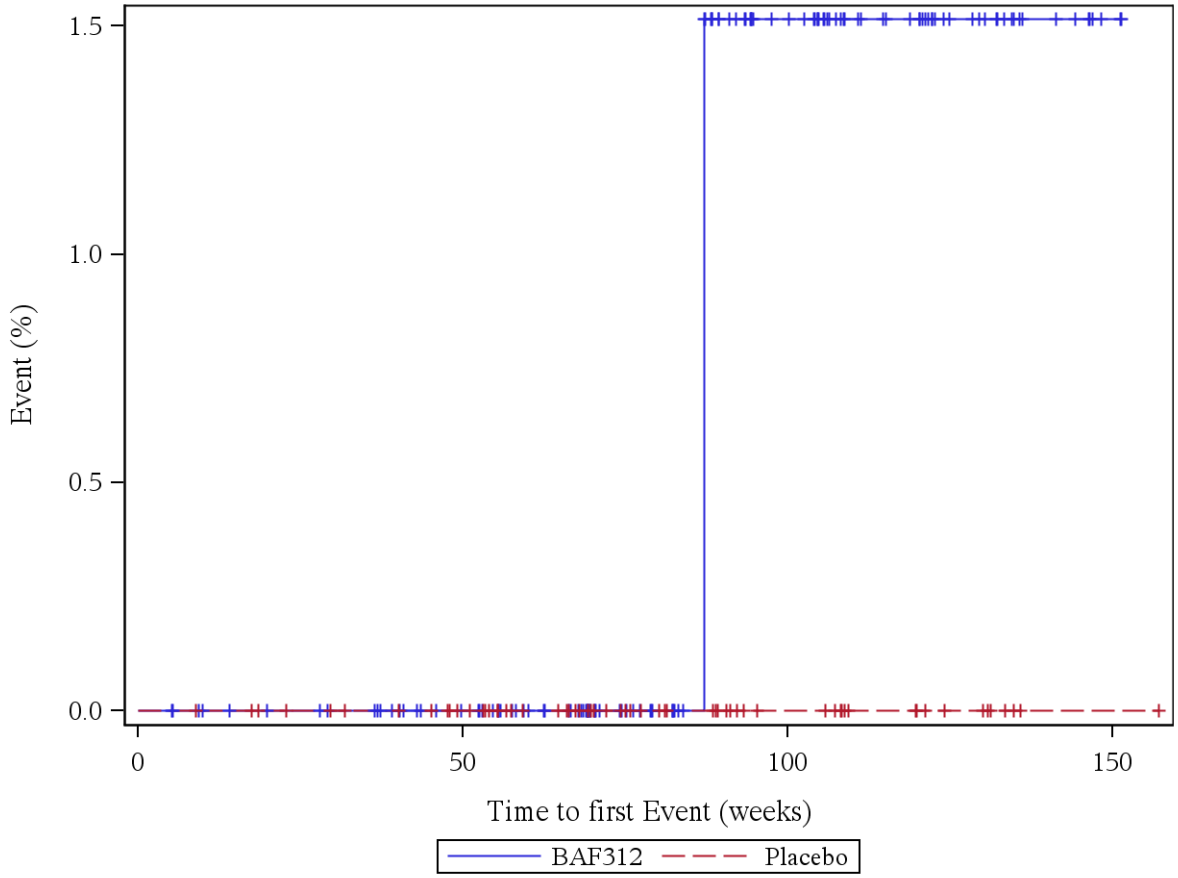


Patients at risk (BAF312/Placebo): Week 0: 127/61, Week 4: 122/59, Week 12: 113/57, Week 24: 110/54, Week 36: 105/51, Week 48: 99/47, Week 60: 84/37, Week 72: 69/28, Week 84: 58/22, Week 96: 43/15, Week 108: 31/13, Week 120: 23/9, Week 132: 11/4, Week 144: 6/1, Week 156: 0/1

Log rank test: p-value = 0,186
*: p < 0,05

Analysis population: A2304 SAF subpopulation "ACTIVE MS WITHOUT RELAPSES"

Figure 12.1.5.76: VASCULAR DISORDERS (SOC, severe)

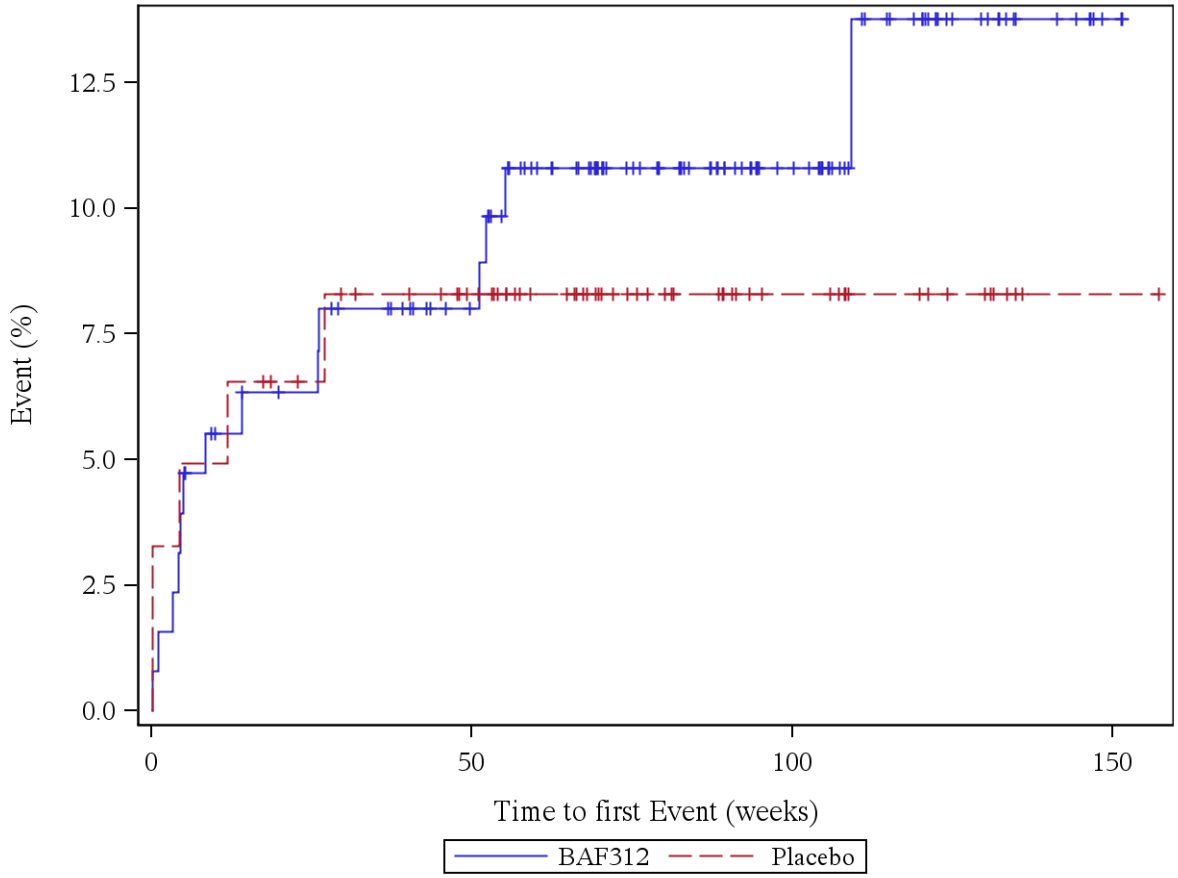


Patients at risk (BAF312/Placebo): Week 0: 127/61, Week 4: 127/61, Week 12: 123/60, Week 24: 121/57, Week 36: 119/55, Week 48: 110/51, Week 60: 99/41, Week 72: 80/32, Week 84: 66/25, Week 96: 49/17, Week 108: 36/15, Week 120: 28/9, Week 132: 15/4, Week 144: 7/1, Week 156: 0/1

Log rank test: p-value = -
*: p < 0,05

Analysis population: A2304 SAF subpopulation "ACTIVE MS WITHOUT RELAPSES"

Figure 12.1.5.77: HYPERTENSION (PT, not severe)

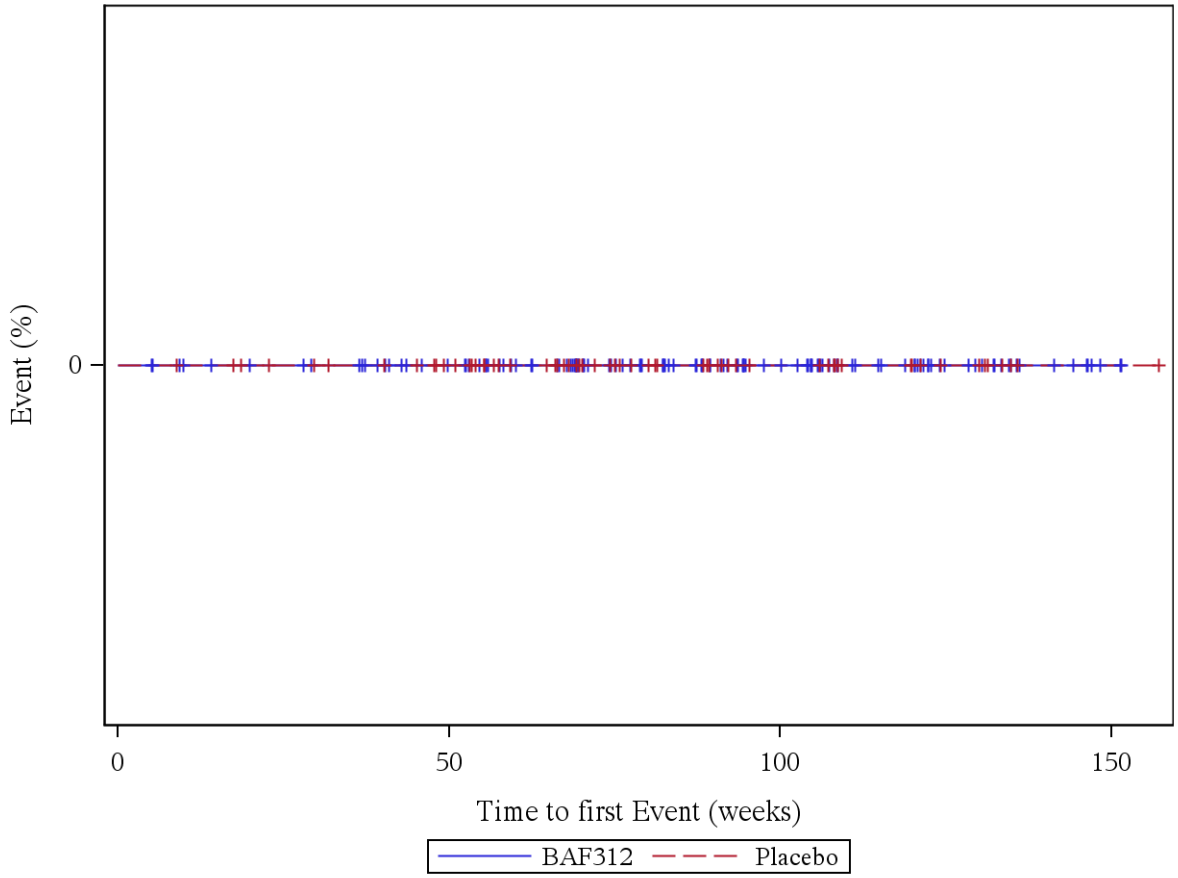


Patients at risk (BAF312/Placebo): Week 0: 127/61, Week 4: 124/59, Week 12: 116/57, Week 24: 113/54, Week 36: 109/51, Week 48: 101/47, Week 60: 87/37, Week 72: 70/28, Week 84: 59/22, Week 96: 44/15, Week 108: 32/13, Week 120: 24/9, Week 132: 13/4, Week 144: 7/1, Week 156: 0/1

Log rank test: p-value = 0,604
*: p < 0,05

Analysis population: A2304 SAF subpopulation "ACTIVE MS WITHOUT RELAPSES"

Figure 12.1.5.78: HYPERTENSION (PT, severe)



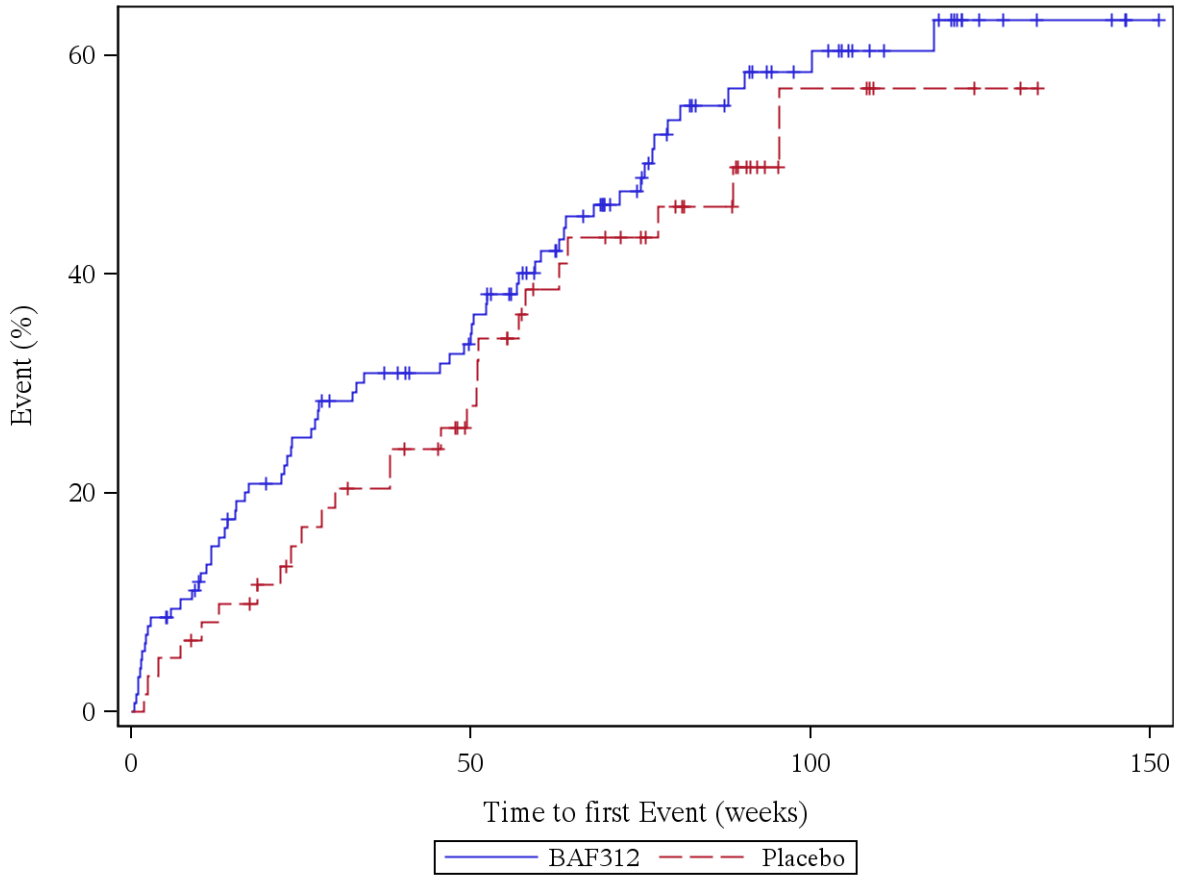
Patients at risk (BAF312/Placebo): Week 0: 127/61, Week 4: 127/61, Week 12: 123/60, Week 24: 121/57, Week 36: 119/55, Week 48: 110/51, Week 60: 99/41, Week 72: 80/32, Week 84: 66/25, Week 96: 49/17, Week 108: 36/15, Week 120: 28/9, Week 132: 15/4, Week 144: 7/1, Week 156: 0/1

Log rank test: p-value = -
*: p < 0,05

Analysis population: A2304 SAF subpopulation "ACTIVE MS WITHOUT RELAPSES"

12.1.6: Time to First Adverse Event of Special Interest by Severity (SAF)

Figure 12.1.6.1: Infections and infestations (AESI, all)

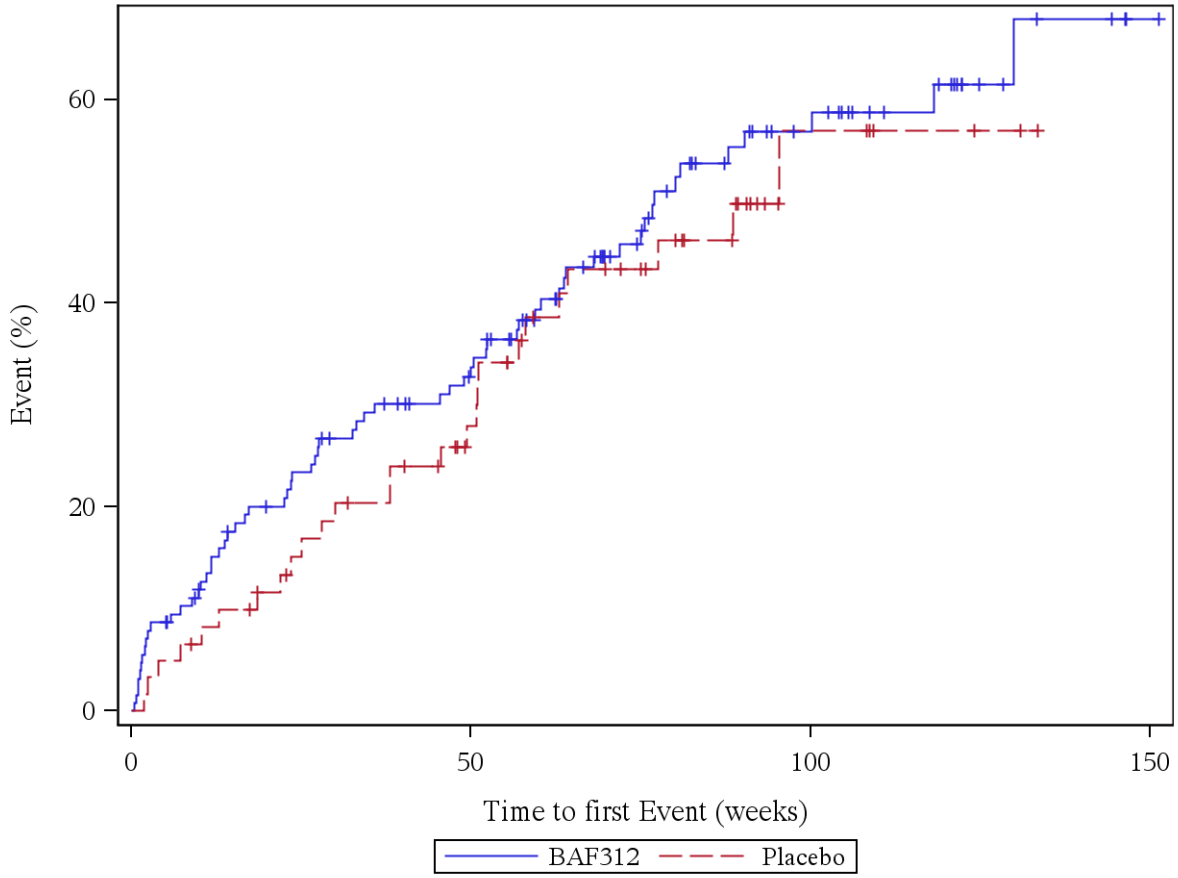


Patients at risk (BAF312/Placebo): Week 0: 127/61, Week 4: 116/58, Week 12: 104/55, Week 24: 90/48, Week 36: 81/44, Week 48: 75/37, Week 60: 58/26, Week 72: 43/22, Week 84: 30/16, Week 96: 23/6, Week 108: 16/6, Week 120: 12/3, Week 132: 5/1, Week 144: 4/0, Week 156: 0/0

Log rank test: p-value = 0,334
*: p < 0,05

Analysis population: A2304 SAF subpopulation "ACTIVE MS WITHOUT RELAPSES"

Figure 12.1.6.2: Infections and infestations (AESI, not severe)

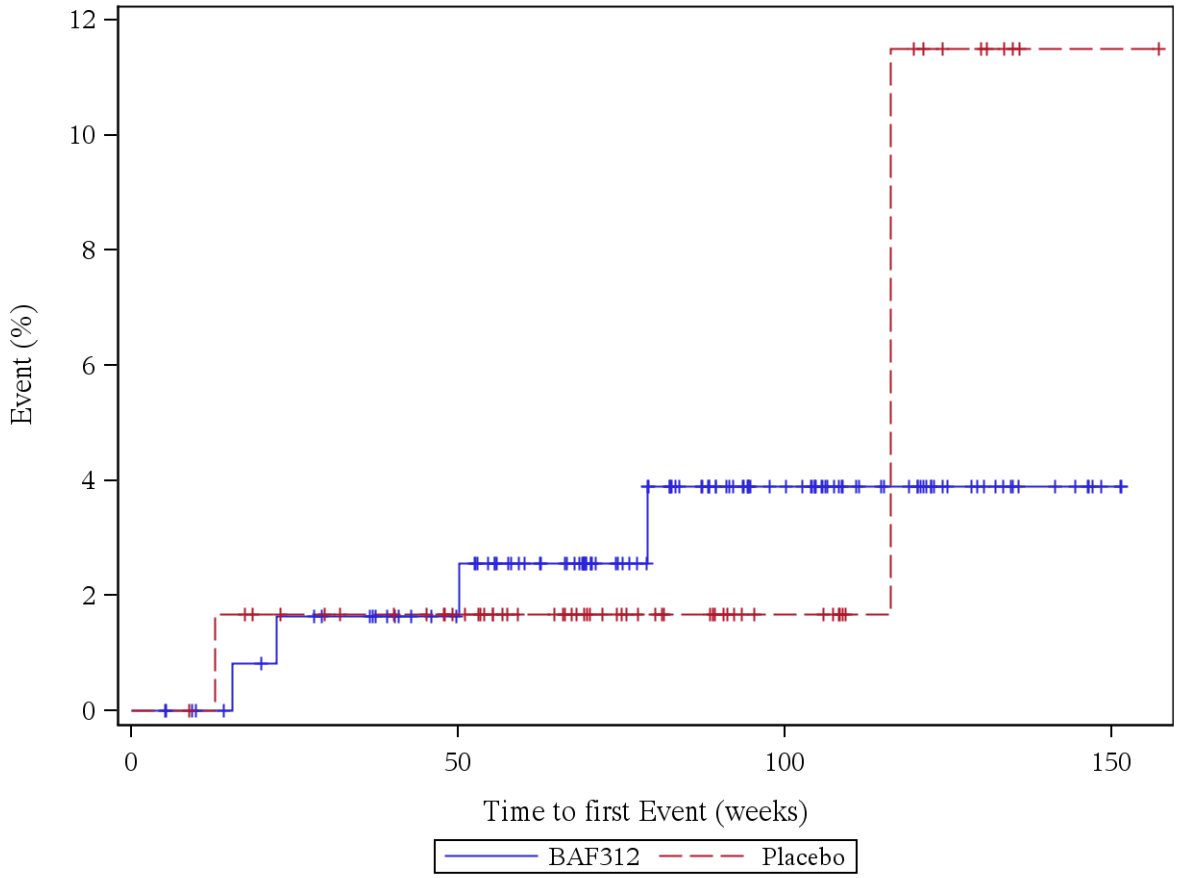


Patients at risk (BAF312/Placebo): Week 0: 127/61, Week 4: 116/58, Week 12: 104/55, Week 24: 92/48, Week 36: 82/44, Week 48: 76/37, Week 60: 60/26, Week 72: 44/22, Week 84: 31/16, Week 96: 24/6, Week 108: 17/6, Week 120: 13/3, Week 132: 5/1, Week 144: 4/0, Week 156: 0/0

Log rank test: p-value = 0,422
*: p < 0,05

Analysis population: A2304 SAF subpopulation "ACTIVE MS WITHOUT RELAPSES"

Figure 12.1.6.3: Infections and infestations (AESI, severe)

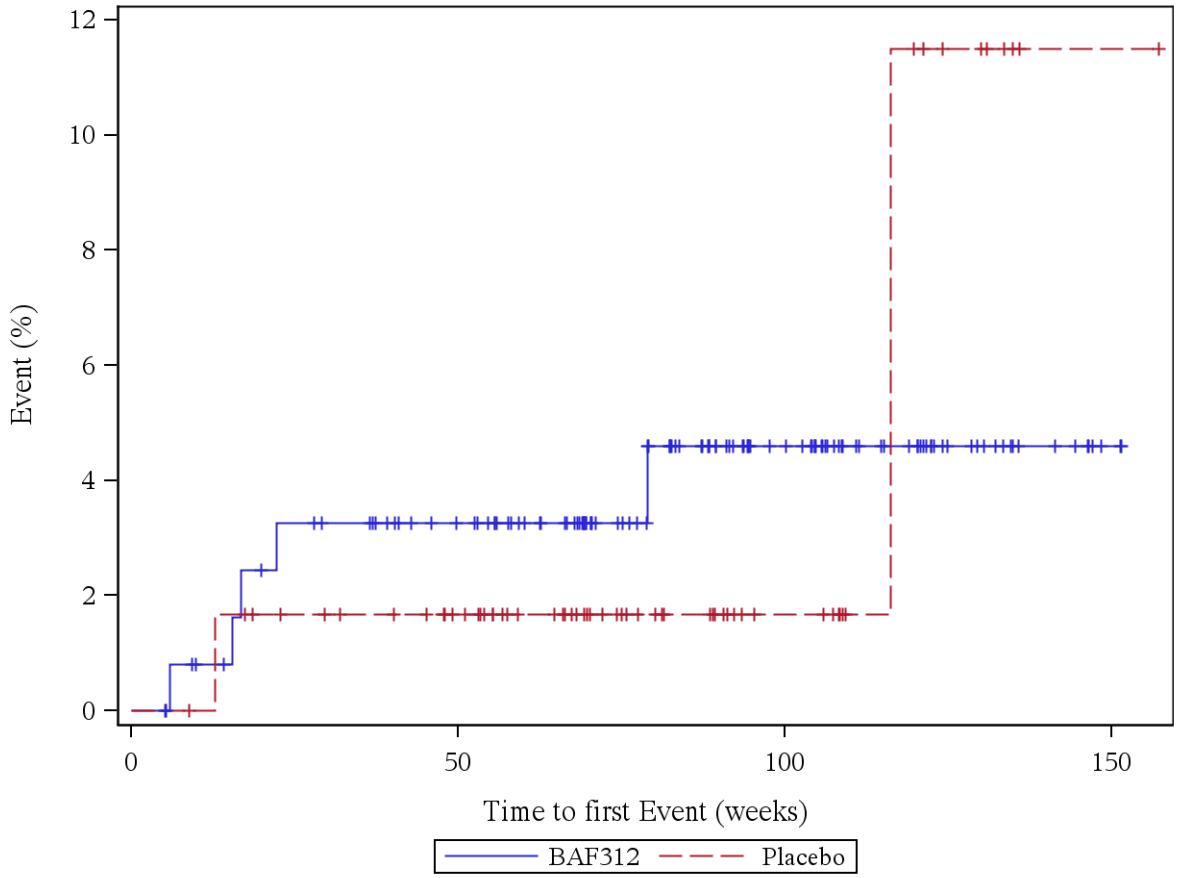


Patients at risk (BAF312/Placebo): Week 0: 127/61, Week 4: 127/61, Week 12: 123/60, Week 24: 119/56, Week 36: 117/54, Week 48: 109/50, Week 60: 97/40, Week 72: 79/31, Week 84: 64/24, Week 96: 47/16, Week 108: 34/14, Week 120: 26/8, Week 132: 13/4, Week 144: 7/1, Week 156: 0/1

Log rank test: p-value = 0,879
*: p < 0,05

Analysis population: A2304 SAF subpopulation "ACTIVE MS WITHOUT RELAPSES"

Figure 12.1.6.4: Infections and infestations (AESI, serious)

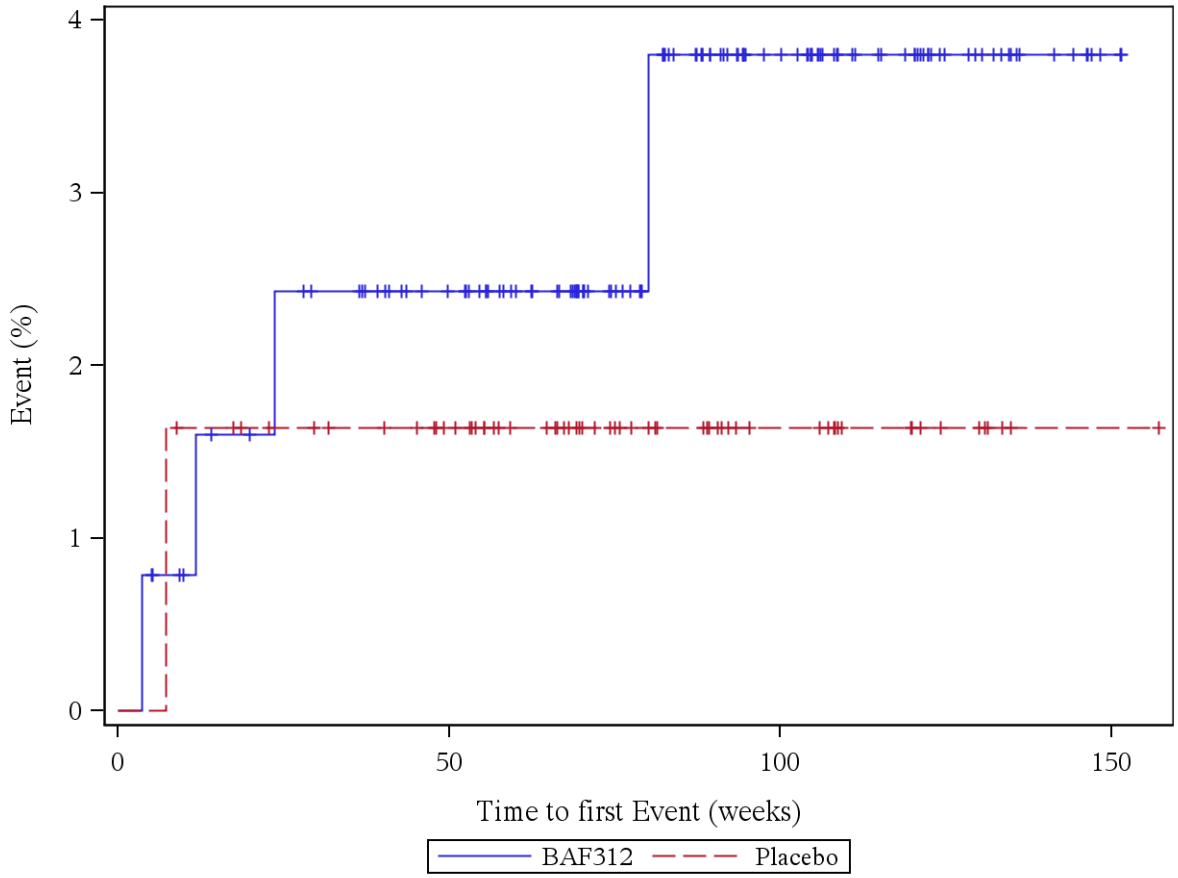


Patients at risk (BAF312/Placebo): Week 0: 127/61, Week 4: 127/61, Week 12: 122/60, Week 24: 117/56, Week 36: 115/54, Week 48: 107/50, Week 60: 97/40, Week 72: 78/31, Week 84: 64/24, Week 96: 47/16, Week 108: 34/14, Week 120: 26/8, Week 132: 13/4, Week 144: 7/1, Week 156: 0/1

Log rank test: p-value = 0,882
*: p < 0,05

Analysis population: A2304 SAF subpopulation "ACTIVE MS WITHOUT RELAPSES"

Figure 12.1.6.5: Herpes simplex virus infections (AESI, all)

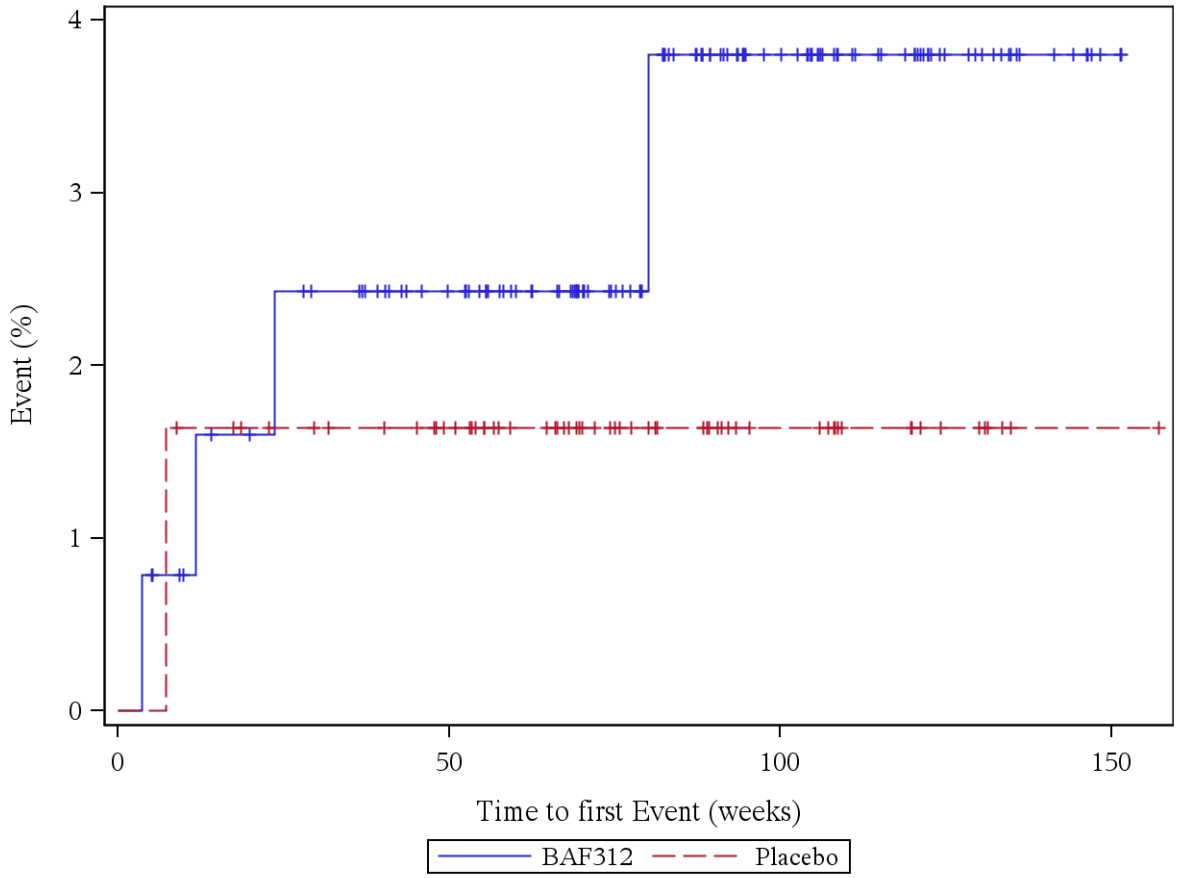


Patients at risk (BAF312/Placebo): Week 0: 127/61, Week 4: 126/61, Week 12: 121/59, Week 24: 118/56, Week 36: 116/54, Week 48: 107/50, Week 60: 96/40, Week 72: 79/31, Week 84: 64/24, Week 96: 47/16, Week 108: 35/14, Week 120: 27/8, Week 132: 14/3, Week 144: 7/1, Week 156: 0/1

Log rank test: p-value = 0,579
*: p < 0,05

Analysis population: A2304 SAF subpopulation "ACTIVE MS WITHOUT RELAPSES"

Figure 12.1.6.6: Herpes simplex virus infections (AESI, not severe)

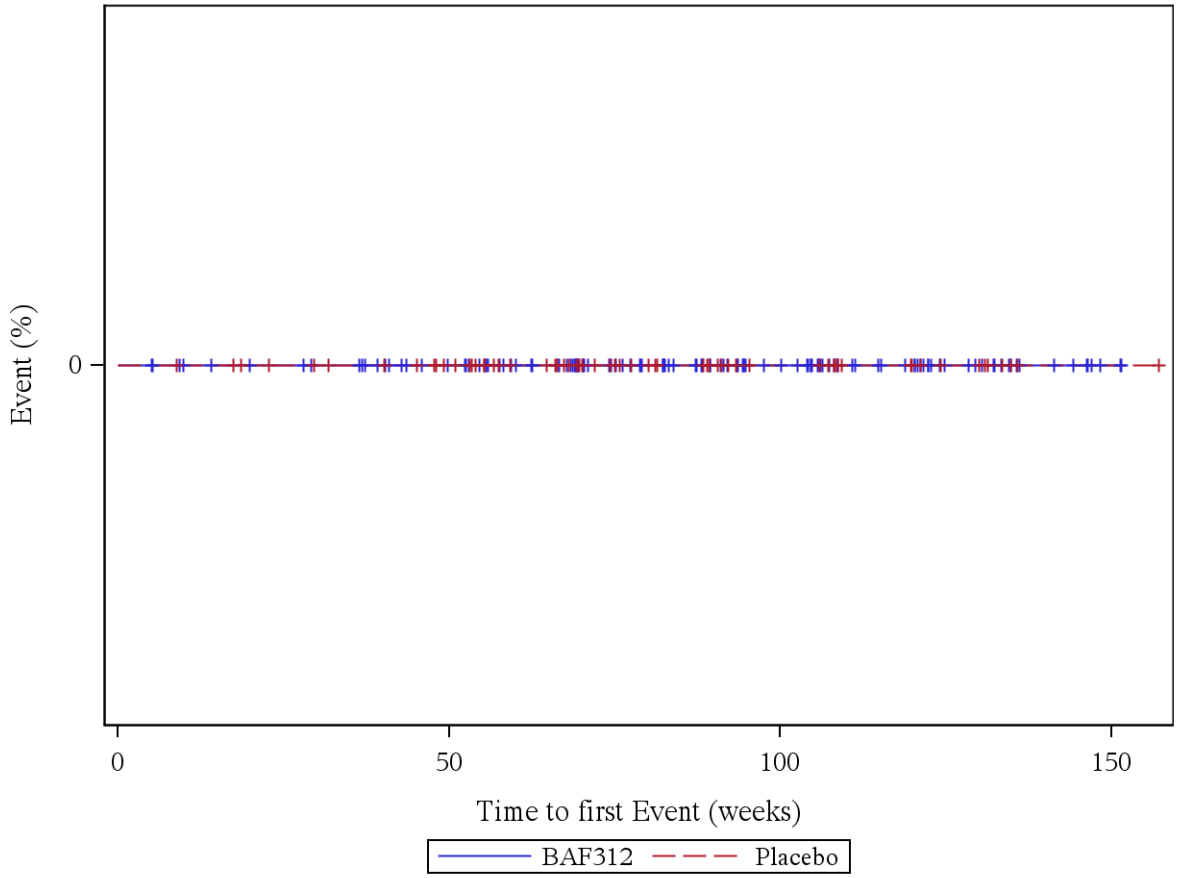


Patients at risk (BAF312/Placebo): Week 0: 127/61, Week 4: 126/61, Week 12: 121/59, Week 24: 118/56, Week 36: 116/54, Week 48: 107/50, Week 60: 96/40, Week 72: 79/31, Week 84: 64/24, Week 96: 47/16, Week 108: 35/14, Week 120: 27/8, Week 132: 14/3, Week 144: 7/1, Week 156: 0/1

Log rank test: p-value = 0,579
*: p < 0,05

Analysis population: A2304 SAF subpopulation "ACTIVE MS WITHOUT RELAPSES"

Figure 12.1.6.7: Herpes simplex virus infections (AESI, severe)

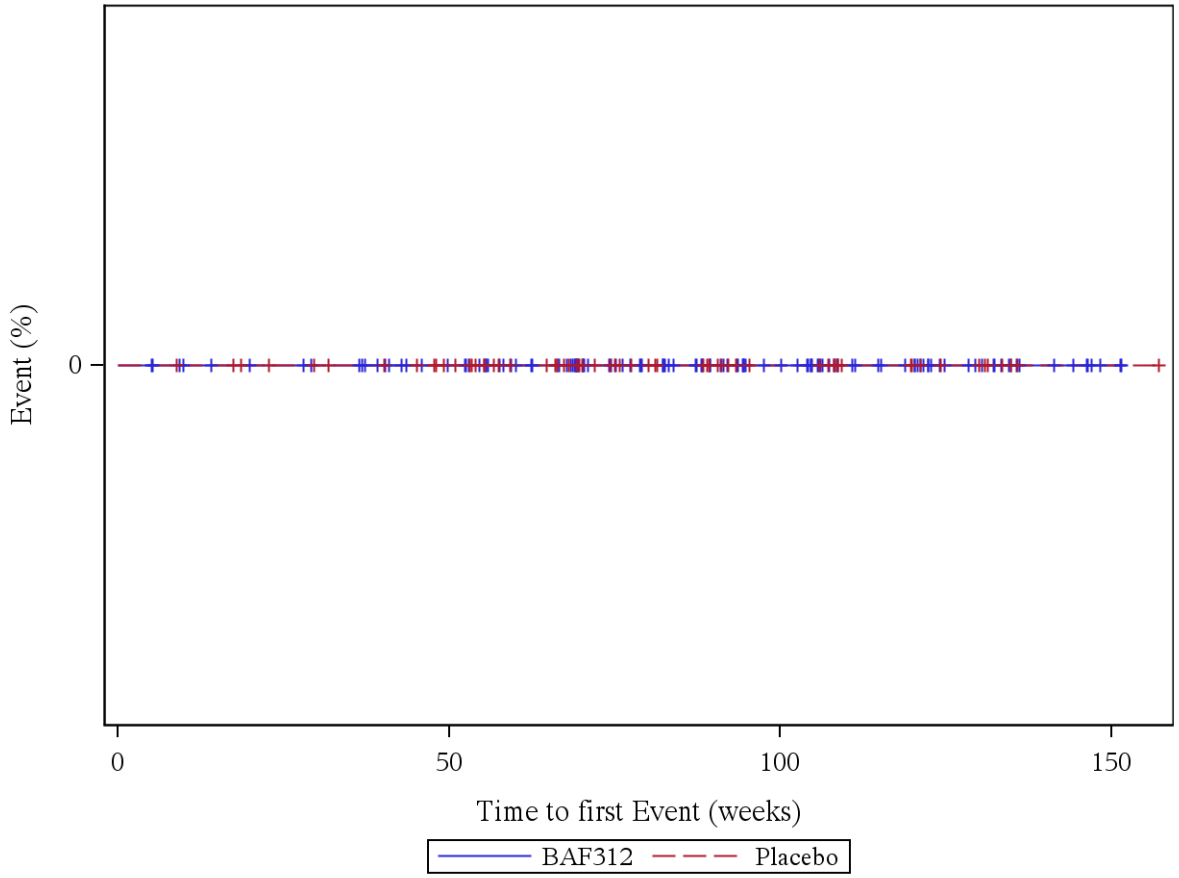


Patients at risk (BAF312/Placebo): Week 0: 127/61, Week 4: 127/61, Week 12: 123/60, Week 24: 121/57, Week 36: 119/55, Week 48: 110/51, Week 60: 99/41, Week 72: 80/32, Week 84: 66/25, Week 96: 49/17, Week 108: 36/15, Week 120: 28/9, Week 132: 15/4, Week 144: 7/1, Week 156: 0/1

Log rank test: p-value = -
*: p < 0,05

Analysis population: A2304 SAF subpopulation "ACTIVE MS WITHOUT RELAPSES"

Figure 12.1.6.8: Herpes simplex virus infections (AESI, serious)

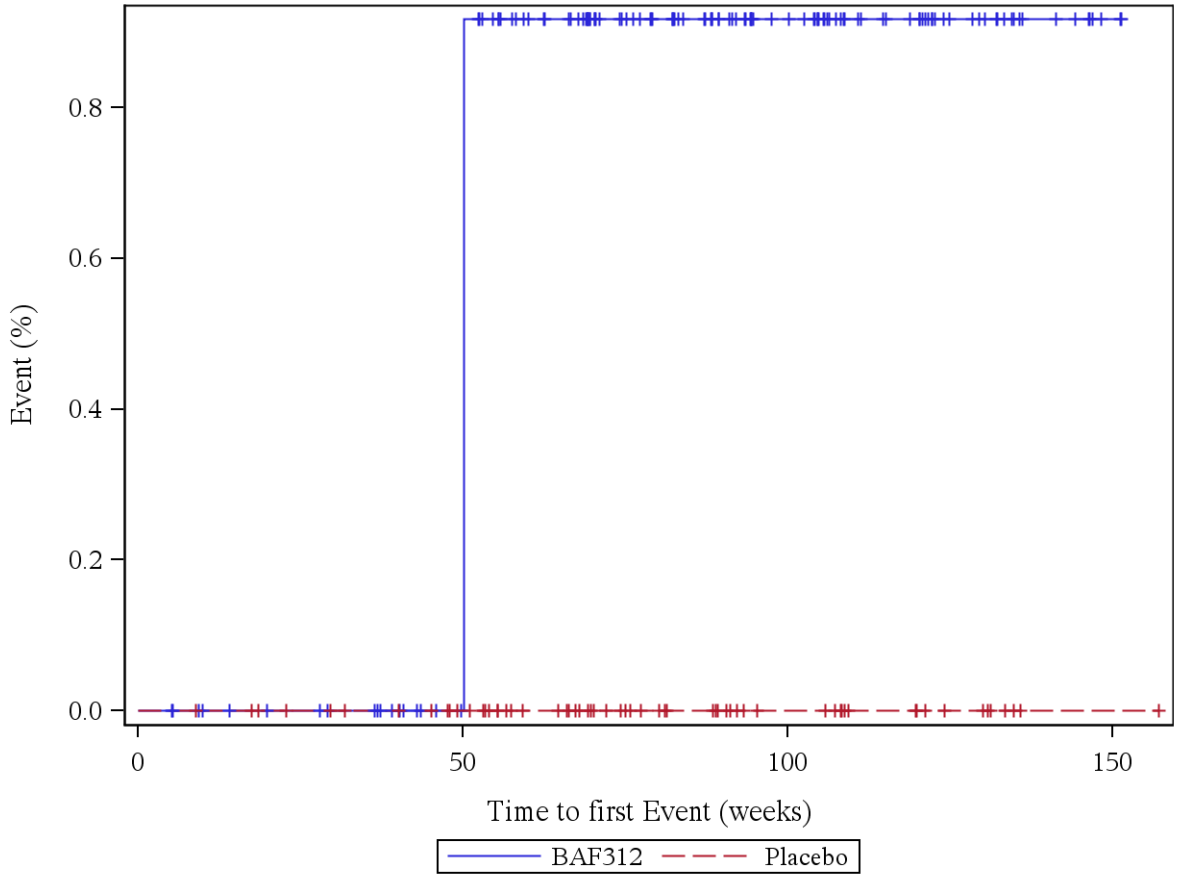


Patients at risk (BAF312/Placebo): Week 0: 127/61, Week 4: 127/61, Week 12: 123/60, Week 24: 121/57, Week 36: 119/55, Week 48: 110/51, Week 60: 99/41, Week 72: 80/32, Week 84: 66/25, Week 96: 49/17, Week 108: 36/15, Week 120: 28/9, Week 132: 15/4, Week 144: 7/1, Week 156: 0/1

Log rank test: p-value = -
*: p < 0,05

Analysis population: A2304 SAF subpopulation "ACTIVE MS WITHOUT RELAPSES"

Figure 12.1.6.9: Varicella-zoster virus infections (AESI, all)

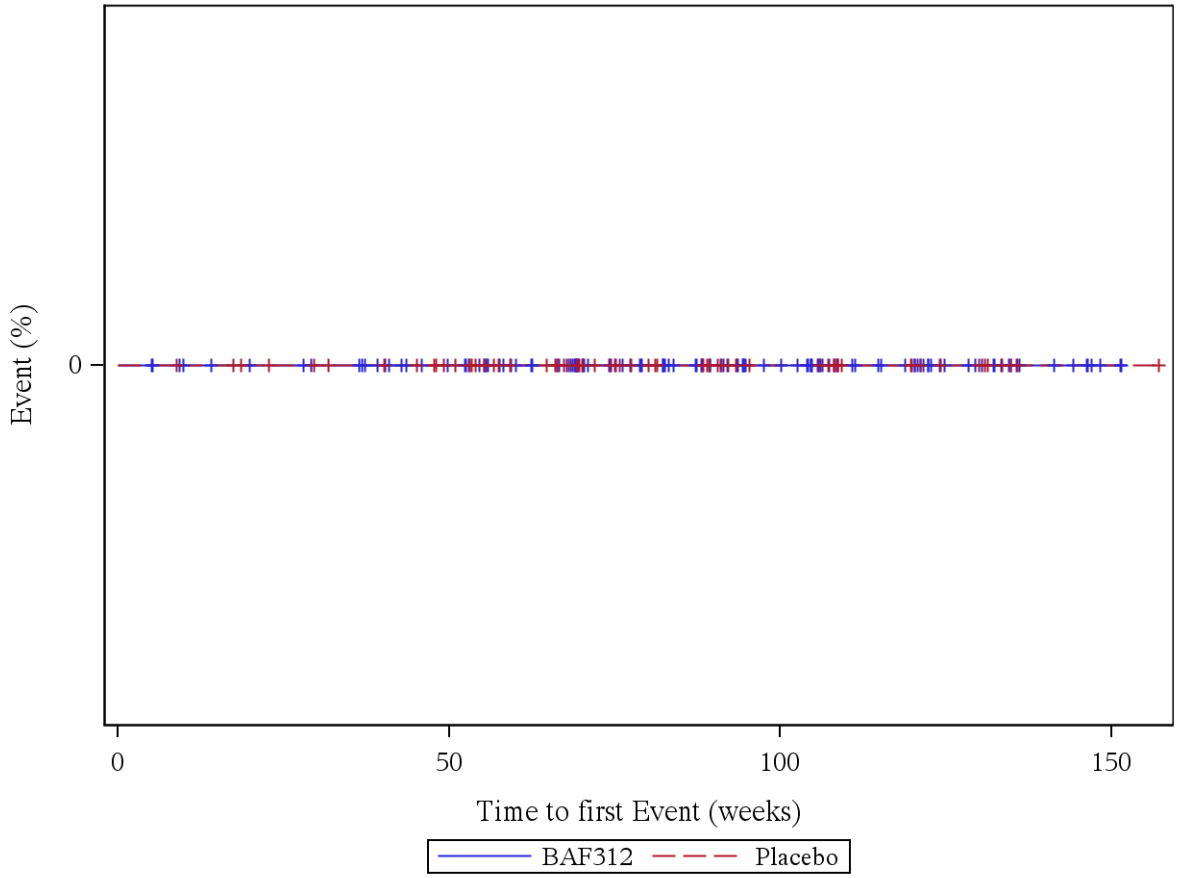


Patients at risk (BAF312/Placebo): Week 0: 127/61, Week 4: 127/61, Week 12: 123/60, Week 24: 121/57, Week 36: 119/55, Week 48: 110/51, Week 60: 98/41, Week 72: 80/32, Week 84: 66/25, Week 96: 49/17, Week 108: 36/15, Week 120: 28/9, Week 132: 15/4, Week 144: 7/1, Week 156: 0/1

Log rank test: p-value = -
*: p < 0,05

Analysis population: A2304 SAF subpopulation "ACTIVE MS WITHOUT RELAPSES"

Figure 12.1.6.10: Varicella-zoster virus infections (AESI, not severe)

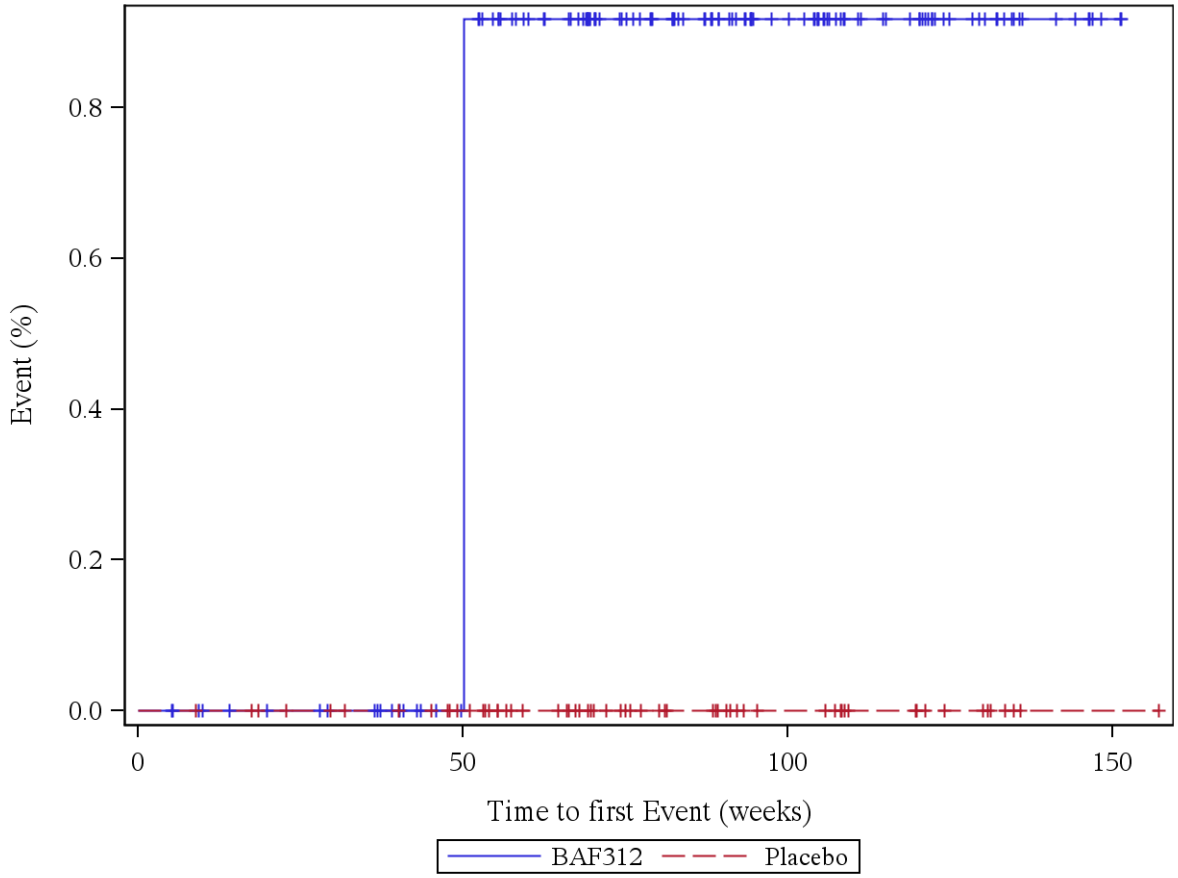


Patients at risk (BAF312/Placebo): Week 0: 127/61, Week 4: 127/61, Week 12: 123/60, Week 24: 121/57, Week 36: 119/55, Week 48: 110/51, Week 60: 99/41, Week 72: 80/32, Week 84: 66/25, Week 96: 49/17, Week 108: 36/15, Week 120: 28/9, Week 132: 15/4, Week 144: 7/1, Week 156: 0/1

Log rank test: p-value = -
*: p < 0,05

Analysis population: A2304 SAF subpopulation "ACTIVE MS WITHOUT RELAPSES"

Figure 12.1.6.11: Varicella-zoster virus infections (AESI, severe)

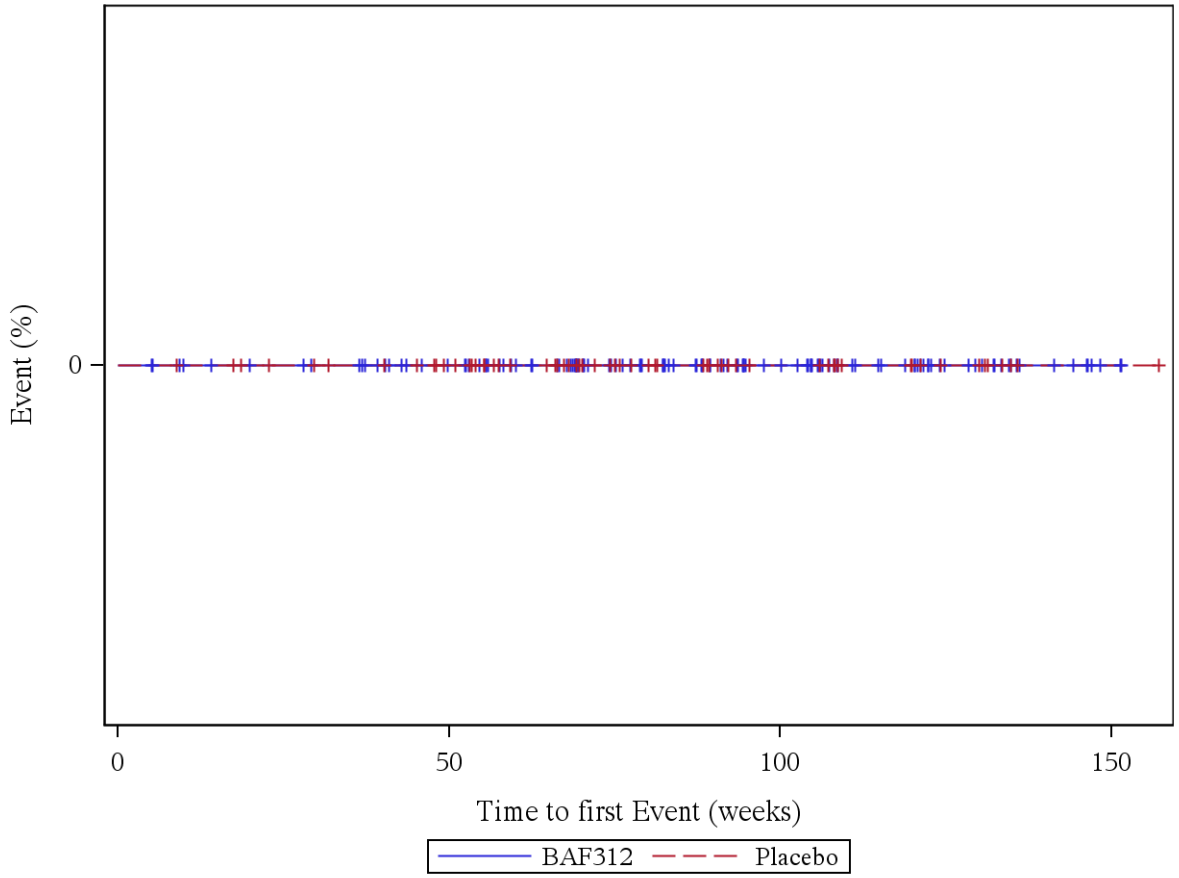


Patients at risk (BAF312/Placebo): Week 0: 127/61, Week 4: 127/61, Week 12: 123/60, Week 24: 121/57, Week 36: 119/55, Week 48: 110/51, Week 60: 98/41, Week 72: 80/32, Week 84: 66/25, Week 96: 49/17, Week 108: 36/15, Week 120: 28/9, Week 132: 15/4, Week 144: 7/1, Week 156: 0/1

Log rank test: p-value = -
*: p < 0,05

Analysis population: A2304 SAF subpopulation "ACTIVE MS WITHOUT RELAPSES"

Figure 12.1.6.12: Varicella-zoster virus infections (AESI, serious)

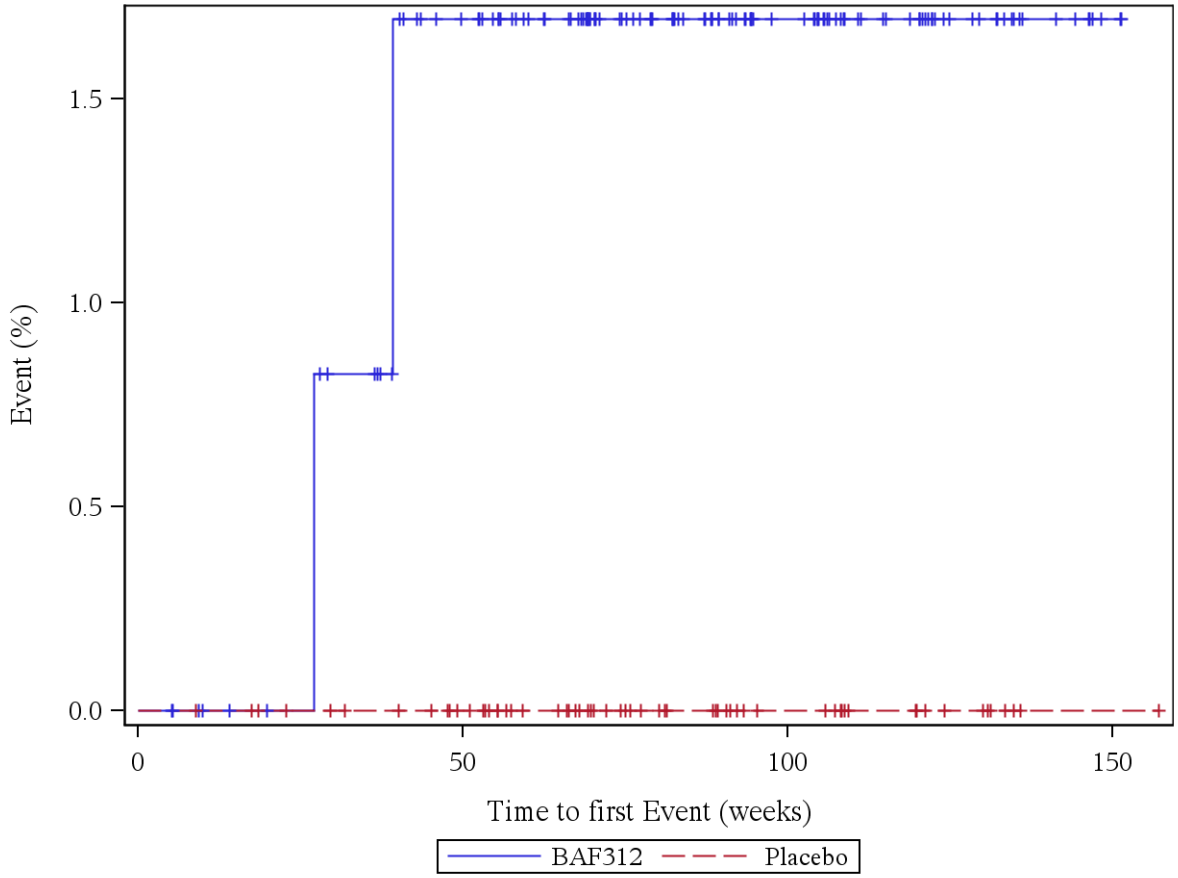


Patients at risk (BAF312/Placebo): Week 0: 127/61, Week 4: 127/61, Week 12: 123/60, Week 24: 121/57, Week 36: 119/55, Week 48: 110/51, Week 60: 99/41, Week 72: 80/32, Week 84: 66/25, Week 96: 49/17, Week 108: 36/15, Week 120: 28/9, Week 132: 15/4, Week 144: 7/1, Week 156: 0/1

Log rank test: p-value = -
*: p < 0,05

Analysis population: A2304 SAF subpopulation "ACTIVE MS WITHOUT RELAPSES"

Figure 12.1.6.13: Lymphopenia (AESI, all)

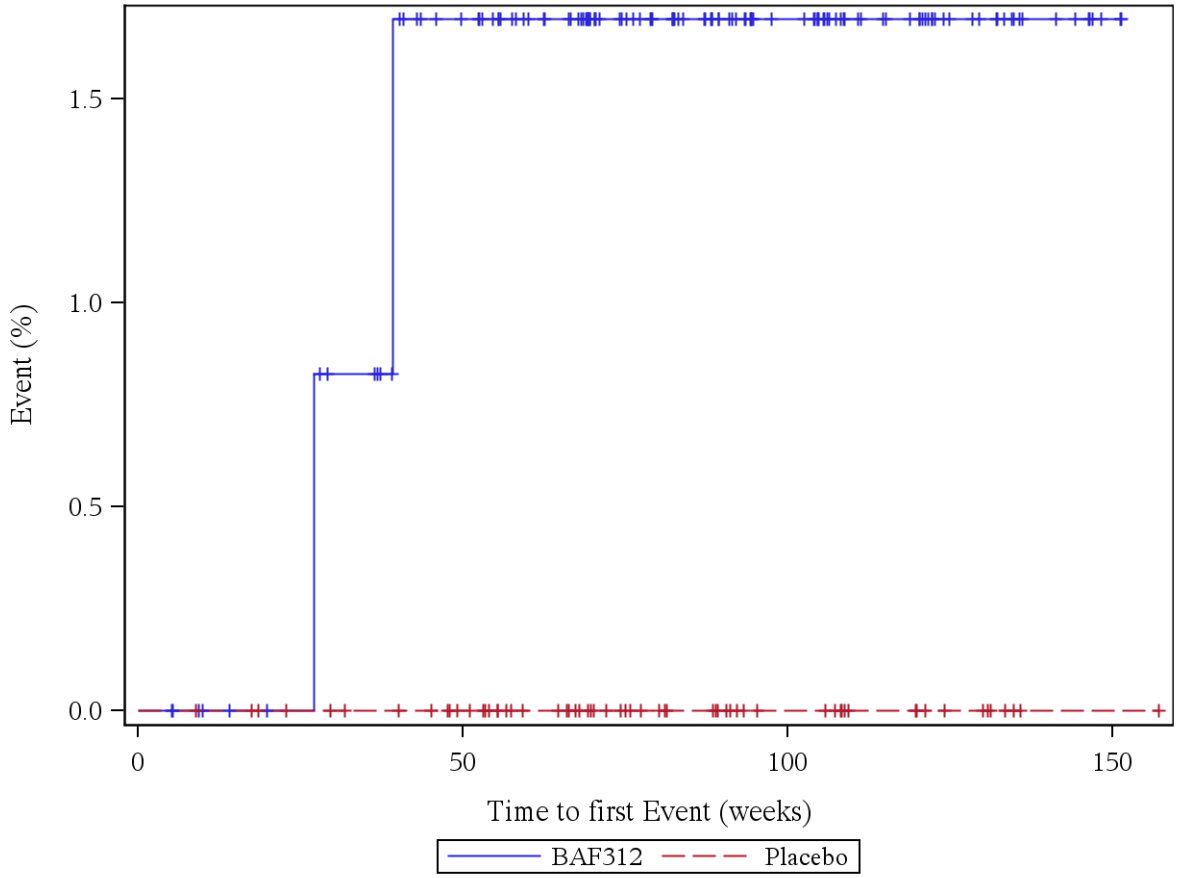


Patients at risk (BAF312/Placebo): Week 0: 127/61, Week 4: 127/61, Week 12: 123/60, Week 24: 121/57, Week 36: 118/55, Week 48: 108/51, Week 60: 97/41, Week 72: 78/32, Week 84: 64/25, Week 96: 47/17, Week 108: 35/15, Week 120: 27/9, Week 132: 15/4, Week 144: 7/1, Week 156: 0/1

Log rank test: p-value = -
*: p < 0,05

Analysis population: A2304 SAF subpopulation "ACTIVE MS WITHOUT RELAPSES"

Figure 12.1.6.14: Lymphopenia (AESI, not severe)

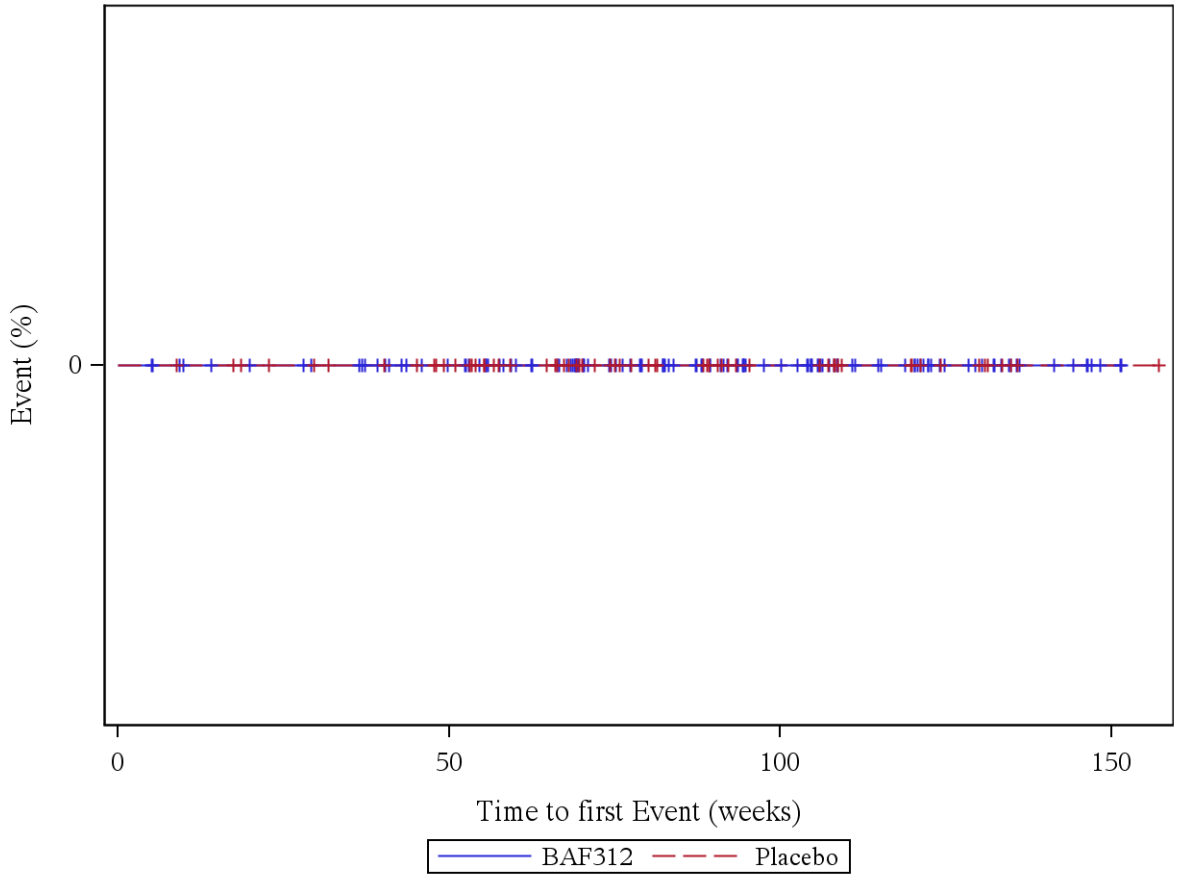


Patients at risk (BAF312/Placebo): Week 0: 127/61, Week 4: 127/61, Week 12: 123/60, Week 24: 121/57, Week 36: 118/55, Week 48: 108/51, Week 60: 97/41, Week 72: 78/32, Week 84: 64/25, Week 96: 47/17, Week 108: 35/15, Week 120: 27/9, Week 132: 15/4, Week 144: 7/1, Week 156: 0/1

Log rank test: p-value = -
*: p < 0,05

Analysis population: A2304 SAF subpopulation "ACTIVE MS WITHOUT RELAPSES"

Figure 12.1.6.15: Lymphopenia (AESI, severe)

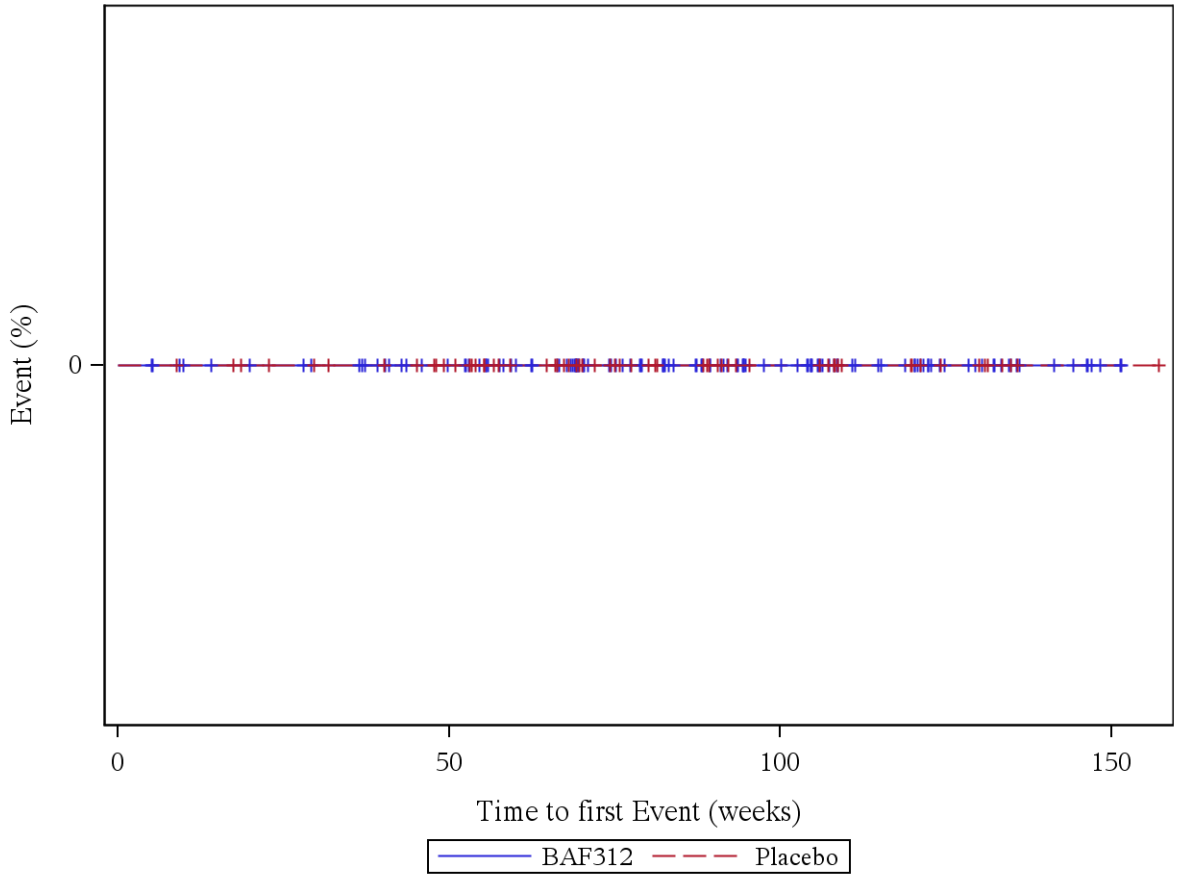


Patients at risk (BAF312/Placebo): Week 0: 127/61, Week 4: 127/61, Week 12: 123/60, Week 24: 121/57, Week 36: 119/55, Week 48: 110/51, Week 60: 99/41, Week 72: 80/32, Week 84: 66/25, Week 96: 49/17, Week 108: 36/15, Week 120: 28/9, Week 132: 15/4, Week 144: 7/1, Week 156: 0/1

Log rank test: p-value = -
*: p < 0,05

Analysis population: A2304 SAF subpopulation "ACTIVE MS WITHOUT RELAPSES"

Figure 12.1.6.16: Lymphopenia (AESI, serious)

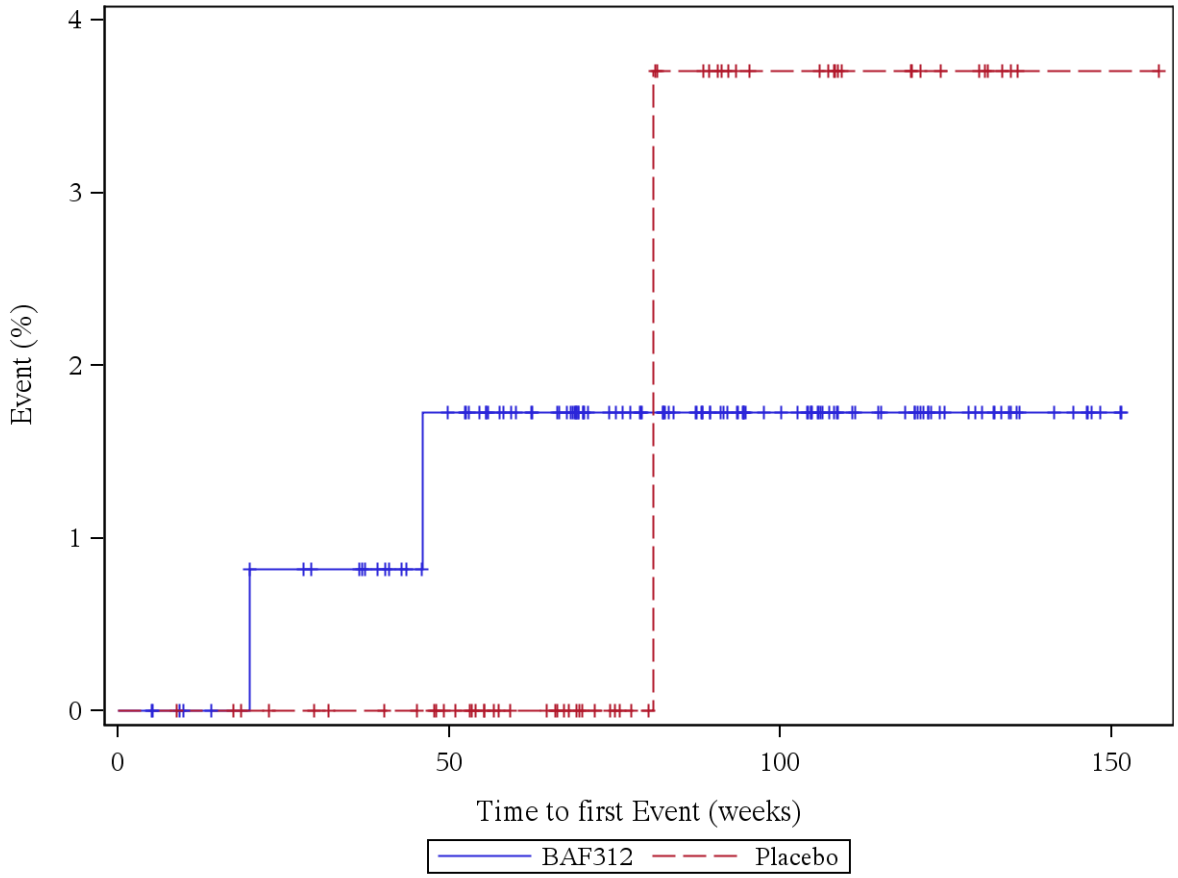


Patients at risk (BAF312/Placebo): Week 0: 127/61, Week 4: 127/61, Week 12: 123/60, Week 24: 121/57, Week 36: 119/55, Week 48: 110/51, Week 60: 99/41, Week 72: 80/32, Week 84: 66/25, Week 96: 49/17, Week 108: 36/15, Week 120: 28/9, Week 132: 15/4, Week 144: 7/1, Week 156: 0/1

Log rank test: p-value = -
*: p < 0,05

Analysis population: A2304 SAF subpopulation "ACTIVE MS WITHOUT RELAPSES"

Figure 12.1.6.17: Macular edema (AESI, all)

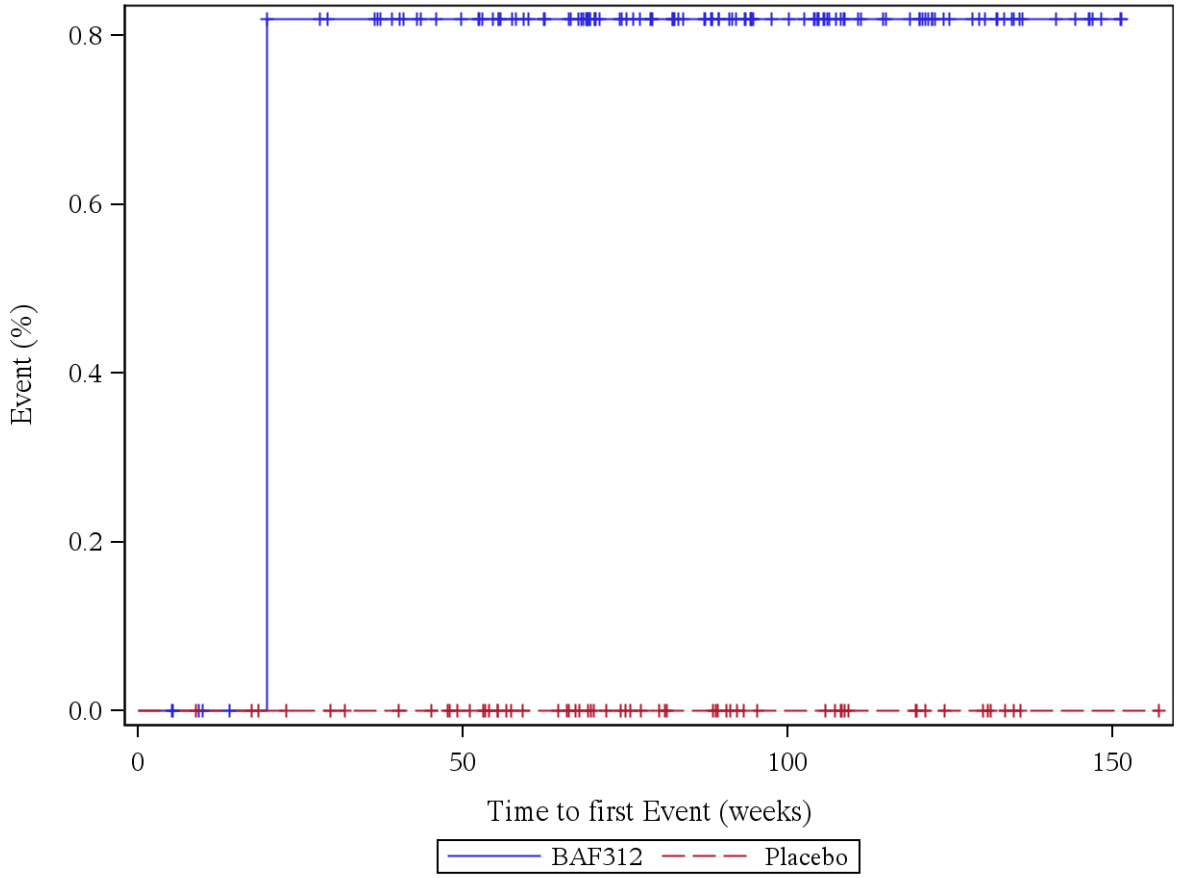


Patients at risk (BAF312/Placebo): Week 0: 127/61, Week 4: 127/61, Week 12: 123/60, Week 24: 120/57, Week 36: 118/55, Week 48: 108/51, Week 60: 97/41, Week 72: 79/32, Week 84: 66/24, Week 96: 49/17, Week 108: 36/15, Week 120: 28/9, Week 132: 15/4, Week 144: 7/1, Week 156: 0/1

Log rank test: p-value = 0,922
*: p < 0,05

Analysis population: A2304 SAF subpopulation "ACTIVE MS WITHOUT RELAPSES"

Figure 12.1.6.18: Macular edema (AESI, not severe)

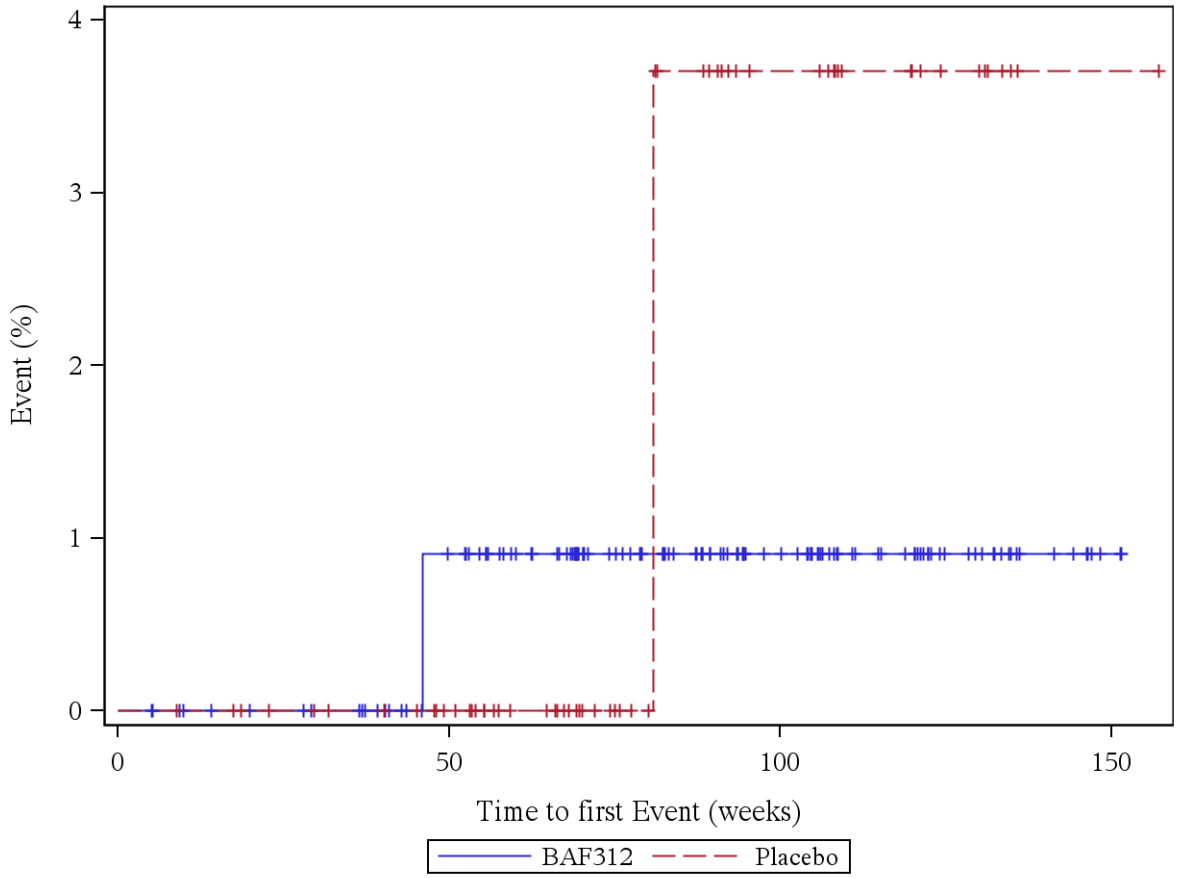


Patients at risk (BAF312/Placebo): Week 0: 127/61, Week 4: 127/61, Week 12: 123/60, Week 24: 120/57, Week 36: 118/55, Week 48: 109/51, Week 60: 98/41, Week 72: 80/32, Week 84: 66/25, Week 96: 49/17, Week 108: 36/15, Week 120: 28/9, Week 132: 15/4, Week 144: 7/1, Week 156: 0/1

Log rank test: p-value = -
*: p < 0,05

Analysis population: A2304 SAF subpopulation "ACTIVE MS WITHOUT RELAPSES"

Figure 12.1.6.19: Macular edema (AESI, severe)

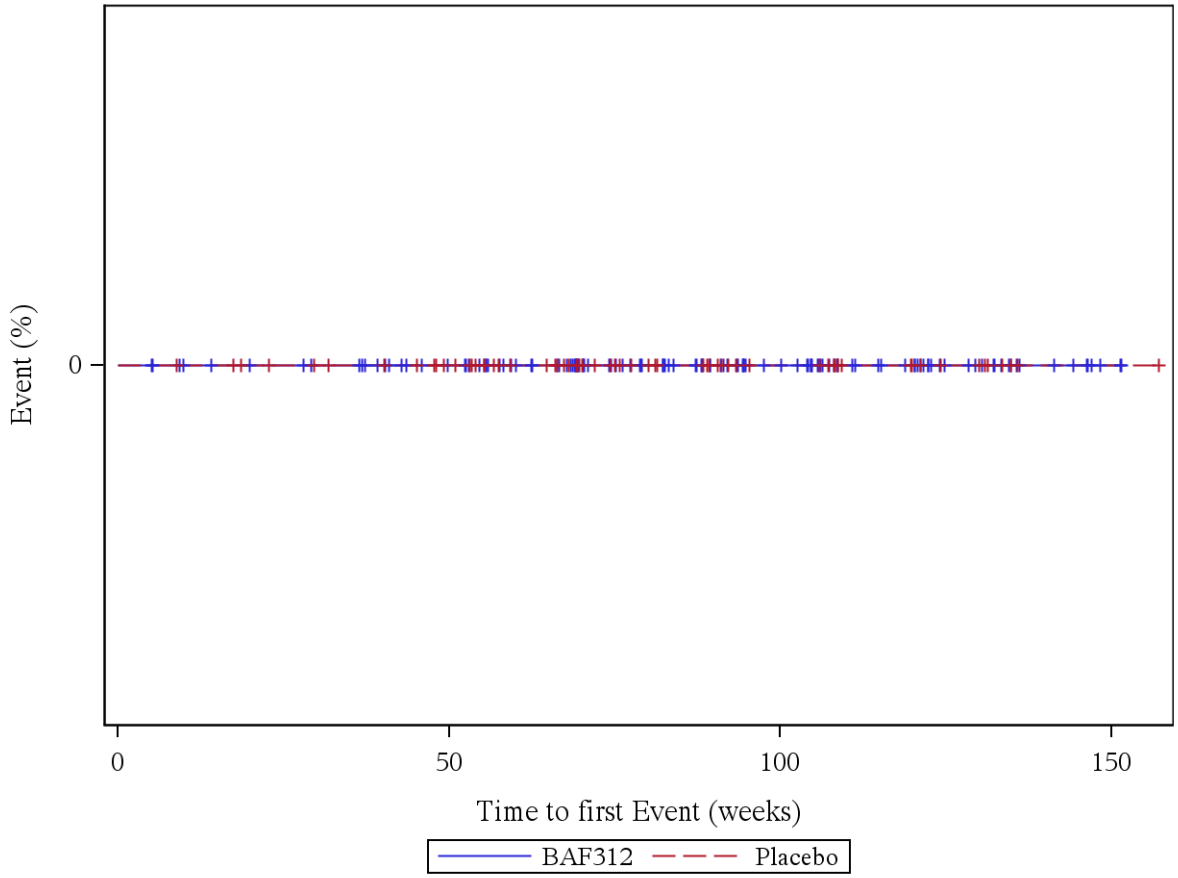


Patients at risk (BAF312/Placebo): Week 0: 127/61, Week 4: 127/61, Week 12: 123/60, Week 24: 121/57, Week 36: 119/55, Week 48: 109/51, Week 60: 98/41, Week 72: 79/32, Week 84: 66/24, Week 96: 49/17, Week 108: 36/15, Week 120: 28/9, Week 132: 15/4, Week 144: 7/1, Week 156: 0/1

Log rank test: p-value = 0,534
*: p < 0,05

Analysis population: A2304 SAF subpopulation "ACTIVE MS WITHOUT RELAPSES"

Figure 12.1.6.20: Macular edema (AESI, serious)

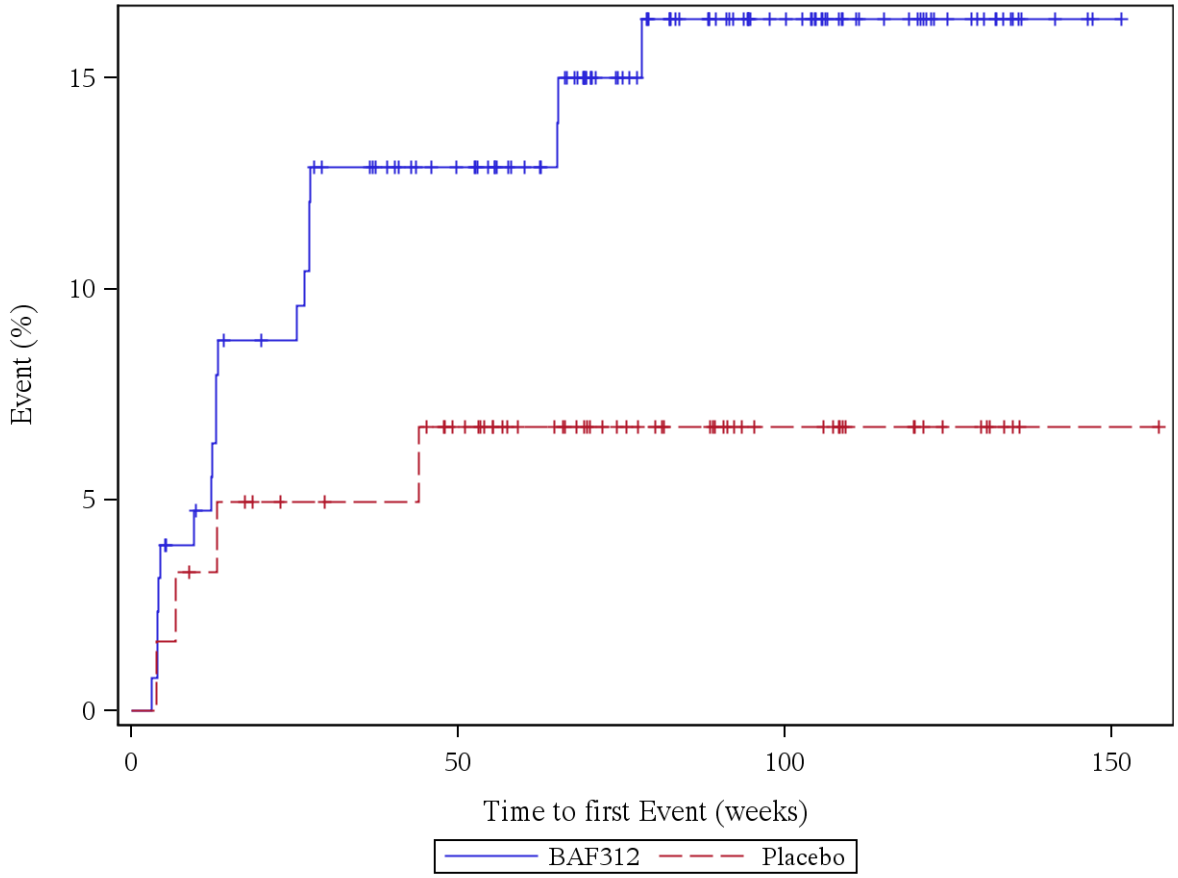


Patients at risk (BAF312/Placebo): Week 0: 127/61, Week 4: 127/61, Week 12: 123/60, Week 24: 121/57, Week 36: 119/55, Week 48: 110/51, Week 60: 99/41, Week 72: 80/32, Week 84: 66/25, Week 96: 49/17, Week 108: 36/15, Week 120: 28/9, Week 132: 15/4, Week 144: 7/1, Week 156: 0/1

Log rank test: p-value = -
*: p < 0,05

Analysis population: A2304 SAF subpopulation "ACTIVE MS WITHOUT RELAPSES"

Figure 12.1.6.21: Abnormal hepatic enzymes (AESI, all)

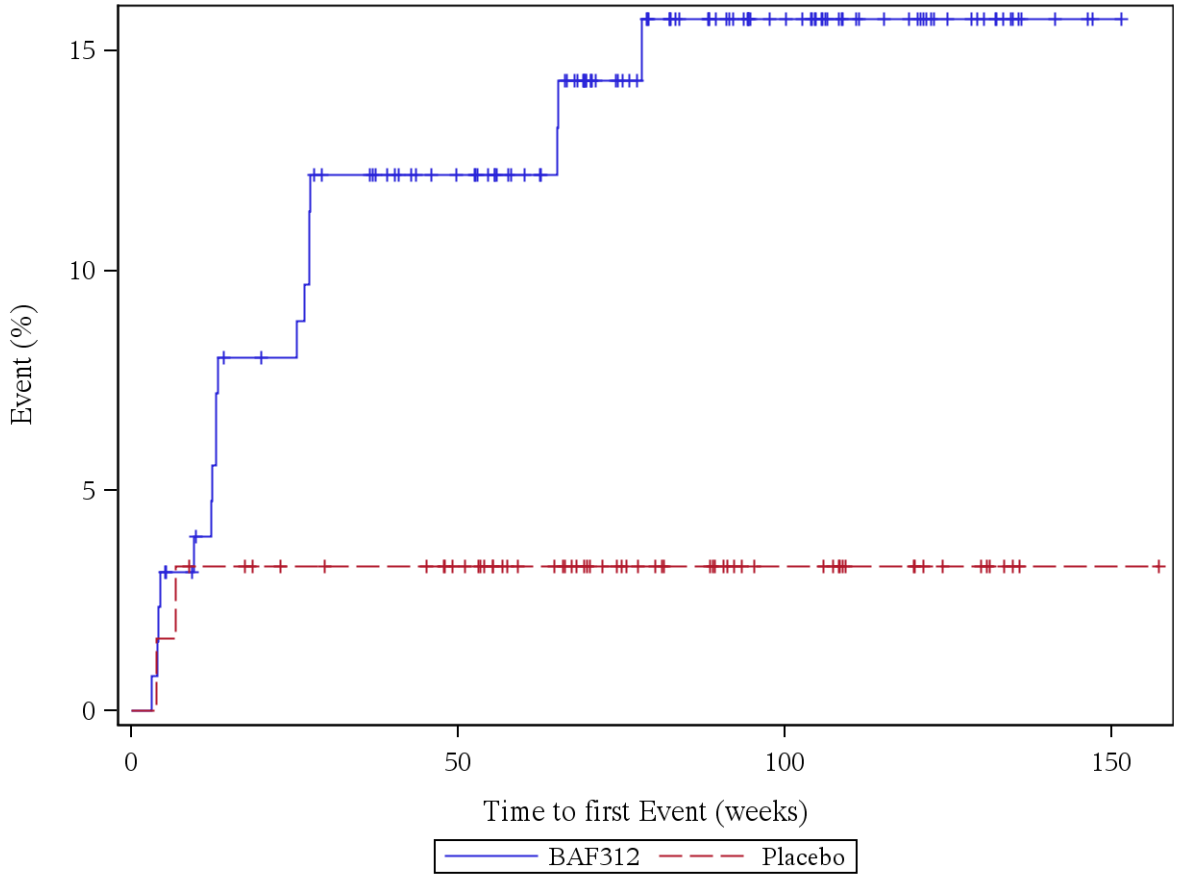


Patients at risk (BAF312/Placebo): Week 0: 127/61, Week 4: 124/60, Week 12: 118/58, Week 24: 111/54, Week 36: 104/53, Week 48: 95/49, Week 60: 85/39, Week 72: 66/31, Week 84: 52/25, Week 96: 39/17, Week 108: 28/15, Week 120: 21/9, Week 132: 11/4, Week 144: 3/1, Week 156: 0/1

Log rank test: p-value = 0,113
*: p < 0,05

Analysis population: A2304 SAF subpopulation "ACTIVE MS WITHOUT RELAPSES"

Figure 12.1.6.22: Abnormal hepatic enzymes (AESI, not severe)

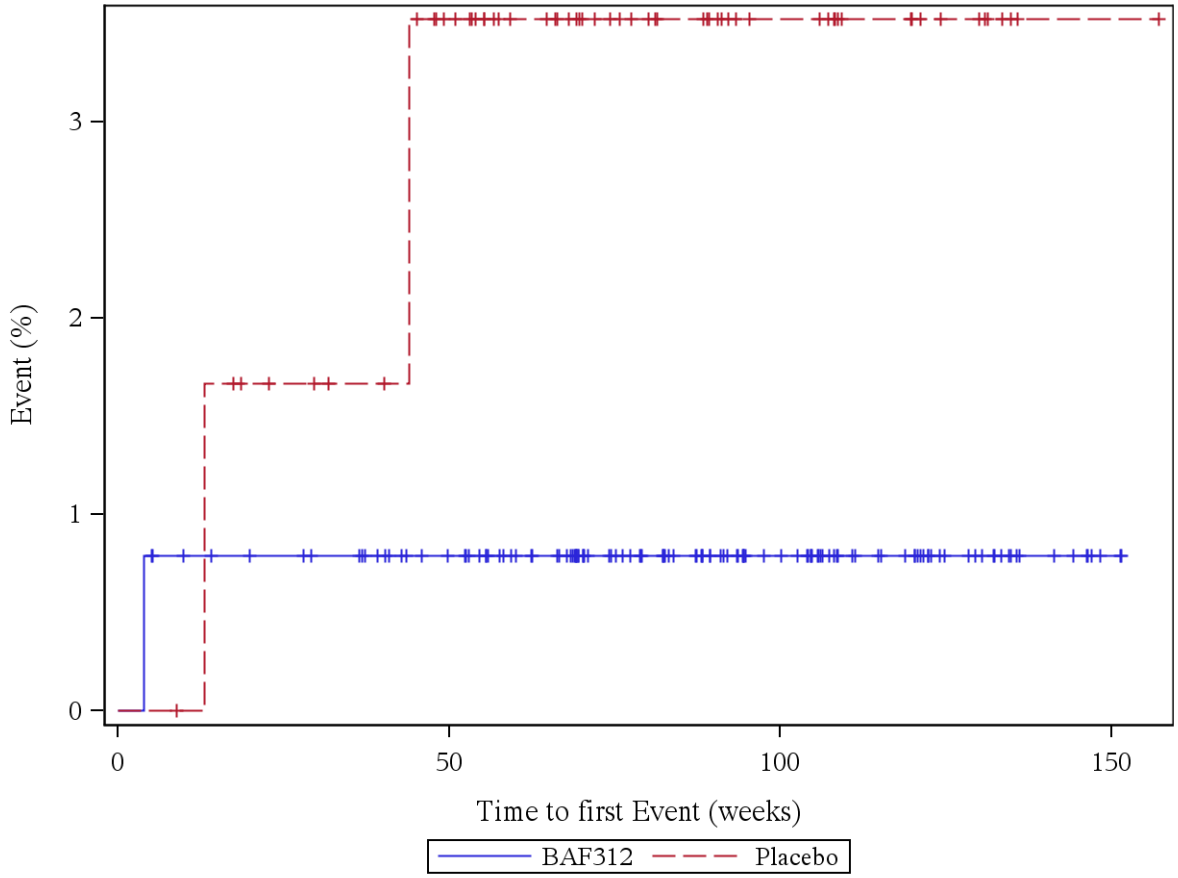


Patients at risk (BAF312/Placebo): Week 0: 127/61, Week 4: 125/60, Week 12: 118/58, Week 24: 111/55, Week 36: 104/54, Week 48: 95/51, Week 60: 85/41, Week 72: 66/32, Week 84: 52/25, Week 96: 39/17, Week 108: 28/15, Week 120: 21/9, Week 132: 11/4, Week 144: 3/1, Week 156: 0/1

Log rank test: p-value = 0,029 *
*: p < 0,05

Analysis population: A2304 SAF subpopulation "ACTIVE MS WITHOUT RELAPSES"

Figure 12.1.6.23: Abnormal hepatic enzymes (AESI, severe)

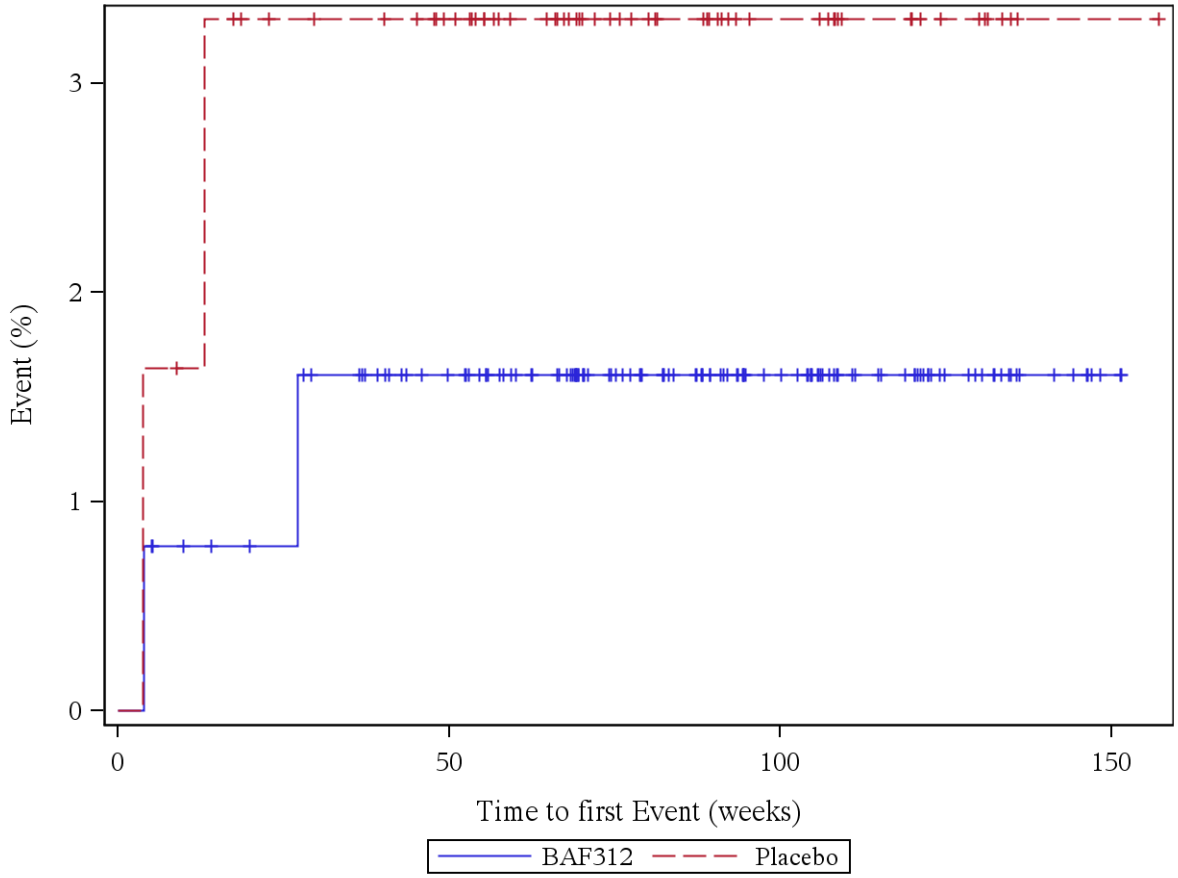


Patients at risk (BAF312/Placebo): Week 0: 127/61, Week 4: 126/61, Week 12: 123/60, Week 24: 121/56, Week 36: 119/54, Week 48: 110/49, Week 60: 99/39, Week 72: 80/31, Week 84: 66/25, Week 96: 49/17, Week 108: 36/15, Week 120: 28/9, Week 132: 15/4, Week 144: 7/1, Week 156: 0/1

Log rank test: p-value = 0,207
*: p < 0,05

Analysis population: A2304 SAF subpopulation "ACTIVE MS WITHOUT RELAPSES"

Figure 12.1.6.24: Abnormal hepatic enzymes (AESI, serious)

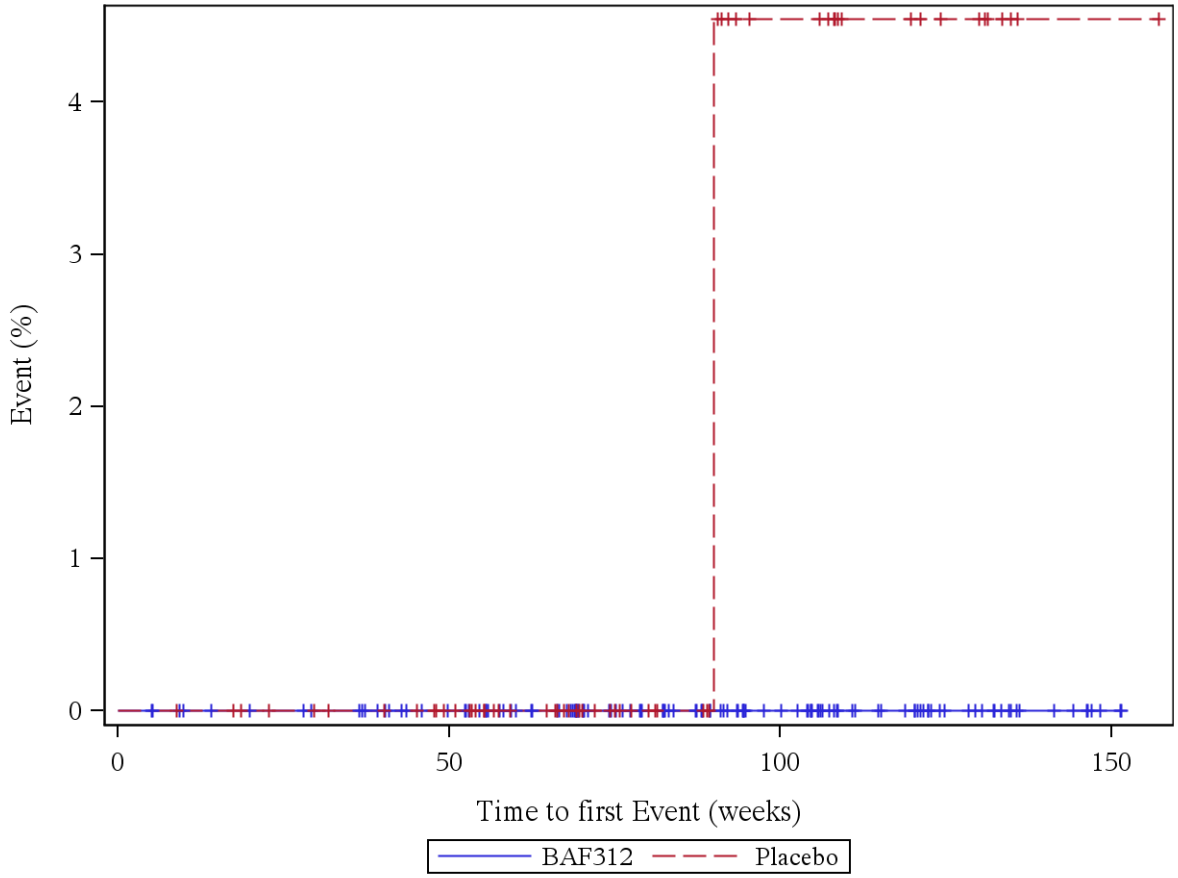


Patients at risk (BAF312/Placebo): Week 0: 127/61, Week 4: 126/60, Week 12: 123/59, Week 24: 121/55, Week 36: 118/54, Week 48: 109/50, Week 60: 98/40, Week 72: 79/31, Week 84: 66/25, Week 96: 49/17, Week 108: 36/15, Week 120: 28/9, Week 132: 15/4, Week 144: 7/1, Week 156: 0/1

Log rank test: p-value = 0,442
*: p < 0,05

Analysis population: A2304 SAF subpopulation "ACTIVE MS WITHOUT RELAPSES"

Figure 12.1.6.25: Malignancies (AESI, all)

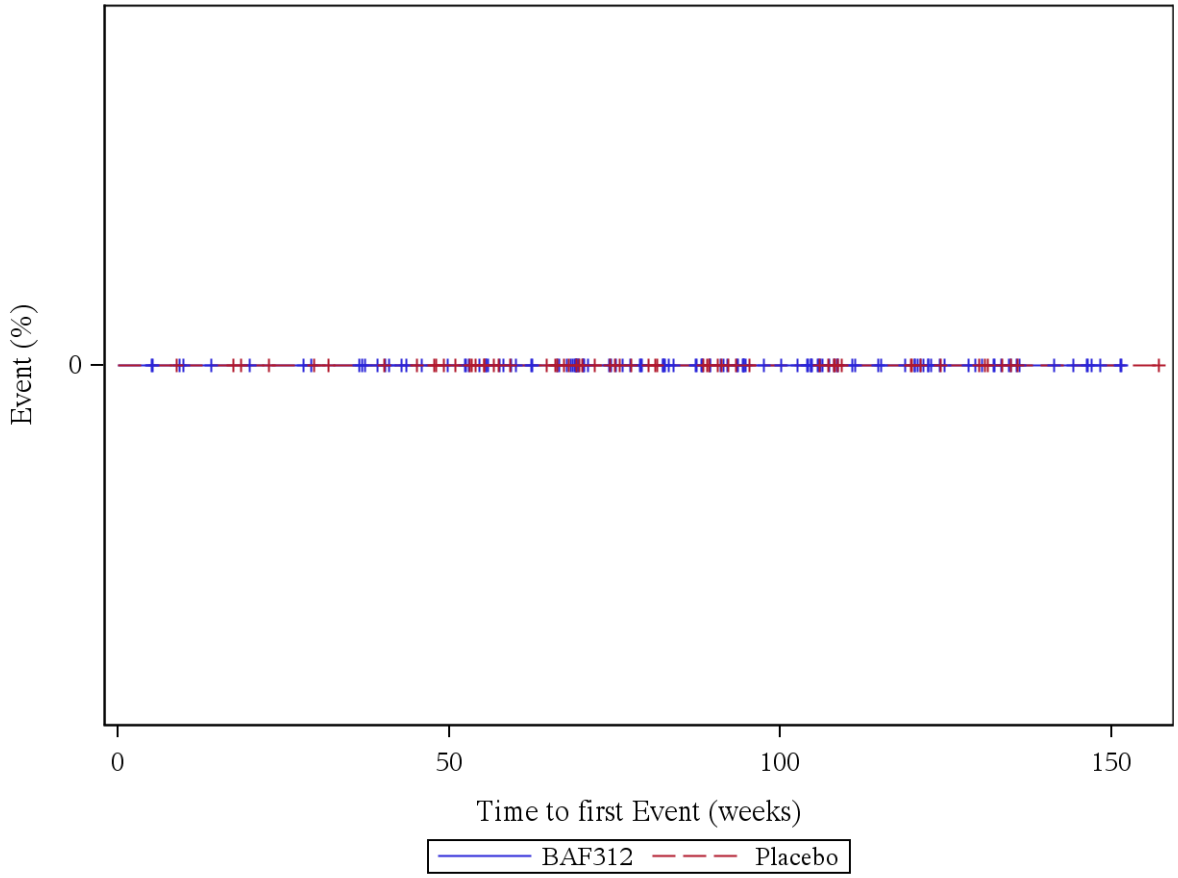


Patients at risk (BAF312/Placebo): Week 0: 127/61, Week 4: 127/61, Week 12: 123/60, Week 24: 121/57, Week 36: 119/55, Week 48: 110/51, Week 60: 99/41, Week 72: 80/32, Week 84: 66/25, Week 96: 49/16, Week 108: 36/14, Week 120: 28/9, Week 132: 15/4, Week 144: 7/1, Week 156: 0/1

Log rank test: p-value = -
*: p < 0,05

Analysis population: A2304 SAF subpopulation "ACTIVE MS WITHOUT RELAPSES"

Figure 12.1.6.26: Malignancies (AESI, not severe)

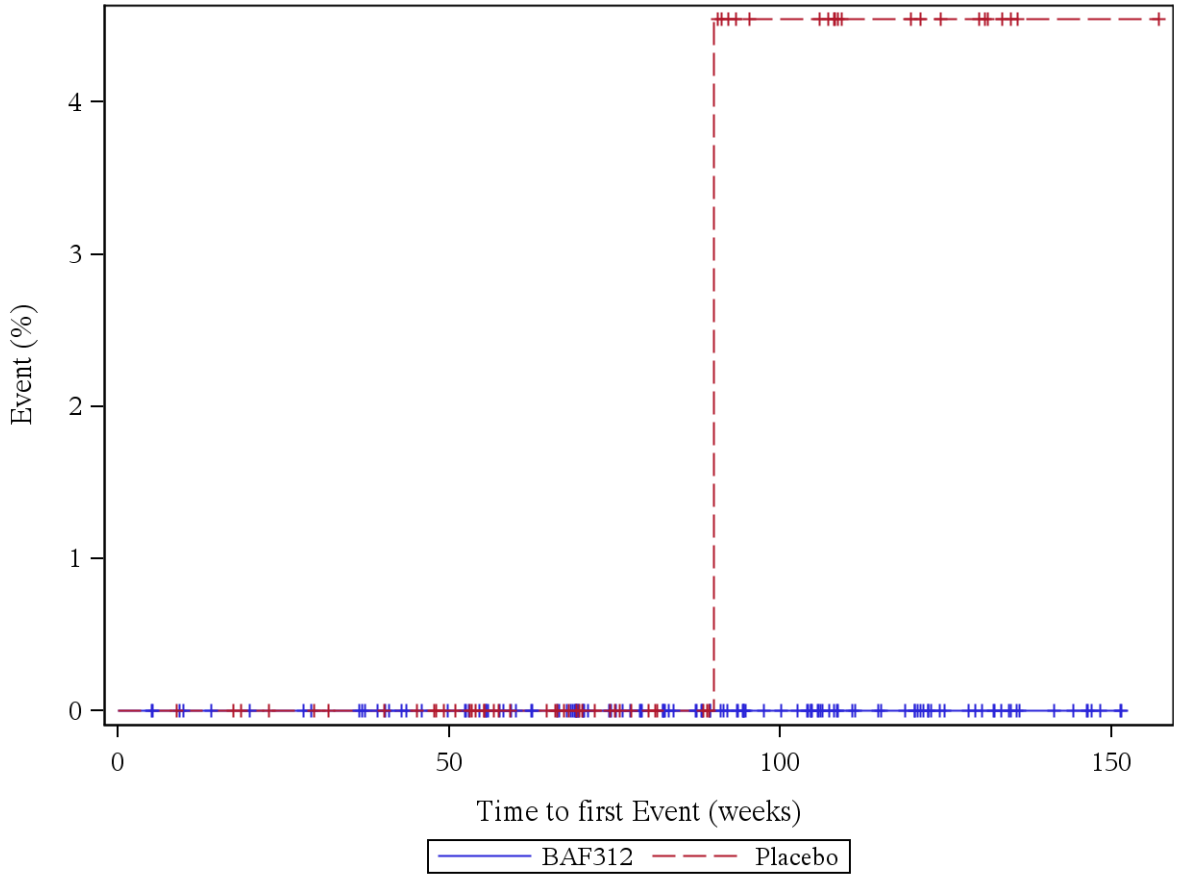


Patients at risk (BAF312/Placebo): Week 0: 127/61, Week 4: 127/61, Week 12: 123/60, Week 24: 121/57, Week 36: 119/55, Week 48: 110/51, Week 60: 99/41, Week 72: 80/32, Week 84: 66/25, Week 96: 49/17, Week 108: 36/15, Week 120: 28/9, Week 132: 15/4, Week 144: 7/1, Week 156: 0/1

Log rank test: p-value = -
*: p < 0,05

Analysis population: A2304 SAF subpopulation "ACTIVE MS WITHOUT RELAPSES"

Figure 12.1.6.27: Malignancies (AESI, severe)

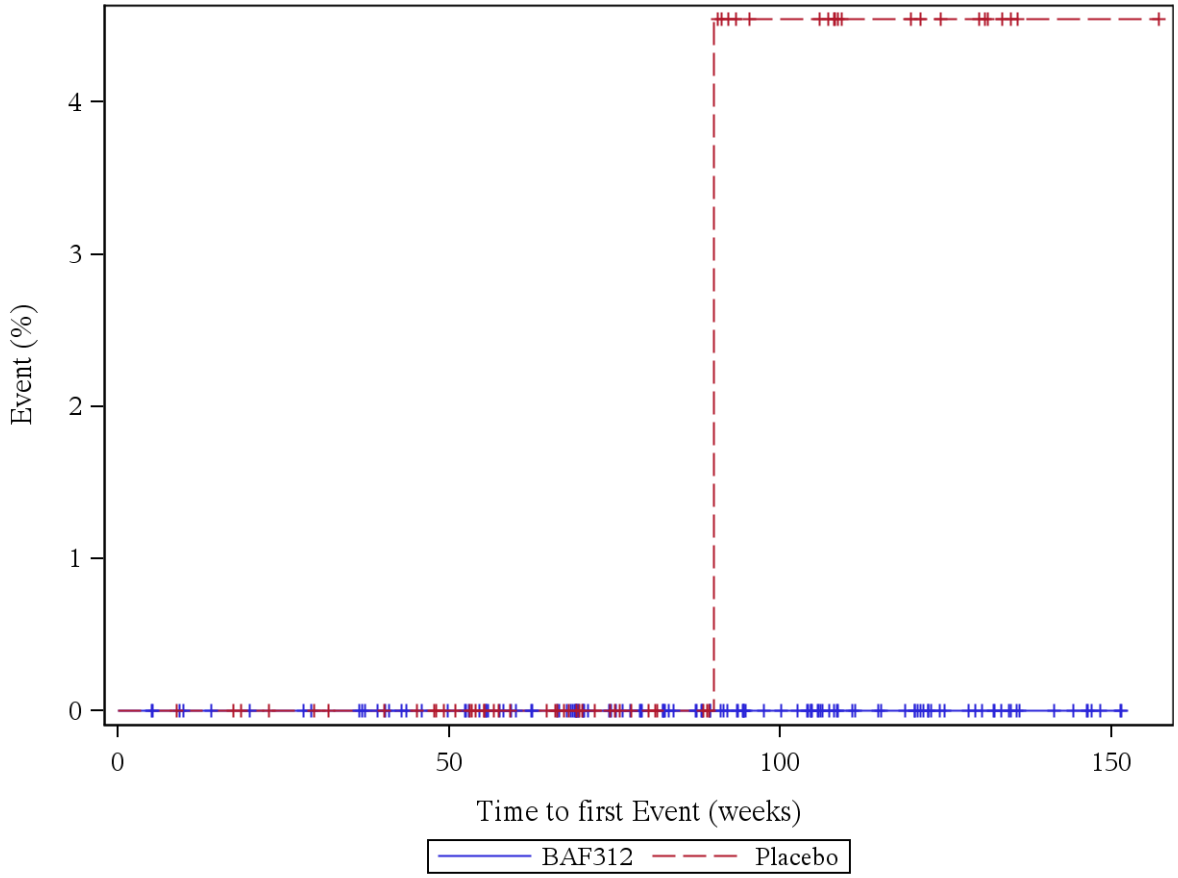


Patients at risk (BAF312/Placebo): Week 0: 127/61, Week 4: 127/61, Week 12: 123/60, Week 24: 121/57, Week 36: 119/55, Week 48: 110/51, Week 60: 99/41, Week 72: 80/32, Week 84: 66/25, Week 96: 49/16, Week 108: 36/14, Week 120: 28/9, Week 132: 15/4, Week 144: 7/1, Week 156: 0/1

Log rank test: p-value = -
*: p < 0,05

Analysis population: A2304 SAF subpopulation "ACTIVE MS WITHOUT RELAPSES"

Figure 12.1.6.28: Malignancies (AESI, serious)

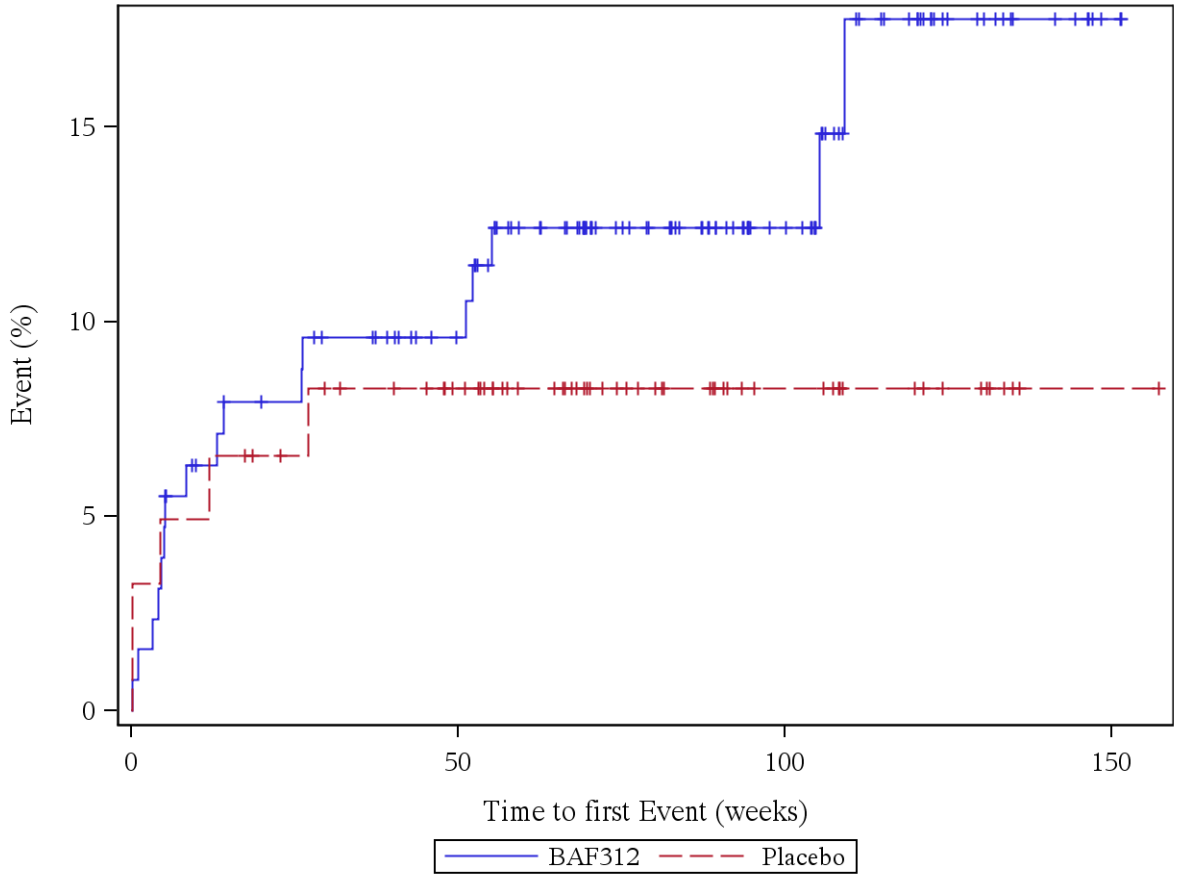


Patients at risk (BAF312/Placebo): Week 0: 127/61, Week 4: 127/61, Week 12: 123/60, Week 24: 121/57, Week 36: 119/55, Week 48: 110/51, Week 60: 99/41, Week 72: 80/32, Week 84: 66/25, Week 96: 49/16, Week 108: 36/14, Week 120: 28/9, Week 132: 15/4, Week 144: 7/1, Week 156: 0/1

Log rank test: p-value = -
*: p < 0,05

Analysis population: A2304 SAF subpopulation "ACTIVE MS WITHOUT RELAPSES"

Figure 12.1.6.29: Hypertension (AESI, all)

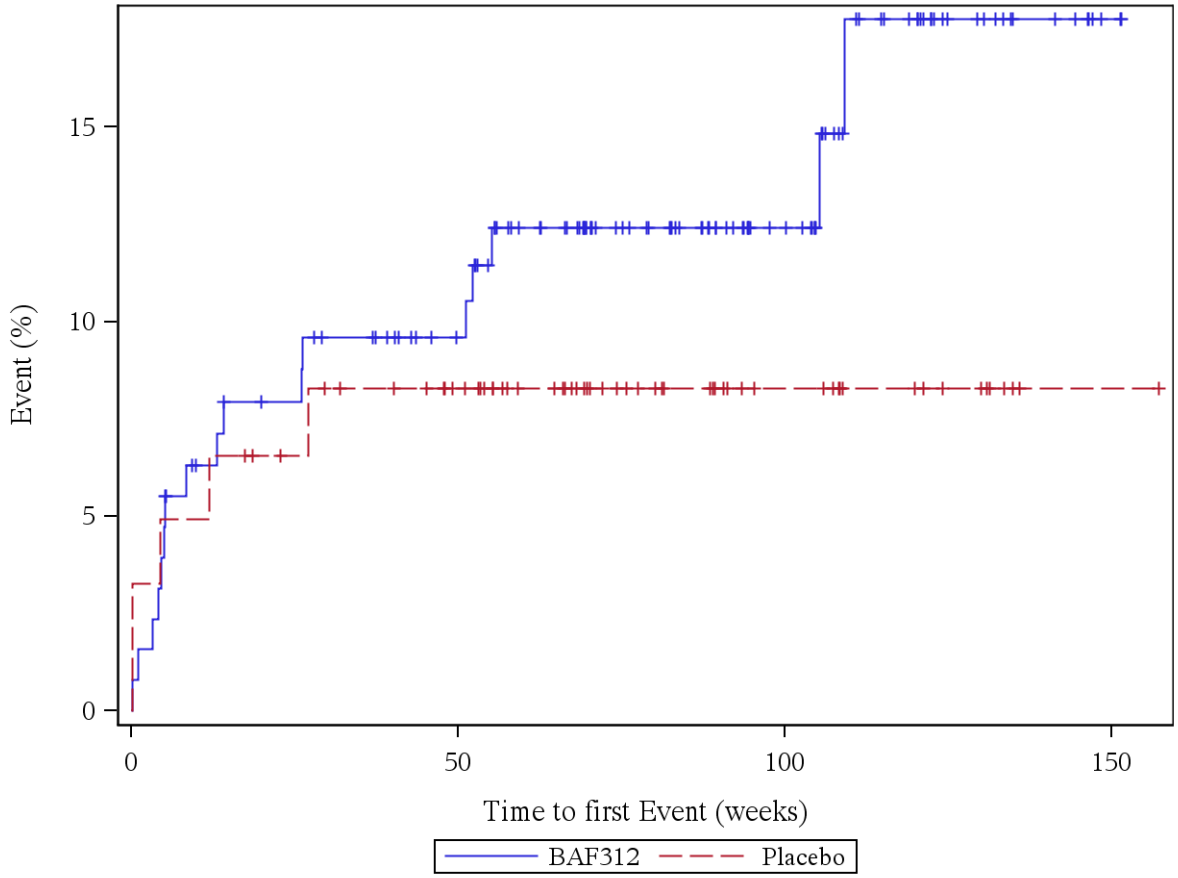


Patients at risk (BAF312/Placebo): Week 0: 127/61, Week 4: 124/59, Week 12: 115/57, Week 24: 111/54, Week 36: 107/51, Week 48: 99/47, Week 60: 85/37, Week 72: 69/28, Week 84: 59/22, Week 96: 44/15, Week 108: 31/13, Week 120: 23/9, Week 132: 12/4, Week 144: 7/1, Week 156: 0/1

Log rank test: p-value = 0,351
*: p < 0,05

Analysis population: A2304 SAF subpopulation "ACTIVE MS WITHOUT RELAPSES"

Figure 12.1.6.30: Hypertension (AESI, not severe)

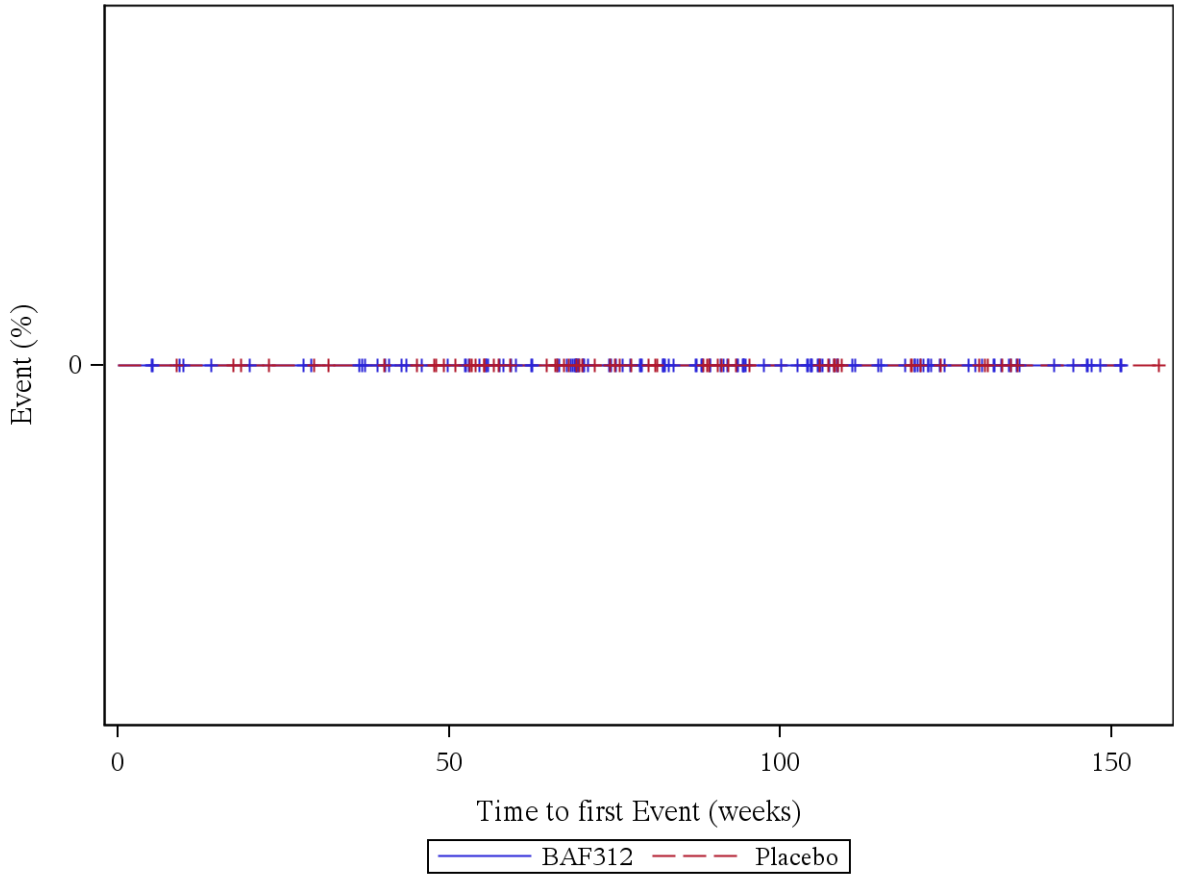


Patients at risk (BAF312/Placebo): Week 0: 127/61, Week 4: 124/59, Week 12: 115/57, Week 24: 111/54, Week 36: 107/51, Week 48: 99/47, Week 60: 85/37, Week 72: 69/28, Week 84: 59/22, Week 96: 44/15, Week 108: 31/13, Week 120: 23/9, Week 132: 12/4, Week 144: 7/1, Week 156: 0/1

Log rank test: p-value = 0,351
*: p < 0,05

Analysis population: A2304 SAF subpopulation "ACTIVE MS WITHOUT RELAPSES"

Figure 12.1.6.31: Hypertension (AESI, severe)

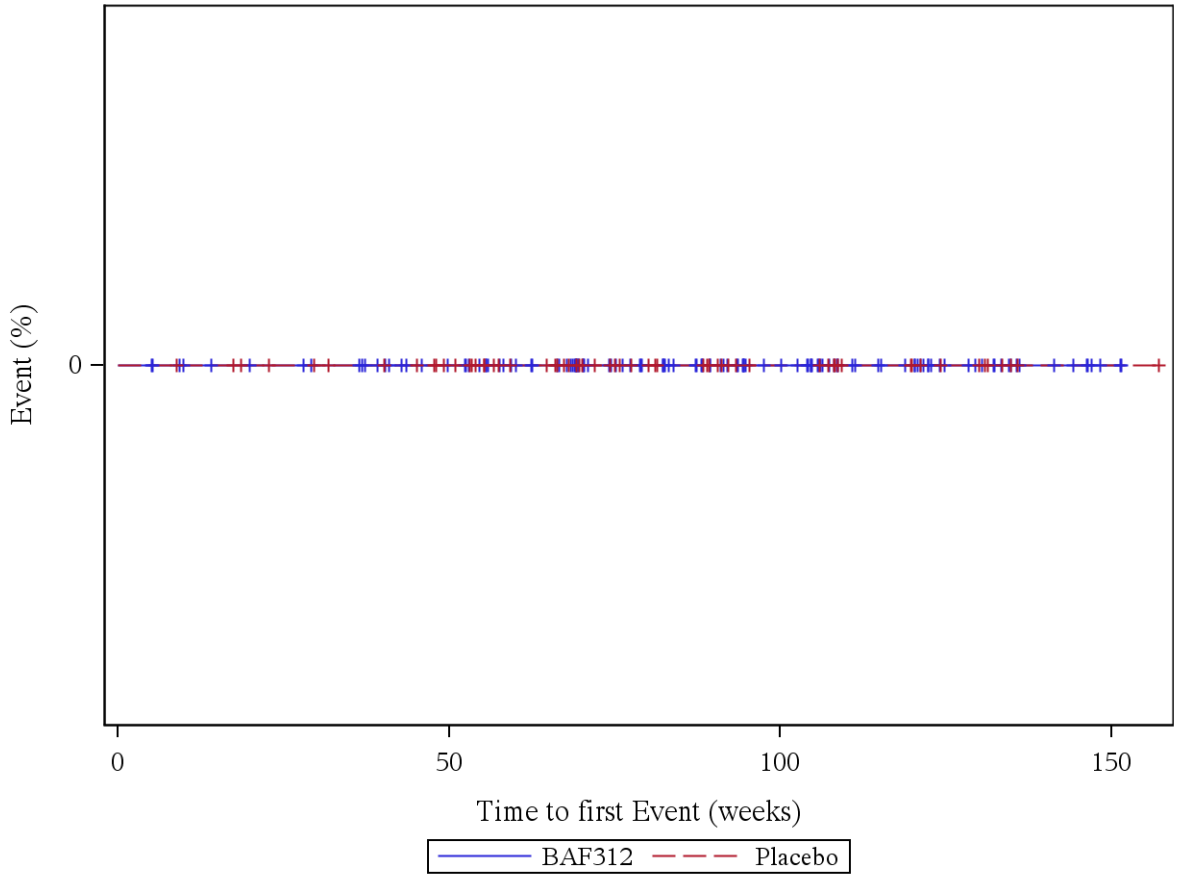


Patients at risk (BAF312/Placebo): Week 0: 127/61, Week 4: 127/61, Week 12: 123/60, Week 24: 121/57, Week 36: 119/55, Week 48: 110/51, Week 60: 99/41, Week 72: 80/32, Week 84: 66/25, Week 96: 49/17, Week 108: 36/15, Week 120: 28/9, Week 132: 15/4, Week 144: 7/1, Week 156: 0/1

Log rank test: p-value = -
*: p < 0,05

Analysis population: A2304 SAF subpopulation "ACTIVE MS WITHOUT RELAPSES"

Figure 12.1.6.32: Hypertension (AESI, serious)

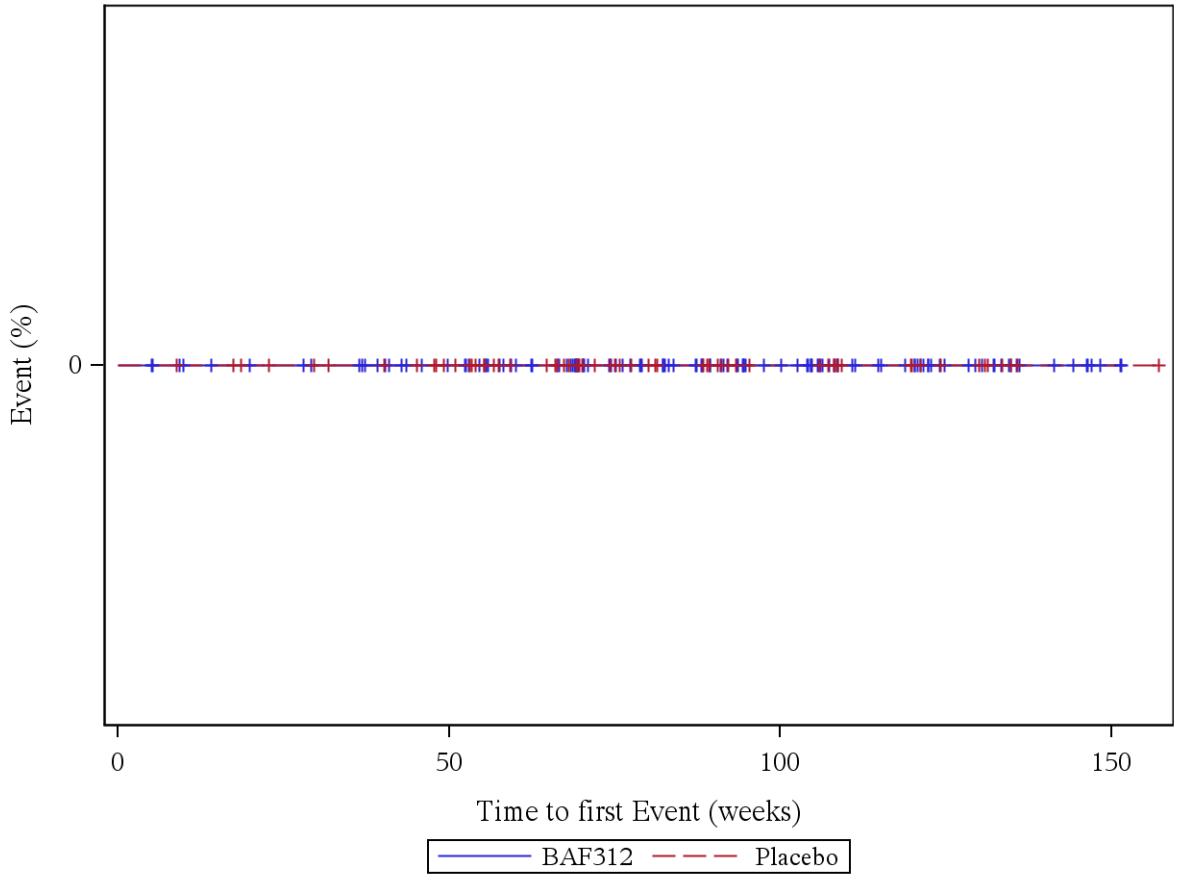


Patients at risk (BAF312/Placebo): Week 0: 127/61, Week 4: 127/61, Week 12: 123/60, Week 24: 121/57, Week 36: 119/55, Week 48: 110/51, Week 60: 99/41, Week 72: 80/32, Week 84: 66/25, Week 96: 49/17, Week 108: 36/15, Week 120: 28/9, Week 132: 15/4, Week 144: 7/1, Week 156: 0/1

Log rank test: p-value = -
*: p < 0,05

Analysis population: A2304 SAF subpopulation "ACTIVE MS WITHOUT RELAPSES"

Figure 12.1.6.33: Seizures (AESI, all)

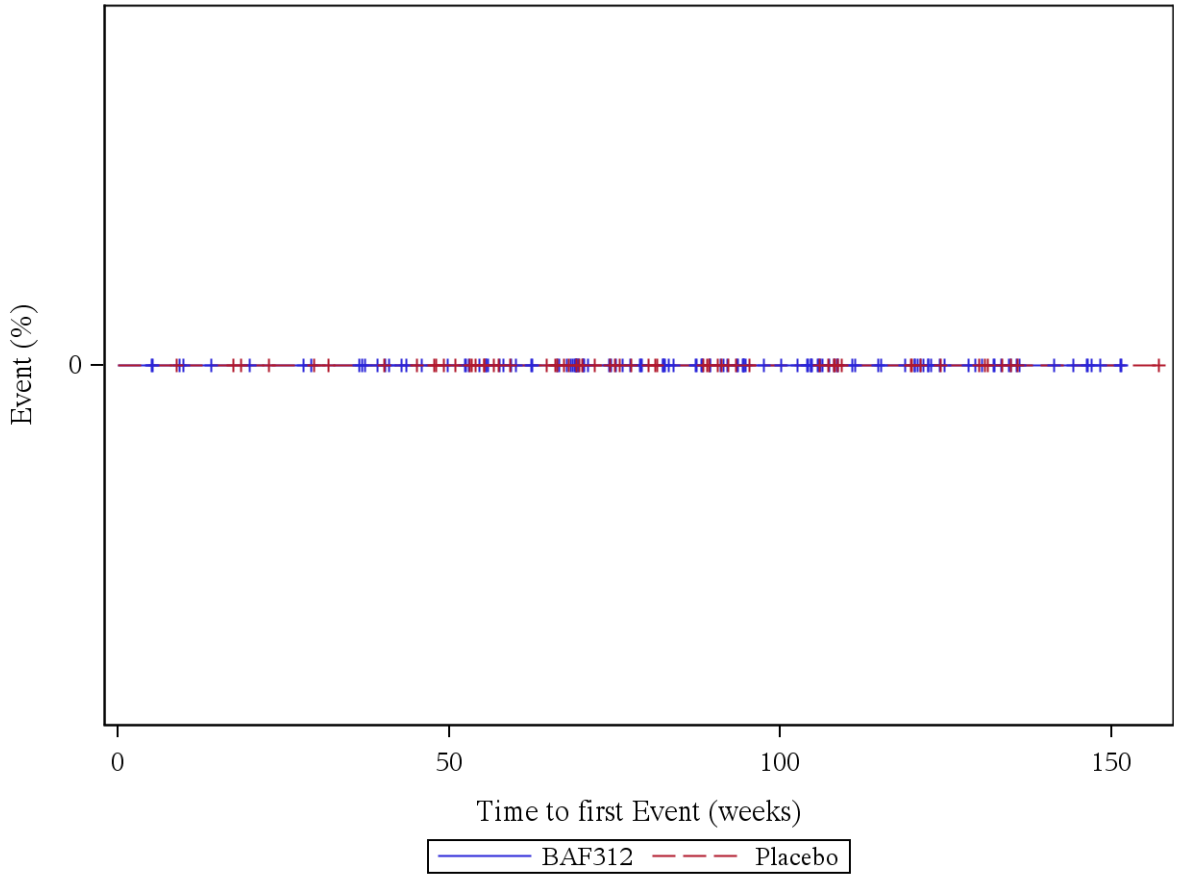


Patients at risk (BAF312/Placebo): Week 0: 127/61, Week 4: 127/61, Week 12: 123/60, Week 24: 121/57, Week 36: 119/55, Week 48: 110/51, Week 60: 99/41, Week 72: 80/32, Week 84: 66/25, Week 96: 49/17, Week 108: 36/15, Week 120: 28/9, Week 132: 15/4, Week 144: 7/1, Week 156: 0/1

Log rank test: p-value = -
*: p < 0,05

Analysis population: A2304 SAF subpopulation "ACTIVE MS WITHOUT RELAPSES"

Figure 12.1.6.34: Seizures (AESI, not severe)

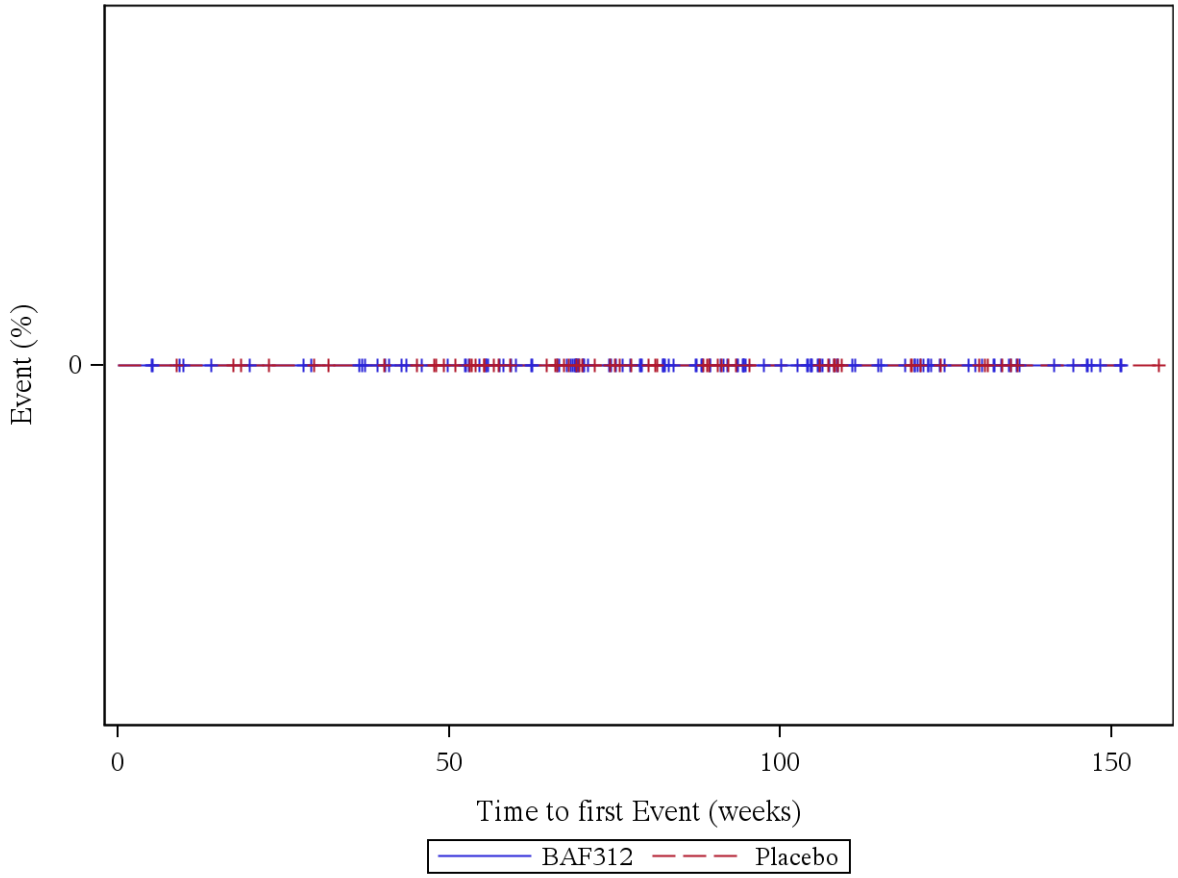


Patients at risk (BAF312/Placebo): Week 0: 127/61, Week 4: 127/61, Week 12: 123/60, Week 24: 121/57, Week 36: 119/55, Week 48: 110/51, Week 60: 99/41, Week 72: 80/32, Week 84: 66/25, Week 96: 49/17, Week 108: 36/15, Week 120: 28/9, Week 132: 15/4, Week 144: 7/1, Week 156: 0/1

Log rank test: p-value = -
*: p < 0,05

Analysis population: A2304 SAF subpopulation "ACTIVE MS WITHOUT RELAPSES"

Figure 12.1.6.35: Seizures (AESI, severe)

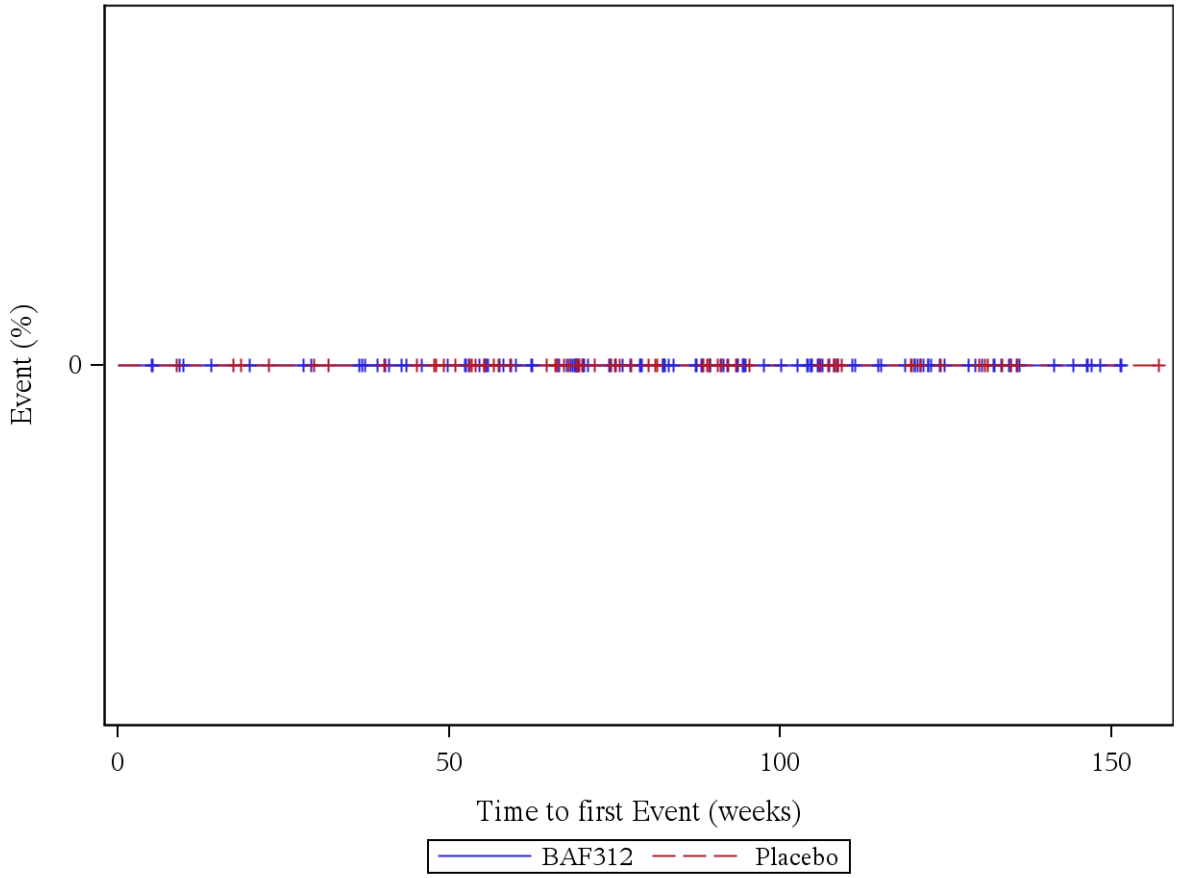


Patients at risk (BAF312/Placebo): Week 0: 127/61, Week 4: 127/61, Week 12: 123/60, Week 24: 121/57, Week 36: 119/55, Week 48: 110/51, Week 60: 99/41, Week 72: 80/32, Week 84: 66/25, Week 96: 49/17, Week 108: 36/15, Week 120: 28/9, Week 132: 15/4, Week 144: 7/1, Week 156: 0/1

Log rank test: p-value = -
*: p < 0,05

Analysis population: A2304 SAF subpopulation "ACTIVE MS WITHOUT RELAPSES"

Figure 12.1.6.36: Seizures (AESI, serious)

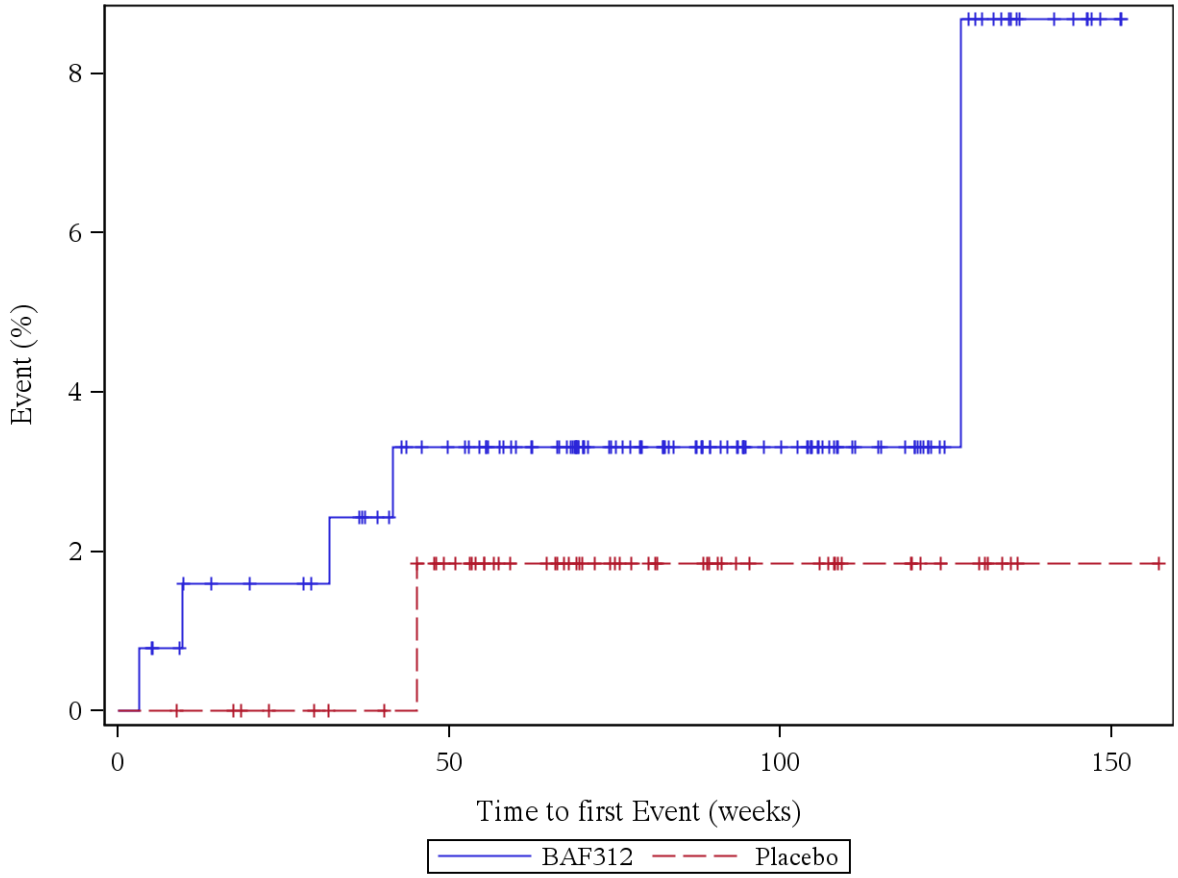


Patients at risk (BAF312/Placebo): Week 0: 127/61, Week 4: 127/61, Week 12: 123/60, Week 24: 121/57, Week 36: 119/55, Week 48: 110/51, Week 60: 99/41, Week 72: 80/32, Week 84: 66/25, Week 96: 49/17, Week 108: 36/15, Week 120: 28/9, Week 132: 15/4, Week 144: 7/1, Week 156: 0/1

Log rank test: p-value = -
*: p < 0,05

Analysis population: A2304 SAF subpopulation "ACTIVE MS WITHOUT RELAPSES"

Figure 12.1.6.37: Thromboembolic events (AESI, all)

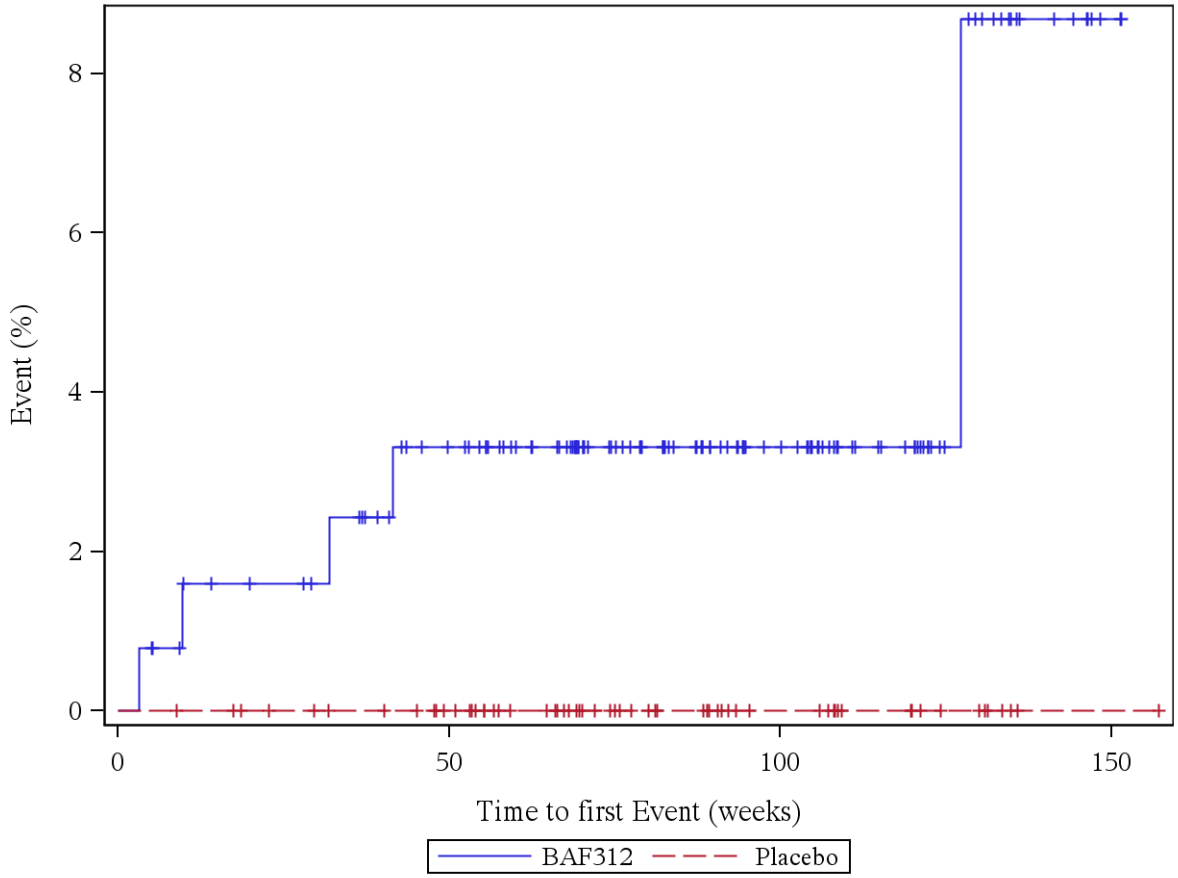


Patients at risk (BAF312/Placebo): Week 0: 127/61, Week 4: 126/61, Week 12: 121/60, Week 24: 119/57, Week 36: 116/55, Week 48: 107/50, Week 60: 97/40, Week 72: 78/31, Week 84: 64/24, Week 96: 48/17, Week 108: 36/15, Week 120: 28/9, Week 132: 14/4, Week 144: 7/1, Week 156: 0/1

Log rank test: p-value = 0,424
*: p < 0,05

Analysis population: A2304 SAF subpopulation "ACTIVE MS WITHOUT RELAPSES"

Figure 12.1.6.38: Thromboembolic events (AESI, not severe)

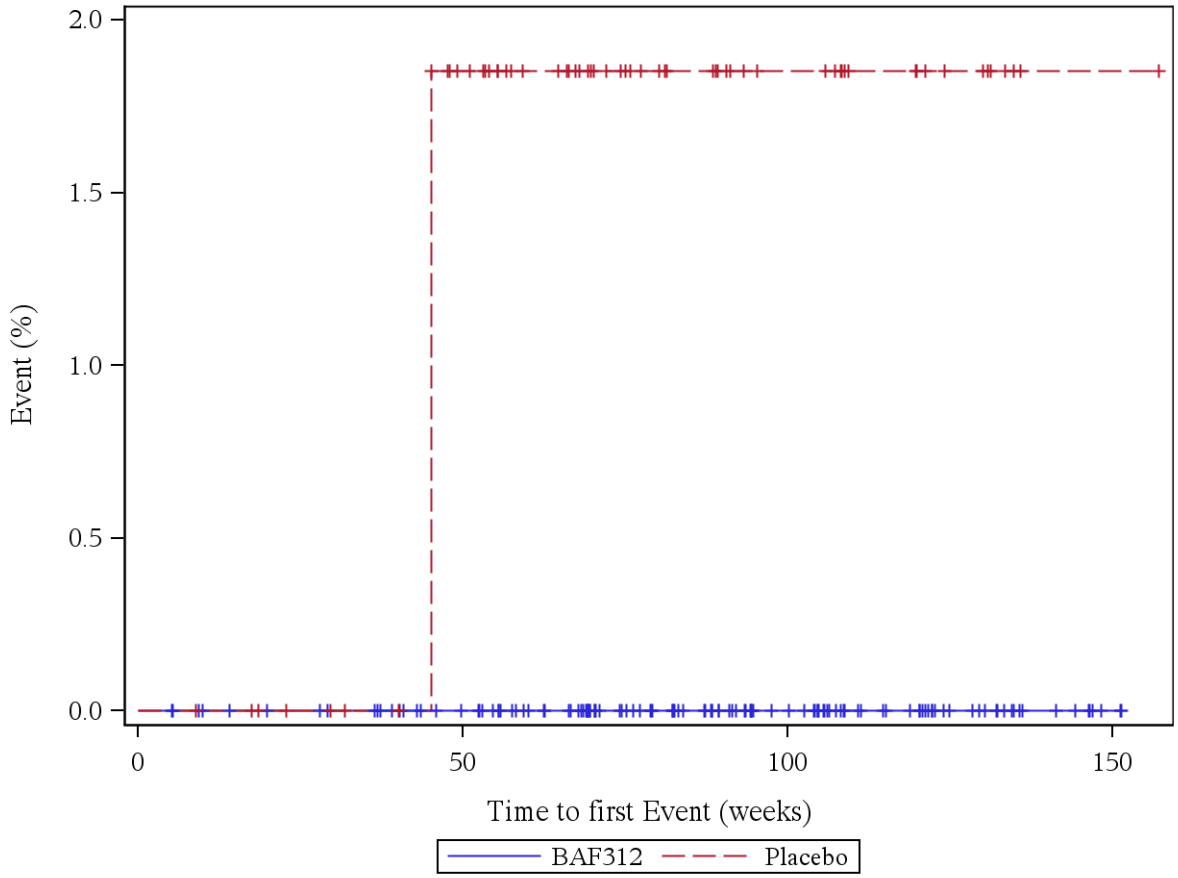


Patients at risk (BAF312/Placebo): Week 0: 127/61, Week 4: 126/61, Week 12: 121/60, Week 24: 119/57, Week 36: 116/55, Week 48: 107/51, Week 60: 97/41, Week 72: 78/32, Week 84: 64/25, Week 96: 48/17, Week 108: 36/15, Week 120: 28/9, Week 132: 14/4, Week 144: 7/1, Week 156: 0/1

Log rank test: p-value = -
*: p < 0,05

Analysis population: A2304 SAF subpopulation "ACTIVE MS WITHOUT RELAPSES"

Figure 12.1.6.39: Thromboembolic events (AESI, severe)

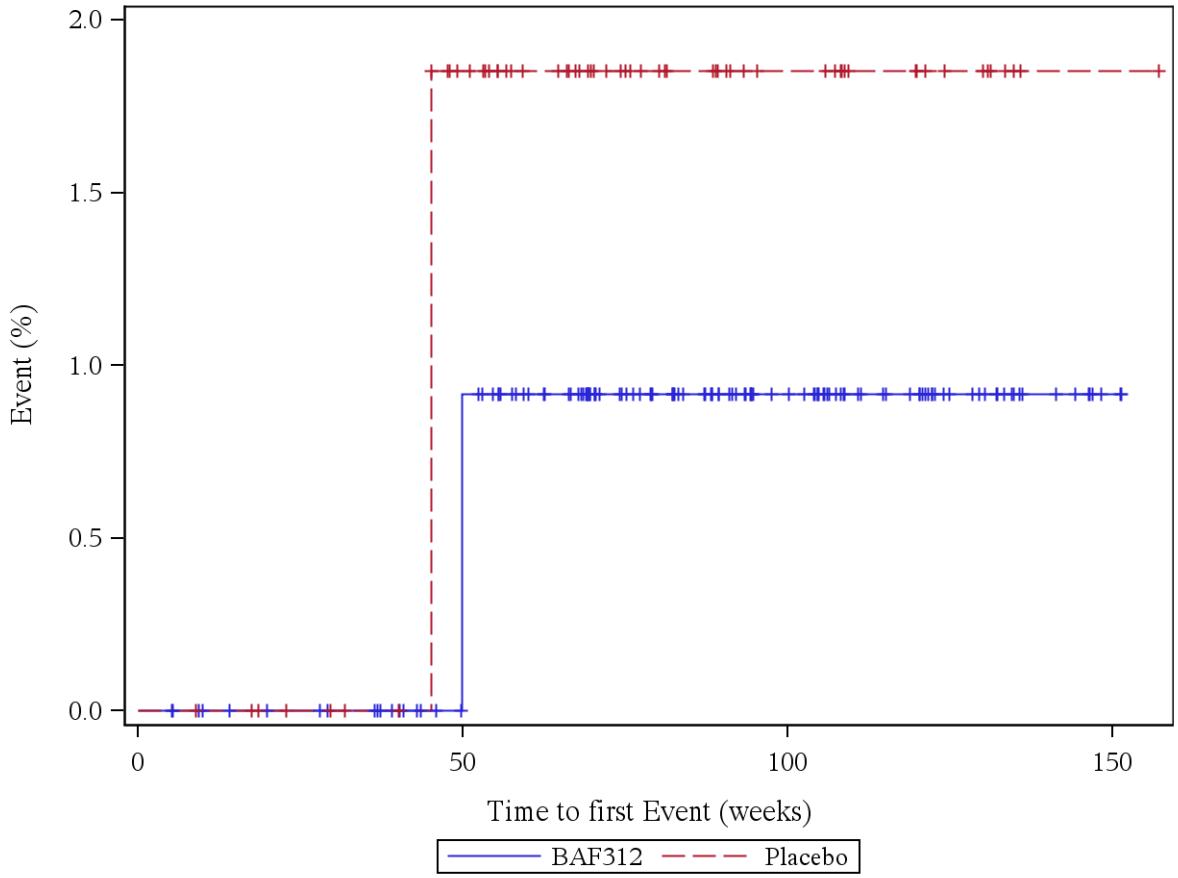


Patients at risk (BAF312/Placebo): Week 0: 127/61, Week 4: 127/61, Week 12: 123/60, Week 24: 121/57, Week 36: 119/55, Week 48: 110/50, Week 60: 99/40, Week 72: 80/31, Week 84: 66/24, Week 96: 49/17, Week 108: 36/15, Week 120: 28/9, Week 132: 15/4, Week 144: 7/1, Week 156: 0/1

Log rank test: p-value = -
*: p < 0,05

Analysis population: A2304 SAF subpopulation "ACTIVE MS WITHOUT RELAPSES"

Figure 12.1.6.40: Thromboembolic events (AESI, serious)

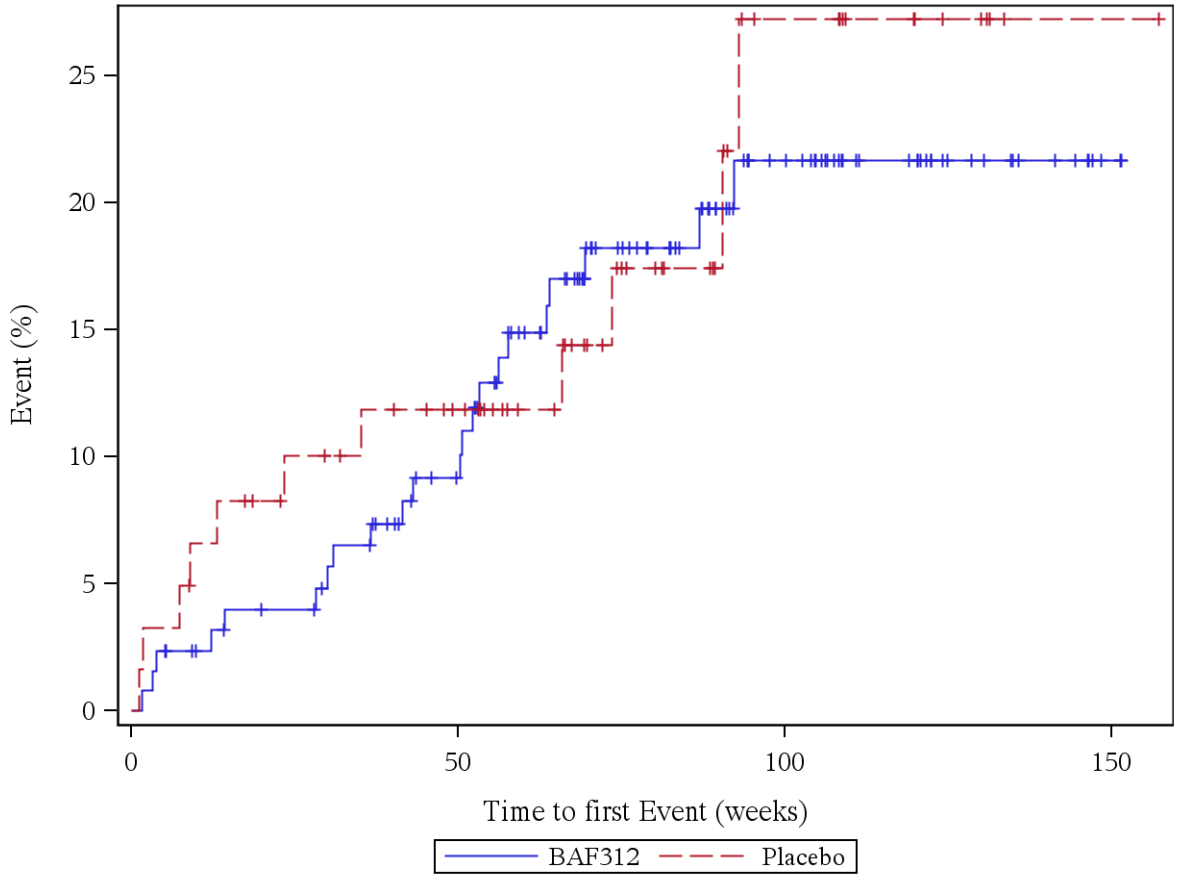


Patients at risk (BAF312/Placebo): Week 0: 127/61, Week 4: 127/61, Week 12: 123/60, Week 24: 121/57, Week 36: 119/55, Week 48: 110/50, Week 60: 99/40, Week 72: 80/31, Week 84: 66/24, Week 96: 49/17, Week 108: 36/15, Week 120: 28/9, Week 132: 15/4, Week 144: 7/1, Week 156: 0/1

Log rank test: p-value = 0,582
*: p < 0,05

Analysis population: A2304 SAF subpopulation "ACTIVE MS WITHOUT RELAPSES"

Figure 12.1.6.41: Respiratory disorders (AESI, all)

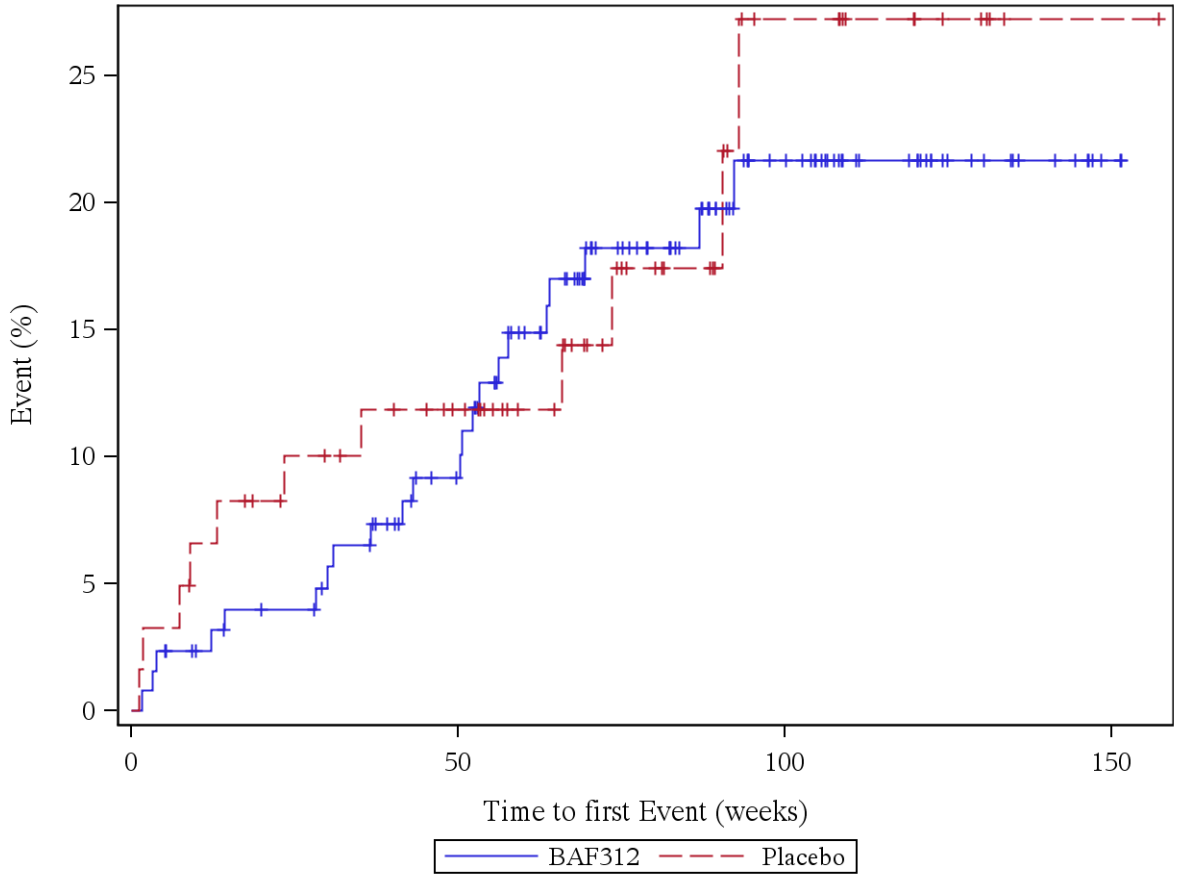


Patients at risk (BAF312/Placebo): Week 0: 127/61, Week 4: 124/59, Week 12: 120/56, Week 24: 116/51, Week 36: 111/48, Week 48: 99/45, Week 60: 83/36, Week 72: 64/28, Week 84: 53/21, Week 96: 37/12, Week 108: 27/12, Week 120: 21/6, Week 132: 11/2, Week 144: 7/1, Week 156: 0/1

Log rank test: p-value = 0,754
*: p < 0,05

Analysis population: A2304 SAF subpopulation "ACTIVE MS WITHOUT RELAPSES"

Figure 12.1.6.42: Respiratory disorders (AESI, not severe)

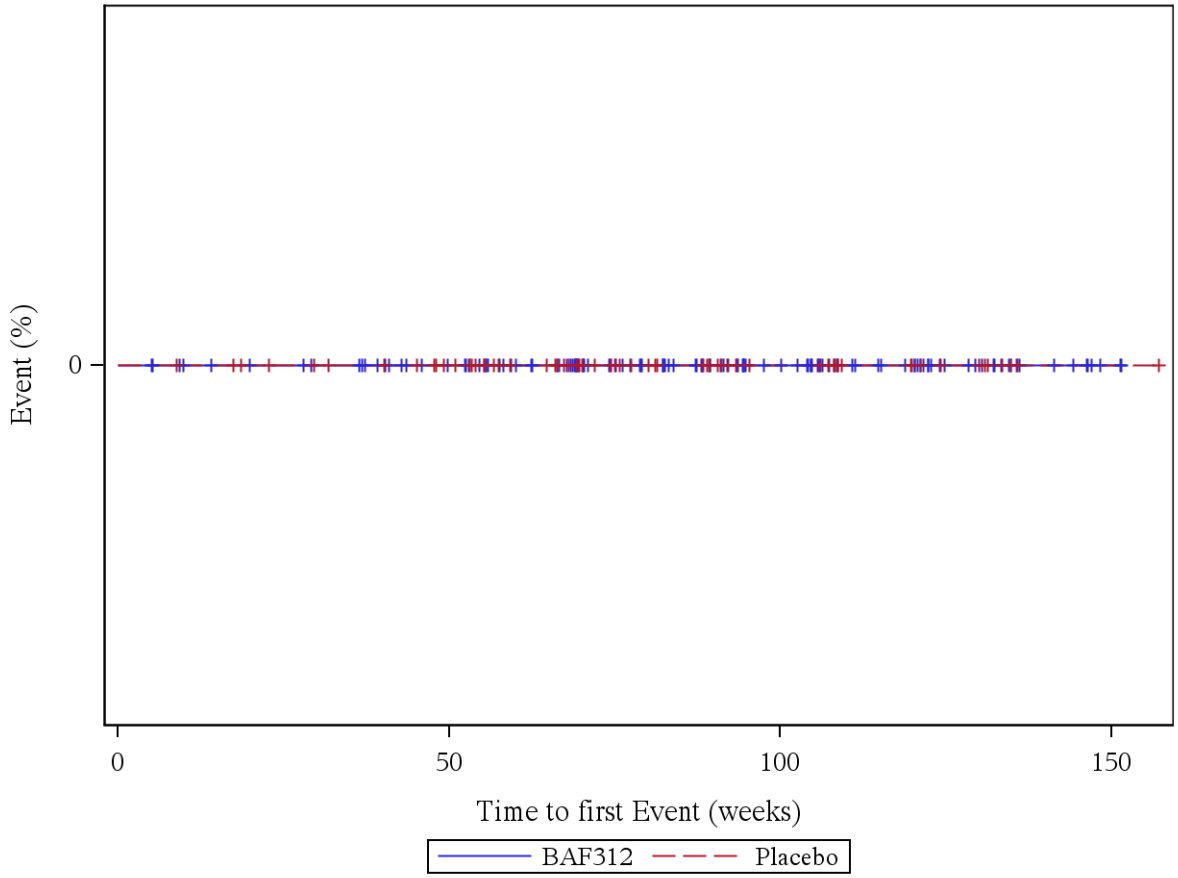


Patients at risk (BAF312/Placebo): Week 0: 127/61, Week 4: 124/59, Week 12: 120/56, Week 24: 116/51, Week 36: 111/48, Week 48: 99/45, Week 60: 83/36, Week 72: 64/28, Week 84: 53/21, Week 96: 37/12, Week 108: 27/12, Week 120: 21/6, Week 132: 11/2, Week 144: 7/1, Week 156: 0/1

Log rank test: p-value = 0,754
*: p < 0,05

Analysis population: A2304 SAF subpopulation "ACTIVE MS WITHOUT RELAPSES"

Figure 12.1.6.43: Respiratory disorders (AESI, severe)

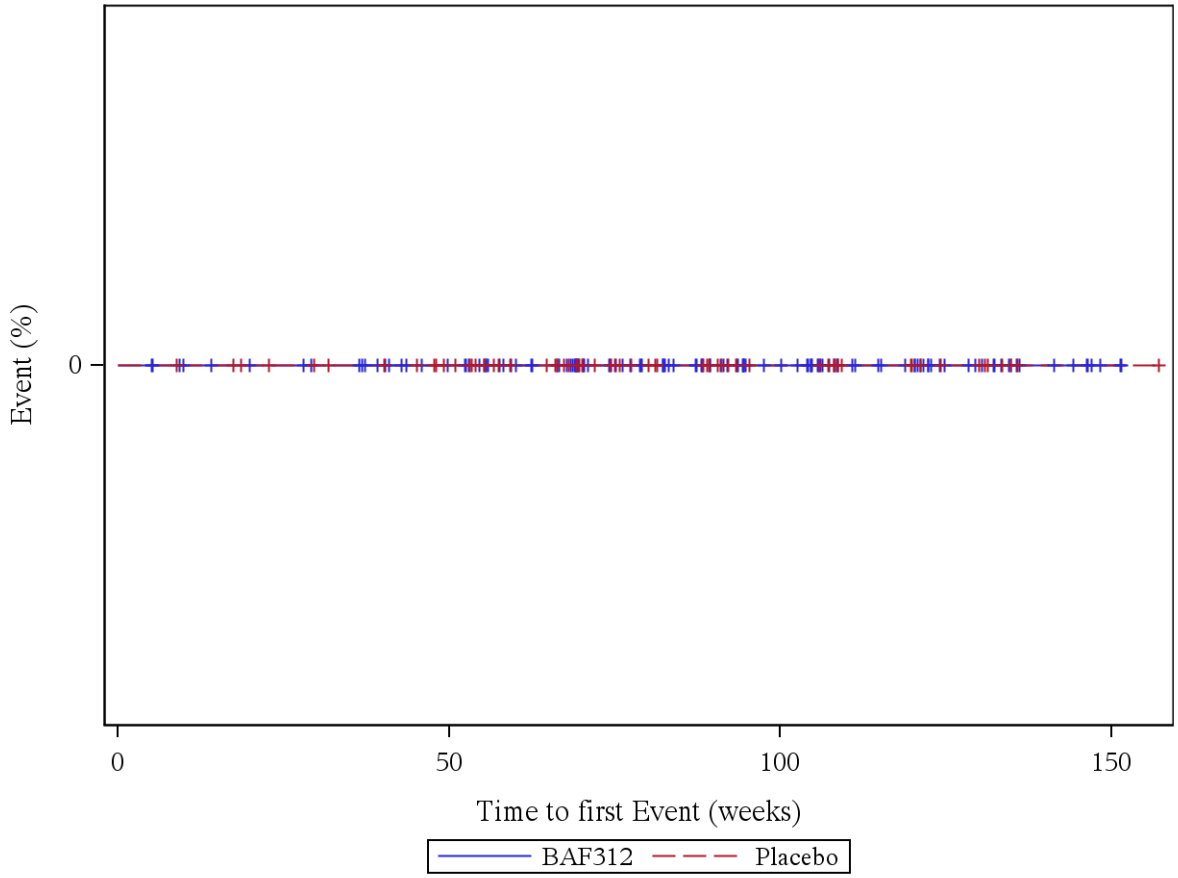


Patients at risk (BAF312/Placebo): Week 0: 127/61, Week 4: 127/61, Week 12: 123/60, Week 24: 121/57, Week 36: 119/55, Week 48: 110/51, Week 60: 99/41, Week 72: 80/32, Week 84: 66/25, Week 96: 49/17, Week 108: 36/15, Week 120: 28/9, Week 132: 15/4, Week 144: 7/1, Week 156: 0/1

Log rank test: p-value = -
*: p < 0,05

Analysis population: A2304 SAF subpopulation "ACTIVE MS WITHOUT RELAPSES"

Figure 12.1.6.44: Respiratory disorders (AESI, serious)

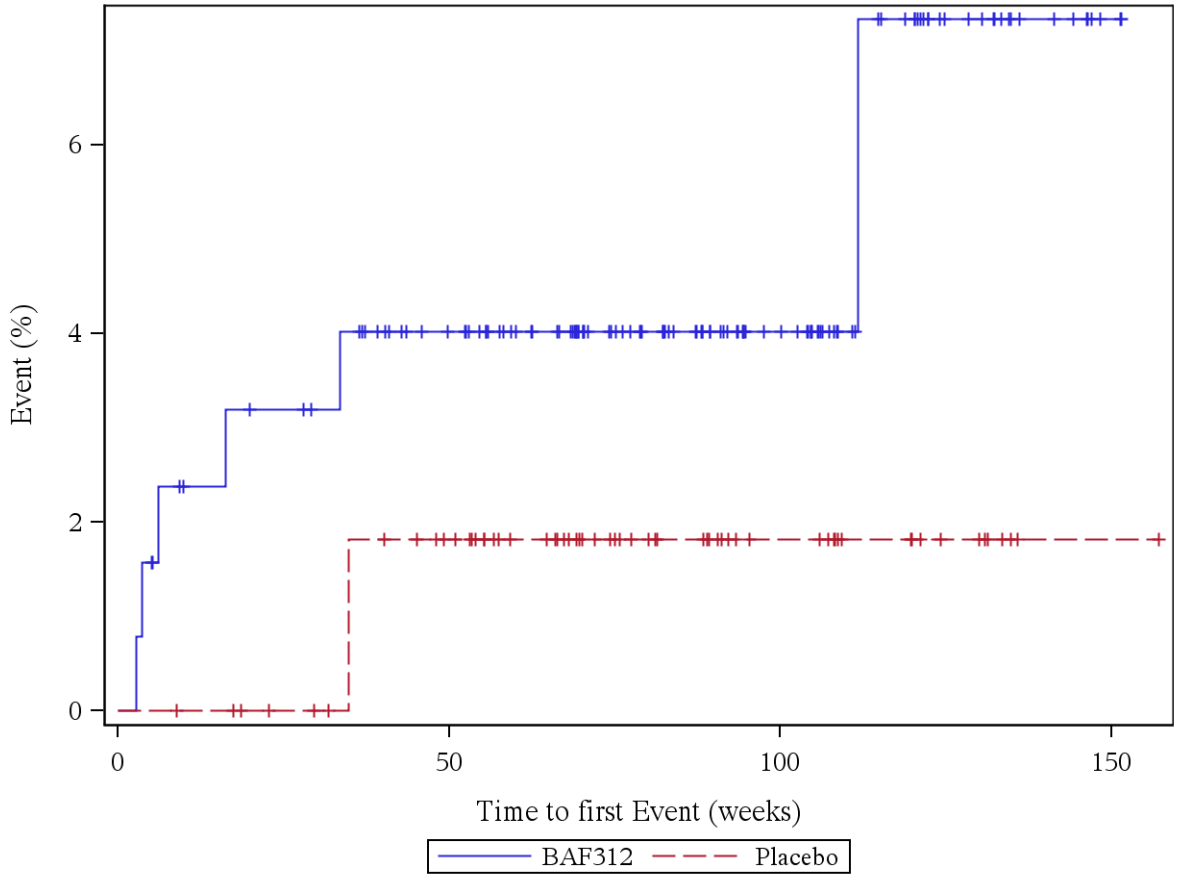


Patients at risk (BAF312/Placebo): Week 0: 127/61, Week 4: 127/61, Week 12: 123/60, Week 24: 121/57, Week 36: 119/55, Week 48: 110/51, Week 60: 99/41, Week 72: 80/32, Week 84: 66/25, Week 96: 49/17, Week 108: 36/15, Week 120: 28/9, Week 132: 15/4, Week 144: 7/1, Week 156: 0/1

Log rank test: p-value = -
*: p < 0,05

Analysis population: A2304 SAF subpopulation "ACTIVE MS WITHOUT RELAPSES"

Figure 12.1.6.45: Peripheral edema/swelling (AESI, all)

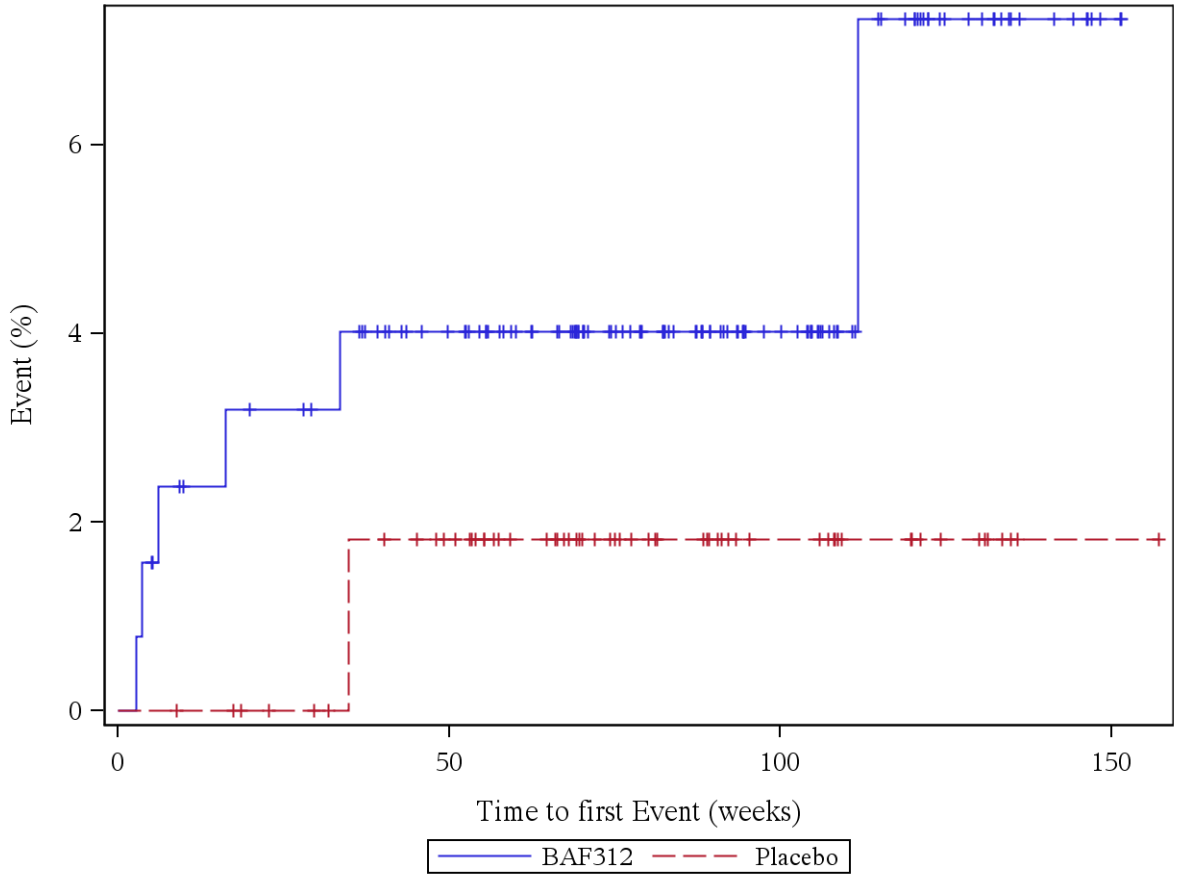


Patients at risk (BAF312/Placebo): Week 0: 127/61, Week 4: 125/61, Week 12: 120/60, Week 24: 118/57, Week 36: 115/54, Week 48: 106/51, Week 60: 95/41, Week 72: 78/32, Week 84: 64/25, Week 96: 47/17, Week 108: 34/15, Week 120: 25/9, Week 132: 14/4, Week 144: 7/1, Week 156: 0/1

Log rank test: p-value = 0,316
*: p < 0,05

Analysis population: A2304 SAF subpopulation "ACTIVE MS WITHOUT RELAPSES"

Figure 12.1.6.46: Peripheral edema/swelling (AESI, not severe)

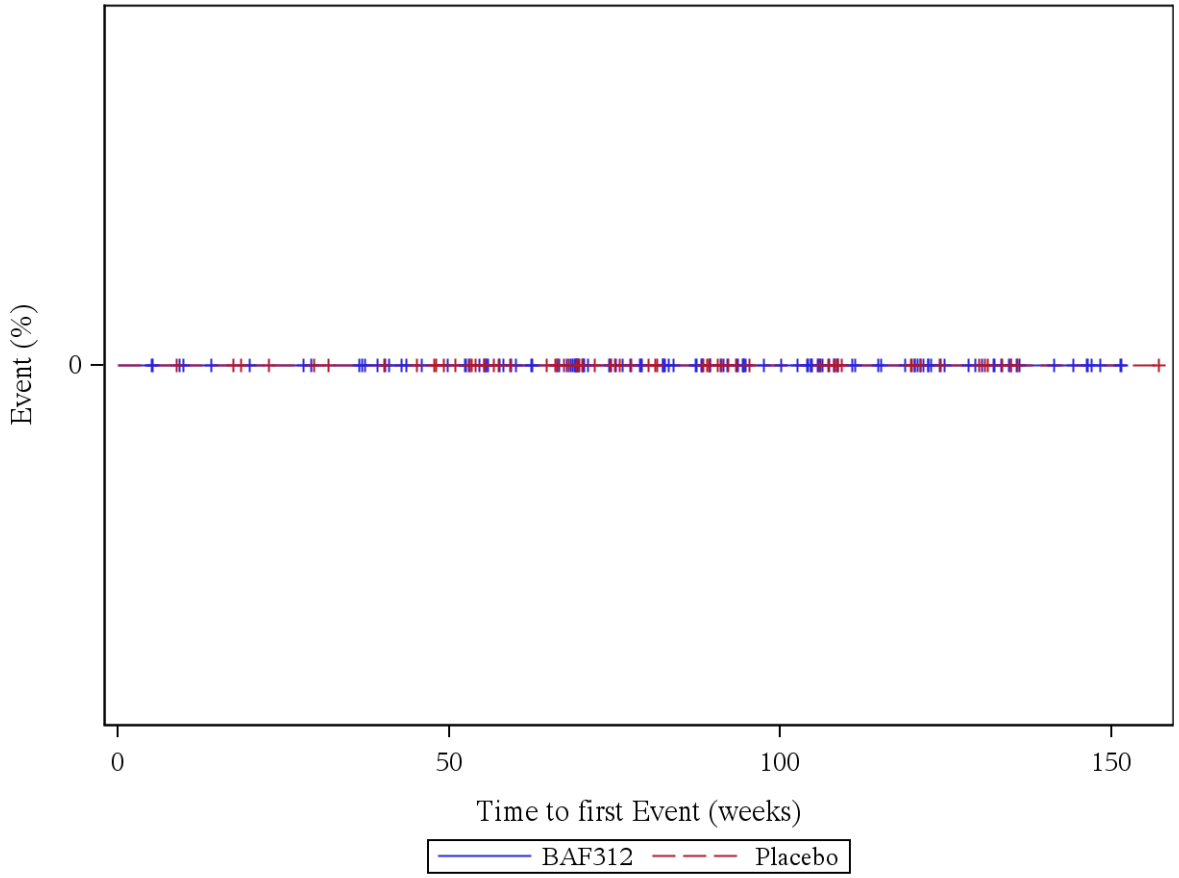


Patients at risk (BAF312/Placebo): Week 0: 127/61, Week 4: 125/61, Week 12: 120/60, Week 24: 118/57, Week 36: 115/54, Week 48: 106/51, Week 60: 95/41, Week 72: 78/32, Week 84: 64/25, Week 96: 47/17, Week 108: 34/15, Week 120: 25/9, Week 132: 14/4, Week 144: 7/1, Week 156: 0/1

Log rank test: p-value = 0,316
*: p < 0,05

Analysis population: A2304 SAF subpopulation "ACTIVE MS WITHOUT RELAPSES"

Figure 12.1.6.47: Peripheral edema/swelling (AESI, severe)

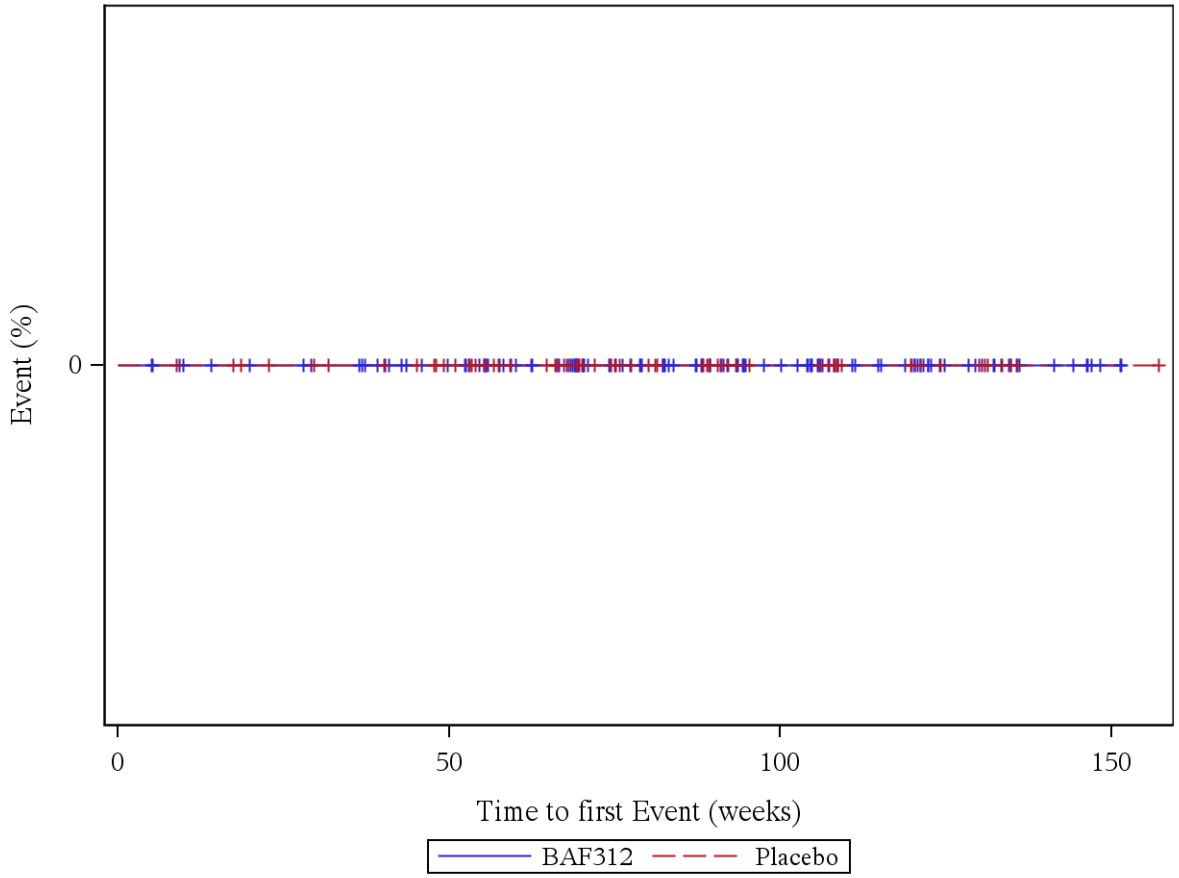


Patients at risk (BAF312/Placebo): Week 0: 127/61, Week 4: 127/61, Week 12: 123/60, Week 24: 121/57, Week 36: 119/55, Week 48: 110/51, Week 60: 99/41, Week 72: 80/32, Week 84: 66/25, Week 96: 49/17, Week 108: 36/15, Week 120: 28/9, Week 132: 15/4, Week 144: 7/1, Week 156: 0/1

Log rank test: p-value = -
*: p < 0,05

Analysis population: A2304 SAF subpopulation "ACTIVE MS WITHOUT RELAPSES"

Figure 12.1.6.48: Peripheral edema/swelling (AESI, serious)

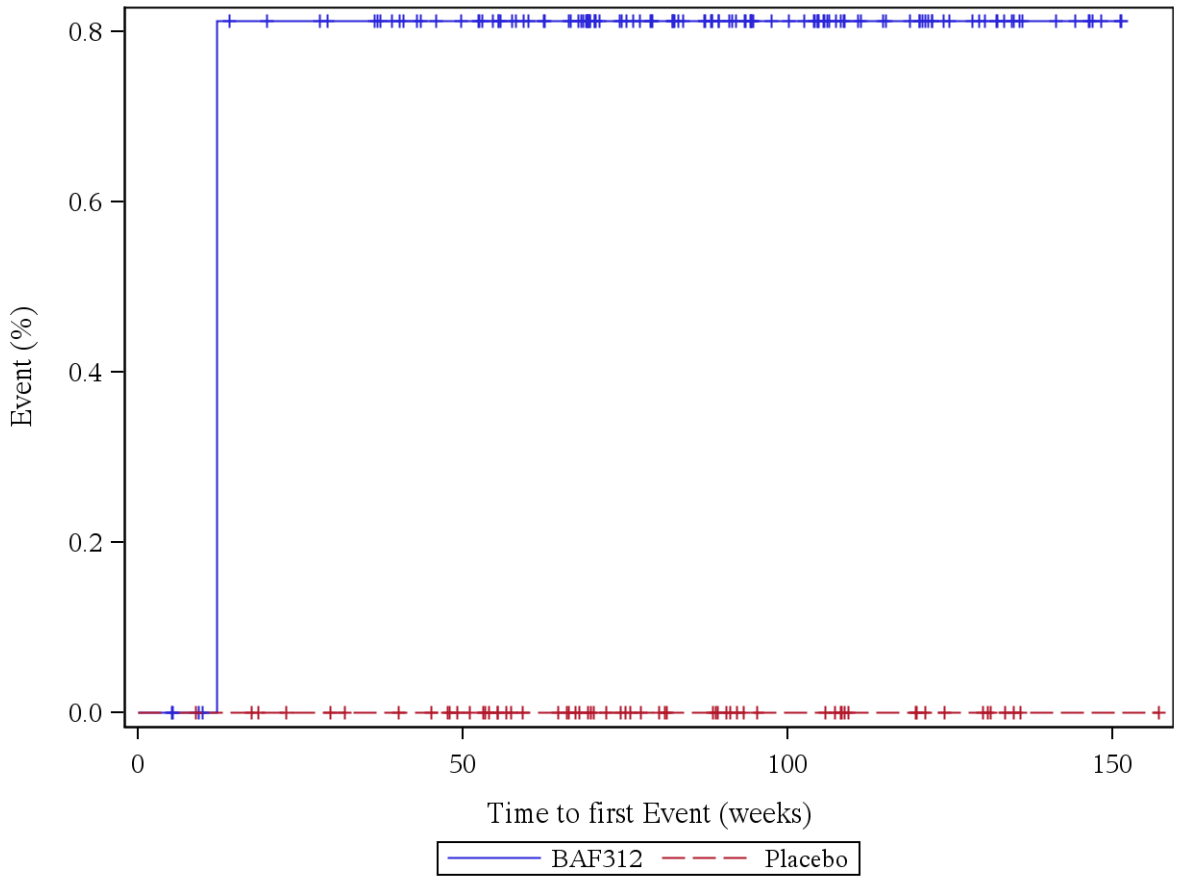


Patients at risk (BAF312/Placebo): Week 0: 127/61, Week 4: 127/61, Week 12: 123/60, Week 24: 121/57, Week 36: 119/55, Week 48: 110/51, Week 60: 99/41, Week 72: 80/32, Week 84: 66/25, Week 96: 49/17, Week 108: 36/15, Week 120: 28/9, Week 132: 15/4, Week 144: 7/1, Week 156: 0/1

Log rank test: p-value = -
*: p < 0,05

Analysis population: A2304 SAF subpopulation "ACTIVE MS WITHOUT RELAPSES"

Figure 12.1.6.49: Asthma/bronchospasm (AESI, all)

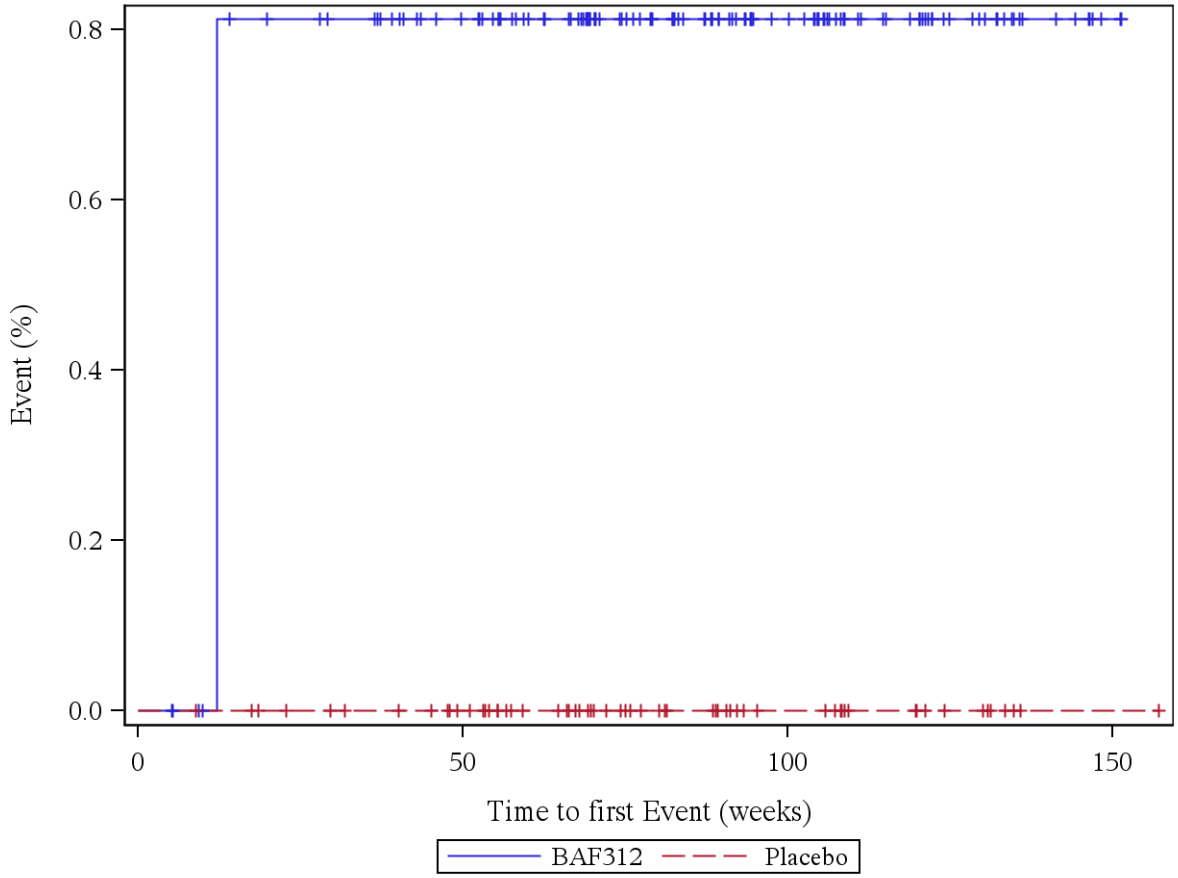


Patients at risk (BAF312/Placebo): Week 0: 127/61, Week 4: 127/61, Week 12: 123/60, Week 24: 120/57, Week 36: 118/55, Week 48: 109/51, Week 60: 98/41, Week 72: 79/32, Week 84: 65/25, Week 96: 48/17, Week 108: 35/15, Week 120: 27/9, Week 132: 15/4, Week 144: 7/1, Week 156: 0/1

Log rank test: p-value = -
*: p < 0,05

Analysis population: A2304 SAF subpopulation "ACTIVE MS WITHOUT RELAPSES"

Figure 12.1.6.50: Asthma/bronchospasm (AESI, not severe)

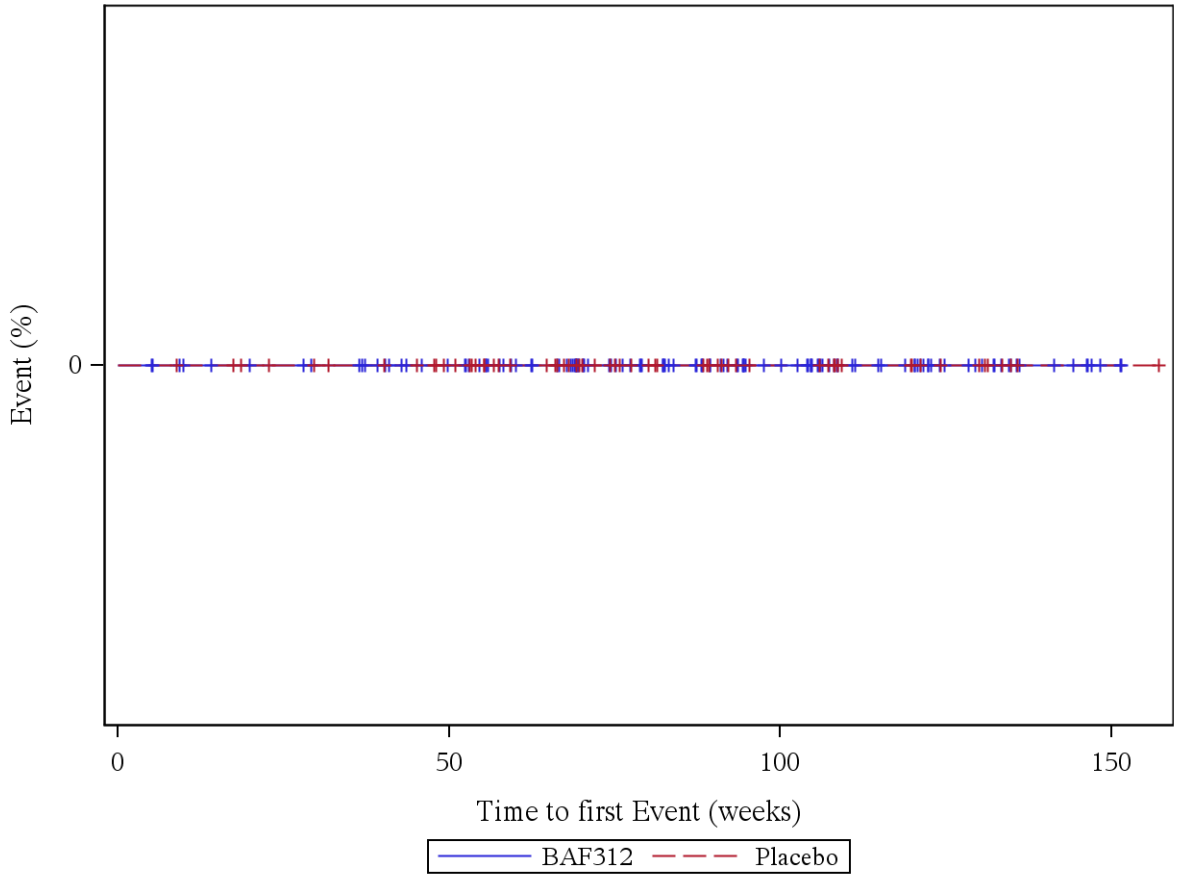


Patients at risk (BAF312/Placebo): Week 0: 127/61, Week 4: 127/61, Week 12: 123/60, Week 24: 120/57, Week 36: 118/55, Week 48: 109/51, Week 60: 98/41, Week 72: 79/32, Week 84: 65/25, Week 96: 48/17, Week 108: 35/15, Week 120: 27/9, Week 132: 15/4, Week 144: 7/1, Week 156: 0/1

Log rank test: p-value = -
*: p < 0,05

Analysis population: A2304 SAF subpopulation "ACTIVE MS WITHOUT RELAPSES"

Figure 12.1.6.51: Asthma/bronchospasm (AESI, severe)

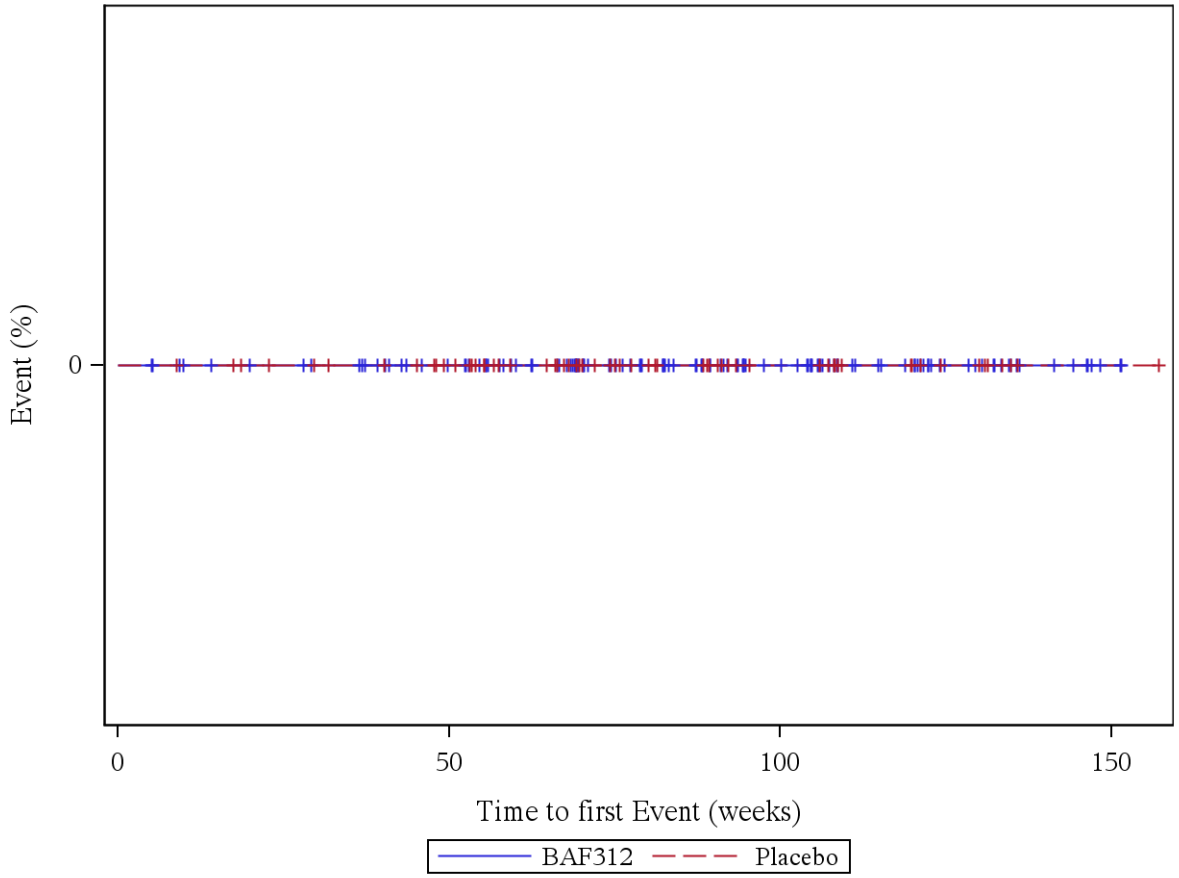


Patients at risk (BAF312/Placebo): Week 0: 127/61, Week 4: 127/61, Week 12: 123/60, Week 24: 121/57, Week 36: 119/55, Week 48: 110/51, Week 60: 99/41, Week 72: 80/32, Week 84: 66/25, Week 96: 49/17, Week 108: 36/15, Week 120: 28/9, Week 132: 15/4, Week 144: 7/1, Week 156: 0/1

Log rank test: p-value = -
*: p < 0,05

Analysis population: A2304 SAF subpopulation "ACTIVE MS WITHOUT RELAPSES"

Figure 12.1.6.52: Asthma/bronchospasm (AESI, serious)

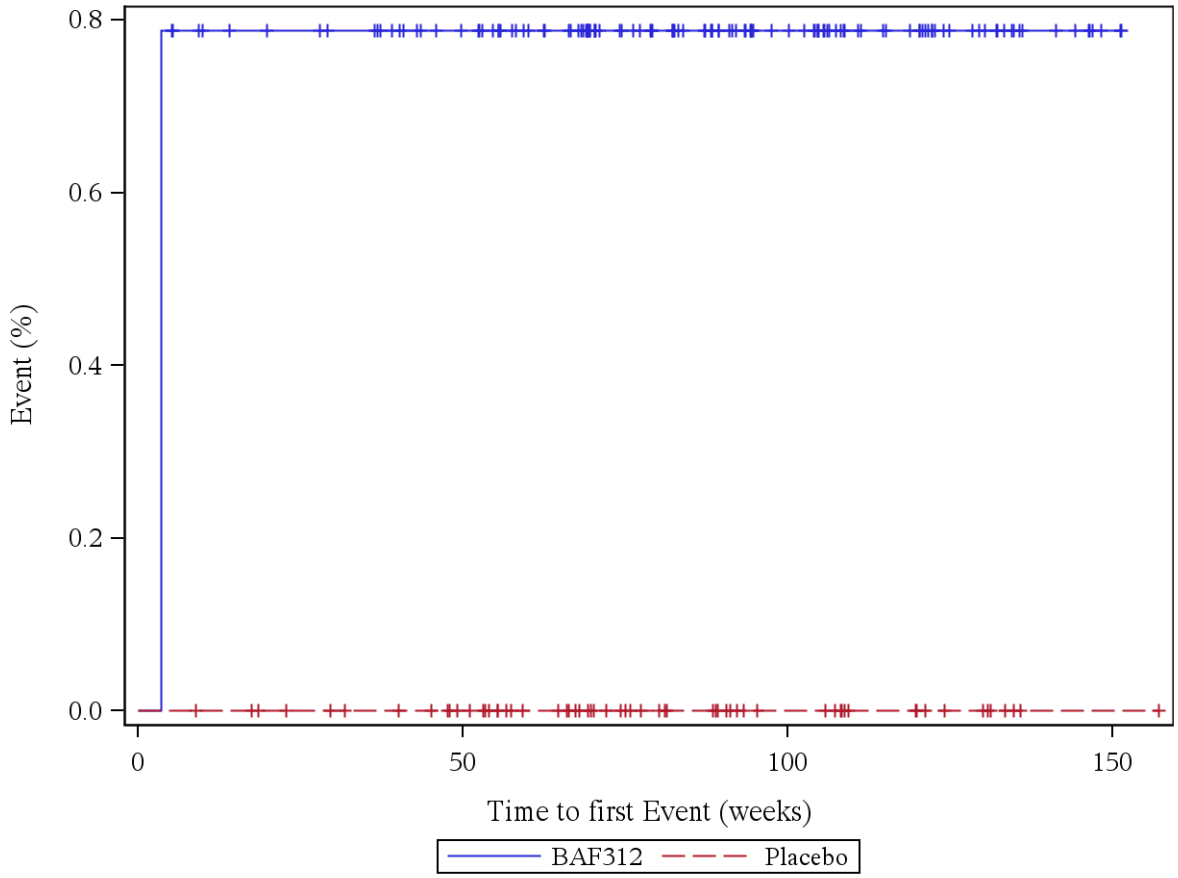


Patients at risk (BAF312/Placebo): Week 0: 127/61, Week 4: 127/61, Week 12: 123/60, Week 24: 121/57, Week 36: 119/55, Week 48: 110/51, Week 60: 99/41, Week 72: 80/32, Week 84: 66/25, Week 96: 49/17, Week 108: 36/15, Week 120: 28/9, Week 132: 15/4, Week 144: 7/1, Week 156: 0/1

Log rank test: p-value = -
*: p < 0,05

Analysis population: A2304 SAF subpopulation "ACTIVE MS WITHOUT RELAPSES"

Figure 12.1.6.53: Pregnancy and neonatal topics (AESI, all)

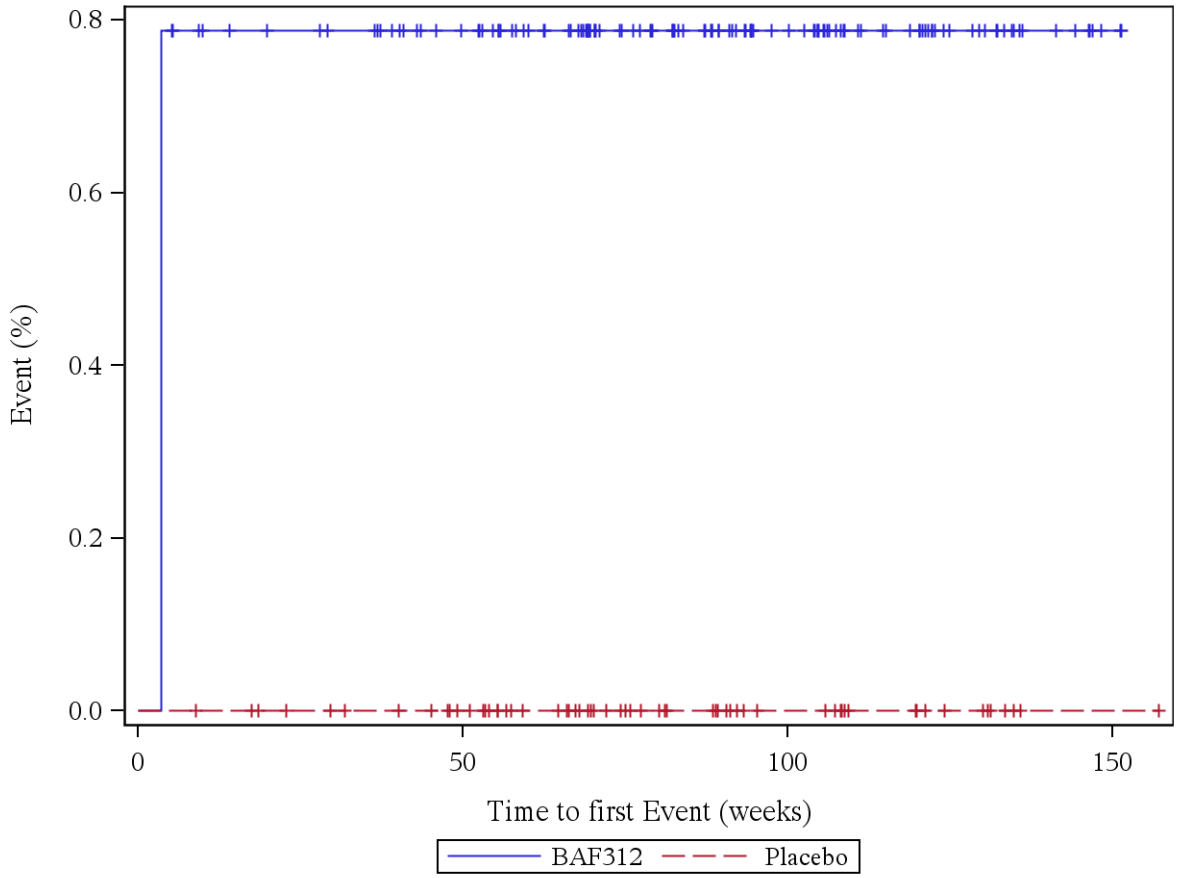


Patients at risk (BAF312/Placebo): Week 0: 127/61, Week 4: 126/61, Week 12: 122/60, Week 24: 120/57, Week 36: 118/55, Week 48: 109/51, Week 60: 98/41, Week 72: 79/32, Week 84: 66/25, Week 96: 49/17, Week 108: 36/15, Week 120: 28/9, Week 132: 15/4, Week 144: 7/1, Week 156: 0/1

Log rank test: p-value = -
*: p < 0,05

Analysis population: A2304 SAF subpopulation "ACTIVE MS WITHOUT RELAPSES"

Figure 12.1.6.54: Pregnancy and neonatal topics (AESI, not severe)

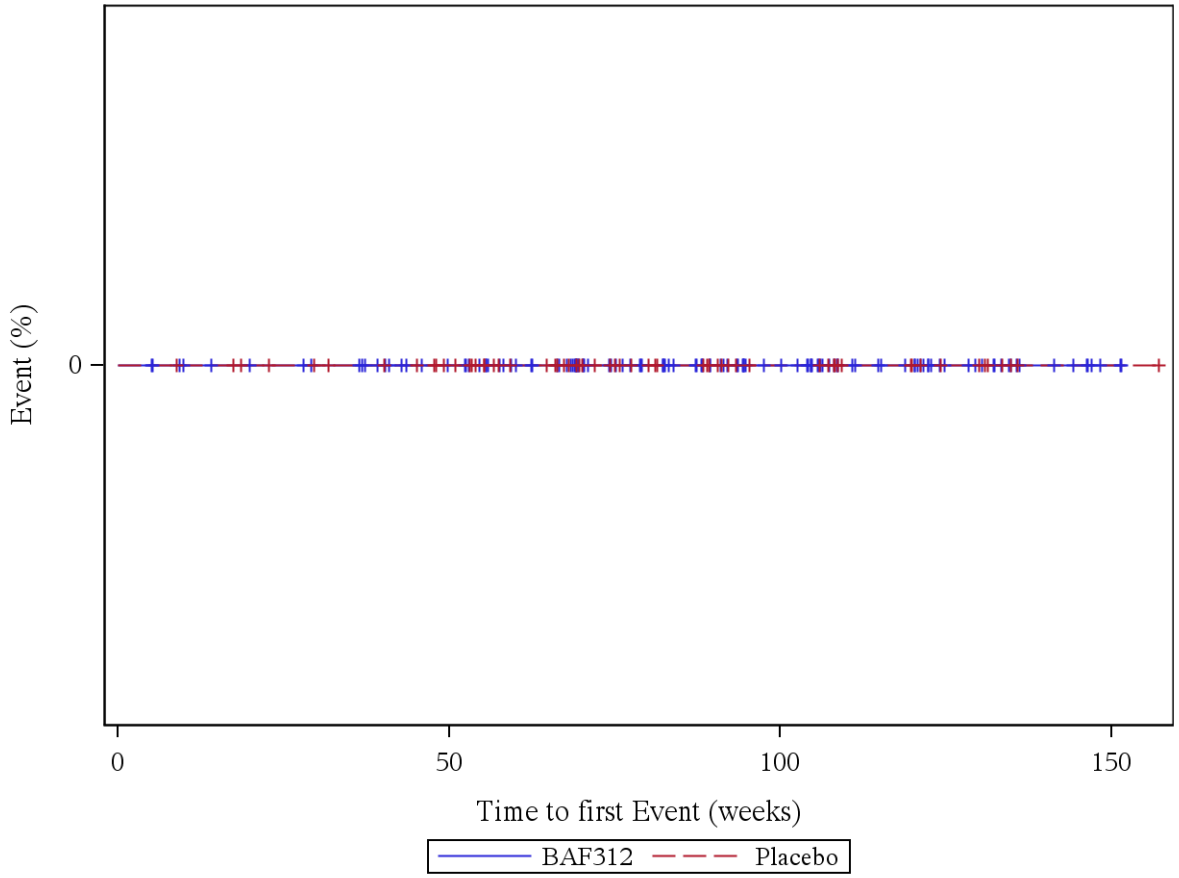


Patients at risk (BAF312/Placebo): Week 0: 127/61, Week 4: 126/61, Week 12: 122/60, Week 24: 120/57, Week 36: 118/55, Week 48: 109/51, Week 60: 98/41, Week 72: 79/32, Week 84: 66/25, Week 96: 49/17, Week 108: 36/15, Week 120: 28/9, Week 132: 15/4, Week 144: 7/1, Week 156: 0/1

Log rank test: p-value = -
*: p < 0,05

Analysis population: A2304 SAF subpopulation "ACTIVE MS WITHOUT RELAPSES"

Figure 12.1.6.55: Pregnancy and neonatal topics (AESI, severe)

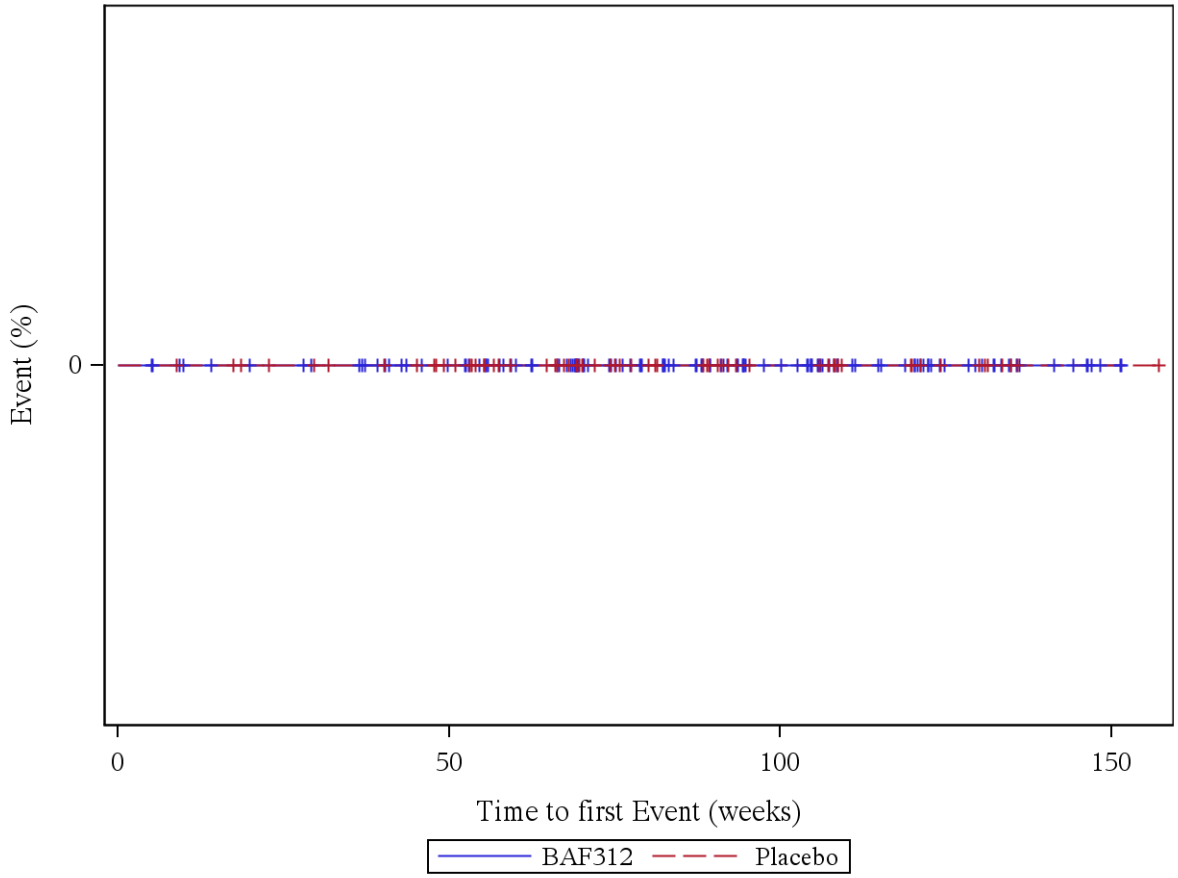


Patients at risk (BAF312/Placebo): Week 0: 127/61, Week 4: 127/61, Week 12: 123/60, Week 24: 121/57, Week 36: 119/55, Week 48: 110/51, Week 60: 99/41, Week 72: 80/32, Week 84: 66/25, Week 96: 49/17, Week 108: 36/15, Week 120: 28/9, Week 132: 15/4, Week 144: 7/1, Week 156: 0/1

Log rank test: p-value = -
*: p < 0,05

Analysis population: A2304 SAF subpopulation "ACTIVE MS WITHOUT RELAPSES"

Figure 12.1.6.56: Pregnancy and neonatal topics (AESI, serious)

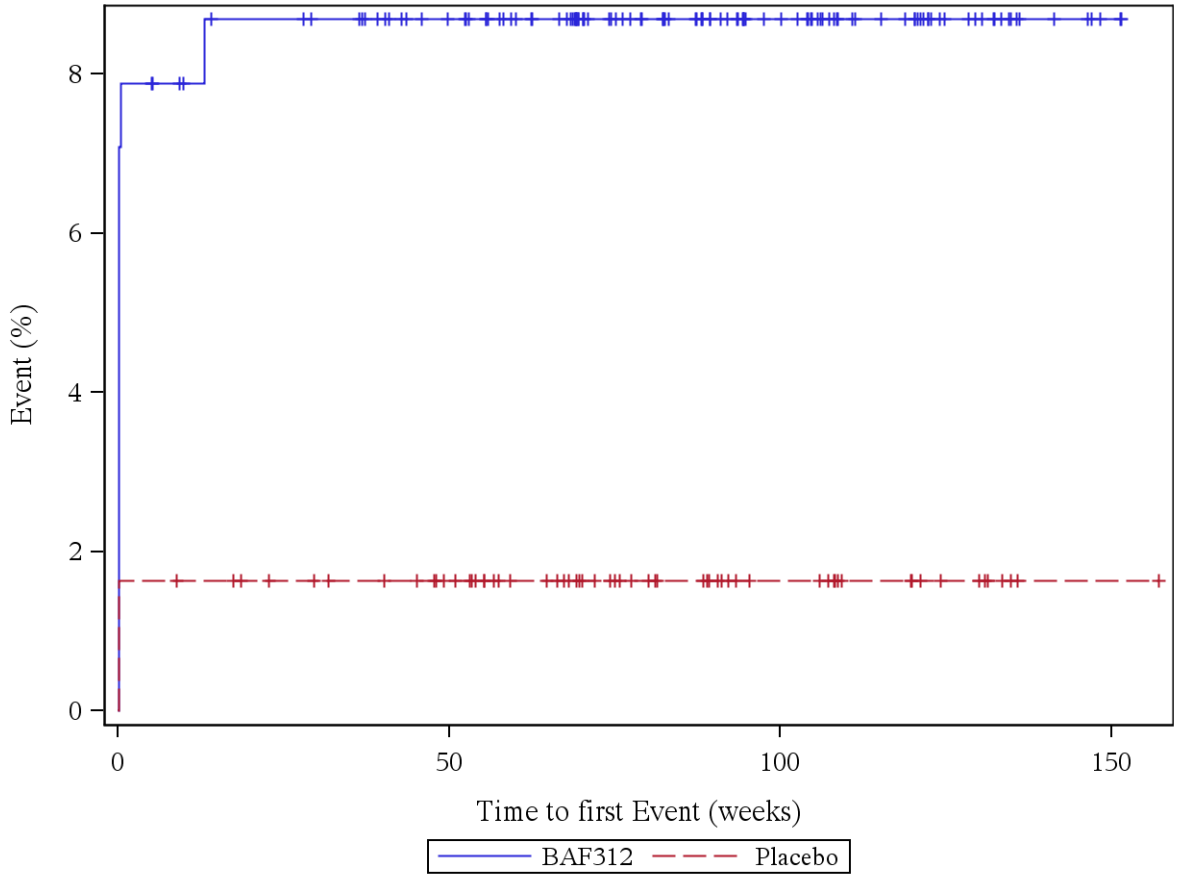


Patients at risk (BAF312/Placebo): Week 0: 127/61, Week 4: 127/61, Week 12: 123/60, Week 24: 121/57, Week 36: 119/55, Week 48: 110/51, Week 60: 99/41, Week 72: 80/32, Week 84: 66/25, Week 96: 49/17, Week 108: 36/15, Week 120: 28/9, Week 132: 15/4, Week 144: 7/1, Week 156: 0/1

Log rank test: p-value = -
*: p < 0,05

Analysis population: A2304 SAF subpopulation "ACTIVE MS WITHOUT RELAPSES"

Figure 12.1.6.57: Bradyarrhythmias and bradycardia (AESI, all)

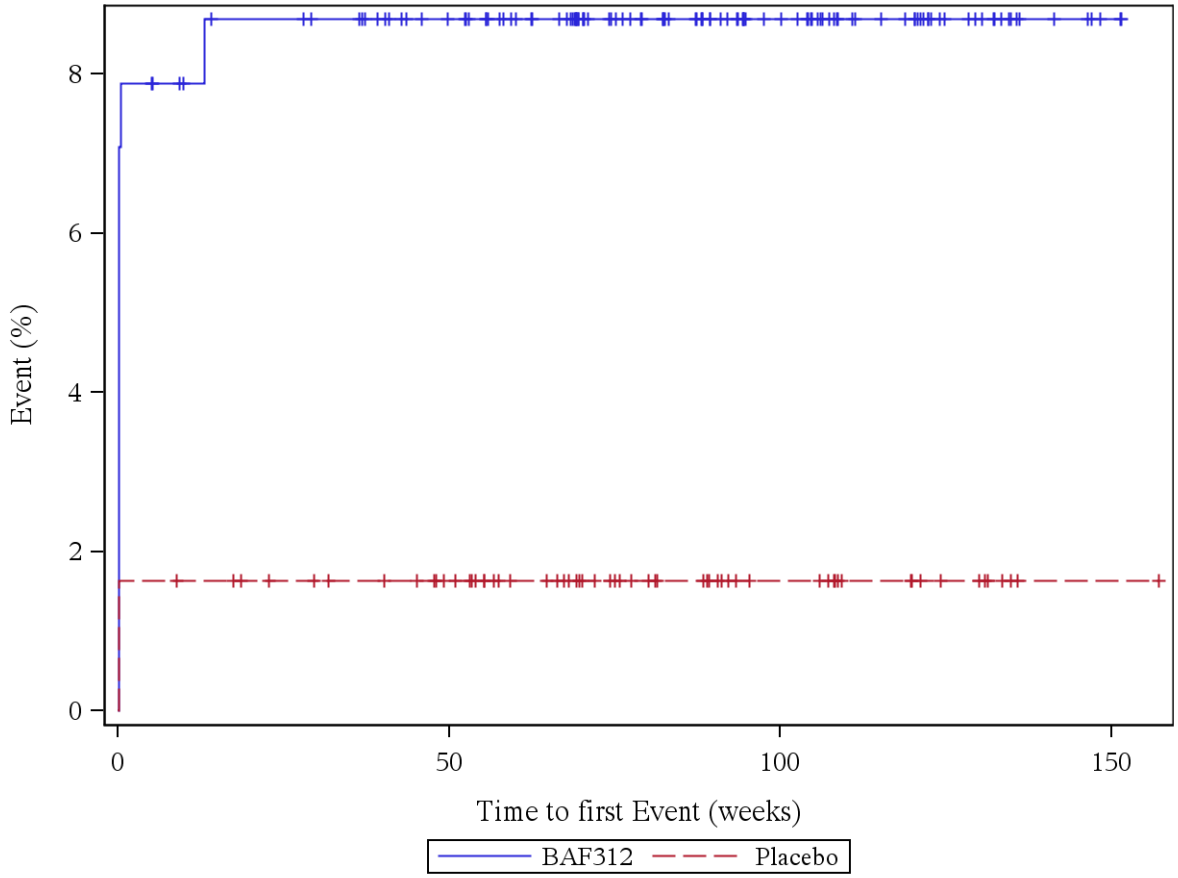


Patients at risk (BAF312/Placebo): Week 0: 127/61, Week 4: 117/60, Week 12: 113/59, Week 24: 111/56, Week 36: 109/54, Week 48: 100/50, Week 60: 90/40, Week 72: 72/32, Week 84: 60/25, Week 96: 44/17, Week 108: 33/15, Week 120: 26/9, Week 132: 13/4, Week 144: 5/1, Week 156: 0/1

Log rank test: p-value = 0,066
*: p < 0,05

Analysis population: A2304 SAF subpopulation "ACTIVE MS WITHOUT RELAPSES"

Figure 12.1.6.58: Bradyarrhythmias and bradycardia (AESI, not severe)

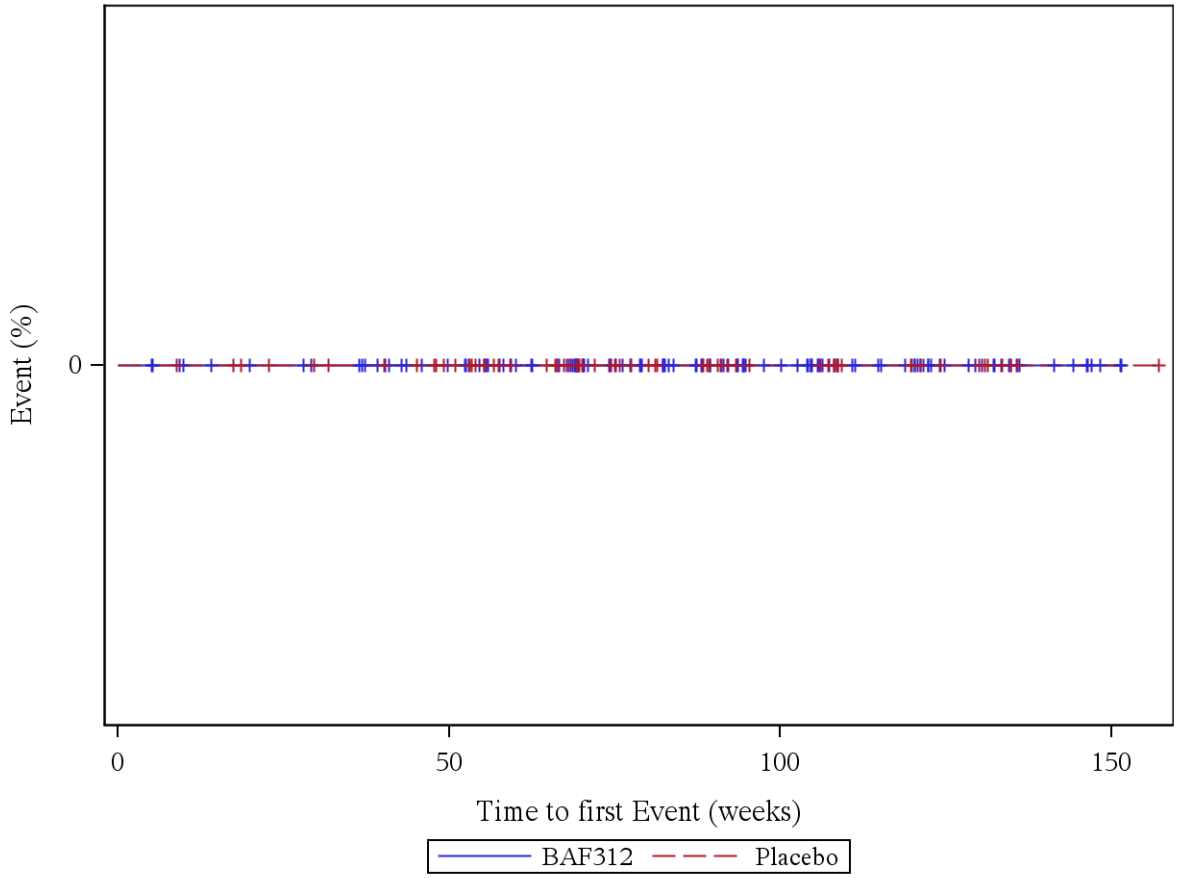


Patients at risk (BAF312/Placebo): Week 0: 127/61, Week 4: 117/60, Week 12: 113/59, Week 24: 111/56, Week 36: 109/54, Week 48: 100/50, Week 60: 90/40, Week 72: 72/32, Week 84: 60/25, Week 96: 44/17, Week 108: 33/15, Week 120: 26/9, Week 132: 13/4, Week 144: 5/1, Week 156: 0/1

Log rank test: p-value = 0,066
*: p < 0,05

Analysis population: A2304 SAF subpopulation "ACTIVE MS WITHOUT RELAPSES"

Figure 12.1.6.59: Bradyarrhythmias and bradycardia (AESI, severe)

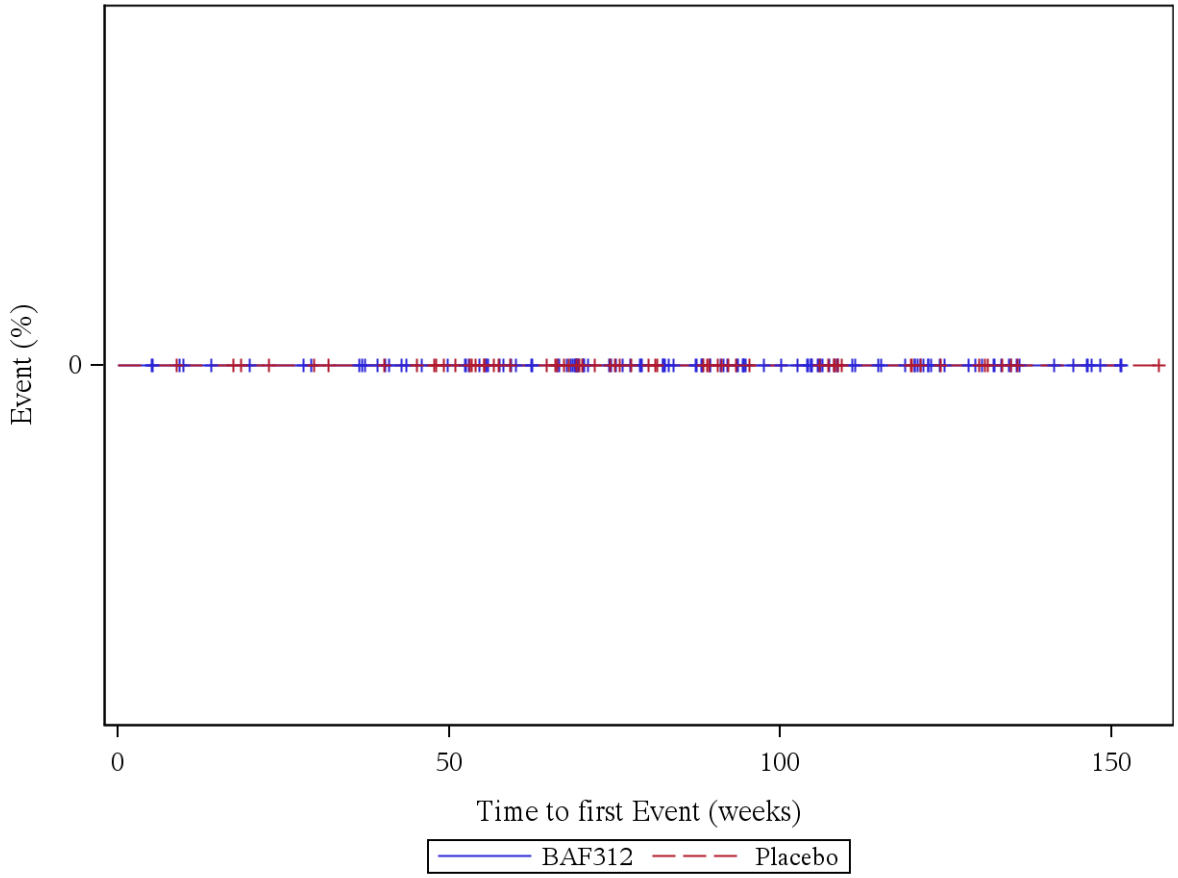


Patients at risk (BAF312/Placebo): Week 0: 127/61, Week 4: 127/61, Week 12: 123/60, Week 24: 121/57, Week 36: 119/55, Week 48: 110/51, Week 60: 99/41, Week 72: 80/32, Week 84: 66/25, Week 96: 49/17, Week 108: 36/15, Week 120: 28/9, Week 132: 15/4, Week 144: 7/1, Week 156: 0/1

Log rank test: p-value = -
*: p < 0,05

Analysis population: A2304 SAF subpopulation "ACTIVE MS WITHOUT RELAPSES"

Figure 12.1.6.60: Bradyarrhythmias and bradycardia (AESI, serious)



Patients at risk (BAF312/Placebo): Week 0: 127/61, Week 4: 127/61, Week 12: 123/60, Week 24: 121/57, Week 36: 119/55, Week 48: 110/51, Week 60: 99/41, Week 72: 80/32, Week 84: 66/25, Week 96: 49/17, Week 108: 36/15, Week 120: 28/9, Week 132: 15/4, Week 144: 7/1, Week 156: 0/1

Log rank test: p-value = -
*: p < 0,05

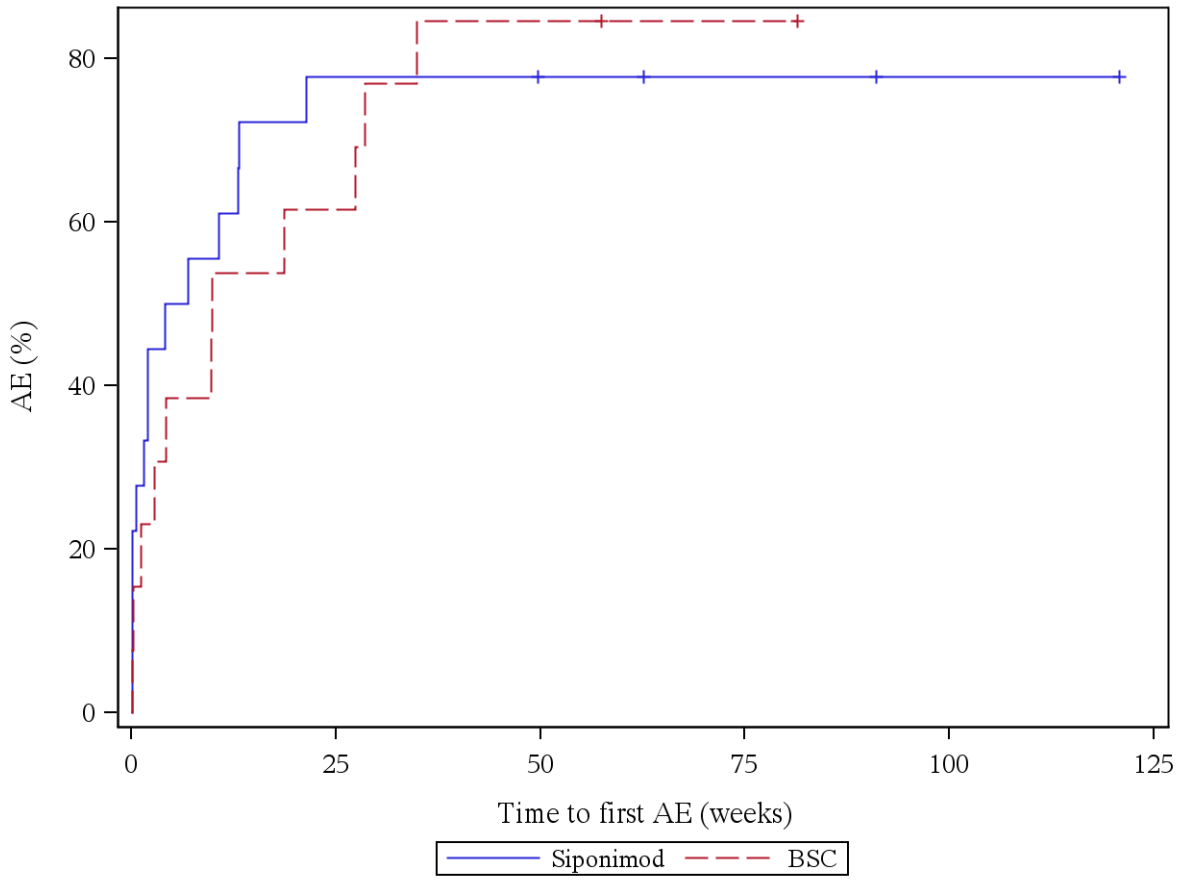
Analysis population: A2304 SAF subpopulation "ACTIVE MS WITHOUT RELAPSES"

12.2 Subgroup: Age

12.2.1: Time to First Adverse Event (SAF) by Age

12.2.1.1: Any AE

Figure 12.2.1.1.1: AE, Age = 18-40 years

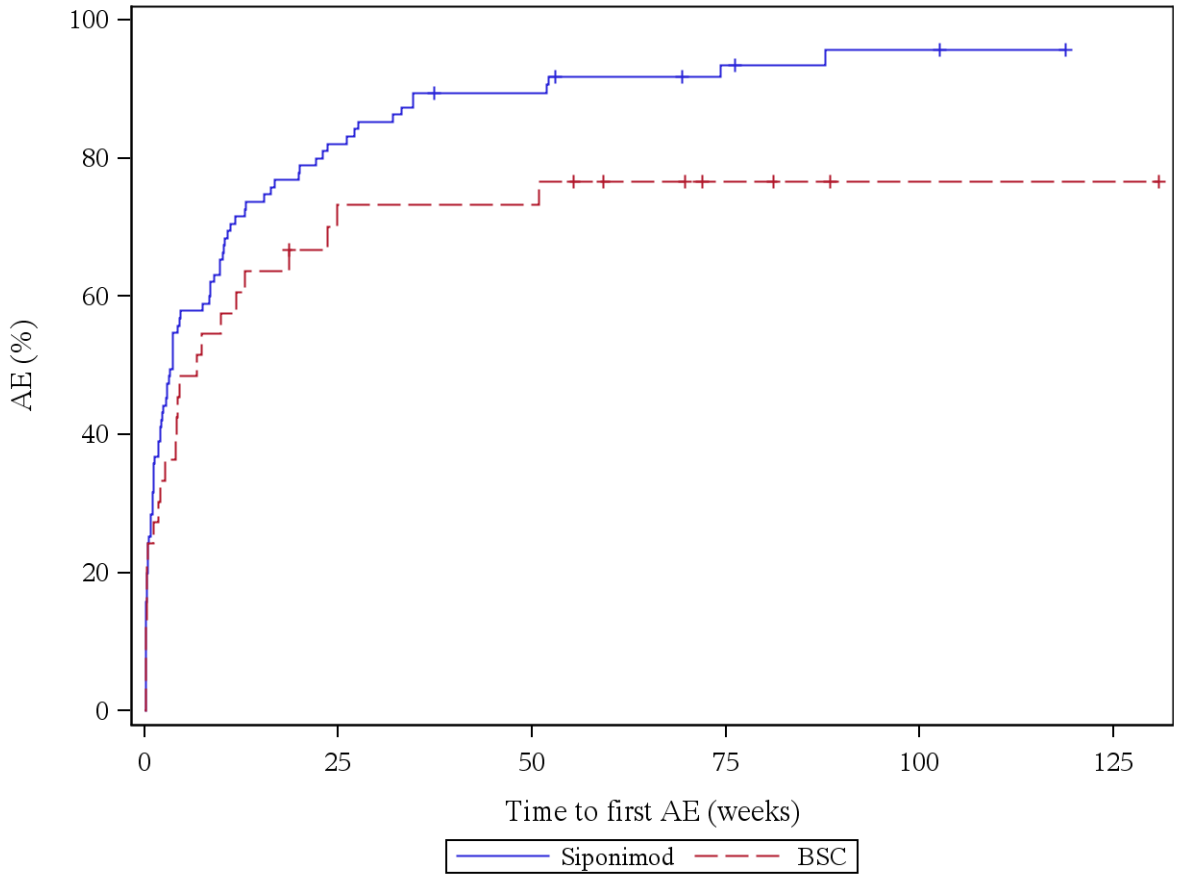


Patients at risk (Siponimod/BSC): Week 0: 18/13, Week 4: 10/9, Week 12: 7/6, Week 24: 4/5, Week 36: 4/2, Week 48: 4/2, Week 60: 3/1, Week 72: 2/1, Week 84: 2/0, Week 96: 1/0, Week 108: 1/0, Week 120: 1/0, Week 132: 0/0

Log rank test: p-value = 0,797
*: p < 0,05

Analysis population: A2304 SAF subpopulation "ACTIVE MS WITHOUT RELAPSES"

Figure 12.2.1.1.2: AE, Age = 41-55 years

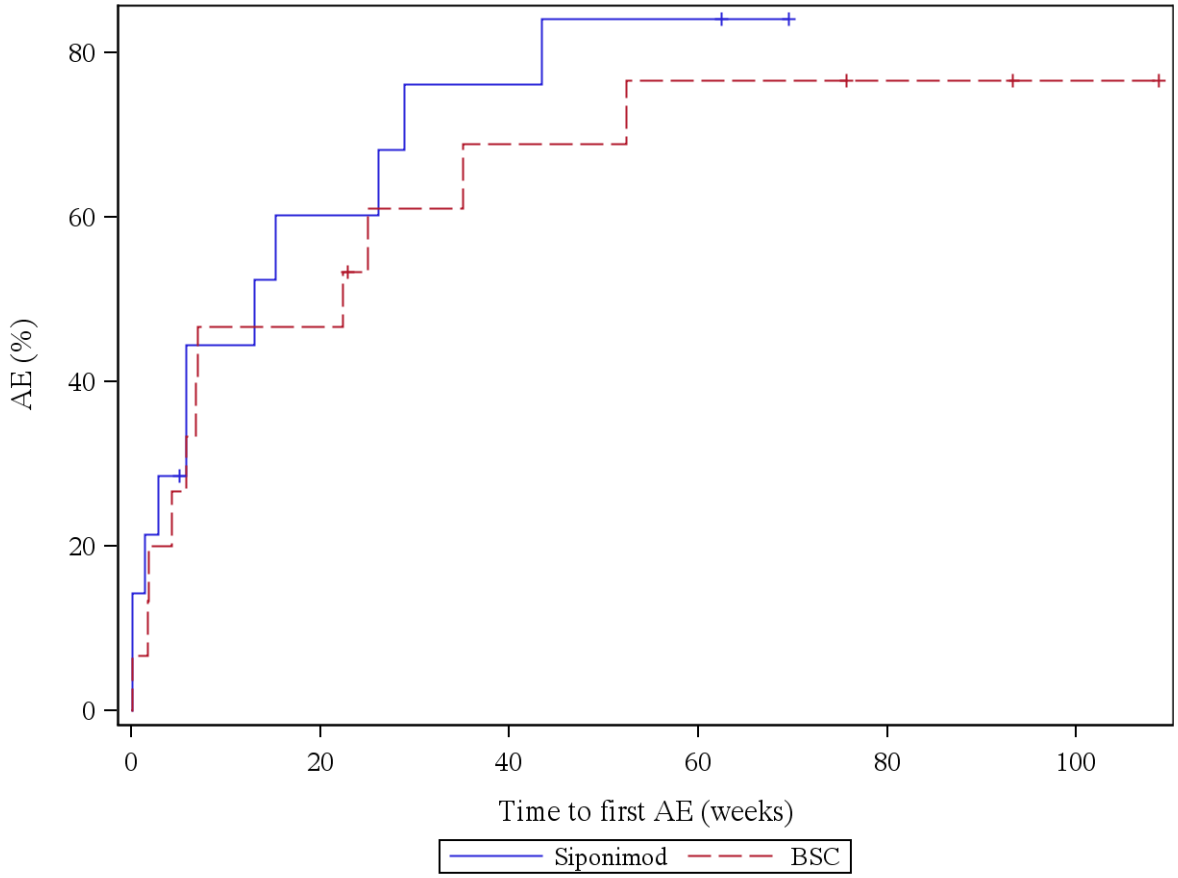


Patients at risk (Siponimod/BSC): Week 0: 95/33, Week 4: 43/20, Week 12: 27/13, Week 24: 17/9, Week 36: 10/8, Week 48: 9/8, Week 60: 6/5, Week 72: 5/3, Week 84: 3/2, Week 96: 2/1, Week 108: 1/1, Week 120: 0/1

Log rank test: p-value = 0,057
*: p < 0,05

Analysis population: A2304 SAF subpopulation "ACTIVE MS WITHOUT RELAPSES"

Figure 12.2.1.1.3: AE, Age = >55 years



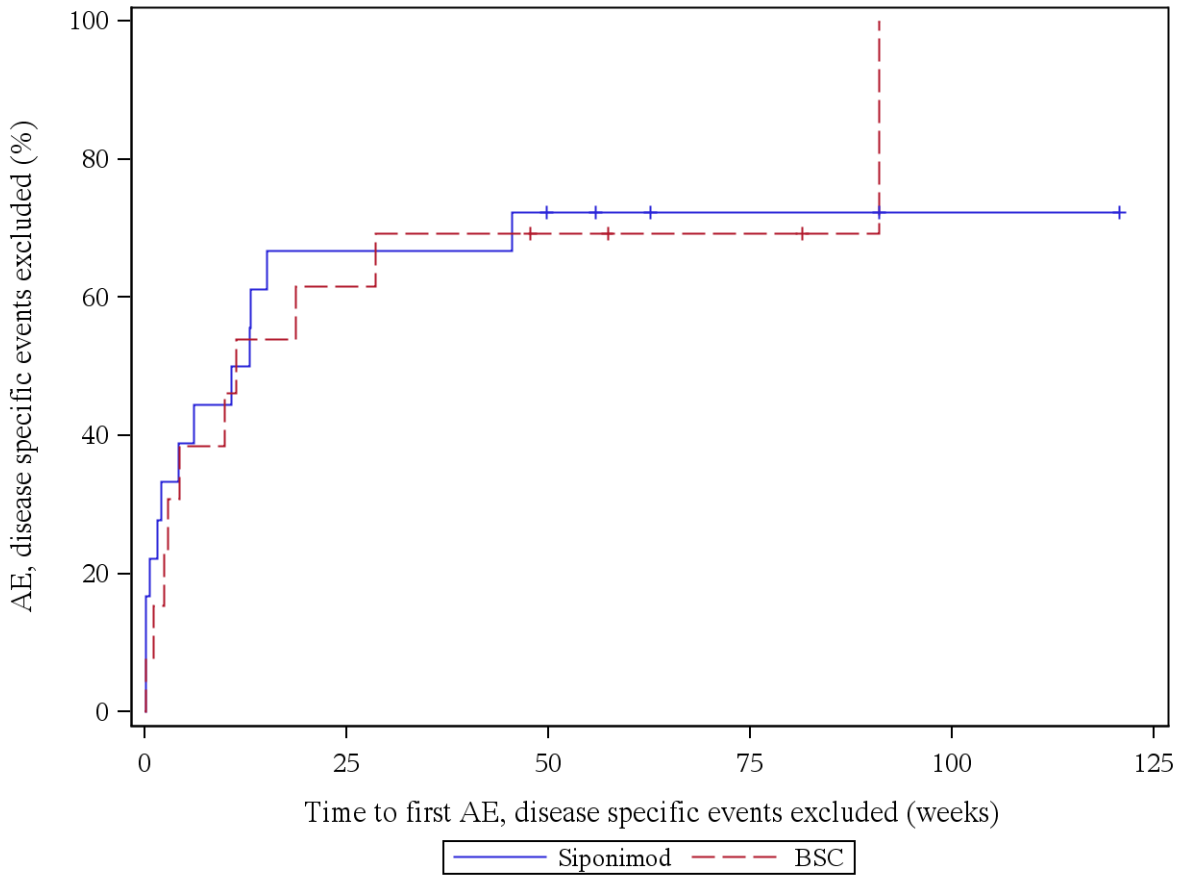
Patients at risk (Siponimod/BSC): Week 0: 14/15, Week 4: 10/12, Week 12: 7/8, Week 24: 5/6, Week 36: 3/4, Week 48: 2/4, Week 60: 2/3, Week 72: 0/3

Log rank test: p-value = 0,588
*: p < 0,05

Analysis population: A2304 SAF subpopulation "ACTIVE MS WITHOUT RELAPSES"

12.2.1.2: Any AE, disease specific events excluded

Figure 12.2.1.2.1: AE, disease specific events excluded, Age = 18-40 years

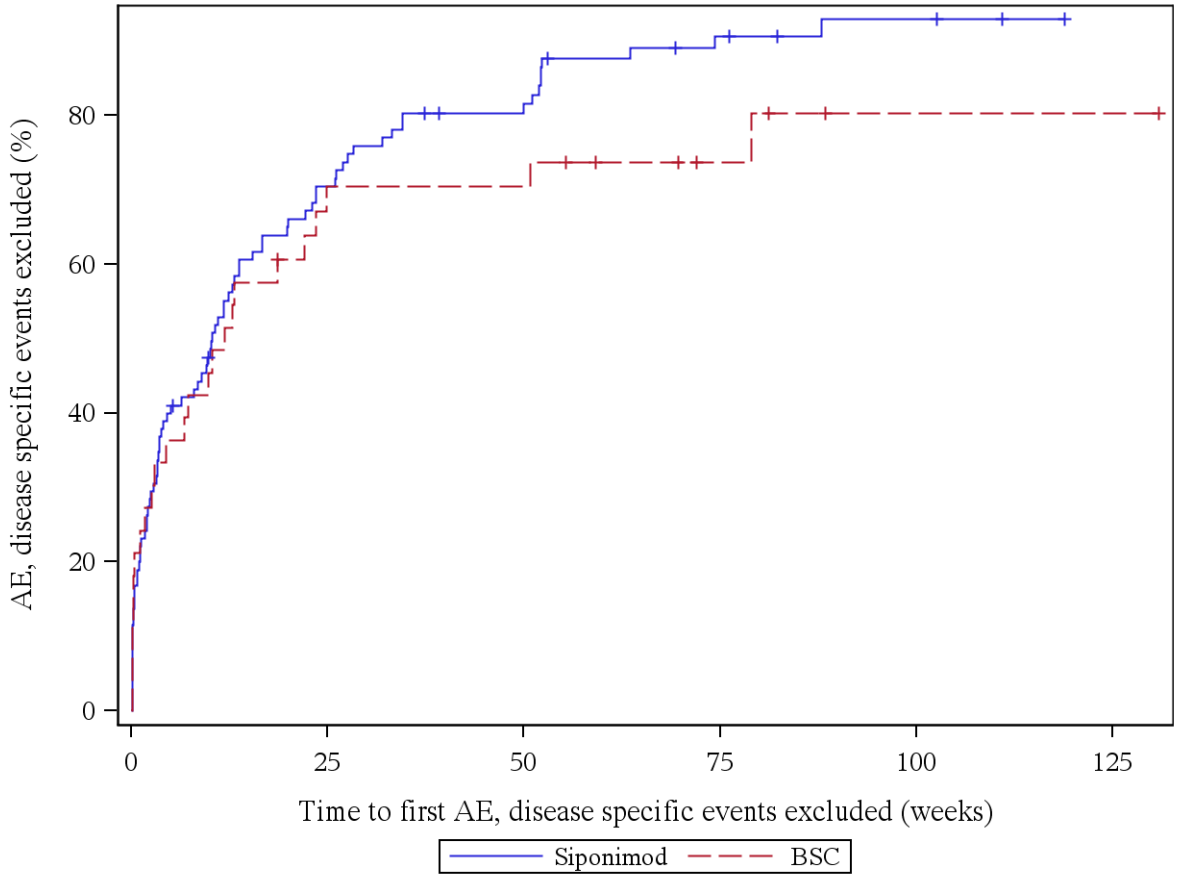


Patients at risk (Siponimod/BSC): Week 0: 18/13, Week 4: 12/9, Week 12: 9/6, Week 24: 6/5, Week 36: 6/4, Week 48: 5/3, Week 60: 3/2, Week 72: 2/2, Week 84: 2/1, Week 96: 1/0, Week 108: 1/0, Week 120: 1/0, Week 132: 0/0

Log rank test: p-value = 0,995
*: p < 0,05

Analysis population: A2304 SAF subpopulation "ACTIVE MS WITHOUT RELAPSES"

Figure 12.2.1.2.2: AE, disease specific events excluded, Age = 41-55 years

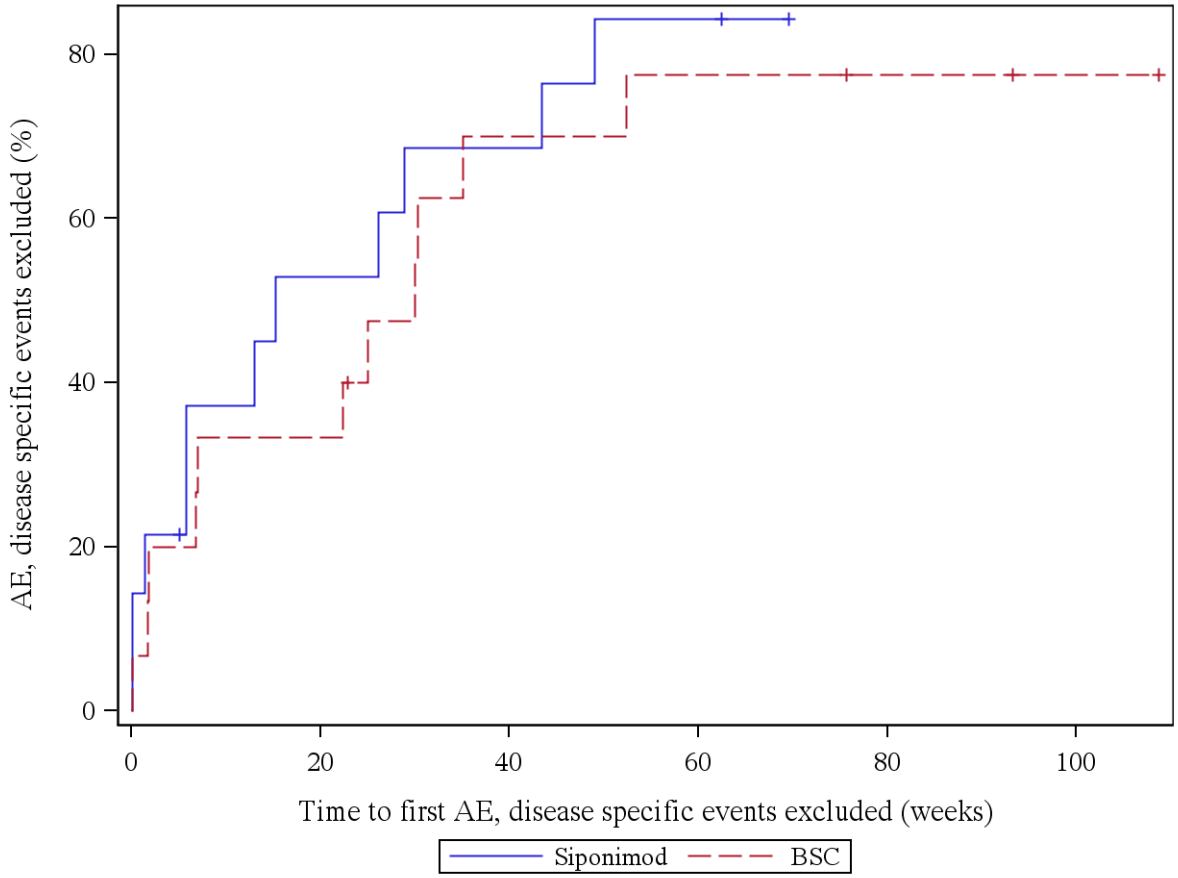


Patients at risk (Siponimod/BSC): Week 0: 95/33, Week 4: 58/22, Week 12: 41/16, Week 24: 27/10, Week 36: 18/9, Week 48: 16/9, Week 60: 9/6, Week 72: 7/4, Week 84: 4/2, Week 96: 3/1, Week 108: 2/1, Week 120: 0/1

Log rank test: p-value = 0,249
*: p < 0,05

Analysis population: A2304 SAF subpopulation "ACTIVE MS WITHOUT RELAPSES"

Figure 12.2.1.2.3: AE, disease specific events excluded, Age = >55 years



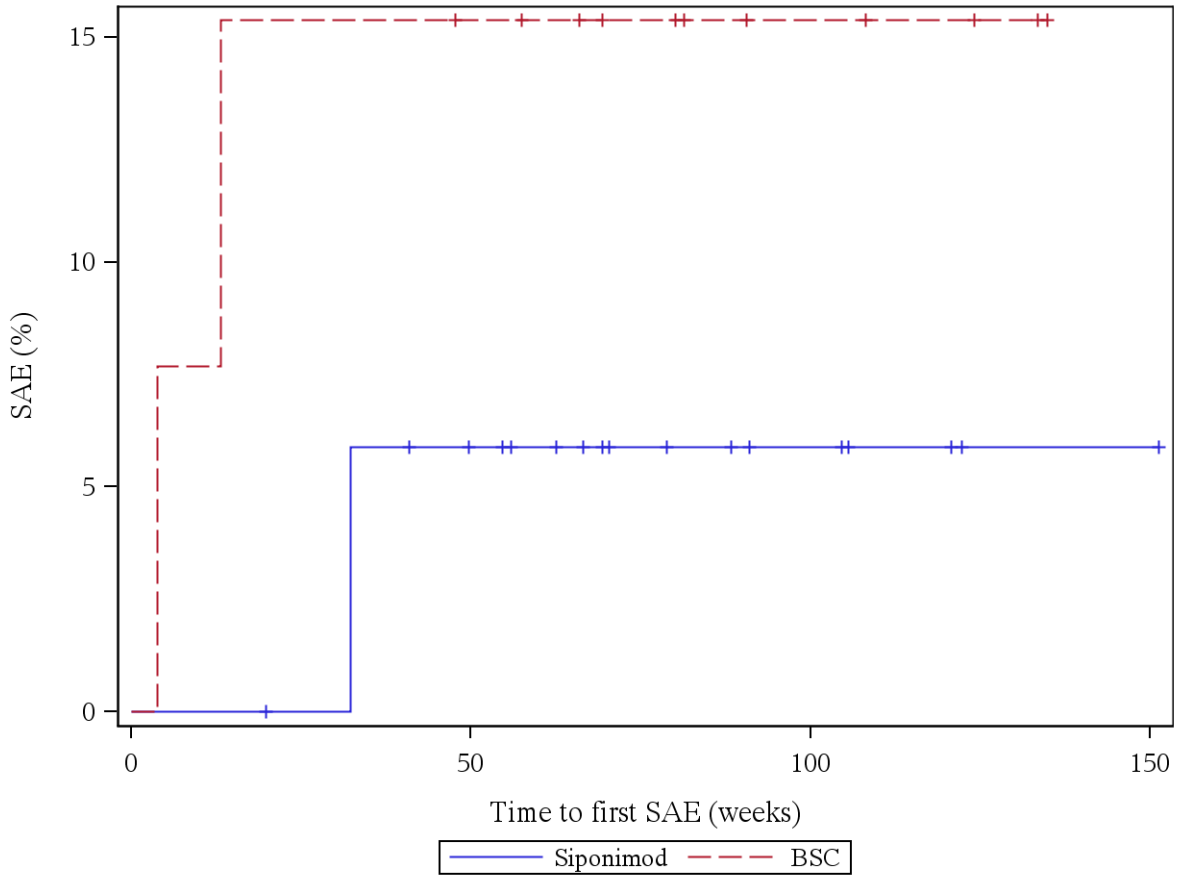
Patients at risk (Siponimod/BSC): Week 0: 14/15, Week 4: 11/12, Week 12: 8/10, Week 24: 6/8, Week 36: 4/4, Week 48: 3/4, Week 60: 2/3, Week 72: 0/3

Log rank test: p-value = 0,527
*: p < 0,05

Analysis population: A2304 SAF subpopulation "ACTIVE MS WITHOUT RELAPSES"

12.2.1.3: Any SAE

Figure 12.2.1.3.1: SAE, Age = 18-40 years

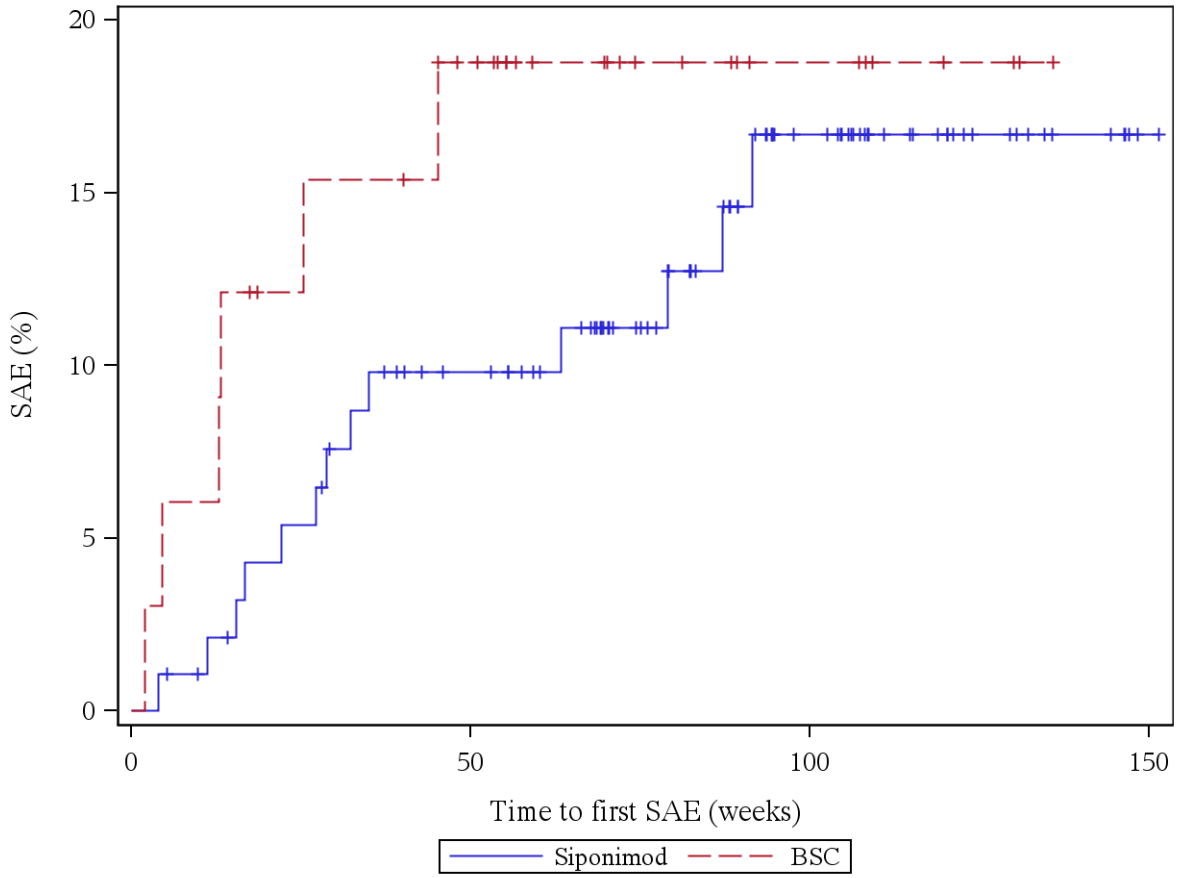


Patients at risk (Siponimod/BSC): Week 0: 18/13, Week 4: 18/12, Week 12: 18/12, Week 24: 17/11, Week 36: 16/11, Week 48: 15/10, Week 60: 12/9, Week 72: 8/7, Week 84: 7/5, Week 96: 5/4, Week 108: 3/4, Week 120: 3/3, Week 132: 1/2, Week 144: 1/0, Week 156: 0/0

Log rank test: p-value = 0,354
*: p < 0,05

Analysis population: A2304 SAF subpopulation "ACTIVE MS WITHOUT RELAPSES"

Figure 12.2.1.3.2: SAE, Age = 41-55 years

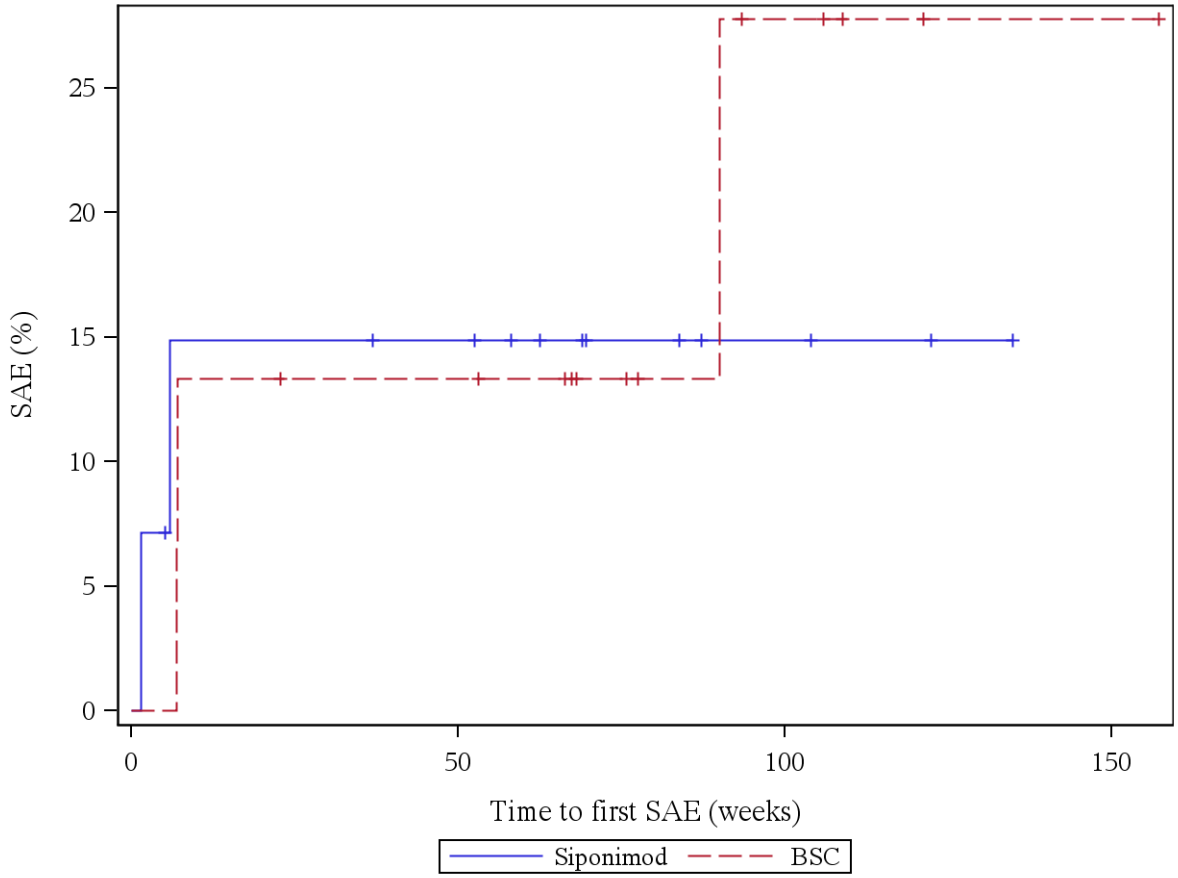


Patients at risk (Siponimod/BSC): Week 0: 95/33, Week 4: 94/32, Week 12: 91/31, Week 24: 87/27, Week 36: 81/26, Week 48: 76/22, Week 60: 71/15, Week 72: 58/12, Week 84: 47/10, Week 96: 32/7, Week 108: 23/6, Week 120: 16/3, Week 132: 9/1, Week 144: 6/0, Week 156: 0/0

Log rank test: p-value = 0,361
*: p < 0,05

Analysis population: A2304 SAF subpopulation "ACTIVE MS WITHOUT RELAPSES"

Figure 12.2.1.3.3: SAE, Age = >55 years



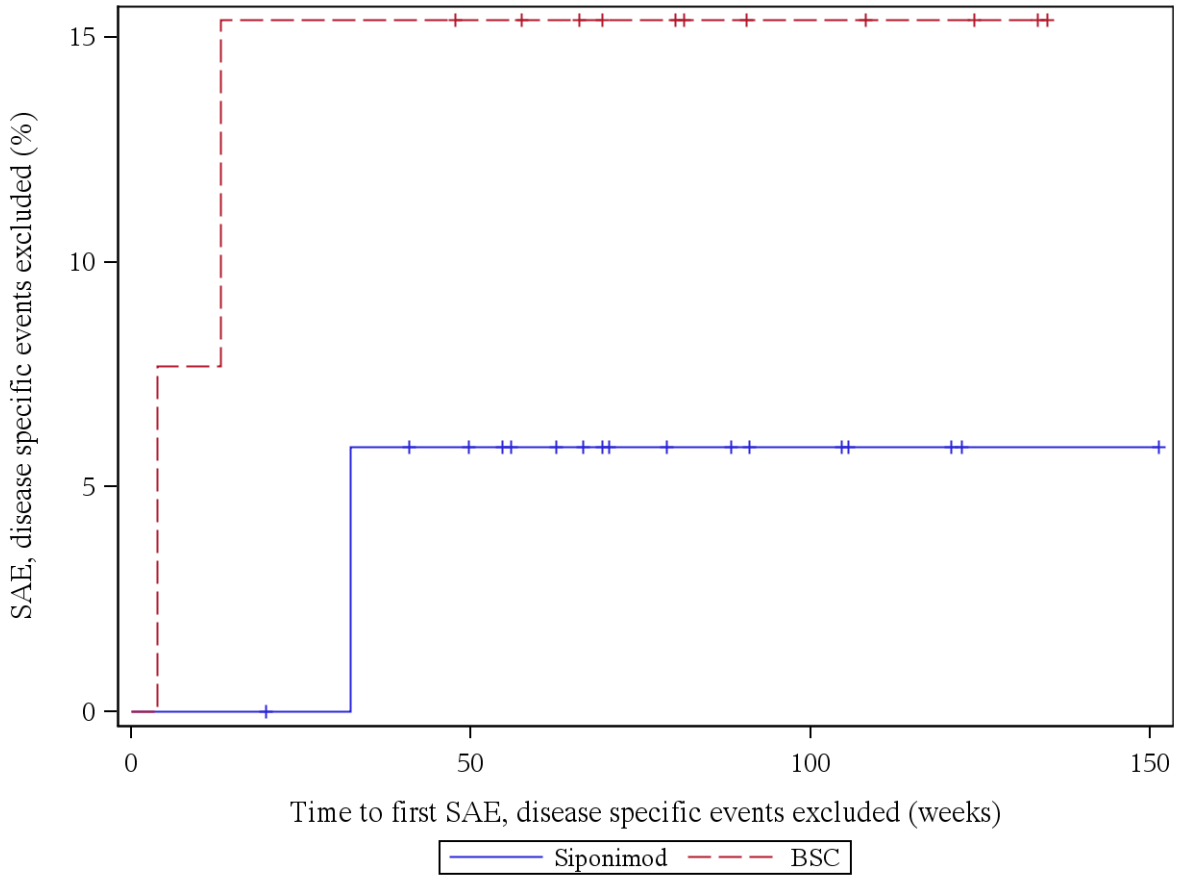
Patients at risk (Siponimod/BSC): Week 0: 14/15, Week 4: 13/15, Week 12: 11/13, Week 24: 11/12, Week 36: 11/12, Week 48: 10/12, Week 60: 8/11, Week 72: 5/8, Week 84: 4/6, Week 96: 3/4, Week 108: 2/3, Week 120: 2/2, Week 132: 1/1, Week 144: 0/1

Log rank test: p-value = 0,911
*: p < 0,05

Analysis population: A2304 SAF subpopulation "ACTIVE MS WITHOUT RELAPSES"

12.2.1.4: Any SAE, disease specific events excluded

Figure 12.2.1.4.1: SAE, disease specific events excluded, Age = 18-40 years

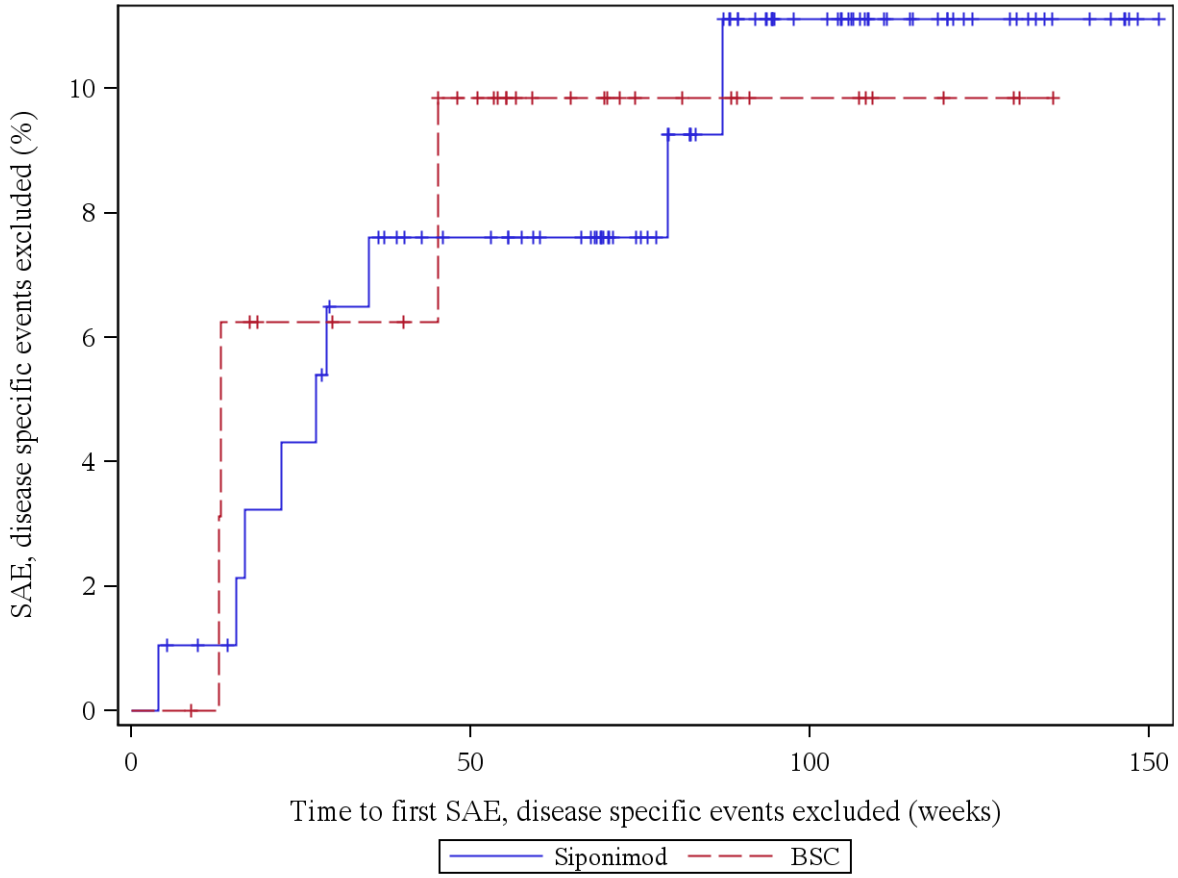


Patients at risk (Siponimod/BSC): Week 0: 18/13, Week 4: 18/12, Week 12: 18/12, Week 24: 17/11, Week 36: 16/11, Week 48: 15/10, Week 60: 12/9, Week 72: 8/7, Week 84: 7/5, Week 96: 5/4, Week 108: 3/4, Week 120: 3/3, Week 132: 1/2, Week 144: 1/0, Week 156: 0/0

Log rank test: p-value = 0,354
*: p < 0,05

Analysis population: A2304 SAF subpopulation "ACTIVE MS WITHOUT RELAPSES"

Figure 12.2.1.4.2: SAE, disease specific events excluded, Age = 41-55 years

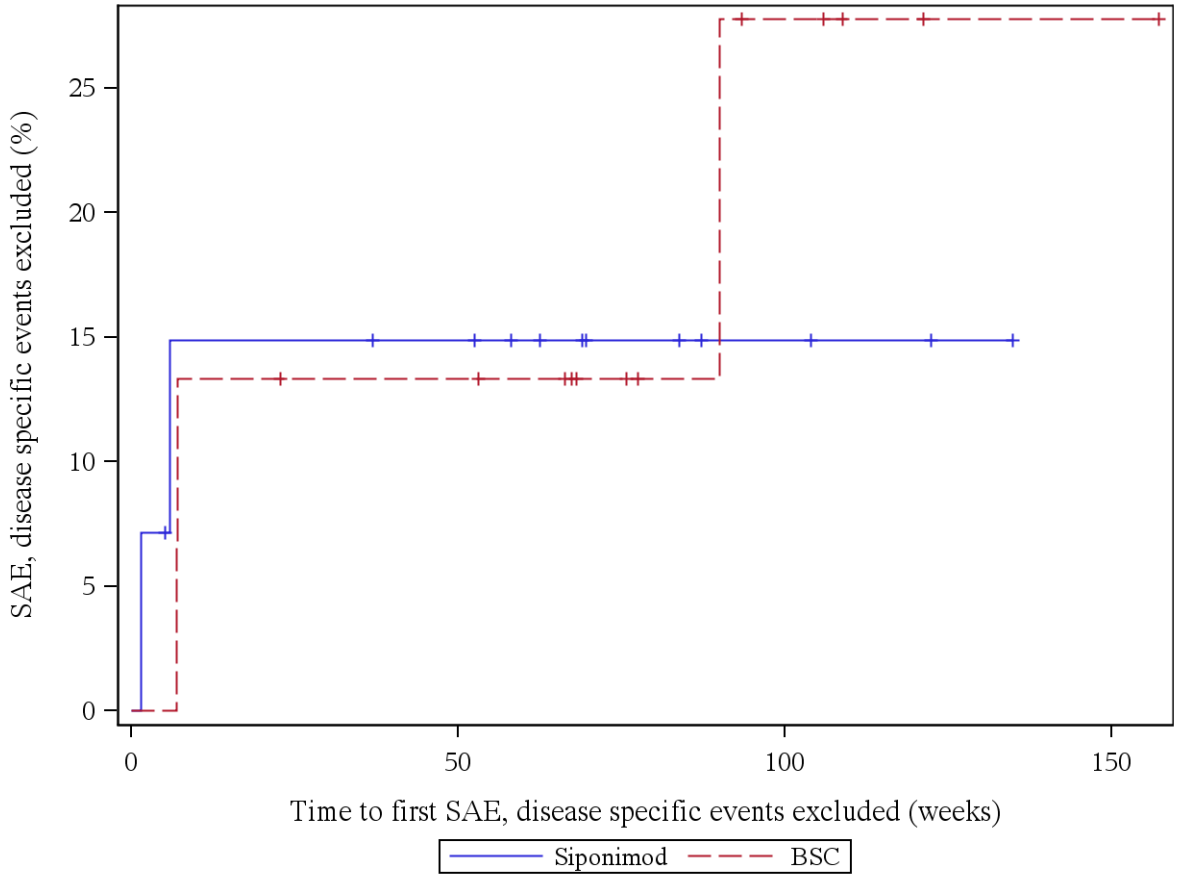


Patients at risk (Siponimod/BSC): Week 0: 95/33, Week 4: 94/33, Week 12: 92/32, Week 24: 88/28, Week 36: 83/27, Week 48: 77/23, Week 60: 72/16, Week 72: 60/12, Week 84: 49/10, Week 96: 35/7, Week 108: 26/6, Week 120: 18/3, Week 132: 11/1, Week 144: 6/0, Week 156: 0/0

Log rank test: p-value = 0,902
*: p < 0,05

Analysis population: A2304 SAF subpopulation "ACTIVE MS WITHOUT RELAPSES"

Figure 12.2.1.4.3: SAE, disease specific events excluded, Age = >55 years



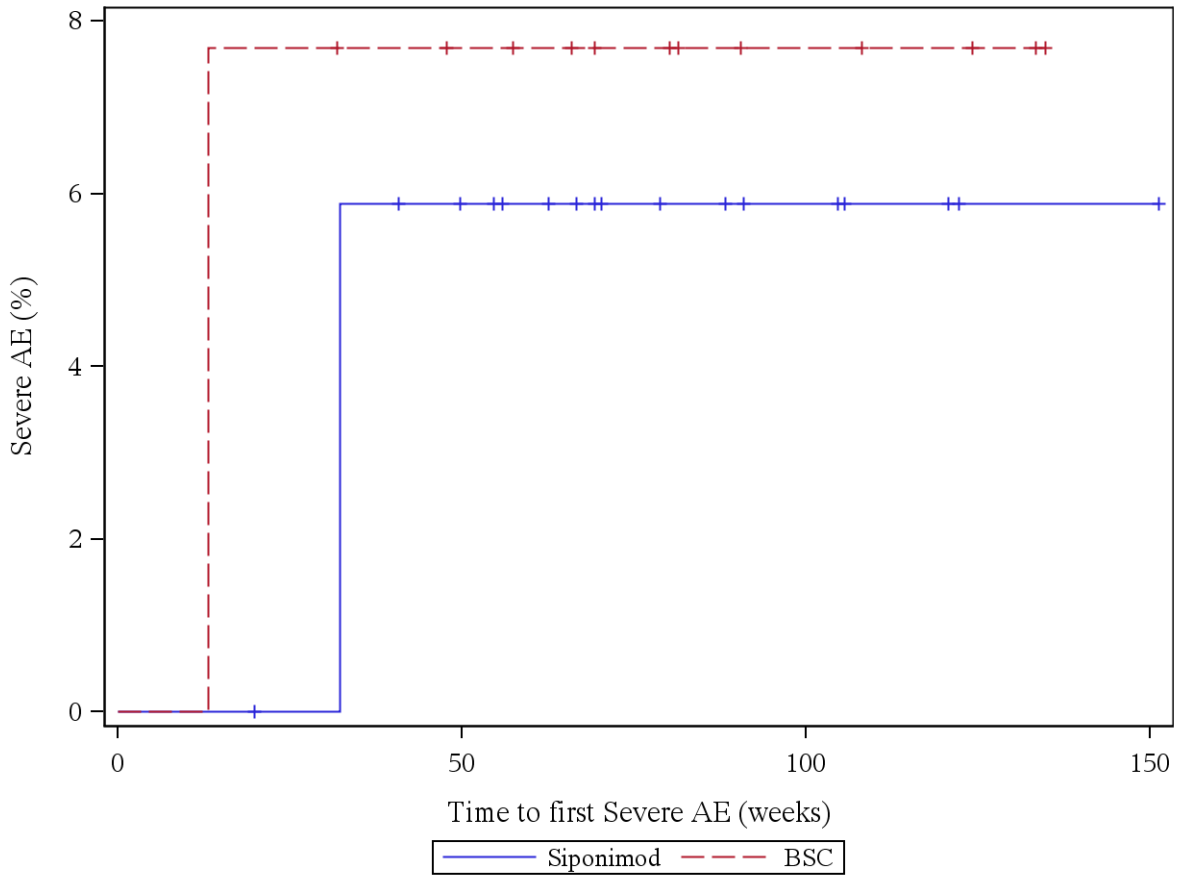
Patients at risk (Siponimod/BSC): Week 0: 14/15, Week 4: 13/15, Week 12: 11/13, Week 24: 11/12, Week 36: 11/12, Week 48: 10/12, Week 60: 8/11, Week 72: 5/8, Week 84: 4/6, Week 96: 3/4, Week 108: 2/3, Week 120: 2/2, Week 132: 1/1, Week 144: 0/1

Log rank test: p-value = 0,911
*: p < 0,05

Analysis population: A2304 SAF subpopulation "ACTIVE MS WITHOUT RELAPSES"

12.2.1.5: Any severe AE

Figure 12.2.1.5.1: Severe AE, Age = 18-40 years

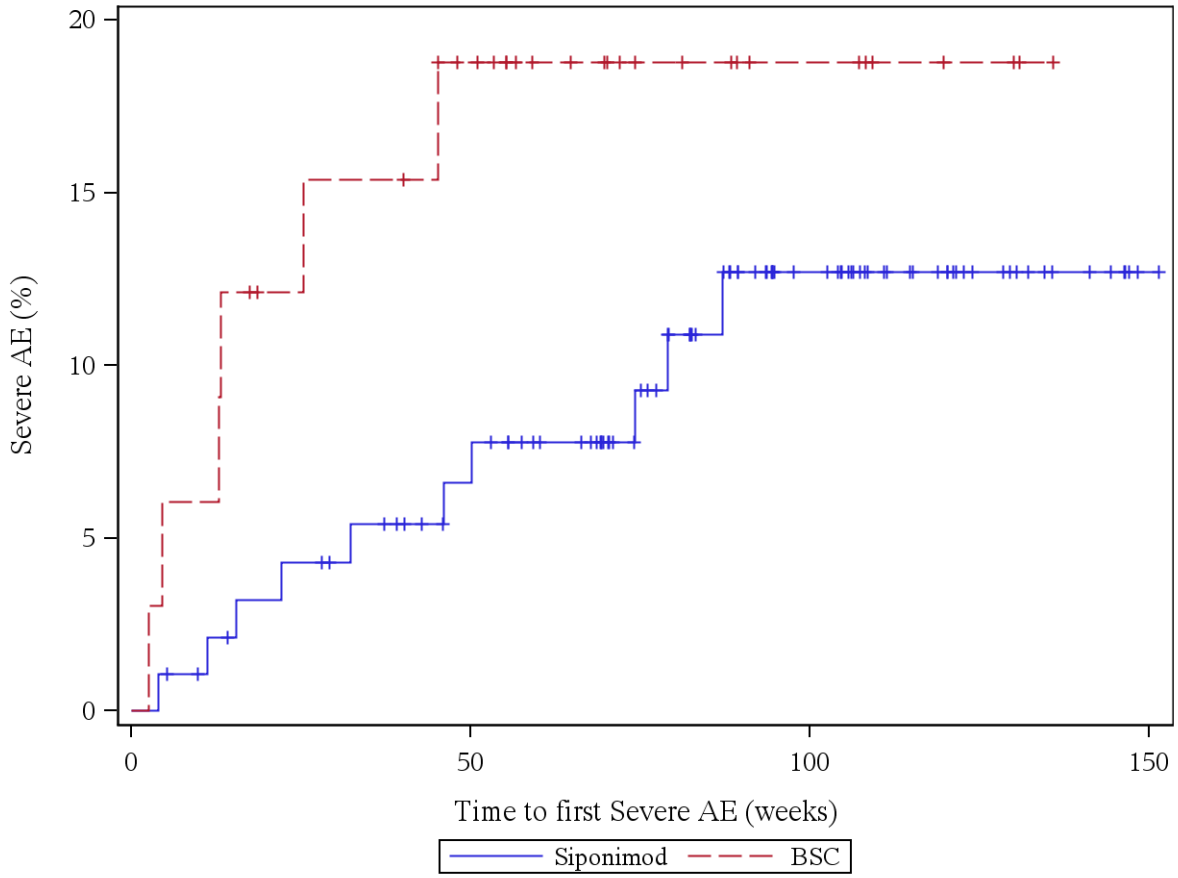


Patients at risk (Siponimod/BSC): Week 0: 18/13, Week 4: 18/13, Week 12: 18/13, Week 24: 17/12, Week 36: 16/11, Week 48: 15/10, Week 60: 12/9, Week 72: 8/7, Week 84: 7/5, Week 96: 5/4, Week 108: 3/4, Week 120: 3/3, Week 132: 1/2, Week 144: 1/0, Week 156: 0/0

Log rank test: p-value = 0,787
*: p < 0,05

Analysis population: A2304 SAF subpopulation "ACTIVE MS WITHOUT RELAPSES"

Figure 12.2.1.5.2: Severe AE, Age = 41-55 years

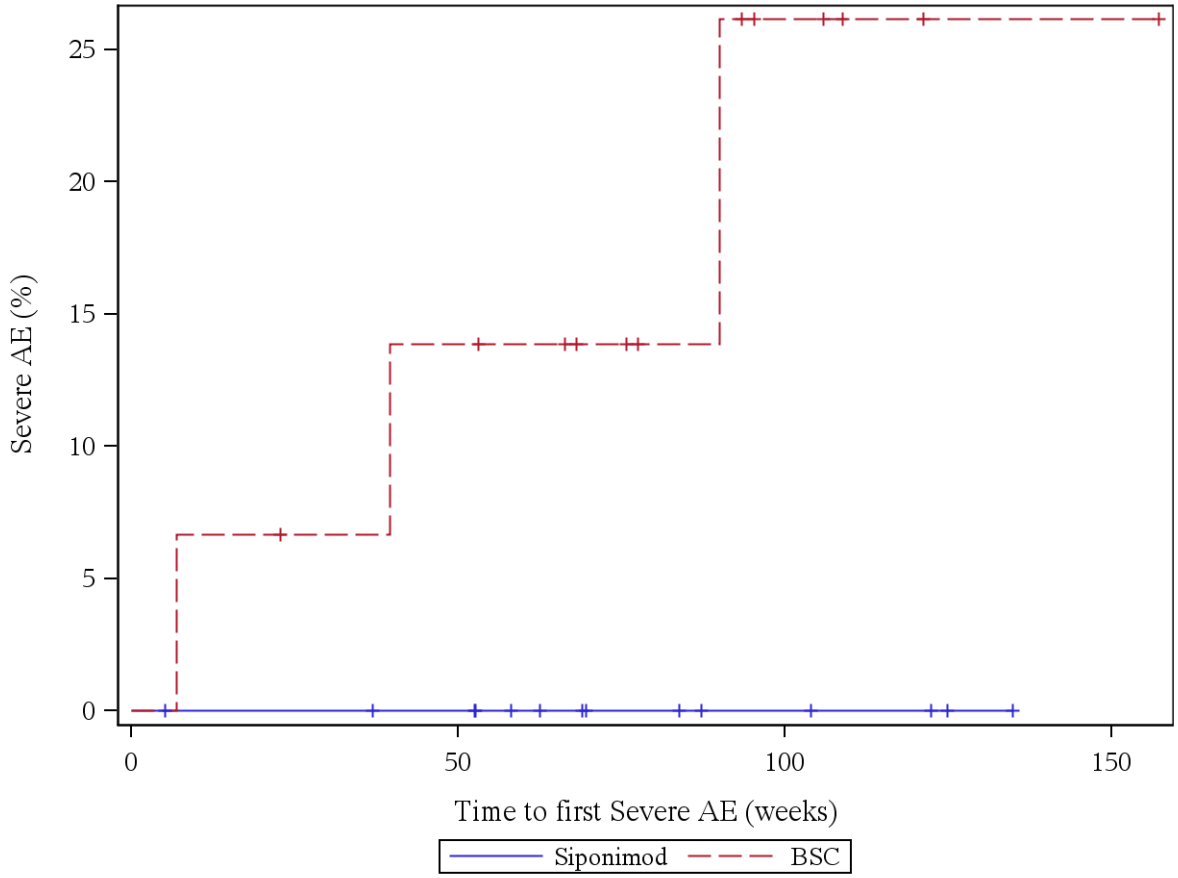


Patients at risk (Siponimod/BSC): Week 0: 95/33, Week 4: 94/32, Week 12: 91/31, Week 24: 88/27, Week 36: 85/26, Week 48: 79/22, Week 60: 73/16, Week 72: 62/12, Week 84: 49/10, Week 96: 35/7, Week 108: 26/6, Week 120: 19/3, Week 132: 10/1, Week 144: 6/0, Week 156: 0/0

Log rank test: p-value = 0,157
*: p < 0,05

Analysis population: A2304 SAF subpopulation "ACTIVE MS WITHOUT RELAPSES"

Figure 12.2.1.5.3: Severe AE, Age = >55 years



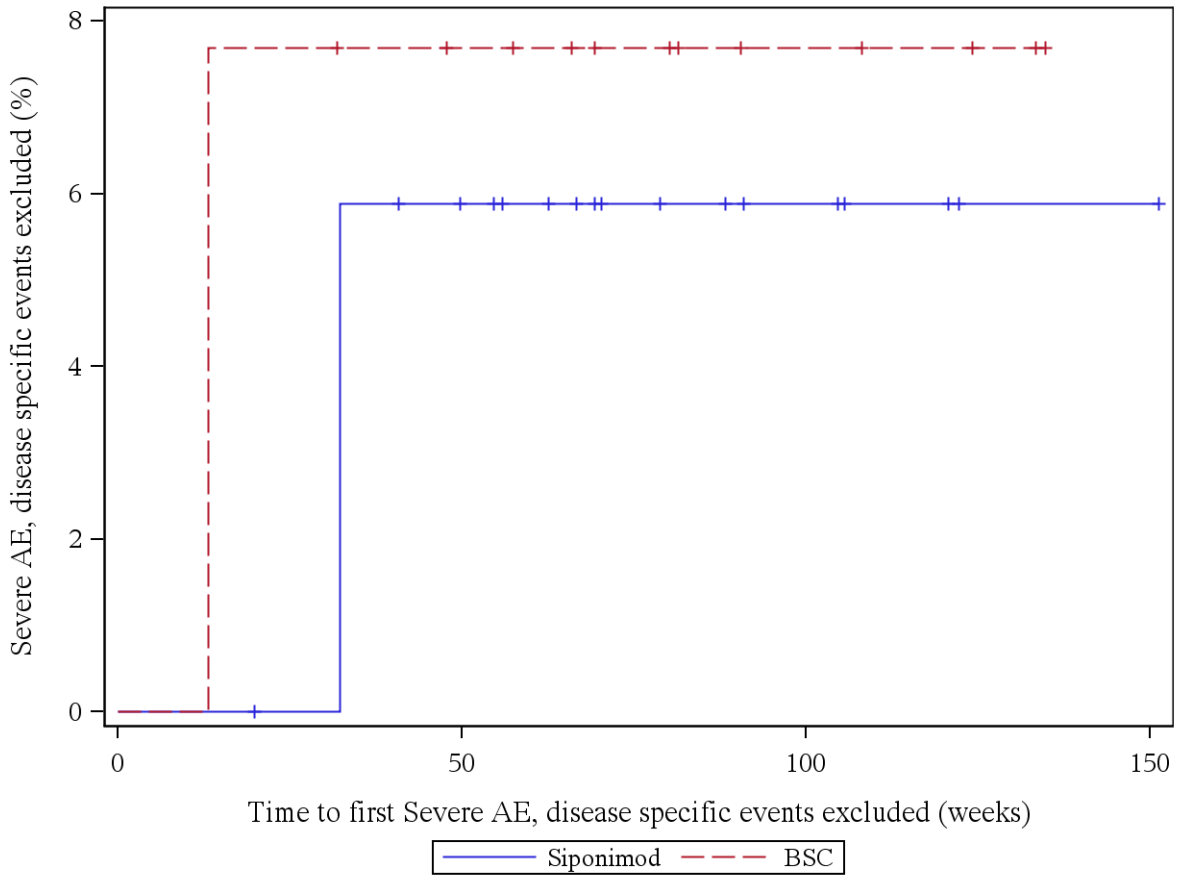
Patients at risk (Siponimod/BSC): Week 0: 14/15, Week 4: 14/15, Week 12: 13/14, Week 24: 13/13, Week 36: 13/13, Week 48: 12/12, Week 60: 9/11, Week 72: 6/9, Week 84: 5/7, Week 96: 4/4, Week 108: 3/3, Week 120: 3/2, Week 132: 1/1, Week 144: 0/1

Log rank test: p-value = -
*: p < 0,05

Analysis population: A2304 SAF subpopulation "ACTIVE MS WITHOUT RELAPSES"

12.2.1.6: Any severe AE, disease specific events excluded

Figure 12.2.1.6.1: Severe AE, disease specific events excluded, Age = 18-40 years

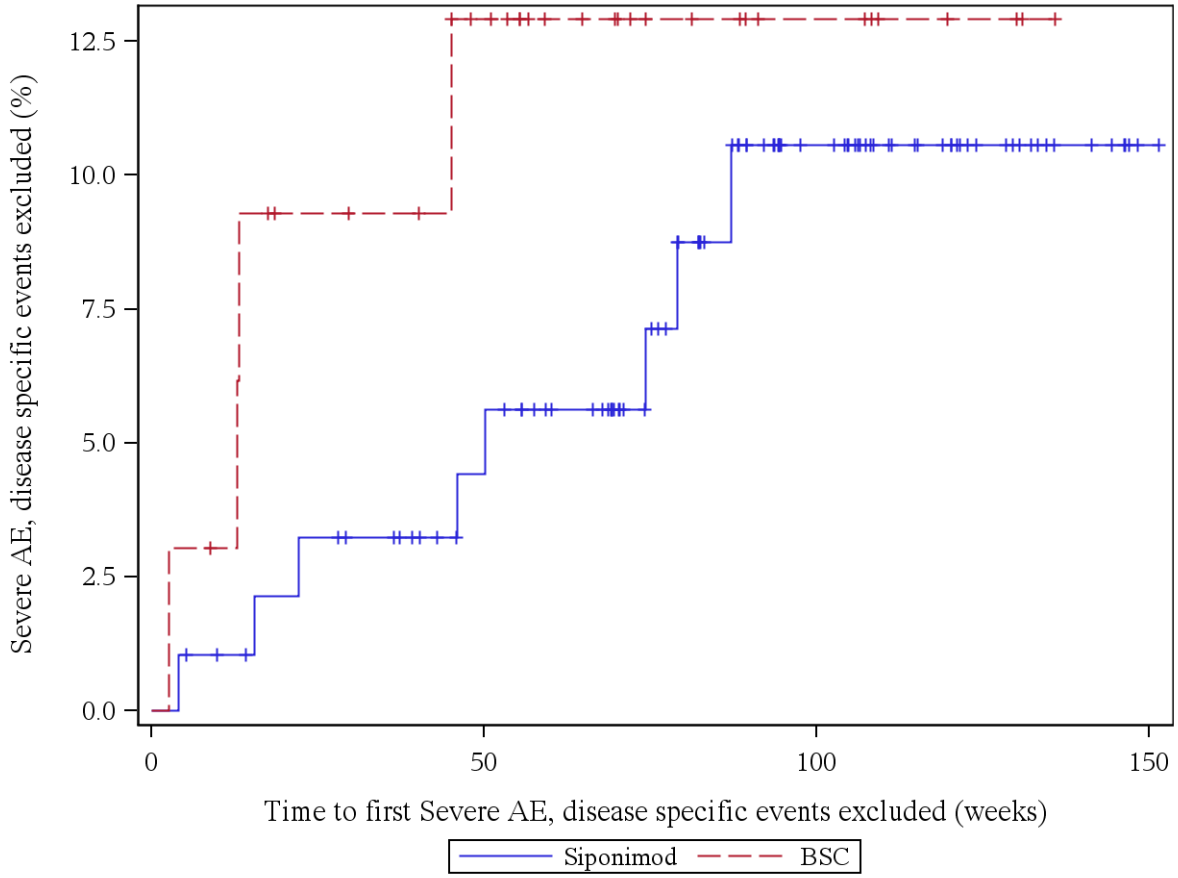


Patients at risk (Siponimod/BSC): Week 0: 18/13, Week 4: 18/13, Week 12: 18/13, Week 24: 17/12, Week 36: 16/11, Week 48: 15/10, Week 60: 12/9, Week 72: 8/7, Week 84: 7/5, Week 96: 5/4, Week 108: 3/4, Week 120: 3/3, Week 132: 1/2, Week 144: 1/0, Week 156: 0/0

Log rank test: p-value = 0,787
*: p < 0,05

Analysis population: A2304 SAF subpopulation "ACTIVE MS WITHOUT RELAPSES"

Figure 12.2.1.6.2: Severe AE, disease specific events excluded, Age = 41-55 years

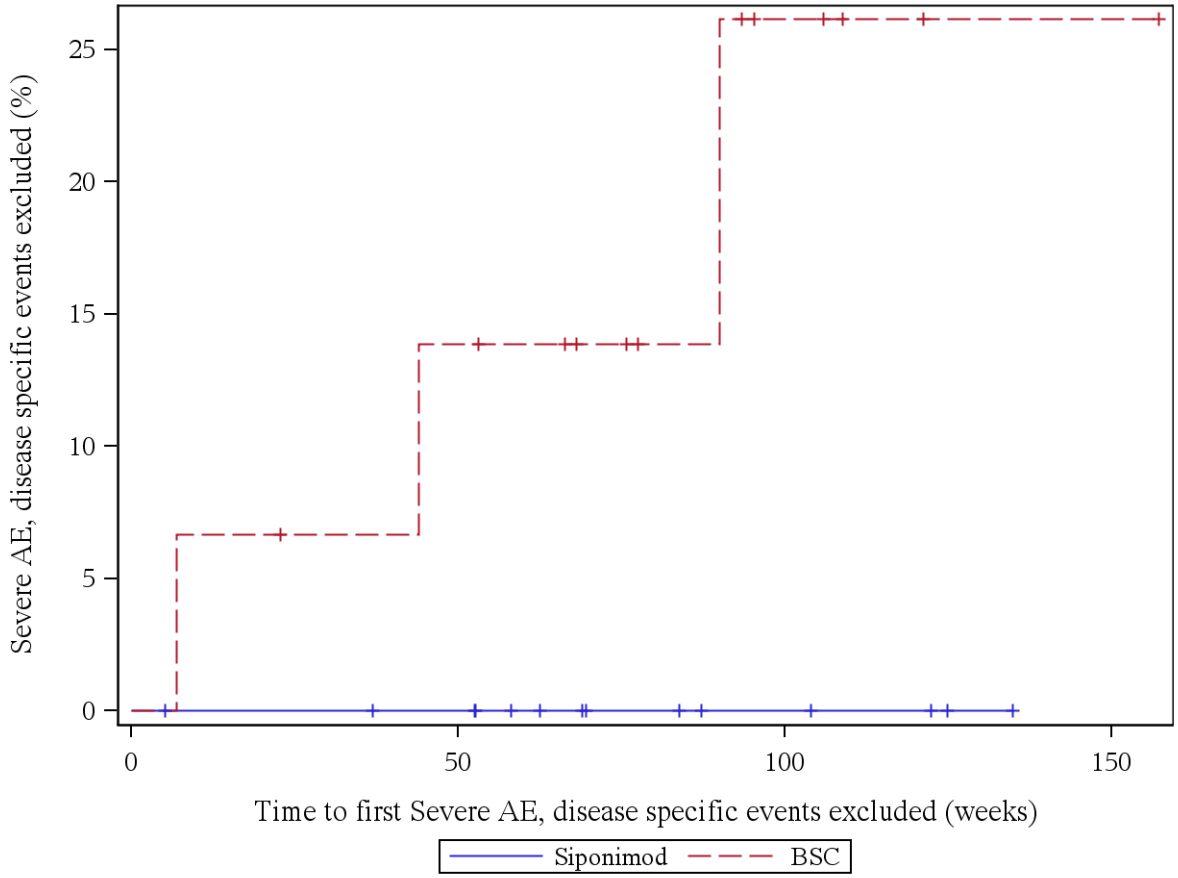


Patients at risk (Siponimod/BSC): Week 0: 95/33, Week 4: 94/32, Week 12: 92/31, Week 24: 89/27, Week 36: 87/26, Week 48: 80/22, Week 60: 74/16, Week 72: 63/12, Week 84: 50/10, Week 96: 36/7, Week 108: 27/6, Week 120: 20/3, Week 132: 11/1, Week 144: 6/0, Week 156: 0/0

Log rank test: p-value = 0,341
*: p < 0,05

Analysis population: A2304 SAF subpopulation "ACTIVE MS WITHOUT RELAPSES"

Figure 12.2.1.6.3: Severe AE, disease specific events excluded, Age = >55 years



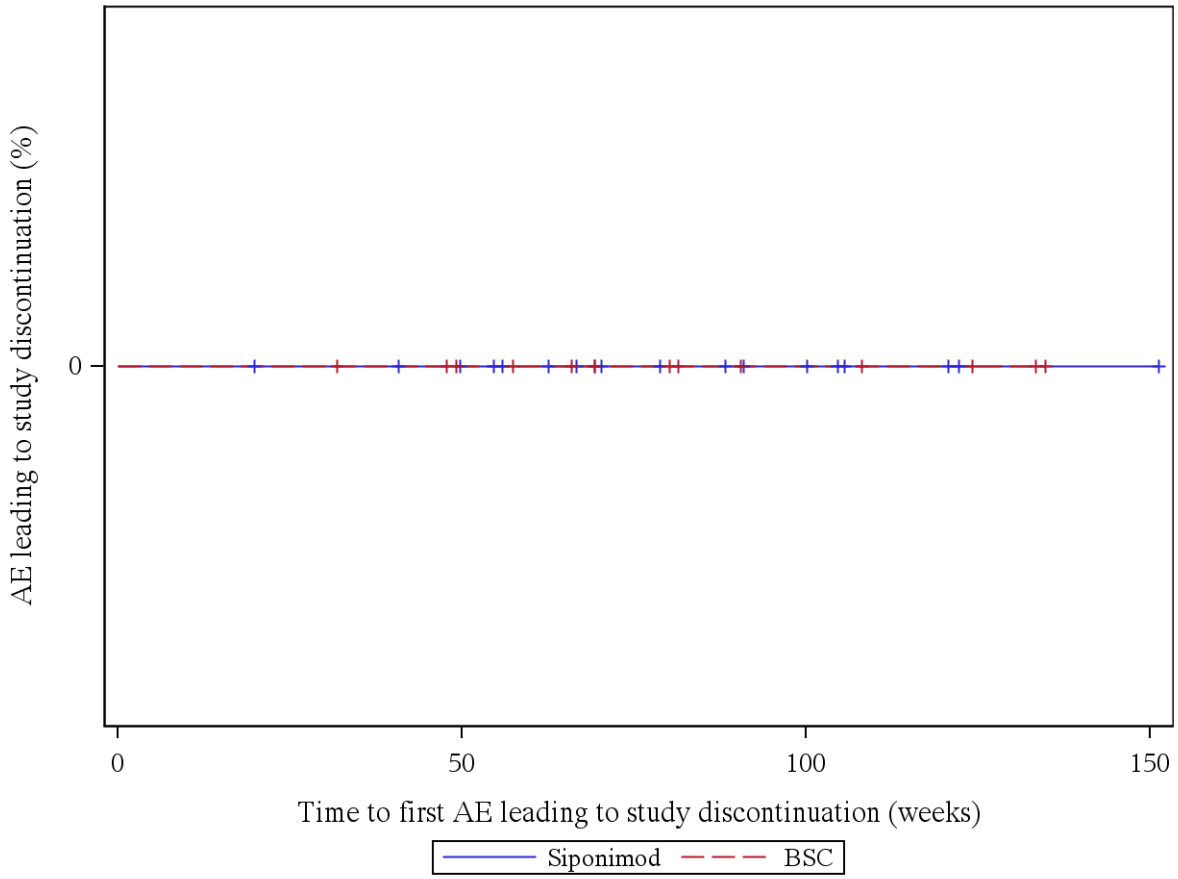
Patients at risk (Siponimod/BSC): Week 0: 14/15, Week 4: 14/15, Week 12: 13/14, Week 24: 13/13, Week 36: 13/13, Week 48: 12/12, Week 60: 9/11, Week 72: 6/9, Week 84: 5/7, Week 96: 4/4, Week 108: 3/3, Week 120: 3/2, Week 132: 1/1, Week 144: 0/1

Log rank test: p-value = -
*: p < 0,05

Analysis population: A2304 SAF subpopulation "ACTIVE MS WITHOUT RELAPSES"

12.2.1.7: Any AE leading to study discontinuation

Figure 12.2.1.7.1: AE leading to study discontinuation, Age = 18-40 years

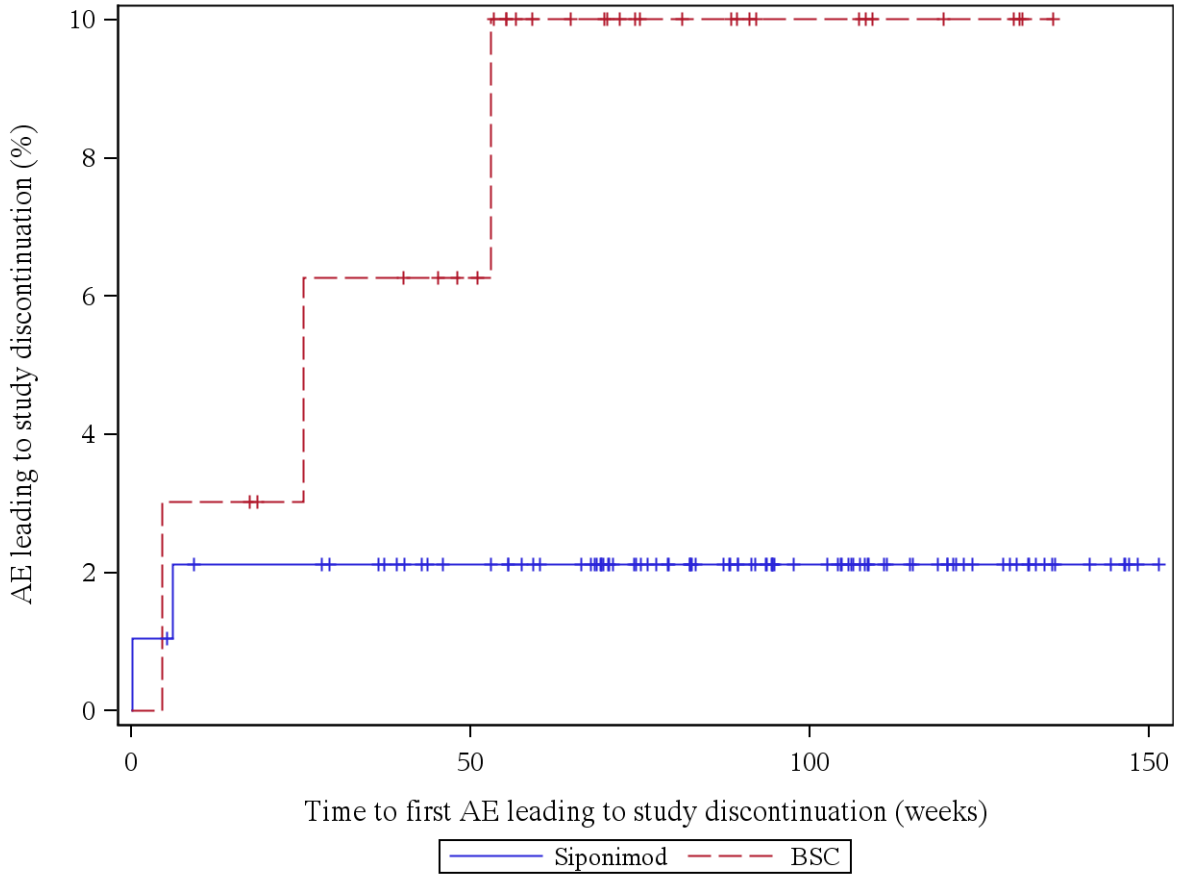


Patients at risk (Siponimod/BSC): Week 0: 18/13, Week 4: 18/13, Week 12: 18/13, Week 24: 17/13, Week 36: 17/12, Week 48: 16/11, Week 60: 13/9, Week 72: 9/7, Week 84: 8/5, Week 96: 6/4, Week 108: 3/4, Week 120: 3/3, Week 132: 1/2, Week 144: 1/0, Week 156: 0/0

Log rank test: p-value = -
*: p < 0,05

Analysis population: A2304 SAF subpopulation "ACTIVE MS WITHOUT RELAPSES"

Figure 12.2.1.7.2: AE leading to study discontinuation, Age = 41-55 years

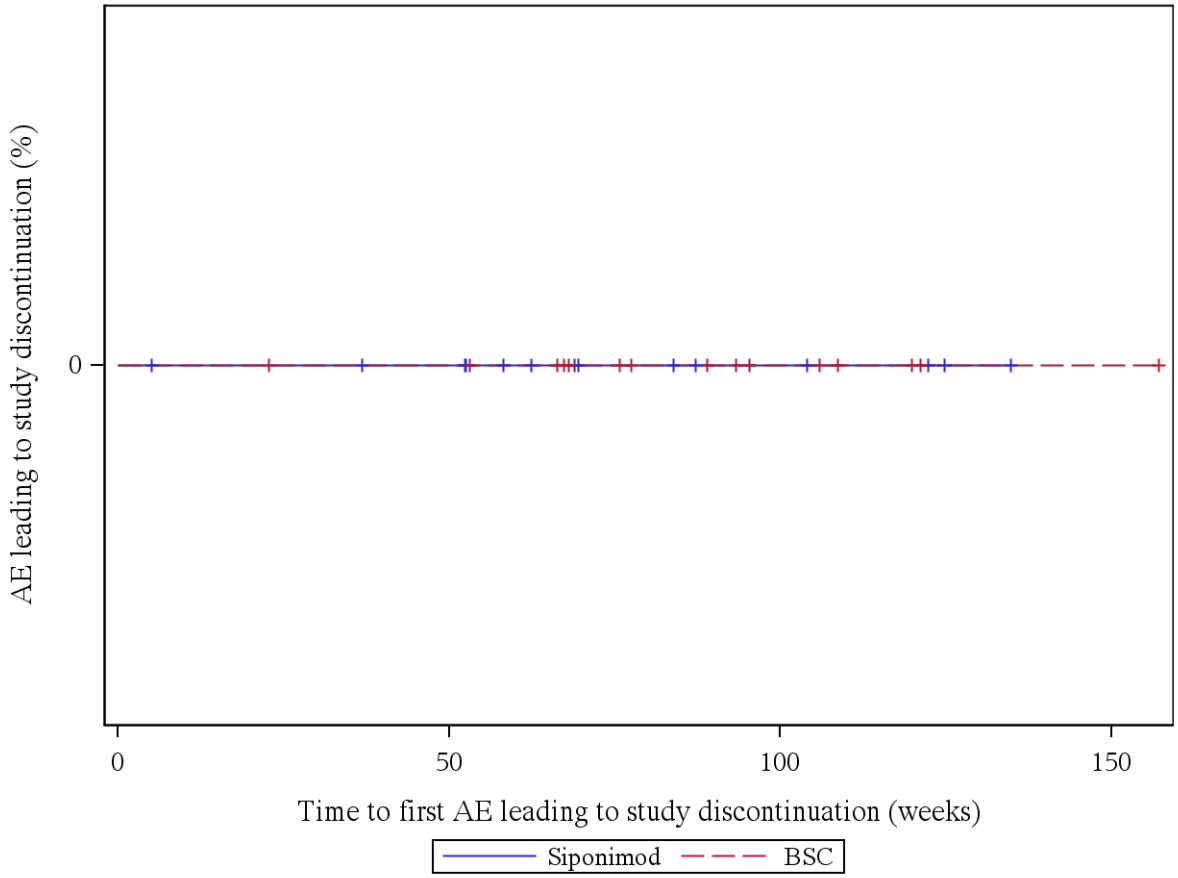


Patients at risk (Siponimod/BSC): Week 0: 95/33, Week 4: 94/33, Week 12: 91/32, Week 24: 91/30, Week 36: 89/29, Week 48: 82/26, Week 60: 77/19, Week 72: 65/15, Week 84: 53/12, Week 96: 39/8, Week 108: 30/7, Week 120: 22/4, Week 132: 13/1, Week 144: 6/0, Week 156: 0/0

Log rank test: p-value = 0,072
*: p < 0,05

Analysis population: A2304 SAF subpopulation "ACTIVE MS WITHOUT RELAPSES"

Figure 12.2.1.7.3: AE leading to study discontinuation, Age = >55 years



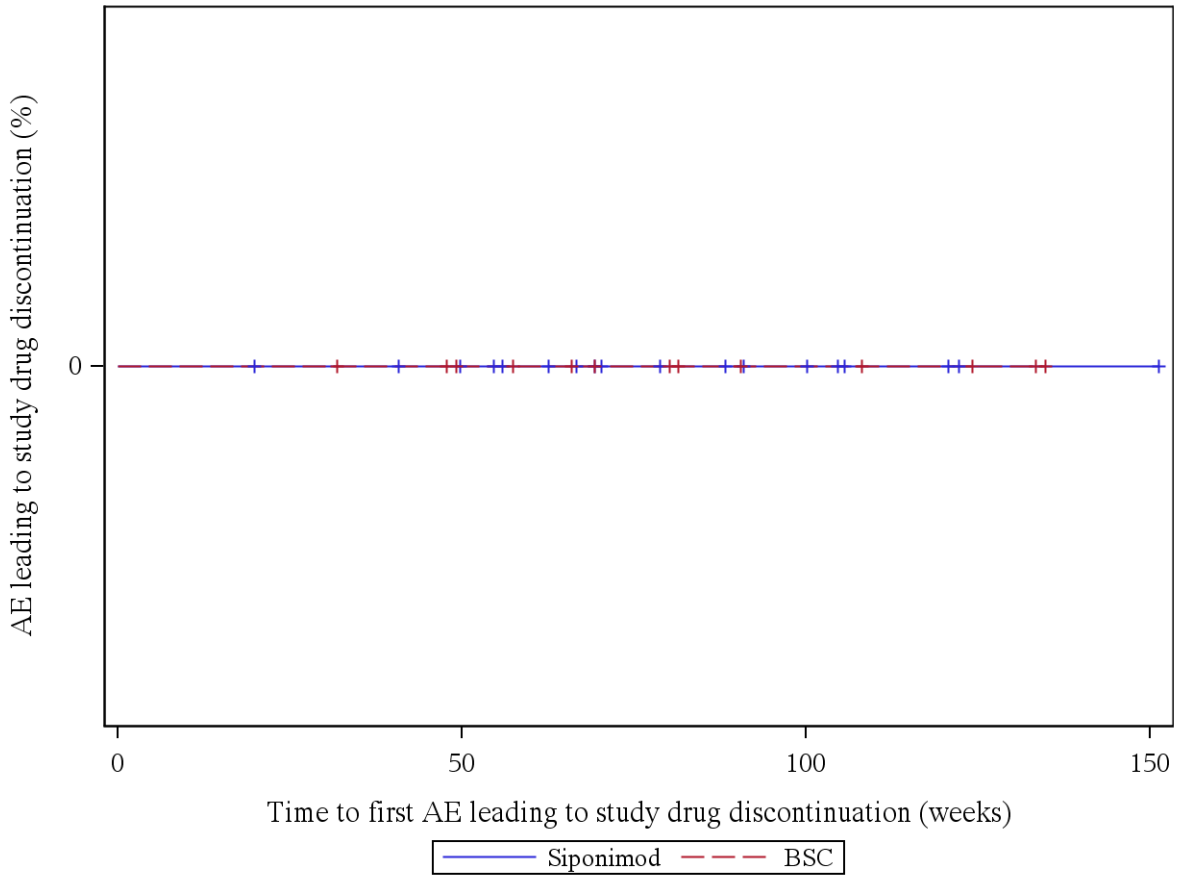
Patients at risk (Siponimod/BSC): Week 0: 14/15, Week 4: 14/15, Week 12: 13/15, Week 24: 13/14, Week 36: 13/14, Week 48: 12/14, Week 60: 9/13, Week 72: 6/10, Week 84: 5/8, Week 96: 4/5, Week 108: 3/4, Week 120: 3/2, Week 132: 1/1, Week 144: 0/1

Log rank test: p-value = -
*: p < 0,05

Analysis population: A2304 SAF subpopulation "ACTIVE MS WITHOUT RELAPSES"

12.2.1.8: Any AE leading to study drug discontinuation

Figure 12.2.1.8.1: AE leading to study drug discontinuation, Age = 18-40 years

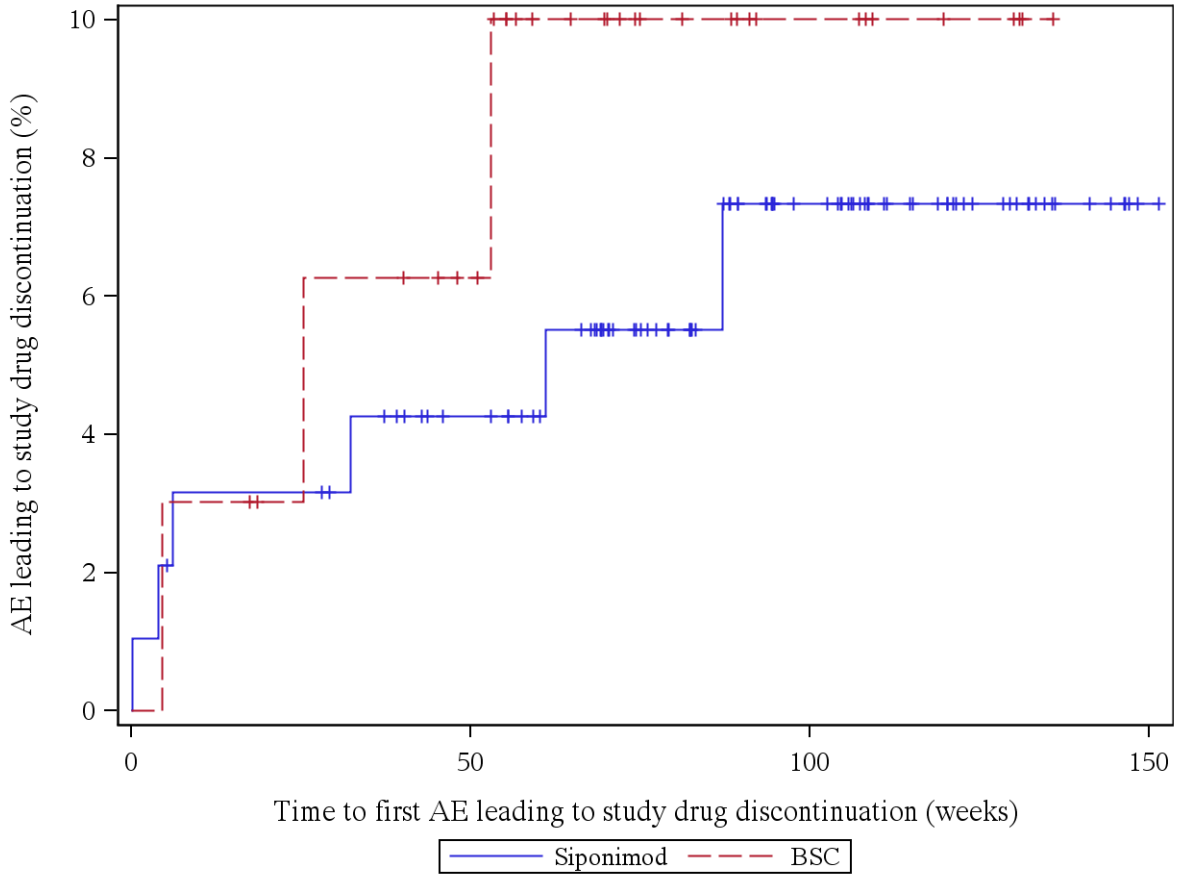


Patients at risk (Siponimod/BSC): Week 0: 18/13, Week 4: 18/13, Week 12: 18/13, Week 24: 17/13, Week 36: 17/12, Week 48: 16/11, Week 60: 13/9, Week 72: 9/7, Week 84: 8/5, Week 96: 6/4, Week 108: 3/4, Week 120: 3/3, Week 132: 1/2, Week 144: 1/0, Week 156: 0/0

Log rank test: p-value = -
*: p < 0,05

Analysis population: A2304 SAF subpopulation "ACTIVE MS WITHOUT RELAPSES"

Figure 12.2.1.8.2: AE leading to study drug discontinuation, Age = 41-55 years

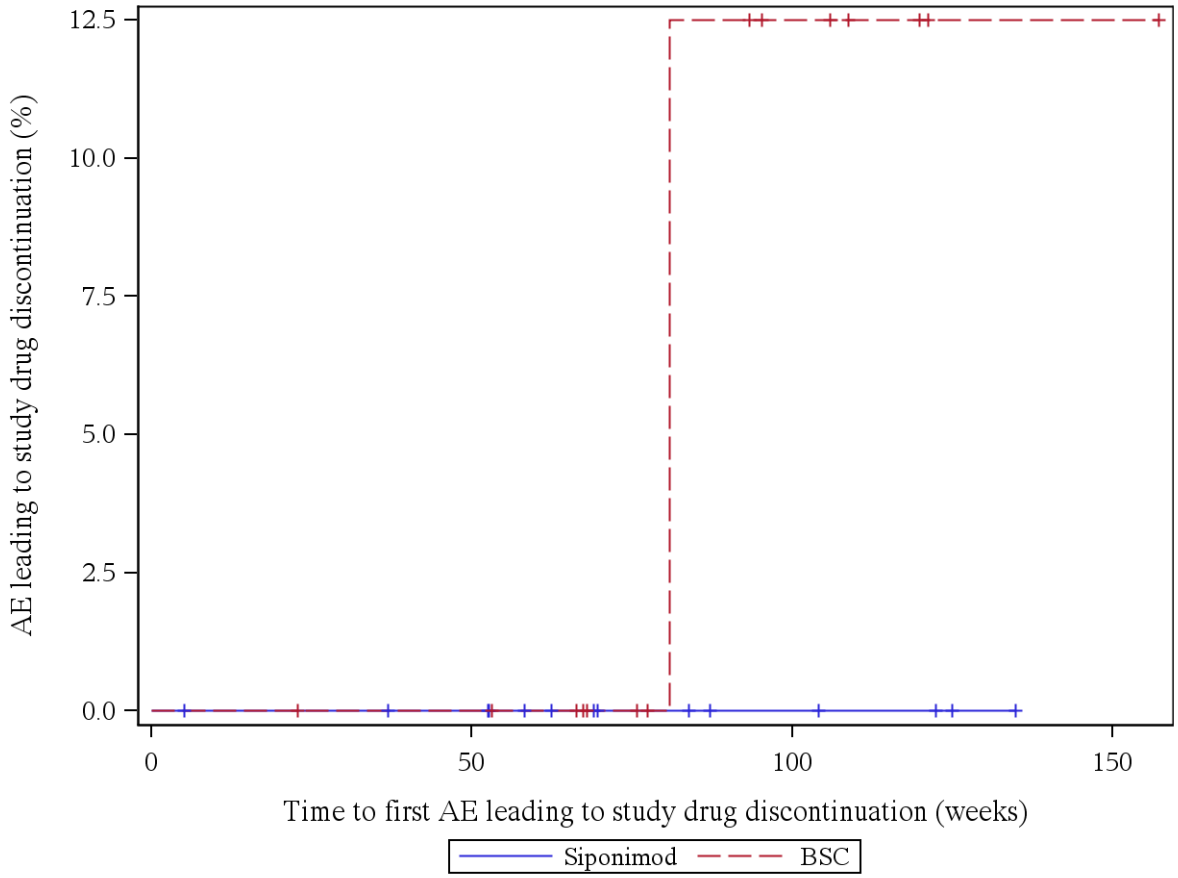


Patients at risk (Siponimod/BSC): Week 0: 95/33, Week 4: 93/33, Week 12: 91/32, Week 24: 91/30, Week 36: 88/29, Week 48: 82/26, Week 60: 77/19, Week 72: 64/15, Week 84: 52/12, Week 96: 39/8, Week 108: 30/7, Week 120: 22/4, Week 132: 13/1, Week 144: 6/0, Week 156: 0/0

Log rank test: p-value = 0,507
*: p < 0,05

Analysis population: A2304 SAF subpopulation "ACTIVE MS WITHOUT RELAPSES"

Figure 12.2.1.8.3: AE leading to study drug discontinuation, Age = >55 years



Patients at risk (Siponimod/BSC): Week 0: 14/15, Week 4: 14/15, Week 12: 13/15, Week 24: 13/14, Week 36: 13/14, Week 48: 12/14, Week 60: 9/13, Week 72: 6/10, Week 84: 5/7, Week 96: 4/5, Week 108: 3/4, Week 120: 3/2, Week 132: 1/1, Week 144: 0/1

Log rank test: p-value = -
*: p < 0,05

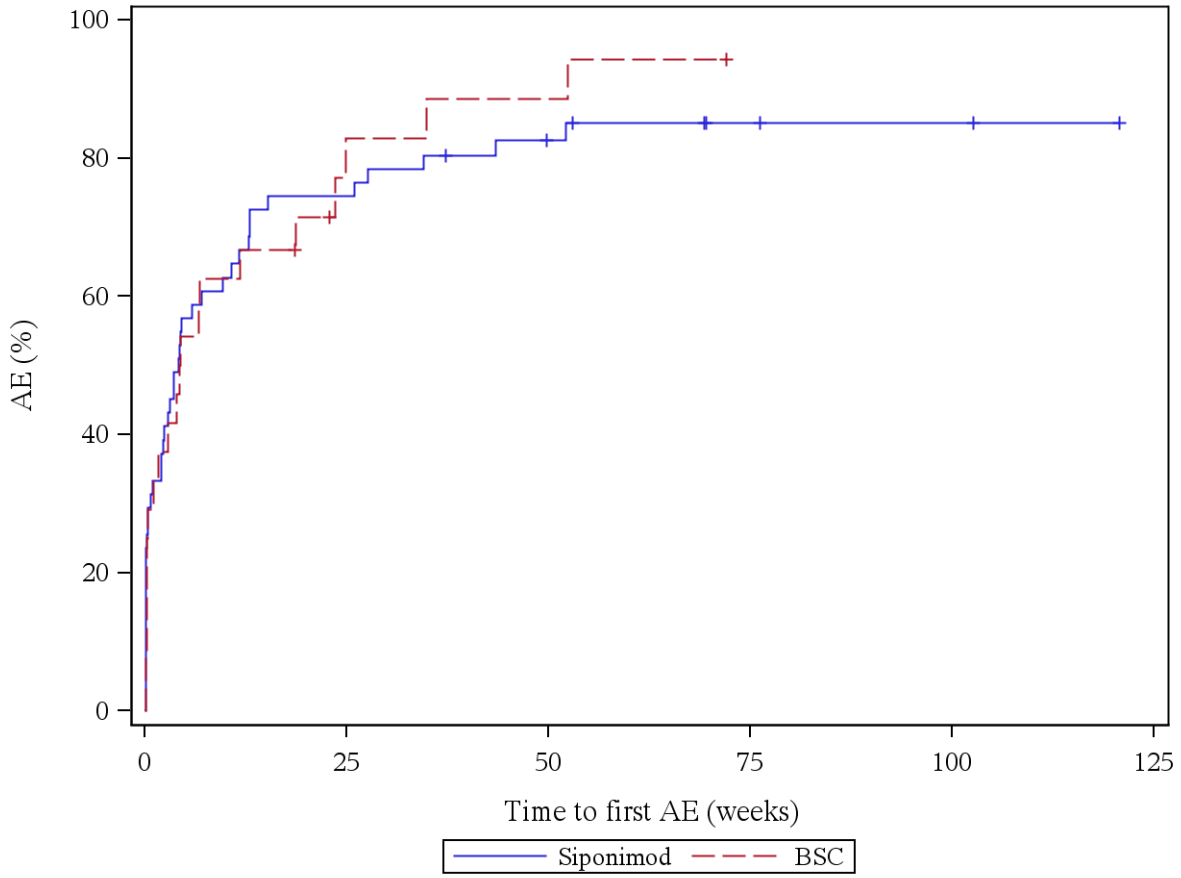
Analysis population: A2304 SAF subpopulation "ACTIVE MS WITHOUT RELAPSES"

12.3 Subgroup: Gender

12.3.1: Time to First Adverse Event (SAF) by Gender

12.3.1.1: Any AE

Figure 12.3.1.1.1: AE, Gender = Male

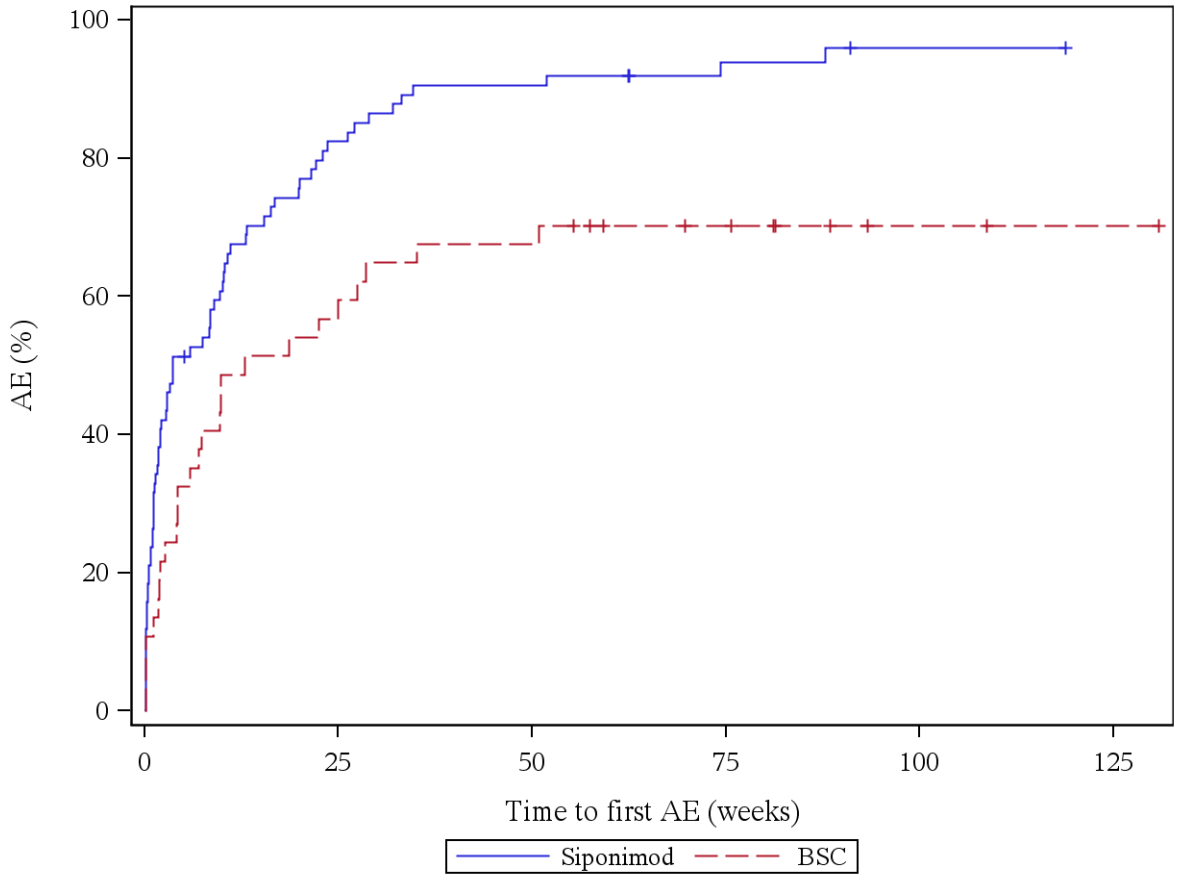


Patients at risk (Siponimod/BSC): Week 0: 51/24, Week 4: 26/13, Week 12: 17/8, Week 24: 13/4, Week 36: 10/2, Week 48: 8/2, Week 60: 5/1, Week 72: 3/0, Week 84: 2/0, Week 96: 2/0, Week 108: 1/0, Week 120: 1/0, Week 132: 0/0

Log rank test: p-value = 0,810
*: p < 0,05

Analysis population: A2304 SAF subpopulation "ACTIVE MS WITHOUT RELAPSES"

Figure 12.3.1.1.2: AE, Gender = Female



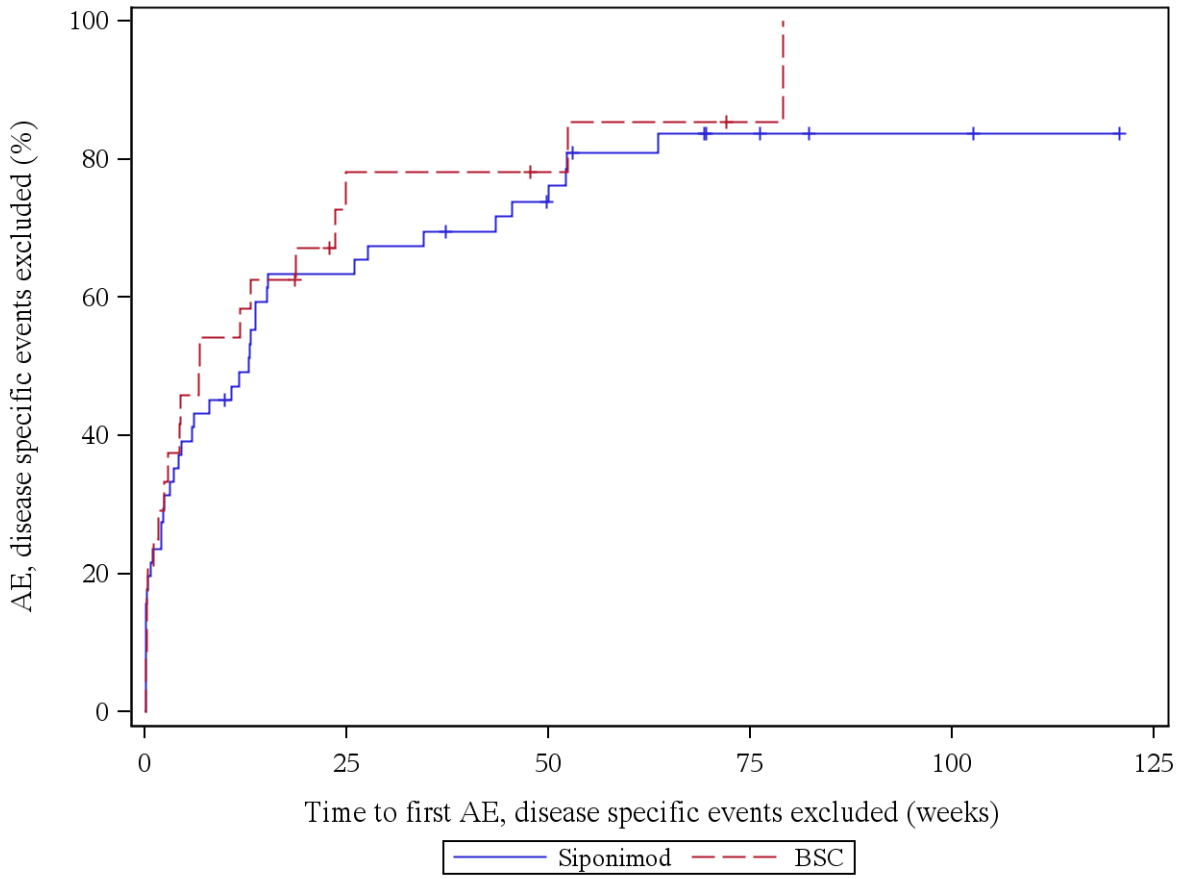
Patients at risk (Siponimod/BSC): Week 0: 76/37, Week 4: 37/28, Week 12: 24/19, Week 24: 13/16, Week 36: 7/12, Week 48: 7/12, Week 60: 6/8, Week 72: 4/7, Week 84: 3/4, Week 96: 1/2, Week 108: 1/2, Week 120: 0/1

Log rank test: p-value = 0,002 *
*: p < 0,05

Analysis population: A2304 SAF subpopulation "ACTIVE MS WITHOUT RELAPSES"

12.3.1.2: Any AE, disease specific events excluded

Figure 12.3.1.2.1: AE, disease specific events excluded, Gender = Male

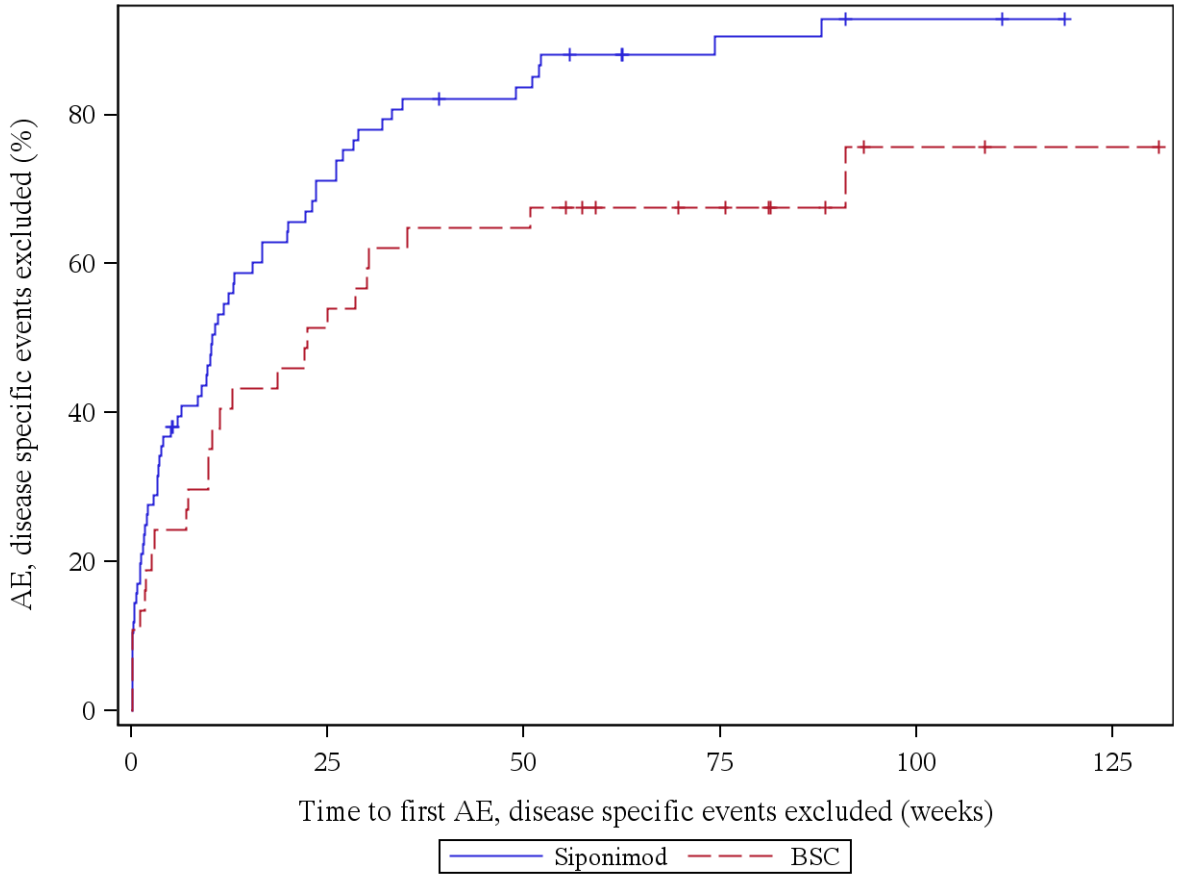


Patients at risk (Siponimod/BSC): Week 0: 51/24, Week 4: 33/15, Week 12: 25/10, Week 24: 18/5, Week 36: 15/4, Week 48: 12/3, Week 60: 7/2, Week 72: 4/1, Week 84: 2/0, Week 96: 2/0, Week 108: 1/0, Week 120: 1/0, Week 132: 0/0

Log rank test: p-value = 0,540
*: p < 0,05

Analysis population: A2304 SAF subpopulation "ACTIVE MS WITHOUT RELAPSES"

Figure 12.3.1.2.2: AE, disease specific events excluded, Gender = Female



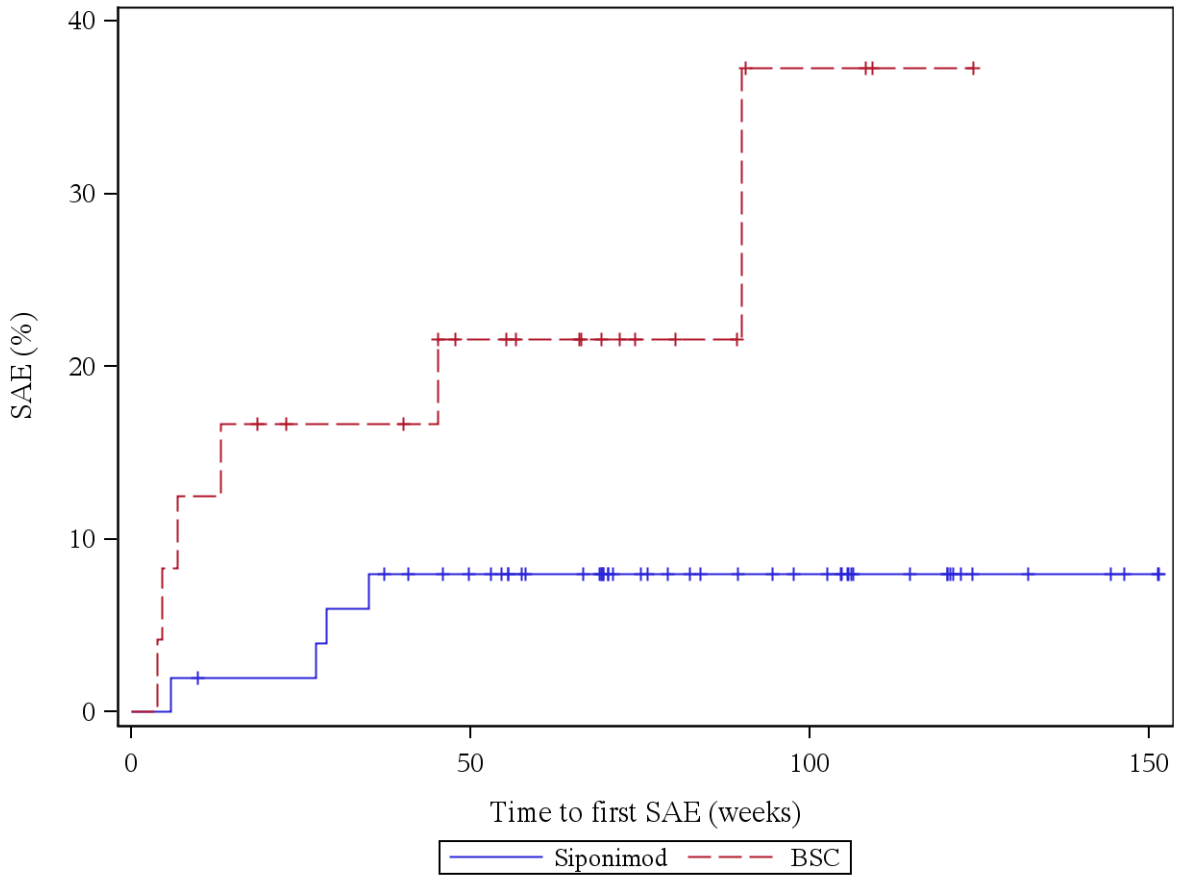
Patients at risk (Siponimod/BSC): Week 0: 76/37, Week 4: 48/28, Week 12: 33/22, Week 24: 21/18, Week 36: 13/13, Week 48: 12/13, Week 60: 7/9, Week 72: 5/8, Week 84: 4/5, Week 96: 2/2, Week 108: 2/2, Week 120: 0/1

Log rank test: p-value = 0,014 *
*: p < 0,05

Analysis population: A2304 SAF subpopulation "ACTIVE MS WITHOUT RELAPSES"

12.3.1.3: Any SAE

Figure 12.3.1.3.1: SAE, Gender = Male

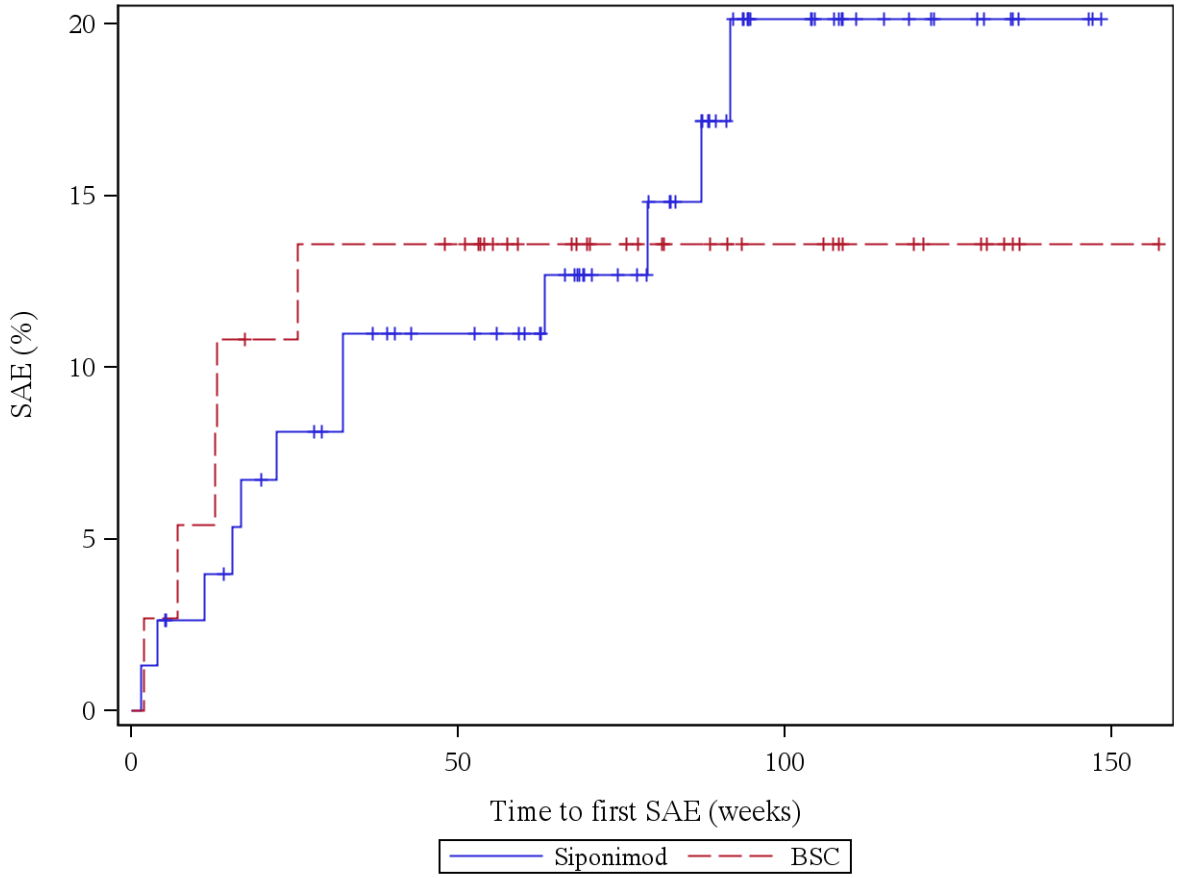


Patients at risk (Siponimod/BSC): Week 0: 51/24, Week 4: 51/23, Week 12: 49/21, Week 24: 49/18, Week 36: 46/18, Week 48: 43/14, Week 60: 36/12, Week 72: 27/8, Week 84: 22/6, Week 96: 20/3, Week 108: 12/3, Week 120: 11/1, Week 132: 5/0, Week 144: 4/0, Week 156: 0/0

Log rank test: p-value = 0,025 *
*: p < 0,05

Analysis population: A2304 SAF subpopulation "ACTIVE MS WITHOUT RELAPSES"

Figure 12.3.1.3.2: SAE, Gender = Female



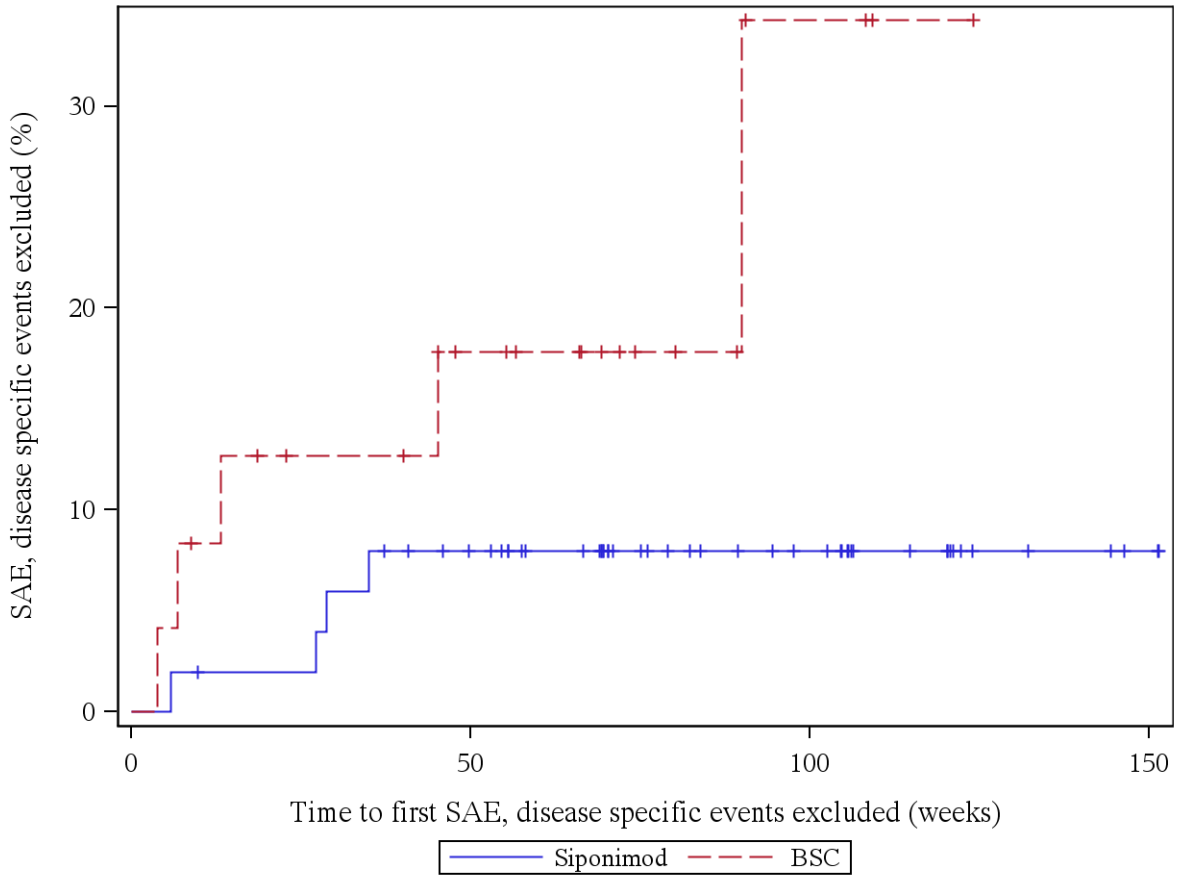
Patients at risk (Siponimod/BSC): Week 0: 76/37, Week 4: 74/36, Week 12: 71/35, Week 24: 66/32, Week 36: 62/31, Week 48: 58/30, Week 60: 55/23, Week 72: 44/19, Week 84: 36/15, Week 96: 20/12, Week 108: 16/10, Week 120: 10/7, Week 132: 6/4, Week 144: 3/1, Week 156: 0/1

Log rank test: p-value = 0,813
*: p < 0,05

Analysis population: A2304 SAF subpopulation "ACTIVE MS WITHOUT RELAPSES"

12.3.1.4: Any SAE, disease specific events excluded

Figure 12.3.1.4.1: SAE, disease specific events excluded, Gender = Male

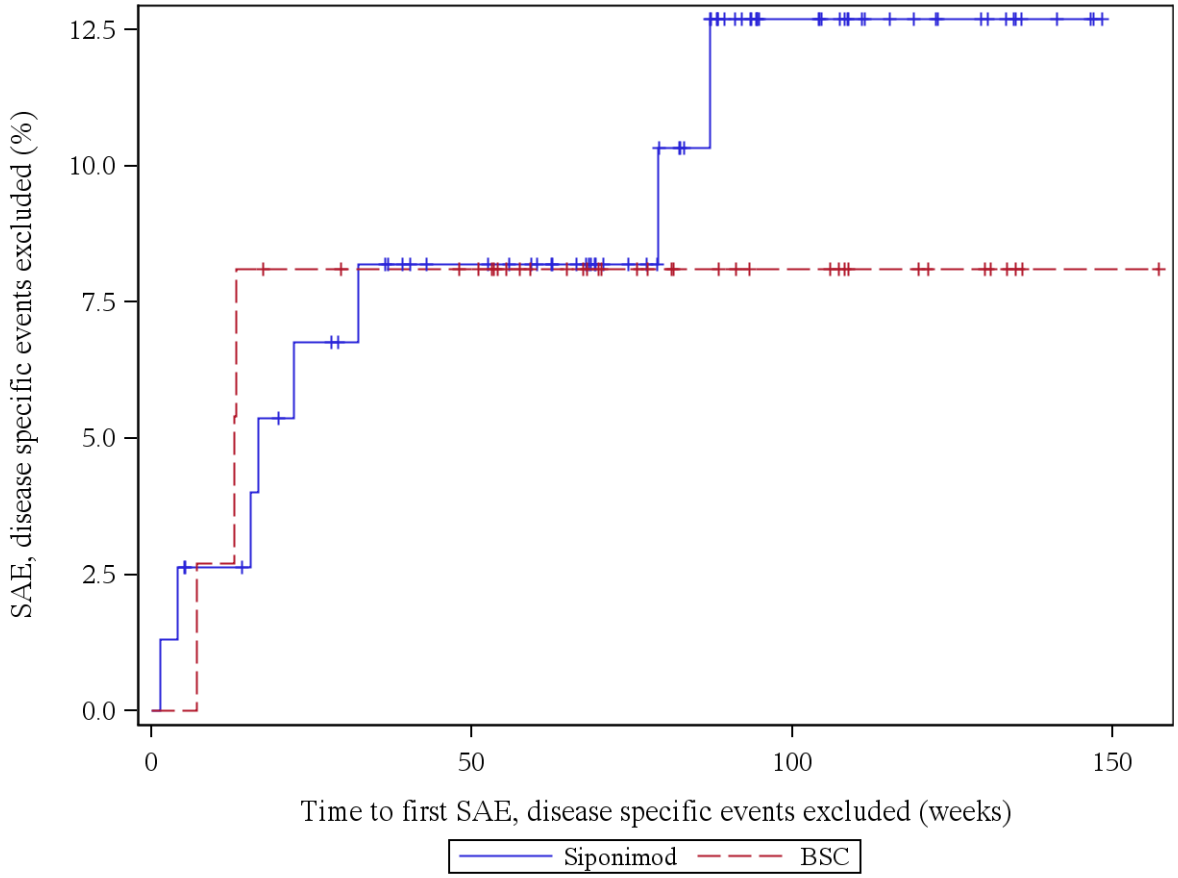


Patients at risk (Siponimod/BSC): Week 0: 51/24, Week 4: 51/23, Week 12: 49/21, Week 24: 49/18, Week 36: 46/18, Week 48: 43/14, Week 60: 36/12, Week 72: 27/8, Week 84: 22/6, Week 96: 20/3, Week 108: 12/3, Week 120: 11/1, Week 132: 5/0, Week 144: 4/0, Week 156: 0/0

Log rank test: p-value = 0,067
*: p < 0,05

Analysis population: A2304 SAF subpopulation "ACTIVE MS WITHOUT RELAPSES"

Figure 12.3.1.4.2: SAE, disease specific events excluded, Gender = Female



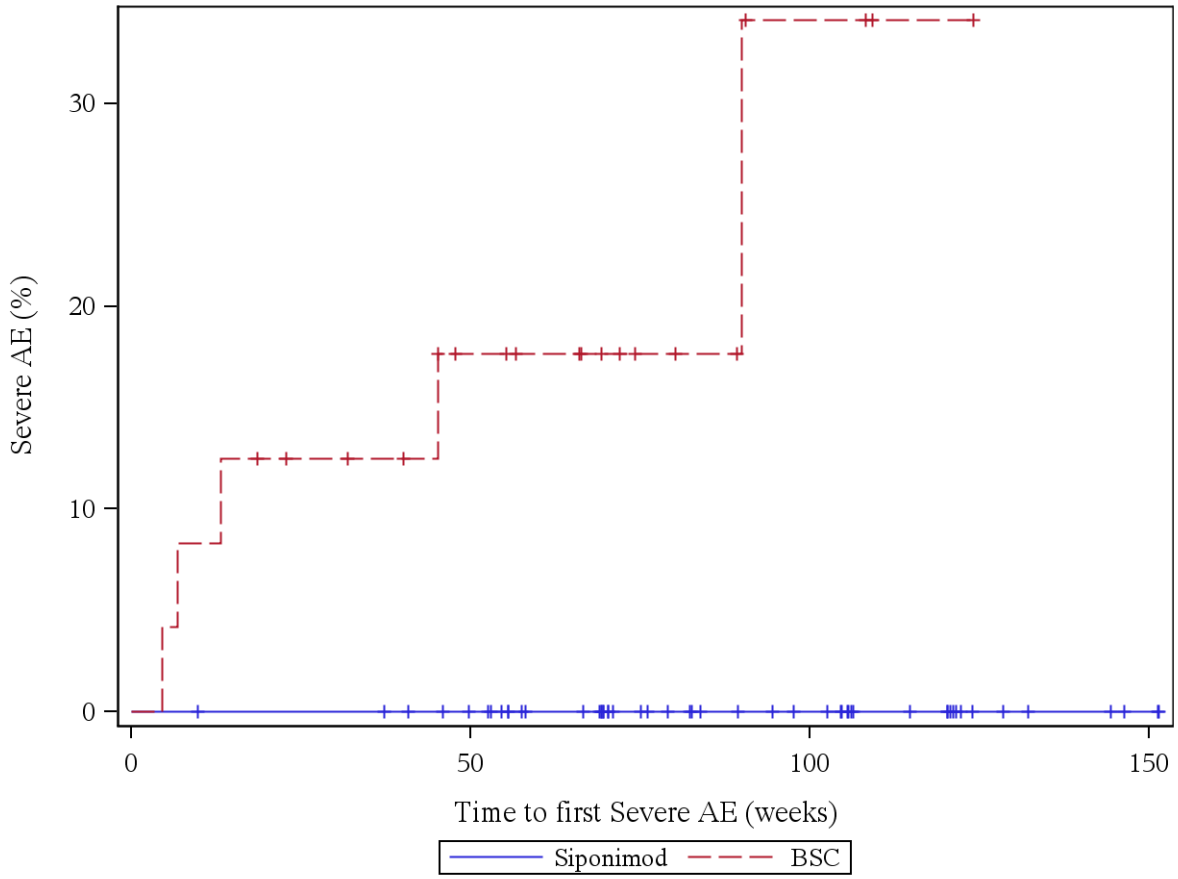
Patients at risk (Siponimod/BSC): Week 0: 76/37, Week 4: 74/37, Week 12: 72/36, Week 24: 67/33, Week 36: 64/32, Week 48: 59/31, Week 60: 56/24, Week 72: 46/19, Week 84: 38/15, Week 96: 23/12, Week 108: 19/10, Week 120: 12/7, Week 132: 8/4, Week 144: 3/1, Week 156: 0/1

Log rank test: p-value = 0,731
*: p < 0,05

Analysis population: A2304 SAF subpopulation "ACTIVE MS WITHOUT RELAPSES"

12.3.1.5: Any severe AE

Figure 12.3.1.5.1: Severe AE, Gender = Male

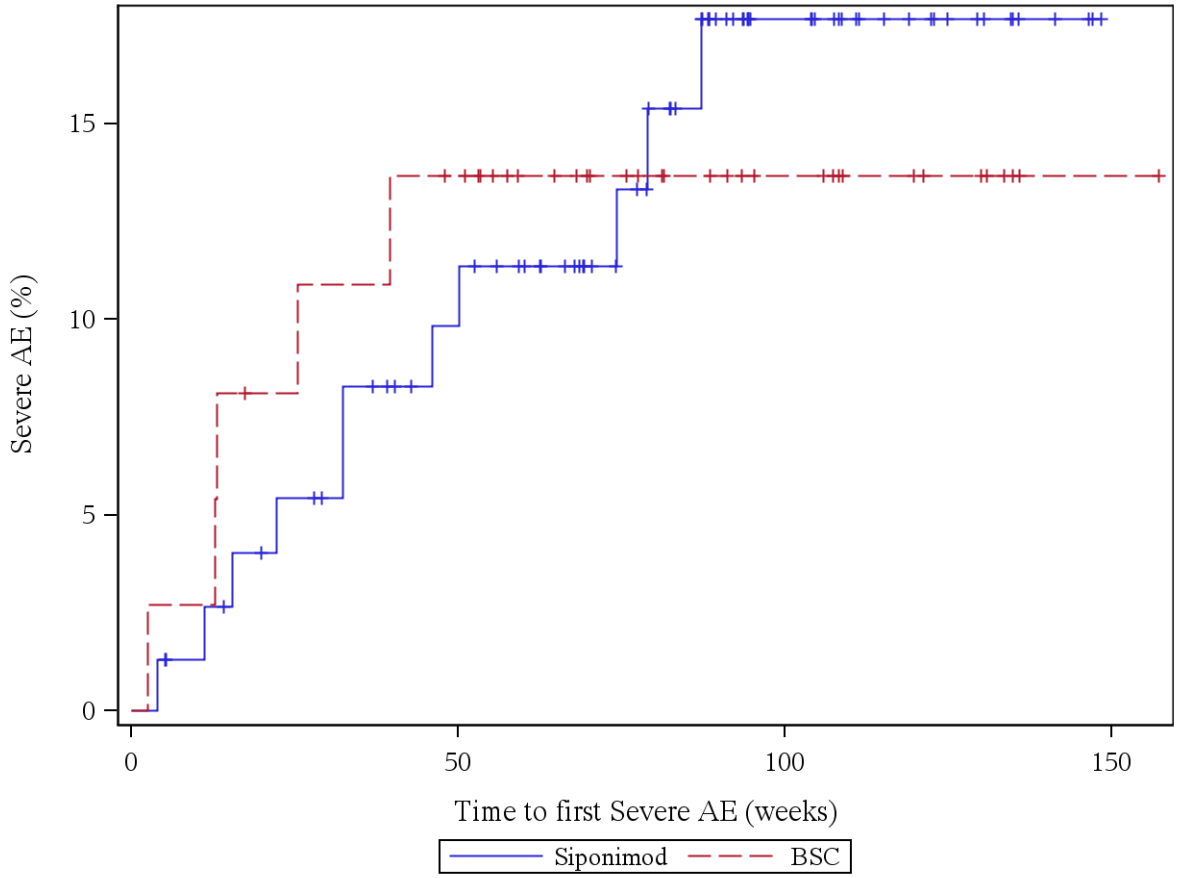


Patients at risk (Siponimod/BSC): Week 0: 51/24, Week 4: 51/24, Week 12: 50/22, Week 24: 50/19, Week 36: 50/18, Week 48: 47/14, Week 60: 39/12, Week 72: 30/8, Week 84: 24/6, Week 96: 22/3, Week 108: 14/3, Week 120: 13/1, Week 132: 5/0, Week 144: 4/0, Week 156: 0/0

Log rank test: p-value = -
*: p < 0,05

Analysis population: A2304 SAF subpopulation "ACTIVE MS WITHOUT RELAPSES"

Figure 12.3.1.5.2: Severe AE, Gender = Female



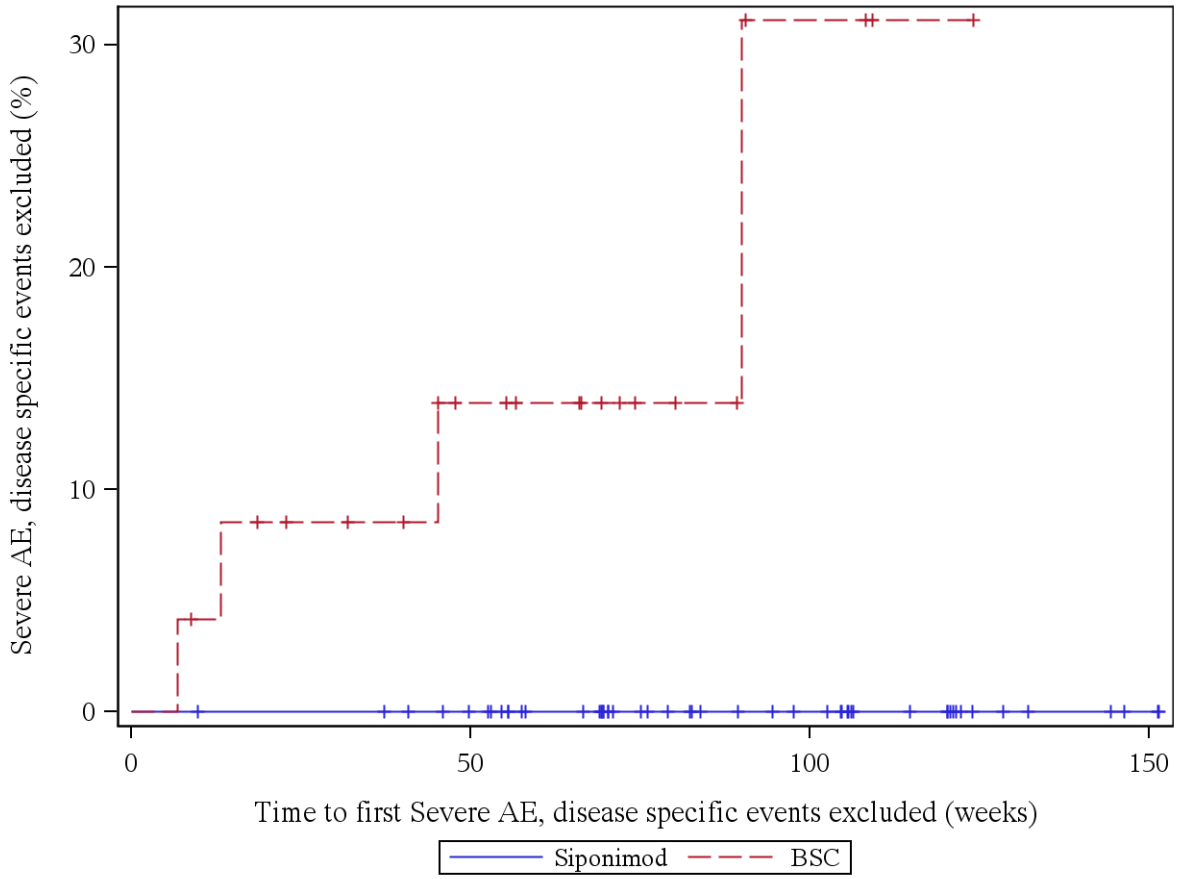
Patients at risk (Siponimod/BSC): Week 0: 76/37, Week 4: 75/36, Week 12: 72/36, Week 24: 68/33, Week 36: 64/32, Week 48: 59/30, Week 60: 55/24, Week 72: 46/20, Week 84: 37/16, Week 96: 22/12, Week 108: 18/10, Week 120: 12/7, Week 132: 7/4, Week 144: 3/1, Week 156: 0/1

Log rank test: p-value = 0,917
*: p < 0,05

Analysis population: A2304 SAF subpopulation "ACTIVE MS WITHOUT RELAPSES"

12.3.1.6: Any severe AE, disease specific events excluded

Figure 12.3.1.6.1: Severe AE, disease specific events excluded, Gender = Male

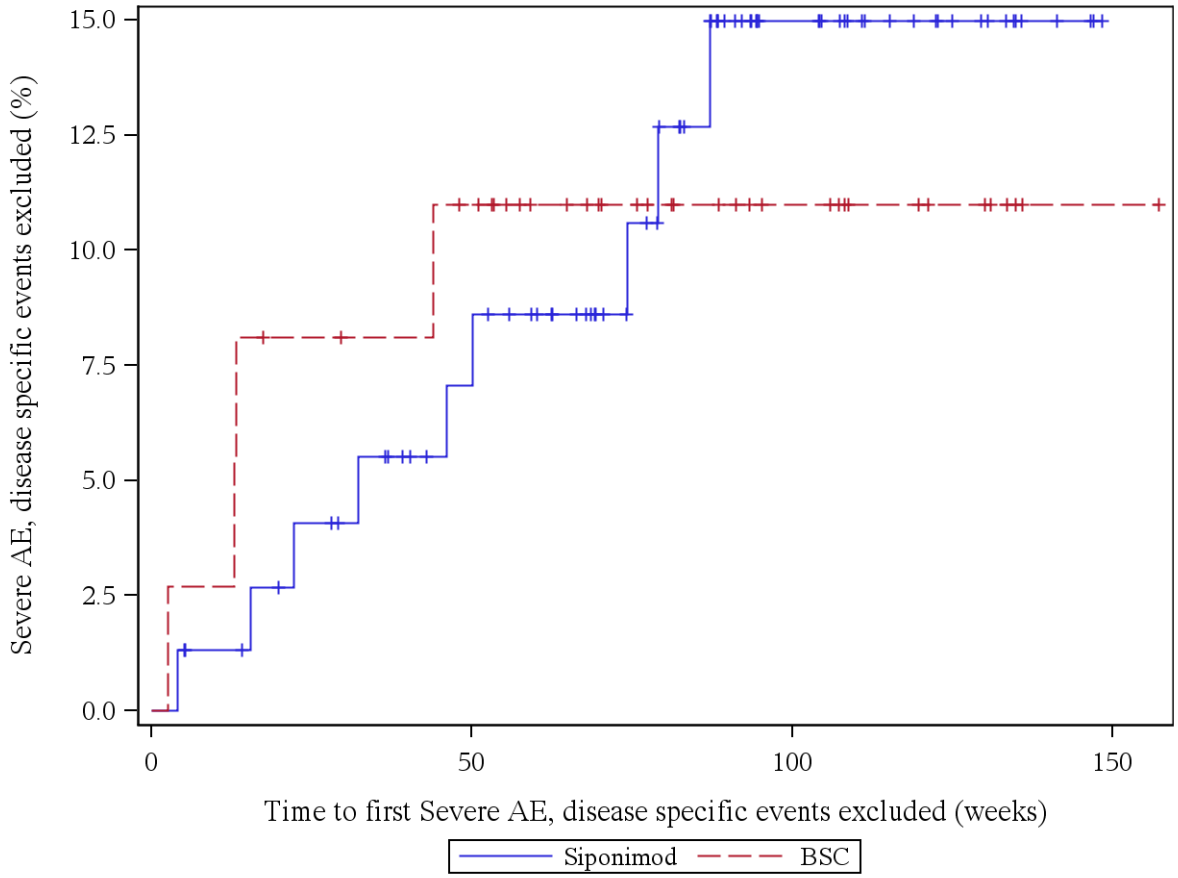


Patients at risk (Siponimod/BSC): Week 0: 51/24, Week 4: 51/24, Week 12: 50/22, Week 24: 50/19, Week 36: 50/18, Week 48: 47/14, Week 60: 39/12, Week 72: 30/8, Week 84: 24/6, Week 96: 22/3, Week 108: 14/3, Week 120: 13/1, Week 132: 5/0, Week 144: 4/0, Week 156: 0/0

Log rank test: p-value = -
*: p < 0,05

Analysis population: A2304 SAF subpopulation "ACTIVE MS WITHOUT RELAPSES"

Figure 12.3.1.6.2: Severe AE, disease specific events excluded, Gender = Female



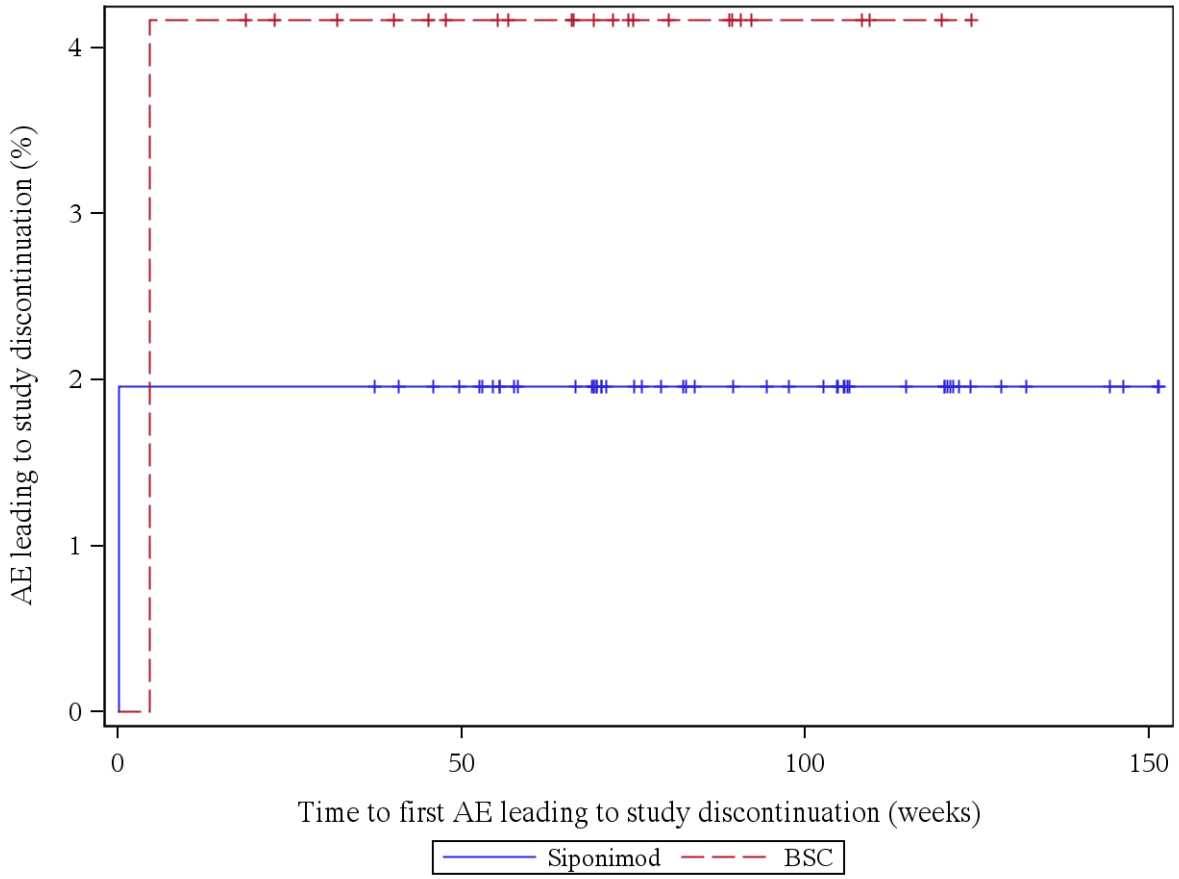
Patients at risk (Siponimod/BSC): Week 0: 76/37, Week 4: 75/36, Week 12: 73/36, Week 24: 69/33, Week 36: 66/32, Week 48: 60/30, Week 60: 56/24, Week 72: 47/20, Week 84: 38/16, Week 96: 23/12, Week 108: 19/10, Week 120: 13/7, Week 132: 8/4, Week 144: 3/1, Week 156: 0/1

Log rank test: p-value = 0,917
*: p < 0,05

Analysis population: A2304 SAF subpopulation "ACTIVE MS WITHOUT RELAPSES"

12.3.1.7: Any AE leading to study discontinuation

Figure 12.3.1.7.1: AE leading to study discontinuation, Gender = Male

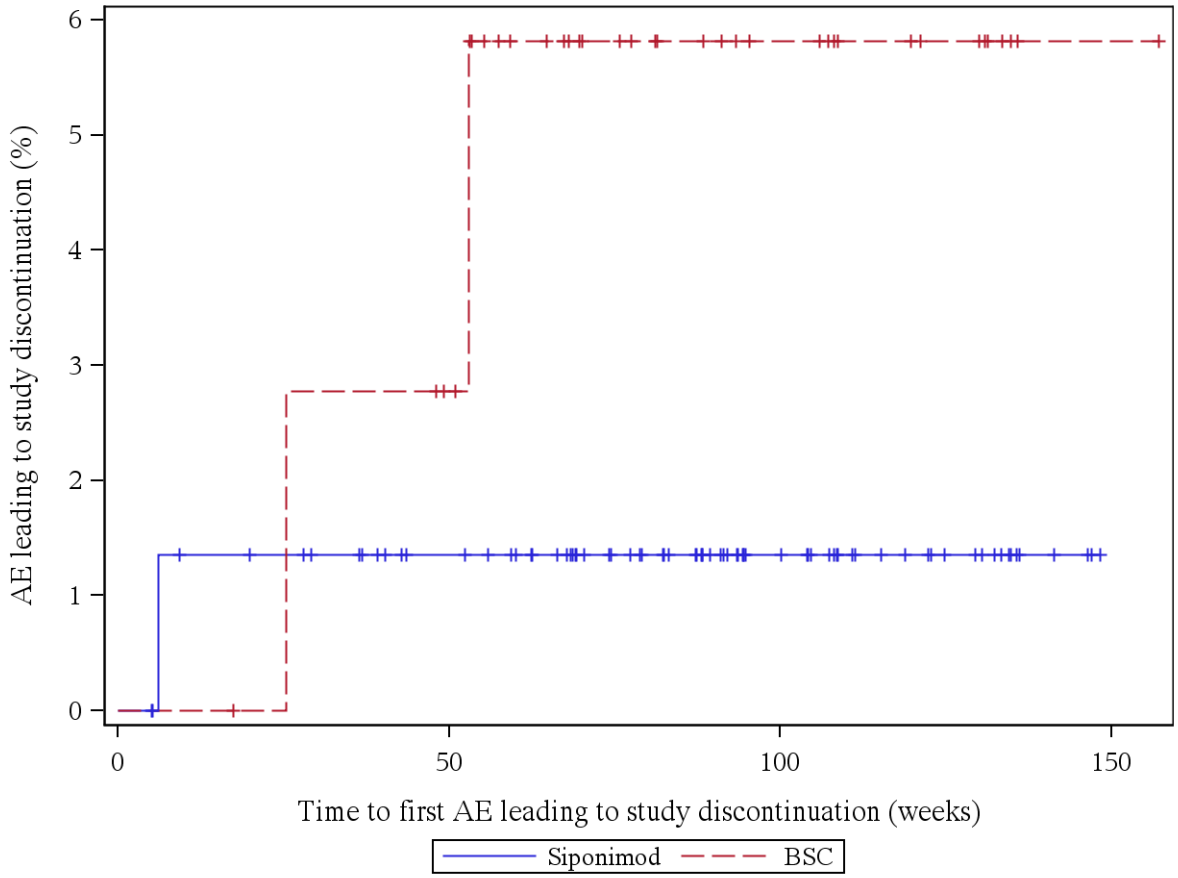


Patients at risk (Siponimod/BSC): Week 0: 51/24, Week 4: 50/24, Week 12: 50/23, Week 24: 50/21, Week 36: 50/20, Week 48: 47/17, Week 60: 39/15, Week 72: 30/11, Week 84: 24/8, Week 96: 22/4, Week 108: 14/4, Week 120: 13/1, Week 132: 5/0, Week 144: 4/0, Week 156: 0/0

Log rank test: p-value = 0,590
*: p < 0,05

Analysis population: A2304 SAF subpopulation "ACTIVE MS WITHOUT RELAPSES"

Figure 12.3.1.7.2: AE leading to study discontinuation, Gender = Female



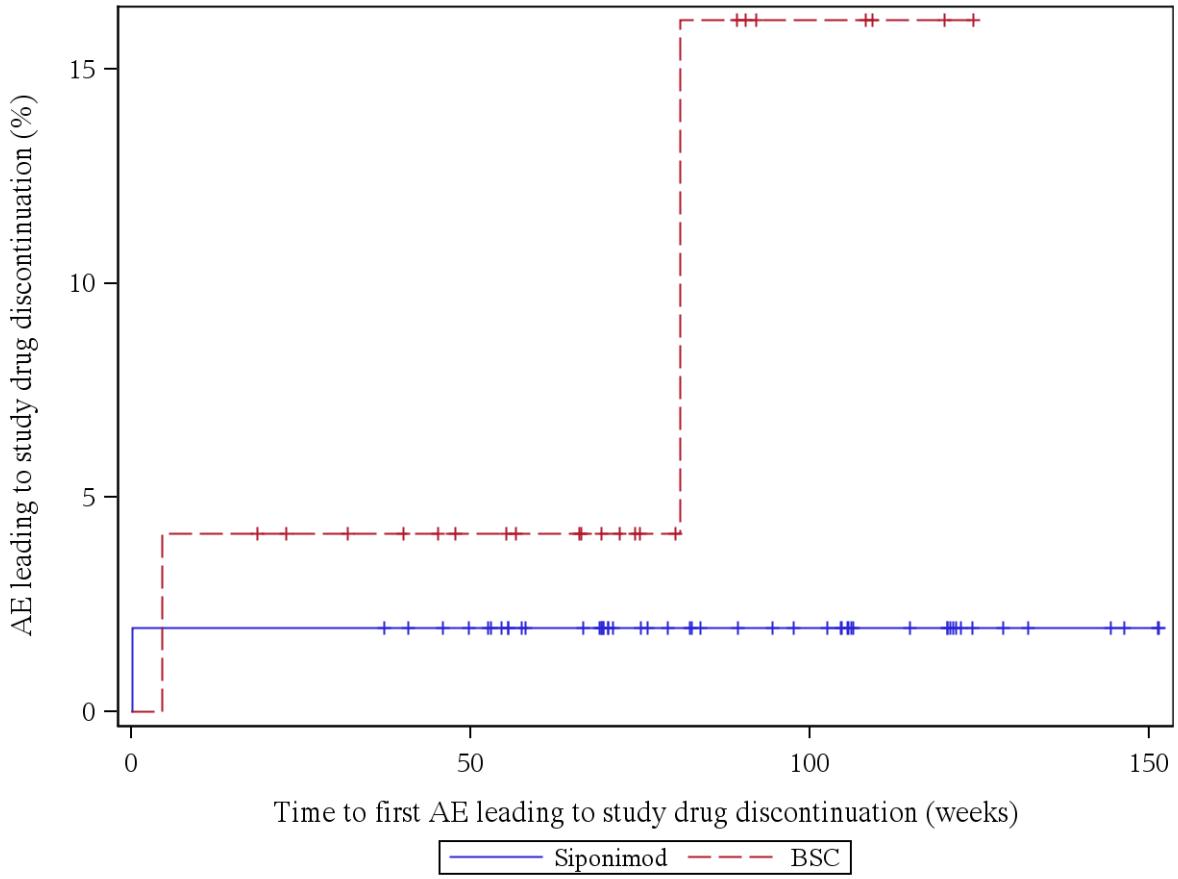
Patients at risk (Siponimod/BSC): Week 0: 76/37, Week 4: 76/37, Week 12: 72/37, Week 24: 71/36, Week 36: 69/35, Week 48: 63/34, Week 60: 60/26, Week 72: 50/21, Week 84: 42/17, Week 96: 27/13, Week 108: 22/11, Week 120: 15/8, Week 132: 10/4, Week 144: 3/1, Week 156: 0/1

Log rank test: p-value = 0,227
*: p < 0,05

Analysis population: A2304 SAF subpopulation "ACTIVE MS WITHOUT RELAPSES"

12.3.1.8: Any AE leading to study drug discontinuation

Figure 12.3.1.8.1: AE leading to study drug discontinuation, Gender = Male

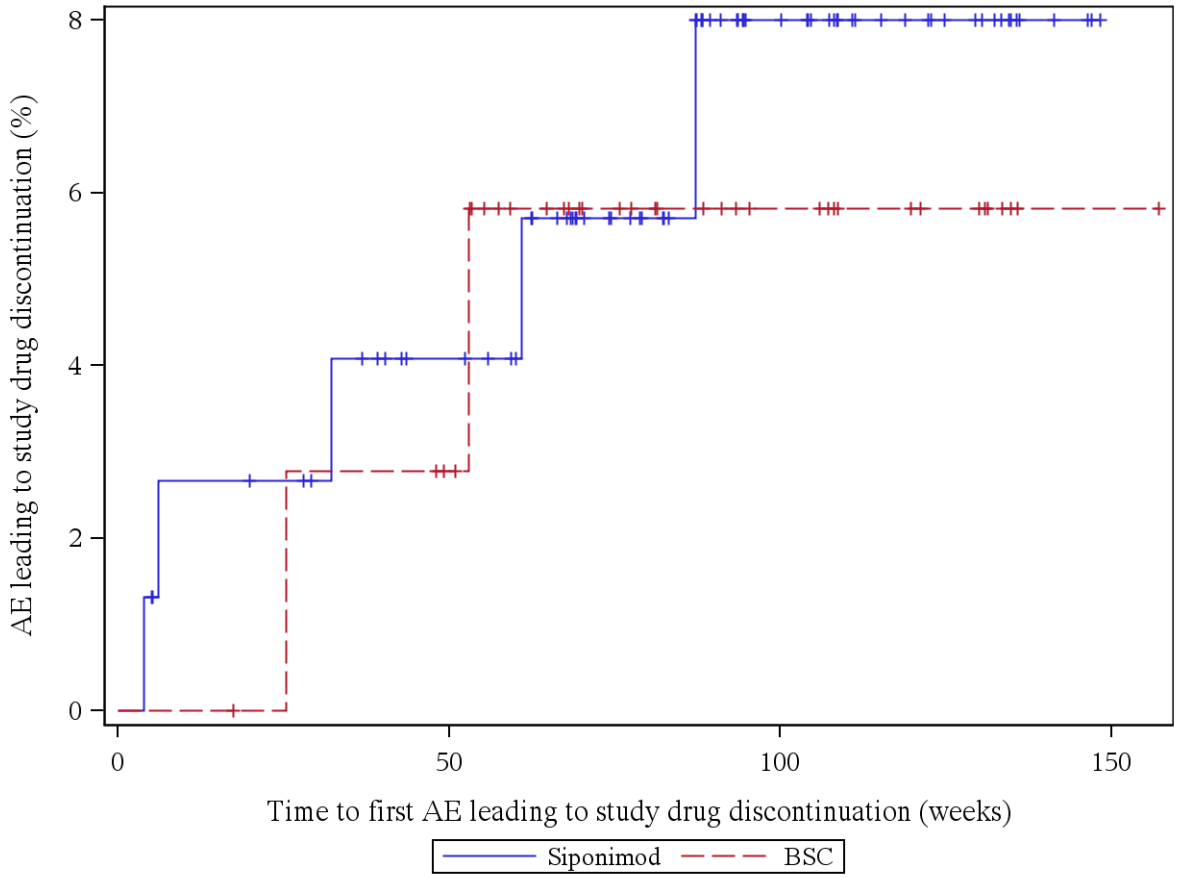


Patients at risk (Siponimod/BSC): Week 0: 51/24, Week 4: 50/24, Week 12: 50/23, Week 24: 50/21, Week 36: 50/20, Week 48: 47/17, Week 60: 39/15, Week 72: 30/11, Week 84: 24/7, Week 96: 22/4, Week 108: 14/4, Week 120: 13/1, Week 132: 5/0, Week 144: 4/0, Week 156: 0/0

Log rank test: p-value = 0,150
*: p < 0,05

Analysis population: A2304 SAF subpopulation "ACTIVE MS WITHOUT RELAPSES"

Figure 12.3.1.8.2: AE leading to study drug discontinuation, Gender = Female



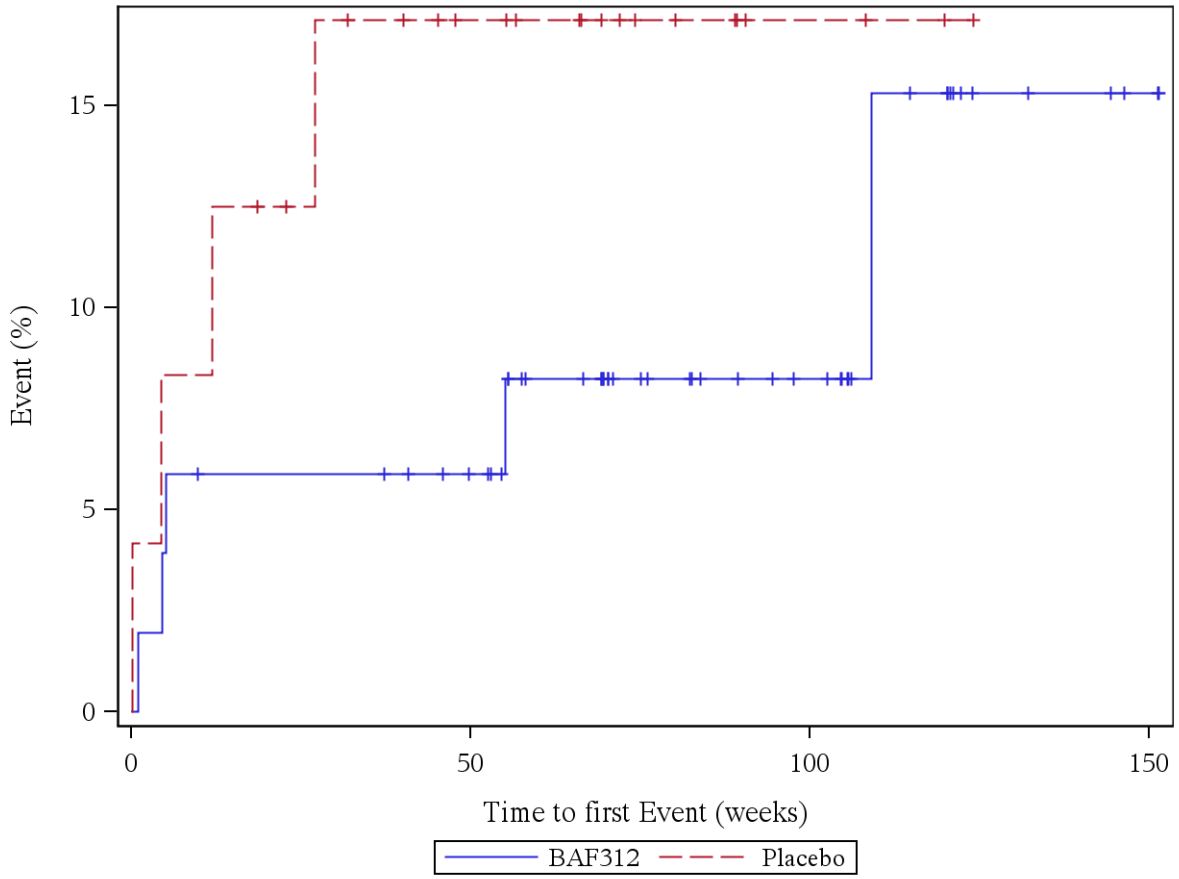
Patients at risk (Siponimod/BSC): Week 0: 76/37, Week 4: 75/37, Week 12: 72/37, Week 24: 71/36, Week 36: 68/35, Week 48: 63/34, Week 60: 60/26, Week 72: 49/21, Week 84: 41/17, Week 96: 27/13, Week 108: 22/11, Week 120: 15/8, Week 132: 10/4, Week 144: 3/1, Week 156: 0/1

Log rank test: p-value = 0,824
*: p < 0,05

Analysis population: A2304 SAF subpopulation "ACTIVE MS WITHOUT RELAPSES"

12.3.5: Time to First Adverse Event of Special Interest (SAF) by Gender

Figure 12.3.5.1.1: Hypertension (AESI), Gender = Male

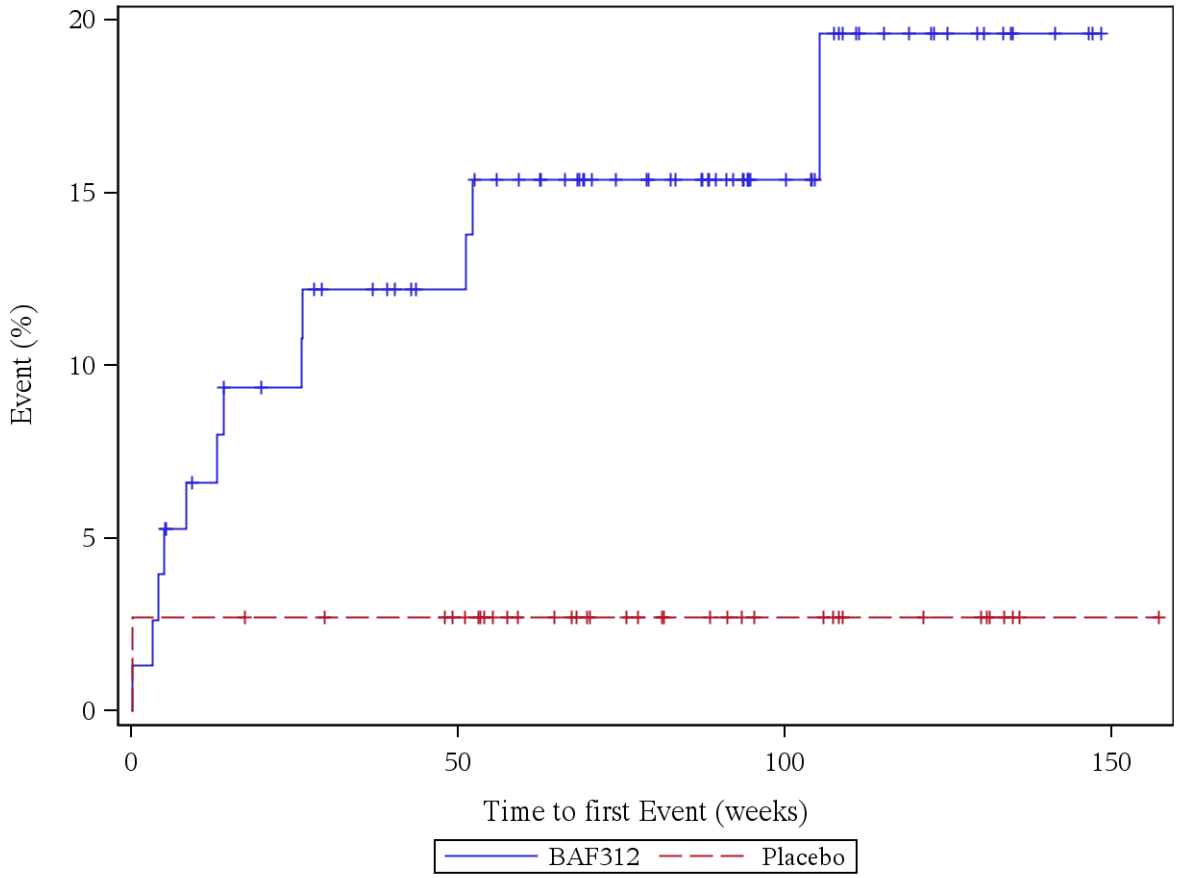


Patients at risk (BAF312/Placebo): Week 0: 51/24, Week 4: 50/23, Week 12: 47/21, Week 24: 47/19, Week 36: 47/17, Week 48: 44/14, Week 60: 35/12, Week 72: 27/8, Week 84: 22/6, Week 96: 20/3, Week 108: 13/3, Week 120: 11/1, Week 132: 5/0, Week 144: 4/0, Week 156: 0/0

Log rank test: p-value = 0,284
*: p < 0,05

Analysis population: A2304 SAF subpopulation "ACTIVE MS WITHOUT RELAPSES"

Figure 12.3.5.1.2: Hypertension (AESI), Gender = Female



Patients at risk (BAF312/Placebo): Week 0: 76/37, Week 4: 74/36, Week 12: 68/36, Week 24: 64/35, Week 36: 60/34, Week 48: 55/33, Week 60: 50/25, Week 72: 42/20, Week 84: 37/16, Week 96: 24/12, Week 108: 18/10, Week 120: 12/8, Week 132: 7/4, Week 144: 3/1, Week 156: 0/1

Log rank test: p-value = 0,042 *
*: p < 0,05

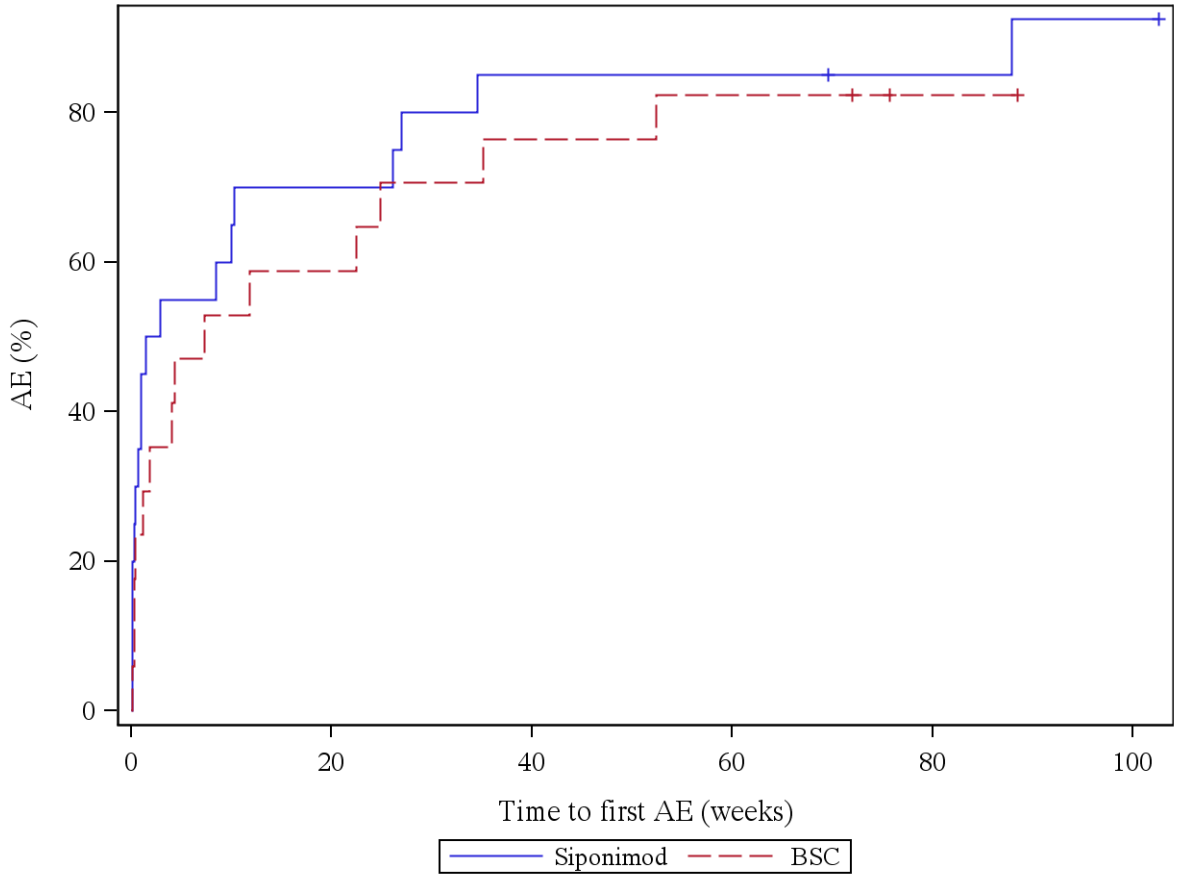
Analysis population: A2304 SAF subpopulation "ACTIVE MS WITHOUT RELAPSES"

12.4 Subgroup: Previous MS DMT

12.4.1: Time to First Adverse Event (SAF) by Previous MS DMT

12.4.1.1: Any AE

Figure 12.4.1.1.1: AE, Previous MS DMT = No

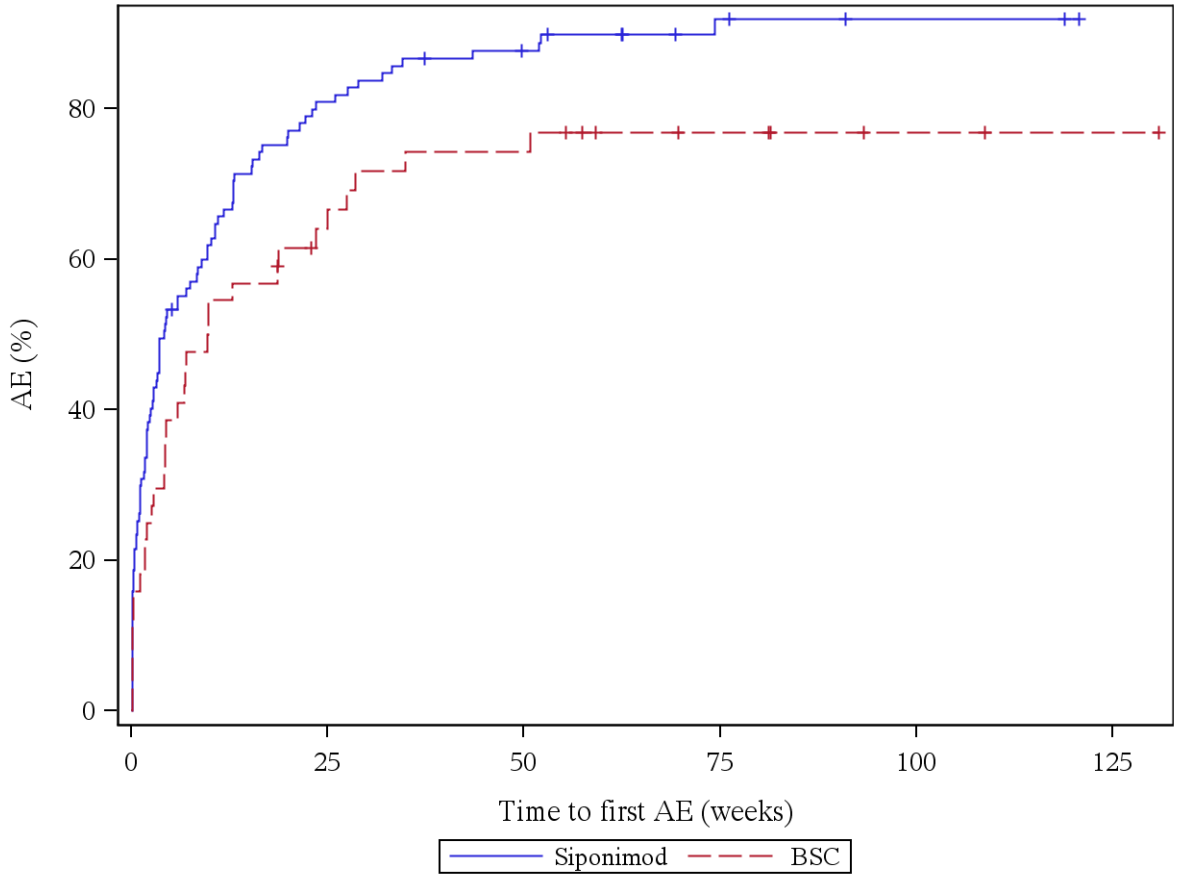


Patients at risk (Siponimod/BSC): Week 0: 20/17, Week 4: 9/10, Week 12: 6/7, Week 24: 6/6, Week 36: 3/4, Week 48: 3/4, Week 60: 3/3, Week 72: 2/2, Week 84: 2/1, Week 96: 1/0, Week 108: 0/0

Log rank test: p-value = 0,448
*: p < 0,05

Analysis population: A2304 SAF subpopulation "ACTIVE MS WITHOUT RELAPSES"

Figure 12.4.1.1.2: AE, Previous MS DMT = Yes



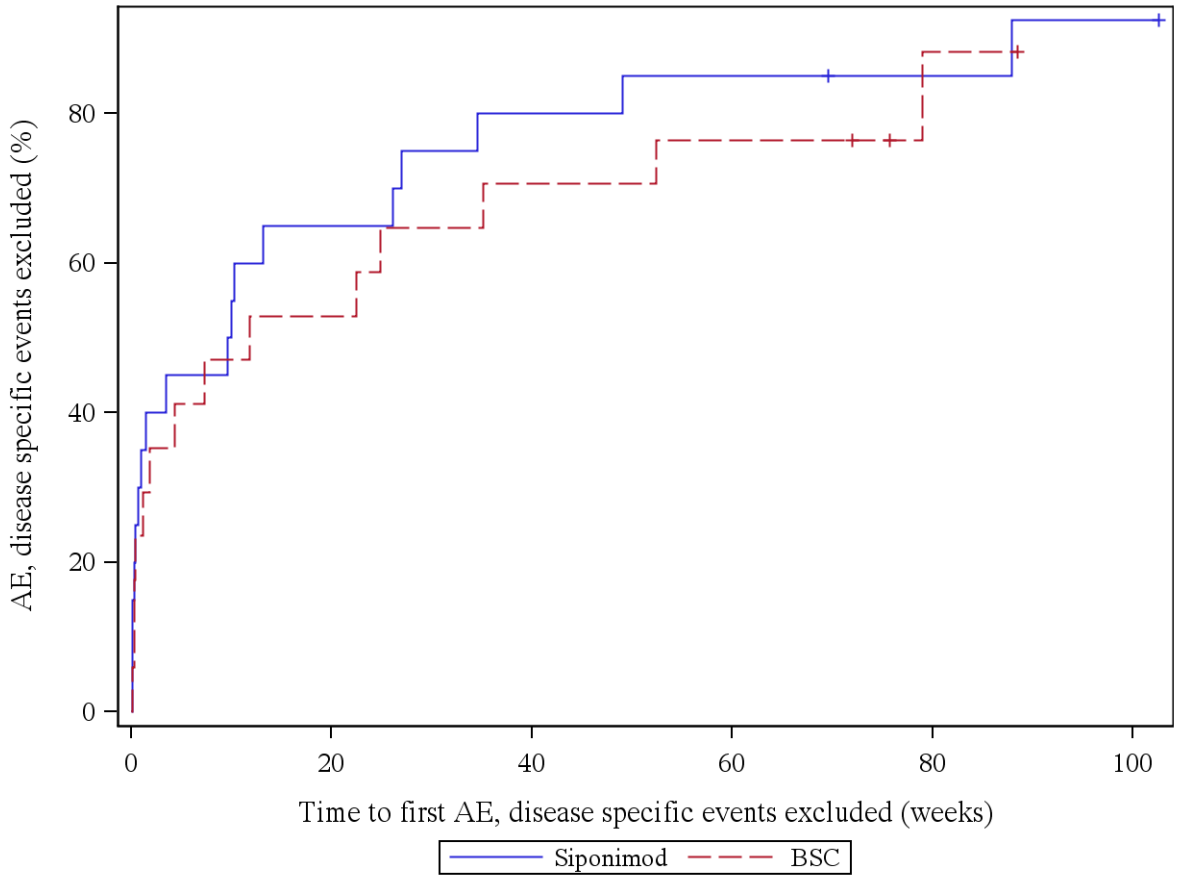
Patients at risk (Siponimod/BSC): Week 0: 107/44, Week 4: 54/31, Week 12: 35/20, Week 24: 20/14, Week 36: 14/10, Week 48: 12/10, Week 60: 8/6, Week 72: 5/5, Week 84: 3/3, Week 96: 2/2, Week 108: 2/2, Week 120: 1/1, Week 132: 0/0

Log rank test: p-value = 0,028 *
*: p < 0,05

Analysis population: A2304 SAF subpopulation "ACTIVE MS WITHOUT RELAPSES"

12.4.1.2: Any AE, disease specific events excluded

Figure 12.4.1.2.1: AE, disease specific events excluded, Previous MS DMT = No

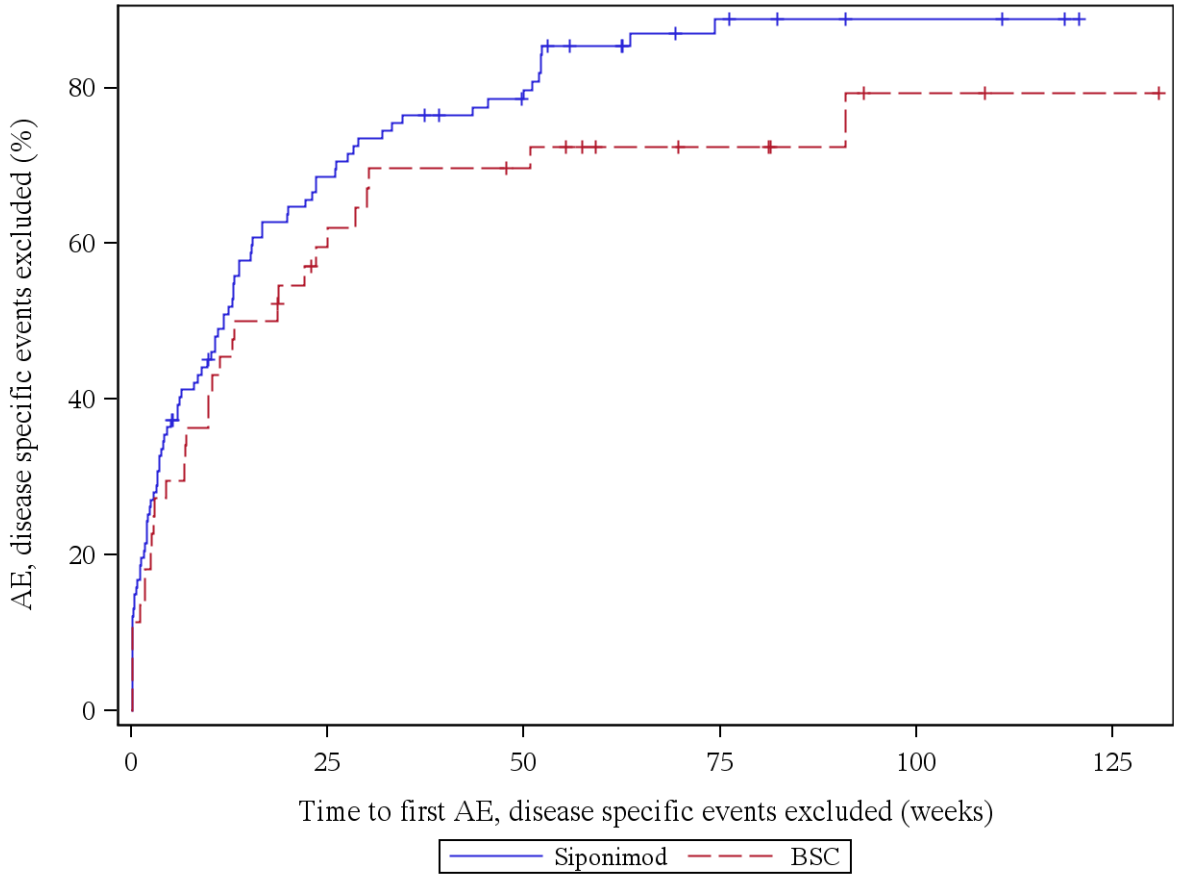


Patients at risk (Siponimod/BSC): Week 0: 20/17, Week 4: 11/11, Week 12: 8/8, Week 24: 7/7, Week 36: 4/5, Week 48: 4/5, Week 60: 3/4, Week 72: 2/3, Week 84: 2/1, Week 96: 1/0, Week 108: 0/0

Log rank test: p-value = 0,539
*: p < 0,05

Analysis population: A2304 SAF subpopulation "ACTIVE MS WITHOUT RELAPSES"

Figure 12.4.1.2.2: AE, disease specific events excluded, Previous MS DMT = Yes



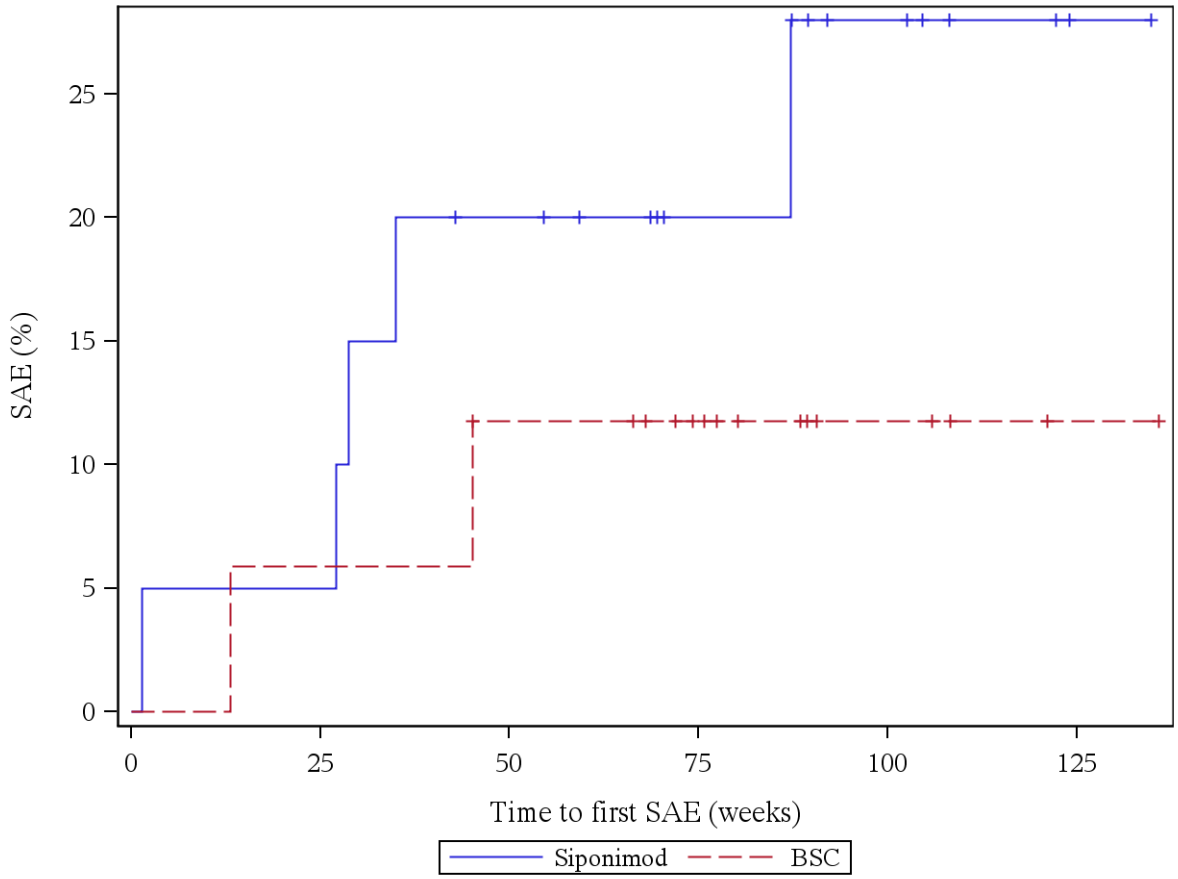
Patients at risk (Siponimod/BSC): Week 0: 107/44, Week 4: 70/32, Week 12: 50/24, Week 24: 32/16, Week 36: 24/12, Week 48: 20/11, Week 60: 11/7, Week 72: 7/6, Week 84: 4/4, Week 96: 3/2, Week 108: 3/2, Week 120: 1/1, Week 132: 0/0

Log rank test: p-value = 0,142
*: p < 0,05

Analysis population: A2304 SAF subpopulation "ACTIVE MS WITHOUT RELAPSES"

12.4.1.3: Any SAE

Figure 12.4.1.3.1: SAE, Previous MS DMT = No

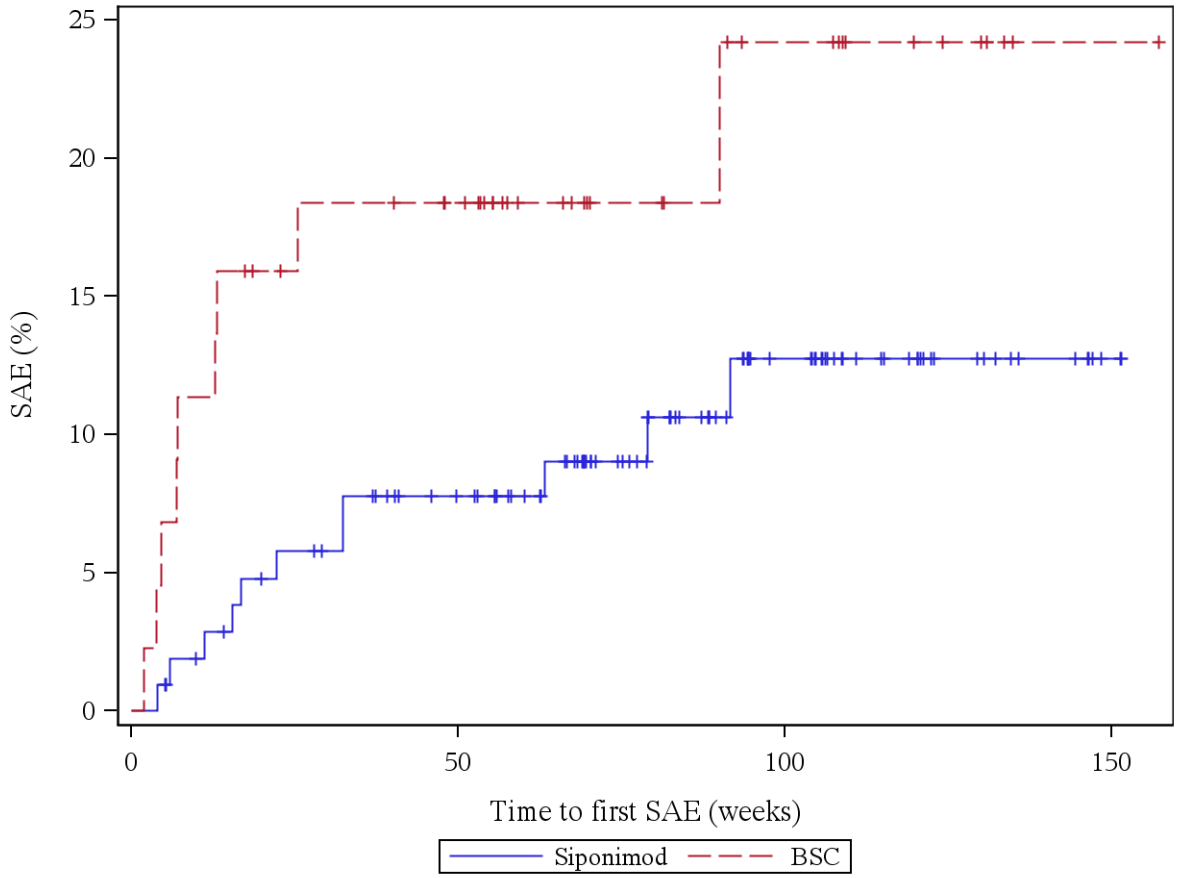


Patients at risk (Siponimod/BSC): Week 0: 20/17, Week 4: 19/17, Week 12: 19/17, Week 24: 19/16, Week 36: 16/16, Week 48: 15/14, Week 60: 13/14, Week 72: 10/11, Week 84: 10/7, Week 96: 6/4, Week 108: 4/3, Week 120: 3/2, Week 132: 1/1, Week 144: 0/0

Log rank test: p-value = 0,334
*: p < 0,05

Analysis population: A2304 SAF subpopulation "ACTIVE MS WITHOUT RELAPSES"

Figure 12.4.1.3.2: SAE, Previous MS DMT = Yes



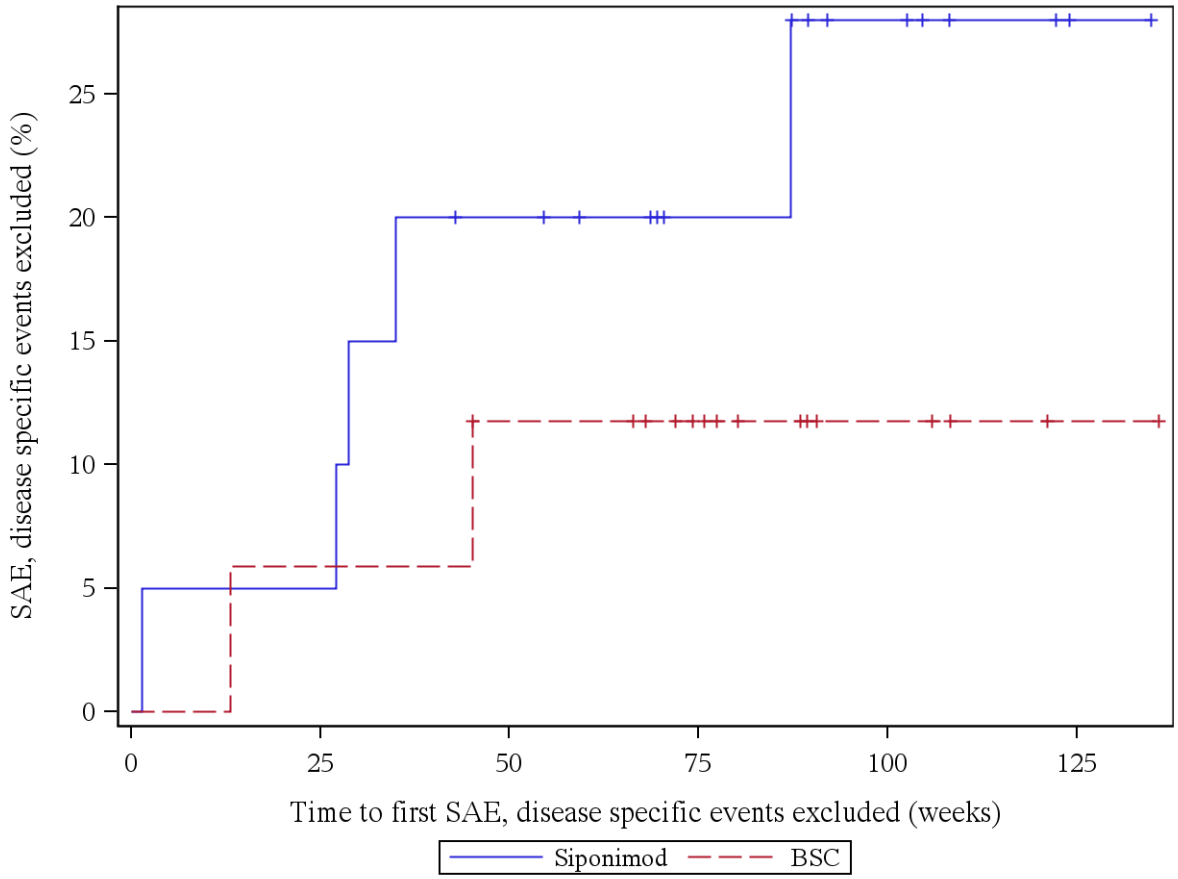
Patients at risk (Siponimod/BSC): Week 0: 107/44, Week 4: 106/42, Week 12: 101/39, Week 24: 96/34, Week 36: 92/33, Week 48: 86/30, Week 60: 78/21, Week 72: 61/16, Week 84: 48/14, Week 96: 34/11, Week 108: 24/10, Week 120: 18/6, Week 132: 10/3, Week 144: 7/1, Week 156: 0/1

Log rank test: p-value = 0,062
*: p < 0,05

Analysis population: A2304 SAF subpopulation "ACTIVE MS WITHOUT RELAPSES"

12.4.1.4: Any SAE, disease specific events excluded

Figure 12.4.1.4.1: SAE, disease specific events excluded, Previous MS DMT = No

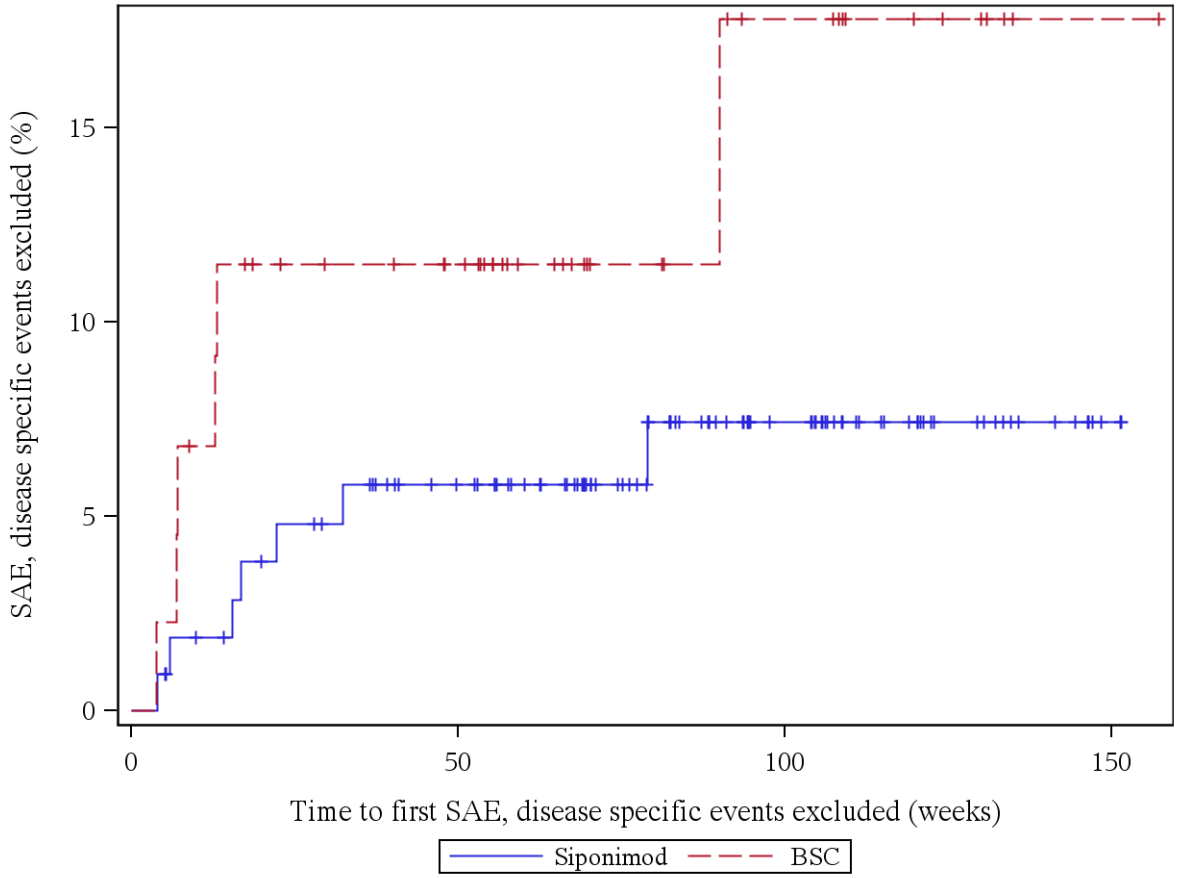


Patients at risk (Siponimod/BSC): Week 0: 20/17, Week 4: 19/17, Week 12: 19/17, Week 24: 19/16, Week 36: 16/16, Week 48: 15/14, Week 60: 13/14, Week 72: 10/11, Week 84: 10/7, Week 96: 6/4, Week 108: 4/3, Week 120: 3/2, Week 132: 1/1, Week 144: 0/0

Log rank test: p-value = 0,334
*: p < 0,05

Analysis population: A2304 SAF subpopulation "ACTIVE MS WITHOUT RELAPSES"

Figure 12.4.1.4.2: SAE, disease specific events excluded, Previous MS DMT = Yes



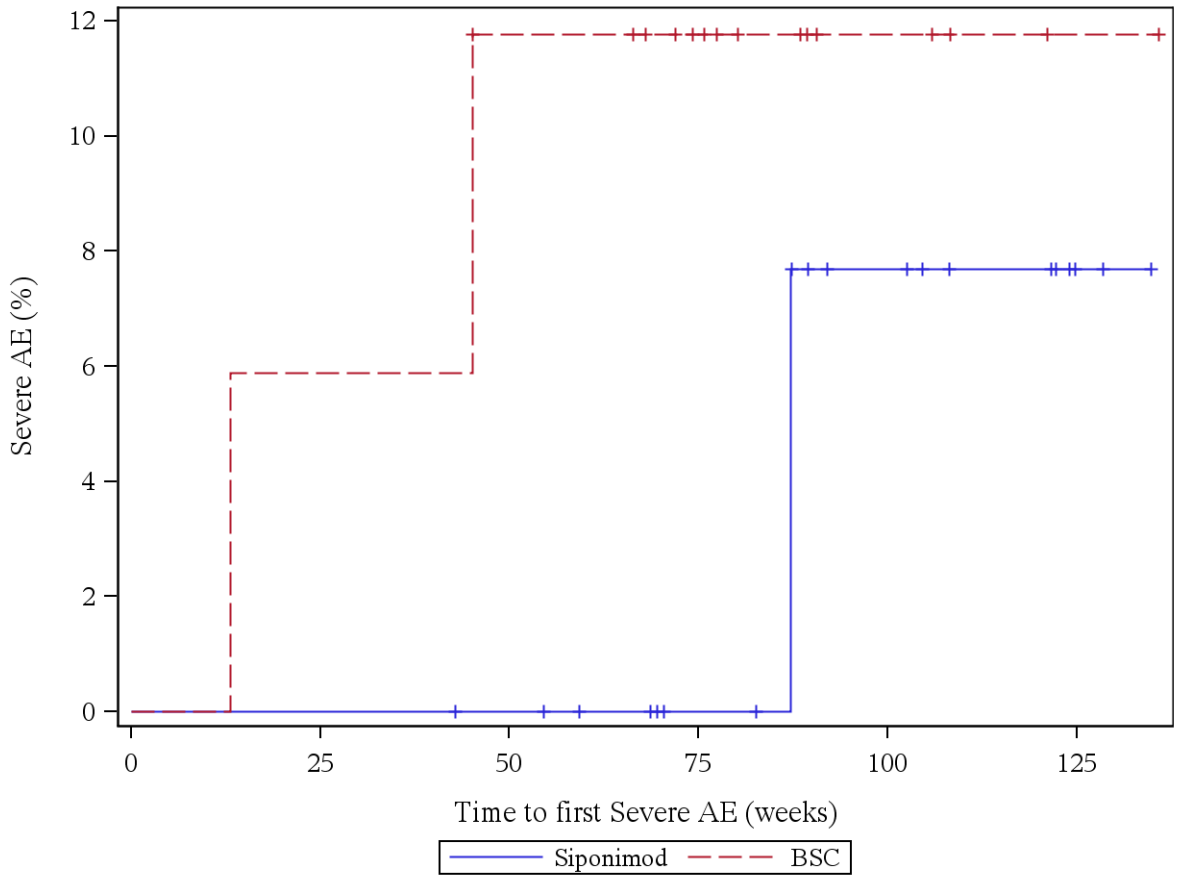
Patients at risk (Siponimod/BSC): Week 0: 107/44, Week 4: 106/43, Week 12: 102/40, Week 24: 97/35, Week 36: 94/34, Week 48: 87/31, Week 60: 79/22, Week 72: 63/16, Week 84: 50/14, Week 96: 37/11, Week 108: 27/10, Week 120: 20/6, Week 132: 12/3, Week 144: 7/1, Week 156: 0/1

Log rank test: p-value = 0,126
*: p < 0,05

Analysis population: A2304 SAF subpopulation "ACTIVE MS WITHOUT RELAPSES"

12.4.1.5: Any severe AE

Figure 12.4.1.5.1: Severe AE, Previous MS DMT = No

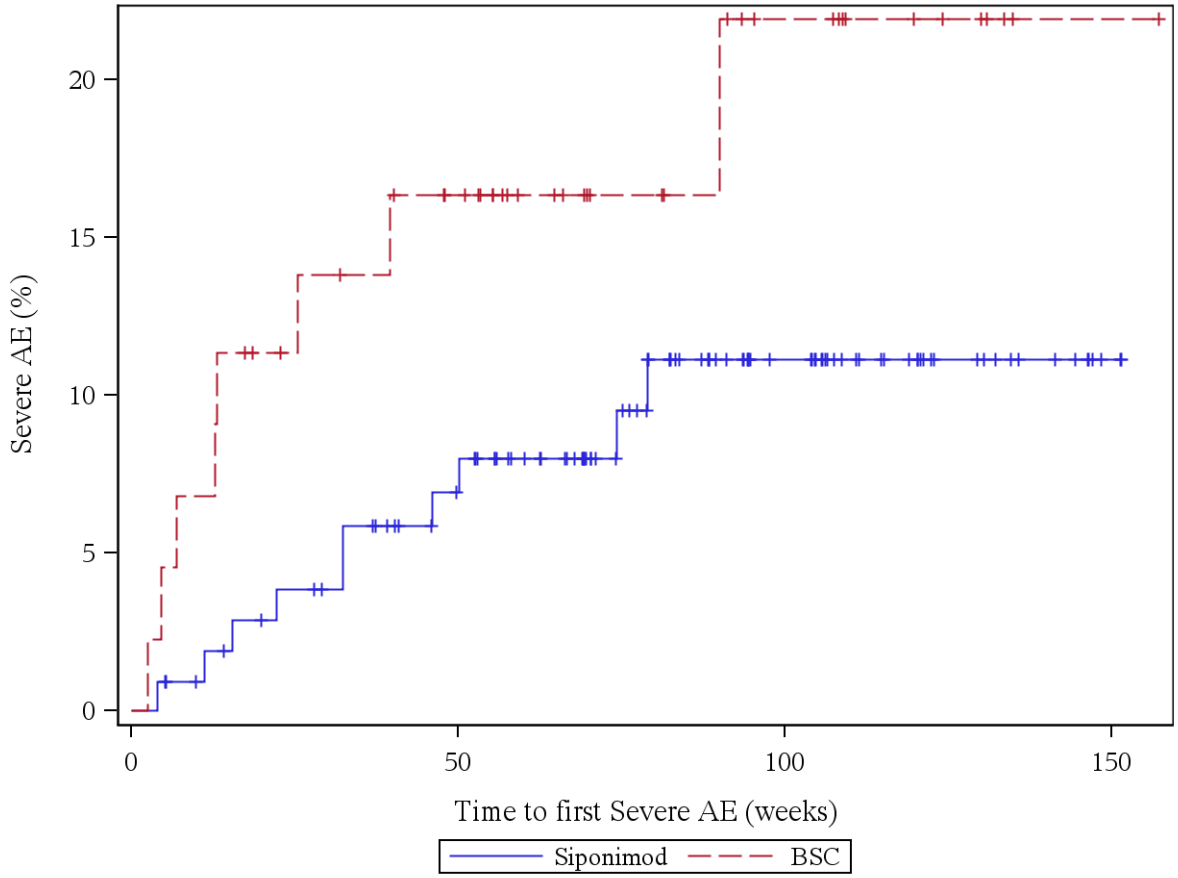


Patients at risk (Siponimod/BSC): Week 0: 20/17, Week 4: 20/17, Week 12: 20/17, Week 24: 20/16, Week 36: 20/16, Week 48: 19/14, Week 60: 17/14, Week 72: 14/11, Week 84: 13/7, Week 96: 9/4, Week 108: 7/3, Week 120: 6/2, Week 132: 1/1, Week 144: 0/0

Log rank test: p-value = 0,389
*: p < 0,05

Analysis population: A2304 SAF subpopulation "ACTIVE MS WITHOUT RELAPSES"

Figure 12.4.1.5.2: Severe AE, Previous MS DMT = Yes



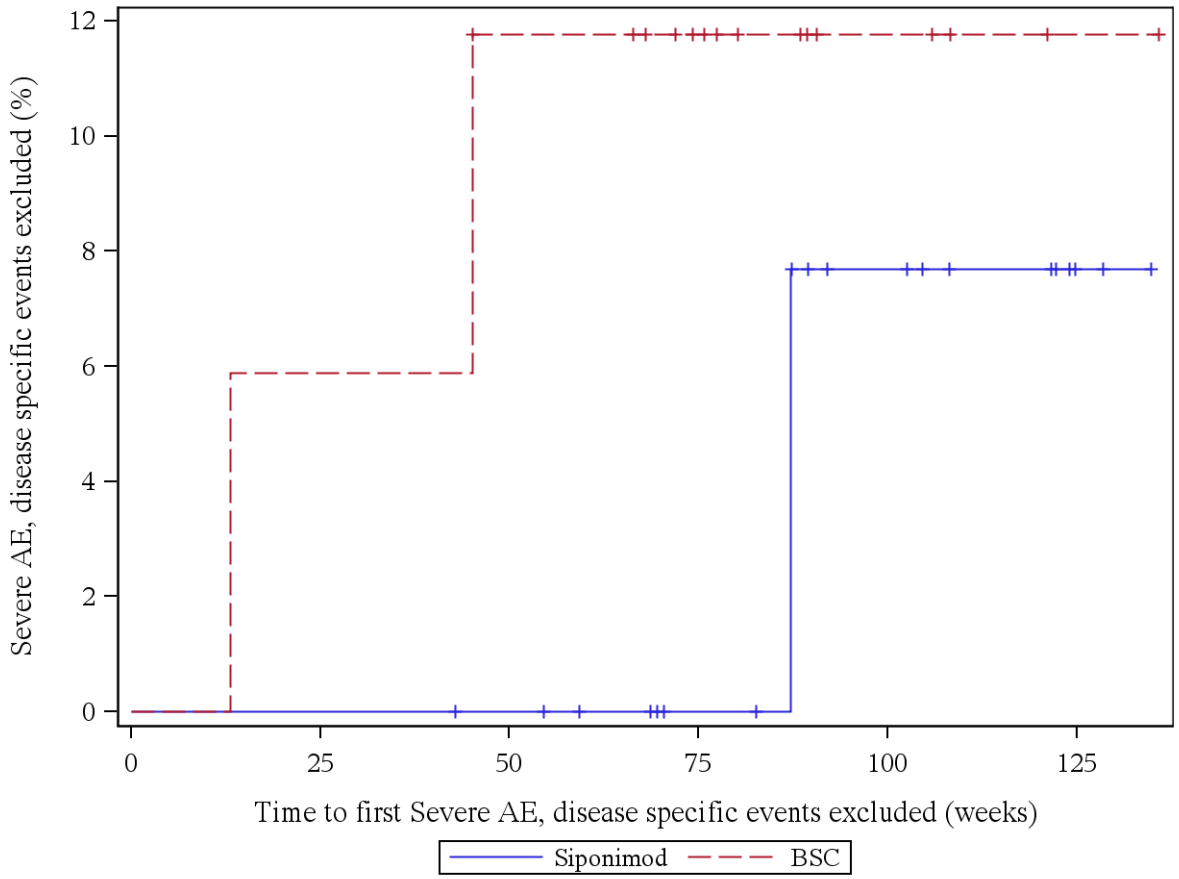
Patients at risk (Siponimod/BSC): Week 0: 107/44, Week 4: 106/43, Week 12: 102/41, Week 24: 98/36, Week 36: 94/34, Week 48: 87/30, Week 60: 77/22, Week 72: 62/17, Week 84: 48/15, Week 96: 35/11, Week 108: 25/10, Week 120: 19/6, Week 132: 11/3, Week 144: 7/1, Week 156: 0/1

Log rank test: p-value = 0,095
*: p < 0,05

Analysis population: A2304 SAF subpopulation "ACTIVE MS WITHOUT RELAPSES"

12.4.1.6: Any severe AE, disease specific events excluded

Figure 12.4.1.6.1: Severe AE, disease specific events excluded, Previous MS DMT = No

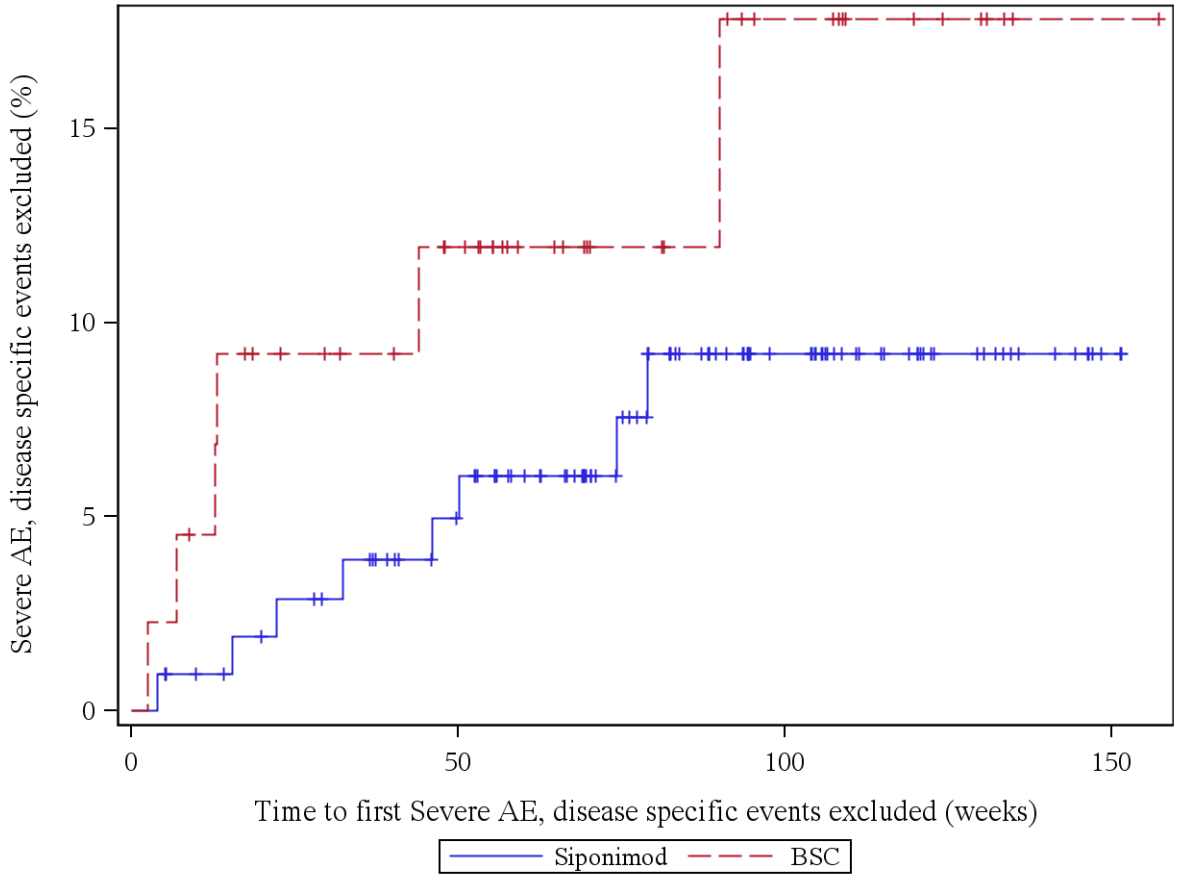


Patients at risk (Siponimod/BSC): Week 0: 20/17, Week 4: 20/17, Week 12: 20/17, Week 24: 20/16, Week 36: 20/16, Week 48: 19/14, Week 60: 17/14, Week 72: 14/11, Week 84: 13/7, Week 96: 9/4, Week 108: 7/3, Week 120: 6/2, Week 132: 1/1, Week 144: 0/0

Log rank test: p-value = 0,389
*: p < 0,05

Analysis population: A2304 SAF subpopulation "ACTIVE MS WITHOUT RELAPSES"

Figure 12.4.1.6.2: Severe AE, disease specific events excluded, Previous MS DMT = Yes



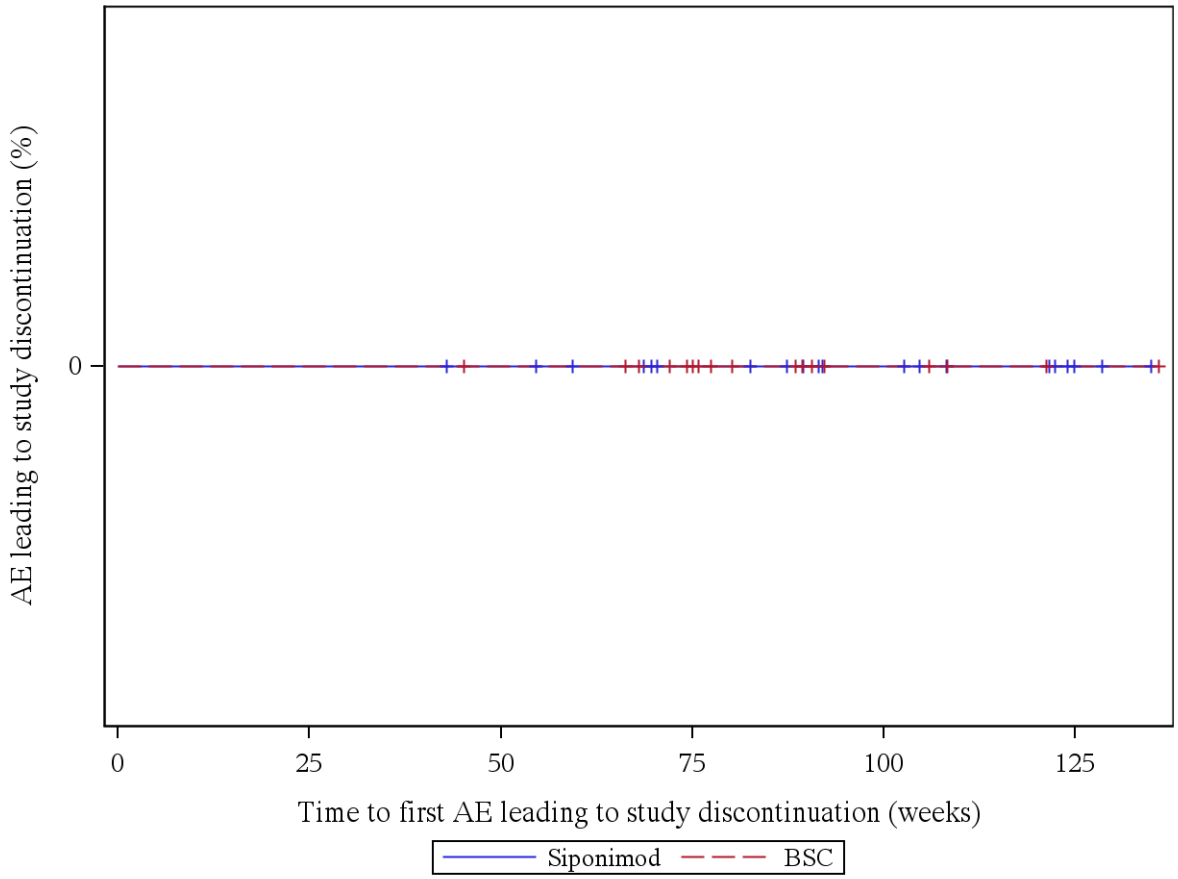
Patients at risk (Siponimod/BSC): Week 0: 107/44, Week 4: 106/43, Week 12: 103/41, Week 24: 99/36, Week 36: 96/34, Week 48: 88/30, Week 60: 78/22, Week 72: 63/17, Week 84: 49/15, Week 96: 36/11, Week 108: 26/10, Week 120: 20/6, Week 132: 12/3, Week 144: 7/1, Week 156: 0/1

Log rank test: p-value = 0,169
*: p < 0,05

Analysis population: A2304 SAF subpopulation "ACTIVE MS WITHOUT RELAPSES"

12.4.1.7: Any AE leading to study discontinuation

Figure 12.4.1.7.1: AE leading to study discontinuation, Previous MS DMT = No

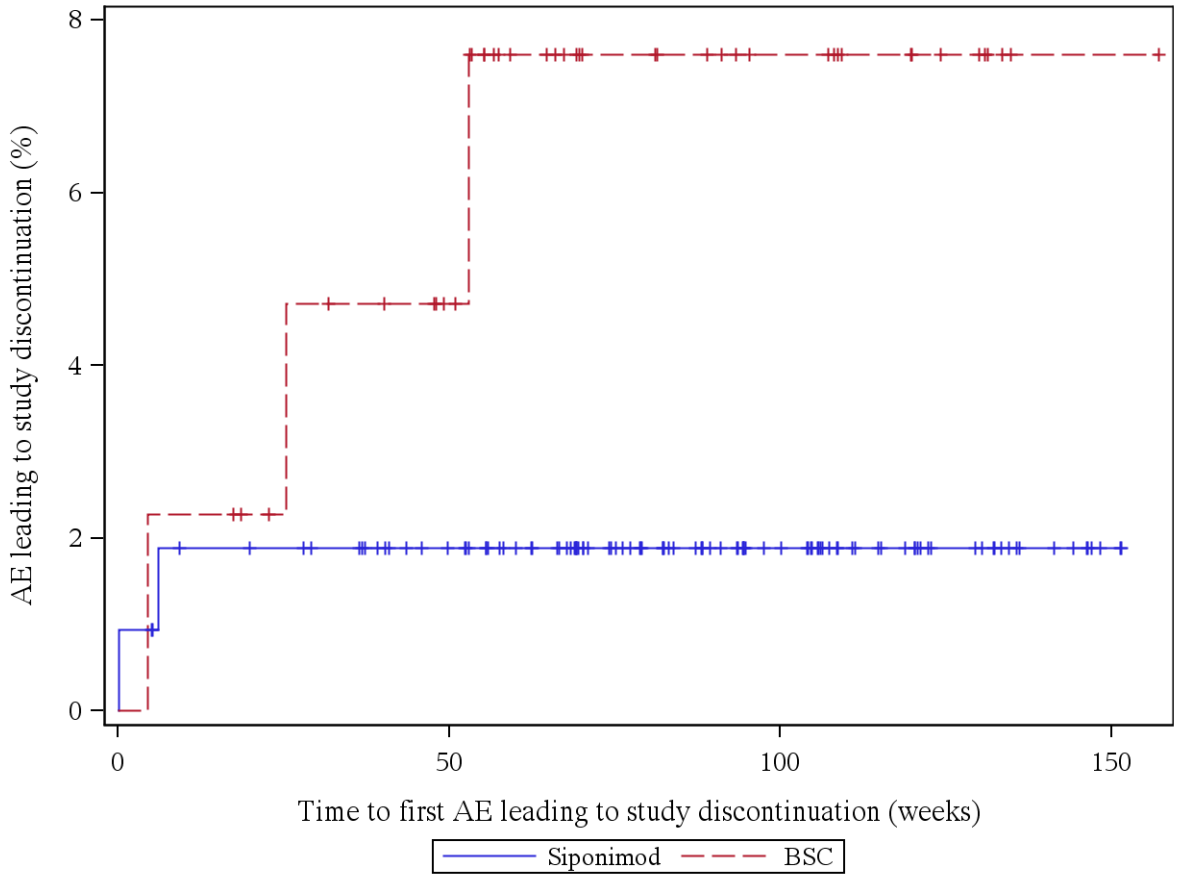


Patients at risk (Siponimod/BSC): Week 0: 20/17, Week 4: 20/17, Week 12: 20/17, Week 24: 20/17, Week 36: 20/17, Week 48: 19/16, Week 60: 17/16, Week 72: 14/13, Week 84: 13/8, Week 96: 9/4, Week 108: 7/3, Week 120: 6/2, Week 132: 1/1, Week 144: 0/0

Log rank test: p-value = -
*: p < 0,05

Analysis population: A2304 SAF subpopulation "ACTIVE MS WITHOUT RELAPSES"

Figure 12.4.1.7.2: AE leading to study discontinuation, Previous MS DMT = Yes



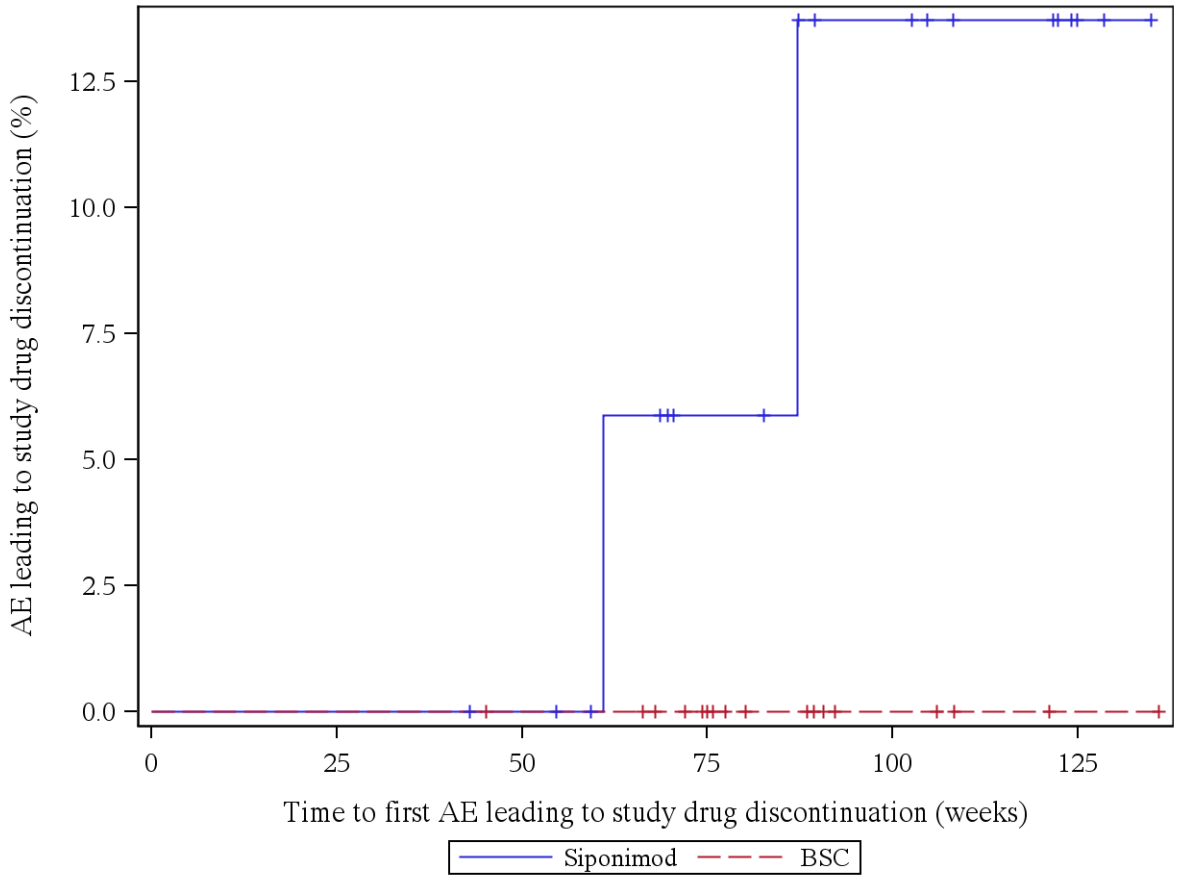
Patients at risk (Siponimod/BSC): Week 0: 107/44, Week 4: 106/44, Week 12: 102/43, Week 24: 101/40, Week 36: 99/38, Week 48: 91/35, Week 60: 82/25, Week 72: 66/19, Week 84: 53/17, Week 96: 40/13, Week 108: 29/12, Week 120: 22/7, Week 132: 14/3, Week 144: 7/1, Week 156: 0/1

Log rank test: p-value = 0,121
*: p < 0,05

Analysis population: A2304 SAF subpopulation "ACTIVE MS WITHOUT RELAPSES"

12.4.1.8: Any AE leading to study drug discontinuation

Figure 12.4.1.8.1: AE leading to study drug discontinuation, Previous MS DMT = No

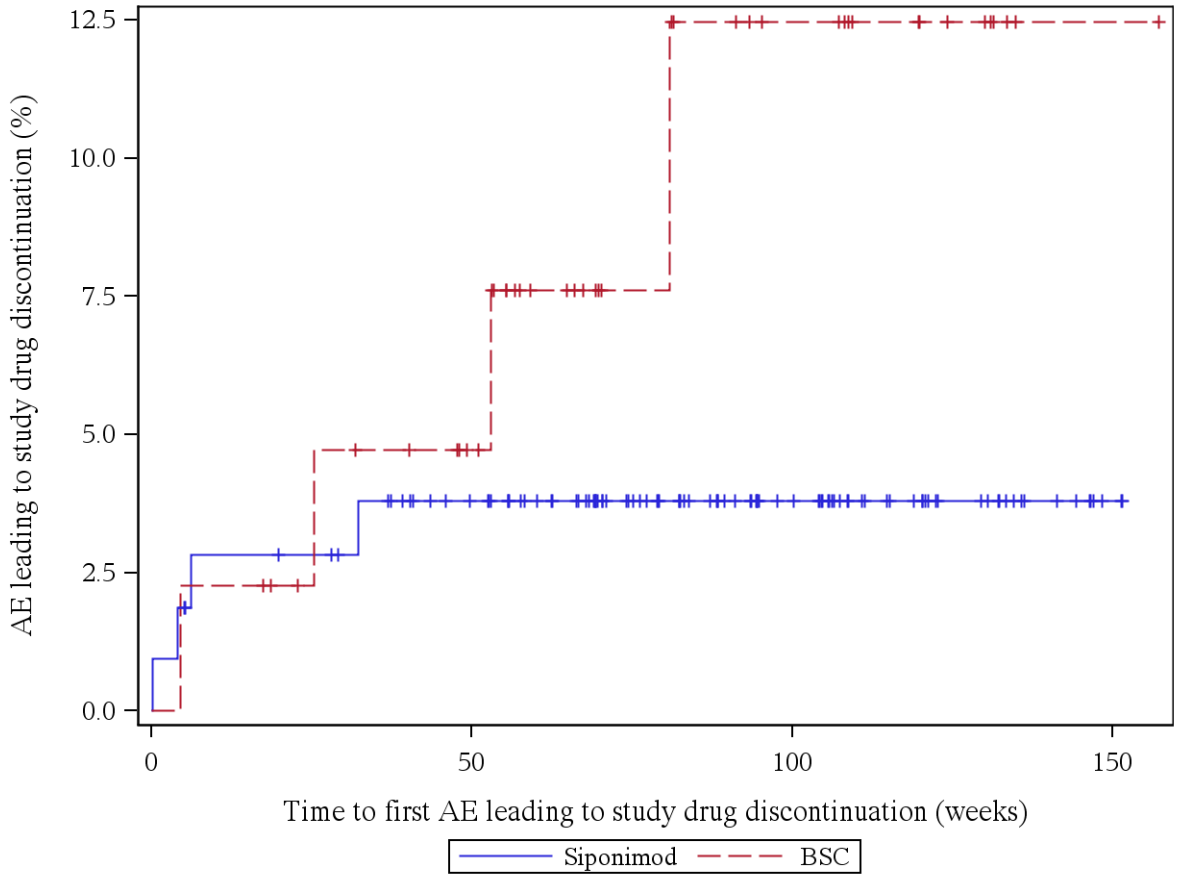


Patients at risk (Siponimod/BSC): Week 0: 20/17, Week 4: 20/17, Week 12: 20/17, Week 24: 20/17, Week 36: 20/17, Week 48: 19/16, Week 60: 17/16, Week 72: 13/13, Week 84: 12/8, Week 96: 9/4, Week 108: 7/3, Week 120: 6/2, Week 132: 1/1, Week 144: 0/0

Log rank test: p-value = -
*: p < 0,05

Analysis population: A2304 SAF subpopulation "ACTIVE MS WITHOUT RELAPSES"

Figure 12.4.1.8.2: AE leading to study drug discontinuation, Previous MS DMT = Yes



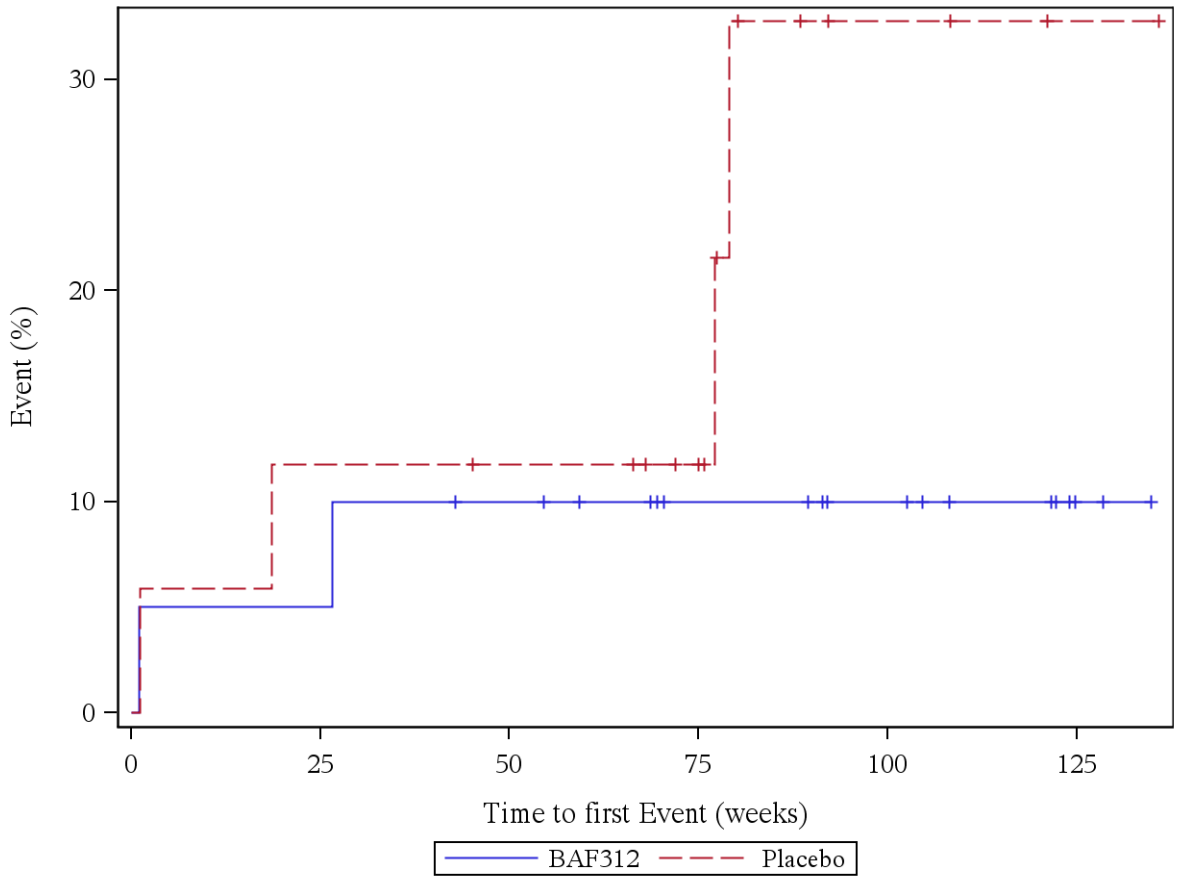
Patients at risk (Siponimod/BSC): Week 0: 107/44, Week 4: 105/44, Week 12: 102/43, Week 24: 101/40, Week 36: 98/38, Week 48: 91/35, Week 60: 82/25, Week 72: 66/19, Week 84: 53/16, Week 96: 40/13, Week 108: 29/12, Week 120: 22/7, Week 132: 14/3, Week 144: 7/1, Week 156: 0/1

Log rank test: p-value = 0,170
*: p < 0,05

Analysis population: A2304 SAF subpopulation "ACTIVE MS WITHOUT RELAPSES"

12.4.2: Time to First Adverse Event by SOC and PT (SAF) by Previous MS DMT

Figure 12.4.2.1.1: GENERAL DISORDERS AND ADMINISTRATION SITE CONDITIONS (SOC), Previous MS DMT = No

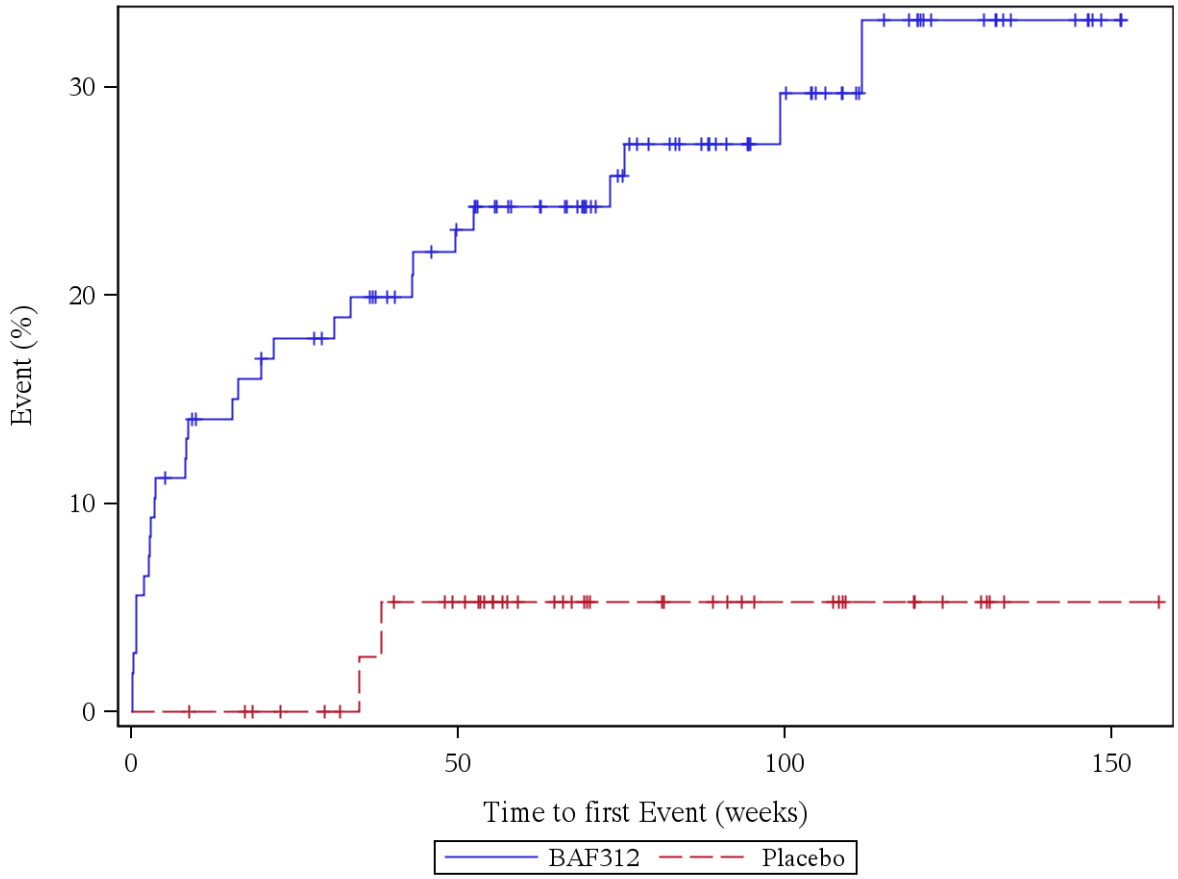


Patients at risk (BAF312/Placebo): Week 0: 20/17, Week 4: 19/16, Week 12: 19/16, Week 24: 19/15, Week 36: 18/15, Week 48: 17/14, Week 60: 15/14, Week 72: 12/11, Week 84: 12/5, Week 96: 9/3, Week 108: 7/3, Week 120: 6/2, Week 132: 1/1, Week 144: 0/0

Log rank test: p-value = 0,257
*: p < 0,05

Analysis population: A2304 SAF subpopulation "ACTIVE MS WITHOUT RELAPSES"

Figure 12.4.2.1.2: GENERAL DISORDERS AND ADMINISTRATION SITE CONDITIONS (SOC), Previous MS DMT = Yes



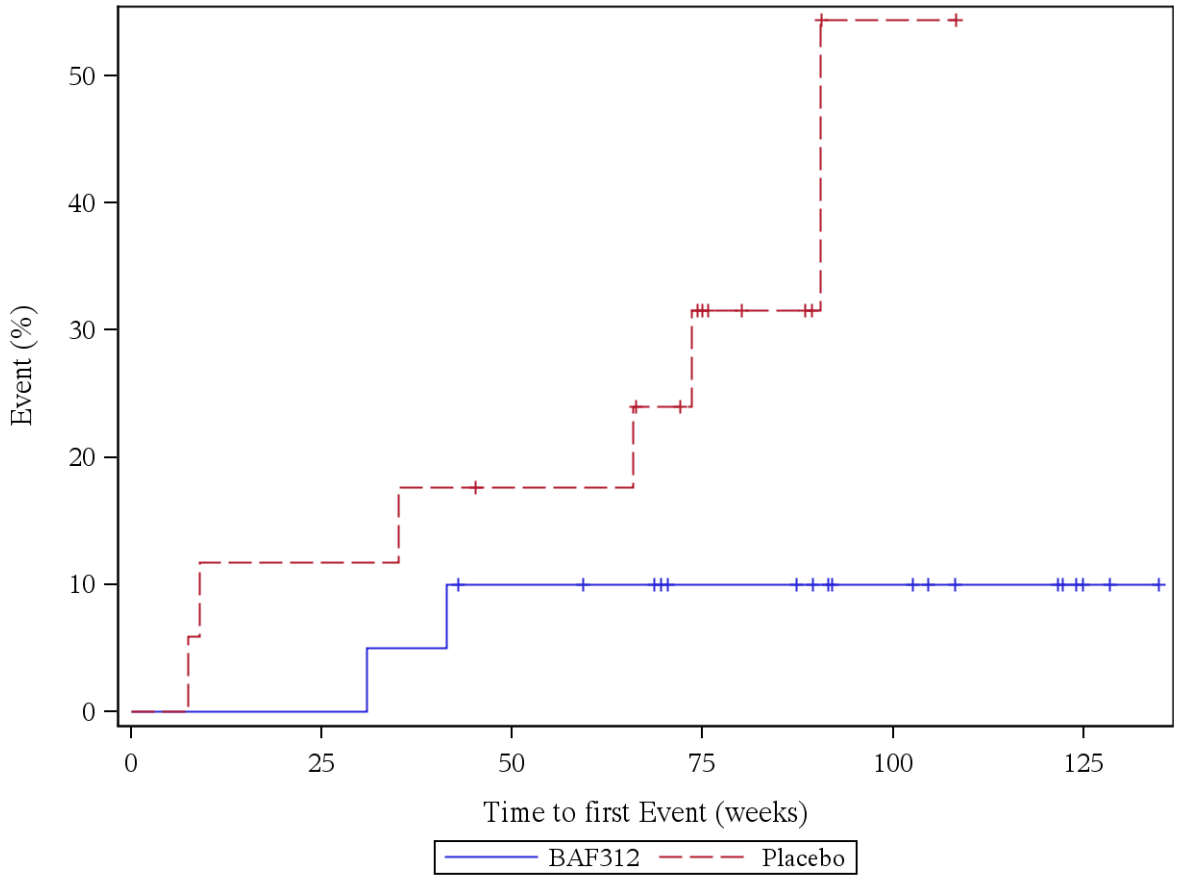
Patients at risk (BAF312/Placebo): Week 0: 107/44, Week 4: 95/44, Week 12: 89/43, Week 24: 84/40, Week 36: 80/37, Week 48: 72/34, Week 60: 62/24, Week 72: 51/18, Week 84: 41/16, Week 96: 30/12, Week 108: 24/11, Week 120: 17/6, Week 132: 11/2, Week 144: 7/1, Week 156: 0/1

Log rank test: p-value = 0,003 *
*: p < 0,05

Analysis population: A2304 SAF subpopulation "ACTIVE MS WITHOUT RELAPSES"

12.4.5: Time to First Adverse Event of Special Interest (SAF) by Previous MS DMT

Figure 12.4.5.1.1: Respiratory disorders (AESI), Previous MS DMT = No

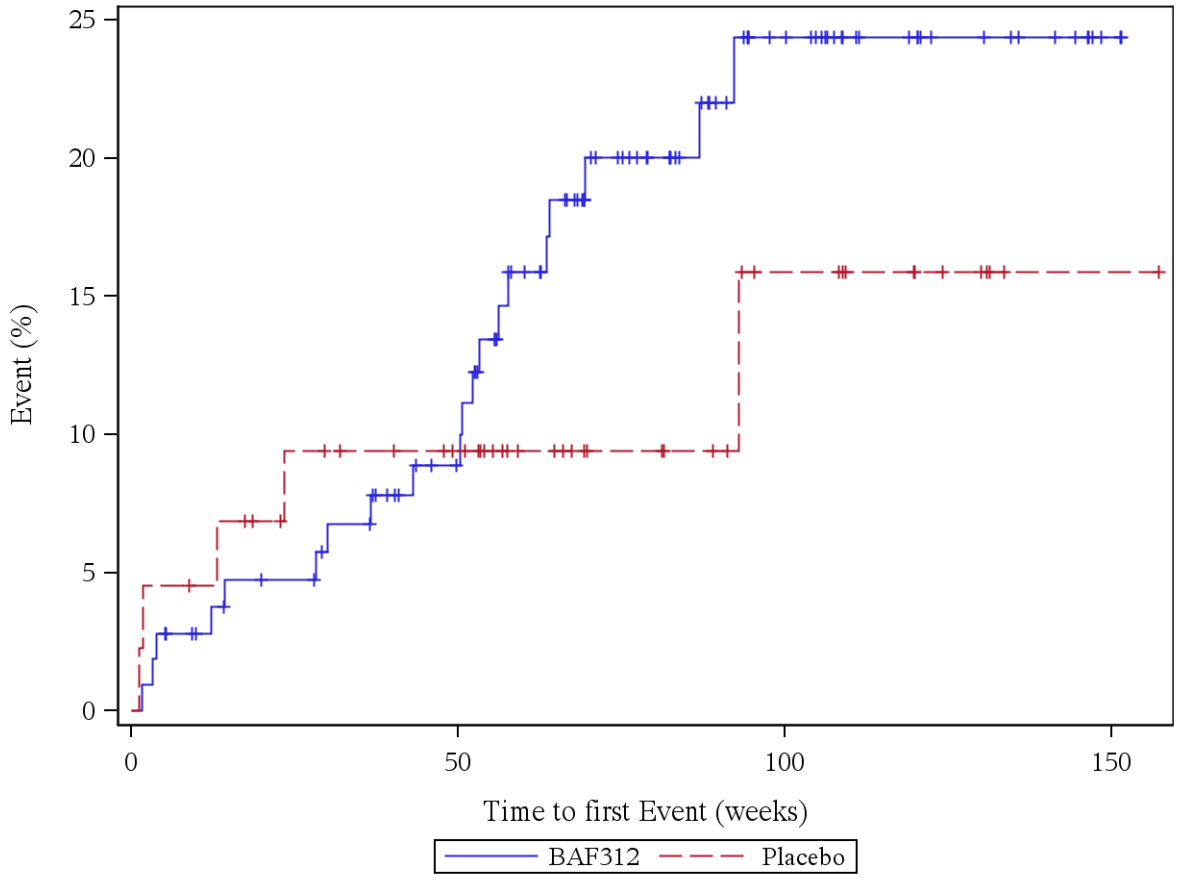


Patients at risk (BAF312/Placebo): Week 0: 20/17, Week 4: 20/17, Week 12: 20/15, Week 24: 20/15, Week 36: 19/14, Week 48: 17/13, Week 60: 16/13, Week 72: 13/10, Week 84: 13/5, Week 96: 9/1, Week 108: 7/1, Week 120: 6/0, Week 132: 1/0, Week 144: 0/0

Log rank test: p-value = 0,049 *
*: p < 0,05

Analysis population: A2304 SAF subpopulation "ACTIVE MS WITHOUT RELAPSES"

Figure 12.4.5.1.2: Respiratory disorders (AESI), Previous MS DMT = Yes



Patients at risk (BAF312/Placebo): Week 0: 107/44, Week 4: 104/42, Week 12: 100/41, Week 24: 96/36, Week 36: 92/34, Week 48: 82/32, Week 60: 67/23, Week 72: 51/18, Week 84: 40/16, Week 96: 28/11, Week 108: 20/11, Week 120: 15/6, Week 132: 10/2, Week 144: 7/1, Week 156: 0/1

Log rank test: p-value = 0,373
*: p < 0,05

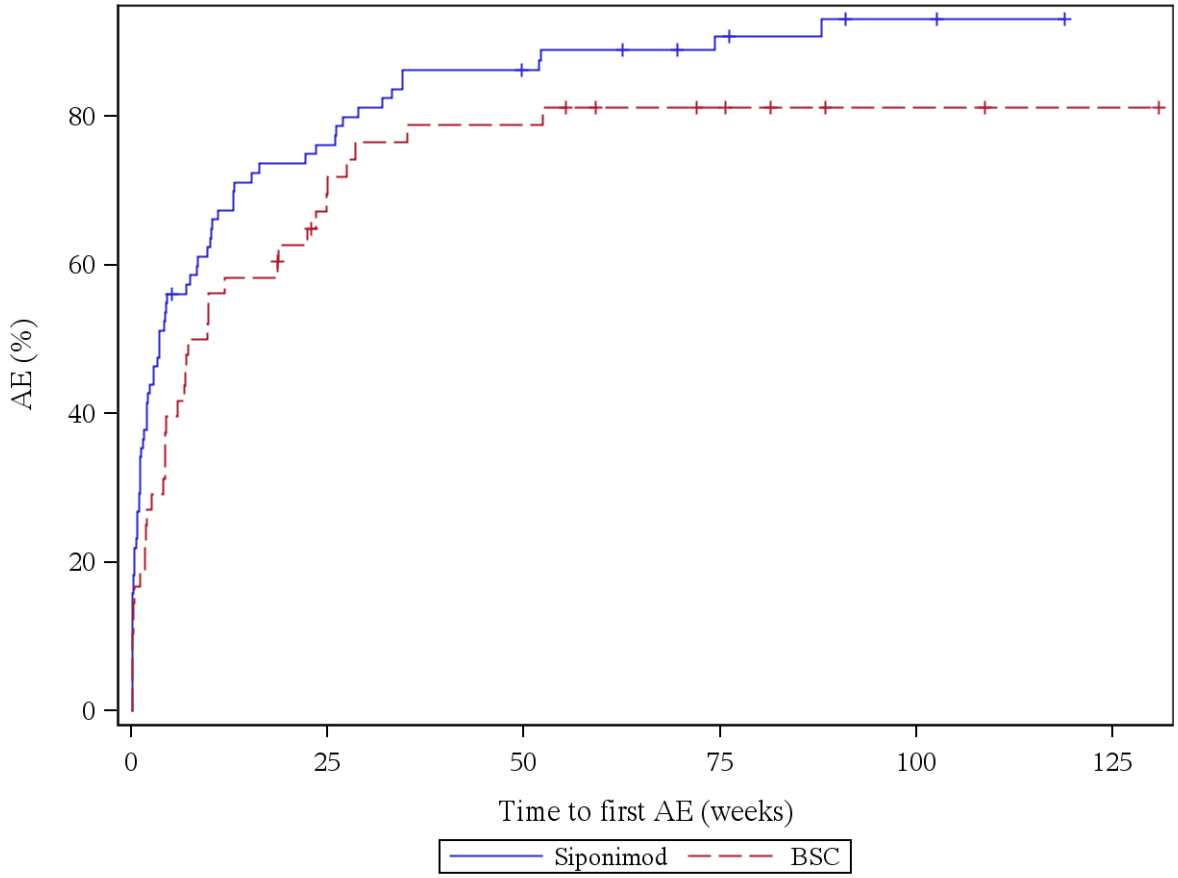
Analysis population: A2304 SAF subpopulation "ACTIVE MS WITHOUT RELAPSES"

12.5 Subgroup: Previous IFN-beta-1b Treatment

12.5.1: Time to First Adverse Event (SAF) by Previous IFN-beta-1b Treatment

12.5.1.1: Any AE

Figure 12.5.1.1.1: AE, Previous IFN-beta-1b Treatment = No

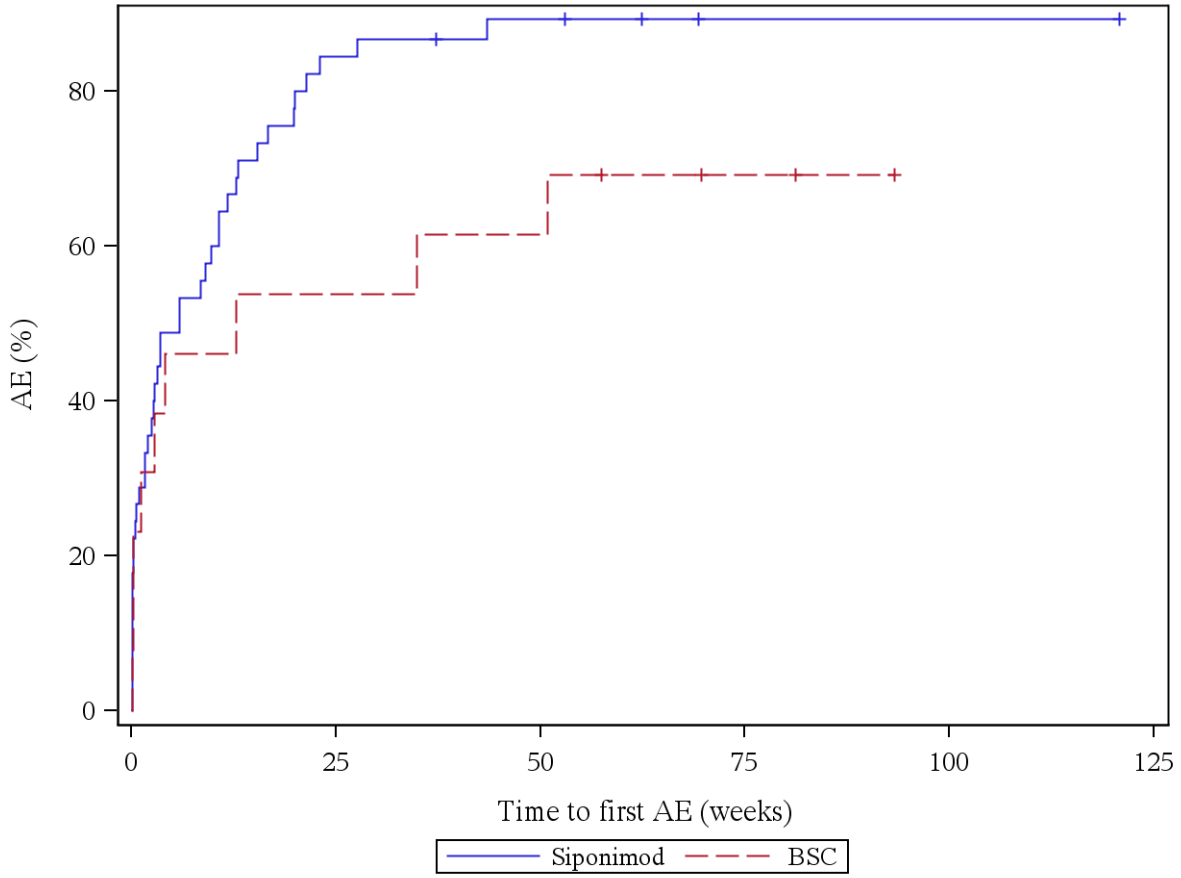


Patients at risk (Siponimod/BSC): Week 0: 82/48, Week 4: 40/33, Week 12: 26/20, Week 24: 19/14, Week 36: 11/9, Week 48: 11/9, Week 60: 8/6, Week 72: 6/5, Week 84: 4/3, Week 96: 2/2, Week 108: 1/2, Week 120: 0/1

Log rank test: p-value = 0,086
*: p < 0,05

Analysis population: A2304 SAF subpopulation "ACTIVE MS WITHOUT RELAPSES"

Figure 12.5.1.1.2: AE, Previous IFN-beta-1b Treatment = Yes



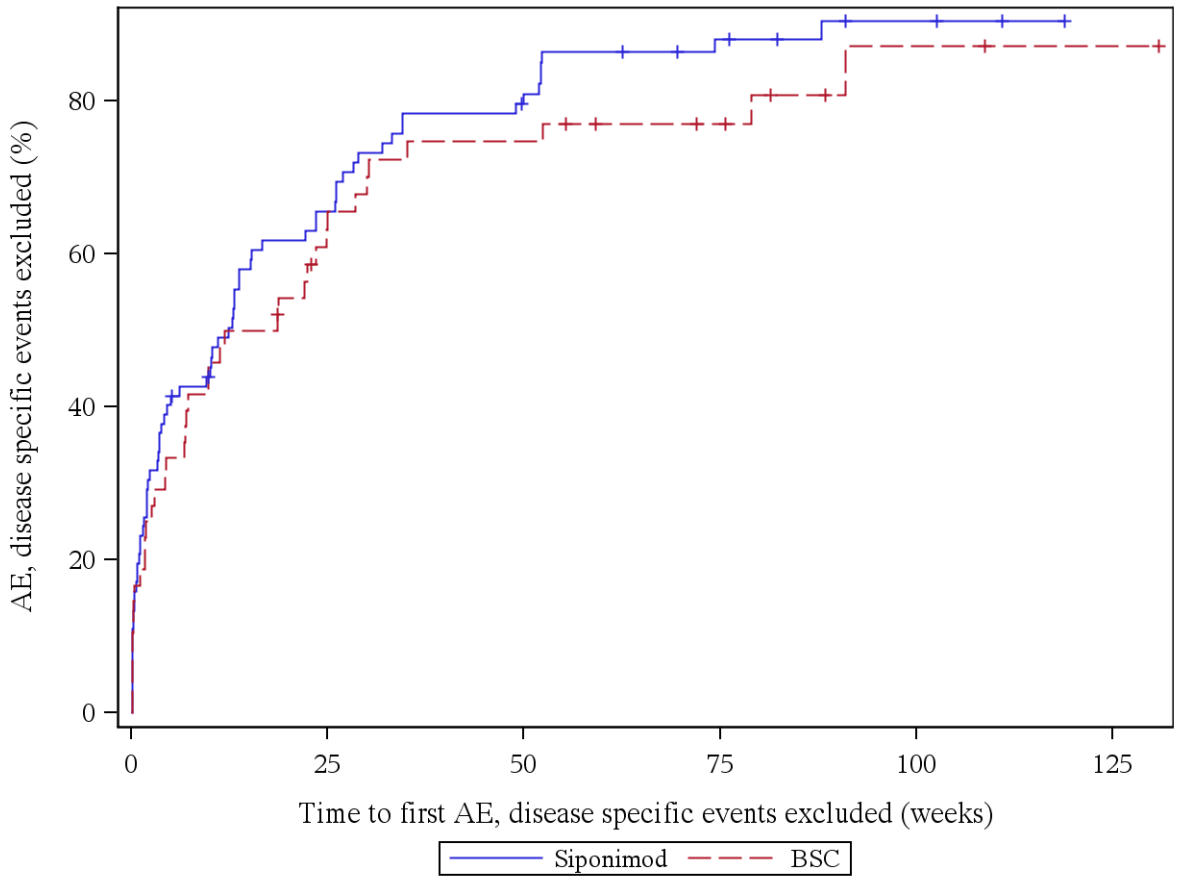
Patients at risk (Siponimod/BSC): Week 0: 45/13, Week 4: 23/8, Week 12: 15/7, Week 24: 7/6, Week 36: 6/5, Week 48: 4/5, Week 60: 3/3, Week 72: 1/2, Week 84: 1/1, Week 96: 1/0, Week 108: 1/0, Week 120: 1/0, Week 132: 0/0

Log rank test: p-value = 0,113
*: p < 0,05

Analysis population: A2304 SAF subpopulation "ACTIVE MS WITHOUT RELAPSES"

12.5.1.2: Any AE, disease specific events excluded

Figure 12.5.1.2.1: AE, disease specific events excluded, Previous IFN-beta-1b Treatment = No

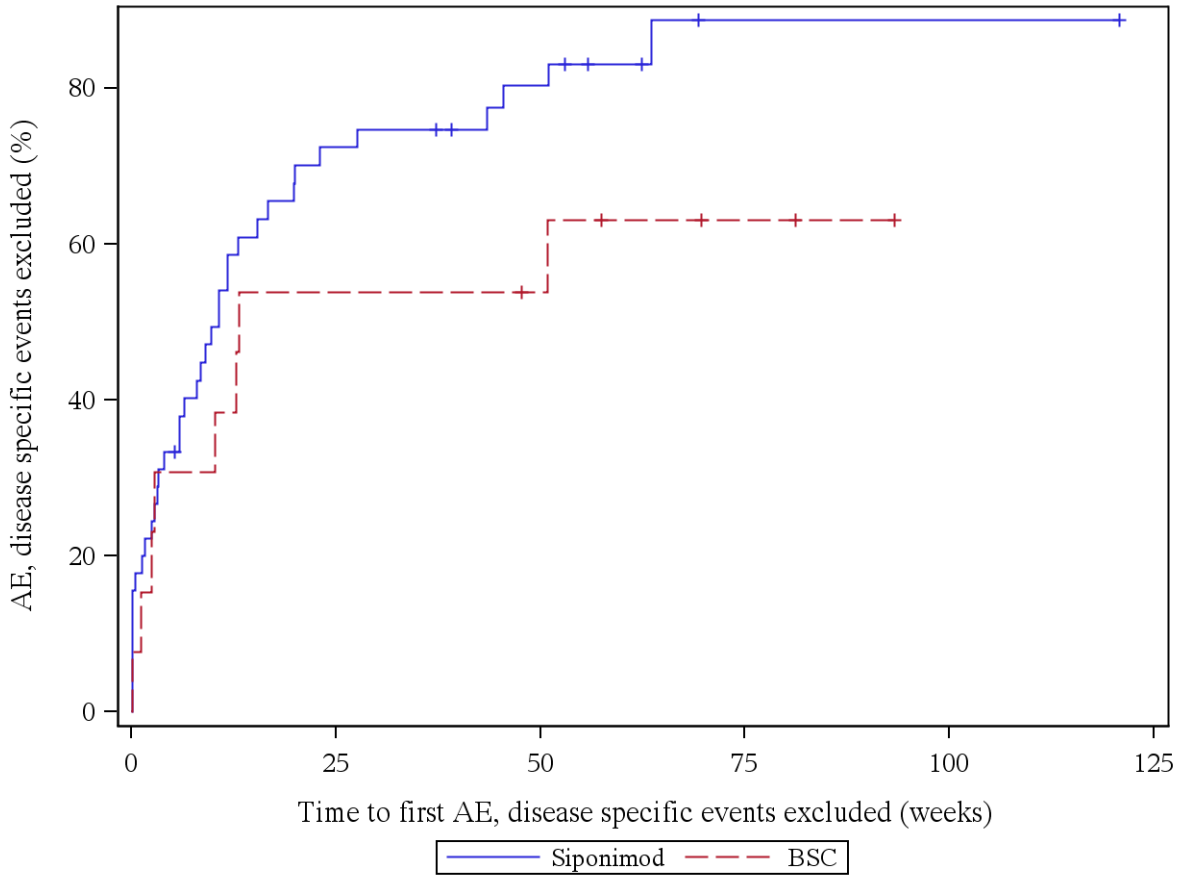


Patients at risk (Siponimod/BSC): Week 0: 82/48, Week 4: 51/34, Week 12: 40/24, Week 24: 27/17, Week 36: 17/11, Week 48: 17/11, Week 60: 10/8, Week 72: 8/7, Week 84: 5/4, Week 96: 3/2, Week 108: 2/2, Week 120: 0/1

Log rank test: p-value = 0,345
*: p < 0,05

Analysis population: A2304 SAF subpopulation "ACTIVE MS WITHOUT RELAPSES"

Figure 12.5.1.2.2: AE, disease specific events excluded, Previous IFN-beta-1b Treatment = Yes



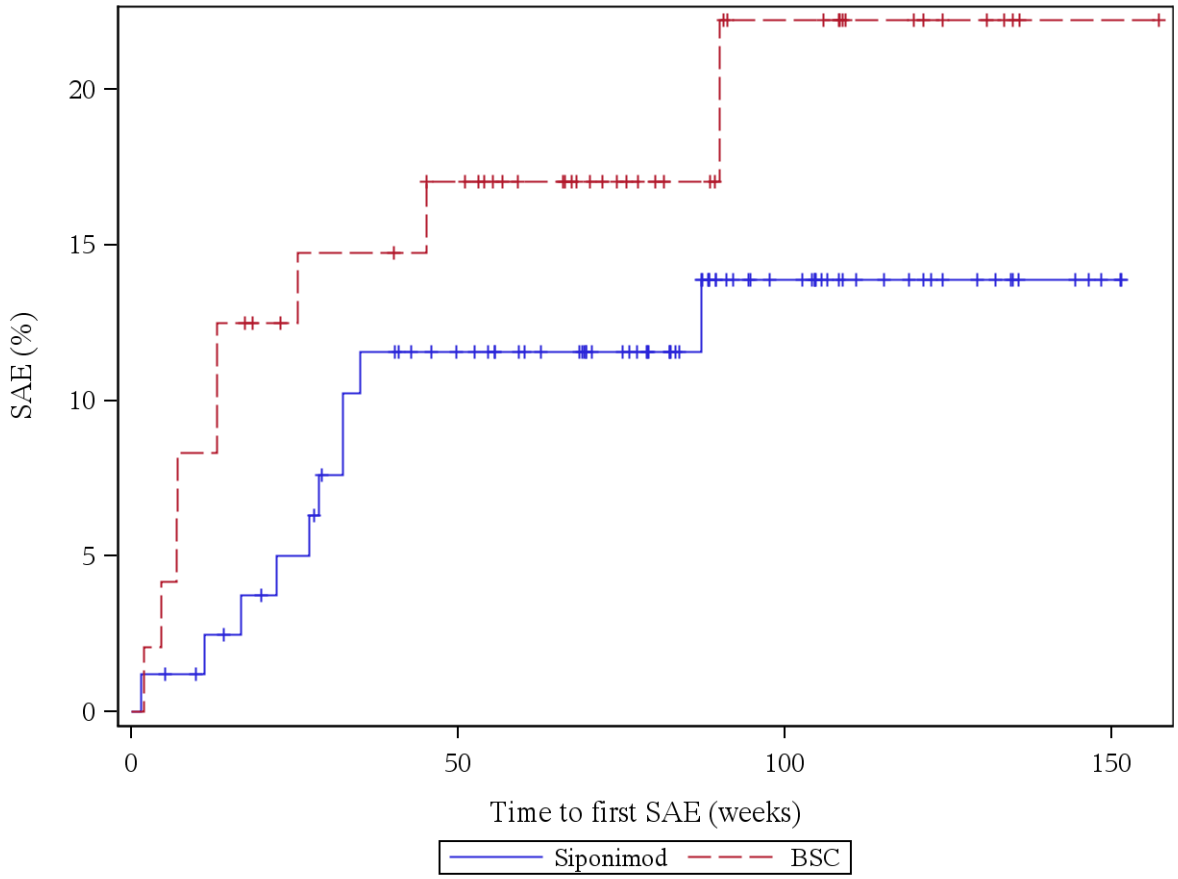
Patients at risk (Siponimod/BSC): Week 0: 45/13, Week 4: 30/9, Week 12: 18/8, Week 24: 12/6, Week 36: 11/6, Week 48: 7/5, Week 60: 4/3, Week 72: 1/2, Week 84: 1/1, Week 96: 1/0, Week 108: 1/0, Week 120: 1/0, Week 132: 0/0

Log rank test: p-value = 0,142
*: p < 0,05

Analysis population: A2304 SAF subpopulation "ACTIVE MS WITHOUT RELAPSES"

12.5.1.3: Any SAE

Figure 12.5.1.3.1: SAE, Previous IFN-beta-1b Treatment = No

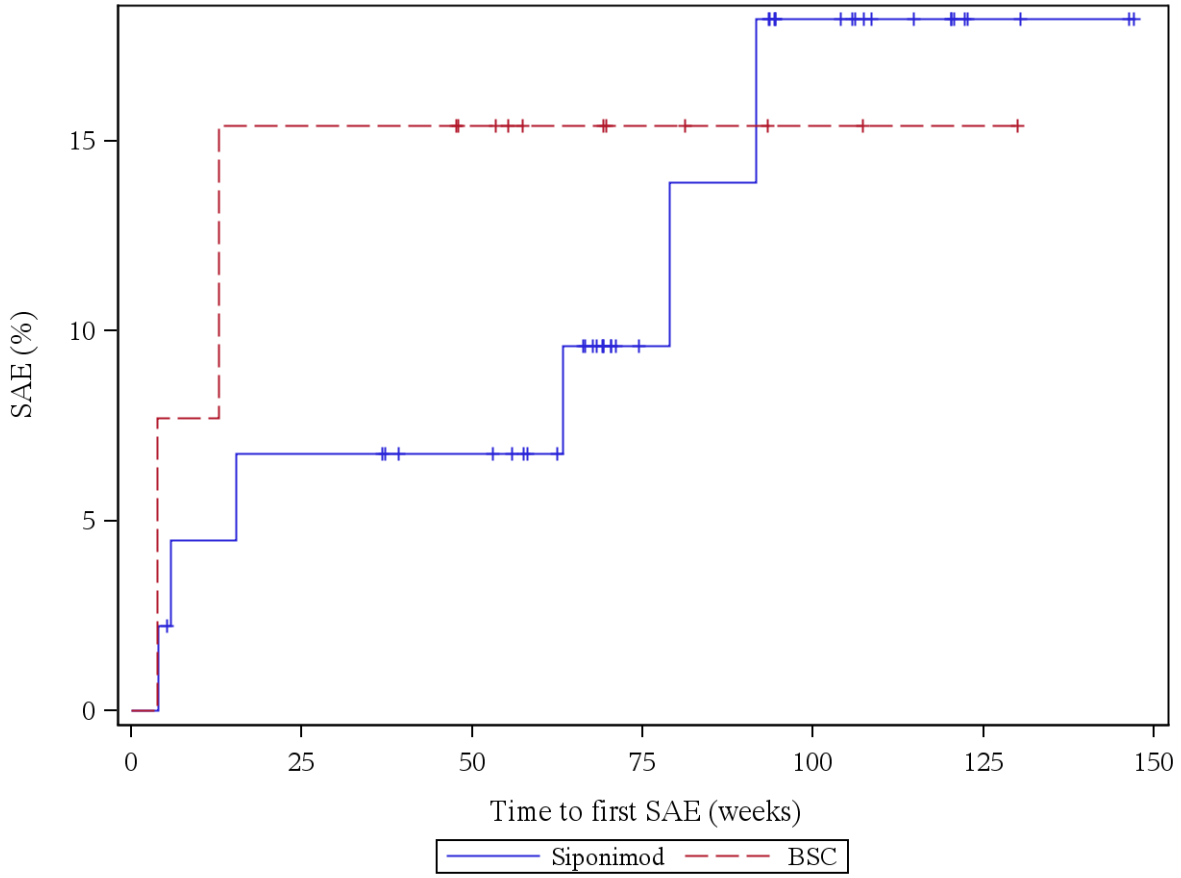


Patients at risk (Siponimod/BSC): Week 0: 82/48, Week 4: 81/47, Week 12: 78/44, Week 24: 74/39, Week 36: 67/38, Week 48: 63/35, Week 60: 57/29, Week 72: 49/23, Week 84: 38/18, Week 96: 26/13, Week 108: 18/12, Week 120: 13/7, Week 132: 9/4, Week 144: 5/1, Week 156: 0/1

Log rank test: p-value = 0,278
*: p < 0,05

Analysis population: A2304 SAF subpopulation "ACTIVE MS WITHOUT RELAPSES"

Figure 12.5.1.3.2: SAE, Previous IFN-beta-1b Treatment = Yes



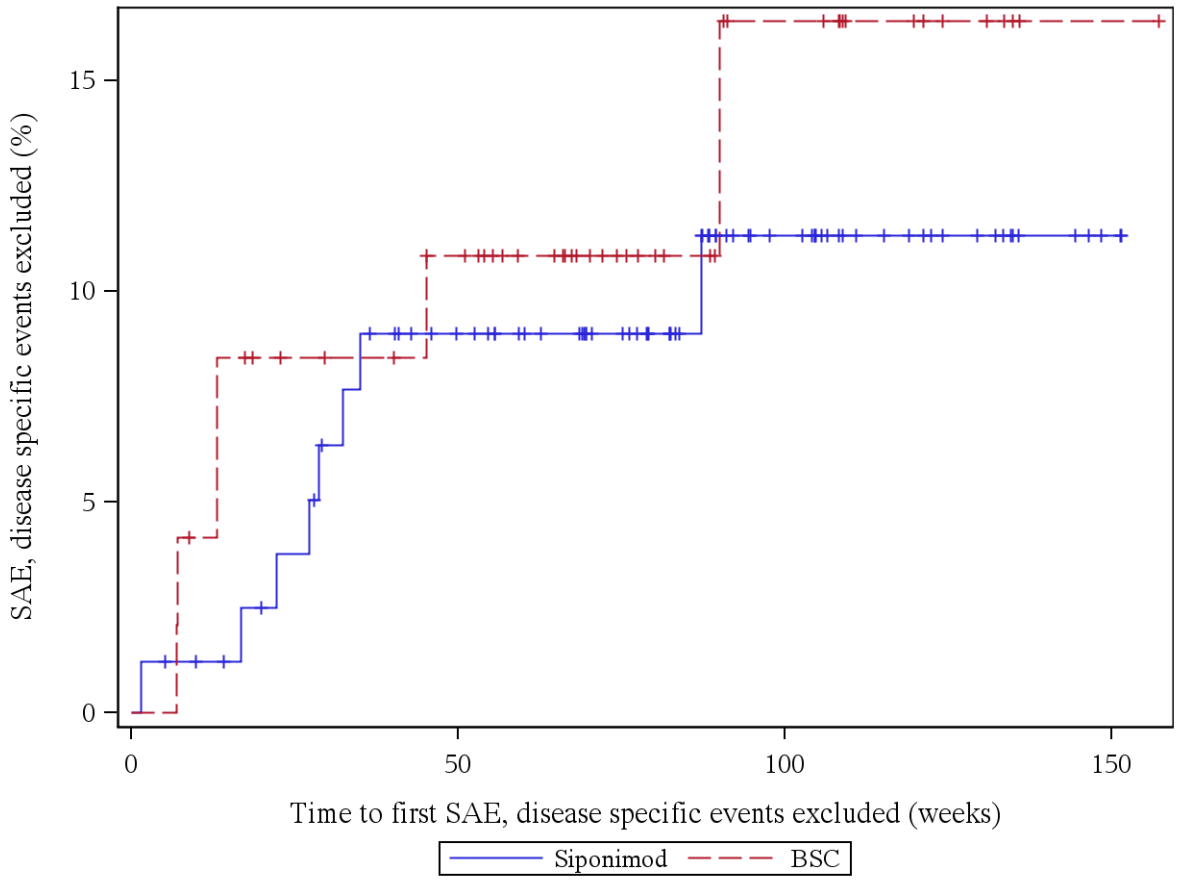
Patients at risk (Siponimod/BSC): Week 0: 45/13, Week 4: 44/12, Week 12: 42/12, Week 24: 41/11, Week 36: 41/11, Week 48: 38/9, Week 60: 34/6, Week 72: 22/4, Week 84: 20/3, Week 96: 14/2, Week 108: 10/1, Week 120: 8/1, Week 132: 2/0, Week 144: 2/0, Week 156: 0/0

Log rank test: p-value = 0,669
*: p < 0,05

Analysis population: A2304 SAF subpopulation "ACTIVE MS WITHOUT RELAPSES"

12.5.1.4: Any SAE, disease specific events excluded

Figure 12.5.1.4.1: SAE, disease specific events excluded, Previous IFN-beta-1b Treatment = No

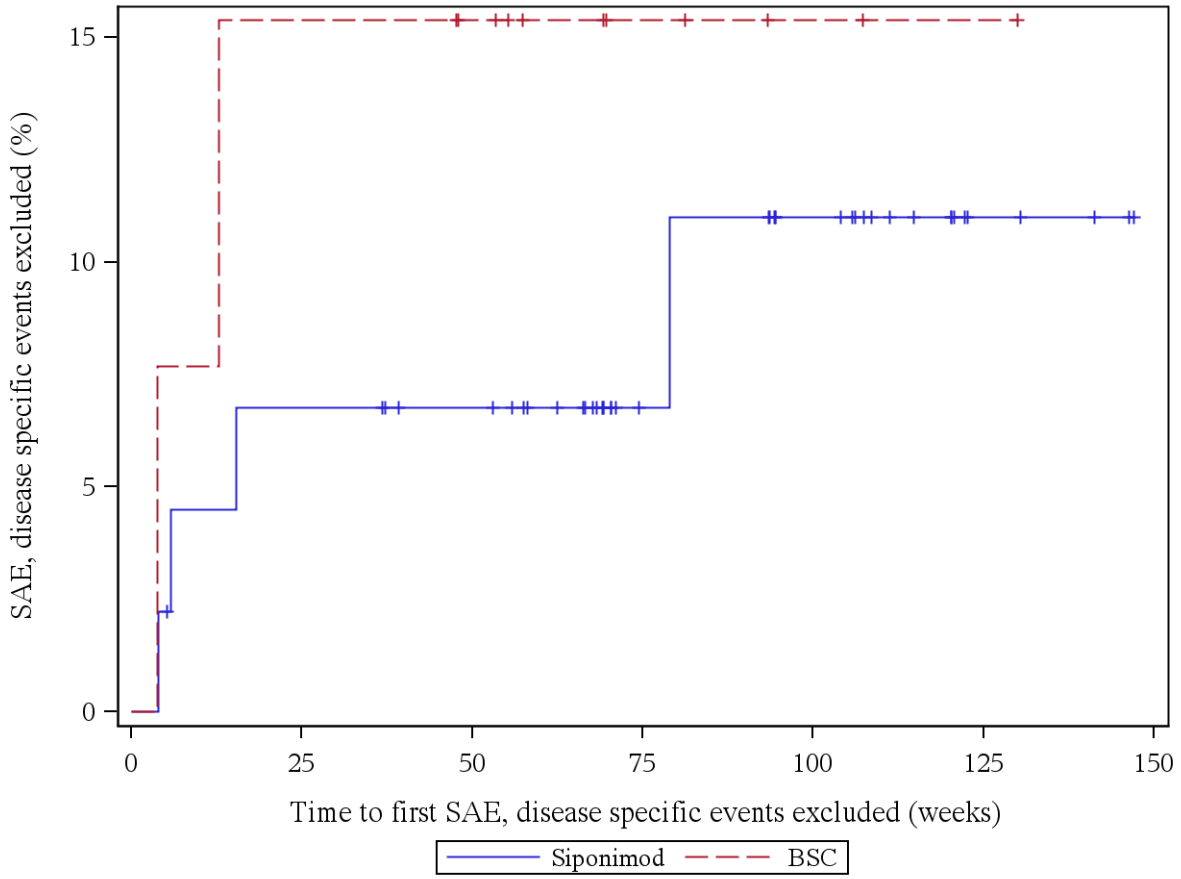


Patients at risk (Siponimod/BSC): Week 0: 82/48, Week 4: 81/48, Week 12: 79/45, Week 24: 75/40, Week 36: 69/39, Week 48: 64/36, Week 60: 58/30, Week 72: 50/23, Week 84: 39/18, Week 96: 27/13, Week 108: 19/12, Week 120: 14/7, Week 132: 10/4, Week 144: 5/1, Week 156: 0/1

Log rank test: p-value = 0,571
*: p < 0,05

Analysis population: A2304 SAF subpopulation "ACTIVE MS WITHOUT RELAPSES"

Figure 12.5.1.4.2: SAE, disease specific events excluded, Previous IFN-beta-1b Treatment = Yes



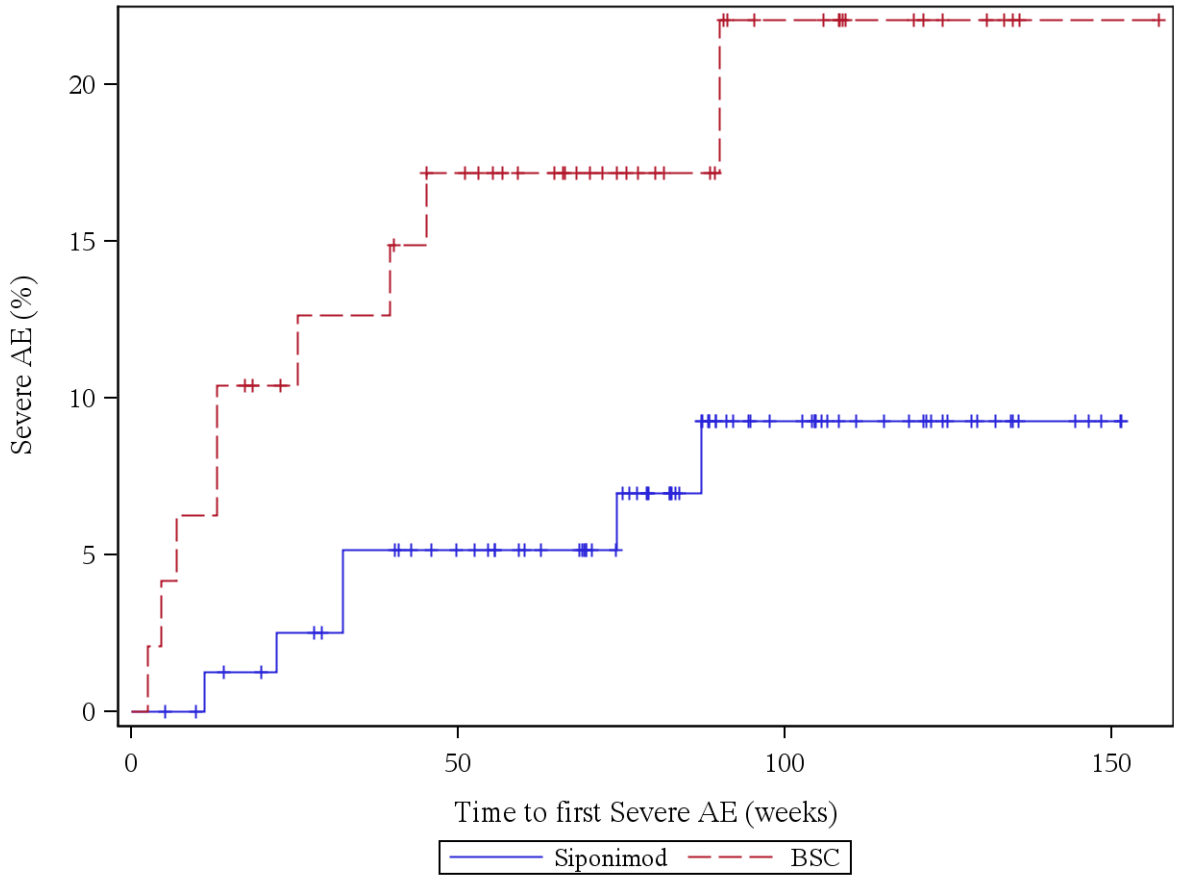
Patients at risk (Siponimod/BSC): Week 0: 45/13, Week 4: 44/12, Week 12: 42/12, Week 24: 41/11, Week 36: 41/11, Week 48: 38/9, Week 60: 34/6, Week 72: 23/4, Week 84: 21/3, Week 96: 16/2, Week 108: 12/1, Week 120: 9/1, Week 132: 3/0, Week 144: 2/0, Week 156: 0/0

Log rank test: p-value = 0,440
*: p < 0,05

Analysis population: A2304 SAF subpopulation "ACTIVE MS WITHOUT RELAPSES"

12.5.1.5: Any severe AE

Figure 12.5.1.5.1: Severe AE, Previous IFN-beta-1b Treatment = No

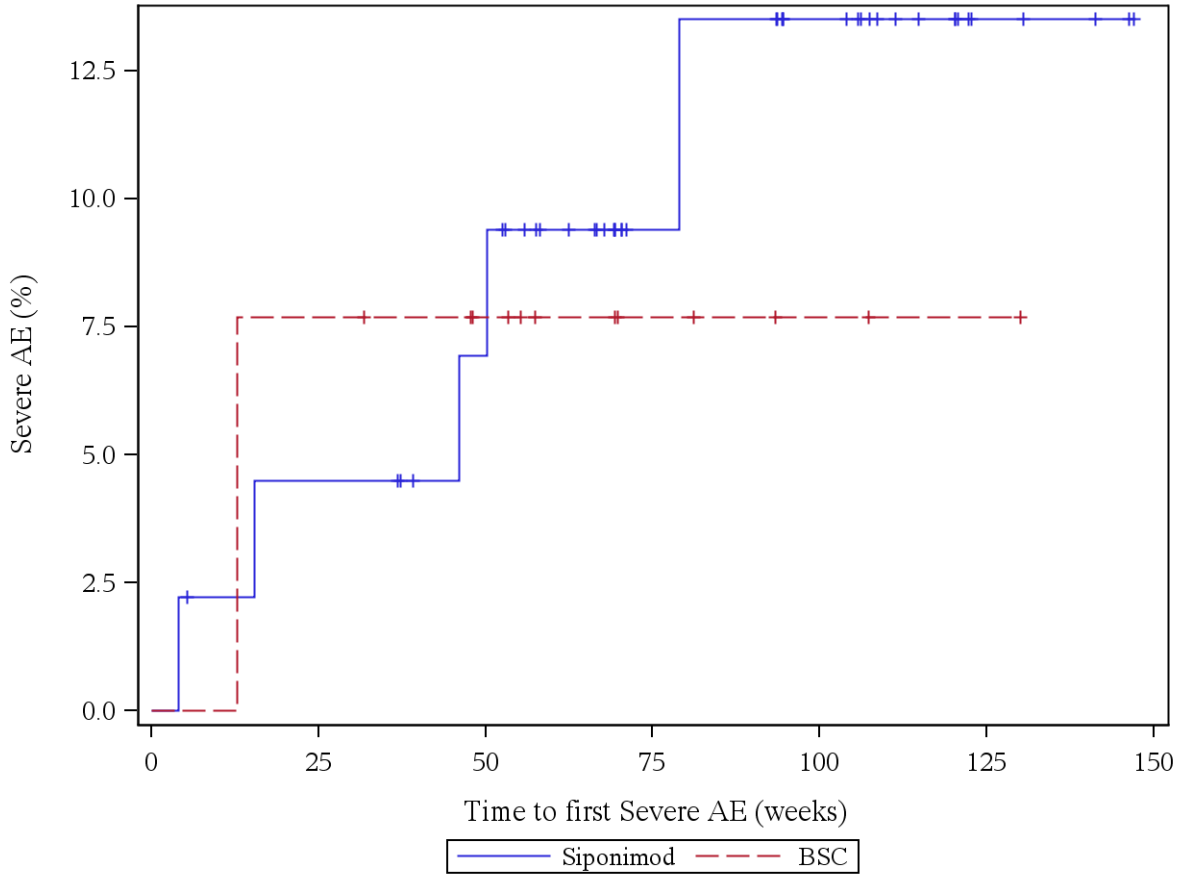


Patients at risk (Siponimod/BSC): Week 0: 82/48, Week 4: 82/47, Week 12: 79/45, Week 24: 76/40, Week 36: 72/39, Week 48: 68/35, Week 60: 62/30, Week 72: 54/24, Week 84: 40/19, Week 96: 28/13, Week 108: 20/12, Week 120: 16/7, Week 132: 9/4, Week 144: 5/1, Week 156: 0/1

Log rank test: p-value = 0,042 *
*: p < 0,05

Analysis population: A2304 SAF subpopulation "ACTIVE MS WITHOUT RELAPSES"

Figure 12.5.1.5.2: Severe AE, Previous IFN-beta-1b Treatment = Yes



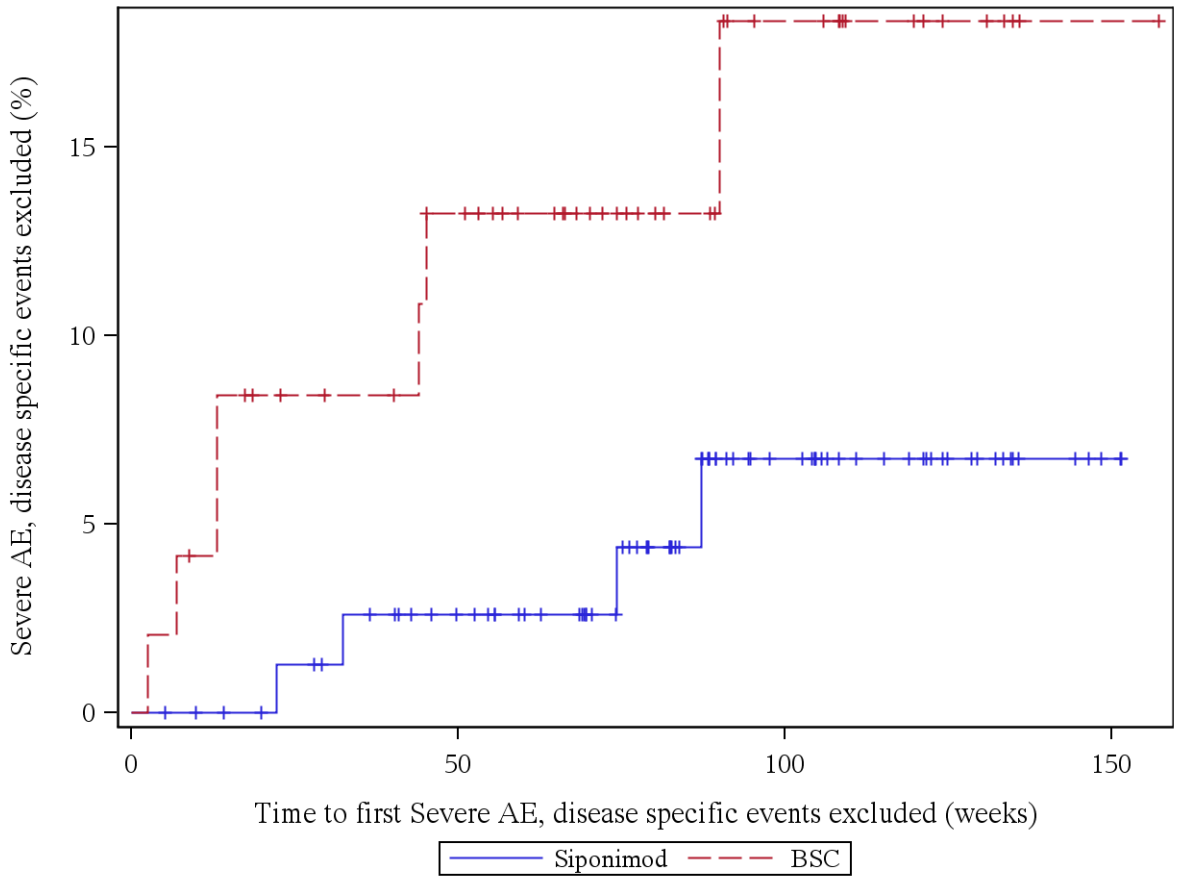
Patients at risk (Siponimod/BSC): Week 0: 45/13, Week 4: 44/13, Week 12: 43/13, Week 24: 42/12, Week 36: 42/11, Week 48: 38/9, Week 60: 32/6, Week 72: 22/4, Week 84: 21/3, Week 96: 16/2, Week 108: 12/1, Week 120: 9/1, Week 132: 3/0, Week 144: 2/0, Week 156: 0/0

Log rank test: p-value = 0,809
*: p < 0,05

Analysis population: A2304 SAF subpopulation "ACTIVE MS WITHOUT RELAPSES"

12.5.1.6: Any severe AE, disease specific events excluded

Figure 12.5.1.6.1: Severe AE, disease specific events excluded, Previous IFN-beta-1b Treatment = No

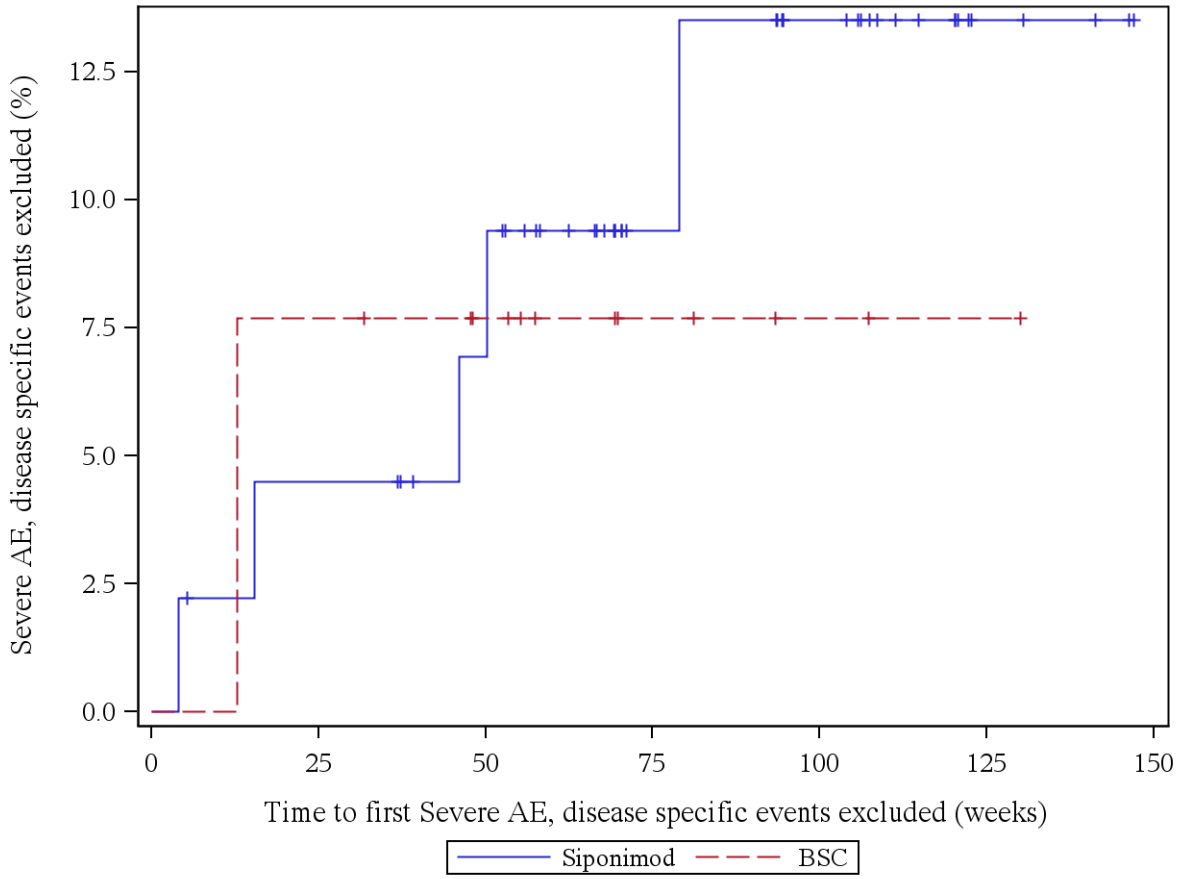


Patients at risk (Siponimod/BSC): Week 0: 82/48, Week 4: 82/47, Week 12: 80/45, Week 24: 77/40, Week 36: 74/39, Week 48: 69/35, Week 60: 63/30, Week 72: 55/24, Week 84: 41/19, Week 96: 29/13, Week 108: 21/12, Week 120: 17/7, Week 132: 10/4, Week 144: 5/1, Week 156: 0/1

Log rank test: p-value = 0,043 *
*: p < 0,05

Analysis population: A2304 SAF subpopulation "ACTIVE MS WITHOUT RELAPSES"

Figure 12.5.1.6.2: Severe AE, disease specific events excluded, Previous IFN-beta-1b Treatment = Yes



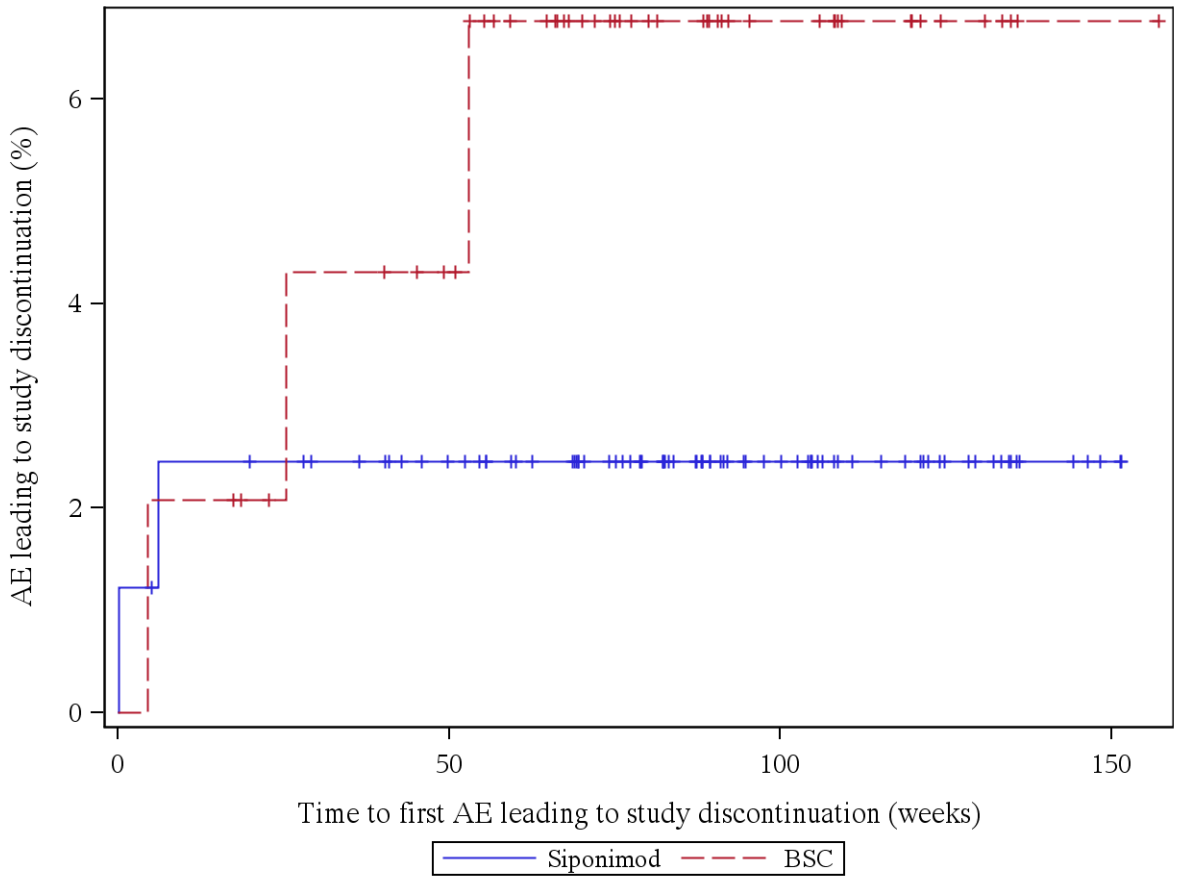
Patients at risk (Siponimod/BSC): Week 0: 45/13, Week 4: 44/13, Week 12: 43/13, Week 24: 42/12, Week 36: 42/11, Week 48: 38/9, Week 60: 32/6, Week 72: 22/4, Week 84: 21/3, Week 96: 16/2, Week 108: 12/1, Week 120: 9/1, Week 132: 3/0, Week 144: 2/0, Week 156: 0/0

Log rank test: p-value = 0,809
*: p < 0,05

Analysis population: A2304 SAF subpopulation "ACTIVE MS WITHOUT RELAPSES"

12.5.1.7: Any AE leading to study discontinuation

Figure 12.5.1.7.1: AE leading to study discontinuation, Previous IFN-beta-1b Treatment = No

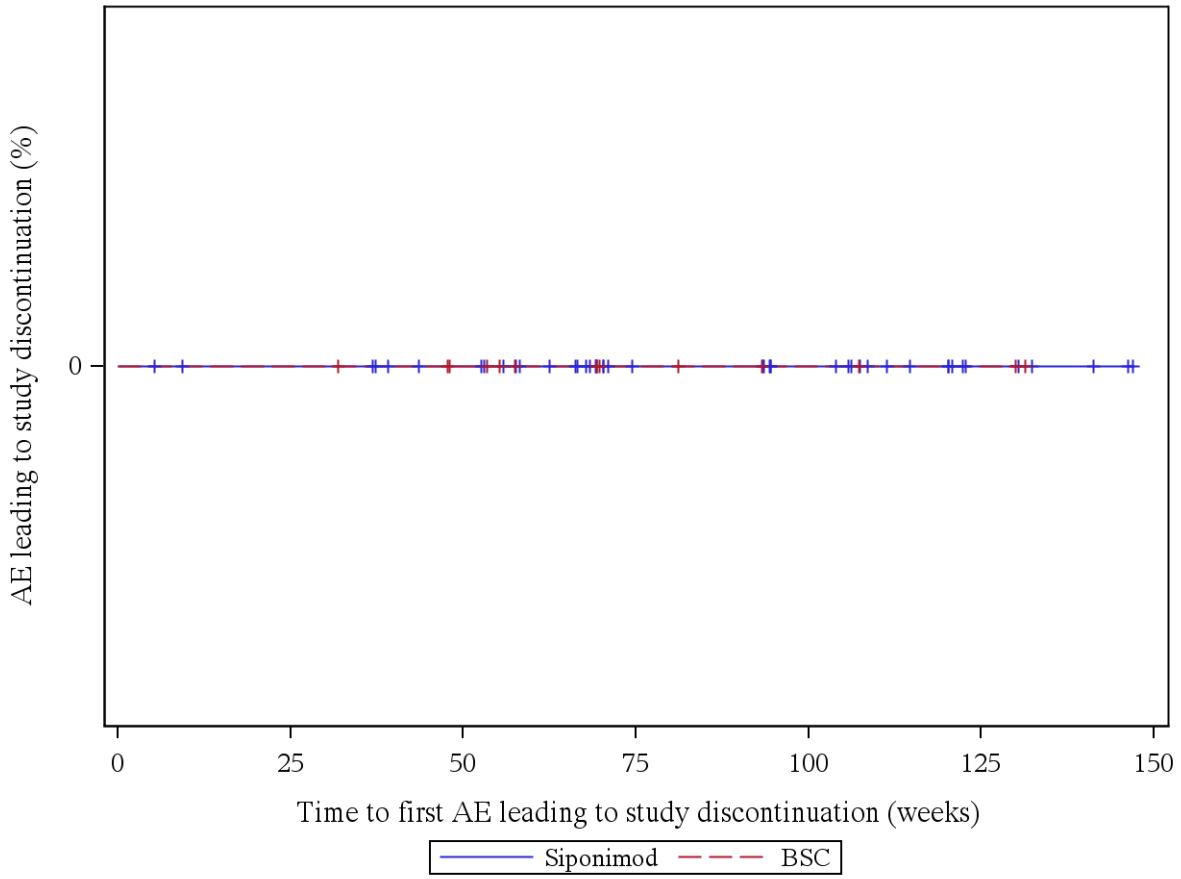


Patients at risk (Siponimod/BSC): Week 0: 82/48, Week 4: 81/48, Week 12: 79/47, Week 24: 78/44, Week 36: 76/43, Week 48: 71/41, Week 60: 65/34, Week 72: 57/27, Week 84: 44/21, Week 96: 32/14, Week 108: 23/13, Week 120: 18/7, Week 132: 11/4, Week 144: 5/1, Week 156: 0/1

Log rank test: p-value = 0,279
*: p < 0,05

Analysis population: A2304 SAF subpopulation "ACTIVE MS WITHOUT RELAPSES"

Figure 12.5.1.7.2: AE leading to study discontinuation, Previous IFN-beta-1b Treatment = Yes



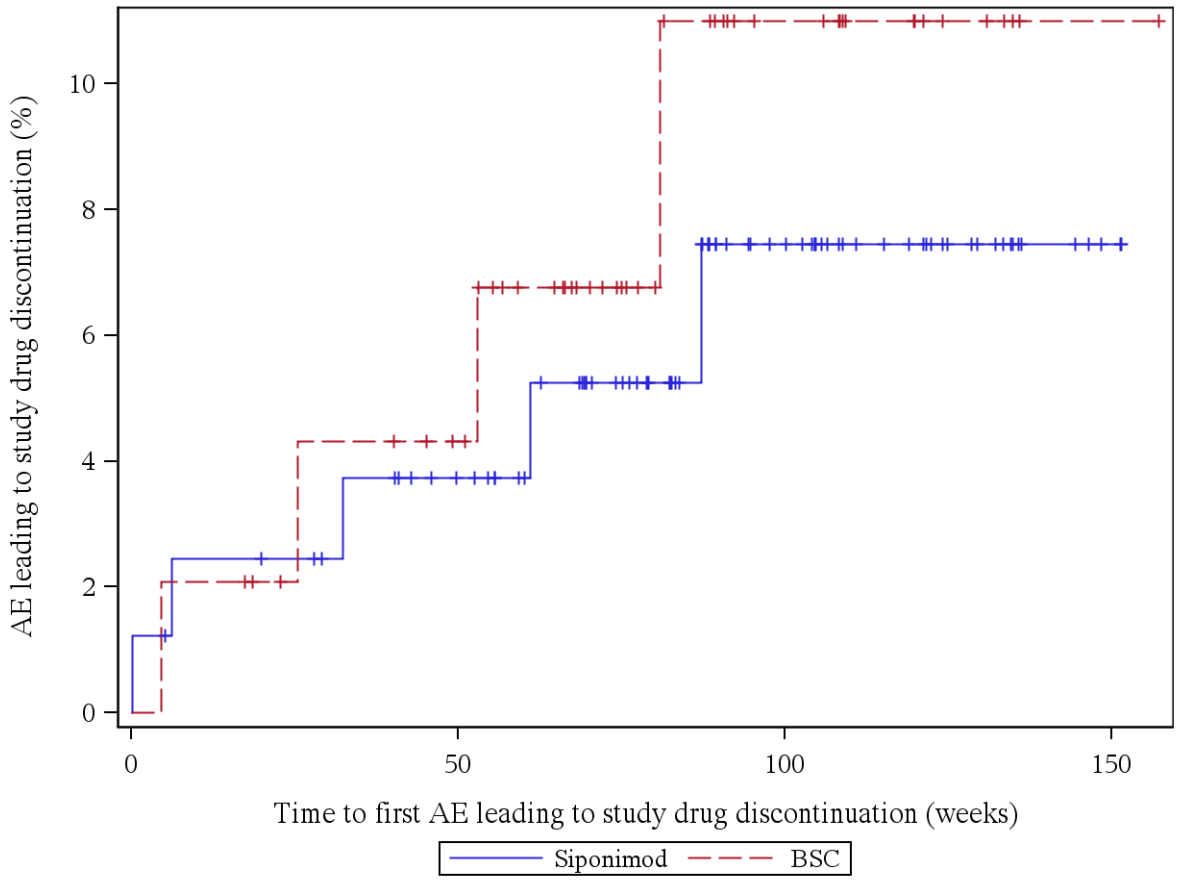
Patients at risk (Siponimod/BSC): Week 0: 45/13, Week 4: 45/13, Week 12: 43/13, Week 24: 43/13, Week 36: 43/12, Week 48: 39/10, Week 60: 34/7, Week 72: 23/5, Week 84: 22/4, Week 96: 17/3, Week 108: 13/2, Week 120: 10/2, Week 132: 4/0, Week 144: 2/0, Week 156: 0/0

Log rank test: p-value = -
*: p < 0,05

Analysis population: A2304 SAF subpopulation "ACTIVE MS WITHOUT RELAPSES"

12.5.1.8: Any AE leading to study drug discontinuation

Figure 12.5.1.8.1: AE leading to study drug discontinuation, Previous IFN-beta-1b Treatment = No

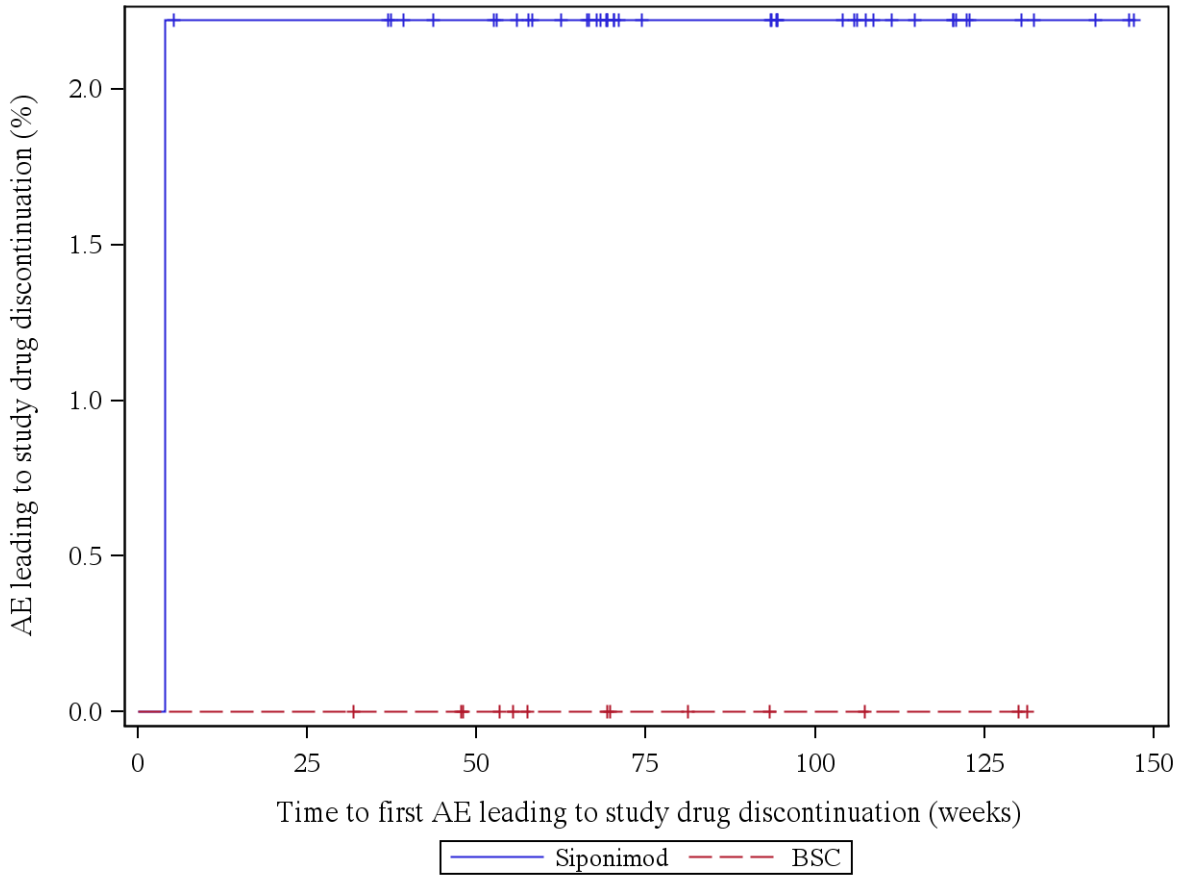


Patients at risk (Siponimod/BSC): Week 0: 82/48, Week 4: 81/48, Week 12: 79/47, Week 24: 78/44, Week 36: 75/43, Week 48: 71/41, Week 60: 65/34, Week 72: 56/27, Week 84: 43/20, Week 96: 32/14, Week 108: 23/13, Week 120: 18/7, Week 132: 11/4, Week 144: 5/1, Week 156: 0/1

Log rank test: p-value = 0,561
*: p < 0,05

Analysis population: A2304 SAF subpopulation "ACTIVE MS WITHOUT RELAPSES"

Figure 12.5.1.8.2: AE leading to study drug discontinuation, Previous IFN-beta-1b Treatment = Yes



Patients at risk (Siponimod/BSC): Week 0: 45/13, Week 4: 44/13, Week 12: 43/13, Week 24: 43/13, Week 36: 43/12, Week 48: 39/10, Week 60: 34/7, Week 72: 23/5, Week 84: 22/4, Week 96: 17/3, Week 108: 13/2, Week 120: 10/2, Week 132: 4/0, Week 144: 2/0, Week 156: 0/0

Log rank test: p-value = -
*: p < 0,05

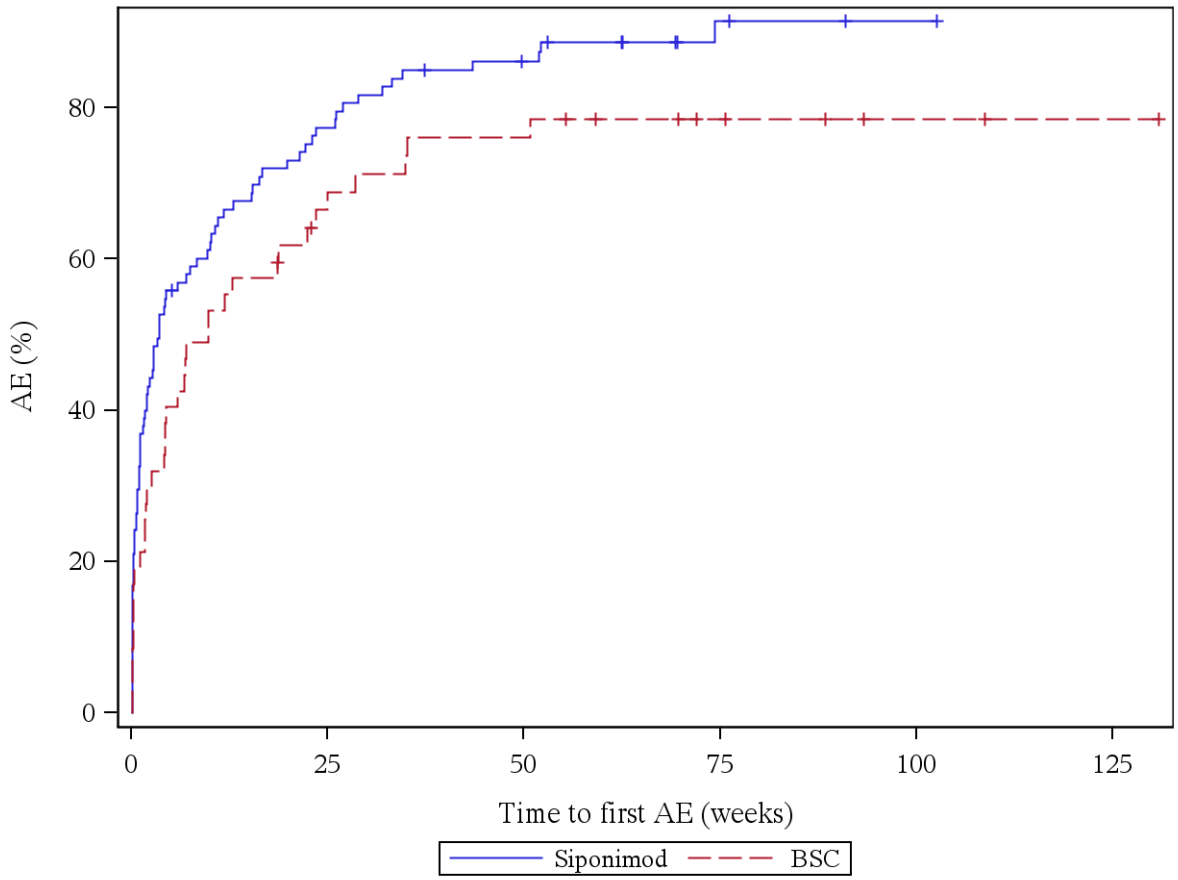
Analysis population: A2304 SAF subpopulation "ACTIVE MS WITHOUT RELAPSES"

12.6 Subgroup: Rapid Evolvement

12.6.1: Time to First Adverse Event (SAF) by Rapid Evolvement

12.6.1.1: Any AE

Figure 12.6.1.1.1: AE, Rapid Evolvement = No

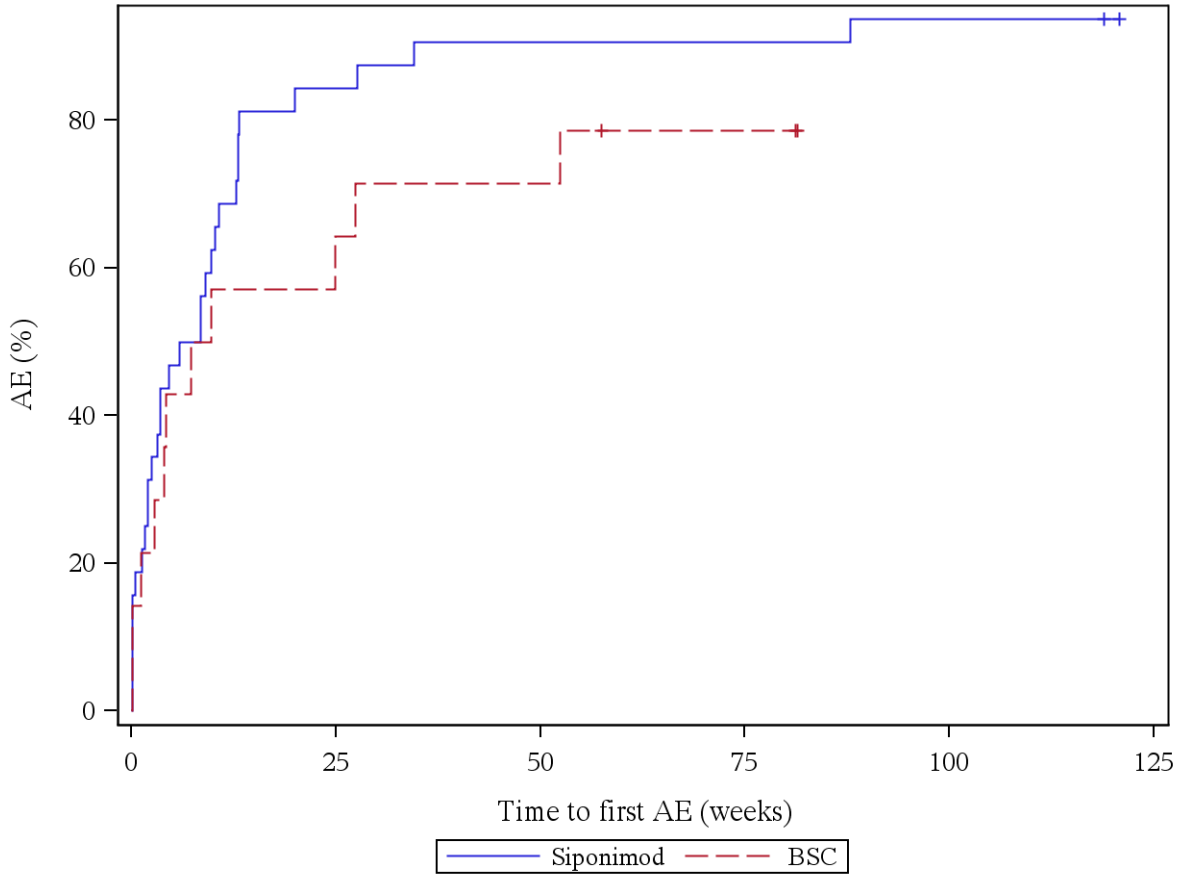


Patients at risk (Siponimod/BSC): Week 0: 95/47, Week 4: 45/32, Week 12: 31/21, Week 24: 21/14, Week 36: 14/10, Week 48: 12/10, Week 60: 8/7, Week 72: 4/5, Week 84: 2/4, Week 96: 1/2, Week 108: 0/2

Log rank test: p-value = 0,058
*: p < 0,05

Analysis population: A2304 SAF subpopulation "ACTIVE MS WITHOUT RELAPSES"

Figure 12.6.1.1.2: AE, Rapid Evolvement = Yes



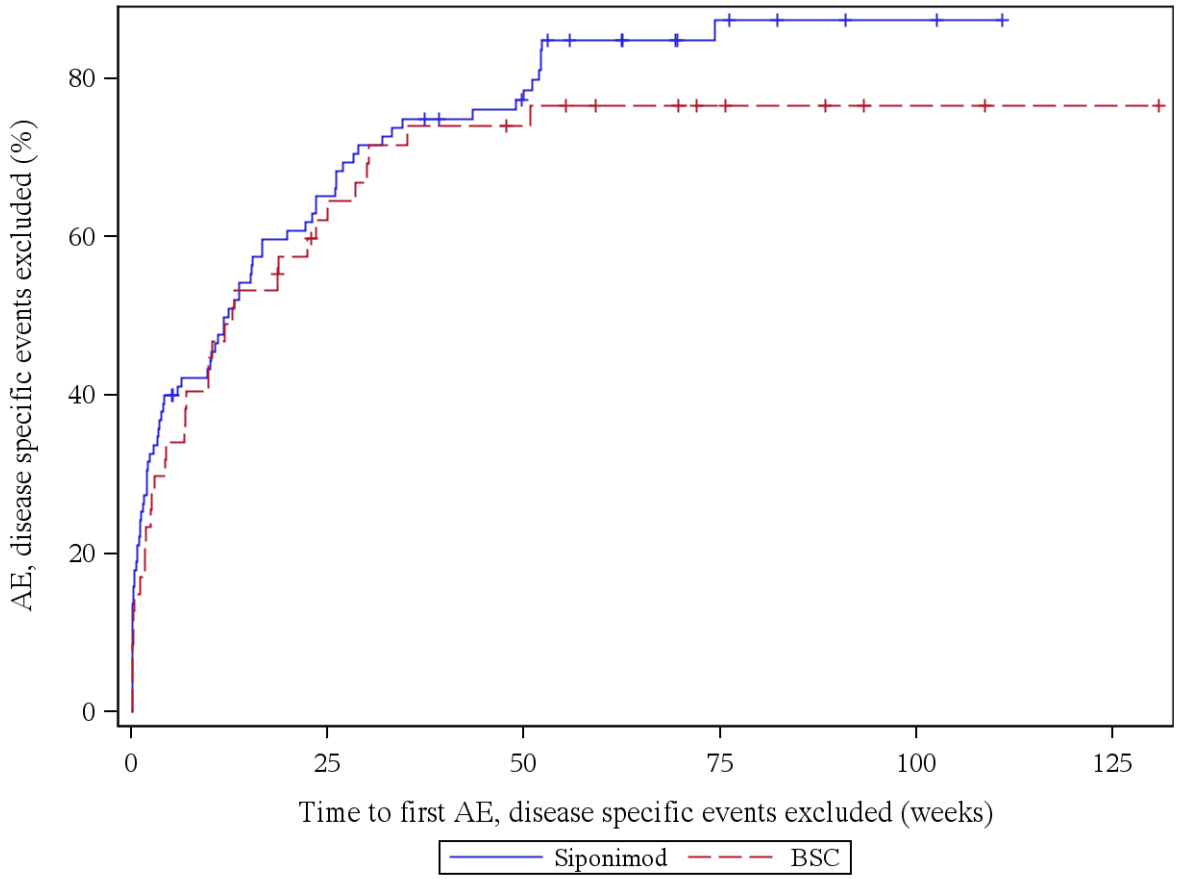
Patients at risk (Siponimod/BSC): Week 0: 32/14, Week 4: 18/9, Week 12: 10/6, Week 24: 5/6, Week 36: 3/4, Week 48: 3/4, Week 60: 3/2, Week 72: 3/2, Week 84: 3/0, Week 96: 2/0, Week 108: 2/0, Week 120: 1/0, Week 132: 0/0

Log rank test: p-value = 0,258
*: p < 0,05

Analysis population: A2304 SAF subpopulation "ACTIVE MS WITHOUT RELAPSES"

12.6.1.2: Any AE, disease specific events excluded

Figure 12.6.1.2.1: AE, disease specific events excluded, Rapid Evolvement = No

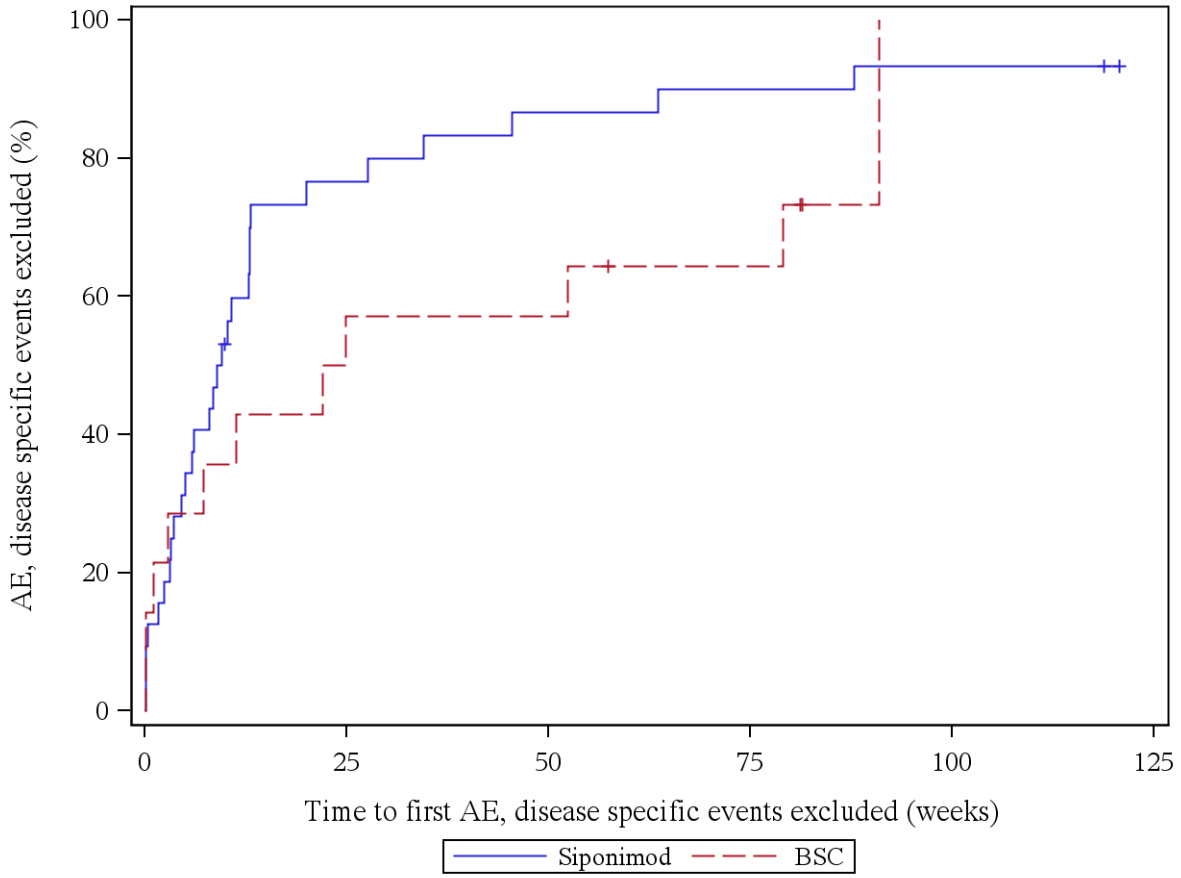


Patients at risk (Siponimod/BSC): Week 0: 95/47, Week 4: 58/33, Week 12: 46/24, Week 24: 32/16, Week 36: 23/11, Week 48: 20/10, Week 60: 10/7, Week 72: 6/5, Week 84: 3/4, Week 96: 2/2, Week 108: 1/2, Week 120: 0/1

Log rank test: p-value = 0,375
*: p < 0,05

Analysis population: A2304 SAF subpopulation "ACTIVE MS WITHOUT RELAPSES"

Figure 12.6.1.2.2: AE, disease specific events excluded, Rapid Evolvement = Yes



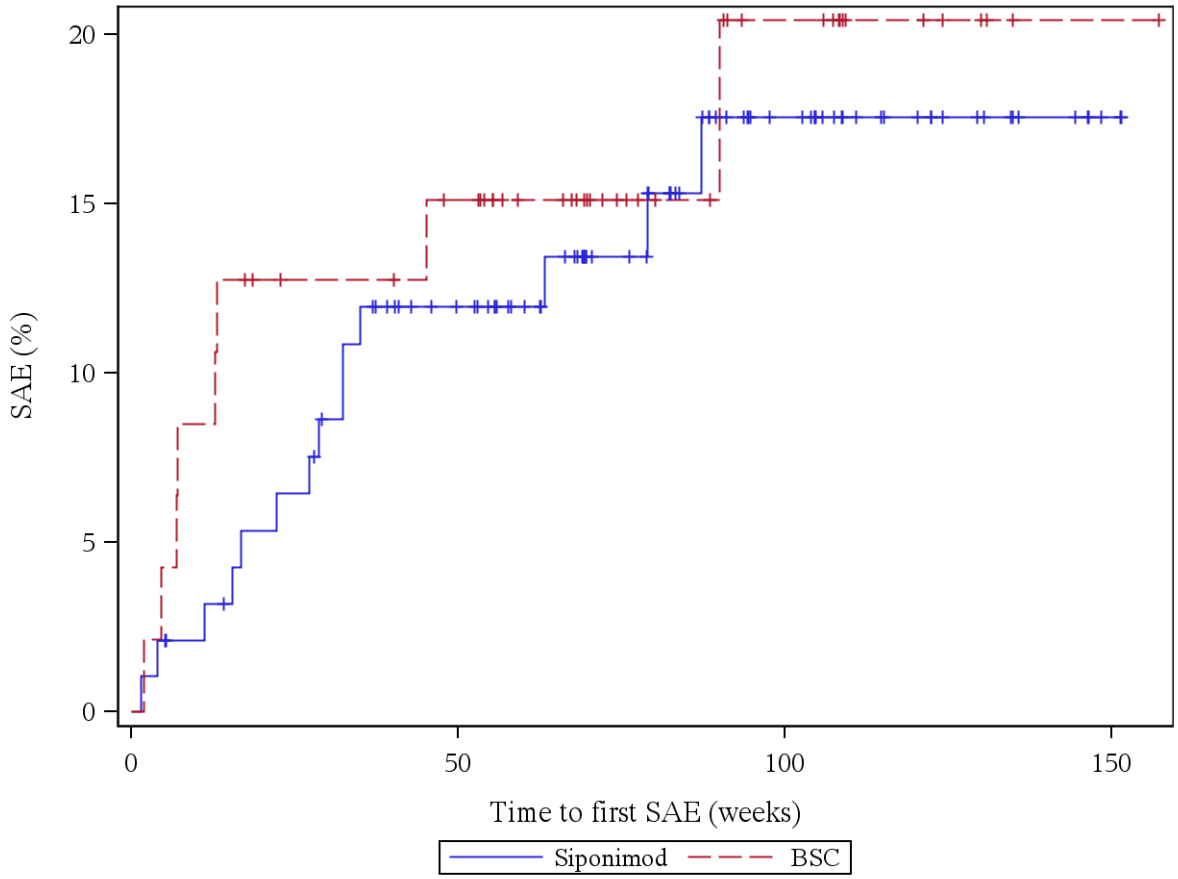
Patients at risk (Siponimod/BSC): Week 0: 32/14, Week 4: 23/10, Week 12: 12/8, Week 24: 7/7, Week 36: 5/6, Week 48: 4/6, Week 60: 4/4, Week 72: 3/4, Week 84: 3/1, Week 96: 2/0, Week 108: 2/0, Week 120: 1/0, Week 132: 0/0

Log rank test: p-value = 0,174
*: p < 0,05

Analysis population: A2304 SAF subpopulation "ACTIVE MS WITHOUT RELAPSES"

12.6.1.3: Any SAE

Figure 12.6.1.3.1: SAE, Rapid Evolvement = No

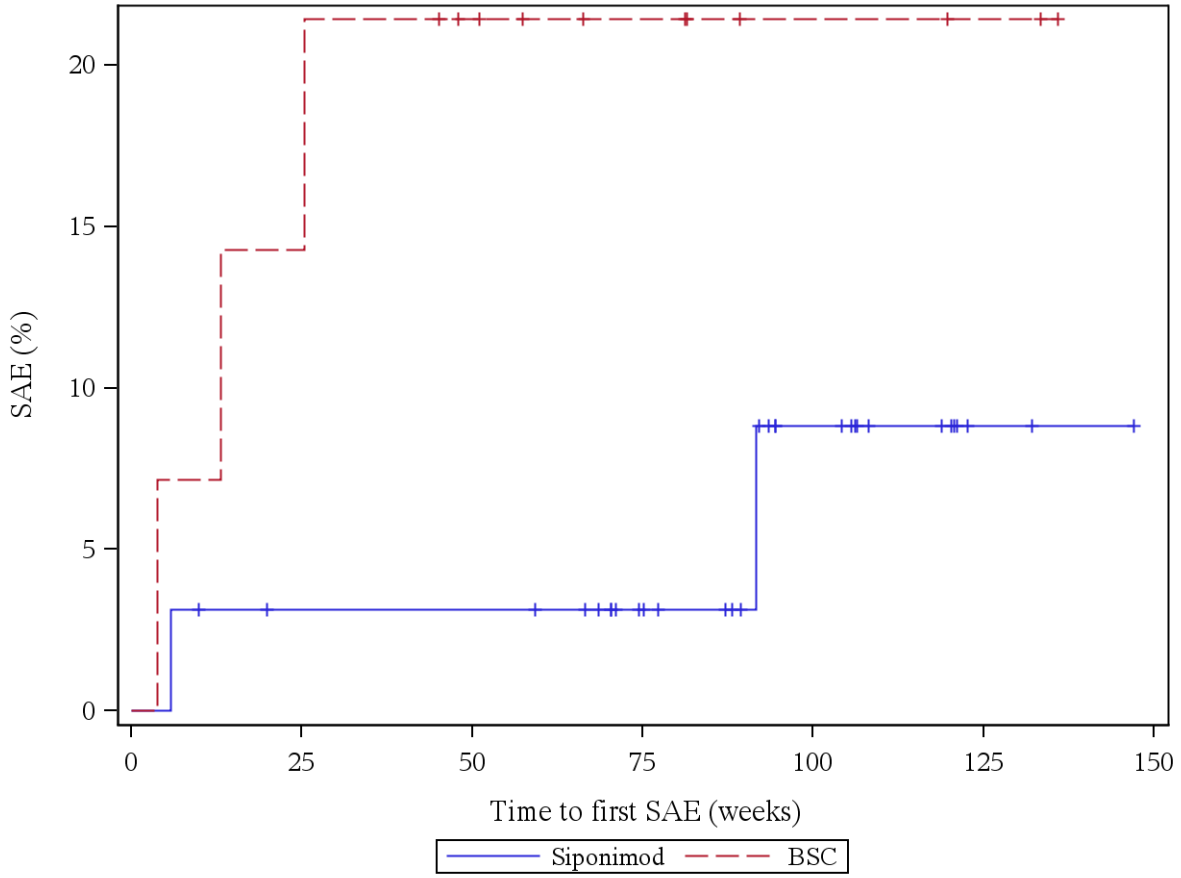


Patients at risk (Siponimod/BSC): Week 0: 95/47, Week 4: 93/46, Week 12: 90/43, Week 24: 86/38, Week 36: 79/38, Week 48: 72/35, Week 60: 63/28, Week 72: 48/21, Week 84: 38/17, Week 96: 28/12, Week 108: 20/10, Week 120: 15/6, Week 132: 9/2, Week 144: 6/1, Week 156: 0/1

Log rank test: p-value = 0,657
*: p < 0,05

Analysis population: A2304 SAF subpopulation "ACTIVE MS WITHOUT RELAPSES"

Figure 12.6.1.3.2: SAE, Rapid Evolvement = Yes



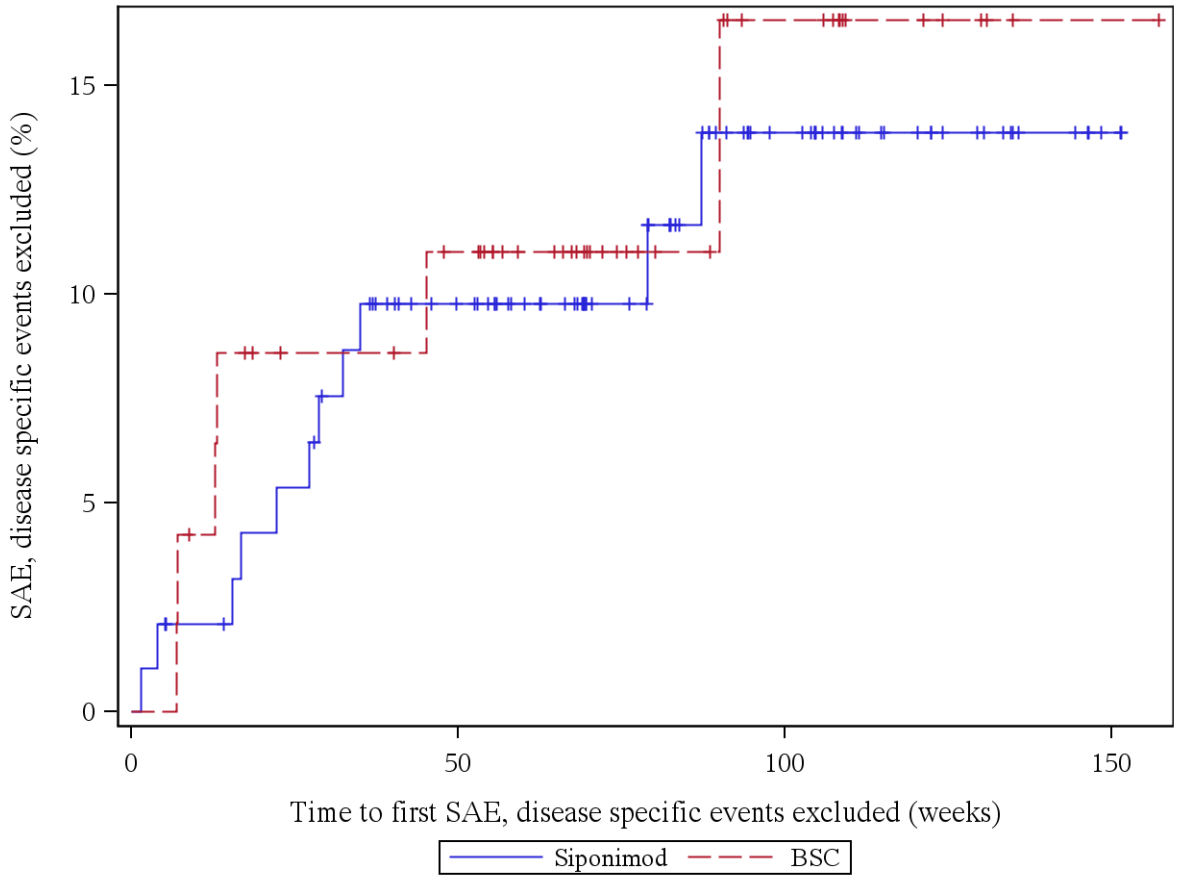
Patients at risk (Siponimod/BSC): Week 0: 32/14, Week 4: 32/13, Week 12: 30/13, Week 24: 29/12, Week 36: 29/11, Week 48: 29/9, Week 60: 28/7, Week 72: 23/6, Week 84: 20/4, Week 96: 12/3, Week 108: 8/3, Week 120: 6/2, Week 132: 2/2, Week 144: 1/0, Week 156: 0/0

Log rank test: p-value = 0,090
*: p < 0,05

Analysis population: A2304 SAF subpopulation "ACTIVE MS WITHOUT RELAPSES"

12.6.1.4: Any SAE, disease specific events excluded

Figure 12.6.1.4.1: SAE, disease specific events excluded, Rapid Evolvement = No

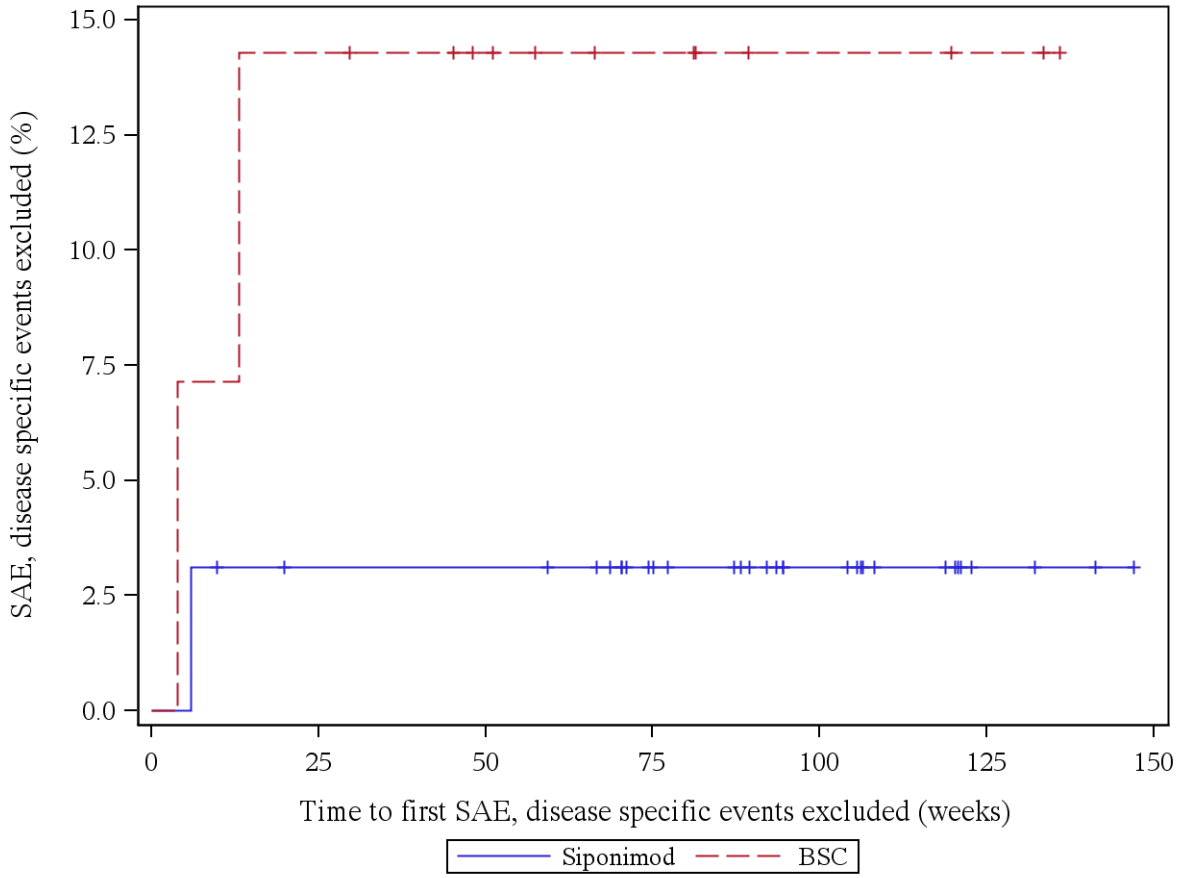


Patients at risk (Siponimod/BSC): Week 0: 95/47, Week 4: 93/47, Week 12: 91/44, Week 24: 87/39, Week 36: 81/39, Week 48: 73/36, Week 60: 64/29, Week 72: 50/21, Week 84: 40/17, Week 96: 30/12, Week 108: 22/10, Week 120: 16/6, Week 132: 10/2, Week 144: 6/1, Week 156: 0/1

Log rank test: p-value = 0,766
*: p < 0,05

Analysis population: A2304 SAF subpopulation "ACTIVE MS WITHOUT RELAPSES"

Figure 12.6.1.4.2: SAE, disease specific events excluded, Rapid Evolvement = Yes



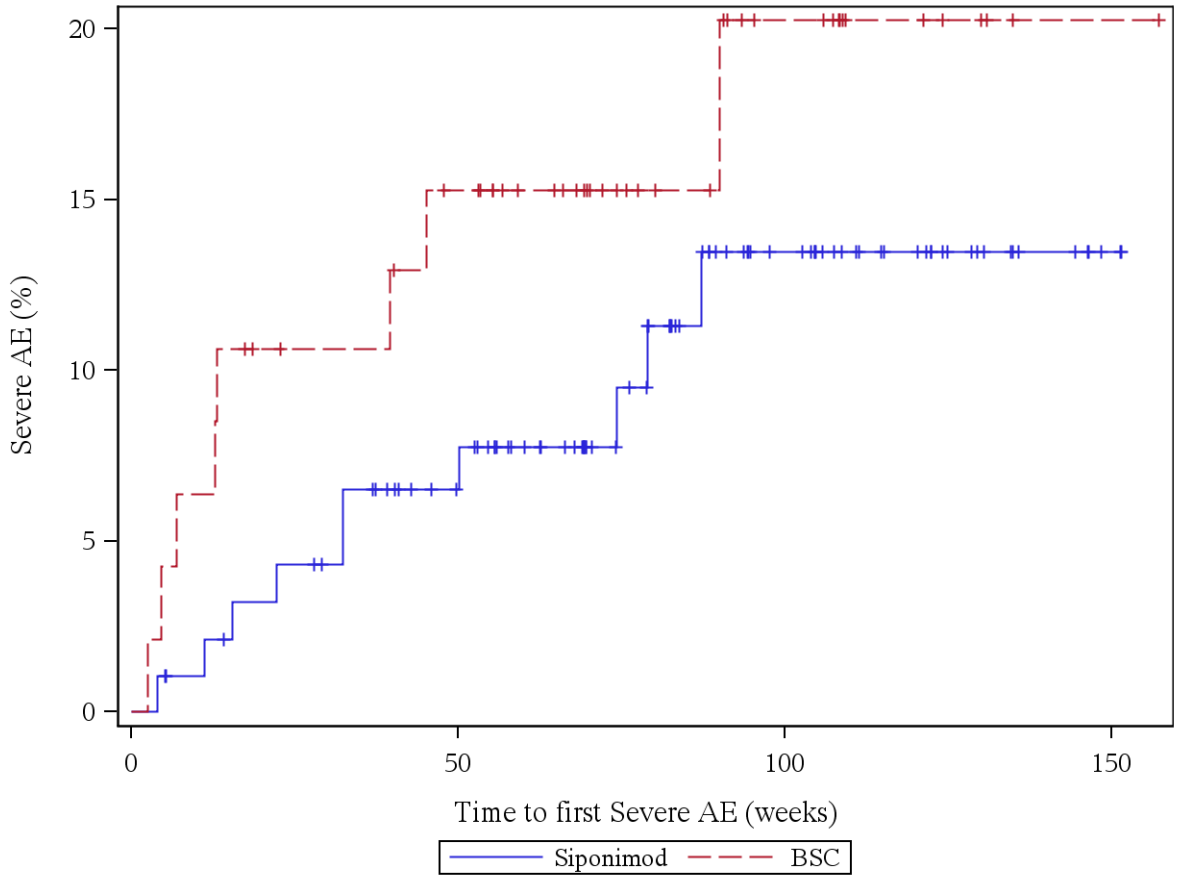
Patients at risk (Siponimod/BSC): Week 0: 32/14, Week 4: 32/13, Week 12: 30/13, Week 24: 29/12, Week 36: 29/11, Week 48: 29/9, Week 60: 28/7, Week 72: 23/6, Week 84: 20/4, Week 96: 13/3, Week 108: 9/3, Week 120: 7/2, Week 132: 3/2, Week 144: 1/0, Week 156: 0/0

Log rank test: p-value = 0,163
*: p < 0,05

Analysis population: A2304 SAF subpopulation "ACTIVE MS WITHOUT RELAPSES"

12.6.1.5: Any severe AE

Figure 12.6.1.5.1: Severe AE, Rapid Evolvement = No

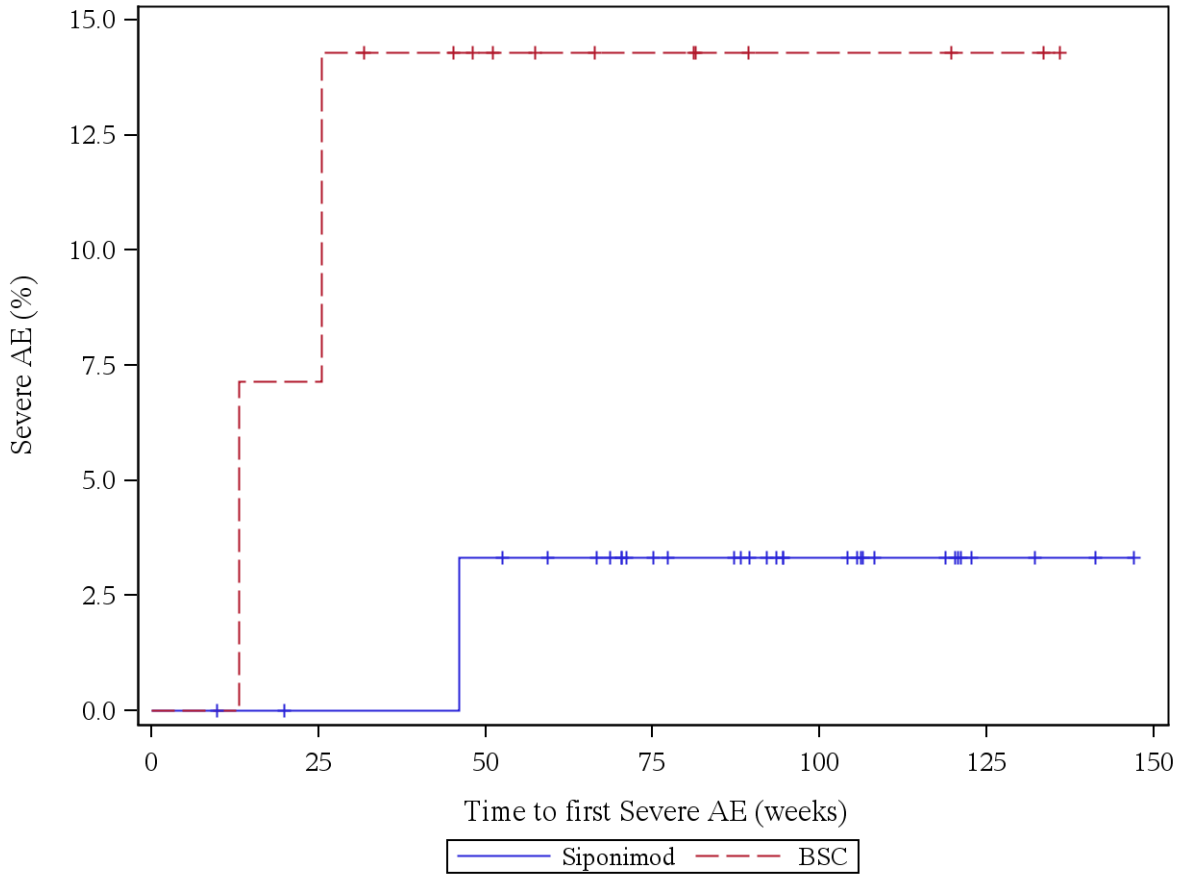


Patients at risk (Siponimod/BSC): Week 0: 95/47, Week 4: 94/46, Week 12: 91/44, Week 24: 88/39, Week 36: 84/39, Week 48: 77/35, Week 60: 67/29, Week 72: 54/22, Week 84: 41/18, Week 96: 31/12, Week 108: 23/10, Week 120: 18/6, Week 132: 9/2, Week 144: 6/1, Week 156: 0/1

Log rank test: p-value = 0,242
*: p < 0,05

Analysis population: A2304 SAF subpopulation "ACTIVE MS WITHOUT RELAPSES"

Figure 12.6.1.5.2: Severe AE, Rapid Evolvement = Yes



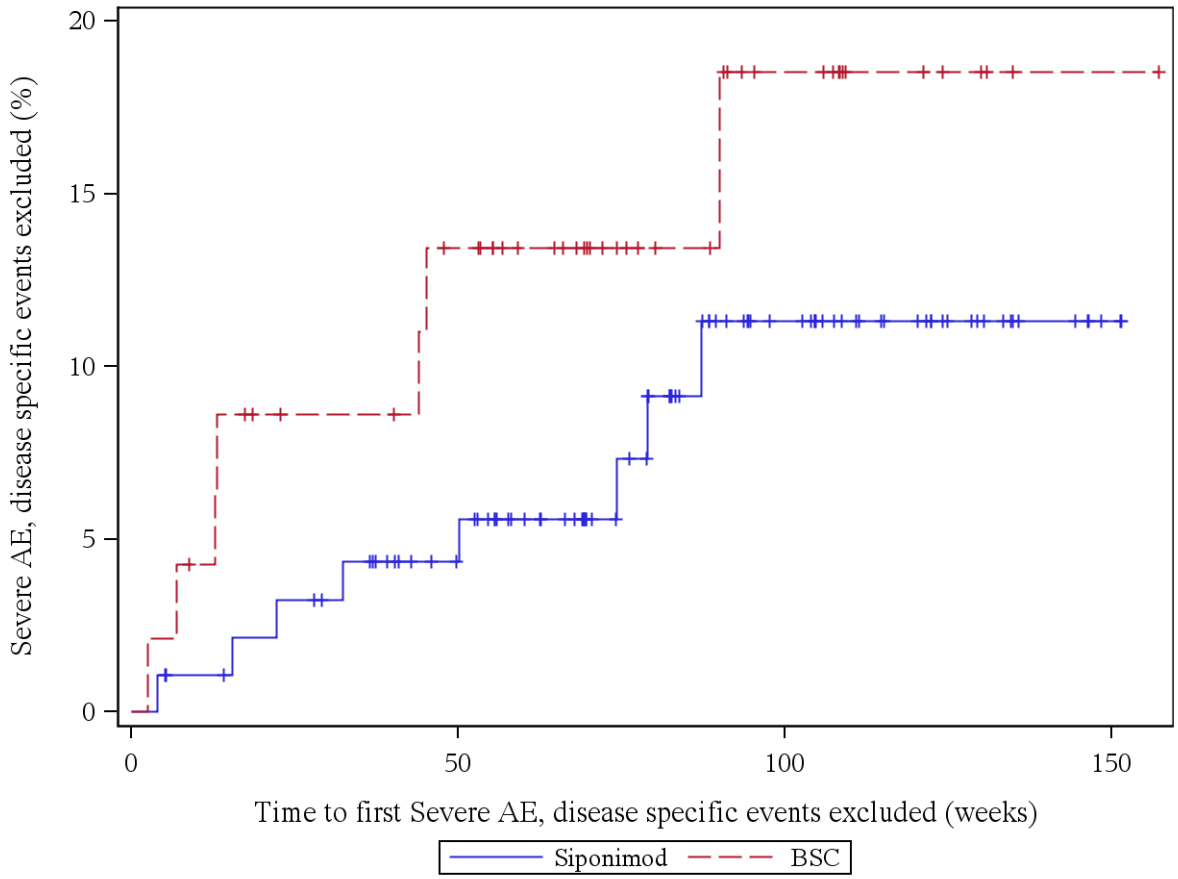
Patients at risk (Siponimod/BSC): Week 0: 32/14, Week 4: 32/14, Week 12: 31/14, Week 24: 30/13, Week 36: 30/11, Week 48: 29/9, Week 60: 27/7, Week 72: 22/6, Week 84: 20/4, Week 96: 13/3, Week 108: 9/3, Week 120: 7/2, Week 132: 3/2, Week 144: 1/0, Week 156: 0/0

Log rank test: p-value = 0,147
*: p < 0,05

Analysis population: A2304 SAF subpopulation "ACTIVE MS WITHOUT RELAPSES"

12.6.1.6: Any severe AE, disease specific events excluded

Figure 12.6.1.6.1: Severe AE, disease specific events excluded, Rapid Evolvement = No

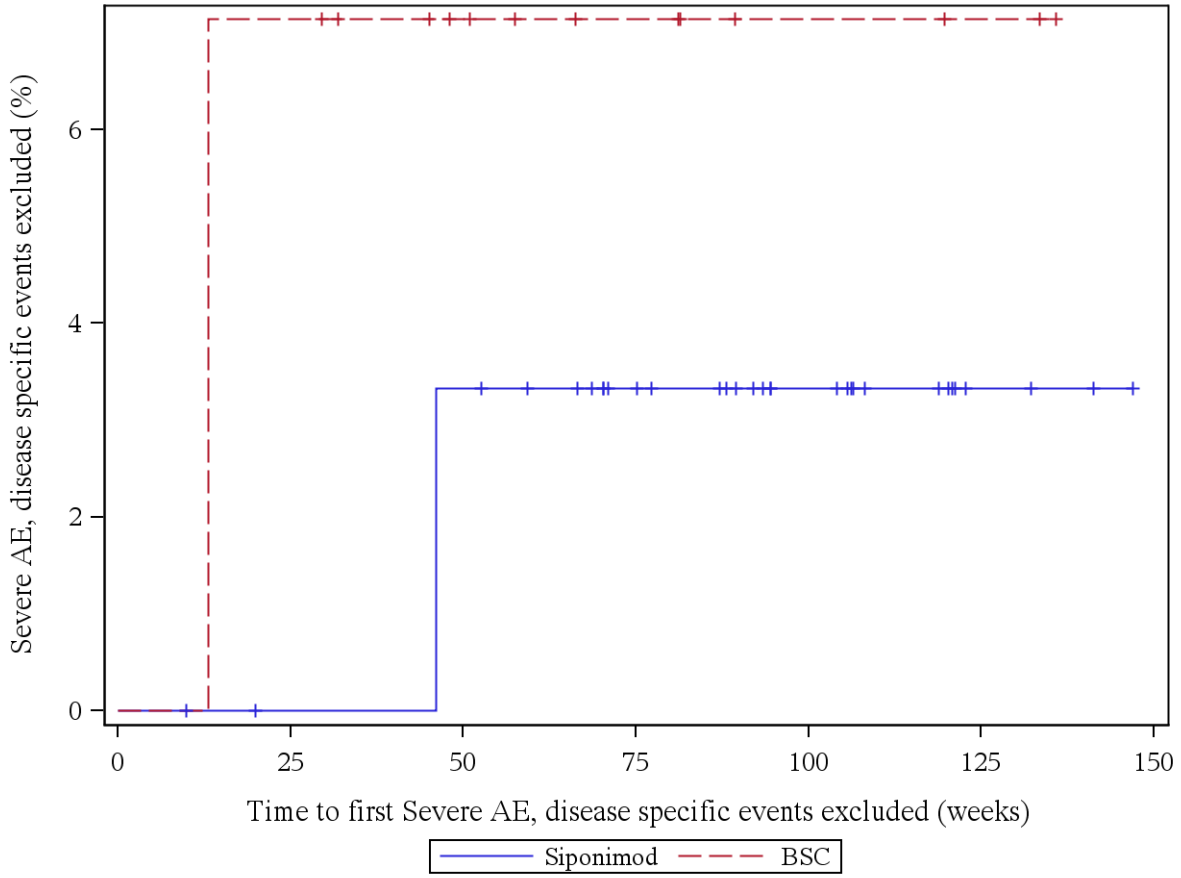


Patients at risk (Siponimod/BSC): Week 0: 95/47, Week 4: 94/46, Week 12: 92/44, Week 24: 89/39, Week 36: 86/39, Week 48: 78/35, Week 60: 68/29, Week 72: 55/22, Week 84: 42/18, Week 96: 32/12, Week 108: 24/10, Week 120: 19/6, Week 132: 10/2, Week 144: 6/1, Week 156: 0/1

Log rank test: p-value = 0,200
*: p < 0,05

Analysis population: A2304 SAF subpopulation "ACTIVE MS WITHOUT RELAPSES"

Figure 12.6.1.6.2: Severe AE, disease specific events excluded, Rapid Evolvement = Yes



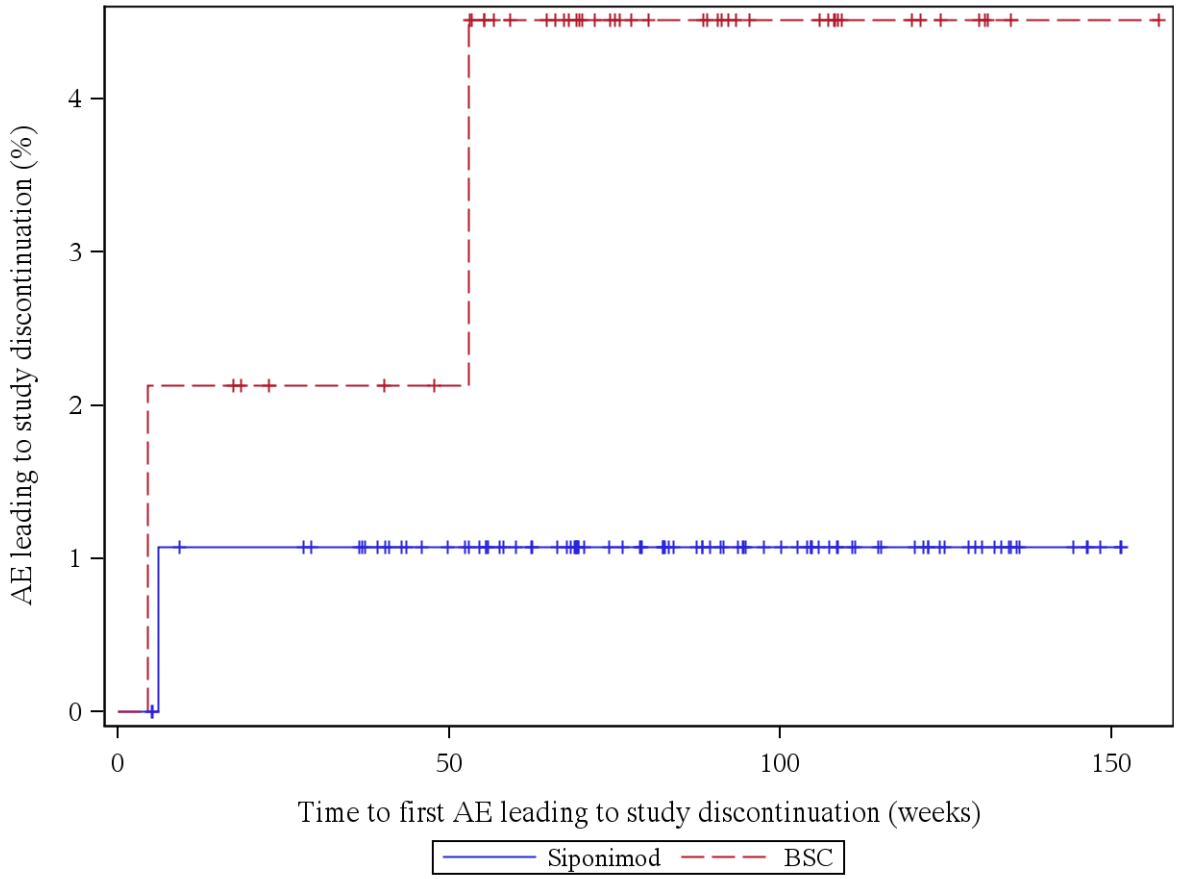
Patients at risk (Siponimod/BSC): Week 0: 32/14, Week 4: 32/14, Week 12: 31/14, Week 24: 30/13, Week 36: 30/11, Week 48: 29/9, Week 60: 27/7, Week 72: 22/6, Week 84: 20/4, Week 96: 13/3, Week 108: 9/3, Week 120: 7/2, Week 132: 3/2, Week 144: 1/0, Week 156: 0/0

Log rank test: p-value = 0,489
*: p < 0,05

Analysis population: A2304 SAF subpopulation "ACTIVE MS WITHOUT RELAPSES"

12.6.1.7: Any AE leading to study discontinuation

Figure 12.6.1.7.1: AE leading to study discontinuation, Rapid Evolvement = No

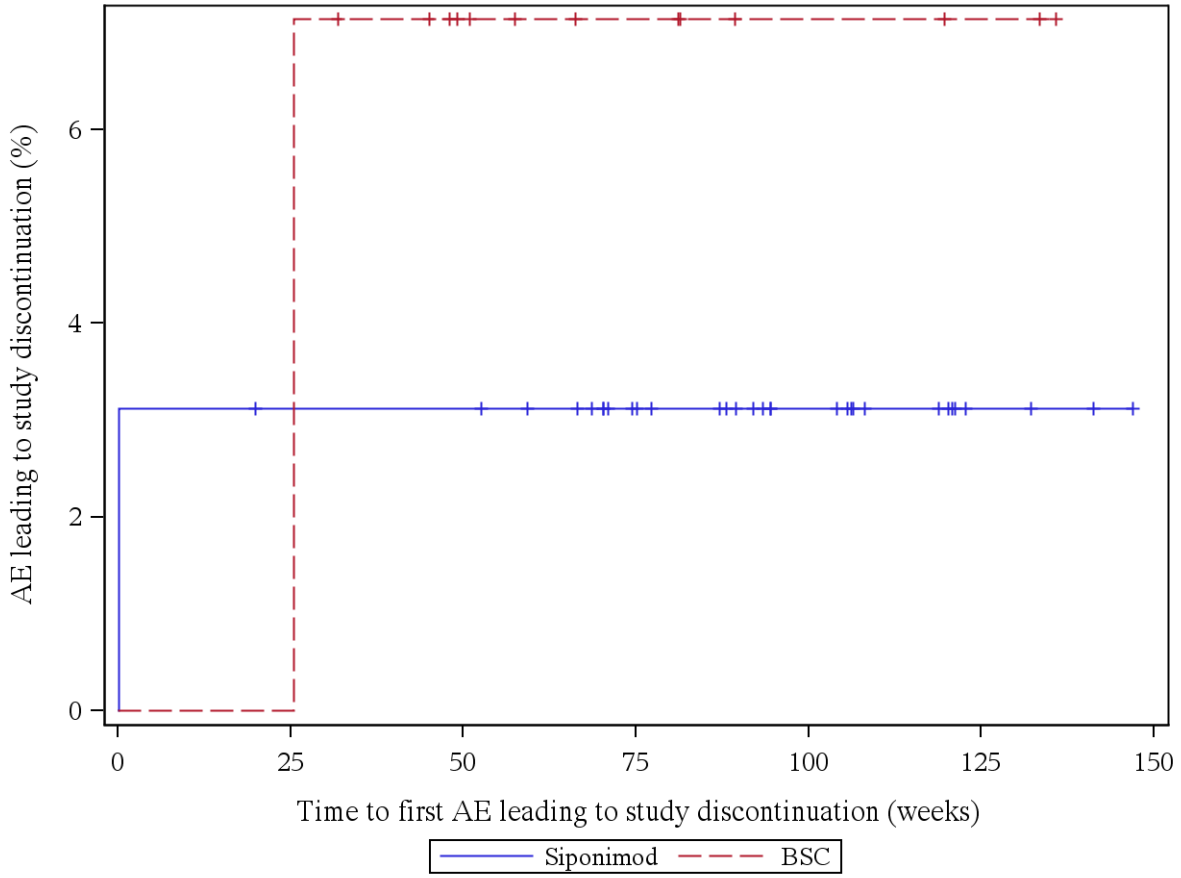


Patients at risk (Siponimod/BSC): Week 0: 95/47, Week 4: 95/47, Week 12: 91/46, Week 24: 91/43, Week 36: 89/43, Week 48: 80/41, Week 60: 71/34, Week 72: 57/26, Week 84: 46/21, Week 96: 36/14, Week 108: 27/12, Week 120: 21/7, Week 132: 12/2, Week 144: 6/1, Week 156: 0/1

Log rank test: p-value = 0,224
*: p < 0,05

Analysis population: A2304 SAF subpopulation "ACTIVE MS WITHOUT RELAPSES"

Figure 12.6.1.7.2: AE leading to study discontinuation, Rapid Evolvement = Yes



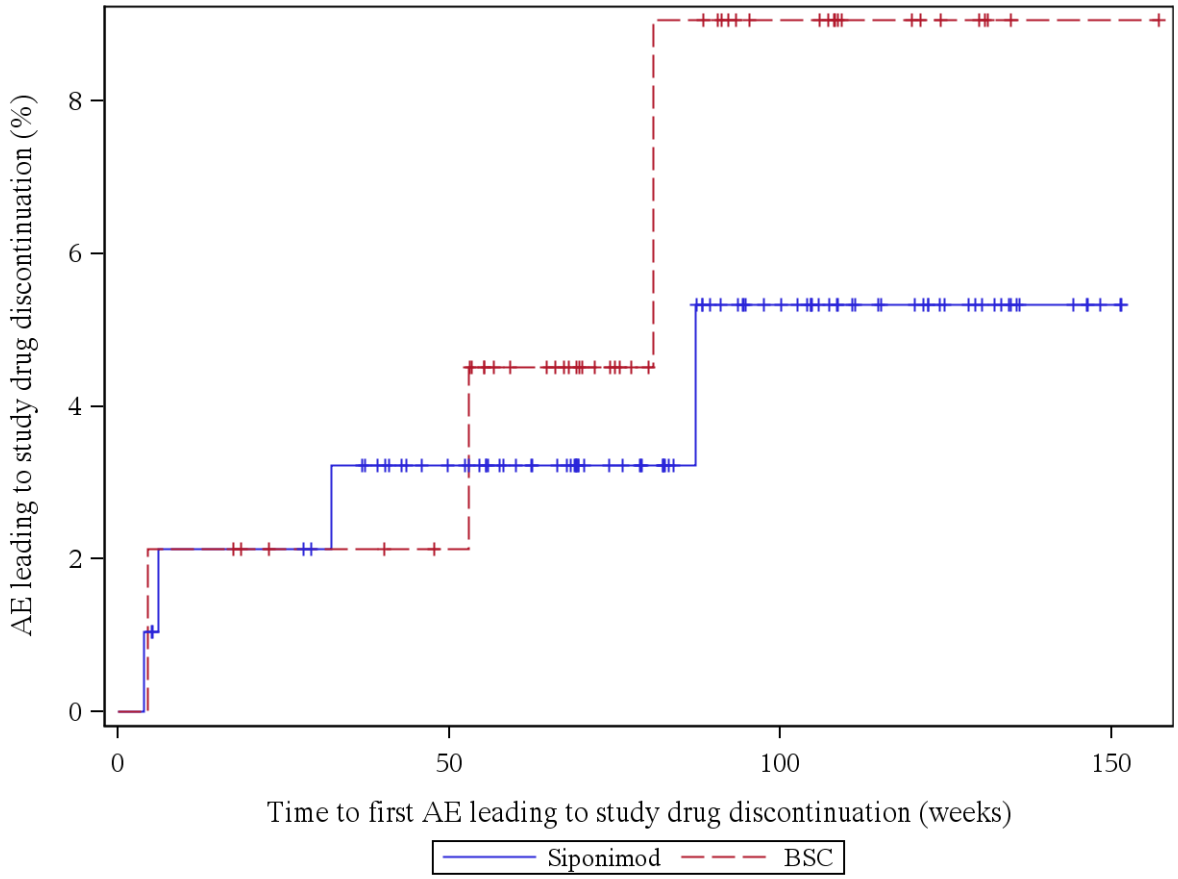
Patients at risk (Siponimod/BSC): Week 0: 32/14, Week 4: 31/14, Week 12: 31/14, Week 24: 30/14, Week 36: 30/12, Week 48: 30/10, Week 60: 28/7, Week 72: 23/6, Week 84: 20/4, Week 96: 13/3, Week 108: 9/3, Week 120: 7/2, Week 132: 3/2, Week 144: 1/0, Week 156: 0/0

Log rank test: p-value = 0,564
*: p < 0,05

Analysis population: A2304 SAF subpopulation "ACTIVE MS WITHOUT RELAPSES"

12.6.1.8: Any AE leading to study drug discontinuation

Figure 12.6.1.8.1: AE leading to study drug discontinuation, Rapid Evolvement = No

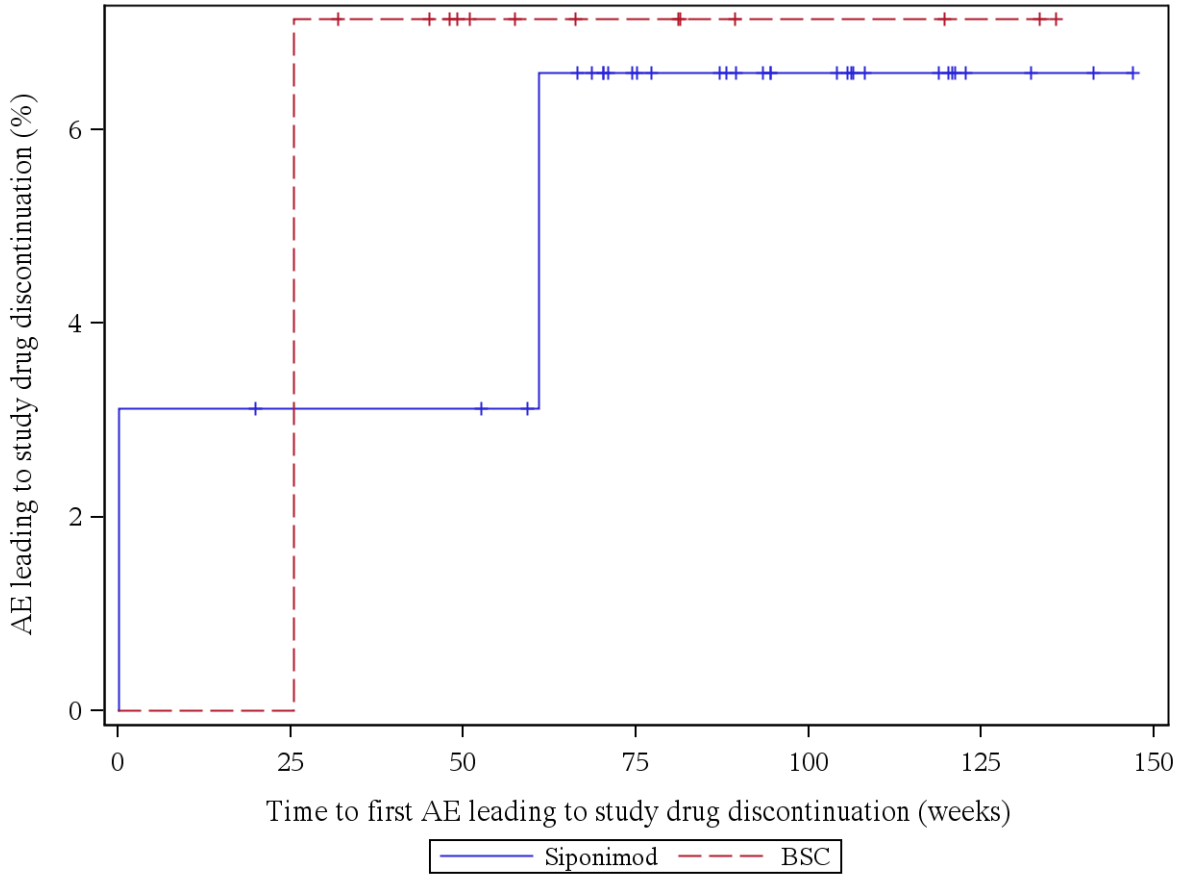


Patients at risk (Siponimod/BSC): Week 0: 95/47, Week 4: 94/47, Week 12: 91/46, Week 24: 91/43, Week 36: 88/43, Week 48: 80/41, Week 60: 71/34, Week 72: 57/26, Week 84: 46/20, Week 96: 36/14, Week 108: 27/12, Week 120: 21/7, Week 132: 12/2, Week 144: 6/1, Week 156: 0/1

Log rank test: p-value = 0,549
*: p < 0,05

Analysis population: A2304 SAF subpopulation "ACTIVE MS WITHOUT RELAPSES"

Figure 12.6.1.8.2: AE leading to study drug discontinuation, Rapid Evolvement = Yes



Patients at risk (Siponimod/BSC): Week 0: 32/14, Week 4: 31/14, Week 12: 31/14, Week 24: 30/14, Week 36: 30/12, Week 48: 30/10, Week 60: 28/7, Week 72: 22/6, Week 84: 19/4, Week 96: 13/3, Week 108: 9/3, Week 120: 7/2, Week 132: 3/2, Week 144: 1/0, Week 156: 0/0

Log rank test: p-value = 0,817
*: p < 0,05

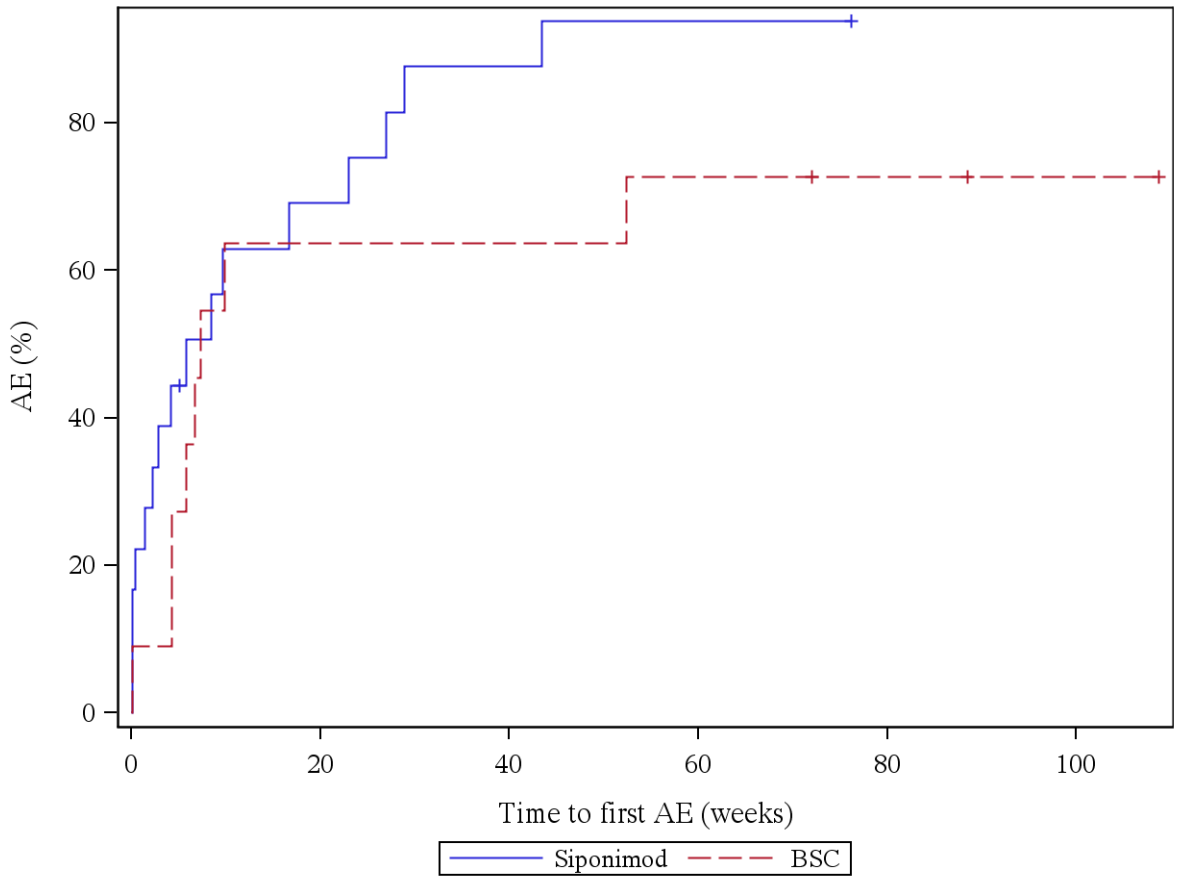
Analysis population: A2304 SAF subpopulation "ACTIVE MS WITHOUT RELAPSES"

12.7 Subgroup: Disease Course

12.7.1: Time to First Adverse Event (SAF) by Disease Course

12.7.1.1: Any AE

Figure 12.7.1.1.1: AE, Moderate or Severe Disease Course = No

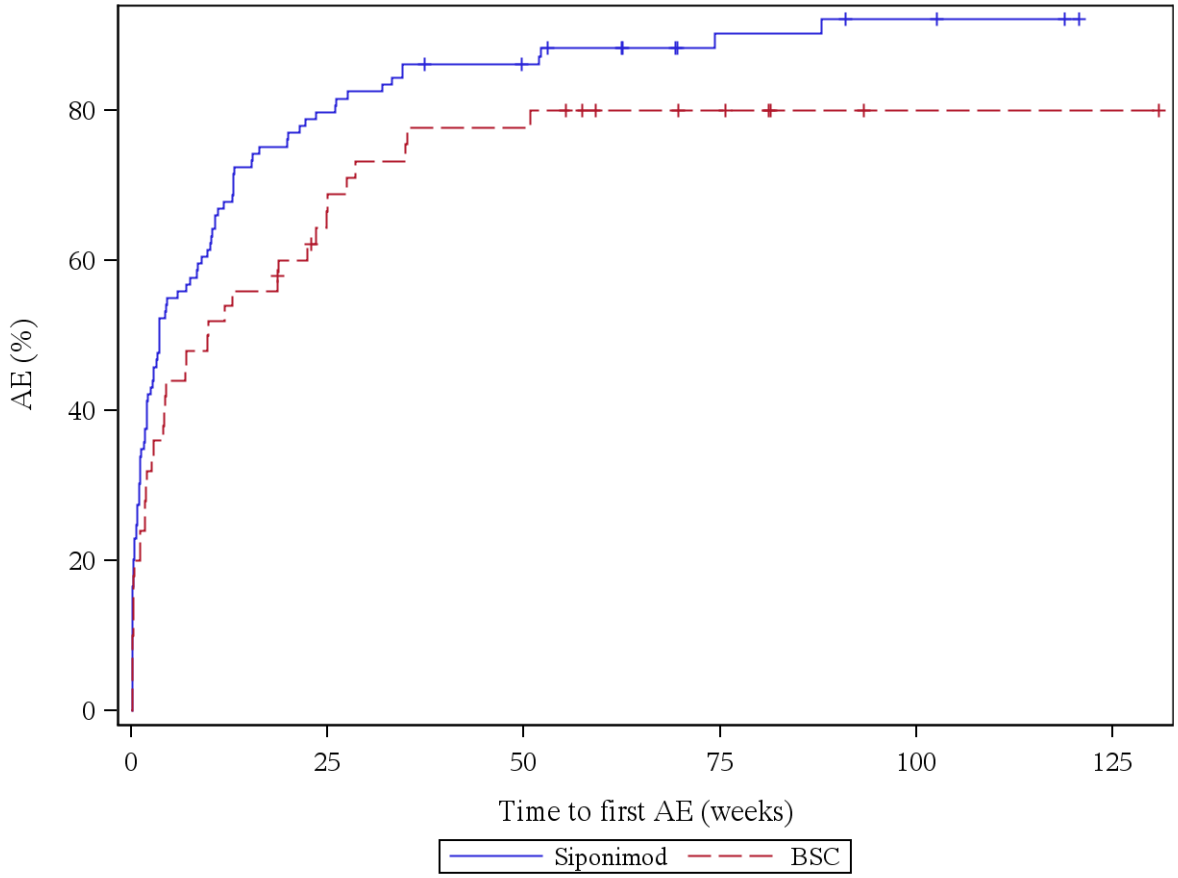


Patients at risk (Siponimod/BSC): Week 0: 18/11, Week 4: 11/10, Week 12: 6/4, Week 24: 4/4, Week 36: 2/4, Week 48: 1/4, Week 60: 1/3, Week 72: 1/2, Week 84: 0/2

Log rank test: p-value = 0,180
*: p < 0,05

Analysis population: A2304 SAF subpopulation "ACTIVE MS WITHOUT RELAPSES"

Figure 12.7.1.1.2: AE, Moderate or Severe Disease Course = Yes



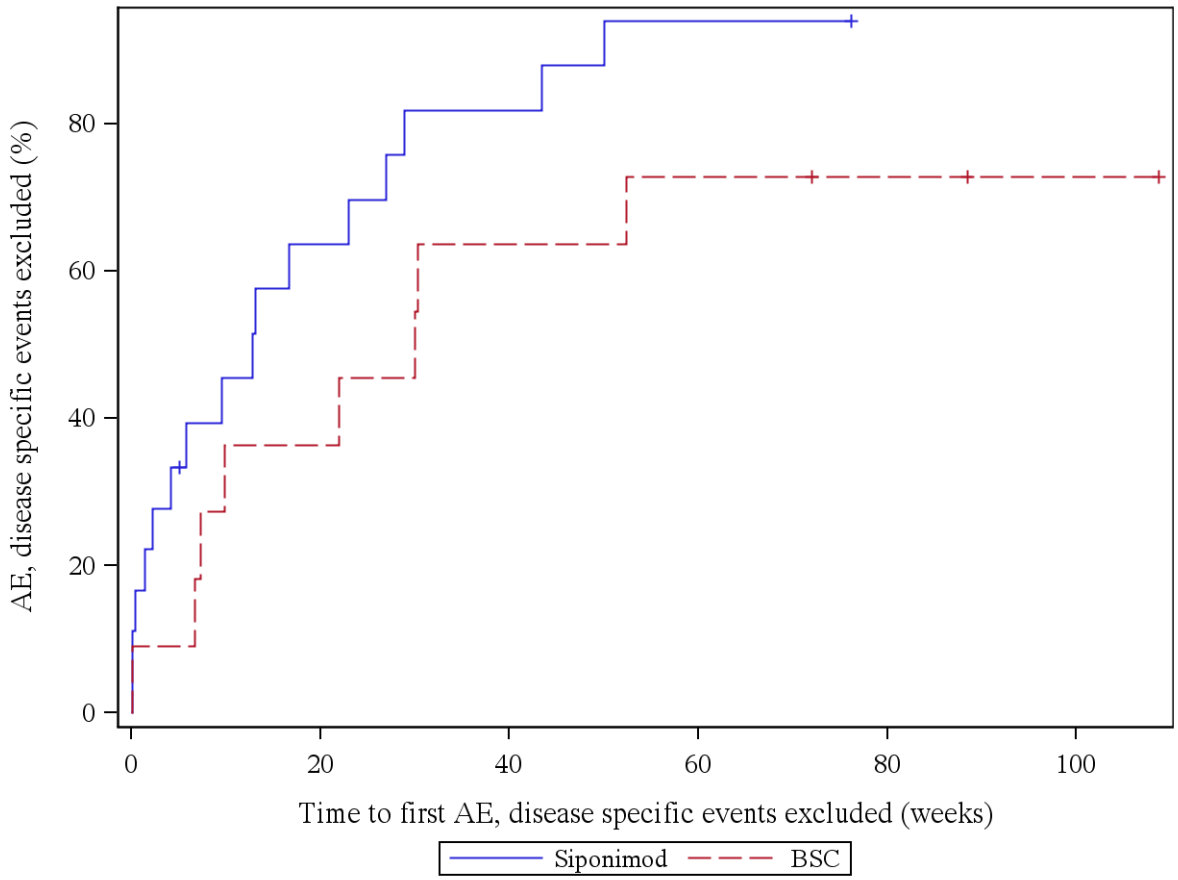
Patients at risk (Siponimod/BSC): Week 0: 109/50, Week 4: 52/31, Week 12: 35/23, Week 24: 22/16, Week 36: 15/10, Week 48: 14/10, Week 60: 10/6, Week 72: 6/5, Week 84: 5/2, Week 96: 3/1, Week 108: 2/1, Week 120: 1/1, Week 132: 0/0

Log rank test: p-value = 0,056
*: p < 0,05

Analysis population: A2304 SAF subpopulation "ACTIVE MS WITHOUT RELAPSES"

12.7.1.2: Any AE, disease specific events excluded

Figure 12.7.1.2.1: AE, disease specific events excluded, Moderate or Severe Disease Course = No

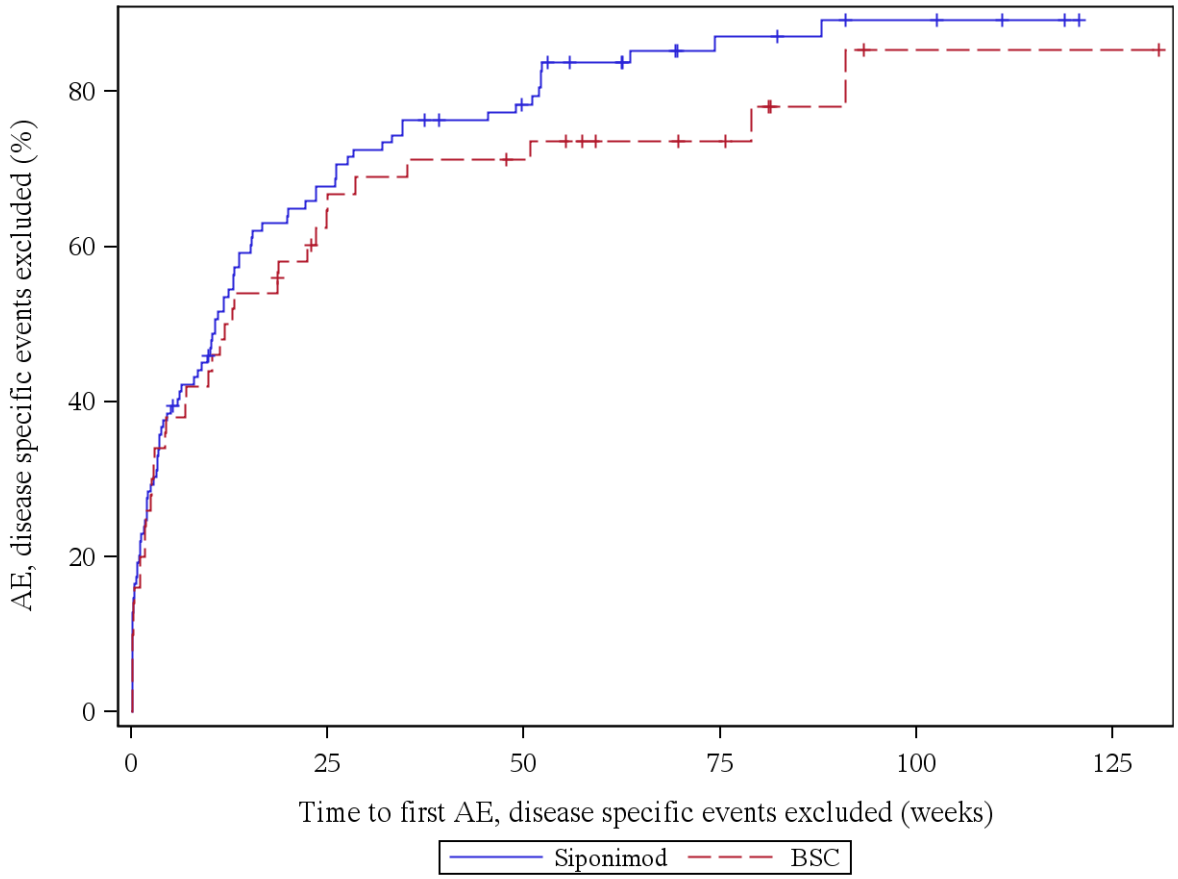


Patients at risk (Siponimod/BSC): Week 0: 18/11, Week 4: 13/10, Week 12: 9/7, Week 24: 5/6, Week 36: 3/4, Week 48: 2/4, Week 60: 1/3, Week 72: 1/2, Week 84: 0/2

Log rank test: p-value = 0,089
*: p < 0,05

Analysis population: A2304 SAF subpopulation "ACTIVE MS WITHOUT RELAPSES"

Figure 12.7.1.2.2: AE, disease specific events excluded, Moderate or Severe Disease Course = Yes



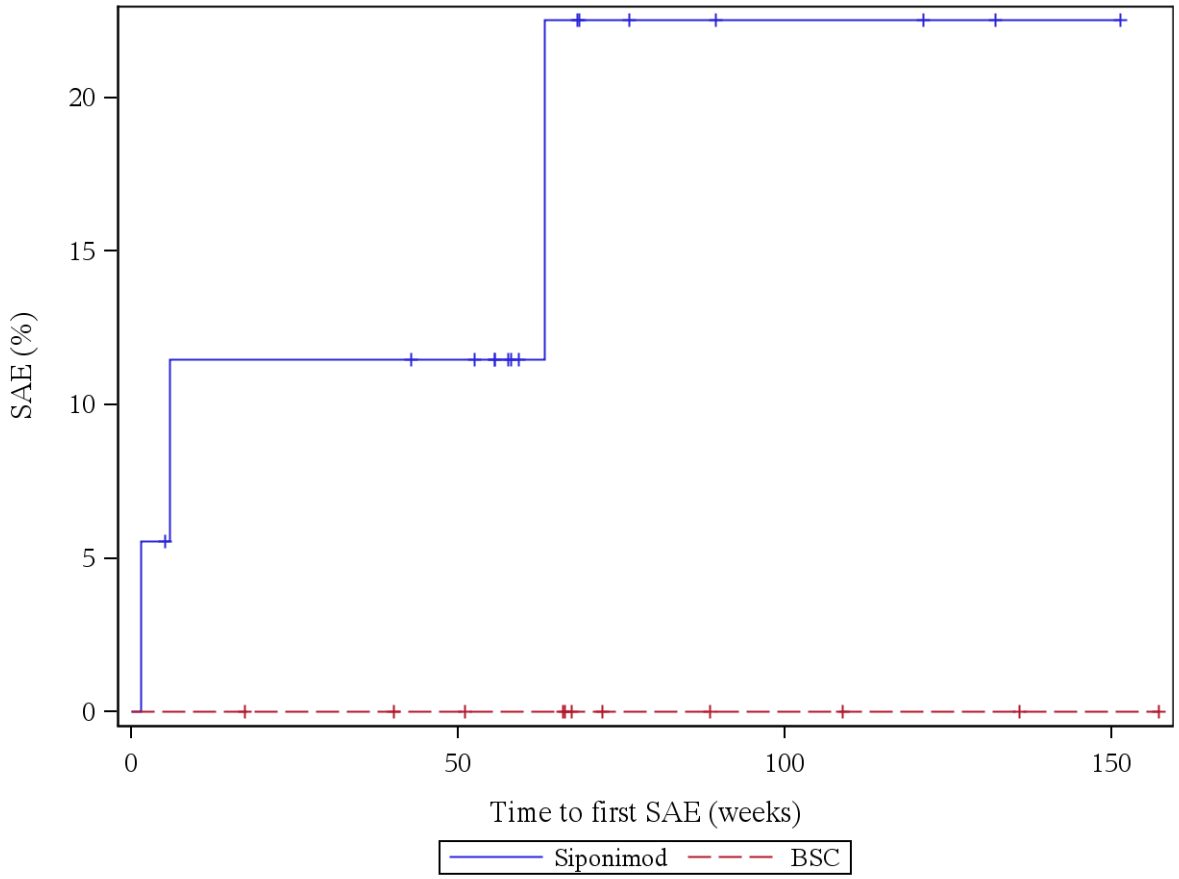
Patients at risk (Siponimod/BSC): Week 0: 109/50, Week 4: 68/33, Week 12: 49/25, Week 24: 34/17, Week 36: 25/13, Week 48: 22/12, Week 60: 13/8, Week 72: 8/7, Week 84: 6/3, Week 96: 4/1, Week 108: 3/1, Week 120: 1/1, Week 132: 0/0

Log rank test: p-value = 0,327
*: p < 0,05

Analysis population: A2304 SAF subpopulation "ACTIVE MS WITHOUT RELAPSES"

12.7.1.3: Any SAE

Figure 12.7.1.3.1: SAE, Moderate or Severe Disease Course = No

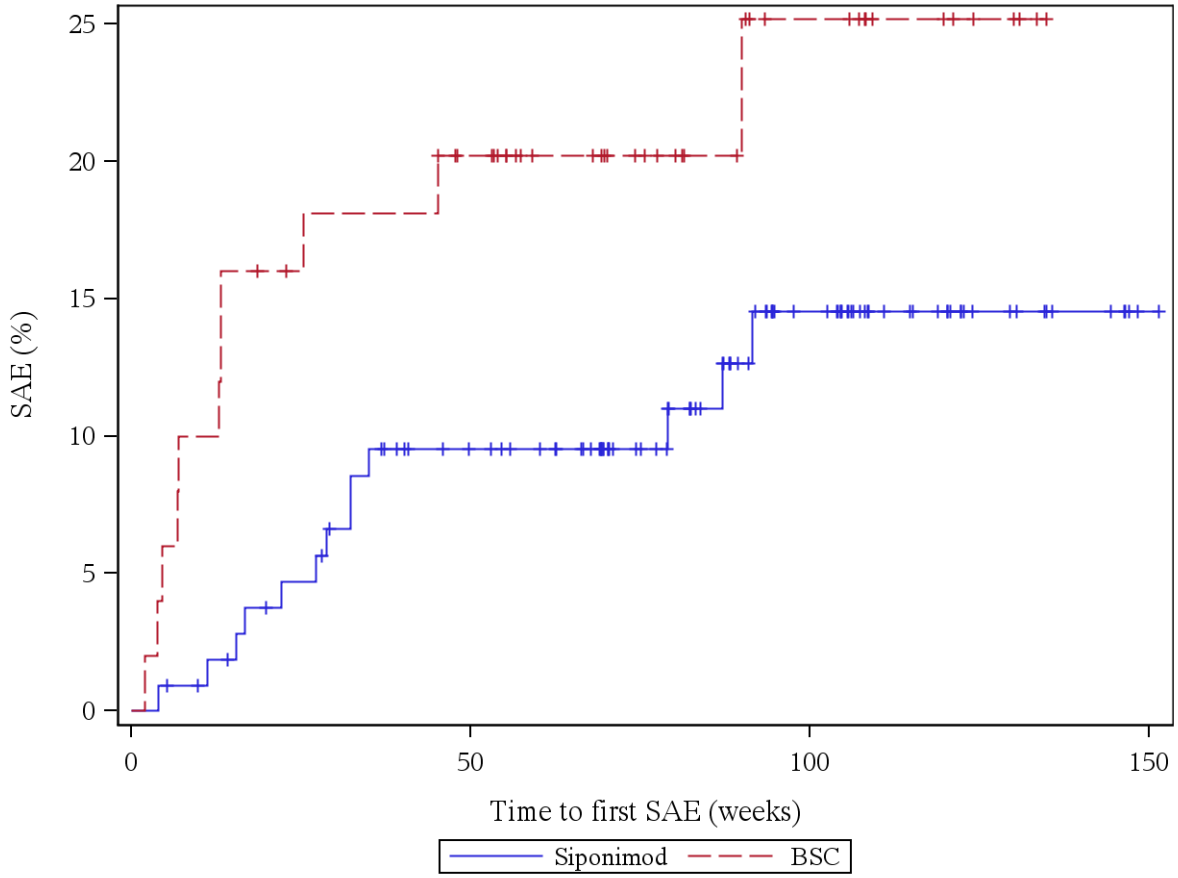


Patients at risk (Siponimod/BSC): Week 0: 18/11, Week 4: 17/11, Week 12: 15/11, Week 24: 15/10, Week 36: 15/10, Week 48: 14/9, Week 60: 8/8, Week 72: 5/4, Week 84: 4/4, Week 96: 3/3, Week 108: 3/3, Week 120: 3/2, Week 132: 2/2, Week 144: 1/1, Week 156: 0/1

Log rank test: p-value = -
*: p < 0,05

Analysis population: A2304 SAF subpopulation "ACTIVE MS WITHOUT RELAPSES"

Figure 12.7.1.3.2: SAE, Moderate or Severe Disease Course = Yes



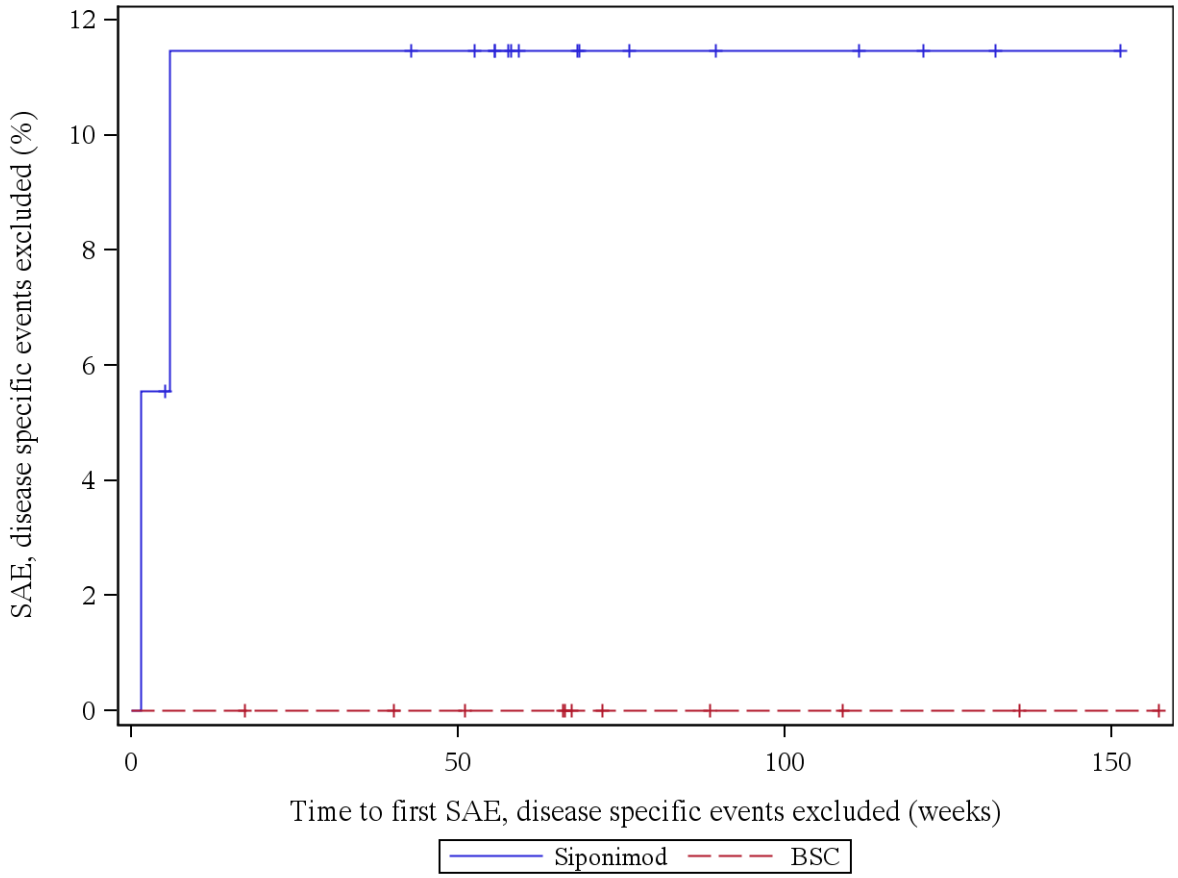
Patients at risk (Siponimod/BSC): Week 0: 109/50, Week 4: 108/48, Week 12: 105/45, Week 24: 100/40, Week 36: 93/39, Week 48: 87/35, Week 60: 83/27, Week 72: 66/23, Week 84: 54/17, Week 96: 37/12, Week 108: 25/10, Week 120: 18/6, Week 132: 9/2, Week 144: 6/0, Week 156: 0/0

Log rank test: p-value = 0,063
*: p < 0,05

Analysis population: A2304 SAF subpopulation "ACTIVE MS WITHOUT RELAPSES"

12.7.1.4: Any SAE, disease specific events excluded

Figure 12.7.1.4.1: SAE, disease specific events excluded, Moderate or Severe Disease Course = No

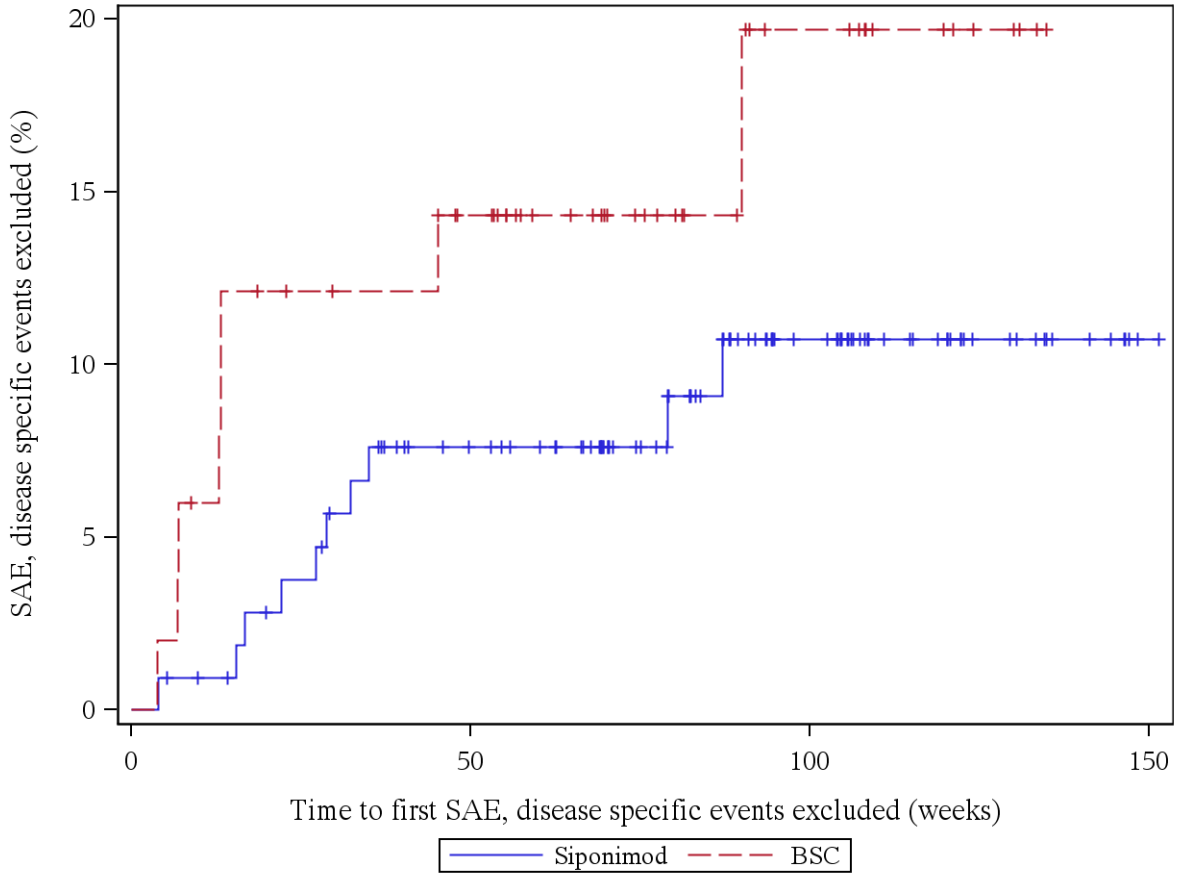


Patients at risk (Siponimod/BSC): Week 0: 18/11, Week 4: 17/11, Week 12: 15/11, Week 24: 15/10, Week 36: 15/10, Week 48: 14/9, Week 60: 8/8, Week 72: 6/4, Week 84: 5/4, Week 96: 4/3, Week 108: 4/3, Week 120: 3/2, Week 132: 2/2, Week 144: 1/1, Week 156: 0/1

Log rank test: p-value = -
*: p < 0,05

Analysis population: A2304 SAF subpopulation "ACTIVE MS WITHOUT RELAPSES"

Figure 12.7.1.4.2: SAE, disease specific events excluded, Moderate or Severe Disease Course = Yes



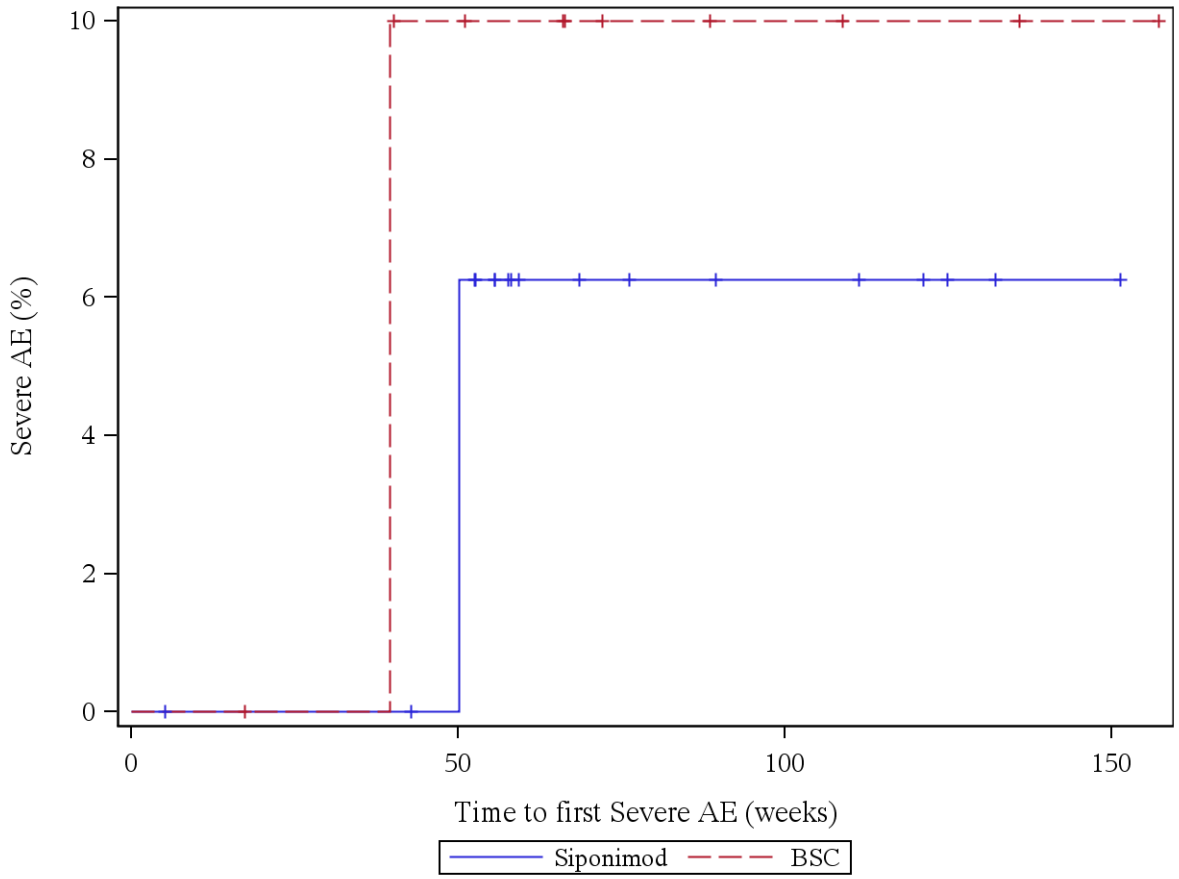
Patients at risk (Siponimod/BSC): Week 0: 109/50, Week 4: 108/49, Week 12: 106/46, Week 24: 101/41, Week 36: 95/40, Week 48: 88/36, Week 60: 84/28, Week 72: 67/23, Week 84: 55/17, Week 96: 39/12, Week 108: 27/10, Week 120: 20/6, Week 132: 11/2, Week 144: 6/0, Week 156: 0/0

Log rank test: p-value = 0,149
*: p < 0,05

Analysis population: A2304 SAF subpopulation "ACTIVE MS WITHOUT RELAPSES"

12.7.1.5: Any severe AE

Figure 12.7.1.5.1: Severe AE, Moderate or Severe Disease Course = No

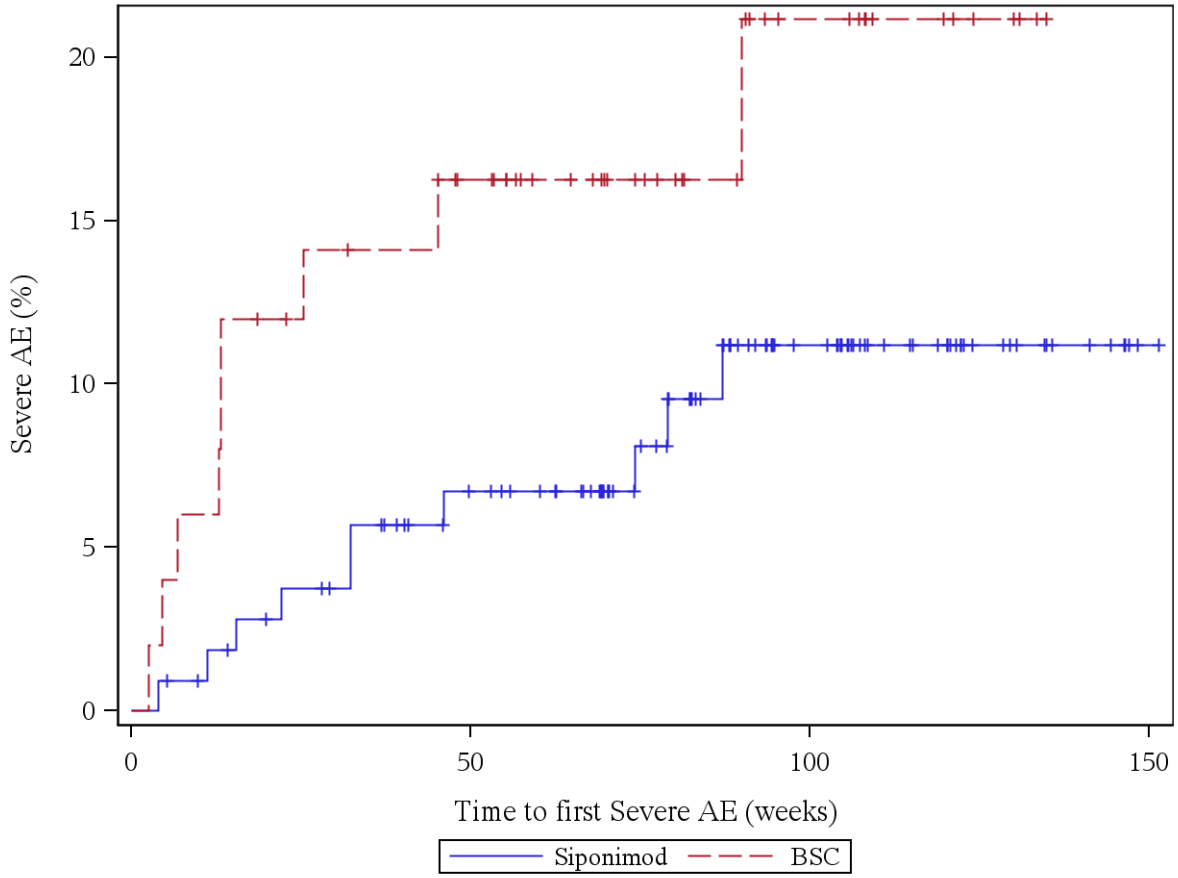


Patients at risk (Siponimod/BSC): Week 0: 18/11, Week 4: 18/11, Week 12: 17/11, Week 24: 17/10, Week 36: 17/10, Week 48: 16/8, Week 60: 8/7, Week 72: 7/4, Week 84: 6/4, Week 96: 5/3, Week 108: 5/3, Week 120: 4/2, Week 132: 2/2, Week 144: 1/1, Week 156: 0/1

Log rank test: p-value = 0,661
*: p < 0,05

Analysis population: A2304 SAF subpopulation "ACTIVE MS WITHOUT RELAPSES"

Figure 12.7.1.5.2: Severe AE, Moderate or Severe Disease Course = Yes



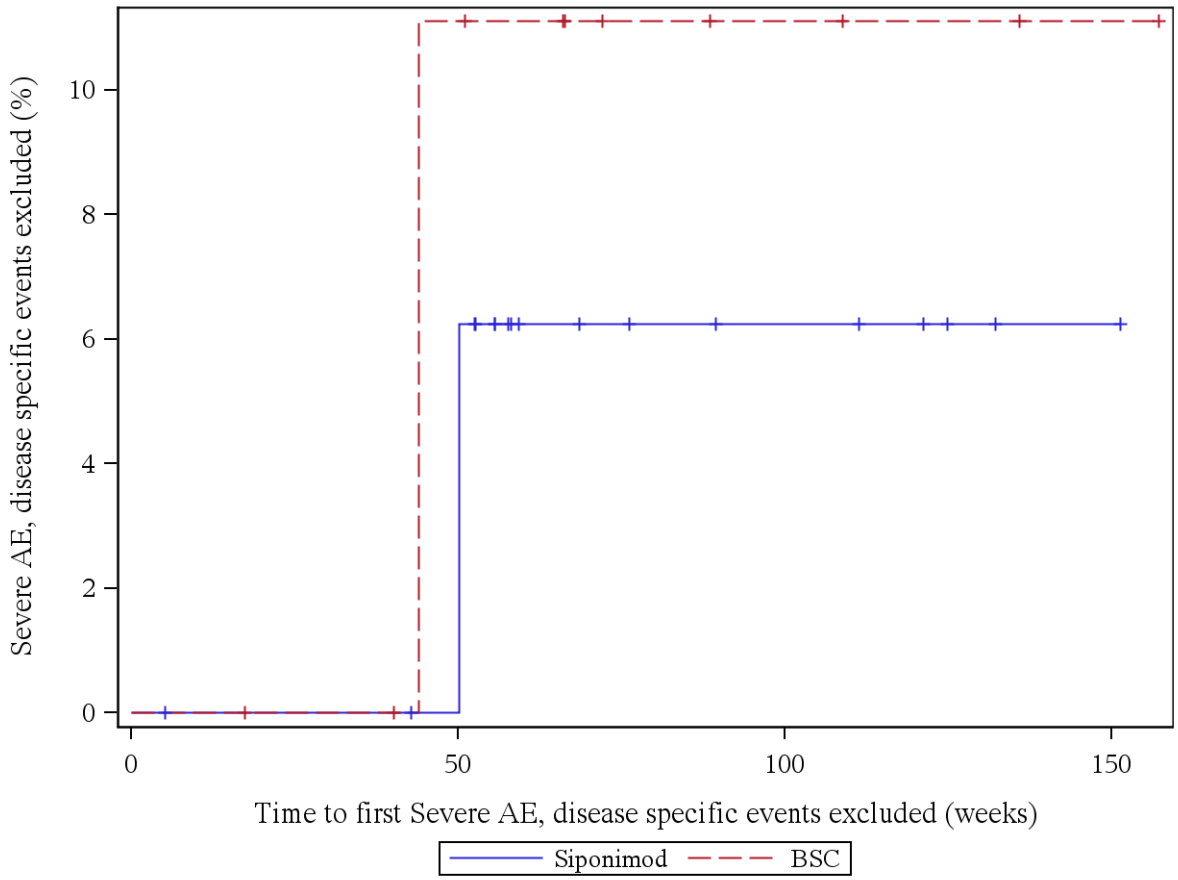
Patients at risk (Siponimod/BSC): Week 0: 109/50, Week 4: 108/49, Week 12: 105/47, Week 24: 101/42, Week 36: 97/40, Week 48: 90/36, Week 60: 86/29, Week 72: 69/24, Week 84: 55/18, Week 96: 39/12, Week 108: 27/10, Week 120: 21/6, Week 132: 10/2, Week 144: 6/0, Week 156: 0/0

Log rank test: p-value = 0,081
*: p < 0,05

Analysis population: A2304 SAF subpopulation "ACTIVE MS WITHOUT RELAPSES"

12.7.1.6: Any severe AE, disease specific events excluded

Figure 12.7.1.6.1: Severe AE, disease specific events excluded, Moderate or Severe Disease Course = No

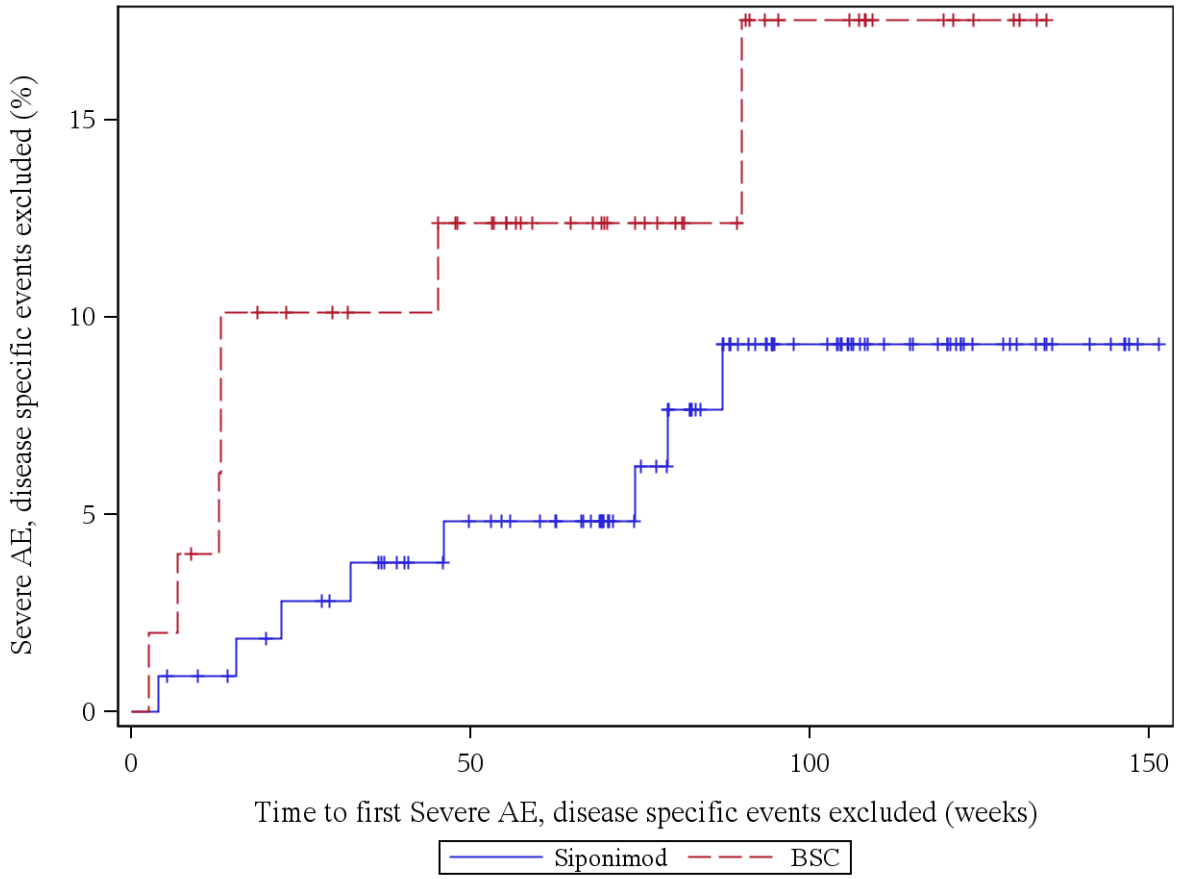


Patients at risk (Siponimod/BSC): Week 0: 18/11, Week 4: 18/11, Week 12: 17/11, Week 24: 17/10, Week 36: 17/10, Week 48: 16/8, Week 60: 8/7, Week 72: 7/4, Week 84: 6/4, Week 96: 5/3, Week 108: 5/3, Week 120: 4/2, Week 132: 2/2, Week 144: 1/1, Week 156: 0/1

Log rank test: p-value = 0,649
*: p < 0,05

Analysis population: A2304 SAF subpopulation "ACTIVE MS WITHOUT RELAPSES"

Figure 12.7.1.6.2: Severe AE, disease specific events excluded, Moderate or Severe Disease Course = Yes



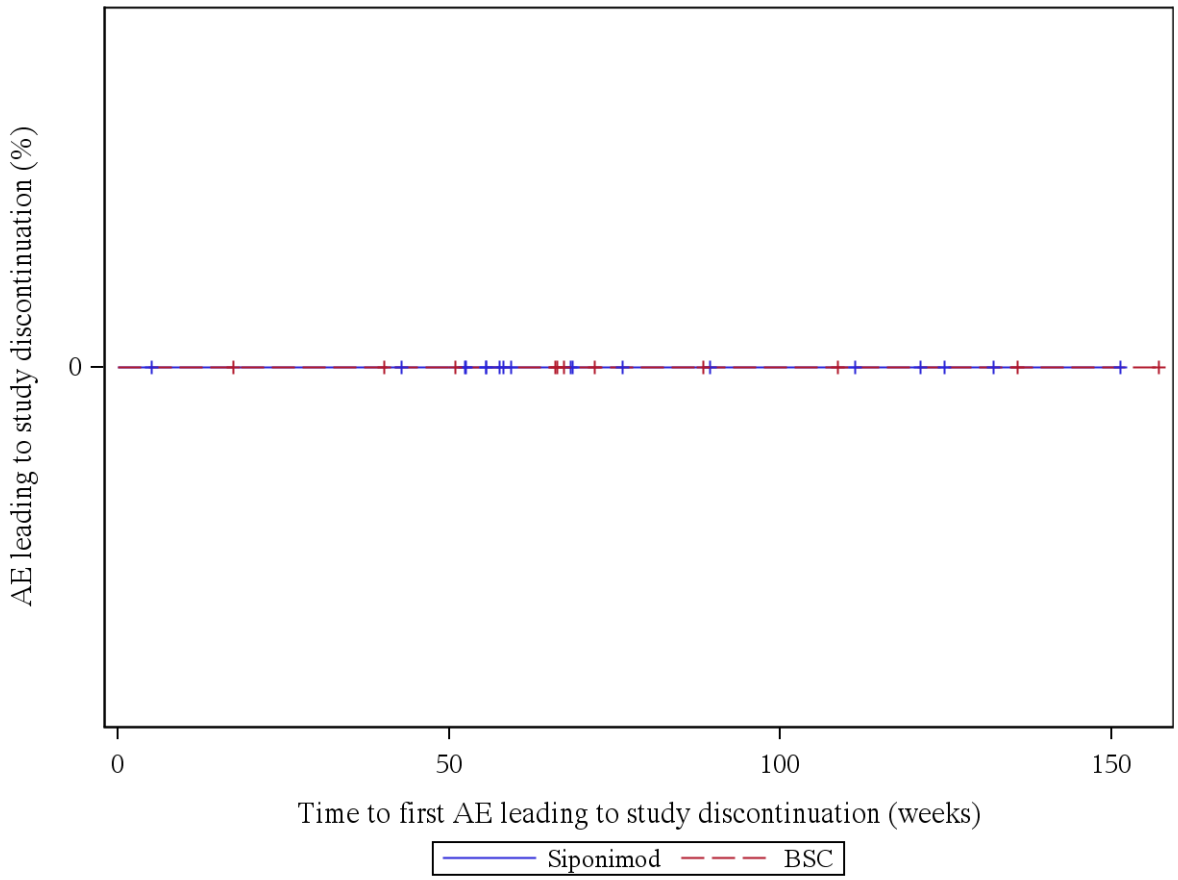
Patients at risk (Siponimod/BSC): Week 0: 109/50, Week 4: 108/49, Week 12: 106/47, Week 24: 102/42, Week 36: 99/40, Week 48: 91/36, Week 60: 87/29, Week 72: 70/24, Week 84: 56/18, Week 96: 40/12, Week 108: 28/10, Week 120: 22/6, Week 132: 11/2, Week 144: 6/0, Week 156: 0/0

Log rank test: p-value = 0,126
*: p < 0,05

Analysis population: A2304 SAF subpopulation "ACTIVE MS WITHOUT RELAPSES"

12.7.1.7: Any AE leading to study discontinuation

Figure 12.7.1.7.1: AE leading to study discontinuation, Moderate or Severe Disease Course = No

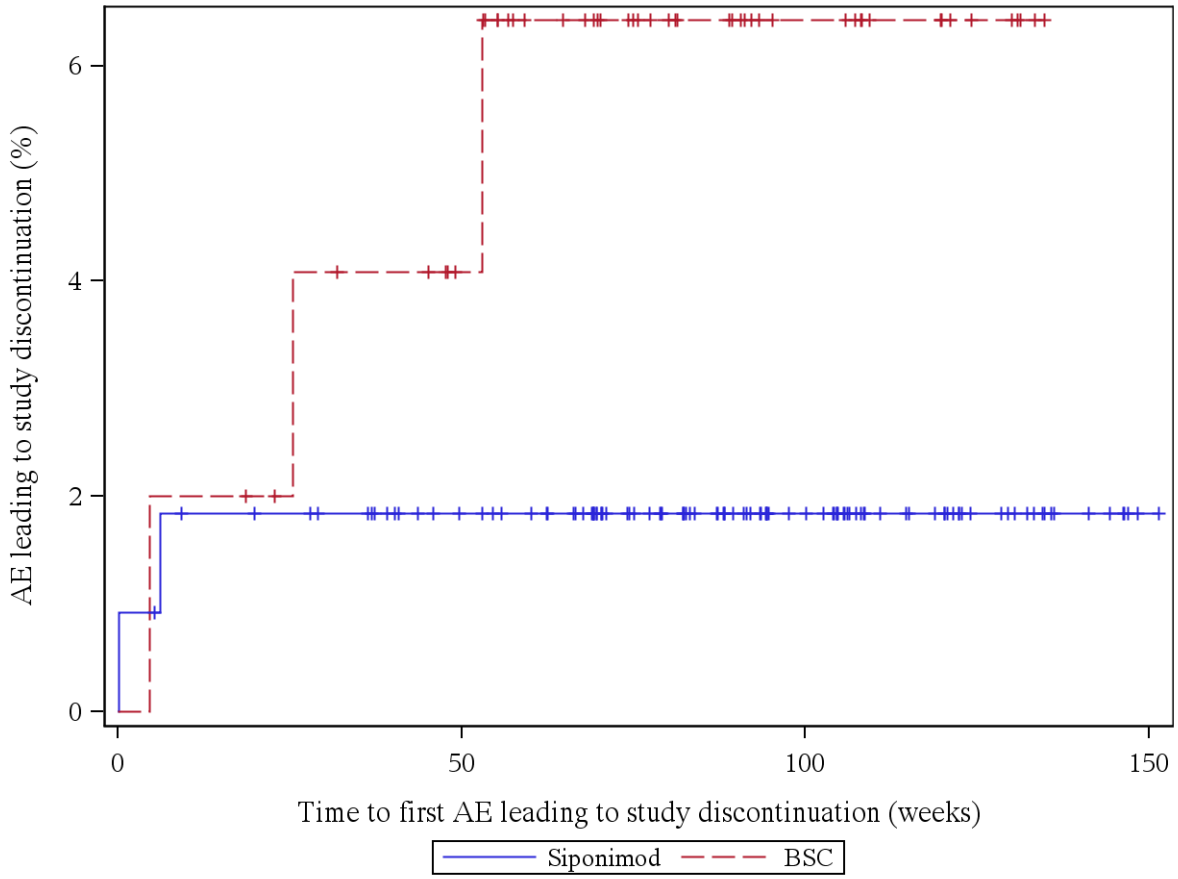


Patients at risk (Siponimod/BSC): Week 0: 18/11, Week 4: 18/11, Week 12: 17/11, Week 24: 17/10, Week 36: 17/10, Week 48: 16/9, Week 60: 9/8, Week 72: 7/4, Week 84: 6/4, Week 96: 5/3, Week 108: 5/3, Week 120: 4/2, Week 132: 2/2, Week 144: 1/1, Week 156: 0/1

Log rank test: p-value = -
*: p < 0,05

Analysis population: A2304 SAF subpopulation "ACTIVE MS WITHOUT RELAPSES"

Figure 12.7.1.7.2: AE leading to study discontinuation, Moderate or Severe Disease Course = Yes



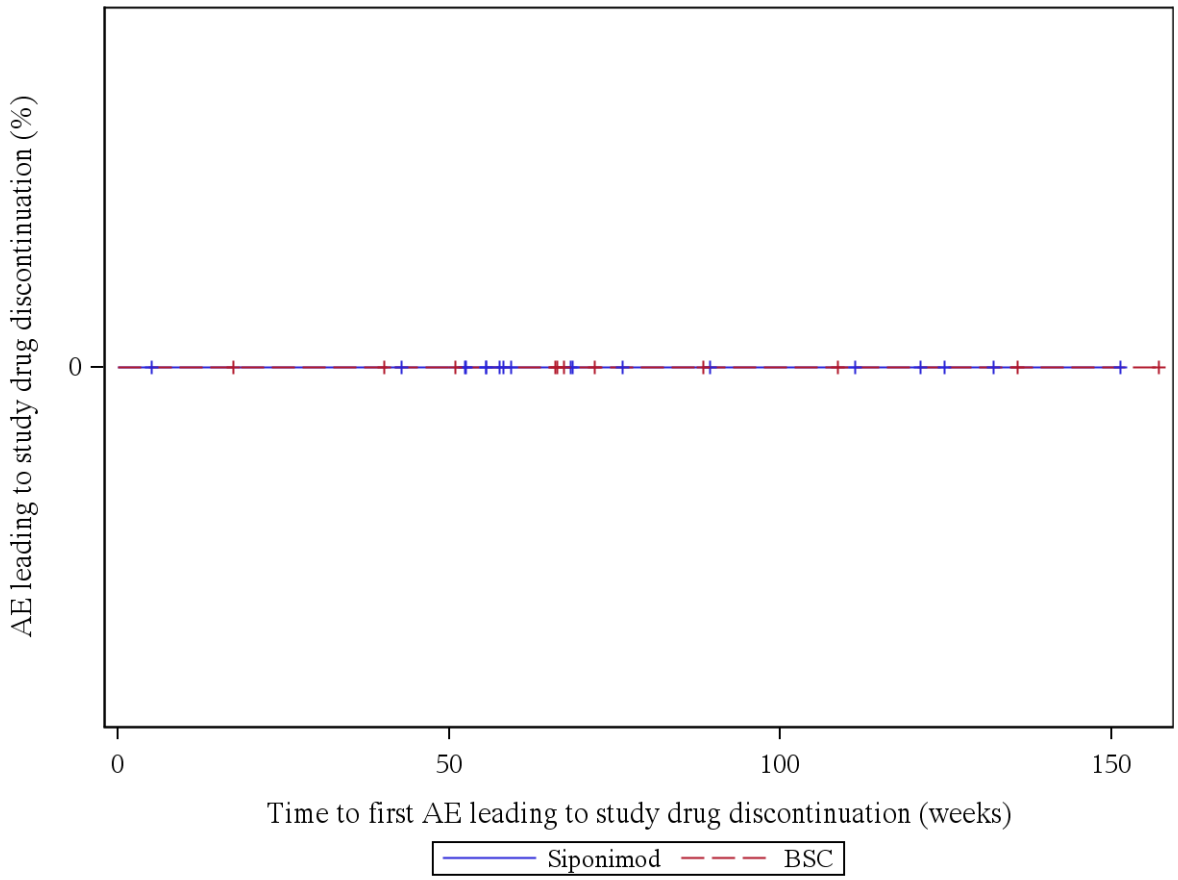
Patients at risk (Siponimod/BSC): Week 0: 109/50, Week 4: 108/50, Week 12: 105/49, Week 24: 104/47, Week 36: 102/45, Week 48: 94/42, Week 60: 90/33, Week 72: 73/28, Week 84: 60/21, Week 96: 44/14, Week 108: 31/12, Week 120: 24/7, Week 132: 13/2, Week 144: 6/0, Week 156: 0/0

Log rank test: p-value = 0,165
*: p < 0,05

Analysis population: A2304 SAF subpopulation "ACTIVE MS WITHOUT RELAPSES"

12.7.1.8: Any AE leading to study drug discontinuation

Figure 12.7.1.8.1: AE leading to study drug discontinuation, Moderate or Severe Disease Course = No

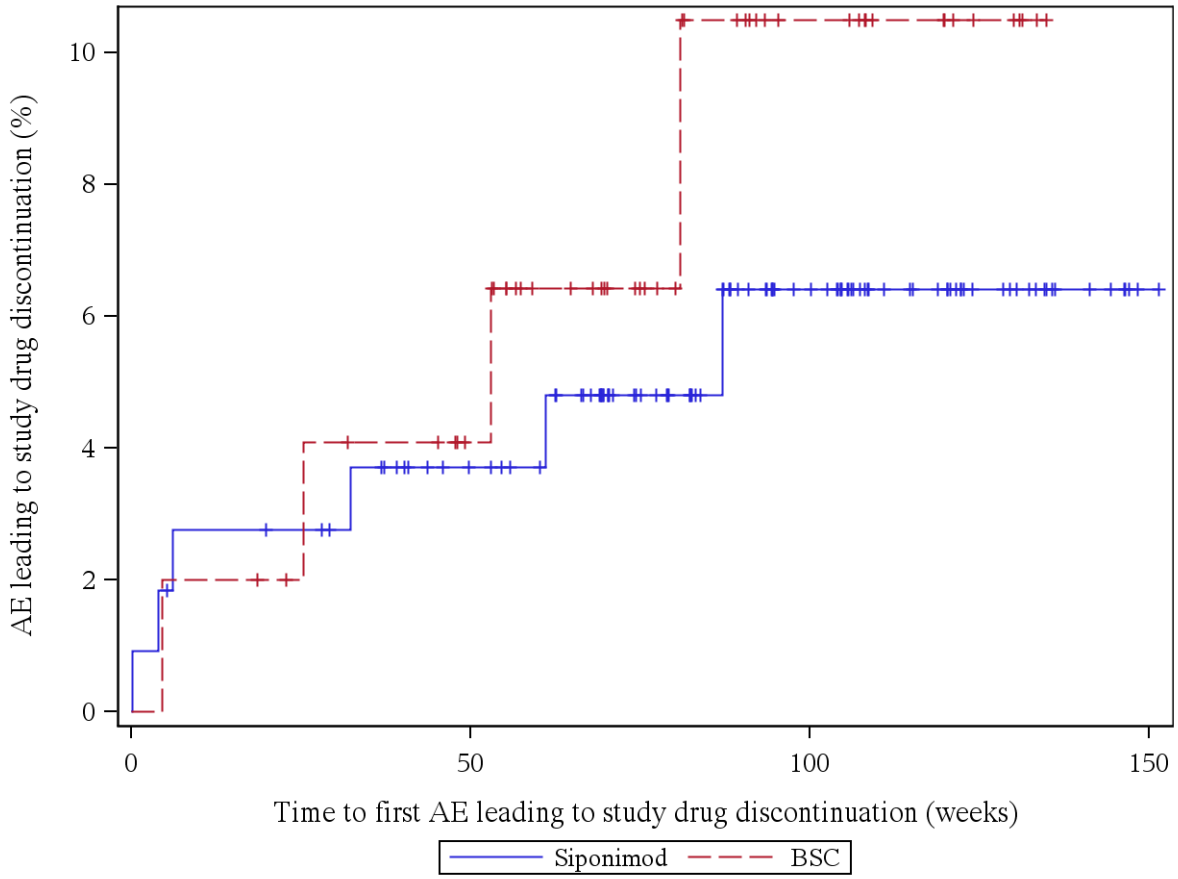


Patients at risk (Siponimod/BSC): Week 0: 18/11, Week 4: 18/11, Week 12: 17/11, Week 24: 17/10, Week 36: 17/10, Week 48: 16/9, Week 60: 9/8, Week 72: 7/4, Week 84: 6/4, Week 96: 5/3, Week 108: 5/3, Week 120: 4/2, Week 132: 2/2, Week 144: 1/1, Week 156: 0/1

Log rank test: p-value = -
*: p < 0,05

Analysis population: A2304 SAF subpopulation "ACTIVE MS WITHOUT RELAPSES"

Figure 12.7.1.8.2: AE leading to study drug discontinuation, Moderate or Severe Disease Course = Yes



Patients at risk (Siponimod/BSC): Week 0: 109/50, Week 4: 107/50, Week 12: 105/49, Week 24: 104/47, Week 36: 101/45, Week 48: 94/42, Week 60: 90/33, Week 72: 72/28, Week 84: 59/20, Week 96: 44/14, Week 108: 31/12, Week 120: 24/7, Week 132: 13/2, Week 144: 6/0, Week 156: 0/0

Log rank test: p-value = 0,477
*: p < 0,05

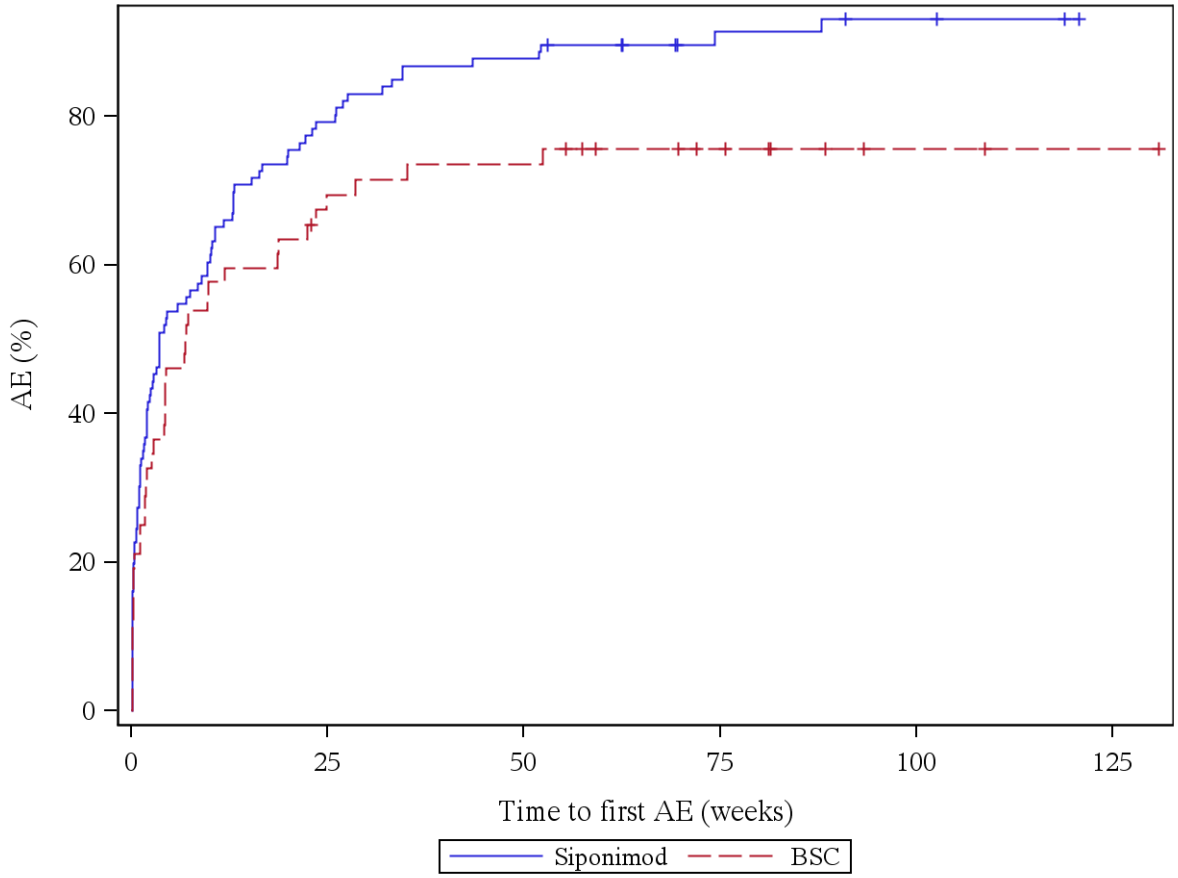
Analysis population: A2304 SAF subpopulation "ACTIVE MS WITHOUT RELAPSES"

12.8 Subgroup: Region

12.8.1: Time to First Adverse Event (SAF) by Region

12.8.1.1: Any AE

Figure 12.8.1.1.1: AE, Region = Europe

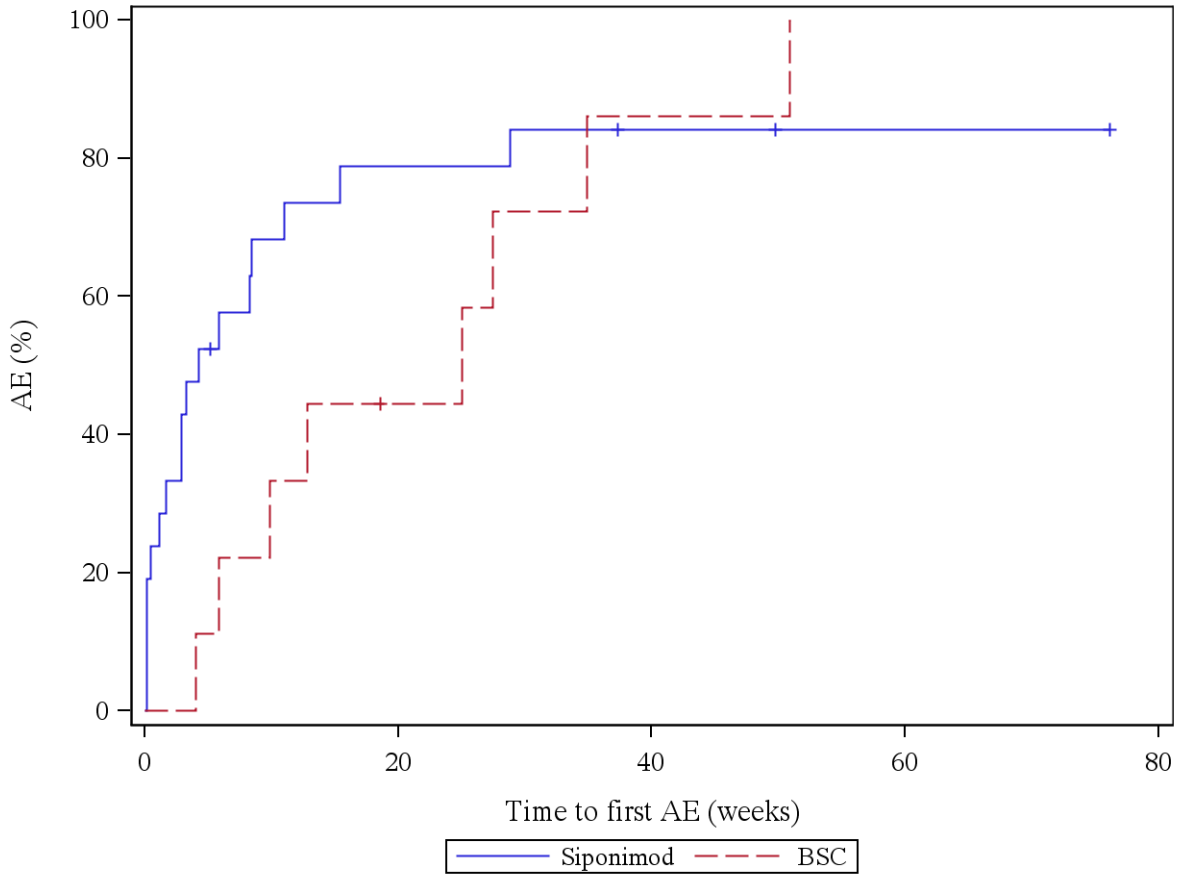


Patients at risk (Siponimod/BSC): Week 0: 106/52, Week 4: 52/33, Week 12: 36/21, Week 24: 22/16, Week 36: 14/13, Week 48: 13/13, Week 60: 10/9, Week 72: 6/7, Week 84: 5/4, Week 96: 3/2, Week 108: 2/2, Week 120: 1/1, Week 132: 0/0

Log rank test: p-value = 0,036 *
*: p < 0,05

Analysis population: A2304 SAF subpopulation "ACTIVE MS WITHOUT RELAPSES"

Figure 12.8.1.1.2: AE, Region = Other



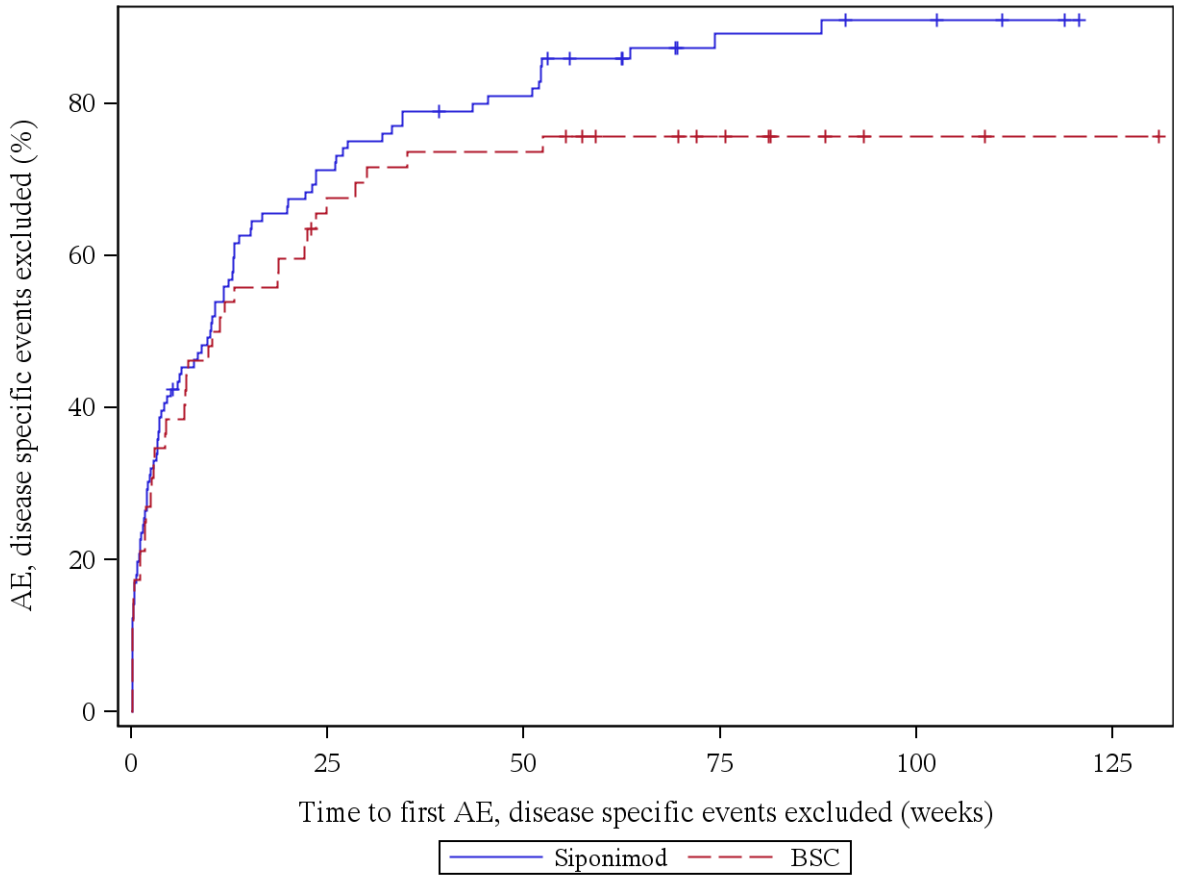
Patients at risk (Siponimod/BSC): Week 0: 21/9, Week 4: 11/8, Week 12: 5/6, Week 24: 4/4, Week 36: 3/1, Week 48: 2/1, Week 60: 1/0, Week 72: 1/0, Week 84: 0/0

Log rank test: p-value = 0,296
*: p < 0,05

Analysis population: A2304 SAF subpopulation "ACTIVE MS WITHOUT RELAPSES"

12.8.1.2: Any AE, disease specific events excluded

Figure 12.8.1.2.1: AE, disease specific events excluded, Region = Europe

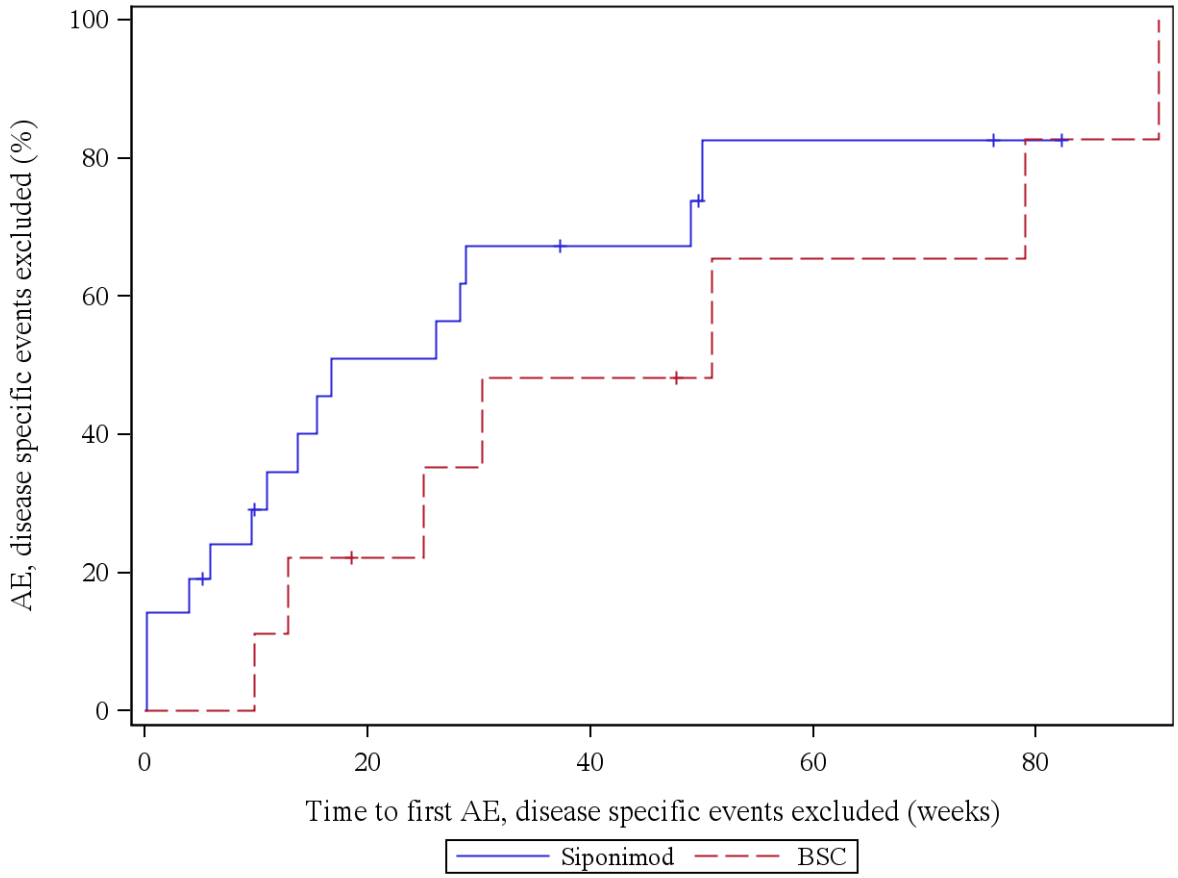


Patients at risk (Siponimod/BSC): Week 0: 106/52, Week 4: 64/34, Week 12: 46/24, Week 24: 30/17, Week 36: 22/13, Week 48: 19/13, Week 60: 12/9, Week 72: 7/7, Week 84: 6/4, Week 96: 4/2, Week 108: 3/2, Week 120: 1/1, Week 132: 0/0

Log rank test: p-value = 0,168
*: p < 0,05

Analysis population: A2304 SAF subpopulation "ACTIVE MS WITHOUT RELAPSES"

Figure 12.8.1.2.2: AE, disease specific events excluded, Region = Other



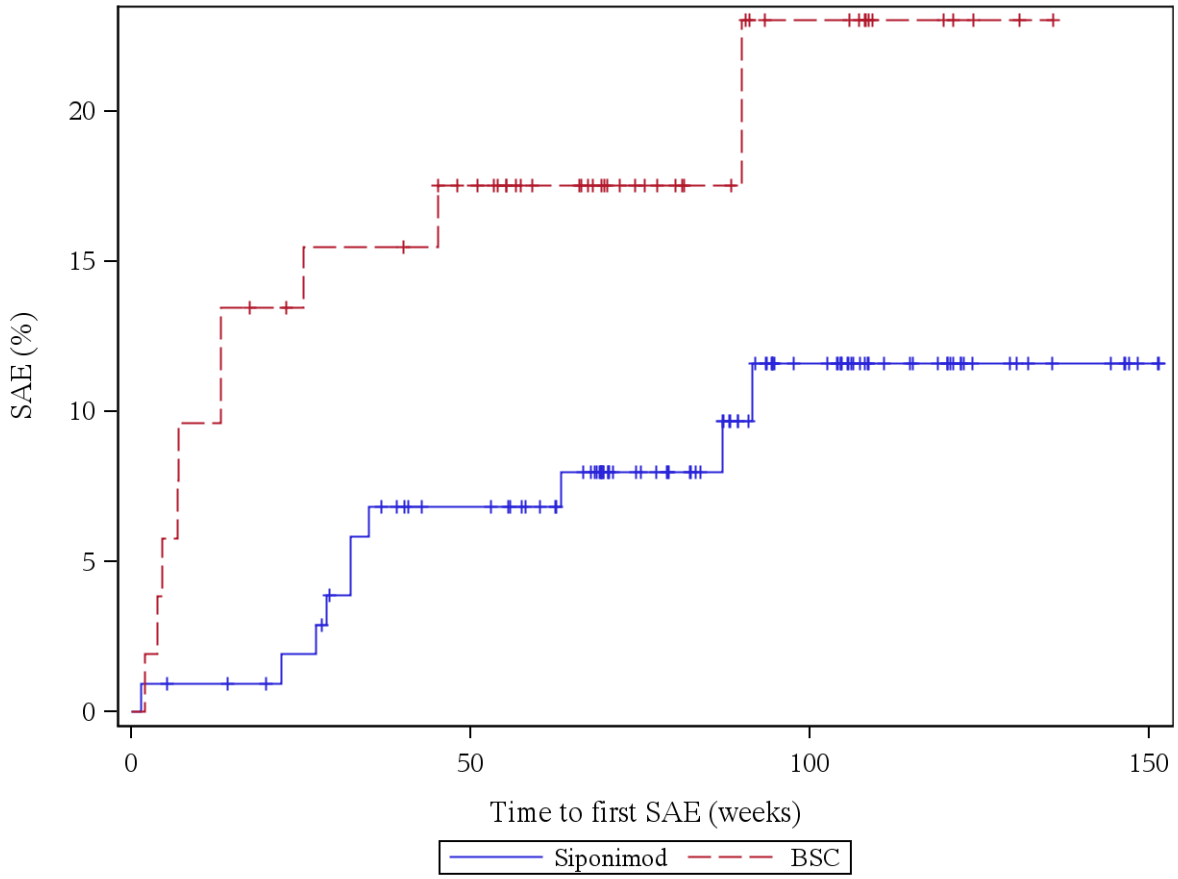
Patients at risk (Siponimod/BSC): Week 0: 21/9, Week 4: 17/9, Week 12: 12/8, Week 24: 9/6, Week 36: 6/4, Week 48: 5/3, Week 60: 2/2, Week 72: 2/2, Week 84: 0/1

Log rank test: p-value = 0,263
*: p < 0,05

Analysis population: A2304 SAF subpopulation "ACTIVE MS WITHOUT RELAPSES"

12.8.1.3: Any SAE

Figure 12.8.1.3.1: SAE, Region = Europe

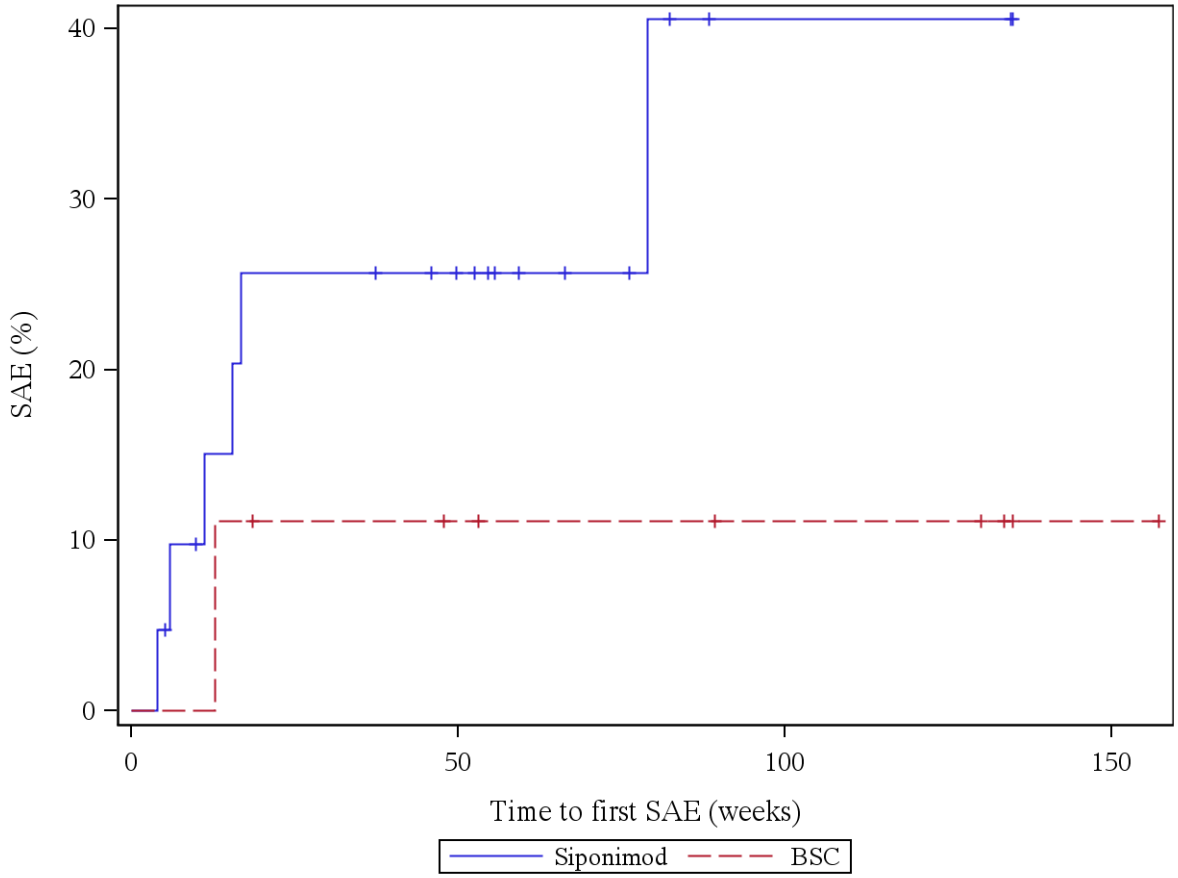


Patients at risk (Siponimod/BSC): Week 0: 106/52, Week 4: 105/50, Week 12: 104/47, Week 24: 101/43, Week 36: 94/42, Week 48: 89/38, Week 60: 84/30, Week 72: 65/22, Week 84: 55/16, Week 96: 38/11, Week 108: 26/9, Week 120: 19/4, Week 132: 9/1, Week 144: 7/0, Week 156: 0/0

Log rank test: p-value = 0,045 *
*: p < 0,05

Analysis population: A2304 SAF subpopulation "ACTIVE MS WITHOUT RELAPSES"

Figure 12.8.1.3.2: SAE, Region = Other



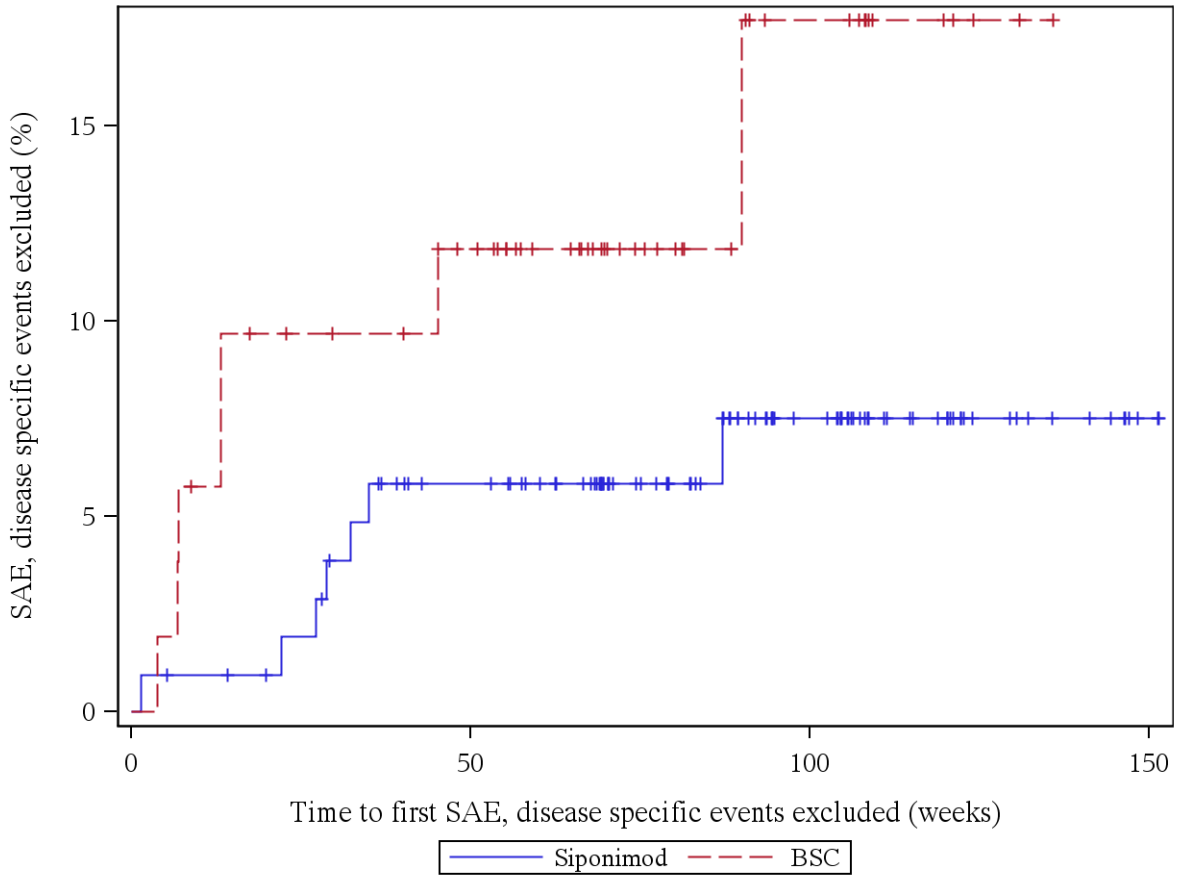
Patients at risk (Siponimod/BSC): Week 0: 21/9, Week 4: 20/9, Week 12: 16/9, Week 24: 14/7, Week 36: 14/7, Week 48: 12/6, Week 60: 7/5, Week 72: 6/5, Week 84: 3/5, Week 96: 2/4, Week 108: 2/4, Week 120: 2/4, Week 132: 2/3, Week 144: 0/1

Log rank test: p-value = 0,231
*: p < 0,05

Analysis population: A2304 SAF subpopulation "ACTIVE MS WITHOUT RELAPSES"

12.8.1.4: Any SAE, disease specific events excluded

Figure 12.8.1.4.1: SAE, disease specific events excluded, Region = Europe

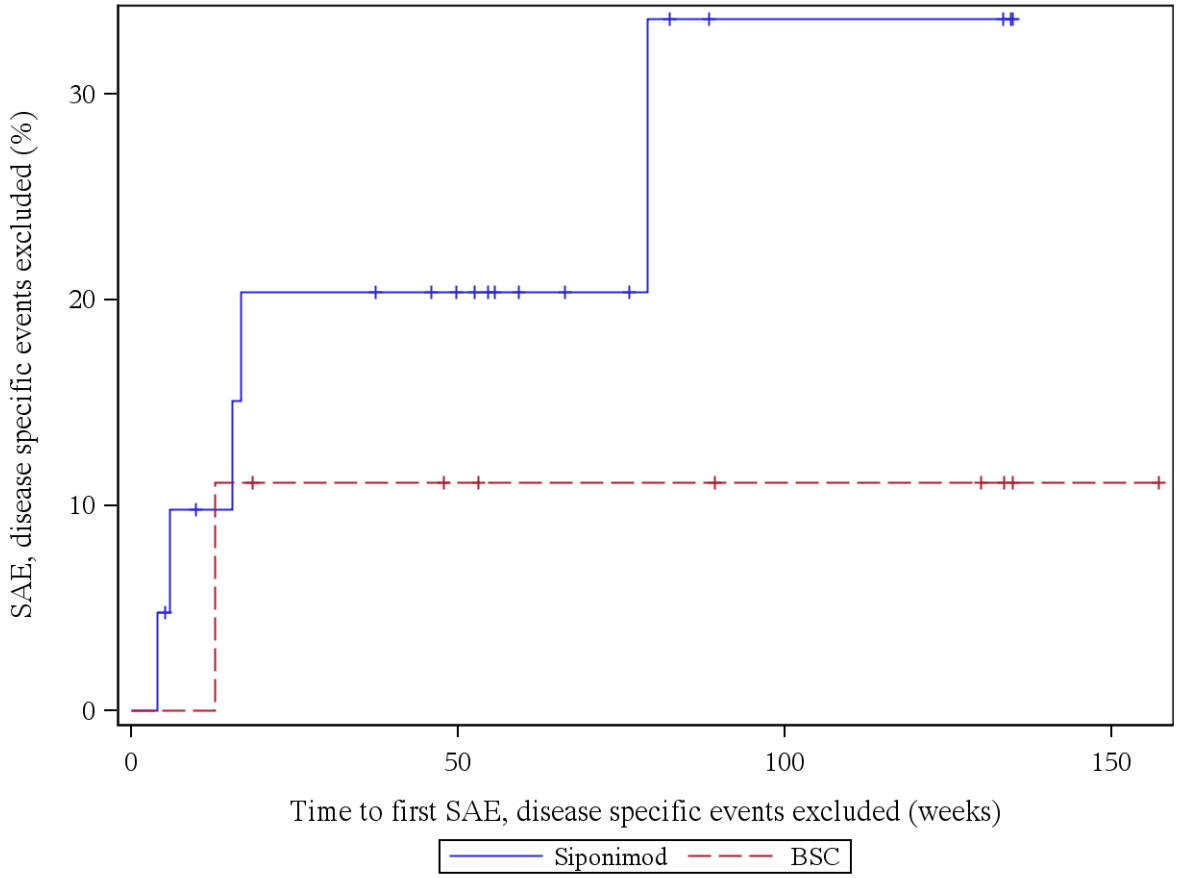


Patients at risk (Siponimod/BSC): Week 0: 106/52, Week 4: 105/51, Week 12: 104/48, Week 24: 101/44, Week 36: 95/43, Week 48: 89/39, Week 60: 84/31, Week 72: 66/22, Week 84: 56/16, Week 96: 40/11, Week 108: 28/9, Week 120: 20/4, Week 132: 10/1, Week 144: 7/0, Week 156: 0/0

Log rank test: p-value = 0,110
*: p < 0,05

Analysis population: A2304 SAF subpopulation "ACTIVE MS WITHOUT RELAPSES"

Figure 12.8.1.4.2: SAE, disease specific events excluded, Region = Other



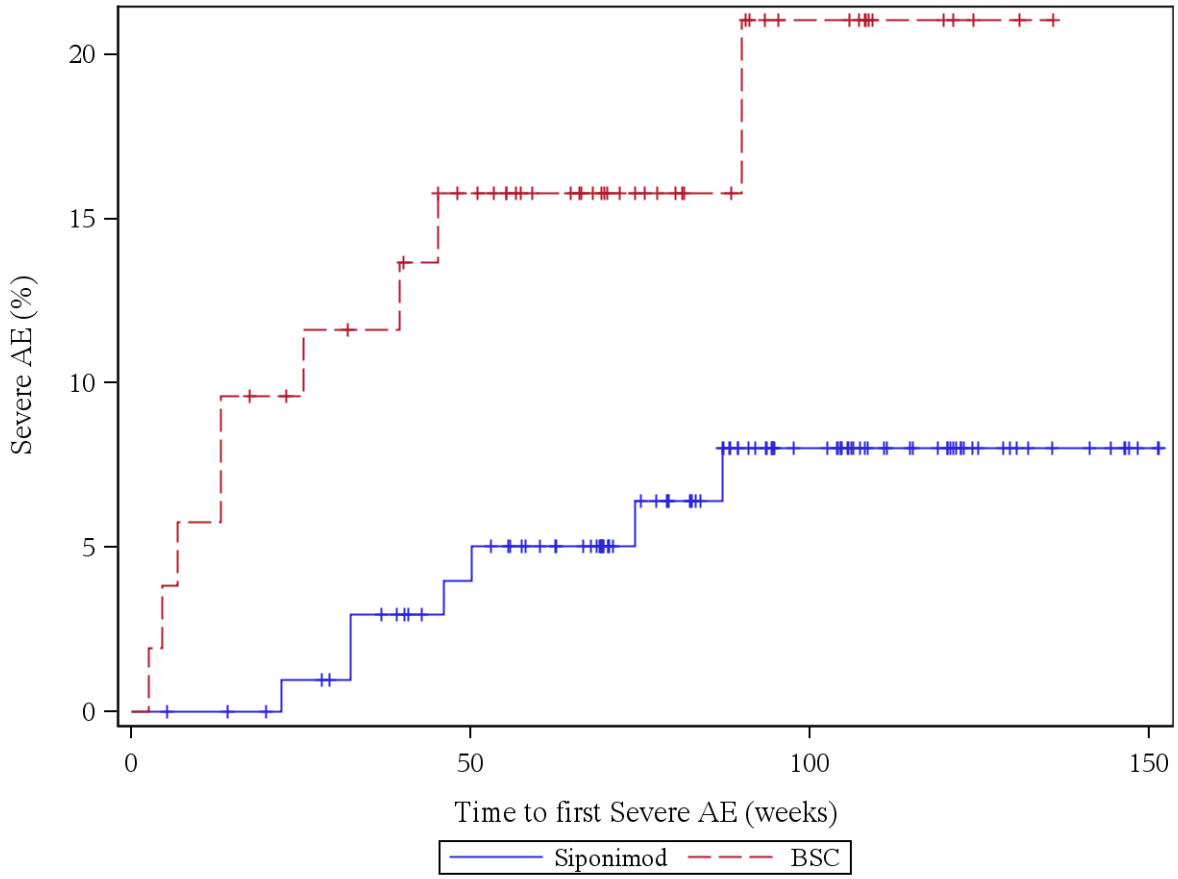
Patients at risk (Siponimod/BSC): Week 0: 21/9, Week 4: 20/9, Week 12: 17/9, Week 24: 15/7, Week 36: 15/7, Week 48: 13/6, Week 60: 8/5, Week 72: 7/5, Week 84: 4/5, Week 96: 3/4, Week 108: 3/4, Week 120: 3/4, Week 132: 3/3, Week 144: 0/1

Log rank test: p-value = 0,353
*: p < 0,05

Analysis population: A2304 SAF subpopulation "ACTIVE MS WITHOUT RELAPSES"

12.8.1.5: Any severe AE

Figure 12.8.1.5.1: Severe AE, Region = Europe

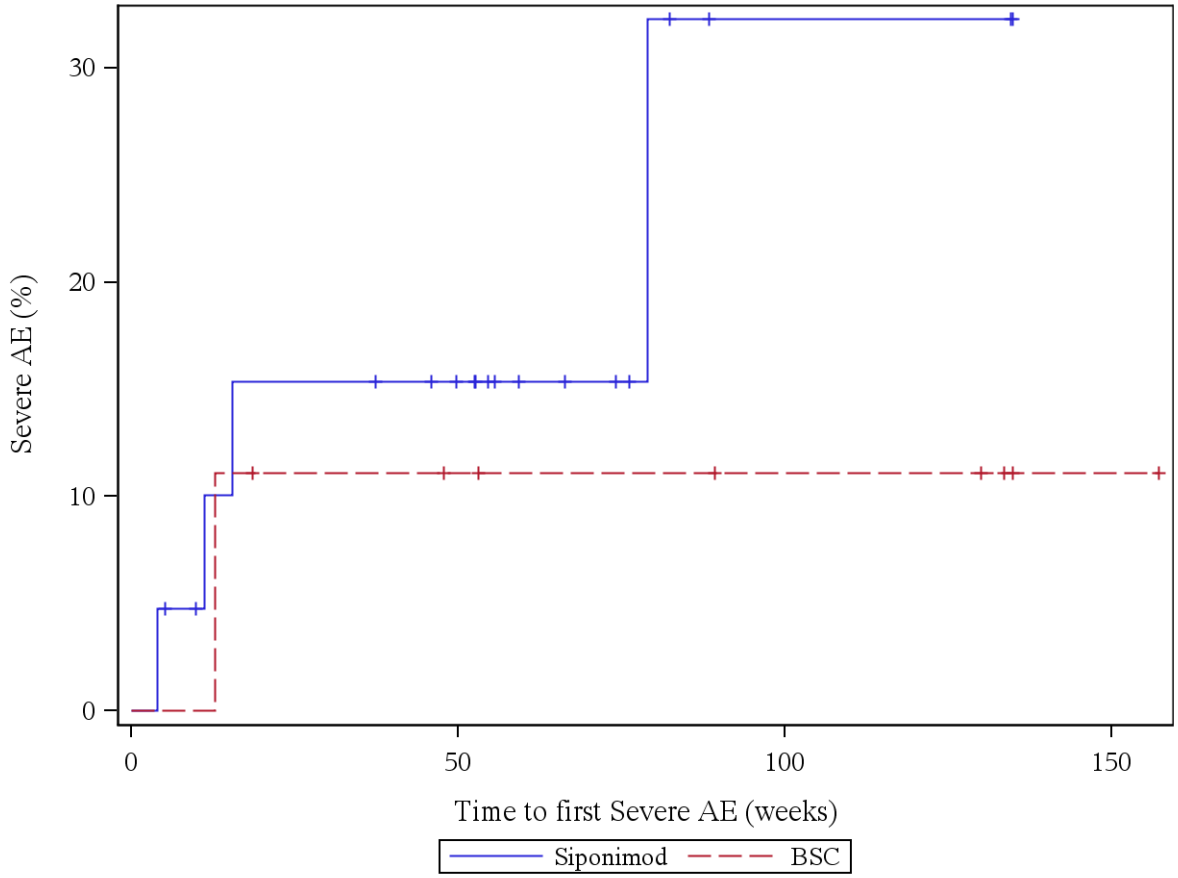


Patients at risk (Siponimod/BSC): Week 0: 106/52, Week 4: 106/51, Week 12: 105/49, Week 24: 102/45, Week 36: 98/43, Week 48: 92/38, Week 60: 86/31, Week 72: 69/23, Week 84: 58/17, Week 96: 42/11, Week 108: 30/9, Week 120: 23/4, Week 132: 10/1, Week 144: 7/0, Week 156: 0/0

Log rank test: p-value = 0,020 *
*: p < 0,05

Analysis population: A2304 SAF subpopulation "ACTIVE MS WITHOUT RELAPSES"

Figure 12.8.1.5.2: Severe AE, Region = Other



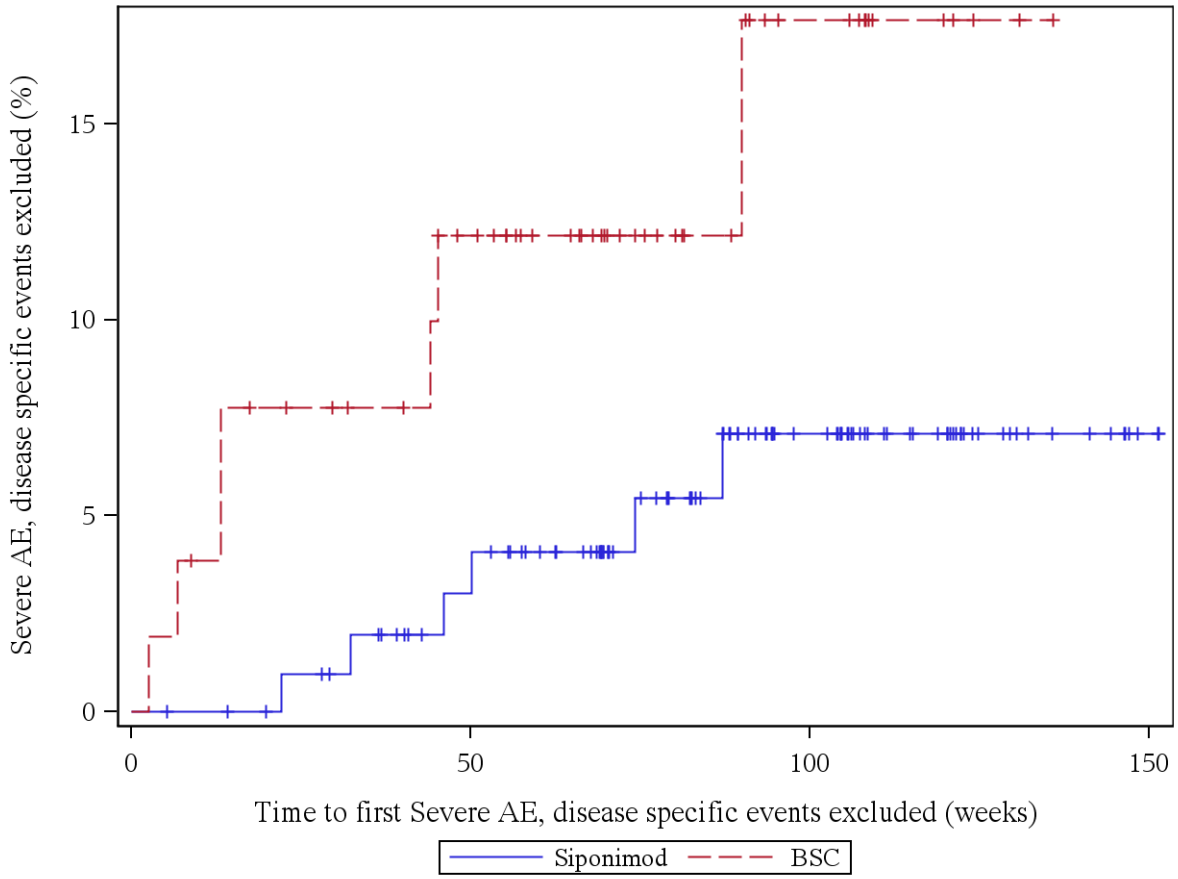
Patients at risk (Siponimod/BSC): Week 0: 21/9, Week 4: 20/9, Week 12: 17/9, Week 24: 16/7, Week 36: 16/7, Week 48: 14/6, Week 60: 8/5, Week 72: 7/5, Week 84: 3/5, Week 96: 2/4, Week 108: 2/4, Week 120: 2/4, Week 132: 2/3, Week 144: 0/1

Log rank test: p-value = 0,451
*: p < 0,05

Analysis population: A2304 SAF subpopulation "ACTIVE MS WITHOUT RELAPSES"

12.8.1.6: Any severe AE, disease specific events excluded

Figure 12.8.1.6.1: Severe AE, disease specific events excluded, Region = Europe

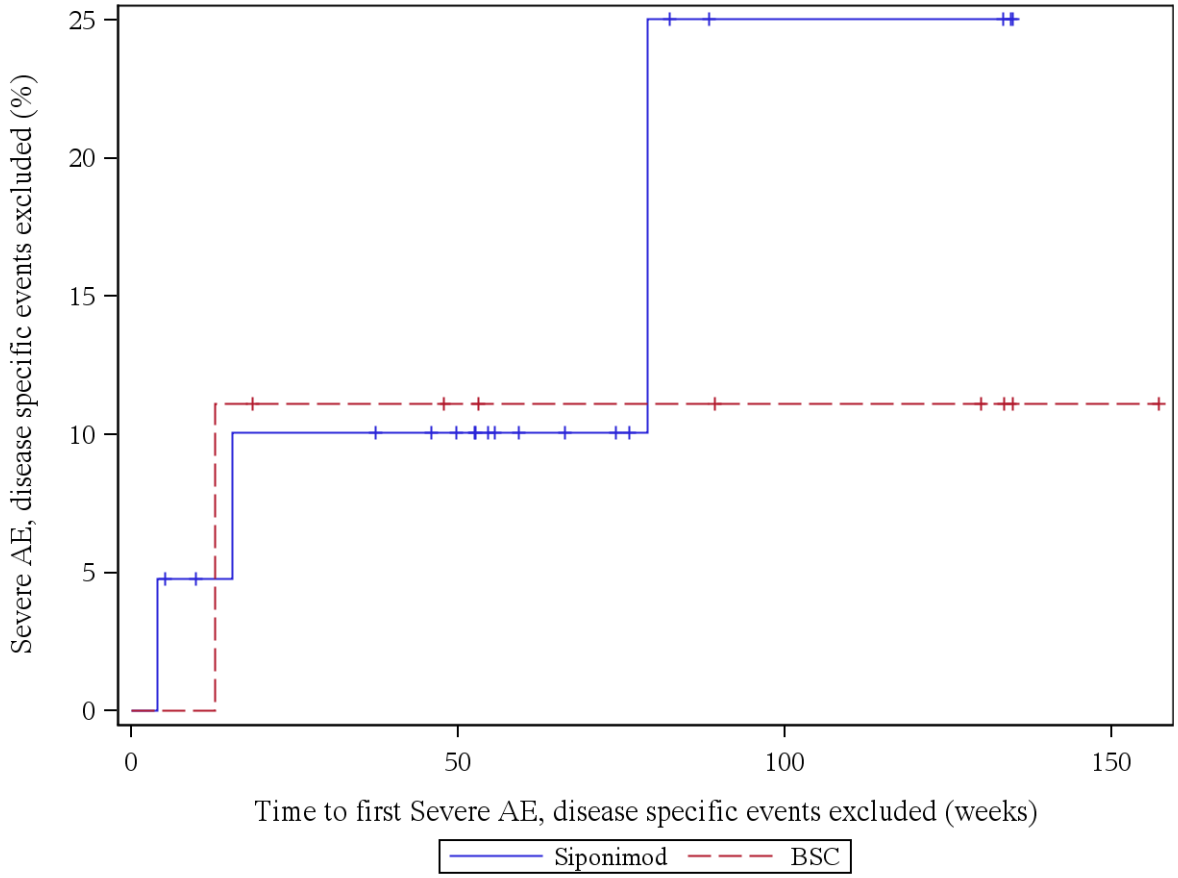


Patients at risk (Siponimod/BSC): Week 0: 106/52, Week 4: 106/51, Week 12: 105/49, Week 24: 102/45, Week 36: 99/43, Week 48: 92/38, Week 60: 86/31, Week 72: 69/23, Week 84: 58/17, Week 96: 42/11, Week 108: 30/9, Week 120: 23/4, Week 132: 10/1, Week 144: 7/0, Week 156: 0/0

Log rank test: p-value = 0,052
*: p < 0,05

Analysis population: A2304 SAF subpopulation "ACTIVE MS WITHOUT RELAPSES"

Figure 12.8.1.6.2: Severe AE, disease specific events excluded, Region = Other



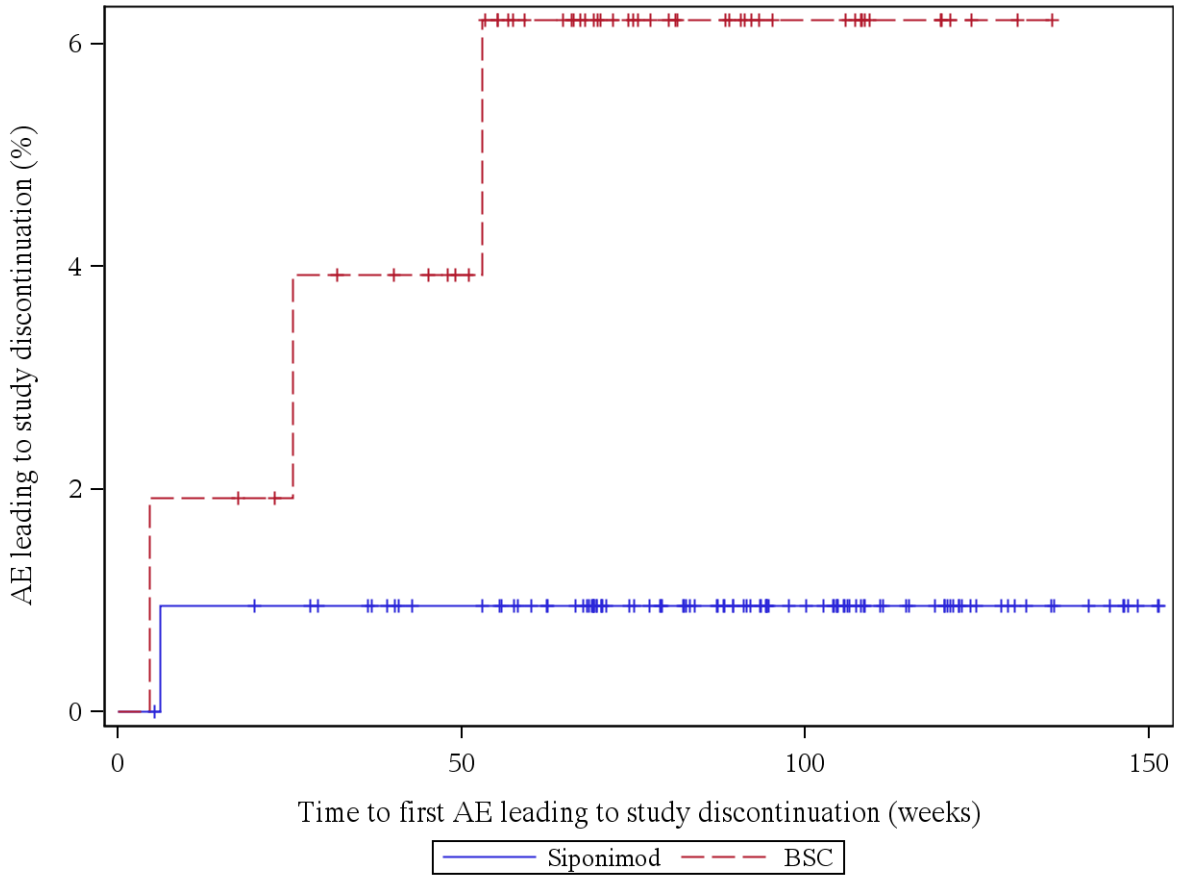
Patients at risk (Siponimod/BSC): Week 0: 21/9, Week 4: 20/9, Week 12: 18/9, Week 24: 17/7, Week 36: 17/7, Week 48: 15/6, Week 60: 9/5, Week 72: 8/5, Week 84: 4/5, Week 96: 3/4, Week 108: 3/4, Week 120: 3/4, Week 132: 3/3, Week 144: 0/1

Log rank test: p-value = 0,676
*: p < 0,05

Analysis population: A2304 SAF subpopulation "ACTIVE MS WITHOUT RELAPSES"

12.8.1.7: Any AE leading to study discontinuation

Figure 12.8.1.7.1: AE leading to study discontinuation, Region = Europe

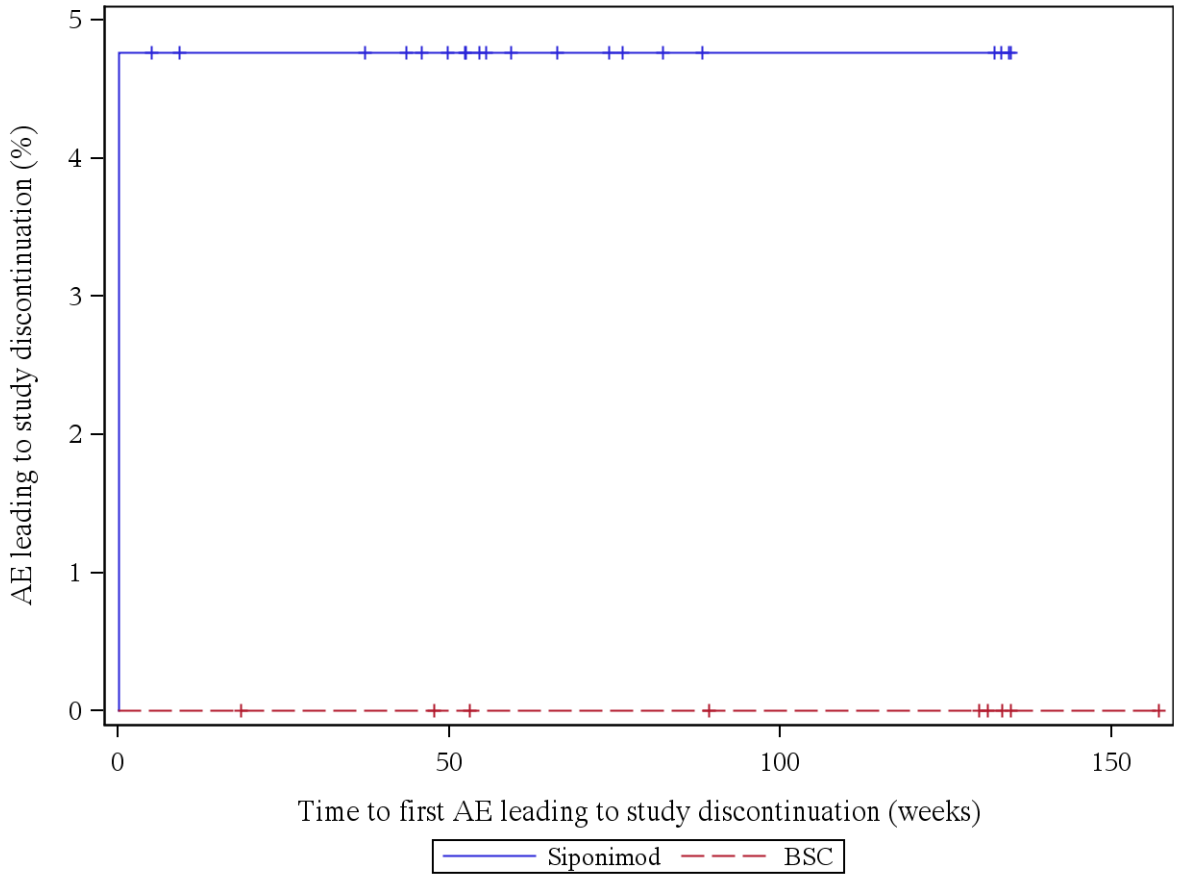


Patients at risk (Siponimod/BSC): Week 0: 106/52, Week 4: 106/52, Week 12: 104/51, Week 24: 103/49, Week 36: 101/47, Week 48: 95/44, Week 60: 90/35, Week 72: 72/26, Week 84: 61/19, Week 96: 45/12, Week 108: 32/10, Week 120: 24/4, Week 132: 11/1, Week 144: 7/0, Week 156: 0/0

Log rank test: p-value = 0,066
*: p < 0,05

Analysis population: A2304 SAF subpopulation "ACTIVE MS WITHOUT RELAPSES"

Figure 12.8.1.7.2: AE leading to study discontinuation, Region = Other



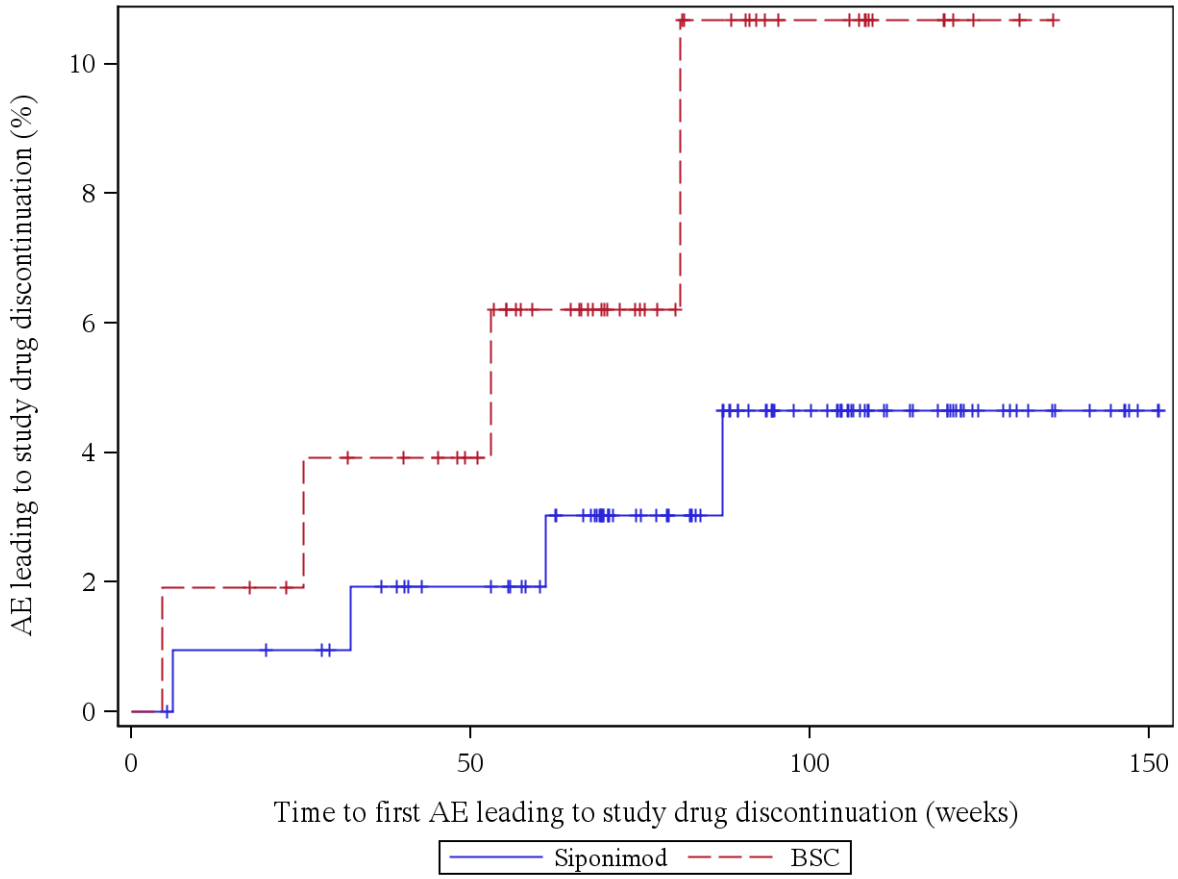
Patients at risk (Siponimod/BSC): Week 0: 21/9, Week 4: 20/9, Week 12: 18/9, Week 24: 18/8, Week 36: 18/8, Week 48: 15/7, Week 60: 9/6, Week 72: 8/6, Week 84: 5/6, Week 96: 4/5, Week 108: 4/5, Week 120: 4/5, Week 132: 4/3, Week 144: 0/1

Log rank test: p-value = -
*: p < 0,05

Analysis population: A2304 SAF subpopulation "ACTIVE MS WITHOUT RELAPSES"

12.8.1.8: Any AE leading to study drug discontinuation

Figure 12.8.1.8.1: AE leading to study drug discontinuation, Region = Europe

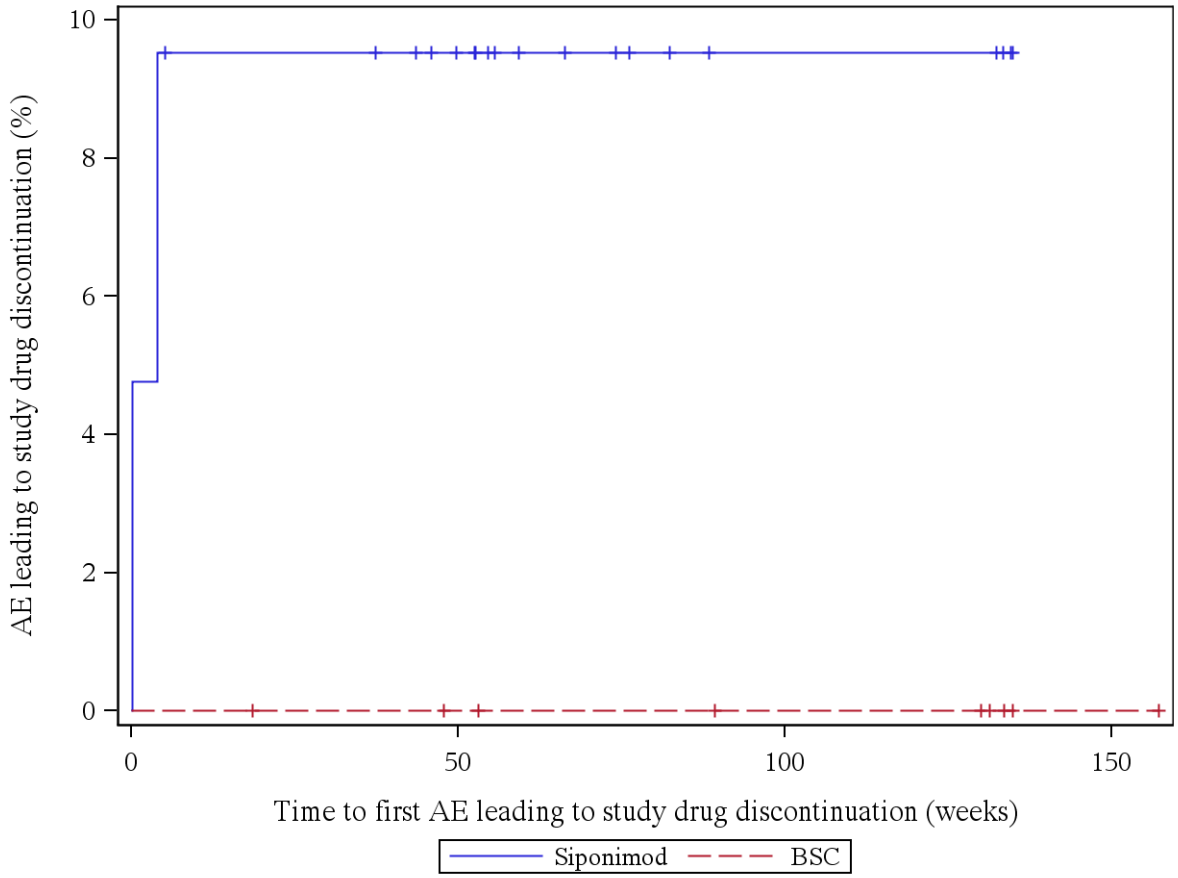


Patients at risk (Siponimod/BSC): Week 0: 106/52, Week 4: 106/52, Week 12: 104/51, Week 24: 103/49, Week 36: 100/47, Week 48: 95/44, Week 60: 90/35, Week 72: 71/26, Week 84: 60/18, Week 96: 45/12, Week 108: 32/10, Week 120: 24/4, Week 132: 11/1, Week 144: 7/0, Week 156: 0/0

Log rank test: p-value = 0,202
*: p < 0,05

Analysis population: A2304 SAF subpopulation "ACTIVE MS WITHOUT RELAPSES"

Figure 12.8.1.8.2: AE leading to study drug discontinuation, Region = Other



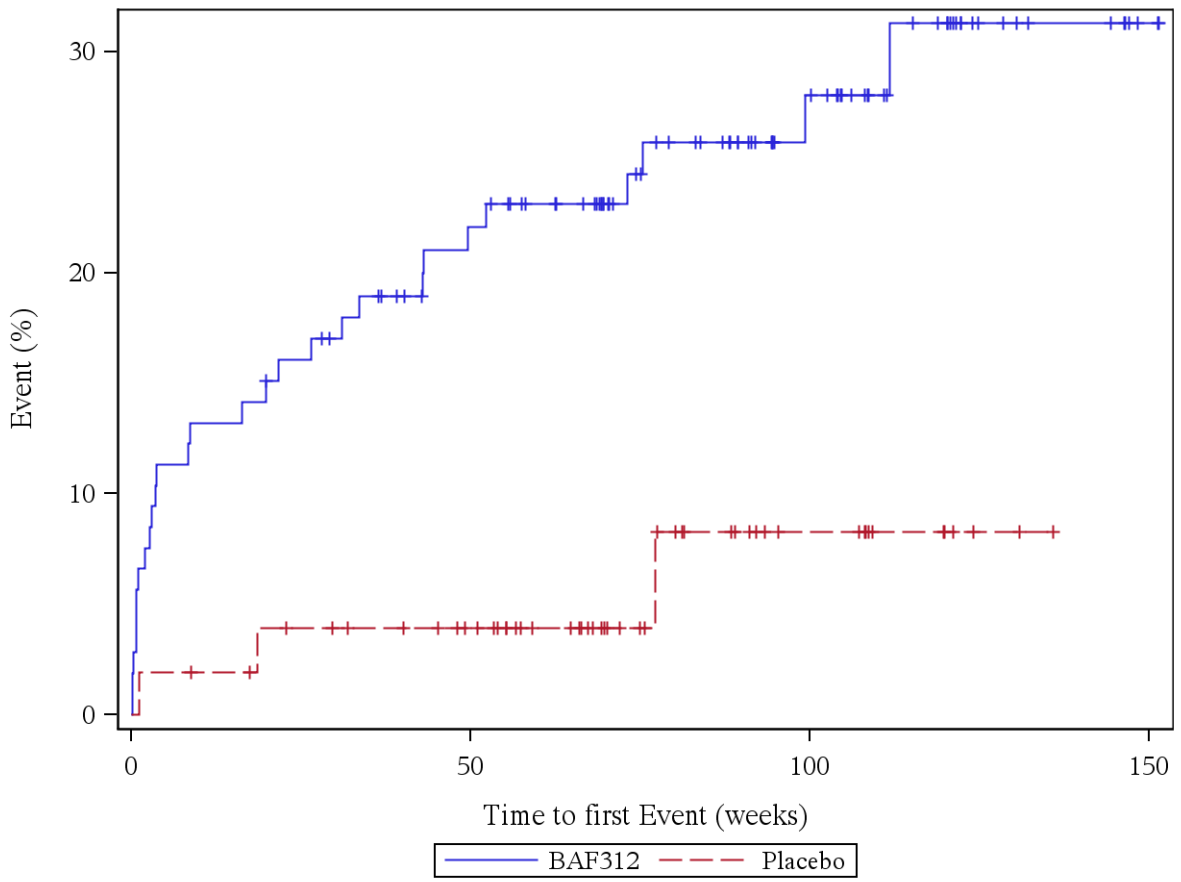
Patients at risk (Siponimod/BSC): Week 0: 21/9, Week 4: 19/9, Week 12: 18/9, Week 24: 18/8, Week 36: 18/8, Week 48: 15/7, Week 60: 9/6, Week 72: 8/6, Week 84: 5/6, Week 96: 4/5, Week 108: 4/5, Week 120: 4/5, Week 132: 4/3, Week 144: 0/1

Log rank test: p-value = -
*: p < 0,05

Analysis population: A2304 SAF subpopulation "ACTIVE MS WITHOUT RELAPSES"

12.8.2: Time to First Adverse Event by SOC and PT (SAF) by Region

Figure 12.8.2.1.1: GENERAL DISORDERS AND ADMINISTRATION SITE CONDITIONS (SOC), Region = Europe

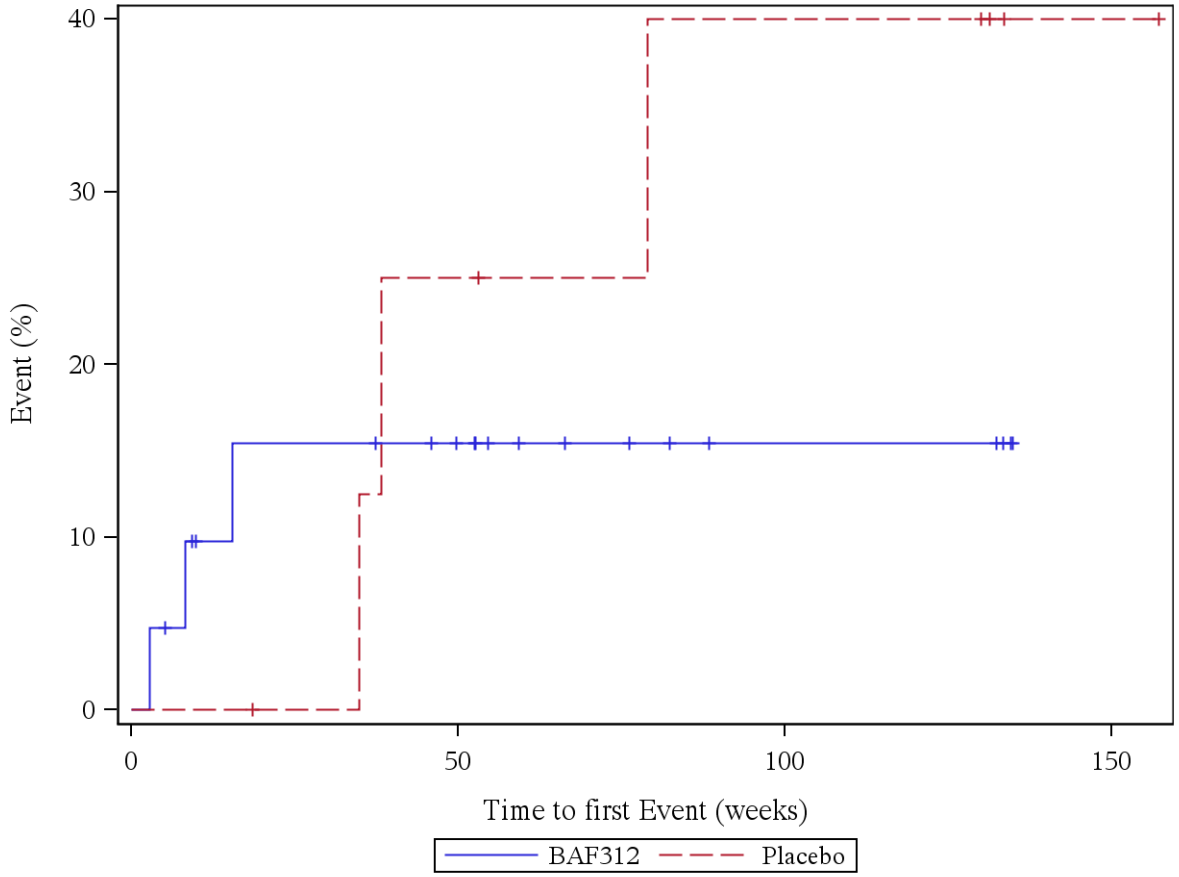


Patients at risk (BAF312/Placebo): Week 0: 106/52, Week 4: 94/51, Week 12: 92/50, Week 24: 88/47, Week 36: 83/45, Week 48: 76/42, Week 60: 69/33, Week 72: 56/24, Week 84: 48/17, Week 96: 35/11, Week 108: 27/10, Week 120: 19/4, Week 132: 8/1, Week 144: 7/0, Week 156: 0/0

Log rank test: p-value = 0,005 *
*: p < 0,05

Analysis population: A2304 SAF subpopulation "ACTIVE MS WITHOUT RELAPSES"

Figure 12.8.2.1.2: GENERAL DISORDERS AND ADMINISTRATION SITE CONDITIONS (SOC), Region = Other



Patients at risk (BAF312/Placebo): Week 0: 21/9, Week 4: 20/9, Week 12: 16/9, Week 24: 15/8, Week 36: 15/7, Week 48: 13/6, Week 60: 8/5, Week 72: 7/5, Week 84: 5/4, Week 96: 4/4, Week 108: 4/4, Week 120: 4/4, Week 132: 4/2, Week 144: 0/1

Log rank test: p-value = 0,448
*: p < 0,05

Analysis population: A2304 SAF subpopulation "ACTIVE MS WITHOUT RELAPSES"

Efficacy Tables

Novartis **Siponimod SPMS**
AMNOG Dossier Subpopulation "ACTIVE SPMS WITHOUT RELAPSES **CBAF312A2304**

Table 2.1: All-cause Mortality (FAS), Binary Analysis

	Treatment groups		Comparison		
	BAF312 (N=127)	**Placebo (N=61)**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
N'	127	61			
All-cause mortality n (%)	1 (0.8)	1 (1.6)	0.48 [0.03;7.74] 0.602	0.48 [0.03;7.55] 0.602	-0.01 [-0.04;0.03] 0.637

N': Number of patients in the analysis
OR: Odds Ratio
RR: Relative Risk
RD: Risk Difference

Novartis **Siponimod SPMS**
AMNOG Dossier Subpopulation "ACTIVE SPMS WITHOUT RELAPSES **CBAF312A2304**

Table 3.1.1: Annualized Relapse Rate (FAS)

	Treatment groups		Comparison	
	BAF312 (N=127)	**Placebo (N=61)**	**RR [95% CI]**	**p-value**
N'	127	61		
Patients with at least one relapse	13	12		
Number of relapses	14	15		
Annualized Relapse Rate* [95% CI]	0.06 [0.03;0.10]	0.14 [0.08;0.26]	0.41 [0.18;0.92]	0.031

N': Number of patients in the analysis
* calculated from negative binomial model including the following variables: Treatment+SPMS Group+BL T1 Lesions category+BL EDSS
RR: Rate Ratio

Table 3.1.2: Annualized Relapse Rate (FAS) by Age

	Treatment groups		Comparison	
	BAF312 (N=127)	**Placebo (N=61)**	**RR [95% CI]**	**p-value**
Interaction Test				0.358
Age = 18-40				
N'	18	13		
Patients with at least one relapse	2	4		
Number of relapses	2	4		
Annualized Relapse Rate* [95% CI]	0.06 [0.01;0.26]	0.17 [0.05;0.52]	0.35 [0.06;2.20]	0.263
Age = 41-55				
N'	95	33		
Patients with at least one relapse	10	7		
Number of relapses	10	10		
Annualized Relapse Rate* [95% CI]	0.06 [0.03;0.11]	0.18 [0.09;0.38]	0.31 [0.12;0.82]	0.018
Age = >55				
N'	14	15		
Patients with at least one relapse	1	1		
Number of relapses	2	1		
Annualized Relapse Rate* [95% CI]	0.08 [0.02;0.37]	0.04 [0.01;0.31]	2.08 [0.17;25.60]	0.568

N': Number of patients in the analysis
* calculated from negative binomial model including the following variables: Treatment+Agegroup+Treatment*Agegroup+SPMS Group+BL T1 Lesions category+BL EDSS
RR: Rate Ratio

Table 3.1.3: Annualized Relapse Rate (FAS) by Gender

	Treatment groups		Comparison	
	BAF312 (N=127)	**Placebo (N=61)**	**RR [95% CI]**	**p-value**
Interaction Test				0.441
Sex = F				
N'	76	37		
Patients with at least one relapse	8	6		
Number of relapses	8	7		
Annualized Relapse Rate* [95% CI]	0.06 [0.03;0.13]	0.11 [0.05;0.26]	0.55 [0.18;1.64]	0.284
Sex = M				
N'	51	24		
Patients with at least one relapse	5	6		
Number of relapses	6	8		
Annualized Relapse Rate* [95% CI]	0.06 [0.02;0.14]	0.19 [0.08;0.45]	0.29 [0.09;0.95]	0.041

N': Number of patients in the analysis
* calculated from negative binomial model including the following variables: Treatment+Sex+Treatment*Sex+SPMS Group+BL T1 Lesions category+BL EDSS
RR: Rate Ratio

Table 3.1.4: Annualized Relapse Rate (FAS) by Previous MS DMT

	Treatment groups		Comparison	
	BAF312 (N=127)	**Placebo (N=61)**	**RR [95% CI]**	**p-value**
Interaction Test				0.380
Previous MS-DMT = N				
N'	20	17		
Patients with at least one relapse	0	1		
Number of relapses	0	1		
Annualized Relapse Rate* [95% CI]	NA	0.03 [0.00;0.21]	NA	.
Previous MS-DMT = Y				
N'	107	44		
Patients with at least one relapse	13	11		
Number of relapses	14	14		
Annualized Relapse Rate* [95% CI]	0.07 [0.04;0.12]	0.19 [0.11;0.33]	0.38 [0.17;0.83]	0.016

N': Number of patients in the analysis
* calculated from negative binomial model including the following variables: Treatment+DMT+Treatment*DMT+SPMS Group+BL T1 Lesions category+BL EDSS
RR: Rate Ratio

Table 3.1.5: Annualized Relapse Rate (FAS) by Previous IFN-beta-1b treatment

	Treatment groups		Comparison	
	BAF312 (N=127)	**Placebo (N=61)**	**RR [95% CI]**	**p-value**
Interaction Test				N.E.
Previous IFN-beta 1b = N				
N'	82	48		
Patients with at least one relapse	6	9		
Number of relapses	6	10		
Annualized Relapse Rate* [95% CI]	0.04 [0.02;0.08]	0.11 [0.05;0.22]	0.33 [0.11;0.96]	0.041
Previous IFN-beta 1b = Y				
N'	45	13		
Patients with at least one relapse	7	3		
Number of relapses	8	5		
Annualized Relapse Rate* [95% CI]	0.10 [0.05;0.21]	0.26 [0.10;0.70]	0.39 [0.11;1.33]	0.133

N': Number of patients in the analysis
* calculated from negative binomial model including the following variables: Treatment+IFN+Treatment*IFN+SPMS Group+BL T1 Lesions category+BL EDSS
RR: Rate Ratio

Table 3.1.6: Annualized Relapse Rate (FAS) by Rapid Evolvement

	Treatment groups		Comparison	
	BAF312 (N=127)	**Placebo (N=61)**	**RR [95% CI]**	**p-value**
Interaction Test				0.690
Rapid evolvement = N				
N'	95	47		
Patients with at least one relapse	9	7		
Number of relapses	9	10		
Annualized Relapse Rate* [95% CI]	0.05 [0.03;0.11]	0.12 [0.06;0.25]	0.45 [0.17;1.18]	0.105
Rapid evolvement = Y				
N'	32	14		
Patients with at least one relapse	4	5		
Number of relapses	5	5		
Annualized Relapse Rate* [95% CI]	0.07 [0.03;0.20]	0.23 [0.08;0.68]	0.31 [0.07;1.34]	0.117

N': Number of patients in the analysis
* calculated from negative binomial model including the following variables: Treatment+Rapid evolvement+Treatment*Rapid evolvement+SPMS Group+BL T1 Lesions category+BL EDSS
RR: Rate Ratio

Table 3.1.7: Annualized Relapse Rate (FAS) by Disease Course

	Treatment groups		Comparison	
	BAF312 (N=127)	**Placebo (N=61)**	**RR [95% CI]**	**p-value**
Interaction Test				0.446
Moderate/severe disease course = N				
N'	18	11		
Patients with at least one relapse	3	3		
Number of relapses	4	3		
Annualized Relapse Rate* [95% CI]	0.09 [0.03;0.33]	0.12 [0.03;0.49]	0.74 [0.14;4.00]	0.725
Moderate/severe disease course = Y				
N'	109	50		
Patients with at least one relapse	10	9		
Number of relapses	10	12		
Annualized Relapse Rate* [95% CI]	0.05 [0.03;0.10]	0.15 [0.08;0.29]	0.35 [0.14;0.87]	0.023

N': Number of patients in the analysis
* calculated from negative binomial model including the following variables: Treatment+Course+Treatment*Course+SPMS Group+BL T1 Lesions category+BL EDSS
RR: Rate Ratio

Table 3.1.8: Annualized Relapse Rate (FAS) by Region

	Treatment groups		Comparison	
	BAF312 (N=127)	**Placebo (N=61)**	**RR [95% CI]**	**p-value**
Interaction Test				0.386
Region = Europe				
N'	106	52		
Patients with at least one relapse	12	11		
Number of relapses	12	14		
Annualized Relapse Rate* [95% CI]	0.06 [0.03;0.11]	0.16 [0.09;0.30]	0.36 [0.16;0.84]	0.018
Region = Others				
N'	21	9		
Patients with at least one relapse	1	1		
Number of relapses	2	1		
Annualized Relapse Rate* [95% CI]	0.07 [0.02;0.28]	0.06 [0.01;0.44]	1.15 [0.09;14.38]	0.914

N': Number of patients in the analysis
* calculated from negative binomial model including the following variables: Treatment+Region+Treatment*Region+SPMS Group+BL T1 Lesions category+BL EDSS
RR: Rate Ratio

Table 3.2.1: Time to First Relapse (FAS)

	Treatment groups		Comparison	
	BAF312 (N=127)	**Placebo (N=61)**	**HR [95% CI]**	**p-value**
N'	127	61		
Patients with at least one relapse	13	12		
Median in days* [95% KI]	[S > 50%]	[S > 50%]		
% of patients without relapse after 24 months* [95% KI]	90.81 [85.63;95.99]	79.47 [69.08;89.86]		
% of patients without relapse at EOS* [95% KI]	80.32 [64.05;96.60]	79.47 [69.08;89.86]		
			0.38 [0.16;0.89]	0.026

N': Number of patients in the analysis
[S > 50%]: Survival curve does not reach 50% level
*: K-M estimate % of outcome-free patients; Greenwood formula is used for CIs
HR calculated from Cox proportional hazards model including the following variables: Treatment+Country+SPMS Group+BL EDSS+BL Number of T1 Lesions

Table 3.2.2: Time to First Relapse (FAS) by Age

	Treatment groups		Comparison	
	BAF312 (N=127)	**Placebo (N=61)**	**HR [95% CI]**	**p-value**
Interaction Test				0.651
Age = 18-40				
N'	18	13		
Patients with at least one relapse	2	4		
Median in days* [95% KI]	[S > 50%]	[S > 50%]		
% of patients without relapse after 24 months* [95% KI]	87.50 [71.29;100.0]	67.69 [41.50;93.89]		
% of patients without relapse at EOS* [95% KI]	87.50 [71.29;100.0]	67.69 [41.50;93.89]		
			0.19 [0.03;1.32]	0.093
Age = 41-55				
N'	95	33		
Patients with at least one relapse	10	7		
Median in days* [95% KI]	[S > 50%]	[S > 50%]		
% of patients without relapse after 24 months* [95% KI]	91.15 [85.28;97.01]	78.20 [63.91;92.49]		
% of patients without relapse at EOS* [95% KI]	78.22 [58.71;97.74]	78.20 [63.91;92.49]		
			0.34 [0.11;1.00]	0.051

N': Number of patients in the analysis
[S > 50%]: Survival curve does not reach 50% level
*: K-M estimate % of outcome-free patients; Greenwood formula is used for CIs
HR calculated from Cox proportional hazards model including the following variables:
Treatment+Agegroup+Treatment*Agegroup+Country+SPMS Group+BL EDSS+BL Number of T1 Lesions

Table 3.2.2: Time to First Relapse (FAS) by Age

	Treatment groups		Comparison	
	BAF312 (N=127)	**Placebo (N=61)**	**HR [95% CI]**	**p-value**
Age = >55				
N'	14	15		
Patients with at least one relapse	1	1		
Median in days* [95% KI]	[S > 50%]	[S > 50%]		
% of patients without relapse after 24 months* [95% KI]	92.31 [77.82;100.0]	92.86 [79.37;100.0]		
% of patients without relapse at EOS* [95% KI]	92.31 [77.82;100.0]	92.86 [79.37;100.0]		
			0.99 [0.05;19.01]	0.996

N': Number of patients in the analysis
[S > 50%]: Survival curve does not reach 50% level
*: K-M estimate % of outcome-free patients; Greenwood formula is used for CIs
HR calculated from Cox proportional hazards model including the following variables:
Treatment+Agegroup+Treatment*Agegroup+Country+SPMS Group+BL EDSS+BL Number of T1 Lesions

Table 3.2.3: Time to First Relapse (FAS) by Gender

	Treatment groups		Comparison	
	BAF312 (N=127)	**Placebo (N=61)**	**HR [95% CI]**	**p-value**
Interaction Test				0.897
Sex = F				
N'	76	37		
Patients with at least one relapse	8	6		
Median in days* [95% KI]	[S > 50%]	[S > 50%]		
% of patients without relapse after 24 months* [95% KI]	90.03 [83.00;97.05]	83.70 [71.76;95.64]		
% of patients without relapse at EOS* [95% KI]	85.52 [74.64;96.41]	83.70 [71.76;95.64]		
			0.36 [0.11;1.17]	0.089
Sex = M				
N'	51	24		
Patients with at least one relapse	5	6		
Median in days* [95% KI]	[S > 50%]	[S > 50%]		
% of patients without relapse after 24 months* [95% KI]	91.85 [84.17;99.52]	71.59 [52.14;91.04]		
% of patients without relapse at EOS* [95% KI]	73.48 [40.70;100.0]	71.59 [52.14;91.04]		
			0.41 [0.11;1.48]	0.173

N': Number of patients in the analysis
[S > 50%]: Survival curve does not reach 50% level
*: K-M estimate % of outcome-free patients; Greenwood formula is used for CIs
HR calculated from Cox proportional hazards model including the following variables: Treatment+Sex+Treatment*Sex+Country+SPMS Group+BL EDSS+BL Number of T1 Lesions

Table 3.2.4: Time to First Relapse (FAS) by Previous MS DMT

	Treatment groups		Comparison	
	BAF312 (N=127)	**Placebo (N=61)**	**HR [95% CI]**	**p-value**
Interaction Test				0.995
Previous MS-DMT = N				
N'	20	17		
Patients with at least one relapse	0	1		
Median in days* [95% KI]	[S > 50%]	[S > 50%]		
% of patients without relapse after 24 months* [95% KI]	100.0 [100.0;100.0]	94.12 [82.93;100.0]		
% of patients without relapse at EOS* [95% KI]	100.0 [100.0;100.0]	94.12 [82.93;100.0]		
			NA	.
Previous MS-DMT = Y				
N'	107	44		
Patients with at least one relapse	13	11		
Median in days* [95% KI]	[S > 50%]	[S > 50%]		
% of patients without relapse after 24 months* [95% KI]	88.97 [82.81;95.13]	73.34 [59.75;86.93]		
% of patients without relapse at EOS* [95% KI]	77.31 [59.65;94.98]	73.34 [59.75;86.93]		
			0.29 [0.12;0.72]	0.007

N': Number of patients in the analysis
[S > 50%]: Survival curve does not reach 50% level
*: K-M estimate % of outcome-free patients; Greenwood formula is used for CIs
HR calculated from Cox proportional hazards model including the following variables: Treatment+DMT+Treatment*DMT+Country+SPMS Group+BL EDSS+BL Number of T1 Lesions

Table 3.2.5: Time to First Relapse (FAS) by Previous IFN-beta-1b treatment

	Treatment groups		Comparison	
	BAF312 (N=127)	**Placebo (N=61)**	**HR [95% CI]**	**p-value**
Interaction Test				0.526
Previous IFN-beta 1b = N				
N'	82	48		
Patients with at least one relapse	6	9		
Median in days* [95% KI]	[S > 50%]	[S > 50%]		
% of patients without relapse after 24 months* [95% KI]	94.82 [89.86;99.77]	80.34 [68.79;91.89]		
% of patients without relapse at EOS* [95% KI]	78.15 [53.42;100.0]	80.34 [68.79;91.89]		
			0.28 [0.09;0.87]	0.027
Previous IFN-beta 1b = Y				
N'	45	13		
Patients with at least one relapse	7	3		
Median in days* [95% KI]	[S > 50%]	[S > 50%]		
% of patients without relapse after 24 months* [95% KI]	83.66 [72.56;94.76]	76.15 [52.51;99.80]		
% of patients without relapse at EOS* [95% KI]	83.66 [72.56;94.76]	76.15 [52.51;99.80]		
			0.50 [0.12;2.10]	0.347

N': Number of patients in the analysis
[S > 50%]: Survival curve does not reach 50% level
*: K-M estimate % of outcome-free patients; Greenwood formula is used for CIs
HR calculated from Cox proportional hazards model including the following variables: Treatment+IFN+Treatment*IFN+Country+SPMS Group+BL EDSS+BL Number of T1 Lesions

Table 3.2.6: Time to First Relapse (FAS) by Rapid Evolvement

	Treatment groups		Comparison	
	BAF312 (N=127)	**Placebo (N=61)**	**HR [95% CI]**	**p-value**
Interaction Test				0.328
Rapid evolvement = N				
N'	95	47		
Patients with at least one relapse	9	7		
Median in days* [95% KI]	[S > 50%]	[S > 50%]		
% of patients without relapse after 24 months* [95% KI]	92.19 [86.63;97.75]	84.23 [73.49;94.98]		
% of patients without relapse at EOS* [95% KI]	79.22 [59.59;98.85]	84.23 [73.49;94.98]		
			0.50 [0.18;1.43]	0.198
Rapid evolvement = Y				
N'	32	14		
Patients with at least one relapse	4	5		
Median in days* [95% KI]	[S > 50%]	[S > 50%]		
% of patients without relapse after 24 months* [95% KI]	87.05 [75.19;98.91]	64.29 [39.19;89.39]		
% of patients without relapse at EOS* [95% KI]	87.05 [75.19;98.91]	64.29 [39.19;89.39]		
			0.21 [0.05;0.87]	0.031

N': Number of patients in the analysis
[S > 50%]: Survival curve does not reach 50% level
*: K-M estimate % of outcome-free patients; Greenwood formula is used for CIs
HR calculated from Cox proportional hazards model including the following variables: Treatment+Rapid evolvement+Treatment*Rapid evolvement+Country+SPMS Group+BL EDSS+BL Number of T1 Lesions

Table 3.2.7: Time to First Relapse (FAS) by Disease Course

	Treatment groups		Comparison	
	BAF312 (N=127)	**Placebo (N=61)**	**HR [95% CI]**	**p-value**
Interaction Test				0.837
Moderate/severe disease course = N				
N'	18	11		
Patients with at least one relapse	3	3		
Median in days* [95% KI]	[S > 50%]	[S > 50%]		
% of patients without relapse after 24 months* [95% KI]	82.35 [64.23;100.0]	71.59 [44.22;98.97]		
% of patients without relapse at EOS* [95% KI]	82.35 [64.23;100.0]	71.59 [44.22;98.97]		
			0.45 [0.08;2.66]	0.378
Moderate/severe disease course = Y				
N'	109	50		
Patients with at least one relapse	10	9		
Median in days* [95% KI]	[S > 50%]	[S > 50%]		
% of patients without relapse after 24 months* [95% KI]	92.10 [86.83;97.36]	81.12 [69.98;92.26]		
% of patients without relapse at EOS* [95% KI]	79.38 [59.90;98.87]	81.12 [69.98;92.26]		
			0.36 [0.14;0.97]	0.042

N': Number of patients in the analysis
[S > 50%]: Survival curve does not reach 50% level
*: K-M estimate % of outcome-free patients; Greenwood formula is used for CIs
HR calculated from Cox proportional hazards model including the following variables: Treatment+Course+Treatment*Course+Country+SPMS Group+BL EDSS+BL Number of T1 Lesions

Table 3.2.8: Time to First Relapse (FAS) by Region

	Treatment groups		Comparison	
	BAF312 (N=127)	**Placebo (N=61)**	**HR [95% CI]**	**p-value**
Interaction Test				0.897
Region = Europe				
N'	106	52		
Patients with at least one relapse	12	11		
Median in days* [95% KI]	[S > 50%]	[S > 50%]		
% of patients without relapse after 24 months* [95% KI]	90.15 [84.35;95.95]	77.87 [66.29;89.45]		
% of patients without relapse at EOS* [95% KI]	78.68 [61.00;96.35]	77.87 [66.29;89.45]		
			0.48 [0.21;1.08]	0.077
Region = Others				
N'	21	9		
Patients with at least one relapse	1	1		
Median in days* [95% KI]	[S > 50%]	[S > 50%]		
% of patients without relapse after 24 months* [95% KI]	95.00 [85.45;100.0]	88.89 [68.36;100.0]		
% of patients without relapse at EOS* [95% KI]	95.00 [85.45;100.0]	88.89 [68.36;100.0]		
			0.58 [0.04;9.25]	0.696

N': Number of patients in the analysis
[S > 50%]: Survival curve does not reach 50% level
*: K-M estimate % of outcome-free patients; Greenwood formula is used for CIs
HR calculated from Cox proportional hazards model including the following variables: Treatment+Region+Treatment*Region+SPMS Group+BL EDSS+BL Number of T1 Lesions

Table 4.1.1: 3-month CDP (FAS), Binary Analysis

	Treatment groups		Comparison		
	BAF312 (N=127)	**Placebo (N=61)**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
N'	127	61			
3-month CDP n (%)	30 (23.6)	19 (31.1)	0.68 [0.35;1.35] 0.272	0.76 [0.47;1.23] 0.266	-0.08 [-0.21;0.06] 0.284

N': Number of patients in the analysis
OR: Odds Ratio
RR: Relative Risk
RD: Risk Difference

Table 4.1.2: 3-month CDP (FAS), Binary Analysis by Age

	Treatment groups		Comparison		
	BAF312 (N=127)	**Placebo (N=61)**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Interaction Test	p= 0.272				
Age = 18-40					
N'	18	13			
3-month CDP n (%)	7 (38.9)	3 (23.1)	2.12 [0.43;10.52] 0.357	1.69 [0.53;5.32] 0.373	0.16 [-0.16;0.48] 0.335
Age = 41-55					
N'	95	33			
3-month CDP n (%)	21 (22.1)	12 (36.4)	0.50 [0.21;1.17] 0.110	0.61 [0.34;1.09] 0.097	-0.14 [-0.33;0.04] 0.129
Age = >55					
N'	14	15			
3-month CDP n (%)	2 (14.3)	4 (26.7)	0.46 [0.07;3.02] 0.417	0.54 [0.12;2.48] 0.425	-0.12 [-0.41;0.17] 0.402

N': Number of patients in the analysis
OR: Odds Ratio
RR: Relative Risk
RD: Risk Difference

Table 4.1.3: 3-month CDP (FAS), Binary Analysis by Gender

	Treatment groups		Comparison		
	BAF312 (N=127)	**Placebo (N=61)**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Interaction Test	p= 0.246				
Sex = F					
N'	76	37			
3-month CDP n (%)	16 (21.1)	13 (35.1)	0.49 [0.21;1.18] 0.111	0.60 [0.32;1.11] 0.104	-0.14 [-0.32;0.04] 0.123
Sex = M					
N'	51	24			
3-month CDP n (%)	14 (27.5)	6 (25.0)	1.14 [0.37;3.44] 0.823	1.10 [0.48;2.50] 0.824	0.02 [-0.19;0.24] 0.821

N': Number of patients in the analysis
OR: Odds Ratio
RR: Relative Risk
RD: Risk Difference

Table 4.1.4: 3-month CDP (FAS), Binary Analysis by Previous MS DMT

	Treatment groups		Comparison		
	BAF312 (N=127)	**Placebo (N=61)**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Interaction Test	p= 0.557				
Previous MS-DMT = N					
N'	20	17			
3-month CDP n (%)	3 (15.0)	5 (29.4)	0.42 [0.08;2.12] 0.296	0.51 [0.14;1.83] 0.301	-0.14 [-0.41;0.12] 0.290
Previous MS-DMT = Y					
N'	107	44			
3-month CDP n (%)	27 (25.2)	14 (31.8)	0.72 [0.33;1.56] 0.409	0.79 [0.46;1.36] 0.402	-0.07 [-0.23;0.09] 0.421

N': Number of patients in the analysis
OR: Odds Ratio
RR: Relative Risk
RD: Risk Difference

Table 4.1.5: 3-month CDP (FAS), Binary Analysis by Previous IFN-beta-1b treatment

	Treatment groups		Comparison		
	BAF312 (N=127)	**Placebo (N=61)**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Interaction Test	p= 0.144				
Previous IFN-beta 1b = N					
N'	82	48			
3-month CDP n (%)	18 (22.0)	17 (35.4)	0.51 [0.23;1.13] 0.097	0.62 [0.35;1.08] 0.094	-0.13 [-0.30;0.03] 0.104
Previous IFN-beta 1b = Y					
N'	45	13			
3-month CDP n (%)	12 (26.7)	2 (15.4)	2.00 [0.39;10.36] 0.409	1.73 [0.44;6.78] 0.429	0.11 [-0.12;0.35] 0.346

N': Number of patients in the analysis
OR: Odds Ratio
RR: Relative Risk
RD: Risk Difference

Table 4.1.6: 3-month CDP (FAS), Binary Analysis by Rapid Evolvement

	Treatment groups		Comparison		
	BAF312 (N=127)	**Placebo (N=61)**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Interaction Test	p= 0.948				
Rapid evolvement = N					
N'	95	47			
3-month CDP n (%)	21 (22.1)	14 (29.8)	0.67 [0.30;1.48] 0.319	0.74 [0.42;1.32] 0.313	-0.08 [-0.23;0.08] 0.332
Rapid evolvement = Y					
N'	32	14			
3-month CDP n (%)	9 (28.1)	5 (35.7)	0.70 [0.18;2.68] 0.607	0.79 [0.32;1.93] 0.601	-0.08 [-0.37;0.22] 0.615

N': Number of patients in the analysis
OR: Odds Ratio
RR: Relative Risk
RD: Risk Difference

Table 4.1.7: 3-month CDP (FAS), Binary Analysis by Disease Course

	Treatment groups		Comparison		
	BAF312 (N=127)	**Placebo (N=61)**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Interaction Test	p= 0.750				
Moderate/severe disease course = N					
N'	18	11			
3-month CDP n (%)	6 (33.3)	4 (36.4)	0.87 [0.18;4.21] 0.868	0.92 [0.33;2.54] 0.867	-0.03 [-0.39;0.33] 0.868
Moderate/severe disease course = Y					
N'	109	50			
3-month CDP n (%)	24 (22.0)	15 (30.0)	0.66 [0.31;1.40] 0.279	0.73 [0.42;1.27] 0.272	-0.08 [-0.23;0.07] 0.294

N': Number of patients in the analysis
OR: Odds Ratio
RR: Relative Risk
RD: Risk Difference

Table 4.1.8: 3-month CDP (FAS), Binary Analysis by Region

	Treatment groups		Comparison		
	BAF312 (N=127)	**Placebo (N=61)**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Interaction Test	p= 0.595				
Region = Europe					
N'	106	52			
3-month CDP n (%)	25 (23.6)	17 (32.7)	0.64 [0.31;1.32] 0.225	0.72 [0.43;1.21] 0.218	-0.09 [-0.24;0.06] 0.237
Region = Others					
N'	21	9			
3-month CDP n (%)	5 (23.8)	2 (22.2)	1.09 [0.17;7.06] 0.925	1.07 [0.25;4.53] 0.925	0.02 [-0.31;0.34] 0.924

N': Number of patients in the analysis
OR: Odds Ratio
RR: Relative Risk
RD: Risk Difference

Table 4.2.1: 3-month CDP (FAS), Time-to-Event Analysis

	Treatment groups		Comparison	
	BAF312 (N=127)	**Placebo (N=61)**	**HR [95% CI]**	**p-value**
N'	127	61		
Patients with at least one CDP	30	19		
Median in days* [95% KI]	[S > 50%]	[S > 50%]		
% of patients without CDP after 24 months* [95% KI]	70.98 [61.77;80.18]	63.25 [47.77;78.73]		
% of patients without CDP at EOS* [95% KI]	70.98 [61.77;80.18]	57.50 [39.79;75.20]		
			0.65 [0.34;1.23]	0.185

N': Number of patients in the analysis
[S > 50%]: Survival curve does not reach 50% level
*: K-M estimate % of outcome-free patients; Greenwood formula is used for CIs
HR calculated from Cox proportional hazards model including the following variables: Treatment+Country+SPMS Group+BL EDSS

Table 4.2.2: 3-month CDP (FAS), Time-to-Event Analysis by Age

	Treatment groups		Comparison	
	BAF312 (N=127)	Placebo (N=61)	HR [95% CI]	p-value
Interaction Test				0.122
Age = 18-40				
N'	18	13		
Patients with at least one CDP	7	3		
Median in days* [95% KI]	631 [366;NA]	[S > 50%]		
% of patients without CDP after 24 months* [95% KI]	46.77 [17.21;76.34]	55.38 [8.80;100.0]		
% of patients without CDP at EOS* [95% KI]	46.77 [17.21;76.34]	55.38 [8.80;100.0]		
			3.09 [0.59;16.07]	0.180
Age = 41-55				
N'	95	33		
Patients with at least one CDP	21	12		
Median in days* [95% KI]	[S > 50%]	[S > 50%]		
% of patients without CDP after 24 months* [95% KI]	73.60 [63.53;83.68]	57.35 [37.72;76.97]		
% of patients without CDP at EOS* [95% KI]	73.60 [63.53;83.68]	57.35 [37.72;76.97]		
			0.48 [0.21;1.08]	0.076

N': Number of patients in the analysis
[S > 50%]: Survival curve does not reach 50% level
*: K-M estimate % of outcome-free patients; Greenwood formula is used for CIs
HR calculated from Cox proportional hazards model including the following variables:
Treatment+Agegroup+Treatment*Agegroup+Country+SPMSGroup+BL EDSS

Table 4.2.2: 3-month CDP (FAS), Time-to-Event Analysis by Age

	Treatment groups		Comparison	
	BAF312 (N=127)	**Placebo (N=61)**	**HR [95% CI]**	**p-value**
Age = >55				
N'	14	15		
Patients with at least one CDP	2	4		
Median in days* [95% KI]	[S > 50%]	[S > 50%]		
% of patients without CDP after 24 months* [95% KI]	84.62 [65.00;100.0]	78.57 [57.08;100.0]		
% of patients without CDP at EOS* [95% KI]	84.62 [65.00;100.0]	58.93 [21.89;95.96]		
			0.48 [0.05;4.30]	0.509

N': Number of patients in the analysis
[S > 50%]: Survival curve does not reach 50% level
*: K-M estimate % of outcome-free patients; Greenwood formula is used for CIs
HR calculated from Cox proportional hazards model including the following variables:
Treatment+Agegroup+Treatment*Agegroup+Country+SPMSGroup+BL EDSS

Table 4.2.3: 3-month CDP (FAS), Time-to-Event Analysis by Gender

	Treatment groups		Comparison	
	BAF312 (N=127)	**Placebo (N=61)**	**HR [95% CI]**	**p-value**
Interaction Test				0.622
Sex = F				
N'	76	37		
Patients with at least one CDP	16	13		
Median in days* [95% KI]	[S > 50%]	736 [549;NA]		
% of patients without CDP after 24 months* [95% KI]	75.73 [65.23;86.23]	58.13 [36.93;79.32]		
% of patients without CDP at EOS* [95% KI]	75.73 [65.23;86.23]	48.44 [23.69;73.19]		
			0.57 [0.24;1.35]	0.202
Sex = M				
N'	51	24		
Patients with at least one CDP	14	6		
Median in days* [95% KI]	[S > 50%]	[S > 50%]		
% of patients without CDP after 24 months* [95% KI]	64.10 [47.95;80.26]	72.82 [54.11;91.53]		
% of patients without CDP at EOS* [95% KI]	64.10 [47.95;80.26]	72.82 [54.11;91.53]		
			0.81 [0.28;2.32]	0.697

N': Number of patients in the analysis
[S > 50%]: Survival curve does not reach 50% level
*: K-M estimate % of outcome-free patients; Greenwood formula is used for CIs
HR calculated from Cox proportional hazards model including the following variables: Treatment+Sex+Treatment*Sex+Country+SPMS Group+BL EDSS

Table 4.2.4: 3-month CDP (FAS), Time-to-Event Analysis by Previous MS DMT

	Treatment groups		Comparison	
	BAF312 (N=127)	**Placebo (N=61)**	**HR [95% CI]**	**p-value**
Interaction Test				0.734
Previous MS-DMT = N				
N'	20	17		
Patients with at least one CDP	3	5		
Median in days* [95% KI]	[S > 50%]	[S > 50%]		
% of patients without CDP after 24 months* [95% KI]	79.39 [57.81;100.0]	76.47 [56.31;96.63]		
% of patients without CDP at EOS* [95% KI]	79.39 [57.81;100.0]	50.98 [8.03;93.93]		
			0.49 [0.11;2.24]	0.360
Previous MS-DMT = Y				
N'	107	44		
Patients with at least one CDP	27	14		
Median in days* [95% KI]	[S > 50%]	[S > 50%]		
% of patients without CDP after 24 months* [95% KI]	69.47 [59.45;79.49]	58.35 [39.35;77.36]		
% of patients without CDP at EOS* [95% KI]	69.47 [59.45;79.49]	58.35 [39.35;77.36]		
			0.67 [0.32;1.40]	0.283

N': Number of patients in the analysis
[S > 50%]: Survival curve does not reach 50% level
*: K-M estimate % of outcome-free patients; Greenwood formula is used for CIs
HR calculated from Cox proportional hazards model including the following variables: Treatment+DMT+Treatment*DMT+Country+SPMS Group+BL EDSS

Table 4.2.5: 3-month CDP (FAS), Time-to-Event Analysis by Previous IFN-beta-1b treatment

	Treatment groups		Comparison	
	BAF312 (N=127)	**Placebo (N=61)**	**HR [95% CI]**	**p-value**
Interaction Test				0.291
Previous IFN-beta 1b = N				
N'	82	48		
Patients with at least one CDP	18	17		
Median in days* [95% KI]	[S > 50%]	[S > 50%]		
% of patients without CDP after 24 months* [95% KI]	72.91 [61.72;84.09]	58.94 [41.56;76.32]		
% of patients without CDP at EOS* [95% KI]	72.91 [61.72;84.09]	52.39 [32.76;72.01]		
			0.53 [0.25;1.11]	0.091
Previous IFN-beta 1b = Y				
N'	45	13		
Patients with at least one CDP	12	2		
Median in days* [95% KI]	[S > 50%]	[S > 50%]		
% of patients without CDP after 24 months* [95% KI]	67.30 [51.20;83.40]	84.62 [65.00;100.0]		
% of patients without CDP at EOS* [95% KI]	67.30 [51.20;83.40]	84.62 [65.00;100.0]		
			1.34 [0.28;6.39]	0.714

N': Number of patients in the analysis
[S > 50%]: Survival curve does not reach 50% level
*: K-M estimate % of outcome-free patients; Greenwood formula is used for CIs
HR calculated from Cox proportional hazards model including the following variables: Treatment+IFN+Treatment*IFN+Country+SPMS Group+BL EDSS

Table 4.2.6: 3-month CDP (FAS), Time-to-Event Analysis by Rapid Evolvement

	Treatment groups		Comparison	
	BAF312 (N=127)	**Placebo (N=61)**	**HR [95% CI]**	**p-value**
Interaction Test				0.699
Rapid evolvement = N				
N'	95	47		
Patients with at least one CDP	21	14		
Median in days* [95% KI]	[S > 50%]	[S > 50%]		
% of patients without CDP after 24 months* [95% KI]	73.57 [63.49;83.65]	69.89 [56.07;83.71]		
% of patients without CDP at EOS* [95% KI]	73.57 [63.49;83.65]	62.90 [44.91;80.89]		
			0.60 [0.29;1.26]	0.175
Rapid evolvement = Y				
N'	32	14		
Patients with at least one CDP	9	5		
Median in days* [95% KI]	[S > 50%]	730 [549;NA]		
% of patients without CDP after 24 months* [95% KI]	63.11 [42.28;83.93]	29.46 [0.00;74.30]		
% of patients without CDP at EOS* [95% KI]	63.11 [42.28;83.93]	29.46 [0.00;74.30]		
			0.80 [0.23;2.81]	0.727

N': Number of patients in the analysis
[S > 50%]: Survival curve does not reach 50% level
*: K-M estimate % of outcome-free patients; Greenwood formula is used for CIs
HR calculated from Cox proportional hazards model including the following variables: Treatment+Rapid evolvement+Treatment*Rapid evolvement+Country+SPMS Group+BL EDSS

Table 4.2.7: 3-month CDP (FAS), Time-to-Event Analysis by Disease Course

	Treatment groups		Comparison	
	BAF312 (N=127)	**Placebo (N=61)**	**HR [95% CI]**	**p-value**
Interaction Test				0.627
Moderate/severe disease course = N				
N'	18	11		
Patients with at least one CDP	6	4		
Median in days* [95% KI]	[S > 50%]	[S > 50%]		
% of patients without CDP after 24 months* [95% KI]	63.53 [40.03;87.03]	61.36 [31.45;91.28]		
% of patients without CDP at EOS* [95% KI]	63.53 [40.03;87.03]	61.36 [31.45;91.28]		
			0.47 [0.11;1.95]	0.297
Moderate/severe disease course = Y				
N'	109	50		
Patients with at least one CDP	24	15		
Median in days* [95% KI]	[S > 50%]	[S > 50%]		
% of patients without CDP after 24 months* [95% KI]	72.76 [63.04;82.47]	63.05 [44.77;81.33]		
% of patients without CDP at EOS* [95% KI]	72.76 [63.04;82.47]	56.04 [35.27;76.82]		
			0.70 [0.34;1.43]	0.327

N': Number of patients in the analysis
[S > 50%]: Survival curve does not reach 50% level
*: K-M estimate % of outcome-free patients; Greenwood formula is used for CIs
HR calculated from Cox proportional hazards model including the following variables: Treatment+Course+Treatment*Course+Country+SPMS Group+BL EDSS

Table 4.2.8: 3-month CDP (FAS), Time-to-Event Analysis by Region

	Treatment groups		Comparison	
	BAF312 (N=127)	**Placebo (N=61)**	**HR [95% CI]**	**p-value**
Interaction Test				0.264
Region = Europe				
N'	106	52		
Patients with at least one CDP	25	17		
Median in days* [95% KI]	[S > 50%]	[S > 50%]		
% of patients without CDP after 24 months* [95% KI]	71.61 [61.75;81.46]	64.53 [49.79;79.27]		
% of patients without CDP at EOS* [95% KI]	71.61 [61.75;81.46]	55.31 [34.35;76.28]		
			0.60 [0.33;1.12]	0.110
Region = Others				
N'	21	9		
Patients with at least one CDP	5	2		
Median in days* [95% KI]	[S > 50%]	[S > 50%]		
% of patients without CDP after 24 months* [95% KI]	66.82 [41.54;92.10]	71.11 [35.88;100.0]		
% of patients without CDP at EOS* [95% KI]	66.82 [41.54;92.10]	71.11 [35.88;100.0]		
			1.65 [0.32;8.53]	0.551

N': Number of patients in the analysis
[S > 50%]: Survival curve does not reach 50% level
*: K-M estimate % of outcome-free patients; Greenwood formula is used for CIs
HR calculated from Cox proportional hazards model including the following variables: Treatment+Region+Treatment*Region+SPMS Group+BL EDSS

Table 5.1.1: 6-month CDP (FAS), Binary Analysis

	Treatment groups		Comparison		
	BAF312 (N=127)	**Placebo (N=61)**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
N'	127	61			
6-month CDP n (%)	24 (18.9)	16 (26.2)	0.66 [0.32;1.35] 0.252	0.72 [0.41;1.25] 0.246	-0.07 [-0.20;0.06] 0.268

N': Number of patients in the analysis
OR: Odds Ratio
RR: Relative Risk
RD: Risk Difference

Table 5.1.2: 6-month CDP (FAS), Binary Analysis by Age

	Treatment groups		Comparison		
	BAF312 (N=127)	**Placebo (N=61)**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Interaction Test	p= 0.406				
Age = 18-40					
N'	18	13			
6-moth CDP n (%)	6 (33.3)	3 (23.1)	1.67 [0.33;8.42] 0.537	1.44 [0.44;4.74] 0.544	0.10 [-0.21;0.42] 0.525
Age = 41-55					
N'	95	33			
6-moth CDP n (%)	16 (16.8)	10 (30.3)	0.47 [0.19;1.16] 0.102	0.56 [0.28;1.10] 0.092	-0.13 [-0.31;0.04] 0.129
Age = >55					
N'	14	15			
6-moth CDP n (%)	2 (14.3)	3 (20.0)	0.67 [0.09;4.73] 0.685	0.71 [0.14;3.66] 0.687	-0.06 [-0.33;0.22] 0.682

N': Number of patients in the analysis
OR: Odds Ratio
RR: Relative Risk
RD: Risk Difference

Table 5.1.3: 6-month CDP (FAS), Binary Analysis by Gender

	Treatment groups		Comparison		
	BAF312 (N=127)	**Placebo (N=61)**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Interaction Test	p= 0.047				
Sex = F					
N'	76	37			
6-moth CDP n (%)	11 (14.5)	12 (32.4)	0.35 [0.14;0.90] 0.030	0.45 [0.22;0.91] 0.028	-0.18 [-0.35;-0.01] 0.039
Sex = M					
N'	51	24			
6-moth CDP n (%)	13 (25.5)	4 (16.7)	1.71 [0.49;5.94] 0.398	1.53 [0.56;4.20] 0.410	0.09 [-0.10;0.28] 0.366

N': Number of patients in the analysis
OR: Odds Ratio
RR: Relative Risk
RD: Risk Difference

Table 5.1.4: 6-month CDP (FAS), Binary Analysis by Previous MS DMT

	Treatment groups		Comparison		
	BAF312 (N=127)	**Placebo (N=61)**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Interaction Test	p= 0.870				
Previous MS-DMT = N					
N'	20	17			
6-moth CDP n (%)	2 (10.0)	3 (17.6)	0.52 [0.08;3.54] 0.503	0.57 [0.11;3.01] 0.505	-0.08 [-0.30;0.15] 0.503
Previous MS-DMT = Y					
N'	107	44			
6-moth CDP n (%)	22 (20.6)	13 (29.5)	0.62 [0.28;1.37] 0.237	0.70 [0.39;1.25] 0.228	-0.09 [-0.24;0.07] 0.256

N': Number of patients in the analysis
OR: Odds Ratio
RR: Relative Risk
RD: Risk Difference

Table 5.1.5: 6-month CDP (FAS), Binary Analysis by Previous IFN-beta-1b treatment

	Treatment groups		Comparison		
	BAF312 (N=127)	**Placebo (N=61)**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Interaction Test	p= 0.229				
Previous IFN-beta 1b = N					
N'	82	48			
6-moth CDP n (%)	14 (17.1)	14 (29.2)	0.50 [0.21;1.17] 0.109	0.59 [0.31;1.12] 0.106	-0.12 [-0.27;0.03] 0.119
Previous IFN-beta 1b = Y					
N'	45	13			
6-moth CDP n (%)	10 (22.2)	2 (15.4)	1.57 [0.30;8.29] 0.594	1.44 [0.36;5.78] 0.603	0.07 [-0.16;0.30] 0.561

N': Number of patients in the analysis
OR: Odds Ratio
RR: Relative Risk
RD: Risk Difference

Table 5.1.6: 6-month CDP (FAS), Binary Analysis by Rapid Evolvement

	Treatment groups		Comparison		
	BAF312 (N=127)	**Placebo (N=61)**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Interaction Test	p= 0.682				
Rapid evolvement = N					
N'	95	47			
6-moth CDP n (%)	16 (16.8)	12 (25.5)	0.59 [0.25;1.38] 0.224	0.66 [0.34;1.28] 0.218	-0.09 [-0.23;0.06] 0.242
Rapid evolvement = Y					
N'	32	14			
6-moth CDP n (%)	8 (25.0)	4 (28.6)	0.83 [0.20;3.41] 0.799	0.88 [0.31;2.43] 0.798	-0.04 [-0.32;0.24] 0.803

N': Number of patients in the analysis
OR: Odds Ratio
RR: Relative Risk
RD: Risk Difference

Table 5.1.7: 6-month CDP (FAS), Binary Analysis by Disease Course

	Treatment groups		Comparison		
	BAF312 (N=127)	**Placebo (N=61)**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Interaction Test	p= 0.574				
Moderate/severe disease course = N					
N'	18	11			
6-moth CDP n (%)	5 (27.8)	3 (27.3)	1.03 [0.19;5.51] 0.976	1.02 [0.30;3.45] 0.976	0.01 [-0.33;0.34] 0.976
Moderate/severe disease course = Y					
N'	109	50			
6-moth CDP n (%)	19 (17.4)	13 (26.0)	0.60 [0.27;1.34] 0.214	0.67 [0.36;1.25] 0.207	-0.09 [-0.23;0.06] 0.233

N': Number of patients in the analysis
OR: Odds Ratio
RR: Relative Risk
RD: Risk Difference

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Table 5.1.8: 6-month CDP (FAS), Binary Analysis by Region

	Treatment groups		Comparison		
	BAF312 (N=127)	**Placebo (N=61)**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Interaction Test	p= 0.898				
Region = Europe					
N'	106	52			
6-moth CDP n (%)	21 (19.8)	14 (26.9)	0.67 [0.31;1.46] 0.313	0.74 [0.41;1.33] 0.308	-0.07 [-0.21;0.07] 0.328
Region = Others					
N'	21	9			
6-moth CDP n (%)	3 (14.3)	2 (22.2)	0.58 [0.08;4.27] 0.596	0.64 [0.13;3.22] 0.591	-0.08 [-0.39;0.23] 0.616

N': Number of patients in the analysis
OR: Odds Ratio
RR: Relative Risk
RD: Risk Difference

Table 5.2.1: 6-month CDP (FAS), Time-to-Event Analysis

	Treatment groups		Comparison	
	BAF312 (N=127)	**Placebo (N=61)**	**HR [95% CI]**	**p-value**
N'	127	61		
Patients with at least one CDP	24	16		
Median in days* [95% KI]	[S > 50%]	[S > 50%]		
% of patients without CDP after 24 months* [95% KI]	76.79 [68.25;85.33]	66.05 [50.38;81.72]		
% of patients without CDP at EOS* [95% KI]	76.79 [68.25;85.33]	66.05 [50.38;81.72]		
			0.57 [0.28;1.16]	0.121

N': Number of patients in the analysis
[S > 50%]: Survival curve does not reach 50% level
*: K-M estimate % of outcome-free patients; Greenwood formula is used for CIs
HR calculated from Cox proportional hazards model including the following variables: Treatment+Country+SPMS Group+BL EDSS

Table 5.2.2: 6-month CDP (FAS), Time-to-Event Analysis by Age

	Treatment groups		Comparison	
	BAF312 (N=127)	**Placebo (N=61)**	**HR [95% CI]**	**p-value**
Interaction Test				0.386
Age = 18-40				
N'	18	13		
Patients with at least one CDP	6	3		
Median in days* [95% KI]	[S > 50%]	[S > 50%]		
% of patients without CDP after 24 months* [95% KI]	56.84 [28.76;84.92]	55.38 [8.80;100.0]		
% of patients without CDP at EOS* [95% KI]	56.84 [28.76;84.92]	55.38 [8.80;100.0]		
			1.74 [0.31;9.92]	0.532
Age = 41-55				
N'	95	33		
Patients with at least one CDP	16	10		
Median in days* [95% KI]	[S > 50%]	[S > 50%]		
% of patients without CDP after 24 months* [95% KI]	79.55 [70.26;88.85]	62.56 [42.53;82.59]		
% of patients without CDP at EOS* [95% KI]	79.55 [70.26;88.85]	62.56 [42.53;82.59]		
			0.46 [0.19;1.12]	0.088

N': Number of patients in the analysis
[S > 50%]: Survival curve does not reach 50% level
*: K-M estimate % of outcome-free patients; Greenwood formula is used for CIs
HR calculated from Cox proportional hazards model including the following variables:
Treatment+Agegroup+Treatment*Agegroup+Country+SPMSGroup+BL EDSS

Table 5.2.2: 6-month CDP (FAS), Time-to-Event Analysis by Age

	Treatment groups		Comparison	
	BAF312 (N=127)	**Placebo (N=61)**	**HR [95% CI]**	**p-value**
Age = >55				
N'	14	15		
Patients with at least one CDP	2	3		
Median in days* [95% KI]	[S > 50%]	[S > 50%]		
% of patients without CDP after 24 months* [95% KI]	84.62 [65.00;100.0]	78.57 [57.08;100.0]		
% of patients without CDP at EOS* [95% KI]	84.62 [65.00;100.0]	78.57 [57.08;100.0]		
			0.51 [0.05;4.98]	0.559

N': Number of patients in the analysis
[S > 50%]: Survival curve does not reach 50% level
*: K-M estimate % of outcome-free patients; Greenwood formula is used for CIs
HR calculated from Cox proportional hazards model including the following variables:
Treatment+Agegroup+Treatment*Agegroup+Country+SPMSGroup+BL EDSS

Table 5.2.3: 6-month CDP (FAS), Time-to-Event Analysis by Gender

	Treatment groups		Comparison	
	BAF312 (N=127)	**Placebo (N=61)**	**HR [95% CI]**	**p-value**
Interaction Test				0.253
Sex = F				
N'	76	37		
Patients with at least one CDP	11	12		
Median in days* [95% KI]	[S > 50%]	[S > 50%]		
% of patients without CDP after 24 months* [95% KI]	83.42 [74.40;92.44]	58.13 [36.93;79.32]		
% of patients without CDP at EOS* [95% KI]	83.42 [74.40;92.44]	58.13 [36.93;79.32]		
			0.40 [0.15;1.04]	0.061
Sex = M				
N'	51	24		
Patients with at least one CDP	13	4		
Median in days* [95% KI]	[S > 50%]	[S > 50%]		
% of patients without CDP after 24 months* [95% KI]	67.32 [51.70;82.94]	81.52 [65.00;98.04]		
% of patients without CDP at EOS* [95% KI]	67.32 [51.70;82.94]	81.52 [65.00;98.04]		
			1.01 [0.30;3.46]	0.982

N': Number of patients in the analysis
[S > 50%]: Survival curve does not reach 50% level
*: K-M estimate % of outcome-free patients; Greenwood formula is used for CIs
HR calculated from Cox proportional hazards model including the following variables: Treatment+Sex+Treatment*Sex+Country+SPMS Group+BL EDSS

Table 5.2.4: 6-month CDP (FAS), Time-to-Event Analysis by Previous MS DMT

	Treatment groups		Comparison	
	BAF312 (N=127)	**Placebo (N=61)**	**HR [95% CI]**	**p-value**
Interaction Test				0.959
Previous MS-DMT = N				
N'	20	17		
Patients with at least one CDP	2	3		
Median in days* [95% KI]	[S > 50%]	[S > 50%]		
% of patients without CDP after 24 months* [95% KI]	86.36 [68.04;100.0]	82.35 [64.23;100.0]		
% of patients without CDP at EOS* [95% KI]	86.36 [68.04;100.0]	82.35 [64.23;100.0]		
			0.52 [0.08;3.41]	0.494
Previous MS-DMT = Y				
N'	107	44		
Patients with at least one CDP	22	13		
Median in days* [95% KI]	[S > 50%]	[S > 50%]		
% of patients without CDP after 24 months* [95% KI]	75.03 [65.63;84.43]	60.13 [40.88;79.39]		
% of patients without CDP at EOS* [95% KI]	75.03 [65.63;84.43]	60.13 [40.88;79.39]		
			0.55 [0.25;1.21]	0.136

N': Number of patients in the analysis
[S > 50%]: Survival curve does not reach 50% level
*: K-M estimate % of outcome-free patients; Greenwood formula is used for CIs
HR calculated from Cox proportional hazards model including the following variables: Treatment+DMT+Treatment*DMT+Country+SPMS Group+BL EDSS

Table 5.2.5: 6-month CDP (FAS), Time-to-Event Analysis by Previous IFN-beta-1b treatment

	Treatment groups		Comparison	
	BAF312 (N=127)	**Placebo (N=61)**	**HR [95% CI]**	**p-value**
Interaction Test				0.399
Previous IFN-beta 1b = N				
N'	82	48		
Patients with at least one CDP	14	14		
Median in days* [95% KI]	[S > 50%]	[S > 50%]		
% of patients without CDP after 24 months* [95% KI]	78.70 [68.35;89.06]	62.38 [44.65;80.10]		
% of patients without CDP at EOS* [95% KI]	78.70 [68.35;89.06]	62.38 [44.65;80.10]		
			0.46 [0.20;1.09]	0.078
Previous IFN-beta 1b = Y				
N'	45	13		
Patients with at least one CDP	10	2		
Median in days* [95% KI]	[S > 50%]	[S > 50%]		
% of patients without CDP after 24 months* [95% KI]	73.54 [58.79;88.29]	84.62 [65.00;100.0]		
% of patients without CDP at EOS* [95% KI]	73.54 [58.79;88.29]	84.62 [65.00;100.0]		
			1.02 [0.20;5.04]	0.985

N': Number of patients in the analysis
[S > 50%]: Survival curve does not reach 50% level
*: K-M estimate % of outcome-free patients; Greenwood formula is used for CIs
HR calculated from Cox proportional hazards model including the following variables: Treatment+IFN+Treatment*IFN+Country+SPMS Group+BL EDSS

Table 5.2.6: 6-month CDP (FAS), Time-to-Event Analysis by Rapid Evolvement

	Treatment groups		Comparison	
	BAF312 (N=127)	**Placebo (N=61)**	**HR [95% CI]**	**p-value**
Interaction Test				0.646
Rapid evolvement = N				
N'	95	47		
Patients with at least one CDP	16	12		
Median in days* [95% KI]	[S > 50%]	[S > 50%]		
% of patients without CDP after 24 months* [95% KI]	79.75 [70.56;88.93]	71.84 [58.18;85.51]		
% of patients without CDP at EOS* [95% KI]	79.75 [70.56;88.93]	71.84 [58.18;85.51]		
			0.51 [0.22;1.16]	0.108
Rapid evolvement = Y				
N'	32	14		
Patients with at least one CDP	8	4		
Median in days* [95% KI]	[S > 50%]	730 [549;NA]		
% of patients without CDP after 24 months* [95% KI]	68.30 [48.64;87.95]	32.14 [0.00;80.75]		
% of patients without CDP at EOS* [95% KI]	68.30 [48.64;87.95]	32.14 [0.00;80.75]		
			0.74 [0.18;3.05]	0.679

N': Number of patients in the analysis
[S > 50%]: Survival curve does not reach 50% level
*: K-M estimate % of outcome-free patients; Greenwood formula is used for CIs
HR calculated from Cox proportional hazards model including the following variables: Treatment+Rapid evolvement+Treatment*Rapid evolvement+Country+SPMS Group+BL EDSS

Table 5.2.7: 6-month CDP (FAS), Time-to-Event Analysis by Disease Course

	Treatment groups		Comparison	
	BAF312 (N=127)	**Placebo (N=61)**	**HR [95% CI]**	**p-value**
Interaction Test				0.953
Moderate/severe disease course = N				
N'	18	11		
Patients with at least one CDP	5	3		
Median in days* [95% KI]	[S > 50%]	[S > 50%]		
% of patients without CDP after 24 months* [95% KI]	69.52 [47.05;91.99]	70.13 [41.29;98.97]		
% of patients without CDP at EOS* [95% KI]	69.52 [47.05;91.99]	70.13 [41.29;98.97]		
			0.55 [0.11;2.81]	0.473
Moderate/severe disease course = Y				
N'	109	50		
Patients with at least one CDP	19	13		
Median in days* [95% KI]	[S > 50%]	[S > 50%]		
% of patients without CDP after 24 months* [95% KI]	78.38 [69.37;87.38]	64.72 [46.25;83.18]		
% of patients without CDP at EOS* [95% KI]	78.38 [69.37;87.38]	64.72 [46.25;83.18]		
			0.58 [0.26;1.28]	0.178

N': Number of patients in the analysis
[S > 50%]: Survival curve does not reach 50% level
*: K-M estimate % of outcome-free patients; Greenwood formula is used for CIs
HR calculated from Cox proportional hazards model including the following variables: Treatment+Course+Treatment*Course+Country+SPMS Group+BL EDSS

Table 5.2.8: 6-month CDP (FAS), Time-to-Event Analysis by Region

	Treatment groups		Comparison	
	BAF312 (N=127)	**Placebo (N=61)**	**HR [95% CI]**	**p-value**
Interaction Test				0.688
Region = Europe				
N'	106	52		
Patients with at least one CDP	21	14		
Median in days* [95% KI]	[S > 50%]	[S > 50%]		
% of patients without CDP after 24 months* [95% KI]	76.20 [66.92;85.48]	68.00 [53.28;82.73]		
% of patients without CDP at EOS* [95% KI]	76.20 [66.92;85.48]	68.00 [53.28;82.73]		
			0.62 [0.31;1.22]	0.164
Region = Others				
N'	21	9		
Patients with at least one CDP	3	2		
Median in days* [95% KI]	[S > 50%]	[S > 50%]		
% of patients without CDP after 24 months* [95% KI]	82.50 [63.97;100.0]	71.11 [35.88;100.0]		
% of patients without CDP at EOS* [95% KI]	82.50 [63.97;100.0]	71.11 [35.88;100.0]		
			0.92 [0.15;5.49]	0.923

N': Number of patients in the analysis
[S > 50%]: Survival curve does not reach 50% level
*: K-M estimate % of outcome-free patients; Greenwood formula is used for CIs
HR calculated from Cox proportional hazards model including the following variables: Treatment+Region+Treatment*Region+SPMS Group+BL EDSS

Table 6.1.0: MSFC Z Score (FAS), Return Rates

	Treatment groups		
	BAF312 (N=127)	**Placebo (N=61)**	**Total (N=188)**
Return Rate n (%)*			
Baseline	125 (98.4)	59 (96.7)	184 (97.9)
Month 06	113 (89.0)	54 (88.5)	167 (88.8)
Month 12	103 (81.1)	41 (67.2)	144 (76.6)
Month 18	75 (59.1)	27 (44.3)	102 (54.3)
Month 24	48 (37.8)	17 (27.9)	65 (34.6)

* Number and percentage of patients with non-missing data at the given time point.

Table 6.1.1: MSFC Z Score (FAS), Change from Baseline

	Treatment groups		Comparison	
	BAF312 (N=127)	**Placebo (N=61)**	**Mean Difference [95% CI]**	**p-value**
N'	113	53		
Baseline Mean (SD)	-0.10 (0.65)	-0.11 (0.60)		
Month 12 Adjusted Mean Change (SE)	0.04 (0.04)	0.02 (0.06)	0.02 [-0.11;0.15]	0.743
Month 24 Adjusted Mean Change (SE)	-0.07 (0.05)	-0.10 (0.08)	0.03 [-0.17;0.22]	0.789

N': Number of patients in the analysis
Adjusted Mean Change calculated by MMRM model including the following variables: Treatment+Visit+Treatment*Visit+BL Value

Table 6.1.2: MSFC Z Score (FAS), Change from Baseline by Age

	Treatment groups		Comparison	
	BAF312 (N=127)	Placebo (N=61)	Mean Difference [95% CI]	p-value
Interaction Test				0.800
Age = 18-40				
N'	16	12		
Baseline Mean (SD)	-0.32 (0.85)	-0.15 (0.75)		
Month 12 Adjusted Mean Change (SE)	0.06 (0.10)	0.14 (0.11)	-0.08 [-0.38;0.22]	0.605
Month 24 Adjusted Mean Change (SE)	-0.10 (0.13)	-0.27 (0.16)	0.17 [-0.25;0.59]	0.422
Age = 41-55				
N'	85	28		
Baseline Mean (SD)	-0.06 (0.61)	-0.07 (0.60)		
Month 12 Adjusted Mean Change (SE)	0.05 (0.04)	-0.01 (0.08)	0.06 [-0.12;0.24]	0.507
Month 24 Adjusted Mean Change (SE)	-0.04 (0.06)	-0.02 (0.11)	-0.01 [-0.26;0.23]	0.911
Age = >55				
N'	12	13		
Baseline Mean (SD)	-0.14 (0.71)	-0.17 (0.46)		
Month 12 Adjusted Mean Change (SE)	-0.07 (0.13)	-0.04 (0.11)	-0.02 [-0.36;0.32]	0.892
Month 24 Adjusted Mean Change (SE)	-0.30 (0.16)	-0.11 (0.18)	-0.18 [-0.66;0.30]	0.454

N': Number of patients in the analysis
Adjusted Mean Change calculated by MMRM model including the following variables:
Treatment+Agegroup+Visit+Treatment*Agegroup+Treatment*Visit+Agegroup*Visit+Treatment*Visit*Agegroup+BL Value

Table 6.1.3: MSFC Z Score (FAS), Change from Baseline by Gender

	Treatment groups		Comparison	
	BAF312 (N=127)	**Placebo (N=61)**	**Mean Difference [95% CI]**	**p-value**
Interaction Test				0.927
Sex = F				
N'	65	33		
Baseline Mean (SD)	-0.11 (0.69)	-0.18 (0.63)		
Month 12 Adjusted Mean Change (SE)	0.02 (0.05)	-0.01 (0.07)	0.03 [-0.14;0.20]	0.711
Month 24 Adjusted Mean Change (SE)	-0.13 (0.07)	-0.12 (0.10)	-0.01 [-0.25;0.23]	0.931
Sex = M				
N'	48	20		
Baseline Mean (SD)	-0.09 (0.61)	0.00 (0.53)		
Month 12 Adjusted Mean Change (SE)	0.07 (0.06)	0.07 (0.09)	0.00 [-0.22;0.21]	0.976
Month 24 Adjusted Mean Change (SE)	0.01 (0.08)	-0.08 (0.15)	0.09 [-0.24;0.43]	0.583

N': Number of patients in the analysis
Adjusted Mean Change calculated by MMRM model including the following variables:
Treatment+Sex+Visit+Treatment*Sex+Treatment*Visit+Sex*Visit+Treatment*Visit*Sex+BL Value

Table 6.1.4 MSFC Z Score (FAS), Change from Baseline by Previous MS DMT

	Treatment groups		Comparison	
	BAF312 (N=127)	**Placebo (N=61)**	**Mean Difference [95% CI]**	**p-value**
Interaction Test				0.905
Previous MS-DMT = N				
N'	20	17		
Baseline Mean (SD)	-0.07 (0.67)	-0.05 (0.33)		
Month 12 Adjusted Mean Change (SE)	0.19 (0.08)	0.06 (0.10)	0.13 [-0.12;0.38]	0.297
Month 24 Adjusted Mean Change (SE)	0.12 (0.12)	0.16 (0.19)	-0.04 [-0.48;0.39]	0.847
Previous MS-DMT = Y				
N'	93	36		
Baseline Mean (SD)	-0.11 (0.65)	-0.14 (0.69)		
Month 12 Adjusted Mean Change (SE)	0.01 (0.04)	0.00 (0.07)	0.00 [-0.15;0.16]	0.964
Month 24 Adjusted Mean Change (SE)	-0.12 (0.06)	-0.17 (0.09)	0.05 [-0.17;0.27]	0.645

N': Number of patients in the analysis
Adjusted Mean Change calculated by MMRM model including the following variables:
Treatment+DMT+Visit+Treatment*DMT+Treatment*Visit+DMT*Visit+Treatment*Visit*DMT+BL Value

Table 6.1.5 MSFC Z Score (FAS), Change from Baseline by Previous IFN-beta-1b treatment

	Treatment groups		Comparison	
	BAF312 (N=127)	**Placebo (N=61)**	**Mean Difference [95% CI]**	**p-value**
Interaction Test				0.543
Previous IFN-beta 1b = N				
N'	73	41		
Baseline Mean (SD)	-0.13 (0.70)	-0.06 (0.61)		
Month 12 Adjusted Mean Change (SE)	-0.01 (0.04)	0.00 (0.06)	-0.02 [-0.17;0.14]	0.840
Month 24 Adjusted Mean Change (SE)	-0.13 (0.06)	-0.12 (0.10)	-0.02 [-0.25;0.21]	0.879
Previous IFN-beta 1b = Y				
N'	40	12		
Baseline Mean (SD)	-0.05 (0.56)	-0.30 (0.51)		
Month 12 Adjusted Mean Change (SE)	0.14 (0.06)	0.09 (0.13)	0.05 [-0.22;0.33]	0.700
Month 24 Adjusted Mean Change (SE)	0.03 (0.08)	-0.04 (0.18)	0.07 [-0.31;0.46]	0.708

N': Number of patients in the analysis
Adjusted Mean Change calculated by MMRM model including the following variables:
Treatment+IFN+Visit+Treatment*IFN+Treatment*Visit+IFN*Visit+Treatment*Visit*IFN+BL Value

Table 6.1.6 MSFC Z Score (FAS), Change from Baseline by Rapid Evolvement

	Treatment groups		Comparison	
	BAF312 (N=127)	**Placebo (N=61)**	**Mean Difference [95% CI]**	**p-value**
Interaction Test				0.834
Rapid evolvement = N				
N'	84	41		
Baseline Mean (SD)	-0.17 (0.64)	-0.07 (0.59)		
Month 12 Adjusted Mean Change (SE)	0.04 (0.04)	0.00 (0.06)	0.04 [-0.11;0.19]	0.615
Month 24 Adjusted Mean Change (SE)	-0.07 (0.06)	-0.07 (0.09)	0.00 [-0.22;0.22]	0.992
Rapid evolvement = Y				
N'	29	12		
Baseline Mean (SD)	0.10 (0.66)	-0.26 (0.62)		
Month 12 Adjusted Mean Change (SE)	0.06 (0.07)	0.11 (0.13)	-0.05 [-0.33;0.24]	0.743
Month 24 Adjusted Mean Change (SE)	-0.08 (0.10)	-0.18 (0.17)	0.10 [-0.29;0.50]	0.602

N': Number of patients in the analysis
Adjusted Mean Change calculated by MMRM model including the following variables:
Treatment+RapEv+Visit+Treatment*RapEv+Treatment*Visit+RapEv*Visit+Treatment*Visit*RapEv+BL Value

Table 6.1.7 MSFC Z Score (FAS), Change from Baseline by Disease Course

	Treatment groups		Comparison	
	BAF312 (N=127)	**Placebo (N=61)**	**Mean Difference [95% CI]**	**p-value**
Interaction Test				0.506
Moderate/severe disease course = N				
N'	17	10		
Baseline Mean (SD)	0.29 (0.47)	0.20 (0.50)		
Month 12 Adjusted Mean Change (SE)	0.03 (0.10)	0.04 (0.13)	-0.01 [-0.34;0.31]	0.945
Month 24 Adjusted Mean Change (SE)	-0.07 (0.14)	0.06 (0.17)	-0.12 [-0.56;0.32]	0.582
Moderate/severe disease course = Y				
N'	96	43		
Baseline Mean (SD)	-0.17 (0.66)	-0.19 (0.60)		
Month 12 Adjusted Mean Change (SE)	0.04 (0.04)	0.01 (0.06)	0.03 [-0.12;0.17]	0.708
Month 24 Adjusted Mean Change (SE)	-0.08 (0.05)	-0.15 (0.10)	0.08 [-0.15;0.30]	0.493

N': Number of patients in the analysis
Adjusted Mean Change calculated by MMRM model including the following variables:
Treatment+DC+Visit+Treatment*DC+Treatment*Visit+DC*Visit+Treatment*Visit*DC+BL Value

Table 6.1.8 MSFC Z Score (FAS), Change from Baseline by Region

	Treatment groups		Comparison	
	BAF312 (N=127)	**Placebo (N=61)**	**Mean Difference [95% CI]**	**p-value**
Interaction Test				0.902
Region = Europe				
N'	97	45		
Baseline Mean (SD)	-0.06 (0.67)	-0.12 (0.58)		
Month 12 Adjusted Mean Change (SE)	0.05 (0.04)	0.03 (0.06)	0.02 [-0.12;0.16]	0.783
Month 24 Adjusted Mean Change (SE)	-0.07 (0.05)	-0.08 (0.10)	0.01 [-0.21;0.24]	0.912
Region = Others				
N'	16	8		
Baseline Mean (SD)	-0.35 (0.49)	-0.04 (0.70)		
Month 12 Adjusted Mean Change (SE)	0.00 (0.11)	-0.03 (0.14)	0.02 [-0.32;0.37]	0.888
Month 24 Adjusted Mean Change (SE)	-0.11 (0.16)	-0.19 (0.17)	0.07 [-0.39;0.53]	0.757

N': Number of patients in the analysis
Adjusted Mean Change calculated by MMRM model including the following variables:
Treatment+Region+Visit+Treatment*Region+Treatment*Visit+Region*Visit+Treatment*Visit*Region+BL Value

Table 6.2.0: PASAT 3 (FAS), Return Rates

	Treatment groups		
	BAF312 (N=127)	**Placebo (N=61)**	**Total (N=188)**
Return Rate n (%)*			
Baseline	126 (99.2)	59 (96.7)	185 (98.4)
Month 06	115 (90.6)	57 (93.4)	172 (91.5)
Month 12	105 (82.7)	47 (77.0)	152 (80.9)
Month 18	77 (60.6)	31 (50.8)	108 (57.4)
Month 24	52 (40.9)	21 (34.4)	73 (38.8)

* Number and percentage of patients with non-missing data at the given time point.

Table 6.2.1: PASAT 3 (FAS), Change from Baseline

	Treatment groups		Comparison	
	BAF312 (N=127)	**Placebo (N=61)**	**Mean Difference [95% CI]**	**p-value**
N'	115	56		
Baseline Mean (SD)	37.80 (14.41)	34.57 (13.48)		
Month 12 Adjusted Mean Change (SE)	3.13 (0.87)	3.44 (1.29)	-0.31 [-3.39;2.77]	0.842
Month 24 Adjusted Mean Change (SE)	2.27 (1.21)	0.96 (1.90)	1.31 [-3.16;5.78]	0.563

N': Number of patients in the analysis
Adjusted Mean Change calculated by MMRM model including the following variables: Treatment+Visit+Treatment*Visit+BL Value

Table 6.2.2: PASAT 3 (FAS), Change from Baseline by Age

	Treatment groups		Comparison	
	BAF312 (N=127)	Placebo (N=61)	Mean Difference [95% CI]	p-value
Interaction Test				0.265
Age = 18-40				
N'	16	13		
Baseline Mean (SD)	36.25 (16.80)	31.15 (14.39)		
Month 12 Adjusted Mean Change (SE)	6.41 (2.20)	11.47 (2.63)	-5.05 [-11.83;1.72]	0.143
Month 24 Adjusted Mean Change (SE)	3.32 (3.16)	-0.39 (4.04)	3.71 [-6.47;13.89]	0.471
Age = 41-55				
N'	87	30		
Baseline Mean (SD)	38.34 (13.76)	36.73 (12.54)		
Month 12 Adjusted Mean Change (SE)	3.04 (0.95)	0.15 (1.73)	2.89 [-1.00;6.78]	0.144
Month 24 Adjusted Mean Change (SE)	2.86 (1.34)	1.69 (2.43)	1.17 [-4.34;6.68]	0.673
Age = >55				
N'	12	13		
Baseline Mean (SD)	35.92 (16.66)	33.00 (14.78)		
Month 12 Adjusted Mean Change (SE)	-1.59 (2.90)	3.05 (2.39)	-4.65 [-12.06;2.76]	0.217
Month 24 Adjusted Mean Change (SE)	-4.94 (3.83)	-0.19 (3.98)	-4.75 [-15.73;6.23]	0.392

N': Number of patients in the analysis
Adjusted Mean Change calculated by MMRM model including the following variables:
Treatment+Agegroup+Visit+Treatment*Agegroup+Treatment*Visit+Agegroup*Visit+Treatment*Visit*Agegroup+BL Value

Table 6.2.3: PASAT 3 (FAS), Change from Baseline by Gender

	Treatment groups		Comparison	
	BAF312 (N=127)	**Placebo (N=61)**	**Mean Difference [95% CI]**	**p-value**
Interaction Test				0.804
Sex = F				
N'	66	35		
Baseline Mean (SD)	37.23 (14.94)	34.03 (13.70)		
Month 12 Adjusted Mean Change (SE)	3.28 (1.15)	2.92 (1.61)	0.36 [-3.55;4.26]	0.857
Month 24 Adjusted Mean Change (SE)	2.82 (1.62)	1.66 (2.23)	1.16 [-4.32;6.63]	0.676
Sex = M				
N'	49	21		
Baseline Mean (SD)	38.57 (13.77)	35.48 (13.39)		
Month 12 Adjusted Mean Change (SE)	2.93 (1.35)	4.44 (2.18)	-1.51 [-6.57;3.55]	0.557
Month 24 Adjusted Mean Change (SE)	1.57 (1.83)	-1.97 (3.66)	3.55 [-4.58;11.67]	0.388

N': Number of patients in the analysis
Adjusted Mean Change calculated by MMRM model including the following variables:
Treatment+Sex+Visit+Treatment*Sex+Treatment*Visit+Sex*Visit+Treatment*Visit*Sex+BL Value

Table 6.2.4 PASAT 3 (FAS), Change from Baseline by Previous MS DMT

	Treatment groups		Comparison	
	BAF312 (N=127)	**Placebo (N=61)**	**Mean Difference [95% CI]**	**p-value**
Interaction Test				0.853
Previous MS-DMT = N				
N'	20	17		
Baseline Mean (SD)	34.20 (15.49)	33.12 (12.52)		
Month 12 Adjusted Mean Change (SE)	2.16 (2.02)	1.38 (2.24)	0.78 [-5.16;6.73]	0.795
Month 24 Adjusted Mean Change (SE)	-0.45 (2.76)	1.91 (4.04)	-2.36 [-12.08;7.37]	0.631
Previous MS-DMT = Y				
N'	95	39		
Baseline Mean (SD)	38.56 (14.14)	35.21 (13.99)		
Month 12 Adjusted Mean Change (SE)	3.36 (0.97)	4.55 (1.58)	-1.19 [-4.84;2.47]	0.522
Month 24 Adjusted Mean Change (SE)	2.96 (1.35)	1.08 (2.16)	1.87 [-3.19;6.94]	0.464

N': Number of patients in the analysis
Adjusted Mean Change calculated by MMRM model including the following variables:
Treatment+DMT+Visit+Treatment*DMT+Treatment*Visit+DMT*Visit+Treatment*Visit*DMT+BL Value

Table 6.2.5 PASAT 3 (FAS), Change from Baseline by Previous IFN-beta-1b treatment

	Treatment groups		Comparison	
	BAF312 (N=127)	**Placebo (N=61)**	**Mean Difference [95% CI]**	**p-value**
Interaction Test				0.335
Previous IFN-beta 1b = N				
N'	74	43		
Baseline Mean (SD)	38.16 (14.10)	35.28 (13.50)		
Month 12 Adjusted Mean Change (SE)	2.43 (1.08)	2.84 (1.43)	-0.42 [-3.96;3.13]	0.817
Month 24 Adjusted Mean Change (SE)	2.68 (1.54)	-1.09 (2.17)	3.78 [-1.51;9.06]	0.159
Previous IFN-beta 1b = Y				
N'	41	13		
Baseline Mean (SD)	37.15 (15.11)	32.23 (13.68)		
Month 12 Adjusted Mean Change (SE)	4.48 (1.47)	5.44 (2.93)	-0.96 [-7.43;5.51]	0.770
Month 24 Adjusted Mean Change (SE)	1.66 (1.98)	8.08 (3.91)	-6.41 [-15.12;2.29]	0.147

N': Number of patients in the analysis
Adjusted Mean Change calculated by MMRM model including the following variables:
Treatment+IFN+Visit+Treatment*IFN+Treatment*Visit+IFN*Visit+Treatment*Visit*IFN+BL Value

Table 6.2.6 PASAT 3 (FAS), Change from Baseline by Rapid Evolvement

	Treatment groups		Comparison	
	BAF312 (N=127)	**Placebo (N=61)**	**Mean Difference [95% CI]**	**p-value**
Interaction Test				0.771
Rapid evolvement = N				
N'	86	42		
Baseline Mean (SD)	36.92 (14.92)	37.19 (12.24)		
Month 12 Adjusted Mean Change (SE)	3.09 (1.01)	2.86 (1.45)	0.23 [-3.26;3.72]	0.897
Month 24 Adjusted Mean Change (SE)	2.48 (1.41)	1.84 (2.14)	0.64 [-4.45;5.73]	0.803
Rapid evolvement = Y				
N'	29	14		
Baseline Mean (SD)	40.41 (12.64)	26.71 (14.41)		
Month 12 Adjusted Mean Change (SE)	3.25 (1.71)	5.75 (2.87)	-2.50 [-9.16;4.16]	0.460
Month 24 Adjusted Mean Change (SE)	1.46 (2.41)	-2.22 (4.22)	3.68 [-5.99;13.35]	0.451

N': Number of patients in the analysis
Adjusted Mean Change calculated by MMRM model including the following variables:
Treatment+RapEv+Visit+Treatment*RapEv+Treatment*Visit+RapEv*Visit+Treatment*Visit*RapEv+BL Value

Table 6.2.7 PASAT 3 (FAS), Change from Baseline by Disease Course

	Treatment groups		Comparison	
	BAF312 (N=127)	**Placebo (N=61)**	**Mean Difference [95% CI]**	**p-value**
Interaction Test				0.957
Moderate/severe disease course = N				
N'	17	10		
Baseline Mean (SD)	38.76 (13.24)	36.60 (14.18)		
Month 12 Adjusted Mean Change (SE)	2.60 (2.38)	-0.43 (2.96)	3.02 [-4.47;10.52]	0.427
Month 24 Adjusted Mean Change (SE)	0.26 (3.54)	-0.24 (3.99)	0.49 [-10.10;11.09]	0.926
Moderate/severe disease course = Y				
N'	98	46		
Baseline Mean (SD)	37.63 (14.66)	34.13 (13.45)		
Month 12 Adjusted Mean Change (SE)	3.24 (0.93)	4.36 (1.43)	-1.13 [-4.50;2.25]	0.510
Month 24 Adjusted Mean Change (SE)	2.49 (1.30)	1.09 (2.19)	1.39 [-3.66;6.45]	0.585

N': Number of patients in the analysis
Adjusted Mean Change calculated by MMRM model including the following variables:
Treatment+DC+Visit+Treatment*DC+Treatment*Visit+DC*Visit+Treatment*Visit*DC+BL Value

Table 6.2.8 PASAT 3 (FAS), Change from Baseline by Region

	Treatment groups		Comparison	
	BAF312 (N=127)	**Placebo (N=61)**	**Mean Difference [95% CI]**	**p-value**
Interaction Test				0.176
Region = Europe				
N'	98	48		
Baseline Mean (SD)	38.36 (14.36)	34.48 (13.16)		
Month 12 Adjusted Mean Change (SE)	2.94 (0.94)	3.93 (1.40)	-0.99 [-4.33;2.35]	0.559
Month 24 Adjusted Mean Change (SE)	1.89 (1.31)	0.42 (2.18)	1.47 [-3.59;6.52]	0.566
Region = Others				
N'	17	8		
Baseline Mean (SD)	34.59 (14.72)	35.13 (16.24)		
Month 12 Adjusted Mean Change (SE)	3.87 (2.50)	0.74 (3.37)	3.13 [-5.16;11.42]	0.456
Month 24 Adjusted Mean Change (SE)	4.70 (3.56)	1.59 (4.15)	3.11 [-7.76;13.98]	0.571

N': Number of patients in the analysis
Adjusted Mean Change calculated by MMRM model including the following variables:
Treatment+Region+Visit+Treatment*Region+Treatment*Visit+Region*Visit+Treatment*Visit*Region+BL Value

Table 6.3.0: 9-Hole Peg Test (FAS), Return Rates

	Treatment groups		
	BAF312 (N=127)	**Placebo (N=61)**	**Total (N=188)**
Return Rate n (%)*			
Baseline	127 (100.0)	61 (100.0)	188 (100.0)
Month 03	121 (95.3)	58 (95.1)	179 (95.2)
Month 06	117 (92.1)	56 (91.8)	173 (92.0)
Month 09	113 (89.0)	54 (88.5)	167 (88.8)
Month 12	108 (85.0)	49 (80.3)	157 (83.5)
Month 15	100 (78.7)	43 (70.5)	143 (76.1)
Month 18	82 (64.6)	29 (47.5)	111 (59.0)
Month 21	71 (55.9)	25 (41.0)	96 (51.1)
Month 24	52 (40.9)	20 (32.8)	72 (38.3)

* Number and percentage of patients with non-missing data at the given time point.

Table 6.3.1: 9-Hole Peg Test (FAS), Change from Baseline

	Treatment groups		Comparison	
	BAF312 (N=127)	**Placebo (N=61)**	**Mean Difference [95% CI]**	**p-value**
N'	124	60		
Baseline Mean (SD)	39.67 (22.21)	34.81 (17.19)		
Month 12 Adjusted Mean Change (SE)	-1.03 (1.16)	0.00 (1.70)	-1.03 [-5.13;3.07]	0.620
Month 24 Adjusted Mean Change (SE)	0.69 (2.30)	3.59 (3.53)	-2.89 [-11.28;5.49]	0.495

N': Number of patients in the analysis
Adjusted Mean Change calculated by MMRM model including the following variables: Treatment+Visit+Treatment*Visit+BL Value

Table 6.3.2: 9-Hole Peg Test (FAS), Change from Baseline by Age

	Treatment groups		Comparison	
	BAF312 (N=127)	Placebo (N=61)	Mean Difference [95% CI]	p-value
Interaction Test				0.719
Age = 18-40				
N'	18	13		
Baseline Mean (SD)	50.07 (29.25)	33.19 (13.15)		
Month 12 Adjusted Mean Change (SE)	-4.60 (3.10)	0.28 (3.57)	-4.87 [-14.27;4.52]	0.307
Month 24 Adjusted Mean Change (SE)	-4.21 (6.15)	0.19 (7.67)	-4.40 [-24.09;15.29]	0.656
Age = 41-55				
N'	93	32		
Baseline Mean (SD)	38.37 (21.19)	36.21 (20.94)		
Month 12 Adjusted Mean Change (SE)	-0.71 (1.29)	-0.30 (2.30)	-0.42 [-5.64;4.81]	0.874
Month 24 Adjusted Mean Change (SE)	1.31 (2.67)	7.96 (5.02)	-6.65 [-18.03;4.73]	0.247
Age = >55				
N'	13	15		
Baseline Mean (SD)	34.63 (14.15)	33.22 (10.82)		
Month 12 Adjusted Mean Change (SE)	1.77 (3.56)	-0.25 (3.21)	2.02 [-7.47;11.51]	0.674
Month 24 Adjusted Mean Change (SE)	3.01 (7.34)	-1.31 (6.96)	4.32 [-15.94;24.59]	0.671

N': Number of patients in the analysis
Adjusted Mean Change calculated by MMRM model including the following variables:
Treatment+Agegroup+Visit+Treatment*Agegroup+Treatment*Visit+Agegroup*Visit+Treatment*Visit*Agegroup+BL Value

Table 6.3.3: 9-Hole Peg Test (FAS), Change from Baseline by Gender

	Treatment groups		Comparison	
	BAF312 (N=127)	**Placebo (N=61)**	**Mean Difference [95% CI]**	**p-value**
Interaction Test				0.390
Sex = F				
N'	73	37		
Baseline Mean (SD)	39.95 (24.84)	35.58 (19.87)		
Month 12 Adjusted Mean Change (SE)	-0.53 (1.51)	1.07 (2.12)	-1.59 [-6.76;3.57]	0.541
Month 24 Adjusted Mean Change (SE)	0.23 (3.17)	5.77 (4.47)	-5.54 [-16.51;5.42]	0.316
Sex = M				
N'	51	23		
Baseline Mean (SD)	39.27 (18.03)	33.58 (12.02)		
Month 12 Adjusted Mean Change (SE)	-1.65 (1.77)	-1.84 (2.77)	0.19 [-6.35;6.73]	0.954
Month 24 Adjusted Mean Change (SE)	1.35 (3.67)	0.58 (6.94)	0.77 [-14.88;16.42]	0.922

N': Number of patients in the analysis
Adjusted Mean Change calculated by MMRM model including the following variables:
Treatment+Sex+Visit+Treatment*Sex+Treatment*Visit+Sex*Visit+Treatment*Visit*Sex+BL Value

Table 6.3.4 9-Hole Peg Test (FAS), Change from Baseline by Previous MS DMT

	Treatment groups		Comparison	
	BAF312 (N=127)	**Placebo (N=61)**	**Mean Difference [95% CI]**	**p-value**
Interaction Test				0.403
Previous MS-DMT = N				
N'	20	17		
Baseline Mean (SD)	35.19 (17.58)	32.12 (10.34)		
Month 12 Adjusted Mean Change (SE)	-3.36 (2.71)	-1.56 (3.00)	-1.79 [-9.78;6.19]	0.658
Month 24 Adjusted Mean Change (SE)	0.34 (5.10)	-6.44 (6.61)	6.78 [-9.84;23.39]	0.419
Previous MS-DMT = Y				
N'	104	43		
Baseline Mean (SD)	40.54 (22.97)	35.88 (19.25)		
Month 12 Adjusted Mean Change (SE)	-0.45 (1.25)	-0.02 (1.99)	-0.43 [-5.07;4.21]	0.856
Month 24 Adjusted Mean Change (SE)	0.76 (2.33)	7.33 (3.80)	-6.57 [-15.47;2.32]	0.145

N': Number of patients in the analysis
Adjusted Mean Change calculated by MMRM model including the following variables:
Treatment+DMT+Visit+Treatment*DMT+Treatment*Visit+DMT*Visit+Treatment*Visit*DMT+BL Value

Table 6.3.5 9-Hole Peg Test (FAS), Change from Baseline by Previous IFN-beta-1b treatment

	Treatment groups		Comparison	
	BAF312 (N=127)	**Placebo (N=61)**	**Mean Difference [95% CI]**	**p-value**
Interaction Test				0.115
Previous IFN-beta 1b = N				
N'	80	47		
Baseline Mean (SD)	39.42 (21.52)	34.24 (18.39)		
Month 12 Adjusted Mean Change (SE)	0.48 (1.39)	-0.44 (1.85)	0.91 [-3.67;5.49]	0.694
Month 24 Adjusted Mean Change (SE)	2.59 (2.64)	0.35 (3.69)	2.24 [-6.80;11.28]	0.623
Previous IFN-beta 1b = Y				
N'	44	13		
Baseline Mean (SD)	40.14 (23.66)	36.89 (12.29)		
Month 12 Adjusted Mean Change (SE)	-3.57 (1.90)	0.23 (3.64)	-3.81 [-11.92;4.31]	0.355
Month 24 Adjusted Mean Change (SE)	-2.44 (3.51)	15.64 (6.76)	-18.09 [-33.27;-2.90]	0.020

N': Number of patients in the analysis
Adjusted Mean Change calculated by MMRM model including the following variables:
Treatment+IFN+Visit+Treatment*IFN+Treatment*Visit+IFN*Visit+Treatment*Visit*IFN+BL Value

Table 6.3.6 9-Hole Peg Test (FAS), Change from Baseline by Rapid Evolvement

	Treatment groups		Comparison	
	BAF312 (N=127)	**Placebo (N=61)**	**Mean Difference [95% CI]**	**p-value**
Interaction Test				0.857
Rapid evolvement = N				
N'	92	46		
Baseline Mean (SD)	41.43 (23.91)	35.44 (18.55)		
Month 12 Adjusted Mean Change (SE)	-0.51 (1.32)	-0.26 (1.86)	-0.25 [-4.76;4.26]	0.913
Month 24 Adjusted Mean Change (SE)	0.53 (2.55)	4.73 (3.81)	-4.19 [-13.35;4.96]	0.364
Rapid evolvement = Y				
N'	32	14		
Baseline Mean (SD)	34.64 (15.65)	32.73 (12.02)		
Month 12 Adjusted Mean Change (SE)	-2.21 (2.19)	-0.31 (3.67)	-1.90 [-10.33;6.53]	0.656
Month 24 Adjusted Mean Change (SE)	1.20 (4.30)	-0.40 (7.42)	1.60 [-15.51;18.70]	0.853

N': Number of patients in the analysis
Adjusted Mean Change calculated by MMRM model including the following variables:
Treatment+RapEv+Visit+Treatment*RapEv+Treatment*Visit+RapEv*Visit+Treatment*Visit*RapEv+BL Value

Table 6.3.7 9-Hole Peg Test (FAS), Change from Baseline by Disease Course

	Treatment groups		Comparison	
	BAF312 (N=127)	**Placebo (N=61)**	**Mean Difference [95% CI]**	**p-value**
Interaction Test				0.572
Moderate/severe disease course = N				
N'	17	11		
Baseline Mean (SD)	26.54 (4.90)	25.79 (3.93)		
Month 12 Adjusted Mean Change (SE)	-2.16 (3.05)	-2.89 (3.95)	0.73 [-9.04;10.50]	0.883
Month 24 Adjusted Mean Change (SE)	-0.43 (6.44)	-0.78 (7.90)	0.35 [-20.00;20.70]	0.973
Moderate/severe disease course = Y				
N'	107	49		
Baseline Mean (SD)	41.76 (23.17)	36.84 (18.37)		
Month 12 Adjusted Mean Change (SE)	-0.77 (1.22)	0.25 (1.83)	-1.02 [-5.37;3.33]	0.644
Month 24 Adjusted Mean Change (SE)	0.83 (2.41)	4.61 (3.90)	-3.79 [-12.96;5.39]	0.413

N': Number of patients in the analysis
Adjusted Mean Change calculated by MMRM model including the following variables:
Treatment+DC+Visit+Treatment*DC+Treatment*Visit+DC*Visit+Treatment*Visit*DC+BL Value

Table 6.3.8 9-Hole Peg Test (FAS), Change from Baseline by Region

	Treatment groups		Comparison	
	BAF312 (N=127)	**Placebo (N=61)**	**Mean Difference [95% CI]**	**p-value**
Interaction Test				0.212
Region = Europe				
N'	104	51		
Baseline Mean (SD)	38.21 (22.61)	34.39 (17.20)		
Month 12 Adjusted Mean Change (SE)	-1.88 (1.24)	-0.08 (1.84)	-1.80 [-6.19;2.58]	0.418
Month 24 Adjusted Mean Change (SE)	0.21 (2.46)	3.92 (3.99)	-3.70 [-13.02;5.61]	0.432
Region = Others				
N'	20	9		
Baseline Mean (SD)	47.30 (18.71)	37.21 (17.97)		
Month 12 Adjusted Mean Change (SE)	3.35 (3.12)	0.03 (4.20)	3.31 [-7.06;13.68]	0.528
Month 24 Adjusted Mean Change (SE)	4.25 (6.53)	4.56 (7.92)	-0.31 [-20.75;20.13]	0.976

N': Number of patients in the analysis
Adjusted Mean Change calculated by MMRM model including the following variables:
Treatment+Region+Visit+Treatment*Region+Treatment*Visit+Region*Visit+Treatment*Visit*Region+BL Value

Table 6.4.0: Timed 25-Foot Walk (FAS), Return Rates

	Treatment groups		
	BAF312 (N=127)	**Placebo (N=61)**	**Total (N=188)**
Return Rate n (%)*			
Baseline	126 (99.2)	61 (100.0)	187 (99.5)
Month 03	119 (93.7)	59 (96.7)	178 (94.7)
Month 06	114 (89.8)	55 (90.2)	169 (89.9)
Month 09	111 (87.4)	52 (85.2)	163 (86.7)
Month 12	107 (84.3)	43 (70.5)	150 (79.8)
Month 15	100 (78.7)	39 (63.9)	139 (73.9)
Month 18	79 (62.2)	27 (44.3)	106 (56.4)
Month 21	66 (52.0)	23 (37.7)	89 (47.3)
Month 24	50 (39.4)	17 (27.9)	67 (35.6)

* Number and percentage of patients with non-missing data at the given time point.

Table 6.4.1: Timed 25-Foot Walk (FAS), Change from Baseline

	Treatment groups		Comparison	
	BAF312 (N=127)	**Placebo (N=61)**	**Mean Difference [95% CI]**	**p-value**
N'	121	60		
Baseline Mean (SD)	16.45 (15.80)	14.44 (12.19)		
Month 12 Adjusted Mean Change (SE)	6.14 (1.76)	7.90 (2.61)	-1.76 [-8.05;4.54]	0.579
Month 24 Adjusted Mean Change (SE)	12.31 (2.94)	13.05 (4.48)	-0.74 [-11.55;10.08]	0.891

N': Number of patients in the analysis
Adjusted Mean Change calculated by MMRM model including the following variables: Treatment+Visit+Treatment*Visit+BL Value

Table 6.4.2: Timed 25-Foot Walk (FAS), Change from Baseline by Age

	Treatment groups		Comparison	
	BAF312 (N=127)	Placebo (N=61)	Mean Difference [95% CI]	p-value
Interaction Test				0.217
Age = 18-40				
N'	18	13		
Baseline Mean (SD)	19.59 (24.28)	13.20 (11.20)		
Month 12 Adjusted Mean Change (SE)	18.13 (4.76)	6.56 (5.47)	11.57 [-2.93;26.06]	0.116
Month 24 Adjusted Mean Change (SE)	30.92 (7.89)	16.20 (9.61)	14.72 [-10.52;39.97]	0.244
Age = 41-55				
N'	90	32		
Baseline Mean (SD)	16.24 (14.56)	13.68 (13.51)		
Month 12 Adjusted Mean Change (SE)	4.52 (2.00)	6.51 (3.56)	-1.99 [-10.15;6.17]	0.627
Month 24 Adjusted Mean Change (SE)	9.90 (3.45)	11.99 (6.31)	-2.09 [-16.68;12.50]	0.773
Age = >55				
N'	13	15		
Baseline Mean (SD)	13.50 (8.06)	17.14 (10.19)		
Month 12 Adjusted Mean Change (SE)	1.81 (5.43)	11.77 (5.19)	-9.96 [-24.95;5.03]	0.189
Month 24 Adjusted Mean Change (SE)	7.04 (9.34)	10.56 (9.41)	-3.52 [-30.36;23.33]	0.792

N': Number of patients in the analysis
Adjusted Mean Change calculated by MMRM model including the following variables:
Treatment+Agegroup+Visit+Treatment*Agegroup+Treatment*Visit+Agegroup*Visit+Treatment*Visit*Agegroup+BL Value

Table 6.4.3: Timed 25-Foot Walk (FAS), Change from Baseline by Gender

	Treatment groups		Comparison	
	BAF312 (N=127)	**Placebo (N=61)**	**Mean Difference [95% CI]**	**p-value**
Interaction Test				0.205
Sex = F				
N'	71	37		
Baseline Mean (SD)	17.89 (14.86)	17.50 (13.76)		
Month 12 Adjusted Mean Change (SE)	6.44 (2.29)	10.62 (3.27)	-4.18 [-12.16;3.81]	0.300
Month 24 Adjusted Mean Change (SE)	15.00 (3.84)	20.01 (5.54)	-5.01 [-18.59;8.57]	0.461
Sex = M				
N'	50	23		
Baseline Mean (SD)	14.40 (17.00)	9.53 (6.88)		
Month 12 Adjusted Mean Change (SE)	5.57 (2.70)	2.69 (4.23)	2.89 [-7.15;12.93]	0.567
Month 24 Adjusted Mean Change (SE)	8.61 (4.54)	-0.93 (7.59)	9.54 [-8.25;27.33]	0.286

N': Number of patients in the analysis
Adjusted Mean Change calculated by MMRM model including the following variables:
Treatment+Sex+Visit+Treatment*Sex+Treatment*Visit+Sex*Visit+Treatment*Visit*Sex+BL Value

Table 6.4.4 Timed 25-Foot Walk (FAS), Change from Baseline by Previous MS DMT

	Treatment groups		Comparison	
	BAF312 (N=127)	**Placebo (N=61)**	**Mean Difference [95% CI]**	**p-value**
Interaction Test				0.767
Previous MS-DMT = N				
N'	20	17		
Baseline Mean (SD)	13.07 (9.54)	10.17 (5.84)		
Month 12 Adjusted Mean Change (SE)	1.45 (4.18)	1.96 (4.72)	-0.51 [-13.13;12.11]	0.936
Month 24 Adjusted Mean Change (SE)	0.29 (6.74)	2.49 (8.82)	-2.20 [-24.57;20.18]	0.844
Previous MS-DMT = Y				
N'	101	43		
Baseline Mean (SD)	17.11 (16.72)	16.13 (13.61)		
Month 12 Adjusted Mean Change (SE)	7.11 (1.93)	10.18 (3.11)	-3.07 [-10.39;4.25]	0.404
Month 24 Adjusted Mean Change (SE)	14.67 (3.15)	16.44 (5.10)	-1.76 [-13.89;10.37]	0.770

N': Number of patients in the analysis
Adjusted Mean Change calculated by MMRM model including the following variables:
Treatment+DMT+Visit+Treatment*DMT+Treatment*Visit+DMT*Visit+Treatment*Visit*DMT+BL Value

Table 6.4.5 Timed 25-Foot Walk (FAS), Change from Baseline by Previous IFN-beta-1b treatment

	Treatment groups		Comparison	
	BAF312 (N=127)	**Placebo (N=61)**	**Mean Difference [95% CI]**	**p-value**
Interaction Test				0.709
Previous IFN-beta 1b = N				
N'	79	47		
Baseline Mean (SD)	18.52 (17.85)	14.05 (12.90)		
Month 12 Adjusted Mean Change (SE)	8.74 (2.19)	9.00 (2.94)	-0.25 [-7.59;7.09]	0.946
Month 24 Adjusted Mean Change (SE)	16.33 (3.70)	14.45 (5.12)	1.88 [-10.87;14.63]	0.767
Previous IFN-beta 1b = Y				
N'	42	13		
Baseline Mean (SD)	12.55 (10.07)	15.85 (9.48)		
Month 12 Adjusted Mean Change (SE)	1.36 (2.99)	3.05 (5.67)	-1.70 [-14.50;11.11]	0.792
Month 24 Adjusted Mean Change (SE)	5.05 (5.01)	7.01 (9.80)	-1.96 [-24.17;20.25]	0.859

N': Number of patients in the analysis
Adjusted Mean Change calculated by MMRM model including the following variables:
Treatment+IFN+Visit+Treatment*IFN+Treatment*Visit+IFN*Visit+Treatment*Visit*IFN+BL Value

Table 6.4.6 Timed 25-Foot Walk (FAS), Change from Baseline by Rapid Evolvement

	Treatment groups		Comparison	
	BAF312 (N=127)	**Placebo (N=61)**	**Mean Difference [95% CI]**	**p-value**
Interaction Test				0.024
Rapid evolvement = N				
N'	89	46		
Baseline Mean (SD)	17.79 (14.94)	15.16 (13.00)		
Month 12 Adjusted Mean Change (SE)	7.94 (2.06)	6.49 (2.92)	1.45 [-5.69;8.59]	0.685
Month 24 Adjusted Mean Change (SE)	15.31 (3.44)	9.55 (5.08)	5.76 [-6.61;18.13]	0.353
Rapid evolvement = Y				
N'	32	14		
Baseline Mean (SD)	12.72 (17.72)	12.07 (9.01)		
Month 12 Adjusted Mean Change (SE)	1.15 (3.39)	12.56 (5.74)	-11.41 [-24.73;1.91]	0.092
Month 24 Adjusted Mean Change (SE)	3.98 (5.72)	25.53 (9.71)	-21.55 [-44.31;1.21]	0.063

N': Number of patients in the analysis
Adjusted Mean Change calculated by MMRM model including the following variables:
Treatment+RapEv+Visit+Treatment*RapEv+Treatment*Visit+RapEv*Visit+Treatment*Visit*RapEv+BL Value

Table 6.4.7 Timed 25-Foot Walk (FAS), Change from Baseline by Disease Course

	Treatment groups		Comparison	
	BAF312 (N=127)	**Placebo (N=61)**	**Mean Difference [95% CI]**	**p-value**
Interaction Test				0.583
Moderate/severe disease course = N				
N'	17	11		
Baseline Mean (SD)	6.41 (1.64)	9.35 (4.42)		
Month 12 Adjusted Mean Change (SE)	1.07 (4.66)	-0.41 (6.17)	1.49 [-13.97;16.95]	0.848
Month 24 Adjusted Mean Change (SE)	1.73 (8.13)	-0.14 (10.18)	1.86 [-24.50;28.22]	0.887
Moderate/severe disease course = Y				
N'	104	49		
Baseline Mean (SD)	18.09 (16.47)	15.59 (13.08)		
Month 12 Adjusted Mean Change (SE)	7.00 (1.90)	9.64 (2.86)	-2.64 [-9.52;4.24]	0.445
Month 24 Adjusted Mean Change (SE)	14.04 (3.17)	15.72 (5.05)	-1.68 [-13.70;10.34]	0.779

N': Number of patients in the analysis
Adjusted Mean Change calculated by MMRM model including the following variables:
Treatment+DC+Visit+Treatment*DC+Treatment*Visit+DC*Visit+Treatment*Visit*DC+BL Value

Table 6.4.8 Timed 25-Foot Walk (FAS), Change from Baseline by Region

	Treatment groups		Comparison	
	BAF312 (N=127)	**Placebo (N=61)**	**Mean Difference [95% CI]**	**p-value**
Interaction Test				0.229
Region = Europe				
N'	103	51		
Baseline Mean (SD)	15.51 (16.01)	14.43 (12.72)		
Month 12 Adjusted Mean Change (SE)	5.56 (1.91)	8.79 (2.87)	-3.23 [-10.12;3.66]	0.352
Month 24 Adjusted Mean Change (SE)	10.89 (3.12)	11.95 (4.98)	-1.05 [-12.90;10.79]	0.858
Region = Others				
N'	18	9		
Baseline Mean (SD)	21.78 (13.78)	14.51 (9.17)		
Month 12 Adjusted Mean Change (SE)	9.44 (4.89)	3.30 (6.58)	6.14 [-10.26;22.54]	0.457
Month 24 Adjusted Mean Change (SE)	20.65 (8.42)	12.83 (10.40)	7.81 [-19.27;34.90]	0.563

N': Number of patients in the analysis
Adjusted Mean Change calculated by MMRM model including the following variables:
Treatment+Region+Visit+Treatment*Region+Treatment*Visit+Region*Visit+Treatment*Visit*Region+BL Value

Table 6.5.1: Worsening of T25W of ≥20% (FAS), Binary Analysis

	Treatment groups		Comparison		
	BAF312 (N=127)	**Placebo (N=61)**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
N'	127	61			
Worsening of T25W of ≥20% n(%)	62 (48.8)	28 (45.9)	1.12 [0.61;2.07] 0.708	1.06 [0.77;1.47] 0.711	0.03 [-0.12;0.18] 0.707

N': Number of patients in the analysis
OR: Odds Ratio
RR: Relative Risk
RD: Risk Difference

Table 6.5.2: Worsening of T25W of ≥20% (FAS), Binary Analysis by Age

	Treatment groups		Comparison		
	BAF312 (N=127)	**Placebo (N=61)**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Interaction Test	p= 0.879				
Age = 18-40					
N'	18	13			
Worsening of T25W of ≥20% n (%)	10 (55.6)	6 (46.2)	1.46 [0.35;6.11] 0.606	1.20 [0.59;2.47] 0.613	0.09 [-0.26;0.45] 0.604
Age = 41-55					
N'	95	33			
Worsening of T25W of ≥20% n (%)	46 (48.4)	15 (45.5)	1.13 [0.51;2.49] 0.769	1.07 [0.69;1.63] 0.772	0.03 [-0.17;0.23] 0.768
Age = >55					
N'	14	15			
Worsening of T25W of ≥20% n (%)	6 (42.9)	7 (46.7)	0.86 [0.20;3.71] 0.837	0.92 [0.41;2.07] 0.837	-0.04 [-0.40;0.32] 0.837

N': Number of patients in the analysis
OR: Odds Ratio
RR: Relative Risk
RD: Risk Difference

Table 6.5.3: Worsening of T25W of ≥20% (FAS), Binary Analysis by Gender

	Treatment groups		Comparison		
	BAF312 (N=127)	**Placebo (N=61)**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Interaction Test	p= 0.384				
Sex = F					
N'	76	37			
Worsening of T25W of ≥20% n (%)	35 (46.1)	18 (48.6)	0.90 [0.41;1.98] 0.795	0.95 [0.63;1.43] 0.794	-0.03 [-0.22;0.17] 0.795
Sex = M					
N'	51	24			
Worsening of T25W of ≥20% n (%)	27 (52.9)	10 (41.7)	1.57 [0.59;4.20] 0.364	1.27 [0.74;2.18] 0.384	0.11 [-0.13;0.35] 0.357

N': Number of patients in the analysis
OR: Odds Ratio
RR: Relative Risk
RD: Risk Difference

Table 6.5.4: Worsening of T25W of ≥20% (FAS), Binary Analysis by Previous MS DMT

	Treatment groups		Comparison		
	BAF312 (N=127)	**Placebo (N=61)**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Interaction Test	p= 0.196				
Previous MS-DMT = N					
N'	20	17			
Worsening of T25W of ≥20% n (%)	6 (30.0)	8 (47.1)	0.48 [0.13;1.86] 0.290	0.64 [0.28;1.47] 0.292	-0.17 [-0.48;0.14] 0.282
Previous MS-DMT = Y					
N'	107	44			
Worsening of T25W of ≥20% n (%)	56 (52.3)	20 (45.5)	1.32 [0.65;2.66] 0.443	1.15 [0.79;1.67] 0.456	0.07 [-0.11;0.24] 0.441

N': Number of patients in the analysis
OR: Odds Ratio
RR: Relative Risk
RD: Risk Difference

Table 6.5.5: Worsening of T25W of ≥20% (FAS), Binary Analysis by Previous IFN-beta-1b treatment

	Treatment groups		Comparison		
	BAF312 (N=127)	**Placebo (N=61)**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Interaction Test	p= 0.353				
Previous IFN-beta 1b = N					
N'	82	48			
Worsening of T25W of ≥20% n (%)	42 (51.2)	21 (43.8)	1.35 [0.66;2.76] 0.411	1.17 [0.80;1.72] 0.421	0.07 [-0.10;0.25] 0.409
Previous IFN-beta 1b = Y					
N'	45	13			
Worsening of T25W of ≥20% n (%)	20 (44.4)	7 (53.8)	0.69 [0.20;2.37] 0.551	0.83 [0.45;1.50] 0.531	-0.09 [-0.40;0.21] 0.549

N': Number of patients in the analysis
OR: Odds Ratio
RR: Relative Risk
RD: Risk Difference

Table 6.5.6: Worsening of T25W of ≥20% (FAS), Binary Analysis by Rapid Evolvement

	Treatment groups		Comparison		
	BAF312 (N=127)	**Placebo (N=61)**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Interaction Test	p= 0.717				
Rapid evolvement = N					
N'	95	47			
Worsening of T25W of ≥20% n (%)	48 (50.5)	23 (48.9)	1.07 [0.53;2.14] 0.858	1.03 [0.73;1.47] 0.859	0.02 [-0.16;0.19] 0.858
Rapid evolvement = Y					
N'	32	14			
Worsening of T25W of ≥20% n (%)	14 (43.8)	5 (35.7)	1.40 [0.38;5.12] 0.611	1.23 [0.55;2.74] 0.621	0.08 [-0.22;0.38] 0.605

N': Number of patients in the analysis
OR: Odds Ratio
RR: Relative Risk
RD: Risk Difference

Table 6.5.7: Worsening of T25W of ≥20% (FAS), Binary Analysis by Disease Course

	Treatment groups		Comparison		
	BAF312 (N=127)	**Placebo (N=61)**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Interaction Test	p= 0.247				
Moderate/severe disease course = N					
N'	18	11			
Worsening of T25W of ≥20% n (%)	5 (27.8)	1 (9.1)	3.85 [0.39;38.36] 0.251	3.06 [0.41;22.85] 0.277	0.19 [-0.08;0.45] 0.171
Moderate/severe disease course = Y					
N'	109	50			
Worsening of T25W of ≥20% n (%)	57 (52.3)	27 (54.0)	0.93 [0.48;1.83] 0.841	0.97 [0.71;1.32] 0.840	-0.02 [-0.18;0.15] 0.841

N': Number of patients in the analysis
OR: Odds Ratio
RR: Relative Risk
RD: Risk Difference

Table 6.5.8: Worsening of T25W of ≥20% (FAS), Binary Analysis by Region

	Treatment groups		Comparison		
	BAF312 (N=127)	**Placebo (N=61)**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Interaction Test	p= 0.152				
Region = Europe					
N'	106	52			
Worsening of T25W of ≥20% n (%)	53 (50.0)	22 (42.3)	1.36 [0.70;2.66] 0.364	1.18 [0.82;1.71] 0.376	0.08 [-0.09;0.24] 0.360
Region = Others					
N'	21	9			
Worsening of T25W of ≥20% n (%)	9 (42.9)	6 (66.7)	0.38 [0.07;1.92] 0.239	0.64 [0.33;1.26] 0.200	-0.24 [-0.61;0.14] 0.212

N': Number of patients in the analysis
OR: Odds Ratio
RR: Relative Risk
RD: Risk Difference

Table 6.6.1: Worsening of T25W of ≥20% (FAS), Time-to-Event Analysis

	Treatment groups		Comparison	
	BAF312 (N=127)	**Placebo (N=61)**	**HR [95% CI]**	**p-value**
N'	126	61		
Patients with at least one worsening	61	28		
Median in days* [95% KI]	633 [444;819]	457 [371;NA]		
% of patients without worsening after 24 months* [95% KI]	43.65 [33.03;54.28]	48.42 [34.39;62.45]		
% of patients without worsening at EOS* [95% KI]	32.91 [19.31;46.51]	43.04 [27.09;58.99]		
			1.27 [0.76;2.11]	0.367

N': Number of patients in the analysis
[S > 50%]: Survival curve does not reach 50% level
*: K-M estimate % of outcome-free patients; Greenwood formula is used for CIs
HR calculated from Cox proportional hazards model including the following variables: Treatment+Country+SPMS Group+BL EDSS+BL Value

Table 6.6.2: Worsening of T25W of ≥20% (FAS), Time-to-Event Analysis by Age

	Treatment groups		Comparison	
	BAF312 (N=127)	**Placebo (N=61)**	**HR [95% CI]**	**p-value**
Interaction Test				0.604
Age = 18-40				
N'	18	13		
Patients with at least one worsening	10	6		
Median in days* [95% KI]	449 [183;NA]	456 [274;NA]		
% of patients without worsening after 24 months* [95% KI]	31.55 [5.33;57.77]	46.89 [16.30;77.47]		
% of patients without worsening at EOS* [95% KI]	31.55 [5.33;57.77]	46.89 [16.30;77.47]		
			2.16 [0.62;7.44]	0.224
Age = 41-55				
N'	94	33		
Patients with at least one worsening	45	15		
Median in days* [95% KI]	717 [449;851]	457 [372;NA]		
% of patients without worsening after 24 months* [95% KI]	45.41 [33.14;57.68]	48.76 [29.58;67.94]		
% of patients without worsening at EOS* [95% KI]	31.22 [14.91;47.53]	40.64 [19.03;62.24]		
			1.09 [0.57;2.09]	0.799

N': Number of patients in the analysis
[S > 50%]: Survival curve does not reach 50% level
*: K-M estimate % of outcome-free patients; Greenwood formula is used for CIs
HR calculated from Cox proportional hazards model including the following variables:
Treatment+Agegroup+Treatment*Agegroup+Country+SPMSGroup+BL EDSS+BL Value

Table 6.6.2: Worsening of T25W of ≥20% (FAS), Time-to-Event Analysis by Age

	Treatment groups		Comparison	
	BAF312 (N=127)	**Placebo (N=61)**	**HR [95% CI]**	**p-value**
Age = >55				
N'	14	15		
Patients with at least one worsening	6	7		
Median in days* [95% KI]	546 [183;NA]	[S > 50%]		
% of patients without worsening after 24 months* [95% KI]	48.46 [18.12;78.80]	50.91 [24.77;77.05]		
% of patients without worsening at EOS* [95% KI]	48.46 [18.12;78.80]	50.91 [24.77;77.05]		
			1.53 [0.37;6.38]	0.556

N': Number of patients in the analysis
[S > 50%]: Survival curve does not reach 50% level
*: K-M estimate % of outcome-free patients; Greenwood formula is used for CIs
HR calculated from Cox proportional hazards model including the following variables:
Treatment+Agegroup+Treatment*Agegroup+Country+SPMS Group+BL EDSS+BL Value

Table 6.6.3: Worsening of T25W of ≥20% (FAS), Time-to-Event Analysis by Gender

	Treatment groups		Comparison	
	BAF312 (N=127)	**Placebo (N=61)**	**HR [95% CI]**	**p-value**
Interaction Test				0.774
Sex = F				
N'	75	37		
Patients with at least one worsening	34	18		
Median in days* [95% KI]	633 [444;NA]	456 [287;NA]		
% of patients without worsening after 24 months* [95% KI]	45.39 [31.53;59.26]	44.73 [27.11;62.35]		
% of patients without worsening at EOS* [95% KI]	38.91 [22.19;55.63]	44.73 [27.11;62.35]		
			1.18 [0.60;2.30]	0.637
Sex = M				
N'	51	24		
Patients with at least one worsening	27	10		
Median in days* [95% KI]	449 [365;851]	804 [372;NA]		
% of patients without worsening after 24 months* [95% KI]	40.93 [24.25;57.62]	54.56 [31.63;77.49]		
% of patients without worsening at EOS* [95% KI]	26.31 [6.31;46.32]	36.37 [3.50;69.25]		
			1.39 [0.58;3.36]	0.461

N': Number of patients in the analysis
[S > 50%]: Survival curve does not reach 50% level
*: K-M estimate % of outcome-free patients; Greenwood formula is used for CIs
HR calculated from Cox proportional hazards model including the following variables: Treatment+Sex+Treatment*Sex+Country+SPMS Group+BL EDSS+BL Value

Table 6.6.4: Worsening of T25W of ≥20% (FAS), Time-to-Event Analysis by Previous MS DMT

	Treatment groups		Comparison	
	BAF312 (N=127)	**Placebo (N=61)**	**HR [95% CI]**	**p-value**
Interaction Test				0.148
Previous MS-DMT = N				
N'	20	17		
Patients with at least one worsening	6	8		
Median in days* [95% KI]	[S > 50%]	804 [372;NA]		
% of patients without worsening after 24 months* [95% KI]	58.12 [29.65;86.59]	57.04 [32.68;81.40]		
% of patients without worsening at EOS* [95% KI]	58.12 [29.65;86.59]	28.52 [0.00;69.88]		
			0.58 [0.18;1.81]	0.344
Previous MS-DMT = Y				
N'	106	44		
Patients with at least one worsening	55	20		
Median in days* [95% KI]	449 [372;806]	456 [287;NA]		
% of patients without worsening after 24 months* [95% KI]	40.71 [29.45;51.97]	44.51 [27.42;61.60]		
% of patients without worsening at EOS* [95% KI]	28.20 [13.92;42.47]	44.51 [27.42;61.60]		
			1.51 [0.83;2.75]	0.182

N': Number of patients in the analysis
[S > 50%]: Survival curve does not reach 50% level
*: K-M estimate % of outcome-free patients; Greenwood formula is used for CIs
HR calculated from Cox proportional hazards model including the following variables: Treatment+DMT+Treatment*DMT+Country+SPMS Group+BL EDSS+BL Value

Table 6.6.5: Worsening of T25W of ≥20% (FAS), Time-to-Event Analysis by Previous IFN-beta-1b treatment

	Treatment groups		Comparison	
	BAF312 (N=127)	**Placebo (N=61)**	**HR [95% CI]**	**p-value**
Interaction Test				0.315
Previous IFN-beta 1b = N				
N'	81	48		
Patients with at least one worsening	41	21		
Median in days* [95% KI]	555 [440;851]	804 [371;NA]		
% of patients without worsening after 24 months* [95% KI]	41.10 [28.08;54.13]	51.74 [36.07;67.41]		
% of patients without worsening at EOS* [95% KI]	30.83 [14.77;46.88]	45.27 [27.14;63.40]		
			1.56 [0.84;2.89]	0.157
Previous IFN-beta 1b = Y				
N'	45	13		
Patients with at least one worsening	20	7		
Median in days* [95% KI]	722 [365;NA]	454 [274;NA]		
% of patients without worsening after 24 months* [95% KI]	49.37 [31.51;67.23]	36.26 [6.15;66.37]		
% of patients without worsening at EOS* [95% KI]	37.03 [12.16;61.90]	36.26 [6.15;66.37]		
			0.88 [0.35;2.23]	0.793

N': Number of patients in the analysis
[S > 50%]: Survival curve does not reach 50% level
*: K-M estimate % of outcome-free patients; Greenwood formula is used for CIs
HR calculated from Cox proportional hazards model including the following variables: Treatment+IFN+Treatment*IFN+Country+SPMS Group+BL EDSS+BL Value

Table 6.6.6: Worsening of T25W of ≥20% (FAS), Time-to-Event Analysis by Rapid Evolvement

	Treatment groups		Comparison	
	BAF312 (N=127)	**Placebo (N=61)**	**HR [95% CI]**	**p-value**
Interaction Test				0.700
Rapid evolvement = N				
N'	94	47		
Patients with at least one worsening	47	23		
Median in days* [95% KI]	553 [372;851]	456 [358;NA]		
% of patients without worsening after 24 months* [95% KI]	44.87 [33.23;56.52]	46.80 [31.15;62.44]		
% of patients without worsening at EOS* [95% KI]	32.28 [17.19;47.36]	39.00 [19.90;58.09]		
			1.33 [0.76;2.33]	0.318
Rapid evolvement = Y				
N'	32	14		
Patients with at least one worsening	14	5		
Median in days* [95% KI]	633 [449;NA]	[S > 50%]		
% of patients without worsening after 24 months* [95% KI]	34.17 [7.19;61.16]	55.10 [24.52;85.68]		
% of patients without worsening at EOS* [95% KI]	34.17 [7.19;61.16]	55.10 [24.52;85.68]		
			1.03 [0.32;3.36]	0.958

N': Number of patients in the analysis
[S > 50%]: Survival curve does not reach 50% level
*: K-M estimate % of outcome-free patients; Greenwood formula is used for CIs
HR calculated from Cox proportional hazards model including the following variables: Treatment+RapEv+Treatment*RapEv+Country+SPMS Group+BL EDSS+BL Value

Table 6.6.7: Worsening of T25W of ≥20% (FAS), Time-to-Event Analysis by Disease Course

	Treatment groups		Comparison	
	BAF312 (N=127)	**Placebo (N=61)**	**HR [95% CI]**	**p-value**
Interaction Test				0.125
Moderate/severe disease course = N				
N'	18	11		
Patients with at least one worsening	5	1		
Median in days* [95% KI]	[S > 50%]	[S > 50%]		
% of patients without worsening after 24 months* [95% KI]	57.35 [21.55;93.15]	100.0 [100.0;100.0]		
% of patients without worsening at EOS* [95% KI]	57.35 [21.55;93.15]	75.00 [32.56;100.0]		
			6.72 [0.70;64.74]	0.100
Moderate/severe disease course = Y				
N'	108	50		
Patients with at least one worsening	56	27		
Median in days* [95% KI]	555 [440;819]	442 [287;NA]		
% of patients without worsening after 24 months* [95% KI]	41.72 [30.68;52.77]	37.52 [22.47;52.58]		
% of patients without worsening at EOS* [95% KI]	30.44 [16.43;44.45]	37.52 [22.47;52.58]		
			1.09 [0.64;1.86]	0.742

N': Number of patients in the analysis
[S > 50%]: Survival curve does not reach 50% level
*: K-M estimate % of outcome-free patients; Greenwood formula is used for CIs
HR calculated from Cox proportional hazards model including the following variables: Treatment+DC+Treatment*DC+Country+SPMS Group+BL EDSS+BL Value

Table 7.1.0: SDMT (FAS), Return Rates

	Treatment groups		
	BAF312 (N=127)	**Placebo (N=61)**	**Total (N=188)**
Return Rate n (%)*			
Baseline	127 (100.0)	60 (98.4)	187 (99.5)
Month 06	116 (91.3)	56 (91.8)	172 (91.5)
Month 12	107 (84.3)	48 (78.7)	155 (82.4)
Month 18	79 (62.2)	30 (49.2)	109 (58.0)
Month 24	41 (32.3)	15 (24.6)	56 (29.8)
Month 30	14 (11.0)	3 (4.9)	17 (9.0)

* Number and percentage of patients with non-missing data at the given time point.

Table 7.1.1: SDMT (FAS), Change from Baseline

	Treatment groups		Comparison	
	BAF312 (N=127)	**Placebo (N=61)**	**Mean Difference [95% CI]**	**p-value**
N'	118	57		
Baseline Mean (SD)	36.54 (13.85)	37.07 (12.14)		
Month 12 Adjusted Mean Change (SE)	-0.16 (0.93)	-3.04 (1.20)	2.89 [0.33;5.44]	0.027
Month 24 Adjusted Mean Change (SE)	-0.34 (1.31)	-4.11 (1.97)	3.77 [-0.70;8.24]	0.097

N': Number of patients in the analysis
Adjusted Mean Change calculated by MMRM model including the following variables: Treatment+Visit+Treatment*Visit+Country+BL Value

Table 7.1.2: SDMT (FAS), Change from Baseline by Age

	Treatment groups		Comparison	
	BAF312 (N=127)	**Placebo (N=61)**	**Mean Difference [95% CI]**	**p-value**
Interaction Test				0.664
Age = 18-40				
N'	16	13		
Baseline Mean (SD)	31.13 (14.44)	36.69 (14.97)		
Month 12 Adjusted Mean Change (SE)	2.37 (2.08)	-1.28 (2.39)	3.66 [-2.55;9.87]	0.246
Month 24 Adjusted Mean Change (SE)	3.50 (3.41)	-1.81 (4.35)	5.31 [-5.72;16.34]	0.340
Age = 41-55				
N'	89	31		
Baseline Mean (SD)	38.04 (13.37)	38.94 (11.81)		
Month 12 Adjusted Mean Change (SE)	-0.46 (1.09)	-4.36 (1.57)	3.89 [0.51;7.28]	0.025
Month 24 Adjusted Mean Change (SE)	-0.48 (1.51)	-5.80 (2.54)	5.32 [-0.35;10.99]	0.065
Age = >55				
N'	13	13		
Baseline Mean (SD)	32.92 (15.09)	33.00 (9.39)		
Month 12 Adjusted Mean Change (SE)	-2.26 (2.70)	-2.70 (2.26)	0.44 [-6.23;7.10]	0.897
Month 24 Adjusted Mean Change (SE)	-4.69 (3.65)	0.28 (4.33)	-4.98 [-16.18;6.22]	0.378

N': Number of patients in the analysis
Adjusted Mean Change calculated by MMRM model including the following variables:
Treatment+Agegroup+Visit+Treatment*Agegroup+Treatment*Visit+Agegroup*Visit+Treatment*Visit*Agegroup+Country+BL Value

Table 7.1.3: SDMT (FAS), Change from Baseline by Gender

	Treatment groups		Comparison	
	BAF312 (N=127)	**Placebo (N=61)**	**Mean Difference [95% CI]**	**p-value**
Interaction Test				0.866
Sex = F				
N'	68	35		
Baseline Mean (SD)	38.06 (14.29)	35.23 (12.84)		
Month 12 Adjusted Mean Change (SE)	0.22 (1.20)	-2.23 (1.49)	2.45 [-0.89;5.79]	0.150
Month 24 Adjusted Mean Change (SE)	-0.54 (1.78)	-3.78 (2.33)	3.24 [-2.37;8.85]	0.253
Sex = M				
N'	50	22		
Baseline Mean (SD)	34.48 (13.08)	40.00 (10.57)		
Month 12 Adjusted Mean Change (SE)	-0.53 (1.23)	-4.05 (1.91)	3.52 [-0.71;7.74]	0.102
Month 24 Adjusted Mean Change (SE)	-0.22 (1.80)	-4.25 (3.78)	4.03 [-4.18;12.23]	0.331

N': Number of patients in the analysis
Adjusted Mean Change calculated by MMRM model including the following variables:
Treatment+Sex+Visit+Treatment*Sex+Treatment*Visit+Sex*Visit+Treatment*Visit*Sex+Country+BL Value

Table 7.1.4 SDMT (FAS), Change from Baseline by Previous MS DMT

	Treatment groups		Comparison	
	BAF312 (N=127)	**Placebo (N=61)**	**Mean Difference [95% CI]**	**p-value**
Interaction Test				0.670
Previous MS-DMT = N				
N'	20	17		
Baseline Mean (SD)	38.10 (16.05)	35.47 (8.92)		
Month 12 Adjusted Mean Change (SE)	-2.82 (1.85)	-2.16 (2.03)	-0.66 [-5.74;4.41]	0.797
Month 24 Adjusted Mean Change (SE)	0.59 (2.80)	-4.00 (4.31)	4.58 [-5.44;14.61]	0.364
Previous MS-DMT = Y				
N'	98	40		
Baseline Mean (SD)	36.22 (13.43)	37.75 (13.32)		
Month 12 Adjusted Mean Change (SE)	0.48 (1.01)	-3.43 (1.39)	3.91 [0.85;6.97]	0.013
Month 24 Adjusted Mean Change (SE)	-0.52 (1.46)	-4.50 (2.25)	3.98 [-1.20;9.16]	0.129

N': Number of patients in the analysis
Adjusted Mean Change calculated by MMRM model including the following variables:
Treatment+DMT+Visit+Treatment*DMT+Treatment*Visit+DMT*Visit+Treatment*Visit*DMT+Country+BL Value

Table 7.1.5 SDMT (FAS), Change from Baseline by Previous IFN-beta-1b treatment

	Treatment groups		Comparison	
	BAF312 (N=127)	**Placebo (N=61)**	**Mean Difference [95% CI]**	**p-value**
Interaction Test				0.771
Previous IFN-beta 1b = N				
N'	75	44		
Baseline Mean (SD)	34.71 (13.26)	38.00 (11.88)		
Month 12 Adjusted Mean Change (SE)	0.75 (1.07)	-2.83 (1.32)	3.58 [0.58;6.57]	0.020
Month 24 Adjusted Mean Change (SE)	1.40 (1.59)	-3.06 (2.15)	4.46 [-0.68;9.59]	0.088
Previous IFN-beta 1b = Y				
N'	43	13		
Baseline Mean (SD)	39.74 (14.43)	33.92 (12.98)		
Month 12 Adjusted Mean Change (SE)	-1.83 (1.38)	-3.93 (2.49)	2.09 [-3.16;7.35]	0.432
Month 24 Adjusted Mean Change (SE)	-3.39 (1.94)	-7.30 (4.25)	3.91 [-5.19;13.01]	0.394

N': Number of patients in the analysis
Adjusted Mean Change calculated by MMRM model including the following variables:
Treatment+IFN+Visit+Treatment*IFN+Treatment*Visit+IFN*Visit+Treatment*Visit*IFN+Country+BL Value

Table 7.1.6 SDMT (FAS), Change from Baseline by Rapid Evolvement

	Treatment groups		Comparison	
	BAF312 (N=127)	**Placebo (N=61)**	**Mean Difference [95% CI]**	**p-value**
Interaction Test				0.619
Rapid evolvement = N				
N'	88	43		
Baseline Mean (SD)	34.49 (13.86)	38.95 (11.44)		
Month 12 Adjusted Mean Change (SE)	0.63 (1.04)	-2.39 (1.33)	3.02 [0.09;5.95]	0.044
Month 24 Adjusted Mean Change (SE)	1.49 (1.44)	-3.42 (2.21)	4.91 [-0.11;9.94]	0.055
Rapid evolvement = Y				
N'	30	14		
Baseline Mean (SD)	42.57 (12.12)	31.29 (12.83)		
Month 12 Adjusted Mean Change (SE)	-2.18 (1.54)	-5.46 (2.46)	3.28 [-2.30;8.85]	0.247
Month 24 Adjusted Mean Change (SE)	-5.81 (2.35)	-6.48 (3.70)	0.67 [-7.98;9.32]	0.877

N': Number of patients in the analysis
Adjusted Mean Change calculated by MMRM model including the following variables:
Treatment+RapEv+Visit+Treatment*RapEv+Treatment*Visit+RapEv*Visit+Treatment*Visit*RapEv+Country+BL Value

Table 7.1.7 SDMT (FAS), Change from Baseline by Disease Course

	Treatment groups		Comparison	
	BAF312 (N=127)	**Placebo (N=61)**	**Mean Difference [95% CI]**	**p-value**
Interaction Test				0.981
Moderate/severe disease course = N				
N'	17	10		
Baseline Mean (SD)	38.29 (11.52)	39.80 (13.44)		
Month 12 Adjusted Mean Change (SE)	-1.03 (2.06)	-2.67 (2.59)	1.64 [-4.67;7.95]	0.609
Month 24 Adjusted Mean Change (SE)	1.12 (3.18)	-1.01 (3.87)	2.12 [-7.71;11.96]	0.667
Moderate/severe disease course = Y				
N'	101	47		
Baseline Mean (SD)	36.25 (14.23)	36.49 (11.93)		
Month 12 Adjusted Mean Change (SE)	0.01 (0.97)	-3.13 (1.31)	3.14 [0.30;5.97]	0.030
Month 24 Adjusted Mean Change (SE)	-0.55 (1.40)	-5.32 (2.29)	4.77 [-0.40;9.95]	0.070

N': Number of patients in the analysis
Adjusted Mean Change calculated by MMRM model including the following variables:
Treatment+DC+Visit+Treatment*DC+Treatment*Visit+DC*Visit+Treatment*Visit*DC+Country+BL Value

Table 7.1.8 SDMT (FAS), Change from Baseline by Region

	Treatment groups		Comparison	
	BAF312 (N=127)	**Placebo (N=61)**	**Mean Difference [95% CI]**	**p-value**
Interaction Test				0.083
Region = Europe				
N'	100	49		
Baseline Mean (SD)	37.34 (13.27)	36.86 (12.02)		
Month 12 Adjusted Mean Change (SE)	1.43 (0.78)	-2.27 (1.16)	3.70 [0.93;6.47]	0.009
Month 24 Adjusted Mean Change (SE)	1.60 (1.29)	-3.80 (2.35)	5.40 [0.04;10.76]	0.049
Region = Others				
N'	18	8		
Baseline Mean (SD)	32.11 (16.45)	38.38 (13.67)		
Month 12 Adjusted Mean Change (SE)	-2.79 (2.02)	-0.91 (2.84)	-1.89 [-8.77;5.00]	0.589
Month 24 Adjusted Mean Change (SE)	-4.62 (3.16)	-0.88 (3.61)	-3.75 [-13.34;5.84]	0.438

N': Number of patients in the analysis
Adjusted Mean Change calculated by MMRM model including the following variables:
Treatment+Region+Visit+Treatment*Region+Treatment*Visit+Region*Visit+Treatment*Visit*Region+BL Value

Table 7.2.1: SDMT Improvement by ≥4 points in 12 Months (FAS), Binary Analysis

	Treatment groups		Comparison		
	BAF312 (N=127)	**Placebo (N=61)**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
N'	127	61			
SDMT improvement by ≥4 points in 12 months	38 (29.9)	16 (26.2)	1.20 [0.61;2.38] 0.601	1.14 [0.69;1.88] 0.604	0.04 [-0.10;0.17] 0.595

N': Number of patients in the analysis
OR: Odds Ratio
RR: Relative Risk
RD: Risk Difference

Table 7.2.2: SDMT Improvement by ≥4 points in 12 Months (FAS), Binary Analysis by Age

	Treatment groups		Comparison		
	BAF312 (N=127)	**Placebo (N=61)**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Interaction Test	p= 0.828				
Age = 18-40					
N'	18	13			
SDMT improvement by ≥4 points in 12 months	6 (33.3)	5 (38.5)	0.80 [0.18;3.54] 0.769	0.87 [0.34;2.24] 0.767	-0.05 [-0.39;0.29] 0.769
Age = 41-55					
N'	95	33			
SDMT improvement by ≥4 points in 12 months	29 (30.5)	8 (24.2)	1.37 [0.55;3.40] 0.494	1.26 [0.64;2.47] 0.503	0.06 [-0.11;0.24] 0.477
Age = >55					
N'	14	15			
SDMT improvement by ≥4 points in 12 months	3 (21.4)	3 (20.0)	1.09 [0.18;6.58] 0.924	1.07 [0.26;4.45] 0.924	0.01 [-0.28;0.31] 0.924

N': Number of patients in the analysis
OR: Odds Ratio
RR: Relative Risk
RD: Risk Difference

Table 7.2.3: SDMT Improvement by ≥4 points in 12 Months (FAS), Binary Analysis by Gender

	Treatment groups		Comparison		
	BAF312 (N=127)	**Placebo (N=61)**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Interaction Test	p= 0.758				
Sex = F					
N'	76	37			
SDMT improvement by ≥4 points in 12 months	22 (28.9)	10 (27.0)	1.10 [0.46;2.65] 0.832	1.07 [0.57;2.02] 0.832	0.02 [-0.16;0.19] 0.830
Sex = M					
N'	51	24			
SDMT improvement by ≥4 points in 12 months	16 (31.4)	6 (25.0)	1.37 [0.46;4.11] 0.573	1.25 [0.56;2.80] 0.579	0.06 [-0.15;0.28] 0.561

N': Number of patients in the analysis
OR: Odds Ratio
RR: Relative Risk
RD: Risk Difference

Table 7.2.4: SDMT Improvement by ≥4 points in 12 Months (FAS), Binary Analysis by Previous MS DMT

	Treatment groups		Comparison		
	BAF312 (N=127)	**Placebo (N=61)**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Interaction Test	p= 0.072				
Previous MS-DMT = N					
N'	20	17			
SDMT improvement by ≥4 points in 12 months	3 (15.0)	6 (35.3)	0.32 [0.07;1.57] 0.162	0.43 [0.12;1.45] 0.171	-0.20 [-0.48;0.07] 0.149
Previous MS-DMT = Y					
N'	107	44			
SDMT improvement by ≥4 points in 12 months	35 (32.7)	10 (22.7)	1.65 [0.73;3.72] 0.226	1.44 [0.78;2.65] 0.241	0.10 [-0.05;0.25] 0.199

N': Number of patients in the analysis
OR: Odds Ratio
RR: Relative Risk
RD: Risk Difference

Table 7.2.5: SDMT Improvement by ≥4 points in 12 Months (FAS), Binary Analysis by Previous IFN-beta-1b treatment

	Treatment groups		Comparison		
	BAF312 (N=127)	**Placebo (N=61)**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Interaction Test	p= 0.862				
Previous IFN-beta 1b = N					
N'	82	48			
SDMT improvement by ≥4 points in 12 months	30 (36.6)	14 (29.2)	1.40 [0.65;3.02] 0.389	1.25 [0.74;2.12] 0.397	0.07 [-0.09;0.24] 0.380
Previous IFN-beta 1b = Y					
N'	45	13			
SDMT improvement by ≥4 points in 12 months	8 (17.8)	2 (15.4)	1.19 [0.22;6.44] 0.841	1.16 [0.28;4.79] 0.842	0.02 [-0.20;0.25] 0.835

N': Number of patients in the analysis
OR: Odds Ratio
RR: Relative Risk
RD: Risk Difference

Table 7.2.6: SDMT Improvement by ≥4 points in 12 Months (FAS), Binary Analysis by Rapid Evolvement

	Treatment groups		Comparison		
	BAF312 (N=127)	**Placebo (N=61)**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Interaction Test	p= 0.093				
Rapid evolvement = N					
N'	95	47			
SDMT improvement by ≥4 points in 12 months	32 (33.7)	11 (23.4)	1.66 [0.75;3.69] 0.212	1.44 [0.80;2.59] 0.226	0.10 [-0.05;0.26] 0.190
Rapid evolvement = Y					
N'	32	14			
SDMT improvement by ≥4 points in 12 months	6 (18.8)	5 (35.7)	0.42 [0.10;1.70] 0.221	0.53 [0.19;1.44] 0.210	-0.17 [-0.45;0.12] 0.244

N': Number of patients in the analysis
OR: Odds Ratio
RR: Relative Risk
RD: Risk Difference

Table 7.2.7: SDMT Improvement by ≥4 points in 12 Months (FAS), Binary Analysis by Disease Course

	Treatment groups		Comparison		
	BAF312 (N=127)	**Placebo (N=61)**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Interaction Test	p= 0.666				
Moderate/severe disease course = N					
N'	18	11			
SDMT improvement by ≥4 points in 12 months	5 (27.8)	2 (18.2)	1.73 [0.27;10.97] 0.560	1.53 [0.36;6.57] 0.569	0.10 [-0.21;0.40] 0.541
Moderate/severe disease course = Y					
N'	109	50			
SDMT improvement by ≥4 points in 12 months	33 (30.3)	14 (28.0)	1.12 [0.53;2.34] 0.770	1.08 [0.64;1.83] 0.772	0.02 [-0.13;0.17] 0.768

N': Number of patients in the analysis
OR: Odds Ratio
RR: Relative Risk
RD: Risk Difference

Table 7.2.8: SDMT Improvement by ≥4 points in 12 Months (FAS), Binary Analysis by Region

	Treatment groups		Comparison		
	BAF312 (N=127)	**Placebo (N=61)**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Interaction Test	p= 0.443				
Region = Europe					
N'	106	52			
SDMT improvement by ≥4 points in 12 months	35 (33.0)	14 (26.9)	1.34 [0.64;2.79] 0.437	1.23 [0.73;2.07] 0.445	0.06 [-0.09;0.21] 0.426
Region = Others					
N'	21	9			
SDMT improvement by ≥4 points in 12 months	3 (14.3)	2 (22.2)	0.58 [0.08;4.27] 0.596	0.64 [0.13;3.22] 0.591	-0.08 [-0.39;0.23] 0.616

N': Number of patients in the analysis
OR: Odds Ratio
RR: Relative Risk
RD: Risk Difference

Table 7.3.1: SDMT Worsening by ≥4 points in 12 Months (FAS), Binary Analysis

	Treatment groups		Comparison		
	BAF312 (N=127)	**Placebo (N=61)**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
N'	127	61			
SDMT worsening by ≥4 points in 12 months n	41 (32.3)	23 (37.7)	0.79 [0.42;1.49] 0.463	0.86 [0.57;1.29] 0.457	-0.05 [-0.20;0.09] 0.468

N': Number of patients in the analysis
OR: Odds Ratio
RR: Relative Risk
RD: Risk Difference

Table 7.3.2: SDMT Worsening by ≥4 points in 12 Months (FAS), Binary Analysis by Age

	Treatment groups		Comparison		
	BAF312 (N=127)	**Placebo (N=61)**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Interaction Test	p= 0.034				
Age = 18-40					
N'	18	13			
SDMT worsening by ≥4 points in 12 months n	4 (22.2)	4 (30.8)	0.64 [0.13;3.25] 0.593	0.72 [0.22;2.37] 0.591	-0.09 [-0.40;0.23] 0.596
Age = 41-55					
N'	95	33			
SDMT worsening by ≥4 points in 12 months n	29 (30.5)	16 (48.5)	0.47 [0.21;1.05] 0.065	0.63 [0.40;1.00] 0.051	-0.18 [-0.37;0.01] 0.070
Age = >55					
N'	14	15			
SDMT worsening by ≥4 points in 12 months n	8 (57.1)	3 (20.0)	5.33 [1.02;27.76] 0.047	2.86 [0.94;8.66] 0.064	0.37 [0.04;0.70] 0.027

N': Number of patients in the analysis
OR: Odds Ratio
RR: Relative Risk
RD: Risk Difference

Table 7.3.3: SDMT Worsening by ≥4 points in 12 Months (FAS), Binary Analysis by Gender

	Treatment groups		Comparison		
	BAF312 (N=127)	**Placebo (N=61)**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Interaction Test	p= 0.610				
Sex = F					
N'	76	37			
SDMT worsening by ≥4 points in 12 months n	23 (30.3)	12 (32.4)	0.90 [0.39;2.10] 0.815	0.93 [0.52;1.66] 0.814	-0.02 [-0.20;0.16] 0.816
Sex = M					
N'	51	24			
SDMT worsening by ≥4 points in 12 months n	18 (35.3)	11 (45.8)	0.64 [0.24;1.73] 0.383	0.77 [0.43;1.36] 0.371	-0.11 [-0.34;0.13] 0.387

N': Number of patients in the analysis
OR: Odds Ratio
RR: Relative Risk
RD: Risk Difference

Table 7.3.4: SDMT Worsening by ≥4 points in 12 Months (FAS), Binary Analysis by Previous MS DMT

	Treatment groups		Comparison		
	BAF312 (N=127)	**Placebo (N=61)**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Interaction Test	p= 0.057				
Previous MS-DMT = N					
N'	20	17			
SDMT worsening by ≥4 points in 12 months n	9 (45.0)	4 (23.5)	2.66 [0.64;11.05] 0.179	1.91 [0.71;5.12] 0.197	0.21 [-0.08;0.51] 0.156
Previous MS-DMT = Y					
N'	107	44			
SDMT worsening by ≥4 points in 12 months n	32 (29.9)	19 (43.2)	0.56 [0.27;1.16] 0.119	0.69 [0.44;1.08] 0.107	-0.13 [-0.30;0.04] 0.126

N': Number of patients in the analysis
OR: Odds Ratio
RR: Relative Risk
RD: Risk Difference

Table 7.3.5: SDMT Worsening by ≥4 points in 12 Months (FAS), Binary Analysis by Previous IFN-beta-1b treatment

	Treatment groups		Comparison		
	BAF312 (N=127)	**Placebo (N=61)**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Interaction Test	p= 0.677				
Previous IFN-beta 1b = N					
N'	82	48			
SDMT worsening by ≥4 points in 12 months n	23 (28.0)	16 (33.3)	0.78 [0.36;1.68] 0.526	0.84 [0.50;1.43] 0.523	-0.05 [-0.22;0.11] 0.530
Previous IFN-beta 1b = Y					
N'	45	13			
SDMT worsening by ≥4 points in 12 months n	18 (40.0)	7 (53.8)	0.57 [0.16;1.98] 0.378	0.74 [0.40;1.38] 0.345	-0.14 [-0.44;0.17] 0.376

N': Number of patients in the analysis
OR: Odds Ratio
RR: Relative Risk
RD: Risk Difference

Table 7.3.6: SDMT Worsening by ≥4 points in 12 Months (FAS), Binary Analysis by Rapid Evolvement

	Treatment groups		Comparison		
	BAF312 (N=127)	**Placebo (N=61)**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Interaction Test	p= 0.601				
Rapid evolvement = N					
N'	95	47			
SDMT worsening by ≥4 points in 12 months n	27 (28.4)	17 (36.2)	0.70 [0.33;1.47] 0.348	0.79 [0.48;1.29] 0.341	-0.08 [-0.24;0.09] 0.356
Rapid evolvement = Y					
N'	32	14			
SDMT worsening by ≥4 points in 12 months n	14 (43.8)	6 (42.9)	1.04 [0.29;3.69] 0.955	1.02 [0.50;2.10] 0.955	0.01 [-0.30;0.32] 0.955

N': Number of patients in the analysis
OR: Odds Ratio
RR: Relative Risk
RD: Risk Difference

Table 7.3.7: SDMT Worsening by ≥4 points in 12 Months (FAS), Binary Analysis by Disease Course

	Treatment groups		Comparison		
	BAF312 (N=127)	**Placebo (N=61)**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Interaction Test	p= 0.430				
Moderate/severe disease course = N					
N'	18	11			
SDMT worsening by ≥4 points in 12 months n	8 (44.4)	4 (36.4)	1.40 [0.30;6.53] 0.669	1.22 [0.48;3.12] 0.675	0.08 [-0.28;0.45] 0.665
Moderate/severe disease course = Y					
N'	109	50			
SDMT worsening by ≥4 points in 12 months n	33 (30.3)	19 (38.0)	0.71 [0.35;1.43] 0.336	0.80 [0.51;1.26] 0.327	-0.08 [-0.24;0.08] 0.343

N': Number of patients in the analysis
OR: Odds Ratio
RR: Relative Risk
RD: Risk Difference

Table 7.3.8: SDMT Worsening by ≥4 points in 12 Months (FAS), Binary Analysis by Region

	Treatment groups		Comparison		
	BAF312 (N=127)	**Placebo (N=61)**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Interaction Test	p= 0.559				
Region = Europe					
N'	106	52			
SDMT worsening by ≥4 points in 12 months n	33 (31.1)	20 (38.5)	0.72 [0.36;1.45] 0.360	0.81 [0.52;1.26] 0.352	-0.07 [-0.23;0.09] 0.366
Region = Others					
N'	21	9			
SDMT worsening by ≥4 points in 12 months n	8 (38.1)	3 (33.3)	1.23 [0.24;6.36] 0.804	1.14 [0.39;3.34] 0.807	0.05 [-0.32;0.42] 0.802

N': Number of patients in the analysis
OR: Odds Ratio
RR: Relative Risk
RD: Risk Difference

Table 8.1.0: BVMT-R Delayed Recall Score (FAS), Return Rates

	Treatment groups		
	BAF312 (N=127)	**Placebo (N=61)**	**Total (N=188)**
Return Rate n (%)*			
Baseline	123 (96.9)	59 (96.7)	182 (96.8)
Month 06	115 (90.6)	56 (91.8)	171 (91.0)
Month 12	107 (84.3)	48 (78.7)	155 (82.4)
Month 18	76 (59.8)	29 (47.5)	105 (55.9)
Month 24	39 (30.7)	15 (24.6)	54 (28.7)
Month 30	14 (11.0)	2 (3.3)	16 (8.5)

* Number and percentage of patients with non-missing data at the given time point.

Table 8.1.1: BVMT-R Delayed Recall Score (FAS), Change from Baseline

	Treatment groups		Comparison	
	BAF312 (N=127)	**Placebo (N=61)**	**Mean Difference [95% CI]**	**p-value**
N'	113	56		
Baseline Mean (SD)	7.9 (3.29)	7.2 (3.28)		
Month 12 Adjusted Mean Change (SE)	-0.53 (0.32)	0.36 (0.42)	-0.89 [-1.79;0.01]	0.052
Month 24 Adjusted Mean Change (SE)	0.47 (0.43)	0.88 (0.64)	-0.41 [-1.84;1.03]	0.574

N': Number of patients in the analysis
Adjusted Mean Change calculated by MMRM model including the following variables: Treatment+Visit+Treatment*Visit+Country+BL Value+Age

Table 8.1.2: BVMT-R Delayed Recall Score (FAS), Change from Baseline by Age

	Treatment groups		Comparison	
	BAF312 (N=127)	Placebo (N=61)	Mean Difference [95% CI]	p-value
Interaction Test				0.393
Age = 18-40				
N'	16	12		
Baseline Mean (SD)	8.00 (3.74)	7.58 (3.23)		
Month 12 Adjusted Mean Change (SE)	-0.58 (0.71)	0.96 (0.88)	-1.54 [-3.76;0.68]	0.172
Month 24 Adjusted Mean Change (SE)	-0.77 (1.08)	2.11 (1.50)	-2.89 [-6.54;0.76]	0.119
Age = 41-55				
N'	86	31		
Baseline Mean (SD)	7.95 (3.13)	7.26 (3.39)		
Month 12 Adjusted Mean Change (SE)	-0.39 (0.38)	0.38 (0.55)	-0.77 [-1.96;0.42]	0.201
Month 24 Adjusted Mean Change (SE)	0.79 (0.51)	0.19 (0.81)	0.60 [-1.20;2.41]	0.509
Age = >55				
N'	11	13		
Baseline Mean (SD)	7.36 (4.08)	6.69 (3.25)		
Month 12 Adjusted Mean Change (SE)	-1.09 (0.99)	-0.13 (0.78)	-0.95 [-3.37;1.47]	0.439
Month 24 Adjusted Mean Change (SE)	0.41 (1.34)	2.23 (1.33)	-1.82 [-5.52;1.88]	0.331

N': Number of patients in the analysis
Adjusted Mean Change calculated by MMRM model including the following variables:
Treatment+Agegroup+Visit+Treatment*Agegroup+Treatment*Visit+Agegroup*Visit+Treatment*Visit*Agegroup+Country+BL Value

Table 8.1.3: BVMT-R Delayed Recall Score (FAS), Change from Baseline by Gender

	Treatment groups		Comparison	
	BAF312 (N=127)	**Placebo (N=61)**	**Mean Difference [95% CI]**	**p-value**
Interaction Test				0.036
Sex = F				
N'	63	34		
Baseline Mean (SD)	7.84 (3.23)	6.71 (3.22)		
Month 12 Adjusted Mean Change (SE)	0.12 (0.41)	0.10 (0.52)	0.02 [-1.14;1.19]	0.969
Month 24 Adjusted Mean Change (SE)	0.97 (0.60)	0.71 (0.78)	0.26 [-1.59;2.11]	0.781
Sex = M				
N'	50	22		
Baseline Mean (SD)	7.98 (3.39)	7.95 (3.29)		
Month 12 Adjusted Mean Change (SE)	-1.13 (0.40)	1.16 (0.64)	-2.29 [-3.71;-0.87]	0.002
Month 24 Adjusted Mean Change (SE)	-0.04 (0.58)	1.76 (1.14)	-1.81 [-4.30;0.69]	0.153

N': Number of patients in the analysis
Adjusted Mean Change calculated by MMRM model including the following variables:
Treatment+Sex+Visit+Treatment*Sex+Treatment*Visit+Sex*Visit+Treatment*Visit*Sex+Country+BL Value+Age

Table 8.1.4 BVMT-R Delayed Recall Score (FAS), Change from Baseline by Previous MS DMT

	Treatment groups		Comparison	
	BAF312 (N=127)	**Placebo (N=61)**	**Mean Difference [95% CI]**	**p-value**
Interaction Test				0.910
Previous MS-DMT = N				
N'	19	17		
Baseline Mean (SD)	8.32 (2.91)	8.59 (2.98)		
Month 12 Adjusted Mean Change (SE)	0.10 (0.65)	0.00 (0.69)	0.10 [-1.66;1.86]	0.908
Month 24 Adjusted Mean Change (SE)	1.60 (0.93)	-0.15 (1.31)	1.75 [-1.39;4.90]	0.270
Previous MS-DMT = Y				
N'	94	39		
Baseline Mean (SD)	7.82 (3.37)	6.59 (3.25)		
Month 12 Adjusted Mean Change (SE)	-0.69 (0.35)	0.51 (0.50)	-1.21 [-2.30;-0.12]	0.030
Month 24 Adjusted Mean Change (SE)	0.20 (0.47)	1.11 (0.72)	-0.91 [-2.54;0.72]	0.269

N': Number of patients in the analysis
Adjusted Mean Change calculated by MMRM model including the following variables:
Treatment+DMT+Visit+Treatment*DMT+Treatment*Visit+DMT*Visit+Treatment*Visit*DMT+Country+BL Value+Age

Table 8.1.5 BVMT-R Delayed Recall Score (FAS), Change from Baseline by Previous IFN-beta-1b treatment

	Treatment groups		Comparison	
	BAF312 (N=127)	**Placebo (N=61)**	**Mean Difference [95% CI]**	**p-value**
Interaction Test				0.079
Previous IFN-beta 1b = N				
N'	72	43		
Baseline Mean (SD)	7.86 (3.11)	7.30 (3.48)		
Month 12 Adjusted Mean Change (SE)	-0.57 (0.37)	0.66 (0.45)	-1.23 [-2.27;-0.20]	0.020
Month 24 Adjusted Mean Change (SE)	0.82 (0.49)	1.62 (0.67)	-0.80 [-2.37;0.77]	0.314
Previous IFN-beta 1b = Y				
N'	41	13		
Baseline Mean (SD)	7.98 (3.63)	6.85 (2.58)		
Month 12 Adjusted Mean Change (SE)	-0.52 (0.47)	-1.19 (0.86)	0.67 [-1.15;2.49]	0.467
Month 24 Adjusted Mean Change (SE)	-0.15 (0.62)	-2.78 (1.24)	2.62 [-0.05;5.30]	0.054

N': Number of patients in the analysis
Adjusted Mean Change calculated by MMRM model including the following variables:
Treatment+IFN+Visit+Treatment*IFN+Treatment*Visit+IFN*Visit+Treatment*Visit*IFN+Country+BL Value+Age

Table 8.1.6 BVMT-R Delayed Recall Score (FAS), Change from Baseline by Rapid Evolvement

	Treatment groups		Comparison	
	BAF312 (N=127)	**Placebo (N=61)**	**Mean Difference [95% CI]**	**p-value**
Interaction Test				0.566
Rapid evolvement = N				
N'	85	42		
Baseline Mean (SD)	7.81 (3.16)	7.02 (3.37)		
Month 12 Adjusted Mean Change (SE)	-0.58 (0.35)	0.45 (0.47)	-1.03 [-2.06;0.01]	0.051
Month 24 Adjusted Mean Change (SE)	0.42 (0.49)	0.89 (0.76)	-0.48 [-2.18;1.23]	0.581
Rapid evolvement = Y				
N'	28	14		
Baseline Mean (SD)	8.18 (3.71)	7.71 (3.02)		
Month 12 Adjusted Mean Change (SE)	-0.33 (0.55)	-0.07 (0.86)	-0.26 [-2.22;1.70]	0.792
Month 24 Adjusted Mean Change (SE)	0.71 (0.83)	0.56 (1.22)	0.15 [-2.73;3.02]	0.918

N': Number of patients in the analysis
Adjusted Mean Change calculated by MMRM model including the following variables:
Treatment+RapEv+Visit+Treatment*RapEv+Treatment*Visit+RapEv*Visit+Treatment*Visit*RapEv+Country+BL Value+Age

Table 8.1.7 BVMT-R Delayed Recall Score (FAS), Change from Baseline by Disease Course

	Treatment groups		Comparison	
	BAF312 (N=127)	**Placebo (N=61)**	**Mean Difference [95% CI]**	**p-value**
Interaction Test				0.377
Moderate/severe disease course = N				
N'	17	10		
Baseline Mean (SD)	7.29 (3.50)	7.90 (3.48)		
Month 12 Adjusted Mean Change (SE)	-0.73 (0.71)	0.68 (0.90)	-1.40 [-3.59;0.78]	0.206
Month 24 Adjusted Mean Change (SE)	0.30 (1.03)	0.45 (1.28)	-0.15 [-3.36;3.07]	0.928
Moderate/severe disease course = Y				
N'	96	46		
Baseline Mean (SD)	8.01 (3.26)	7.04 (3.25)		
Month 12 Adjusted Mean Change (SE)	-0.52 (0.33)	0.27 (0.45)	-0.78 [-1.79;0.22]	0.123
Month 24 Adjusted Mean Change (SE)	0.44 (0.46)	0.96 (0.74)	-0.52 [-2.17;1.13]	0.532

N': Number of patients in the analysis
Adjusted Mean Change calculated by MMRM model including the following variables:
Treatment+DC+Visit+Treatment*DC+Treatment*Visit+DC*Visit+Treatment*Visit*DC+Country+BL Value+Age

Table 8.1.8 BVMT-R Delayed Recall Score (FAS), Change from Baseline by Region

	Treatment groups		Comparison	
	BAF312 (N=127)	**Placebo (N=61)**	**Mean Difference [95% CI]**	**p-value**
Interaction Test				0.901
Region = Europe				
N'	95	49		
Baseline Mean (SD)	8.09 (3.14)	7.24 (3.21)		
Month 12 Adjusted Mean Change (SE)	-0.31 (0.27)	0.51 (0.40)	-0.83 [-1.79;0.13]	0.091
Month 24 Adjusted Mean Change (SE)	0.77 (0.40)	1.33 (0.67)	-0.55 [-2.11;1.01]	0.483
Region = Others				
N'	18	7		
Baseline Mean (SD)	6.89 (3.92)	6.86 (4.02)		
Month 12 Adjusted Mean Change (SE)	-0.85 (0.70)	0.89 (1.05)	-1.74 [-4.23;0.74]	0.167
Month 24 Adjusted Mean Change (SE)	-0.32 (0.94)	-0.18 (1.24)	-0.14 [-3.24;2.95]	0.927

N': Number of patients in the analysis
Adjusted Mean Change calculated by MMRM model including the following variables:
Treatment+Region+Visit+Treatment*Region+Treatment*Visit+Region*Visit+Treatment*Visit*Region+BL Value+Age

Table 8.2.0: BVMT-R Total Recall Score (FAS), Return Rates

	Treatment groups		
	BAF312 (N=127)	**Placebo (N=61)**	**Total (N=188)**
Return Rate n (%)*			
Baseline	123 (96.9)	59 (96.7)	182 (96.8)
Month 06	115 (90.6)	56 (91.8)	171 (91.0)
Month 12	108 (85.0)	48 (78.7)	156 (83.0)
Month 18	77 (60.6)	30 (49.2)	107 (56.9)
Month 24	40 (31.5)	15 (24.6)	55 (29.3)
Month 30	14 (11.0)	2 (3.3)	16 (8.5)

* Number and percentage of patients with non-missing data at the given time point.

Table 8.2.1: BVMT-R Total Recall Score (FAS), Change from Baseline

	Treatment groups		Comparison	
	BAF312 (N=127)	**Placebo (N=61)**	**Mean Difference [95% CI]**	**p-value**
N'	113	56		
Baseline Mean (SD)	20.33 (8.91)	18.18 (7.87)		
Month 12 Adjusted Mean Change (SE)	-0.72 (0.74)	-0.21 (0.96)	-0.52 [-2.55;1.52]	0.616
Month 24 Adjusted Mean Change (SE)	0.93 (0.99)	1.06 (1.47)	-0.13 [-3.43;3.16]	0.937

N': Number of patients in the analysis
Adjusted Mean Change calculated by MMRM model including the following variables: Treatment+Visit+Treatment*Visit+Country+BL Value+Age

Table 8.2.2: BVMT-R Total Recall Score (FAS), Change from Baseline by Age

	Treatment groups		Comparison	
	BAF312 (N=127)	**Placebo (N=61)**	**Mean Difference [95% CI]**	**p-value**
Interaction Test				0.016
Age = 18-40				
N'	16	12		
Baseline Mean (SD)	21.44 (9.67)	19.92 (7.46)		
Month 12 Adjusted Mean Change (SE)	-2.92 (1.58)	1.11 (1.95)	-4.03 [-8.96;0.90]	0.108
Month 24 Adjusted Mean Change (SE)	-0.72 (2.45)	9.02 (3.50)	-9.74 [-18.21;-1.26]	0.025
Age = 41-55				
N'	86	31		
Baseline Mean (SD)	20.37 (8.77)	18.00 (8.27)		
Month 12 Adjusted Mean Change (SE)	-0.53 (0.88)	1.12 (1.24)	-1.64 [-4.26;0.98]	0.217
Month 24 Adjusted Mean Change (SE)	0.87 (1.14)	0.08 (1.87)	0.79 [-3.32;4.90]	0.703
Age = >55				
N'	11	13		
Baseline Mean (SD)	18.36 (9.39)	17.00 (7.57)		
Month 12 Adjusted Mean Change (SE)	0.96 (2.22)	-3.78 (1.72)	4.75 [-0.63;10.12]	0.083
Month 24 Adjusted Mean Change (SE)	4.06 (3.11)	-0.79 (2.95)	4.85 [-3.60;13.30]	0.257

N': Number of patients in the analysis
Adjusted Mean Change calculated by MMRM model including the following variables:
Treatment+Agegroup+Visit+Treatment*Agegroup+Treatment*Visit+Agegroup*Visit+Treatment*Visit*Agegroup+Country+BL Value

Table 8.2.3: BVMT-R Total Recall Score (FAS), Change from Baseline by Gender

	Treatment groups		Comparison	
	BAF312 (N=127)	**Placebo (N=61)**	**Mean Difference [95% CI]**	**p-value**
Interaction Test				0.014
Sex = F				
N'	63	34		
Baseline Mean (SD)	20.43 (8.97)	16.85 (7.48)		
Month 12 Adjusted Mean Change (SE)	0.68 (0.95)	-1.43 (1.18)	2.11 [-0.50;4.72]	0.113
Month 24 Adjusted Mean Change (SE)	1.91 (1.35)	-0.29 (1.76)	2.20 [-1.99;6.38]	0.299
Sex = M				
N'	50	22		
Baseline Mean (SD)	20.20 (8.92)	20.23 (8.19)		
Month 12 Adjusted Mean Change (SE)	-2.09 (0.92)	2.21 (1.46)	-4.30 [-7.50;-1.11]	0.009
Month 24 Adjusted Mean Change (SE)	0.00 (1.32)	4.54 (2.65)	-4.54 [-10.31;1.22]	0.121

N': Number of patients in the analysis
Adjusted Mean Change calculated by MMRM model including the following variables:
Treatment+Sex+Visit+Treatment*Sex+Treatment*Visit+Sex*Visit+Treatment*Visit*Sex+Country+BL Value+Age

Table 8.2.4 BVMT-R Total Recall Score (FAS), Change from Baseline by Previous MS DMT

	Treatment groups		Comparison	
	BAF312 (N=127)	**Placebo (N=61)**	**Mean Difference [95% CI]**	**p-value**
Interaction Test				0.177
Previous MS-DMT = N				
N'	19	17		
Baseline Mean (SD)	21.89 (8.72)	21.00 (7.93)		
Month 12 Adjusted Mean Change (SE)	-0.57 (1.48)	-0.45 (1.59)	-0.12 [-4.09;3.86]	0.953
Month 24 Adjusted Mean Change (SE)	0.91 (2.15)	-0.70 (3.06)	1.61 [-5.63;8.84]	0.659
Previous MS-DMT = Y				
N'	94	39		
Baseline Mean (SD)	20.01 (8.96)	16.95 (7.62)		
Month 12 Adjusted Mean Change (SE)	-0.81 (0.81)	-0.28 (1.14)	-0.53 [-3.01;1.96]	0.676
Month 24 Adjusted Mean Change (SE)	0.82 (1.09)	1.28 (1.69)	-0.46 [-4.29;3.37]	0.813

N': Number of patients in the analysis
Adjusted Mean Change calculated by MMRM model including the following variables:
Treatment+DMT+Visit+Treatment*DMT+Treatment*Visit+DMT*Visit+Treatment*Visit*DMT+Country+BL Value+Age

Table 8.2.5 BVMT-R Total Recall Score (FAS), Change from Baseline by Previous IFN-beta-1b treatment

	Treatment groups		Comparison	
	BAF312 (N=127)	**Placebo (N=61)**	**Mean Difference [95% CI]**	**p-value**
Interaction Test				0.034
Previous IFN-beta 1b = N				
N'	72	43		
Baseline Mean (SD)	20.76 (8.79)	18.51 (8.46)		
Month 12 Adjusted Mean Change (SE)	-0.82 (0.85)	0.35 (1.05)	-1.17 [-3.54;1.20]	0.330
Month 24 Adjusted Mean Change (SE)	0.49 (1.17)	2.72 (1.61)	-2.23 [-6.01;1.55]	0.243
Previous IFN-beta 1b = Y				
N'	41	13		
Baseline Mean (SD)	19.56 (9.17)	17.08 (5.62)		
Month 12 Adjusted Mean Change (SE)	-0.59 (1.10)	-2.46 (2.00)	1.87 [-2.28;6.02]	0.375
Month 24 Adjusted Mean Change (SE)	1.78 (1.49)	-5.33 (3.02)	7.11 [0.65;13.58]	0.031

N': Number of patients in the analysis
Adjusted Mean Change calculated by MMRM model including the following variables:
Treatment+IFN+Visit+Treatment*IFN+Treatment*Visit+IFN*Visit+Treatment*Visit*IFN+Country+BL Value+Age

Table 8.2.6 BVMT-R Total Recall Score (FAS), Change from Baseline by Rapid Evolvement

	Treatment groups		Comparison	
	BAF312 (N=127)	**Placebo (N=61)**	**Mean Difference [95% CI]**	**p-value**
Interaction Test				0.123
Rapid evolvement = N				
N'	85	42		
Baseline Mean (SD)	20.04 (8.63)	18.74 (8.41)		
Month 12 Adjusted Mean Change (SE)	-0.44 (0.81)	-0.64 (1.06)	0.20 [-2.11;2.51]	0.863
Month 24 Adjusted Mean Change (SE)	0.89 (1.08)	-0.71 (1.69)	1.60 [-2.20;5.41]	0.403
Rapid evolvement = Y				
N'	28	14		
Baseline Mean (SD)	21.21 (9.81)	16.50 (5.92)		
Month 12 Adjusted Mean Change (SE)	-1.29 (1.24)	1.14 (1.98)	-2.44 [-6.88;2.00]	0.280
Month 24 Adjusted Mean Change (SE)	1.25 (1.83)	5.11 (2.77)	-3.86 [-10.37;2.65]	0.241

N': Number of patients in the analysis
Adjusted Mean Change calculated by MMRM model including the following variables:
Treatment+RapEv+Visit+Treatment*RapEv+Treatment*Visit+RapEv*Visit+Treatment*Visit*RapEv+Country+BL Value+Age

Table 8.2.7 BVMT-R Total Recall Score (FAS), Change from Baseline by Disease Course

	Treatment groups		Comparison	
	BAF312 (N=127)	**Placebo (N=61)**	**Mean Difference [95% CI]**	**p-value**
Interaction Test				0.059
Moderate/severe disease course = N				
N'	17	10		
Baseline Mean (SD)	19.41 (9.04)	20.60 (8.98)		
Month 12 Adjusted Mean Change (SE)	-0.12 (1.61)	0.70 (2.04)	-0.82 [-5.75;4.12]	0.744
Month 24 Adjusted Mean Change (SE)	-1.30 (2.38)	1.65 (2.90)	-2.95 [-10.27;4.37]	0.425
Moderate/severe disease course = Y				
N'	96	46		
Baseline Mean (SD)	20.49 (8.92)	17.65 (7.62)		
Month 12 Adjusted Mean Change (SE)	-0.76 (0.78)	-0.48 (1.05)	-0.28 [-2.56;1.99]	0.805
Month 24 Adjusted Mean Change (SE)	1.27 (1.05)	1.01 (1.69)	0.27 [-3.53;4.06]	0.889

N': Number of patients in the analysis
Adjusted Mean Change calculated by MMRM model including the following variables:
Treatment+DC+Visit+Treatment*DC+Treatment*Visit+DC*Visit+Treatment*Visit*DC+Country+BL Value+Age

Table 8.2.8 BVMT-R Total Recall Score (FAS), Change from Baseline by Region

	Treatment groups		Comparison	
	BAF312 (N=127)	**Placebo (N=61)**	**Mean Difference [95% CI]**	**p-value**
Interaction Test				0.297
Region = Europe				
N'	95	49		
Baseline Mean (SD)	20.96 (8.75)	18.12 (8.13)		
Month 12 Adjusted Mean Change (SE)	0.03 (0.61)	0.81 (0.90)	-0.78 [-2.95;1.38]	0.476
Month 24 Adjusted Mean Change (SE)	1.93 (0.94)	2.75 (1.63)	-0.82 [-4.56;2.92]	0.663
Region = Others				
N'	18	7		
Baseline Mean (SD)	17.00 (9.26)	18.57 (6.29)		
Month 12 Adjusted Mean Change (SE)	-1.32 (1.59)	-0.77 (2.36)	-0.55 [-6.17;5.06]	0.846
Month 24 Adjusted Mean Change (SE)	-0.91 (2.32)	-2.32 (2.99)	1.41 [-6.10;8.93]	0.709

N': Number of patients in the analysis
Adjusted Mean Change calculated by MMRM model including the following variables:
Treatment+Region+Visit+Treatment*Region+Treatment*Visit+Region*Visit+Treatment*Visit*Region+BL Value+Age

Table 8.3.0: LCVA (FAS), Return Rates

	Treatment groups		
	BAF312 (N=127)	**Placebo (N=61)**	**Total (N=188)**
Return Rate n (%)*			
Baseline	121 (95.3)	60 (98.4)	181 (96.3)
Month 06	111 (87.4)	56 (91.8)	167 (88.8)
Month 12	103 (81.1)	46 (75.4)	149 (79.3)
Month 18	70 (55.1)	23 (37.7)	93 (49.5)
Month 24	41 (32.3)	16 (26.2)	57 (30.3)
Month 30	15 (11.8)	6 (9.8)	21 (11.2)

* Number and percentage of patients with non-missing data at the given time point.

Table 8.3.1: LCVA (FAS), Change from Baseline

	Treatment groups		Comparison	
	BAF312 (N=127)	**Placebo (N=61)**	**Mean Difference [95% CI]**	**p-value**
N'	110	55		
Baseline Mean (SD)	0.39 (0.26)	0.39 (0.26)		
Month 12 Adjusted Mean Change (SE)	0.00 (0.03)	-0.01 (0.03)	0.02 [-0.06;0.09]	0.632
Month 24 Adjusted Mean Change (SE)	0.00 (0.03)	0.04 (0.05)	-0.04 [-0.15;0.06]	0.401

N': Number of patients in the analysis
Adjusted Mean Change calculated by MMRM model including the following variables: Treatment+Visit+Treatment*Visit+Country+BL Value

Table 8.3.2: LCVA (FAS), Change from Baseline by Age

	Treatment groups		Comparison	
	BAF312 (N=127)	**Placebo (N=61)**	**Mean Difference [95% CI]**	**p-value**
Interaction Test				0.303
Age = 18-40				
N'	14	13		
Baseline Mean (SD)	0.52 (0.32)	0.34 (0.23)		
Month 12 Adjusted Mean Change (SE)	-0.06 (0.06)	0.05 (0.07)	-0.12 [-0.30;0.06]	0.193
Month 24 Adjusted Mean Change (SE)	-0.03 (0.10)	0.01 (0.09)	-0.05 [-0.33;0.23]	0.737
Age = 41-55				
N'	84	28		
Baseline Mean (SD)	0.36 (0.24)	0.38 (0.30)		
Month 12 Adjusted Mean Change (SE)	-0.01 (0.03)	-0.05 (0.04)	0.04 [-0.05;0.14]	0.387
Month 24 Adjusted Mean Change (SE)	-0.03 (0.04)	0.08 (0.06)	-0.11 [-0.25;0.03]	0.133
Age = >55				
N'	12	14		
Baseline Mean (SD)	0.43 (0.27)	0.46 (0.20)		
Month 12 Adjusted Mean Change (SE)	0.11 (0.07)	-0.01 (0.06)	0.12 [-0.06;0.30]	0.194
Month 24 Adjusted Mean Change (SE)	0.21 (0.11)	0.00 (0.09)	0.21 [-0.07;0.48]	0.137

N': Number of patients in the analysis
Adjusted Mean Change calculated by MMRM model including the following variables:
Treatment+Agegroup+Visit+Treatment*Agegroup+Treatment*Visit+Agegroup*Visit+Treatment*Visit*Agegroup+Country+BL Value

Table 8.3.3: LCVA (FAS), Change from Baseline by Gender

	Treatment groups		Comparison	
	BAF312 (N=127)	**Placebo (N=61)**	**Mean Difference [95% CI]**	**p-value**
Interaction Test				0.117
Sex = F				
N'	63	35		
Baseline Mean (SD)	0.40 (0.28)	0.43 (0.26)		
Month 12 Adjusted Mean Change (SE)	0.01 (0.03)	-0.01 (0.04)	0.02 [-0.07;0.11]	0.656
Month 24 Adjusted Mean Change (SE)	0.02 (0.04)	0.01 (0.05)	0.00 [-0.12;0.13]	0.938
Sex = M				
N'	47	20		
Baseline Mean (SD)	0.38 (0.23)	0.33 (0.26)		
Month 12 Adjusted Mean Change (SE)	0.00 (0.03)	-0.01 (0.06)	0.01 [-0.12;0.13]	0.892
Month 24 Adjusted Mean Change (SE)	-0.02 (0.05)	0.12 (0.09)	-0.15 [-0.35;0.06]	0.166

N': Number of patients in the analysis
Adjusted Mean Change calculated by MMRM model including the following variables:
Treatment+Sex+Visit+Treatment*Sex+Treatment*Visit+Sex*Visit+Treatment*Visit*Sex+Country+BL Value

Table 8.3.4 LCVA (FAS), Change from Baseline by Previous MS DMT

	Treatment groups		Comparison	
	BAF312 (N=127)	**Placebo (N=61)**	**Mean Difference [95% CI]**	**p-value**
Interaction Test				0.845
Previous MS-DMT = N				
N'	20	16		
Baseline Mean (SD)	0.41 (0.32)	0.31 (0.17)		
Month 12 Adjusted Mean Change (SE)	0.05 (0.05)	-0.01 (0.06)	0.05 [-0.09;0.20]	0.463
Month 24 Adjusted Mean Change (SE)	0.05 (0.07)	0.05 (0.10)	0.00 [-0.24;0.24]	0.990
Previous MS-DMT = Y				
N'	90	39		
Baseline Mean (SD)	0.39 (0.24)	0.43 (0.28)		
Month 12 Adjusted Mean Change (SE)	-0.01 (0.03)	-0.02 (0.04)	0.01 [-0.08;0.10]	0.816
Month 24 Adjusted Mean Change (SE)	-0.01 (0.04)	0.04 (0.05)	-0.06 [-0.18;0.07]	0.363

N': Number of patients in the analysis
Adjusted Mean Change calculated by MMRM model including the following variables:
Treatment+DMT+Visit+Treatment*DMT+Treatment*Visit+DMT*Visit+Treatment*Visit*DMT+Country+BL Value

Table 8.3.5 LCVA (FAS), Change from Baseline by Previous IFN-beta-1b treatment

	Treatment groups		Comparison	
	BAF312 (N=127)	**Placebo (N=61)**	**Mean Difference [95% CI]**	**p-value**
Interaction Test				0.038
Previous IFN-beta 1b = N				
N'	70	42		
Baseline Mean (SD)	0.42 (0.27)	0.39 (0.23)		
Month 12 Adjusted Mean Change (SE)	0.02 (0.03)	-0.01 (0.04)	0.03 [-0.06;0.11]	0.495
Month 24 Adjusted Mean Change (SE)	0.00 (0.04)	0.00 (0.05)	0.00 [-0.12;0.12]	0.978
Previous IFN-beta 1b = Y				
N'	40	13		
Baseline Mean (SD)	0.35 (0.25)	0.40 (0.36)		
Month 12 Adjusted Mean Change (SE)	-0.02 (0.04)	-0.03 (0.07)	0.01 [-0.14;0.16]	0.886
Month 24 Adjusted Mean Change (SE)	0.01 (0.05)	0.23 (0.10)	-0.22 [-0.44;0.00]	0.048

N': Number of patients in the analysis
Adjusted Mean Change calculated by MMRM model including the following variables:
Treatment+IFN+Visit+Treatment*IFN+Treatment*Visit+IFN*Visit+Treatment*Visit*IFN+Country+BL Value

Table 8.3.6 LCVA (FAS), Change from Baseline by Rapid Evolvement

	Treatment groups		Comparison	
	BAF312 (N=127)	**Placebo (N=61)**	**Mean Difference [95% CI]**	**p-value**
Interaction Test				0.394
Rapid evolvement = N				
N'	82	41		
Baseline Mean (SD)	0.39 (0.28)	0.39 (0.26)		
Month 12 Adjusted Mean Change (SE)	0.03 (0.03)	-0.04 (0.04)	0.07 [-0.01;0.15]	0.084
Month 24 Adjusted Mean Change (SE)	0.03 (0.04)	0.07 (0.05)	-0.04 [-0.16;0.08]	0.510
Rapid evolvement = Y				
N'	28	14		
Baseline Mean (SD)	0.39 (0.19)	0.40 (0.27)		
Month 12 Adjusted Mean Change (SE)	-0.08 (0.04)	0.05 (0.07)	-0.13 [-0.29;0.03]	0.101
Month 24 Adjusted Mean Change (SE)	-0.06 (0.05)	-0.12 (0.10)	0.06 [-0.17;0.29]	0.602

N': Number of patients in the analysis
Adjusted Mean Change calculated by MMRM model including the following variables:
Treatment+RapEv+Visit+Treatment*RapEv+Treatment*Visit+RapEv*Visit+Treatment*Visit*RapEv+Country+BL Value

Table 8.3.7 LCVA (FAS), Change from Baseline by Disease Course

	Treatment groups		Comparison	
	BAF312 (N=127)	**Placebo (N=61)**	**Mean Difference [95% CI]**	**p-value**
Interaction Test				0.131
Moderate/severe disease course = N				
N'	16	10		
Baseline Mean (SD)	0.33 (0.20)	0.31 (0.21)		
Month 12 Adjusted Mean Change (SE)	0.01 (0.06)	-0.11 (0.07)	0.11 [-0.07;0.29]	0.217
Month 24 Adjusted Mean Change (SE)	-0.02 (0.08)	-0.09 (0.11)	0.07 [-0.19;0.33]	0.596
Moderate/severe disease course = Y				
N'	94	45		
Baseline Mean (SD)	0.40 (0.27)	0.41 (0.27)		
Month 12 Adjusted Mean Change (SE)	0.00 (0.03)	0.00 (0.04)	-0.01 [-0.09;0.07]	0.867
Month 24 Adjusted Mean Change (SE)	0.00 (0.03)	0.07 (0.05)	-0.07 [-0.19;0.04]	0.213

N': Number of patients in the analysis
Adjusted Mean Change calculated by MMRM model including the following variables:
Treatment+DC+Visit+Treatment*DC+Treatment*Visit+DC*Visit+Treatment*Visit*DC+Country+BL Value

Table 8.3.8 LCVA (FAS), Change from Baseline by Region

	Treatment groups		Comparison	
	BAF312 (N=127)	**Placebo (N=61)**	**Mean Difference [95% CI]**	**p-value**
Interaction Test				0.162
Region = Europe				
N'	93	47		
Baseline Mean (SD)	0.38 (0.26)	0.38 (0.25)		
Month 12 Adjusted Mean Change (SE)	-0.01 (0.02)	0.00 (0.03)	-0.01 [-0.08;0.07]	0.812
Month 24 Adjusted Mean Change (SE)	0.00 (0.03)	0.01 (0.05)	0.00 [-0.12;0.12]	0.957
Region = Others				
N'	17	8		
Baseline Mean (SD)	0.43 (0.27)	0.45 (0.34)		
Month 12 Adjusted Mean Change (SE)	0.03 (0.05)	-0.21 (0.07)	0.25 [0.07;0.42]	0.008
Month 24 Adjusted Mean Change (SE)	-0.03 (0.09)	0.01 (0.08)	-0.04 [-0.27;0.20]	0.765

N': Number of patients in the analysis
Adjusted Mean Change calculated by MMRM model including the following variables:
Treatment+Region+Visit+Treatment*Region+Treatment*Visit+Region*Visit+Treatment*Visit*Region+BL Value

Table 9.1.0: T2 Lesion Volume (FAS), Return Rates

	Treatment groups		
	BAF312 (N=127)	**Placebo (N=61)**	**Total (N=188)**
Return Rate n (%)*			
Baseline	127 (100.0)	61 (100.0)	188 (100.0)
Month 12	118 (92.9)	56 (91.8)	174 (92.6)
Month 24	81 (63.8)	33 (54.1)	114 (60.6)
Month 36	18 (14.2)	5 (8.2)	23 (12.2)

* Number and percentage of patients with non-missing data at the given time point.

Table 9.1.1: T2 Lesion Volume (FAS), Change from Baseline

	Treatment groups		Comparison	
	BAF312 (N=127)	**Placebo (N=61)**	**Mean Difference [95% CI]**	**p-value**
N'	119	56		
Baseline Mean (SD)	21244.56 (17083.27)	20928.18 (18321.47)		
Month 12 Adjusted Mean Change (SE)	-24.02 (231.83)	953.81 (303.79)	-977.83 [-1604.94;-350.73]	0.002
Month 24 Adjusted Mean Change (SE)	-224.07 (240.63)	1379.89 (324.06)	-1603.96 [-2284.99;-922.93]	<.001

N': Number of patients in the analysis
Adjusted Mean Change calculated by MMRM model including the following variables: Treatment+Visit+Treatment*Visit+Country+SPMS Group+BL Value+Age+BL Number of T1 Lesions

Table 9.1.2: T2 Lesion Volume (FAS), Change from Baseline by Age

	Treatment groups		Comparison	
	BAF312 (N=127)	**Placebo (N=61)**	**Mean Difference [95% CI]**	**p-value**
Interaction Test				0.659
Age = 18-40				
N'	17	11		
Baseline Mean (SD)	21766.88 (12164.65)	20998.55 (13986.71)		
Month 12 Adjusted Mean Change (SE)	-148.88 (523.76)	1655.11 (615.88)	-1803.99 [-3382.22;-225.75]	0.025
Month 24 Adjusted Mean Change (SE)	-602.95 (527.95)	1140.39 (623.38)	-1743.34 [-3331.57;-155.10]	0.032
Age = 41-55				
N'	89	31		
Baseline Mean (SD)	20613.39 (17187.96)	15780.68 (13308.32)		
Month 12 Adjusted Mean Change (SE)	149.60 (278.45)	804.12 (392.55)	-654.53 [-1501.57;192.51]	0.129
Month 24 Adjusted Mean Change (SE)	4.08 (282.96)	1142.49 (420.12)	-1138.41 [-2042.08;-234.74]	0.014

N': Number of patients in the analysis
Adjusted Mean Change calculated by MMRM model including the following variables:
Treatment+Agegroup+Visit+Treatment*Agegroup+Treatment*Visit+Agegroup*Visit+Treatment*Visit*Agegroup+Country+SPMSGroup+BL Value+BL Number of T1 Lesions

Table 9.1.2: T2 Lesion Volume (FAS), Change from Baseline by Age

	Treatment groups		Comparison	
	BAF312 (N=127)	**Placebo (N=61)**	**Mean Difference [95% CI]**	**p-value**
Age = >55				
N'	13	14		
Baseline Mean (SD)	24882.62 (22097.54)	32270.93 (25675.36)		
Month 12 Adjusted Mean Change (SE)	-531.35 (680.76)	795.72 (572.01)	-1327.07 [-3008.08;353.94]	0.121
Month 24 Adjusted Mean Change (SE)	-806.75 (704.15)	2337.33 (616.30)	-3144.08 [-4944.08;-1344.07]	<.001

N': Number of patients in the analysis
Adjusted Mean Change calculated by MMRM model including the following variables:
Treatment+Agegroup+Visit+Treatment*Agegroup+Treatment*Visit+Agegroup*Visit+Treatment*Visit*Agegroup+Country+SPMSGroup+BL Value+BL Number of T1 Lesions

Table 9.1.3: T2 Lesion Volume (FAS), Change from Baseline by Gender

	Treatment groups		Comparison	
	BAF312 (N=127)	**Placebo (N=61)**	**Mean Difference [95% CI]**	**p-value**
Interaction Test				0.337
Sex = F				
N'	69	37		
Baseline Mean (SD)	19527.91 (15302.86)	25051.14 (20160.55)		
Month 12 Adjusted Mean Change (SE)	95.25 (300.72)	1123.94 (363.58)	-1028.69 [-1828.20;-229.18]	0.012
Month 24 Adjusted Mean Change (SE)	-17.75 (309.69)	1570.58 (391.21)	-1588.33 [-2451.77;-724.89]	<.001
Sex = M				
N'	50	19		
Baseline Mean (SD)	23613.54 (19181.68)	12899.26 (10478.35)		
Month 12 Adjusted Mean Change (SE)	-129.92 (304.91)	739.97 (498.45)	-869.88 [-1964.53;224.77]	0.118
Month 24 Adjusted Mean Change (SE)	-476.24 (325.00)	1131.61 (535.30)	-1607.85 [-2790.75;-424.95]	0.008

N': Number of patients in the analysis
Adjusted Mean Change calculated by MMRM model including the following variables:
Treatment+Sex+Visit+Treatment*Sex+Treatment*Visit+Sex*Visit+Treatment*Visit*Sex+Country+SPMS Group+BL Value+Age+BL Number of T1 Lesions

Table 9.1.4 T2 Lesion Volume (FAS), Change from Baseline by Previous MS DMT

	Treatment groups		Comparison	
	BAF312 (N=127)	**Placebo (N=61)**	**Mean Difference [95% CI]**	**p-value**
Interaction Test				0.676
Previous MS-DMT = N				
N'	20	16		
Baseline Mean (SD)	19852.10 (17863.21)	19769.38 (14440.40)		
Month 12 Adjusted Mean Change (SE)	494.95 (481.38)	1356.74 (528.76)	-861.79 [-2158.71;435.13]	0.191
Month 24 Adjusted Mean Change (SE)	72.88 (492.04)	2022.82 (585.80)	-1949.94 [-3340.13;-559.76]	0.006
Previous MS-DMT = Y				
N'	99	40		
Baseline Mean (SD)	21525.87 (17001.65)	21391.70 (19809.50)		
Month 12 Adjusted Mean Change (SE)	-111.41 (248.17)	820.14 (344.09)	-931.55 [-1673.03;-190.06]	0.014
Month 24 Adjusted Mean Change (SE)	-260.01 (256.82)	1154.91 (368.62)	-1414.92 [-2216.94;-612.90]	<.001

N': Number of patients in the analysis
Adjusted Mean Change calculated by MMRM model including the following variables:
Treatment+DMT+Visit+Treatment*DMT+Treatment*Visit+DMT*Visit+Treatment*Visit*DMT+Country+SPMS Group+BL Value+Age+BL Number of T1 Lesions

Table 9.1.5 T2 Lesion Volume (FAS), Change from Baseline by Previous IFN-beta-1b treatment

	Treatment groups		Comparison	
	BAF312 (N=127)	**Placebo (N=61)**	**Mean Difference [95% CI]**	**p-value**
Interaction Test				0.896
Previous IFN-beta 1b = N				
N'	77	45		
Baseline Mean (SD)	21366.53 (15850.69)	22457.44 (19750.03)		
Month 12 Adjusted Mean Change (SE)	188.93 (266.75)	971.31 (329.39)	-782.38 [-1512.53;-52.22]	0.036
Month 24 Adjusted Mean Change (SE)	-106.12 (277.81)	1502.74 (355.15)	-1608.86 [-2402.10;-815.62]	<.001
Previous IFN-beta 1b = Y				
N'	42	11		
Baseline Mean (SD)	21020.95 (19342.29)	14672.09 (8738.66)		
Month 12 Adjusted Mean Change (SE)	-428.61 (340.23)	869.24 (615.29)	-1297.84 [-2589.03;-6.66]	0.049
Month 24 Adjusted Mean Change (SE)	-459.21 (361.74)	824.28 (695.21)	-1283.49 [-2740.35;173.38]	0.084

N': Number of patients in the analysis
Adjusted Mean Change calculated by MMRM model including the following variables:
Treatment+IFN+Visit+Treatment*IFN+Treatment*Visit+IFN*Visit+Treatment*Visit*IFN+Country+SPMS Group+BL Value+Age+BL Number of T1 Lesions

Table 9.1.6 T2 Lesion Volume (FAS), Change from Baseline by Rapid Evolvement

	Treatment groups		Comparison	
	BAF312 (N=127)	**Placebo (N=61)**	**Mean Difference [95% CI]**	**p-value**
Interaction Test				0.505
Rapid evolvement = N				
N'	87	44		
Baseline Mean (SD)	21669.20 (17881.93)	21279.11 (19752.36)		
Month 12 Adjusted Mean Change (SE)	-71.76 (255.17)	755.40 (336.38)	-827.16 [-1549.77;-104.56]	0.025
Month 24 Adjusted Mean Change (SE)	-221.95 (266.85)	1335.46 (362.47)	-1557.41 [-2345.98;-768.84]	<.001
Rapid evolvement = Y				
N'	32	12		
Baseline Mean (SD)	20090.09 (14896.31)	19641.42 (12285.31)		
Month 12 Adjusted Mean Change (SE)	130.71 (389.68)	1675.30 (588.35)	-1544.58 [-2862.43;-226.74]	0.022
Month 24 Adjusted Mean Change (SE)	-195.33 (407.30)	1532.62 (647.87)	-1727.95 [-3174.19;-281.71]	0.020

N': Number of patients in the analysis
Adjusted Mean Change calculated by MMRM model including the following variables:
Treatment+RapEv+Visit+Treatment*RapEv+Treatment*Visit+RapEv*Visit+Treatment*Visit*RapEv+Country+SPMS Group+BL Value+Age+BL Number of T1 Lesions

Table 9.1.7 T2 Lesion Volume (FAS), Change from Baseline by Disease Course

	Treatment groups		Comparison	
	BAF312 (N=127)	**Placebo (N=61)**	**Mean Difference [95% CI]**	**p-value**
Interaction Test				0.051
Moderate/severe disease course = N				
N'	17	10		
Baseline Mean (SD)	19642.94 (13551.79)	24603.20 (19238.86)		
Month 12 Adjusted Mean Change (SE)	294.24 (516.02)	973.16 (659.35)	-678.92 [-2258.70;900.86]	0.397
Month 24 Adjusted Mean Change (SE)	-503.09 (587.52)	645.52 (680.26)	-1148.62 [-2850.13;552.89]	0.184
Moderate/severe disease course = Y				
N'	102	46		
Baseline Mean (SD)	21511.50 (17645.47)	20129.26 (18237.07)		
Month 12 Adjusted Mean Change (SE)	-109.98 (243.37)	930.77 (326.45)	-1040.74 [-1737.27;-344.22]	0.004
Month 24 Adjusted Mean Change (SE)	-238.56 (249.06)	1562.36 (352.13)	-1800.92 [-2556.99;-1044.85]	<.001

N': Number of patients in the analysis
Adjusted Mean Change calculated by MMRM model including the following variables:
Treatment+DC+Visit+Treatment*DC+Treatment*Visit+DC*Visit+Treatment*Visit*DC+Country+SPMS Group+BL Value+Age+BL Number of T1 Lesions

Table 9.1.8 T2 Lesion Volume (FAS), Change from Baseline by Region

	Treatment groups		Comparison	
	BAF312 (N=127)	**Placebo (N=61)**	**Mean Difference [95% CI]**	**p-value**
Interaction Test				0.625
Region = Europe				
N'	101	48		
Baseline Mean (SD)	21612.18 (17793.54)	20380.75 (14856.25)		
Month 12 Adjusted Mean Change (SE)	0.72 (185.37)	1318.74 (269.20)	-1318.02 [-1965.65;-670.40]	<.001
Month 24 Adjusted Mean Change (SE)	-193.69 (196.96)	1309.56 (309.28)	-1503.25 [-2229.06;-777.44]	<.001
Region = Others				
N'	18	8		
Baseline Mean (SD)	19181.83 (12569.04)	24212.75 (33781.29)		
Month 12 Adjusted Mean Change (SE)	355.73 (447.38)	439.02 (659.25)	-83.29 [-1655.48; 1488.91]	0.917
Month 24 Adjusted Mean Change (SE)	183.57 (542.51)	2494.73 (667.89)	-2311.16 [-4010.87;-611.46]	0.008

N': Number of patients in the analysis
Adjusted Mean Change calculated by MMRM model including the following variables:
Treatment+Region+Visit+Treatment*Region+Treatment*Visit+Region*Visit+Treatment*Visit*Region+SPMS Group+BL Value+Age+BL Number of T1 Lesions

Table 9.2.0: Number of New or Enlarging T2 Lesions (FAS), Return Rates

	Treatment groups		
	BAF312 (N=127)	**Placebo (N=61)**	**Total (N=188)**
Return Rate n (%)*			
Month 12	118 (92.9)	56 (91.8)	174 (92.6)
Month 24	81 (63.8)	33 (54.1)	114 (60.6)

* Number and percentage of patients with non-missing data at the given time point.

Table 9.2.1: Number of New or Enlarging T2 Lesions (FAS)

	Treatment groups		Comparison	
	BAF312 (N=127)	**Placebo (N=61)**	**RR [95% CI]**	**p-value**
N'	119	56		
Month 12: Number of lesions relative to baseline [95% CI]*	3.33 [2.14;5.18]	9.61 [7.04;13.11]	0.35 [0.20;0.60]	<.001
Month 24: Number of lesions relative to Month 12 [95% CI]*	0.69 [0.31;1.51]	8.09 [5.18;12.64]	0.08 [0.03;0.21]	<.001

N': Number of patients in the analysis
RR: Rate ratio
*: Adjusted means obtained from repeated measures negative binomial regression including the following variables:
Treatment+Visit+Treatment*Visit+Age+BL Number of T1 Lesions

Table 9.2.2: Number of New or Enlarging T2 Lesions (FAS) by Age

	Treatment groups		Comparison	
	BAF312 (N=127)	**Placebo (N=61)**	**RR [95% CI]**	**p-value**
Interaction Test				0.356
Age = 18-40				
N'	17	11		
Month 12: Number of lesions relative to baseline [95% CI]*	5.94 [3.19;11.06]	16.50 [11.04;24.65]	0.36 [0.17;0.75]	0.007
Month 24: Number of lesions relative to Month 12 [95% CI]*	0.39 [0.19;0.82]	11.95 [7.65;18.66]	0.03 [0.01;0.08]	<.001
Age = 41-55				
N'	89	31		
Month 12: Number of lesions relative to baseline [95% CI]*	3.53 [2.05;6.08]	10.49 [6.55;16.79]	0.34 [0.16;0.70]	0.003
Month 24: Number of lesions relative to Month 12 [95% CI]*	0.82 [0.38;1.76]	8.91 [4.87;16.29]	0.09 [0.03;0.24]	<.001
Age = >55				
N'	13	14		
Month 12: Number of lesions relative to baseline [95% CI]*	0.59 [0.32;1.10]	5.22 [2.29;11.89]	0.11 [0.04;0.32]	<.001
Month 24: Number of lesions relative to Month 12 [95% CI]*	0.17 [0.05;0.56]	4.83 [1.07;21.75]	0.03 [0.01;0.24]	<.001

N': Number of patients in the analysis
RR: Rate ratio
*: Adjusted means obtained from repeated measures negative binomial regression including the following variables:
Treatment+Agegroup+Visit+Treatment*Agegroup+Treatment*Visit+Agegroup*Visit+Treatment*Visit*Agegroup+BL Number of T1 Lesions

Table 9.2.3: Number of New or Enlarging T2 Lesions (FAS) by Gender

	Treatment groups		Comparison	
	BAF312 (N=127)	**Placebo (N=61)**	**RR [95% CI]**	**p-value**
Interaction Test				0.706
Sex = F				
N'	69	37		
Month 12: Number of lesions relative to baseline [95% CI]*	2.49 [1.64;3.79]	8.76 [5.67;13.54]	0.28 [0.15;0.53]	<.001
Month 24: Number of lesions relative to Month 12 [95% CI]*	0.83 [0.28;2.42]	7.59 [4.24;13.58]	0.11 [0.03;0.37]	<.001
Sex = M				
N'	50	19		
Month 12: Number of lesions relative to baseline [95% CI]*	4.46 [2.16;9.20]	11.69 [7.52;18.16]	0.38 [0.16;0.89]	0.025
Month 24: Number of lesions relative to Month 12 [95% CI]*	0.52 [0.30;0.89]	9.53 [4.94;18.42]	0.05 [0.02;0.13]	<.001

N': Number of patients in the analysis
RR: Rate ratio
*: Adjusted means obtained from repeated measures negative binomial regression including the following variables:
Treatment+Sex+Visit+Treatment*Sex+Treatment*Visit+Sex*Visit+Treatment*Visit*Sex+Age+BL Number of T1 Lesions

Table 9.2.4: Number of New or Enlarging T2 Lesions (FAS) by Previous MS DMT

	Treatment groups		Comparison	
	BAF312 (N=127)	**Placebo (N=61)**	**RR [95% CI]**	**p-value**
Interaction Test				<.001
Previous MS-DMT = N				
N'	20	16		
Month 12: Number of lesions relative to baseline [95% CI]*	1.91 [1.27;2.87]	16.39 [11.19;24.03]	0.12 [0.07;0.20]	<.001
Month 24: Number of lesions relative to Month 12 [95% CI]*	0.40 [0.12;1.34]	19.79 [12.53;31.28]	0.02 [0.01;0.07]	<.001
Previous MS-DMT = Y				
N'	99	40		
Month 12: Number of lesions relative to baseline [95% CI]*	3.57 [2.20;5.80]	6.96 [4.43;10.93]	0.51 [0.26;1.01]	0.052
Month 24: Number of lesions relative to Month 12 [95% CI]*	0.75 [0.30;1.86]	3.77 [2.16;6.59]	0.20 [0.07;0.57]	0.003

N': Number of patients in the analysis
RR: Rate ratio
*: Adjusted means obtained from repeated measures negative binomial regression including the following variables:
Treatment+DMT+Visit+Treatment*DMT+Treatment*Visit+DMT*Visit+Treatment*Visit*DMT+Age+BL Number of T1 Lesions

Table 9.2.5: Number of New or Enlarging T2 Lesions (FAS) by Previous IFN-beta-1b treatment

	Treatment groups		Comparison	
	BAF312 (N=127)	**Placebo (N=61)**	**RR [95% CI]**	**p-value**
Interaction Test				0.233
Previous IFN-beta 1b = N				
N'	77	45		
Month 12: Number of lesions relative to baseline [95% CI]*	3.51 [1.95;6.32]	10.07 [7.07;14.33]	0.35 [0.18;0.69]	0.003
Month 24: Number of lesions relative to Month 12 [95% CI]*	0.43 [0.27;0.69]	8.44 [5.10;13.96]	0.05 [0.03;0.10]	<.001
Previous IFN-beta 1b = Y				
N'	42	11		
Month 12: Number of lesions relative to baseline [95% CI]*	2.95 [1.65;5.28]	7.87 [4.39;14.09]	0.37 [0.17;0.85]	0.019
Month 24: Number of lesions relative to Month 12 [95% CI]*	1.29 [0.36;4.57]	6.98 [2.85;17.11]	0.18 [0.04;0.90]	0.036

N': Number of patients in the analysis
RR: Rate ratio
*: Adjusted means obtained from repeated measures negative binomial regression including the following variables:
Treatment+IFN+Visit+Treatment*IFN+Treatment*Visit+IFN*Visit+Treatment*Visit*IFN+Age+BL Number of T1 Lesions

Table 9.2.6: Number of New or Enlarging T2 Lesions (FAS) by Rapid Evolvement

	Treatment groups		Comparison	
	BAF312 (N=127)	**Placebo (N=61)**	**RR [95% CI]**	**p-value**
Interaction Test				0.822
Rapid evolvement = N				
N'	87	44		
Month 12: Number of lesions relative to baseline [95% CI]*	2.50 [1.74;3.58]	8.85 [6.00;13.06]	0.28 [0.16;0.48]	<.001
Month 24: Number of lesions relative to Month 12 [95% CI]*	0.74 [0.28;1.97]	8.28 [4.91;13.94]	0.09 [0.03;0.28]	<.001
Rapid evolvement = Y				
N'	32	12		
Month 12: Number of lesions relative to baseline [95% CI]*	5.73 [2.35;13.97]	12.59 [7.66;20.69]	0.45 [0.16;1.26]	0.128
Month 24: Number of lesions relative to Month 12 [95% CI]*	0.56 [0.30;1.05]	7.87 [4.11;15.07]	0.07 [0.03;0.17]	<.001

N': Number of patients in the analysis
RR: Rate ratio
*: Adjusted means obtained from repeated measures negative binomial regression including the following variables:
Treatment+RapEv+Visit+Treatment*RapEv+Treatment*Visit+RapEv*Visit+Treatment*Visit*RapEv+Age+BL Number of T1 Lesions

Table 9.2.7: Number of New or Enlarging T2 Lesions (FAS) by Disease Course

	Treatment groups		Comparison	
	BAF312 (N=127)	**Placebo (N=61)**	**RR [95% CI]**	**p-value**
Interaction Test				0.786
Moderate/severe disease course = N				
N'	17	10		
Month 12: Number of lesions relative to baseline [95% CI]*	1.81 [0.97;3.38]	5.75 [2.61;12.66]	0.32 [0.12;0.85]	0.023
Month 24: Number of lesions relative to Month 12 [95% CI]*	0.37 [0.17;0.82]	5.41 [2.25;13.04]	0.07 [0.02;0.22]	<.001
Moderate/severe disease course = Y				
N'	102	46		
Month 12: Number of lesions relative to baseline [95% CI]*	3.64 [2.26;5.87]	10.38 [7.45;14.46]	0.35 [0.19;0.63]	<.001
Month 24: Number of lesions relative to Month 12 [95% CI]*	0.72 [0.32;1.65]	8.69 [5.29;14.26]	0.08 [0.03;0.22]	<.001

N': Number of patients in the analysis
RR: Rate ratio
*: Adjusted means obtained from repeated measures negative binomial regression including the following variables:
Treatment+DC+Visit+Treatment*DC+Treatment*Visit+DC*Visit+Treatment*Visit*DC+Age+BL Number of T1 Lesions

Table 9.2.8: Number of New or Enlarging T2 Lesions (FAS) by Region

	Treatment groups		Comparison	
	BAF312 (N=127)	**Placebo (N=61)**	**RR [95% CI]**	**p-value**
Interaction Test				<.001
Region = Europe				
N'	101	48		
Month 12: Number of lesions relative to baseline [95% CI]*	2.35 [1.76;3.14]	9.57 [6.97;13.14]	0.25 [0.16;0.38]	<.001
Month 24: Number of lesions relative to Month 12 [95% CI]*	0.39 [0.25;0.61]	8.31 [5.15;13.43]	0.05 [0.02;0.09]	<.001
Region = Others				
N'	18	8		
Month 12: Number of lesions relative to baseline [95% CI]*	11.06 [4.00;30.58]	7.23 [2.80;18.64]	1.53 [0.38;6.08]	0.546
Month 24: Number of lesions relative to Month 12 [95% CI]*	4.64 [1.28;16.76]	5.86 [2.36;14.57]	0.79 [0.16;3.83]	0.771

N': Number of patients in the analysis
RR: Rate ratio
*: Adjusted means obtained from repeated measures negative binomial regression including the following variables:
Treatment+Region+Visit+Treatment*Region+Treatment*Visit+Region*Visit+Treatment*Visit*Region+Age+BL Number of T1 Lesions

Table 9.3.0: Number of T1 GD-enhancing Lesions (FAS), Return Rates

	Treatment groups		
	BAF312 (N=127)	**Placebo (N=61)**	**Total (N=188)**
Return Rate n (%)*			
Month 12	118 (92.9)	56 (91.8)	174 (92.6)
Month 24	80 (63.0)	33 (54.1)	113 (60.1)

* Number and percentage of patients with non-missing data at the given time point.

Table 9.3.1: Number of T1 Gd-enhancing Lesions (FAS)

	Treatment groups		Comparison	
	BAF312 (N=127)	**Placebo (N=61)**	**RR [95% CI]**	**p-value**
N'	119	56		
Month 12: Number of lesions [95% CI]*	0.27 [0.12;0.57]	1.76 [1.10;2.81]	0.15 [0.06;0.38]	<.001
Month 24: Number of lesions [95% CI]*	0.32 [0.10;1.05]	1.05 [0.67;1.65]	0.30 [0.08;1.10]	0.069

N': Number of patients in the analysis
RR: Rate ratio
*: Adjusted means obtained from repeated measures negative binomial regression including the following variables:
Treatment+Visit+Treatment*Visit+Age+BL Number of T1 Lesions

Table 9.3.2: Number of T1 Gd-enhancing Lesions (FAS) by Age

	Treatment groups		Comparison	
	BAF312 (N=127)	**Placebo (N=61)**	**RR [95% CI]**	**p-value**
Interaction Test				N.E.
Age = 18-40				
N'	17	11		
Month 12: Number of lesions [95% CI]*	0.18 [0.06;0.50]	3.73 [2.61;5.34]	0.05 [0.02;0.14]	<.001
Month 24: Number of lesions [95% CI]*	0.12 [0.01;1.52]	0.96 [0.41;2.26]	0.13 [0.01;1.84]	0.132
Age = 41-55				
N'	89	31		
Month 12: Number of lesions [95% CI]*	0.31 [0.13;0.71]	1.50 [0.59;3.84]	0.20 [0.06;0.73]	0.015
Month 24: Number of lesions [95% CI]*	0.39 [0.12;1.30]	1.15 [0.64;2.06]	0.34 [0.09;1.31]	0.118
Age = >55				
N'	13	14		

N': Number of patients in the analysis
RR: Rate ratio
*: Adjusted means obtained from repeated measures negative binomial regression including the following variables:
Treatment+Agegroup+Visit+Treatment*Agegroup+Treatment*Visit+Agegroup*Visit+Treatment*Visit*Agegroup+BL Number of T1 Lesions

Table 9.3.3: Number of T1 Gd-enhancing Lesions (FAS) by Gender

	Treatment groups		Comparison	
	BAF312 (N=127)	Placebo (N=61)	RR [95% CI]	p-value
Interaction Test				0.508
Sex = F				
N'	69	37		
Month 12: Number of lesions [95% CI]*	0.23 [0.10;0.55]	1.61 [0.87;2.97]	0.14 [0.05;0.43]	<.001
Month 24: Number of lesions [95% CI]*	0.47 [0.12;1.83]	1.19 [0.69;2.06]	0.40 [0.09;1.71]	0.215
Sex = M				
N'	50	19		
Month 12: Number of lesions [95% CI]*	0.30 [0.09;1.07]	2.02 [0.99;4.12]	0.15 [0.03;0.64]	0.010
Month 24: Number of lesions [95% CI]*	0.12 [0.03;0.45]	0.88 [0.38;2.05]	0.14 [0.03;0.66]	0.013

N': Number of patients in the analysis
RR: Rate ratio
*: Adjusted means obtained from repeated measures negative binomial regression including the following variables:
Treatment+Sex+Visit+Treatment*Sex+Treatment*Visit+Sex*Visit+Treatment*Visit*Sex+Age+BL Number of T1 Lesions

Table 9.3.4: Number of T1 Gd-enhancing Lesions (FAS) by Previous MS DMT

	Treatment groups		Comparison	
	BAF312 (N=127)	**Placebo (N=61)**	**RR [95% CI]**	**p-value**
Interaction Test				0.006
Previous MS-DMT = N				
N'	20	16		
Month 12: Number of lesions [95% CI]*	0.03 [0.01;0.19]	2.37 [1.07;5.23]	0.01 [0.00;0.09]	<.001
Month 24: Number of lesions [95% CI]*	0.25 [0.04;1.68]	2.44 [1.42;4.18]	0.10 [0.01;0.75]	0.025
Previous MS-DMT = Y				
N'	99	40		
Month 12: Number of lesions [95% CI]*	0.31 [0.14;0.68]	1.50 [0.85;2.64]	0.21 [0.08;0.56]	0.002
Month 24: Number of lesions [95% CI]*	0.33 [0.08;1.35]	0.56 [0.32;0.98]	0.58 [0.13;2.54]	0.474

N': Number of patients in the analysis
RR: Rate ratio
*: Adjusted means obtained from repeated measures negative binomial regression including the following variables:
Treatment+DMT+Visit+Treatment*DMT+Treatment*Visit+DMT*Visit+Treatment*Visit*DMT+Age+BL Number of T1 Lesions

Table 9.3.5: Number of T1 Gd-enhancing Lesions (FAS) by Previous IFN-beta-1b treatment

	Treatment groups		Comparison	
	BAF312 (N=127)	**Placebo (N=61)**	**RR [95% CI]**	**p-value**
Interaction Test				0.027
Previous IFN-beta 1b = N				
N'	77	45		
Month 12: Number of lesions [95% CI]*	0.24 [0.08;0.70]	1.88 [1.16;3.08]	0.13 [0.04;0.41]	<.001
Month 24: Number of lesions [95% CI]*	0.16 [0.06;0.41]	1.18 [0.72;1.94]	0.13 [0.04;0.38]	<.001
Previous IFN-beta 1b = Y				
N'	42	11		
Month 12: Number of lesions [95% CI]*	0.33 [0.11;1.01]	0.94 [0.29;3.03]	0.35 [0.07;1.75]	0.202
Month 24: Number of lesions [95% CI]*	0.69 [0.13;3.70]	0.44 [0.14;1.39]	1.58 [0.20;12.73]	0.668

N': Number of patients in the analysis
RR: Rate ratio
*: Adjusted means obtained from repeated measures negative binomial regression including the following variables:
Treatment+IFN+Visit+Treatment*IFN+Treatment*Visit+IFN*Visit+Treatment*Visit*IFN+Age+BL Number of T1 Lesions

Table 9.3.6: Number of T1 Gd-enhancing Lesions (FAS) by Rapid Evolvement

	Treatment groups		Comparison	
	BAF312 (N=127)	**Placebo (N=61)**	**RR [95% CI]**	**p-value**
Interaction Test				0.895
Rapid evolvement = N				
N'	87	44		
Month 12: Number of lesions [95% CI]*	0.17 [0.06;0.45]	1.78 [0.98;3.21]	0.10 [0.03;0.30]	<.001
Month 24: Number of lesions [95% CI]*	0.40 [0.10;1.53]	1.04 [0.59;1.81]	0.38 [0.08;1.73]	0.212
Rapid evolvement = Y				
N'	32	12		
Month 12: Number of lesions [95% CI]*	0.49 [0.16;1.51]	1.84 [0.95;3.59]	0.27 [0.07;0.98]	0.047
Month 24: Number of lesions [95% CI]*	0.14 [0.02;0.95]	1.27 [0.57;2.83]	0.11 [0.01;0.83]	0.032

N': Number of patients in the analysis
RR: Rate ratio
*: Adjusted means obtained from repeated measures negative binomial regression including the following variables:
Treatment+RapEv+Visit+Treatment*RapEv+Treatment*Visit+RapEv*Visit+Treatment*Visit*RapEv+Age+BL Number of T1 Lesions

Table 9.3.7: Number of T1 Gd-enhancing Lesions (FAS) by Disease Course

	Treatment groups		Comparison	
	BAF312 (N=127)	**Placebo (N=61)**	**RR [95% CI]**	**p-value**
Interaction Test				0.723
Moderate/severe disease course = N				
N'	17	10		
Month 12: Number of lesions [95% CI]*	0.13 [0.03;0.46]	0.92 [0.53;1.61]	0.14 [0.04;0.54]	0.004
Month 24: Number of lesions [95% CI]*	0.21 [0.03;1.29]	1.07 [0.31;3.69]	0.19 [0.02;1.71]	0.140
Moderate/severe disease course = Y				
N'	102	46		
Month 12: Number of lesions [95% CI]*	0.29 [0.13;0.66]	1.93 [1.16;3.19]	0.15 [0.06;0.41]	<.001
Month 24: Number of lesions [95% CI]*	0.33 [0.09;1.18]	1.03 [0.64;1.65]	0.32 [0.08;1.21]	0.094

N': Number of patients in the analysis
RR: Rate ratio
*: Adjusted means obtained from repeated measures negative binomial regression including the following variables:
Treatment+DC+Visit+Treatment*DC+Treatment*Visit+DC*Visit+Treatment*Visit*DC+Age+BL Number of T1 Lesions

Table 9.3.8: Number of T1 Gd-enhancing Lesions (FAS) by Region

	Treatment groups		Comparison	
	BAF312 (N=127)	**Placebo (N=61)**	**RR [95% CI]**	**p-value**
Interaction Test				<.001
Region = Europe				
N'	101	48		
Month 12: Number of lesions [95% CI]*	0.12 [0.07;0.22]	1.58 [0.98;2.54]	0.08 [0.04;0.16]	<.001
Month 24: Number of lesions [95% CI]*	0.11 [0.04;0.30]	0.97 [0.56;1.66]	0.11 [0.03;0.35]	<.001
Region = Others				
N'	18	8		
Month 12: Number of lesions [95% CI]*	1.57 [0.47;5.20]	1.91 [0.51;7.18]	0.82 [0.14;4.90]	0.830
Month 24: Number of lesions [95% CI]*	2.50 [0.52;11.99]	0.83 [0.35;1.99]	3.01 [0.50;18.24]	0.230

N': Number of patients in the analysis
RR: Rate ratio
*: Adjusted means obtained from repeated measures negative binomial regression including the following variables:
Treatment+Region+Visit+Treatment*Region+Treatment*Visit+Region*Visit+Treatment*Visit*Region+Age+BL Number of T1 Lesions

Table 9.4.0: Percent Brain Volume Change (FAS), Return Rates

	Treatment groups		
	BAF312 (N=127)	**Placebo (N=61)**	**Total (N=188)**
Return Rate n (%)*			
Month 12	105 (82.7)	50 (82.0)	155 (82.4)
Month 24	59 (46.5)	26 (42.6)	85 (45.2)
Month 36	8 (6.3)	3 (4.9)	11 (5.9)

* Number and percentage of patients with non-missing data at the given time point.

Table 9.4.1: Percent Brain Volume Change (FAS)

	Treatment groups		Comparison	
	BAF312 (N=127)	**Placebo (N=61)**	**Mean Difference [95% CI]**	**p-value**
N'	106	52		
Normalized Brain Volume at Baseline (SD)	1417.21 (89.02)	1418.54 (88.14)		
Month 12 Adjusted Mean Change (SE)	-0.41 (0.07)	-0.68 (0.09)	0.27 [0.07;0.47]	0.009
Month 24 Adjusted Mean Change (SE)	-0.87 (0.09)	-1.24 (0.13)	0.37 [0.08;0.66]	0.014

N': Number of patients in the analysis
Adjusted Mean Change calculated by MMRM model including the following variables: Treatment+Visit+Treatment*Visit+Country+SPMS Group+Age+BL Number of T1 Lesions+BLT2VOL+BL Normalized Brain Volume

Table 9.4.2: Percent Brain Volume Change (FAS) by Age

	Treatment groups		Comparison	
	BAF312 (N=127)	**Placebo (N=61)**	**Mean Difference [95% CI]**	**p-value**
Interaction Test				0.101
Age = 18-40				
N'	15	10		
Baseline Mean (SD)	1423.31 (113.86)	1468.03 (93.00)		
Month 12 Adjusted Mean Change (SE)	-0.64 (0.16)	-0.65 (0.20)	0.02 [-0.49;0.52]	0.951
Month 24 Adjusted Mean Change (SE)	-1.38 (0.25)	-1.00 (0.26)	-0.38 [-1.09;0.32]	0.283
Age = 41-55				
N'	80	29		
Baseline Mean (SD)	1420.34 (81.46)	1426.00 (85.23)		
Month 12 Adjusted Mean Change (SE)	-0.37 (0.09)	-0.78 (0.12)	0.41 [0.14;0.67]	0.003
Month 24 Adjusted Mean Change (SE)	-0.81 (0.11)	-1.42 (0.17)	0.60 [0.22;0.98]	0.002
Age = >55				
N'	11	13		
Baseline Mean (SD)	1386.16 (106.93)	1363.82 (64.52)		
Month 12 Adjusted Mean Change (SE)	-0.29 (0.24)	-0.40 (0.18)	0.12 [-0.47;0.70]	0.691
Month 24 Adjusted Mean Change (SE)	-0.66 (0.30)	-1.00 (0.24)	0.34 [-0.42;1.10]	0.384

N': Number of patients in the analysis
Adjusted Mean Change calculated by MMRM model including the following variables:
Treatment+Agegroup+Visit+Treatment*Agegroup+Treatment*Visit+Agegroup*Visit+Treatment*Visit*Agegroup+Country+SPMSGroup+BL Number of T1 Lesions+BLT2VOL+BL Normalized Brain Volume

Table 9.4.3: Percent Brain Volume Change (FAS) by Gender

	Treatment groups		Comparison	
	BAF312 (N=127)	**Placebo (N=61)**	**Mean Difference [95% CI]**	**p-value**
Interaction Test				0.852
Sex = F				
N'	60	33		
Baseline Mean (SD)	1411.26 (94.80)	1407.55 (89.70)		
Month 12 Adjusted Mean Change (SE)	-0.43 (0.10)	-0.70 (0.12)	0.27 [0.01;0.53]	0.044
Month 24 Adjusted Mean Change (SE)	-0.79 (0.13)	-1.21 (0.16)	0.42 [0.04;0.80]	0.029
Sex = M				
N'	46	19		
Baseline Mean (SD)	1424.98 (81.22)	1437.62 (84.28)		
Month 12 Adjusted Mean Change (SE)	-0.38 (0.10)	-0.65 (0.15)	0.27 [-0.06;0.60]	0.112
Month 24 Adjusted Mean Change (SE)	-0.96 (0.13)	-1.30 (0.21)	0.34 [-0.13;0.80]	0.157

N': Number of patients in the analysis
Adjusted Mean Change calculated by MMRM model including the following variables:
Treatment+Sex+Visit+Treatment*Sex+Treatment*Visit+Sex*Visit+Treatment*Visit*Sex+Country+SPMS Group+Age+BL Number of T1 Lesions+BL T2 VOL+BL Normalized Brain Volume

Table 9.4.4 Percent Brain Volume Change (FAS) by Previous MS DMT

	Treatment groups		Comparison	
	BAF312 (N=127)	**Placebo (N=61)**	**Mean Difference [95% CI]**	**p-value**
Interaction Test				0.149
Previous MS-DMT = N				
N'	19	15		
Baseline Mean (SD)	1452.96 (91.61)	1422.58 (70.90)		
Month 12 Adjusted Mean Change (SE)	-0.38 (0.15)	-0.67 (0.17)	0.30 [-0.11;0.70]	0.149
Month 24 Adjusted Mean Change (SE)	-0.79 (0.19)	-1.45 (0.23)	0.65 [0.09;1.22]	0.024
Previous MS-DMT = Y				
N'	87	37		
Baseline Mean (SD)	1409.41 (87.03)	1416.90 (95.09)		
Month 12 Adjusted Mean Change (SE)	-0.41 (0.08)	-0.68 (0.11)	0.26 [0.02;0.50]	0.031
Month 24 Adjusted Mean Change (SE)	-0.89 (0.10)	-1.15 (0.15)	0.26 [-0.09;0.60]	0.142

N': Number of patients in the analysis
Adjusted Mean Change calculated by MMRM model including the following variables:
Treatment+DMT+Visit+Treatment*DMT+Treatment*Visit+DMT*Visit+Treatment*Visit*DMT+Country+SPMSGroup+Age+BL Number of T1 Lesions+BLT2VOL+BL Normalized Brain Volume

Table 9.4.5 Percent Brain Volume Change (FAS) by Previous IFN-beta-1b treatment

	Treatment groups		Comparison	
	BAF312 (N=127)	**Placebo (N=61)**	**Mean Difference [95% CI]**	**p-value**
Interaction Test				0.619
Previous IFN-beta 1b = N				
N'	70	42		
Baseline Mean (SD)	1413.02 (97.38)	1408.69 (85.00)		
Month 12 Adjusted Mean Change (SE)	-0.43 (0.08)	-0.62 (0.10)	0.19 [-0.04;0.42]	0.104
Month 24 Adjusted Mean Change (SE)	-0.89 (0.11)	-1.24 (0.14)	0.34 [0.02;0.67]	0.040
Previous IFN-beta 1b = Y				
N'	36	10		
Baseline Mean (SD)	1425.36 (70.52)	1459.90 (93.62)		
Month 12 Adjusted Mean Change (SE)	-0.37 (0.11)	-0.93 (0.19)	0.55 [0.14;0.97]	0.009
Month 24 Adjusted Mean Change (SE)	-0.83 (0.15)	-1.09 (0.33)	0.26 [-0.45;0.96]	0.471

N': Number of patients in the analysis
Adjusted Mean Change calculated by MMRM model including the following variables:
Treatment+IFN+Visit+Treatment*IFN+Treatment*Visit+IFN*Visit+Treatment*Visit*IFN+Country+SPMS Group+Age+BL Number of T1 Lesions+BL T2 VOL+BL Normalized Brain Volume

Table 9.4.6 Percent Brain Volume Change (FAS) by Rapid Evolvement

	Treatment groups		Comparison	
	BAF312 (N=127)	**Placebo (N=61)**	**Mean Difference [95% CI]**	**p-value**
Interaction Test				0.345
Rapid evolvement = N				
N'	75	41		
Baseline Mean (SD)	1417.86 (91.92)	1416.68 (88.55)		
Month 12 Adjusted Mean Change (SE)	-0.38 (0.08)	-0.61 (0.10)	0.22 [-0.01;0.46]	0.056
Month 24 Adjusted Mean Change (SE)	-0.86 (0.11)	-1.15 (0.15)	0.29 [-0.05;0.62]	0.091
Rapid evolvement = Y				
N'	31	11		
Baseline Mean (SD)	1415.64 (82.99)	1425.47 (90.53)		
Month 12 Adjusted Mean Change (SE)	-0.46 (0.12)	-0.92 (0.19)	0.46 [0.04;0.88]	0.031
Month 24 Adjusted Mean Change (SE)	-0.90 (0.16)	-1.54 (0.26)	0.64 [0.05;1.23]	0.034

N': Number of patients in the analysis
Adjusted Mean Change calculated by MMRM model including the following variables:
Treatment+RapEv+Visit+Treatment*RapEv+Treatment*Visit+RapEv*Visit+Treatment*Visit*RapEv+Country+SPMS Group+Age+BL Number of T1 Lesions+BLT2VOL+BL Normalized Brain Volume

Table 9.4.7 Percent Brain Volume Change (FAS) by Disease Course

	Treatment groups		Comparison	
	BAF312 (N=127)	**Placebo (N=61)**	**Mean Difference [95% CI]**	**p-value**
Interaction Test				0.125
Moderate/severe disease course = N				
N'	17	10		
Baseline Mean (SD)	1402.86 (67.31)	1370.25 (64.91)		
Month 12 Adjusted Mean Change (SE)	-0.46 (0.15)	-0.33 (0.20)	-0.13 [-0.60;0.33]	0.576
Month 24 Adjusted Mean Change (SE)	-1.04 (0.23)	-0.66 (0.25)	-0.38 [-1.03;0.28]	0.257
Moderate/severe disease course = Y				
N'	89	42		
Baseline Mean (SD)	1419.95 (92.65)	1430.03 (89.64)		
Month 12 Adjusted Mean Change (SE)	-0.38 (0.08)	-0.75 (0.10)	0.36 [0.14;0.58]	0.001
Month 24 Adjusted Mean Change (SE)	-0.83 (0.10)	-1.40 (0.14)	0.57 [0.25;0.89]	<.001

N': Number of patients in the analysis
Adjusted Mean Change calculated by MMRM model including the following variables:
Treatment+DC+Visit+Treatment*DC+Treatment*Visit+DC*Visit+Treatment*Visit*DC+Country+SPMS Group+Age+BL Number of T1 Lesions+BL T2 VOL+BL Normalized Brain Volume

Table 9.4.8 Percent Brain Volume Change (FAS) by Region

	Treatment groups		Comparison	
	BAF312 (N=127)	**Placebo (N=61)**	**Mean Difference [95% CI]**	**p-value**
Interaction Test				0.761
Region = Europe				
N'	90	45		
Baseline Mean (SD)	1417.97 (87.08)	1411.46 (86.59)		
Month 12 Adjusted Mean Change (SE)	-0.42 (0.06)	-0.54 (0.09)	0.11 [-0.09;0.32]	0.277
Month 24 Adjusted Mean Change (SE)	-0.90 (0.09)	-1.19 (0.13)	0.30 [-0.02;0.61]	0.064
Region = Others				
N'	16	7		
Baseline Mean (SD)	1412.95 (102.22)	1464.00 (90.96)		
Month 12 Adjusted Mean Change (SE)	-0.51 (0.14)	-0.83 (0.22)	0.33 [-0.19;0.84]	0.210
Month 24 Adjusted Mean Change (SE)	-0.91 (0.24)	-0.93 (0.32)	0.03 [-0.76;0.82]	0.948

N': Number of patients in the analysis
Adjusted Mean Change calculated by MMRM model including the following variables:
Treatment+Region+Visit+Treatment*Region+Treatment*Visit+Region*Visit+Treatment*Visit*Region+SPMS Group+Age+BL Number of T1 Lesions+BL T2 VOL+BL Normalized Brain Volume

Table 10.1.0: MSIS-29 Physical Impact Scale (FAS), Return Rates

	Treatment groups		
	BAF312 (N=127)	**Placebo (N=61)**	**Total (N=188)**
Return Rate n (%)*			
Baseline	126 (99.2)	59 (96.7)	185 (98.4)
Month 06	117 (92.1)	56 (91.8)	173 (92.0)
Month 12	107 (84.3)	44 (72.1)	151 (80.3)
Month 18	81 (63.8)	29 (47.5)	110 (58.5)
Month 24	50 (39.4)	19 (31.1)	69 (36.7)
Month 30	20 (15.7)	9 (14.8)	29 (15.4)

* Number and percentage of patients with non-missing data at the given time point.

Table 10.1.1: MSIS-29 Physical Impact Scale (FAS), Change from Baseline

	Treatment groups		Comparison	
	BAF312 (N=127)	**Placebo (N=61)**	**Mean Difference [95% CI]**	**p-value**
N'	117	56		
Baseline Mean (SD)	52.15 (21.74)	53.61 (23.26)		
Month 06 Adjusted Mean Change (SE)	3.23 (2.32)	0.77 (2.98)		.
Month 12 Adjusted Mean Change (SE)	1.53 (2.28)	0.41 (3.00)	1.12 [-5.22;7.46]	0.727
Month 18 Adjusted Mean Change (SE)	7.29 (2.32)	4.65 (3.17)		.
Month 24 Adjusted Mean Change (SE)	7.25 (2.60)	-0.92 (3.65)	8.16 [0.17;16.16]	0.045
Month 30 Adjusted Mean Change (SE)	8.16 (3.29)	2.62 (4.67)		.

N': Number of patients in the analysis
Adjusted Mean Change calculated by MMRM model including the following variables: Treatment+Visit+Treatment*Visit+Country+BL Value

Table 10.1.2: MSIS-29 Physical Impact Scale (FAS), Change from Baseline by Age

	Treatment groups		Comparison	
	BAF312 (N=127)	**Placebo (N=61)**	**Mean Difference [95% CI]**	**p-value**
Interaction Test				0.490
Age = 18-40				
N'	16	12		
Baseline Mean (SD)	51.88 (18.70)	54.72 (27.94)		
Month 06 Adjusted Mean Change (SE)	3.91 (5.31)	3.33 (6.04)	.	.
Month 12 Adjusted Mean Change (SE)	-0.70 (5.08)	0.68 (6.17)	-1.38 [-17.08;14.32]	0.862
Month 18 Adjusted Mean Change (SE)	10.37 (5.04)	4.97 (5.99)	.	.
Month 24 Adjusted Mean Change (SE)	3.18 (6.14)	-1.50 (8.54)	4.67 [-16.10;25.44]	0.657
Month 30 Adjusted Mean Change (SE)	9.16 (9.45)	5.70 (9.97)	.	.
Age = 41-55				
N'	88	31		
Baseline Mean (SD)	50.91 (22.13)	54.27 (24.39)		
Month 06 Adjusted Mean Change (SE)	4.14 (2.78)	-1.76 (3.85)	.	.
Month 12 Adjusted Mean Change (SE)	3.17 (2.71)	-2.25 (3.90)	5.42 [-2.92;13.75]	0.201
Month 18 Adjusted Mean Change (SE)	6.40 (2.71)	3.32 (4.34)	.	.
Month 24 Adjusted Mean Change (SE)	8.76 (3.10)	-0.79 (4.73)	9.55 [-0.81;19.90]	0.070
Month 30 Adjusted Mean Change (SE)	9.38 (3.83)	-1.13 (6.46)	.	.

N': Number of patients in the analysis
Adjusted Mean Change calculated by MMRM model including the following variables:
Treatment+Agegroup+Visit+Treatment*Agegroup+Treatment*Visit+Agegroup*Visit+Treatment*Visit*Agegroup+Country+BL Value

Table 10.1.2: MSIS-29 Physical Impact Scale (FAS), Change from Baseline by Age

	Treatment groups		Comparison	
	BAF312 (N=127)	**Placebo (N=61)**	**Mean Difference [95% CI]**	**p-value**
Age = >55				
N'	13	13		
Baseline Mean (SD)	60.90 (22.04)	51.03 (16.38)		
Month 06 Adjusted Mean Change (SE)	-2.79 (6.92)	4.64 (5.80)	.	.
Month 12 Adjusted Mean Change (SE)	-6.60 (6.92)	6.24 (5.68)	-12.84 [-30.13;4.46]	0.145
Month 18 Adjusted Mean Change (SE)	12.74 (7.11)	8.62 (5.86)	.	.
Month 24 Adjusted Mean Change (SE)	3.07 (8.06)	-2.80 (7.68)	5.88 [-16.01;27.77]	0.596
Month 30 Adjusted Mean Change (SE)	-6.75 (13.26)	5.57 (9.84)	.	.

N': Number of patients in the analysis
Adjusted Mean Change calculated by MMRM model including the following variables:
Treatment+Agegroup+Visit+Treatment*Agegroup+Treatment*Visit+Agegroup*Visit+Treatment*Visit*Agegroup+Country+BL Value

Table 10.1.3: MSIS-29 Physical Impact Scale (FAS), Change from Baseline by Gender

	Treatment groups		Comparison	
	BAF312 (N=127)	Placebo (N=61)	Mean Difference [95% CI]	p-value
Interaction Test				0.423
Sex = F				
N'	67	34		
Baseline Mean (SD)	54.05 (22.62)	59.63 (22.28)		
Month 06 Adjusted Mean Change (SE)	2.59 (3.05)	1.19 (3.72)	.	.
Month 12 Adjusted Mean Change (SE)	0.23 (2.99)	1.50 (3.70)	-1.27 [-9.54;7.01]	0.762
Month 18 Adjusted Mean Change (SE)	6.46 (3.00)	4.90 (3.83)	.	.
Month 24 Adjusted Mean Change (SE)	7.17 (3.46)	-0.73 (4.34)	7.90 [-2.18;17.97]	0.123
Month 30 Adjusted Mean Change (SE)	4.85 (4.28)	4.27 (5.39)	.	.
Sex = M				
N'	50	22		
Baseline Mean (SD)	49.60 (20.44)	44.32 (22.09)		
Month 06 Adjusted Mean Change (SE)	3.58 (3.06)	-0.44 (4.68)	.	.
Month 12 Adjusted Mean Change (SE)	2.75 (2.97)	-2.06 (4.77)	4.81 [-5.60;15.22]	0.363
Month 18 Adjusted Mean Change (SE)	7.93 (3.17)	4.05 (5.53)	.	.
Month 24 Adjusted Mean Change (SE)	7.01 (3.50)	-1.32 (6.73)	8.33 [-6.22;22.88]	0.259
Month 30 Adjusted Mean Change (SE)	12.28 (4.80)	-3.00 (9.52)	.	.

N': Number of patients in the analysis
Adjusted Mean Change calculated by MMRM model including the following variables:
Treatment+Sex+Visit+Treatment*Sex+Treatment*Visit+Sex*Visit+Treatment*Visit*Sex+Country+BL Value

Table 10.1.4 MSIS-29 Physical Impact Scale (FAS), Change from Baseline by Previous MS DMT

	Treatment groups		Comparison	
	BAF312 (N=127)	**Placebo (N=61)**	**Mean Difference [95% CI]**	**p-value**
Interaction Test				0.565
Previous MS-DMT = N				
N'	20	17		
Baseline Mean (SD)	50.83 (24.34)	44.31 (22.79)		
Month 06 Adjusted Mean Change (SE)	4.48 (4.86)	0.97 (5.19)	.	.
Month 12 Adjusted Mean Change (SE)	1.00 (4.64)	-0.04 (5.10)	1.04 [-11.56;13.65]	0.870
Month 18 Adjusted Mean Change (SE)	10.11 (4.73)	3.76 (6.06)	.	.
Month 24 Adjusted Mean Change (SE)	9.66 (5.47)	-0.62 (7.27)	10.28 [-6.89;27.44]	0.238
Month 30 Adjusted Mean Change (SE)	8.19 (12.01)	-8.45 (12.96)	.	.
Previous MS-DMT = Y				
N'	97	39		
Baseline Mean (SD)	52.42 (21.29)	57.67 (22.56)		
Month 06 Adjusted Mean Change (SE)	3.01 (2.50)	0.78 (3.45)	.	.
Month 12 Adjusted Mean Change (SE)	1.71 (2.47)	0.74 (3.52)	0.98 [-6.69;8.64]	0.802
Month 18 Adjusted Mean Change (SE)	6.70 (2.50)	5.20 (3.65)	.	.
Month 24 Adjusted Mean Change (SE)	6.77 (2.82)	-0.85 (4.16)	7.62 [-1.68;16.93]	0.107
Month 30 Adjusted Mean Change (SE)	7.70 (3.48)	3.98 (5.13)	.	.

N': Number of patients in the analysis
Adjusted Mean Change calculated by MMRM model including the following variables:
Treatment+DMT+Visit+Treatment*DMT+Treatment*Visit+DMT*Visit+Treatment*Visit*DMT+Country+BL Value

Table 10.1.5 MSIS-29 Physical Impact Scale (FAS), Change from Baseline by Previous IFN-beta-1b treatment

	Treatment groups		Comparison	
	BAF312 (N=127)	**Placebo (N=61)**	**Mean Difference [95% CI]**	**p-value**
Interaction Test				0.692
Previous IFN-beta 1b = N				
N'	74	43		
Baseline Mean (SD)	52.73 (23.07)	50.98 (23.05)		
Month 06 Adjusted Mean Change (SE)	2.30 (2.71)	0.83 (3.33)	.	.
Month 12 Adjusted Mean Change (SE)	0.89 (2.64)	-0.64 (3.33)	1.53 [-6.00;9.06]	0.689
Month 18 Adjusted Mean Change (SE)	7.14 (2.68)	4.70 (3.54)	.	.
Month 24 Adjusted Mean Change (SE)	6.43 (3.08)	-4.18 (4.14)	10.61 [1.04;20.17]	0.030
Month 30 Adjusted Mean Change (SE)	7.59 (3.88)	1.47 (5.38)	.	.
Previous IFN-beta 1b = Y				
N'	43	13		
Baseline Mean (SD)	51.16 (19.46)	62.31 (22.66)		
Month 06 Adjusted Mean Change (SE)	5.16 (3.44)	0.97 (5.82)	.	.
Month 12 Adjusted Mean Change (SE)	2.99 (3.39)	4.58 (6.09)	-1.59 [-14.33;11.14]	0.805
Month 18 Adjusted Mean Change (SE)	7.80 (3.49)	4.81 (6.52)	.	.
Month 24 Adjusted Mean Change (SE)	8.84 (3.88)	8.64 (7.13)	0.20 [-14.98;15.39]	0.979
Month 30 Adjusted Mean Change (SE)	9.34 (6.04)	6.55 (9.99)	.	.

N': Number of patients in the analysis
Adjusted Mean Change calculated by MMRM model including the following variables:
Treatment+IFN+Visit+Treatment*IFN+Treatment*Visit+IFN*Visit+Treatment*Visit*IFN+Country+BL Value

Table 10.1.6 MSIS-29 Physical Impact Scale (FAS), Change from Baseline by Rapid Evolvement

	Treatment groups		Comparison	
	BAF312 (N=127)	**Placebo (N=61)**	**Mean Difference [95% CI]**	**p-value**
Interaction Test				0.168
Rapid evolvement = N				
N'	87	42		
Baseline Mean (SD)	54.90 (21.07)	54.02 (20.58)		
Month 06 Adjusted Mean Change (SE)	2.86 (2.55)	-2.18 (3.37)	.	.
Month 12 Adjusted Mean Change (SE)	1.09 (2.51)	-3.29 (3.33)	4.38 [-2.81;11.57]	0.231
Month 18 Adjusted Mean Change (SE)	7.09 (2.57)	4.12 (3.69)	.	.
Month 24 Adjusted Mean Change (SE)	6.70 (2.95)	-3.69 (4.17)	10.39 [1.08;19.70]	0.029
Month 30 Adjusted Mean Change (SE)	8.09 (3.83)	0.12 (5.25)	.	.
Rapid evolvement = Y				
N'	30	14		
Baseline Mean (SD)	44.17 (22.01)	52.38 (30.85)		
Month 06 Adjusted Mean Change (SE)	3.55 (3.98)	9.20 (5.53)	.	.
Month 12 Adjusted Mean Change (SE)	2.11 (3.78)	12.73 (5.92)	-10.63 [-23.96;2.71]	0.118
Month 18 Adjusted Mean Change (SE)	7.35 (3.97)	6.89 (5.91)	.	.
Month 24 Adjusted Mean Change (SE)	8.14 (4.50)	8.74 (7.60)	-0.61 [-17.72;16.51]	0.944
Month 30 Adjusted Mean Change (SE)	7.85 (6.31)	11.37 (12.42)	.	.

N': Number of patients in the analysis
Adjusted Mean Change calculated by MMRM model including the following variables:
Treatment+RapEv+Visit+Treatment*RapEv+Treatment*Visit+RapEv*Visit+Treatment*Visit*RapEv+Country+BL Value

Table 10.1.7 MSIS-29 Physical Impact Scale (FAS), Change from Baseline by Disease Course

	Treatment groups		Comparison	
	BAF312 (N=127)	**Placebo (N=61)**	**Mean Difference [95% CI]**	**p-value**
Interaction Test				0.866
Moderate/severe disease course = N				
N'	17	9		
Baseline Mean (SD)	41.86 (21.09)	38.70 (19.63)		
Month 06 Adjusted Mean Change (SE)	5.41 (5.24)	-2.84 (6.85)	.	.
Month 12 Adjusted Mean Change (SE)	0.82 (5.13)	-2.43 (6.72)	3.24 [-12.72;19.21]	0.688
Month 18 Adjusted Mean Change (SE)	6.71 (5.82)	3.41 (7.74)	.	.
Month 24 Adjusted Mean Change (SE)	1.52 (6.40)	0.13 (7.93)	1.38 [-18.16;20.92]	0.889
Month 30 Adjusted Mean Change (SE)	3.67 (7.58)	-4.92 (10.32)	.	.
Moderate/severe disease course = Y				
N'	100	47		
Baseline Mean (SD)	53.90 (21.46)	56.47 (22.98)		
Month 06 Adjusted Mean Change (SE)	2.79 (2.46)	1.43 (3.20)	.	.
Month 12 Adjusted Mean Change (SE)	1.57 (2.42)	0.98 (3.25)	0.59 [-6.46;7.64]	0.870
Month 18 Adjusted Mean Change (SE)	7.24 (2.43)	4.96 (3.42)	.	.
Month 24 Adjusted Mean Change (SE)	7.93 (2.75)	-1.45 (4.03)	9.38 [0.44;18.33]	0.040
Month 30 Adjusted Mean Change (SE)	8.94 (3.64)	4.76 (5.28)	.	.

N': Number of patients in the analysis
Adjusted Mean Change calculated by MMRM model including the following variables:
Treatment+DC+Visit+Treatment*DC+Treatment*Visit+DC*Visit+Treatment*Visit*DC+Country+BL Value

Table 10.1.8 MSIS-29 Physical Impact Scale (FAS), Change from Baseline by Region

	Treatment groups		Comparison	
	BAF312 (N=127)	Placebo (N=61)	Mean Difference [95% CI]	p-value
Interaction Test				0.861
Region = Europe				
N'	99	47		
Baseline Mean (SD)	50.89 (21.95)	51.64 (23.56)		
Month 06 Adjusted Mean Change (SE)	0.84 (1.92)	1.65 (2.78)	.	.
Month 12 Adjusted Mean Change (SE)	-0.11 (1.86)	2.08 (2.86)	-2.19 [-8.93;4.54]	0.521
Month 18 Adjusted Mean Change (SE)	5.36 (1.84)	3.75 (3.12)	.	.
Month 24 Adjusted Mean Change (SE)	6.03 (2.30)	-1.72 (4.00)	7.75 [-1.39;16.89]	0.096
Month 30 Adjusted Mean Change (SE)	7.40 (3.27)	1.36 (6.50)	.	.
Region = Others				
N'	18	9		
Baseline Mean (SD)	59.07 (19.66)	63.89 (19.67)		
Month 06 Adjusted Mean Change (SE)	7.63 (4.51)	-1.34 (6.38)	.	.
Month 12 Adjusted Mean Change (SE)	1.15 (4.76)	-3.71 (6.30)	4.86 [-10.68;20.40]	0.538
Month 18 Adjusted Mean Change (SE)	8.60 (4.96)	7.60 (6.00)	.	.
Month 24 Adjusted Mean Change (SE)	3.87 (6.07)	0.47 (6.86)	3.39 [-14.72;21.51]	0.711
Month 30 Adjusted Mean Change (SE)	5.33 (8.02)	4.41 (7.79)	.	.

N': Number of patients in the analysis
Adjusted Mean Change calculated by MMRM model including the following variables:
Treatment+Region+Visit+Treatment*Region+Treatment*Visit+Region*Visit+Treatment*Visit*Region+BL Value

Table 10.2.0: MSIS-29 Psychological Impact Scale (FAS), Return Rates

	Treatment groups		
	BAF312 (N=127)	**Placebo (N=61)**	**Total (N=188)**
Return Rate n (%)*			
Baseline	126 (99.2)	59 (96.7)	185 (98.4)
Month 06	116 (91.3)	55 (90.2)	171 (91.0)
Month 12	107 (84.3)	44 (72.1)	151 (80.3)
Month 18	81 (63.8)	29 (47.5)	110 (58.5)
Month 24	50 (39.4)	19 (31.1)	69 (36.7)
Month 30	20 (15.7)	9 (14.8)	29 (15.4)

* Number and percentage of patients with non-missing data at the given time point.

Table 10.2.1: MSIS-29 Psychological Impact Scale (FAS), Change from Baseline

	Treatment groups		Comparison	
	BAF312 (N=127)	**Placebo (N=61)**	**Mean Difference [95% CI]**	**p-value**
N'	117	55		
Baseline Mean (SD)	34.73 (21.90)	41.68 (24.26)		
Month 06 Adjusted Mean Change (SE)	2.22 (2.44)	-0.36 (3.20)		.
Month 12 Adjusted Mean Change (SE)	3.33 (2.39)	1.35 (3.21)	1.98 [-4.77;8.73]	0.563
Month 18 Adjusted Mean Change (SE)	5.85 (2.53)	4.69 (3.61)		.
Month 24 Adjusted Mean Change (SE)	7.51 (2.93)	-3.24 (4.25)	10.75 [1.34;20.16]	0.026
Month 30 Adjusted Mean Change (SE)	7.71 (3.77)	-2.13 (5.34)		.

N': Number of patients in the analysis
Adjusted Mean Change calculated by MMRM model including the following variables: Treatment+Visit+Treatment*Visit+Country+BL Value

Table 10.2.2: MSIS-29 Psychological Impact Scale (FAS), Change from Baseline by Age

	Treatment groups		Comparison	
	BAF312 (N=127)	Placebo (N=61)	Mean Difference [95% CI]	p-value
Interaction Test				0.777
Age = 18-40				
N'	16	11		
Baseline Mean (SD)	38.43 (19.50)	44.44 (25.55)		
Month 06 Adjusted Mean Change (SE)	0.41 (5.63)	-2.11 (6.74)	.	.
Month 12 Adjusted Mean Change (SE)	8.27 (5.29)	3.14 (6.62)	5.13 [-11.50;21.75]	0.543
Month 18 Adjusted Mean Change (SE)	11.53 (5.66)	-0.88 (6.89)	.	.
Month 24 Adjusted Mean Change (SE)	5.44 (6.98)	-11.33 (9.93)	16.77 [-7.20;40.74]	0.168
Month 30 Adjusted Mean Change (SE)	20.32 (11.44)	4.26 (11.51)	.	.
Age = 41-55				
N'	88	31		
Baseline Mean (SD)	33.63 (22.41)	41.70 (25.28)		
Month 06 Adjusted Mean Change (SE)	1.90 (2.94)	-1.56 (4.11)	.	.
Month 12 Adjusted Mean Change (SE)	1.49 (2.82)	-2.77 (4.14)	4.26 [-4.54;13.05]	0.340
Month 18 Adjusted Mean Change (SE)	3.42 (2.97)	8.68 (5.02)	.	.
Month 24 Adjusted Mean Change (SE)	7.40 (3.44)	-0.73 (5.45)	8.13 [-3.83;20.09]	0.180
Month 30 Adjusted Mean Change (SE)	4.60 (4.37)	-6.78 (7.45)	.	.

N': Number of patients in the analysis
Adjusted Mean Change calculated by MMRM model including the following variables:
Treatment+Agegroup+Visit+Treatment*Agegroup+Treatment*Visit+Agegroup*Visit+Treatment*Visit*Agegroup+Country+BL Value

Table 10.2.2: MSIS-29 Psychological Impact Scale (FAS), Change from Baseline by Age

	Treatment groups		Comparison	
	BAF312 (N=127)	**Placebo (N=61)**	**Mean Difference [95% CI]**	**p-value**
Age = >55				
N'	13	13		
Baseline Mean (SD)	37.61 (22.01)	39.32 (22.20)		
Month 06 Adjusted Mean Change (SE)	4.17 (7.21)	3.22 (6.16)	.	.
Month 12 Adjusted Mean Change (SE)	7.06 (7.14)	8.07 (5.97)	-1.01 [-18.91;16.89]	0.912
Month 18 Adjusted Mean Change (SE)	13.53 (7.85)	3.72 (6.68)	.	.
Month 24 Adjusted Mean Change (SE)	8.92 (8.99)	-4.59 (8.85)	13.52 [-11.28;38.31]	0.283
Month 30 Adjusted Mean Change (SE)	14.75 (16.28)	-0.26 (11.46)	.	.

N': Number of patients in the analysis
Adjusted Mean Change calculated by MMRM model including the following variables:
Treatment+Agegroup+Visit+Treatment*Agegroup+Treatment*Visit+Agegroup*Visit+Treatment*Visit*Agegroup+Country+BL Value

Table 10.2.3: MSIS-29 Psychological Impact Scale (FAS), Change from Baseline by Gender

	Treatment groups		Comparison	
	BAF312 (N=127)	Placebo (N=61)	Mean Difference [95% CI]	p-value
Interaction Test				0.388
Sex = F				
N'	67	34		
Baseline Mean (SD)	35.88 (22.53)	47.60 (23.64)		
Month 06 Adjusted Mean Change (SE)	2.28 (3.19)	-2.70 (3.96)	.	.
Month 12 Adjusted Mean Change (SE)	2.27 (3.11)	1.68 (3.93)	0.59 [-8.18;9.35]	0.895
Month 18 Adjusted Mean Change (SE)	5.05 (3.22)	6.64 (4.26)	.	.
Month 24 Adjusted Mean Change (SE)	7.29 (3.91)	-2.11 (5.04)	9.40 [-2.39;21.20]	0.117
Month 30 Adjusted Mean Change (SE)	-1.10 (4.42)	-3.10 (5.50)	.	.
Sex = M				
N'	50	21		
Baseline Mean (SD)	33.19 (21.15)	32.10 (22.60)		
Month 06 Adjusted Mean Change (SE)	2.20 (3.22)	2.96 (5.03)	.	.
Month 12 Adjusted Mean Change (SE)	4.77 (3.11)	0.28 (5.07)	4.49 [-6.58;15.57]	0.424
Month 18 Adjusted Mean Change (SE)	7.01 (3.48)	-0.81 (6.22)	.	.
Month 24 Adjusted Mean Change (SE)	7.96 (4.02)	-5.29 (7.95)	13.25 [-4.01;30.52]	0.131
Month 30 Adjusted Mean Change (SE)	17.30 (5.04)	-2.07 (9.57)	.	.

N': Number of patients in the analysis
Adjusted Mean Change calculated by MMRM model including the following variables:
Treatment+Sex+Visit+Treatment*Sex+Treatment*Visit+Sex*Visit+Treatment*Visit*Sex+Country+BL Value

Table 10.2.4 MSIS-29 Psychological Impact Scale (FAS), Change from Baseline by Previous MS DMT

	Treatment groups		Comparison	
	BAF312 (N=127)	**Placebo (N=61)**	**Mean Difference [95% CI]**	**p-value**
Interaction Test				0.869
Previous MS-DMT = N				
N'	20	17		
Baseline Mean (SD)	34.26 (22.89)	34.42 (25.92)		
Month 06 Adjusted Mean Change (SE)	4.27 (5.13)	-3.98 (5.45)	.	.
Month 12 Adjusted Mean Change (SE)	3.55 (4.84)	3.62 (5.34)	-0.07 [-13.27;13.13]	0.992
Month 18 Adjusted Mean Change (SE)	7.57 (5.25)	2.58 (6.86)	.	.
Month 24 Adjusted Mean Change (SE)	9.88 (6.31)	-4.59 (8.63)	14.47 [-5.96;34.91]	0.163
Month 30 Adjusted Mean Change (SE)	3.95 (15.27)	0.51 (15.52)	.	.
Previous MS-DMT = Y				
N'	97	38		
Baseline Mean (SD)	34.82 (21.81)	44.93 (23.09)		
Month 06 Adjusted Mean Change (SE)	1.70 (2.64)	1.24 (3.72)	.	.
Month 12 Adjusted Mean Change (SE)	3.21 (2.59)	0.00 (3.79)	3.21 [-4.98;11.40]	0.440
Month 18 Adjusted Mean Change (SE)	5.40 (2.75)	5.37 (4.16)	.	.
Month 24 Adjusted Mean Change (SE)	6.94 (3.20)	-2.93 (4.86)	9.87 [-1.06;20.80]	0.076
Month 30 Adjusted Mean Change (SE)	7.82 (4.01)	-2.94 (5.94)	.	.

N': Number of patients in the analysis
Adjusted Mean Change calculated by MMRM model including the following variables:
Treatment+DMT+Visit+Treatment*DMT+Treatment*Visit+DMT*Visit+Treatment*Visit*DMT+Country+BL Value

Table 10.2.5 MSIS-29 Psychological Impact Scale (FAS), Change from Baseline by Previous IFN-beta-1b treatment

	Treatment groups		Comparison	
	BAF312 (N=127)	**Placebo (N=61)**	**Mean Difference [95% CI]**	**p-value**
Interaction Test				0.390
Previous IFN-beta 1b = N				
N'	74	43		
Baseline Mean (SD)	35.94 (20.80)	40.91 (24.55)		
Month 06 Adjusted Mean Change (SE)	2.30 (2.84)	-1.70 (3.53)	.	.
Month 12 Adjusted Mean Change (SE)	3.27 (2.76)	2.41 (3.53)	0.87 [-7.06;8.79]	0.829
Month 18 Adjusted Mean Change (SE)	5.15 (2.93)	3.22 (4.00)	.	.
Month 24 Adjusted Mean Change (SE)	9.63 (3.44)	-6.88 (4.73)	16.51 [5.56;27.47]	0.003
Month 30 Adjusted Mean Change (SE)	9.20 (4.39)	-2.83 (6.12)	.	.
Previous IFN-beta 1b = Y				
N'	43	12		
Baseline Mean (SD)	32.64 (23.79)	44.44 (24.00)		
Month 06 Adjusted Mean Change (SE)	2.80 (3.64)	5.17 (6.34)	.	.
Month 12 Adjusted Mean Change (SE)	4.18 (3.56)	-2.41 (6.54)	6.58 [-7.09;20.25]	0.343
Month 18 Adjusted Mean Change (SE)	8.01 (3.87)	10.16 (7.44)	.	.
Month 24 Adjusted Mean Change (SE)	5.23 (4.35)	7.67 (8.13)	-2.44 [-19.89;15.02]	0.782
Month 30 Adjusted Mean Change (SE)	4.38 (7.12)	-0.24 (11.55)	.	.

N': Number of patients in the analysis
Adjusted Mean Change calculated by MMRM model including the following variables:
Treatment+IFN+Visit+Treatment*IFN+Treatment*Visit+IFN*Visit+Treatment*Visit*IFN+Country+BL Value

Table 10.2.6 MSIS-29 Psychological Impact Scale (FAS), Change from Baseline by Rapid Evolvement

	Treatment groups		Comparison	
	BAF312 (N=127)	**Placebo (N=61)**	**Mean Difference [95% CI]**	**p-value**
Interaction Test				0.143
Rapid evolvement = N				
N'	87	41		
Baseline Mean (SD)	35.63 (21.44)	41.82 (22.27)		
Month 06 Adjusted Mean Change (SE)	2.46 (2.70)	-2.44 (3.66)	.	.
Month 12 Adjusted Mean Change (SE)	3.78 (2.64)	-1.59 (3.60)	5.36 [-2.34;13.07]	0.171
Month 18 Adjusted Mean Change (SE)	4.07 (2.80)	3.32 (4.17)	.	.
Month 24 Adjusted Mean Change (SE)	6.87 (3.32)	-6.74 (4.84)	13.61 [2.74;24.48]	0.015
Month 30 Adjusted Mean Change (SE)	8.04 (4.35)	-5.68 (5.88)	.	.
Rapid evolvement = Y				
N'	30	14		
Baseline Mean (SD)	32.10 (23.35)	41.27 (30.29)		
Month 06 Adjusted Mean Change (SE)	0.58 (4.21)	4.75 (5.87)	.	.
Month 12 Adjusted Mean Change (SE)	1.32 (3.95)	10.73 (6.35)	-9.42 [-23.70;4.87]	0.195
Month 18 Adjusted Mean Change (SE)	10.15 (4.35)	8.56 (6.65)	.	.
Month 24 Adjusted Mean Change (SE)	8.44 (5.12)	8.24 (8.79)	0.19 [-19.65;20.03]	0.985
Month 30 Adjusted Mean Change (SE)	6.16 (7.25)	13.61 (14.95)	.	.

N': Number of patients in the analysis
Adjusted Mean Change calculated by MMRM model including the following variables:
Treatment+RapEv+Visit+Treatment*RapEv+Treatment*Visit+RapEv*Visit+Treatment*Visit*RapEv+Country+BL Value

Table 10.2.7 MSIS-29 Psychological Impact Scale (FAS), Change from Baseline by Disease Course

	Treatment groups		Comparison	
	BAF312 (N=127)	**Placebo (N=61)**	**Mean Difference [95% CI]**	**p-value**
Interaction Test				0.522
Moderate/severe disease course = N				
N'	17	9		
Baseline Mean (SD)	36.38 (29.14)	37.04 (24.43)		
Month 06 Adjusted Mean Change (SE)	2.05 (5.43)	-9.78 (7.17)	.	.
Month 12 Adjusted Mean Change (SE)	6.04 (5.30)	2.72 (7.00)	3.31 [-13.41;20.04]	0.696
Month 18 Adjusted Mean Change (SE)	8.82 (6.50)	5.19 (8.80)	.	.
Month 24 Adjusted Mean Change (SE)	8.16 (7.45)	0.83 (9.24)	7.33 [-15.74;30.41]	0.529
Month 30 Adjusted Mean Change (SE)	17.26 (8.09)	-5.45 (11.22)	.	.
Moderate/severe disease course = Y				
N'	100	46		
Baseline Mean (SD)	34.44 (20.59)	42.59 (24.39)		
Month 06 Adjusted Mean Change (SE)	2.36 (2.57)	1.60 (3.43)	.	.
Month 12 Adjusted Mean Change (SE)	2.99 (2.51)	1.11 (3.48)	1.89 [-5.62;9.39]	0.620
Month 18 Adjusted Mean Change (SE)	5.55 (2.64)	4.72 (3.89)	.	.
Month 24 Adjusted Mean Change (SE)	7.45 (3.10)	-4.21 (4.74)	11.66 [1.08;22.24]	0.031
Month 30 Adjusted Mean Change (SE)	4.76 (4.14)	-1.59 (5.93)	.	.

N': Number of patients in the analysis
Adjusted Mean Change calculated by MMRM model including the following variables:
Treatment+DC+Visit+Treatment*DC+Treatment*Visit+DC*Visit+Treatment*Visit*DC+Country+BL Value

Table 10.2.8 MSIS-29 Psychological Impact Scale (FAS), Change from Baseline by Region

	Treatment groups		Comparison	
	BAF312 (N=127)	Placebo (N=61)	Mean Difference [95% CI]	p-value
Interaction Test				0.412
Region = Europe				
N'	99	47		
Baseline Mean (SD)	33.11 (21.86)	40.03 (24.21)		
Month 06 Adjusted Mean Change (SE)	-0.81 (2.00)	-2.41 (2.88)	.	.
Month 12 Adjusted Mean Change (SE)	1.80 (1.95)	0.57 (3.04)	1.23 [-5.93;8.38]	0.736
Month 18 Adjusted Mean Change (SE)	4.61 (2.08)	5.31 (3.57)	.	.
Month 24 Adjusted Mean Change (SE)	6.77 (2.63)	-6.56 (4.64)	13.34 [2.73;23.94]	0.014
Month 30 Adjusted Mean Change (SE)	8.86 (3.81)	-11.19 (7.88)	.	.
Region = Others				
N'	18	8		
Baseline Mean (SD)	43.62 (20.47)	51.39 (23.71)		
Month 06 Adjusted Mean Change (SE)	7.63 (4.66)	3.74 (7.01)	.	.
Month 12 Adjusted Mean Change (SE)	-0.29 (5.05)	-0.43 (6.73)	0.14 [-16.39;16.67]	0.986
Month 18 Adjusted Mean Change (SE)	0.04 (5.69)	-1.89 (6.84)	.	.
Month 24 Adjusted Mean Change (SE)	-2.65 (7.01)	-2.16 (7.78)	-0.49 [-21.23;20.24]	0.963
Month 30 Adjusted Mean Change (SE)	-5.99 (9.16)	-2.93 (8.34)	.	.

N': Number of patients in the analysis
Adjusted Mean Change calculated by MMRM model including the following variables:
Treatment+Region+Visit+Treatment*Region+Treatment*Visit+Region*Visit+Treatment*Visit*Region+BL Value

Table 10.3.0: EQ-5D Utility Score (FAS), Return Rates

	Treatment groups		
	BAF312 (N=127)	**Placebo (N=61)**	**Total (N=188)**
Return Rate n (%)*			
Baseline	127 (100.0)	61 (100.0)	188 (100.0)
Month 06	118 (92.9)	57 (93.4)	175 (93.1)
Month 12	107 (84.3)	47 (77.0)	154 (81.9)
Month 18	81 (63.8)	31 (50.8)	112 (59.6)
Month 24	40 (31.5)	16 (26.2)	56 (29.8)
Month 30	14 (11.0)	3 (4.9)	17 (9.0)

* Number and percentage of patients with non-missing data at the given time point.

Table 10.3.1: EQ-5D Utility Score (FAS), Change from Baseline

	Treatment groups		Comparison	
	BAF312 (N=127)	**Placebo (N=61)**	**Mean Difference [95% CI]**	**p-value**
N'	118	58		
Baseline Mean (SD)	0.62 (0.24)	0.59 (0.27)		
Month 06 Adjusted Mean Change (SE)	-0.03 (0.02)	-0.03 (0.03)		.
Month 12 Adjusted Mean Change (SE)	-0.01 (0.02)	-0.06 (0.03)	0.04 [-0.02;0.11]	0.188
Month 18 Adjusted Mean Change (SE)	-0.04 (0.02)	-0.06 (0.04)		.
Month 24 Adjusted Mean Change (SE)	-0.05 (0.03)	-0.10 (0.05)	0.05 [-0.07;0.17]	0.413
Month 30 Adjusted Mean Change (SE)	-0.04 (0.03)	-0.03 (0.08)		.

N': Number of patients in the analysis
Adjusted Mean Change calculated by MMRM model including the following variables: Treatment+Visit+Treatment*Visit+BL Value

Table 10.3.2: EQ-5D Utility Score (FAS), Change from Baseline by Age

	Treatment groups		Comparison	
	BAF312 (N=127)	Placebo (N=61)	Mean Difference [95% CI]	p-value
Interaction Test				0.743
Age = 18-40				
N'	16	13		
Baseline Mean (SD)	0.63 (0.12)	0.59 (0.31)		
Month 06 Adjusted Mean Change (SE)	-0.02 (0.05)	-0.09 (0.06)	.	.
Month 12 Adjusted Mean Change (SE)	-0.02 (0.05)	-0.07 (0.06)	0.05 [-0.11;0.21]	0.526
Month 18 Adjusted Mean Change (SE)	-0.16 (0.06)	-0.19 (0.07)	.	.
Month 24 Adjusted Mean Change (SE)	-0.16 (0.09)	-0.14 (0.12)	-0.02 [-0.32;0.28]	0.890
Age = 41-55				
N'	89	31		
Baseline Mean (SD)	0.63 (0.24)	0.58 (0.26)		
Month 06 Adjusted Mean Change (SE)	-0.02 (0.02)	0.00 (0.04)	.	.
Month 12 Adjusted Mean Change (SE)	-0.02 (0.02)	-0.07 (0.04)	0.05 [-0.04;0.14]	0.259
Month 18 Adjusted Mean Change (SE)	-0.01 (0.03)	0.01 (0.05)	.	.
Month 24 Adjusted Mean Change (SE)	-0.04 (0.04)	-0.12 (0.07)	0.09 [-0.07;0.24]	0.277
Month 30 Adjusted Mean Change (SE)	-0.02 (0.04)	-0.13 (0.10)	.	.

N': Number of patients in the analysis
Adjusted Mean Change calculated by MMRM model including the following variables:
Treatment+Agegroup+Visit+Treatment*Agegroup+Treatment*Visit+Agegroup*Visit+Treatment*Visit*Agegroup+BL Value

Table 10.3.2: EQ-5D Utility Score (FAS), Change from Baseline by Age

	Treatment groups		Comparison	
	BAF312 (N=127)	**Placebo (N=61)**	**Mean Difference [95% CI]**	**p-value**
Age = >55				
N'	13	14		
Baseline Mean (SD)	0.57 (0.32)	0.60 (0.28)		
Month 06 Adjusted Mean Change (SE)	-0.04 (0.06)	-0.03 (0.06)	.	.
Month 12 Adjusted Mean Change (SE)	0.05 (0.06)	-0.02 (0.05)	0.07 [-0.09;0.23]	0.380
Month 18 Adjusted Mean Change (SE)	-0.10 (0.08)	-0.02 (0.07)	.	.
Month 24 Adjusted Mean Change (SE)	-0.01 (0.09)	-0.02 (0.10)	0.00 [-0.28;0.28]	0.995
Month 30 Adjusted Mean Change (SE)	-0.06 (0.14)	0.07 (0.14)	.	.

N': Number of patients in the analysis
Adjusted Mean Change calculated by MMRM model including the following variables:
Treatment+Agegroup+Visit+Treatment*Agegroup+Treatment*Visit+Agegroup*Visit+Treatment*Visit*Agegroup+BL Value

Table 10.3.3: EQ-5D Utility Score (FAS), Change from Baseline by Gender

	Treatment groups		Comparison	
	BAF312 (N=127)	Placebo (N=61)	Mean Difference [95% CI]	p-value
Interaction Test				0.425
Sex = F				
N'	68	36		
Baseline Mean (SD)	0.60 (0.25)	0.54 (0.28)		
Month 06 Adjusted Mean Change (SE)	-0.03 (0.02)	-0.03 (0.03)	.	.
Month 12 Adjusted Mean Change (SE)	0.00 (0.02)	-0.09 (0.03)	0.09 [0.01;0.18]	0.030
Month 18 Adjusted Mean Change (SE)	-0.04 (0.03)	-0.10 (0.04)	.	.
Month 24 Adjusted Mean Change (SE)	-0.06 (0.04)	-0.13 (0.06)	0.07 [-0.08;0.22]	0.343
Month 30 Adjusted Mean Change (SE)	-0.03 (0.05)	-0.08 (0.10)	.	.
Sex = M				
N'	50	22		
Baseline Mean (SD)	0.65 (0.22)	0.66 (0.25)		
Month 06 Adjusted Mean Change (SE)	-0.02 (0.03)	-0.04 (0.04)	.	.
Month 12 Adjusted Mean Change (SE)	-0.02 (0.03)	0.01 (0.05)	-0.04 [-0.15;0.07]	0.497
Month 18 Adjusted Mean Change (SE)	-0.03 (0.04)	0.04 (0.07)	.	.
Month 24 Adjusted Mean Change (SE)	-0.04 (0.05)	-0.04 (0.10)	0.00 [-0.22;0.22]	0.994
Month 30 Adjusted Mean Change (SE)	-0.07 (0.06)	-0.10 (0.19)	.	.

N': Number of patients in the analysis
Adjusted Mean Change calculated by MMRM model including the following variables:
Treatment+Sex+Visit+Treatment*Sex+Treatment*Visit+Sex*Visit+Treatment*Visit*Sex+BL Value

Table 10.3.4 EQ-5D Utility Score (FAS), Change from Baseline by Previous MS DMT

	Treatment groups		Comparison	
	BAF312 (N=127)	Placebo (N=61)	Mean Difference [95% CI]	p-value
Interaction Test				0.947
Previous MS-DMT = N				
N'	20	17		
Baseline Mean (SD)	0.56 (0.32)	0.66 (0.24)		
Month 06 Adjusted Mean Change (SE)	-0.04 (0.05)	0.00 (0.05)	.	.
Month 12 Adjusted Mean Change (SE)	0.03 (0.04)	0.01 (0.05)	0.02 [-0.11;0.15]	0.771
Month 18 Adjusted Mean Change (SE)	-0.05 (0.06)	0.08 (0.07)	.	.
Month 24 Adjusted Mean Change (SE)	0.00 (0.08)	-0.17 (0.11)	0.17 [-0.10;0.44]	0.215
Month 30 Adjusted Mean Change (SE)	0.00 (0.13)	-0.13 (0.18)	.	.
Previous MS-DMT = Y				
N'	98	41		
Baseline Mean (SD)	0.63 (0.22)	0.56 (0.28)		
Month 06 Adjusted Mean Change (SE)	-0.02 (0.02)	-0.04 (0.03)	.	.
Month 12 Adjusted Mean Change (SE)	-0.02 (0.02)	-0.09 (0.03)	0.07 [-0.01;0.15]	0.093
Month 18 Adjusted Mean Change (SE)	-0.04 (0.03)	-0.10 (0.04)	.	.
Month 24 Adjusted Mean Change (SE)	-0.06 (0.04)	-0.09 (0.06)	0.03 [-0.10;0.17]	0.623
Month 30 Adjusted Mean Change (SE)	-0.04 (0.04)	-0.05 (0.09)	.	.

N': Number of patients in the analysis
Adjusted Mean Change calculated by MMRM model including the following variables:
Treatment+DMT+Visit+Treatment*DMT+Treatment*Visit+DMT*Visit+Treatment*Visit*DMT+BL Value

Table 10.3.5 EQ-5D Utility Score (FAS), Change from Baseline by Previous IFN-beta-1b treatment

	Treatment groups		Comparison	
	BAF312 (N=127)	**Placebo (N=61)**	**Mean Difference [95% CI]**	**p-value**
Interaction Test				0.207
Previous IFN-beta 1b = N				
N'	75	45		
Baseline Mean (SD)	0.62 (0.26)	0.59 (0.29)		
Month 06 Adjusted Mean Change (SE)	-0.03 (0.02)	-0.01 (0.03)	.	.
Month 12 Adjusted Mean Change (SE)	-0.01 (0.02)	-0.04 (0.03)	0.03 [-0.05;0.11]	0.452
Month 18 Adjusted Mean Change (SE)	-0.05 (0.03)	-0.06 (0.04)	.	.
Month 24 Adjusted Mean Change (SE)	-0.07 (0.04)	-0.08 (0.06)	0.01 [-0.13;0.15]	0.883
Month 30 Adjusted Mean Change (SE)	-0.04 (0.04)	-0.02 (0.08)	.	.
Previous IFN-beta 1b = Y				
N'	43	13		
Baseline Mean (SD)	0.62 (0.20)	0.56 (0.21)		
Month 06 Adjusted Mean Change (SE)	-0.01 (0.03)	-0.10 (0.06)	.	.
Month 12 Adjusted Mean Change (SE)	-0.02 (0.03)	-0.13 (0.06)	0.11 [-0.03;0.25]	0.121
Month 18 Adjusted Mean Change (SE)	-0.02 (0.04)	-0.06 (0.08)	.	.
Month 24 Adjusted Mean Change (SE)	-0.02 (0.05)	-0.18 (0.12)	0.16 [-0.10;0.41]	0.221

N': Number of patients in the analysis
Adjusted Mean Change calculated by MMRM model including the following variables:
Treatment+IFN+Visit+Treatment*IFN+Treatment*Visit+IFN*Visit+Treatment*Visit*IFN+BL Value

Table 10.3.6 EQ-5D Utility Score (FAS), Change from Baseline by Rapid Evolvement

	Treatment groups		Comparison	
	BAF312 (N=127)	**Placebo (N=61)**	**Mean Difference [95% CI]**	**p-value**
Interaction Test				0.037
Rapid evolvement = N				
N'	88	44		
Baseline Mean (SD)	0.60 (0.24)	0.61 (0.24)		
Month 06 Adjusted Mean Change (SE)	-0.03 (0.02)	-0.01 (0.03)	.	.
Month 12 Adjusted Mean Change (SE)	-0.01 (0.02)	-0.04 (0.03)	0.03 [-0.04;0.11]	0.381
Month 18 Adjusted Mean Change (SE)	-0.05 (0.03)	-0.03 (0.04)	.	.
Month 24 Adjusted Mean Change (SE)	-0.06 (0.04)	-0.04 (0.06)	-0.02 [-0.16;0.11]	0.744
Month 30 Adjusted Mean Change (SE)	-0.07 (0.04)	0.01 (0.08)	.	.
Rapid evolvement = Y				
N'	30	14		
Baseline Mean (SD)	0.68 (0.22)	0.52 (0.35)		
Month 06 Adjusted Mean Change (SE)	-0.01 (0.04)	-0.08 (0.06)	.	.
Month 12 Adjusted Mean Change (SE)	-0.02 (0.04)	-0.11 (0.06)	0.09 [-0.05;0.24]	0.203
Month 18 Adjusted Mean Change (SE)	-0.01 (0.05)	-0.16 (0.07)	.	.
Month 24 Adjusted Mean Change (SE)	0.00 (0.06)	-0.28 (0.10)	0.27 [0.04;0.51]	0.024

N': Number of patients in the analysis
Adjusted Mean Change calculated by MMRM model including the following variables:
Treatment+RapEv+Visit+Treatment*RapEv+Treatment*Visit+RapEv*Visit+Treatment*Visit*RapEv+BL Value

Table 10.3.7 EQ-5D Utility Score (FAS), Change from Baseline by Disease Course

	Treatment groups		Comparison	
	BAF312 (N=127)	Placebo (N=61)	Mean Difference [95% CI]	p-value
Interaction Test				0.441
Moderate/severe disease course = N				
N'	17	10		
Baseline Mean (SD)	0.71 (0.21)	0.74 (0.14)		
Month 06 Adjusted Mean Change (SE)	-0.04 (0.05)	0.02 (0.07)	.	.
Month 12 Adjusted Mean Change (SE)	-0.03 (0.05)	0.00 (0.07)	-0.03 [-0.19;0.13]	0.732
Month 18 Adjusted Mean Change (SE)	-0.03 (0.07)	-0.06 (0.09)	.	.
Month 24 Adjusted Mean Change (SE)	-0.08 (0.08)	-0.12 (0.10)	0.04 [-0.23;0.30]	0.794
Month 30 Adjusted Mean Change (SE)	-0.04 (0.08)	0.00 (0.10)	.	.
Moderate/severe disease course = Y				
N'	101	48		
Baseline Mean (SD)	0.61 (0.24)	0.55 (0.28)		
Month 06 Adjusted Mean Change (SE)	-0.02 (0.02)	-0.04 (0.03)	.	.
Month 12 Adjusted Mean Change (SE)	-0.01 (0.02)	-0.07 (0.03)	0.06 [-0.01;0.13]	0.107
Month 18 Adjusted Mean Change (SE)	-0.04 (0.02)	-0.06 (0.04)	.	.
Month 24 Adjusted Mean Change (SE)	-0.04 (0.04)	-0.09 (0.06)	0.04 [-0.09;0.18]	0.519
Month 30 Adjusted Mean Change (SE)	-0.04 (0.04)	-0.18 (0.13)	.	.

N': Number of patients in the analysis
Adjusted Mean Change calculated by MMRM model including the following variables:
Treatment+DC+Visit+Treatment*DC+Treatment*Visit+DC*Visit+Treatment*Visit*DC+BL Value

Table 10.3.8 EQ-5D Utility Score (FAS), Change from Baseline by Region

	Treatment groups		Comparison	
	BAF312 (N=127)	Placebo (N=61)	Mean Difference [95% CI]	p-value
Interaction Test				0.423
Region = Europe				
N'	100	49		
Baseline Mean (SD)	0.64 (0.21)	0.62 (0.26)		
Month 06 Adjusted Mean Change (SE)	0.00 (0.02)	-0.03 (0.03)	.	.
Month 12 Adjusted Mean Change (SE)	-0.02 (0.02)	-0.06 (0.03)	0.04 [-0.03;0.11]	0.291
Month 18 Adjusted Mean Change (SE)	-0.03 (0.02)	-0.04 (0.04)	.	.
Month 24 Adjusted Mean Change (SE)	-0.04 (0.04)	-0.10 (0.06)	0.06 [-0.08;0.21]	0.378
Month 30 Adjusted Mean Change (SE)	-0.03 (0.04)	-0.14 (0.10)	.	.
Region = Others				
N'	18	9		
Baseline Mean (SD)	0.50 (0.32)	0.43 (0.32)		
Month 06 Adjusted Mean Change (SE)	-0.15 (0.05)	-0.03 (0.07)	.	.
Month 12 Adjusted Mean Change (SE)	0.05 (0.05)	-0.06 (0.07)	0.11 [-0.06;0.28]	0.212
Month 18 Adjusted Mean Change (SE)	-0.10 (0.07)	-0.11 (0.08)	.	.
Month 24 Adjusted Mean Change (SE)	-0.09 (0.08)	-0.10 (0.09)	0.00 [-0.24;0.25]	0.971
Month 30 Adjusted Mean Change (SE)	-0.08 (0.13)	0.02 (0.13)	.	.

N': Number of patients in the analysis
Adjusted Mean Change calculated by MMRM model including the following variables:
Treatment+Region+Visit+Treatment*Region+Treatment*Visit+Region*Visit+Treatment*Visit*Region+BL Value

Table 10.4.0: EQ-5D VAS Thermometer (FAS), Return Rates

	Treatment groups		
	BAF312 (N=127)	**Placebo (N=61)**	**Total (N=188)**
Return Rate n (%)*			
Baseline	125 (98.4)	61 (100.0)	186 (98.9)
Month 06	117 (92.1)	57 (93.4)	174 (92.6)
Month 12	106 (83.5)	47 (77.0)	153 (81.4)
Month 18	82 (64.6)	31 (50.8)	113 (60.1)
Month 24	40 (31.5)	16 (26.2)	56 (29.8)
Month 30	14 (11.0)	3 (4.9)	17 (9.0)

* Number and percentage of patients with non-missing data at the given time point.

Table 10.4.1: EQ-5D VAS Thermometer (FAS), Change from Baseline

	Treatment groups		Comparison	
	BAF312 (N=127)	**Placebo (N=61)**	**Mean Difference [95% CI]**	**p-value**
N'	117	58		
Baseline Mean (SD)	58.76 (18.96)	56.52 (20.22)		
Month 06 Adjusted Mean Change (SE)	-1.93 (1.67)	1.96 (2.38)		.
Month 12 Adjusted Mean Change (SE)	-2.27 (1.68)	-0.16 (2.48)	-2.11 [-8.02;3.80]	0.482
Month 18 Adjusted Mean Change (SE)	-4.27 (1.85)	-1.29 (2.93)		.
Month 24 Adjusted Mean Change (SE)	-6.01 (2.27)	-1.68 (3.49)	-4.33 [-12.61;3.96]	0.302
Month 30 Adjusted Mean Change (SE)	-1.16 (3.65)	0.14 (7.81)		.

N': Number of patients in the analysis
Adjusted Mean Change calculated by MMRM model including the following variables: Treatment+Visit+Treatment*Visit+BL Value

Table 10.4.2: EQ-5D VAS Thermometer (FAS), Change from Baseline by Age

	Treatment groups		Comparison	
	BAF312 (N=127)	Placebo (N=61)	Mean Difference [95% CI]	p-value
Interaction Test				0.789
Age = 18-40				
N'	16	13		
Baseline Mean (SD)	49.44 (20.67)	59.23 (25.56)		
Month 06 Adjusted Mean Change (SE)	-9.33 (4.49)	-6.04 (4.94)	.	.
Month 12 Adjusted Mean Change (SE)	-7.48 (4.63)	-0.61 (5.40)	-6.87 [-20.95;7.22]	0.337
Month 18 Adjusted Mean Change (SE)	-4.36 (4.97)	-0.46 (5.68)	.	.
Month 24 Adjusted Mean Change (SE)	-3.95 (6.21)	-12.08 (7.75)	8.13 [-11.72;27.98]	0.417
Age = 41-55				
N'	89	31		
Baseline Mean (SD)	59.96 (17.94)	54.52 (18.56)		
Month 06 Adjusted Mean Change (SE)	-0.64 (1.90)	3.80 (3.25)	.	.
Month 12 Adjusted Mean Change (SE)	-1.96 (1.93)	1.26 (3.49)	-3.22 [-11.12;4.68]	0.422
Month 18 Adjusted Mean Change (SE)	-4.23 (2.15)	-2.08 (4.53)	.	.
Month 24 Adjusted Mean Change (SE)	-6.98 (2.54)	-0.07 (4.61)	-6.92 [-17.42;3.59]	0.193
Month 30 Adjusted Mean Change (SE)	-0.80 (4.03)	1.68 (9.32)	.	.

N': Number of patients in the analysis
Adjusted Mean Change calculated by MMRM model including the following variables:
Treatment+Agegroup+Visit+Treatment*Agegroup+Treatment*Visit+Agegroup*Visit+Treatment*Visit*Agegroup+BL Value

Table 10.4.2: EQ-5D VAS Thermometer (FAS), Change from Baseline by Age

	Treatment groups		Comparison	
	BAF312 (N=127)	**Placebo (N=61)**	**Mean Difference [95% CI]**	**p-value**
Age = >55				
N'	12	14		
Baseline Mean (SD)	62.33 (21.91)	58.43 (19.32)		
Month 06 Adjusted Mean Change (SE)	-1.31 (5.15)	5.15 (4.76)	.	.
Month 12 Adjusted Mean Change (SE)	3.26 (5.69)	-2.27 (4.83)	5.53 [-9.22;20.28]	0.460
Month 18 Adjusted Mean Change (SE)	-5.43 (6.76)	-1.82 (5.61)	.	.
Month 24 Adjusted Mean Change (SE)	-0.17 (7.04)	4.51 (6.79)	-4.68 [-24.22;14.85]	0.634
Month 30 Adjusted Mean Change (SE)	17.48 (13.54)	7.97 (13.51)	.	.

N': Number of patients in the analysis
Adjusted Mean Change calculated by MMRM model including the following variables:
Treatment+Agegroup+Visit+Treatment*Agegroup+Treatment*Visit+Agegroup*Visit+Treatment*Visit*Agegroup+BL Value

Table 10.4.3: EQ-5D VAS Thermometer (FAS), Change from Baseline by Gender

	Treatment groups		Comparison	
	BAF312 (N=127)	**Placebo (N=61)**	**Mean Difference [95% CI]**	**p-value**
Interaction Test				0.845
Sex = F				
N'	67	36		
Baseline Mean (SD)	60.01 (18.16)	53.72 (20.75)		
Month 06 Adjusted Mean Change (SE)	0.77 (2.20)	2.76 (3.03)	.	.
Month 12 Adjusted Mean Change (SE)	-0.32 (2.22)	-0.45 (3.09)	0.13 [-7.39;7.66]	0.972
Month 18 Adjusted Mean Change (SE)	-3.13 (2.37)	-3.65 (3.50)	.	.
Month 24 Adjusted Mean Change (SE)	-5.85 (3.16)	-3.79 (4.15)	-2.06 [-12.45;8.34]	0.695
Month 30 Adjusted Mean Change (SE)	0.47 (5.69)	5.26 (11.00)	.	.
Sex = M				
N'	50	22		
Baseline Mean (SD)	57.08 (20.04)	61.09 (18.89)		
Month 06 Adjusted Mean Change (SE)	-5.56 (2.53)	0.63 (3.81)	.	.
Month 12 Adjusted Mean Change (SE)	-4.89 (2.56)	0.39 (4.21)	-5.28 [-15.03;4.47]	0.286
Month 18 Adjusted Mean Change (SE)	-5.71 (2.95)	3.82 (5.32)	.	.
Month 24 Adjusted Mean Change (SE)	-6.29 (3.36)	3.29 (6.88)	-9.58 [-24.83;5.67]	0.215
Month 30 Adjusted Mean Change (SE)	-5.42 (6.41)	-21.58 (15.27)	.	.

N': Number of patients in the analysis
Adjusted Mean Change calculated by MMRM model including the following variables:
Treatment+Sex+Visit+Treatment*Sex+Treatment*Visit+Sex*Visit+Treatment*Visit*Sex+BL Value

Table 10.4.4 EQ-5D VAS Thermometer (FAS), Change from Baseline by Previous MS DMT

	Treatment groups		Comparison	
	BAF312 (N=127)	**Placebo (N=61)**	**Mean Difference [95% CI]**	**p-value**
Interaction Test				0.827
Previous MS-DMT = N				
N'	19	17		
Baseline Mean (SD)	59.05 (20.60)	66.06 (18.31)		
Month 06 Adjusted Mean Change (SE)	-2.14 (4.14)	3.99 (4.51)	.	.
Month 12 Adjusted Mean Change (SE)	0.33 (4.03)	0.32 (4.38)	0.01 [-11.74;11.76]	0.998
Month 18 Adjusted Mean Change (SE)	-6.26 (4.47)	4.09 (6.06)	.	.
Month 24 Adjusted Mean Change (SE)	-5.05 (5.76)	3.45 (7.86)	-8.50 [-27.93;10.93]	0.386
Month 30 Adjusted Mean Change (SE)	-2.76 (15.80)	-19.70 (15.45)	.	.
Previous MS-DMT = Y				
N'	98	41		
Baseline Mean (SD)	58.70 (18.74)	52.56 (19.84)		
Month 06 Adjusted Mean Change (SE)	-1.89 (1.83)	1.13 (2.84)	.	.
Month 12 Adjusted Mean Change (SE)	-2.86 (1.86)	-0.27 (3.06)	-2.58 [-9.66;4.50]	0.472
Month 18 Adjusted Mean Change (SE)	-3.85 (2.04)	-3.12 (3.36)	.	.
Month 24 Adjusted Mean Change (SE)	-6.03 (2.50)	-2.94 (3.98)	-3.08 [-12.46;6.29]	0.514
Month 30 Adjusted Mean Change (SE)	-1.80 (4.46)	5.04 (11.14)	.	.

N': Number of patients in the analysis
Adjusted Mean Change calculated by MMRM model including the following variables:
Treatment+DMT+Visit+Treatment*DMT+Treatment*Visit+DMT*Visit+Treatment*Visit*DMT+BL Value

Table 10.4.5 EQ-5D VAS Thermometer (FAS), Change from Baseline by Previous IFN-beta-1b treatment

	Treatment groups		Comparison	
	BAF312 (N=127)	**Placebo (N=61)**	**Mean Difference [95% CI]**	**p-value**
Interaction Test				0.874
Previous IFN-beta 1b = N				
N'	74	45		
Baseline Mean (SD)	59.58 (18.76)	58.84 (20.96)		
Month 06 Adjusted Mean Change (SE)	-2.30 (2.10)	2.52 (2.72)	.	.
Month 12 Adjusted Mean Change (SE)	-3.03 (2.10)	-0.10 (2.78)	-2.93 [-9.82;3.95]	0.402
Month 18 Adjusted Mean Change (SE)	-3.93 (2.30)	-1.75 (3.30)	.	.
Month 24 Adjusted Mean Change (SE)	-6.50 (2.98)	-1.65 (3.95)	-4.85 [-14.71;5.01]	0.330
Month 30 Adjusted Mean Change (SE)	-2.94 (4.37)	1.63 (7.85)	.	.
Previous IFN-beta 1b = Y				
N'	43	13		
Baseline Mean (SD)	57.35 (19.43)	48.46 (15.50)		
Month 06 Adjusted Mean Change (SE)	-1.34 (2.78)	0.08 (5.05)	.	.
Month 12 Adjusted Mean Change (SE)	-0.93 (2.82)	-0.21 (5.63)	-0.71 [-13.14;11.72]	0.910
Month 18 Adjusted Mean Change (SE)	-5.02 (3.21)	0.39 (6.65)	.	.
Month 24 Adjusted Mean Change (SE)	-5.20 (3.68)	-1.76 (8.15)	-3.44 [-21.26;14.38]	0.701

N': Number of patients in the analysis
Adjusted Mean Change calculated by MMRM model including the following variables:
Treatment+IFN+Visit+Treatment*IFN+Treatment*Visit+IFN*Visit+Treatment*Visit*IFN+BL Value

Table 10.4.6 EQ-5D VAS Thermometer (FAS), Change from Baseline by Rapid Evolvement

	Treatment groups		Comparison	
	BAF312 (N=127)	**Placebo (N=61)**	**Mean Difference [95% CI]**	**p-value**
Interaction Test				0.082
Rapid evolvement = N				
N'	87	44		
Baseline Mean (SD)	58.87 (19.08)	58.45 (19.93)		
Month 06 Adjusted Mean Change (SE)	-2.57 (1.90)	5.27 (2.70)	.	.
Month 12 Adjusted Mean Change (SE)	-2.43 (1.97)	0.82 (2.79)	-3.26 [-10.01;3.50]	0.342
Month 18 Adjusted Mean Change (SE)	-4.78 (2.16)	1.43 (3.40)	.	.
Month 24 Adjusted Mean Change (SE)	-5.71 (2.67)	0.46 (4.06)	-6.17 [-15.85;3.52]	0.208
Month 30 Adjusted Mean Change (SE)	-3.30 (4.10)	2.84 (7.70)	.	.
Rapid evolvement = Y				
N'	30	14		
Baseline Mean (SD)	58.43 (18.92)	50.43 (20.63)		
Month 06 Adjusted Mean Change (SE)	-0.13 (3.28)	-8.39 (4.76)	.	.
Month 12 Adjusted Mean Change (SE)	-1.74 (3.23)	-2.71 (5.59)	0.97 [-11.78;13.73]	0.880
Month 18 Adjusted Mean Change (SE)	-2.77 (3.64)	-9.59 (5.85)	.	.
Month 24 Adjusted Mean Change (SE)	-6.84 (4.53)	-8.66 (7.20)	1.81 [-15.14;18.77]	0.832

N': Number of patients in the analysis
Adjusted Mean Change calculated by MMRM model including the following variables:
Treatment+RapEv+Visit+Treatment*RapEv+Treatment*Visit+RapEv*Visit+Treatment*Visit*RapEv+BL Value

Table 10.4.7 EQ-5D VAS Thermometer (FAS), Change from Baseline by Disease Course

	Treatment groups		Comparison	
	BAF312 (N=127)	Placebo (N=61)	Mean Difference [95% CI]	p-value
Interaction Test				0.465
Moderate/severe disease course = N				
N'	17	10		
Baseline Mean (SD)	70.88 (13.29)	65.00 (11.85)		
Month 06 Adjusted Mean Change (SE)	-0.45 (4.42)	10.61 (5.92)	.	.
Month 12 Adjusted Mean Change (SE)	0.10 (4.49)	8.56 (5.74)	-8.46 [-22.79;5.87]	0.245
Month 18 Adjusted Mean Change (SE)	-3.94 (5.80)	2.19 (7.37)	.	.
Month 24 Adjusted Mean Change (SE)	-6.46 (5.95)	8.68 (7.32)	-15.13 [-33.88;3.61]	0.112
Month 30 Adjusted Mean Change (SE)	-3.84 (8.65)	-1.36 (10.36)	.	.
Moderate/severe disease course = Y				
N'	100	48		
Baseline Mean (SD)	56.70 (19.05)	54.75 (21.22)		
Month 06 Adjusted Mean Change (SE)	-2.17 (1.80)	0.21 (2.60)	.	.
Month 12 Adjusted Mean Change (SE)	-2.65 (1.81)	-2.11 (2.75)	-0.54 [-7.03;5.96]	0.870
Month 18 Adjusted Mean Change (SE)	-4.38 (1.98)	-2.14 (3.22)	.	.
Month 24 Adjusted Mean Change (SE)	-5.87 (2.48)	-4.11 (4.01)	-1.77 [-11.15;7.62]	0.708
Month 30 Adjusted Mean Change (SE)	-0.62 (4.66)	9.65 (15.45)	.	.

N': Number of patients in the analysis
Adjusted Mean Change calculated by MMRM model including the following variables:
Treatment+DC+Visit+Treatment*DC+Treatment*Visit+DC*Visit+Treatment*Visit*DC+BL Value

Table 10.4.8 EQ-5D VAS Thermometer (FAS), Change from Baseline by Region

	Treatment groups		Comparison	
	BAF312 (N=127)	Placebo (N=61)	Mean Difference [95% CI]	p-value
Interaction Test				0.631
Region = Europe				
N'	100	49		
Baseline Mean (SD)	59.36 (18.64)	56.39 (19.81)		
Month 06 Adjusted Mean Change (SE)	-2.61 (1.81)	2.11 (2.60)	.	.
Month 12 Adjusted Mean Change (SE)	-2.71 (1.80)	-1.75 (2.73)	-0.97 [-7.43;5.49]	0.768
Month 18 Adjusted Mean Change (SE)	-5.22 (1.97)	-3.17 (3.31)	.	.
Month 24 Adjusted Mean Change (SE)	-6.26 (2.46)	-0.31 (4.34)	-5.95 [-15.90;3.99]	0.237
Month 30 Adjusted Mean Change (SE)	-2.34 (3.75)	-0.63 (9.53)	.	.
Region = Others				
N'	17	9		
Baseline Mean (SD)	55.24 (21.00)	57.22 (23.60)		
Month 06 Adjusted Mean Change (SE)	2.13 (4.37)	1.14 (6.01)	.	.
Month 12 Adjusted Mean Change (SE)	0.40 (4.86)	7.68 (6.11)	-7.28 [-22.70;8.15]	0.353
Month 18 Adjusted Mean Change (SE)	3.38 (5.74)	5.93 (6.41)	.	.
Month 24 Adjusted Mean Change (SE)	-4.08 (6.43)	0.26 (6.56)	-4.34 [-22.66;13.98]	0.638
Month 30 Adjusted Mean Change (SE)	16.28 (13.73)	1.71 (13.62)	.	.

N': Number of patients in the analysis
Adjusted Mean Change calculated by MMRM model including the following variables:
Treatment+Region+Visit+Treatment*Region+Treatment*Visit+Region*Visit+Treatment*Visit*Region+BL Value

Table 10.5.0: MSWS-12 Converted Score (FAS), Return Rates

	Treatment groups		
	BAF312 (N=127)	**Placebo (N=61)**	**Total (N=188)**
Return Rate n (%)*			
Baseline	127 (100.0)	60 (98.4)	187 (99.5)
Month 06	118 (92.9)	58 (95.1)	176 (93.6)
Month 12	107 (84.3)	47 (77.0)	154 (81.9)
Month 18	66 (52.0)	26 (42.6)	92 (48.9)
Month 24	51 (40.2)	20 (32.8)	71 (37.8)
Month 30	19 (15.0)	9 (14.8)	28 (14.9)

* Number and percentage of patients with non-missing data at the given time point.

Table 10.5.1: MSWS-12 Converted Score (FAS), Change from Baseline

	Treatment groups		Comparison	
	BAF312 (N=127)	**Placebo (N=61)**	**Mean Difference [95% CI]**	**p-value**
N'	118	57		
Baseline Mean (SD)	70.06 (24.52)	68.25 (23.57)		
Month 06 Adjusted Mean Change (SE)	1.98 (2.31)	1.02 (2.99)		.
Month 12 Adjusted Mean Change (SE)	4.46 (2.32)	4.72 (3.08)	-0.26 [-6.89;6.36]	0.938
Month 18 Adjusted Mean Change (SE)	8.73 (2.30)	6.71 (3.09)		.
Month 24 Adjusted Mean Change (SE)	9.99 (2.64)	-0.14 (3.70)	10.13 [1.96;18.29]	0.016
Month 30 Adjusted Mean Change (SE)	7.90 (3.06)	8.98 (4.04)		.

N': Number of patients in the analysis
Adjusted Mean Change calculated by MMRM model including the following variables: Treatment+Visit+Treatment*Visit+Country+BL Value

Table 10.5.2: MSWS-12 Converted Score (FAS), Change from Baseline by Age

	Treatment groups		Comparison	
	BAF312 (N=127)	**Placebo (N=61)**	**Mean Difference [95% CI]**	**p-value**
Interaction Test				0.515
Age = 18-40				
N'	16	13		
Baseline Mean (SD)	66.80 (25.49)	66.67 (26.16)		
Month 06 Adjusted Mean Change (SE)	-2.77 (5.37)	0.94 (5.85)	.	.
Month 12 Adjusted Mean Change (SE)	2.95 (5.40)	0.68 (6.19)	2.26 [-13.87;18.40]	0.782
Month 18 Adjusted Mean Change (SE)	8.81 (5.02)	4.77 (5.57)	.	.
Month 24 Adjusted Mean Change (SE)	7.03 (6.24)	-8.00 (7.81)	15.03 [-4.69;34.75]	0.134
Month 30 Adjusted Mean Change (SE)	14.23 (7.89)	1.61 (8.27)	.	.
Age = 41-55				
N'	89	30		
Baseline Mean (SD)	69.85 (24.53)	67.36 (25.65)		
Month 06 Adjusted Mean Change (SE)	3.37 (2.80)	-0.98 (3.94)	.	.
Month 12 Adjusted Mean Change (SE)	5.62 (2.82)	5.81 (4.16)	-0.18 [-9.18;8.81]	0.968
Month 18 Adjusted Mean Change (SE)	8.12 (2.74)	7.20 (4.51)	.	.
Month 24 Adjusted Mean Change (SE)	11.13 (3.12)	0.65 (4.90)	10.49 [-0.26;21.24]	0.056
Month 30 Adjusted Mean Change (SE)	9.60 (3.35)	11.77 (5.25)	.	.

N': Number of patients in the analysis
Adjusted Mean Change calculated by MMRM model including the following variables:
Treatment+Agegroup+Visit+Treatment*Agegroup+Treatment*Visit+Agegroup*Visit+Treatment*Visit*Agegroup+Country+BL Value

Table 10.5.2: MSWS-12 Converted Score (FAS), Change from Baseline by Age

	Treatment groups		Comparison	
	BAF312 (N=127)	**Placebo (N=61)**	**Mean Difference [95% CI]**	**p-value**
Age = >55				
N'	13	14		
Baseline Mean (SD)	75.48 (24.34)	71.63 (16.64)		
Month 06 Adjusted Mean Change (SE)	2.25 (6.82)	7.93 (5.68)	.	.
Month 12 Adjusted Mean Change (SE)	1.67 (7.05)	8.94 (5.74)	-7.28 [-24.77;10.21]	0.412
Month 18 Adjusted Mean Change (SE)	19.44 (6.84)	10.24 (5.56)	.	.
Month 24 Adjusted Mean Change (SE)	7.93 (8.11)	6.33 (7.64)	1.61 [-20.21;23.43]	0.884
Month 30 Adjusted Mean Change (SE)	-15.54 (11.42)	11.91 (7.96)	.	.

N': Number of patients in the analysis
Adjusted Mean Change calculated by MMRM model including the following variables:
Treatment+Agegroup+Visit+Treatment*Agegroup+Treatment*Visit+Agegroup*Visit+Treatment*Visit*Agegroup+Country+BL Value

Table 10.5.3: MSWS-12 Converted Score (FAS), Change from Baseline by Gender

	Treatment groups		Comparison	
	BAF312 (N=127)	Placebo (N=61)	Mean Difference [95% CI]	p-value
Interaction Test				0.138
Sex = F				
N'	68	36		
Baseline Mean (SD)	72.15 (25.69)	72.69 (23.45)		
Month 06 Adjusted Mean Change (SE)	1.76 (3.03)	0.35 (3.68)	.	.
Month 12 Adjusted Mean Change (SE)	2.36 (3.03)	5.97 (3.73)	-3.61 [-12.03;4.81]	0.398
Month 18 Adjusted Mean Change (SE)	7.69 (2.97)	8.28 (3.73)	.	.
Month 24 Adjusted Mean Change (SE)	7.74 (3.48)	2.61 (4.26)	5.13 [-4.85;15.12]	0.310
Month 30 Adjusted Mean Change (SE)	1.97 (3.79)	8.93 (4.42)	.	.
Sex = M				
N'	50	21		
Baseline Mean (SD)	67.21 (22.79)	60.65 (22.30)		
Month 06 Adjusted Mean Change (SE)	1.09 (3.07)	0.93 (4.82)	.	.
Month 12 Adjusted Mean Change (SE)	6.04 (3.05)	0.94 (4.99)	5.10 [-5.92;16.13]	0.362
Month 18 Adjusted Mean Change (SE)	8.79 (3.13)	2.57 (5.27)	.	.
Month 24 Adjusted Mean Change (SE)	11.66 (3.60)	-9.48 (7.54)	21.14 [5.03;37.26]	0.011
Month 30 Adjusted Mean Change (SE)	13.89 (4.06)	7.27 (7.43)	.	.

N': Number of patients in the analysis
Adjusted Mean Change calculated by MMRM model including the following variables:
Treatment+Sex+Visit+Treatment*Sex+Treatment*Visit+Sex*Visit+Treatment*Visit*Sex+Country+BL Value

Table 10.5.4 MSWS-12 Converted Score (FAS), Change from Baseline by Previous MS DMT

	Treatment groups		Comparison	
	BAF312 (N=127)	**Placebo (N=61)**	**Mean Difference [95% CI]**	**p-value**
Interaction Test				0.786
Previous MS-DMT = N				
N'	20	16		
Baseline Mean (SD)	66.04 (21.25)	57.29 (21.31)		
Month 06 Adjusted Mean Change (SE)	-1.56 (4.88)	1.85 (5.37)	.	.
Month 12 Adjusted Mean Change (SE)	3.13 (4.81)	6.29 (5.46)	-3.17 [-16.73;10.40]	0.645
Month 18 Adjusted Mean Change (SE)	9.93 (4.44)	1.60 (5.97)	.	.
Month 24 Adjusted Mean Change (SE)	12.41 (5.57)	-2.13 (7.70)	14.54 [-3.53;32.61]	0.113
Month 30 Adjusted Mean Change (SE)	-2.42 (11.83)	12.00 (10.98)	.	.
Previous MS-DMT = Y				
N'	98	41		
Baseline Mean (SD)	70.88 (25.16)	72.53 (23.25)		
Month 06 Adjusted Mean Change (SE)	2.61 (2.49)	0.75 (3.42)	.	.
Month 12 Adjusted Mean Change (SE)	4.61 (2.52)	4.05 (3.55)	0.56 [-7.26;8.38]	0.887
Month 18 Adjusted Mean Change (SE)	8.17 (2.48)	8.33 (3.50)	.	.
Month 24 Adjusted Mean Change (SE)	9.36 (2.86)	0.63 (4.16)	8.74 [-0.65;18.12]	0.068
Month 30 Adjusted Mean Change (SE)	8.59 (3.21)	8.28 (4.46)	.	.

N': Number of patients in the analysis
Adjusted Mean Change calculated by MMRM model including the following variables:
Treatment+DMT+Visit+Treatment*DMT+Treatment*Visit+DMT*Visit+Treatment*Visit*DMT+Country+BL Value

Table 10.5.5 MSWS-12 Converted Score (FAS), Change from Baseline by Previous IFN-beta-1b treatment

	Treatment groups		Comparison	
	BAF312 (N=127)	**Placebo (N=61)**	**Mean Difference [95% CI]**	**p-value**
Interaction Test				0.437
Previous IFN-beta 1b = N				
N'	75	44		
Baseline Mean (SD)	68.89 (26.20)	66.49 (22.16)		
Month 06 Adjusted Mean Change (SE)	2.39 (2.71)	1.62 (3.35)	.	.
Month 12 Adjusted Mean Change (SE)	4.75 (2.71)	4.90 (3.42)	-0.14 [-8.01;7.73]	0.972
Month 18 Adjusted Mean Change (SE)	8.32 (2.64)	5.57 (3.35)	.	.
Month 24 Adjusted Mean Change (SE)	9.84 (3.17)	-0.64 (4.23)	10.48 [0.64;20.31]	0.037
Month 30 Adjusted Mean Change (SE)	10.17 (3.14)	9.13 (4.20)	.	.
Previous IFN-beta 1b = Y				
N'	43	13		
Baseline Mean (SD)	72.09 (21.43)	74.20 (27.98)		
Month 06 Adjusted Mean Change (SE)	2.43 (3.46)	1.08 (5.87)	.	.
Month 12 Adjusted Mean Change (SE)	5.11 (3.51)	6.39 (6.32)	-1.28 [-14.64;12.09]	0.851
Month 18 Adjusted Mean Change (SE)	11.27 (3.43)	15.14 (6.92)	.	.
Month 24 Adjusted Mean Change (SE)	11.24 (4.02)	4.32 (7.60)	6.91 [-9.33;23.16]	0.400
Month 30 Adjusted Mean Change (SE)	-3.13 (5.41)	9.43 (7.77)	.	.

N': Number of patients in the analysis
Adjusted Mean Change calculated by MMRM model including the following variables:
Treatment+IFN+Visit+Treatment*IFN+Treatment*Visit+IFN*Visit+Treatment*Visit*IFN+Country+BL Value

Table 10.5.6 MSWS-12 Converted Score (FAS), Change from Baseline by Rapid Evolvement

	Treatment groups		Comparison	
	BAF312 (N=127)	**Placebo (N=61)**	**Mean Difference [95% CI]**	**p-value**
Interaction Test				0.775
Rapid evolvement = N				
N'	88	43		
Baseline Mean (SD)	72.40 (23.44)	70.36 (21.21)		
Month 06 Adjusted Mean Change (SE)	1.62 (2.59)	0.83 (3.41)	.	.
Month 12 Adjusted Mean Change (SE)	4.56 (2.62)	4.10 (3.47)	0.46 [-7.21;8.12]	0.906
Month 18 Adjusted Mean Change (SE)	8.12 (2.59)	7.86 (3.56)	.	.
Month 24 Adjusted Mean Change (SE)	8.78 (3.00)	-0.11 (4.17)	8.89 [-0.49;18.28]	0.063
Month 30 Adjusted Mean Change (SE)	8.71 (3.53)	9.01 (4.51)	.	.
Rapid evolvement = Y				
N'	30	14		
Baseline Mean (SD)	63.19 (26.69)	61.76 (29.66)		
Month 06 Adjusted Mean Change (SE)	3.70 (4.05)	2.21 (5.69)	.	.
Month 12 Adjusted Mean Change (SE)	4.98 (4.00)	7.95 (6.26)	-2.97 [-17.14;11.19]	0.679
Month 18 Adjusted Mean Change (SE)	10.98 (3.88)	3.44 (6.16)	.	.
Month 24 Adjusted Mean Change (SE)	14.00 (4.57)	1.47 (7.92)	12.53 [-5.21;30.27]	0.164
Month 30 Adjusted Mean Change (SE)	5.05 (6.16)	3.22 (13.06)	.	.

N': Number of patients in the analysis
Adjusted Mean Change calculated by MMRM model including the following variables:
Treatment+RapEv+Visit+Treatment*RapEv+Treatment*Visit+RapEv*Visit+Treatment*Visit*RapEv+Country+BL Value

Table 10.5.7 MSWS-12 Converted Score (FAS), Change from Baseline by Disease Course

	Treatment groups		Comparison	
	BAF312 (N=127)	Placebo (N=61)	Mean Difference [95% CI]	p-value
Interaction Test				0.292
Moderate/severe disease course = N				
N'	17	10		
Baseline Mean (SD)	51.10 (23.86)	49.17 (16.08)		
Month 06 Adjusted Mean Change (SE)	2.75 (5.37)	-7.54 (6.68)	.	.
Month 12 Adjusted Mean Change (SE)	3.23 (5.42)	-1.64 (6.74)	4.87 [-11.40;21.13]	0.555
Month 18 Adjusted Mean Change (SE)	7.57 (6.08)	-0.82 (7.16)	.	.
Month 24 Adjusted Mean Change (SE)	13.55 (6.84)	-0.92 (7.61)	14.47 [-4.98;33.92]	0.143
Month 30 Adjusted Mean Change (SE)	9.54 (6.48)	3.44 (8.65)	.	.
Moderate/severe disease course = Y				
N'	101	47		
Baseline Mean (SD)	73.25 (23.26)	72.31 (23.02)		
Month 06 Adjusted Mean Change (SE)	1.55 (2.47)	2.57 (3.22)	.	.
Month 12 Adjusted Mean Change (SE)	4.36 (2.48)	5.83 (3.34)	-1.47 [-8.84;5.89]	0.693
Month 18 Adjusted Mean Change (SE)	8.48 (2.41)	8.02 (3.33)	.	.
Month 24 Adjusted Mean Change (SE)	9.18 (2.79)	-0.76 (4.15)	9.94 [0.68;19.20]	0.036
Month 30 Adjusted Mean Change (SE)	7.22 (3.53)	10.07 (4.73)	.	.

N': Number of patients in the analysis
Adjusted Mean Change calculated by MMRM model including the following variables:
Treatment+DC+Visit+Treatment*DC+Treatment*Visit+DC*Visit+Treatment*Visit*DC+Country+BL Value

Table 10.5.8 MSWS-12 Converted Score (FAS), Change from Baseline by Region

	Treatment groups		Comparison	
	BAF312 (N=127)	Placebo (N=61)	Mean Difference [95% CI]	p-value
Interaction Test				0.814
Region = Europe				
N'	100	48		
Baseline Mean (SD)	69.40 (24.69)	66.59 (24.21)		
Month 06 Adjusted Mean Change (SE)	-0.55 (1.92)	1.00 (2.77)	.	.
Month 12 Adjusted Mean Change (SE)	2.08 (1.94)	4.69 (2.94)	-2.62 [-9.56;4.33]	0.458
Month 18 Adjusted Mean Change (SE)	6.40 (1.86)	4.92 (3.03)	.	.
Month 24 Adjusted Mean Change (SE)	7.63 (2.30)	-4.39 (3.96)	12.03 [2.94;21.12]	0.010
Month 30 Adjusted Mean Change (SE)	6.87 (3.11)	9.11 (6.03)	.	.
Region = Others				
N'	18	9		
Baseline Mean (SD)	73.73 (23.89)	77.08 (18.46)		
Month 06 Adjusted Mean Change (SE)	3.02 (4.52)	-5.48 (6.40)	.	.
Month 12 Adjusted Mean Change (SE)	4.72 (5.06)	-0.20 (6.59)	4.93 [-11.46;21.31]	0.554
Month 18 Adjusted Mean Change (SE)	8.83 (5.21)	7.50 (6.35)	.	.
Month 24 Adjusted Mean Change (SE)	10.46 (6.26)	5.34 (6.83)	5.12 [-13.24;23.47]	0.581
Month 30 Adjusted Mean Change (SE)	2.18 (7.19)	6.58 (6.13)	.	.

N': Number of patients in the analysis
Adjusted Mean Change calculated by MMRM model including the following variables:
Treatment+Region+Visit+Treatment*Region+Treatment*Visit+Region*Visit+Treatment*Visit*Region+BL Value

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Table 13.1: C-SSRS (FAS), Binary Analysis

	Treatment groups		Comparison		
	BAF312 (N=127)	Placebo (N=61)	OR [95% CI] p-value	RR [95% CI] p-value	RD [95% CI] p-value
N'	125	61			
Any suicidal ideation (Cat.1-5)	20 (16.0)	6 (9.8)	1.75 [0.66;4.60] 0.255	1.63 [0.69;3.84] 0.267	0.06 [-0.04;0.16] 0.220
Cat.1 - Wish to be dead	20 (16.0)	5 (8.2)	2.13 [0.76;5.99] 0.143	1.95 [0.77;4.95] 0.159	0.08 [-0.02;0.17] 0.104
Cat.2 - Non-specific active suicidal thoughts	6 (4.8)	3 (4.9)	0.97 [0.24;4.04] 0.972	0.98 [0.25;3.77] 0.972	0.00 [-0.07;0.06] 0.972
Cat.3 - Active suicidal ideation with any methods (not plan) without intent to act	5 (4.0)	2 (3.3)	1.23 [0.23;6.52] 0.808	1.22 [0.24;6.11] 0.809	0.01 [-0.05;0.06] 0.802
Cat.4 - Active suicidal ideation with some intent to act, without specific plan	1 (0.8)	1 (1.6)	0.48 [0.03;7.87] 0.602	0.49 [0.03;7.67] 0.610	-0.01 [-0.04;0.03] 0.643
Cat.5 - Active suicidal ideation with specific plan and intent	0 (0)	0 (0)	-	-	-
Any suicidal behavior (Cat.6-10)	1 (0.8)	0 (0.0)	1.48 [0.06;36.91] 0.484	1.48 [0.06;35.72] 0.811	0.01 [-0.01;0.02] 0.315
Cat.6 - Preparatory acts or behavior	1 (0.8)	0 (0.0)	1.48 [0.06;36.91] 0.484	1.48 [0.06;35.72] 0.811	0.01 [-0.01;0.02] 0.315
Cat.7 - Aborted attempt	1 (0.8)	0 (0.0)	1.48 [0.06;36.91] 0.484	1.48 [0.06;35.72] 0.811	0.01 [-0.01;0.02] 0.315
Cat.8 - Interrupted attempt	1 (0.8)	0 (0.0)	1.48 [0.06;36.91] 0.484	1.48 [0.06;35.72] 0.811	0.01 [-0.01;0.02] 0.315
Cat.9 - Actual attempt	0 (0)	0 (0)	-	-	-
Cat.10 - Completed suicide	0 (0)	0 (0)	-	-	-

Table 13.1: C-SSRS (FAS), Binary Analysis

	Treatment groups		Comparison		
	BAF312 (N=127)	**Placebo (N=61)**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Any suicidal ideation or behavior (Cat.1-10)	20 (16.0)	6 (9.8)	1.75 [0.66;4.60] 0.255	1.63 [0.69;3.84] 0.267	0.06 [-0.04;0.16] 0.220
Self-injurious behavior, without suicidal intent	0 (0)	0 (0)	-	-	-

N': Number of patients in the analysis
OR: Odds Ratio
RR: Relative Risk
RD: Risk Difference

Table 13.2: C-SSRS (FAS), Binary Analysis by Age

	Treatment groups		Comparison		
	BAF312 (N=127)	**Placebo (N=61)**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
N' Age=18-40	18	13			
N' Age=41-55	94	33			
N' Age=>55	13	15			
Any suicidal ideation or behavior (Cat.1-10)					
Interaction Test	p= 0.696				
Age = 18-40	3 (16.7)	2 (15.4)	1.10 [0.16;7.74] 0.924	1.08 [0.21;5.59] 0.924	0.01 [-0.25;0.27] 0.923
Age = 41-55	14 (14.9)	3 (9.1)	1.75 [0.47;6.52] 0.404	1.64 [0.50;5.34] 0.413	0.06 [-0.06;0.18] 0.350
Age = >55	3 (23.1)	1 (6.7)	4.20 [0.38;46.48] 0.242	3.46 [0.41;29.36] 0.255	0.16 [-0.10;0.43] 0.219

N': Number of patients in the analysis
OR: Odds Ratio
RR: Relative Risk
RD: Risk Difference

Table 13.3: C-SSRS (FAS), Binary Analysis by Gender

	Treatment groups		Comparison		
	BAF312 (N=127)	**Placebo (N=61)**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
N' Sex=F	74	37			
N' Sex=M	51	24			
Any suicidal ideation or behavior (Cat.1-10)					
Interaction Test	p= 0.796				
Sex = F	14 (18.9)	4 (10.8)	1.93 [0.59;6.33] 0.281	1.75 [0.62;4.95] 0.291	0.08 [-0.05;0.22] 0.236
Sex = M	6 (11.8)	2 (8.3)	1.47 [0.27;7.87] 0.655	1.41 [0.31;6.49] 0.658	0.03 [-0.11;0.18] 0.635

N': Number of patients in the analysis
OR: Odds Ratio
RR: Relative Risk
RD: Risk Difference

Table 13.4: C-SSRS (FAS), Binary Analysis by Previous MS DMT

	Treatment groups		Comparison		
	BAF312 (N=127)	**Placebo (N=61)**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
N' Previous MS-DMT=N	20	17			
N' Previous MS-DMT=Y	105	44			
Any suicidal ideation or behavior (Cat.1-10)					
Interaction Test	p= 0.218				
Previous MS-DMT = N	1 (5.0)	2 (11.8)	0.39 [0.03;4.78] 0.465	0.43 [0.04;4.29] 0.468	-0.07 [-0.25;0.11] 0.463
Previous MS-DMT = Y	19 (18.1)	4 (9.1)	2.21 [0.71;6.92] 0.174	1.99 [0.72;5.52] 0.186	0.09 [-0.02;0.20] 0.116

N': Number of patients in the analysis
OR: Odds Ratio
RR: Relative Risk
RD: Risk Difference

Table 13.5: C-SSRS (FAS), Binary Analysis by Previous IFN-beta-1b treatment

	Treatment groups		Comparison		
	BAF312 (N=127)	**Placebo (N=61)**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
N' Previous IFN-beta 1b=N	81	48			
N' Previous IFN-beta 1b=Y	44	13			
Any suicidal ideation or behavior (Cat.1-10)					
Interaction Test	p= 0.952				
Previous IFN-beta 1b = N	12 (14.8)	6 (12.5)	1.22 [0.42;3.49] 0.714	1.19 [0.48;2.95] 0.715	0.02 [-0.10;0.14] 0.709
Previous IFN-beta 1b = Y	8 (18.2)	0 (0.0)	-	5.29 [0.33;85.97] 0.242	0.18 [0.07;0.30] 0.002

N': Number of patients in the analysis
OR: Odds Ratio
RR: Relative Risk
RD: Risk Difference

Table 13.6: C-SSRS (FAS), Binary Analysis by Rapid Evolvement

	Treatment groups		Comparison		
	BAF312 (N=127)	**Placebo (N=61)**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
N' Rapid evolvement=N	93	47			
N' Rapid evolvement=Y	32	14			
Any suicidal ideation or behavior (Cat.1-10)					
Interaction Test	p= 0.234				
Rapid evolvement = N	17 (18.3)	4 (8.5)	2.40 [0.76;7.61] 0.135	2.15 [0.77;6.02] 0.146	0.10 [-0.01;0.21] 0.087
Rapid evolvement = Y	3 (9.4)	2 (14.3)	0.62 [0.09;4.20] 0.625	0.66 [0.12;3.50] 0.622	-0.05 [-0.26;0.16] 0.646

N': Number of patients in the analysis
OR: Odds Ratio
RR: Relative Risk
RD: Risk Difference

Table 13.7: C-SSRS (FAS), Binary Analysis by Disease Course

	Treatment groups		Comparison		
	BAF312 (N=127)	**Placebo (N=61)**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
N' Moderate/severe disease course=N	17	11			
N' Moderate/severe disease course=Y	108	50			
Any suicidal ideation or behavior (Cat.1-10)					
Interaction Test	p= 0.959				
Moderate/severe disease course = N	2 (11.8)	0 (0.0)	-	3.33 [0.17;63.51] 0.423	0.12 [-0.04;0.27] 0.132
Moderate/severe disease course = Y	18 (16.7)	6 (12.0)	1.47 [0.54;3.95] 0.449	1.39 [0.59;3.29] 0.455	0.05 [-0.07;0.16] 0.423

N': Number of patients in the analysis
OR: Odds Ratio
RR: Relative Risk
RD: Risk Difference

Table 13.8: C-SSRS (FAS), Binary Analysis by Region

	Treatment groups		Comparison		
	BAF312 (N=127)	**Placebo (N=61)**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
N' Region=Europe	105	52			
N' Region=Others	20	9			
Any suicidal ideation or behavior (Cat.1-10)					
Interaction Test	p= 0.852				
Region = Europe	17 (16.2)	5 (9.6)	1.82 [0.63;5.23] 0.269	1.68 [0.66;4.31] 0.277	0.07 [-0.04;0.17] 0.227
Region = Others	3 (15.0)	1 (11.1)	1.41 [0.13;15.78] 0.780	1.35 [0.16;11.27] 0.782	0.04 [-0.22;0.30] 0.768

N': Number of patients in the analysis
OR: Odds Ratio
RR: Relative Risk
RD: Risk Difference

Efficacy Figures

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Figure 3.2.1: Time to First Relapse (FAS)

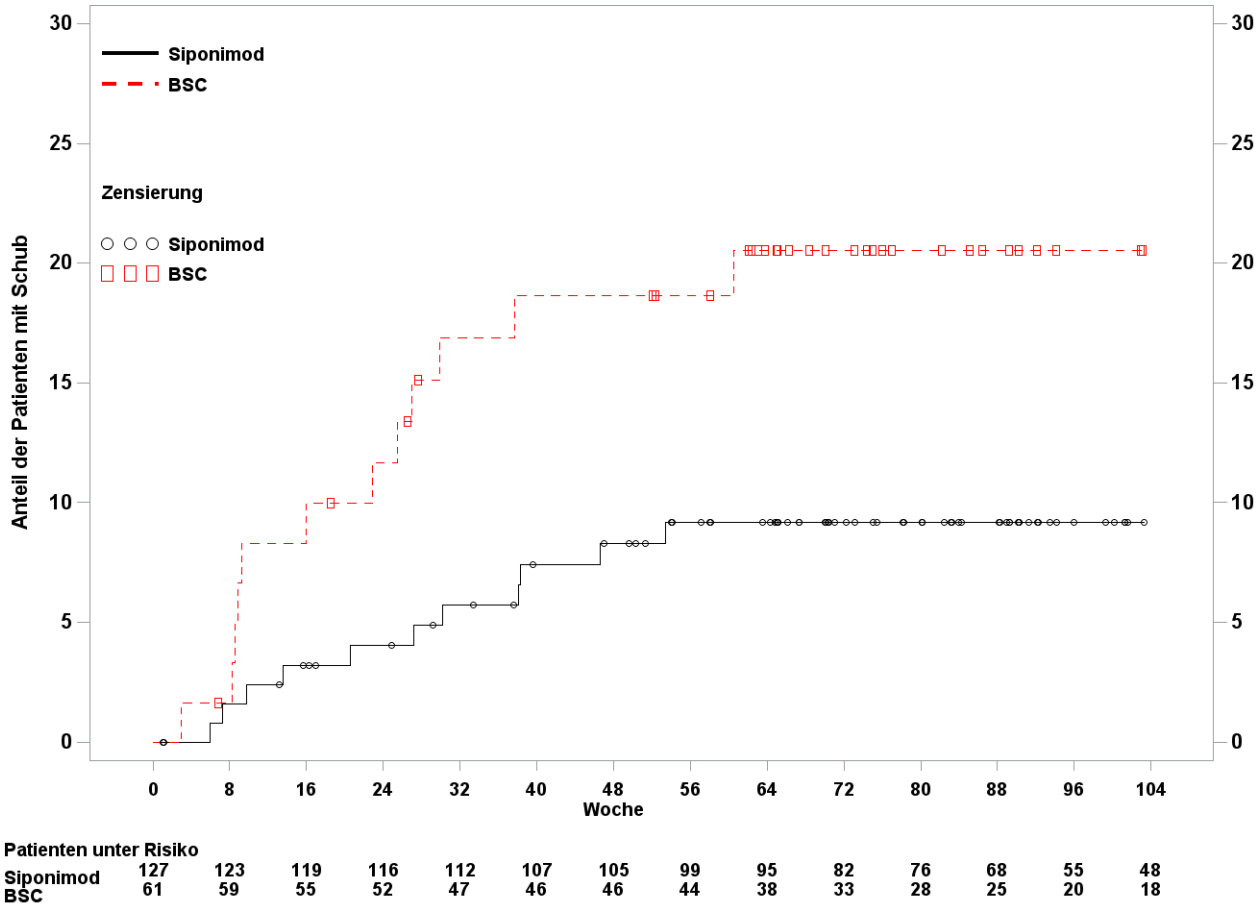

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Figure 4.2.1: Time to First 3-month CDP (FAS)

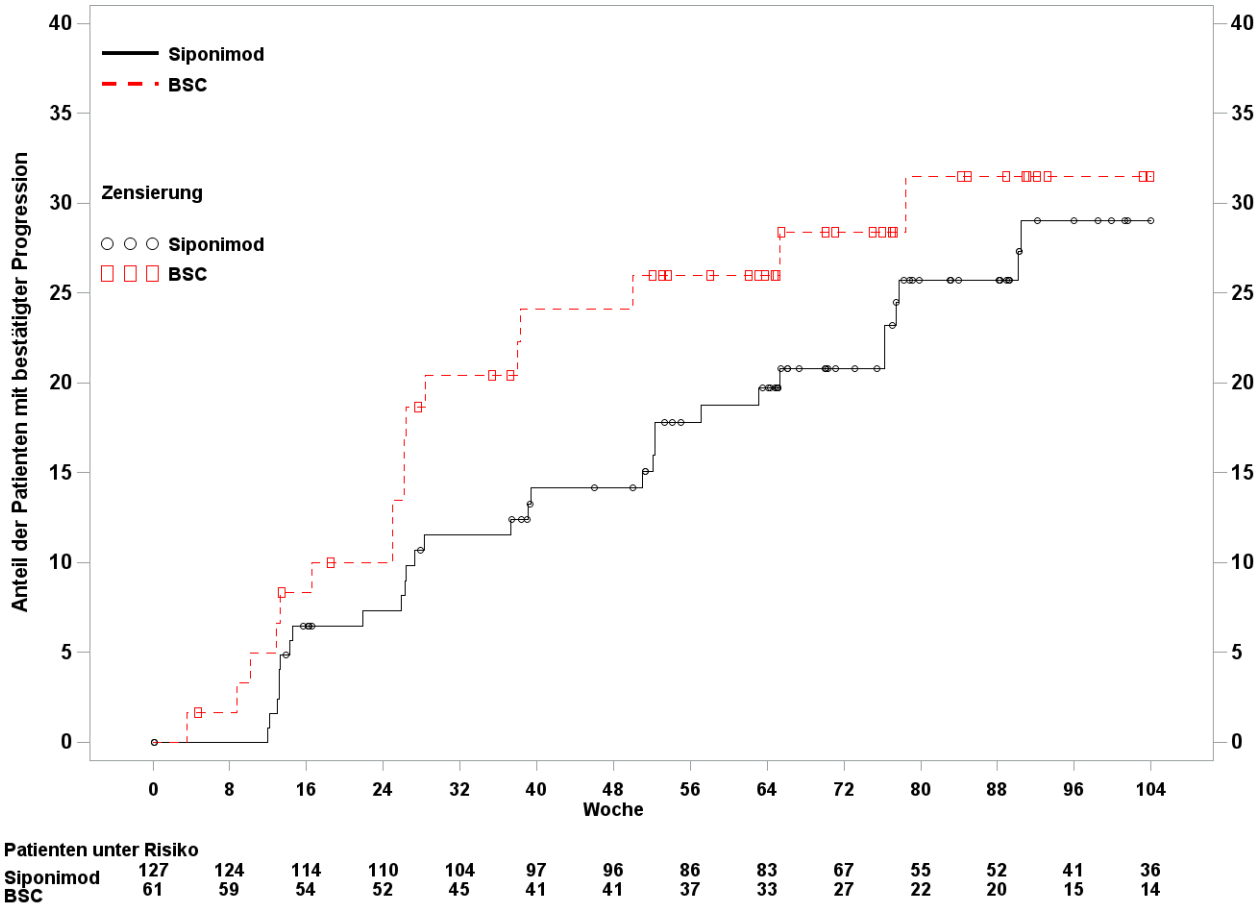

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Figure 5.2.1: Time to First 6-month CDP (FAS)

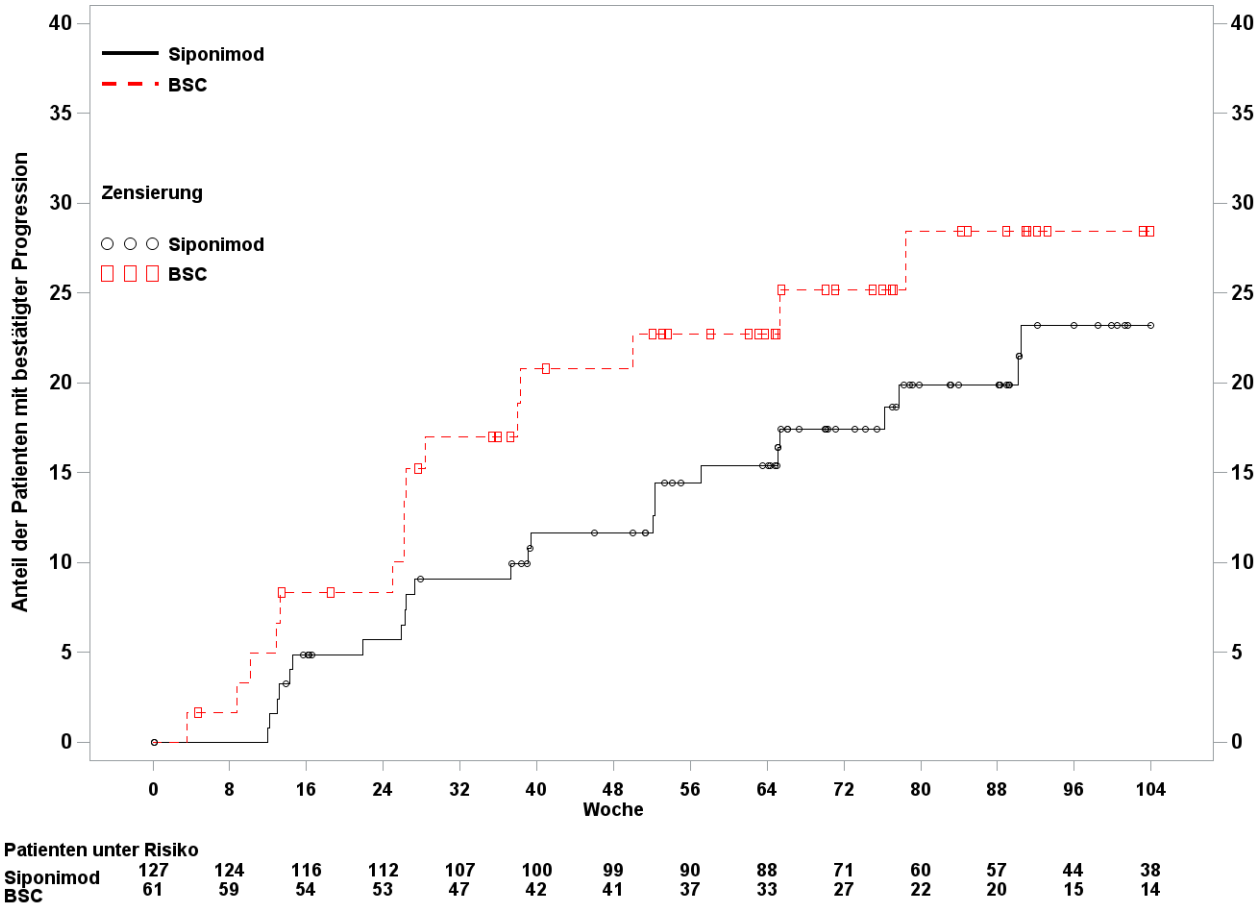

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Figure 6.6.1: Time to First Worsening of T25W of ≥20% (FAS)

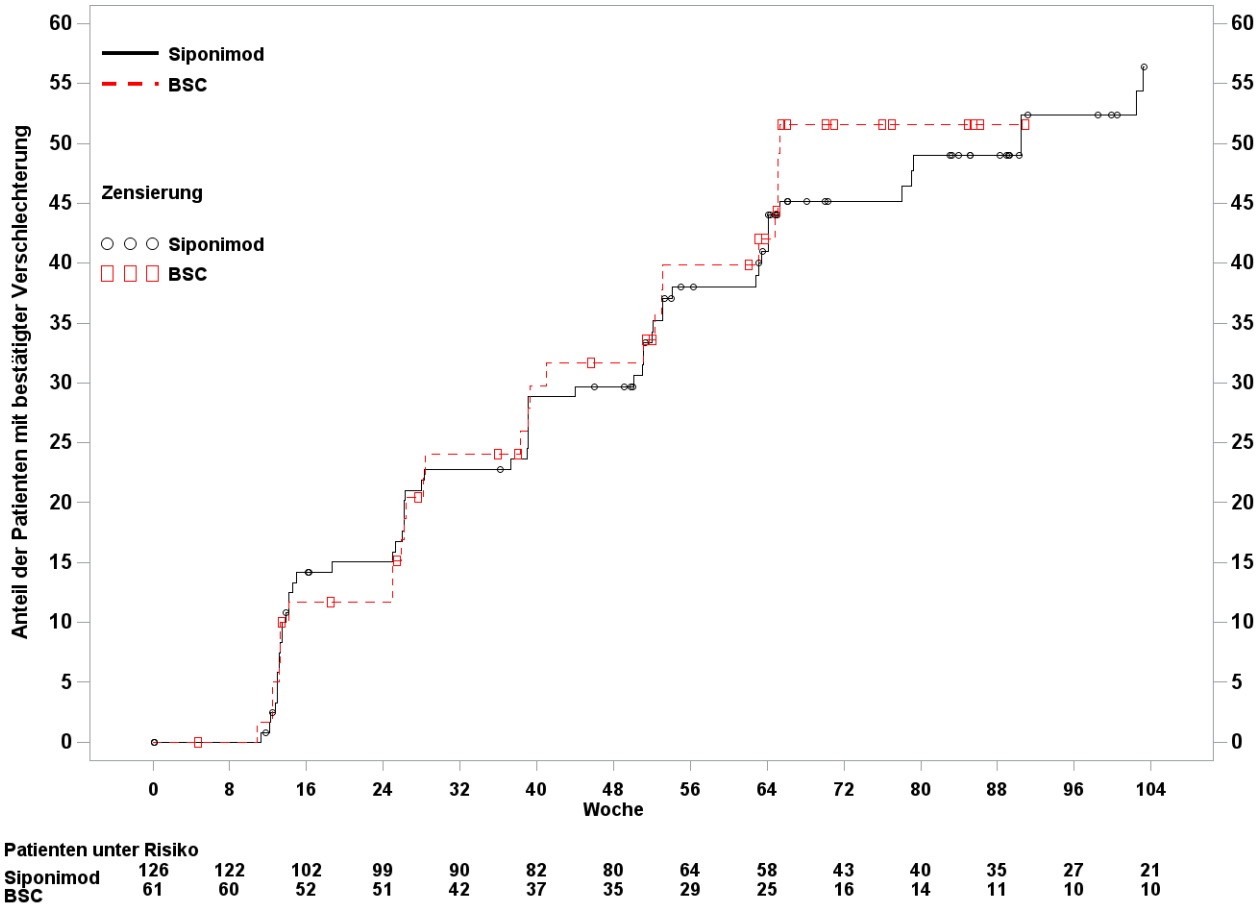

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Figure 10.1.1: MSIS-29 Physical Impact Scale, Time course (FAS)

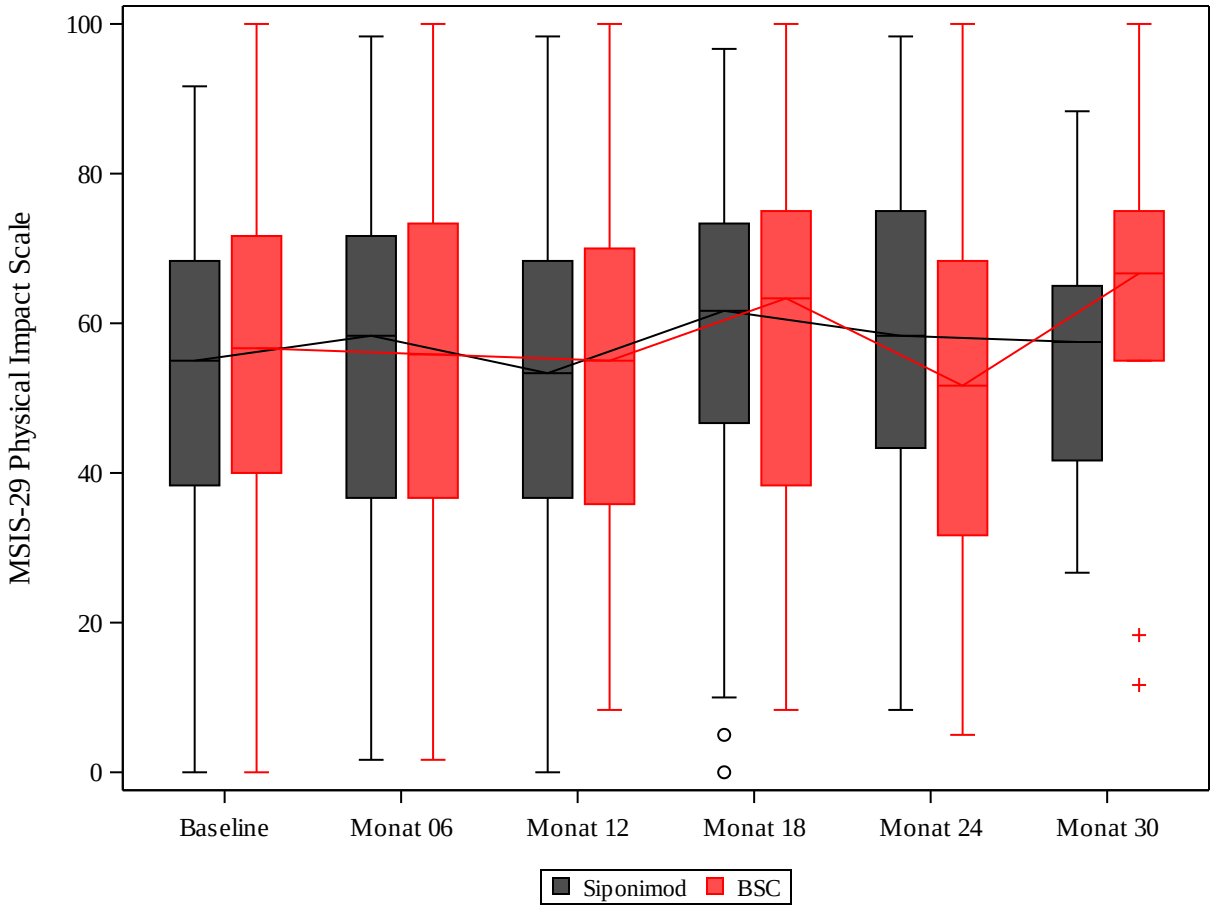

Figure 10.2.1: MSIS-29 Psychological Impact Scale, Time course (FAS)

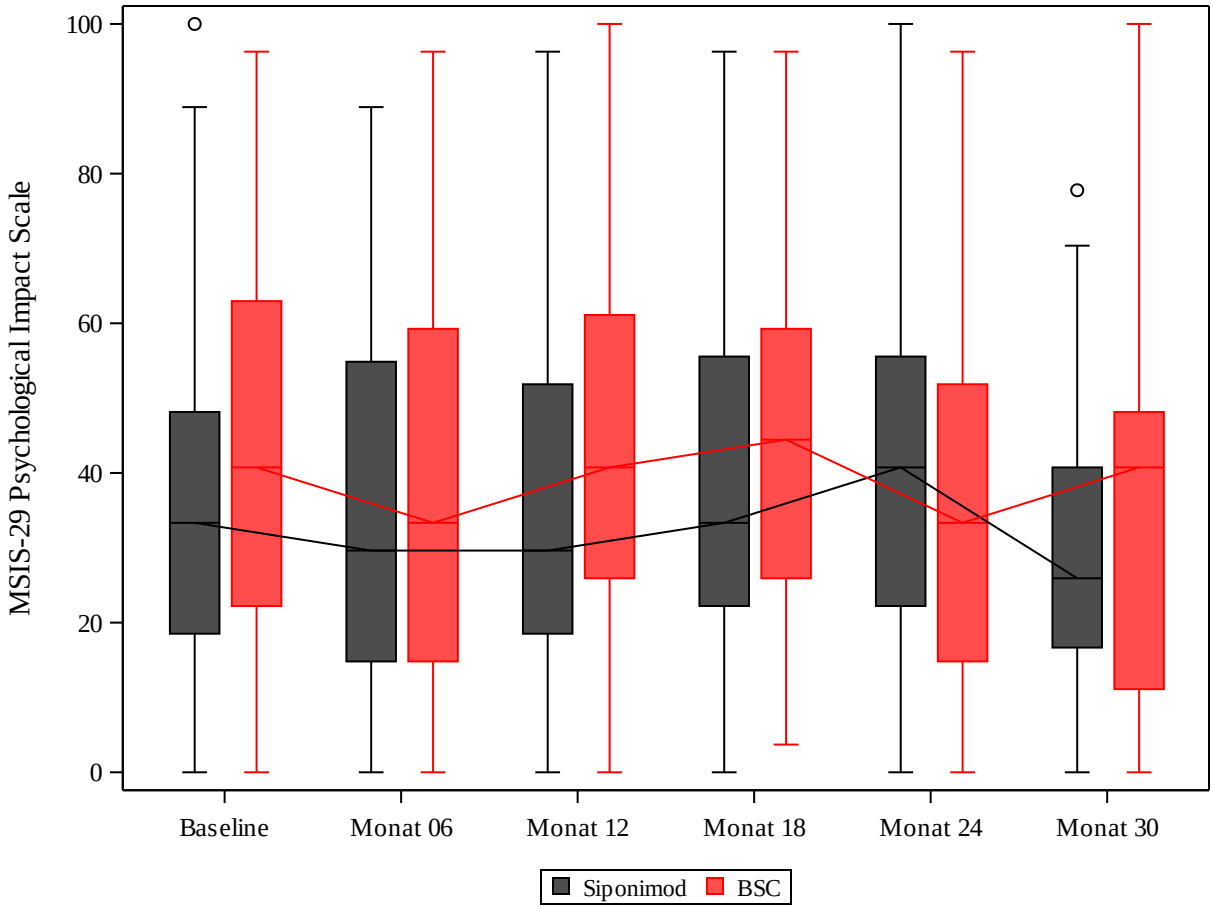

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Figure 10.3.1: EQ-5D Utility Score, Time course (FAS)

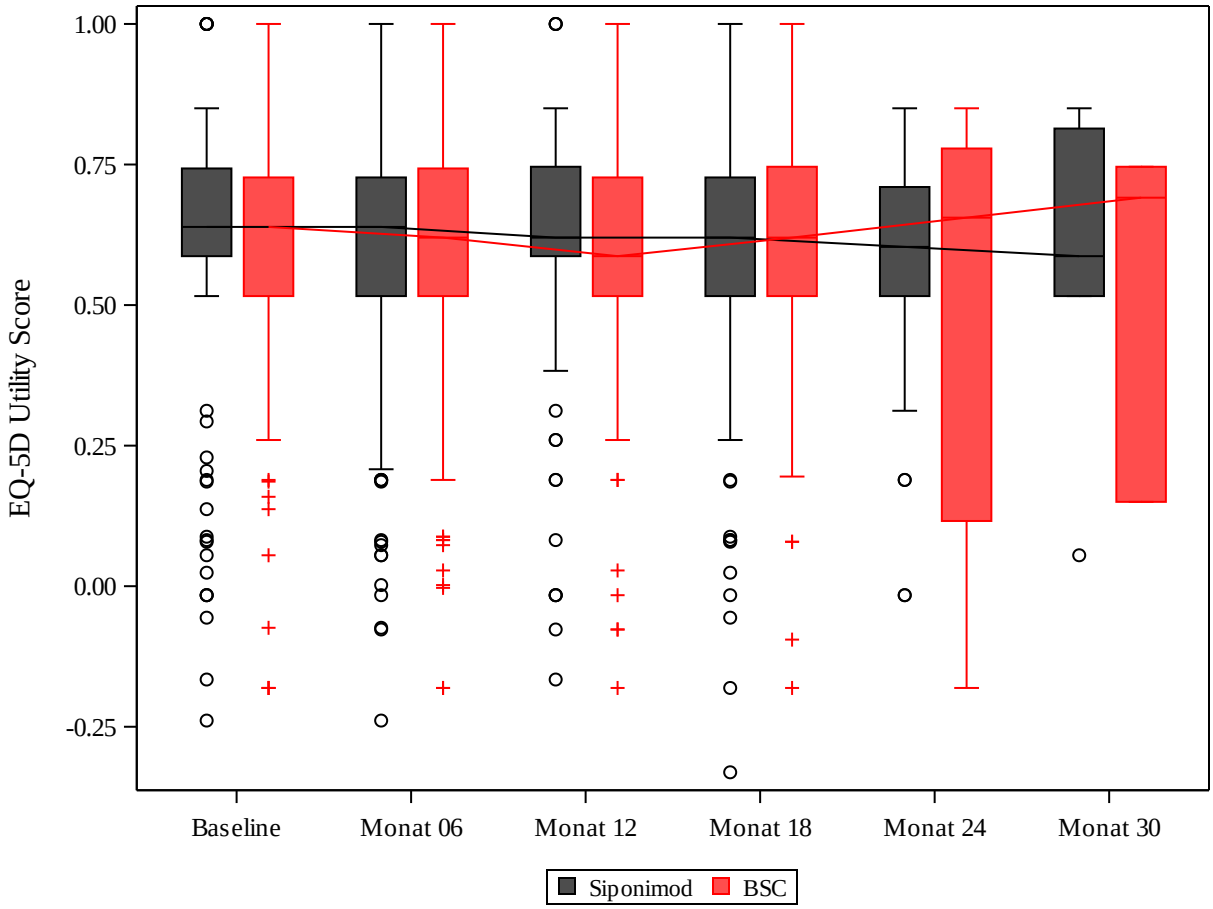


Figure 10.3.6: EQ-5D Utility Score, Time course (FAS) by Rapid Evolvement

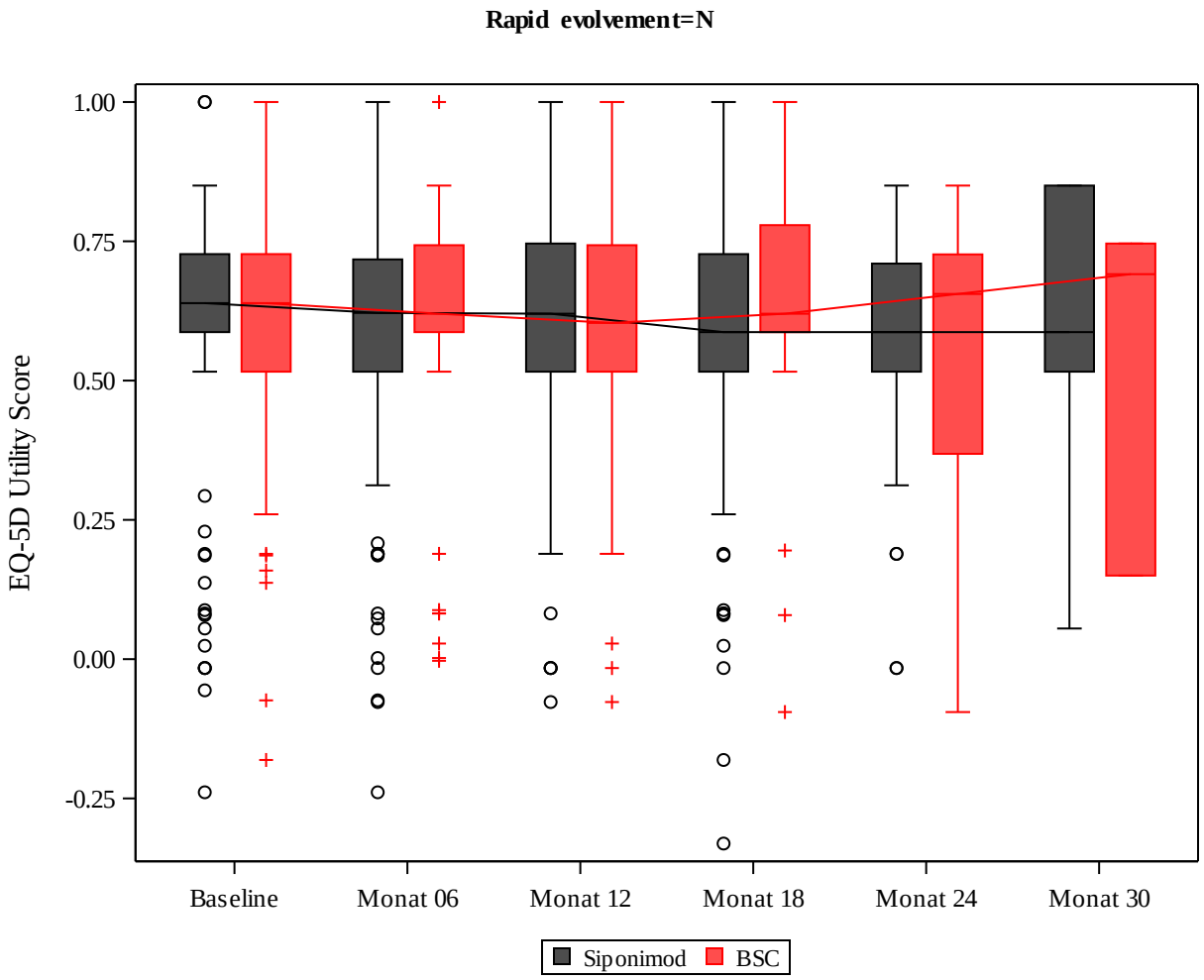


Figure 10.3.6: EQ-5D Utility Score, Time course (FAS) by Rapid Evolvement

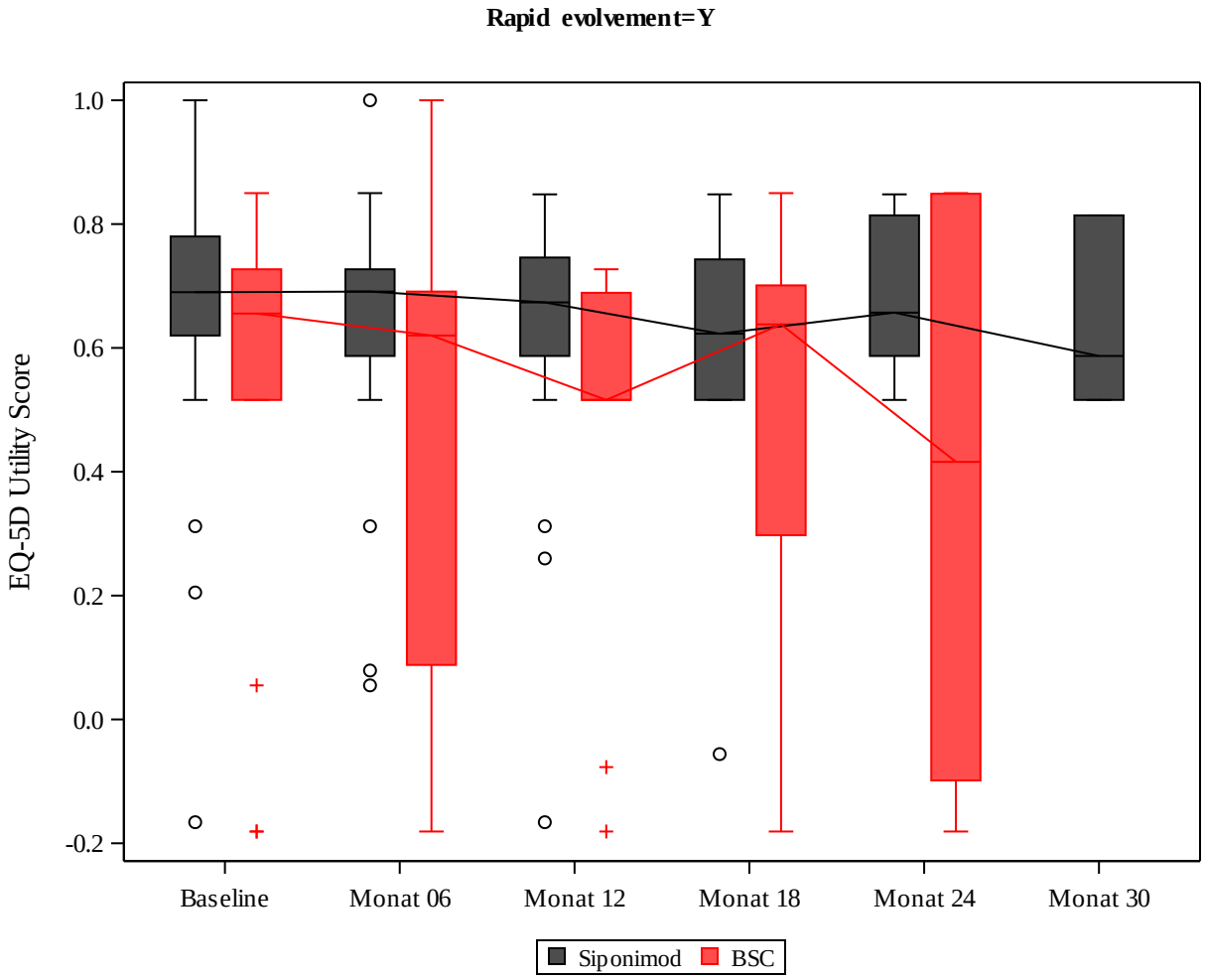
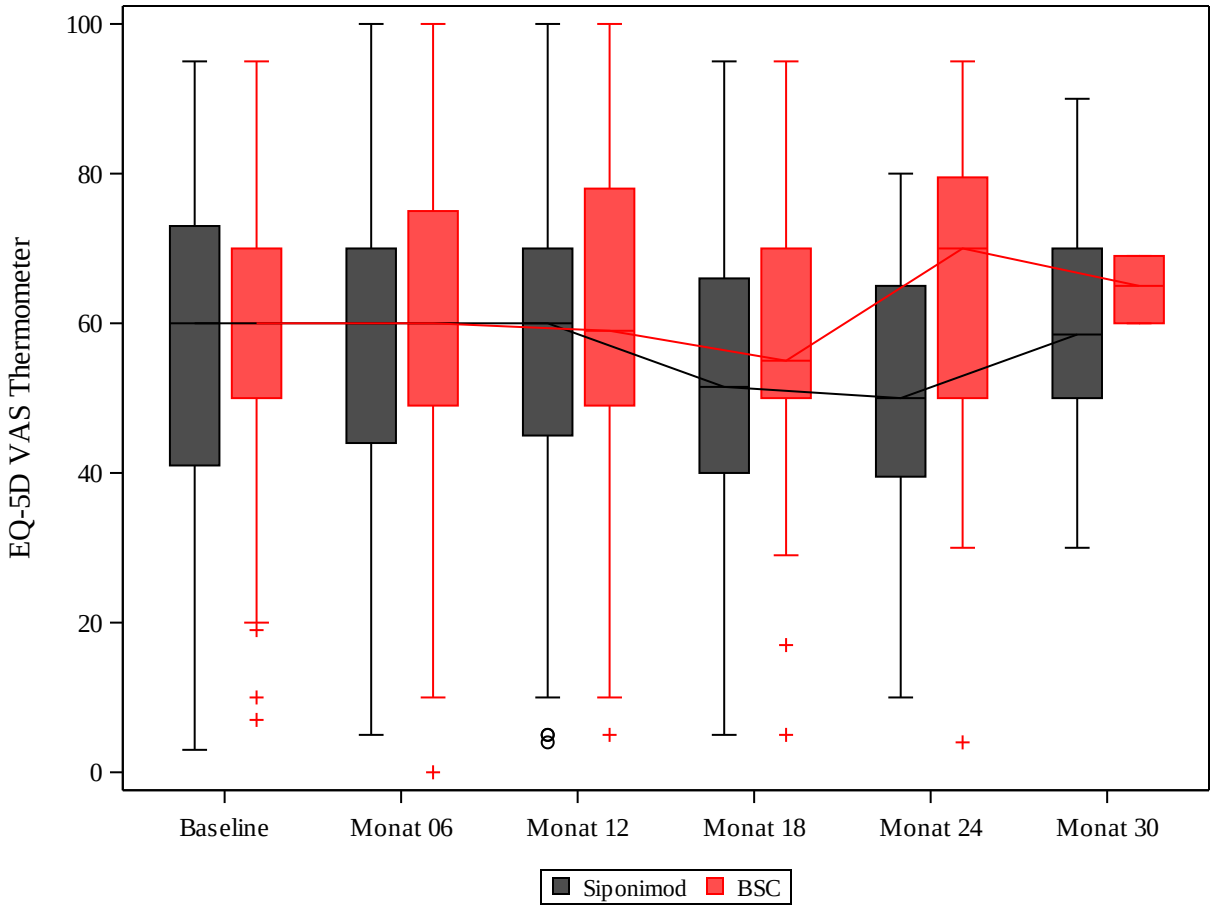


Figure 10.4.1: EQ-5D VAS Thermometer, Time course (FAS)



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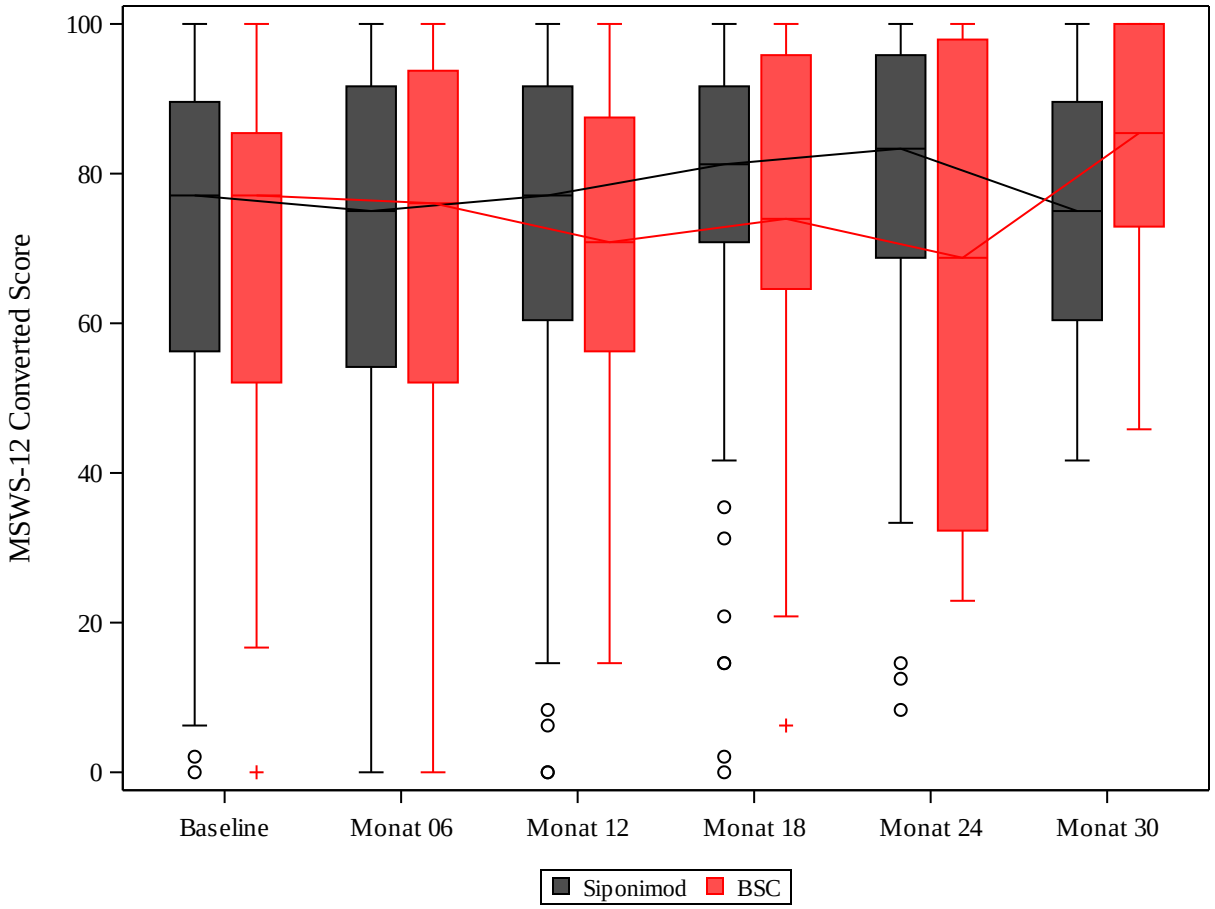
Figure 10.5.1: MSWS-12 Converted Score, Time course (FAS)