SIPONIMOD/Mayzent®

CBAF312A2304 (EXPAND) AMNOG Analysis

Modul 4A, Anhang 1 Gesamtpopulation

Patient Disposition Tables

1. Patient Disposition and Baseline Characteristics

Table 1.1 Patient Disposition and Compliance (RAN, FAS)

	Treatment groups		
Disposition/Reason	**BAF312 (N=1105) n (%)**	**Placebo (N=546) n (%)**	**Total (N=1651) n (%)**
Randomized (RAN)	**1105**	**546**	**1651**
Full Analysis Set (FAS)	**1099 (99,5)**	**546 (100,0)**	**1645 (99,6)**
Reasons for exclusion			
Subject was randomized but did not receive any study drug	5 (0,5)	0 (0,0)	5 (0,3)
Subject did not sign the informed consent prior to initiation of study procedures	1 (0,1)	0 (0,0)	1 (0,1)
Study Discontinuation (RAN)	**202 (18,3)**	**122 (22,3)**	**324 (19,6)**
Reasons for study discontinuation			
Subject/guardian decision	**96 (8,7)**	**77 (14,1)**	**173 (10,5)**
Adverse event	**45 (4,1)**	**18 (3,3)**	**63 (3,8)**
Lack of efficacy	**16 (1,4)**	**11 (2,0)**	**27 (1,6)**
Physician decision	**13 (1,2)**	**1 (0,2)**	**14 (0,8)**
Lost to follow-up	**9 (0,8)**	**8 (1,5)**	**17 (1,0)**
Progressive disease	**8 (0,7)**	**4 (0,7)**	**12 (0,7)**
Non-compliance with study treatment	**5 (0,5)**	**0 (0,0)**	**5 (0,3)**
Death	**3 (0,3)**	**1 (0,2)**	**4 (0,2)**
Protocol deviation	**3 (0,3)**	**1 (0,2)**	**4 (0,2)**
New therapy for study indication	**2 (0,2)**	**1 (0,2)**	**3 (0,2)**
Technical problems	**2 (0,2)**	**0 (0,0)**	**2 (0,1)**
Received study drug	**1100 (99,5)**	**546 (100,0)**	**1646 (99,7)**
Did not receive study drug	**5 (0,5)**	**0 (0,0)**	**5 (0,3)**
Completed Treatment Epoch on double-blind study drug	**737 (66,7)**	**322 (59,0)**	**1059 (64,1)**
Prematurely discontinued double-blind study drug during Treatment Epoch[1]	**368 (33,3)**	**224 (41,0)**	**592 (35,9)**
Continued on open-label siponimod treatment	116 (10,5)	94 (17,2)	210 (12,7)
Continued on abbreviated visit schedule	64 (5,8)	25 (4,6)	89 (5,4)
Discontinued Treatment Epoch directly from study drug	188 (17,0)	105 (19,2)	293 (17,7)
Primary reason for premature discontinuation from double-blind study drug			
Subject/guardian decision	115 (10,4)	71 (13,0)	186 (11,3)
Disease progression	101 (9,1)	81 (14,8)	182 (11,0)
Adverse event	94 (8,5)	28 (5,1)	122 (7,4)

	Treatment groups		
Disposition/Reason	**BAF312 (N=1105) n (%)**	**Placebo (N=546) n (%)**	**Total (N=1651) n (%)**
Lack of efficacy	36 (3,3)	27 (4,9)	63 (3,8)
Physician decision	14 (1,3)	13 (2,4)	27 (1,6)
As per protocol	3 (0,3)	2 (0,4)	5 (0,3)
Protocol deviation	3 (0,3)	0 (0,0)	3 (0,2)
Technical problems	2 (0,2)	1 (0,2)	3 (0,2)
Dosing error	0 (0,0)	1 (0,2)	1 (0,1)
Subject with at least one protocol deviation	**682 (61,7)**	**328 (60,1)**	**1010 (61,2)**
Key procedures not performed as per protocol	415 (37,6)	198 (36,3)	613 (37,1)
Other GCP deviation	296 (26,8)	143 (26,2)	439 (26,6)
Prohibited concomitant medication	74 (6,7)	38 (7,0)	112 (6,8)
Selection criteria not met	99 (9,0)	35 (6,4)	134 (8,1)
Subject not withdrawn as per protocol	3 (0,3)	2 (0,4)	5 (0,3)
Treatment deviation	85 (7,7)	38 (7,0)	123 (7,5)

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

Percentages refer to the number of randomized patients.

Analysis population: A2304 RAN total population

Table 1.2 Length of Study Participation (FAS)

	Treatment groups		
Study participation (FAS)	**BAF312 (N=1099)**	**Placebo (N=546)**	**Total (N=1645)**
Mean ± SD (in days)	629,6 ± 237,25	628,7 ± 227,31	629,3 ± 233,93
Median (in days)	638,0	640,5	639,0
Minimum, Maximum (in days)	7; 1109	16; 1087	7; 1109
Patients ≥ 365 days in study, n (%)	969 (88,2)	480 (87,9)	1449 (88,1)
Patients < 365 days in study, n (%)	130 (11,8)	66 (12,1)	196 (11,9)
Patients ≥ 730 days in study, n (%)	399 (36,3)	195 (35,7)	594 (36,1)
Patients < 730 days in study, n (%)	700 (63,7)	351 (64,3)	1051 (63,9)
Analysis population: A2304 FAS total population			

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

	Treatment Groups		
Patient characteristics	**BAF312 (N=1099)**	**Placebo (N=546)**	**Total (N=1645)**
Age (years)			
Mean ± SD	48,0 ± 7,84	48,1 ± 7,94	48,0 ± 7,87
Median	49,0	49,0	49,0
Range	22 to 61	21 to 61	21 to 61
Age group (years), n (%)			
18-30	26 (2,4)	12 (2,2)	38 (2,3)
31-40	161 (14,6)	91 (16,7)	252 (15,3)
41-55	712 (64,8)	331 (60,6)	1043 (63,4)
>55	200 (18,2)	112 (20,5)	312 (19,0)
Sex, n (%)			
Female	664 (60,4)	323 (59,2)	987 (60,0)
Male	435 (39,6)	223 (40,8)	658 (40,0)
Weight (kg)			
Mean ± SD	71,6 ± 15,69	71,5 ± 16,00	71,5 ± 15,79
Median	70,0	70,0	70,0
Range	40,0 to 142,1	38,5 to 145,3	38,5 to 145,3
Height (cm)			
Mean ± SD	169,3 ± 9,37	169,4 ± 9,87	169,3 ± 9,54
Median	169,0	170,0	169,0
Range	142,2 to 196,0	145,0 to 198,0	142,2 to 198,0
BMI (kg/m^2)			
Mean ± SD	24,9 ± 4,85	24,8 ± 4,77	24,9 ± 4,82
Median	24,1	24,2	24,1
Range	15,1 to 52,2	15,5 to 53,3	15,1 to 53,3
Race, n (%)			
Asian	30 (2,7)	18 (3,3)	48 (2,9)
Black or African American	7 (0,6)	3 (0,5)	10 (0,6)
Other	11 (1,0)	7 (1,3)	18 (1,1)
Unknown	5 (0,5)	5 (0,9)	10 (0,6)
White	1046 (95,2)	513 (94,0)	1559 (94,8)

	Treatment Groups		
Patient characteristics	**BAF312 (N=1099)**	**Placebo (N=546)**	**Total (N=1645)**
Ethnicity, n (%)			
Hispanic or Latino	74 (6,7)	32 (5,9)	106 (6,4)
Not Hispanic or Latino	823 (74,9)	410 (75,1)	1233 (75,0)
Not Reported	95 (8,6)	58 (10,6)	153 (9,3)
Unknown	107 (9,7)	46 (8,4)	153 (9,3)
Analysis population: A2304 FAS total population			

Table 1.4 MS Disease History (FAS)

	Treatment Groups		
	BAF312 (N=1099)	**Placebo (N=546)**	**Total (N=1645)**
Duration of MS since first diagnosis (years)			
Mean ± SD	12,9 ± 7,89	12,1 ± 7,48	12,6 ± 7,76
Median	11,9	11,2	11,7
Range	0,1 to 44,4	0,4 to 39,4	0,1 to 44,4
Duration of MS since first symptom (years)			
Mean ± SD	17,1 ± 8,37	16,2 ± 8,23	16,8 ± 8,33
Median	16,3	15,4	16,0
Range	1,4 to 45,0	1,3 to 43,0	1,3 to 45,0
Time since conversion to SPMS (years)			
Mean ± SD	3,9 ± 3,61	3,6 ± 3,28	3,8 ± 3,51
Median	2,6	2,5	2,6
Range	0,1 to 24,2	0,1 to 21,7	0,1 to 24,2
Number of relapses in the last 24 months prior to screening			
Mean ± SD	0,7 ± 1,21	0,7 ± 1,16	0,7 ± 1,19
Median	0,0	0,0	0,0
Range	0 to 12	0 to 8	0 to 12
Number of relapses in the last 24 months prior to screening (categories), n (%)			
0	708 (64,4)	343 (62,8)	1051 (63,9)
1	198 (18,0)	104 (19,0)	302 (18,4)
2-3	157 (14,3)	81 (14,8)	238 (14,5)
4-5	26 (2,4)	13 (2,4)	39 (2,4)
>5	7 (0,6)	4 (0,7)	11 (0,7)
Missing	3 (0,3)	1 (0,2)	4 (0,2)
Number of relapses in the last 12 months prior to screening			
Mean ± SD	0,2 ± 0,54	0,3 ± 0,57	0,3 ± 0,55
Median	0,0	0,0	0,0
Range	0 to 4	0 to 4	0 to 4
Number of relapses in the last 12 months prior to screening (categories), n (%)			
0	874 (79,5)	416 (76,2)	1290 (78,4)
1	187 (17,0)	111 (20,3)	298 (18,1)
2-3	35 (3,2)	16 (2,9)	51 (3,1)
4-5	2 (0,2)	2 (0,4)	4 (0,2)
Missing	1 (0,1)	1 (0,2)	2 (0,1)

Analysis population: A2304 FAS total population

Table 1.5 Clinical MS Baseline Characteristics (FAS)

	Treatment Groups		
	BAF312 (N=1099)	**Placebo (N=546)**	**Total (N=1645)**
EDSS			
Mean ± SD	5,4 ± 1,08	5,4 ± 1,03	5,4 ± 1,06
Median	6,0	6,0	6,0
Range	2,0 to 7,0	2,5 to 7,0	2,0 to 7,0
EDSS categories, n (%)			
<3.0	6 (0,5)	2 (0,4)	8 (0,5)
3.0-4.5	310 (28,2)	148 (27,1)	458 (27,8)
5.0-5.5	165 (15,0)	100 (18,3)	265 (16,1)
6.0-6.5	616 (56,1)	295 (54,0)	911 (55,4)
>6.5	2 (0,2)	1 (0,2)	3 (0,2)
Number of Gd-enhancing T1 lesions			
Mean ± SD	0,9 ± 3,56	0,7 ± 3,55	0,9 ± 3,56
Median	0,0	0,0	0,0
Range	0 to 55	0 to 65	0 to 65
Number of Gd-enhancing T1 lesions (categories), n (%)			
0	828 (75,3)	415 (76,0)	1243 (75,6)
≥ 1	236 (21,5)	114 (20,9)	350 (21,3)
Missing	35 (3,2)	17 (3,1)	52 (3,2)
Volume of T2 lesions (mm^3)			
Mean ± SD	15598,8 ± 16199,68	14694,0 ± 15619,84	15298,3 ± 16010,24
Median	10286,0	9994,0	10083,0
Range	23,0 to 116664,0	0,0 to 103560,0	0,0 to 116664,0
Normalized brain volume (cc)			
Mean ± SD	1422,0 ± 86,37	1424,5 ± 87,59	1422,8 ± 86,76
Median	1420,5	1425,2	1422,3
Range	1136,1 to 1723,2	1198,8 to 1691,2	1136,1 to 1723,2

Analysis population: A2304 FAS total population

Table 1.6 Definition of Active MS Subpopulation (FAS)

		Treatment Groups		
Relapses in the last 24 months prior to screening	**Gd-enhancing T1 lesions**	**BAF312 (N=1099) n (%)**	**Placebo (N=546) n (%)**	**Total (N=1645) n (%)**
≥ 1	0	269 (24,5)	144 (26,4)	413 (25,1)
≥ 1	≥ 1	108 (9,8)	53 (9,7)	161 (9,8)
0	0	557 (50,7)	270 (49,5)	827 (50,3)
0	≥ 1	127 (11,6)	61 (11,2)	188 (11,4)
Analysis population: A2304 FAS total population				

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

Preferred Terms (grouped by System Organ Class)
PERIPHERAL SWELLING
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

Preferred Terms (grouped by System Organ Class)
DIZZINESS
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

Preferred Terms (grouped by System Organ Class)
PARTIAL SEIZURES
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

Preferred Terms (grouped by System Organ Class)
HALLUCINATION, AUDITORY
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=1099)	**Placebo (N=546)**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
N'	1099	546			
Any AE n (%)	975 (88,7)	445 (81,5)	1,78 [1,34; 2,37] <0,001 *	1,09 [1,04; 1,14] <0,001 *	0,07 [0,03; 0,11] <0,001 *
Any AE, disease specific events excluded[1] n (%)	918 (83,5)	418 (76,6)	1,55 [1,20; 2,00] 0,001 *	1,09 [1,03; 1,15] 0,001 *	0,07 [0,03; 0,11] 0,001 *
Any SAE n (%)	186 (16,9)	74 (13,6)	1,30 [0,97; 1,74] 0,078	1,25 [0,97; 1,60] 0,080	0,03 [-0,00; 0,07] 0,069
Any SAE, disease specific events excluded[1] n (%)	146 (13,3)	53 (9,7)	1,43 [1,02; 1,99] 0,036 *	1,37 [1,02; 1,84] 0,038 *	0,04 [0,00; 0,07] 0,028 *
Any severe AE[2] n (%)	139 (12,6)	61 (11,2)	1,15 [0,84; 1,59] 0,388	1,13 [0,85; 1,50] 0,390	0,01 [-0,02; 0,05] 0,380
Any severe AE[2], disease specific events excluded[1] n (%)	110 (10,0)	44 (8,1)	1,27 [0,88; 1,83] 0,201	1,24 [0,89; 1,73] 0,204	0,02 [-0,01; 0,05] 0,186
Any AE leading to study discontinuation n (%)	46 (4,2)	16 (2,9)	1,45 [0,81; 2,58] 0,208	1,43 [0,82; 2,50] 0,212	0,01 [-0,01; 0,03] 0,182
Any AE leading to study drug discontinuation n (%)	84 (7,6)	28 (5,1)	1,53 [0,99; 2,38] 0,057	1,49 [0,98; 2,26] 0,060	0,03 [0,00; 0,05] 0,042 *

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 total population

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

	Treatment groups		Comparison		
	BAF312 (N=1099)	**Placebo (N=546)**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
N'	1099	546			
Grade 1 n (%)	900 (81,9)	405 (74,2)	1,57 [1,23; 2,01] <0,001 *	1,10 [1,04; 1,17] 0,001 *	0,08 [0,03; 0,12] <0,001 *
Grade 2 n (%)	520 (47,3)	239 (43,8)	1,15 [0,94; 1,42] 0,175	1,08 [0,96; 1,21] 0,180	0,04 [-0,02; 0,09] 0,174
Grade 3 n (%)	121 (11,0)	55 (10,1)	1,10 [0,79; 1,55] 0,563	1,09 [0,81; 1,48] 0,564	0,01 [-0,02; 0,04] 0,558
Grade 4 n (%)	23 (2,1)	7 (1,3)	1,65 [0,70; 3,86] 0,247	1,63 [0,70; 3,78] 0,253	0,01 [-0,00; 0,02] 0,210
Severe (Grade ≥ 3) n (%)	139 (12,6)	61 (11,2)	1,15 [0,84; 1,59] 0,388	1,13 [0,85; 1,50] 0,390	0,01 [-0,02; 0,05] 0,380
Not severe (Grade < 3) n (%)	965 (87,8)	438 (80,2)	1,78 [1,35; 2,34] <0,001 *	1,09 [1,04; 1,15] <0,001 *	0,08 [0,04; 0,11] <0,001 *

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 total population

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

	Treatment groups		Comparison		
	BAF312 (N=1099)	**Placebo (N=546)**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
N'	1099	546			
BLOOD AND LYMPHATIC SYSTEM DISORDERS, n (%)	46 (4,2)	10 (1,8)	2,34 [1,17; 4,68] 0,013 *	2,29 [1,16; 4,49] 0,017 *	0,02 [0,01; 0,04] 0,005 *
ANAEMIA, n (%)	17 (1,5)	6 (1,1)	1,41 [0,55; 3,61] 0,466	1,41 [0,56; 3,55] 0,469	0,00 [-0,01; 0,02] 0,441
CARDIAC DISORDERS, n (%)	130 (11,8)	55 (10,1)	1,20 [0,86; 1,67] 0,289	1,17 [0,87; 1,58] 0,291	0,02 [-0,01; 0,05] 0,277
ATRIOVENTRICULAR BLOCK FIRST DEGREE, n (%)	14 (1,3)	4 (0,7)	1,75 [0,57; 5,34] 0,320	1,74 [0,58; 5,26] 0,327	0,01 [-0,00; 0,02] 0,277
BRADYCARDIA, n (%)	50 (4,5)	14 (2,6)	1,81 [0,99; 3,31] 0,050 *	1,77 [0,99; 3,18] 0,054	0,02 [0,00; 0,04] 0,032 *
PALPITATIONS, n (%)	20 (1,8)	10 (1,8)	0,99 [0,46; 2,14] 0,987	0,99 [0,47; 2,11] 0,987	-0,00 [-0,01; 0,01] 0,987
SINUS BRADYCARDIA, n (%)	14 (1,3)	4 (0,7)	1,75 [0,57; 5,34] 0,320	1,74 [0,58; 5,26] 0,327	0,01 [-0,00; 0,02] 0,277
EAR AND LABYRINTH DISORDERS, n (%)	55 (5,0)	38 (7,0)	0,70 [0,46; 1,08] 0,106	0,72 [0,48; 1,07] 0,107	-0,02 [-0,04; 0,01] 0,124
TINNITUS, n (%)	13 (1,2)	2 (0,4)	3,26 [0,73; 14,48] 0,101	3,23 [0,73; 14,26] 0,122	0,01 [0,00; 0,02] 0,050 *
VERTIGO, n (%)	25 (2,3)	26 (4,8)	0,47 [0,27; 0,81] 0,006 *	0,48 [0,28; 0,82] 0,007 *	-0,02 [-0,04; -0,00] 0,014 *
ENDOCRINE DISORDERS, n (%)	11 (1,0)	4 (0,7)	1,37 [0,43; 4,32] 0,590	1,37 [0,44; 4,27] 0,592	0,00 [-0,01; 0,01] 0,570
EYE DISORDERS, n (%)	111 (10,1)	54 (9,9)	1,02 [0,73; 1,44] 0,894	1,02 [0,75; 1,39] 0,894	0,00 [-0,03; 0,03] 0,893
MACULAR OEDEMA, n (%)	18 (1,6)	1 (0,2)	9,07 [1,21; 68,16] 0,009 *	8,94 [1,20; 66,81] 0,033 *	0,01 [0,01; 0,02] 0,001 *
VISION BLURRED, n (%)	13 (1,2)	9 (1,6)	0,71 [0,30; 1,68] 0,439	0,72 [0,31; 1,67] 0,441	-0,00 [-0,02; 0,01] 0,464

	Treatment groups		Comparison		
	BAF312 (N=1099)	**Placebo (N=546)**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
GASTROINTESTINAL DISORDERS, n (%)	269 (24,5)	110 (20,1)	1,28 [1,00; 1,65] 0,050 *	1,21 [1,00; 1,48] 0,052	0,04 [0,00; 0,09] 0,044 *
ABDOMINAL PAIN, n (%)	12 (1,1)	3 (0,5)	2,00 [0,56; 7,11] 0,276	1,99 [0,56; 7,01] 0,286	0,01 [-0,00; 0,01] 0,223
ABDOMINAL PAIN UPPER, n (%)	23 (2,1)	11 (2,0)	1,04 [0,50; 2,15] 0,916	1,04 [0,51; 2,12] 0,916	0,00 [-0,01; 0,02] 0,916
CONSTIPATION, n (%)	41 (3,7)	22 (4,0)	0,92 [0,54; 1,57] 0,766	0,93 [0,56; 1,54] 0,766	-0,00 [-0,02; 0,02] 0,769
DIARRHOEA, n (%)	70 (6,4)	23 (4,2)	1,55 [0,95; 2,51] 0,074	1,51 [0,95; 2,39] 0,078	0,02 [-0,00; 0,04] 0,057
DYSPEPSIA, n (%)	11 (1,0)	7 (1,3)	0,78 [0,30; 2,02] 0,606	0,78 [0,30; 2,00] 0,607	-0,00 [-0,01; 0,01] 0,620
NAUSEA, n (%)	74 (6,7)	19 (3,5)	2,00 [1,20; 3,35] 0,007 *	1,93 [1,18; 3,17] 0,009 *	0,03 [0,01; 0,05] 0,003 *
VOMITING, n (%)	33 (3,0)	13 (2,4)	1,27 [0,66; 2,43] 0,471	1,26 [0,67; 2,38] 0,473	0,01 [-0,01; 0,02] 0,454
GENERAL DISORDERS AND ADMINISTRATION SITE CONDITIONS, n (%)	268 (24,4)	110 (20,1)	1,28 [1,00; 1,64] 0,054	1,21 [0,99; 1,47] 0,057	0,04 [0,00; 0,08] 0,049 *
ASTHENIA, n (%)	26 (2,4)	7 (1,3)	1,87 [0,80; 4,33] 0,140	1,85 [0,81; 4,22] 0,147	0,01 [-0,00; 0,02] 0,103
CHEST DISCOMFORT, n (%)	11 (1,0)	4 (0,7)	1,37 [0,43; 4,32] 0,590	1,37 [0,44; 4,27] 0,592	0,00 [-0,01; 0,01] 0,570
FATIGUE, n (%)	100 (9,1)	51 (9,3)	0,97 [0,68; 1,38] 0,873	0,97 [0,71; 1,34] 0,873	-0,00 [-0,03; 0,03] 0,874
GAIT DISTURBANCE, n (%)	24 (2,2)	22 (4,0)	0,53 [0,30; 0,96] 0,033 *	0,54 [0,31; 0,96] 0,035 *	-0,02 [-0,04; 0,00] 0,052
INFLUENZA LIKE ILLNESS, n (%)	14 (1,3)	7 (1,3)	0,99 [0,40; 2,48] 0,989	0,99 [0,40; 2,45] 0,989	-0,00 [-0,01; 0,01] 0,989
NON-CARDIAC CHEST PAIN, n (%)	14 (1,3)	6 (1,1)	1,16 [0,44; 3,04] 0,760	1,16 [0,45; 3,00] 0,761	0,00 [-0,01; 0,01] 0,755

	Treatment groups		Comparison		
	BAF312 (N=1099)	**Placebo (N=546)**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
OEDEMA PERIPHERAL, n (%)	50 (4,5)	13 (2,4)	1,95 [1,05; 3,63] 0,031 *	1,91 [1,05; 3,49] 0,035 *	0,02 [0,00; 0,04] 0,017 *
PAIN, n (%)	11 (1,0)	4 (0,7)	1,37 [0,43; 4,32] 0,590	1,37 [0,44; 4,27] 0,592	0,00 [-0,01; 0,01] 0,570
PERIPHERAL SWELLING, n (%)	25 (2,3)	6 (1,1)	2,09 [0,85; 5,14] 0,099	2,07 [0,85; 5,02] 0,107	0,01 [-0,00; 0,02] 0,063
PYREXIA, n (%)	23 (2,1)	8 (1,5)	1,44 [0,64; 3,23] 0,378	1,43 [0,64; 3,17] 0,381	0,01 [-0,01; 0,02] 0,350
HEPATOBILIARY DISORDERS, n (%)	27 (2,5)	4 (0,7)	3,41 [1,19; 9,80] 0,015 *	3,35 [1,18; 9,54] 0,023 *	0,02 [0,01; 0,03] 0,004 *
INFECTIONS AND INFESTATIONS, n (%)	539 (49,0)	268 (49,1)	1,00 [0,81; 1,23] 0,988	1,00 [0,90; 1,11] 0,988	-0,00 [-0,05; 0,05] 0,988
BRONCHITIS, n (%)	36 (3,3)	16 (2,9)	1,12 [0,62; 2,04] 0,706	1,12 [0,63; 2,00] 0,707	0,00 [-0,01; 0,02] 0,701
CYSTITIS, n (%)	28 (2,5)	13 (2,4)	1,07 [0,55; 2,09] 0,838	1,07 [0,56; 2,05] 0,838	0,00 [-0,01; 0,02] 0,836
GASTROENTERITIS, n (%)	16 (1,5)	9 (1,6)	0,88 [0,39; 2,01] 0,764	0,88 [0,39; 1,99] 0,764	-0,00 [-0,01; 0,01] 0,768
HERPES ZOSTER, n (%)	25 (2,3)	4 (0,7)	3,15 [1,09; 9,11] 0,025 *	3,11 [1,09; 8,88] 0,035 *	0,02 [0,00; 0,03] 0,008 *
INFLUENZA, n (%)	73 (6,6)	40 (7,3)	0,90 [0,60; 1,34] 0,606	0,91 [0,63; 1,31] 0,605	-0,01 [-0,03; 0,02] 0,611
NASOPHARYNGITIS, n (%)	149 (13,6)	79 (14,5)	0,93 [0,69; 1,24] 0,615	0,94 [0,73; 1,21] 0,614	-0,01 [-0,04; 0,03] 0,618
ORAL HERPES, n (%)	18 (1,6)	10 (1,8)	0,89 [0,41; 1,95] 0,775	0,89 [0,42; 1,92] 0,775	-0,00 [-0,02; 0,01] 0,779
PHARYNGITIS, n (%)	20 (1,8)	11 (2,0)	0,90 [0,43; 1,90] 0,784	0,90 [0,44; 1,87] 0,784	-0,00 [-0,02; 0,01] 0,788
RHINITIS, n (%)	14 (1,3)	10 (1,8)	0,69 [0,31; 1,57] 0,374	0,70 [0,31; 1,56] 0,377	-0,01 [-0,02; 0,01] 0,403
SINUSITIS, n (%)	21 (1,9)	9 (1,6)	1,16 [0,53; 2,56] 0,708	1,16 [0,53; 2,51] 0,708	0,00 [-0,01; 0,02] 0,701

	Treatment groups		Comparison		
	BAF312 (N=1099)	Placebo (N=546)	OR [95% CI] p-value	RR [95% CI] p-value	RD [95% CI] p-value
UPPER RESPIRATORY TRACT INFECTION, n (%)	91 (8,3)	41 (7,5)	1,11 [0,76; 1,63] 0,588	1,10 [0,77; 1,57] 0,588	0,01 [-0,02; 0,04] 0,582
URINARY TRACT INFECTION, n (%)	133 (12,1)	80 (14,7)	0,80 [0,60; 1,08] 0,147	0,83 [0,64; 1,07] 0,146	-0,03 [-0,06; 0,01] 0,158
INJURY, POISONING AND PROCEDURAL COMPLICATIONS, n (%)	238 (21,7)	114 (20,9)	1,05 [0,81; 1,35] 0,717	1,04 [0,85; 1,26] 0,718	0,01 [-0,03; 0,05] 0,716
CONTUSION, n (%)	35 (3,2)	15 (2,7)	1,16 [0,63; 2,15] 0,626	1,16 [0,64; 2,10] 0,627	0,00 [-0,01; 0,02] 0,618
FALL, n (%)	128 (11,6)	59 (10,8)	1,09 [0,78; 1,51] 0,613	1,08 [0,81; 1,44] 0,613	0,01 [-0,02; 0,04] 0,609
LACERATION, n (%)	18 (1,6)	4 (0,7)	2,26 [0,76; 6,70] 0,132	2,24 [0,76; 6,57] 0,144	0,01 [-0,00; 0,02] 0,087
LIGAMENT SPRAIN, n (%)	12 (1,1)	6 (1,1)	0,99 [0,37; 2,66] 0,990	0,99 [0,37; 2,63] 0,990	-0,00 [-0,01; 0,01] 0,990
INVESTIGATIONS, n (%)	263 (23,9)	80 (14,7)	1,83 [1,39; 2,41] <0,001 *	1,63 [1,30; 2,05] <0,001 *	0,09 [0,05; 0,13] <0,001 *
ALANINE AMINOTRANSFERASE INCREASED, n (%)	65 (5,9)	8 (1,5)	4,23 [2,01; 8,88] <0,001 *	4,04 [1,95; 8,35] <0,001 *	0,04 [0,03; 0,06] <0,001 *
ASPARTATE AMINOTRANSFERASE INCREASED, n (%)	15 (1,4)	4 (0,7)	1,88 [0,62; 5,68] 0,258	1,86 [0,62; 5,59] 0,267	0,01 [-0,00; 0,02] 0,211
BLOOD ALKALINE PHOSPHATASE INCREASED, n (%)	12 (1,1)	0 (0,0)	12,56 [0,74; 212,58] 0,014 *	12,43 [0,74; 209,58] 0,080	0,01 [0,00; 0,02] <0,001 *
BLOOD BILIRUBIN INCREASED, n (%)	12 (1,1)	2 (0,4)	3,00 [0,67; 13,46] 0,131	2,98 [0,67; 13,27] 0,152	0,01 [-0,00; 0,02] 0,074
BLOOD CHOLESTEROL INCREASED, n (%)	20 (1,8)	6 (1,1)	1,67 [0,67; 4,18] 0,270	1,66 [0,67; 4,10] 0,275	0,01 [-0,00; 0,02] 0,231
BLOOD PRESSURE INCREASED, n (%)	19 (1,7)	7 (1,3)	1,35 [0,57; 3,24] 0,494	1,35 [0,57; 3,19] 0,496	0,00 [-0,01; 0,02] 0,472

	Treatment groups		Comparison		
	BAF312 (N=1099)	**Placebo (N=546)**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
GAMMA-GLUTAMYLTRANSFERASE INCREASED, n (%)	43 (3,9)	6 (1,1)	3,66 [1,55; 8,66] 0,002 *	3,56 [1,52; 8,31] 0,003 *	0,03 [0,01; 0,04] <0,001 *
HEPATIC ENZYME INCREASED, n (%)	16 (1,5)	1 (0,2)	8,05 [1,07; 60,87] 0,016 *	7,95 [1,06; 59,78] 0,044 *	0,01 [0,00; 0,02] 0,002 *
WEIGHT DECREASED, n (%)	22 (2,0)	9 (1,6)	1,22 [0,56; 2,67] 0,620	1,21 [0,56; 2,62] 0,620	0,00 [-0,01; 0,02] 0,608
WEIGHT INCREASED, n (%)	27 (2,5)	13 (2,4)	1,03 [0,53; 2,02] 0,925	1,03 [0,54; 1,98] 0,925	0,00 [-0,01; 0,02] 0,925
METABOLISM AND NUTRITION DISORDERS, n (%)	85 (7,7)	28 (5,1)	1,55 [1,00; 2,41] 0,049 *	1,51 [1,00; 2,28] 0,052	0,03 [0,00; 0,05] 0,036 *
HYPERCHOLESTEROLAEMIA, n (%)	28 (2,5)	11 (2,0)	1,27 [0,63; 2,57] 0,503	1,26 [0,63; 2,52] 0,505	0,01 [-0,01; 0,02] 0,487
VITAMIN D DEFICIENCY, n (%)	11 (1,0)	7 (1,3)	0,78 [0,30; 2,02] 0,606	0,78 [0,30; 2,00] 0,607	-0,00 [-0,01; 0,01] 0,620
MUSCULOSKELETAL AND CONNECTIVE TISSUE DISORDERS, n (%)	289 (26,3)	149 (27,3)	0,95 [0,75; 1,20] 0,668	0,96 [0,81; 1,14] 0,667	-0,01 [-0,06; 0,04] 0,669
ARTHRALGIA, n (%)	49 (4,5)	35 (6,4)	0,68 [0,44; 1,06] 0,090	0,70 [0,46; 1,06] 0,091	-0,02 [-0,04; 0,00] 0,109
BACK PAIN, n (%)	67 (6,1)	43 (7,9)	0,76 [0,51; 1,13] 0,174	0,77 [0,54; 1,12] 0,174	-0,02 [-0,04; 0,01] 0,191
JOINT SWELLING, n (%)	17 (1,5)	7 (1,3)	1,21 [0,50; 2,93] 0,673	1,21 [0,50; 2,89] 0,674	0,00 [-0,01; 0,01] 0,663
MUSCLE SPASMS, n (%)	37 (3,4)	19 (3,5)	0,97 [0,55; 1,70] 0,905	0,97 [0,56; 1,67] 0,905	-0,00 [-0,02; 0,02] 0,906
MUSCULAR WEAKNESS, n (%)	17 (1,5)	13 (2,4)	0,64 [0,31; 1,34] 0,234	0,65 [0,32; 1,33] 0,237	-0,01 [-0,02; 0,01] 0,267
MUSCULOSKELETAL PAIN, n (%)	27 (2,5)	14 (2,6)	0,96 [0,50; 1,84] 0,895	0,96 [0,51; 1,81] 0,895	-0,00 [-0,02; 0,02] 0,896
MYALGIA, n (%)	13 (1,2)	8 (1,5)	0,81 [0,33; 1,95] 0,631	0,81 [0,34; 1,94] 0,632	-0,00 [-0,01; 0,01] 0,643

	Treatment groups		Comparison		
	BAF312 (N=1099)	**Placebo (N=546)**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
NECK PAIN, n (%)	13 (1,2)	7 (1,3)	0,92 [0,37; 2,32] 0,863	0,92 [0,37; 2,30] 0,863	-0,00 [-0,01; 0,01] 0,865
PAIN IN EXTREMITY, n (%)	60 (5,5)	21 (3,8)	1,44 [0,87; 2,40] 0,154	1,42 [0,87; 2,31] 0,158	0,02 [-0,00; 0,04] 0,132
NEOPLASMS BENIGN, MALIGNANT AND UNSPECIFIED (INCL CYSTS AND POLYPS), n (%)	113 (10,3)	45 (8,2)	1,28 [0,89; 1,83] 0,186	1,25 [0,90; 1,74] 0,189	0,02 [-0,01; 0,05] 0,171
BASAL CELL CARCINOMA, n (%)	12 (1,1)	7 (1,3)	0,85 [0,33; 2,17] 0,734	0,85 [0,34; 2,15] 0,734	-0,00 [-0,01; 0,01] 0,741
MELANOCYTIC NAEVUS, n (%)	47 (4,3)	17 (3,1)	1,39 [0,79; 2,44] 0,251	1,37 [0,80; 2,37] 0,254	0,01 [-0,01; 0,03] 0,227
NERVOUS SYSTEM DISORDERS, n (%)	416 (37,9)	175 (32,1)	1,29 [1,04; 1,60] 0,021 *	1,18 [1,02; 1,36] 0,023 *	0,06 [0,01; 0,11] 0,019 *
BALANCE DISORDER, n (%)	13 (1,2)	5 (0,9)	1,30 [0,46; 3,65] 0,624	1,29 [0,46; 3,60] 0,625	0,00 [-0,01; 0,01] 0,609
DIZZINESS, n (%)	75 (6,8)	26 (4,8)	1,46 [0,93; 2,32] 0,101	1,43 [0,93; 2,21] 0,104	0,02 [-0,00; 0,04] 0,082
HEADACHE, n (%)	159 (14,5)	71 (13,0)	1,13 [0,84; 1,53] 0,420	1,11 [0,86; 1,44] 0,422	0,01 [-0,02; 0,05] 0,413
HYPOAESTHESIA, n (%)	15 (1,4)	15 (2,7)	0,49 [0,24; 1,01] 0,048 *	0,50 [0,24; 1,01] 0,053	-0,01 [-0,03; 0,00] 0,077
MIGRAINE, n (%)	16 (1,5)	8 (1,5)	0,99 [0,42; 2,34] 0,988	0,99 [0,43; 2,31] 0,988	-0,00 [-0,01; 0,01] 0,988
MUSCLE SPASTICITY, n (%)	43 (3,9)	23 (4,2)	0,93 [0,55; 1,55] 0,770	0,93 [0,57; 1,52] 0,770	-0,00 [-0,02; 0,02] 0,773
NEURALGIA, n (%)	14 (1,3)	5 (0,9)	1,40 [0,50; 3,90] 0,522	1,39 [0,50; 3,84] 0,524	0,00 [-0,01; 0,01] 0,499
PARAESTHESIA, n (%)	18 (1,6)	20 (3,7)	0,44 [0,23; 0,83] 0,010 *	0,45 [0,24; 0,84] 0,012 *	-0,02 [-0,04; -0,00] 0,023 *
SCIATICA, n (%)	18 (1,6)	5 (0,9)	1,80 [0,67; 4,88] 0,240	1,79 [0,67; 4,79] 0,248	0,01 [-0,00; 0,02] 0,197

	Treatment groups		Comparison		
	BAF312 (N=1099)	**Placebo (N=546)**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
SOMNOLENCE, n (%)	11 (1,0)	5 (0,9)	1,09 [0,38; 3,16] 0,868	1,09 [0,38; 3,13] 0,868	0,00 [-0,01; 0,01] 0,866
SYNCOPE, n (%)	14 (1,3)	7 (1,3)	0,99 [0,40; 2,48] 0,989	0,99 [0,40; 2,45] 0,989	-0,00 [-0,01; 0,01] 0,989
TREMOR, n (%)	17 (1,5)	3 (0,5)	2,84 [0,83; 9,75] 0,082	2,82 [0,83; 9,57] 0,097	0,01 [0,00; 0,02] 0,041 *
TRIGEMINAL NEURALGIA, n (%)	17 (1,5)	5 (0,9)	1,70 [0,62; 4,63] 0,294	1,69 [0,63; 4,55] 0,300	0,01 [-0,00; 0,02] 0,253
PSYCHIATRIC DISORDERS, n (%)	169 (15,4)	83 (15,2)	1,01 [0,76; 1,35] 0,926	1,01 [0,79; 1,29] 0,926	0,00 [-0,04; 0,04] 0,925
ANXIETY, n (%)	23 (2,1)	14 (2,6)	0,81 [0,41; 1,59] 0,544	0,82 [0,42; 1,57] 0,544	-0,00 [-0,02; 0,01] 0,557
DEPRESSED MOOD, n (%)	16 (1,5)	7 (1,3)	1,14 [0,47; 2,78] 0,777	1,14 [0,47; 2,74] 0,778	0,00 [-0,01; 0,01] 0,773
DEPRESSION, n (%)	49 (4,5)	30 (5,5)	0,80 [0,50; 1,28] 0,355	0,81 [0,52; 1,26] 0,355	-0,01 [-0,03; 0,01] 0,371
INSOMNIA, n (%)	38 (3,5)	19 (3,5)	0,99 [0,57; 1,74] 0,982	0,99 [0,58; 1,71] 0,982	-0,00 [-0,02; 0,02] 0,982
SLEEP DISORDER, n (%)	11 (1,0)	5 (0,9)	1,09 [0,38; 3,16] 0,868	1,09 [0,38; 3,13] 0,868	0,00 [-0,01; 0,01] 0,866
RENAL AND URINARY DISORDERS, n (%)	84 (7,6)	37 (6,8)	1,14 [0,76; 1,70] 0,526	1,13 [0,78; 1,64] 0,527	0,01 [-0,02; 0,03] 0,518
DYSURIA, n (%)	11 (1,0)	3 (0,5)	1,83 [0,51; 6,59] 0,348	1,82 [0,51; 6,50] 0,356	0,00 [-0,00; 0,01] 0,301
URINARY INCONTINENCE, n (%)	13 (1,2)	12 (2,2)	0,53 [0,24; 1,18] 0,113	0,54 [0,25; 1,17] 0,119	-0,01 [-0,02; 0,00] 0,151
URINARY RETENTION, n (%)	14 (1,3)	8 (1,5)	0,87 [0,36; 2,08] 0,750	0,87 [0,37; 2,06] 0,751	-0,00 [-0,01; 0,01] 0,756
REPRODUCTIVE SYSTEM AND BREAST DISORDERS, n (%)	36 (3,3)	24 (4,4)	0,74 [0,43; 1,25] 0,254	0,75 [0,45; 1,24] 0,255	-0,01 [-0,03; 0,01] 0,276

	Treatment groups		Comparison		
	BAF312 (N=1099)	**Placebo (N=546)**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
RESPIRATORY, THORACIC AND MEDIASTINAL DISORDERS, n (%)	117 (10,6)	71 (13,0)	0,80 [0,58; 1,09] 0,157	0,82 [0,62; 1,08] 0,156	-0,02 [-0,06; 0,01] 0,169
COUGH, n (%)	35 (3,2)	18 (3,3)	0,96 [0,54; 1,72] 0,904	0,97 [0,55; 1,69] 0,904	-0,00 [-0,02; 0,02] 0,904
DYSPNOEA, n (%)	19 (1,7)	10 (1,8)	0,94 [0,44; 2,04] 0,882	0,94 [0,44; 2,02] 0,882	-0,00 [-0,01; 0,01] 0,883
OROPHARYNGEAL PAIN, n (%)	20 (1,8)	17 (3,1)	0,58 [0,30; 1,11] 0,096	0,58 [0,31; 1,11] 0,099	-0,01 [-0,03; 0,00] 0,126
SKIN AND SUBCUTANEOUS TISSUE DISORDERS, n (%)	188 (17,1)	93 (17,0)	1,01 [0,77; 1,32] 0,970	1,00 [0,80; 1,26] 0,970	0,00 [-0,04; 0,04] 0,970
ACTINIC KERATOSIS, n (%)	15 (1,4)	6 (1,1)	1,25 [0,48; 3,23] 0,651	1,24 [0,48; 3,18] 0,652	0,00 [-0,01; 0,01] 0,639
ECZEMA, n (%)	17 (1,5)	5 (0,9)	1,70 [0,62; 4,63] 0,294	1,69 [0,63; 4,55] 0,300	0,01 [-0,00; 0,02] 0,253
RASH, n (%)	20 (1,8)	13 (2,4)	0,76 [0,38; 1,54] 0,445	0,76 [0,38; 1,52] 0,446	-0,01 [-0,02; 0,01] 0,464
VASCULAR DISORDERS, n (%)	160 (14,6)	60 (11,0)	1,38 [1,01; 1,89] 0,045 *	1,32 [1,00; 1,75] 0,048 *	0,04 [0,00; 0,07] 0,037 *
HAEMATOMA, n (%)	15 (1,4)	3 (0,5)	2,50 [0,72; 8,69] 0,134	2,48 [0,72; 8,54] 0,149	0,01 [-0,00; 0,02] 0,084
HYPERTENSION, n (%)	115 (10,5)	41 (7,5)	1,44 [0,99; 2,09] 0,054	1,39 [0,99; 1,96] 0,057	0,03 [0,00; 0,06] 0,043 *

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 total population

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

	Treatment groups		Comparison		
	BAF312 (N=1099)	Placebo (N=546)	OR [95% CI] p-value	RR [95% CI] p-value	RD [95% CI] p-value
N'	1099	546			
INFECTIONS AND INFESTATIONS, n (%)	33 (3,0)	15 (2,7)	1,10 [0,59; 2,04] 0,772	1,09 [0,60; 1,99] 0,772	0,00 [-0,01; 0,02] 0,769
URINARY TRACT INFECTION, n (%)	13 (1,2)	6 (1,1)	1,08 [0,41; 2,85] 0,881	1,08 [0,41; 2,82] 0,881	0,00 [-0,01; 0,01] 0,879
INJURY, POISONING AND PROCEDURAL COMPLICATIONS, n (%)	20 (1,8)	5 (0,9)	2,01 [0,75; 5,37] 0,158	1,99 [0,75; 5,27] 0,167	0,01 [-0,00; 0,02] 0,115
INVESTIGATIONS, n (%)	21 (1,9)	3 (0,5)	3,53 [1,05; 11,87] 0,030 *	3,48 [1,04; 11,61] 0,043 *	0,01 [0,00; 0,02] 0,009 *
MUSCULOSKELETAL AND CONNECTIVE TISSUE DISORDERS, n (%)	12 (1,1)	3 (0,5)	2,00 [0,56; 7,11] 0,276	1,99 [0,56; 7,01] 0,286	0,01 [-0,00; 0,01] 0,223
NEOPLASMS BENIGN, MALIGNANT AND UNSPECIFIED (INCL CYSTS AND POLYPS), n (%)	23 (2,1)	15 (2,7)	0,76 [0,39; 1,46] 0,405	0,76 [0,40; 1,45] 0,406	-0,01 [-0,02; 0,01] 0,426
BASAL CELL CARCINOMA, n (%)	11 (1,0)	6 (1,1)	0,91 [0,33; 2,47] 0,853	0,91 [0,34; 2,45] 0,853	-0,00 [-0,01; 0,01] 0,855
NERVOUS SYSTEM DISORDERS, n (%)	40 (3,6)	17 (3,1)	1,18 [0,66; 2,09] 0,583	1,17 [0,67; 2,04] 0,583	0,01 [-0,01; 0,02] 0,573
PSYCHIATRIC DISORDERS, n (%)	22 (2,0)	7 (1,3)	1,57 [0,67; 3,71] 0,296	1,56 [0,67; 3,63] 0,301	0,01 [-0,01; 0,02] 0,261
RENAL AND URINARY DISORDERS, n (%)	14 (1,3)	3 (0,5)	2,34 [0,67; 8,16] 0,171	2,32 [0,67; 8,03] 0,185	0,01 [-0,00; 0,02] 0,118

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 ≥ 5% in at least one treatment arm are displayed.

Analysis population: A2304 SAF total population

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

	Treatment groups		Comparison		
	BAF312 (N=1099)	Placebo (N=546)	OR [95% CI] p-value	RR [95% CI] p-value	RD [95% CI] p-value
N'	1099	546			
BLOOD AND LYMPHATIC SYSTEM DISORDERS					
not severe[1]	41 (3,7)	8 (1,5)	2,61 [1,21; 5,60] 0,011 *	2,55 [1,20; 5,39] 0,015 *	0,02 [0,01; 0,04] 0,003 *
severe[1]	5 (0,5)	2 (0,4)	1,24 [0,24; 6,43] 0,795	1,24 [0,24; 6,38] 0,795	0,00 [-0,01; 0,01] 0,787
ANAEMIA					
not severe[1]	17 (1,5)	4 (0,7)	2,13 [0,71; 6,36] 0,166	2,11 [0,71; 6,24] 0,177	0,01 [-0,00; 0,02] 0,118
severe[1]	0 (0,0)	2 (0,4)	0,10 [0,00; 2,07] 0,045 *	0,10 [0,00; 2,07] 0,136	-0,00 [-0,01; 0,00] 0,157
CARDIAC DISORDERS					
not severe[1]	127 (11,6)	53 (9,7)	1,22 [0,87; 1,70] 0,258	1,19 [0,88; 1,61] 0,260	0,02 [-0,01; 0,05] 0,246
severe[1]	6 (0,5)	3 (0,5)	0,99 [0,25; 3,99] 0,993	0,99 [0,25; 3,96] 0,993	-0,00 [-0,01; 0,01] 0,993
ATRIOVENTRICULAR BLOCK FIRST DEGREE					
not severe[1]	14 (1,3)	4 (0,7)	1,75 [0,57; 5,34] 0,320	1,74 [0,58; 5,26] 0,327	0,01 [-0,00; 0,02] 0,277
severe[1]	0 (0,0)	0 (0,0)	-	-	-
BRADYCARDIA					
not severe[1]	48 (4,4)	14 (2,6)	1,74 [0,95; 3,18] 0,071	1,70 [0,95; 3,06] 0,075	0,02 [0,00; 0,04] 0,049 *
severe[1]	2 (0,2)	0 (0,0)	2,49 [0,12; 51,95] 0,319	2,49 [0,12; 51,70] 0,556	0,00 [-0,00; 0,00] 0,157
PALPITATIONS					
not severe[1]	19 (1,7)	10 (1,8)	0,94 [0,44; 2,04] 0,882	0,94 [0,44; 2,02] 0,882	-0,00 [-0,01; 0,01] 0,883
severe[1]	1 (0,1)	0 (0,0)	1,49 [0,06; 36,70] 0,481	1,49 [0,06; 36,56] 0,806	0,00 [-0,00; 0,00] 0,317

	Treatment groups		Comparison		
	BAF312 (N=1099)	**Placebo (N=546)**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
SINUS BRADYCARDIA					
not severe[1]	14 (1,3)	4 (0,7)	1,75 [0,57; 5,34] 0,320	1,74 [0,58; 5,26] 0,327	0,01 [-0,00; 0,02] 0,277
severe[1]	0 (0,0)	0 (0,0)	-	-	-
EAR AND LABYRINTH DISORDERS					
not severe[1]	55 (5,0)	36 (6,6)	0,75 [0,48; 1,15] 0,184	0,76 [0,51; 1,14] 0,185	-0,02 [-0,04; 0,01] 0,203
severe[1]	0 (0,0)	2 (0,4)	0,10 [0,00; 2,07] 0,045 *	0,10 [0,00; 2,07] 0,136	-0,00 [-0,01; 0,00] 0,157
TINNITUS					
not severe[1]	13 (1,2)	2 (0,4)	3,26 [0,73; 14,48] 0,101	3,23 [0,73; 14,26] 0,122	0,01 [0,00; 0,02] 0,050 *
severe[1]	0 (0,0)	0 (0,0)	-	-	-
VERTIGO					
not severe[1]	25 (2,3)	25 (4,6)	0,49 [0,28; 0,85] 0,010 *	0,50 [0,29; 0,86] 0,012 *	-0,02 [-0,04; -0,00] 0,021 *
severe[1]	0 (0,0)	1 (0,2)	0,17 [0,01; 4,07] 0,156	0,17 [0,01; 4,06] 0,271	-0,00 [-0,01; 0,00] 0,317
ENDOCRINE DISORDERS					
not severe[1]	11 (1,0)	4 (0,7)	1,37 [0,43; 4,32] 0,590	1,37 [0,44; 4,27] 0,592	0,00 [-0,01; 0,01] 0,570
severe[1]	0 (0,0)	0 (0,0)	-	-	-
EYE DISORDERS					
not severe[1]	107 (9,7)	54 (9,9)	0,98 [0,70; 1,39] 0,921	0,98 [0,72; 1,34] 0,921	-0,00 [-0,03; 0,03] 0,921
severe[1]	7 (0,6)	1 (0,2)	3,49 [0,43; 28,47] 0,213	3,48 [0,43; 28,20] 0,243	0,00 [-0,00; 0,01] 0,133
MACULAR OEDEMA					
not severe[1]	14 (1,3)	0 (0,0)	14,60 [0,87; 245,21] 0,008 *	14,42 [0,86; 241,29] 0,063	0,01 [0,01; 0,02] <0,001 *
severe[1]	4 (0,4)	1 (0,2)	1,99 [0,22; 17,86] 0,530	1,99 [0,22; 17,74] 0,539	0,00 [-0,00; 0,01] 0,483

	Treatment groups		Comparison		
	BAF312 (N=1099)	**Placebo (N=546)**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
VISION BLURRED					
not severe[1]	13 (1,2)	9 (1,6)	0,71 [0,30; 1,68] 0,439	0,72 [0,31; 1,67] 0,441	-0,00 [-0,02; 0,01] 0,464
severe[1]	0 (0,0)	0 (0,0)	-	-	-
GASTROINTESTINAL DISORDERS					
not severe[1]	268 (24,4)	107 (19,6)	1,32 [1,03; 1,70] 0,029 *	1,24 [1,02; 1,52] 0,032 *	0,05 [0,01; 0,09] 0,025 *
severe[1]	5 (0,5)	4 (0,7)	0,62 [0,17; 2,32] 0,472	0,62 [0,17; 2,30] 0,476	-0,00 [-0,01; 0,01] 0,506
ABDOMINAL PAIN					
not severe[1]	12 (1,1)	3 (0,5)	2,00 [0,56; 7,11] 0,276	1,99 [0,56; 7,01] 0,286	0,01 [-0,00; 0,01] 0,223
severe[1]	0 (0,0)	0 (0,0)	-	-	-
ABDOMINAL PAIN UPPER					
not severe[1]	23 (2,1)	11 (2,0)	1,04 [0,50; 2,15] 0,916	1,04 [0,51; 2,12] 0,916	0,00 [-0,01; 0,02] 0,916
severe[1]	1 (0,1)	0 (0,0)	1,49 [0,06; 36,70] 0,481	1,49 [0,06; 36,56] 0,806	0,00 [-0,00; 0,00] 0,317
CONSTIPATION					
not severe[1]	41 (3,7)	22 (4,0)	0,92 [0,54; 1,57] 0,766	0,93 [0,56; 1,54] 0,766	-0,00 [-0,02; 0,02] 0,769
severe[1]	0 (0,0)	0 (0,0)	-	-	-
DIARRHOEA					
not severe[1]	69 (6,3)	23 (4,2)	1,52 [0,94; 2,47] 0,086	1,49 [0,94; 2,36] 0,089	0,02 [-0,00; 0,04] 0,067
severe[1]	2 (0,2)	0 (0,0)	2,49 [0,12; 51,95] 0,319	2,49 [0,12; 51,70] 0,556	0,00 [-0,00; 0,00] 0,157
DYSPEPSIA					
not severe[1]	11 (1,0)	7 (1,3)	0,78 [0,30; 2,02] 0,606	0,78 [0,30; 2,00] 0,607	-0,00 [-0,01; 0,01] 0,620
severe[1]	0 (0,0)	0 (0,0)	-	-	-

	Treatment groups		Comparison		
	BAF312 (N=1099)	**Placebo (N=546)**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
NAUSEA					
not severe[1]	73 (6,6)	19 (3,5)	1,97 [1,18; 3,30] 0,009 *	1,91 [1,16; 3,13] 0,010 *	0,03 [0,01; 0,05] 0,004 *
severe[1]	2 (0,2)	0 (0,0)	2,49 [0,12; 51,95] 0,319	2,49 [0,12; 51,70] 0,556	0,00 [-0,00; 0,00] 0,157
VOMITING					
not severe[1]	33 (3,0)	13 (2,4)	1,27 [0,66; 2,43] 0,471	1,26 [0,67; 2,38] 0,473	0,01 [-0,01; 0,02] 0,454
severe[1]	0 (0,0)	0 (0,0)	-	-	-
GENERAL DISORDERS AND ADMINISTRATION SITE CONDITIONS					
not severe[1]	265 (24,1)	108 (19,8)	1,29 [1,00; 1,66] 0,048 *	1,22 [1,00; 1,49] 0,051	0,04 [0,00; 0,09] 0,043 *
severe[1]	6 (0,5)	3 (0,5)	0,99 [0,25; 3,99] 0,993	0,99 [0,25; 3,96] 0,993	-0,00 [-0,01; 0,01] 0,993
ASTHENIA					
not severe[1]	25 (2,3)	7 (1,3)	1,79 [0,77; 4,17] 0,170	1,77 [0,77; 4,08] 0,177	0,01 [-0,00; 0,02] 0,132
severe[1]	1 (0,1)	0 (0,0)	1,49 [0,06; 36,70] 0,481	1,49 [0,06; 36,56] 0,806	0,00 [-0,00; 0,00] 0,317
CHEST DISCOMFORT					
not severe[1]	11 (1,0)	4 (0,7)	1,37 [0,43; 4,32] 0,590	1,37 [0,44; 4,27] 0,592	0,00 [-0,01; 0,01] 0,570
severe[1]	0 (0,0)	0 (0,0)	-	-	-
FATIGUE					
not severe[1]	98 (8,9)	50 (9,2)	0,97 [0,68; 1,39] 0,873	0,97 [0,70; 1,35] 0,873	-0,00 [-0,03; 0,03] 0,873
severe[1]	4 (0,4)	1 (0,2)	1,99 [0,22; 17,86] 0,530	1,99 [0,22; 17,74] 0,539	0,00 [-0,00; 0,01] 0,483
GAIT DISTURBANCE					
not severe[1]	24 (2,2)	21 (3,8)	0,56 [0,31; 1,01] 0,052	0,57 [0,32; 1,01] 0,054	-0,02 [-0,03; 0,00] 0,075
severe[1]	0 (0,0)	1 (0,2)	0,17 [0,01; 4,07] 0,156	0,17 [0,01; 4,06] 0,271	-0,00 [-0,01; 0,00] 0,317

	Treatment groups		Comparison		
	BAF312 (N=1099)	**Placebo (N=546)**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
INFLUENZA LIKE ILLNESS					
not severe[1]	14 (1,3)	7 (1,3)	0,99 [0,40; 2,48] 0,989	0,99 [0,40; 2,45] 0,989	-0,00 [-0,01; 0,01] 0,989
severe[1]	0 (0,0)	0 (0,0)	-	-	-
NON-CARDIAC CHEST PAIN					
not severe[1]	13 (1,2)	6 (1,1)	1,08 [0,41; 2,85] 0,881	1,08 [0,41; 2,82] 0,881	0,00 [-0,01; 0,01] 0,879
severe[1]	1 (0,1)	0 (0,0)	1,49 [0,06; 36,70] 0,481	1,49 [0,06; 36,56] 0,806	0,00 [-0,00; 0,00] 0,317
OEDEMA PERIPHERAL					
not severe[1]	50 (4,5)	13 (2,4)	1,95 [1,05; 3,63] 0,031 *	1,91 [1,05; 3,49] 0,035 *	0,02 [0,00; 0,04] 0,017 *
severe[1]	0 (0,0)	0 (0,0)	-	-	-
PAIN					
not severe[1]	11 (1,0)	4 (0,7)	1,37 [0,43; 4,32] 0,590	1,37 [0,44; 4,27] 0,592	0,00 [-0,01; 0,01] 0,570
severe[1]	0 (0,0)	0 (0,0)	-	-	-
PERIPHERAL SWELLING					
not severe[1]	25 (2,3)	6 (1,1)	2,09 [0,85; 5,14] 0,099	2,07 [0,85; 5,02] 0,107	0,01 [-0,00; 0,02] 0,063
severe[1]	0 (0,0)	0 (0,0)	-	-	-
PYREXIA					
not severe[1]	23 (2,1)	8 (1,5)	1,44 [0,64; 3,23] 0,378	1,43 [0,64; 3,17] 0,381	0,01 [-0,01; 0,02] 0,350
severe[1]	0 (0,0)	0 (0,0)	-	-	-
HEPATOBILIARY DISORDERS					
not severe[1]	22 (2,0)	4 (0,7)	2,77 [0,95; 8,07] 0,052	2,73 [0,95; 7,89] 0,063	0,01 [0,00; 0,02] 0,023 *
severe[1]	5 (0,5)	0 (0,0)	5,49 [0,30; 99,51] 0,114	5,47 [0,30; 98,74] 0,250	0,00 [0,00; 0,01] 0,025 *

	Treatment groups		Comparison		
	BAF312 (N=1099)	**Placebo (N=546)**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
INFECTIONS AND INFESTATIONS					
not severe[1]	528 (48,0)	262 (48,0)	1,00 [0,82; 1,23] 0,982	1,00 [0,90; 1,11] 0,982	0,00 [-0,05; 0,05] 0,982
severe[1]	24 (2,2)	11 (2,0)	1,09 [0,53; 2,23] 0,823	1,08 [0,53; 2,20] 0,823	0,00 [-0,01; 0,02] 0,821
BRONCHITIS					
not severe[1]	36 (3,3)	16 (2,9)	1,12 [0,62; 2,04] 0,706	1,12 [0,63; 2,00] 0,707	0,00 [-0,01; 0,02] 0,701
severe[1]	0 (0,0)	0 (0,0)	-	-	-
CYSTITIS					
not severe[1]	28 (2,5)	13 (2,4)	1,07 [0,55; 2,09] 0,838	1,07 [0,56; 2,05] 0,838	0,00 [-0,01; 0,02] 0,836
severe[1]	0 (0,0)	0 (0,0)	-	-	-
GASTROENTERITIS					
not severe[1]	16 (1,5)	8 (1,5)	0,99 [0,42; 2,34] 0,988	0,99 [0,43; 2,31] 0,988	-0,00 [-0,01; 0,01] 0,988
severe[1]	0 (0,0)	1 (0,2)	0,17 [0,01; 4,07] 0,156	0,17 [0,01; 4,06] 0,271	-0,00 [-0,01; 0,00] 0,317
HERPES ZOSTER					
not severe[1]	22 (2,0)	4 (0,7)	2,77 [0,95; 8,07] 0,052	2,73 [0,95; 7,89] 0,063	0,01 [0,00; 0,02] 0,023 *
severe[1]	3 (0,3)	0 (0,0)	3,49 [0,18; 67,66] 0,222	3,48 [0,18; 67,27] 0,409	0,00 [-0,00; 0,01] 0,083
INFLUENZA					
not severe[1]	72 (6,6)	39 (7,1)	0,91 [0,61; 1,37] 0,652	0,92 [0,63; 1,34] 0,652	-0,01 [-0,03; 0,02] 0,657
severe[1]	1 (0,1)	2 (0,4)	0,25 [0,02; 2,74] 0,218	0,25 [0,02; 2,73] 0,255	-0,00 [-0,01; 0,00] 0,315
NASOPHARYNGITIS					
not severe[1]	149 (13,6)	79 (14,5)	0,93 [0,69; 1,24] 0,615	0,94 [0,73; 1,21] 0,614	-0,01 [-0,04; 0,03] 0,618
severe[1]	1 (0,1)	0 (0,0)	1,49 [0,06; 36,70] 0,481	1,49 [0,06; 36,56] 0,806	0,00 [-0,00; 0,00] 0,317

	Treatment groups		Comparison		
	BAF312 (N=1099)	**Placebo (N=546)**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
ORAL HERPES					
not severe[1]	18 (1,6)	10 (1,8)	0,89 [0,41; 1,95] 0,775	0,89 [0,42; 1,92] 0,775	-0,00 [-0,02; 0,01] 0,779
severe[1]	1 (0,1)	0 (0,0)	1,49 [0,06; 36,70] 0,481	1,49 [0,06; 36,56] 0,806	0,00 [-0,00; 0,00] 0,317
PHARYNGITIS					
not severe[1]	20 (1,8)	11 (2,0)	0,90 [0,43; 1,90] 0,784	0,90 [0,44; 1,87] 0,784	-0,00 [-0,02; 0,01] 0,788
severe[1]	0 (0,0)	0 (0,0)	-	-	-
RHINITIS					
not severe[1]	14 (1,3)	10 (1,8)	0,69 [0,31; 1,57] 0,374	0,70 [0,31; 1,56] 0,377	-0,01 [-0,02; 0,01] 0,403
severe[1]	0 (0,0)	0 (0,0)	-	-	-
SINUSITIS					
not severe[1]	21 (1,9)	9 (1,6)	1,16 [0,53; 2,56] 0,708	1,16 [0,53; 2,51] 0,708	0,00 [-0,01; 0,02] 0,701
severe[1]	0 (0,0)	0 (0,0)	-	-	-
UPPER RESPIRATORY TRACT INFECTION					
not severe[1]	91 (8,3)	41 (7,5)	1,11 [0,76; 1,63] 0,588	1,10 [0,77; 1,57] 0,588	0,01 [-0,02; 0,04] 0,582
severe[1]	0 (0,0)	0 (0,0)	-	-	-
URINARY TRACT INFECTION					
not severe[1]	130 (11,8)	77 (14,1)	0,82 [0,60; 1,11] 0,190	0,84 [0,65; 1,09] 0,189	-0,02 [-0,06; 0,01] 0,201
severe[1]	9 (0,8)	4 (0,7)	1,12 [0,34; 3,65] 0,852	1,12 [0,35; 3,61] 0,852	0,00 [-0,01; 0,01] 0,850
INJURY, POISONING AND PROCEDURAL COMPLICATIONS					
not severe[1]	233 (21,2)	111 (20,3)	1,05 [0,82; 1,36] 0,682	1,04 [0,85; 1,28] 0,683	0,01 [-0,03; 0,05] 0,681
severe[1]	15 (1,4)	4 (0,7)	1,88 [0,62; 5,68] 0,258	1,86 [0,62; 5,59] 0,267	0,01 [-0,00; 0,02] 0,211

	Treatment groups		Comparison		
	BAF312 (N=1099)	**Placebo (N=546)**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
CONTUSION					
not severe[1]	35 (3,2)	15 (2,7)	1,16 [0,63; 2,15] 0,626	1,16 [0,64; 2,10] 0,627	0,00 [-0,01; 0,02] 0,618
severe[1]	0 (0,0)	0 (0,0)	-	-	-
FALL					
not severe[1]	125 (11,4)	59 (10,8)	1,06 [0,76; 1,47] 0,731	1,05 [0,79; 1,41] 0,731	0,01 [-0,03; 0,04] 0,729
severe[1]	5 (0,5)	0 (0,0)	5,49 [0,30; 99,51] 0,114	5,47 [0,30; 98,74] 0,250	0,00 [0,00; 0,01] 0,025 *
LACERATION					
not severe[1]	18 (1,6)	4 (0,7)	2,26 [0,76; 6,70] 0,132	2,24 [0,76; 6,57] 0,144	0,01 [-0,00; 0,02] 0,087
severe[1]	1 (0,1)	0 (0,0)	1,49 [0,06; 36,70] 0,481	1,49 [0,06; 36,56] 0,806	0,00 [-0,00; 0,00] 0,317
LIGAMENT SPRAIN					
not severe[1]	12 (1,1)	6 (1,1)	0,99 [0,37; 2,66] 0,990	0,99 [0,37; 2,63] 0,990	-0,00 [-0,01; 0,01] 0,990
severe[1]	0 (0,0)	0 (0,0)	-	-	-
INVESTIGATIONS					
not severe[1]	252 (22,9)	77 (14,1)	1,81 [1,37; 2,40] <0,001 *	1,63 [1,29; 2,05] <0,001 *	0,09 [0,05; 0,13] <0,001 *
severe[1]	17 (1,5)	5 (0,9)	1,70 [0,62; 4,63] 0,294	1,69 [0,63; 4,55] 0,300	0,01 [-0,00; 0,02] 0,253
ALANINE AMINOTRANSFERASE INCREASED					
not severe[1]	59 (5,4)	7 (1,3)	4,37 [1,98; 9,63] <0,001 *	4,19 [1,93; 9,11] <0,001 *	0,04 [0,02; 0,06] <0,001 *
severe[1]	8 (0,7)	2 (0,4)	1,99 [0,42; 9,42] 0,374	1,99 [0,42; 9,33] 0,384	0,00 [-0,00; 0,01] 0,321
ASPARTATE AMINOTRANSFERASE INCREASED					
not severe[1]	14 (1,3)	3 (0,5)	2,34 [0,67; 8,16] 0,171	2,32 [0,67; 8,03] 0,185	0,01 [-0,00; 0,02] 0,118
severe[1]	1 (0,1)	2 (0,4)	0,25 [0,02; 2,74] 0,218	0,25 [0,02; 2,73] 0,255	-0,00 [-0,01; 0,00] 0,315

	Treatment groups		Comparison		
	BAF312 (N=1099)	Placebo (N=546)	OR [95% CI] p-value	RR [95% CI] p-value	RD [95% CI] p-value
BLOOD ALKALINE PHOSPHATASE INCREASED					
not severe[1]	12 (1,1)	0 (0,0)	12,56 [0,74; 212,58] 0,014 *	12,43 [0,74; 209,58] 0,080	0,01 [0,00; 0,02] <0,001 *
severe[1]	0 (0,0)	0 (0,0)	-	-	-
BLOOD BILIRUBIN INCREASED					
not severe[1]	11 (1,0)	2 (0,4)	2,75 [0,61; 12,45] 0,171	2,73 [0,61; 12,28] 0,190	0,01 [-0,00; 0,01] 0,109
severe[1]	1 (0,1)	0 (0,0)	1,49 [0,06; 36,70] 0,481	1,49 [0,06; 36,56] 0,806	0,00 [-0,00; 0,00] 0,317
BLOOD CHOLESTEROL INCREASED					
not severe[1]	20 (1,8)	5 (0,9)	2,01 [0,75; 5,37] 0,158	1,99 [0,75; 5,27] 0,167	0,01 [-0,00; 0,02] 0,115
severe[1]	0 (0,0)	1 (0,2)	0,17 [0,01; 4,07] 0,156	0,17 [0,01; 4,06] 0,271	-0,00 [-0,01; 0,00] 0,317
BLOOD PRESSURE INCREASED					
not severe[1]	19 (1,7)	7 (1,3)	1,35 [0,57; 3,24] 0,494	1,35 [0,57; 3,19] 0,496	0,00 [-0,01; 0,02] 0,472
severe[1]	0 (0,0)	0 (0,0)	-	-	-
GAMMA-GLUTAMYLTRANSFERASE INCREASED					
not severe[1]	42 (3,8)	6 (1,1)	3,58 [1,51; 8,47] 0,002 *	3,48 [1,49; 8,13] 0,004 *	0,03 [0,01; 0,04] <0,001 *
severe[1]	1 (0,1)	0 (0,0)	1,49 [0,06; 36,70] 0,481	1,49 [0,06; 36,56] 0,806	0,00 [-0,00; 0,00] 0,317
HEPATIC ENZYME INCREASED					
not severe[1]	15 (1,4)	1 (0,2)	7,54 [0,99; 57,24] 0,021 *	7,45 [0,99; 56,27] 0,052	0,01 [0,00; 0,02] 0,003 *
severe[1]	1 (0,1)	0 (0,0)	1,49 [0,06; 36,70] 0,481	1,49 [0,06; 36,56] 0,806	0,00 [-0,00; 0,00] 0,317
WEIGHT DECREASED					
not severe[1]	22 (2,0)	9 (1,6)	1,22 [0,56; 2,67] 0,620	1,21 [0,56; 2,62] 0,620	0,00 [-0,01; 0,02] 0,608
severe[1]	0 (0,0)	0 (0,0)	-	-	-

	Treatment groups		Comparison		
	BAF312 (N=1099)	**Placebo (N=546)**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
WEIGHT INCREASED					
not severe[1]	27 (2,5)	13 (2,4)	1,03 [0,53; 2,02] 0,925	1,03 [0,54; 1,98] 0,925	0,00 [-0,01; 0,02] 0,925
severe[1]	0 (0,0)	0 (0,0)	-	-	-
METABOLISM AND NUTRITION DISORDERS					
not severe[1]	83 (7,6)	27 (4,9)	1,57 [1,00; 2,46] 0,046 *	1,53 [1,00; 2,33] 0,049 *	0,03 [0,00; 0,05] 0,033 *
severe[1]	3 (0,3)	1 (0,2)	1,49 [0,15; 14,37] 0,728	1,49 [0,16; 14,30] 0,729	0,00 [-0,00; 0,01] 0,710
HYPERCHOLESTEROLAEMIA					
not severe[1]	28 (2,5)	11 (2,0)	1,27 [0,63; 2,57] 0,503	1,26 [0,63; 2,52] 0,505	0,01 [-0,01; 0,02] 0,487
severe[1]	0 (0,0)	0 (0,0)	-	-	-
VITAMIN D DEFICIENCY					
not severe[1]	11 (1,0)	7 (1,3)	0,78 [0,30; 2,02] 0,606	0,78 [0,30; 2,00] 0,607	-0,00 [-0,01; 0,01] 0,620
severe[1]	0 (0,0)	0 (0,0)	-	-	-
MUSCULOSKELETAL AND CONNECTIVE TISSUE DISORDERS					
not severe[1]	280 (25,5)	144 (26,4)	0,95 [0,76; 1,21] 0,696	0,97 [0,81; 1,15] 0,695	-0,01 [-0,05; 0,04] 0,697
severe[1]	11 (1,0)	8 (1,5)	0,68 [0,27; 1,70] 0,407	0,68 [0,28; 1,69] 0,409	-0,00 [-0,02; 0,01] 0,436
ARTHRALGIA					
not severe[1]	49 (4,5)	34 (6,2)	0,70 [0,45; 1,10] 0,123	0,72 [0,47; 1,10] 0,124	-0,02 [-0,04; 0,01] 0,143
severe[1]	1 (0,1)	1 (0,2)	0,50 [0,03; 7,95] 0,613	0,50 [0,03; 7,93] 0,621	-0,00 [-0,00; 0,00] 0,652
BACK PAIN					
not severe[1]	64 (5,8)	43 (7,9)	0,72 [0,48; 1,08] 0,112	0,74 [0,51; 1,07] 0,112	-0,02 [-0,05; 0,01] 0,129
severe[1]	3 (0,3)	0 (0,0)	3,49 [0,18; 67,66] 0,222	3,48 [0,18; 67,27] 0,409	0,00 [-0,00; 0,01] 0,083

	Treatment groups		Comparison		
	BAF312 (N=1099)	**Placebo (N=546)**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
JOINT SWELLING					
not severe[1]	16 (1,5)	7 (1,3)	1,14 [0,47; 2,78] 0,777	1,14 [0,47; 2,74] 0,778	0,00 [-0,01; 0,01] 0,773
severe[1]	1 (0,1)	0 (0,0)	1,49 [0,06; 36,70] 0,481	1,49 [0,06; 36,56] 0,806	0,00 [-0,00; 0,00] 0,317
MUSCLE SPASMS					
not severe[1]	37 (3,4)	19 (3,5)	0,97 [0,55; 1,70] 0,905	0,97 [0,56; 1,67] 0,905	-0,00 [-0,02; 0,02] 0,906
severe[1]	0 (0,0)	1 (0,2)	0,17 [0,01; 4,07] 0,156	0,17 [0,01; 4,06] 0,271	-0,00 [-0,01; 0,00] 0,317
MUSCULAR WEAKNESS					
not severe[1]	15 (1,4)	11 (2,0)	0,67 [0,31; 1,48] 0,320	0,68 [0,31; 1,46] 0,322	-0,01 [-0,02; 0,01] 0,350
severe[1]	2 (0,2)	2 (0,4)	0,50 [0,07; 3,53] 0,475	0,50 [0,07; 3,52] 0,484	-0,00 [-0,01; 0,00] 0,523
MUSCULOSKELETAL PAIN					
not severe[1]	27 (2,5)	14 (2,6)	0,96 [0,50; 1,84] 0,895	0,96 [0,51; 1,81] 0,895	-0,00 [-0,02; 0,02] 0,896
severe[1]	0 (0,0)	0 (0,0)	-	-	-
MYALGIA					
not severe[1]	13 (1,2)	7 (1,3)	0,92 [0,37; 2,32] 0,863	0,92 [0,37; 2,30] 0,863	-0,00 [-0,01; 0,01] 0,865
severe[1]	0 (0,0)	1 (0,2)	0,17 [0,01; 4,07] 0,156	0,17 [0,01; 4,06] 0,271	-0,00 [-0,01; 0,00] 0,317
NECK PAIN					
not severe[1]	13 (1,2)	7 (1,3)	0,92 [0,37; 2,32] 0,863	0,92 [0,37; 2,30] 0,863	-0,00 [-0,01; 0,01] 0,865
severe[1]	0 (0,0)	0 (0,0)	-	-	-
PAIN IN EXTREMITY					
not severe[1]	60 (5,5)	20 (3,7)	1,52 [0,91; 2,55] 0,111	1,49 [0,91; 2,45] 0,114	0,02 [-0,00; 0,04] 0,089
severe[1]	0 (0,0)	1 (0,2)	0,17 [0,01; 4,07] 0,156	0,17 [0,01; 4,06] 0,271	-0,00 [-0,01; 0,00] 0,317

	Treatment groups		Comparison		
	BAF312 (N=1099)	**Placebo (N=546)**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
NEOPLASMS BENIGN, MALIGNANT AND UNSPECIFIED (INCL CYSTS AND POLYPS)					
not severe[1]	102 (9,3)	36 (6,6)	1,45 [0,98; 2,15] 0,064	1,41 [0,98; 2,03] 0,067	0,03 [-0,00; 0,05] 0,051
severe[1]	14 (1,3)	9 (1,6)	0,77 [0,33; 1,79] 0,542	0,77 [0,34; 1,77] 0,543	-0,00 [-0,02; 0,01] 0,559
BASAL CELL CARCINOMA					
not severe[1]	9 (0,8)	6 (1,1)	0,74 [0,26; 2,10] 0,574	0,75 [0,27; 2,08] 0,575	-0,00 [-0,01; 0,01] 0,592
severe[1]	4 (0,4)	1 (0,2)	1,99 [0,22; 17,86] 0,530	1,99 [0,22; 17,74] 0,539	0,00 [-0,00; 0,01] 0,483
MELANOCYTIC NAEVUS					
not severe[1]	46 (4,2)	17 (3,1)	1,36 [0,77; 2,39] 0,286	1,34 [0,78; 2,32] 0,289	0,01 [-0,01; 0,03] 0,263
severe[1]	1 (0,1)	0 (0,0)	1,49 [0,06; 36,70] 0,481	1,49 [0,06; 36,56] 0,806	0,00 [-0,00; 0,00] 0,317
NERVOUS SYSTEM DISORDERS					
not severe[1]	408 (37,1)	171 (31,3)	1,29 [1,04; 1,61] 0,020 *	1,19 [1,02; 1,37] 0,023 *	0,06 [0,01; 0,11] 0,018 *
severe[1]	27 (2,5)	15 (2,7)	0,89 [0,47; 1,69] 0,725	0,89 [0,48; 1,67] 0,725	-0,00 [-0,02; 0,01] 0,730
BALANCE DISORDER					
not severe[1]	13 (1,2)	5 (0,9)	1,30 [0,46; 3,65] 0,624	1,29 [0,46; 3,60] 0,625	0,00 [-0,01; 0,01] 0,609
severe[1]	0 (0,0)	0 (0,0)	-	-	-
DIZZINESS					
not severe[1]	75 (6,8)	26 (4,8)	1,46 [0,93; 2,32] 0,101	1,43 [0,93; 2,21] 0,104	0,02 [-0,00; 0,04] 0,082
severe[1]	1 (0,1)	0 (0,0)	1,49 [0,06; 36,70] 0,481	1,49 [0,06; 36,56] 0,806	0,00 [-0,00; 0,00] 0,317

	Treatment groups		Comparison		
	BAF312 (N=1099)	**Placebo (N=546)**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
HEADACHE					
not severe[1]	158 (14,4)	71 (13,0)	1,12 [0,83; 1,52] 0,449	1,11 [0,85; 1,43] 0,450	0,01 [-0,02; 0,05] 0,442
severe[1]	2 (0,2)	0 (0,0)	2,49 [0,12; 51,95] 0,319	2,49 [0,12; 51,70] 0,556	0,00 [-0,00; 0,00] 0,157
HYPOAESTHESIA					
not severe[1]	14 (1,3)	14 (2,6)	0,49 [0,23; 1,04] 0,057	0,50 [0,24; 1,03] 0,062	-0,01 [-0,03; 0,00] 0,088
severe[1]	1 (0,1)	1 (0,2)	0,50 [0,03; 7,95] 0,613	0,50 [0,03; 7,93] 0,621	-0,00 [-0,00; 0,00] 0,652
MIGRAINE					
not severe[1]	16 (1,5)	8 (1,5)	0,99 [0,42; 2,34] 0,988	0,99 [0,43; 2,31] 0,988	-0,00 [-0,01; 0,01] 0,988
severe[1]	0 (0,0)	0 (0,0)	-	-	-
MUSCLE SPASTICITY					
not severe[1]	42 (3,8)	23 (4,2)	0,90 [0,54; 1,52] 0,702	0,91 [0,55; 1,49] 0,702	-0,00 [-0,02; 0,02] 0,706
severe[1]	2 (0,2)	0 (0,0)	2,49 [0,12; 51,95] 0,319	2,49 [0,12; 51,70] 0,556	0,00 [-0,00; 0,00] 0,157
NEURALGIA					
not severe[1]	13 (1,2)	5 (0,9)	1,30 [0,46; 3,65] 0,624	1,29 [0,46; 3,60] 0,625	0,00 [-0,01; 0,01] 0,609
severe[1]	1 (0,1)	0 (0,0)	1,49 [0,06; 36,70] 0,481	1,49 [0,06; 36,56] 0,806	0,00 [-0,00; 0,00] 0,317
PARAESTHESIA					
not severe[1]	18 (1,6)	20 (3,7)	0,44 [0,23; 0,83] 0,010 *	0,45 [0,24; 0,84] 0,012 *	-0,02 [-0,04; -0,00] 0,023 *
severe[1]	0 (0,0)	0 (0,0)	-	-	-
SCIATICA					
not severe[1]	18 (1,6)	5 (0,9)	1,80 [0,67; 4,88] 0,240	1,79 [0,67; 4,79] 0,248	0,01 [-0,00; 0,02] 0,197
severe[1]	0 (0,0)	0 (0,0)	-	-	-

	Treatment groups		Comparison		
	BAF312 (N=1099)	**Placebo (N=546)**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
SOMNOLENCE					
not severe[1]	11 (1,0)	5 (0,9)	1,09 [0,38; 3,16] 0,868	1,09 [0,38; 3,13] 0,868	0,00 [-0,01; 0,01] 0,866
severe[1]	0 (0,0)	0 (0,0)	-	-	-
SYNCOPE					
not severe[1]	13 (1,2)	6 (1,1)	1,08 [0,41; 2,85] 0,881	1,08 [0,41; 2,82] 0,881	0,00 [-0,01; 0,01] 0,879
severe[1]	1 (0,1)	1 (0,2)	0,50 [0,03; 7,95] 0,613	0,50 [0,03; 7,93] 0,621	-0,00 [-0,00; 0,00] 0,652
TREMOR					
not severe[1]	16 (1,5)	3 (0,5)	2,67 [0,78; 9,22] 0,105	2,65 [0,78; 9,05] 0,120	0,01 [-0,00; 0,02] 0,059
severe[1]	1 (0,1)	0 (0,0)	1,49 [0,06; 36,70] 0,481	1,49 [0,06; 36,56] 0,806	0,00 [-0,00; 0,00] 0,317
TRIGEMINAL NEURALGIA					
not severe[1]	17 (1,5)	5 (0,9)	1,70 [0,62; 4,63] 0,294	1,69 [0,63; 4,55] 0,300	0,01 [-0,00; 0,02] 0,253
severe[1]	3 (0,3)	1 (0,2)	1,49 [0,15; 14,37] 0,728	1,49 [0,16; 14,30] 0,729	0,00 [-0,00; 0,01] 0,710
PSYCHIATRIC DISORDERS					
not severe[1]	158 (14,4)	78 (14,3)	1,01 [0,75; 1,35] 0,960	1,01 [0,78; 1,29] 0,960	0,00 [-0,04; 0,04] 0,960
severe[1]	17 (1,5)	6 (1,1)	1,41 [0,55; 3,61] 0,466	1,41 [0,56; 3,55] 0,469	0,00 [-0,01; 0,02] 0,441
ANXIETY					
not severe[1]	22 (2,0)	14 (2,6)	0,78 [0,39; 1,53] 0,463	0,78 [0,40; 1,51] 0,464	-0,01 [-0,02; 0,01] 0,481
severe[1]	1 (0,1)	0 (0,0)	1,49 [0,06; 36,70] 0,481	1,49 [0,06; 36,56] 0,806	0,00 [-0,00; 0,00] 0,317
DEPRESSED MOOD					
not severe[1]	16 (1,5)	7 (1,3)	1,14 [0,47; 2,78] 0,777	1,14 [0,47; 2,74] 0,778	0,00 [-0,01; 0,01] 0,773
severe[1]	0 (0,0)	0 (0,0)	-	-	-

	Treatment groups		Comparison		
	BAF312 (N=1099)	**Placebo (N=546)**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
DEPRESSION					
not severe[1]	44 (4,0)	28 (5,1)	0,77 [0,47; 1,25] 0,294	0,78 [0,49; 1,24] 0,294	-0,01 [-0,03; 0,01] 0,313
severe[1]	5 (0,5)	2 (0,4)	1,24 [0,24; 6,43] 0,795	1,24 [0,24; 6,38] 0,795	0,00 [-0,01; 0,01] 0,787
INSOMNIA					
not severe[1]	38 (3,5)	17 (3,1)	1,11 [0,62; 1,99] 0,715	1,11 [0,63; 1,95] 0,715	0,00 [-0,01; 0,02] 0,710
severe[1]	0 (0,0)	2 (0,4)	0,10 [0,00; 2,07] 0,045 *	0,10 [0,00; 2,07] 0,136	-0,00 [-0,01; 0,00] 0,157
SLEEP DISORDER					
not severe[1]	11 (1,0)	5 (0,9)	1,09 [0,38; 3,16] 0,868	1,09 [0,38; 3,13] 0,868	0,00 [-0,01; 0,01] 0,866
severe[1]	0 (0,0)	0 (0,0)	-	-	-
RENAL AND URINARY DISORDERS					
not severe[1]	78 (7,1)	35 (6,4)	1,12 [0,74; 1,69] 0,604	1,11 [0,75; 1,63] 0,605	0,01 [-0,02; 0,03] 0,598
severe[1]	9 (0,8)	3 (0,5)	1,49 [0,40; 5,54] 0,545	1,49 [0,41; 5,48] 0,548	0,00 [-0,01; 0,01] 0,518
DYSURIA					
not severe[1]	11 (1,0)	3 (0,5)	1,83 [0,51; 6,59] 0,348	1,82 [0,51; 6,50] 0,356	0,00 [-0,00; 0,01] 0,301
severe[1]	0 (0,0)	0 (0,0)	-	-	-
URINARY INCONTINENCE					
not severe[1]	12 (1,1)	12 (2,2)	0,49 [0,22; 1,10] 0,078	0,50 [0,22; 1,10] 0,084	-0,01 [-0,02; 0,00] 0,115
severe[1]	2 (0,2)	0 (0,0)	2,49 [0,12; 51,95] 0,319	2,49 [0,12; 51,70] 0,556	0,00 [-0,00; 0,00] 0,157
URINARY RETENTION					
not severe[1]	11 (1,0)	6 (1,1)	0,91 [0,33; 2,47] 0,853	0,91 [0,34; 2,45] 0,853	-0,00 [-0,01; 0,01] 0,855
severe[1]	3 (0,3)	2 (0,4)	0,74 [0,12; 4,47] 0,746	0,75 [0,12; 4,45] 0,747	-0,00 [-0,01; 0,00] 0,758

	Treatment groups		Comparison		
	BAF312 (N=1099)	**Placebo (N=546)**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
REPRODUCTIVE SYSTEM AND BREAST DISORDERS					
not severe[1]	36 (3,3)	23 (4,2)	0,77 [0,45; 1,31] 0,336	0,78 [0,47; 1,30] 0,337	-0,01 [-0,03; 0,01] 0,355
severe[1]	0 (0,0)	2 (0,4)	0,10 [0,00; 2,07] 0,045 *	0,10 [0,00; 2,07] 0,136	-0,00 [-0,01; 0,00] 0,157
RESPIRATORY, THORACIC AND MEDIASTINAL DISORDERS					
not severe[1]	114 (10,4)	70 (12,8)	0,79 [0,57; 1,08] 0,138	0,81 [0,61; 1,07] 0,137	-0,02 [-0,06; 0,01] 0,150
severe[1]	3 (0,3)	1 (0,2)	1,49 [0,15; 14,37] 0,728	1,49 [0,16; 14,30] 0,729	0,00 [-0,00; 0,01] 0,710
COUGH					
not severe[1]	35 (3,2)	18 (3,3)	0,96 [0,54; 1,72] 0,904	0,97 [0,55; 1,69] 0,904	-0,00 [-0,02; 0,02] 0,904
severe[1]	0 (0,0)	0 (0,0)	-	-	-
DYSPNOEA					
not severe[1]	19 (1,7)	10 (1,8)	0,94 [0,44; 2,04] 0,882	0,94 [0,44; 2,02] 0,882	-0,00 [-0,01; 0,01] 0,883
severe[1]	0 (0,0)	0 (0,0)	-	-	-
OROPHARYNGEAL PAIN					
not severe[1]	20 (1,8)	17 (3,1)	0,58 [0,30; 1,11] 0,096	0,58 [0,31; 1,11] 0,099	-0,01 [-0,03; 0,00] 0,126
severe[1]	0 (0,0)	0 (0,0)	-	-	-
SKIN AND SUBCUTANEOUS TISSUE DISORDERS					
not severe[1]	188 (17,1)	92 (16,8)	1,02 [0,77; 1,34] 0,896	1,02 [0,81; 1,27] 0,896	0,00 [-0,04; 0,04] 0,896
severe[1]	1 (0,1)	2 (0,4)	0,25 [0,02; 2,74] 0,218	0,25 [0,02; 2,73] 0,255	-0,00 [-0,01; 0,00] 0,315
ACTINIC KERATOSIS					
not severe[1]	15 (1,4)	6 (1,1)	1,25 [0,48; 3,23] 0,651	1,24 [0,48; 3,18] 0,652	0,00 [-0,01; 0,01] 0,639
severe[1]	0 (0,0)	0 (0,0)	-	-	-

	Treatment groups		Comparison		
	BAF312 (N=1099)	**Placebo (N=546)**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
ECZEMA					
not severe[1]	17 (1,5)	5 (0,9)	1,70 [0,62; 4,63] 0,294	1,69 [0,63; 4,55] 0,300	0,01 [-0,00; 0,02] 0,253
severe[1]	0 (0,0)	0 (0,0)	-	-	-
RASH					
not severe[1]	20 (1,8)	13 (2,4)	0,76 [0,38; 1,54] 0,445	0,76 [0,38; 1,52] 0,446	-0,01 [-0,02; 0,01] 0,464
severe[1]	0 (0,0)	0 (0,0)	-	-	-
VASCULAR DISORDERS					
not severe[1]	160 (14,6)	59 (10,8)	1,41 [1,02; 1,93] 0,035 *	1,35 [1,02; 1,78] 0,037 *	0,04 [0,00; 0,07] 0,027 *
severe[1]	3 (0,3)	2 (0,4)	0,74 [0,12; 4,47] 0,746	0,75 [0,12; 4,45] 0,747	-0,00 [-0,01; 0,00] 0,758
HAEMATOMA					
not severe[1]	15 (1,4)	3 (0,5)	2,50 [0,72; 8,69] 0,134	2,48 [0,72; 8,54] 0,149	0,01 [-0,00; 0,02] 0,084
severe[1]	1 (0,1)	0 (0,0)	1,49 [0,06; 36,70] 0,481	1,49 [0,06; 36,56] 0,806	0,00 [-0,00; 0,00] 0,317
HYPERTENSION					
not severe[1]	115 (10,5)	40 (7,3)	1,48 [1,02; 2,15] 0,040 *	1,43 [1,01; 2,02] 0,043 *	0,03 [0,00; 0,06] 0,030 *
severe[1]	1 (0,1)	1 (0,2)	0,50 [0,03; 7,95] 0,613	0,50 [0,03; 7,93] 0,621	-0,00 [-0,00; 0,00] 0,652

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 total population

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

	Treatment groups	
	BAF312 (N=1099)	Placebo (N=546)
N'	1099	546
BLOOD AND LYMPHATIC SYSTEM DISORDERS, n (%)	2 (0,2)	0 (0,0)
LEUKOPENIA, n (%)	1 (0,1)	0 (0,0)
THROMBOCYTOPENIA, n (%)	1 (0,1)	0 (0,0)
CARDIAC DISORDERS, n (%)	9 (0,8)	0 (0,0)
ACUTE CORONARY SYNDROME, n (%)	1 (0,1)	0 (0,0)
ANGINA PECTORIS, n (%)	2 (0,2)	0 (0,0)
ATRIOVENTRICULAR BLOCK FIRST DEGREE, n (%)	2 (0,2)	0 (0,0)
ATRIOVENTRICULAR BLOCK SECOND DEGREE, n (%)	2 (0,2)	0 (0,0)
BRADYCARDIA, n (%)	4 (0,4)	0 (0,0)
MYOCARDIAL ISCHAEMIA, n (%)	1 (0,1)	0 (0,0)
SUPRAVENTRICULAR TACHYCARDIA, n (%)	1 (0,1)	0 (0,0)
EAR AND LABYRINTH DISORDERS, n (%)	1 (0,1)	0 (0,0)
VERTIGO, n (%)	1 (0,1)	0 (0,0)
EYE DISORDERS, n (%)	8 (0,7)	0 (0,0)
BLINDNESS, n (%)	1 (0,1)	0 (0,0)
EYELID OEDEMA, n (%)	1 (0,1)	0 (0,0)
MACULAR OEDEMA, n (%)	5 (0,5)	0 (0,0)
UVEITIS, n (%)	1 (0,1)	0 (0,0)
GASTROINTESTINAL DISORDERS, n (%)	0 (0,0)	1 (0,2)
NAUSEA, n (%)	0 (0,0)	1 (0,2)
GENERAL DISORDERS AND ADMINISTRATION SITE CONDITIONS, n (%)	3 (0,3)	3 (0,5)
FATIGUE, n (%)	2 (0,2)	3 (0,5)
MALAISE, n (%)	1 (0,1)	0 (0,0)
OEDEMA PERIPHERAL, n (%)	1 (0,1)	0 (0,0)
IMMUNE SYSTEM DISORDERS, n (%)	1 (0,1)	0 (0,0)
HYPERSENSITIVITY, n (%)	1 (0,1)	0 (0,0)
INFECTIONS AND INFESTATIONS, n (%)	1 (0,1)	0 (0,0)
URINARY TRACT INFECTION, n (%)	1 (0,1)	0 (0,0)
INVESTIGATIONS, n (%)	4 (0,4)	0 (0,0)

	Treatment groups	
	BAF312 (N=1099)	**Placebo (N=546)**
ALANINE AMINOTRANSFERASE INCREASED, n (%)	1 (0,1)	0 (0,0)
ASPARTATE AMINOTRANSFERASE INCREASED, n (%)	1 (0,1)	0 (0,0)
CD4 LYMPHOCYTES DECREASED, n (%)	1 (0,1)	0 (0,0)
HEART RATE INCREASED, n (%)	1 (0,1)	0 (0,0)
PULMONARY FUNCTION TEST DECREASED, n (%)	1 (0,1)	0 (0,0)
MUSCULOSKELETAL AND CONNECTIVE TISSUE DISORDERS, n (%)	1 (0,1)	2 (0,4)
MUSCLE SPASMS, n (%)	1 (0,1)	1 (0,2)
MUSCULAR WEAKNESS, n (%)	1 (0,1)	1 (0,2)
MYALGIA, n (%)	0 (0,0)	1 (0,2)
NEOPLASMS BENIGN, MALIGNANT AND UNSPECIFIED (INCL CYSTS AND POLYPS), n (%)	6 (0,5)	4 (0,7)
BREAST CANCER, n (%)	1 (0,1)	0 (0,0)
ENDOMETRIAL CANCER, n (%)	1 (0,1)	0 (0,0)
GASTRIC CANCER, n (%)	0 (0,0)	1 (0,2)
GASTROINTESTINAL MELANOMA, n (%)	1 (0,1)	0 (0,0)
LUNG ADENOCARCINOMA, n (%)	0 (0,0)	1 (0,2)
LUNG ADENOCARCINOMA METASTATIC, n (%)	1 (0,1)	0 (0,0)
MALIGNANT MELANOMA IN SITU, n (%)	1 (0,1)	0 (0,0)
PROSTATE CANCER, n (%)	0 (0,0)	2 (0,4)
SEMINOMA, n (%)	1 (0,1)	0 (0,0)
NERVOUS SYSTEM DISORDERS, n (%)	9 (0,8)	6 (1,1)
ATAXIA, n (%)	0 (0,0)	1 (0,2)
CENTRAL NERVOUS SYSTEM LESION, n (%)	0 (0,0)	1 (0,2)
DIZZINESS, n (%)	2 (0,2)	0 (0,0)
HAEMORRHAGIC STROKE, n (%)	0 (0,0)	1 (0,2)
HEADACHE, n (%)	0 (0,0)	2 (0,4)
INTENTION TREMOR, n (%)	1 (0,1)	0 (0,0)
ISCHAEMIC STROKE, n (%)	1 (0,1)	0 (0,0)
MENTAL IMPAIRMENT, n (%)	0 (0,0)	1 (0,2)
MULTIPLE SCLEROSIS, n (%)	1 (0,1)	0 (0,0)

	Treatment groups	
	BAF312 (N=1099)	**Placebo (N=546)**
MULTIPLE SCLEROSIS RELAPSE, n (%)	1 (0,1)	0 (0,0)
MUSCLE SPASTICITY, n (%)	1 (0,1)	0 (0,0)
NYSTAGMUS, n (%)	0 (0,0)	1 (0,2)
PARAPARESIS, n (%)	0 (0,0)	1 (0,2)
POLYNEUROPATHY, n (%)	1 (0,1)	0 (0,0)
SOMNOLENCE, n (%)	1 (0,1)	0 (0,0)
PSYCHIATRIC DISORDERS, n (%)	4 (0,4)	3 (0,5)
COMPLETED SUICIDE, n (%)	1 (0,1)	0 (0,0)
DEPRESSION, n (%)	1 (0,1)	1 (0,2)
INSOMNIA, n (%)	0 (0,0)	1 (0,2)
MANIA, n (%)	1 (0,1)	0 (0,0)
PANIC ATTACK, n (%)	1 (0,1)	0 (0,0)
PSYCHOTIC DISORDER, n (%)	1 (0,1)	0 (0,0)
SUICIDAL IDEATION, n (%)	0 (0,0)	1 (0,2)
SUICIDE ATTEMPT, n (%)	0 (0,0)	1 (0,2)
RESPIRATORY, THORACIC AND MEDIASTINAL DISORDERS, n (%)	1 (0,1)	0 (0,0)
COUGH, n (%)	1 (0,1)	0 (0,0)
SKIN AND SUBCUTANEOUS TISSUE DISORDERS, n (%)	1 (0,1)	0 (0,0)
ECZEMA, n (%)	1 (0,1)	0 (0,0)
TOXIC SKIN ERUPTION, n (%)	1 (0,1)	0 (0,0)
SOCIAL CIRCUMSTANCES, n (%)	0 (0,0)	1 (0,2)
WALKING DISABILITY, n (%)	0 (0,0)	1 (0,2)

N': Number of patients in the analysis
Analysis population: A2304 SAF total population

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

	Treatment groups	
	BAF312 (N=1099)	Placebo (N=546)
N'	1099	546
BLOOD AND LYMPHATIC SYSTEM DISORDERS, n (%)	2 (0,2)	0 (0,0)
LEUKOPENIA, n (%)	1 (0,1)	0 (0,0)
THROMBOCYTOPENIA, n (%)	1 (0,1)	0 (0,0)
CARDIAC DISORDERS, n (%)	11 (1,0)	1 (0,2)
ACUTE CORONARY SYNDROME, n (%)	1 (0,1)	0 (0,0)
ANGINA PECTORIS, n (%)	2 (0,2)	0 (0,0)
ATRIOVENTRICULAR BLOCK FIRST DEGREE, n (%)	2 (0,2)	0 (0,0)
ATRIOVENTRICULAR BLOCK SECOND DEGREE, n (%)	2 (0,2)	0 (0,0)
BRADYCARDIA, n (%)	4 (0,4)	0 (0,0)
MYOCARDIAL ISCHAEMIA, n (%)	1 (0,1)	0 (0,0)
PALPITATIONS, n (%)	1 (0,1)	0 (0,0)
SINUS BRADYCARDIA, n (%)	1 (0,1)	0 (0,0)
SUPRAVENTRICULAR TACHYCARDIA, n (%)	1 (0,1)	1 (0,2)
EAR AND LABYRINTH DISORDERS, n (%)	1 (0,1)	0 (0,0)
VERTIGO, n (%)	1 (0,1)	0 (0,0)
EYE DISORDERS, n (%)	17 (1,5)	2 (0,4)
BLINDNESS, n (%)	1 (0,1)	0 (0,0)
CYSTOID MACULAR OEDEMA, n (%)	1 (0,1)	0 (0,0)
EYE PAIN, n (%)	1 (0,1)	0 (0,0)
EYELID OEDEMA, n (%)	1 (0,1)	0 (0,0)
EYELIDS PRURITUS, n (%)	0 (0,0)	1 (0,2)
MACULAR OEDEMA, n (%)	11 (1,0)	1 (0,2)
UVEITIS, n (%)	2 (0,2)	0 (0,0)
GASTROINTESTINAL DISORDERS, n (%)	0 (0,0)	2 (0,4)
HYPOAESTHESIA ORAL, n (%)	0 (0,0)	1 (0,2)
NAUSEA, n (%)	0 (0,0)	1 (0,2)
GENERAL DISORDERS AND ADMINISTRATION SITE CONDITIONS, n (%)	6 (0,5)	6 (1,1)
ASTHENIA, n (%)	0 (0,0)	1 (0,2)
FATIGUE, n (%)	3 (0,3)	4 (0,7)
GAIT DISTURBANCE, n (%)	0 (0,0)	1 (0,2)

	Treatment groups	
	BAF312 (N=1099)	**Placebo (N=546)**
MALAISE, n (%)	1 (0,1)	0 (0,0)
OEDEMA PERIPHERAL, n (%)	2 (0,2)	0 (0,0)
PAIN, n (%)	1 (0,1)	0 (0,0)
IMMUNE SYSTEM DISORDERS, n (%)	1 (0,1)	0 (0,0)
HYPERSENSITIVITY, n (%)	1 (0,1)	0 (0,0)
INFECTIONS AND INFESTATIONS, n (%)	2 (0,2)	4 (0,7)
BURSITIS INFECTIVE, n (%)	1 (0,1)	0 (0,0)
CYSTITIS, n (%)	0 (0,0)	1 (0,2)
PNEUMONIA, n (%)	0 (0,0)	1 (0,2)
URINARY TRACT INFECTION, n (%)	1 (0,1)	2 (0,4)
INJURY, POISONING AND PROCEDURAL COMPLICATIONS, n (%)	1 (0,1)	0 (0,0)
CERVICAL VERTEBRAL FRACTURE, n (%)	1 (0,1)	0 (0,0)
INVESTIGATIONS, n (%)	16 (1,5)	0 (0,0)
ALANINE AMINOTRANSFERASE INCREASED, n (%)	5 (0,5)	0 (0,0)
ASPARTATE AMINOTRANSFERASE INCREASED, n (%)	3 (0,3)	0 (0,0)
BLOOD ALKALINE PHOSPHATASE INCREASED, n (%)	1 (0,1)	0 (0,0)
CARBON MONOXIDE DIFFUSING CAPACITY DECREASED, n (%)	2 (0,2)	0 (0,0)
CD4 LYMPHOCYTES DECREASED, n (%)	1 (0,1)	0 (0,0)
GAMMA-GLUTAMYLTRANSFERASE INCREASED, n (%)	3 (0,3)	0 (0,0)
HEART RATE INCREASED, n (%)	1 (0,1)	0 (0,0)
HEPATIC ENZYME INCREASED, n (%)	2 (0,2)	0 (0,0)
INTERNATIONAL NORMALISED RATIO INCREASED, n (%)	1 (0,1)	0 (0,0)
LYMPHOCYTE COUNT DECREASED, n (%)	1 (0,1)	0 (0,0)
PULMONARY FUNCTION TEST DECREASED, n (%)	3 (0,3)	0 (0,0)
MUSCULOSKELETAL AND CONNECTIVE TISSUE DISORDERS, n (%)	1 (0,1)	2 (0,4)
MUSCLE SPASMS, n (%)	1 (0,1)	1 (0,2)
MUSCLE TIGHTNESS, n (%)	0 (0,0)	1 (0,2)
MUSCULAR WEAKNESS, n (%)	1 (0,1)	1 (0,2)
MYALGIA, n (%)	0 (0,0)	1 (0,2)

	Treatment groups	
	BAF312 (N=1099)	**Placebo (N=546)**
NEOPLASMS BENIGN, MALIGNANT AND UNSPECIFIED (INCL CYSTS AND POLYPS), n (%)	9 (0,8)	5 (0,9)
BREAST CANCER, n (%)	1 (0,1)	1 (0,2)
ENDOMETRIAL CANCER, n (%)	1 (0,1)	0 (0,0)
GASTRIC CANCER, n (%)	0 (0,0)	1 (0,2)
GASTROINTESTINAL MELANOMA, n (%)	1 (0,1)	0 (0,0)
LIP SQUAMOUS CELL CARCINOMA, n (%)	1 (0,1)	0 (0,0)
LUNG ADENOCARCINOMA, n (%)	0 (0,0)	1 (0,2)
LUNG ADENOCARCINOMA METASTATIC, n (%)	1 (0,1)	0 (0,0)
MALIGNANT MELANOMA IN SITU, n (%)	2 (0,2)	0 (0,0)
PROSTATE CANCER, n (%)	0 (0,0)	2 (0,4)
SEMINOMA, n (%)	2 (0,2)	0 (0,0)
SQUAMOUS CELL CARCINOMA, n (%)	1 (0,1)	0 (0,0)
NERVOUS SYSTEM DISORDERS, n (%)	13 (1,2)	10 (1,8)
ATAXIA, n (%)	0 (0,0)	1 (0,2)
BURNING SENSATION, n (%)	0 (0,0)	1 (0,2)
CENTRAL NERVOUS SYSTEM LESION, n (%)	0 (0,0)	1 (0,2)
DIZZINESS, n (%)	3 (0,3)	0 (0,0)
GENERALISED TONIC-CLONIC SEIZURE, n (%)	1 (0,1)	0 (0,0)
HAEMORRHAGIC STROKE, n (%)	0 (0,0)	1 (0,2)
HEADACHE, n (%)	1 (0,1)	2 (0,4)
HYPOAESTHESIA, n (%)	1 (0,1)	1 (0,2)
INTENTION TREMOR, n (%)	1 (0,1)	0 (0,0)
ISCHAEMIC STROKE, n (%)	1 (0,1)	0 (0,0)
MENTAL IMPAIRMENT, n (%)	0 (0,0)	1 (0,2)
MULTIPLE SCLEROSIS, n (%)	1 (0,1)	1 (0,2)
MULTIPLE SCLEROSIS RELAPSE, n (%)	1 (0,1)	2 (0,4)
MUSCLE SPASTICITY, n (%)	1 (0,1)	0 (0,0)
NYSTAGMUS, n (%)	0 (0,0)	1 (0,2)
OPTIC NEURITIS, n (%)	1 (0,1)	0 (0,0)
PARAPARESIS, n (%)	0 (0,0)	1 (0,2)
POLYNEUROPATHY, n (%)	1 (0,1)	0 (0,0)

	Treatment groups	
	BAF312 (N=1099)	**Placebo (N=546)**
SOMNOLENCE, n (%)	1 (0,1)	0 (0,0)
PSYCHIATRIC DISORDERS, n (%)	9 (0,8)	6 (1,1)
ANXIETY, n (%)	1 (0,1)	1 (0,2)
COMPLETED SUICIDE, n (%)	1 (0,1)	0 (0,0)
DEPRESSED MOOD, n (%)	1 (0,1)	0 (0,0)
DEPRESSION, n (%)	3 (0,3)	1 (0,2)
HALLUCINATION, n (%)	1 (0,1)	0 (0,0)
INSOMNIA, n (%)	0 (0,0)	3 (0,5)
MANIA, n (%)	1 (0,1)	0 (0,0)
PANIC ATTACK, n (%)	1 (0,1)	0 (0,0)
PSYCHOTIC DISORDER, n (%)	1 (0,1)	0 (0,0)
SLEEP DISORDER, n (%)	1 (0,1)	0 (0,0)
SUICIDAL IDEATION, n (%)	0 (0,0)	1 (0,2)
SUICIDE ATTEMPT, n (%)	1 (0,1)	1 (0,2)
RENAL AND URINARY DISORDERS, n (%)	0 (0,0)	1 (0,2)
HYDRONEPHROSIS, n (%)	0 (0,0)	1 (0,2)
URINARY RETENTION, n (%)	0 (0,0)	1 (0,2)
RESPIRATORY, THORACIC AND MEDIASTINAL DISORDERS, n (%)	3 (0,3)	2 (0,4)
COUGH, n (%)	1 (0,1)	0 (0,0)
DYSPNOEA, n (%)	1 (0,1)	0 (0,0)
NASAL PRURITUS, n (%)	0 (0,0)	1 (0,2)
OROPHARYNGEAL PAIN, n (%)	0 (0,0)	1 (0,2)
PULMONARY EMBOLISM, n (%)	0 (0,0)	1 (0,2)
RESPIRATORY DISORDER, n (%)	1 (0,1)	0 (0,0)
SKIN AND SUBCUTANEOUS TISSUE DISORDERS, n (%)	4 (0,4)	1 (0,2)
ECZEMA, n (%)	1 (0,1)	0 (0,0)
PRURITUS, n (%)	0 (0,0)	1 (0,2)
RASH, n (%)	1 (0,1)	0 (0,0)
RASH PAPULAR, n (%)	1 (0,1)	0 (0,0)
TOXIC SKIN ERUPTION, n (%)	1 (0,1)	0 (0,0)
SOCIAL CIRCUMSTANCES, n (%)	0 (0,0)	1 (0,2)
WALKING DISABILITY, n (%)	0 (0,0)	1 (0,2)
VASCULAR DISORDERS, n (%)	1 (0,1)	0 (0,0)
DEEP VEIN THROMBOSIS, n (%)	1 (0,1)	0 (0,0)

N': Number of patients in the analysis
Analysis population: A2304 SAF total population

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

	Treatment groups		Comparison		
	BAF312 (N=1099)	**Placebo (N=546)**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
N'	1099	546			
Infections and infestations, n (%)	539 (49,0)	268 (49,1)	1,00 [0,81; 1,23] 0,988	1,00 [0,90; 1,11] 0,988	-0,00 [-0,05; 0,05] 0,988
not severe	528 (48,0)	262 (48,0)	1,00 [0,82; 1,23] 0,982	1,00 [0,90; 1,11] 0,982	0,00 [-0,05; 0,05] 0,982
severe	24 (2,2)	11 (2,0)	1,09 [0,53; 2,23] 0,823	1,08 [0,53; 2,20] 0,823	0,00 [-0,01; 0,02] 0,821
serious	33 (3,0)	15 (2,7)	1,10 [0,59; 2,04] 0,772	1,09 [0,60; 1,99] 0,772	0,00 [-0,01; 0,02] 0,769
Herpes simplex virus infections, n (%)	25 (2,3)	11 (2,0)	1,13 [0,55; 2,32] 0,734	1,13 [0,56; 2,28] 0,734	0,00 [-0,01; 0,02] 0,729
not severe	25 (2,3)	11 (2,0)	1,13 [0,55; 2,32] 0,734	1,13 [0,56; 2,28] 0,734	0,00 [-0,01; 0,02] 0,729
severe	1 (0,1)	0 (0,0)	1,49 [0,06; 36,70] 0,481	1,49 [0,06; 36,56] 0,806	0,00 [-0,00; 0,00] 0,317
serious	0 (0,0)	0 (0,0)	-	-	-
Varicella-zoster virus infections, n (%)	33 (3,0)	4 (0,7)	4,19 [1,48; 11,90] 0,003 *	4,10 [1,46; 11,51] 0,007 *	0,02 [0,01; 0,04] <0,001 *
not severe	30 (2,7)	4 (0,7)	3,80 [1,33; 10,85] 0,007 *	3,73 [1,32; 10,52] 0,013 *	0,02 [0,01; 0,03] 0,001 *
severe	3 (0,3)	0 (0,0)	3,49 [0,18; 67,66] 0,222	3,48 [0,18; 67,27] 0,409	0,00 [-0,00; 0,01] 0,083
serious	2 (0,2)	0 (0,0)	2,49 [0,12; 51,95] 0,319	2,49 [0,12; 51,70] 0,556	0,00 [-0,00; 0,00] 0,157
Lymphopenia, n (%)	14 (1,3)	0 (0,0)	14,60 [0,87; 245,21] 0,008 *	14,42 [0,86; 241,29] 0,063	0,01 [0,01; 0,02] <0,001 *
not severe	10 (0,9)	0 (0,0)	10,53 [0,62; 180,09] 0,025 *	10,44 [0,61; 177,88] 0,105	0,01 [0,00; 0,01] 0,001 *
severe	4 (0,4)	0 (0,0)	4,49 [0,24; 83,54] 0,158	4,48 [0,24; 82,98] 0,314	0,00 [0,00; 0,01] 0,045 *
serious	0 (0,0)	0 (0,0)	-	-	-

	Treatment groups		Comparison		
	BAF312 (N=1099)	**Placebo (N=546)**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Macular edema, n (%)	20 (1,8)	1 (0,2)	10,10 [1,35; 75,47] 0,005 *	9,94 [1,34; 73,84] 0,025 *	0,02 [0,01; 0,03] <0,001 *
not severe	15 (1,4)	0 (0,0)	15,62 [0,93; 261,57] 0,006 *	15,42 [0,92; 257,15] 0,057	0,01 [0,01; 0,02] <0,001 *
severe	5 (0,5)	1 (0,2)	2,49 [0,29; 21,37] 0,389	2,48 [0,29; 21,21] 0,406	0,00 [-0,00; 0,01] 0,320
serious	3 (0,3)	0 (0,0)	3,49 [0,18; 67,66] 0,222	3,48 [0,18; 67,27] 0,409	0,00 [-0,00; 0,01] 0,083
Abnormal hepatic enzymes, n (%)	135 (12,3)	21 (3,8)	3,50 [2,18; 5,61] <0,001 *	3,19 [2,04; 5,00] <0,001 *	0,08 [0,06; 0,11] <0,001 *
not severe	125 (11,4)	19 (3,5)	3,56 [2,17; 5,83] <0,001 *	3,27 [2,04; 5,24] <0,001 *	0,08 [0,05; 0,10] <0,001 *
severe	13 (1,2)	3 (0,5)	2,17 [0,61; 7,64] 0,218	2,15 [0,62; 7,52] 0,230	0,01 [-0,00; 0,02] 0,163
serious	14 (1,3)	3 (0,5)	2,34 [0,67; 8,16] 0,171	2,32 [0,67; 8,03] 0,185	0,01 [-0,00; 0,02] 0,118
Malignancies, n (%)	20 (1,8)	14 (2,6)	0,70 [0,35; 1,41] 0,318	0,71 [0,36; 1,39] 0,320	-0,01 [-0,02; 0,01] 0,345
not severe	11 (1,0)	7 (1,3)	0,78 [0,30; 2,02] 0,606	0,78 [0,30; 2,00] 0,607	-0,00 [-0,01; 0,01] 0,620
severe	11 (1,0)	7 (1,3)	0,78 [0,30; 2,02] 0,606	0,78 [0,30; 2,00] 0,607	-0,00 [-0,01; 0,01] 0,620
serious	19 (1,7)	13 (2,4)	0,72 [0,35; 1,47] 0,367	0,73 [0,36; 1,46] 0,369	-0,01 [-0,02; 0,01] 0,392
Hypertension, n (%)	137 (12,5)	50 (9,2)	1,41 [1,00; 1,99] 0,047 *	1,36 [1,00; 1,85] 0,049 *	0,03 [0,00; 0,06] 0,037 *
not severe	137 (12,5)	49 (9,0)	1,44 [1,02; 2,04] 0,035 *	1,39 [1,02; 1,89] 0,038 *	0,03 [0,00; 0,07] 0,027 *
severe	1 (0,1)	1 (0,2)	0,50 [0,03; 7,95] 0,613	0,50 [0,03; 7,93] 0,621	-0,00 [-0,00; 0,00] 0,652
serious	1 (0,1)	0 (0,0)	1,49 [0,06; 36,70] 0,481	1,49 [0,06; 36,56] 0,806	0,00 [-0,00; 0,00] 0,317

	Treatment groups		Comparison		
	BAF312 (N=1099)	**Placebo (N=546)**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Seizures, n (%)	19 (1,7)	2 (0,4)	4,79 [1,11; 20,62] 0,020 *	4,72 [1,10; 20,19] 0,036 *	0,01 [0,00; 0,02] 0,004 *
not severe	16 (1,5)	2 (0,4)	4,02 [0,92; 17,54] 0,045 *	3,97 [0,92; 17,22] 0,065	0,01 [0,00; 0,02] 0,014 *
severe	5 (0,5)	0 (0,0)	5,49 [0,30; 99,51] 0,114	5,47 [0,30; 98,74] 0,250	0,00 [0,00; 0,01] 0,025 *
serious	9 (0,8)	0 (0,0)	9,52 [0,55; 163,90] 0,034 *	9,45 [0,55; 162,03] 0,121	0,01 [0,00; 0,01] 0,003 *
Thromboembolic events, n (%)	33 (3,0)	15 (2,7)	1,10 [0,59; 2,04] 0,772	1,09 [0,60; 1,99] 0,772	0,00 [-0,01; 0,02] 0,769
not severe	25 (2,3)	12 (2,2)	1,04 [0,52; 2,08] 0,921	1,04 [0,52; 2,04] 0,921	0,00 [-0,01; 0,02] 0,921
severe	9 (0,8)	5 (0,9)	0,89 [0,30; 2,68] 0,840	0,89 [0,30; 2,66] 0,841	-0,00 [-0,01; 0,01] 0,843
serious	15 (1,4)	7 (1,3)	1,07 [0,43; 2,63] 0,890	1,06 [0,44; 2,60] 0,891	0,00 [-0,01; 0,01] 0,889
Respiratory disorders, n (%)	117 (10,6)	71 (13,0)	0,80 [0,58; 1,09] 0,157	0,82 [0,62; 1,08] 0,156	-0,02 [-0,06; 0,01] 0,169
not severe	114 (10,4)	70 (12,8)	0,79 [0,57; 1,08] 0,138	0,81 [0,61; 1,07] 0,137	-0,02 [-0,06; 0,01] 0,150
severe	3 (0,3)	1 (0,2)	1,49 [0,15; 14,37] 0,728	1,49 [0,16; 14,30] 0,729	0,00 [-0,00; 0,01] 0,710
serious	2 (0,2)	1 (0,2)	0,99 [0,09; 10,98] 0,996	0,99 [0,09; 10,93] 0,996	-0,00 [-0,00; 0,00] 0,996

	Treatment groups		Comparison		
	BAF312 (N=1099)	**Placebo (N=546)**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Peripheral edema/swelling, n (%)	74 (6,7)	18 (3,3)	2,12 [1,25; 3,58] 0,004 *	2,04 [1,23; 3,38] 0,006 *	0,03 [0,01; 0,06] 0,001 *
not severe	74 (6,7)	18 (3,3)	2,12 [1,25; 3,58] 0,004 *	2,04 [1,23; 3,38] 0,006 *	0,03 [0,01; 0,06] 0,001 *
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 total population

	Treatment groups		Comparison		
	BAF312 (N=1099)	**Placebo (N=546)**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
N'	1099	546			
Asthma/bronchospasm, n (%)	8 (0,7)	2 (0,4)	1,99 [0,42; 9,42] 0,374	1,99 [0,42; 9,33] 0,384	0,00 [-0,00; 0,01] 0,321
not severe	8 (0,7)	2 (0,4)	1,99 [0,42; 9,42] 0,374	1,99 [0,42; 9,33] 0,384	0,00 [-0,00; 0,01] 0,321
severe	0 (0,0)	0 (0,0)	-	-	-
serious	0 (0,0)	0 (0,0)	-	-	-
Pregnancy and neonatal topics, n (%)	6 (0,5)	0 (0,0)	6,50 [0,37; 115,54] 0,084	6,46 [0,36; 114,54] 0,203	0,01 [0,00; 0,01] 0,014 *
not severe	6 (0,5)	0 (0,0)	6,50 [0,37; 115,54] 0,084	6,46 [0,36; 114,54] 0,203	0,01 [0,00; 0,01] 0,014 *
severe	0 (0,0)	0 (0,0)	-	-	-
serious	0 (0,0)	0 (0,0)	-	-	-
Bradyarrhythmias and bradycardia, n (%)	103 (9,4)	31 (5,7)	1,72 [1,13; 2,60] 0,010 *	1,65 [1,12; 2,43] 0,011 *	0,04 [0,01; 0,06] 0,005 *
not severe	101 (9,2)	30 (5,5)	1,74 [1,14; 2,65] 0,009 *	1,67 [1,13; 2,48] 0,011 *	0,04 [0,01; 0,06] 0,005 *
severe	5 (0,5)	1 (0,2)	2,49 [0,29; 21,37] 0,389	2,48 [0,29; 21,21] 0,406	0,00 [-0,00; 0,01] 0,320
serious	10 (0,9)	1 (0,2)	5,00 [0,64; 39,20] 0,089	4,97 [0,64; 38,71] 0,126	0,01 [0,00; 0,01] 0,032 *

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 total population

11.2 Subgroup: Age

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

	Treatment groups		Comparison		
	BAF312 (N=1099)	**Placebo (N=546)**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
N'	1099	546			
N' Age = 18-30 years	26	12			
N' Age = 31-40 years	161	91			
N' Age = 41-55 years	712	331			
N' Age = >55 years	200	112			
Any AE					
Interaction test:	p=0,760				
Age = 18-30 years	21 (80,8)	9 (75,0)	1,40 [0,27; 7,15] 0,685	1,08 [0,74; 1,57] 0,700	0,06 [-0,23; 0,35] 0,695
Age = 31-40 years	133 (82,6)	71 (78,0)	1,34 [0,70; 2,54] 0,373	1,06 [0,93; 1,21] 0,389	0,05 [-0,06; 0,15] 0,384
Age = 41-55 years	636 (89,3)	269 (81,3)	1,93 [1,34; 2,78] <0,001 *	1,10 [1,04; 1,16] 0,001 *	0,08 [0,03; 0,13] 0,001 *
Age = >55 years	185 (92,5)	96 (85,7)	2,06 [0,97; 4,34] 0,055	1,08 [0,99; 1,18] 0,080	0,07 [-0,01; 0,14] 0,074
Any AE, disease specific events excluded[1]					
Interaction test:	p=0,977				
Age = 18-30 years	18 (69,2)	8 (66,7)	1,13 [0,26; 4,85] 0,874	1,04 [0,65; 1,67] 0,876	0,03 [-0,29; 0,35] 0,875
Age = 31-40 years	127 (78,9)	64 (70,3)	1,58 [0,88; 2,84] 0,128	1,12 [0,96; 1,31] 0,148	0,09 [-0,03; 0,20] 0,138
Age = 41-55 years	598 (84,0)	255 (77,0)	1,56 [1,13; 2,16] 0,007 *	1,09 [1,02; 1,17] 0,012 *	0,07 [0,02; 0,12] 0,010 *
Age = >55 years	175 (87,5)	91 (81,3)	1,62 [0,86; 3,04] 0,135	1,08 [0,97; 1,19] 0,159	0,06 [-0,02; 0,15] 0,152

	Treatment groups		Comparison		
	BAF312 (N=1099)	**Placebo (N=546)**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Any SAE					
Interaction test:	p=0,062				
Age = 18-30 years	2 (7,7)	2 (16,7)	0,42 [0,05; 3,38] 0,402	0,46 [0,07; 2,90] 0,409	-0,09 [-0,32; 0,14] 0,453
Age = 31-40 years	12 (7,5)	11 (12,1)	0,59 [0,25; 1,39] 0,220	0,62 [0,28; 1,34] 0,222	-0,05 [-0,12; 0,03] 0,246
Age = 41-55 years	118 (16,6)	45 (13,6)	1,26 [0,87; 1,83] 0,218	1,22 [0,89; 1,67] 0,222	0,03 [-0,02; 0,08] 0,204
Age = >55 years	54 (27,0)	16 (14,3)	2,22 [1,20; 4,10] 0,010 *	1,89 [1,14; 3,14] 0,014 *	0,13 [0,04; 0,22] 0,005 *
Any SAE, disease specific events excluded[1]					
Interaction test:	p=0,349				
Age = 18-30 years	1 (3,8)	2 (16,7)	0,20 [0,02; 2,46] 0,173	0,23 [0,02; 2,30] 0,212	-0,13 [-0,35; 0,10] 0,261
Age = 31-40 years	11 (6,8)	6 (6,6)	1,04 [0,37; 2,91] 0,942	1,04 [0,40; 2,71] 0,942	0,00 [-0,06; 0,07] 0,942
Age = 41-55 years	90 (12,6)	30 (9,1)	1,45 [0,94; 2,24] 0,092	1,39 [0,94; 2,06] 0,096	0,04 [-0,00; 0,08] 0,075
Age = >55 years	44 (22,0)	15 (13,4)	1,82 [0,96; 3,45] 0,063	1,64 [0,96; 2,81] 0,071	0,09 [0,00; 0,17] 0,048 *
Any severe AE[2]					
Interaction test:	p=0,236				
Age = 18-30 years	2 (7,7)	3 (25,0)	0,25 [0,04; 1,75] 0,142	0,31 [0,06; 1,61] 0,162	-0,17 [-0,44; 0,09] 0,201
Age = 31-40 years	11 (6,8)	5 (5,5)	1,26 [0,42; 3,75] 0,676	1,24 [0,45; 3,47] 0,677	0,01 [-0,05; 0,07] 0,667
Age = 41-55 years	86 (12,1)	39 (11,8)	1,03 [0,69; 1,54] 0,891	1,03 [0,72; 1,46] 0,891	0,00 [-0,04; 0,05] 0,891
Age = >55 years	40 (20,0)	14 (12,5)	1,75 [0,91; 3,38] 0,093	1,60 [0,91; 2,81] 0,102	0,08 [-0,01; 0,16] 0,075

	Treatment groups		Comparison		
	BAF312 (N=1099)	**Placebo (N=546)**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Any severe AE[2], disease specific events excluded[1]					
Interaction test:	p=0,243				
Age = 18-30 years	1 (3,8)	3 (25,0)	0,12 [0,01; 1,31] 0,048 *	0,15 [0,02; 1,33] 0,089	-0,21 [-0,47; 0,04] 0,105
Age = 31-40 years	9 (5,6)	5 (5,5)	1,02 [0,33; 3,14] 0,975	1,02 [0,35; 2,94] 0,975	0,00 [-0,06; 0,06] 0,975
Age = 41-55 years	71 (10,0)	24 (7,3)	1,42 [0,87; 2,30] 0,155	1,38 [0,88; 2,14] 0,160	0,03 [-0,01; 0,06] 0,134
Age = >55 years	29 (14,5)	12 (10,7)	1,41 [0,69; 2,89] 0,342	1,35 [0,72; 2,55] 0,348	0,04 [-0,04; 0,11] 0,324
Any AE leading to study discontinuation					
Interaction test:	N.E.				
Age = 18-30 years	1 (3,8)	0 (0,0)	1,47 [0,06; 38,75] 0,491	1,44 [0,06; 33,09] 0,818	0,04 [-0,04; 0,11] 0,308
Age = 31-40 years	0 (0,0)	1 (1,1)	0,19 [0,01; 4,63] 0,183	0,19 [0,01; 4,60] 0,307	-0,01 [-0,03; 0,01] 0,315
Age = 41-55 years	30 (4,2)	13 (3,9)	1,08 [0,55; 2,09] 0,829	1,07 [0,57; 2,03] 0,829	0,00 [-0,02; 0,03] 0,827
Age = >55 years	15 (7,5)	2 (1,8)	4,46 [1,00; 19,87] 0,033 *	4,20 [0,98; 18,03] 0,054	0,06 [0,01; 0,10] 0,011 *

	Treatment groups		Comparison		
	BAF312 (N=1099)	**Placebo (N=546)**	**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 = 18-30 years	1 (3,8)	0 (0,0)	1,47 [0,06; 38,75] 0,491	1,44 [0,06; 33,09] 0,818	0,04 [-0,04; 0,11] 0,308
Age = 31-40 years	2 (1,2)	1 (1,1)	1,13 [0,10; 12,66] 0,920	1,13 [0,10; 12,30] 0,920	0,00 [-0,03; 0,03] 0,918
Age = 41-55 years	59 (8,3)	21 (6,3)	1,33 [0,80; 2,23] 0,273	1,31 [0,81; 2,11] 0,276	0,02 [-0,01; 0,05] 0,251
Age = >55 years	22 (11,0)	6 (5,4)	2,18 [0,86; 5,56] 0,094	2,05 [0,86; 4,91] 0,106	0,06 [-0,00; 0,12] 0,066

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 total population

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

	Treatment groups		Comparison		
	BAF312 (N=1099)	**Placebo (N=546)**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
N'	1099	546			
N' Age = 18-30 years	26	12			
N' Age = 31-40 years	161	91			
N' Age = 41-55 years	712	331			
N' Age = >55 years	200	112			
BLOOD AND LYMPHATIC SYSTEM DISORDERS					
Interaction test:	N.E.				
Age = 18-30 years	1 (3,8)	0 (0,0)	1,47 [0,06; 38,75] 0,491	1,44 [0,06; 33,09] 0,818	0,04 [-0,04; 0,11] 0,308
Age = 31-40 years	10 (6,2)	4 (4,4)	1,44 [0,44; 4,73] 0,546	1,41 [0,46; 4,38] 0,549	0,02 [-0,04; 0,07] 0,527
Age = 41-55 years	28 (3,9)	4 (1,2)	3,35 [1,16; 9,62] 0,018 *	3,25 [1,15; 9,20] 0,026 *	0,03 [0,01; 0,05] 0,004 *
Age = >55 years	7 (3,5)	2 (1,8)	1,99 [0,41; 9,77] 0,385	1,96 [0,41; 9,27] 0,396	0,02 [-0,02; 0,05] 0,342
EAR AND LABYRINTH DISORDERS					
VERTIGO					
Interaction test:	N.E.				
Age = 18-30 years	1 (3,8)	0 (0,0)	1,47 [0,06; 38,75] 0,491	1,44 [0,06; 33,09] 0,818	0,04 [-0,04; 0,11] 0,308
Age = 31-40 years	2 (1,2)	3 (3,3)	0,37 [0,06; 2,25] 0,261	0,38 [0,06; 2,21] 0,280	-0,02 [-0,06; 0,02] 0,320
Age = 41-55 years	21 (2,9)	19 (5,7)	0,50 [0,26; 0,94] 0,029 *	0,51 [0,28; 0,94] 0,031 *	-0,03 [-0,06; 0,00] 0,051
Age = >55 years	1 (0,5)	4 (3,6)	0,14 [0,01; 1,23] 0,038 *	0,14 [0,02; 1,24] 0,077	-0,03 [-0,07; 0,01] 0,092

	Treatment groups		Comparison		
	BAF312 (N=1099)	**Placebo (N=546)**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
EYE DISORDERS					
MACULAR OEDEMA					
Interaction test:	N.E.				
Age = 18-30 years	0 (0,0)	0 (0,0)	-	-	-
Age = 31-40 years	0 (0,0)	0 (0,0)	-	-	-
Age = 41-55 years	13 (1,8)	0 (0,0)	12,80 [0,76; 215,90] 0,013 *	12,57 [0,75; 210,85] 0,078	0,02 [0,01; 0,03] <0,001 *
Age = >55 years	5 (2,5)	1 (0,9)	2,85 [0,33; 24,67] 0,321	2,80 [0,33; 23,67] 0,344	0,02 [-0,01; 0,04] 0,257
GASTROINTESTINAL DISORDERS					
NAUSEA					
Interaction test:	N.E.				
Age = 18-30 years	2 (7,7)	0 (0,0)	2,55 [0,11; 57,30] 0,324	2,41 [0,12; 46,62] 0,561	0,08 [-0,03; 0,18] 0,141
Age = 31-40 years	9 (5,6)	2 (2,2)	2,63 [0,56; 12,47] 0,206	2,54 [0,56; 11,52] 0,226	0,03 [-0,01; 0,08] 0,153
Age = 41-55 years	47 (6,6)	13 (3,9)	1,73 [0,92; 3,24] 0,084	1,68 [0,92; 3,06] 0,090	0,03 [-0,00; 0,05] 0,059
Age = >55 years	16 (8,0)	4 (3,6)	2,35 [0,77; 7,20] 0,126	2,24 [0,77; 6,54] 0,140	0,04 [-0,01; 0,10] 0,088
GENERAL DISORDERS AND ADMINISTRATION SITE CONDITIONS					
GAIT DISTURBANCE					
Interaction test:	N.E.				
Age = 18-30 years	0 (0,0)	0 (0,0)	-	-	-
Age = 31-40 years	4 (2,5)	3 (3,3)	0,75 [0,16; 3,42] 0,706	0,75 [0,17; 3,29] 0,707	-0,01 [-0,05; 0,04] 0,717
Age = 41-55 years	14 (2,0)	13 (3,9)	0,49 [0,23; 1,06] 0,063	0,50 [0,24; 1,05] 0,068	-0,02 [-0,04; 0,00] 0,099
Age = >55 years	6 (3,0)	6 (5,4)	0,55 [0,17; 1,74] 0,299	0,56 [0,18; 1,70] 0,305	-0,02 [-0,07; 0,02] 0,335

	Treatment groups		Comparison		
	BAF312 (N=1099)	**Placebo (N=546)**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
OEDEMA PERIPHERAL					
Interaction test:	N.E.				
Age = 18-30 years	0 (0,0)	0 (0,0)	-	-	-
Age = 31-40 years	0 (0,0)	0 (0,0)	-	-	-
Age = 41-55 years	34 (4,8)	10 (3,0)	1,61 [0,79; 3,30] 0,190	1,58 [0,79; 3,16] 0,195	0,02 [-0,01; 0,04] 0,155
Age = >55 years	16 (8,0)	3 (2,7)	3,16 [0,90; 11,09] 0,059	2,99 [0,89; 10,03] 0,077	0,05 [0,01; 0,10] 0,030 *
HEPATOBILIARY DISORDERS					
Interaction test:	N.E.				
Age = 18-30 years	0 (0,0)	0 (0,0)	-	-	-
Age = 31-40 years	1 (0,6)	0 (0,0)	1,71 [0,07; 42,42] 0,451	1,70 [0,07; 41,40] 0,743	0,01 [-0,01; 0,02] 0,316
Age = 41-55 years	20 (2,8)	3 (0,9)	3,16 [0,93; 10,71] 0,051	3,10 [0,93; 10,36] 0,066	0,02 [0,00; 0,03] 0,019 *
Age = >55 years	6 (3,0)	1 (0,9)	3,43 [0,41; 28,88] 0,228	3,36 [0,41; 27,56] 0,259	0,02 [-0,01; 0,05] 0,160
INFECTIONS AND INFESTATIONS					
HERPES ZOSTER					
Interaction test:	N.E.				
Age = 18-30 years	1 (3,8)	0 (0,0)	1,47 [0,06; 38,75] 0,491	1,44 [0,06; 33,09] 0,818	0,04 [-0,04; 0,11] 0,308
Age = 31-40 years	1 (0,6)	0 (0,0)	1,71 [0,07; 42,42] 0,451	1,70 [0,07; 41,40] 0,743	0,01 [-0,01; 0,02] 0,316
Age = 41-55 years	16 (2,2)	2 (0,6)	3,78 [0,86; 16,54] 0,058	3,72 [0,86; 16,08] 0,079	0,02 [0,00; 0,03] 0,019 *
Age = >55 years	7 (3,5)	2 (1,8)	1,99 [0,41; 9,77] 0,385	1,96 [0,41; 9,27] 0,396	0,02 [-0,02; 0,05] 0,342

	Treatment groups		Comparison		
	BAF312 (N=1099)	**Placebo (N=546)**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
INVESTIGATIONS					
Interaction test:	p=0,977				
Age = 18-30 years	4 (15,4)	1 (8,3)	2,00 [0,20; 20,10] 0,550	1,85 [0,23; 14,80] 0,564	0,07 [-0,14; 0,28] 0,508
Age = 31-40 years	39 (24,2)	12 (13,2)	2,10 [1,04; 4,26] 0,036 *	1,84 [1,01; 3,33] 0,045 *	0,11 [0,01; 0,21] 0,024 *
Age = 41-55 years	176 (24,7)	52 (15,7)	1,76 [1,25; 2,48] 0,001 *	1,57 [1,19; 2,08] 0,002 *	0,09 [0,04; 0,14] <0,001 *
Age = >55 years	44 (22,0)	15 (13,4)	1,82 [0,96; 3,45] 0,063	1,64 [0,96; 2,81] 0,071	0,09 [0,00; 0,17] 0,048 *
ALANINE AMINOTRANSFERASE INCREASED					
Interaction test:	N.E.				
Age = 18-30 years	0 (0,0)	0 (0,0)	-	-	-
Age = 31-40 years	17 (10,6)	4 (4,4)	2,57 [0,84; 7,88] 0,089	2,40 [0,83; 6,92] 0,105	0,06 [-0,00; 0,13] 0,057
Age = 41-55 years	40 (5,6)	2 (0,6)	9,79 [2,35; 40,76] <0,001 *	9,30 [2,26; 38,24] 0,002 *	0,05 [0,03; 0,07] <0,001 *
Age = >55 years	8 (4,0)	2 (1,8)	2,29 [0,48; 10,98] 0,287	2,24 [0,48; 10,37] 0,302	0,02 [-0,01; 0,06] 0,236
GAMMA-GLUTAMYLTRANSFERASE INCREASED					
Interaction test:	N.E.				
Age = 18-30 years	0 (0,0)	0 (0,0)	-	-	-
Age = 31-40 years	6 (3,7)	1 (1,1)	3,48 [0,41; 29,40] 0,223	3,39 [0,41; 27,73] 0,255	0,03 [-0,01; 0,06] 0,155
Age = 41-55 years	31 (4,4)	5 (1,5)	2,97 [1,14; 7,70] 0,019 *	2,88 [1,13; 7,35] 0,027 *	0,03 [0,01; 0,05] 0,005 *
Age = >55 years	6 (3,0)	0 (0,0)	7,52 [0,42; 134,73] 0,064	7,31 [0,42; 128,54] 0,174	0,03 [0,01; 0,05] 0,013 *

	Treatment groups		Comparison		
	BAF312 (N=1099)	**Placebo (N=546)**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
HEPATIC ENZYME INCREASED					
Interaction test:	N.E.				
Age = 18-30 years	0 (0,0)	0 (0,0)	-	-	-
Age = 31-40 years	2 (1,2)	0 (0,0)	2,87 [0,14; 60,40] 0,286	2,84 [0,14; 58,51] 0,499	0,01 [-0,00; 0,03] 0,155
Age = 41-55 years	9 (1,3)	1 (0,3)	4,22 [0,53; 33,48] 0,138	4,18 [0,53; 32,89] 0,174	0,01 [-0,00; 0,02] 0,062
Age = >55 years	5 (2,5)	0 (0,0)	6,33 [0,35; 115,54] 0,092	6,18 [0,35; 110,81] 0,216	0,03 [0,00; 0,05] 0,024 *
NERVOUS SYSTEM DISORDERS					
Interaction test:	p=0,798				
Age = 18-30 years	8 (30,8)	0 (0,0)	11,49 [0,61; 217,51] 0,031 *	8,19 [0,51; 131,20] 0,137	0,31 [0,13; 0,49] 0,001 *
Age = 31-40 years	47 (29,2)	27 (29,7)	0,98 [0,56; 1,72] 0,936	0,98 [0,66; 1,46] 0,936	-0,00 [-0,12; 0,11] 0,936
Age = 41-55 years	287 (40,3)	111 (33,5)	1,34 [1,02; 1,76] 0,036 *	1,20 [1,01; 1,43] 0,041 *	0,07 [0,01; 0,13] 0,033 *
Age = >55 years	74 (37,0)	37 (33,0)	1,19 [0,73; 1,94] 0,483	1,12 [0,81; 1,54] 0,487	0,04 [-0,07; 0,15] 0,479
PARAESTHESIA					
Interaction test:	N.E.				
Age = 18-30 years	1 (3,8)	0 (0,0)	1,47 [0,06; 38,75] 0,491	1,44 [0,06; 33,09] 0,818	0,04 [-0,04; 0,11] 0,308
Age = 31-40 years	2 (1,2)	3 (3,3)	0,37 [0,06; 2,25] 0,261	0,38 [0,06; 2,21] 0,280	-0,02 [-0,06; 0,02] 0,320
Age = 41-55 years	13 (1,8)	13 (3,9)	0,45 [0,21; 0,99] 0,043 *	0,46 [0,22; 0,99] 0,048 *	-0,02 [-0,04; 0,00] 0,075
Age = >55 years	2 (1,0)	4 (3,6)	0,27 [0,05; 1,51] 0,113	0,28 [0,05; 1,50] 0,138	-0,03 [-0,06; 0,01] 0,174

	Treatment groups		Comparison		
	BAF312 (N=1099)	**Placebo (N=546)**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
VASCULAR DISORDERS					
Interaction test:	p=0,370				
Age = 18-30 years	1 (3,8)	0 (0,0)	1,47 [0,06; 38,75] 0,491	1,44 [0,06; 33,09] 0,818	0,04 [-0,04; 0,11] 0,308
Age = 31-40 years	13 (8,1)	4 (4,4)	1,91 [0,60; 6,04] 0,263	1,84 [0,62; 5,47] 0,275	0,04 [-0,02; 0,10] 0,226
Age = 41-55 years	107 (15,0)	45 (13,6)	1,12 [0,77; 1,64] 0,542	1,11 [0,80; 1,53] 0,543	0,01 [-0,03; 0,06] 0,535
Age = >55 years	39 (19,5)	11 (9,8)	2,22 [1,09; 4,54] 0,025 *	1,99 [1,06; 3,72] 0,032 *	0,10 [0,02; 0,17] 0,015 *

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 total population

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

	Treatment groups		Comparison		
	BAF312 (N=1099)	**Placebo (N=546)**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
N'	1099	546			
N' Age = 18-30 years	26	12			
N' Age = 31-40 years	161	91			
N' Age = 41-55 years	712	331			
N' Age = >55 years	200	112			
INVESTIGATIONS					
Interaction test:	N.E.				
Age = 18-30 years	0 (0,0)	0 (0,0)	-	-	-
Age = 31-40 years	5 (3,1)	1 (1,1)	2,88 [0,33; 25,08] 0,316	2,83 [0,34; 23,82] 0,339	0,02 [-0,01; 0,05] 0,252
Age = 41-55 years	14 (2,0)	2 (0,6)	3,30 [0,75; 14,60] 0,096	3,25 [0,74; 14,24] 0,117	0,01 [0,00; 0,03] 0,043 *
Age = >55 years	2 (1,0)	0 (0,0)	2,83 [0,13; 59,55] 0,288	2,81 [0,14; 58,04] 0,503	0,01 [-0,00; 0,02] 0,155

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 total population

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=1099)	**Placebo (N=546)**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
N'	1099	546			
N' Age = 18-30 years	26	12			
N' Age = 31-40 years	161	91			
N' Age = 41-55 years	712	331			
N' Age = >55 years	200	112			
Infections and infestations					
Interaction test:	p=0,684				
Age = 18-30 years	10 (38,5)	3 (25,0)	1,88 [0,41; 8,63] 0,416	1,54 [0,52; 4,59] 0,440	0,13 [-0,17; 0,44] 0,392
Age = 31-40 years	64 (39,8)	39 (42,9)	0,88 [0,52; 1,48] 0,630	0,93 [0,68; 1,26] 0,628	-0,03 [-0,16; 0,10] 0,631
Age = 41-55 years	366 (51,4)	166 (50,2)	1,05 [0,81; 1,36] 0,706	1,02 [0,90; 1,17] 0,708	0,01 [-0,05; 0,08] 0,706
Age = >55 years	99 (49,5)	60 (53,6)	0,85 [0,53; 1,35] 0,490	0,92 [0,74; 1,15] 0,485	-0,04 [-0,16; 0,07] 0,490
Herpes simplex virus infections					
Interaction test:	N.E.				
Age = 18-30 years	0 (0,0)	0 (0,0)	-	-	-
Age = 31-40 years	2 (1,2)	1 (1,1)	1,13 [0,10; 12,66] 0,920	1,13 [0,10; 12,30] 0,920	0,00 [-0,03; 0,03] 0,918
Age = 41-55 years	20 (2,8)	8 (2,4)	1,17 [0,51; 2,68] 0,715	1,16 [0,52; 2,61] 0,716	0,00 [-0,02; 0,02] 0,708
Age = >55 years	3 (1,5)	2 (1,8)	0,84 [0,14; 5,09] 0,847	0,84 [0,14; 4,95] 0,847	-0,00 [-0,03; 0,03] 0,851

	Treatment groups		Comparison		
	BAF312 (N=1099)	**Placebo (N=546)**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Varicella-zoster virus infections					
Interaction test:	N.E.				
Age = 18-30 years	1 (3,8)	0 (0,0)	1,47 [0,06; 38,75] 0,491	1,44 [0,06; 33,09] 0,818	0,04 [-0,04; 0,11] 0,308
Age = 31-40 years	2 (1,2)	0 (0,0)	2,87 [0,14; 60,40] 0,286	2,84 [0,14; 58,51] 0,499	0,01 [-0,00; 0,03] 0,155
Age = 41-55 years	21 (2,9)	2 (0,6)	5,00 [1,17; 21,45] 0,016 *	4,88 [1,15; 20,70] 0,031 *	0,02 [0,01; 0,04] 0,002 *
Age = >55 years	9 (4,5)	2 (1,8)	2,59 [0,55; 12,21] 0,212	2,52 [0,55; 11,46] 0,232	0,03 [-0,01; 0,06] 0,159
Lymphopenia					
Interaction test:	N.E.				
Age = 18-30 years	1 (3,8)	0 (0,0)	1,47 [0,06; 38,75] 0,491	1,44 [0,06; 33,09] 0,818	0,04 [-0,04; 0,11] 0,308
Age = 31-40 years	3 (1,9)	0 (0,0)	4,04 [0,21; 79,11] 0,190	3,98 [0,21; 76,11] 0,360	0,02 [-0,00; 0,04] 0,080
Age = 41-55 years	8 (1,1)	0 (0,0)	8,00 [0,46; 139,00] 0,053	7,92 [0,46; 136,74] 0,155	0,01 [0,00; 0,02] 0,004 *
Age = >55 years	2 (1,0)	0 (0,0)	2,83 [0,13; 59,55] 0,288	2,81 [0,14; 58,04] 0,503	0,01 [-0,00; 0,02] 0,155
Macular edema					
Interaction test:	N.E.				
Age = 18-30 years	0 (0,0)	0 (0,0)	-	-	-
Age = 31-40 years	0 (0,0)	0 (0,0)	-	-	-
Age = 41-55 years	15 (2,1)	0 (0,0)	14,73 [0,88; 246,98] 0,008 *	14,43 [0,87; 240,52] 0,063	0,02 [0,01; 0,03] <0,001 *
Age = >55 years	5 (2,5)	1 (0,9)	2,85 [0,33; 24,67] 0,321	2,80 [0,33; 23,67] 0,344	0,02 [-0,01; 0,04] 0,257

	Treatment groups		Comparison		
	BAF312 (N=1099)	**Placebo (N=546)**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Abnormal hepatic enzymes					
Interaction test:	p=0,991				
Age = 18-30 years	1 (3,8)	0 (0,0)	1,47 [0,06; 38,75] 0,491	1,44 [0,06; 33,09] 0,818	0,04 [-0,04; 0,11] 0,308
Age = 31-40 years	24 (14,9)	5 (5,5)	3,01 [1,11; 8,19] 0,025 *	2,71 [1,07; 6,87] 0,035 *	0,09 [0,02; 0,17] 0,011 *
Age = 41-55 years	91 (12,8)	13 (3,9)	3,58 [1,97; 6,51] <0,001 *	3,25 [1,85; 5,73] <0,001 *	0,09 [0,06; 0,12] <0,001 *
Age = >55 years	19 (9,5)	3 (2,7)	3,81 [1,10; 13,19] 0,024 *	3,55 [1,07; 11,72] 0,038 *	0,07 [0,02; 0,12] 0,008 *
Malignancies					
Interaction test:	N.E.				
Age = 18-30 years	0 (0,0)	0 (0,0)	-	-	-
Age = 31-40 years	2 (1,2)	1 (1,1)	1,13 [0,10; 12,66] 0,920	1,13 [0,10; 12,30] 0,920	0,00 [-0,03; 0,03] 0,918
Age = 41-55 years	4 (0,6)	8 (2,4)	0,23 [0,07; 0,76] 0,009 *	0,23 [0,07; 0,77] 0,017 *	-0,02 [-0,04; -0,00] 0,037 *
Age = >55 years	14 (7,0)	5 (4,5)	1,61 [0,56; 4,60] 0,369	1,57 [0,58; 4,24] 0,375	0,03 [-0,03; 0,08] 0,340
Hypertension					
Interaction test:	p=0,502				
Age = 18-30 years	1 (3,8)	0 (0,0)	1,47 [0,06; 38,75] 0,491	1,44 [0,06; 33,09] 0,818	0,04 [-0,04; 0,11] 0,308
Age = 31-40 years	10 (6,2)	2 (2,2)	2,95 [0,63; 13,76] 0,151	2,83 [0,63; 12,62] 0,174	0,04 [-0,01; 0,09] 0,101
Age = 41-55 years	94 (13,2)	38 (11,5)	1,17 [0,78; 1,75] 0,436	1,15 [0,81; 1,64] 0,438	0,02 [-0,03; 0,06] 0,426
Age = >55 years	32 (16,0)	10 (8,9)	1,94 [0,92; 4,12] 0,079	1,79 [0,92; 3,51] 0,089	0,07 [-0,00; 0,14] 0,059

	Treatment groups		Comparison		
	BAF312 (N=1099)	**Placebo (N=546)**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Seizures					
Interaction test:	N.E.				
Age = 18-30 years	0 (0,0)	0 (0,0)	-	-	-
Age = 31-40 years	0 (0,0)	1 (1,1)	0,19 [0,01; 4,63] 0,183	0,19 [0,01; 4,60] 0,307	-0,01 [-0,03; 0,01] 0,315
Age = 41-55 years	17 (2,4)	0 (0,0)	16,68 [1,00; 278,25] 0,005 *	16,30 [0,98; 270,19] 0,051	0,02 [0,01; 0,04] <0,001 *
Age = >55 years	2 (1,0)	1 (0,9)	1,12 [0,10; 12,50] 0,926	1,12 [0,10; 12,21] 0,926	0,00 [-0,02; 0,02] 0,925
Thromboembolic events					
Interaction test:	N.E.				
Age = 18-30 years	1 (3,8)	0 (0,0)	1,47 [0,06; 38,75] 0,491	1,44 [0,06; 33,09] 0,818	0,04 [-0,04; 0,11] 0,308
Age = 31-40 years	4 (2,5)	2 (2,2)	1,13 [0,20; 6,31] 0,886	1,13 [0,21; 6,05] 0,886	0,00 [-0,04; 0,04] 0,884
Age = 41-55 years	19 (2,7)	10 (3,0)	0,88 [0,40; 1,91] 0,747	0,88 [0,42; 1,88] 0,747	-0,00 [-0,03; 0,02] 0,752
Age = >55 years	9 (4,5)	3 (2,7)	1,71 [0,45; 6,46] 0,422	1,68 [0,46; 6,08] 0,429	0,02 [-0,02; 0,06] 0,389
Respiratory disorders					
Interaction test:	p=0,470				
Age = 18-30 years	2 (7,7)	2 (16,7)	0,42 [0,05; 3,38] 0,402	0,46 [0,07; 2,90] 0,409	-0,09 [-0,32; 0,14] 0,453
Age = 31-40 years	10 (6,2)	4 (4,4)	1,44 [0,44; 4,73] 0,546	1,41 [0,46; 4,38] 0,549	0,02 [-0,04; 0,07] 0,527
Age = 41-55 years	82 (11,5)	44 (13,3)	0,85 [0,57; 1,26] 0,413	0,87 [0,62; 1,22] 0,411	-0,02 [-0,06; 0,03] 0,423
Age = >55 years	23 (11,5)	21 (18,8)	0,56 [0,30; 1,07] 0,078	0,61 [0,36; 1,06] 0,078	-0,07 [-0,16; 0,01] 0,094

	Treatment groups		Comparison		
	BAF312 (N=1099)	**Placebo (N=546)**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Peripheral edema/swelling					
Interaction test:	N.E.				
Age = 18-30 years	0 (0,0)	0 (0,0)	-	-	-
Age = 31-40 years	0 (0,0)	2 (2,2)	0,11 [0,01; 2,33] 0,059	0,11 [0,01; 2,34] 0,159	-0,02 [-0,05; 0,01] 0,153
Age = 41-55 years	55 (7,7)	13 (3,9)	2,05 [1,10; 3,80] 0,021 *	1,97 [1,09; 3,55] 0,025 *	0,04 [0,01; 0,07] 0,009 *
Age = >55 years	19 (9,5)	3 (2,7)	3,81 [1,10; 13,19] 0,024 *	3,55 [1,07; 11,72] 0,038 *	0,07 [0,02; 0,12] 0,008 *

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 total population

	Treatment groups		Comparison		
	BAF312 (N=1099)	**Placebo (N=546)**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
N'	1099	546			
N' Age = 18-30 years	26	12			
N' Age = 31-40 years	161	91			
N' Age = 41-55 years	712	331			
N' Age = >55 years	200	112			
Asthma/bronchospasm					
Interaction test:	N.E.				
Age = 18-30 years	0 (0,0)	0 (0,0)	-	-	-
Age = 31-40 years	2 (1,2)	0 (0,0)	2,87 [0,14; 60,40] 0,286	2,84 [0,14; 58,51] 0,499	0,01 [-0,00; 0,03] 0,155
Age = 41-55 years	4 (0,6)	2 (0,6)	0,93 [0,17; 5,10] 0,933	0,93 [0,17; 5,05] 0,933	-0,00 [-0,01; 0,01] 0,934
Age = >55 years	2 (1,0)	0 (0,0)	2,83 [0,13; 59,55] 0,288	2,81 [0,14; 58,04] 0,503	0,01 [-0,00; 0,02] 0,155
Pregnancy and neonatal topics					
Interaction test:	N.E.				
Age = 18-30 years	0 (0,0)	0 (0,0)	-	-	-
Age = 31-40 years	2 (1,2)	0 (0,0)	2,87 [0,14; 60,40] 0,286	2,84 [0,14; 58,51] 0,499	0,01 [-0,00; 0,03] 0,155
Age = 41-55 years	3 (0,4)	0 (0,0)	3,27 [0,17; 63,50] 0,237	3,26 [0,17; 62,92] 0,434	0,00 [-0,00; 0,01] 0,083
Age = >55 years	1 (0,5)	0 (0,0)	1,69 [0,07; 41,88] 0,454	1,69 [0,07; 41,06] 0,748	0,01 [-0,00; 0,01] 0,316

	Treatment groups		Comparison		
	BAF312 (N=1099)	**Placebo (N=546)**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Bradyarrhythmias and bradycardia					
Interaction test:	p=0,750				
Age = 18-30 years	3 (11,5)	1 (8,3)	1,43 [0,13; 15,42] 0,765	1,38 [0,16; 11,97] 0,767	0,03 [-0,17; 0,23] 0,752
Age = 31-40 years	18 (11,2)	4 (4,4)	2,74 [0,90; 8,35] 0,067	2,54 [0,89; 7,29] 0,082	0,07 [0,00; 0,13] 0,039 *
Age = 41-55 years	62 (8,7)	17 (5,1)	1,76 [1,01; 3,06] 0,042 *	1,70 [1,01; 2,85] 0,047 *	0,04 [0,00; 0,07] 0,026 *
Age = >55 years	20 (10,0)	9 (8,0)	1,27 [0,56; 2,90] 0,567	1,24 [0,59; 2,64] 0,569	0,02 [-0,05; 0,08] 0,555

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 total population

11.3 Subgroup: Gender

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

	Treatment groups		Comparison		
	BAF312 (N=1099)	**Placebo (N=546)**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
N'	1099	546			
N' Gender = Male	435	223			
N' Gender = Female	664	323			
Any AE					
Interaction test:	p=0,274				
Gender = Male	383 (88,0)	186 (83,4)	1,47 [0,93; 2,31] 0,100	1,06 [0,99; 1,13] 0,119	0,05 [-0,01; 0,10] 0,114
Gender = Female	592 (89,2)	259 (80,2)	2,03 [1,41; 2,93] <0,001 *	1,11 [1,05; 1,18] 0,001 *	0,09 [0,04; 0,14] <0,001 *
Any AE, disease specific events excluded[1]					
Interaction test:	p=0,579				
Gender = Male	360 (82,8)	172 (77,1)	1,42 [0,95; 2,12] 0,082	1,07 [0,99; 1,17] 0,098	0,06 [-0,01; 0,12] 0,092
Gender = Female	558 (84,0)	246 (76,2)	1,65 [1,19; 2,29] 0,003 *	1,10 [1,03; 1,18] 0,005 *	0,08 [0,02; 0,13] 0,004 *
Any SAE					
Interaction test:	p=0,089				
Gender = Male	73 (16,8)	38 (17,0)	0,98 [0,64; 1,51] 0,933	0,98 [0,69; 1,41] 0,933	-0,00 [-0,06; 0,06] 0,933
Gender = Female	113 (17,0)	36 (11,1)	1,63 [1,09; 2,44] 0,016 *	1,53 [1,08; 2,17] 0,018 *	0,06 [0,01; 0,10] 0,010 *
Any SAE, disease specific events excluded[1]					
Interaction test:	p=0,134				
Gender = Male	56 (12,9)	27 (12,1)	1,07 [0,66; 1,75] 0,779	1,06 [0,69; 1,63] 0,780	0,01 [-0,05; 0,06] 0,778
Gender = Female	90 (13,6)	26 (8,0)	1,79 [1,13; 2,83] 0,012 *	1,68 [1,11; 2,55] 0,014 *	0,06 [0,02; 0,09] 0,006 *

	Treatment groups		Comparison		
	BAF312 (N=1099)	**Placebo (N=546)**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Any severe AE[2]					
Interaction test:	p=0,093				
Gender = Male	50 (11,5)	30 (13,5)	0,84 [0,51; 1,36] 0,467	0,85 [0,56; 1,30] 0,466	-0,02 [-0,07; 0,03] 0,476
Gender = Female	89 (13,4)	31 (9,6)	1,46 [0,95; 2,25] 0,086	1,40 [0,95; 2,06] 0,090	0,04 [-0,00; 0,08] 0,071
Any severe AE[2], disease specific events excluded[1]					
Interaction test:	p=0,065				
Gender = Male	39 (9,0)	23 (10,3)	0,86 [0,50; 1,47] 0,575	0,87 [0,53; 1,42] 0,575	-0,01 [-0,06; 0,03] 0,583
Gender = Female	71 (10,7)	21 (6,5)	1,72 [1,04; 2,86] 0,034 *	1,64 [1,03; 2,63] 0,037 *	0,04 [0,01; 0,08] 0,021 *
Any AE leading to study discontinuation					
Interaction test:	p=0,909				
Gender = Male	16 (3,7)	6 (2,7)	1,38 [0,53; 3,58] 0,505	1,37 [0,54; 3,45] 0,507	0,01 [-0,02; 0,04] 0,484
Gender = Female	30 (4,5)	10 (3,1)	1,48 [0,71; 3,07] 0,288	1,46 [0,72; 2,95] 0,292	0,01 [-0,01; 0,04] 0,258

	Treatment groups		Comparison		
	BAF312 (N=1099)	**Placebo (N=546)**	**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=0,703				
Gender = Male	26 (6,0)	10 (4,5)	1,35 [0,64; 2,86] 0,425	1,33 [0,65; 2,71] 0,428	0,01 [-0,02; 0,05] 0,405
Gender = Female	58 (8,7)	18 (5,6)	1,62 [0,94; 2,80] 0,080	1,57 [0,94; 2,62] 0,085	0,03 [-0,00; 0,06] 0,060

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 + 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 total population

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

	Treatment groups		Comparison		
	BAF312 (N=1099)	**Placebo (N=546)**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
N'	1099	546			
N' Gender = Male	435	223			
N' Gender = Female	664	323			
BLOOD AND LYMPHATIC SYSTEM DISORDERS					
Interaction test:	p=0,996				
Gender = Male	9 (2,1)	2 (0,9)	2,33 [0,50; 10,90] 0,267	2,31 [0,50; 10,59] 0,282	0,01 [-0,01; 0,03] 0,207
Gender = Female	37 (5,6)	8 (2,5)	2,32 [1,07; 5,05] 0,029 *	2,25 [1,06; 4,77] 0,035 *	0,03 [0,01; 0,06] 0,013 *
EAR AND LABYRINTH DISORDERS					
VERTIGO					
Interaction test:	p=0,845				
Gender = Male	7 (1,6)	7 (3,1)	0,50 [0,17; 1,46] 0,198	0,51 [0,18; 1,44] 0,206	-0,02 [-0,04; 0,01] 0,244
Gender = Female	18 (2,7)	19 (5,9)	0,45 [0,23; 0,86] 0,014 *	0,46 [0,25; 0,87] 0,016 *	-0,03 [-0,06; -0,00] 0,029 *
EYE DISORDERS					
MACULAR OEDEMA					
Interaction test:	N.E.				
Gender = Male	6 (1,4)	1 (0,4)	3,10 [0,37; 25,95] 0,271	3,08 [0,37; 25,39] 0,297	0,01 [-0,00; 0,02] 0,194
Gender = Female	12 (1,8)	0 (0,0)	12,39 [0,73; 210,00] 0,015 *	12,18 [0,72; 205,08] 0,083	0,02 [0,01; 0,03] <0,001 *
GASTROINTESTINAL DISORDERS					
NAUSEA					
Interaction test:	p=0,860				
Gender = Male	14 (3,2)	4 (1,8)	1,82 [0,59; 5,60] 0,289	1,79 [0,60; 5,39] 0,297	0,01 [-0,01; 0,04] 0,246
Gender = Female	60 (9,0)	15 (4,6)	2,04 [1,14; 3,65] 0,015 *	1,95 [1,12; 3,37] 0,018 *	0,04 [0,01; 0,08] 0,007 *

	Treatment groups		Comparison		
	BAF312 (N=1099)	**Placebo (N=546)**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
GENERAL DISORDERS AND ADMINISTRATION SITE CONDITIONS					
GAIT DISTURBANCE					
Interaction test:	p=0,304				
Gender = Male	12 (2,8)	8 (3,6)	0,76 [0,31; 1,89] 0,558	0,77 [0,32; 1,85] 0,558	-0,01 [-0,04; 0,02] 0,573
Gender = Female	12 (1,8)	14 (4,3)	0,41 [0,19; 0,89] 0,020 *	0,42 [0,20; 0,89] 0,024 *	-0,03 [-0,05; -0,00] 0,042 *
OEDEMA PERIPHERAL					
Interaction test:	p=0,128				
Gender = Male	15 (3,4)	7 (3,1)	1,10 [0,44; 2,74] 0,835	1,10 [0,45; 2,66] 0,835	0,00 [-0,03; 0,03] 0,832
Gender = Female	35 (5,3)	6 (1,9)	2,94 [1,22; 7,06] 0,012 *	2,84 [1,21; 6,68] 0,017 *	0,03 [0,01; 0,06] 0,003 *
HEPATOBILIARY DISORDERS					
Interaction test:	p=0,309				
Gender = Male	14 (3,2)	1 (0,4)	7,38 [0,96; 56,51] 0,024 *	7,18 [0,95; 54,23] 0,056	0,03 [0,01; 0,05] 0,004 *
Gender = Female	13 (2,0)	3 (0,9)	2,13 [0,60; 7,53] 0,230	2,11 [0,60; 7,35] 0,242	0,01 [-0,00; 0,03] 0,174
INFECTIONS AND INFESTATIONS					
HERPES ZOSTER					
Interaction test:	p=0,992				
Gender = Male	6 (1,4)	1 (0,4)	3,10 [0,37; 25,95] 0,271	3,08 [0,37; 25,39] 0,297	0,01 [-0,00; 0,02] 0,194
Gender = Female	19 (2,9)	3 (0,9)	3,14 [0,92; 10,70] 0,054	3,08 [0,92; 10,34] 0,068	0,02 [0,00; 0,04] 0,021 *
INVESTIGATIONS					
Interaction test:	p=0,196				
Gender = Male	120 (27,6)	32 (14,3)	2,27 [1,48; 3,49] <0,001 *	1,92 [1,35; 2,74] <0,001 *	0,13 [0,07; 0,19] <0,001 *
Gender = Female	143 (21,5)	48 (14,9)	1,57 [1,10; 2,25] 0,013 *	1,45 [1,08; 1,95] 0,015 *	0,07 [0,02; 0,12] 0,009 *

	Treatment groups		Comparison		
	BAF312 (N=1099)	**Placebo (N=546)**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
ALANINE AMINOTRANSFERASE INCREASED					
Interaction test:	p=0,563				
Gender = Male	38 (8,7)	4 (1,8)	5,24 [1,85; 14,88] 0,001 *	4,87 [1,76; 13,47] 0,002 *	0,07 [0,04; 0,10] <0,001 *
Gender = Female	27 (4,1)	4 (1,2)	3,38 [1,17; 9,74] 0,017 *	3,28 [1,16; 9,30] 0,025 *	0,03 [0,01; 0,05] 0,004 *
GAMMA-GLUTAMYLTRANSFERASE INCREASED					
Interaction test:	p=0,752				
Gender = Male	25 (5,7)	4 (1,8)	3,34 [1,15; 9,71] 0,019 *	3,20 [1,13; 9,09] 0,029 *	0,04 [0,01; 0,07] 0,006 *
Gender = Female	18 (2,7)	2 (0,6)	4,47 [1,03; 19,39] 0,029 *	4,38 [1,02; 18,75] 0,047 *	0,02 [0,01; 0,04] 0,006 *
HEPATIC ENZYME INCREASED					
Interaction test:	N.E.				
Gender = Male	9 (2,1)	0 (0,0)	9,96 [0,58; 171,86] 0,031 *	9,76 [0,57; 166,95] 0,116	0,02 [0,01; 0,03] 0,002 *
Gender = Female	7 (1,1)	1 (0,3)	3,43 [0,42; 28,00] 0,221	3,41 [0,42; 27,56] 0,251	0,01 [-0,00; 0,02] 0,138
NERVOUS SYSTEM DISORDERS					
Interaction test:	p=0,077				
Gender = Male	135 (31,0)	69 (30,9)	1,00 [0,71; 1,42] 0,981	1,00 [0,79; 1,28] 0,981	0,00 [-0,07; 0,08] 0,981
Gender = Female	281 (42,3)	106 (32,8)	1,50 [1,14; 1,98] 0,004 *	1,29 [1,08; 1,54] 0,006 *	0,10 [0,03; 0,16] 0,003 *
PARAESTHESIA					
Interaction test:	p=0,090				
Gender = Male	1 (0,2)	6 (2,7)	0,08 [0,01; 0,70] 0,004 *	0,09 [0,01; 0,71] 0,022 *	-0,02 [-0,05; -0,00] 0,026 *
Gender = Female	17 (2,6)	14 (4,3)	0,58 [0,28; 1,19] 0,134	0,59 [0,29; 1,18] 0,137	-0,02 [-0,04; 0,01] 0,168

	Treatment groups		Comparison		
	BAF312 (N=1099)	**Placebo (N=546)**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
VASCULAR DISORDERS					
Interaction test:	p=0,297				
Gender = Male	56 (12,9)	26 (11,7)	1,12 [0,68; 1,84] 0,655	1,10 [0,71; 1,71] 0,656	0,01 [-0,04; 0,06] 0,651
Gender = Female	104 (15,7)	34 (10,5)	1,58 [1,05; 2,38] 0,029 *	1,49 [1,03; 2,14] 0,032 *	0,05 [0,01; 0,09] 0,020 *

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

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 total population

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

	Treatment groups		Comparison		
	BAF312 (N=1099)	**Placebo (N=546)**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
N'	1099	546			
N' Gender = Male	435	223			
N' Gender = Female	664	323			
INVESTIGATIONS					
Interaction test:	p=0,573				
Gender = Male	10 (2,3)	2 (0,9)	2,60 [0,56; 11,97] 0,203	2,56 [0,57; 11,60] 0,222	0,01 [-0,00; 0,03] 0,143
Gender = Female	11 (1,7)	1 (0,3)	5,42 [0,70; 42,20] 0,070	5,35 [0,69; 41,27] 0,108	0,01 [0,00; 0,02] 0,021 *

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 total population

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=1099)	**Placebo (N=546)**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
N'	1099	546			
N' Gender = Male	435	223			
N' Gender = Female	664	323			
Infections and infestations					
Interaction test:	p=0,915				
Gender = Male	197 (45,3)	102 (45,7)	0,98 [0,71; 1,36] 0,912	0,99 [0,83; 1,18] 0,912	-0,00 [-0,08; 0,08] 0,912
Gender = Female	342 (51,5)	166 (51,4)	1,00 [0,77; 1,31] 0,973	1,00 [0,88; 1,14] 0,973	0,00 [-0,07; 0,07] 0,973
Herpes simplex virus infections					
Interaction test:	p=0,913				
Gender = Male	4 (0,9)	2 (0,9)	1,03 [0,19; 5,64] 0,977	1,03 [0,19; 5,55] 0,977	0,00 [-0,02; 0,02] 0,977
Gender = Female	21 (3,2)	9 (2,8)	1,14 [0,52; 2,52] 0,747	1,14 [0,53; 2,45] 0,747	0,00 [-0,02; 0,03] 0,741
Varicella-zoster virus infections					
Interaction test:	p=0,897				
Gender = Male	9 (2,1)	1 (0,4)	4,69 [0,59; 37,26] 0,108	4,61 [0,59; 36,19] 0,146	0,02 [0,00; 0,03] 0,047 *
Gender = Female	24 (3,6)	3 (0,9)	4,00 [1,20; 13,38] 0,015 *	3,89 [1,18; 12,83] 0,026 *	0,03 [0,01; 0,04] 0,003 *
Lymphopenia					
Interaction test:	N.E.				
Gender = Male	5 (1,1)	0 (0,0)	5,71 [0,31; 103,74] 0,108	5,65 [0,31; 101,75] 0,240	0,01 [0,00; 0,02] 0,025 *
Gender = Female	9 (1,4)	0 (0,0)	9,38 [0,54; 161,61] 0,036 *	9,26 [0,54; 158,56] 0,125	0,01 [0,00; 0,02] 0,003 *

	Treatment groups		Comparison		
	BAF312 (N=1099)	**Placebo (N=546)**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Macular edema					
Interaction test:	N.E.				
Gender = Male	6 (1,4)	1 (0,4)	3,10 [0,37; 25,95] 0,271	3,08 [0,37; 25,39] 0,297	0,01 [-0,00; 0,02] 0,194
Gender = Female	14 (2,1)	0 (0,0)	14,42 [0,86; 242,52] 0,009 *	14,13 [0,85; 236,11] 0,065	0,02 [0,01; 0,03] <0,001 *
Abnormal hepatic enzymes					
Interaction test:	p=0,597				
Gender = Male	75 (17,2)	11 (4,9)	4,02 [2,09; 7,73] <0,001 *	3,50 [1,90; 6,44] <0,001 *	0,12 [0,08; 0,17] <0,001 *
Gender = Female	60 (9,0)	10 (3,1)	3,11 [1,57; 6,16] 0,001 *	2,92 [1,51; 5,63] 0,001 *	0,06 [0,03; 0,09] <0,001 *
Malignancies					
Interaction test:	p=0,420				
Gender = Male	7 (1,6)	7 (3,1)	0,50 [0,17; 1,46] 0,198	0,51 [0,18; 1,44] 0,206	-0,02 [-0,04; 0,01] 0,244
Gender = Female	13 (2,0)	7 (2,2)	0,90 [0,36; 2,28] 0,827	0,90 [0,36; 2,24] 0,827	-0,00 [-0,02; 0,02] 0,830
Hypertension					
Interaction test:	p=0,138				
Gender = Male	51 (11,7)	25 (11,2)	1,05 [0,63; 1,75] 0,845	1,05 [0,67; 1,64] 0,846	0,01 [-0,05; 0,06] 0,844
Gender = Female	86 (13,0)	25 (7,7)	1,77 [1,11; 2,83] 0,015 *	1,67 [1,09; 2,56] 0,018 *	0,05 [0,01; 0,09] 0,008 *
Seizures					
Interaction test:	N.E.				
Gender = Male	4 (0,9)	0 (0,0)	4,66 [0,25; 86,97] 0,151	4,62 [0,25; 85,50] 0,304	0,01 [0,00; 0,02] 0,045 *
Gender = Female	15 (2,3)	2 (0,6)	3,71 [0,84; 16,32] 0,063	3,65 [0,84; 15,86] 0,084	0,02 [0,00; 0,03] 0,023 *

	Treatment groups		Comparison		
	BAF312 (N=1099)	**Placebo (N=546)**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Thromboembolic events					
Interaction test:	p=0,409				
Gender = Male	13 (3,0)	8 (3,6)	0,83 [0,34; 2,03] 0,679	0,83 [0,35; 1,98] 0,679	-0,01 [-0,04; 0,02] 0,688
Gender = Female	20 (3,0)	7 (2,2)	1,40 [0,59; 3,35] 0,445	1,39 [0,59; 3,25] 0,448	0,01 [-0,01; 0,03] 0,420
Respiratory disorders					
Interaction test:	p=0,904				
Gender = Male	42 (9,7)	27 (12,1)	0,78 [0,46; 1,30] 0,331	0,80 [0,51; 1,26] 0,330	-0,02 [-0,08; 0,03] 0,346
Gender = Female	75 (11,3)	44 (13,6)	0,81 [0,54; 1,20] 0,292	0,83 [0,59; 1,17] 0,291	-0,02 [-0,07; 0,02] 0,305
Peripheral edema/swelling					
Interaction test:	p=0,006 *				
Gender = Male	19 (4,4)	11 (4,9)	0,88 [0,41; 1,88] 0,742	0,89 [0,43; 1,83] 0,742	-0,01 [-0,04; 0,03] 0,747
Gender = Female	55 (8,3)	7 (2,2)	4,08 [1,84; 9,06] <0,001 *	3,82 [1,76; 8,30] 0,001 *	0,06 [0,03; 0,09] <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 + gender + treatment * gender

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

Analysis population: A2304 SAF total population

	Treatment groups		Comparison		
	BAF312 (N=1099)	**Placebo (N=546)**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
N'	1099	546			
N' Gender = Male	435	223			
N' Gender = Female	664	323			
Asthma/bronchospasm					
Interaction test:	p=0,773				
Gender = Male	3 (0,7)	1 (0,4)	1,54 [0,16; 14,91] 0,706	1,54 [0,16; 14,70] 0,709	0,00 [-0,01; 0,01] 0,687
Gender = Female	5 (0,8)	1 (0,3)	2,44 [0,28; 21,00] 0,400	2,43 [0,29; 20,73] 0,416	0,00 [-0,00; 0,01] 0,331
Pregnancy and neonatal topics					
Interaction test:	N.E.				
Gender = Male	3 (0,7)	0 (0,0)	3,62 [0,19; 70,34] 0,214	3,60 [0,19; 69,32] 0,397	0,01 [-0,00; 0,01] 0,082
Gender = Female	3 (0,5)	0 (0,0)	3,42 [0,18; 66,47] 0,226	3,41 [0,18; 65,83] 0,417	0,00 [-0,00; 0,01] 0,083
Bradyarrhythmias and bradycardia					
Interaction test:	p=0,031 *				
Gender = Male	57 (13,1)	11 (4,9)	2,91 [1,49; 5,66] 0,001 *	2,66 [1,42; 4,96] 0,002 *	0,08 [0,04; 0,12] <0,001 *
Gender = Female	46 (6,9)	20 (6,2)	1,13 [0,66; 1,94] 0,664	1,12 [0,67; 1,86] 0,665	0,01 [-0,03; 0,04] 0,658

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 total population

11.4 Subgroup: Previous MS DMT

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

	Treatment groups		Comparison		
	BAF312 (N=1099)	**Placebo (N=546)**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
N'	1099	546			
N' Previous MS DMT = No	242	114			
N' Previous MS DMT = Yes	857	432			
Any AE					
Interaction test:	p=0,144				
Previous MS DMT = No	210 (86,8)	82 (71,9)	2,56 [1,47; 4,45] 0,001 *	1,21 [1,06; 1,37] 0,003 *	0,15 [0,06; 0,24] 0,002 *
Previous MS DMT = Yes	765 (89,3)	363 (84,0)	1,58 [1,13; 2,21] 0,007 *	1,06 [1,01; 1,11] 0,012 *	0,05 [0,01; 0,09] 0,011 *
Any AE, disease specific events excluded[1]					
Interaction test:	p=0,036 *				
Previous MS DMT = No	205 (84,7)	78 (68,4)	2,56 [1,51; 4,33] <0,001 *	1,24 [1,08; 1,42] 0,002 *	0,16 [0,07; 0,26] 0,001 *
Previous MS DMT = Yes	713 (83,2)	340 (78,7)	1,34 [1,00; 1,79] 0,049 *	1,06 [1,00; 1,12] 0,059	0,04 [-0,00; 0,09] 0,056
Any SAE					
Interaction test:	p=0,986				
Previous MS DMT = No	45 (18,6)	17 (14,9)	1,30 [0,71; 2,40] 0,393	1,25 [0,75; 2,08] 0,398	0,04 [-0,04; 0,12] 0,377
Previous MS DMT = Yes	141 (16,5)	57 (13,2)	1,30 [0,93; 1,81] 0,126	1,25 [0,94; 1,66] 0,129	0,03 [-0,01; 0,07] 0,114
Any SAE, disease specific events excluded[1]					
Interaction test:	p=0,952				
Previous MS DMT = No	38 (15,7)	13 (11,4)	1,45 [0,74; 2,84] 0,280	1,38 [0,76; 2,48] 0,287	0,04 [-0,03; 0,12] 0,256
Previous MS DMT = Yes	108 (12,6)	40 (9,3)	1,41 [0,96; 2,07] 0,076	1,36 [0,97; 1,92] 0,079	0,03 [-0,00; 0,07] 0,063

	Treatment groups		Comparison		
	BAF312 (N=1099)	**Placebo (N=546)**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Any severe AE[2]					
Interaction test:	p=0,234				
Previous MS DMT = No	24 (9,9)	14 (12,3)	0,79 [0,39; 1,58] 0,500	0,81 [0,43; 1,50] 0,500	-0,02 [-0,09; 0,05] 0,514
Previous MS DMT = Yes	115 (13,4)	47 (10,9)	1,27 [0,88; 1,82] 0,194	1,23 [0,90; 1,70] 0,197	0,03 [-0,01; 0,06] 0,181
Any severe AE[2], disease specific events excluded[1]					
Interaction test:	p=0,077				
Previous MS DMT = No	18 (7,4)	12 (10,5)	0,68 [0,32; 1,47] 0,328	0,71 [0,35; 1,42] 0,328	-0,03 [-0,10; 0,03] 0,354
Previous MS DMT = Yes	92 (10,7)	32 (7,4)	1,50 [0,99; 2,29] 0,056	1,45 [0,99; 2,13] 0,059	0,03 [0,00; 0,07] 0,043 *
Any AE leading to study discontinuation					
Interaction test:	p=0,612				
Previous MS DMT = No	12 (5,0)	5 (4,4)	1,14 [0,39; 3,31] 0,813	1,13 [0,41; 3,13] 0,813	0,01 [-0,04; 0,05] 0,809
Previous MS DMT = Yes	34 (4,0)	11 (2,5)	1,58 [0,79; 3,15] 0,190	1,56 [0,80; 3,04] 0,195	0,01 [-0,01; 0,03] 0,159

	Treatment groups		Comparison		
	BAF312 (N=1099)	**Placebo (N=546)**	**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=0,514				
Previous MS DMT = No	20 (8,3)	8 (7,0)	1,19 [0,51; 2,80] 0,683	1,18 [0,53; 2,59] 0,685	0,01 [-0,05; 0,07] 0,675
Previous MS DMT = Yes	64 (7,5)	20 (4,6)	1,66 [0,99; 2,79] 0,051	1,61 [0,99; 2,63] 0,055	0,03 [0,00; 0,05] 0,036 *

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 + 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 total population

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

	Treatment groups		Comparison		
	BAF312 (N=1099)	**Placebo (N=546)**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
N'	1099	546			
N' Previous MS DMT = No	242	114			
N' Previous MS DMT = Yes	857	432			
BLOOD AND LYMPHATIC SYSTEM DISORDERS					
Interaction test:	N.E.				
Previous MS DMT = No	8 (3,3)	0 (0,0)	8,30 [0,47; 145,07] 0,050 *	8,05 [0,47; 138,19] 0,151	0,03 [0,01; 0,06] 0,004 *
Previous MS DMT = Yes	38 (4,4)	10 (2,3)	1,96 [0,97; 3,97] 0,058	1,92 [0,96; 3,81] 0,064	0,02 [0,00; 0,04] 0,036 *
EAR AND LABYRINTH DISORDERS					
VERTIGO					
Interaction test:	p=0,195				
Previous MS DMT = No	8 (3,3)	4 (3,5)	0,94 [0,28; 3,19] 0,921	0,94 [0,29; 3,06] 0,921	-0,00 [-0,04; 0,04] 0,922
Previous MS DMT = Yes	17 (2,0)	22 (5,1)	0,38 [0,20; 0,72] 0,002 *	0,39 [0,21; 0,73] 0,003 *	-0,03 [-0,05; -0,01] 0,007 *
EYE DISORDERS					
MACULAR OEDEMA					
Interaction test:	N.E.				
Previous MS DMT = No	4 (1,7)	0 (0,0)	4,32 [0,23; 80,94] 0,167	4,26 [0,23; 78,45] 0,330	0,02 [0,00; 0,03] 0,044 *
Previous MS DMT = Yes	14 (1,6)	1 (0,2)	7,16 [0,94; 54,61] 0,027 *	7,06 [0,93; 53,49] 0,059	0,01 [0,00; 0,02] 0,004 *
GASTROINTESTINAL DISORDERS					
NAUSEA					
Interaction test:	p=0,733				
Previous MS DMT = No	15 (6,2)	3 (2,6)	2,44 [0,69; 8,62] 0,152	2,36 [0,70; 7,97] 0,169	0,04 [-0,01; 0,08] 0,098
Previous MS DMT = Yes	59 (6,9)	16 (3,7)	1,92 [1,09; 3,38] 0,021 *	1,86 [1,08; 3,19] 0,024 *	0,03 [0,01; 0,06] 0,011 *

	Treatment groups		Comparison		
	BAF312 (N=1099)	**Placebo (N=546)**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
GENERAL DISORDERS AND ADMINISTRATION SITE CONDITIONS					
GAIT DISTURBANCE					
Interaction test:	p=0,799				
Previous MS DMT = No	5 (2,1)	5 (4,4)	0,46 [0,13; 1,62] 0,216	0,47 [0,14; 1,59] 0,226	-0,02 [-0,06; 0,02] 0,275
Previous MS DMT = Yes	19 (2,2)	17 (3,9)	0,55 [0,28; 1,08] 0,077	0,56 [0,30; 1,07] 0,081	-0,02 [-0,04; 0,00] 0,106
OEDEMA PERIPHERAL					
Interaction test:	p=0,594				
Previous MS DMT = No	7 (2,9)	1 (0,9)	3,37 [0,41; 27,69] 0,231	3,30 [0,41; 26,49] 0,262	0,02 [-0,01; 0,05] 0,146
Previous MS DMT = Yes	43 (5,0)	12 (2,8)	1,85 [0,96; 3,54] 0,060	1,81 [0,96; 3,39] 0,066	0,02 [0,00; 0,04] 0,039 *
HEPATOBILIARY DISORDERS					
Interaction test:	N.E.				
Previous MS DMT = No	3 (1,2)	0 (0,0)	3,35 [0,17; 65,33] 0,233	3,31 [0,17; 63,60] 0,427	0,01 [-0,00; 0,03] 0,081
Previous MS DMT = Yes	24 (2,8)	4 (0,9)	3,08 [1,06; 8,94] 0,029 *	3,02 [1,06; 8,66] 0,039 *	0,02 [0,00; 0,03] 0,010 *
INFECTIONS AND INFESTATIONS					
HERPES ZOSTER					
Interaction test:	p=0,087				
Previous MS DMT = No	7 (2,9)	3 (2,6)	1,10 [0,28; 4,34] 0,889	1,10 [0,29; 4,17] 0,890	0,00 [-0,03; 0,04] 0,888
Previous MS DMT = Yes	18 (2,1)	1 (0,2)	9,25 [1,23; 69,50] 0,009 *	9,07 [1,22; 67,74] 0,032 *	0,02 [0,01; 0,03] 0,001 *
INVESTIGATIONS					
Interaction test:	p=0,389				
Previous MS DMT = No	69 (28,5)	24 (21,1)	1,50 [0,88; 2,54] 0,135	1,35 [0,90; 2,04] 0,145	0,07 [-0,02; 0,17] 0,120
Previous MS DMT = Yes	194 (22,6)	56 (13,0)	1,96 [1,42; 2,71] <0,001 *	1,75 [1,33; 2,30] <0,001 *	0,10 [0,05; 0,14] <0,001 *

	Treatment groups		Comparison		
	BAF312 (N=1099)	**Placebo (N=546)**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
ALANINE AMINOTRANSFERASE INCREASED					
Interaction test:	p=0,319				
Previous MS DMT = No	20 (8,3)	1 (0,9)	10,18 [1,35; 76,83] 0,006 *	9,42 [1,28; 69,34] 0,028 *	0,07 [0,04; 0,11] <0,001 *
Previous MS DMT = Yes	45 (5,3)	7 (1,6)	3,36 [1,50; 7,53] 0,002 *	3,24 [1,47; 7,13] 0,003 *	0,04 [0,02; 0,06] <0,001 *
GAMMA-GLUTAMYLTRANSFERASE INCREASED					
Interaction test:	p=0,366				
Previous MS DMT = No	8 (3,3)	2 (1,8)	1,91 [0,40; 9,16] 0,408	1,88 [0,41; 8,73] 0,418	0,02 [-0,02; 0,05] 0,357
Previous MS DMT = Yes	35 (4,1)	4 (0,9)	4,56 [1,61; 12,90] 0,002 *	4,41 [1,58; 12,33] 0,005 *	0,03 [0,02; 0,05] <0,001 *
HEPATIC ENZYME INCREASED					
Interaction test:	N.E.				
Previous MS DMT = No	4 (1,7)	0 (0,0)	4,32 [0,23; 80,94] 0,167	4,26 [0,23; 78,45] 0,330	0,02 [0,00; 0,03] 0,044 *
Previous MS DMT = Yes	12 (1,4)	1 (0,2)	6,12 [0,79; 47,23] 0,047 *	6,05 [0,79; 46,37] 0,083	0,01 [0,00; 0,02] 0,012 *
NERVOUS SYSTEM DISORDERS					
Interaction test:	p=0,455				
Previous MS DMT = No	68 (28,1)	30 (26,3)	1,09 [0,66; 1,81] 0,725	1,07 [0,74; 1,54] 0,726	0,02 [-0,08; 0,12] 0,723
Previous MS DMT = Yes	348 (40,6)	145 (33,6)	1,35 [1,06; 1,72] 0,014 *	1,21 [1,04; 1,41] 0,016 *	0,07 [0,02; 0,13] 0,013 *
PARAESTHESIA					
Interaction test:	p=0,290				
Previous MS DMT = No	3 (1,2)	6 (5,3)	0,23 [0,06; 0,92] 0,024 *	0,24 [0,06; 0,92] 0,038 *	-0,04 [-0,08; 0,00] 0,069
Previous MS DMT = Yes	15 (1,8)	14 (3,2)	0,53 [0,25; 1,11] 0,089	0,54 [0,26; 1,11] 0,093	-0,01 [-0,03; 0,00] 0,122

	Treatment groups		Comparison		
	BAF312 (N=1099)	**Placebo (N=546)**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
VASCULAR DISORDERS					
Interaction test:	p=0,838				
Previous MS DMT = No	33 (13,6)	11 (9,6)	1,48 [0,72; 3,04] 0,286	1,41 [0,74; 2,69] 0,293	0,04 [-0,03; 0,11] 0,260
Previous MS DMT = Yes	127 (14,8)	49 (11,3)	1,36 [0,96; 1,93] 0,086	1,31 [0,96; 1,78] 0,090	0,03 [-0,00; 0,07] 0,075

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

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 total population

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

	Treatment groups		Comparison		
	BAF312 (N=1099)	**Placebo (N=546)**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
N'	1099	546			
N' Previous MS DMT = No	242	114			
N' Previous MS DMT = Yes	857	432			
INVESTIGATIONS					
Interaction test:	p=0,686				
Previous MS DMT = No	5 (2,1)	1 (0,9)	2,38 [0,28; 20,64] 0,416	2,36 [0,28; 19,93] 0,432	0,01 [-0,01; 0,04] 0,347
Previous MS DMT = Yes	16 (1,9)	2 (0,5)	4,09 [0,94; 17,87] 0,043 *	4,03 [0,93; 17,46] 0,062	0,01 [0,00; 0,03] 0,013 *

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 total population

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=1099)	**Placebo (N=546)**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
N'	1099	546			
N' Previous MS DMT = No	242	114			
N' Previous MS DMT = Yes	857	432			
Infections and infestations					
Interaction test:	p=0,502				
Previous MS DMT = No	108 (44,6)	47 (41,2)	1,15 [0,73; 1,80] 0,546	1,08 [0,83; 1,40] 0,551	0,03 [-0,08; 0,14] 0,544
Previous MS DMT = Yes	431 (50,3)	221 (51,2)	0,97 [0,77; 1,22] 0,769	0,98 [0,88; 1,10] 0,769	-0,01 [-0,07; 0,05] 0,769
Herpes simplex virus infections					
Interaction test:	p=0,014 *				
Previous MS DMT = No	2 (0,8)	5 (4,4)	0,18 [0,03; 0,95] 0,024 *	0,19 [0,04; 0,96] 0,044 *	-0,04 [-0,07; 0,00] 0,076
Previous MS DMT = Yes	23 (2,7)	6 (1,4)	1,96 [0,79; 4,85] 0,139	1,93 [0,79; 4,71] 0,147	0,01 [-0,00; 0,03] 0,101
Varicella-zoster virus infections					
Interaction test:	p=0,059				
Previous MS DMT = No	8 (3,3)	3 (2,6)	1,26 [0,33; 4,86] 0,732	1,26 [0,34; 4,65] 0,733	0,01 [-0,03; 0,04] 0,721
Previous MS DMT = Yes	25 (2,9)	1 (0,2)	12,95 [1,75; 95,90] 0,001 *	12,60 [1,71; 92,69] 0,013 *	0,03 [0,01; 0,04] <0,001 *
Lymphopenia					
Interaction test:	N.E.				
Previous MS DMT = No	3 (1,2)	0 (0,0)	3,35 [0,17; 65,33] 0,233	3,31 [0,17; 63,60] 0,427	0,01 [-0,00; 0,03] 0,081
Previous MS DMT = Yes	11 (1,3)	0 (0,0)	11,75 [0,69; 199,89] 0,018 *	11,61 [0,69; 196,51] 0,089	0,01 [0,01; 0,02] 0,001 *

	Treatment groups		Comparison		
	BAF312 (N=1099)	**Placebo (N=546)**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Macular edema					
Interaction test:	N.E.				
Previous MS DMT = No	4 (1,7)	0 (0,0)	4,32 [0,23; 80,94] 0,167	4,26 [0,23; 78,45] 0,330	0,02 [0,00; 0,03] 0,044 *
Previous MS DMT = Yes	16 (1,9)	1 (0,2)	8,20 [1,08; 62,04] 0,015 *	8,07 [1,07; 60,62] 0,043 *	0,02 [0,01; 0,03] 0,002 *
Abnormal hepatic enzymes					
Interaction test:	p=0,417				
Previous MS DMT = No	35 (14,5)	7 (6,1)	2,58 [1,11; 6,01] 0,023 *	2,36 [1,08; 5,14] 0,031 *	0,08 [0,02; 0,15] 0,009 *
Previous MS DMT = Yes	100 (11,7)	14 (3,2)	3,94 [2,23; 6,99] <0,001 *	3,60 [2,08; 6,22] <0,001 *	0,08 [0,06; 0,11] <0,001 *
Malignancies					
Interaction test:	p=0,856				
Previous MS DMT = No	4 (1,7)	3 (2,6)	0,62 [0,14; 2,83] 0,535	0,63 [0,14; 2,76] 0,538	-0,01 [-0,04; 0,02] 0,567
Previous MS DMT = Yes	16 (1,9)	11 (2,5)	0,73 [0,33; 1,58] 0,421	0,73 [0,34; 1,57] 0,423	-0,01 [-0,02; 0,01] 0,444
Hypertension					
Interaction test:	p=0,327				
Previous MS DMT = No	26 (10,7)	12 (10,5)	1,02 [0,50; 2,11] 0,951	1,02 [0,53; 1,95] 0,951	0,00 [-0,07; 0,07] 0,950
Previous MS DMT = Yes	111 (13,0)	38 (8,8)	1,54 [1,05; 2,27] 0,028 *	1,47 [1,04; 2,09] 0,030 *	0,04 [0,01; 0,08] 0,020 *
Seizures					
Interaction test:	N.E.				
Previous MS DMT = No	0 (0,0)	1 (0,9)	0,16 [0,01; 3,86] 0,145	0,16 [0,01; 3,84] 0,257	-0,01 [-0,03; 0,01] 0,315
Previous MS DMT = Yes	19 (2,2)	1 (0,2)	9,77 [1,30; 73,24] 0,006 *	9,58 [1,29; 71,31] 0,027 *	0,02 [0,01; 0,03] <0,001 *

	Treatment groups		Comparison		
	BAF312 (N=1099)	**Placebo (N=546)**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Thromboembolic events					
Interaction test:	p=0,434				
Previous MS DMT = No	8 (3,3)	2 (1,8)	1,91 [0,40; 9,16] 0,408	1,88 [0,41; 8,73] 0,418	0,02 [-0,02; 0,05] 0,357
Previous MS DMT = Yes	25 (2,9)	13 (3,0)	0,97 [0,49; 1,91] 0,926	0,97 [0,50; 1,88] 0,926	-0,00 [-0,02; 0,02] 0,927
Respiratory disorders					
Interaction test:	p=0,019 *				
Previous MS DMT = No	17 (7,0)	19 (16,7)	0,38 [0,19; 0,76] 0,005 *	0,42 [0,23; 0,78] 0,006 *	-0,10 [-0,17; -0,02] 0,012 *
Previous MS DMT = Yes	100 (11,7)	52 (12,0)	0,97 [0,68; 1,38] 0,846	0,97 [0,71; 1,33] 0,846	-0,00 [-0,04; 0,03] 0,847
Peripheral edema/swelling					
Interaction test:	p=0,490				
Previous MS DMT = No	14 (5,8)	2 (1,8)	3,44 [0,77; 15,39] 0,087	3,30 [0,76; 14,27] 0,110	0,04 [0,00; 0,08] 0,038 *
Previous MS DMT = Yes	60 (7,0)	16 (3,7)	1,96 [1,11; 3,44] 0,018 *	1,89 [1,10; 3,24] 0,021 *	0,03 [0,01; 0,06] 0,009 *

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 total population

	Treatment groups		Comparison		
	BAF312 (N=1099)	**Placebo (N=546)**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
N'	1099	546			
N' Previous MS DMT = No	242	114			
N' Previous MS DMT = Yes	857	432			
Asthma/bronchospasm					
Interaction test:	N.E.				
Previous MS DMT = No	0 (0,0)	1 (0,9)	0,16 [0,01; 3,86] 0,145	0,16 [0,01; 3,84] 0,257	-0,01 [-0,03; 0,01] 0,315
Previous MS DMT = Yes	8 (0,9)	1 (0,2)	4,06 [0,51; 32,58] 0,153	4,03 [0,51; 32,14] 0,188	0,01 [-0,00; 0,01] 0,081
Pregnancy and neonatal topics					
Interaction test:	N.E.				
Previous MS DMT = No	2 (0,8)	0 (0,0)	2,38 [0,11; 49,99] 0,330	2,37 [0,11; 48,89] 0,577	0,01 [-0,00; 0,02] 0,156
Previous MS DMT = Yes	4 (0,5)	0 (0,0)	4,56 [0,24; 84,90] 0,155	4,54 [0,25; 84,17] 0,310	0,00 [0,00; 0,01] 0,045 *
Bradyarrhythmias and bradycardia					
Interaction test:	p=0,561				
Previous MS DMT = No	33 (13,6)	8 (7,0)	2,09 [0,93; 4,69] 0,068	1,94 [0,93; 4,07] 0,078	0,07 [0,00; 0,13] 0,042 *
Previous MS DMT = Yes	70 (8,2)	23 (5,3)	1,58 [0,97; 2,57] 0,062	1,53 [0,97; 2,42] 0,066	0,03 [0,00; 0,06] 0,047 *

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 total population

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=1099)	Placebo (N=546)	OR [95% CI] p-value	RR [95% CI] p-value	RD [95% CI] p-value
N'	1099	546			
N' Previous IFN-beta-1b Treatment = No	755	392			
N' Previous IFN-beta-1b Treatment = Yes	344	154			
Any AE					
Interaction test:	p=0,804				
Previous IFN-beta-1b Treatment = No	671 (88,9)	319 (81,4)	1,83 [1,30; 2,57] <0,001 *	1,09 [1,04; 1,15] 0,001 *	0,07 [0,03; 0,12] 0,001 *
Previous IFN-beta-1b Treatment = Yes	304 (88,4)	126 (81,8)	1,69 [1,00; 2,86] 0,049 *	1,08 [0,99; 1,17] 0,071	0,07 [-0,00; 0,14] 0,065
Any AE, disease specific events excluded[1]					
Interaction test:	p=0,604				
Previous IFN-beta-1b Treatment = No	632 (83,7)	298 (76,0)	1,62 [1,20; 2,19] 0,002 *	1,10 [1,03; 1,17] 0,003 *	0,08 [0,03; 0,13] 0,002 *
Previous IFN-beta-1b Treatment = Yes	286 (83,1)	120 (77,9)	1,40 [0,87; 2,24] 0,166	1,07 [0,97; 1,18] 0,189	0,05 [-0,02; 0,13] 0,181
Any SAE					
Interaction test:	p=0,640				
Previous IFN-beta-1b Treatment = No	135 (17,9)	54 (13,8)	1,36 [0,97; 1,92] 0,075	1,30 [0,97; 1,74] 0,079	0,04 [-0,00; 0,08] 0,066
Previous IFN-beta-1b Treatment = Yes	51 (14,8)	20 (13,0)	1,17 [0,67; 2,03] 0,588	1,14 [0,71; 1,85] 0,589	0,02 [-0,05; 0,08] 0,579
Any SAE, disease specific events excluded[1]					
Interaction test:	p=0,446				
Previous IFN-beta-1b Treatment = No	105 (13,9)	37 (9,4)	1,55 [1,04; 2,30] 0,029 *	1,47 [1,03; 2,10] 0,032 *	0,04 [0,01; 0,08] 0,021 *
Previous IFN-beta-1b Treatment = Yes	41 (11,9)	16 (10,4)	1,17 [0,63; 2,15] 0,620	1,15 [0,66; 1,98] 0,622	0,02 [-0,04; 0,07] 0,612

	Treatment groups		Comparison		
	BAF312 (N=1099)	**Placebo (N=546)**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Any severe AE[2]					
Interaction test:	p=0,079				
Previous IFN-beta-1b Treatment = No	94 (12,5)	50 (12,8)	0,97 [0,67; 1,40] 0,883	0,98 [0,71; 1,35] 0,882	-0,00 [-0,04; 0,04] 0,883
Previous IFN-beta-1b Treatment = Yes	45 (13,1)	11 (7,1)	1,96 [0,98; 3,90] 0,053	1,83 [0,97; 3,44] 0,060	0,06 [0,01; 0,11] 0,031 *
Any severe AE[2], disease specific events excluded[1]					
Interaction test:	p=0,089				
Previous IFN-beta-1b Treatment = No	75 (9,9)	37 (9,4)	1,06 [0,70; 1,60] 0,789	1,05 [0,72; 1,53] 0,789	0,00 [-0,03; 0,04] 0,787
Previous IFN-beta-1b Treatment = Yes	35 (10,2)	7 (4,5)	2,38 [1,03; 5,48] 0,037 *	2,24 [1,02; 4,93] 0,045 *	0,06 [0,01; 0,10] 0,016 *
Any AE leading to study discontinuation					
Interaction test:	p=0,228				
Previous IFN-beta-1b Treatment = No	37 (4,9)	11 (2,8)	1,78 [0,90; 3,54] 0,093	1,75 [0,90; 3,39] 0,099	0,02 [-0,00; 0,04] 0,068
Previous IFN-beta-1b Treatment = Yes	9 (2,6)	5 (3,2)	0,80 [0,26; 2,43] 0,694	0,81 [0,27; 2,36] 0,694	-0,01 [-0,04; 0,03] 0,705

	Treatment groups		Comparison		
	BAF312 (N=1099)	**Placebo (N=546)**	**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=0,560				
Previous IFN-beta-1b Treatment = No	65 (8,6)	21 (5,4)	1,66 [1,00; 2,77] 0,047 *	1,61 [1,00; 2,59] 0,051	0,03 [0,00; 0,06] 0,033 *
Previous IFN-beta-1b Treatment = Yes	19 (5,5)	7 (4,5)	1,23 [0,51; 2,98] 0,650	1,22 [0,52; 2,83] 0,652	0,01 [-0,03; 0,05] 0,639

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 + 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 total population

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

	Treatment groups		Comparison		
	BAF312 (N=1099)	**Placebo (N=546)**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
N'	1099	546			
N' Previous IFN-beta-1b Treatment = No	755	392			
N' Previous IFN-beta-1b Treatment = Yes	344	154			
BLOOD AND LYMPHATIC SYSTEM DISORDERS					
Interaction test:	p=0,346				
Previous IFN-beta-1b Treatment = No	33 (4,4)	6 (1,5)	2,94 [1,22; 7,08] 0,012 *	2,86 [1,21; 6,76] 0,017 *	0,03 [0,01; 0,05] 0,003 *
Previous IFN-beta-1b Treatment = Yes	13 (3,8)	4 (2,6)	1,47 [0,47; 4,59] 0,502	1,45 [0,48; 4,39] 0,506	0,01 [-0,02; 0,04] 0,472
EAR AND LABYRINTH DISORDERS					
VERTIGO					
Interaction test:	p=0,643				
Previous IFN-beta-1b Treatment = No	17 (2,3)	17 (4,3)	0,51 [0,26; 1,01] 0,048 *	0,52 [0,27; 1,01] 0,052	-0,02 [-0,04; 0,00] 0,073
Previous IFN-beta-1b Treatment = Yes	8 (2,3)	9 (5,8)	0,38 [0,15; 1,01] 0,046 *	0,40 [0,16; 1,01] 0,053	-0,04 [-0,08; 0,01] 0,087
EYE DISORDERS					
MACULAR OEDEMA					
Interaction test:	N.E.				
Previous IFN-beta-1b Treatment = No	11 (1,5)	1 (0,3)	5,78 [0,74; 44,94] 0,058	5,71 [0,74; 44,08] 0,095	0,01 [0,00; 0,02] 0,017 *
Previous IFN-beta-1b Treatment = Yes	7 (2,0)	0 (0,0)	6,87 [0,39; 120,99] 0,075	6,74 [0,39; 117,26] 0,190	0,02 [0,01; 0,04] 0,008 *
GASTROINTESTINAL DISORDERS					
NAUSEA					
Interaction test:	p=0,557				
Previous IFN-beta-1b Treatment = No	57 (7,5)	14 (3,6)	2,20 [1,21; 4,01] 0,008 *	2,11 [1,19; 3,74] 0,010 *	0,04 [0,01; 0,07] 0,003 *
Previous IFN-beta-1b Treatment = Yes	17 (4,9)	5 (3,2)	1,55 [0,56; 4,28] 0,395	1,52 [0,57; 4,05] 0,400	0,02 [-0,02; 0,05] 0,358

	Treatment groups		Comparison		
	BAF312 (N=1099)	**Placebo (N=546)**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
GENERAL DISORDERS AND ADMINISTRATION SITE CONDITIONS					
GAIT DISTURBANCE					
Interaction test:	p=0,284				
Previous IFN-beta-1b Treatment = No	19 (2,5)	15 (3,8)	0,65 [0,33; 1,29] 0,215	0,66 [0,34; 1,28] 0,217	-0,01 [-0,04; 0,01] 0,244
Previous IFN-beta-1b Treatment = Yes	5 (1,5)	7 (4,5)	0,31 [0,10; 0,99] 0,038 *	0,32 [0,10; 0,99] 0,048 *	-0,03 [-0,07; 0,00] 0,086
OEDEMA PERIPHERAL					
Interaction test:	p=0,594				
Previous IFN-beta-1b Treatment = No	29 (3,8)	9 (2,3)	1,70 [0,80; 3,63] 0,166	1,67 [0,80; 3,50] 0,172	0,02 [-0,00; 0,04] 0,134
Previous IFN-beta-1b Treatment = Yes	21 (6,1)	4 (2,6)	2,44 [0,82; 7,23] 0,098	2,35 [0,82; 6,73] 0,111	0,04 [-0,00; 0,07] 0,054
HEPATOBILIARY DISORDERS					
Interaction test:	p=0,631				
Previous IFN-beta-1b Treatment = No	16 (2,1)	3 (0,8)	2,81 [0,81; 9,69] 0,088	2,77 [0,81; 9,45] 0,104	0,01 [0,00; 0,03] 0,048 *
Previous IFN-beta-1b Treatment = Yes	11 (3,2)	1 (0,6)	5,05 [0,65; 39,50] 0,087	4,92 [0,64; 37,81] 0,125	0,03 [0,00; 0,05] 0,026 *
INFECTIONS AND INFESTATIONS					
HERPES ZOSTER					
Interaction test:	N.E.				
Previous IFN-beta-1b Treatment = No	18 (2,4)	4 (1,0)	2,37 [0,80; 7,05] 0,110	2,34 [0,80; 6,86] 0,122	0,01 [-0,00; 0,03] 0,070
Previous IFN-beta-1b Treatment = Yes	7 (2,0)	0 (0,0)	6,87 [0,39; 120,99] 0,075	6,74 [0,39; 117,26] 0,190	0,02 [0,01; 0,04] 0,008 *
INVESTIGATIONS					
Interaction test:	p=0,613				
Previous IFN-beta-1b Treatment = No	182 (24,1)	60 (15,3)	1,76 [1,27; 2,42] 0,001 *	1,57 [1,21; 2,05] 0,001 *	0,09 [0,04; 0,13] <0,001 *
Previous IFN-beta-1b Treatment = Yes	81 (23,5)	20 (13,0)	2,06 [1,21; 3,51] 0,007 *	1,81 [1,15; 2,85] 0,010 *	0,11 [0,04; 0,18] 0,003 *

	Treatment groups		Comparison		
	BAF312 (N=1099)	**Placebo (N=546)**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
ALANINE AMINOTRANSFERASE INCREASED					
Interaction test:	p=0,835				
Previous IFN-beta-1b Treatment = No	41 (5,4)	5 (1,3)	4,44 [1,74; 11,34] 0,001 *	4,26 [1,70; 10,69] 0,002 *	0,04 [0,02; 0,06] <0,001 *
Previous IFN-beta-1b Treatment = Yes	24 (7,0)	3 (1,9)	3,78 [1,12; 12,73] 0,022 *	3,58 [1,09; 11,71] 0,035 *	0,05 [0,02; 0,08] 0,004 *
GAMMA-GLUTAMYLTRANSFERASE INCREASED					
Interaction test:	p=0,936				
Previous IFN-beta-1b Treatment = No	28 (3,7)	4 (1,0)	3,74 [1,30; 10,73] 0,009 *	3,63 [1,28; 10,29] 0,015 *	0,03 [0,01; 0,04] 0,002 *
Previous IFN-beta-1b Treatment = Yes	15 (4,4)	2 (1,3)	3,47 [0,78; 15,34] 0,082	3,36 [0,78; 14,50] 0,105	0,03 [0,00; 0,06] 0,032 *
HEPATIC ENZYME INCREASED					
Interaction test:	N.E.				
Previous IFN-beta-1b Treatment = No	12 (1,6)	1 (0,3)	6,31 [0,82; 48,74] 0,043 *	6,23 [0,81; 47,74] 0,078	0,01 [0,00; 0,02] 0,011 *
Previous IFN-beta-1b Treatment = Yes	4 (1,2)	0 (0,0)	4,08 [0,22; 76,32] 0,179	4,04 [0,22; 74,64] 0,348	0,01 [0,00; 0,02] 0,044 *
NERVOUS SYSTEM DISORDERS					
Interaction test:	p=0,663				
Previous IFN-beta-1b Treatment = No	283 (37,5)	127 (32,4)	1,25 [0,97; 1,62] 0,088	1,16 [0,98; 1,37] 0,093	0,05 [-0,01; 0,11] 0,085
Previous IFN-beta-1b Treatment = Yes	133 (38,7)	48 (31,2)	1,39 [0,93; 2,09] 0,108	1,24 [0,95; 1,62] 0,118	0,07 [-0,01; 0,16] 0,101
PARAESTHESIA					
Interaction test:	p=0,456				
Previous IFN-beta-1b Treatment = No	14 (1,9)	14 (3,6)	0,51 [0,24; 1,08] 0,074	0,52 [0,25; 1,08] 0,079	-0,02 [-0,04; 0,00] 0,105
Previous IFN-beta-1b Treatment = Yes	4 (1,2)	6 (3,9)	0,29 [0,08; 1,04] 0,044 *	0,30 [0,09; 1,04] 0,058	-0,03 [-0,06; 0,01] 0,100

	Treatment groups		Comparison		
	BAF312 (N=1099)	**Placebo (N=546)**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
VASCULAR DISORDERS					
Interaction test:	p=0,544				
Previous IFN-beta-1b Treatment = No	106 (14,0)	44 (11,2)	1,29 [0,89; 1,88] 0,180	1,25 [0,90; 1,74] 0,183	0,03 [-0,01; 0,07] 0,167
Previous IFN-beta-1b Treatment = Yes	54 (15,7)	16 (10,4)	1,61 [0,89; 2,91] 0,115	1,51 [0,89; 2,55] 0,123	0,05 [-0,01; 0,11] 0,091

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

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 total population

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

	Treatment groups		Comparison		
	BAF312 (N=1099)	**Placebo (N=546)**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
N'	1099	546			
N' Previous IFN-beta-1b Treatment = No	755	392			
N' Previous IFN-beta-1b Treatment = Yes	344	154			
INVESTIGATIONS					
Interaction test:	p=0,180				
Previous IFN-beta-1b Treatment = No	15 (2,0)	1 (0,3)	7,93 [1,04; 60,22] 0,018 *	7,79 [1,03; 58,74] 0,046 *	0,02 [0,01; 0,03] 0,002 *
Previous IFN-beta-1b Treatment = Yes	6 (1,7)	2 (1,3)	1,35 [0,27; 6,76] 0,715	1,34 [0,27; 6,58] 0,716	0,00 [-0,02; 0,03] 0,699

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 total population

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=1099)	**Placebo (N=546)**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
N'	1099	546			
N' Previous IFN-beta-1b Treatment = No	755	392			
N' Previous IFN-beta-1b Treatment = Yes	344	154			
Infections and infestations					
Interaction test:	p=0,754				
Previous IFN-beta-1b Treatment = No	363 (48,1)	191 (48,7)	0,97 [0,76; 1,24] 0,836	0,99 [0,87; 1,12] 0,835	-0,01 [-0,07; 0,05] 0,836
Previous IFN-beta-1b Treatment = Yes	176 (51,2)	77 (50,0)	1,05 [0,72; 1,53] 0,810	1,02 [0,85; 1,24] 0,811	0,01 [-0,08; 0,11] 0,810
Herpes simplex virus infections					
Interaction test:	p=0,276				
Previous IFN-beta-1b Treatment = No	15 (2,0)	9 (2,3)	0,86 [0,37; 1,99] 0,729	0,87 [0,38; 1,96] 0,729	-0,00 [-0,02; 0,01] 0,734
Previous IFN-beta-1b Treatment = Yes	10 (2,9)	2 (1,3)	2,28 [0,49; 10,51] 0,279	2,24 [0,50; 10,09] 0,294	0,02 [-0,01; 0,04] 0,211
Varicella-zoster virus infections					
Interaction test:	N.E.				
Previous IFN-beta-1b Treatment = No	24 (3,2)	4 (1,0)	3,18 [1,10; 9,24] 0,025 *	3,12 [1,09; 8,92] 0,034 *	0,02 [0,01; 0,04] 0,008 *
Previous IFN-beta-1b Treatment = Yes	9 (2,6)	0 (0,0)	8,75 [0,51; 151,29] 0,043 *	8,54 [0,50; 145,74] 0,139	0,03 [0,01; 0,04] 0,002 *
Lymphopenia					
Interaction test:	N.E.				
Previous IFN-beta-1b Treatment = No	11 (1,5)	0 (0,0)	12,13 [0,71; 206,31] 0,016 *	11,96 [0,71; 202,36] 0,086	0,01 [0,01; 0,02] 0,001 *
Previous IFN-beta-1b Treatment = Yes	3 (0,9)	0 (0,0)	3,17 [0,16; 61,68] 0,245	3,14 [0,16; 60,52] 0,448	0,01 [-0,00; 0,02] 0,082

	Treatment groups		Comparison		
	BAF312 (N=1099)	**Placebo (N=546)**	**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	13 (1,7)	1 (0,3)	6,85 [0,89; 52,56] 0,032 *	6,75 [0,89; 51,41] 0,065	0,01 [0,00; 0,03] 0,006 *
Previous IFN-beta-1b Treatment = Yes	7 (2,0)	0 (0,0)	6,87 [0,39; 120,99] 0,075	6,74 [0,39; 117,26] 0,190	0,02 [0,01; 0,04] 0,008 *
Abnormal hepatic enzymes					
Interaction test:	p=0,758				
Previous IFN-beta-1b Treatment = No	88 (11,7)	15 (3,8)	3,32 [1,89; 5,82] <0,001 *	3,05 [1,79; 5,19] <0,001 *	0,08 [0,05; 0,11] <0,001 *
Previous IFN-beta-1b Treatment = Yes	47 (13,7)	6 (3,9)	3,90 [1,63; 9,34] 0,001 *	3,51 [1,53; 8,03] 0,003 *	0,10 [0,05; 0,15] <0,001 *
Malignancies					
Interaction test:	p=0,044 *				
Previous IFN-beta-1b Treatment = No	16 (2,1)	7 (1,8)	1,19 [0,49; 2,92] 0,702	1,19 [0,49; 2,86] 0,703	0,00 [-0,01; 0,02] 0,695
Previous IFN-beta-1b Treatment = Yes	4 (1,2)	7 (4,5)	0,25 [0,07; 0,86] 0,018 *	0,26 [0,08; 0,86] 0,028 *	-0,03 [-0,07; 0,00] 0,057
Hypertension					
Interaction test:	p=0,310				
Previous IFN-beta-1b Treatment = No	84 (11,1)	36 (9,2)	1,24 [0,82; 1,87] 0,308	1,21 [0,84; 1,76] 0,311	0,02 [-0,02; 0,06] 0,295
Previous IFN-beta-1b Treatment = Yes	53 (15,4)	14 (9,1)	1,82 [0,98; 3,39] 0,056	1,69 [0,97; 2,96] 0,064	0,06 [0,00; 0,12] 0,037 *
Seizures					
Interaction test:	N.E.				
Previous IFN-beta-1b Treatment = No	12 (1,6)	2 (0,5)	3,15 [0,70; 14,14] 0,114	3,12 [0,70; 13,85] 0,136	0,01 [-0,00; 0,02] 0,063
Previous IFN-beta-1b Treatment = Yes	7 (2,0)	0 (0,0)	6,87 [0,39; 120,99] 0,075	6,74 [0,39; 117,26] 0,190	0,02 [0,01; 0,04] 0,008 *

	Treatment groups		Comparison		
	BAF312 (N=1099)	**Placebo (N=546)**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Thromboembolic events					
Interaction test:	p=0,458				
Previous IFN-beta-1b Treatment = No	22 (2,9)	12 (3,1)	0,95 [0,47; 1,94] 0,889	0,95 [0,48; 1,90] 0,889	-0,00 [-0,02; 0,02] 0,890
Previous IFN-beta-1b Treatment = Yes	11 (3,2)	3 (1,9)	1,66 [0,46; 6,05] 0,436	1,64 [0,46; 5,80] 0,442	0,01 [-0,02; 0,04] 0,393
Respiratory disorders					
Interaction test:	p=0,055				
Previous IFN-beta-1b Treatment = No	85 (11,3)	45 (11,5)	0,98 [0,67; 1,44] 0,911	0,98 [0,70; 1,38] 0,911	-0,00 [-0,04; 0,04] 0,911
Previous IFN-beta-1b Treatment = Yes	32 (9,3)	26 (16,9)	0,50 [0,29; 0,88] 0,015 *	0,55 [0,34; 0,89] 0,015 *	-0,08 [-0,14; -0,01] 0,026 *
Peripheral edema/swelling					
Interaction test:	p=0,734				
Previous IFN-beta-1b Treatment = No	50 (6,6)	12 (3,1)	2,25 [1,18; 4,27] 0,011 *	2,16 [1,17; 4,01] 0,014 *	0,04 [0,01; 0,06] 0,005 *
Previous IFN-beta-1b Treatment = Yes	24 (7,0)	6 (3,9)	1,85 [0,74; 4,62] 0,182	1,79 [0,75; 4,29] 0,191	0,03 [-0,01; 0,07] 0,138

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 total population

	Treatment groups		Comparison		
	BAF312 (N=1099)	**Placebo (N=546)**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
N'	1099	546			
N' Previous IFN-beta-1b Treatment = No	755	392			
N' Previous IFN-beta-1b Treatment = Yes	344	154			
Asthma/bronchospasm					
Interaction test:	p=0,444				
Previous IFN-beta-1b Treatment = No	6 (0,8)	1 (0,3)	3,13 [0,38; 26,11] 0,266	3,12 [0,38; 25,78] 0,292	0,01 [-0,00; 0,01] 0,190
Previous IFN-beta-1b Treatment = Yes	2 (0,6)	1 (0,6)	0,89 [0,08; 9,94] 0,928	0,90 [0,08; 9,80] 0,928	-0,00 [-0,02; 0,01] 0,929
Pregnancy and neonatal topics					
Interaction test:	N.E.				
Previous IFN-beta-1b Treatment = No	5 (0,7)	0 (0,0)	5,75 [0,32; 104,31] 0,106	5,72 [0,32; 103,15] 0,237	0,01 [0,00; 0,01] 0,025 *
Previous IFN-beta-1b Treatment = Yes	1 (0,3)	0 (0,0)	1,35 [0,05; 33,31] 0,503	1,35 [0,06; 32,90] 0,855	0,00 [-0,00; 0,01] 0,317
Bradyarrhythmias and bradycardia					
Interaction test:	p=0,049 *				
Previous IFN-beta-1b Treatment = No	72 (9,5)	28 (7,1)	1,37 [0,87; 2,16] 0,173	1,34 [0,88; 2,03] 0,177	0,02 [-0,01; 0,06] 0,155
Previous IFN-beta-1b Treatment = Yes	31 (9,0)	3 (1,9)	4,99 [1,50; 16,57] 0,004 *	4,63 [1,44; 14,90] 0,010 *	0,07 [0,03; 0,11] <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 + 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 total population

11.6 Subgroup: Rapid Evolvement

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

	Treatment groups		Comparison		
	BAF312 (N=1099)	**Placebo (N=546)**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
N'	1099	546			
N' Rapid Evolvement = No	835	401			
N' Rapid Evolvement = Yes	264	145			
Any AE					
Interaction test:	p=0,682				
Rapid Evolvement = No	747 (89,5)	334 (83,3)	1,70 [1,21; 2,40] 0,002 *	1,07 [1,02; 1,13] 0,005 *	0,06 [0,02; 0,10] 0,004 *
Rapid Evolvement = Yes	228 (86,4)	111 (76,6)	1,94 [1,15; 3,27] 0,012 *	1,13 [1,02; 1,25] 0,021 *	0,10 [0,02; 0,18] 0,017 *
Any AE, disease specific events excluded[1]					
Interaction test:	p=0,537				
Rapid Evolvement = No	701 (84,0)	313 (78,1)	1,47 [1,09; 1,99] 0,011 *	1,08 [1,01; 1,14] 0,017 *	0,06 [0,01; 0,11] 0,015 *
Rapid Evolvement = Yes	217 (82,2)	105 (72,4)	1,76 [1,09; 2,85] 0,021 *	1,14 [1,01; 1,27] 0,031 *	0,10 [0,01; 0,18] 0,026 *
Any SAE					
Interaction test:	p=0,050				
Rapid Evolvement = No	152 (18,2)	51 (12,7)	1,53 [1,08; 2,15] 0,015 *	1,43 [1,07; 1,92] 0,017 *	0,05 [0,01; 0,10] 0,010 *
Rapid Evolvement = Yes	34 (12,9)	23 (15,9)	0,78 [0,44; 1,39] 0,405	0,81 [0,50; 1,32] 0,404	-0,03 [-0,10; 0,04] 0,416
Any SAE, disease specific events excluded[1]					
Interaction test:	p=0,421				
Rapid Evolvement = No	118 (14,1)	39 (9,7)	1,53 [1,04; 2,24] 0,029 *	1,45 [1,03; 2,05] 0,032 *	0,04 [0,01; 0,08] 0,021 *
Rapid Evolvement = Yes	28 (10,6)	14 (9,7)	1,11 [0,56; 2,18] 0,762	1,10 [0,60; 2,02] 0,762	0,01 [-0,05; 0,07] 0,759

	Treatment groups		Comparison		
	BAF312 (N=1099)	**Placebo (N=546)**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Any severe AE[2]					
Interaction test:	p=0,534				
Rapid Evolvement = No	111 (13,3)	45 (11,2)	1,21 [0,84; 1,75] 0,305	1,18 [0,86; 1,64] 0,307	0,02 [-0,02; 0,06] 0,292
Rapid Evolvement = Yes	28 (10,6)	16 (11,0)	0,96 [0,50; 1,83] 0,894	0,96 [0,54; 1,72] 0,894	-0,00 [-0,07; 0,06] 0,894
Any severe AE[2], disease specific events excluded[1]					
Interaction test:	p=0,678				
Rapid Evolvement = No	86 (10,3)	32 (8,0)	1,32 [0,87; 2,02] 0,194	1,29 [0,88; 1,90] 0,197	0,02 [-0,01; 0,06] 0,176
Rapid Evolvement = Yes	24 (9,1)	12 (8,3)	1,11 [0,54; 2,29] 0,781	1,10 [0,57; 2,13] 0,781	0,01 [-0,05; 0,06] 0,778
Any AE leading to study discontinuation					
Interaction test:	p=0,840				
Rapid Evolvement = No	40 (4,8)	14 (3,5)	1,39 [0,75; 2,59] 0,296	1,37 [0,76; 2,49] 0,299	0,01 [-0,01; 0,04] 0,270
Rapid Evolvement = Yes	6 (2,3)	2 (1,4)	1,66 [0,33; 8,35] 0,533	1,65 [0,34; 8,06] 0,538	0,01 [-0,02; 0,04] 0,503

	Treatment groups		Comparison		
	BAF312 (N=1099)	**Placebo (N=546)**	**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=0,225				
Rapid Evolvement = No	68 (8,1)	25 (6,2)	1,33 [0,83; 2,14] 0,234	1,31 [0,84; 2,03] 0,237	0,02 [-0,01; 0,05] 0,213
Rapid Evolvement = Yes	16 (6,1)	3 (2,1)	3,05 [0,87; 10,66] 0,067	2,93 [0,87; 9,89] 0,083	0,04 [0,00; 0,08] 0,034 *

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 total population

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

	Treatment groups		Comparison		
	BAF312 (N=1099)	Placebo (N=546)	OR [95% CI] p-value	RR [95% CI] p-value	RD [95% CI] p-value
N'	1099	546			
N' Rapid Evolvement = No	835	401			
N' Rapid Evolvement = Yes	264	145			
BLOOD AND LYMPHATIC SYSTEM DISORDERS					
Interaction test:	p=0,020 *				
Rapid Evolvement = No	40 (4,8)	5 (1,2)	3,98 [1,56; 10,18] 0,002 *	3,84 [1,53; 9,66] 0,004 *	0,04 [0,02; 0,05] <0,001 *
Rapid Evolvement = Yes	6 (2,3)	5 (3,4)	0,65 [0,20; 2,17] 0,482	0,66 [0,20; 2,12] 0,485	-0,01 [-0,05; 0,02] 0,507
EAR AND LABYRINTH DISORDERS					
VERTIGO					
Interaction test:	p=0,915				
Rapid Evolvement = No	21 (2,5)	21 (5,2)	0,47 [0,25; 0,87] 0,013 *	0,48 [0,27; 0,87] 0,015 *	-0,03 [-0,05; -0,00] 0,028 *
Rapid Evolvement = Yes	4 (1,5)	5 (3,4)	0,43 [0,11; 1,63] 0,202	0,44 [0,12; 1,61] 0,215	-0,02 [-0,05; 0,01] 0,253
EYE DISORDERS					
MACULAR OEDEMA					
Interaction test:	N.E.				
Rapid Evolvement = No	15 (1,8)	1 (0,2)	7,32 [0,96; 55,59] 0,024 *	7,20 [0,95; 54,34] 0,055	0,02 [0,01; 0,03] 0,003 *
Rapid Evolvement = Yes	3 (1,1)	0 (0,0)	3,89 [0,20; 75,93] 0,198	3,86 [0,20; 74,15] 0,371	0,01 [-0,00; 0,02] 0,082
GASTROINTESTINAL DISORDERS					
NAUSEA					
Interaction test:	p=0,602				
Rapid Evolvement = No	56 (6,7)	15 (3,7)	1,85 [1,03; 3,31] 0,036 *	1,79 [1,03; 3,13] 0,040 *	0,03 [0,00; 0,05] 0,021 *
Rapid Evolvement = Yes	18 (6,8)	4 (2,8)	2,58 [0,86; 7,77] 0,082	2,47 [0,85; 7,16] 0,096	0,04 [0,00; 0,08] 0,049 *

	Treatment groups		Comparison		
	BAF312 (N=1099)	**Placebo (N=546)**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
GENERAL DISORDERS AND ADMINISTRATION SITE CONDITIONS					
GAIT DISTURBANCE					
Interaction test:	p=0,464				
Rapid Evolvement = No	21 (2,5)	17 (4,2)	0,58 [0,30; 1,12] 0,100	0,59 [0,32; 1,11] 0,103	-0,02 [-0,04; 0,01] 0,131
Rapid Evolvement = Yes	3 (1,1)	5 (3,4)	0,32 [0,08; 1,37] 0,106	0,33 [0,08; 1,36] 0,125	-0,02 [-0,06; 0,01] 0,161
OEDEMA PERIPHERAL					
Interaction test:	p=0,014 *				
Rapid Evolvement = No	44 (5,3)	7 (1,7)	3,13 [1,40; 7,01] 0,004 *	3,02 [1,37; 6,64] 0,006 *	0,04 [0,02; 0,06] 0,001 *
Rapid Evolvement = Yes	6 (2,3)	6 (4,1)	0,54 [0,17; 1,70] 0,285	0,55 [0,18; 1,67] 0,291	-0,02 [-0,06; 0,02] 0,324
HEPATOBILIARY DISORDERS					
Interaction test:	p=0,308				
Rapid Evolvement = No	21 (2,5)	2 (0,5)	5,15 [1,20; 22,06] 0,014 *	5,04 [1,19; 21,40] 0,028 *	0,02 [0,01; 0,03] 0,002 *
Rapid Evolvement = Yes	6 (2,3)	2 (1,4)	1,66 [0,33; 8,35] 0,533	1,65 [0,34; 8,06] 0,538	0,01 [-0,02; 0,04] 0,503
INFECTIONS AND INFESTATIONS					
HERPES ZOSTER					
Interaction test:	p=0,901				
Rapid Evolvement = No	20 (2,4)	3 (0,7)	3,26 [0,96; 11,02] 0,045 *	3,20 [0,96; 10,71] 0,059	0,02 [0,00; 0,03] 0,016 *
Rapid Evolvement = Yes	5 (1,9)	1 (0,7)	2,78 [0,32; 24,03] 0,333	2,75 [0,32; 23,28] 0,354	0,01 [-0,01; 0,03] 0,267
INVESTIGATIONS					
Interaction test:	p=0,609				
Rapid Evolvement = No	201 (24,1)	57 (14,2)	1,91 [1,39; 2,64] <0,001 *	1,69 [1,29; 2,22] <0,001 *	0,10 [0,05; 0,14] <0,001 *
Rapid Evolvement = Yes	62 (23,5)	23 (15,9)	1,63 [0,96; 2,76] 0,069	1,48 [0,96; 2,28] 0,076	0,08 [-0,00; 0,15] 0,057

	Treatment groups		Comparison		
	BAF312 (N=1099)	**Placebo (N=546)**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
ALANINE AMINOTRANSFERASE INCREASED					
Interaction test:	p=0,185				
Rapid Evolvement = No	43 (5,1)	3 (0,7)	7,20 [2,22; 23,36] <0,001 *	6,88 [2,15; 22,05] 0,001 *	0,04 [0,03; 0,06] <0,001 *
Rapid Evolvement = Yes	22 (8,3)	5 (3,4)	2,55 [0,94; 6,87] 0,057	2,42 [0,93; 6,25] 0,069	0,05 [0,00; 0,09] 0,032 *
GAMMA-GLUTAMYLTRANSFERASE INCREASED					
Interaction test:	p=0,421				
Rapid Evolvement = No	30 (3,6)	5 (1,2)	2,95 [1,14; 7,67] 0,020 *	2,88 [1,13; 7,37] 0,027 *	0,02 [0,01; 0,04] 0,006 *
Rapid Evolvement = Yes	13 (4,9)	1 (0,7)	7,46 [0,97; 57,60] 0,024 *	7,14 [0,94; 54,03] 0,057	0,04 [0,01; 0,07] 0,005 *
HEPATIC ENZYME INCREASED					
Interaction test:	N.E.				
Rapid Evolvement = No	10 (1,2)	0 (0,0)	10,21 [0,60; 174,74] 0,028 *	10,10 [0,59; 171,90] 0,110	0,01 [0,00; 0,02] 0,001 *
Rapid Evolvement = Yes	6 (2,3)	1 (0,7)	3,35 [0,40; 28,09] 0,238	3,30 [0,40; 27,11] 0,267	0,02 [-0,01; 0,04] 0,167
NERVOUS SYSTEM DISORDERS					
Interaction test:	p=0,810				
Rapid Evolvement = No	326 (39,0)	132 (32,9)	1,31 [1,02; 1,68] 0,037 *	1,19 [1,01; 1,40] 0,041 *	0,06 [0,00; 0,12] 0,034 *
Rapid Evolvement = Yes	90 (34,1)	43 (29,7)	1,23 [0,79; 1,90] 0,360	1,15 [0,85; 1,55] 0,365	0,04 [-0,05; 0,14] 0,354
PARAESTHESIA					
Interaction test:	p=0,981				
Rapid Evolvement = No	14 (1,7)	15 (3,7)	0,44 [0,21; 0,92] 0,025 *	0,45 [0,22; 0,92] 0,029 *	-0,02 [-0,04; -0,00] 0,049 *
Rapid Evolvement = Yes	4 (1,5)	5 (3,4)	0,43 [0,11; 1,63] 0,202	0,44 [0,12; 1,61] 0,215	-0,02 [-0,05; 0,01] 0,253

	Treatment groups		Comparison		
	BAF312 (N=1099)	**Placebo (N=546)**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
VASCULAR DISORDERS					
Interaction test:	p=0,949				
Rapid Evolvement = No	122 (14,6)	44 (11,0)	1,39 [0,96; 2,00] 0,079	1,33 [0,96; 1,84] 0,083	0,04 [-0,00; 0,08] 0,066
Rapid Evolvement = Yes	38 (14,4)	16 (11,0)	1,36 [0,73; 2,53] 0,337	1,30 [0,75; 2,26] 0,342	0,03 [-0,03; 0,10] 0,321

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

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 total population

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

	Treatment groups		Comparison		
	BAF312 (N=1099)	**Placebo (N=546)**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
N'	1099	546			
N' Rapid Evolvement = No	835	401			
N' Rapid Evolvement = Yes	264	145			
INVESTIGATIONS					
Interaction test:	p=0,193				
Rapid Evolvement = No	16 (1,9)	1 (0,2)	7,81 [1,03; 59,13] 0,018 *	7,68 [1,02; 57,74] 0,048 *	0,02 [0,01; 0,03] 0,002 *
Rapid Evolvement = Yes	5 (1,9)	2 (1,4)	1,38 [0,26; 7,21] 0,701	1,37 [0,27; 6,99] 0,703	0,01 [-0,02; 0,03] 0,688

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 total population

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=1099)	**Placebo (N=546)**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
N'	1099	546			
N' Rapid Evolvement = No	835	401			
N' Rapid Evolvement = Yes	264	145			
Infections and infestations					
Interaction test:	p=0,339				
Rapid Evolvement = No	404 (48,4)	200 (49,9)	0,94 [0,74; 1,20] 0,623	0,97 [0,86; 1,09] 0,621	-0,01 [-0,07; 0,04] 0,623
Rapid Evolvement = Yes	135 (51,1)	68 (46,9)	1,19 [0,79; 1,78] 0,412	1,09 [0,88; 1,34] 0,418	0,04 [-0,06; 0,14] 0,411
Herpes simplex virus infections					
Interaction test:	p=0,269				
Rapid Evolvement = No	19 (2,3)	6 (1,5)	1,53 [0,61; 3,87] 0,362	1,52 [0,61; 3,78] 0,367	0,01 [-0,01; 0,02] 0,328
Rapid Evolvement = Yes	6 (2,3)	5 (3,4)	0,65 [0,20; 2,17] 0,482	0,66 [0,20; 2,12] 0,485	-0,01 [-0,05; 0,02] 0,507
Varicella-zoster virus infections					
Interaction test:	p=0,822				
Rapid Evolvement = No	27 (3,2)	3 (0,7)	4,43 [1,34; 14,70] 0,008 *	4,32 [1,32; 14,16] 0,016 *	0,02 [0,01; 0,04] 0,001 *
Rapid Evolvement = Yes	6 (2,3)	1 (0,7)	3,35 [0,40; 28,09] 0,238	3,30 [0,40; 27,11] 0,267	0,02 [-0,01; 0,04] 0,167
Lymphopenia					
Interaction test:	N.E.				
Rapid Evolvement = No	12 (1,4)	0 (0,0)	12,19 [0,72; 206,38] 0,016 *	12,02 [0,71; 202,53] 0,084	0,01 [0,01; 0,02] <0,001 *
Rapid Evolvement = Yes	2 (0,8)	0 (0,0)	2,77 [0,13; 58,12] 0,293	2,75 [0,13; 56,99] 0,512	0,01 [-0,00; 0,02] 0,156

	Treatment groups		Comparison		
	BAF312 (N=1099)	**Placebo (N=546)**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Macular edema					
Interaction test:	N.E.				
Rapid Evolvement = No	17 (2,0)	1 (0,2)	8,31 [1,10; 62,69] 0,014 *	8,16 [1,09; 61,13] 0,041 *	0,02 [0,01; 0,03] 0,001 *
Rapid Evolvement = Yes	3 (1,1)	0 (0,0)	3,89 [0,20; 75,93] 0,198	3,86 [0,20; 74,15] 0,371	0,01 [-0,00; 0,02] 0,082
Abnormal hepatic enzymes					
Interaction test:	p=0,428				
Rapid Evolvement = No	94 (11,3)	12 (3,0)	4,11 [2,23; 7,59] <0,001 *	3,76 [2,09; 6,78] <0,001 *	0,08 [0,06; 0,11] <0,001 *
Rapid Evolvement = Yes	41 (15,5)	9 (6,2)	2,78 [1,31; 5,90] 0,006 *	2,50 [1,25; 5,00] 0,009 *	0,09 [0,03; 0,15] 0,002 *
Malignancies					
Interaction test:	p=0,802				
Rapid Evolvement = No	18 (2,2)	12 (3,0)	0,71 [0,34; 1,50] 0,371	0,72 [0,35; 1,48] 0,372	-0,01 [-0,03; 0,01] 0,397
Rapid Evolvement = Yes	2 (0,8)	2 (1,4)	0,55 [0,08; 3,92] 0,541	0,55 [0,08; 3,86] 0,547	-0,01 [-0,03; 0,02] 0,574
Hypertension					
Interaction test:	p=0,535				
Rapid Evolvement = No	107 (12,8)	40 (10,0)	1,33 [0,90; 1,95] 0,149	1,28 [0,91; 1,81] 0,153	0,03 [-0,01; 0,07] 0,133
Rapid Evolvement = Yes	30 (11,4)	10 (6,9)	1,73 [0,82; 3,65] 0,146	1,65 [0,83; 3,27] 0,154	0,04 [-0,01; 0,10] 0,120
Seizures					
Interaction test:	p=0,553				
Rapid Evolvement = No	14 (1,7)	1 (0,2)	6,82 [0,89; 52,05] 0,032 *	6,72 [0,89; 50,95] 0,065	0,01 [0,00; 0,02] 0,005 *
Rapid Evolvement = Yes	5 (1,9)	1 (0,7)	2,78 [0,32; 24,03] 0,333	2,75 [0,32; 23,28] 0,354	0,01 [-0,01; 0,03] 0,267

	Treatment groups		Comparison		
	BAF312 (N=1099)	**Placebo (N=546)**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Thromboembolic events					
Interaction test:	p=0,752				
Rapid Evolvement = No	28 (3,4)	13 (3,2)	1,04 [0,53; 2,02] 0,918	1,03 [0,54; 1,98] 0,918	0,00 [-0,02; 0,02] 0,918
Rapid Evolvement = Yes	5 (1,9)	2 (1,4)	1,38 [0,26; 7,21] 0,701	1,37 [0,27; 6,99] 0,703	0,01 [-0,02; 0,03] 0,688
Respiratory disorders					
Interaction test:	p=0,858				
Rapid Evolvement = No	89 (10,7)	53 (13,2)	0,78 [0,54; 1,13] 0,187	0,81 [0,59; 1,11] 0,186	-0,03 [-0,06; 0,01] 0,201
Rapid Evolvement = Yes	28 (10,6)	18 (12,4)	0,84 [0,45; 1,57] 0,580	0,85 [0,49; 1,49] 0,579	-0,02 [-0,08; 0,05] 0,587
Peripheral edema/swelling					
Interaction test:	p=0,085				
Rapid Evolvement = No	61 (7,3)	11 (2,7)	2,79 [1,45; 5,37] 0,001 *	2,66 [1,42; 5,00] 0,002 *	0,05 [0,02; 0,07] <0,001 *
Rapid Evolvement = Yes	13 (4,9)	7 (4,8)	1,02 [0,40; 2,62] 0,965	1,02 [0,42; 2,50] 0,965	0,00 [-0,04; 0,04] 0,965

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 total population

	Treatment groups		Comparison		
	BAF312 (N=1099)	**Placebo (N=546)**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
N'	1099	546			
N' Rapid Evolvement = No	835	401			
N' Rapid Evolvement = Yes	264	145			
Asthma/bronchospasm					
Interaction test:	p=0,929				
Rapid Evolvement = No	4 (0,5)	1 (0,2)	1,93 [0,21; 17,28] 0,551	1,92 [0,22; 17,13] 0,559	0,00 [-0,00; 0,01] 0,506
Rapid Evolvement = Yes	4 (1,5)	1 (0,7)	2,22 [0,25; 20,01] 0,467	2,20 [0,25; 19,47] 0,480	0,01 [-0,01; 0,03] 0,418
Pregnancy and neonatal topics					
Interaction test:	N.E.				
Rapid Evolvement = No	4 (0,5)	0 (0,0)	4,35 [0,23; 80,91] 0,165	4,33 [0,23; 80,19] 0,325	0,00 [0,00; 0,01] 0,045 *
Rapid Evolvement = Yes	2 (0,8)	0 (0,0)	2,77 [0,13; 58,12] 0,293	2,75 [0,13; 56,99] 0,512	0,01 [-0,00; 0,02] 0,156
Bradyarrhythmias and bradycardia					
Interaction test:	p=0,605				
Rapid Evolvement = No	83 (9,9)	23 (5,7)	1,81 [1,12; 2,93] 0,013 *	1,73 [1,11; 2,71] 0,016 *	0,04 [0,01; 0,07] 0,007 *
Rapid Evolvement = Yes	20 (7,6)	8 (5,5)	1,40 [0,60; 3,27] 0,430	1,37 [0,62; 3,04] 0,434	0,02 [-0,03; 0,07] 0,410

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 total population

11.7 Subgroup: Disease Course

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

	Treatment groups		Comparison		
	BAF312 (N=1099)	**Placebo (N=546)**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
N'	1099	546			
N' Moderate or Severe Disease Course = No	195	87			
N' Moderate or Severe Disease Course = Yes	904	459			
Any AE					
Interaction test:	p=0,148				
Moderate or Severe Disease Course = No	179 (91,8)	69 (79,3)	2,92 [1,41; 6,05] 0,003 *	1,16 [1,03; 1,30] 0,013 *	0,12 [0,03; 0,22] 0,009 *
Moderate or Severe Disease Course = Yes	796 (88,1)	376 (81,9)	1,63 [1,19; 2,22] 0,002 *	1,07 [1,02; 1,13] 0,004 *	0,06 [0,02; 0,10] 0,003 *
Any AE, disease specific events excluded[1]					
Interaction test:	p=0,079				
Moderate or Severe Disease Course = No	173 (88,7)	65 (74,7)	2,66 [1,38; 5,13] 0,003 *	1,19 [1,04; 1,36] 0,011 *	0,14 [0,04; 0,24] 0,007 *
Moderate or Severe Disease Course = Yes	745 (82,4)	353 (76,9)	1,41 [1,07; 1,86] 0,015 *	1,07 [1,01; 1,14] 0,020 *	0,06 [0,01; 0,10] 0,019 *
Any SAE					
Interaction test:	p=0,527				
Moderate or Severe Disease Course = No	34 (17,4)	10 (11,5)	1,63 [0,76; 3,46] 0,204	1,52 [0,79; 2,93] 0,215	0,06 [-0,03; 0,15] 0,174
Moderate or Severe Disease Course = Yes	152 (16,8)	64 (13,9)	1,25 [0,91; 1,71] 0,170	1,21 [0,92; 1,58] 0,173	0,03 [-0,01; 0,07] 0,159
Any SAE, disease specific events excluded[1]					
Interaction test:	p=0,238				
Moderate or Severe Disease Course = No	29 (14,9)	6 (6,9)	2,36 [0,94; 5,91] 0,061	2,16 [0,93; 5,00] 0,074	0,08 [0,01; 0,15] 0,032 *
Moderate or Severe Disease Course = Yes	117 (12,9)	47 (10,2)	1,30 [0,91; 1,87] 0,147	1,26 [0,92; 1,74] 0,150	0,03 [-0,01; 0,06] 0,134

	Treatment groups		Comparison		
	BAF312 (N=1099)	**Placebo (N=546)**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Any severe AE[2]					
Interaction test:	p=0,616				
Moderate or Severe Disease Course = No	19 (9,7)	6 (6,9)	1,46 [0,56; 3,79] 0,437	1,41 [0,58; 3,41] 0,443	0,03 [-0,04; 0,10] 0,409
Moderate or Severe Disease Course = Yes	120 (13,3)	55 (12,0)	1,12 [0,80; 1,58] 0,500	1,11 [0,82; 1,49] 0,502	0,01 [-0,02; 0,05] 0,494
Any severe AE[2], disease specific events excluded[1]					
Interaction test:	p=0,176				
Moderate or Severe Disease Course = No	18 (9,2)	3 (3,4)	2,85 [0,82; 9,93] 0,088	2,68 [0,81; 8,85] 0,107	0,06 [0,00; 0,11] 0,042 *
Moderate or Severe Disease Course = Yes	92 (10,2)	41 (8,9)	1,16 [0,78; 1,70] 0,464	1,14 [0,80; 1,62] 0,466	0,01 [-0,02; 0,05] 0,456
Any AE leading to study discontinuation					
Interaction test:	p=0,765				
Moderate or Severe Disease Course = No	8 (4,1)	3 (3,4)	1,20 [0,31; 4,63] 0,793	1,19 [0,32; 4,38] 0,794	0,01 [-0,04; 0,05] 0,787
Moderate or Severe Disease Course = Yes	38 (4,2)	13 (2,8)	1,51 [0,79; 2,86] 0,207	1,48 [0,80; 2,76] 0,212	0,01 [-0,01; 0,03] 0,180

	Treatment groups		Comparison		
	BAF312 (N=1099)	**Placebo (N=546)**	**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=0,590				
Moderate or Severe Disease Course = No	13 (6,7)	5 (5,7)	1,17 [0,40; 3,39] 0,770	1,16 [0,43; 3,15] 0,771	0,01 [-0,05; 0,07] 0,764
Moderate or Severe Disease Course = Yes	71 (7,9)	23 (5,0)	1,62 [1,00; 2,62] 0,050	1,57 [0,99; 2,47] 0,054	0,03 [0,00; 0,05] 0,036 *

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 + 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 total population

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

	Treatment groups		Comparison		
	BAF312 (N=1099)	**Placebo (N=546)**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
N'	1099	546			
N' Moderate or Severe Disease Course = No	195	87			
N' Moderate or Severe Disease Course = Yes	904	459			
BLOOD AND LYMPHATIC SYSTEM DISORDERS					
Interaction test:	p=0,349				
Moderate or Severe Disease Course = No	5 (2,6)	2 (2,3)	1,12 [0,21; 5,88] 0,895	1,12 [0,22; 5,64] 0,895	0,00 [-0,04; 0,04] 0,893
Moderate or Severe Disease Course = Yes	41 (4,5)	8 (1,7)	2,68 [1,24; 5,76] 0,009 *	2,60 [1,23; 5,50] 0,012 *	0,03 [0,01; 0,05] 0,002 *
EAR AND LABYRINTH DISORDERS					
VERTIGO					
Interaction test:	p=0,582				
Moderate or Severe Disease Course = No	2 (1,0)	3 (3,4)	0,29 [0,05; 1,77] 0,154	0,30 [0,05; 1,75] 0,180	-0,02 [-0,07; 0,02] 0,245
Moderate or Severe Disease Course = Yes	23 (2,5)	23 (5,0)	0,49 [0,27; 0,89] 0,017 *	0,51 [0,29; 0,90] 0,019 *	-0,02 [-0,05; -0,00] 0,031 *
EYE DISORDERS					
MACULAR OEDEMA					
Interaction test:	N.E.				
Moderate or Severe Disease Course = No	3 (1,5)	0 (0,0)	3,18 [0,16; 62,26] 0,245	3,14 [0,16; 60,20] 0,447	0,02 [-0,00; 0,03] 0,081
Moderate or Severe Disease Course = Yes	15 (1,7)	1 (0,2)	7,73 [1,02; 58,69] 0,020 *	7,62 [1,01; 57,48] 0,049 *	0,01 [0,01; 0,02] 0,003 *
GASTROINTESTINAL DISORDERS					
NAUSEA					
Interaction test:	p=0,981				
Moderate or Severe Disease Course = No	9 (4,6)	2 (2,3)	2,06 [0,43; 9,72] 0,353	2,01 [0,44; 9,10] 0,366	0,02 [-0,02; 0,07] 0,292
Moderate or Severe Disease Course = Yes	65 (7,2)	17 (3,7)	2,01 [1,17; 3,48] 0,011 *	1,94 [1,15; 3,27] 0,013 *	0,03 [0,01; 0,06] 0,005 *

	Treatment groups		Comparison		
	BAF312 (N=1099)	**Placebo (N=546)**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
GENERAL DISORDERS AND ADMINISTRATION SITE CONDITIONS					
GAIT DISTURBANCE					
Interaction test:	p=0,692				
Moderate or Severe Disease Course = No	6 (3,1)	6 (6,9)	0,43 [0,13; 1,37] 0,142	0,45 [0,15; 1,34] 0,152	-0,04 [-0,10; 0,02] 0,201
Moderate or Severe Disease Course = Yes	18 (2,0)	16 (3,5)	0,56 [0,28; 1,11] 0,094	0,57 [0,29; 1,11] 0,098	-0,01 [-0,03; 0,00] 0,125
OEDEMA PERIPHERAL					
Interaction test:	p=0,442				
Moderate or Severe Disease Course = No	9 (4,6)	1 (1,1)	4,16 [0,52; 33,37] 0,146	4,02 [0,52; 31,21] 0,184	0,03 [-0,00; 0,07] 0,066
Moderate or Severe Disease Course = Yes	41 (4,5)	12 (2,6)	1,77 [0,92; 3,40] 0,083	1,73 [0,92; 3,27] 0,088	0,02 [-0,00; 0,04] 0,059
HEPATOBILIARY DISORDERS					
Interaction test:	N.E.				
Moderate or Severe Disease Course = No	5 (2,6)	0 (0,0)	5,05 [0,28; 92,39] 0,132	4,94 [0,28; 88,34] 0,278	0,03 [0,00; 0,05] 0,023 *
Moderate or Severe Disease Course = Yes	22 (2,4)	4 (0,9)	2,84 [0,97; 8,28] 0,046 *	2,79 [0,97; 8,06] 0,057	0,02 [0,00; 0,03] 0,020 *
INFECTIONS AND INFESTATIONS					
HERPES ZOSTER					
Interaction test:	p=0,115				
Moderate or Severe Disease Course = No	4 (2,1)	2 (2,3)	0,89 [0,16; 4,95] 0,894	0,89 [0,17; 4,78] 0,894	-0,00 [-0,04; 0,03] 0,896
Moderate or Severe Disease Course = Yes	21 (2,3)	2 (0,4)	5,43 [1,27; 23,28] 0,011 *	5,33 [1,26; 22,64] 0,023 *	0,02 [0,01; 0,03] 0,001 *
INVESTIGATIONS					
Interaction test:	p=0,966				
Moderate or Severe Disease Course = No	47 (24,1)	13 (14,9)	1,81 [0,92; 3,55] 0,083	1,61 [0,92; 2,82] 0,094	0,09 [-0,00; 0,19] 0,061
Moderate or Severe Disease Course = Yes	216 (23,9)	67 (14,6)	1,84 [1,36; 2,48] <0,001 *	1,64 [1,27; 2,10] <0,001 *	0,09 [0,05; 0,14] <0,001 *

	Treatment groups		Comparison		
	BAF312 (N=1099)	**Placebo (N=546)**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
ALANINE AMINOTRANSFERASE INCREASED					
Interaction test:	p=0,962				
Moderate or Severe Disease Course = No	17 (8,7)	2 (2,3)	4,06 [0,92; 17,97] 0,047 *	3,79 [0,90; 16,06] 0,070	0,06 [0,01; 0,11] 0,013 *
Moderate or Severe Disease Course = Yes	48 (5,3)	6 (1,3)	4,23 [1,80; 9,97] <0,001 *	4,06 [1,75; 9,42] 0,001 *	0,04 [0,02; 0,06] <0,001 *
GAMMA-GLUTAMYLTRANSFERASE INCREASED					
Interaction test:	p=0,104				
Moderate or Severe Disease Course = No	9 (4,6)	3 (3,4)	1,35 [0,36; 5,13] 0,654	1,34 [0,37; 4,82] 0,656	0,01 [-0,04; 0,06] 0,636
Moderate or Severe Disease Course = Yes	34 (3,8)	3 (0,7)	5,94 [1,81; 19,45] 0,001 *	5,75 [1,78; 18,64] 0,004 *	0,03 [0,02; 0,05] <0,001 *
HEPATIC ENZYME INCREASED					
Interaction test:	N.E.				
Moderate or Severe Disease Course = No	2 (1,0)	0 (0,0)	2,26 [0,11; 47,59] 0,343	2,24 [0,11; 46,27] 0,600	0,01 [-0,00; 0,02] 0,155
Moderate or Severe Disease Course = Yes	14 (1,5)	1 (0,2)	7,20 [0,94; 54,96] 0,026 *	7,11 [0,94; 53,89] 0,058	0,01 [0,00; 0,02] 0,004 *
NERVOUS SYSTEM DISORDERS					
Interaction test:	p=0,717				
Moderate or Severe Disease Course = No	71 (36,4)	25 (28,7)	1,42 [0,82; 2,46] 0,209	1,27 [0,87; 1,85] 0,221	0,08 [-0,04; 0,19] 0,197
Moderate or Severe Disease Course = Yes	345 (38,2)	150 (32,7)	1,27 [1,00; 1,61] 0,047 *	1,17 [1,00; 1,36] 0,050	0,05 [0,00; 0,11] 0,044 *
PARAESTHESIA					
Interaction test:	p=0,998				
Moderate or Severe Disease Course = No	3 (1,5)	3 (3,4)	0,44 [0,09; 2,21] 0,305	0,45 [0,09; 2,17] 0,317	-0,02 [-0,06; 0,02] 0,373
Moderate or Severe Disease Course = Yes	15 (1,7)	17 (3,7)	0,44 [0,22; 0,89] 0,018 *	0,45 [0,23; 0,89] 0,022 *	-0,02 [-0,04; -0,00] 0,037 *

	Treatment groups		Comparison		
	BAF312 (N=1099)	**Placebo (N=546)**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
VASCULAR DISORDERS					
Interaction test:	p=0,828				
Moderate or Severe Disease Course = No	25 (12,8)	9 (10,3)	1,27 [0,57; 2,86] 0,555	1,24 [0,60; 2,54] 0,559	0,02 [-0,05; 0,10] 0,541
Moderate or Severe Disease Course = Yes	135 (14,9)	51 (11,1)	1,40 [1,00; 1,98] 0,052	1,34 [0,99; 1,82] 0,055	0,04 [0,00; 0,08] 0,043 *

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 total population

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

	Treatment groups		Comparison		
	BAF312 (N=1099)	**Placebo (N=546)**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
N'	1099	546			
N' Moderate or Severe Disease Course = No	195	87			
N' Moderate or Severe Disease Course = Yes	904	459			
INVESTIGATIONS					
Interaction test:	N.E.				
Moderate or Severe Disease Course = No	2 (1,0)	0 (0,0)	2,26 [0,11; 47,59] 0,343	2,24 [0,11; 46,27] 0,600	0,01 [-0,00; 0,02] 0,155
Moderate or Severe Disease Course = Yes	19 (2,1)	3 (0,7)	3,26 [0,96; 11,09] 0,045 *	3,22 [0,96; 10,81] 0,059	0,01 [0,00; 0,03] 0,017 *

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 total population

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=1099)	**Placebo (N=546)**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
N'	1099	546			
N' Moderate or Severe Disease Course = No	195	87			
N' Moderate or Severe Disease Course = Yes	904	459			
Infections and infestations					
Interaction test:	p=0,422				
Moderate or Severe Disease Course = No	101 (51,8)	41 (47,1)	1,21 [0,73; 2,00] 0,469	1,10 [0,85; 1,43] 0,477	0,05 [-0,08; 0,17] 0,468
Moderate or Severe Disease Course = Yes	438 (48,5)	227 (49,5)	0,96 [0,77; 1,20] 0,726	0,98 [0,87; 1,10] 0,725	-0,01 [-0,07; 0,05] 0,726
Herpes simplex virus infections					
Interaction test:	p=0,046 *				
Moderate or Severe Disease Course = No	4 (2,1)	5 (5,7)	0,34 [0,09; 1,31] 0,103	0,36 [0,10; 1,30] 0,118	-0,04 [-0,09; 0,02] 0,170
Moderate or Severe Disease Course = Yes	21 (2,3)	6 (1,3)	1,80 [0,72; 4,48] 0,203	1,78 [0,72; 4,37] 0,211	0,01 [-0,00; 0,02] 0,164
Varicella-zoster virus infections					
Interaction test:	p=0,136				
Moderate or Severe Disease Course = No	6 (3,1)	2 (2,3)	1,35 [0,27; 6,82] 0,716	1,34 [0,28; 6,50] 0,718	0,01 [-0,03; 0,05] 0,701
Moderate or Severe Disease Course = Yes	27 (3,0)	2 (0,4)	7,03 [1,67; 29,71] 0,002 *	6,85 [1,64; 28,70] 0,008 *	0,03 [0,01; 0,04] <0,001 *
Lymphopenia					
Interaction test:	N.E.				
Moderate or Severe Disease Course = No	1 (0,5)	0 (0,0)	1,35 [0,05; 33,46] 0,503	1,35 [0,06; 32,74] 0,855	0,01 [-0,00; 0,02] 0,316
Moderate or Severe Disease Course = Yes	13 (1,4)	0 (0,0)	13,92 [0,83; 234,62] 0,010 *	13,72 [0,82; 230,34] 0,069	0,01 [0,01; 0,02] <0,001 *

	Treatment groups		Comparison		
	BAF312 (N=1099)	**Placebo (N=546)**	**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	4 (2,1)	0 (0,0)	4,11 [0,22; 77,22] 0,178	4,04 [0,22; 74,24] 0,347	0,02 [0,00; 0,04] 0,043 *
Moderate or Severe Disease Course = Yes	16 (1,8)	1 (0,2)	8,25 [1,09; 62,42] 0,015 *	8,12 [1,08; 61,07] 0,042 *	0,02 [0,01; 0,03] 0,002 *
Abnormal hepatic enzymes					
Interaction test:	p=0,057				
Moderate or Severe Disease Course = No	24 (12,3)	7 (8,0)	1,60 [0,66; 3,88] 0,291	1,53 [0,69; 3,41] 0,300	0,04 [-0,03; 0,12] 0,255
Moderate or Severe Disease Course = Yes	111 (12,3)	14 (3,1)	4,45 [2,52; 7,85] <0,001 *	4,03 [2,34; 6,94] <0,001 *	0,09 [0,07; 0,12] <0,001 *
Malignancies					
Interaction test:	p=0,363				
Moderate or Severe Disease Course = No	6 (3,1)	2 (2,3)	1,35 [0,27; 6,82] 0,716	1,34 [0,28; 6,50] 0,718	0,01 [-0,03; 0,05] 0,701
Moderate or Severe Disease Course = Yes	14 (1,5)	12 (2,6)	0,59 [0,27; 1,28] 0,174	0,59 [0,28; 1,27] 0,178	-0,01 [-0,03; 0,01] 0,210
Hypertension					
Interaction test:	p=0,943				
Moderate or Severe Disease Course = No	25 (12,8)	8 (9,2)	1,45 [0,63; 3,36] 0,382	1,39 [0,66; 2,97] 0,388	0,04 [-0,04; 0,11] 0,355
Moderate or Severe Disease Course = Yes	112 (12,4)	42 (9,2)	1,40 [0,97; 2,04] 0,074	1,35 [0,97; 1,90] 0,077	0,03 [-0,00; 0,07] 0,062
Seizures					
Interaction test:	N.E.				
Moderate or Severe Disease Course = No	3 (1,5)	0 (0,0)	3,18 [0,16; 62,26] 0,245	3,14 [0,16; 60,20] 0,447	0,02 [-0,00; 0,03] 0,081
Moderate or Severe Disease Course = Yes	16 (1,8)	2 (0,4)	4,12 [0,94; 17,98] 0,041 *	4,06 [0,94; 17,59] 0,061	0,01 [0,00; 0,02] 0,013 *

	Treatment groups		Comparison		
	BAF312 (N=1099)	**Placebo (N=546)**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Thromboembolic events					
Interaction test:	p=0,616				
Moderate or Severe Disease Course = No	7 (3,6)	2 (2,3)	1,58 [0,32; 7,78] 0,569	1,56 [0,33; 7,36] 0,573	0,01 [-0,03; 0,05] 0,536
Moderate or Severe Disease Course = Yes	26 (2,9)	13 (2,8)	1,02 [0,52; 2,00] 0,963	1,02 [0,53; 1,96] 0,963	0,00 [-0,02; 0,02] 0,963
Respiratory disorders					
Interaction test:	p=0,675				
Moderate or Severe Disease Course = No	23 (11,8)	11 (12,6)	0,92 [0,43; 1,99] 0,840	0,93 [0,48; 1,83] 0,840	-0,01 [-0,09; 0,07] 0,842
Moderate or Severe Disease Course = Yes	94 (10,4)	60 (13,1)	0,77 [0,55; 1,09] 0,141	0,80 [0,59; 1,08] 0,140	-0,03 [-0,06; 0,01] 0,153
Peripheral edema/swelling					
Interaction test:	p=0,320				
Moderate or Severe Disease Course = No	12 (6,2)	1 (1,1)	5,64 [0,72; 44,07] 0,064	5,35 [0,71; 40,53] 0,104	0,05 [0,01; 0,09] 0,015 *
Moderate or Severe Disease Course = Yes	62 (6,9)	17 (3,7)	1,91 [1,11; 3,31] 0,018 *	1,85 [1,10; 3,13] 0,021 *	0,03 [0,01; 0,06] 0,010 *

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 total population

	Treatment groups		Comparison		
	BAF312 (N=1099)	**Placebo (N=546)**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
N'	1099	546			
N' Moderate or Severe Disease Course = No	195	87			
N' Moderate or Severe Disease Course = Yes	904	459			
Asthma/bronchospasm					
Interaction test:	p=0,241				
Moderate or Severe Disease Course = No	1 (0,5)	1 (1,1)	0,44 [0,03; 7,17] 0,556	0,45 [0,03; 7,05] 0,567	-0,01 [-0,03; 0,02] 0,611
Moderate or Severe Disease Course = Yes	7 (0,8)	1 (0,2)	3,57 [0,44; 29,14] 0,204	3,55 [0,44; 28,80] 0,235	0,01 [-0,00; 0,01] 0,126
Pregnancy and neonatal topics					
Interaction test:	N.E.				
Moderate or Severe Disease Course = No	1 (0,5)	0 (0,0)	1,35 [0,05; 33,46] 0,503	1,35 [0,06; 32,74] 0,855	0,01 [-0,00; 0,02] 0,316
Moderate or Severe Disease Course = Yes	5 (0,6)	0 (0,0)	5,62 [0,31; 101,84] 0,110	5,59 [0,31; 100,89] 0,244	0,01 [0,00; 0,01] 0,025 *
Bradyarrhythmias and bradycardia					
Interaction test:	p=0,235				
Moderate or Severe Disease Course = No	19 (9,7)	8 (9,2)	1,07 [0,45; 2,54] 0,885	1,06 [0,48; 2,33] 0,885	0,01 [-0,07; 0,08] 0,884
Moderate or Severe Disease Course = Yes	84 (9,3)	23 (5,0)	1,94 [1,21; 3,12] 0,005 *	1,85 [1,19; 2,90] 0,007 *	0,04 [0,02; 0,07] 0,002 *

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 total population

11.8 Subgroup: Region

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

	Treatment groups		Comparison		
	BAF312 (N=1099)	**Placebo (N=546)**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
N'	1099	546			
N' Region = Europe	860	427			
N' Region = Other	239	119			
Any AE					
Interaction test:	p=0,440				
Region = Europe	764 (88,8)	345 (80,8)	1,89 [1,37; 2,61] <0,001 *	1,10 [1,04; 1,16] <0,001 *	0,08 [0,04; 0,12] <0,001 *
Region = Other	211 (88,3)	100 (84,0)	1,43 [0,76; 2,69] 0,262	1,05 [0,96; 1,15] 0,287	0,04 [-0,03; 0,12] 0,282
Any AE, disease specific events excluded[1]					
Interaction test:	p=0,899				
Region = Europe	718 (83,5)	326 (76,3)	1,57 [1,18; 2,09] 0,002 *	1,09 [1,03; 1,16] 0,004 *	0,07 [0,02; 0,12] 0,003 *
Region = Other	200 (83,7)	92 (77,3)	1,51 [0,87; 2,61] 0,143	1,08 [0,97; 1,21] 0,167	0,06 [-0,02; 0,15] 0,159
Any SAE					
Interaction test:	p=0,772				
Region = Europe	148 (17,2)	60 (14,1)	1,27 [0,92; 1,76] 0,147	1,22 [0,93; 1,62] 0,151	0,03 [-0,01; 0,07] 0,136
Region = Other	38 (15,9)	14 (11,8)	1,42 [0,74; 2,73] 0,296	1,35 [0,76; 2,39] 0,302	0,04 [-0,03; 0,12] 0,275
Any SAE, disease specific events excluded[1]					
Interaction test:	p=0,917				
Region = Europe	114 (13,3)	41 (9,6)	1,44 [0,99; 2,10] 0,058	1,38 [0,99; 1,93] 0,061	0,04 [0,00; 0,07] 0,047 *
Region = Other	32 (13,4)	12 (10,1)	1,38 [0,68; 2,78] 0,370	1,33 [0,71; 2,48] 0,375	0,03 [-0,04; 0,10] 0,349

	Treatment groups		Comparison		
	BAF312 (N=1099)	**Placebo (N=546)**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Any severe AE[2]					
Interaction test:	p=0,570				
Region = Europe	107 (12,4)	49 (11,5)	1,10 [0,76; 1,57] 0,617	1,08 [0,79; 1,49] 0,618	0,01 [-0,03; 0,05] 0,613
Region = Other	32 (13,4)	12 (10,1)	1,38 [0,68; 2,78] 0,370	1,33 [0,71; 2,48] 0,375	0,03 [-0,04; 0,10] 0,349
Any severe AE[2], disease specific events excluded[1]					
Interaction test:	p=0,841				
Region = Europe	86 (10,0)	35 (8,2)	1,24 [0,82; 1,88] 0,297	1,22 [0,84; 1,78] 0,299	0,02 [-0,01; 0,05] 0,282
Region = Other	24 (10,0)	9 (7,6)	1,36 [0,61; 3,04] 0,445	1,33 [0,64; 2,77] 0,449	0,02 [-0,04; 0,09] 0,425
Any AE leading to study discontinuation					
Interaction test:	p=0,828				
Region = Europe	33 (3,8)	11 (2,6)	1,51 [0,76; 3,02] 0,241	1,49 [0,76; 2,92] 0,245	0,01 [-0,01; 0,03] 0,211
Region = Other	13 (5,4)	5 (4,2)	1,31 [0,46; 3,77] 0,614	1,29 [0,47; 3,55] 0,616	0,01 [-0,03; 0,06] 0,599

	Treatment groups		Comparison		
	BAF312 (N=1099)	**Placebo (N=546)**	**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=0,592				
Region = Europe	62 (7,2)	22 (5,2)	1,43 [0,87; 2,36] 0,159	1,40 [0,87; 2,24] 0,163	0,02 [-0,01; 0,05] 0,138
Region = Other	22 (9,2)	6 (5,0)	1,91 [0,75; 4,84] 0,167	1,83 [0,76; 4,38] 0,178	0,04 [-0,01; 0,10] 0,129

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 + 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 total population

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

	Treatment groups		Comparison		
	BAF312 (N=1099)	**Placebo (N=546)**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
N'	1099	546			
N' Region = Europe	860	427			
N' Region = Other	239	119			
BLOOD AND LYMPHATIC SYSTEM DISORDERS					
Interaction test:	p=0,243				
Region = Europe	33 (3,8)	9 (2,1)	1,85 [0,88; 3,91] 0,100	1,82 [0,88; 3,77] 0,107	0,02 [-0,00; 0,04] 0,070
Region = Other	13 (5,4)	1 (0,8)	6,79 [0,88; 52,52] 0,034 *	6,47 [0,86; 48,89] 0,070	0,05 [0,01; 0,08] 0,006 *
EAR AND LABYRINTH DISORDERS					
VERTIGO					
Interaction test:	p=0,521				
Region = Europe	23 (2,7)	25 (5,9)	0,44 [0,25; 0,79] 0,005 *	0,46 [0,26; 0,80] 0,006 *	-0,03 [-0,06; -0,01] 0,012 *
Region = Other	2 (0,8)	1 (0,8)	1,00 [0,09; 11,09] 0,997	1,00 [0,09; 10,87] 0,997	-0,00 [-0,02; 0,02] 0,997
EYE DISORDERS					
MACULAR OEDEMA					
Interaction test:	N.E.				
Region = Europe	15 (1,7)	1 (0,2)	7,56 [1,00; 57,44] 0,021 *	7,45 [0,99; 56,19] 0,051	0,02 [0,01; 0,02] 0,003 *
Region = Other	3 (1,3)	0 (0,0)	3,54 [0,18; 69,04] 0,220	3,50 [0,18; 67,21] 0,406	0,01 [-0,00; 0,03] 0,081
GASTROINTESTINAL DISORDERS					
NAUSEA					
Interaction test:	p=0,693				
Region = Europe	47 (5,5)	11 (2,6)	2,19 [1,12; 4,26] 0,019 *	2,12 [1,11; 4,05] 0,023 *	0,03 [0,01; 0,05] 0,008 *
Region = Other	27 (11,3)	8 (6,7)	1,77 [0,78; 4,02] 0,170	1,68 [0,79; 3,58] 0,179	0,05 [-0,01; 0,11] 0,137

	Treatment groups		Comparison		
	BAF312 (N=1099)	**Placebo (N=546)**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
GENERAL DISORDERS AND ADMINISTRATION SITE CONDITIONS					
GAIT DISTURBANCE					
Interaction test:	p=0,121				
Region = Europe	16 (1,9)	19 (4,4)	0,41 [0,21; 0,80] 0,007 *	0,42 [0,22; 0,80] 0,009 *	-0,03 [-0,05; -0,00] 0,018 *
Region = Other	8 (3,3)	3 (2,5)	1,34 [0,35; 5,14] 0,670	1,33 [0,36; 4,91] 0,671	0,01 [-0,03; 0,04] 0,655
OEDEMA PERIPHERAL					
Interaction test:	p=0,042 *				
Region = Europe	38 (4,4)	6 (1,4)	3,24 [1,36; 7,73] 0,005 *	3,14 [1,34; 7,38] 0,008 *	0,03 [0,01; 0,05] 0,001 *
Region = Other	12 (5,0)	7 (5,9)	0,85 [0,32; 2,21] 0,732	0,85 [0,35; 2,11] 0,732	-0,01 [-0,06; 0,04] 0,738
HEPATOBILIARY DISORDERS					
Interaction test:	N.E.				
Region = Europe	24 (2,8)	4 (0,9)	3,04 [1,05; 8,81] 0,032 *	2,98 [1,04; 8,53] 0,042 *	0,02 [0,00; 0,03] 0,011 *
Region = Other	3 (1,3)	0 (0,0)	3,54 [0,18; 69,04] 0,220	3,50 [0,18; 67,21] 0,406	0,01 [-0,00; 0,03] 0,081
INFECTIONS AND INFESTATIONS					
HERPES ZOSTER					
Interaction test:	N.E.				
Region = Europe	19 (2,2)	4 (0,9)	2,39 [0,81; 7,07] 0,105	2,36 [0,81; 6,89] 0,117	0,01 [-0,00; 0,03] 0,063
Region = Other	6 (2,5)	0 (0,0)	6,65 [0,37; 119,10] 0,081	6,50 [0,37; 114,42] 0,201	0,03 [0,01; 0,04] 0,013 *
INVESTIGATIONS					
Interaction test:	p=0,788				
Region = Europe	213 (24,8)	66 (15,5)	1,80 [1,33; 2,44] <0,001 *	1,60 [1,25; 2,06] <0,001 *	0,09 [0,05; 0,14] <0,001 *
Region = Other	50 (20,9)	14 (11,8)	1,98 [1,05; 3,76] 0,033 *	1,78 [1,03; 3,08] 0,040 *	0,09 [0,01; 0,17] 0,021 *

	Treatment groups		Comparison		
	BAF312 (N=1099)	**Placebo (N=546)**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
ALANINE AMINOTRANSFERASE INCREASED					
Interaction test:	p=0,746				
Region = Europe	59 (6,9)	7 (1,6)	4,42 [2,00; 9,76] <0,001 *	4,18 [1,93; 9,08] <0,001 *	0,05 [0,03; 0,07] <0,001 *
Region = Other	6 (2,5)	1 (0,8)	3,04 [0,36; 25,53] 0,282	2,99 [0,36; 24,53] 0,308	0,02 [-0,01; 0,04] 0,203
GAMMA-GLUTAMYLTRANSFERASE INCREASED					
Interaction test:	p=0,037 *				
Region = Europe	41 (4,8)	4 (0,9)	5,29 [1,88; 14,88] <0,001 *	5,09 [1,83; 14,11] 0,002 *	0,04 [0,02; 0,06] <0,001 *
Region = Other	2 (0,8)	2 (1,7)	0,49 [0,07; 3,55] 0,474	0,50 [0,07; 3,49] 0,483	-0,01 [-0,03; 0,02] 0,522
HEPATIC ENZYME INCREASED					
Interaction test:	N.E.				
Region = Europe	13 (1,5)	1 (0,2)	6,54 [0,85; 50,15] 0,038 *	6,45 [0,85; 49,18] 0,072	0,01 [0,00; 0,02] 0,007 *
Region = Other	3 (1,3)	0 (0,0)	3,54 [0,18; 69,04] 0,220	3,50 [0,18; 67,21] 0,406	0,01 [-0,00; 0,03] 0,081
NERVOUS SYSTEM DISORDERS					
Interaction test:	p=0,181				
Region = Europe	312 (36,3)	138 (32,3)	1,19 [0,93; 1,52] 0,161	1,12 [0,95; 1,32] 0,165	0,04 [-0,02; 0,09] 0,156
Region = Other	104 (43,5)	37 (31,1)	1,71 [1,07; 2,72] 0,023 *	1,40 [1,03; 1,90] 0,030 *	0,12 [0,02; 0,23] 0,020 *
PARAESTHESIA					
Interaction test:	p=0,279				
Region = Europe	16 (1,9)	15 (3,5)	0,52 [0,25; 1,06] 0,069	0,53 [0,26; 1,06] 0,073	-0,02 [-0,04; 0,00] 0,099
Region = Other	2 (0,8)	5 (4,2)	0,19 [0,04; 1,01] 0,030 *	0,20 [0,04; 1,01] 0,052	-0,03 [-0,07; 0,00] 0,081

	Treatment groups		Comparison		
	BAF312 (N=1099)	**Placebo (N=546)**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
VASCULAR DISORDERS					
Interaction test:	p=0,490				
Region = Europe	141 (16,4)	51 (11,9)	1,45 [1,03; 2,04] 0,035 *	1,37 [1,02; 1,85] 0,038 *	0,04 [0,01; 0,08] 0,027 *
Region = Other	19 (7,9)	9 (7,6)	1,06 [0,46; 2,41] 0,898	1,05 [0,49; 2,25] 0,898	0,00 [-0,05; 0,06] 0,897

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 total population

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

	Treatment groups		Comparison		
	BAF312 (N=1099)	**Placebo (N=546)**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
N'	1099	546			
N' Region = Europe	860	427			
N' Region = Other	239	119			
INVESTIGATIONS					
Interaction test:	p=0,422				
Region = Europe	18 (2,1)	2 (0,5)	4,54 [1,05; 19,67] 0,027 *	4,47 [1,04; 19,17] 0,044 *	0,02 [0,00; 0,03] 0,006 *
Region = Other	3 (1,3)	1 (0,8)	1,50 [0,15; 14,58] 0,725	1,49 [0,16; 14,21] 0,727	0,00 [-0,02; 0,03] 0,707

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 + 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 total population

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=1099)	**Placebo (N=546)**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
N'	1099	546			
N' Region = Europe	860	427			
N' Region = Other	239	119			
Infections and infestations					
Interaction test:	p=0,574				
Region = Europe	426 (49,5)	215 (50,4)	0,97 [0,77; 1,22] 0,783	0,98 [0,88; 1,10] 0,782	-0,01 [-0,07; 0,05] 0,783
Region = Other	113 (47,3)	53 (44,5)	1,12 [0,72; 1,74] 0,624	1,06 [0,83; 1,35] 0,627	0,03 [-0,08; 0,14] 0,623
Herpes simplex virus infections					
Interaction test:	p=0,380				
Region = Europe	23 (2,7)	9 (2,1)	1,28 [0,59; 2,78] 0,539	1,27 [0,59; 2,72] 0,540	0,01 [-0,01; 0,02] 0,523
Region = Other	2 (0,8)	2 (1,7)	0,49 [0,07; 3,55] 0,474	0,50 [0,07; 3,49] 0,483	-0,01 [-0,03; 0,02] 0,522
Varicella-zoster virus infections					
Interaction test:	N.E.				
Region = Europe	27 (3,1)	4 (0,9)	3,43 [1,19; 9,86] 0,015 *	3,35 [1,18; 9,52] 0,023 *	0,02 [0,01; 0,04] 0,004 *
Region = Other	6 (2,5)	0 (0,0)	6,65 [0,37; 119,10] 0,081	6,50 [0,37; 114,42] 0,201	0,03 [0,01; 0,04] 0,013 *
Lymphopenia					
Interaction test:	N.E.				
Region = Europe	10 (1,2)	0 (0,0)	10,56 [0,62; 180,56] 0,025 *	10,44 [0,61; 177,72] 0,105	0,01 [0,00; 0,02] 0,001 *
Region = Other	4 (1,7)	0 (0,0)	4,57 [0,24; 85,53] 0,156	4,50 [0,24; 82,90] 0,312	0,02 [0,00; 0,03] 0,044 *

	Treatment groups		Comparison		
	BAF312 (N=1099)	**Placebo (N=546)**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Macular edema					
Interaction test:	N.E.				
Region = Europe	16 (1,9)	1 (0,2)	8,08 [1,07; 61,10] 0,016 *	7,94 [1,06; 59,70] 0,044 *	0,02 [0,01; 0,03] 0,002 *
Region = Other	4 (1,7)	0 (0,0)	4,57 [0,24; 85,53] 0,156	4,50 [0,24; 82,90] 0,312	0,02 [0,00; 0,03] 0,044 *
Abnormal hepatic enzymes					
Interaction test:	p=0,852				
Region = Europe	117 (13,6)	18 (4,2)	3,58 [2,15; 5,96] <0,001 *	3,23 [1,99; 5,23] <0,001 *	0,09 [0,06; 0,12] <0,001 *
Region = Other	18 (7,5)	3 (2,5)	3,15 [0,91; 10,91] 0,057	2,99 [0,90; 9,94] 0,074	0,05 [0,01; 0,09] 0,025 *
Malignancies					
Interaction test:	p=0,962				
Region = Europe	13 (1,5)	9 (2,1)	0,71 [0,30; 1,68] 0,437	0,72 [0,31; 1,66] 0,439	-0,01 [-0,02; 0,01] 0,462
Region = Other	7 (2,9)	5 (4,2)	0,69 [0,21; 2,22] 0,528	0,70 [0,23; 2,15] 0,530	-0,01 [-0,05; 0,03] 0,552
Hypertension					
Interaction test:	p=0,956				
Region = Europe	118 (13,7)	43 (10,1)	1,42 [0,98; 2,06] 0,062	1,36 [0,98; 1,89] 0,066	0,04 [-0,00; 0,07] 0,051
Region = Other	19 (7,9)	7 (5,9)	1,38 [0,56; 3,38] 0,478	1,35 [0,58; 3,12] 0,481	0,02 [-0,03; 0,08] 0,457
Seizures					
Interaction test:	N.E.				
Region = Europe	15 (1,7)	2 (0,5)	3,77 [0,86; 16,57] 0,059	3,72 [0,86; 16,21] 0,080	0,01 [0,00; 0,02] 0,022 *
Region = Other	4 (1,7)	0 (0,0)	4,57 [0,24; 85,53] 0,156	4,50 [0,24; 82,90] 0,312	0,02 [0,00; 0,03] 0,044 *

	Treatment groups		Comparison		
	BAF312 (N=1099)	**Placebo (N=546)**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Thromboembolic events					
Interaction test:	p=0,497				
Region = Europe	21 (2,4)	8 (1,9)	1,31 [0,58; 2,98] 0,518	1,30 [0,58; 2,92] 0,519	0,01 [-0,01; 0,02] 0,499
Region = Other	12 (5,0)	7 (5,9)	0,85 [0,32; 2,21] 0,732	0,85 [0,35; 2,11] 0,732	-0,01 [-0,06; 0,04] 0,738
Respiratory disorders					
Interaction test:	p=0,633				
Region = Europe	89 (10,3)	56 (13,1)	0,76 [0,54; 1,09] 0,139	0,79 [0,58; 1,08] 0,139	-0,03 [-0,07; 0,01] 0,153
Region = Other	28 (11,7)	15 (12,6)	0,92 [0,47; 1,80] 0,807	0,93 [0,52; 1,67] 0,807	-0,01 [-0,08; 0,06] 0,809
Peripheral edema/swelling					
Interaction test:	p=0,065				
Region = Europe	54 (6,3)	9 (2,1)	3,11 [1,52; 6,36] 0,001 *	2,98 [1,49; 5,98] 0,002 *	0,04 [0,02; 0,06] <0,001 *
Region = Other	20 (8,4)	9 (7,6)	1,12 [0,49; 2,53] 0,793	1,11 [0,52; 2,35] 0,793	0,01 [-0,05; 0,07] 0,789

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 total population

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

	Treatment groups		Comparison		
	BAF312 (N=1099)	**Placebo (N=546)**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
N'	1099	546			
N' Region = Europe	860	427			
N' Region = Other	239	119			
Asthma/bronchospasm					
Interaction test:	N.E.				
Region = Europe	5 (0,6)	2 (0,5)	1,24 [0,24; 6,43] 0,795	1,24 [0,24; 6,37] 0,796	0,00 [-0,01; 0,01] 0,788
Region = Other	3 (1,3)	0 (0,0)	3,54 [0,18; 69,04] 0,220	3,50 [0,18; 67,21] 0,406	0,01 [-0,00; 0,03] 0,081
Pregnancy and neonatal topics					
Interaction test:	N.E.				
Region = Europe	5 (0,6)	0 (0,0)	5,50 [0,30; 99,64] 0,114	5,47 [0,30; 98,66] 0,250	0,01 [0,00; 0,01] 0,025 *
Region = Other	1 (0,4)	0 (0,0)	1,50 [0,06; 37,18] 0,480	1,50 [0,06; 36,55] 0,803	0,00 [-0,00; 0,01] 0,316
Bradyarrhythmias and bradycardia					
Interaction test:	p=0,549				
Region = Europe	85 (9,9)	27 (6,3)	1,62 [1,04; 2,55] 0,033 *	1,56 [1,03; 2,37] 0,036 *	0,04 [0,01; 0,07] 0,022 *
Region = Other	18 (7,5)	4 (3,4)	2,34 [0,77; 7,08] 0,122	2,24 [0,78; 6,47] 0,136	0,04 [-0,00; 0,09] 0,079

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 total population

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=1099)	**Placebo (N=546)**	**HR [95% CI]**	**p-value**
N'	1099	546		
Any AE				
Number of patients with event	975	445		
Median (in weeks)	4,1 [3,6; 5,3]	7,3 [5,0; 11,1]		
% of event-free patients+	6,82 [4,36; 9,27]	13,39 [9,40; 17,37]		
			1,26 [1,13; 1,41]	<0,001 *
Any AE, disease specific events excluded[1]				
Number of patients with event	918	418		
Median (in weeks)	11,0 [9,0; 12,6]	13,0 [10,9; 17,0]		
% of event-free patients+	10,14 [7,33; 12,95]	16,95 [12,46; 21,44]		
			1,22 [1,09; 1,37]	0,001 *
Any SAE				
Number of patients with event	186	74		
Median (in weeks)	-	-		
% of event-free patients+	75,71 [70,68; 80,74]	79,69 [71,61; 87,78]		
			1,26 [0,96; 1,65]	0,095
Any SAE, disease specific events excluded[1]				
Number of patients with event	146	53		
Median (in weeks)	-	-		
% of event-free patients+	82,01 [78,87; 85,15]	84,05 [76,06; 92,03]		
			1,37 [1,00; 1,87]	0,050
Any severe AE[2]				
Number of patients with event	139	61		
Median (in weeks)	-	-		
% of event-free patients+	83,41 [80,29; 86,53]	85,27 [81,28; 89,25]		
			1,13 [0,84; 1,53]	0,423

	Treatment groups		Comparison	
	BAF312 (N=1099)	**Placebo (N=546)**	**HR [95% CI]**	**p-value**
Any severe AE[2], disease specific events excluded[1]				
Number of patients with event	110	44		
Median (in weeks)	-	-		
% of event-free patients[+]	86,19 [83,17; 89,22]	88,75 [85,04; 92,45]		
			1,23 [0,87; 1,75]	0,244
Any AE leading to study discontinuation				
Number of patients with event	46	16		
Median (in weeks)	-	-		
% of event-free patients[+]	95,50 [94,20; 96,79]	96,24 [94,18; 98,30]		
			1,43 [0,81; 2,53]	0,216
Any AE leading to study drug discontinuation				
Number of patients with event	84	28		
Median (in weeks)	-	-		
% of event-free patients[+]	91,70 [89,97; 93,43]	93,52 [90,99; 96,06]		
			1,49 [0,97; 2,29]	0,066

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 total population

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

	Treatment groups		Comparison	
	BAF312 (N=1099)	**Placebo (N=546)**	**HR [95% CI]**	**p-value**
N'	1099	546		
Grade 1				
Number of patients with event	900	405		
Median (in weeks)	8,4 [5,3; 10,6]	13,0 [10,4; 17,6]		
% of event-free patients+	11,49 [8,42; 14,57]	19,50 [14,76; 24,23]		
			1,25 [1,12; 1,41]	<0,001 *
Grade 2				
Number of patients with event	520	239		
Median (in weeks)	91,6 [77,7; 114,9]	105,0 [85,6; -]		
% of event-free patients+	37,74 [27,13; 48,35]	46,91 [41,25; 52,57]		
			1,09 [0,93; 1,27]	0,280
Grade 3				
Number of patients with event	121	55		
Median (in weeks)	-	-		
% of event-free patients+	85,09 [82,00; 88,18]	86,96 [83,22; 90,71]		
			1,09 [0,79; 1,50]	0,592
Grade 4				
Number of patients with event	23	7		
Median (in weeks)	-	-		
% of event-free patients+	97,56 [96,56; 98,55]	98,03 [96,37; 99,68]		
			1,62 [0,70; 3,78]	0,263
Severe (Grade ≥ 3)				
Number of patients with event	139	61		
Median (in weeks)	-	-		
% of event-free patients+	83,41 [80,29; 86,53]	85,27 [81,28; 89,25]		
			1,13 [0,84; 1,53]	0,423

	Treatment groups		Comparison	
	BAF312 (N=1099)	**Placebo (N=546)**	**HR [95% CI]**	**p-value**
Not severe (Grade < 3)				
Number of patients with event	965	438		
Median (in weeks)	4,3 [3,7; 5,9]	8,1 [5,1; 11,1]		
% of event-free patients+	7,28 [4,74; 9,83]	14,10 [9,93; 18,27]		
			1,26 [1,13; 1,42]	<0,001 *

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 total population

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

	Treatment groups		Comparison	
	BAF312 (N=1099)	Placebo (N=546)	HR [95% CI]	p-value
N'	1099	546		
BLOOD AND LYMPHATIC SYSTEM DISORDERS				
Number of patients with event	46	10		
Median (in weeks)	-	-		
% of event-free patients+	94,62 [92,99; 96,26]	98,05 [96,84; 99,25]		
			2,29 [1,15; 4,53]	0,018 *
ANAEMIA				
Number of patients with event	17	6		
Median (in weeks)	-	-		
% of event-free patients+	98,31 [97,50; 99,11]	98,88 [97,99; 99,77]		
			1,41 [0,56; 3,59]	0,465
CARDIAC DISORDERS				
Number of patients with event	130	55		
Median (in weeks)	-	-		
% of event-free patients+	86,28 [83,61; 88,95]	82,68 [73,23; 92,13]		
			1,19 [0,87; 1,63]	0,280
ATRIOVENTRICULAR BLOCK FIRST DEGREE				
Number of patients with event	14	4		
Median (in weeks)	-	-		
% of event-free patients+	98,50 [97,65; 99,36]	98,79 [97,43; 100,00]		
			1,72 [0,57; 5,23]	0,339
BRADYCARDIA				
Number of patients with event	50	14		
Median (in weeks)	-	-		
% of event-free patients+	95,41 [94,16; 96,65]	97,44 [96,11; 98,76]		
			1,78 [0,99; 3,23]	0,055
PALPITATIONS				
Number of patients with event	20	10		
Median (in weeks)	-	-		
% of event-free patients+	97,98 [97,07; 98,88]	97,93 [96,64; 99,23]		
			0,99 [0,46; 2,12]	0,982

	Treatment groups		Comparison	
	BAF312 (N=1099)	**Placebo (N=546)**	**HR [95% CI]**	**p-value**
SINUS BRADYCARDIA				
Number of patients with event	14	4		
Median (in weeks)	-	-		
% of event-free patients+	98,73 [98,06; 99,39]	99,13 [98,28; 99,99]		
			1,74 [0,57; 5,30]	0,327
EAR AND LABYRINTH DISORDERS				
Number of patients with event	55	38		
Median (in weeks)	-	-		
% of event-free patients+	92,30 [89,18; 95,42]	92,14 [89,69; 94,59]		
			0,70 [0,47; 1,07]	0,097
TINNITUS				
Number of patients with event	13	2		
Median (in weeks)	-	-		
% of event-free patients+	97,16 [94,48; 99,85]	99,59 [99,03; 100,00]		
			3,13 [0,71; 13,90]	0,133
VERTIGO				
Number of patients with event	25	26		
Median (in weeks)	-	-		
% of event-free patients+	97,23 [95,99; 98,47]	94,49 [92,37; 96,60]		
			0,47 [0,27; 0,82]	0,007 *
ENDOCRINE DISORDERS				
Number of patients with event	11	4		
Median (in weeks)	-	-		
% of event-free patients+	96,70 [92,75; 100,00]	99,19 [98,39; 99,99]		
			1,33 [0,42; 4,18]	0,626
EYE DISORDERS				
Number of patients with event	111	54		
Median (in weeks)	-	-		
% of event-free patients+	83,95 [78,25; 89,65]	84,61 [79,51; 89,72]		
			1,00 [0,72; 1,39]	0,993
MACULAR OEDEMA				
Number of patients with event	18	1		
Median (in weeks)	-	-		
% of event-free patients+	98,05 [97,09; 99,00]	99,61 [98,85; 100,00]		
			8,92 [1,19; 66,79]	0,033 *

	Treatment groups		Comparison	
	BAF312 (N=1099)	**Placebo (N=546)**	**HR [95% CI]**	**p-value**
VISION BLURRED				
Number of patients with event	13	9		
Median (in weeks)	-	-		
% of event-free patients+	98,62 [97,84; 99,40]	98,24 [97,10; 99,39]		
			0,72 [0,31; 1,68]	0,443
GASTROINTESTINAL DISORDERS				
Number of patients with event	269	110		
Median (in weeks)	-	-		
% of event-free patients+	69,18 [64,40; 73,96]	76,55 [72,41; 80,69]		
			1,25 [1,00; 1,56]	0,052
ABDOMINAL PAIN				
Number of patients with event	12	3		
Median (in weeks)	-	-		
% of event-free patients+	98,61 [97,78; 99,43]	98,74 [96,95; 100,00]		
			1,96 [0,55; 6,96]	0,296
ABDOMINAL PAIN UPPER				
Number of patients with event	23	11		
Median (in weeks)	-	-		
% of event-free patients+	97,32 [96,12; 98,51]	97,71 [96,29; 99,12]		
			1,03 [0,50; 2,11]	0,941
CONSTIPATION				
Number of patients with event	41	22		
Median (in weeks)	-	-		
% of event-free patients+	93,25 [89,22; 97,28]	95,37 [93,38; 97,36]		
			0,91 [0,54; 1,53]	0,728
DIARRHOEA				
Number of patients with event	70	23		
Median (in weeks)	-	-		
% of event-free patients+	91,44 [89,15; 93,73]	95,18 [93,09; 97,28]		
			1,50 [0,94; 2,41]	0,090
DYSPEPSIA				
Number of patients with event	11	7		
Median (in weeks)	-	-		
% of event-free patients+	98,84 [98,10; 99,57]	97,83 [95,69; 99,96]		
			0,77 [0,30; 2,00]	0,597

	Treatment groups		Comparison	
	BAF312 (N=1099)	**Placebo (N=546)**	**HR [95% CI]**	**p-value**
NAUSEA				
Number of patients with event	74	19		
Median (in weeks)	-	-		
% of event-free patients+	92,64 [90,94; 94,34]	95,82 [93,80; 97,85]		
			1,96 [1,19; 3,25]	0,009 *
VOMITING				
Number of patients with event	33	13		
Median (in weeks)	-	-		
% of event-free patients+	96,53 [95,30; 97,76]	96,94 [95,12; 98,76]		
			1,26 [0,66; 2,40]	0,478
GENERAL DISORDERS AND ADMINISTRATION SITE CONDITIONS				
Number of patients with event	268	110		
Median (in weeks)	-	-		
% of event-free patients+	58,86 [42,56; 75,17]	74,34 [68,32; 80,36]		
			1,25 [1,00; 1,56]	0,053
ASTHENIA				
Number of patients with event	26	7		
Median (in weeks)	-	-		
% of event-free patients+	97,35 [96,33; 98,37]	98,69 [97,73; 99,66]		
			1,85 [0,80; 4,26]	0,149
CHEST DISCOMFORT				
Number of patients with event	11	4		
Median (in weeks)	-	-		
% of event-free patients+	98,87 [98,18; 99,56]	99,23 [98,48; 99,98]		
			1,37 [0,44; 4,31]	0,588
FATIGUE				
Number of patients with event	100	51		
Median (in weeks)	-	-		
% of event-free patients+	89,82 [87,86; 91,79]	86,30 [81,01; 91,59]		
			0,97 [0,70; 1,36]	0,878
GAIT DISTURBANCE				
Number of patients with event	24	22		
Median (in weeks)	-	-		
% of event-free patients+	91,17 [78,80; 100,00]	94,12 [91,43; 96,81]		
			0,53 [0,30; 0,94]	0,030 *

	Treatment groups		Comparison	
	BAF312 (N=1099)	**Placebo (N=546)**	**HR [95% CI]**	**p-value**
INFLUENZA LIKE ILLNESS				
Number of patients with event	14	7		
Median (in weeks)	-	-		
% of event-free patients+	98,67 [97,98; 99,36]	98,67 [97,69; 99,65]		
			1,01 [0,41; 2,49]	0,989
NON-CARDIAC CHEST PAIN				
Number of patients with event	14	6		
Median (in weeks)	-	-		
% of event-free patients+	98,30 [97,23; 99,37]	98,13 [96,55; 99,70]		
			1,14 [0,44; 2,97]	0,786
OEDEMA PERIPHERAL				
Number of patients with event	50	13		
Median (in weeks)	-	-		
% of event-free patients+	88,65 [77,33; 99,96]	97,24 [95,68; 98,79]		
			1,92 [1,04; 3,53]	0,036 *
PAIN				
Number of patients with event	11	4		
Median (in weeks)	-	-		
% of event-free patients+	98,82 [98,11; 99,53]	99,17 [98,36; 99,99]		
			1,37 [0,44; 4,30]	0,591
PERIPHERAL SWELLING				
Number of patients with event	25	6		
Median (in weeks)	-	-		
% of event-free patients+	96,95 [95,59; 98,30]	98,53 [97,30; 99,77]		
			2,06 [0,85; 5,03]	0,111
PYREXIA				
Number of patients with event	23	8		
Median (in weeks)	-	-		
% of event-free patients+	95,69 [93,44; 97,93]	98,39 [97,28; 99,51]		
			1,37 [0,61; 3,07]	0,439
HEPATOBILIARY DISORDERS				
Number of patients with event	27	4		
Median (in weeks)	-	-		
% of event-free patients+	96,69 [95,33; 98,06]	98,89 [97,78; 99,99]		
			3,35 [1,17; 9,57]	0,024 *

	Treatment groups		Comparison	
	BAF312 (N=1099)	**Placebo (N=546)**	**HR [95% CI]**	**p-value**
INFECTIONS AND INFESTATIONS				
Number of patients with event	539	268		
Median (in weeks)	75,6 [66,1; 87,9]	74,1 [62,6; 95,4]		
% of event-free patients+	39,57 [35,34; 43,80]	42,56 [37,22; 47,90]		
			0,99 [0,85; 1,14]	0,874
BRONCHITIS				
Number of patients with event	36	16		
Median (in weeks)	-	-		
% of event-free patients+	95,82 [94,41; 97,22]	94,99 [92,18; 97,81]		
			1,11 [0,61; 2,00]	0,734
CYSTITIS				
Number of patients with event	28	13		
Median (in weeks)	-	-		
% of event-free patients+	96,06 [94,12; 98,00]	97,48 [96,12; 98,83]		
			1,05 [0,55; 2,04]	0,875
GASTROENTERITIS				
Number of patients with event	16	9		
Median (in weeks)	-	-		
% of event-free patients+	98,07 [97,10; 99,03]	97,86 [96,40; 99,32]		
			0,87 [0,38; 1,96]	0,733
HERPES ZOSTER				
Number of patients with event	25	4		
Median (in weeks)	-	-		
% of event-free patients+	97,16 [96,01; 98,31]	98,96 [97,92; 100,00]		
			3,12 [1,09; 8,97]	0,035 *
INFLUENZA				
Number of patients with event	73	40		
Median (in weeks)	-	-		
% of event-free patients+	89,35 [85,29; 93,41]	89,01 [85,03; 92,99]		
			0,89 [0,60; 1,31]	0,548
NASOPHARYNGITIS				
Number of patients with event	149	79		
Median (in weeks)	-	-		
% of event-free patients+	77,00 [70,84; 83,16]	78,63 [69,62; 87,65]		
			0,92 [0,70; 1,21]	0,563

	Treatment groups		Comparison	
	BAF312 (N=1099)	Placebo (N=546)	HR [95% CI]	p-value
ORAL HERPES				
Number of patients with event	18	10		
Median (in weeks)	-	-		
% of event-free patients+	97,99 [97,02; 98,96]	97,10 [94,76; 99,44]		
			0,89 [0,41; 1,93]	0,766
PHARYNGITIS				
Number of patients with event	20	11		
Median (in weeks)	-	-		
% of event-free patients+	97,61 [96,40; 98,82]	96,96 [94,97; 98,95]		
			0,89 [0,43; 1,86]	0,762
RHINITIS				
Number of patients with event	14	10		
Median (in weeks)	-	-		
% of event-free patients+	97,80 [96,44; 99,16]	97,73 [96,19; 99,28]		
			0,68 [0,30; 1,53]	0,349
SINUSITIS				
Number of patients with event	21	9		
Median (in weeks)	-	-		
% of event-free patients+	97,57 [96,47; 98,66]	97,93 [96,52; 99,33]		
			1,15 [0,53; 2,52]	0,719
UPPER RESPIRATORY TRACT INFECTION				
Number of patients with event	91	41		
Median (in weeks)	-	-		
% of event-free patients+	87,41 [84,42; 90,39]	90,77 [87,86; 93,67]		
			1,08 [0,75; 1,56]	0,682
URINARY TRACT INFECTION				
Number of patients with event	133	80		
Median (in weeks)	-	-		
% of event-free patients+	82,96 [79,64; 86,28]	81,93 [77,79; 86,07]		
			0,80 [0,60; 1,05]	0,107
INJURY, POISONING AND PROCEDURAL COMPLICATIONS				
Number of patients with event	238	114		
Median (in weeks)	-	-		
% of event-free patients+	62,00 [48,48; 75,53]	66,96 [56,68; 77,23]		
			1,02 [0,82; 1,28]	0,845

	Treatment groups		Comparison	
	BAF312 (N=1099)	Placebo (N=546)	HR [95% CI]	p-value
CONTUSION				
Number of patients with event	35	15		
Median (in weeks)	-	-		
% of event-free patients+	95,56 [93,87; 97,25]	95,27 [92,36; 98,19]		
			1,14 [0,62; 2,09]	0,664
FALL				
Number of patients with event	128	59		
Median (in weeks)	-	-		
% of event-free patients+	83,22 [79,32; 87,11]	79,08 [68,77; 89,38]		
			1,07 [0,78; 1,45]	0,674
LACERATION				
Number of patients with event	18	4		
Median (in weeks)	-	-		
% of event-free patients+	96,32 [93,34; 99,30]	99,08 [98,15; 100,00]		
			2,19 [0,74; 6,47]	0,157
LIGAMENT SPRAIN				
Number of patients with event	12	6		
Median (in weeks)	-	-		
% of event-free patients+	98,70 [97,95; 99,46]	96,70 [92,34; 100,00]		
			0,98 [0,37; 2,62]	0,972
INVESTIGATIONS				
Number of patients with event	263	80		
Median (in weeks)	-	-		
% of event-free patients+	67,73 [63,75; 71,70]	75,51 [68,98; 82,04]		
			1,72 [1,34; 2,21]	<0,001 *
ALANINE AMINOTRANSFERASE INCREASED				
Number of patients with event	65	8		
Median (in weeks)	-	-		
% of event-free patients+	92,20 [90,17; 94,24]	98,46 [97,39; 99,52]		
			4,09 [1,96; 8,53]	<0,001 *
ASPARTATE AMINOTRANSFERASE INCREASED				
Number of patients with event	15	4		
Median (in weeks)	-	-		
% of event-free patients+	98,36 [97,50; 99,21]	99,17 [98,36; 99,98]		
			1,86 [0,62; 5,60]	0,270

	Treatment groups		Comparison	
	BAF312 (N=1099)	Placebo (N=546)	HR [95% CI]	p-value
BLOOD ALKALINE PHOSPHATASE INCREASED				
Number of patients with event	12	0		
Median (in weeks)	-	-		
% of event-free patients+	98,00 [96,25; 99,75]	100,00 [100,00; 100,00]		
			-	-
BLOOD BILIRUBIN INCREASED				
Number of patients with event	12	2		
Median (in weeks)	-	-		
% of event-free patients+	98,82 [98,16; 99,49]	99,63 [99,11; 100,00]		
			3,01 [0,67; 13,44]	0,149
BLOOD CHOLESTEROL INCREASED				
Number of patients with event	20	6		
Median (in weeks)	-	-		
% of event-free patients+	97,15 [95,71; 98,59]	97,90 [95,65; 100,00]		
			1,63 [0,65; 4,06]	0,295
BLOOD PRESSURE INCREASED				
Number of patients with event	19	7		
Median (in weeks)	-	-		
% of event-free patients+	97,93 [96,94; 98,92]	98,08 [96,61; 99,55]		
			1,34 [0,56; 3,19]	0,505
GAMMA-GLUTAMYLTRANSFERASE INCREASED				
Number of patients with event	43	6		
Median (in weeks)	-	-		
% of event-free patients+	94,49 [92,42; 96,55]	97,99 [96,19; 99,79]		
			3,57 [1,52; 8,38]	0,004 *
HEPATIC ENZYME INCREASED				
Number of patients with event	16	1		
Median (in weeks)	-	-		
% of event-free patients+	98,31 [97,47; 99,15]	99,73 [99,19; 100,00]		
			7,97 [1,06; 60,10]	0,044 *
WEIGHT DECREASED				
Number of patients with event	22	9		
Median (in weeks)	-	-		
% of event-free patients+	96,94 [95,56; 98,32]	96,51 [93,67; 99,35]		
			1,19 [0,55; 2,58]	0,662

	Treatment groups		Comparison	
	BAF312 (N=1099)	**Placebo (N=546)**	**HR [95% CI]**	**p-value**
WEIGHT INCREASED				
Number of patients with event	27	13		
Median (in weeks)	-	-		
% of event-free patients+	95,18 [93,06; 97,31]	96,06 [93,36; 98,76]		
			0,99 [0,51; 1,92]	0,982
METABOLISM AND NUTRITION DISORDERS				
Number of patients with event	85	28		
Median (in weeks)	-	-		
% of event-free patients+	89,16 [86,46; 91,85]	93,49 [90,93; 96,04]		
			1,52 [0,99; 2,33]	0,055
HYPERCHOLESTEROLAEMIA				
Number of patients with event	28	11		
Median (in weeks)	-	-		
% of event-free patients+	96,20 [94,34; 98,05]	97,15 [95,23; 99,07]		
			1,25 [0,62; 2,52]	0,528
VITAMIN D DEFICIENCY				
Number of patients with event	11	7		
Median (in weeks)	-	-		
% of event-free patients+	98,47 [97,52; 99,42]	98,42 [97,23; 99,61]		
			0,77 [0,30; 1,97]	0,580
MUSCULOSKELETAL AND CONNECTIVE TISSUE DISORDERS				
Number of patients with event	289	149		
Median (in weeks)	-	-		
% of event-free patients+	67,76 [64,24; 71,27]	62,77 [55,78; 69,77]		
			0,95 [0,78; 1,15]	0,578
ARTHRALGIA				
Number of patients with event	49	35		
Median (in weeks)	-	-		
% of event-free patients+	94,56 [92,96; 96,15]	91,50 [88,56; 94,45]		
			0,69 [0,45; 1,06]	0,090
BACK PAIN				
Number of patients with event	67	43		
Median (in weeks)	-	-		
% of event-free patients+	92,10 [90,08; 94,12]	87,70 [82,99; 92,40]		
			0,76 [0,52; 1,11]	0,156

	Treatment groups		Comparison	
	BAF312 (N=1099)	**Placebo (N=546)**	**HR [95% CI]**	**p-value**
JOINT SWELLING				
Number of patients with event	17	7		
Median (in weeks)	-	-		
% of event-free patients+	98,22 [97,35; 99,08]	98,57 [97,51; 99,63]		
			1,22 [0,50; 2,93]	0,662
MUSCLE SPASMS				
Number of patients with event	37	19		
Median (in weeks)	-	-		
% of event-free patients+	95,52 [93,97; 97,07]	95,16 [92,44; 97,87]		
			0,95 [0,55; 1,65]	0,858
MUSCULAR WEAKNESS				
Number of patients with event	17	13		
Median (in weeks)	-	-		
% of event-free patients+	98,14 [97,22; 99,06]	96,88 [95,15; 98,61]		
			0,64 [0,31; 1,32]	0,227
MUSCULOSKELETAL PAIN				
Number of patients with event	27	14		
Median (in weeks)	-	-		
% of event-free patients+	96,54 [95,04; 98,04]	95,24 [92,15; 98,33]		
			0,94 [0,49; 1,80]	0,860
MYALGIA				
Number of patients with event	13	8		
Median (in weeks)	-	-		
% of event-free patients+	98,74 [98,05; 99,42]	98,32 [97,12; 99,53]		
			0,81 [0,33; 1,95]	0,633
NECK PAIN				
Number of patients with event	13	7		
Median (in weeks)	-	-		
% of event-free patients+	98,52 [97,71; 99,34]	98,37 [97,03; 99,70]		
			0,91 [0,36; 2,28]	0,840
PAIN IN EXTREMITY				
Number of patients with event	60	21		
Median (in weeks)	-	-		
% of event-free patients+	91,78 [89,28; 94,28]	94,24 [91,42; 97,07]		
			1,40 [0,85; 2,31]	0,180

	Treatment groups		Comparison	
	BAF312 (N=1099)	**Placebo (N=546)**	**HR [95% CI]**	**p-value**
NEOPLASMS BENIGN, MALIGNANT AND UNSPECIFIED (INCL CYSTS AND POLYPS)				
Number of patients with event	113	45		
Median (in weeks)	-	-		
% of event-free patients+	71,57 [52,37; 90,78]	78,80 [67,85; 89,75]		
			1,21 [0,85; 1,71]	0,285
BASAL CELL CARCINOMA				
Number of patients with event	12	7		
Median (in weeks)	-	-		
% of event-free patients+	97,74 [95,97; 99,51]	94,18 [85,88; 100,00]		
			0,80 [0,32; 2,04]	0,646
MELANOCYTIC NAEVUS				
Number of patients with event	47	17		
Median (in weeks)	-	-		
% of event-free patients+	90,95 [87,59; 94,30]	92,03 [87,01; 97,05]		
			1,30 [0,74; 2,26]	0,361
NERVOUS SYSTEM DISORDERS				
Number of patients with event	416	175		
Median (in weeks)	-	-		
% of event-free patients+	51,57 [43,12; 60,02]	62,75 [57,53; 67,96]		
			1,22 [1,02; 1,45]	0,028 *
BALANCE DISORDER				
Number of patients with event	13	5		
Median (in weeks)	-	-		
% of event-free patients+	98,63 [97,88; 99,39]	97,83 [95,44; 100,00]		
			1,27 [0,45; 3,57]	0,647
DIZZINESS				
Number of patients with event	75	26		
Median (in weeks)	-	-		
% of event-free patients+	92,36 [90,55; 94,17]	94,53 [92,32; 96,75]		
			1,45 [0,93; 2,26]	0,106
HEADACHE				
Number of patients with event	159	71		
Median (in weeks)	-	-		
% of event-free patients+	82,42 [79,06; 85,79]	82,61 [77,82; 87,40]		
			1,11 [0,84; 1,47]	0,461

	Treatment groups		Comparison	
	BAF312 (N=1099)	**Placebo (N=546)**	**HR [95% CI]**	**p-value**
HYPOAESTHESIA				
Number of patients with event	15	15		
Median (in weeks)	-	-		
% of event-free patients+	98,41 [97,58; 99,25]	96,17 [93,66; 98,68]		
			0,49 [0,24; 1,01]	0,052
MIGRAINE				
Number of patients with event	16	8		
Median (in weeks)	-	-		
% of event-free patients+	98,21 [97,28; 99,13]	98,01 [96,52; 99,50]		
			0,99 [0,42; 2,32]	0,984
MUSCLE SPASTICITY				
Number of patients with event	43	23		
Median (in weeks)	-	-		
% of event-free patients+	95,05 [93,38; 96,72]	93,27 [89,32; 97,23]		
			0,92 [0,55; 1,53]	0,750
NEURALGIA				
Number of patients with event	14	5		
Median (in weeks)	-	-		
% of event-free patients+	97,99 [96,77; 99,21]	99,02 [98,16; 99,88]		
			1,37 [0,49; 3,79]	0,550
PARAESTHESIA				
Number of patients with event	18	20		
Median (in weeks)	-	-		
% of event-free patients+	97,28 [95,52; 99,04]	95,32 [93,06; 97,59]		
			0,44 [0,23; 0,82]	0,011 *
SCIATICA				
Number of patients with event	18	5		
Median (in weeks)	-	-		
% of event-free patients+	96,06 [91,92; 100,00]	98,99 [98,11; 99,87]		
			1,78 [0,66; 4,79]	0,256
SOMNOLENCE				
Number of patients with event	11	5		
Median (in weeks)	-	-		
% of event-free patients+	98,98 [98,38; 99,58]	98,17 [96,07; 100,00]		
			1,08 [0,38; 3,12]	0,881

	Treatment groups		Comparison	
	BAF312 (N=1099)	**Placebo (N=546)**	**HR [95% CI]**	**p-value**
SYNCOPE				
Number of patients with event	14	7		
Median (in weeks)	-	-		
% of event-free patients+	97,04 [94,16; 99,92]	97,97 [96,32; 99,63]		
			0,96 [0,39; 2,38]	0,932
TREMOR				
Number of patients with event	17	3		
Median (in weeks)	-	-		
% of event-free patients+	97,82 [96,49; 99,16]	99,43 [98,78; 100,00]		
			2,81 [0,82; 9,60]	0,099
TRIGEMINAL NEURALGIA				
Number of patients with event	17	5		
Median (in weeks)	-	-		
% of event-free patients+	92,53 [82,64; 100,00]	99,06 [98,24; 99,88]		
			1,64 [0,60; 4,45]	0,332
PSYCHIATRIC DISORDERS				
Number of patients with event	169	83		
Median (in weeks)	-	-		
% of event-free patients+	78,50 [73,55; 83,46]	80,77 [76,47; 85,07]		
			1,01 [0,78; 1,32]	0,912
ANXIETY				
Number of patients with event	23	14		
Median (in weeks)	-	-		
% of event-free patients+	97,64 [96,67; 98,61]	96,57 [94,62; 98,52]		
			0,82 [0,42; 1,59]	0,555
DEPRESSED MOOD				
Number of patients with event	16	7		
Median (in weeks)	-	-		
% of event-free patients+	97,75 [96,43; 99,08]	98,52 [97,39; 99,64]		
			1,12 [0,46; 2,73]	0,797
DEPRESSION				
Number of patients with event	49	30		
Median (in weeks)	-	-		
% of event-free patients+	94,22 [92,45; 96,00]	92,28 [89,06; 95,50]		
			0,80 [0,51; 1,27]	0,348

	Treatment groups		Comparison	
	BAF312 (N=1099)	**Placebo (N=546)**	**HR [95% CI]**	**p-value**
INSOMNIA				
Number of patients with event	38	19		
Median (in weeks)	-	-		
% of event-free patients+	93,80 [89,81; 97,78]	96,06 [94,26; 97,86]		
			0,99 [0,57; 1,72]	0,970
SLEEP DISORDER				
Number of patients with event	11	5		
Median (in weeks)	-	-		
% of event-free patients+	98,74 [97,97; 99,52]	98,85 [97,81; 99,89]		
			1,08 [0,38; 3,11]	0,884
RENAL AND URINARY DISORDERS				
Number of patients with event	84	37		
Median (in weeks)	-	-		
% of event-free patients+	89,72 [87,39; 92,05]	90,73 [87,60; 93,86]		
			1,13 [0,76; 1,66]	0,549
DYSURIA				
Number of patients with event	11	3		
Median (in weeks)	-	-		
% of event-free patients+	98,93 [98,30; 99,56]	99,41 [98,73; 100,00]		
			1,85 [0,52; 6,64]	0,344
URINARY INCONTINENCE				
Number of patients with event	13	12		
Median (in weeks)	-	-		
% of event-free patients+	98,61 [97,85; 99,37]	96,53 [94,41; 98,64]		
			0,53 [0,24; 1,16]	0,113
URINARY RETENTION				
Number of patients with event	14	8		
Median (in weeks)	-	-		
% of event-free patients+	98,02 [96,83; 99,22]	97,76 [96,04; 99,49]		
			0,84 [0,35; 2,01]	0,701
REPRODUCTIVE SYSTEM AND BREAST DISORDERS				
Number of patients with event	36	24		
Median (in weeks)	-	-		
% of event-free patients+	95,37 [93,67; 97,07]	93,32 [90,14; 96,50]		
			0,73 [0,43; 1,22]	0,226

	Treatment groups		Comparison	
	BAF312 (N=1099)	**Placebo (N=546)**	**HR [95% CI]**	**p-value**
RESPIRATORY, THORACIC AND MEDIASTINAL DISORDERS				
Number of patients with event	117	71		
Median (in weeks)	-	-		
% of event-free patients+	87,31 [85,06; 89,55]	76,70 [66,49; 86,92]		
			0,80 [0,60; 1,08]	0,140
COUGH				
Number of patients with event	35	18		
Median (in weeks)	-	-		
% of event-free patients+	95,93 [94,52; 97,33]	95,83 [93,76; 97,89]		
			0,96 [0,54; 1,69]	0,875
DYSPNOEA				
Number of patients with event	19	10		
Median (in weeks)	-	-		
% of event-free patients+	98,03 [97,13; 98,92]	96,69 [93,91; 99,46]		
			0,94 [0,43; 2,01]	0,864
OROPHARYNGEAL PAIN				
Number of patients with event	20	17		
Median (in weeks)	-	-		
% of event-free patients+	97,30 [95,82; 98,79]	96,33 [94,44; 98,22]		
			0,57 [0,30; 1,09]	0,091
SKIN AND SUBCUTANEOUS TISSUE DISORDERS				
Number of patients with event	188	93		
Median (in weeks)	-	-		
% of event-free patients+	70,86 [61,91; 79,82]	72,15 [64,84; 79,47]		
			0,96 [0,75; 1,24]	0,770
ACTINIC KERATOSIS				
Number of patients with event	15	6		
Median (in weeks)	-	-		
% of event-free patients+	92,63 [82,74; 100,00]	98,29 [96,76; 99,83]		
			1,16 [0,45; 2,99]	0,760
ECZEMA				
Number of patients with event	17	5		
Median (in weeks)	-	-		
% of event-free patients+	97,70 [96,11; 99,29]	98,06 [95,86; 100,00]		
			1,66 [0,61; 4,51]	0,317

	Treatment groups		Comparison	
	BAF312 (N=1099)	**Placebo (N=546)**	**HR [95% CI]**	**p-value**
RASH				
Number of patients with event	20	13		
Median (in weeks)	-	-		
% of event-free patients+	97,67 [96,57; 98,77]	94,96 [90,40; 99,52]		
			0,74 [0,37; 1,50]	0,408
VASCULAR DISORDERS				
Number of patients with event	160	60		
Median (in weeks)	-	-		
% of event-free patients+	79,26 [74,48; 84,04]	80,67 [71,83; 89,50]		
			1,32 [0,98; 1,78]	0,065
HAEMATOMA				
Number of patients with event	15	3		
Median (in weeks)	-	-		
% of event-free patients+	98,29 [97,39; 99,18]	99,03 [97,88; 100,00]		
			2,47 [0,72; 8,54]	0,153
HYPERTENSION				
Number of patients with event	115	41		
Median (in weeks)	-	-		
% of event-free patients+	84,83 [80,48; 89,19]	86,19 [77,37; 95,01]		
			1,39 [0,97; 1,98]	0,073

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 total population

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

	Treatment groups		Comparison	
	BAF312 (N=1099)	Placebo (N=546)	HR [95% CI]	p-value
N'	1099	546		
INFECTIONS AND INFESTATIONS				
Number of patients with event	33	15		
Median (in weeks)	-	-		
% of event-free patients+	95,86 [94,36; 97,37]	95,56 [92,76; 98,35]		
			1,08 [0,59; 1,99]	0,799
URINARY TRACT INFECTION				
Number of patients with event	13	6		
Median (in weeks)	-	-		
% of event-free patients+	98,62 [97,85; 99,39]	98,85 [97,93; 99,76]		
			1,09 [0,41; 2,86]	0,866
INJURY, POISONING AND PROCEDURAL COMPLICATIONS				
Number of patients with event	20	5		
Median (in weeks)	-	-		
% of event-free patients+	97,00 [95,54; 98,45]	98,83 [97,77; 99,89]		
			1,93 [0,73; 5,16]	0,187
INVESTIGATIONS				
Number of patients with event	21	3		
Median (in weeks)	-	-		
% of event-free patients+	97,74 [96,75; 98,73]	99,40 [98,72; 100,00]		
			3,46 [1,03; 11,61]	0,044 *
MUSCULOSKELETAL AND CONNECTIVE TISSUE DISORDERS				
Number of patients with event	12	3		
Median (in weeks)	-	-		
% of event-free patients+	98,21 [97,12; 99,29]	99,35 [98,61; 100,00]		
			1,92 [0,54; 6,82]	0,311
NEOPLASMS BENIGN, MALIGNANT AND UNSPECIFIED (INCL CYSTS AND POLYPS)				
Number of patients with event	23	15		
Median (in weeks)	-	-		
% of event-free patients+	96,61 [94,72; 98,49]	91,96 [83,66; 100,00]		
			0,74 [0,38; 1,41]	0,357

	Treatment groups		Comparison	
	BAF312 (N=1099)	**Placebo (N=546)**	**HR [95% CI]**	**p-value**
BASAL CELL CARCINOMA				
Number of patients with event	11	6		
Median (in weeks)	-	-		
% of event-free patients+	97,86 [96,11; 99,61]	94,37 [86,06; 100,00]		
			0,85 [0,32; 2,31]	0,757
NERVOUS SYSTEM DISORDERS				
Number of patients with event	40	17		
Median (in weeks)	-	-		
% of event-free patients+	93,67 [90,33; 97,01]	95,85 [93,81; 97,90]		
			1,15 [0,65; 2,03]	0,623
PSYCHIATRIC DISORDERS				
Number of patients with event	22	7		
Median (in weeks)	-	-		
% of event-free patients+	97,68 [96,69; 98,66]	98,66 [97,67; 99,65]		
			1,57 [0,67; 3,68]	0,297
RENAL AND URINARY DISORDERS				
Number of patients with event	14	3		
Median (in weeks)	-	-		
% of event-free patients+	98,30 [97,40; 99,21]	99,30 [98,50; 100,00]		
			2,28 [0,66; 7,95]	0,194

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 ≥ 5% in at least one treatment arm are displayed.

Analysis population: A2304 SAF total population

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

	Treatment groups		Comparison	
	BAF312 (N=1099)	**Placebo (N=546)**	**HR [95% CI]**	**p-value**
N'	1099	546		
BLOOD AND LYMPHATIC SYSTEM DISORDERS				
not severe[1]				
Number of patients with event	41	8		
Median (in weeks)	-	-		
% of event-free patients+	95,15 [93,57; 96,73]	98,42 [97,33; 99,51]		
			2,55 [1,19; 5,43]	0,016 *
severe[1]				
Number of patients with event	5	2		
Median (in weeks)	-	-		
% of event-free patients+	99,47 [99,00; 99,94]	99,62 [99,10; 100,00]		
			1,24 [0,24; 6,40]	0,796
ANAEMIA				
not severe[1]				
Number of patients with event	17	4		
Median (in weeks)	-	-		
% of event-free patients+	98,31 [97,50; 99,11]	99,26 [98,53; 99,98]		
			2,12 [0,71; 6,31]	0,175
severe[1]				
Number of patients with event	0	2		
Median (in weeks)	-	-		
% of event-free patients+	100,00 [100,00; 100,00]	99,62 [99,10; 100,00]		
			-	-
CARDIAC DISORDERS				
not severe[1]				
Number of patients with event	127	53		
Median (in weeks)	-	-		
% of event-free patients+	86,54 [83,88; 89,21]	83,32 [73,84; 92,79]		
			1,21 [0,88; 1,66]	0,253

	Treatment groups		Comparison	
	BAF312 (N=1099)	**Placebo (N=546)**	**HR [95% CI]**	**p-value**
severe[1]				
Number of patients with event	6	3		
Median (in weeks)	-	-		
% of event-free patients+	99,43 [98,98; 99,89]	99,11 [98,02; 100,00]		
			0,99 [0,25; 3,97]	0,990
ATRIOVENTRICULAR BLOCK FIRST DEGREE				
not severe[1]				
Number of patients with event	14	4		
Median (in weeks)	-	-		
% of event-free patients+	98,50 [97,65; 99,36]	98,79 [97,43; 100,00]		
			1,72 [0,57; 5,23]	0,339
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]		
			-	-
BRADYCARDIA				
not severe[1]				
Number of patients with event	48	14		
Median (in weeks)	-	-		
% of event-free patients+	95,59 [94,37; 96,81]	97,44 [96,11; 98,76]		
			1,71 [0,94; 3,11]	0,077
severe[1]				
Number of patients with event	2	0		
Median (in weeks)	-	-		
% of event-free patients+	99,82 [99,57; 100,00]	100,00 [100,00; 100,00]		
			-	-
PALPITATIONS				
not severe[1]				
Number of patients with event	19	10		
Median (in weeks)	-	-		
% of event-free patients+	98,08 [97,20; 98,96]	97,93 [96,64; 99,23]		
			0,94 [0,44; 2,03]	0,878

	Treatment groups		Comparison	
	BAF312 (N=1099)	**Placebo (N=546)**	**HR [95% CI]**	**p-value**
severe[1]				
Number of patients with event	1	0		
Median (in weeks)	-	-		
% of event-free patients+	99,89 [99,68; 100,00]	100,00 [100,00; 100,00]		
			-	-
SINUS BRADYCARDIA				
not severe[1]				
Number of patients with event	14	4		
Median (in weeks)	-	-		
% of event-free patients+	98,73 [98,06; 99,39]	99,13 [98,28; 99,99]		
			1,74 [0,57; 5,30]	0,327
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]		
			-	-
EAR AND LABYRINTH DISORDERS				
not severe[1]				
Number of patients with event	55	36		
Median (in weeks)	-	-		
% of event-free patients+	92,30 [89,18; 95,42]	92,51 [90,10; 94,92]		
			0,75 [0,49; 1,13]	0,171
severe[1]				
Number of patients with event	0	2		
Median (in weeks)	-	-		
% of event-free patients+	100,00 [100,00; 100,00]	99,63 [99,12; 100,00]		
			-	-
TINNITUS				
not severe[1]				
Number of patients with event	13	2		
Median (in weeks)	-	-		
% of event-free patients+	97,16 [94,48; 99,85]	99,59 [99,03; 100,00]		
			3,13 [0,71; 13,90]	0,133

	Treatment groups		Comparison	
	BAF312 (N=1099)	**Placebo (N=546)**	**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]		
			-	-
VERTIGO				
not severe[1]				
Number of patients with event	25	25		
Median (in weeks)	-	-		
% of event-free patients+	97,23 [95,99; 98,47]	94,67 [92,58; 96,75]		
			0,49 [0,28; 0,85]	0,012 *
severe[1]				
Number of patients with event	0	1		
Median (in weeks)	-	-		
% of event-free patients+	100,00 [100,00; 100,00]	99,82 [99,46; 100,00]		
			-	-
ENDOCRINE DISORDERS				
not severe[1]				
Number of patients with event	11	4		
Median (in weeks)	-	-		
% of event-free patients+	96,70 [92,75; 100,00]	99,19 [98,39; 99,99]		
			1,33 [0,42; 4,18]	0,626
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	107	54		
Median (in weeks)	-	-		
% of event-free patients+	84,27 [78,56; 89,99]	84,61 [79,50; 89,72]		
			0,96 [0,69; 1,34]	0,824

	Treatment groups		Comparison	
	BAF312 (N=1099)	**Placebo (N=546)**	**HR [95% CI]**	**p-value**
severe[1]				
Number of patients with event	7	1		
Median (in weeks)	-	-		
% of event-free patients+	99,33 [98,83; 99,82]	99,82 [99,46; 100,00]		
			3,50 [0,43; 28,48]	0,241
MACULAR OEDEMA				
not severe[1]				
Number of patients with event	14	0		
Median (in weeks)	-	-		
% of event-free patients+	98,43 [97,54; 99,31]	100,00 [100,00; 100,00]		
			-	-
severe[1]				
Number of patients with event	4	1		
Median (in weeks)	-	-		
% of event-free patients+	99,62 [99,24; 99,99]	99,61 [98,85; 100,00]		
			1,97 [0,22; 17,61]	0,545
VISION BLURRED				
not severe[1]				
Number of patients with event	13	9		
Median (in weeks)	-	-		
% of event-free patients+	98,62 [97,84; 99,40]	98,24 [97,10; 99,39]		
			0,72 [0,31; 1,68]	0,443
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]		
			-	-
GASTROINTESTINAL DISORDERS				
not severe[1]				
Number of patients with event	268	107		
Median (in weeks)	-	-		
% of event-free patients+	69,22 [64,43; 74,00]	77,17 [73,06; 81,29]		
			1,27 [1,02; 1,59]	0,034 *

	Treatment groups		Comparison	
	BAF312 (N=1099)	**Placebo (N=546)**	**HR [95% CI]**	**p-value**
severe[1]				
Number of patients with event	5	4		
Median (in weeks)	-	-		
% of event-free patients+	99,41 [98,86; 99,96]	99,15 [98,31; 99,98]		
			0,62 [0,17; 2,32]	0,480
ABDOMINAL PAIN				
not severe[1]				
Number of patients with event	12	3		
Median (in weeks)	-	-		
% of event-free patients+	98,61 [97,78; 99,43]	98,74 [96,95; 100,00]		
			1,96 [0,55; 6,96]	0,296
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]		
			-	-
ABDOMINAL PAIN UPPER				
not severe[1]				
Number of patients with event	23	11		
Median (in weeks)	-	-		
% of event-free patients+	97,32 [96,12; 98,51]	97,71 [96,29; 99,12]		
			1,03 [0,50; 2,11]	0,940
severe[1]				
Number of patients with event	1	0		
Median (in weeks)	-	-		
% of event-free patients+	99,91 [99,73; 100,00]	100,00 [100,00; 100,00]		
			-	-
CONSTIPATION				
not severe[1]				
Number of patients with event	41	22		
Median (in weeks)	-	-		
% of event-free patients+	93,25 [89,22; 97,28]	95,37 [93,38; 97,36]		
			0,91 [0,54; 1,53]	0,728

	Treatment groups		Comparison	
	BAF312 (N=1099)	**Placebo (N=546)**	**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]		
			-	-
DIARRHOEA				
not severe[1]				
Number of patients with event	69	23		
Median (in weeks)	-	-		
% of event-free patients+	91,55 [89,27; 93,83]	95,18 [93,09; 97,28]		
			1,48 [0,92; 2,37]	0,103
severe[1]				
Number of patients with event	2	0		
Median (in weeks)	-	-		
% of event-free patients+	99,81 [99,54; 100,00]	100,00 [100,00; 100,00]		
			-	-
DYSPEPSIA				
not severe[1]				
Number of patients with event	11	7		
Median (in weeks)	-	-		
% of event-free patients+	98,84 [98,10; 99,57]	97,83 [95,69; 99,96]		
			0,77 [0,30; 2,00]	0,597
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]		
			-	-
NAUSEA				
not severe[1]				
Number of patients with event	73	19		
Median (in weeks)	-	-		
% of event-free patients+	92,74 [91,04; 94,43]	95,82 [93,80; 97,85]		
			1,93 [1,17; 3,21]	0,010 *

	Treatment groups		Comparison	
	BAF312 (N=1099)	**Placebo (N=546)**	**HR [95% CI]**	**p-value**
severe[1]				
Number of patients with event	2	0		
Median (in weeks)	-	-		
% of event-free patients+	99,81 [99,55; 100,00]	100,00 [100,00; 100,00]		
			-	-
VOMITING				
not severe[1]				
Number of patients with event	33	13		
Median (in weeks)	-	-		
% of event-free patients+	96,53 [95,30; 97,76]	96,94 [95,12; 98,76]		
			1,26 [0,66; 2,40]	0,478
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	265	108		
Median (in weeks)	-	-		
% of event-free patients+	58,80 [42,49; 75,10]	74,66 [68,63; 80,69]		
			1,25 [1,00; 1,57]	0,048 *
severe[1]				
Number of patients with event	6	3		
Median (in weeks)	-	-		
% of event-free patients+	99,28 [98,67; 99,89]	99,45 [98,82; 100,00]		
			0,99 [0,25; 3,96]	0,989
ASTHENIA				
not severe[1]				
Number of patients with event	25	7		
Median (in weeks)	-	-		
% of event-free patients+	97,44 [96,44; 98,45]	98,69 [97,73; 99,66]		
			1,78 [0,77; 4,11]	0,179

	Treatment groups		Comparison	
	BAF312 (N=1099)	**Placebo (N=546)**	**HR [95% CI]**	**p-value**
severe[1]				
Number of patients with event	1	0		
Median (in weeks)	-	-		
% of event-free patients+	99,90 [99,72; 100,00]	100,00 [100,00; 100,00]		
			-	-
CHEST DISCOMFORT				
not severe[1]				
Number of patients with event	11	4		
Median (in weeks)	-	-		
% of event-free patients+	98,87 [98,18; 99,56]	99,23 [98,48; 99,98]		
			1,37 [0,44; 4,31]	0,588
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]		
			-	-
FATIGUE				
not severe[1]				
Number of patients with event	98	50		
Median (in weeks)	-	-		
% of event-free patients+	89,66 [87,48; 91,85]	86,47 [81,18; 91,76]		
			0,97 [0,69; 1,37]	0,866
severe[1]				
Number of patients with event	4	1		
Median (in weeks)	-	-		
% of event-free patients+	99,50 [98,97; 100,00]	99,82 [99,46; 100,00]		
			1,98 [0,22; 17,72]	0,541
GAIT DISTURBANCE				
not severe[1]				
Number of patients with event	24	21		
Median (in weeks)	-	-		
% of event-free patients+	91,17 [78,80; 100,00]	94,30 [91,63; 96,97]		
			0,55 [0,31; 0,99]	0,048 *

	Treatment groups		Comparison	
	BAF312 (N=1099)	**Placebo (N=546)**	**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]	99,82 [99,46; 100,00]		
			-	-
INFLUENZA LIKE ILLNESS				
not severe[1]				
Number of patients with event	14	7		
Median (in weeks)	-	-		
% of event-free patients+	98,67 [97,98; 99,36]	98,67 [97,69; 99,65]		
			1,01 [0,41; 2,49]	0,989
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]		
			-	-
NON-CARDIAC CHEST PAIN				
not severe[1]				
Number of patients with event	13	6		
Median (in weeks)	-	-		
% of event-free patients+	98,42 [97,38; 99,47]	98,13 [96,55; 99,70]		
			1,06 [0,40; 2,79]	0,905
severe[1]				
Number of patients with event	1	0		
Median (in weeks)	-	-		
% of event-free patients+	99,88 [99,64; 100,00]	100,00 [100,00; 100,00]		
			-	-
OEDEMA PERIPHERAL				
not severe[1]				
Number of patients with event	50	13		
Median (in weeks)	-	-		
% of event-free patients+	88,65 [77,33; 99,96]	97,24 [95,68; 98,79]		
			1,92 [1,04; 3,53]	0,036 *

	Treatment groups		Comparison	
	BAF312 (N=1099)	**Placebo (N=546)**	**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]		
			-	-
PAIN				
not severe[1]				
Number of patients with event	11	4		
Median (in weeks)	-	-		
% of event-free patients+	98,82 [98,11; 99,53]	99,17 [98,36; 99,99]		
			1,37 [0,44; 4,30]	0,591
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]		
			-	-
PERIPHERAL SWELLING				
not severe[1]				
Number of patients with event	25	6		
Median (in weeks)	-	-		
% of event-free patients+	96,95 [95,59; 98,30]	98,53 [97,30; 99,77]		
			2,06 [0,85; 5,03]	0,111
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]		
			-	-
PYREXIA				
not severe[1]				
Number of patients with event	23	8		
Median (in weeks)	-	-		
% of event-free patients+	95,69 [93,44; 97,93]	98,39 [97,28; 99,51]		
			1,37 [0,61; 3,07]	0,439

	Treatment groups		Comparison	
	BAF312 (N=1099)	**Placebo (N=546)**	**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]		
			-	-
HEPATOBILIARY DISORDERS				
not severe[1]				
Number of patients with event	22	4		
Median (in weeks)	-	-		
% of event-free patients+	97,30 [96,06; 98,55]	98,89 [97,78; 99,99]		
			2,72 [0,94; 7,89]	0,066
severe[1]				
Number of patients with event	5	0		
Median (in weeks)	-	-		
% of event-free patients+	99,39 [98,81; 99,96]	100,00 [100,00; 100,00]		
			-	-
INFECTIONS AND INFESTATIONS				
not severe[1]				
Number of patients with event	528	262		
Median (in weeks)	80,1 [71,9; 98,0]	77,6 [63,1; 105,0]		
% of event-free patients+	40,33 [36,00; 44,66]	43,59 [38,22; 48,96]		
			0,99 [0,85; 1,14]	0,844
severe[1]				
Number of patients with event	24	11		
Median (in weeks)	-	-		
% of event-free patients+	97,20 [96,02; 98,38]	96,91 [94,51; 99,31]		
			1,08 [0,53; 2,21]	0,831
BRONCHITIS				
not severe[1]				
Number of patients with event	36	16		
Median (in weeks)	-	-		
% of event-free patients+	95,82 [94,41; 97,22]	94,99 [92,18; 97,81]		
			1,11 [0,61; 2,00]	0,734

	Treatment groups		Comparison	
	BAF312 (N=1099)	**Placebo (N=546)**	**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]		
			-	-
CYSTITIS				
not severe[1]				
Number of patients with event	28	13		
Median (in weeks)	-	-		
% of event-free patients+	96,06 [94,12; 98,00]	97,48 [96,12; 98,83]		
			1,05 [0,55; 2,04]	0,875
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]		
			-	-
GASTROENTERITIS				
not severe[1]				
Number of patients with event	16	8		
Median (in weeks)	-	-		
% of event-free patients+	98,07 [97,10; 99,03]	98,12 [96,75; 99,49]		
			0,98 [0,42; 2,29]	0,960
severe[1]				
Number of patients with event	0	1		
Median (in weeks)	-	-		
% of event-free patients+	100,00 [100,00; 100,00]	99,74 [99,23; 100,00]		
			-	-
HERPES ZOSTER				
not severe[1]				
Number of patients with event	22	4		
Median (in weeks)	-	-		
% of event-free patients+	97,46 [96,36; 98,56]	98,96 [97,92; 100,00]		
			2,74 [0,94; 7,95]	0,064

	Treatment groups		Comparison	
	BAF312 (N=1099)	**Placebo (N=546)**	**HR [95% CI]**	**p-value**
severe[1]				
Number of patients with event	3	0		
Median (in weeks)	-	-		
% of event-free patients+	99,70 [99,37; 100,00]	100,00 [100,00; 100,00]		
			-	-
INFLUENZA				
not severe[1]				
Number of patients with event	72	39		
Median (in weeks)	-	-		
% of event-free patients+	89,44 [85,38; 93,50]	89,19 [85,22; 93,16]		
			0,90 [0,61; 1,33]	0,590
severe[1]				
Number of patients with event	1	2		
Median (in weeks)	-	-		
% of event-free patients+	99,91 [99,72; 100,00]	98,77 [96,71; 100,00]		
			0,24 [0,02; 2,60]	0,238
NASOPHARYNGITIS				
not severe[1]				
Number of patients with event	149	79		
Median (in weeks)	-	-		
% of event-free patients+	76,82 [70,65; 82,98]	78,63 [69,62; 87,65]		
			0,92 [0,70; 1,21]	0,557
severe[1]				
Number of patients with event	1	0		
Median (in weeks)	-	-		
% of event-free patients+	99,90 [99,70; 100,00]	100,00 [100,00; 100,00]		
			-	-
ORAL HERPES				
not severe[1]				
Number of patients with event	18	10		
Median (in weeks)	-	-		
% of event-free patients+	97,99 [97,02; 98,95]	97,10 [94,76; 99,44]		
			0,89 [0,41; 1,93]	0,766

	Treatment groups		Comparison	
	BAF312 (N=1099)	**Placebo (N=546)**	**HR [95% CI]**	**p-value**
severe[1]				
Number of patients with event	1	0		
Median (in weeks)	-	-		
% of event-free patients+	99,91 [99,72; 100,00]	100,00 [100,00; 100,00]		
			-	-
PHARYNGITIS				
not severe[1]				
Number of patients with event	20	11		
Median (in weeks)	-	-		
% of event-free patients+	97,61 [96,40; 98,82]	96,96 [94,97; 98,95]		
			0,89 [0,43; 1,86]	0,762
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]		
			-	-
RHINITIS				
not severe[1]				
Number of patients with event	14	10		
Median (in weeks)	-	-		
% of event-free patients+	97,80 [96,44; 99,16]	97,73 [96,19; 99,28]		
			0,68 [0,30; 1,53]	0,349
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]		
			-	-
SINUSITIS				
not severe[1]				
Number of patients with event	21	9		
Median (in weeks)	-	-		
% of event-free patients+	97,57 [96,47; 98,66]	97,93 [96,52; 99,33]		
			1,15 [0,53; 2,52]	0,719

	Treatment groups		Comparison	
	BAF312 (N=1099)	**Placebo (N=546)**	**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]		
			-	-
UPPER RESPIRATORY TRACT INFECTION				
not severe[1]				
Number of patients with event	91	41		
Median (in weeks)	-	-		
% of event-free patients+	87,41 [84,42; 90,39]	90,77 [87,86; 93,67]		
			1,08 [0,75; 1,56]	0,682
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	130	77		
Median (in weeks)	-	-		
% of event-free patients+	83,36 [80,08; 86,65]	82,53 [78,42; 86,63]		
			0,81 [0,61; 1,07]	0,138
severe[1]				
Number of patients with event	9	4		
Median (in weeks)	-	-		
% of event-free patients+	99,02 [98,35; 99,68]	99,21 [98,43; 99,98]		
			1,13 [0,35; 3,67]	0,838
INJURY, POISONING AND PROCEDURAL COMPLICATIONS				
not severe[1]				
Number of patients with event	233	111		
Median (in weeks)	-	-		
% of event-free patients+	62,62 [48,98; 76,25]	67,70 [57,36; 78,04]		
			1,03 [0,82; 1,29]	0,804

	Treatment groups		Comparison	
	BAF312 (N=1099)	**Placebo (N=546)**	**HR [95% CI]**	**p-value**
severe[1]				
Number of patients with event	15	4		
Median (in weeks)	-	-		
% of event-free patients+	97,79 [96,63; 98,95]	98,98 [97,96; 100,00]		
			1,80 [0,60; 5,42]	0,297
CONTUSION				
not severe[1]				
Number of patients with event	35	15		
Median (in weeks)	-	-		
% of event-free patients+	95,56 [93,87; 97,25]	95,27 [92,36; 98,19]		
			1,14 [0,62; 2,09]	0,664
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	125	59		
Median (in weeks)	-	-		
% of event-free patients+	83,62 [79,74; 87,50]	79,08 [68,77; 89,38]		
			1,04 [0,76; 1,42]	0,793
severe[1]				
Number of patients with event	5	0		
Median (in weeks)	-	-		
% of event-free patients+	99,36 [98,78; 99,94]	100,00 [100,00; 100,00]		
			-	-
LACERATION				
not severe[1]				
Number of patients with event	18	4		
Median (in weeks)	-	-		
% of event-free patients+	96,32 [93,34; 99,30]	99,08 [98,15; 100,00]		
			2,19 [0,74; 6,47]	0,157

	Treatment groups		Comparison	
	BAF312 (N=1099)	**Placebo (N=546)**	**HR [95% CI]**	**p-value**
severe[1]				
Number of patients with event	1	0		
Median (in weeks)	-	-		
% of event-free patients+	99,90 [99,71; 100,00]	100,00 [100,00; 100,00]		
			-	-
LIGAMENT SPRAIN				
not severe[1]				
Number of patients with event	12	6		
Median (in weeks)	-	-		
% of event-free patients+	98,70 [97,95; 99,46]	96,70 [92,34; 100,00]		
			0,98 [0,37; 2,62]	0,972
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	252	77		
Median (in weeks)	-	-		
% of event-free patients+	68,64 [64,66; 72,62]	76,94 [70,64; 83,23]		
			1,70 [1,32; 2,20]	<0,001 *
severe[1]				
Number of patients with event	17	5		
Median (in weeks)	-	-		
% of event-free patients+	98,18 [97,30; 99,06]	98,09 [95,87; 100,00]		
			1,67 [0,62; 4,52]	0,314
ALANINE AMINOTRANSFERASE INCREASED				
not severe[1]				
Number of patients with event	59	7		
Median (in weeks)	-	-		
% of event-free patients+	92,82 [90,84; 94,80]	98,66 [97,68; 99,65]		
			4,23 [1,93; 9,26]	<0,001 *

	Treatment groups		Comparison	
	BAF312 (N=1099)	**Placebo (N=546)**	**HR [95% CI]**	**p-value**
severe[1]				
Number of patients with event	8	2		
Median (in weeks)	-	-		
% of event-free patients+	99,16 [98,57; 99,75]	99,56 [98,96; 100,00]		
			1,98 [0,42; 9,34]	0,387
ASPARTATE AMINOTRANSFERASE INCREASED				
not severe[1]				
Number of patients with event	14	3		
Median (in weeks)	-	-		
% of event-free patients+	98,45 [97,61; 99,29]	99,38 [98,68; 100,00]		
			2,31 [0,66; 8,05]	0,188
severe[1]				
Number of patients with event	1	2		
Median (in weeks)	-	-		
% of event-free patients+	99,91 [99,73; 100,00]	99,56 [98,94; 100,00]		
			0,25 [0,02; 2,72]	0,252
BLOOD ALKALINE PHOSPHATASE INCREASED				
not severe[1]				
Number of patients with event	12	0		
Median (in weeks)	-	-		
% of event-free patients+	98,00 [96,25; 99,75]	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]		
			-	-
BLOOD BILIRUBIN INCREASED				
not severe[1]				
Number of patients with event	11	2		
Median (in weeks)	-	-		
% of event-free patients+	98,91 [98,27; 99,55]	99,63 [99,11; 100,00]		
			2,76 [0,61; 12,44]	0,187

	Treatment groups		Comparison	
	BAF312 (N=1099)	**Placebo (N=546)**	**HR [95% CI]**	**p-value**
severe[1]				
Number of patients with event	1	0		
Median (in weeks)	-	-		
% of event-free patients+	99,91 [99,73; 100,00]	100,00 [100,00; 100,00]		
			-	-
BLOOD CHOLESTEROL INCREASED				
not severe[1]				
Number of patients with event	20	5		
Median (in weeks)	-	-		
% of event-free patients+	97,15 [95,71; 98,59]	98,95 [98,03; 99,88]		
			1,96 [0,74; 5,24]	0,177
severe[1]				
Number of patients with event	0	1		
Median (in weeks)	-	-		
% of event-free patients+	100,00 [100,00; 100,00]	98,94 [96,86; 100,00]		
			-	-
BLOOD PRESSURE INCREASED				
not severe[1]				
Number of patients with event	19	7		
Median (in weeks)	-	-		
% of event-free patients+	97,93 [96,94; 98,92]	98,08 [96,61; 99,55]		
			1,34 [0,56; 3,19]	0,505
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]		
			-	-
GAMMA-GLUTAMYLTRANSFERASE INCREASED				
not severe[1]				
Number of patients with event	42	6		
Median (in weeks)	-	-		
% of event-free patients+	94,61 [92,55; 96,66]	97,99 [96,19; 99,79]		
			3,49 [1,48; 8,20]	0,004 *

	Treatment groups		Comparison	
	BAF312 (N=1099)	**Placebo (N=546)**	**HR [95% CI]**	**p-value**
severe[1]				
Number of patients with event	1	0		
Median (in weeks)	-	-		
% of event-free patients+	99,88 [99,63; 100,00]	100,00 [100,00; 100,00]		
			-	-
HEPATIC ENZYME INCREASED				
not severe[1]				
Number of patients with event	15	1		
Median (in weeks)	-	-		
% of event-free patients+	98,40 [97,58; 99,23]	99,73 [99,19; 100,00]		
			7,47 [0,99; 56,55]	0,052
severe[1]				
Number of patients with event	1	0		
Median (in weeks)	-	-		
% of event-free patients+	99,91 [99,73; 100,00]	100,00 [100,00; 100,00]		
			-	-
WEIGHT DECREASED				
not severe[1]				
Number of patients with event	22	9		
Median (in weeks)	-	-		
% of event-free patients+	96,94 [95,56; 98,32]	96,51 [93,67; 99,35]		
			1,19 [0,55; 2,58]	0,662
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	27	13		
Median (in weeks)	-	-		
% of event-free patients+	95,18 [93,06; 97,31]	96,06 [93,36; 98,76]		
			0,99 [0,51; 1,92]	0,982

	Treatment groups		Comparison	
	BAF312 (N=1099)	**Placebo (N=546)**	**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	83	27		
Median (in weeks)	-	-		
% of event-free patients+	89,35 [86,66; 92,04]	93,68 [91,16; 96,21]		
			1,54 [0,99; 2,37]	0,053
severe[1]				
Number of patients with event	3	1		
Median (in weeks)	-	-		
% of event-free patients+	99,67 [99,31; 100,00]	99,79 [99,39; 100,00]		
			1,49 [0,16; 14,32]	0,730
HYPERCHOLESTEROLAEMIA				
not severe[1]				
Number of patients with event	28	11		
Median (in weeks)	-	-		
% of event-free patients+	96,20 [94,34; 98,05]	97,15 [95,23; 99,07]		
			1,25 [0,62; 2,52]	0,528
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]		
			-	-
VITAMIN D DEFICIENCY				
not severe[1]				
Number of patients with event	11	7		
Median (in weeks)	-	-		
% of event-free patients+	98,47 [97,52; 99,42]	98,42 [97,23; 99,61]		
			0,77 [0,30; 1,97]	0,580

	Treatment groups		Comparison	
	BAF312 (N=1099)	**Placebo (N=546)**	**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]		
			-	-
MUSCULOSKELETAL AND CONNECTIVE TISSUE DISORDERS				
not severe[1]				
Number of patients with event	280	144		
Median (in weeks)	-	-		
% of event-free patients+	68,68 [65,17; 72,18]	63,98 [56,98; 70,98]		
			0,95 [0,78; 1,16]	0,606
severe[1]				
Number of patients with event	11	8		
Median (in weeks)	-	-		
% of event-free patients+	98,71 [97,93; 99,49]	97,78 [96,05; 99,51]		
			0,67 [0,27; 1,66]	0,381
ARTHRALGIA				
not severe[1]				
Number of patients with event	49	34		
Median (in weeks)	-	-		
% of event-free patients+	94,56 [92,96; 96,15]	92,17 [89,51; 94,83]		
			0,71 [0,46; 1,10]	0,124
severe[1]				
Number of patients with event	1	1		
Median (in weeks)	-	-		
% of event-free patients+	99,87 [99,62; 100,00]	99,34 [98,06; 100,00]		
			0,45 [0,03; 7,19]	0,572
BACK PAIN				
not severe[1]				
Number of patients with event	64	43		
Median (in weeks)	-	-		
% of event-free patients+	92,43 [90,44; 94,41]	87,70 [82,99; 92,40]		
			0,72 [0,49; 1,06]	0,099

	Treatment groups		Comparison	
	BAF312 (N=1099)	**Placebo (N=546)**	**HR [95% CI]**	**p-value**
severe[1]				
Number of patients with event	3	0		
Median (in weeks)	-	-		
% of event-free patients+	99,68 [99,32; 100,00]	100,00 [100,00; 100,00]		
			-	-
JOINT SWELLING				
not severe[1]				
Number of patients with event	16	7		
Median (in weeks)	-	-		
% of event-free patients+	98,35 [97,52; 99,18]	98,57 [97,51; 99,63]		
			1,15 [0,47; 2,79]	0,761
severe[1]				
Number of patients with event	1	0		
Median (in weeks)	-	-		
% of event-free patients+	99,87 [99,62; 100,00]	100,00 [100,00; 100,00]		
			-	-
MUSCLE SPASMS				
not severe[1]				
Number of patients with event	37	19		
Median (in weeks)	-	-		
% of event-free patients+	95,52 [93,97; 97,07]	93,52 [89,10; 97,94]		
			0,95 [0,54; 1,65]	0,849
severe[1]				
Number of patients with event	0	1		
Median (in weeks)	-	-		
% of event-free patients+	100,00 [100,00; 100,00]	99,81 [99,45; 100,00]		
			-	-
MUSCULAR WEAKNESS				
not severe[1]				
Number of patients with event	15	11		
Median (in weeks)	-	-		
% of event-free patients+	98,35 [97,47; 99,22]	97,29 [95,66; 98,93]		
			0,67 [0,31; 1,45]	0,310

	Treatment groups		Comparison	
	BAF312 (N=1099)	**Placebo (N=546)**	**HR [95% CI]**	**p-value**
severe[1]				
Number of patients with event	2	2		
Median (in weeks)	-	-		
% of event-free patients+	99,79 [99,50; 100,00]	99,58 [98,99; 100,00]		
			0,49 [0,07; 3,49]	0,477
MUSCULOSKELETAL PAIN				
not severe[1]				
Number of patients with event	27	14		
Median (in weeks)	-	-		
% of event-free patients+	96,54 [95,04; 98,04]	95,24 [92,15; 98,33]		
			0,94 [0,49; 1,80]	0,860
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]		
			-	-
MYALGIA				
not severe[1]				
Number of patients with event	13	7		
Median (in weeks)	-	-		
% of event-free patients+	98,74 [98,05; 99,42]	98,51 [97,36; 99,66]		
			0,92 [0,37; 2,31]	0,863
severe[1]				
Number of patients with event	0	1		
Median (in weeks)	-	-		
% of event-free patients+	100,00 [100,00; 100,00]	99,82 [99,45; 100,00]		
			-	-
NECK PAIN				
not severe[1]				
Number of patients with event	13	7		
Median (in weeks)	-	-		
% of event-free patients+	98,52 [97,71; 99,34]	98,37 [97,03; 99,70]		
			0,91 [0,36; 2,28]	0,840

	Treatment groups		Comparison	
	BAF312 (N=1099)	**Placebo (N=546)**	**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]		
			-	-
PAIN IN EXTREMITY				
not severe[1]				
Number of patients with event	60	20		
Median (in weeks)	-	-		
% of event-free patients+	91,78 [89,28; 94,28]	94,43 [91,63; 97,23]		
			1,48 [0,89; 2,45]	0,132
severe[1]				
Number of patients with event	0	1		
Median (in weeks)	-	-		
% of event-free patients+	100,00 [100,00; 100,00]	99,81 [99,44; 100,00]		
			-	-
NEOPLASMS BENIGN, MALIGNANT AND UNSPECIFIED (INCL CYSTS AND POLYPS)				
not severe[1]				
Number of patients with event	102	36		
Median (in weeks)	-	-		
% of event-free patients+	72,49 [53,04; 91,94]	81,09 [69,99; 92,18]		
			1,36 [0,93; 1,99]	0,110
severe[1]				
Number of patients with event	14	9		
Median (in weeks)	-	-		
% of event-free patients+	97,79 [96,09; 99,48]	97,24 [95,20; 99,28]		
			0,75 [0,32; 1,73]	0,502
BASAL CELL CARCINOMA				
not severe[1]				
Number of patients with event	9	6		
Median (in weeks)	-	-		
% of event-free patients+	98,72 [97,83; 99,61]	94,62 [86,33; 100,00]		
			0,71 [0,25; 2,00]	0,519

	Treatment groups		Comparison	
	BAF312 (N=1099)	**Placebo (N=546)**	**HR [95% CI]**	**p-value**
severe[1]				
Number of patients with event	4	1		
Median (in weeks)	-	-		
% of event-free patients+	98,85 [97,28; 100,00]	99,54 [98,64; 100,00]		
			1,81 [0,20; 16,23]	0,597
MELANOCYTIC NAEVUS				
not severe[1]				
Number of patients with event	46	17		
Median (in weeks)	-	-		
% of event-free patients+	91,04 [87,69; 94,40]	92,03 [87,01; 97,05]		
			1,27 [0,73; 2,21]	0,406
severe[1]				
Number of patients with event	1	0		
Median (in weeks)	-	-		
% of event-free patients+	99,89 [99,69; 100,00]	100,00 [100,00; 100,00]		
			-	-
NERVOUS SYSTEM DISORDERS				
not severe[1]				
Number of patients with event	408	171		
Median (in weeks)	-	-		
% of event-free patients+	52,14 [43,60; 60,67]	62,78 [57,32; 68,25]		
			1,22 [1,02; 1,46]	0,029 *
severe[1]				
Number of patients with event	27	15		
Median (in weeks)	-	-		
% of event-free patients+	96,33 [94,49; 98,18]	96,60 [94,86; 98,35]		
			0,89 [0,47; 1,66]	0,705
BALANCE DISORDER				
not severe[1]				
Number of patients with event	13	5		
Median (in weeks)	-	-		
% of event-free patients+	98,63 [97,88; 99,39]	97,83 [95,44; 100,00]		
			1,27 [0,45; 3,57]	0,647

	Treatment groups		Comparison	
	BAF312 (N=1099)	**Placebo (N=546)**	**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]		
			-	-
DIZZINESS				
not severe[1]				
Number of patients with event	75	26		
Median (in weeks)	-	-		
% of event-free patients+	92,36 [90,55; 94,17]	94,53 [92,32; 96,75]		
			1,45 [0,93; 2,26]	0,106
severe[1]				
Number of patients with event	1	0		
Median (in weeks)	-	-		
% of event-free patients+	99,91 [99,72; 100,00]	100,00 [100,00; 100,00]		
			-	-
HEADACHE				
not severe[1]				
Number of patients with event	158	71		
Median (in weeks)	-	-		
% of event-free patients+	82,51 [79,15; 85,88]	82,61 [77,82; 87,40]		
			1,10 [0,83; 1,46]	0,490
severe[1]				
Number of patients with event	2	0		
Median (in weeks)	-	-		
% of event-free patients+	99,62 [99,03; 100,00]	100,00 [100,00; 100,00]		
			-	-
HYPOAESTHESIA				
not severe[1]				
Number of patients with event	14	14		
Median (in weeks)	-	-		
% of event-free patients+	98,51 [97,69; 99,32]	96,36 [93,89; 98,83]		
			0,49 [0,23; 1,03]	0,060

	Treatment groups		Comparison	
	BAF312 (N=1099)	**Placebo (N=546)**	**HR [95% CI]**	**p-value**
severe[1]				
Number of patients with event	1	1		
Median (in weeks)	-	-		
% of event-free patients+	99,91 [99,73; 100,00]	99,82 [99,46; 100,00]		
			0,50 [0,03; 7,99]	0,624
MIGRAINE				
not severe[1]				
Number of patients with event	16	8		
Median (in weeks)	-	-		
% of event-free patients+	98,21 [97,28; 99,13]	98,01 [96,52; 99,50]		
			0,99 [0,42; 2,32]	0,984
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]		
			-	-
MUSCLE SPASTICITY				
not severe[1]				
Number of patients with event	42	23		
Median (in weeks)	-	-		
% of event-free patients+	95,14 [93,48; 96,80]	93,27 [89,32; 97,23]		
			0,90 [0,54; 1,50]	0,682
severe[1]				
Number of patients with event	2	0		
Median (in weeks)	-	-		
% of event-free patients+	99,80 [99,53; 100,00]	100,00 [100,00; 100,00]		
			-	-
NEURALGIA				
not severe[1]				
Number of patients with event	13	5		
Median (in weeks)	-	-		
% of event-free patients+	98,08 [96,87; 99,29]	99,02 [98,16; 99,88]		
			1,27 [0,45; 3,55]	0,655

	Treatment groups		Comparison	
	BAF312 (N=1099)	**Placebo (N=546)**	**HR [95% CI]**	**p-value**
severe[1]				
Number of patients with event	1	0		
Median (in weeks)	-	-		
% of event-free patients+	99,91 [99,73; 100,00]	100,00 [100,00; 100,00]		
			-	-
PARAESTHESIA				
not severe[1]				
Number of patients with event	18	20		
Median (in weeks)	-	-		
% of event-free patients+	97,28 [95,52; 99,04]	95,32 [93,06; 97,59]		
			0,44 [0,23; 0,82]	0,011 *
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]		
			-	-
SCIATICA				
not severe[1]				
Number of patients with event	18	5		
Median (in weeks)	-	-		
% of event-free patients+	96,06 [91,92; 100,00]	98,99 [98,11; 99,87]		
			1,78 [0,66; 4,79]	0,256
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]		
			-	-
SOMNOLENCE				
not severe[1]				
Number of patients with event	11	5		
Median (in weeks)	-	-		
% of event-free patients+	98,98 [98,38; 99,58]	98,17 [96,07; 100,00]		
			1,08 [0,38; 3,12]	0,881

	Treatment groups		Comparison	
	BAF312 (N=1099)	**Placebo (N=546)**	**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]		
			-	-
SYNCOPE				
not severe[1]				
Number of patients with event	13	6		
Median (in weeks)	-	-		
% of event-free patients+	97,13 [94,26; 100,00]	98,35 [96,86; 99,83]		
			1,04 [0,40; 2,74]	0,936
severe[1]				
Number of patients with event	1	1		
Median (in weeks)	-	-		
% of event-free patients+	99,91 [99,73; 100,00]	99,63 [98,90; 100,00]		
			0,49 [0,03; 7,76]	0,609
TREMOR				
not severe[1]				
Number of patients with event	16	3		
Median (in weeks)	-	-		
% of event-free patients+	97,92 [96,60; 99,25]	99,43 [98,78; 100,00]		
			2,65 [0,77; 9,08]	0,122
severe[1]				
Number of patients with event	1	0		
Median (in weeks)	-	-		
% of event-free patients+	99,90 [99,70; 100,00]	100,00 [100,00; 100,00]		
			-	-
TRIGEMINAL NEURALGIA				
not severe[1]				
Number of patients with event	17	5		
Median (in weeks)	-	-		
% of event-free patients+	92,53 [82,63; 100,00]	99,06 [98,24; 99,88]		
			1,64 [0,60; 4,45]	0,331

	Treatment groups		Comparison	
	BAF312 (N=1099)	**Placebo (N=546)**	**HR [95% CI]**	**p-value**
severe[1]				
Number of patients with event	3	1		
Median (in weeks)	-	-		
% of event-free patients+	99,71 [99,38; 100,00]	99,78 [99,35; 100,00]		
			1,49 [0,16; 14,35]	0,729
PSYCHIATRIC DISORDERS				
not severe[1]				
Number of patients with event	158	78		
Median (in weeks)	-	-		
% of event-free patients+	79,02 [73,87; 84,16]	81,93 [77,73; 86,14]		
			1,01 [0,77; 1,32]	0,966
severe[1]				
Number of patients with event	17	6		
Median (in weeks)	-	-		
% of event-free patients+	98,11 [97,19; 99,03]	98,58 [97,36; 99,81]		
			1,41 [0,55; 3,57]	0,472
ANXIETY				
not severe[1]				
Number of patients with event	22	14		
Median (in weeks)	-	-		
% of event-free patients+	97,76 [96,82; 98,70]	96,57 [94,62; 98,52]		
			0,78 [0,40; 1,53]	0,476
severe[1]				
Number of patients with event	1	0		
Median (in weeks)	-	-		
% of event-free patients+	99,88 [99,64; 100,00]	100,00 [100,00; 100,00]		
			-	-
DEPRESSED MOOD				
not severe[1]				
Number of patients with event	16	7		
Median (in weeks)	-	-		
% of event-free patients+	97,75 [96,43; 99,08]	98,52 [97,39; 99,64]		
			1,12 [0,46; 2,73]	0,797

	Treatment groups		Comparison	
	BAF312 (N=1099)	**Placebo (N=546)**	**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]		
			-	-
DEPRESSION				
not severe[1]				
Number of patients with event	44	28		
Median (in weeks)	-	-		
% of event-free patients+	94,73 [93,00; 96,45]	92,95 [89,87; 96,03]		
			0,77 [0,48; 1,24]	0,289
severe[1]				
Number of patients with event	5	2		
Median (in weeks)	-	-		
% of event-free patients+	99,49 [99,05; 99,94]	99,34 [98,35; 100,00]		
			1,24 [0,24; 6,37]	0,801
INSOMNIA				
not severe[1]				
Number of patients with event	38	17		
Median (in weeks)	-	-		
% of event-free patients+	93,80 [89,81; 97,78]	96,44 [94,70; 98,17]		
			1,11 [0,62; 1,96]	0,730
severe[1]				
Number of patients with event	0	2		
Median (in weeks)	-	-		
% of event-free patients+	100,00 [100,00; 100,00]	99,62 [99,09; 100,00]		
			-	-
SLEEP DISORDER				
not severe[1]				
Number of patients with event	11	5		
Median (in weeks)	-	-		
% of event-free patients+	98,74 [97,97; 99,52]	98,85 [97,81; 99,89]		
			1,08 [0,38; 3,11]	0,884

	Treatment groups		Comparison	
	BAF312 (N=1099)	**Placebo (N=546)**	**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]		
			-	-
RENAL AND URINARY DISORDERS				
not severe[1]				
Number of patients with event	78	35		
Median (in weeks)	-	-		
% of event-free patients[+]	90,28 [87,98; 92,59]	91,13 [88,03; 94,22]		
			1,10 [0,74; 1,64]	0,632
severe[1]				
Number of patients with event	9	3		
Median (in weeks)	-	-		
% of event-free patients[+]	98,94 [98,24; 99,64]	99,38 [98,69; 100,00]		
			1,47 [0,40; 5,44]	0,561
DYSURIA				
not severe[1]				
Number of patients with event	11	3		
Median (in weeks)	-	-		
% of event-free patients[+]	98,93 [98,30; 99,56]	99,41 [98,73; 100,00]		
			1,85 [0,52; 6,64]	0,344
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 INCONTINENCE				
not severe[1]				
Number of patients with event	12	12		
Median (in weeks)	-	-		
% of event-free patients[+]	98,71 [97,98; 99,44]	96,53 [94,41; 98,64]		
			0,49 [0,22; 1,09]	0,079

	Treatment groups		Comparison	
	BAF312 (N=1099)	**Placebo (N=546)**	**HR [95% CI]**	**p-value**
severe[1]				
Number of patients with event	2	0		
Median (in weeks)	-	-		
% of event-free patients+	99,79 [99,50; 100,00]	100,00 [100,00; 100,00]		
			-	-
URINARY RETENTION				
not severe[1]				
Number of patients with event	11	6		
Median (in weeks)	-	-		
% of event-free patients+	98,35 [97,22; 99,49]	98,18 [96,55; 99,80]		
			0,88 [0,32; 2,38]	0,798
severe[1]				
Number of patients with event	3	2		
Median (in weeks)	-	-		
% of event-free patients+	99,66 [99,28; 100,00]	99,59 [99,01; 100,00]		
			0,74 [0,12; 4,43]	0,742
REPRODUCTIVE SYSTEM AND BREAST DISORDERS				
not severe[1]				
Number of patients with event	36	23		
Median (in weeks)	-	-		
% of event-free patients+	95,37 [93,67; 97,07]	93,51 [90,35; 96,68]		
			0,76 [0,45; 1,28]	0,299
severe[1]				
Number of patients with event	0	2		
Median (in weeks)	-	-		
% of event-free patients+	100,00 [100,00; 100,00]	99,61 [99,07; 100,00]		
			-	-
RESPIRATORY, THORACIC AND MEDIASTINAL DISORDERS				
not severe[1]				
Number of patients with event	114	70		
Median (in weeks)	-	-		
% of event-free patients+	87,65 [85,43; 89,87]	77,33 [67,10; 87,55]		
			0,79 [0,59; 1,07]	0,124

	Treatment groups		Comparison	
	BAF312 (N=1099)	**Placebo (N=546)**	**HR [95% CI]**	**p-value**
severe[1]				
Number of patients with event	3	1		
Median (in weeks)	-	-		
% of event-free patients+	99,65 [99,26; 100,00]	99,34 [98,04; 100,00]		
			1,42 [0,15; 13,63]	0,763
COUGH				
not severe[1]				
Number of patients with event	35	18		
Median (in weeks)	-	-		
% of event-free patients+	95,93 [94,52; 97,33]	95,83 [93,76; 97,89]		
			0,96 [0,54; 1,69]	0,875
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]		
			-	-
DYSPNOEA				
not severe[1]				
Number of patients with event	19	10		
Median (in weeks)	-	-		
% of event-free patients+	98,03 [97,13; 98,92]	96,69 [93,91; 99,46]		
			0,94 [0,43; 2,01]	0,864
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]		
			-	-
OROPHARYNGEAL PAIN				
not severe[1]				
Number of patients with event	20	17		
Median (in weeks)	-	-		
% of event-free patients+	97,30 [95,82; 98,79]	96,33 [94,44; 98,22]		
			0,57 [0,30; 1,09]	0,091

	Treatment groups		Comparison	
	BAF312 (N=1099)	**Placebo (N=546)**	**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	188	92		
Median (in weeks)	-	-		
% of event-free patients+	70,86 [61,91; 79,82]	72,35 [65,03; 79,67]		
			0,98 [0,76; 1,25]	0,845
severe[1]				
Number of patients with event	1	2		
Median (in weeks)	-	-		
% of event-free patients+	99,90 [99,70; 100,00]	99,58 [99,00; 100,00]		
			0,25 [0,02; 2,72]	0,253
ACTINIC KERATOSIS				
not severe[1]				
Number of patients with event	15	6		
Median (in weeks)	-	-		
% of event-free patients+	92,63 [82,74; 100,00]	98,29 [96,76; 99,83]		
			1,16 [0,45; 2,99]	0,760
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]		
			-	-
ECZEMA				
not severe[1]				
Number of patients with event	17	5		
Median (in weeks)	-	-		
% of event-free patients+	97,70 [96,11; 99,29]	98,06 [95,86; 100,00]		
			1,66 [0,61; 4,51]	0,317

	Treatment groups		Comparison	
	BAF312 (N=1099)	**Placebo (N=546)**	**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]		
			-	-
RASH				
not severe[1]				
Number of patients with event	20	13		
Median (in weeks)	-	-		
% of event-free patients+	97,67 [96,57; 98,77]	94,96 [90,40; 99,52]		
			0,74 [0,37; 1,50]	0,408
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]		
			-	-
VASCULAR DISORDERS				
not severe[1]				
Number of patients with event	160	59		
Median (in weeks)	-	-		
% of event-free patients+	79,26 [74,48; 84,04]	80,87 [72,02; 89,71]		
			1,35 [1,00; 1,81]	0,051
severe[1]				
Number of patients with event	3	2		
Median (in weeks)	-	-		
% of event-free patients+	99,59 [99,10; 100,00]	99,45 [98,66; 100,00]		
			0,72 [0,12; 4,33]	0,723
HAEMATOMA				
not severe[1]				
Number of patients with event	15	3		
Median (in weeks)	-	-		
% of event-free patients+	98,28 [97,39; 99,18]	99,03 [97,88; 100,00]		
			2,47 [0,72; 8,54]	0,152

	Treatment groups		Comparison	
	BAF312 (N=1099)	**Placebo (N=546)**	**HR [95% CI]**	**p-value**
severe[1]				
Number of patients with event	1	0		
Median (in weeks)	-	-		
% of event-free patients[+]	99,88 [99,65; 100,00]	100,00 [100,00; 100,00]		
			-	-
HYPERTENSION				
not severe[1]				
Number of patients with event	115	40		
Median (in weeks)	-	-		
% of event-free patients[+]	84,83 [80,48; 89,19]	86,39 [77,56; 95,22]		
			1,42 [0,99; 2,04]	0,056
severe[1]				
Number of patients with event	1	1		
Median (in weeks)	-	-		
% of event-free patients[+]	99,91 [99,73; 100,00]	99,81 [99,43; 100,00]		
			0,51 [0,03; 8,08]	0,629

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 total population

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

	Treatment groups		Comparison	
	BAF312 (N=1099)	**Placebo (N=546)**	**HR [95% CI]**	**p-value**
N'	1099	546		
Infections and infestations				
Number of patients with event	539	268		
Median (in weeks)	75,6 [66,1; 87,9]	74,1 [62,6; 95,4]		
% of event-free patients+	39,57 [35,34; 43,80]	42,56 [37,22; 47,90]		
			0,99 [0,85; 1,14]	0,874
not severe				
Number of patients with event	528	262		
Median (in weeks)	80,1 [71,9; 98,0]	77,6 [63,1; 105,0]		
% of event-free patients+	40,33 [36,00; 44,66]	43,59 [38,22; 48,96]		
			0,99 [0,85; 1,14]	0,844
severe				
Number of patients with event	24	11		
Median (in weeks)	-	-		
% of event-free patients+	97,20 [96,02; 98,38]	96,91 [94,51; 99,31]		
			1,08 [0,53; 2,21]	0,831
serious				
Number of patients with event	33	15		
Median (in weeks)	-	-		
% of event-free patients+	95,86 [94,36; 97,37]	95,56 [92,76; 98,35]		
			1,08 [0,59; 1,99]	0,799
Herpes simplex virus infections				
Number of patients with event	25	11		
Median (in weeks)	-	-		
% of event-free patients+	96,99 [95,66; 98,32]	96,74 [94,31; 99,18]		
			1,12 [0,55; 2,28]	0,755
not severe				
Number of patients with event	25	11		
Median (in weeks)	-	-		
% of event-free patients+	96,99 [95,65; 98,32]	96,74 [94,31; 99,18]		
			1,12 [0,55; 2,28]	0,755

	Treatment groups		Comparison	
	BAF312 (N=1099)	**Placebo (N=546)**	**HR [95% CI]**	**p-value**
severe				
Number of patients with event	1	0		
Median (in weeks)	-	-		
% of event-free patients+	99,91 [99,72; 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	33	4		
Median (in weeks)	-	-		
% of event-free patients+	95,86 [94,30; 97,42]	98,96 [97,92; 100,00]		
			4,11 [1,46; 11,60]	0,008 *
not severe				
Number of patients with event	30	4		
Median (in weeks)	-	-		
% of event-free patients+	96,16 [94,63; 97,69]	98,96 [97,92; 100,00]		
			3,72 [1,31; 10,56]	0,014 *
severe				
Number of patients with event	3	0		
Median (in weeks)	-	-		
% of event-free patients+	99,70 [99,37; 100,00]	100,00 [100,00; 100,00]		
			-	-
serious				
Number of patients with event	2	0		
Median (in weeks)	-	-		
% of event-free patients+	99,74 [99,38; 100,00]	100,00 [100,00; 100,00]		
			-	-

	Treatment groups		Comparison	
	BAF312 (N=1099)	**Placebo (N=546)**	**HR [95% CI]**	**p-value**
Lymphopenia				
Number of patients with event	14	0		
Median (in weeks)	-	-		
% of event-free patients+	98,56 [97,81; 99,31]	100,00 [100,00; 100,00]		
			-	-
not severe				
Number of patients with event	10	0		
Median (in weeks)	-	-		
% of event-free patients+	98,95 [98,31; 99,60]	100,00 [100,00; 100,00]		
			-	-
severe				
Number of patients with event	4	0		
Median (in weeks)	-	-		
% of event-free patients+	99,61 [99,22; 99,99]	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	20	1		
Median (in weeks)	-	-		
% of event-free patients+	97,84 [96,84; 98,83]	99,61 [98,85; 100,00]		
			9,91 [1,33; 73,76]	0,025 *
not severe				
Number of patients with event	15	0		
Median (in weeks)	-	-		
% of event-free patients+	98,32 [97,41; 99,22]	100,00 [100,00; 100,00]		
			-	-

	Treatment groups		Comparison	
	BAF312 (N=1099)	**Placebo (N=546)**	**HR [95% CI]**	**p-value**
severe				
Number of patients with event	5	1		
Median (in weeks)	-	-		
% of event-free patients+	99,51 [99,09; 99,94]	99,61 [98,85; 100,00]		
			2,47 [0,29; 21,14]	0,409
serious				
Number of patients with event	3	0		
Median (in weeks)	-	-		
% of event-free patients+	99,70 [99,36; 100,00]	100,00 [100,00; 100,00]		
			-	-
Abnormal hepatic enzymes				
Number of patients with event	135	21		
Median (in weeks)	-	-		
% of event-free patients+	83,60 [80,34; 86,86]	94,41 [91,76; 97,06]		
			3,31 [2,09; 5,24]	<0,001 *
not severe				
Number of patients with event	125	19		
Median (in weeks)	-	-		
% of event-free patients+	84,56 [81,32; 87,79]	94,80 [92,20; 97,41]		
			3,38 [2,08; 5,47]	<0,001 *
severe				
Number of patients with event	13	3		
Median (in weeks)	-	-		
% of event-free patients+	98,67 [97,94; 99,39]	99,37 [98,66; 100,00]		
			2,15 [0,61; 7,55]	0,232
serious				
Number of patients with event	14	3		
Median (in weeks)	-	-		
% of event-free patients+	98,62 [97,89; 99,34]	99,40 [98,72; 100,00]		
			2,32 [0,67; 8,06]	0,187

	Treatment groups		Comparison	
	BAF312 (N=1099)	**Placebo (N=546)**	**HR [95% CI]**	**p-value**
Malignancies				
Number of patients with event	20	14		
Median (in weeks)	-	-		
% of event-free patients+	97,57 [96,45; 98,68]	92,17 [83,87; 100,00]		
			0,69 [0,35; 1,37]	0,287
not severe				
Number of patients with event	11	7		
Median (in weeks)	-	-		
% of event-free patients+	98,53 [97,61; 99,45]	94,41 [86,13; 100,00]		
			0,75 [0,29; 1,94]	0,555
severe				
Number of patients with event	11	7		
Median (in weeks)	-	-		
% of event-free patients+	98,10 [96,44; 99,75]	97,66 [95,71; 99,61]		
			0,75 [0,29; 1,94]	0,558
serious				
Number of patients with event	19	13		
Median (in weeks)	-	-		
% of event-free patients+	97,02 [95,19; 98,85]	92,36 [84,05; 100,00]		
			0,70 [0,34; 1,41]	0,316
Hypertension				
Number of patients with event	137	50		
Median (in weeks)	-	-		
% of event-free patients+	82,57 [78,15; 87,00]	83,96 [75,21; 92,70]		
			1,36 [0,98; 1,88]	0,064
not severe				
Number of patients with event	137	49		
Median (in weeks)	-	-		
% of event-free patients+	82,57 [78,15; 87,00]	84,15 [75,40; 92,90]		
			1,39 [1,00; 1,92]	0,049 *
severe				
Number of patients with event	1	1		
Median (in weeks)	-	-		
% of event-free patients+	99,91 [99,73; 100,00]	99,81 [99,43; 100,00]		
			0,51 [0,03; 8,08]	0,629

	Treatment groups		Comparison	
	BAF312 (N=1099)	**Placebo (N=546)**	**HR [95% CI]**	**p-value**
serious				
Number of patients with event	1	0		
Median (in weeks)	-	-		
% of event-free patients+	99,91 [99,73; 100,00]	100,00 [100,00; 100,00]		
			-	-
Seizures				
Number of patients with event	19	2		
Median (in weeks)	-	-		
% of event-free patients+	97,16 [95,40; 98,92]	99,62 [99,09; 100,00]		
			4,66 [1,09; 20,02]	0,038 *
not severe				
Number of patients with event	16	2		
Median (in weeks)	-	-		
% of event-free patients+	96,51 [93,27; 99,75]	99,62 [99,09; 100,00]		
			3,88 [0,89; 16,88]	0,071
severe				
Number of patients with event	5	0		
Median (in weeks)	-	-		
% of event-free patients+	98,91 [97,45; 100,00]	100,00 [100,00; 100,00]		
			-	-
serious				
Number of patients with event	9	0		
Median (in weeks)	-	-		
% of event-free patients+	97,55 [94,43; 100,00]	100,00 [100,00; 100,00]		
			-	-
Thromboembolic events				
Number of patients with event	33	15		
Median (in weeks)	-	-		
% of event-free patients+	95,49 [93,27; 97,71]	94,76 [90,35; 99,18]		
			1,08 [0,58; 1,98]	0,811

	Treatment groups		Comparison	
	BAF312 (N=1099)	**Placebo (N=546)**	**HR [95% CI]**	**p-value**
not severe				
Number of patients with event	25	12		
Median (in weeks)	-	-		
% of event-free patients+	96,87 [95,20; 98,54]	95,37 [90,98; 99,75]		
			1,02 [0,51; 2,03]	0,958
severe				
Number of patients with event	9	5		
Median (in weeks)	-	-		
% of event-free patients+	98,49 [96,98; 99,99]	99,00 [98,12; 99,87]		
			0,88 [0,30; 2,64]	0,826
serious				
Number of patients with event	15	7		
Median (in weeks)	-	-		
% of event-free patients+	97,88 [96,29; 99,46]	98,27 [96,90; 99,64]		
			1,05 [0,43; 2,57]	0,917
Respiratory disorders				
Number of patients with event	117	71		
Median (in weeks)	-	-		
% of event-free patients+	87,31 [85,06; 89,55]	76,70 [66,49; 86,92]		
			0,80 [0,60; 1,08]	0,140
not severe				
Number of patients with event	114	70		
Median (in weeks)	-	-		
% of event-free patients+	87,65 [85,43; 89,87]	77,33 [67,10; 87,55]		
			0,79 [0,59; 1,07]	0,124
severe				
Number of patients with event	3	1		
Median (in weeks)	-	-		
% of event-free patients+	99,65 [99,26; 100,00]	99,34 [98,04; 100,00]		
			1,42 [0,15; 13,63]	0,763
serious				
Number of patients with event	2	1		
Median (in weeks)	-	-		
% of event-free patients+	99,77 [99,45; 100,00]	99,34 [98,04; 100,00]		
			0,94 [0,09; 10,40]	0,961

	Treatment groups		Comparison	
	BAF312 (N=1099)	**Placebo (N=546)**	**HR [95% CI]**	**p-value**
Peripheral edema/swelling				
Number of patients with event	74	18		
Median (in weeks)	-	-		
% of event-free patients+	85,87 [74,84; 96,91]	95,97 [94,03; 97,90]		
			2,06 [1,23; 3,45]	0,006 *
not severe				
Number of patients with event	74	18		
Median (in weeks)	-	-		
% of event-free patients+	85,87 [74,84; 96,91]	95,97 [94,03; 97,90]		
			2,06 [1,23; 3,45]	0,006 *
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]		
			-	-

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 total population

	Treatment groups		Comparison	
	BAF312 (N=1099)	**Placebo (N=546)**	**HR [95% CI]**	**p-value**
N'	1099	546		
Asthma/bronchospasm				
Number of patients with event	8	2		
Median (in weeks)	-	-		
% of event-free patients+	99,18 [98,61; 99,75]	99,49 [98,76; 100,00]		
			2,00 [0,42; 9,41]	0,382
not severe				
Number of patients with event	8	2		
Median (in weeks)	-	-		
% of event-free patients+	99,18 [98,61; 99,75]	99,49 [98,76; 100,00]		
			2,00 [0,42; 9,41]	0,382
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	6	0		
Median (in weeks)	-	-		
% of event-free patients+	99,38 [98,88; 99,87]	100,00 [100,00; 100,00]		
			-	-
not severe				
Number of patients with event	6	0		
Median (in weeks)	-	-		
% of event-free patients+	99,38 [98,88; 99,87]	100,00 [100,00; 100,00]		
			-	-

	Treatment groups		Comparison	
	BAF312 (N=1099)	**Placebo (N=546)**	**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	103	31		
Median (in weeks)	-	-		
% of event-free patients+	87,53 [83,83; 91,23]	92,98 [90,32; 95,63]		
			1,67 [1,12; 2,49]	0,013 *
not severe				
Number of patients with event	101	30		
Median (in weeks)	-	-		
% of event-free patients+	87,70 [84,00; 91,40]	93,35 [90,79; 95,91]		
			1,69 [1,12; 2,54]	0,012 *
severe				
Number of patients with event	5	1		
Median (in weeks)	-	-		
% of event-free patients+	99,53 [99,12; 99,94]	99,63 [98,90; 100,00]		
			2,47 [0,29; 21,14]	0,409

	Treatment groups		Comparison	
	BAF312 (N=1099)	**Placebo (N=546)**	**HR [95% CI]**	**p-value**
serious				
Number of patients with event	10	1		
Median (in weeks)	-	-		
% of event-free patients+	97,74 [94,96; 100,00]	99,63 [98,90; 100,00]		
			4,83 [0,62; 37,72]	0,134

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 total population

12.2 Subgroup: Age

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

	Treatment groups		Comparison	
	BAF312 (N=1099)	**Placebo (N=546)**	**HR [95% CI]**	**p-value**
N'	1099	546		
N' Age = 18-30 years	26	12		
N' Age = 31-40 years	161	91		
N' Age = 41-55 years	712	331		
N' Age = >55 years	200	112		
Any AE				
Interaction test:	p=0,978			
Age = 18-30 years				
Number of patients with event	21	9		
Median (in weeks)	3,1 [1,4; 26,6]	19,6 [7,4; 50,0]		
% of event-free patients+	14,42 [0,00; 30,27]	25,00 [0,50; 49,50]		
			1,40 [0,64; 3,07]	0,393
Age = 31-40 years				
Number of patients with event	133	71		
Median (in weeks)	7,0 [3,9; 12,4]	12,4 [4,1; 22,6]		
% of event-free patients+	13,96 [7,80; 20,12]	17,12 [7,43; 26,81]		
			1,21 [0,91; 1,62]	0,191
Age = 41-55 years				
Number of patients with event	636	269		
Median (in weeks)	4,0 [3,1; 5,1]	7,3 [4,4; 11,3]		
% of event-free patients+	6,14 [3,13; 9,16]	13,69 [8,67; 18,71]		
			1,28 [1,11; 1,47]	0,001 *
Age = >55 years				
Number of patients with event	185	96		
Median (in weeks)	4,4 [3,1; 7,9]	5,6 [3,3; 9,9]		
% of event-free patients+	3,70 [0,00; 7,45]	8,71 [0,39; 17,03]		
			1,24 [0,97; 1,59]	0,087

	Treatment groups		Comparison	
	BAF312 (N=1099)	**Placebo (N=546)**	**HR [95% CI]**	**p-value**
Any AE, disease specific events excluded[1]				
Interaction test:	p=0,991			
Age = 18-30 years				
Number of patients with event	18	8		
Median (in weeks)	20,6 [3,0; 50,7]	20,9 [8,9; -]		
% of event-free patients+	20,20 [0,00; 40,77]	33,33 [6,66; 60,01]		
			1,21 [0,52; 2,77]	0,660
Age = 31-40 years				
Number of patients with event	127	64		
Median (in weeks)	12,1 [6,4; 16,7]	14,0 [10,3; 41,1]		
% of event-free patients+	16,94 [10,08; 23,80]	23,77 [13,24; 34,30]		
			1,28 [0,95; 1,73]	0,106
Age = 41-55 years				
Number of patients with event	598	255		
Median (in weeks)	11,0 [8,6; 12,7]	12,9 [10,3; 17,6]		
% of event-free patients+	9,30 [5,74; 12,85]	17,00 [11,54; 22,47]		
			1,21 [1,05; 1,40]	0,010 *
Age = >55 years				
Number of patients with event	175	91		
Median (in weeks)	9,3 [5,3; 13,0]	8,9 [6,7; 21,0]		
% of event-free patients+	7,83 [2,81; 12,85]	10,63 [0,72; 20,55]		
			1,21 [0,94; 1,56]	0,138
Any SAE				
Interaction test:	p=0,040 *			
Age = 18-30 years				
Number of patients with event	2	2		
Median (in weeks)	-	-		
% of event-free patients+	91,27 [79,69; 100,00]	83,33 [62,25; 100,00]		
			0,45 [0,06; 3,16]	0,419
Age = 31-40 years				
Number of patients with event	12	11		
Median (in weeks)	-	-		
% of event-free patients+	89,51 [83,60; 95,42]	83,55 [73,77; 93,32]		
			0,58 [0,26; 1,31]	0,191

	Treatment groups		Comparison	
	BAF312 (N=1099)	**Placebo (N=546)**	**HR [95% CI]**	**p-value**
Age = 41-55 years				
Number of patients with event	118	45		
Median (in weeks)	-	-		
% of event-free patients+	75,52 [68,81; 82,23]	77,18 [62,26; 92,10]		
			1,20 [0,85; 1,70]	0,291
Age = >55 years				
Number of patients with event	54	16		
Median (in weeks)	-	-		
% of event-free patients+	63,93 [53,48; 74,38]	79,40 [69,29; 89,50]		
			2,18 [1,25; 3,80]	0,006 *
Any SAE, disease specific events excluded[1]				
Interaction test:	p=0,317			
Age = 18-30 years				
Number of patients with event	1	2		
Median (in weeks)	-	-		
% of event-free patients+	95,24 [86,13; 100,00]	83,33 [62,25; 100,00]		
			0,22 [0,02; 2,44]	0,218
Age = 31-40 years				
Number of patients with event	11	6		
Median (in weeks)	-	-		
% of event-free patients+	90,30 [84,57; 96,04]	91,74 [85,14; 98,35]		
			0,99 [0,37; 2,69]	0,990
Age = 41-55 years				
Number of patients with event	90	30		
Median (in weeks)	-	-		
% of event-free patients+	83,36 [79,89; 86,83]	82,18 [67,77; 96,60]		
			1,37 [0,91; 2,07]	0,135
Age = >55 years				
Number of patients with event	44	15		
Median (in weeks)	-	-		
% of event-free patients+	68,49 [57,74; 79,25]	80,55 [70,59; 90,51]		
			1,83 [1,02; 3,28]	0,044 *

	Treatment groups		Comparison	
	BAF312 (N=1099)	**Placebo (N=546)**	**HR [95% CI]**	**p-value**
Any severe AE[2]				
Interaction test:	p=0,201			
Age = 18-30 years				
Number of patients with event	2	3		
Median (in weeks)	-	-		
% of event-free patients[+]	91,43 [80,03; 100,00]	72,92 [46,36; 99,47]		
			0,30 [0,05; 1,80]	0,187
Age = 31-40 years				
Number of patients with event	11	5		
Median (in weeks)	-	-		
% of event-free patients[+]	91,75 [86,93; 96,58]	93,41 [87,70; 99,13]		
			1,21 [0,42; 3,48]	0,724
Age = 41-55 years				
Number of patients with event	86	39		
Median (in weeks)	-	-		
% of event-free patients[+]	84,34 [80,78; 87,90]	86,06 [81,84; 90,28]		
			1,00 [0,69; 1,46]	0,998
Age = >55 years				
Number of patients with event	40	14		
Median (in weeks)	-	-		
% of event-free patients[+]	72,68 [62,86; 82,50]	78,86 [66,65; 91,07]		
			1,77 [0,97; 3,26]	0,065
Any severe AE[2], disease specific events excluded[1]				
Interaction test:	p=0,269			
Age = 18-30 years				
Number of patients with event	1	3		
Median (in weeks)	-	-		
% of event-free patients[+]	95,24 [86,13; 100,00]	72,92 [46,36; 99,47]		
			0,15 [0,02; 1,41]	0,096
Age = 31-40 years				
Number of patients with event	9	5		
Median (in weeks)	-	-		
% of event-free patients[+]	93,05 [88,51; 97,59]	93,40 [87,68; 99,13]		
			0,98 [0,33; 2,92]	0,969

	Treatment groups		Comparison	
	BAF312 (N=1099)	**Placebo (N=546)**	**HR [95% CI]**	**p-value**
Age = 41-55 years				
Number of patients with event	71	24		
Median (in weeks)	-	-		
% of event-free patients+	86,74 [83,34; 90,14]	91,44 [88,07; 94,81]		
			1,34 [0,84; 2,13]	0,215
Age = >55 years				
Number of patients with event	29	12		
Median (in weeks)	-	-		
% of event-free patients+	77,71 [67,69; 87,73]	80,44 [68,49; 92,39]		
			1,46 [0,75; 2,87]	0,268
Any AE leading to study discontinuation				
Interaction test:	p=0,392			
Age = 18-30 years				
Number of patients with event	1	0		
Median (in weeks)	-	-		
% of event-free patients+	96,15 [88,76; 100,00]	100,00 [100,00; 100,00]		
			-	-
Age = 31-40 years				
Number of patients with event	0	1		
Median (in weeks)	-	-		
% of event-free patients+	100,00 [100,00; 100,00]	98,25 [94,84; 100,00]		
			-	-
Age = 41-55 years				
Number of patients with event	30	13		
Median (in weeks)	-	-		
% of event-free patients+	95,40 [93,77; 97,04]	95,71 [93,42; 98,01]		
			1,06 [0,56; 2,04]	0,851
Age = >55 years				
Number of patients with event	15	2		
Median (in weeks)	-	-		
% of event-free patients+	92,17 [88,36; 95,98]	95,69 [88,90; 100,00]		
			4,42 [1,01; 19,34]	0,048 *

	Treatment groups		Comparison	
	BAF312 (N=1099)	**Placebo (N=546)**	**HR [95% CI]**	**p-value**
Any AE leading to study drug discontinuation				
Interaction test:	p=0,792			
Age = 18-30 years				
Number of patients with event	1	0		
Median (in weeks)	-	-		
% of event-free patients+	96,15 [88,76; 100,00]	100,00 [100,00; 100,00]		
			-	-
Age = 31-40 years				
Number of patients with event	2	1		
Median (in weeks)	-	-		
% of event-free patients+	98,36 [96,05; 100,00]	98,25 [94,84; 100,00]		
			1,11 [0,10; 12,19]	0,935
Age = 41-55 years				
Number of patients with event	59	21		
Median (in weeks)	-	-		
% of event-free patients+	90,99 [88,75; 93,22]	93,08 [90,20; 95,96]		
			1,29 [0,79; 2,13]	0,312
Age = >55 years				
Number of patients with event	22	6		
Median (in weeks)	-	-		
% of event-free patients+	88,38 [83,79; 92,97]	90,76 [82,90; 98,61]		
			2,18 [0,88; 5,38]	0,090

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 total population

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

	Treatment groups		Comparison	
	BAF312 (N=1099)	**Placebo (N=546)**	**HR [95% CI]**	**p-value**
N'	1099	546		
N' Age = 18-30 years	26	12		
N' Age = 31-40 years	161	91		
N' Age = 41-55 years	712	331		
N' Age = >55 years	200	112		
BLOOD AND LYMPHATIC SYSTEM DISORDERS				
Interaction test:	p=0,770			
Age = 18-30 years				
Number of patients with event	1	0		
Median (in weeks)	-	-		
% of event-free patients+	96,00 [88,32; 100,00]	100,00 [100,00; 100,00]		
			-	-
Age = 31-40 years				
Number of patients with event	10	4		
Median (in weeks)	-	-		
% of event-free patients+	93,51 [89,61; 97,41]	95,53 [91,24; 99,81]		
			1,38 [0,43; 4,40]	0,585
Age = 41-55 years				
Number of patients with event	28	4		
Median (in weeks)	-	-		
% of event-free patients+	95,23 [93,41; 97,05]	98,66 [97,34; 99,98]		
			3,22 [1,13; 9,17]	0,029 *
Age = >55 years				
Number of patients with event	7	2		
Median (in weeks)	-	-		
% of event-free patients+	93,06 [87,62; 98,50]	98,12 [95,54; 100,00]		
			2,07 [0,43; 9,95]	0,365

	Treatment groups		Comparison	
	BAF312 (N=1099)	**Placebo (N=546)**	**HR [95% CI]**	**p-value**
EAR AND LABYRINTH DISORDERS				
VERTIGO				
Interaction test:	p=0,752			
Age = 18-30 years				
Number of patients with event	1	0		
Median (in weeks)	-	-		
% of event-free patients+	96,15 [88,76; 100,00]	100,00 [100,00; 100,00]		
			-	-
Age = 31-40 years				
Number of patients with event	2	3		
Median (in weeks)	-	-		
% of event-free patients+	98,73 [96,97; 100,00]	96,01 [91,53; 100,00]		
			0,37 [0,06; 2,20]	0,273
Age = 41-55 years				
Number of patients with event	21	19		
Median (in weeks)	-	-		
% of event-free patients+	96,35 [94,57; 98,13]	93,34 [90,37; 96,32]		
			0,50 [0,27; 0,93]	0,029 *
Age = >55 years				
Number of patients with event	1	4		
Median (in weeks)	-	-		
% of event-free patients+	99,48 [98,48; 100,00]	96,03 [92,17; 99,90]		
			0,14 [0,02; 1,29]	0,083
EYE DISORDERS				
MACULAR OEDEMA				
Interaction test:	p=1,000			
Age = 18-30 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=1099)	**Placebo (N=546)**	**HR [95% CI]**	**p-value**
Age = 31-40 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	13	0		
Median (in weeks)	-	-		
% of event-free patients+	97,74 [96,43; 99,04]	100,00 [100,00; 100,00]		
			-	-
Age = >55 years				
Number of patients with event	5	1		
Median (in weeks)	-	-		
% of event-free patients+	97,37 [95,09; 99,65]	98,21 [94,75; 100,00]		
			2,94 [0,34; 25,16]	0,325
GASTROINTESTINAL DISORDERS				
NAUSEA				
Interaction test:	p=0,931			
Age = 18-30 years				
Number of patients with event	2	0		
Median (in weeks)	-	-		
% of event-free patients+	91,09 [79,17; 100,00]	100,00 [100,00; 100,00]		
			-	-
Age = 31-40 years				
Number of patients with event	9	2		
Median (in weeks)	-	-		
% of event-free patients+	92,56 [87,23; 97,89]	94,74 [86,56; 100,00]		
			2,57 [0,56; 11,92]	0,226
Age = 41-55 years				
Number of patients with event	47	13		
Median (in weeks)	-	-		
% of event-free patients+	92,95 [90,93; 94,97]	96,04 [93,93; 98,15]		
			1,69 [0,91; 3,11]	0,096

	Treatment groups		Comparison	
	BAF312 (N=1099)	**Placebo (N=546)**	**HR [95% CI]**	**p-value**
Age = >55 years				
Number of patients with event	16	4		
Median (in weeks)	-	-		
% of event-free patients+	91,66 [87,74; 95,59]	95,36 [90,83; 99,89]		
			2,36 [0,79; 7,05]	0,125
GENERAL DISORDERS AND ADMINISTRATION SITE CONDITIONS				
GAIT DISTURBANCE				
Interaction test:	p=0,966			
Age = 18-30 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 = 31-40 years				
Number of patients with event	4	3		
Median (in weeks)	-	-		
% of event-free patients+	97,34 [94,75; 99,92]	95,02 [88,97; 100,00]		
			0,73 [0,16; 3,24]	0,674
Age = 41-55 years				
Number of patients with event	14	13		
Median (in weeks)	-	-		
% of event-free patients+	88,13 [69,89; 100,00]	94,88 [91,90; 97,86]		
			0,48 [0,22; 1,02]	0,056
Age = >55 years				
Number of patients with event	6	6		
Median (in weeks)	-	-		
% of event-free patients+	96,91 [94,47; 99,35]	90,82 [82,87; 98,76]		
			0,59 [0,19; 1,82]	0,356
OEDEMA PERIPHERAL				
Interaction test:	p=0,783			
Age = 18-30 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=1099)	**Placebo (N=546)**	**HR [95% CI]**	**p-value**
Age = 31-40 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	34	10		
Median (in weeks)	-	-		
% of event-free patients+	86,75 [71,85; 100,00]	96,33 [93,95; 98,70]		
			1,56 [0,77; 3,15]	0,220
Age = >55 years				
Number of patients with event	16	3		
Median (in weeks)	-	-		
% of event-free patients+	88,95 [83,10; 94,80]	97,24 [94,16; 100,00]		
			3,30 [0,96; 11,33]	0,058
HEPATOBILIARY DISORDERS				
Interaction test:	p=0,999			
Age = 18-30 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 = 31-40 years				
Number of patients with event	1	0		
Median (in weeks)	-	-		
% of event-free patients+	99,34 [98,06; 100,00]	100,00 [100,00; 100,00]		
			-	-
Age = 41-55 years				
Number of patients with event	20	3		
Median (in weeks)	-	-		
% of event-free patients+	96,24 [94,45; 98,04]	98,59 [96,96; 100,00]		
			3,03 [0,90; 10,21]	0,073

	Treatment groups		Comparison	
	BAF312 (N=1099)	**Placebo (N=546)**	**HR [95% CI]**	**p-value**
Age = >55 years				
Number of patients with event	6	1		
Median (in weeks)	-	-		
% of event-free patients+	95,69 [92,04; 99,34]	98,75 [96,32; 100,00]		
			3,69 [0,44; 30,69]	0,226
INFECTIONS AND INFESTATIONS				
HERPES ZOSTER				
Interaction test:	p=0,971			
Age = 18-30 years				
Number of patients with event	1	0		
Median (in weeks)	-	-		
% of event-free patients+	94,74 [84,70; 100,00]	100,00 [100,00; 100,00]		
			-	-
Age = 31-40 years				
Number of patients with event	1	0		
Median (in weeks)	-	-		
% of event-free patients+	98,94 [96,86; 100,00]	100,00 [100,00; 100,00]		
			-	-
Age = 41-55 years				
Number of patients with event	16	2		
Median (in weeks)	-	-		
% of event-free patients+	97,43 [96,16; 98,69]	99,30 [98,33; 100,00]		
			3,67 [0,84; 15,98]	0,083
Age = >55 years				
Number of patients with event	7	2		
Median (in weeks)	-	-		
% of event-free patients+	94,82 [90,81; 98,84]	97,12 [93,14; 100,00]		
			2,14 [0,45; 10,32]	0,342

	Treatment groups		Comparison	
	BAF312 (N=1099)	**Placebo (N=546)**	**HR [95% CI]**	**p-value**
INVESTIGATIONS				
Interaction test:	p=0,950			
Age = 18-30 years				
Number of patients with event	4	1		
Median (in weeks)	-	-		
% of event-free patients+	68,75 [36,35; 100,00]	87,50 [64,58; 100,00]		
			1,93 [0,22; 17,23]	0,558
Age = 31-40 years				
Number of patients with event	39	12		
Median (in weeks)	-	-		
% of event-free patients+	70,22 [61,33; 79,11]	79,65 [65,25; 94,05]		
			1,97 [1,03; 3,77]	0,040 *
Age = 41-55 years				
Number of patients with event	176	52		
Median (in weeks)	-	-		
% of event-free patients+	67,47 [62,52; 72,42]	74,49 [66,01; 82,97]		
			1,62 [1,19; 2,21]	0,002 *
Age = >55 years				
Number of patients with event	44	15		
Median (in weeks)	-	-		
% of event-free patients+	66,93 [57,56; 76,30]	74,50 [60,28; 88,73]		
			1,81 [1,01; 3,26]	0,047 *
ALANINE AMINOTRANSFERASE INCREASED				
Interaction test:	p=0,484			
Age = 18-30 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 = 31-40 years				
Number of patients with event	17	4		
Median (in weeks)	-	-		
% of event-free patients+	86,11 [79,12; 93,11]	95,46 [91,10; 99,81]		
			2,44 [0,82; 7,25]	0,109

	Treatment groups		Comparison	
	BAF312 (N=1099)	**Placebo (N=546)**	**HR [95% CI]**	**p-value**
Age = 41-55 years				
Number of patients with event	40	2		
Median (in weeks)	-	-		
% of event-free patients+	92,69 [90,24; 95,15]	99,37 [98,50; 100,00]		
			9,27 [2,24; 38,35]	0,002 *
Age = >55 years				
Number of patients with event	8	2		
Median (in weeks)	-	-		
% of event-free patients+	94,36 [90,23; 98,48]	98,10 [95,50; 100,00]		
			2,40 [0,51; 11,32]	0,267
GAMMA-GLUTAMYLTRANSFERASE INCREASED				
Interaction test:	p=0,999			
Age = 18-30 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 = 31-40 years				
Number of patients with event	6	1		
Median (in weeks)	-	-		
% of event-free patients+	95,83 [92,53; 99,12]	97,22 [91,85; 100,00]		
			3,38 [0,41; 28,05]	0,260
Age = 41-55 years				
Number of patients with event	31	5		
Median (in weeks)	-	-		
% of event-free patients+	93,76 [90,99; 96,54]	97,44 [94,88; 99,99]		
			2,84 [1,11; 7,31]	0,030 *
Age = >55 years				
Number of patients with event	6	0		
Median (in weeks)	-	-		
% of event-free patients+	95,78 [92,04; 99,53]	100,00 [100,00; 100,00]		
			-	-

	Treatment groups		Comparison	
	BAF312 (N=1099)	**Placebo (N=546)**	**HR [95% CI]**	**p-value**
HEPATIC ENZYME INCREASED				
Interaction test:	p=1,000			
Age = 18-30 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 = 31-40 years				
Number of patients with event	2	0		
Median (in weeks)	-	-		
% of event-free patients+	98,75 [97,02; 100,00]	100,00 [100,00; 100,00]		
			-	-
Age = 41-55 years				
Number of patients with event	9	1		
Median (in weeks)	-	-		
% of event-free patients+	98,62 [97,71; 99,52]	99,55 [98,66; 100,00]		
			4,13 [0,52; 32,57]	0,179
Age = >55 years				
Number of patients with event	5	0		
Median (in weeks)	-	-		
% of event-free patients+	96,59 [93,50; 99,68]	100,00 [100,00; 100,00]		
			-	-
NERVOUS SYSTEM DISORDERS				
Interaction test:	p=0,798			
Age = 18-30 years				
Number of patients with event	8	0		
Median (in weeks)	-	-		
% of event-free patients+	67,60 [48,99; 86,21]	100,00 [100,00; 100,00]		
			-	-
Age = 31-40 years				
Number of patients with event	47	27		
Median (in weeks)	-	-		
% of event-free patients+	67,21 [58,75; 75,66]	66,55 [55,27; 77,83]		
			0,96 [0,59; 1,53]	0,849

	Treatment groups		Comparison	
	BAF312 (N=1099)	**Placebo (N=546)**	**HR [95% CI]**	**p-value**
Age = 41-55 years				
Number of patients with event	287	111		
Median (in weeks)	150,9 [133,9; -]	-		
% of event-free patients+	47,33 [35,43; 59,24]	61,28 [54,69; 67,86]		
			1,25 [1,00; 1,55]	0,048 *
Age = >55 years				
Number of patients with event	74	37		
Median (in weeks)	-	-		
% of event-free patients+	53,69 [43,43; 63,95]	60,89 [48,42; 73,35]		
			1,17 [0,79; 1,74]	0,437
PARAESTHESIA				
Interaction test:	p=0,970			
Age = 18-30 years				
Number of patients with event	1	0		
Median (in weeks)	-	-		
% of event-free patients+	95,45 [86,75; 100,00]	100,00 [100,00; 100,00]		
			-	-
Age = 31-40 years				
Number of patients with event	2	3		
Median (in weeks)	-	-		
% of event-free patients+	98,75 [97,04; 100,00]	93,60 [85,21; 100,00]		
			0,36 [0,06; 2,18]	0,268
Age = 41-55 years				
Number of patients with event	13	13		
Median (in weeks)	-	-		
% of event-free patients+	97,51 [95,96; 99,06]	95,93 [93,76; 98,10]		
			0,45 [0,21; 0,97]	0,041 *

	Treatment groups		Comparison	
	BAF312 (N=1099)	**Placebo (N=546)**	**HR [95% CI]**	**p-value**
Age = >55 years				
Number of patients with event	2	4		
Median (in weeks)	-	-		
% of event-free patients+	95,52 [87,82; 100,00]	94,26 [88,15; 100,00]		
			0,28 [0,05; 1,56]	0,147

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 total population

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

	Treatment groups		Comparison	
	BAF312 (N=1099)	**Placebo (N=546)**	**HR [95% CI]**	**p-value**
N'	1099	546		
N' Age = 18-30 years	26	12		
N' Age = 31-40 years	161	91		
N' Age = 41-55 years	712	331		
N' Age = >55 years	200	112		
INVESTIGATIONS				
Interaction test:	p=1,000			
Age = 18-30 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 = 31-40 years				
Number of patients with event	5	1		
Median (in weeks)	-	-		
% of event-free patients+	96,39 [93,24; 99,54]	98,90 [96,76; 100,00]		
			2,79 [0,33; 23,89]	0,349
Age = 41-55 years				
Number of patients with event	14	2		
Median (in weeks)	-	-		
% of event-free patients+	97,65 [96,39; 98,91]	99,31 [98,35; 100,00]		
			3,20 [0,73; 14,07]	0,124

	Treatment groups		Comparison	
	BAF312 (N=1099)	**Placebo (N=546)**	**HR [95% CI]**	**p-value**
Age = >55 years				
Number of patients with event	2	0		
Median (in weeks)	-	-		
% of event-free patients+	98,98 [97,58; 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.

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 total population

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=1099)	**Placebo (N=546)**	**HR [95% CI]**	**p-value**
N'	1099	546		
N' Age = 18-30 years	26	12		
N' Age = 31-40 years	161	91		
N' Age = 41-55 years	712	331		
N' Age = >55 years	200	112		
Infections and infestations				
Interaction test:	p=0,745			
Age = 18-30 years				
Number of patients with event	10	3		
Median (in weeks)	99,0 [64,3; -]	-		
% of event-free patients+	42,98 [13,13; 72,83]	75,00 [50,50; 99,50]		
			1,76 [0,48; 6,40]	0,390
Age = 31-40 years				
Number of patients with event	64	39		
Median (in weeks)	-	-		
% of event-free patients+	50,93 [40,09; 61,76]	51,95 [40,45; 63,46]		
			0,86 [0,58; 1,29]	0,468
Age = 41-55 years				
Number of patients with event	366	166		
Median (in weeks)	74,1 [61,4; 85,9]	68,1 [51,0; 102,6]		
% of event-free patients+	37,69 [32,47; 42,91]	41,74 [34,96; 48,53]		
			1,00 [0,83; 1,20]	0,990
Age = >55 years				
Number of patients with event	99	60		
Median (in weeks)	66,0 [50,0; 100,1]	64,9 [49,4; 88,6]		
% of event-free patients+	37,40 [28,64; 46,15]	35,76 [24,07; 47,45]		
			0,98 [0,71; 1,35]	0,914
Herpes simplex virus infections				
Interaction test:	p=0,996			
Age = 18-30 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=1099)	**Placebo (N=546)**	**HR [95% CI]**	**p-value**
Age = 31-40 years				
Number of patients with event	2	1		
Median (in weeks)	-	-		
% of event-free patients+	98,74 [97,00; 100,00]	97,87 [93,75; 100,00]		
			1,11 [0,10; 12,29]	0,930
Age = 41-55 years				
Number of patients with event	20	8		
Median (in weeks)	-	-		
% of event-free patients+	96,64 [95,13; 98,15]	97,20 [95,26; 99,15]		
			1,13 [0,50; 2,58]	0,763
Age = >55 years				
Number of patients with event	3	2		
Median (in weeks)	-	-		
% of event-free patients+	96,53 [91,99; 100,00]	94,98 [86,88; 100,00]		
			0,88 [0,15; 5,27]	0,888
Varicella-zoster virus infections				
Interaction test:	p=0,966			
Age = 18-30 years				
Number of patients with event	1	0		
Median (in weeks)	-	-		
% of event-free patients+	94,74 [84,70; 100,00]	100,00 [100,00; 100,00]		
			-	-
Age = 31-40 years				
Number of patients with event	2	0		
Median (in weeks)	-	-		
% of event-free patients+	97,20 [93,26; 100,00]	100,00 [100,00; 100,00]		
			-	-
Age = 41-55 years				
Number of patients with event	21	2		
Median (in weeks)	-	-		
% of event-free patients+	96,69 [95,28; 98,10]	99,30 [98,33; 100,00]		
			4,81 [1,13; 20,51]	0,034 *

	Treatment groups		Comparison	
	BAF312 (N=1099)	**Placebo (N=546)**	**HR [95% CI]**	**p-value**
Age = >55 years				
Number of patients with event	9	2		
Median (in weeks)	-	-		
% of event-free patients+	91,66 [85,62; 97,70]	97,12 [93,14; 100,00]		
			2,75 [0,59; 12,73]	0,196
Lymphopenia				
Interaction test:	p=1,000			
Age = 18-30 years				
Number of patients with event	1	0		
Median (in weeks)	-	-		
% of event-free patients+	96,00 [88,32; 100,00]	100,00 [100,00; 100,00]		
			-	-
Age = 31-40 years				
Number of patients with event	3	0		
Median (in weeks)	-	-		
% of event-free patients+	98,10 [95,97; 100,00]	100,00 [100,00; 100,00]		
			-	-
Age = 41-55 years				
Number of patients with event	8	0		
Median (in weeks)	-	-		
% of event-free patients+	98,74 [97,87; 99,61]	100,00 [100,00; 100,00]		
			-	-
Age = >55 years				
Number of patients with event	2	0		
Median (in weeks)	-	-		
% of event-free patients+	98,55 [96,56; 100,00]	100,00 [100,00; 100,00]		
			-	-

	Treatment groups		Comparison	
	BAF312 (N=1099)	**Placebo (N=546)**	**HR [95% CI]**	**p-value**
Macular edema				
Interaction test:	p=1,000			
Age = 18-30 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 = 31-40 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	15	0		
Median (in weeks)	-	-		
% of event-free patients+	97,41 [96,04; 98,79]	100,00 [100,00; 100,00]		
			-	-
Age = >55 years				
Number of patients with event	5	1		
Median (in weeks)	-	-		
% of event-free patients+	97,37 [95,09; 99,65]	98,21 [94,75; 100,00]		
			2,95 [0,34; 25,23]	0,324
Abnormal hepatic enzymes				
Interaction test:	p=0,983			
Age = 18-30 years				
Number of patients with event	1	0		
Median (in weeks)	-	-		
% of event-free patients+	95,65 [87,32; 100,00]	100,00 [100,00; 100,00]		
			-	-
Age = 31-40 years				
Number of patients with event	24	5		
Median (in weeks)	-	-		
% of event-free patients+	83,00 [76,44; 89,56]	92,73 [85,97; 99,49]		
			2,83 [1,08; 7,42]	0,034 *

	Treatment groups		Comparison	
	BAF312 (N=1099)	**Placebo (N=546)**	**HR [95% CI]**	**p-value**
Age = 41-55 years				
Number of patients with event	91	13		
Median (in weeks)	-	-		
% of event-free patients+	82,70 [78,37; 87,03]	93,76 [89,97; 97,55]		
			3,32 [1,85; 5,93]	<0,001 *
Age = >55 years				
Number of patients with event	19	3		
Median (in weeks)	-	-		
% of event-free patients+	86,44 [80,22; 92,67]	97,13 [93,93; 100,00]		
			3,87 [1,15; 13,09]	0,029 *
Malignancies				
Interaction test:	p=0,080			
Age = 18-30 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 = 31-40 years				
Number of patients with event	2	1		
Median (in weeks)	-	-		
% of event-free patients+	97,60 [94,29; 100,00]	98,25 [94,84; 100,00]		
			1,06 [0,10; 11,72]	0,961
Age = 41-55 years				
Number of patients with event	4	8		
Median (in weeks)	-	-		
% of event-free patients+	99,33 [98,68; 99,99]	89,42 [74,07; 100,00]		
			0,22 [0,07; 0,73]	0,013 *
Age = >55 years				
Number of patients with event	14	5		
Median (in weeks)	-	-		
% of event-free patients+	90,43 [85,30; 95,55]	91,23 [82,78; 99,67]		
			1,74 [0,63; 4,84]	0,286

	Treatment groups		Comparison	
	BAF312 (N=1099)	**Placebo (N=546)**	**HR [95% CI]**	**p-value**
Hypertension				
Interaction test:	p=0,392			
Age = 18-30 years				
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]		
			60946,09 [0,00; I]	0,976
Age = 31-40 years				
Number of patients with event	10	2		
Median (in weeks)	-	-		
% of event-free patients+	92,07 [86,97; 97,17]	94,41 [85,56; 100,00]		
			2,79 [0,61; 12,72]	0,186
Age = 41-55 years				
Number of patients with event	94	38		
Median (in weeks)	-	-		
% of event-free patients+	83,57 [80,03; 87,10]	76,94 [60,42; 93,45]		
			1,11 [0,76; 1,62]	0,583
Age = >55 years				
Number of patients with event	32	10		
Median (in weeks)	-	-		
% of event-free patients+	68,17 [46,63; 89,71]	89,77 [83,55; 95,98]		
			1,99 [0,98; 4,04]	0,058
Seizures				
Interaction test:	p=1,000			
Age = 18-30 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 = 31-40 years				
Number of patients with event	0	1		
Median (in weeks)	-	-		
% of event-free patients+	100,00 [100,00; 100,00]	98,88 [96,69; 100,00]		
			-	-

	Treatment groups		Comparison	
	BAF312 (N=1099)	**Placebo (N=546)**	**HR [95% CI]**	**p-value**
Age = 41-55 years				
Number of patients with event	17	0		
Median (in weeks)	-	-		
% of event-free patients+	96,03 [93,50; 98,56]	100,00 [100,00; 100,00]		
			-	-
Age = >55 years				
Number of patients with event	2	1		
Median (in weeks)	-	-		
% of event-free patients+	98,97 [97,55; 100,00]	99,07 [97,27; 100,00]		
			1,16 [0,11; 12,82]	0,903
Thromboembolic events				
Interaction test:	p=0,822			
Age = 18-30 years				
Number of patients with event	1	0		
Median (in weeks)	-	-		
% of event-free patients+	95,83 [87,84; 100,00]	100,00 [100,00; 100,00]		
			-	-
Age = 31-40 years				
Number of patients with event	4	2		
Median (in weeks)	-	-		
% of event-free patients+	97,44 [94,96; 99,92]	95,71 [89,22; 100,00]		
			1,11 [0,20; 6,05]	0,905
Age = 41-55 years				
Number of patients with event	19	10		
Median (in weeks)	-	-		
% of event-free patients+	95,37 [92,40; 98,34]	96,63 [94,55; 98,70]		
			0,85 [0,40; 1,84]	0,685
Age = >55 years				
Number of patients with event	9	3		
Median (in weeks)	-	-		
% of event-free patients+	94,97 [91,74; 98,21]	88,13 [69,74; 100,00]		
			1,78 [0,48; 6,58]	0,387

	Treatment groups		Comparison	
	BAF312 (N=1099)	**Placebo (N=546)**	**HR [95% CI]**	**p-value**
Respiratory disorders				
Interaction test:	p=0,612			
Age = 18-30 years				
Number of patients with event	2	2		
Median (in weeks)	-	-		
% of event-free patients+	91,20 [79,48; 100,00]	61,11 [11,11; 100,00]		
			0,44 [0,06; 3,12]	0,411
Age = 31-40 years				
Number of patients with event	10	4		
Median (in weeks)	-	-		
% of event-free patients+	93,37 [89,39; 97,36]	64,41 [12,81; 100,00]		
			1,39 [0,44; 4,42]	0,580
Age = 41-55 years				
Number of patients with event	82	44		
Median (in weeks)	-	-		
% of event-free patients+	86,19 [83,31; 89,08]	81,28 [74,87; 87,70]		
			0,83 [0,58; 1,20]	0,320
Age = >55 years				
Number of patients with event	23	21		
Median (in weeks)	-	-		
% of event-free patients+	86,09 [80,43; 91,74]	72,06 [60,04; 84,08]		
			0,64 [0,35; 1,15]	0,138
Peripheral edema/swelling				
Interaction test:	p=0,795			
Age = 18-30 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 = 31-40 years				
Number of patients with event	0	2		
Median (in weeks)	-	-		
% of event-free patients+	100,00 [100,00; 100,00]	97,65 [94,42; 100,00]		
			-	-

	Treatment groups		Comparison	
	BAF312 (N=1099)	**Placebo (N=546)**	**HR [95% CI]**	**p-value**
Age = 41-55 years				
Number of patients with event	55	13		
Median (in weeks)	-	-		
% of event-free patients+	83,12 [68,74; 97,51]	94,85 [91,92; 97,79]		
			1,95 [1,07; 3,57]	0,030 *
Age = >55 years				
Number of patients with event	19	3		
Median (in weeks)	-	-		
% of event-free patients+	86,99 [80,78; 93,19]	97,24 [94,16; 100,00]		
			3,94 [1,17; 13,31]	0,027 *

N': Number of patients in the analysis
CI: Confidence Interval
HR: Hazard Ratio
I: upper limit of confidence interval >1E6
*: $p < 0,05$

+ 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 total population

	Treatment groups		Comparison	
	BAF312 (N=1099)	**Placebo (N=546)**	**HR [95% CI]**	**p-value**
N'	1099	546		
N' Age = 18-30 years	26	12		
N' Age = 31-40 years	161	91		
N' Age = 41-55 years	712	331		
N' Age = >55 years	200	112		
Asthma/bronchospasm				
Interaction test:	p=1,000			
Age = 18-30 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 = 31-40 years				
Number of patients with event	2	0		
Median (in weeks)	-	-		
% of event-free patients+	98,58 [96,63; 100,00]	100,00 [100,00; 100,00]		
			-	-
Age = 41-55 years				
Number of patients with event	4	2		
Median (in weeks)	-	-		
% of event-free patients+	99,38 [98,77; 99,99]	99,15 [97,94; 100,00]		
			0,92 [0,17; 5,01]	0,921
Age = >55 years				
Number of patients with event	2	0		
Median (in weeks)	-	-		
% of event-free patients+	98,86 [97,29; 100,00]	100,00 [100,00; 100,00]		
			-	-

	Treatment groups		Comparison	
	BAF312 (N=1099)	**Placebo (N=546)**	**HR [95% CI]**	**p-value**
Pregnancy and neonatal topics				
Interaction test:	p=1,000			
Age = 18-30 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 = 31-40 years				
Number of patients with event	2	0		
Median (in weeks)	-	-		
% of event-free patients+	98,61 [96,69; 100,00]	100,00 [100,00; 100,00]		
			-	-
Age = 41-55 years				
Number of patients with event	3	0		
Median (in weeks)	-	-		
% of event-free patients+	99,52 [98,98; 100,00]	100,00 [100,00; 100,00]		
			-	-
Age = >55 years				
Number of patients with event	1	0		
Median (in weeks)	-	-		
% of event-free patients+	99,41 [98,26; 100,00]	100,00 [100,00; 100,00]		
			-	-
Bradyarrhythmias and bradycardia				
Interaction test:	p=0,776			
Age = 18-30 years				
Number of patients with event	3	1		
Median (in weeks)	-	-		
% of event-free patients+	88,46 [76,18; 100,00]	91,67 [76,03; 100,00]		
			1,34 [0,14; 12,88]	0,800

	Treatment groups		Comparison	
	BAF312 (N=1099)	**Placebo (N=546)**	**HR [95% CI]**	**p-value**
Age = 31-40 years				
Number of patients with event	18	4		
Median (in weeks)	-	-		
% of event-free patients+	87,35 [81,20; 93,49]	95,58 [91,34; 99,82]		
			2,61 [0,88; 7,71]	0,083
Age = 41-55 years				
Number of patients with event	62	17		
Median (in weeks)	-	-		
% of event-free patients+	89,06 [85,75; 92,37]	94,17 [91,40; 96,94]		
			1,70 [0,99; 2,90]	0,054
Age = >55 years				
Number of patients with event	20	9		
Median (in weeks)	-	-		
% of event-free patients+	82,63 [68,01; 97,25]	87,68 [78,77; 96,58]		
			1,29 [0,59; 2,83]	0,526

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 total population

12.3 Subgroup: Gender

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

	Treatment groups		Comparison	
	BAF312 (N=1099)	**Placebo (N=546)**	**HR [95% CI]**	**p-value**
N'	1099	546		
N' Gender = Male	435	223		
N' Gender = Female	664	323		
Any AE				
Interaction test:	p=0,321			
Gender = Male				
Number of patients with event	383	186		
Median (in weeks)	4,7 [4,0; 8,3]	8,1 [4,4; 12,7]		
% of event-free patients+	4,44 [0,10; 8,78]	12,61 [7,61; 17,61]		
			1,18 [0,99; 1,41]	0,063
Gender = Female				
Number of patients with event	592	259		
Median (in weeks)	3,7 [3,0; 5,3]	7,3 [4,7; 11,1]		
% of event-free patients+	8,47 [6,08; 10,87]	13,04 [6,84; 19,23]		
			1,33 [1,14; 1,53]	<0,001 *
Any AE, disease specific events excluded[1]				
Interaction test:	p=0,650			
Gender = Male				
Number of patients with event	360	172		
Median (in weeks)	12,1 [8,9; 13,1]	14,1 [11,0; 24,9]		
% of event-free patients+	9,17 [4,40; 13,95]	18,12 [12,38; 23,86]		
			1,18 [0,99; 1,42]	0,069
Gender = Female				
Number of patients with event	558	246		
Median (in weeks)	10,3 [8,0; 12,6]	11,7 [8,9; 16,3]		
% of event-free patients+	11,17 [8,13; 14,21]	15,86 [9,45; 22,27]		
			1,25 [1,08; 1,45]	0,004 *

	Treatment groups		Comparison	
	BAF312 (N=1099)	**Placebo (N=546)**	**HR [95% CI]**	**p-value**
Any SAE				
Interaction test:	p=0,098			
Gender = Male				
Number of patients with event	73	38		
Median (in weeks)	-	-		
% of event-free patients+	74,59 [65,48; 83,70]	69,93 [52,76; 87,10]		
			0,98 [0,66; 1,45]	0,921
Gender = Female				
Number of patients with event	113	36		
Median (in weeks)	-	-		
% of event-free patients+	77,00 [72,44; 81,56]	86,89 [82,61; 91,16]		
			1,55 [1,06; 2,25]	0,022 *
Any SAE, disease specific events excluded[1]				
Interaction test:	p=0,133			
Gender = Male				
Number of patients with event	56	27		
Median (in weeks)	-	-		
% of event-free patients+	82,42 [77,23; 87,61]	76,24 [59,66; 92,82]		
			1,05 [0,66; 1,66]	0,844
Gender = Female				
Number of patients with event	90	26		
Median (in weeks)	-	-		
% of event-free patients+	81,85 [78,13; 85,57]	90,10 [86,18; 94,03]		
			1,70 [1,10; 2,63]	0,017 *
Any severe AE[2]				
Interaction test:	p=0,084			
Gender = Male				
Number of patients with event	50	30		
Median (in weeks)	-	-		
% of event-free patients+	84,91 [80,05; 89,77]	82,85 [76,84; 88,86]		
			0,83 [0,53; 1,31]	0,420

	Treatment groups		Comparison	
	BAF312 (N=1099)	**Placebo (N=546)**	**HR [95% CI]**	**p-value**
Gender = Female				
Number of patients with event	89	31		
Median (in weeks)	-	-		
% of event-free patients+	82,41 [78,38; 86,43]	86,98 [81,74; 92,23]		
			1,42 [0,94; 2,14]	0,092
Any severe AE[2], disease specific events excluded[1]				
Interaction test:	p=0,055			
Gender = Male				
Number of patients with event	39	23		
Median (in weeks)	-	-		
% of event-free patients+	87,81 [83,18; 92,45]	86,49 [81,00; 91,97]		
			0,83 [0,50; 1,40]	0,488
Gender = Female				
Number of patients with event	71	21		
Median (in weeks)	-	-		
% of event-free patients+	85,06 [81,11; 89,00]	90,33 [85,36; 95,30]		
			1,67 [1,02; 2,71]	0,040 *
Any AE leading to study discontinuation				
Interaction test:	p=0,905			
Gender = Male				
Number of patients with event	16	6		
Median (in weeks)	-	-		
% of event-free patients+	96,01 [94,04; 97,98]	97,11 [94,83; 99,40]		
			1,37 [0,53; 3,49]	0,515
Gender = Female				
Number of patients with event	30	10		
Median (in weeks)	-	-		
% of event-free patients+	95,18 [93,49; 96,87]	95,65 [92,57; 98,73]		
			1,47 [0,72; 3,00]	0,294
Any AE leading to study drug discontinuation				
Interaction test:	p=0,705			
Gender = Male				
Number of patients with event	26	10		
Median (in weeks)	-	-		
% of event-free patients+	93,55 [91,10; 96,00]	94,06 [90,18; 97,93]		
			1,33 [0,64; 2,75]	0,448

	Treatment groups		Comparison	
	BAF312 (N=1099)	**Placebo (N=546)**	**HR [95% CI]**	**p-value**
Gender = Female				
Number of patients with event	58	18		
Median (in weeks)	-	-		
% of event-free patients+	90,49 [88,12; 92,85]	93,14 [89,81; 96,48]		
			1,58 [0,93; 2,68]	0,091

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 total population

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

	Treatment groups		Comparison	
	BAF312 (N=1099)	**Placebo (N=546)**	**HR [95% CI]**	**p-value**
N'	1099	546		
N' Gender = Male	435	223		
N' Gender = Female	664	323		
BLOOD AND LYMPHATIC SYSTEM DISORDERS				
Interaction test:	p=0,994			
Gender = Male				
Number of patients with event	9	2		
Median (in weeks)	-	-		
% of event-free patients+	97,33 [95,49; 99,17]	99,05 [97,73; 100,00]		
			2,26 [0,49; 10,48]	0,296
Gender = Female				
Number of patients with event	37	8		
Median (in weeks)	-	-		
% of event-free patients+	92,79 [90,33; 95,24]	97,36 [95,55; 99,18]		
			2,28 [1,06; 4,89]	0,035 *
EAR AND LABYRINTH DISORDERS				
VERTIGO				
Interaction test:	p=0,876			
Gender = Male				
Number of patients with event	7	7		
Median (in weeks)	-	-		
% of event-free patients+	98,33 [97,11; 99,56]	96,56 [94,03; 99,09]		
			0,50 [0,18; 1,43]	0,199
Gender = Female				
Number of patients with event	18	19		
Median (in weeks)	-	-		
% of event-free patients+	96,46 [94,51; 98,41]	93,07 [89,98; 96,16]		
			0,46 [0,24; 0,87]	0,017 *

	Treatment groups		Comparison	
	BAF312 (N=1099)	**Placebo (N=546)**	**HR [95% CI]**	**p-value**
EYE DISORDERS				
MACULAR OEDEMA				
Interaction test:	p=0,989			
Gender = Male				
Number of patients with event	6	1		
Median (in weeks)	-	-		
% of event-free patients+	98,41 [97,11; 99,71]	99,00 [97,05; 100,00]		
			3,01 [0,36; 25,00]	0,308
Gender = Female				
Number of patients with event	12	0		
Median (in weeks)	-	-		
% of event-free patients+	97,78 [96,41; 99,15]	100,00 [100,00; 100,00]		
			-	-
GASTROINTESTINAL DISORDERS				
NAUSEA				
Interaction test:	p=0,850			
Gender = Male				
Number of patients with event	14	4		
Median (in weeks)	-	-		
% of event-free patients+	96,32 [94,29; 98,35]	98,17 [96,39; 99,95]		
			1,78 [0,58; 5,39]	0,311
Gender = Female				
Number of patients with event	60	15		
Median (in weeks)	-	-		
% of event-free patients+	90,22 [87,75; 92,69]	94,27 [91,16; 97,38]		
			2,00 [1,14; 3,53]	0,016 *
GENERAL DISORDERS AND ADMINISTRATION SITE CONDITIONS				
GAIT DISTURBANCE				
Interaction test:	p=0,332			
Gender = Male				
Number of patients with event	12	8		
Median (in weeks)	-	-		
% of event-free patients+	83,26 [58,04; 100,00]	94,40 [90,09; 98,70]		
			0,74 [0,30; 1,80]	0,503

	Treatment groups		Comparison	
	BAF312 (N=1099)	**Placebo (N=546)**	**HR [95% CI]**	**p-value**
Gender = Female				
Number of patients with event	12	14		
Median (in weeks)	-	-		
% of event-free patients+	98,04 [96,93; 99,15]	93,94 [90,52; 97,36]		
			0,41 [0,19; 0,89]	0,024 *
OEDEMA PERIPHERAL				
Interaction test:	p=0,113			
Gender = Male				
Number of patients with event	15	7		
Median (in weeks)	-	-		
% of event-free patients+	95,37 [92,82; 97,91]	96,11 [93,07; 99,16]		
			1,07 [0,43; 2,61]	0,891
Gender = Female				
Number of patients with event	35	6		
Median (in weeks)	-	-		
% of event-free patients+	80,63 [56,18; 100,00]	98,00 [96,40; 99,59]		
			2,92 [1,23; 6,94]	0,015 *
HEPATOBILIARY DISORDERS				
Interaction test:	p=0,325			
Gender = Male				
Number of patients with event	14	1		
Median (in weeks)	-	-		
% of event-free patients+	95,45 [92,84; 98,07]	99,09 [97,32; 100,00]		
			7,05 [0,93; 53,64]	0,059
Gender = Female				
Number of patients with event	13	3		
Median (in weeks)	-	-		
% of event-free patients+	97,59 [96,22; 98,95]	98,74 [97,30; 100,00]		
			2,13 [0,61; 7,48]	0,238

	Treatment groups		Comparison	
	BAF312 (N=1099)	**Placebo (N=546)**	**HR [95% CI]**	**p-value**
INFECTIONS AND INFESTATIONS				
HERPES ZOSTER				
Interaction test:	p=0,974			
Gender = Male				
Number of patients with event	6	1		
Median (in weeks)	-	-		
% of event-free patients+	98,37 [97,05; 99,69]	99,54 [98,63; 100,00]		
			3,02 [0,36; 25,08]	0,306
Gender = Female				
Number of patients with event	19	3		
Median (in weeks)	-	-		
% of event-free patients+	96,32 [94,59; 98,05]	98,58 [96,96; 100,00]		
			3,15 [0,93; 10,63]	0,065
INVESTIGATIONS				
Interaction test:	p=0,281			
Gender = Male				
Number of patients with event	120	32		
Median (in weeks)	-	-		
% of event-free patients+	63,50 [57,25; 69,74]	77,08 [65,55; 88,61]		
			2,02 [1,37; 2,98]	<0,001 *
Gender = Female				
Number of patients with event	143	48		
Median (in weeks)	-	-		
% of event-free patients+	70,51 [65,35; 75,68]	74,42 [66,33; 82,50]		
			1,53 [1,10; 2,12]	0,011 *
ALANINE AMINOTRANSFERASE INCREASED				
Interaction test:	p=0,601			
Gender = Male				
Number of patients with event	38	4		
Median (in weeks)	-	-		
% of event-free patients+	88,46 [84,51; 92,41]	98,15 [96,35; 99,95]		
			4,93 [1,76; 13,82]	0,002 *

	Treatment groups		Comparison	
	BAF312 (N=1099)	**Placebo (N=546)**	**HR [95% CI]**	**p-value**
Gender = Female				
Number of patients with event	27	4		
Median (in weeks)	-	-		
% of event-free patients+	94,70 [92,60; 96,81]	98,67 [97,37; 99,97]		
			3,33 [1,17; 9,51]	0,025 *
GAMMA-GLUTAMYLTRANSFERASE INCREASED				
Interaction test:	p=0,712			
Gender = Male				
Number of patients with event	25	4		
Median (in weeks)	-	-		
% of event-free patients+	92,90 [90,06; 95,74]	97,10 [94,09; 100,00]		
			3,16 [1,10; 9,08]	0,033 *
Gender = Female				
Number of patients with event	18	2		
Median (in weeks)	-	-		
% of event-free patients+	95,55 [92,66; 98,43]	98,61 [96,45; 100,00]		
			4,44 [1,03; 19,12]	0,046 *
HEPATIC ENZYME INCREASED				
Interaction test:	p=0,991			
Gender = Male				
Number of patients with event	9	0		
Median (in weeks)	-	-		
% of event-free patients+	97,71 [96,21; 99,20]	100,00 [100,00; 100,00]		
			-	-
Gender = Female				
Number of patients with event	7	1		
Median (in weeks)	-	-		
% of event-free patients+	98,69 [97,68; 99,70]	99,55 [98,66; 100,00]		
			3,42 [0,42; 27,84]	0,250

	Treatment groups		Comparison	
	BAF312 (N=1099)	**Placebo (N=546)**	**HR [95% CI]**	**p-value**
NERVOUS SYSTEM DISORDERS				
Interaction test:	p=0,095			
Gender = Male				
Number of patients with event	135	69		
Median (in weeks)	-	-		
% of event-free patients+	54,74 [38,97; 70,51]	63,21 [55,04; 71,37]		
			1,00 [0,75; 1,33]	0,991
Gender = Female				
Number of patients with event	281	106		
Median (in weeks)	-	-		
% of event-free patients+	50,48 [45,35; 55,62]	62,50 [55,77; 69,24]		
			1,36 [1,09; 1,71]	0,007 *
PARAESTHESIA				
Interaction test:	p=0,084			
Gender = Male				
Number of patients with event	1	6		
Median (in weeks)	-	-		
% of event-free patients+	99,75 [99,26; 100,00]	97,14 [94,88; 99,40]		
			0,08 [0,01; 0,68]	0,020 *
Gender = Female				
Number of patients with event	17	14		
Median (in weeks)	-	-		
% of event-free patients+	95,58 [92,64; 98,52]	94,16 [90,78; 97,55]		
			0,58 [0,29; 1,18]	0,136

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 total population

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

	Treatment groups		Comparison	
	BAF312 (N=1099)	**Placebo (N=546)**	**HR [95% CI]**	**p-value**
N'	1099	546		
N' Gender = Male	435	223		
N' Gender = Female	664	323		
INVESTIGATIONS				
Interaction test:	p=0,567			
Gender = Male				
Number of patients with event	10	2		
Median (in weeks)	-	-		
% of event-free patients+	97,25 [95,53; 98,98]	99,09 [97,84; 100,00]		
			2,54 [0,56; 11,59]	0,229
Gender = Female				
Number of patients with event	11	1		
Median (in weeks)	-	-		
% of event-free patients+	98,05 [96,86; 99,24]	99,61 [98,85; 100,00]		
			5,35 [0,69; 41,43]	0,108

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 total population

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=1099)	**Placebo (N=546)**	**HR [95% CI]**	**p-value**
N'	1099	546		
N' Gender = Male	435	223		
N' Gender = Female	664	323		
Infections and infestations				
Interaction test:	p=0,878			
Gender = Male				
Number of patients with event	197	102		
Median (in weeks)	98,0 [73,7; -]	74,3 [61,0; -]		
% of event-free patients+	42,24 [34,35; 50,13]	47,72 [40,22; 55,23]		
			0,97 [0,76; 1,23]	0,813
Gender = Female				
Number of patients with event	342	166		
Median (in weeks)	68,1 [56,7; 79,0]	72,1 [49,3; 95,4]		
% of event-free patients+	37,32 [32,40; 42,24]	39,12 [31,89; 46,34]		
			0,99 [0,83; 1,20]	0,957
Herpes simplex virus infections				
Interaction test:	p=0,880			
Gender = Male				
Number of patients with event	4	2		
Median (in weeks)	-	-		
% of event-free patients+	98,31 [96,29; 100,00]	99,09 [97,85; 100,00]		
			0,99 [0,18; 5,41]	0,992
Gender = Female				
Number of patients with event	21	9		
Median (in weeks)	-	-		
% of event-free patients+	96,12 [94,40; 97,84]	95,20 [91,30; 99,10]		
			1,14 [0,52; 2,50]	0,736
Varicella-zoster virus infections				
Interaction test:	p=0,923			
Gender = Male				
Number of patients with event	9	1		
Median (in weeks)	-	-		
% of event-free patients+	96,94 [94,61; 99,28]	99,54 [98,63; 100,00]		
			4,48 [0,57; 35,39]	0,155

	Treatment groups		Comparison	
	BAF312 (N=1099)	**Placebo (N=546)**	**HR [95% CI]**	**p-value**
Gender = Female				
Number of patients with event	24	3		
Median (in weeks)	-	-		
% of event-free patients+	95,13 [93,06; 97,19]	98,58 [96,96; 100,00]		
			3,99 [1,20; 13,24]	0,024 *
Lymphopenia				
Interaction test:	p=1,000			
Gender = Male				
Number of patients with event	5	0		
Median (in weeks)	-	-		
% of event-free patients+	98,79 [97,74; 99,85]	100,00 [100,00; 100,00]		
			-	-
Gender = Female				
Number of patients with event	9	0		
Median (in weeks)	-	-		
% of event-free patients+	98,41 [97,37; 99,45]	100,00 [100,00; 100,00]		
			-	-
Macular edema				
Interaction test:	p=0,988			
Gender = Male				
Number of patients with event	6	1		
Median (in weeks)	-	-		
% of event-free patients+	98,41 [97,11; 99,71]	99,00 [97,05; 100,00]		
			3,01 [0,36; 25,03]	0,307
Gender = Female				
Number of patients with event	14	0		
Median (in weeks)	-	-		
% of event-free patients+	97,43 [95,98; 98,88]	100,00 [100,00; 100,00]		
			-	-

	Treatment groups		Comparison	
	BAF312 (N=1099)	**Placebo (N=546)**	**HR [95% CI]**	**p-value**
Abnormal hepatic enzymes				
Interaction test:	p=0,674			
Gender = Male				
Number of patients with event	75	11		
Median (in weeks)	-	-		
% of event-free patients+	78,76 [73,96; 83,56]	93,44 [89,39; 97,49]		
			3,66 [1,95; 6,90]	<0,001 *
Gender = Female				
Number of patients with event	60	10		
Median (in weeks)	-	-		
% of event-free patients+	86,66 [82,17; 91,15]	95,13 [91,72; 98,55]		
			3,01 [1,54; 5,87]	0,001 *
Malignancies				
Interaction test:	p=0,403			
Gender = Male				
Number of patients with event	7	7		
Median (in weeks)	-	-		
% of event-free patients+	98,02 [96,54; 99,49]	86,45 [68,35; 100,00]		
			0,49 [0,17; 1,40]	0,182
Gender = Female				
Number of patients with event	13	7		
Median (in weeks)	-	-		
% of event-free patients+	97,21 [95,58; 98,84]	96,58 [93,65; 99,51]		
			0,89 [0,35; 2,23]	0,800
Hypertension				
Interaction test:	p=0,114			
Gender = Male				
Number of patients with event	51	25		
Median (in weeks)	-	-		
% of event-free patients+	85,18 [81,09; 89,27]	74,47 [54,12; 94,82]		
			1,01 [0,62; 1,63]	0,974
Gender = Female				
Number of patients with event	86	25		
Median (in weeks)	-	-		
% of event-free patients+	80,52 [73,12; 87,93]	90,24 [86,18; 94,30]		
			1,71 [1,09; 2,67]	0,018 *

	Treatment groups		Comparison	
	BAF312 (N=1099)	**Placebo (N=546)**	**HR [95% CI]**	**p-value**
Seizures				
Interaction test:	p=0,991			
Gender = Male				
Number of patients with event	4	0		
Median (in weeks)	-	-		
% of event-free patients+	99,01 [98,05; 99,98]	100,00 [100,00; 100,00]		
			-	-
Gender = Female				
Number of patients with event	15	2		
Median (in weeks)	-	-		
% of event-free patients+	95,86 [92,96; 98,76]	99,35 [98,46; 100,00]		
			3,67 [0,84; 16,03]	0,084
Thromboembolic events				
Interaction test:	p=0,381			
Gender = Male				
Number of patients with event	13	8		
Median (in weeks)	-	-		
% of event-free patients+	96,65 [94,83; 98,47]	95,30 [91,83; 98,76]		
			0,80 [0,33; 1,94]	0,624
Gender = Female				
Number of patients with event	20	7		
Median (in weeks)	-	-		
% of event-free patients+	94,67 [91,12; 98,22]	94,87 [88,75; 100,00]		
			1,39 [0,59; 3,29]	0,453
Respiratory disorders				
Interaction test:	p=0,798			
Gender = Male				
Number of patients with event	42	27		
Median (in weeks)	-	-		
% of event-free patients+	88,33 [84,83; 91,82]	83,22 [75,60; 90,84]		
			0,76 [0,47; 1,23]	0,269

	Treatment groups		Comparison	
	BAF312 (N=1099)	**Placebo (N=546)**	**HR [95% CI]**	**p-value**
Gender = Female				
Number of patients with event	75	44		
Median (in weeks)	-	-		
% of event-free patients+	86,70 [83,80; 89,60]	73,05 [58,22; 87,87]		
			0,82 [0,57; 1,20]	0,309
Peripheral edema/swelling				
Interaction test:	p=0,005 *			
Gender = Male				
Number of patients with event	19	11		
Median (in weeks)	-	-		
% of event-free patients+	94,13 [91,32; 96,95]	93,44 [89,38; 97,50]		
			0,85 [0,41; 1,79]	0,676
Gender = Female				
Number of patients with event	55	7		
Median (in weeks)	-	-		
% of event-free patients+	77,08 [53,64; 100,00]	97,67 [95,96; 99,38]		
			3,98 [1,81; 8,75]	0,001 *

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 total population

	Treatment groups		Comparison	
	BAF312 (N=1099)	**Placebo (N=546)**	**HR [95% CI]**	**p-value**
N'	1099	546		
N' Gender = Male	435	223		
N' Gender = Female	664	323		
Asthma/bronchospasm				
Interaction test:	p=0,767			
Gender = Male				
Number of patients with event	3	1		
Median (in weeks)	-	-		
% of event-free patients+	99,19 [98,26; 100,00]	99,22 [97,69; 100,00]		
			1,53 [0,16; 14,74]	0,711
Gender = Female				
Number of patients with event	5	1		
Median (in weeks)	-	-		
% of event-free patients+	99,17 [98,44; 99,90]	99,67 [99,03; 100,00]		
			2,46 [0,29; 21,03]	0,412
Pregnancy and neonatal topics				
Interaction test:	p=1,000			
Gender = Male				
Number of patients with event	3	0		
Median (in weeks)	-	-		
% of event-free patients+	99,24 [98,38; 100,00]	100,00 [100,00; 100,00]		
			-	-
Gender = Female				
Number of patients with event	3	0		
Median (in weeks)	-	-		
% of event-free patients+	99,47 [98,86; 100,00]	100,00 [100,00; 100,00]		
			-	-

	Treatment groups		Comparison	
	BAF312 (N=1099)	**Placebo (N=546)**	**HR [95% CI]**	**p-value**
Bradyarrhythmias and bradycardia				
Interaction test:	p=0,038 *			
Gender = Male				
Number of patients with event	57	11		
Median (in weeks)	-	-		
% of event-free patients+	83,27 [77,95; 88,60]	94,97 [92,07; 97,87]		
			2,71 [1,42; 5,17]	0,002 *
Gender = Female				
Number of patients with event	46	20		
Median (in weeks)	-	-		
% of event-free patients+	90,51 [85,60; 95,42]	91,68 [87,73; 95,62]		
			1,12 [0,66; 1,90]	0,664

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 total population

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=1099)	**Placebo (N=546)**	**HR [95% CI]**	**p-value**
N'	1099	546		
N' Previous MS DMT = No	242	114		
N' Previous MS DMT = Yes	857	432		
Any AE				
Interaction test:	p=0,313			
Previous MS DMT = No				
Number of patients with event	210	82		
Median (in weeks)	8,3 [3,3; 12,7]	11,3 [5,0; 22,6]		
% of event-free patients+	7,46 [2,64; 12,29]	25,06 [15,99; 34,13]		
			1,42 [1,10; 1,84]	0,007 *
Previous MS DMT = Yes				
Number of patients with event	765	363		
Median (in weeks)	4,0 [3,3; 4,9]	6,7 [4,4; 10,4]		
% of event-free patients+	6,70 [3,92; 9,49]	10,29 [5,98; 14,61]		
			1,23 [1,09; 1,39]	0,001 *
Any AE, disease specific events excluded[1]				
Interaction test:	p=0,204			
Previous MS DMT = No				
Number of patients with event	205	78		
Median (in weeks)	13,0 [8,9; 19,4]	15,7 [8,1; 34,0]		
% of event-free patients+	8,45 [3,66; 13,24]	27,37 [17,86; 36,87]		
			1,42 [1,10; 1,85]	0,008 *
Previous MS DMT = Yes				
Number of patients with event	713	340		
Median (in weeks)	10,4 [8,4; 12,1]	12,7 [10,3; 16,3]		
% of event-free patients+	10,84 [7,44; 14,24]	14,09 [9,08; 19,11]		
			1,18 [1,03; 1,34]	0,013 *

	Treatment groups		Comparison	
	BAF312 (N=1099)	**Placebo (N=546)**	**HR [95% CI]**	**p-value**
Any SAE				
Interaction test:	p=0,917			
Previous MS DMT = No				
Number of patients with event	45	17		
Median (in weeks)	-	-		
% of event-free patients+	77,06 [70,85; 83,27]	82,51 [74,66; 90,37]		
			1,29 [0,74; 2,25]	0,372
Previous MS DMT = Yes				
Number of patients with event	141	57		
Median (in weeks)	-	-		
% of event-free patients+	75,41 [69,31; 81,51]	79,58 [70,62; 88,53]		
			1,25 [0,92; 1,70]	0,160
Any SAE, disease specific events excluded[1]				
Interaction test:	p=0,877			
Previous MS DMT = No				
Number of patients with event	38	13		
Median (in weeks)	-	-		
% of event-free patients+	80,28 [74,34; 86,22]	86,13 [78,82; 93,44]		
			1,43 [0,76; 2,68]	0,268
Previous MS DMT = Yes				
Number of patients with event	108	40		
Median (in weeks)	-	-		
% of event-free patients+	82,53 [78,87; 86,20]	84,15 [75,34; 92,96]		
			1,35 [0,94; 1,94]	0,106
Any severe AE[2]				
Interaction test:	p=0,242			
Previous MS DMT = No				
Number of patients with event	24	14		
Median (in weeks)	-	-		
% of event-free patients+	86,60 [81,35; 91,86]	85,38 [77,98; 92,79]		
			0,80 [0,41; 1,54]	0,496

	Treatment groups		Comparison	
	BAF312 (N=1099)	**Placebo (N=546)**	**HR [95% CI]**	**p-value**
Previous MS DMT = Yes				
Number of patients with event	115	47		
Median (in weeks)	-	-		
% of event-free patients+	82,58 [78,85; 86,31]	85,25 [80,61; 89,89]		
			1,24 [0,88; 1,74]	0,218
Any severe AE[2], disease specific events excluded[1]				
Interaction test:	p=0,085			
Previous MS DMT = No				
Number of patients with event	18	12		
Median (in weeks)	-	-		
% of event-free patients+	89,43 [84,55; 94,31]	87,17 [80,04; 94,29]		
			0,69 [0,33; 1,44]	0,324
Previous MS DMT = Yes				
Number of patients with event	92	32		
Median (in weeks)	-	-		
% of event-free patients+	85,34 [81,70; 88,99]	89,21 [84,94; 93,49]		
			1,44 [0,96; 2,16]	0,075
Any AE leading to study discontinuation				
Interaction test:	p=0,624			
Previous MS DMT = No				
Number of patients with event	12	5		
Median (in weeks)	-	-		
% of event-free patients+	94,58 [91,51; 97,65]	95,48 [91,60; 99,35]		
			1,14 [0,40; 3,24]	0,803
Previous MS DMT = Yes				
Number of patients with event	34	11		
Median (in weeks)	-	-		
% of event-free patients+	95,78 [94,38; 97,17]	96,42 [94,01; 98,83]		
			1,56 [0,79; 3,08]	0,200
Any AE leading to study drug discontinuation				
Interaction test:	p=0,538			
Previous MS DMT = No				
Number of patients with event	20	8		
Median (in weeks)	-	-		
% of event-free patients+	90,64 [86,60; 94,67]	91,76 [85,92; 97,61]		
			1,19 [0,53; 2,71]	0,674

	Treatment groups		Comparison	
	BAF312 (N=1099)	**Placebo (N=546)**	**HR [95% CI]**	**p-value**
Previous MS DMT = Yes				
Number of patients with event	64	20		
Median (in weeks)	-	-		
% of event-free patients[+]	92,05 [90,17; 93,93]	93,97 [91,16; 96,79]		
			1,61 [0,98; 2,66]	0,062

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 total population

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

	Treatment groups		Comparison	
	BAF312 (N=1099)	**Placebo (N=546)**	**HR [95% CI]**	**p-value**
N'	1099	546		
N' Previous MS DMT = No	242	114		
N' Previous MS DMT = Yes	857	432		
BLOOD AND LYMPHATIC SYSTEM DISORDERS				
Interaction test:	p=0,981			
Previous MS DMT = No				
Number of patients with event	8	0		
Median (in weeks)	-	-		
% of event-free patients+	95,64 [92,43; 98,86]	100,00 [100,00; 100,00]		
			-	-
Previous MS DMT = Yes				
Number of patients with event	38	10		
Median (in weeks)	-	-		
% of event-free patients+	94,33 [92,44; 96,22]	97,52 [96,00; 99,05]		
			1,91 [0,95; 3,82]	0,070
EAR AND LABYRINTH DISORDERS				
VERTIGO				
Interaction test:	p=0,191			
Previous MS DMT = No				
Number of patients with event	8	4		
Median (in weeks)	-	-		
% of event-free patients+	95,50 [91,89; 99,12]	95,61 [91,34; 99,88]		
			0,95 [0,28; 3,14]	0,928
Previous MS DMT = Yes				
Number of patients with event	17	22		
Median (in weeks)	-	-		
% of event-free patients+	97,83 [96,79; 98,87]	94,22 [91,81; 96,62]		
			0,38 [0,20; 0,72]	0,003 *

	Treatment groups		Comparison	
	BAF312 (N=1099)	**Placebo (N=546)**	**HR [95% CI]**	**p-value**
EYE DISORDERS				
MACULAR OEDEMA				
Interaction test:	p=0,990			
Previous MS DMT = No				
Number of patients with event	4	0		
Median (in weeks)	-	-		
% of event-free patients+	97,31 [94,49; 100,00]	100,00 [100,00; 100,00]		
			-	-
Previous MS DMT = Yes				
Number of patients with event	14	1		
Median (in weeks)	-	-		
% of event-free patients+	98,28 [97,38; 99,17]	99,50 [98,54; 100,00]		
			7,03 [0,92; 53,44]	0,060
GASTROINTESTINAL DISORDERS				
NAUSEA				
Interaction test:	p=0,721			
Previous MS DMT = No				
Number of patients with event	15	3		
Median (in weeks)	-	-		
% of event-free patients+	92,89 [89,17; 96,62]	97,33 [94,34; 100,00]		
			2,41 [0,70; 8,32]	0,164
Previous MS DMT = Yes				
Number of patients with event	59	16		
Median (in weeks)	-	-		
% of event-free patients+	92,59 [90,69; 94,49]	95,37 [92,89; 97,86]		
			1,88 [1,08; 3,27]	0,025 *
GENERAL DISORDERS AND ADMINISTRATION SITE CONDITIONS				
GAIT DISTURBANCE				
Interaction test:	p=0,802			
Previous MS DMT = No				
Number of patients with event	5	5		
Median (in weeks)	-	-		
% of event-free patients+	65,45 [13,07; 100,00]	91,59 [83,78; 99,39]		
			0,46 [0,13; 1,58]	0,218

	Treatment groups		Comparison	
	BAF312 (N=1099)	**Placebo (N=546)**	**HR [95% CI]**	**p-value**
Previous MS DMT = Yes				
Number of patients with event	19	17		
Median (in weeks)	-	-		
% of event-free patients+	97,54 [96,42; 98,65]	94,89 [92,30; 97,48]		
			0,55 [0,28; 1,06]	0,072
OEDEMA PERIPHERAL				
Interaction test:	p=0,582			
Previous MS DMT = No				
Number of patients with event	7	1		
Median (in weeks)	-	-		
% of event-free patients+	96,02 [92,77; 99,27]	99,07 [97,24; 100,00]		
			3,35 [0,41; 27,21]	0,258
Previous MS DMT = Yes				
Number of patients with event	43	12		
Median (in weeks)	-	-		
% of event-free patients+	87,90 [75,89; 99,91]	96,73 [94,80; 98,66]		
			1,81 [0,95; 3,43]	0,069
HEPATOBILIARY DISORDERS				
Interaction test:	p=0,987			
Previous MS DMT = No				
Number of patients with event	3	0		
Median (in weeks)	-	-		
% of event-free patients+	98,25 [96,18; 100,00]	100,00 [100,00; 100,00]		
			-	-
Previous MS DMT = Yes				
Number of patients with event	24	4		
Median (in weeks)	-	-		
% of event-free patients+	96,25 [94,59; 97,91]	98,57 [97,15; 99,99]		
			3,01 [1,05; 8,68]	0,041 *

	Treatment groups		Comparison	
	BAF312 (N=1099)	**Placebo (N=546)**	**HR [95% CI]**	**p-value**
INFECTIONS AND INFESTATIONS				
HERPES ZOSTER				
Interaction test:	p=0,092			
Previous MS DMT = No				
Number of patients with event	7	3		
Median (in weeks)	-	-		
% of event-free patients+	96,76 [94,39; 99,13]	96,44 [92,34; 100,00]		
			1,13 [0,29; 4,37]	0,860
Previous MS DMT = Yes				
Number of patients with event	18	1		
Median (in weeks)	-	-		
% of event-free patients+	97,26 [95,94; 98,58]	99,67 [99,01; 100,00]		
			9,07 [1,21; 67,95]	0,032 *
INVESTIGATIONS				
Interaction test:	p=0,270			
Previous MS DMT = No				
Number of patients with event	69	24		
Median (in weeks)	-	-		
% of event-free patients+	61,18 [52,78; 69,58]	64,88 [49,31; 80,45]		
			1,36 [0,86; 2,17]	0,192
Previous MS DMT = Yes				
Number of patients with event	194	56		
Median (in weeks)	-	-		
% of event-free patients+	69,80 [65,34; 74,26]	78,22 [71,04; 85,40]		
			1,86 [1,38; 2,50]	<0,001 *
ALANINE AMINOTRANSFERASE INCREASED				
Interaction test:	p=0,324			
Previous MS DMT = No				
Number of patients with event	20	1		
Median (in weeks)	-	-		
% of event-free patients+	88,56 [83,27; 93,85]	99,07 [97,27; 100,00]		
			9,70 [1,30; 72,28]	0,027 *

	Treatment groups		Comparison	
	BAF312 (N=1099)	**Placebo (N=546)**	**HR [95% CI]**	**p-value**
Previous MS DMT = Yes				
Number of patients with event	45	7		
Median (in weeks)	-	-		
% of event-free patients+	93,36 [91,32; 95,39]	98,29 [97,03; 99,55]		
			3,27 [1,48; 7,25]	0,004 *
GAMMA-GLUTAMYLTRANSFERASE INCREASED				
Interaction test:	p=0,368			
Previous MS DMT = No				
Number of patients with event	8	2		
Median (in weeks)	-	-		
% of event-free patients+	93,87 [87,77; 99,97]	97,13 [92,97; 100,00]		
			1,88 [0,40; 8,87]	0,424
Previous MS DMT = Yes				
Number of patients with event	35	4		
Median (in weeks)	-	-		
% of event-free patients+	94,74 [92,89; 96,58]	98,24 [96,27; 100,00]		
			4,43 [1,57; 12,46]	0,005 *
HEPATIC ENZYME INCREASED				
Interaction test:	p=0,991			
Previous MS DMT = No				
Number of patients with event	4	0		
Median (in weeks)	-	-		
% of event-free patients+	98,09 [96,23; 99,95]	100,00 [100,00; 100,00]		
			-	-
Previous MS DMT = Yes				
Number of patients with event	12	1		
Median (in weeks)	-	-		
% of event-free patients+	98,36 [97,41; 99,32]	99,65 [98,96; 100,00]		
			6,05 [0,79; 46,50]	0,084

	Treatment groups		Comparison	
	BAF312 (N=1099)	**Placebo (N=546)**	**HR [95% CI]**	**p-value**
NERVOUS SYSTEM DISORDERS				
Interaction test:	p=0,517			
Previous MS DMT = No				
Number of patients with event	68	30		
Median (in weeks)	-	-		
% of event-free patients+	66,95 [59,54; 74,36]	71,43 [62,46; 80,39]		
			1,08 [0,70; 1,65]	0,735
Previous MS DMT = Yes				
Number of patients with event	348	145		
Median (in weeks)	150,9 [127,9; -]	-		
% of event-free patients+	48,43 [39,61; 57,25]	60,48 [54,38; 66,57]		
			1,26 [1,04; 1,53]	0,020 *
PARAESTHESIA				
Interaction test:	p=0,288			
Previous MS DMT = No				
Number of patients with event	3	6		
Median (in weeks)	-	-		
% of event-free patients+	98,71 [97,25; 100,00]	92,79 [86,49; 99,10]		
			0,23 [0,06; 0,90]	0,036 *
Previous MS DMT = Yes				
Number of patients with event	15	14		
Median (in weeks)	-	-		
% of event-free patients+	96,82 [94,54; 99,09]	96,02 [93,74; 98,31]		
			0,53 [0,25; 1,10]	0,086

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 total population

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

	Treatment groups		Comparison	
	BAF312 (N=1099)	**Placebo (N=546)**	**HR [95% CI]**	**p-value**
N'	1099	546		
N' Previous MS DMT = No	242	114		
N' Previous MS DMT = Yes	857	432		
INVESTIGATIONS				
Interaction test:	p=0,695			
Previous MS DMT = No				
Number of patients with event	5	1		
Median (in weeks)	-	-		
% of event-free patients+	97,77 [95,83; 99,71]	99,10 [97,34; 100,00]		
			2,38 [0,28; 20,36]	0,429
Previous MS DMT = Yes				
Number of patients with event	16	2		
Median (in weeks)	-	-		
% of event-free patients+	97,72 [96,57; 98,87]	99,48 [98,75; 100,00]		
			4,00 [0,92; 17,41]	0,064

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 total population

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=1099)	**Placebo (N=546)**	**HR [95% CI]**	**p-value**
N'	1099	546		
N' Previous MS DMT = No	242	114		
N' Previous MS DMT = Yes	857	432		
Infections and infestations				
Interaction test:	p=0,398			
Previous MS DMT = No				
Number of patients with event	108	47		
Median (in weeks)	98,0 [73,7; -]	102,6 [77,6; -]		
% of event-free patients+	46,21 [38,52; 53,91]	48,45 [36,44; 60,46]		
			1,13 [0,80; 1,59]	0,490
Previous MS DMT = Yes				
Number of patients with event	431	221		
Median (in weeks)	73,4 [63,0; 86,0]	64,3 [51,0; 83,9]		
% of event-free patients+	37,51 [32,43; 42,58]	41,10 [35,20; 47,01]		
			0,96 [0,81; 1,13]	0,605
Herpes simplex virus infections				
Interaction test:	p=0,013 *			
Previous MS DMT = No				
Number of patients with event	2	5		
Median (in weeks)	-	-		
% of event-free patients+	99,07 [97,79; 100,00]	90,82 [80,06; 100,00]		
			0,18 [0,04; 0,93]	0,041 *
Previous MS DMT = Yes				
Number of patients with event	23	6		
Median (in weeks)	-	-		
% of event-free patients+	96,35 [94,63; 98,07]	98,20 [96,71; 99,69]		
			1,93 [0,79; 4,75]	0,151
Varicella-zoster virus infections				
Interaction test:	p=0,061			
Previous MS DMT = No				
Number of patients with event	8	3		
Median (in weeks)	-	-		
% of event-free patients+	96,29 [93,76; 98,82]	96,44 [92,34; 100,00]		
			1,27 [0,34; 4,79]	0,724

	Treatment groups		Comparison	
	BAF312 (N=1099)	**Placebo (N=546)**	**HR [95% CI]**	**p-value**
Previous MS DMT = Yes				
Number of patients with event	25	1		
Median (in weeks)	-	-		
% of event-free patients+	95,67 [93,73; 97,60]	99,67 [99,01; 100,00]		
			12,61 [1,71; 93,09]	0,013 *
Lymphopenia				
Interaction test:	p=1,000			
Previous MS DMT = No				
Number of patients with event	3	0		
Median (in weeks)	-	-		
% of event-free patients+	98,43 [96,65; 100,00]	100,00 [100,00; 100,00]		
			-	-
Previous MS DMT = Yes				
Number of patients with event	11	0		
Median (in weeks)	-	-		
% of event-free patients+	98,61 [97,80; 99,43]	100,00 [100,00; 100,00]		
			-	-
Macular edema				
Interaction test:	p=0,990			
Previous MS DMT = No				
Number of patients with event	4	0		
Median (in weeks)	-	-		
% of event-free patients+	97,31 [94,49; 100,00]	100,00 [100,00; 100,00]		
			-	-
Previous MS DMT = Yes				
Number of patients with event	16	1		
Median (in weeks)	-	-		
% of event-free patients+	98,01 [97,04; 98,98]	99,50 [98,54; 100,00]		
			8,03 [1,06; 60,54]	0,043 *

	Treatment groups		Comparison	
	BAF312 (N=1099)	**Placebo (N=546)**	**HR [95% CI]**	**p-value**
Abnormal hepatic enzymes				
Interaction test:	p=0,376			
Previous MS DMT = No				
Number of patients with event	35	7		
Median (in weeks)	-	-		
% of event-free patients+	76,47 [66,63; 86,32]	90,68 [83,14; 98,23]		
			2,40 [1,07; 5,41]	0,034 *
Previous MS DMT = Yes				
Number of patients with event	100	14		
Median (in weeks)	-	-		
% of event-free patients+	85,92 [83,17; 88,66]	95,45 [92,83; 98,08]		
			3,75 [2,14; 6,56]	<0,001 *
Malignancies				
Interaction test:	p=0,858			
Previous MS DMT = No				
Number of patients with event	4	3		
Median (in weeks)	-	-		
% of event-free patients+	97,97 [95,99; 99,95]	96,76 [93,13; 100,00]		
			0,61 [0,14; 2,73]	0,519
Previous MS DMT = Yes				
Number of patients with event	16	11		
Median (in weeks)	-	-		
% of event-free patients+	97,44 [96,12; 98,77]	91,68 [82,57; 100,00]		
			0,71 [0,33; 1,54]	0,387
Hypertension				
Interaction test:	p=0,321			
Previous MS DMT = No				
Number of patients with event	26	12		
Median (in weeks)	-	-		
% of event-free patients+	74,93 [54,64; 95,23]	86,21 [77,90; 94,52]		
			1,00 [0,50; 1,98]	0,993
Previous MS DMT = Yes				
Number of patients with event	111	38		
Median (in weeks)	-	-		
% of event-free patients+	84,10 [80,96; 87,25]	84,28 [74,99; 93,56]		
			1,48 [1,02; 2,14]	0,038 *

	Treatment groups		Comparison	
	BAF312 (N=1099)	**Placebo (N=546)**	**HR [95% CI]**	**p-value**
Seizures				
Interaction test:	p=0,988			
Previous MS DMT = No				
Number of patients with event	0	1		
Median (in weeks)	-	-		
% of event-free patients+	100,00 [100,00; 100,00]	99,10 [97,34; 100,00]		
			-	-
Previous MS DMT = Yes				
Number of patients with event	19	1		
Median (in weeks)	-	-		
% of event-free patients+	96,31 [93,98; 98,63]	99,76 [99,28; 100,00]		
			9,50 [1,27; 70,96]	0,028 *
Thromboembolic events				
Interaction test:	p=0,433			
Previous MS DMT = No				
Number of patients with event	8	2		
Median (in weeks)	-	-		
% of event-free patients+	96,41 [93,96; 98,87]	98,12 [95,53; 100,00]		
			1,87 [0,40; 8,83]	0,427
Previous MS DMT = Yes				
Number of patients with event	25	13		
Median (in weeks)	-	-		
% of event-free patients+	95,22 [92,45; 97,99]	94,10 [89,02; 99,19]		
			0,95 [0,49; 1,86]	0,889
Respiratory disorders				
Interaction test:	p=0,016 *			
Previous MS DMT = No				
Number of patients with event	17	19		
Median (in weeks)	-	-		
% of event-free patients+	92,20 [88,61; 95,79]	79,19 [70,18; 88,21]		
			0,39 [0,20; 0,75]	0,005 *

	Treatment groups		Comparison	
	BAF312 (N=1099)	**Placebo (N=546)**	**HR [95% CI]**	**p-value**
Previous MS DMT = Yes				
Number of patients with event	100	52		
Median (in weeks)	-	-		
% of event-free patients+	85,87 [83,17; 88,58]	76,67 [65,01; 88,33]		
			0,96 [0,69; 1,34]	0,820
Peripheral edema/swelling				
Interaction test:	p=0,478			
Previous MS DMT = No				
Number of patients with event	14	2		
Median (in weeks)	-	-		
% of event-free patients+	92,40 [88,21; 96,58]	97,93 [95,06; 100,00]		
			3,37 [0,77; 14,85]	0,108
Previous MS DMT = Yes				
Number of patients with event	60	16		
Median (in weeks)	-	-		
% of event-free patients+	85,26 [73,51; 97,00]	95,43 [93,08; 97,78]		
			1,90 [1,10; 3,31]	0,022 *

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 total population

	Treatment groups		Comparison	
	BAF312 (N=1099)	**Placebo (N=546)**	**HR [95% CI]**	**p-value**
N'	1099	546		
N' Previous MS DMT = No	242	114		
N' Previous MS DMT = Yes	857	432		
Asthma/bronchospasm				
Interaction test:	p=0,992			
Previous MS DMT = No				
Number of patients with event	0	1		
Median (in weeks)	-	-		
% of event-free patients+	100,00 [100,00; 100,00]	99,07 [97,27; 100,00]		
			-	-
Previous MS DMT = Yes				
Number of patients with event	8	1		
Median (in weeks)	-	-		
% of event-free patients+	98,94 [98,21; 99,68]	99,59 [98,79; 100,00]		
			4,04 [0,51; 32,31]	0,188
Pregnancy and neonatal topics				
Interaction test:	p=1,000			
Previous MS DMT = No				
Number of patients with event	2	0		
Median (in weeks)	-	-		
% of event-free patients+	98,99 [97,60; 100,00]	100,00 [100,00; 100,00]		
			-	-
Previous MS DMT = Yes				
Number of patients with event	4	0		
Median (in weeks)	-	-		
% of event-free patients+	99,48 [98,98; 99,99]	100,00 [100,00; 100,00]		
			-	-

	Treatment groups		Comparison	
	BAF312 (N=1099)	**Placebo (N=546)**	**HR [95% CI]**	**p-value**
Bradyarrhythmias and bradycardia				
Interaction test:	p=0,585			
Previous MS DMT = No				
Number of patients with event	33	8		
Median (in weeks)	-	-		
% of event-free patients+	83,57 [76,30; 90,83]	91,10 [84,26; 97,93]		
			1,99 [0,92; 4,30]	0,082
Previous MS DMT = Yes				
Number of patients with event	70	23		
Median (in weeks)	-	-		
% of event-free patients+	88,76 [84,65; 92,87]	93,48 [90,66; 96,29]		
			1,54 [0,96; 2,47]	0,071

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 total population

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=1099)	**Placebo (N=546)**	**HR [95% CI]**	**p-value**
N'	1099	546		
N' Previous IFN-beta-1b Treatment = No	755	392		
N' Previous IFN-beta-1b Treatment = Yes	344	154		
Any AE				
Interaction test:	p=0,736			
Previous IFN-beta-1b Treatment = No				
Number of patients with event	671	319		
Median (in weeks)	4,3 [3,4; 6,9]	7,0 [5,0; 11,3]		
% of event-free patients+	6,87 [3,95; 9,78]	12,87 [8,05; 17,68]		
			1,25 [1,09; 1,43]	0,001 *
Previous IFN-beta-1b Treatment = Yes				
Number of patients with event	304	126		
Median (in weeks)	4,1 [3,1; 5,9]	8,8 [4,1; 12,9]		
% of event-free patients+	6,47 [1,73; 11,21]	15,55 [9,40; 21,69]		
			1,30 [1,06; 1,60]	0,013 *
Any AE, disease specific events excluded[1]				
Interaction test:	p=0,960			
Previous IFN-beta-1b Treatment = No				
Number of patients with event	632	298		
Median (in weeks)	11,9 [9,0; 13,1]	12,9 [10,0; 18,3]		
% of event-free patients+	10,24 [6,89; 13,59]	16,70 [11,28; 22,13]		
			1,22 [1,06; 1,40]	0,005 *
Previous IFN-beta-1b Treatment = Yes				
Number of patients with event	286	120		
Median (in weeks)	9,9 [6,9; 12,3]	13,0 [9,4; 19,6]		
% of event-free patients+	9,74 [4,28; 15,20]	18,37 [11,66; 25,07]		
			1,23 [0,99; 1,52]	0,059

	Treatment groups		Comparison	
	BAF312 (N=1099)	**Placebo (N=546)**	**HR [95% CI]**	**p-value**
Any SAE				
Interaction test:	p=0,698			
Previous IFN-beta-1b Treatment = No				
Number of patients with event	135	54		
Median (in weeks)	-	-		
% of event-free patients+	77,37 [73,49; 81,26]	83,19 [78,82; 87,56]		
			1,30 [0,95; 1,79]	0,099
Previous IFN-beta-1b Treatment = Yes				
Number of patients with event	51	20		
Median (in weeks)	-	-		
% of event-free patients+	71,20 [57,11; 85,30]	63,12 [27,01; 99,23]		
			1,16 [0,69; 1,94]	0,580
Any SAE, disease specific events excluded[1]				
Interaction test:	p=0,525			
Previous IFN-beta-1b Treatment = No				
Number of patients with event	105	37		
Median (in weeks)	-	-		
% of event-free patients+	82,43 [79,19; 85,68]	88,12 [84,28; 91,96]		
			1,46 [1,01; 2,13]	0,047 *
Previous IFN-beta-1b Treatment = Yes				
Number of patients with event	41	16		
Median (in weeks)	-	-		
% of event-free patients+	80,43 [72,73; 88,13]	69,81 [38,76; 100,00]		
			1,17 [0,66; 2,08]	0,595
Any severe AE[2]				
Interaction test:	p=0,069			
Previous IFN-beta-1b Treatment = No				
Number of patients with event	94	50		
Median (in weeks)	-	-		
% of event-free patients+	83,84 [80,35; 87,34]	83,30 [78,39; 88,22]		
			0,96 [0,68; 1,35]	0,806

	Treatment groups		Comparison	
	BAF312 (N=1099)	**Placebo (N=546)**	**HR [95% CI]**	**p-value**
Previous IFN-beta-1b Treatment = Yes				
Number of patients with event	45	11		
Median (in weeks)	-	-		
% of event-free patients+	82,30 [75,68; 88,91]	90,29 [84,24; 96,34]		
			1,91 [0,99; 3,69]	0,054
Any severe AE[2], disease specific events excluded[1]				
Interaction test:	p=0,076			
Previous IFN-beta-1b Treatment = No				
Number of patients with event	75	37		
Median (in weeks)	-	-		
% of event-free patients+	86,56 [83,21; 89,91]	87,09 [82,52; 91,66]		
			1,03 [0,69; 1,52]	0,902
Previous IFN-beta-1b Treatment = Yes				
Number of patients with event	35	7		
Median (in weeks)	-	-		
% of event-free patients+	85,21 [78,64; 91,78]	93,07 [87,54; 98,60]		
			2,32 [1,03; 5,22]	0,042 *
Any AE leading to study discontinuation				
Interaction test:	p=0,243			
Previous IFN-beta-1b Treatment = No				
Number of patients with event	37	11		
Median (in weeks)	-	-		
% of event-free patients+	94,79 [93,12; 96,45]	96,96 [95,17; 98,74]		
			1,75 [0,89; 3,43]	0,104
Previous IFN-beta-1b Treatment = Yes				
Number of patients with event	9	5		
Median (in weeks)	-	-		
% of event-free patients+	97,05 [95,13; 98,97]	94,61 [89,26; 99,96]		
			0,81 [0,27; 2,43]	0,711
Any AE leading to study drug discontinuation				
Interaction test:	p=0,602			
Previous IFN-beta-1b Treatment = No				
Number of patients with event	65	21		
Median (in weeks)	-	-		
% of event-free patients+	90,63 [88,42; 92,84]	93,59 [90,77; 96,40]		
			1,60 [0,98; 2,62]	0,060

	Treatment groups		Comparison	
	BAF312 (N=1099)	**Placebo (N=546)**	**HR [95% CI]**	**p-value**
Previous IFN-beta-1b Treatment = Yes				
Number of patients with event	19	7		
Median (in weeks)	-	-		
% of event-free patients[+]	94,09 [91,49; 96,69]	93,46 [88,19; 98,72]		
			1,23 [0,52; 2,93]	0,639

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 total population

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=1099)	**Placebo (N=546)**	**HR [95% CI]**	**p-value**
N'	1099	546		
N' Previous IFN-beta-1b Treatment = No	755	392		
N' Previous IFN-beta-1b Treatment = Yes	344	154		
BLOOD AND LYMPHATIC SYSTEM DISORDERS				
Interaction test:	p=0,364			
Previous IFN-beta-1b Treatment = No				
Number of patients with event	33	6		
Median (in weeks)	-	-		
% of event-free patients+	94,20 [92,09; 96,31]	98,34 [97,02; 99,67]		
			2,84 [1,19; 6,78]	0,019 *
Previous IFN-beta-1b Treatment = Yes				
Number of patients with event	13	4		
Median (in weeks)	-	-		
% of event-free patients+	95,57 [93,16; 97,98]	97,30 [94,68; 99,91]		
			1,47 [0,48; 4,52]	0,498
EAR AND LABYRINTH DISORDERS				
VERTIGO				
Interaction test:	p=0,672			
Previous IFN-beta-1b Treatment = No				
Number of patients with event	17	17		
Median (in weeks)	-	-		
% of event-free patients+	97,19 [95,63; 98,75]	95,12 [92,82; 97,42]		
			0,51 [0,26; 1,00]	0,050 *
Previous IFN-beta-1b Treatment = Yes				
Number of patients with event	8	9		
Median (in weeks)	-	-		
% of event-free patients+	97,38 [95,53; 99,22]	93,06 [88,57; 97,55]		
			0,40 [0,15; 1,03]	0,057

	Treatment groups		Comparison	
	BAF312 (N=1099)	**Placebo (N=546)**	**HR [95% CI]**	**p-value**
EYE DISORDERS				
MACULAR OEDEMA				
Interaction test:	p=0,988			
Previous IFN-beta-1b Treatment = No				
Number of patients with event	11	1		
Median (in weeks)	-	-		
% of event-free patients+	98,13 [96,93; 99,32]	99,44 [98,35; 100,00]		
			5,66 [0,73; 43,84]	0,097
Previous IFN-beta-1b Treatment = Yes				
Number of patients with event	7	0		
Median (in weeks)	-	-		
% of event-free patients+	97,87 [96,31; 99,43]	100,00 [100,00; 100,00]		
			-	-
GASTROINTESTINAL DISORDERS				
NAUSEA				
Interaction test:	p=0,570			
Previous IFN-beta-1b Treatment = No				
Number of patients with event	57	14		
Median (in weeks)	-	-		
% of event-free patients+	92,00 [89,93; 94,06]	95,47 [92,84; 98,09]		
			2,15 [1,20; 3,86]	0,010 *
Previous IFN-beta-1b Treatment = Yes				
Number of patients with event	17	5		
Median (in weeks)	-	-		
% of event-free patients+	94,05 [91,05; 97,04]	96,62 [93,70; 99,54]		
			1,54 [0,57; 4,17]	0,398
GENERAL DISORDERS AND ADMINISTRATION SITE CONDITIONS				
GAIT DISTURBANCE				
Interaction test:	p=0,322			
Previous IFN-beta-1b Treatment = No				
Number of patients with event	19	15		
Median (in weeks)	-	-		
% of event-free patients+	89,87 [75,72; 100,00]	94,54 [91,47; 97,62]		
			0,63 [0,32; 1,24]	0,184

	Treatment groups		Comparison	
	BAF312 (N=1099)	**Placebo (N=546)**	**HR [95% CI]**	**p-value**
Previous IFN-beta-1b Treatment = Yes				
Number of patients with event	5	7		
Median (in weeks)	-	-		
% of event-free patients+	98,38 [96,96; 99,81]	93,18 [87,87; 98,50]		
			0,32 [0,10; 1,01]	0,053
OEDEMA PERIPHERAL				
Interaction test:	p=0,566			
Previous IFN-beta-1b Treatment = No				
Number of patients with event	29	9		
Median (in weeks)	-	-		
% of event-free patients+	88,08 [74,15; 100,00]	97,16 [95,21; 99,11]		
			1,66 [0,79; 3,51]	0,185
Previous IFN-beta-1b Treatment = Yes				
Number of patients with event	21	4		
Median (in weeks)	-	-		
% of event-free patients+	92,66 [89,37; 95,96]	97,36 [94,81; 99,91]		
			2,43 [0,83; 7,08]	0,103
HEPATOBILIARY DISORDERS				
Interaction test:	p=0,615			
Previous IFN-beta-1b Treatment = No				
Number of patients with event	16	3		
Median (in weeks)	-	-		
% of event-free patients+	97,45 [96,17; 98,73]	98,94 [97,75; 100,00]		
			2,74 [0,80; 9,39]	0,110
Previous IFN-beta-1b Treatment = Yes				
Number of patients with event	11	1		
Median (in weeks)	-	-		
% of event-free patients+	94,97 [91,58; 98,36]	98,88 [96,69; 100,00]		
			5,05 [0,65; 39,09]	0,121

	Treatment groups		Comparison	
	BAF312 (N=1099)	**Placebo (N=546)**	**HR [95% CI]**	**p-value**
INFECTIONS AND INFESTATIONS				
HERPES ZOSTER				
Interaction test:	p=0,990			
Previous IFN-beta-1b Treatment = No				
Number of patients with event	18	4		
Median (in weeks)	-	-		
% of event-free patients+	97,14 [95,80; 98,47]	98,52 [97,04; 100,00]		
			2,33 [0,79; 6,87]	0,127
Previous IFN-beta-1b Treatment = Yes				
Number of patients with event	7	0		
Median (in weeks)	-	-		
% of event-free patients+	97,21 [94,99; 99,44]	100,00 [100,00; 100,00]		
			-	-
INVESTIGATIONS				
Interaction test:	p=0,450			
Previous IFN-beta-1b Treatment = No				
Number of patients with event	182	60		
Median (in weeks)	-	-		
% of event-free patients+	66,88 [61,96; 71,80]	75,35 [68,27; 82,42]		
			1,62 [1,21; 2,17]	0,001 *
Previous IFN-beta-1b Treatment = Yes				
Number of patients with event	81	20		
Median (in weeks)	-	-		
% of event-free patients+	69,64 [63,02; 76,25]	73,81 [57,09; 90,54]		
			2,02 [1,24; 3,29]	0,005 *
ALANINE AMINOTRANSFERASE INCREASED				
Interaction test:	p=0,869			
Previous IFN-beta-1b Treatment = No				
Number of patients with event	41	5		
Median (in weeks)	-	-		
% of event-free patients+	92,62 [90,17; 95,06]	98,62 [97,41; 99,82]		
			4,26 [1,68; 10,77]	0,002 *

	Treatment groups		Comparison	
	BAF312 (N=1099)	**Placebo (N=546)**	**HR [95% CI]**	**p-value**
Previous IFN-beta-1b Treatment = Yes				
Number of patients with event	24	3		
Median (in weeks)	-	-		
% of event-free patients+	91,36 [87,76; 94,95]	98,03 [95,81; 100,00]		
			3,75 [1,13; 12,44]	0,031 *
GAMMA-GLUTAMYLTRANSFERASE INCREASED				
Interaction test:	p=0,968			
Previous IFN-beta-1b Treatment = No				
Number of patients with event	28	4		
Median (in weeks)	-	-		
% of event-free patients+	94,42 [91,78; 97,06]	98,31 [96,55; 100,00]		
			3,60 [1,26; 10,25]	0,017 *
Previous IFN-beta-1b Treatment = Yes				
Number of patients with event	15	2		
Median (in weeks)	-	-		
% of event-free patients+	94,79 [92,11; 97,48]	97,24 [92,95; 100,00]		
			3,47 [0,79; 15,16]	0,099
HEPATIC ENZYME INCREASED				
Interaction test:	p=0,990			
Previous IFN-beta-1b Treatment = No				
Number of patients with event	12	1		
Median (in weeks)	-	-		
% of event-free patients+	98,10 [97,01; 99,20]	99,62 [98,88; 100,00]		
			6,22 [0,81; 47,83]	0,079
Previous IFN-beta-1b Treatment = Yes				
Number of patients with event	4	0		
Median (in weeks)	-	-		
% of event-free patients+	98,77 [97,58; 99,97]	100,00 [100,00; 100,00]		
			-	-

	Treatment groups		Comparison	
	BAF312 (N=1099)	**Placebo (N=546)**	**HR [95% CI]**	**p-value**
NERVOUS SYSTEM DISORDERS				
Interaction test:	p=0,653			
Previous IFN-beta-1b Treatment = No				
Number of patients with event	283	127		
Median (in weeks)	-	-		
% of event-free patients+	52,17 [41,66; 62,68]	61,96 [55,65; 68,27]		
			1,19 [0,96; 1,46]	0,109
Previous IFN-beta-1b Treatment = Yes				
Number of patients with event	133	48		
Median (in weeks)	-	-		
% of event-free patients+	51,03 [41,25; 60,82]	65,30 [56,78; 73,81]		
			1,30 [0,93; 1,81]	0,121
PARAESTHESIA				
Interaction test:	p=0,476			
Previous IFN-beta-1b Treatment = No				
Number of patients with event	14	14		
Median (in weeks)	-	-		
% of event-free patients+	97,73 [96,39; 99,07]	95,06 [92,10; 98,01]		
			0,50 [0,24; 1,06]	0,069
Previous IFN-beta-1b Treatment = Yes				
Number of patients with event	4	6		
Median (in weeks)	-	-		
% of event-free patients+	95,82 [90,23; 100,00]	95,80 [92,49; 99,12]		
			0,30 [0,08; 1,05]	0,059

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 total population

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

	Treatment groups		Comparison	
	BAF312 (N=1099)	**Placebo (N=546)**	**HR [95% CI]**	**p-value**
N'	1099	546		
N' Previous IFN-beta-1b Treatment = No	755	392		
N' Previous IFN-beta-1b Treatment = Yes	344	154		
INVESTIGATIONS				
Interaction test:	p=0,188			
Previous IFN-beta-1b Treatment = No				
Number of patients with event	15	1		
Median (in weeks)	-	-		
% of event-free patients+	97,59 [96,33; 98,84]	99,74 [99,23; 100,00]		
			7,71 [1,02; 58,32]	0,048 *
Previous IFN-beta-1b Treatment = Yes				
Number of patients with event	6	2		
Median (in weeks)	-	-		
% of event-free patients+	98,07 [96,51; 99,62]	98,56 [96,56; 100,00]		
			1,36 [0,27; 6,74]	0,707

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 total population

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=1099)	**Placebo (N=546)**	**HR [95% CI]**	**p-value**
N'	1099	546		
N' Previous IFN-beta-1b Treatment = No	755	392		
N' Previous IFN-beta-1b Treatment = Yes	344	154		
Infections and infestations				
Interaction test:	p=0,550			
Previous IFN-beta-1b Treatment = No				
Number of patients with event	363	191		
Median (in weeks)	80,9 [70,6; 98,3]	73,4 [61,4; 95,4]		
% of event-free patients+	39,53 [34,30; 44,76]	43,08 [37,03; 49,13]		
			0,96 [0,80; 1,14]	0,632
Previous IFN-beta-1b Treatment = Yes				
Number of patients with event	176	77		
Median (in weeks)	65,9 [54,6; 96,3]	74,1 [45,7; -]		
% of event-free patients+	40,08 [33,34; 46,81]	40,79 [29,46; 52,13]		
			1,06 [0,81; 1,38]	0,688
Herpes simplex virus infections				
Interaction test:	p=0,265			
Previous IFN-beta-1b Treatment = No				
Number of patients with event	15	9		
Median (in weeks)	-	-		
% of event-free patients+	97,32 [95,75; 98,90]	96,28 [93,18; 99,38]		
			0,85 [0,37; 1,94]	0,700
Previous IFN-beta-1b Treatment = Yes				
Number of patients with event	10	2		
Median (in weeks)	-	-		
% of event-free patients+	96,28 [93,89; 98,68]	98,21 [95,65; 100,00]		
			2,27 [0,50; 10,36]	0,290

	Treatment groups		Comparison	
	BAF312 (N=1099)	**Placebo (N=546)**	**HR [95% CI]**	**p-value**
Varicella-zoster virus infections				
Interaction test:	p=0,989			
Previous IFN-beta-1b Treatment = No				
Number of patients with event	24	4		
Median (in weeks)	-	-		
% of event-free patients+	95,64 [93,69; 97,59]	98,52 [97,04; 100,00]		
			3,09 [1,07; 8,91]	0,037 *
Previous IFN-beta-1b Treatment = Yes				
Number of patients with event	9	0		
Median (in weeks)	-	-		
% of event-free patients+	96,39 [93,89; 98,89]	100,00 [100,00; 100,00]		
			-	-
Lymphopenia				
Interaction test:	p=1,000			
Previous IFN-beta-1b Treatment = No				
Number of patients with event	11	0		
Median (in weeks)	-	-		
% of event-free patients+	98,34 [97,36; 99,32]	100,00 [100,00; 100,00]		
			-	-
Previous IFN-beta-1b Treatment = Yes				
Number of patients with event	3	0		
Median (in weeks)	-	-		
% of event-free patients+	99,05 [97,98; 100,00]	100,00 [100,00; 100,00]		
			-	-
Macular edema				
Interaction test:	p=0,988			
Previous IFN-beta-1b Treatment = No				
Number of patients with event	13	1		
Median (in weeks)	-	-		
% of event-free patients+	97,82 [96,56; 99,09]	99,44 [98,35; 100,00]		
			6,69 [0,87; 51,11]	0,067

	Treatment groups		Comparison	
	BAF312 (N=1099)	**Placebo (N=546)**	**HR [95% CI]**	**p-value**
Previous IFN-beta-1b Treatment = Yes				
Number of patients with event	7	0		
Median (in weeks)	-	-		
% of event-free patients+	97,87 [96,31; 99,43]	100,00 [100,00; 100,00]		
			-	-
Abnormal hepatic enzymes				
Interaction test:	p=0,695			
Previous IFN-beta-1b Treatment = No				
Number of patients with event	88	15		
Median (in weeks)	-	-		
% of event-free patients+	83,41 [79,20; 87,62]	94,56 [91,53; 97,58]		
			3,10 [1,79; 5,36]	<0,001 *
Previous IFN-beta-1b Treatment = Yes				
Number of patients with event	47	6		
Median (in weeks)	-	-		
% of event-free patients+	84,30 [79,98; 88,62]	94,16 [88,97; 99,36]		
			3,79 [1,62; 8,87]	0,002 *
Malignancies				
Interaction test:	p=0,052			
Previous IFN-beta-1b Treatment = No				
Number of patients with event	16	7		
Median (in weeks)	-	-		
% of event-free patients+	97,10 [95,61; 98,59]	97,53 [95,58; 99,47]		
			1,14 [0,47; 2,78]	0,770
Previous IFN-beta-1b Treatment = Yes				
Number of patients with event	4	7		
Median (in weeks)	-	-		
% of event-free patients+	98,60 [97,23; 99,98]	74,87 [41,75; 100,00]		
			0,25 [0,07; 0,87]	0,029 *
Hypertension				
Interaction test:	p=0,272			
Previous IFN-beta-1b Treatment = No				
Number of patients with event	84	36		
Median (in weeks)	-	-		
% of event-free patients+	83,70 [77,98; 89,42]	87,42 [82,79; 92,06]		
			1,19 [0,80; 1,75]	0,389

	Treatment groups		Comparison	
	BAF312 (N=1099)	**Placebo (N=546)**	**HR [95% CI]**	**p-value**
Previous IFN-beta-1b Treatment = Yes				
Number of patients with event	53	14		
Median (in weeks)	-	-		
% of event-free patients+	79,85 [73,51; 86,18]	71,91 [40,09; 100,00]		
			1,76 [0,98; 3,18]	0,059
Seizures				
Interaction test:	p=0,987			
Previous IFN-beta-1b Treatment = No				
Number of patients with event	12	2		
Median (in weeks)	-	-		
% of event-free patients+	97,15 [94,91; 99,39]	99,47 [98,73; 100,00]		
			3,05 [0,68; 13,62]	0,145
Previous IFN-beta-1b Treatment = Yes				
Number of patients with event	7	0		
Median (in weeks)	-	-		
% of event-free patients+	97,35 [95,18; 99,52]	100,00 [100,00; 100,00]		
			-	-
Thromboembolic events				
Interaction test:	p=0,449			
Previous IFN-beta-1b Treatment = No				
Number of patients with event	22	12		
Median (in weeks)	-	-		
% of event-free patients+	96,02 [93,74; 98,31]	93,87 [88,27; 99,46]		
			0,93 [0,46; 1,89]	0,847
Previous IFN-beta-1b Treatment = Yes				
Number of patients with event	11	3		
Median (in weeks)	-	-		
% of event-free patients+	94,05 [88,61; 99,49]	97,59 [94,87; 100,00]		
			1,64 [0,46; 5,87]	0,449

	Treatment groups		Comparison	
	BAF312 (N=1099)	**Placebo (N=546)**	**HR [95% CI]**	**p-value**
Respiratory disorders				
Interaction test:	p=0,074			
Previous IFN-beta-1b Treatment = No				
Number of patients with event	85	45		
Median (in weeks)	-	-		
% of event-free patients+	86,68 [83,92; 89,44]	84,29 [79,27; 89,31]		
			0,96 [0,67; 1,38]	0,820
Previous IFN-beta-1b Treatment = Yes				
Number of patients with event	32	26		
Median (in weeks)	-	143,0 [143,0; -]		
% of event-free patients+	88,68 [84,84; 92,51]	37,24 [0,00; 89,19]		
			0,54 [0,32; 0,91]	0,020 *
Peripheral edema/swelling				
Interaction test:	p=0,777			
Previous IFN-beta-1b Treatment = No				
Number of patients with event	50	12		
Median (in weeks)	-	-		
% of event-free patients+	84,93 [71,43; 98,43]	95,92 [93,49; 98,36]		
			2,17 [1,15; 4,07]	0,016 *
Previous IFN-beta-1b Treatment = Yes				
Number of patients with event	24	6		
Median (in weeks)	-	-		
% of event-free patients+	90,56 [86,19; 94,92]	95,95 [92,78; 99,13]		
			1,85 [0,76; 4,52]	0,178

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 total population

	Treatment groups		Comparison	
	BAF312 (N=1099)	**Placebo (N=546)**	**HR [95% CI]**	**p-value**
N'	1099	546		
N' Previous IFN-beta-1b Treatment = No	755	392		
N' Previous IFN-beta-1b Treatment = Yes	344	154		
Asthma/bronchospasm				
Interaction test:	p=0,455			
Previous IFN-beta-1b Treatment = No				
Number of patients with event	6	1		
Median (in weeks)	-	-		
% of event-free patients+	99,11 [98,40; 99,82]	99,73 [99,20; 100,00]		
			3,11 [0,37; 25,81]	0,294
Previous IFN-beta-1b Treatment = Yes				
Number of patients with event	2	1		
Median (in weeks)	-	-		
% of event-free patients+	99,31 [98,36; 100,00]	98,95 [96,90; 100,00]		
			0,92 [0,08; 10,10]	0,943
Pregnancy and neonatal topics				
Interaction test:	p=1,000			
Previous IFN-beta-1b Treatment = No				
Number of patients with event	5	0		
Median (in weeks)	-	-		
% of event-free patients+	99,24 [98,58; 99,91]	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+	99,67 [99,02; 100,00]	100,00 [100,00; 100,00]		
			-	-

	Treatment groups		Comparison	
	BAF312 (N=1099)	**Placebo (N=546)**	**HR [95% CI]**	**p-value**
Bradyarrhythmias and bradycardia				
Interaction test:	p=0,049 *			
Previous IFN-beta-1b Treatment = No				
Number of patients with event	72	28		
Median (in weeks)	-	-		
% of event-free patients+	88,23 [84,99; 91,46]	90,97 [87,35; 94,58]		
			1,34 [0,87; 2,07]	0,190
Previous IFN-beta-1b Treatment = Yes				
Number of patients with event	31	3		
Median (in weeks)	-	-		
% of event-free patients+	85,09 [73,91; 96,26]	97,91 [95,55; 100,00]		
			4,76 [1,45; 15,56]	0,010 *

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 total population

12.6 Subgroup: Rapid Evolvement

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

	Treatment groups		Comparison	
	BAF312 (N=1099)	**Placebo (N=546)**	**HR [95% CI]**	**p-value**
N'	1099	546		
N' Rapid Evolvement = No	835	401		
N' Rapid Evolvement = Yes	264	145		
Any AE				
Interaction test:	p=0,259			
Rapid Evolvement = No				
Number of patients with event	747	334		
Median (in weeks)	4,1 [3,3; 5,0]	5,9 [4,3; 9,9]		
% of event-free patients+	6,09 [3,32; 8,85]	10,79 [5,94; 15,64]		
			1,21 [1,06; 1,38]	0,004 *
Rapid Evolvement = Yes				
Number of patients with event	228	111		
Median (in weeks)	5,9 [3,4; 8,9]	11,3 [6,3; 22,6]		
% of event-free patients+	9,48 [4,96; 14,00]	19,53 [11,77; 27,30]		
			1,41 [1,12; 1,76]	0,003 *
Any AE, disease specific events excluded[1]				
Interaction test:	p=0,191			
Rapid Evolvement = No				
Number of patients with event	701	313		
Median (in weeks)	11,0 [8,7; 12,6]	11,9 [8,9; 14,1]		
% of event-free patients+	9,52 [6,14; 12,89]	15,01 [9,53; 20,50]		
			1,16 [1,02; 1,33]	0,028 *
Rapid Evolvement = Yes				
Number of patients with event	217	105		
Median (in weeks)	11,9 [8,1; 13,1]	22,0 [11,7; 34,3]		
% of event-free patients+	12,01 [6,96; 17,05]	21,71 [13,15; 30,27]		
			1,39 [1,10; 1,75]	0,006 *

	Treatment groups		Comparison	
	BAF312 (N=1099)	**Placebo (N=546)**	**HR [95% CI]**	**p-value**
Any SAE				
Interaction test:	p=0,050 *			
Rapid Evolvement = No				
Number of patients with event	152	51		
Median (in weeks)	-	-		
% of event-free patients+	72,63 [65,85; 79,41]	79,47 [69,65; 89,30]		
			1,46 [1,06; 2,00]	0,020 *
Rapid Evolvement = Yes				
Number of patients with event	34	23		
Median (in weeks)	-	-		
% of event-free patients+	83,85 [78,60; 89,10]	81,85 [74,94; 88,77]		
			0,79 [0,46; 1,34]	0,374
Any SAE, disease specific events excluded[1]				
Interaction test:	p=0,418			
Rapid Evolvement = No				
Number of patients with event	118	39		
Median (in weeks)	-	-		
% of event-free patients+	80,31 [76,33; 84,29]	82,71 [72,69; 92,74]		
			1,46 [1,02; 2,10]	0,040 *
Rapid Evolvement = Yes				
Number of patients with event	28	14		
Median (in weeks)	-	-		
% of event-free patients+	86,69 [81,86; 91,52]	88,56 [82,72; 94,40]		
			1,08 [0,57; 2,05]	0,820
Any severe AE[2]				
Interaction test:	p=0,536			
Rapid Evolvement = No				
Number of patients with event	111	45		
Median (in weeks)	-	-		
% of event-free patients+	82,01 [77,95; 86,06]	85,90 [81,73; 90,07]		
			1,19 [0,84; 1,68]	0,334

	Treatment groups		Comparison	
	BAF312 (N=1099)	**Placebo (N=546)**	**HR [95% CI]**	**p-value**
Rapid Evolvement = Yes				
Number of patients with event	28	16		
Median (in weeks)	-	-		
% of event-free patients+	87,04 [82,38; 91,70]	84,39 [75,96; 92,81]		
			0,95 [0,51; 1,75]	0,868
Any severe AE[2], disease specific events excluded[1]				
Interaction test:	p=0,694			
Rapid Evolvement = No				
Number of patients with event	86	32		
Median (in weeks)	-	-		
% of event-free patients+	85,11 [81,16; 89,06]	89,54 [85,75; 93,32]		
			1,28 [0,85; 1,92]	0,236
Rapid Evolvement = Yes				
Number of patients with event	24	12		
Median (in weeks)	-	-		
% of event-free patients+	88,82 [84,43; 93,21]	87,46 [79,55; 95,37]		
			1,09 [0,54; 2,17]	0,813
Any AE leading to study discontinuation				
Interaction test:	p=0,839			
Rapid Evolvement = No				
Number of patients with event	40	14		
Median (in weeks)	-	-		
% of event-free patients+	94,79 [93,18; 96,40]	95,33 [92,58; 98,09]		
			1,38 [0,75; 2,53]	0,303
Rapid Evolvement = Yes				
Number of patients with event	6	2		
Median (in weeks)	-	-		
% of event-free patients+	97,67 [95,82; 99,51]	98,58 [96,63; 100,00]		
			1,64 [0,33; 8,14]	0,542

	Treatment groups		Comparison	
	BAF312 (N=1099)	**Placebo (N=546)**	**HR [95% CI]**	**p-value**
Any AE leading to study drug discontinuation				
Interaction test:	p=0,231			
Rapid Evolvement = No				
Number of patients with event	68	25		
Median (in weeks)	-	-		
% of event-free patients+	91,06 [88,99; 93,14]	92,00 [88,69; 95,32]		
			1,31 [0,83; 2,07]	0,249
Rapid Evolvement = Yes				
Number of patients with event	16	3		
Median (in weeks)	-	-		
% of event-free patients+	93,61 [90,55; 96,66]	97,66 [95,02; 100,00]		
			2,93 [0,85; 10,04]	0,088

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 total population

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

	Treatment groups		Comparison	
	BAF312 (N=1099)	**Placebo (N=546)**	**HR [95% CI]**	**p-value**
N'	1099	546		
N' Rapid Evolvement = No	835	401		
N' Rapid Evolvement = Yes	264	145		
BLOOD AND LYMPHATIC SYSTEM DISORDERS				
Interaction test:	p=0,019 *			
Rapid Evolvement = No				
Number of patients with event	40	5		
Median (in weeks)	-	-		
% of event-free patients+	93,99 [92,05; 95,93]	98,63 [97,43; 99,83]		
			3,88 [1,53; 9,82]	0,004 *
Rapid Evolvement = Yes				
Number of patients with event	6	5		
Median (in weeks)	-	-		
% of event-free patients+	96,63 [93,75; 99,52]	96,44 [93,37; 99,51]		
			0,64 [0,20; 2,10]	0,460
EAR AND LABYRINTH DISORDERS				
VERTIGO				
Interaction test:	p=0,896			
Rapid Evolvement = No				
Number of patients with event	21	21		
Median (in weeks)	-	-		
% of event-free patients+	96,89 [95,31; 98,48]	93,69 [91,00; 96,38]		
			0,47 [0,26; 0,87]	0,016 *
Rapid Evolvement = Yes				
Number of patients with event	4	5		
Median (in weeks)	-	-		
% of event-free patients+	98,21 [96,42; 100,00]	96,53 [93,53; 99,52]		
			0,43 [0,12; 1,60]	0,209

	Treatment groups		Comparison	
	BAF312 (N=1099)	**Placebo (N=546)**	**HR [95% CI]**	**p-value**
EYE DISORDERS				
MACULAR OEDEMA				
Interaction test:	p=0,990			
Rapid Evolvement = No				
Number of patients with event	15	1		
Median (in weeks)	-	-		
% of event-free patients+	98,03 [97,02; 99,03]	99,47 [98,42; 100,00]		
			7,20 [0,95; 54,52]	0,056
Rapid Evolvement = Yes				
Number of patients with event	3	0		
Median (in weeks)	-	-		
% of event-free patients+	98,22 [96,05; 100,00]	100,00 [100,00; 100,00]		
			-	-
GASTROINTESTINAL DISORDERS				
NAUSEA				
Interaction test:	p=0,609			
Rapid Evolvement = No				
Number of patients with event	56	15		
Median (in weeks)	-	-		
% of event-free patients+	92,48 [90,45; 94,52]	95,87 [93,77; 97,96]		
			1,82 [1,03; 3,22]	0,040 *
Rapid Evolvement = Yes				
Number of patients with event	18	4		
Median (in weeks)	-	-		
% of event-free patients+	93,03 [89,92; 96,14]	95,85 [91,21; 100,00]		
			2,50 [0,85; 7,39]	0,097
GENERAL DISORDERS AND ADMINISTRATION SITE CONDITIONS				
GAIT DISTURBANCE				
Interaction test:	p=0,425			
Rapid Evolvement = No				
Number of patients with event	21	17		
Median (in weeks)	-	-		
% of event-free patients+	85,21 [62,87; 100,00]	93,74 [90,52; 96,97]		
			0,58 [0,31; 1,11]	0,099

	Treatment groups		Comparison	
	BAF312 (N=1099)	**Placebo (N=546)**	**HR [95% CI]**	**p-value**
Rapid Evolvement = Yes				
Number of patients with event	3	5		
Median (in weeks)	-	-		
% of event-free patients+	98,60 [96,97; 100,00]	95,11 [90,29; 99,93]		
			0,31 [0,07; 1,29]	0,107
OEDEMA PERIPHERAL				
Interaction test:	p=0,013 *			
Rapid Evolvement = No				
Number of patients with event	44	7		
Median (in weeks)	-	-		
% of event-free patients+	84,15 [66,66; 100,00]	97,76 [96,02; 99,51]		
			3,07 [1,38; 6,82]	0,006 *
Rapid Evolvement = Yes				
Number of patients with event	6	6		
Median (in weeks)	-	-		
% of event-free patients+	97,63 [95,75; 99,50]	95,80 [92,51; 99,09]		
			0,53 [0,17; 1,64]	0,270
HEPATOBILIARY DISORDERS				
Interaction test:	p=0,305			
Rapid Evolvement = No				
Number of patients with event	21	2		
Median (in weeks)	-	-		
% of event-free patients+	96,51 [94,83; 98,18]	99,34 [98,42; 100,00]		
			5,05 [1,18; 21,53]	0,029 *
Rapid Evolvement = Yes				
Number of patients with event	6	2		
Median (in weeks)	-	-		
% of event-free patients+	97,20 [94,92; 99,48]	97,74 [94,62; 100,00]		
			1,63 [0,33; 8,07]	0,550

	Treatment groups		Comparison	
	BAF312 (N=1099)	**Placebo (N=546)**	**HR [95% CI]**	**p-value**
INFECTIONS AND INFESTATIONS				
HERPES ZOSTER				
Interaction test:	p=0,899			
Rapid Evolvement = No				
Number of patients with event	20	3		
Median (in weeks)	-	-		
% of event-free patients+	97,06 [95,76; 98,36]	99,06 [98,00; 100,00]		
			3,22 [0,96; 10,83]	0,059
Rapid Evolvement = Yes				
Number of patients with event	5	1		
Median (in weeks)	-	-		
% of event-free patients+	97,48 [95,10; 99,85]	98,72 [96,22; 100,00]		
			2,75 [0,32; 23,49]	0,357
INVESTIGATIONS				
Interaction test:	p=0,562			
Rapid Evolvement = No				
Number of patients with event	201	57		
Median (in weeks)	-	-		
% of event-free patients+	67,54 [62,85; 72,22]	78,01 [71,75; 84,26]		
			1,79 [1,34; 2,41]	<0,001 *
Rapid Evolvement = Yes				
Number of patients with event	62	23		
Median (in weeks)	-	-		
% of event-free patients+	68,73 [61,13; 76,34]	72,34 [58,87; 85,81]		
			1,52 [0,94; 2,45]	0,087
ALANINE AMINOTRANSFERASE INCREASED				
Interaction test:	p=0,176			
Rapid Evolvement = No				
Number of patients with event	43	3		
Median (in weeks)	-	-		
% of event-free patients+	93,06 [90,88; 95,24]	99,20 [98,29; 100,00]		
			6,98 [2,17; 22,50]	0,001 *

	Treatment groups		Comparison	
	BAF312 (N=1099)	**Placebo (N=546)**	**HR [95% CI]**	**p-value**
Rapid Evolvement = Yes				
Number of patients with event	22	5		
Median (in weeks)	-	-		
% of event-free patients+	89,80 [85,33; 94,28]	96,45 [93,39; 99,51]		
			2,44 [0,92; 6,45]	0,072
GAMMA-GLUTAMYLTRANSFERASE INCREASED				
Interaction test:	p=0,432			
Rapid Evolvement = No				
Number of patients with event	30	5		
Median (in weeks)	-	-		
% of event-free patients+	94,45 [91,72; 97,19]	97,47 [95,02; 99,91]		
			2,89 [1,12; 7,45]	0,028 *
Rapid Evolvement = Yes				
Number of patients with event	13	1		
Median (in weeks)	-	-		
% of event-free patients+	94,15 [90,88; 97,42]	99,31 [97,96; 100,00]		
			7,11 [0,93; 54,36]	0,059
HEPATIC ENZYME INCREASED				
Interaction test:	p=0,989			
Rapid Evolvement = No				
Number of patients with event	10	0		
Median (in weeks)	-	-		
% of event-free patients+	98,51 [97,57; 99,46]	100,00 [100,00; 100,00]		
			-	-
Rapid Evolvement = Yes				
Number of patients with event	6	1		
Median (in weeks)	-	-		
% of event-free patients+	97,62 [95,74; 99,50]	99,07 [97,24; 100,00]		
			3,30 [0,40; 27,45]	0,269

	Treatment groups		Comparison	
	BAF312 (N=1099)	**Placebo (N=546)**	**HR [95% CI]**	**p-value**
NERVOUS SYSTEM DISORDERS				
Interaction test:	p=0,853			
Rapid Evolvement = No				
Number of patients with event	326	132		
Median (in weeks)	-	-		
% of event-free patients+	53,19 [47,99; 58,39]	62,10 [56,02; 68,18]		
			1,22 [1,00; 1,50]	0,049 *
Rapid Evolvement = Yes				
Number of patients with event	90	43		
Median (in weeks)	150,9 [150,9; -]	-		
% of event-free patients+	49,72 [27,27; 72,16]	65,16 [55,31; 75,01]		
			1,18 [0,82; 1,69]	0,378
PARAESTHESIA				
Interaction test:	p=0,970			
Rapid Evolvement = No				
Number of patients with event	14	15		
Median (in weeks)	-	-		
% of event-free patients+	96,96 [94,54; 99,38]	95,57 [93,14; 98,00]		
			0,44 [0,21; 0,91]	0,026 *
Rapid Evolvement = Yes				
Number of patients with event	4	5		
Median (in weeks)	-	-		
% of event-free patients+	97,89 [95,63; 100,00]	94,79 [89,76; 99,83]		
			0,42 [0,11; 1,58]	0,202

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 total population

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

	Treatment groups		Comparison	
	BAF312 (N=1099)	**Placebo (N=546)**	**HR [95% CI]**	**p-value**
N'	1099	546		
N' Rapid Evolvement = No	835	401		
N' Rapid Evolvement = Yes	264	145		
INVESTIGATIONS				
Interaction test:	p=0,189			
Rapid Evolvement = No				
Number of patients with event	16	1		
Median (in weeks)	-	-		
% of event-free patients+	97,83 [96,75; 98,91]	99,74 [99,24; 100,00]		
			7,69 [1,02; 57,96]	0,048 *
Rapid Evolvement = Yes				
Number of patients with event	5	2		
Median (in weeks)	-	-		
% of event-free patients+	97,55 [95,36; 99,74]	98,48 [96,37; 100,00]		
			1,35 [0,26; 6,94]	0,723

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 total population

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=1099)	**Placebo (N=546)**	**HR [95% CI]**	**p-value**
N'	1099	546		
N' Rapid Evolvement = No	835	401		
N' Rapid Evolvement = Yes	264	145		
Infections and infestations				
Interaction test:	p=0,386			
Rapid Evolvement = No				
Number of patients with event	404	200		
Median (in weeks)	77,0 [64,4; 96,3]	69,1 [53,3; 88,6]		
% of event-free patients+	39,81 [34,77; 44,85]	41,59 [35,55; 47,63]		
			0,95 [0,80; 1,13]	0,551
Rapid Evolvement = Yes				
Number of patients with event	135	68		
Median (in weeks)	75,0 [64,0; 99,0]	95,4 [57,0; -]		
% of event-free patients+	39,18 [31,42; 46,94]	46,13 [36,02; 56,24]		
			1,10 [0,82; 1,48]	0,511
Herpes simplex virus infections				
Interaction test:	p=0,260			
Rapid Evolvement = No				
Number of patients with event	19	6		
Median (in weeks)	-	-		
% of event-free patients+	96,89 [95,24; 98,54]	97,06 [93,86; 100,00]		
			1,52 [0,61; 3,80]	0,374
Rapid Evolvement = Yes				
Number of patients with event	6	5		
Median (in weeks)	-	-		
% of event-free patients+	97,22 [94,92; 99,51]	95,61 [91,69; 99,52]		
			0,64 [0,20; 2,10]	0,462
Varicella-zoster virus infections				
Interaction test:	p=0,820			
Rapid Evolvement = No				
Number of patients with event	27	3		
Median (in weeks)	-	-		
% of event-free patients+	95,41 [93,46; 97,36]	99,06 [98,00; 100,00]		
			4,34 [1,32; 14,31]	0,016 *

	Treatment groups		Comparison	
	BAF312 (N=1099)	**Placebo (N=546)**	**HR [95% CI]**	**p-value**
Rapid Evolvement = Yes				
Number of patients with event	6	1		
Median (in weeks)	-	-		
% of event-free patients+	97,08 [94,59; 99,57]	98,72 [96,22; 100,00]		
			3,28 [0,39; 27,21]	0,272
Lymphopenia				
Interaction test:	p=1,000			
Rapid Evolvement = No				
Number of patients with event	12	0		
Median (in weeks)	-	-		
% of event-free patients+	98,35 [97,41; 99,28]	100,00 [100,00; 100,00]		
			-	-
Rapid Evolvement = Yes				
Number of patients with event	2	0		
Median (in weeks)	-	-		
% of event-free patients+	99,19 [98,07; 100,00]	100,00 [100,00; 100,00]		
			-	-
Macular edema				
Interaction test:	p=0,989			
Rapid Evolvement = No				
Number of patients with event	17	1		
Median (in weeks)	-	-		
% of event-free patients+	97,75 [96,67; 98,82]	99,47 [98,42; 100,00]		
			8,16 [1,09; 61,32]	0,041 *
Rapid Evolvement = Yes				
Number of patients with event	3	0		
Median (in weeks)	-	-		
% of event-free patients+	98,22 [96,05; 100,00]	100,00 [100,00; 100,00]		
			-	-

	Treatment groups		Comparison	
	BAF312 (N=1099)	**Placebo (N=546)**	**HR [95% CI]**	**p-value**
Abnormal hepatic enzymes				
Interaction test:	p=0,371			
Rapid Evolvement = No				
Number of patients with event	94	12		
Median (in weeks)	-	-		
% of event-free patients+	85,09 [81,60; 88,58]	95,00 [91,79; 98,20]		
			3,92 [2,15; 7,15]	<0,001 *
Rapid Evolvement = Yes				
Number of patients with event	41	9		
Median (in weeks)	-	-		
% of event-free patients+	80,10 [73,45; 86,74]	92,83 [88,16; 97,50]		
			2,55 [1,24; 5,25]	0,011 *
Malignancies				
Interaction test:	p=0,768			
Rapid Evolvement = No				
Number of patients with event	18	12		
Median (in weeks)	-	-		
% of event-free patients+	97,07 [95,65; 98,50]	90,31 [79,82; 100,00]		
			0,71 [0,34; 1,47]	0,352
Rapid Evolvement = Yes				
Number of patients with event	2	2		
Median (in weeks)	-	-		
% of event-free patients+	99,01 [97,64; 100,00]	98,30 [95,93; 100,00]		
			0,52 [0,07; 3,66]	0,508
Hypertension				
Interaction test:	p=0,534			
Rapid Evolvement = No				
Number of patients with event	107	40		
Median (in weeks)	-	-		
% of event-free patients+	83,92 [80,81; 87,03]	86,20 [81,44; 90,96]		
			1,28 [0,89; 1,84]	0,186

	Treatment groups		Comparison	
	BAF312 (N=1099)	**Placebo (N=546)**	**HR [95% CI]**	**p-value**
Rapid Evolvement = Yes				
Number of patients with event	30	10		
Median (in weeks)	-	-		
% of event-free patients+	80,32 [68,27; 92,37]	74,54 [41,68; 100,00]		
			1,65 [0,81; 3,37]	0,171
Seizures				
Interaction test:	p=0,541			
Rapid Evolvement = No				
Number of patients with event	14	1		
Median (in weeks)	-	-		
% of event-free patients+	96,84 [94,38; 99,30]	99,73 [99,22; 100,00]		
			6,68 [0,88; 50,80]	0,067
Rapid Evolvement = Yes				
Number of patients with event	5	1		
Median (in weeks)	-	-		
% of event-free patients+	97,73 [95,68; 99,78]	99,29 [97,91; 100,00]		
			2,66 [0,31; 22,77]	0,372
Thromboembolic events				
Interaction test:	p=0,776			
Rapid Evolvement = No				
Number of patients with event	28	13		
Median (in weeks)	-	-		
% of event-free patients+	94,47 [91,30; 97,64]	93,21 [87,02; 99,40]		
			1,02 [0,53; 1,98]	0,943
Rapid Evolvement = Yes				
Number of patients with event	5	2		
Median (in weeks)	-	-		
% of event-free patients+	97,92 [96,11; 99,73]	98,60 [96,66; 100,00]		
			1,32 [0,26; 6,83]	0,737

	Treatment groups		Comparison	
	BAF312 (N=1099)	**Placebo (N=546)**	**HR [95% CI]**	**p-value**
Respiratory disorders				
Interaction test:	p=0,868			
Rapid Evolvement = No				
Number of patients with event	89	53		
Median (in weeks)	-	-		
% of event-free patients+	87,14 [84,50; 89,77]	74,79 [61,93; 87,65]		
			0,79 [0,56; 1,11]	0,169
Rapid Evolvement = Yes				
Number of patients with event	28	18		
Median (in weeks)	-	-		
% of event-free patients+	87,84 [83,54; 92,14]	83,08 [74,27; 91,89]		
			0,83 [0,46; 1,51]	0,550
Peripheral edema/swelling				
Interaction test:	p=0,076			
Rapid Evolvement = No				
Number of patients with event	61	11		
Median (in weeks)	-	-		
% of event-free patients+	82,08 [64,99; 99,17]	96,30 [94,00; 98,59]		
			2,73 [1,44; 5,18]	0,002 *
Rapid Evolvement = Yes				
Number of patients with event	13	7		
Median (in weeks)	-	-		
% of event-free patients+	93,10 [88,97; 97,22]	95,06 [91,49; 98,63]		
			0,99 [0,39; 2,48]	0,978

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 total population

	Treatment groups		Comparison	
	BAF312 (N=1099)	**Placebo (N=546)**	**HR [95% CI]**	**p-value**
N'	1099	546		
N' Rapid Evolvement = No	835	401		
N' Rapid Evolvement = Yes	264	145		
Asthma/bronchospasm				
Interaction test:	p=0,929			
Rapid Evolvement = No				
Number of patients with event	4	1		
Median (in weeks)	-	-		
% of event-free patients+	99,48 [98,98; 99,99]	99,73 [99,22; 100,00]		
			1,93 [0,22; 17,22]	0,558
Rapid Evolvement = Yes				
Number of patients with event	4	1		
Median (in weeks)	-	-		
% of event-free patients+	98,28 [96,60; 99,96]	98,88 [96,69; 100,00]		
			2,22 [0,25; 19,83]	0,477
Pregnancy and neonatal topics				
Interaction test:	p=1,000			
Rapid Evolvement = No				
Number of patients with event	4	0		
Median (in weeks)	-	-		
% of event-free patients+	99,43 [98,87; 99,99]	100,00 [100,00; 100,00]		
			-	-
Rapid Evolvement = Yes				
Number of patients with event	2	0		
Median (in weeks)	-	-		
% of event-free patients+	99,20 [98,10; 100,00]	100,00 [100,00; 100,00]		
			-	-

	Treatment groups		Comparison	
	BAF312 (N=1099)	**Placebo (N=546)**	**HR [95% CI]**	**p-value**
Bradyarrhythmias and bradycardia				
Interaction test:	p=0,606			
Rapid Evolvement = No				
Number of patients with event	83	23		
Median (in weeks)	-	-		
% of event-free patients+	87,77 [84,49; 91,05]	92,75 [89,47; 96,03]		
			1,76 [1,11; 2,79]	0,017 *
Rapid Evolvement = Yes				
Number of patients with event	20	8		
Median (in weeks)	-	-		
% of event-free patients+	87,93 [79,19; 96,66]	93,51 [89,00; 98,02]		
			1,37 [0,60; 3,11]	0,452

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 total population

12.7 Subgroup: Disease Course

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

	Treatment groups		Comparison	
	BAF312 (N=1099)	**Placebo (N=546)**	**HR [95% CI]**	**p-value**
N'	1099	546		
N' Moderate or Severe Disease Course = No	195	87		
N' Moderate or Severe Disease Course = Yes	904	459		
Any AE				
Interaction test:	p=0,377			
Moderate or Severe Disease Course = No				
Number of patients with event	179	69		
Median (in weeks)	4,1 [2,7; 7,9]	5,9 [3,3; 11,6]		
% of event-free patients+	2,63 [0,00; 6,71]	11,98 [1,81; 22,16]		
			1,42 [1,07; 1,87]	0,014 *
Moderate or Severe Disease Course = Yes				
Number of patients with event	796	376		
Median (in weeks)	4,2 [3,6; 6,0]	8,1 [5,1; 11,9]		
% of event-free patients+	7,90 [5,24; 10,56]	14,16 [10,08; 18,23]		
			1,23 [1,09; 1,40]	0,001 *
Any AE, disease specific events excluded[1]				
Interaction test:	p=0,201			
Moderate or Severe Disease Course = No				
Number of patients with event	173	65		
Median (in weeks)	11,4 [4,9; 13,1]	12,9 [6,7; 30,0]		
% of event-free patients+	2,92 [0,00; 7,49]	16,09 [4,87; 27,30]		
			1,45 [1,09; 1,93]	0,011 *
Moderate or Severe Disease Course = Yes				
Number of patients with event	745	353		
Median (in weeks)	11,0 [8,9; 12,7]	13,0 [10,9; 17,0]		
% of event-free patients+	11,83 [8,75; 14,91]	17,77 [13,17; 22,37]		
			1,18 [1,04; 1,34]	0,010 *

	Treatment groups		Comparison	
	BAF312 (N=1099)	**Placebo (N=546)**	**HR [95% CI]**	**p-value**
Any SAE				
Interaction test:	p=0,459			
Moderate or Severe Disease Course = No				
Number of patients with event	34	10		
Median (in weeks)	-	-		
% of event-free patients+	73,12 [61,25; 85,00]	87,12 [79,59; 94,64]		
			1,60 [0,79; 3,24]	0,189
Moderate or Severe Disease Course = Yes				
Number of patients with event	152	64		
Median (in weeks)	-	-		
% of event-free patients+	76,21 [70,74; 81,68]	78,37 [69,16; 87,59]		
			1,20 [0,90; 1,61]	0,216
Any SAE, disease specific events excluded[1]				
Interaction test:	p=0,208			
Moderate or Severe Disease Course = No				
Number of patients with event	29	6		
Median (in weeks)	-	-		
% of event-free patients+	76,42 [64,44; 88,39]	92,07 [85,91; 98,24]		
			2,29 [0,95; 5,51]	0,065
Moderate or Severe Disease Course = Yes				
Number of patients with event	117	47		
Median (in weeks)	-	-		
% of event-free patients+	82,96 [79,87; 86,06]	82,67 [73,60; 91,73]		
			1,25 [0,89; 1,75]	0,197
Any severe AE[2]				
Interaction test:	p=0,554			
Moderate or Severe Disease Course = No				
Number of patients with event	19	6		
Median (in weeks)	-	-		
% of event-free patients+	84,40 [74,29; 94,52]	92,00 [85,80; 98,20]		
			1,47 [0,59; 3,69]	0,409

	Treatment groups		Comparison	
	BAF312 (N=1099)	**Placebo (N=546)**	**HR [95% CI]**	**p-value**
Moderate or Severe Disease Course = Yes				
Number of patients with event	120	55		
Median (in weeks)	-	-		
% of event-free patients+	83,15 [79,97; 86,34]	83,89 [79,26; 88,51]		
			1,10 [0,80; 1,51]	0,567
Any severe AE[2], disease specific events excluded[1]				
Interaction test:	p=0,157			
Moderate or Severe Disease Course = No				
Number of patients with event	18	3		
Median (in weeks)	-	-		
% of event-free patients+	84,89 [74,76; 95,02]	95,70 [90,87; 100,00]		
			2,81 [0,83; 9,52]	0,098
Moderate or Severe Disease Course = Yes				
Number of patients with event	92	41		
Median (in weeks)	-	-		
% of event-free patients+	86,42 [83,39; 89,46]	87,37 [83,04; 91,70]		
			1,12 [0,77; 1,61]	0,558
Any AE leading to study discontinuation				
Interaction test:	p=0,784			
Moderate or Severe Disease Course = No				
Number of patients with event	8	3		
Median (in weeks)	-	-		
% of event-free patients+	95,58 [92,56; 98,60]	96,30 [92,17; 100,00]		
			1,21 [0,32; 4,56]	0,779
Moderate or Severe Disease Course = Yes				
Number of patients with event	38	13		
Median (in weeks)	-	-		
% of event-free patients+	95,48 [94,05; 96,91]	96,21 [93,88; 98,55]		
			1,48 [0,79; 2,79]	0,219

	Treatment groups		Comparison	
	BAF312 (N=1099)	**Placebo (N=546)**	**HR [95% CI]**	**p-value**
Any AE leading to study drug discontinuation				
Interaction test:	p=0,631			
Moderate or Severe Disease Course = No				
Number of patients with event	13	5		
Median (in weeks)	-	-		
% of event-free patients+	92,98 [89,27; 96,68]	93,90 [88,72; 99,09]		
			1,19 [0,42; 3,33]	0,747
Moderate or Severe Disease Course = Yes				
Number of patients with event	71	23		
Median (in weeks)	-	-		
% of event-free patients+	91,44 [89,50; 93,38]	93,41 [90,54; 96,29]		
			1,56 [0,98; 2,50]	0,062

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 total population

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

	Treatment groups		Comparison	
	BAF312 (N=1099)	**Placebo (N=546)**	**HR [95% CI]**	**p-value**
N'	1099	546		
N' Moderate or Severe Disease Course = No	195	87		
N' Moderate or Severe Disease Course = Yes	904	459		
BLOOD AND LYMPHATIC SYSTEM DISORDERS				
Interaction test:	p=0,362			
Moderate or Severe Disease Course = No				
Number of patients with event	5	2		
Median (in weeks)	-	-		
% of event-free patients+	96,93 [94,23; 99,62]	97,63 [94,39; 100,00]		
			1,12 [0,22; 5,78]	0,891
Moderate or Severe Disease Course = Yes				
Number of patients with event	41	8		
Median (in weeks)	-	-		
% of event-free patients+	94,13 [92,22; 96,03]	98,12 [96,83; 99,42]		
			2,60 [1,22; 5,55]	0,013 *
EAR AND LABYRINTH DISORDERS				
VERTIGO				
Interaction test:	p=0,595			
Moderate or Severe Disease Course = No				
Number of patients with event	2	3		
Median (in weeks)	-	-		
% of event-free patients+	98,96 [97,51; 100,00]	96,09 [91,69; 100,00]		
			0,30 [0,05; 1,79]	0,186
Moderate or Severe Disease Course = Yes				
Number of patients with event	23	23		
Median (in weeks)	-	-		
% of event-free patients+	96,86 [95,39; 98,34]	94,17 [91,80; 96,55]		
			0,50 [0,28; 0,89]	0,018 *

	Treatment groups		Comparison	
	BAF312 (N=1099)	**Placebo (N=546)**	**HR [95% CI]**	**p-value**
EYE DISORDERS				
MACULAR OEDEMA				
Interaction test:	p=0,992			
Moderate or Severe Disease Course = No				
Number of patients with event	3	0		
Median (in weeks)	-	-		
% of event-free patients+	97,46 [94,24; 100,00]	100,00 [100,00; 100,00]		
			-	-
Moderate or Severe Disease Course = Yes				
Number of patients with event	15	1		
Median (in weeks)	-	-		
% of event-free patients+	98,17 [97,24; 99,10]	99,53 [98,62; 100,00]		
			7,57 [1,00; 57,31]	0,050
GASTROINTESTINAL DISORDERS				
NAUSEA				
Interaction test:	p=0,975			
Moderate or Severe Disease Course = No				
Number of patients with event	9	2		
Median (in weeks)	-	-		
% of event-free patients+	95,23 [92,19; 98,28]	97,26 [93,45; 100,00]		
			2,02 [0,44; 9,36]	0,367
Moderate or Severe Disease Course = Yes				
Number of patients with event	65	17		
Median (in weeks)	-	-		
% of event-free patients+	92,08 [90,12; 94,04]	95,55 [93,25; 97,85]		
			1,97 [1,16; 3,36]	0,013 *
GENERAL DISORDERS AND ADMINISTRATION SITE CONDITIONS				
GAIT DISTURBANCE				
Interaction test:	p=0,758			
Moderate or Severe Disease Course = No				
Number of patients with event	6	6		
Median (in weeks)	-	-		
% of event-free patients+	64,91 [12,95; 100,00]	88,49 [78,62; 98,37]		
			0,45 [0,14; 1,39]	0,166

	Treatment groups		Comparison	
	BAF312 (N=1099)	**Placebo (N=546)**	**HR [95% CI]**	**p-value**
Moderate or Severe Disease Course = Yes				
Number of patients with event	18	16		
Median (in weeks)	-	-		
% of event-free patients+	97,75 [96,70; 98,80]	95,30 [92,82; 97,77]		
			0,55 [0,28; 1,08]	0,085
OEDEMA PERIPHERAL				
Interaction test:	p=0,430			
Moderate or Severe Disease Course = No				
Number of patients with event	9	1		
Median (in weeks)	-	-		
% of event-free patients+	94,26 [90,18; 98,35]	98,85 [96,61; 100,00]		
			4,14 [0,52; 32,68]	0,178
Moderate or Severe Disease Course = Yes				
Number of patients with event	41	12		
Median (in weeks)	-	-		
% of event-free patients+	87,34 [73,54; 100,00]	96,92 [95,10; 98,73]		
			1,73 [0,91; 3,30]	0,094
HEPATOBILIARY DISORDERS				
Interaction test:	p=0,988			
Moderate or Severe Disease Course = No				
Number of patients with event	5	0		
Median (in weeks)	-	-		
% of event-free patients+	96,46 [93,26; 99,67]	100,00 [100,00; 100,00]		
			-	-
Moderate or Severe Disease Course = Yes				
Number of patients with event	22	4		
Median (in weeks)	-	-		
% of event-free patients+	96,73 [95,22; 98,24]	98,67 [97,34; 99,99]		
			2,77 [0,95; 8,03]	0,061

	Treatment groups		Comparison	
	BAF312 (N=1099)	**Placebo (N=546)**	**HR [95% CI]**	**p-value**
INFECTIONS AND INFESTATIONS				
HERPES ZOSTER				
Interaction test:	p=0,122			
Moderate or Severe Disease Course = No				
Number of patients with event	4	2		
Median (in weeks)	-	-		
% of event-free patients+	96,94 [93,68; 100,00]	96,97 [92,82; 100,00]		
			0,92 [0,17; 5,00]	0,919
Moderate or Severe Disease Course = Yes				
Number of patients with event	21	2		
Median (in weeks)	-	-		
% of event-free patients+	97,22 [96,03; 98,42]	99,35 [98,40; 100,00]		
			5,34 [1,25; 22,77]	0,024 *
INVESTIGATIONS				
Interaction test:	p=0,995			
Moderate or Severe Disease Course = No				
Number of patients with event	47	13		
Median (in weeks)	-	-		
% of event-free patients+	69,32 [61,07; 77,57]	81,28 [70,76; 91,80]		
			1,72 [0,93; 3,18]	0,083
Moderate or Severe Disease Course = Yes				
Number of patients with event	216	67		
Median (in weeks)	-	-		
% of event-free patients+	67,36 [62,86; 71,86]	74,39 [66,91; 81,87]		
			1,72 [1,31; 2,26]	<0,001 *
ALANINE AMINOTRANSFERASE INCREASED				
Interaction test:	p=0,988			
Moderate or Severe Disease Course = No				
Number of patients with event	17	2		
Median (in weeks)	-	-		
% of event-free patients+	89,51 [84,41; 94,62]	97,51 [94,10; 100,00]		
			4,03 [0,93; 17,43]	0,062

	Treatment groups		Comparison	
	BAF312 (N=1099)	**Placebo (N=546)**	**HR [95% CI]**	**p-value**
Moderate or Severe Disease Course = Yes				
Number of patients with event	48	6		
Median (in weeks)	-	-		
% of event-free patients+	92,80 [90,59; 95,01]	98,64 [97,56; 99,72]		
			4,08 [1,75; 9,53]	0,001 *
GAMMA-GLUTAMYLTRANSFERASE INCREASED				
Interaction test:	p=0,112			
Moderate or Severe Disease Course = No				
Number of patients with event	9	3		
Median (in weeks)	-	-		
% of event-free patients+	95,14 [92,03; 98,25]	95,14 [89,37; 100,00]		
			1,37 [0,37; 5,08]	0,633
Moderate or Severe Disease Course = Yes				
Number of patients with event	34	3		
Median (in weeks)	-	-		
% of event-free patients+	94,36 [91,95; 96,77]	98,58 [96,80; 100,00]		
			5,74 [1,76; 18,69]	0,004 *
HEPATIC ENZYME INCREASED				
Interaction test:	p=0,992			
Moderate or Severe Disease Course = No				
Number of patients with event	2	0		
Median (in weeks)	-	-		
% of event-free patients+	98,63 [96,72; 100,00]	100,00 [100,00; 100,00]		
			-	-
Moderate or Severe Disease Course = Yes				
Number of patients with event	14	1		
Median (in weeks)	-	-		
% of event-free patients+	98,24 [97,30; 99,18]	99,67 [99,03; 100,00]		
			7,10 [0,93; 54,00]	0,058

	Treatment groups		Comparison	
	BAF312 (N=1099)	**Placebo (N=546)**	**HR [95% CI]**	**p-value**
NERVOUS SYSTEM DISORDERS				
Interaction test:	p=0,698			
Moderate or Severe Disease Course = No				
Number of patients with event	71	25		
Median (in weeks)	-	-		
% of event-free patients+	51,41 [37,83; 65,00]	65,25 [50,24; 80,25]		
			1,33 [0,84; 2,09]	0,225
Moderate or Severe Disease Course = Yes				
Number of patients with event	345	150		
Median (in weeks)	-	-		
% of event-free patients+	51,81 [42,21; 61,40]	62,10 [56,55; 67,66]		
			1,20 [0,99; 1,46]	0,060
PARAESTHESIA				
Interaction test:	p=0,983			
Moderate or Severe Disease Course = No				
Number of patients with event	3	3		
Median (in weeks)	-	-		
% of event-free patients+	98,46 [96,73; 100,00]	94,50 [87,67; 100,00]		
			0,44 [0,09; 2,20]	0,319
Moderate or Severe Disease Course = Yes				
Number of patients with event	15	17		
Median (in weeks)	-	-		
% of event-free patients+	97,04 [94,96; 99,12]	95,56 [93,28; 97,83]		
			0,43 [0,22; 0,87]	0,019 *

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 total population

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

	Treatment groups		Comparison	
	BAF312 (N=1099)	**Placebo (N=546)**	**HR [95% CI]**	**p-value**
N'	1099	546		
N' Moderate or Severe Disease Course = No	195	87		
N' Moderate or Severe Disease Course = Yes	904	459		
INVESTIGATIONS				
Interaction test:	p=0,990			
Moderate or Severe Disease Course = No				
Number of patients with event	2	0		
Median (in weeks)	-	-		
% of event-free patients+	98,86 [97,27; 100,00]	100,00 [100,00; 100,00]		
			-	-
Moderate or Severe Disease Course = Yes				
Number of patients with event	19	3		
Median (in weeks)	-	-		
% of event-free patients+	97,51 [96,37; 98,65]	99,29 [98,48; 100,00]		
			3,19 [0,94; 10,77]	0,062

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 total population

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=1099)	**Placebo (N=546)**	**HR [95% CI]**	**p-value**
N'	1099	546		
N' Moderate or Severe Disease Course = No	195	87		
N' Moderate or Severe Disease Course = Yes	904	459		
Infections and infestations				
Interaction test:	p=0,205			
Moderate or Severe Disease Course = No				
Number of patients with event	101	41		
Median (in weeks)	66,0 [51,6; 86,0]	81,1 [61,4; -]		
% of event-free patients+	31,37 [19,06; 43,69]	43,30 [30,85; 55,74]		
			1,22 [0,85; 1,76]	0,277
Moderate or Severe Disease Course = Yes				
Number of patients with event	438	227		
Median (in weeks)	79,0 [70,6; 98,0]	74,1 [56,0; 102,6]		
% of event-free patients+	41,00 [36,48; 45,52]	42,44 [36,51; 48,37]		
			0,95 [0,81; 1,11]	0,497
Herpes simplex virus infections				
Interaction test:	p=0,049 *			
Moderate or Severe Disease Course = No				
Number of patients with event	4	5		
Median (in weeks)	-	-		
% of event-free patients+	97,27 [94,41; 100,00]	88,09 [74,48; 100,00]		
			0,35 [0,10; 1,32]	0,122
Moderate or Severe Disease Course = Yes				
Number of patients with event	21	6		
Median (in weeks)	-	-		
% of event-free patients+	96,91 [95,41; 98,42]	98,31 [96,91; 99,71]		
			1,76 [0,71; 4,36]	0,222

	Treatment groups		Comparison	
	BAF312 (N=1099)	**Placebo (N=546)**	**HR [95% CI]**	**p-value**
Varicella-zoster virus infections				
Interaction test:	p=0,143			
Moderate or Severe Disease Course = No				
Number of patients with event	6	2		
Median (in weeks)	-	-		
% of event-free patients+	95,45 [91,58; 99,31]	96,97 [92,82; 100,00]		
			1,37 [0,28; 6,80]	0,698
Moderate or Severe Disease Course = Yes				
Number of patients with event	27	2		
Median (in weeks)	-	-		
% of event-free patients+	95,95 [94,24; 97,66]	99,35 [98,40; 100,00]		
			6,84 [1,63; 28,78]	0,009 *
Lymphopenia				
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+	99,49 [98,48; 100,00]	100,00 [100,00; 100,00]		
			-	-
Moderate or Severe Disease Course = Yes				
Number of patients with event	13	0		
Median (in weeks)	-	-		
% of event-free patients+	98,37 [97,48; 99,25]	100,00 [100,00; 100,00]		
			-	-
Macular edema				
Interaction test:	p=0,991			
Moderate or Severe Disease Course = No				
Number of patients with event	4	0		
Median (in weeks)	-	-		
% of event-free patients+	96,84 [93,43; 100,00]	100,00 [100,00; 100,00]		
			-	-

	Treatment groups		Comparison	
	BAF312 (N=1099)	**Placebo (N=546)**	**HR [95% CI]**	**p-value**
Moderate or Severe Disease Course = Yes				
Number of patients with event	16	1		
Median (in weeks)	-	-		
% of event-free patients+	98,05 [97,09; 99,01]	99,53 [98,62; 100,00]		
			8,07 [1,07; 60,88]	0,043 *
Abnormal hepatic enzymes				
Interaction test:	p=0,068			
Moderate or Severe Disease Course = No				
Number of patients with event	24	7		
Median (in weeks)	-	-		
% of event-free patients+	86,67 [81,65; 91,68]	87,60 [77,71; 97,50]		
			1,62 [0,70; 3,77]	0,259
Moderate or Severe Disease Course = Yes				
Number of patients with event	111	14		
Median (in weeks)	-	-		
% of event-free patients+	82,97 [79,18; 86,76]	95,78 [93,34; 98,22]		
			4,15 [2,38; 7,24]	<0,001 *
Malignancies				
Interaction test:	p=0,344			
Moderate or Severe Disease Course = No				
Number of patients with event	6	2		
Median (in weeks)	-	-		
% of event-free patients+	95,55 [91,71; 99,38]	96,90 [92,64; 100,00]		
			1,35 [0,27; 6,68]	0,714
Moderate or Severe Disease Course = Yes				
Number of patients with event	14	12		
Median (in weeks)	-	-		
% of event-free patients+	98,01 [96,95; 99,07]	91,43 [81,93; 100,00]		
			0,57 [0,26; 1,24]	0,155

	Treatment groups		Comparison	
	BAF312 (N=1099)	**Placebo (N=546)**	**HR [95% CI]**	**p-value**
Hypertension				
Interaction test:	p=0,899			
Moderate or Severe Disease Course = No				
Number of patients with event	25	8		
Median (in weeks)	-	-		
% of event-free patients+	72,04 [53,36; 90,71]	86,96 [76,97; 96,96]		
			1,42 [0,64; 3,15]	0,386
Moderate or Severe Disease Course = Yes				
Number of patients with event	112	42		
Median (in weeks)	-	-		
% of event-free patients+	84,92 [82,12; 87,73]	83,47 [73,43; 93,52]		
			1,34 [0,94; 1,92]	0,102
Seizures				
Interaction test:	p=0,991			
Moderate or Severe Disease Course = No				
Number of patients with event	3	0		
Median (in weeks)	-	-		
% of event-free patients+	97,07 [93,63; 100,00]	100,00 [100,00; 100,00]		
			-	-
Moderate or Severe Disease Course = Yes				
Number of patients with event	16	2		
Median (in weeks)	-	-		
% of event-free patients+	97,16 [95,15; 99,16]	99,55 [98,92; 100,00]		
			3,99 [0,92; 17,36]	0,065
Thromboembolic events				
Interaction test:	p=0,594			
Moderate or Severe Disease Course = No				
Number of patients with event	7	2		
Median (in weeks)	-	-		
% of event-free patients+	96,00 [93,07; 98,92]	97,50 [94,06; 100,00]		
			1,58 [0,33; 7,62]	0,567

	Treatment groups		Comparison	
	BAF312 (N=1099)	**Placebo (N=546)**	**HR [95% CI]**	**p-value**
Moderate or Severe Disease Course = Yes				
Number of patients with event	26	13		
Median (in weeks)	-	-		
% of event-free patients+	95,42 [92,86; 97,98]	94,25 [89,08; 99,41]		
			1,00 [0,51; 1,94]	0,989
Respiratory disorders				
Interaction test:	p=0,644			
Moderate or Severe Disease Course = No				
Number of patients with event	23	11		
Median (in weeks)	-	-		
% of event-free patients+	86,11 [80,58; 91,64]	85,63 [77,53; 93,74]		
			0,93 [0,45; 1,91]	0,848
Moderate or Severe Disease Course = Yes				
Number of patients with event	94	60		
Median (in weeks)	-	-		
% of event-free patients+	87,55 [85,08; 90,01]	75,01 [62,95; 87,06]		
			0,77 [0,56; 1,07]	0,122
Peripheral edema/swelling				
Interaction test:	p=0,305			
Moderate or Severe Disease Course = No				
Number of patients with event	12	1		
Median (in weeks)	-	-		
% of event-free patients+	92,68 [88,27; 97,09]	98,85 [96,61; 100,00]		
			5,61 [0,73; 43,12]	0,098
Moderate or Severe Disease Course = Yes				
Number of patients with event	62	17		
Median (in weeks)	-	-		
% of event-free patients+	84,36 [70,95; 97,77]	95,39 [93,11; 97,67]		
			1,86 [1,09; 3,18]	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 + disease course + disease course * treatment
If it was not possible to fit the minimal model, the HR is not given.

Analysis population: A2304 SAF total population

	Treatment groups		Comparison	
	BAF312 (N=1099)	**Placebo (N=546)**	**HR [95% CI]**	**p-value**
N'	1099	546		
N' Moderate or Severe Disease Course = No	195	87		
N' Moderate or Severe Disease Course = Yes	904	459		
Asthma/bronchospasm				
Interaction test:	p=0,249			
Moderate or Severe Disease Course = No				
Number of patients with event	1	1		
Median (in weeks)	-	-		
% of event-free patients+	99,30 [97,92; 100,00]	98,04 [94,23; 100,00]		
			0,46 [0,03; 7,35]	0,583
Moderate or Severe Disease Course = Yes				
Number of patients with event	7	1		
Median (in weeks)	-	-		
% of event-free patients+	99,15 [98,51; 99,78]	99,77 [99,32; 100,00]		
			3,55 [0,44; 28,87]	0,236
Pregnancy and neonatal topics				
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+	99,37 [98,13; 100,00]	100,00 [100,00; 100,00]		
			-	-
Moderate or Severe Disease Course = Yes				
Number of patients with event	5	0		
Median (in weeks)	-	-		
% of event-free patients+	99,38 [98,83; 99,92]	100,00 [100,00; 100,00]		
			-	-

	Treatment groups		Comparison	
	BAF312 (N=1099)	**Placebo (N=546)**	**HR [95% CI]**	**p-value**
Bradyarrhythmias and bradycardia				
Interaction test:	p=0,231			
Moderate or Severe Disease Course = No				
Number of patients with event	19	8		
Median (in weeks)	-	-		
% of event-free patients+	88,53 [83,01; 94,05]	90,78 [84,68; 96,87]		
			1,05 [0,46; 2,41]	0,901
Moderate or Severe Disease Course = Yes				
Number of patients with event	84	23		
Median (in weeks)	-	-		
% of event-free patients+	87,34 [83,03; 91,66]	93,36 [90,40; 96,32]		
			1,88 [1,18; 2,98]	0,007 *

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 total population

12.8 Subgroup: Region

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

	Treatment groups		Comparison	
	BAF312 (N=1099)	**Placebo (N=546)**	**HR [95% CI]**	**p-value**
N'	1099	546		
N' Region = Europe	860	427		
N' Region = Other	239	119		
Any AE				
Interaction test:	p=0,792			
Region = Europe				
Number of patients with event	764	345		
Median (in weeks)	4,6 [3,9; 7,1]	7,0 [4,7; 11,7]		
% of event-free patients+	7,03 [4,42; 9,64]	14,52 [10,09; 18,94]		
			1,26 [1,11; 1,43]	<0,001 *
Region = Other				
Number of patients with event	211	100		
Median (in weeks)	3,1 [2,3; 4,4]	8,7 [4,6; 12,9]		
% of event-free patients+	7,52 [2,27; 12,78]	9,67 [2,36; 16,97]		
			1,30 [1,03; 1,65]	0,029 *
Any AE, disease specific events excluded[1]				
Interaction test:	p=0,578			
Region = Europe				
Number of patients with event	718	326		
Median (in weeks)	11,7 [9,0; 12,7]	12,9 [10,3; 17,3]		
% of event-free patients+	10,52 [7,50; 13,54]	17,98 [13,09; 22,87]		
			1,20 [1,06; 1,37]	0,006 *
Region = Other				
Number of patients with event	200	92		
Median (in weeks)	9,9 [5,0; 13,1]	13,1 [9,9; 24,4]		
% of event-free patients+	9,88 [3,26; 16,51]	11,02 [0,57; 21,47]		
			1,30 [1,02; 1,67]	0,036 *

	Treatment groups		Comparison	
	BAF312 (N=1099)	**Placebo (N=546)**	**HR [95% CI]**	**p-value**
Any SAE				
Interaction test:	p=0,675			
Region = Europe				
Number of patients with event	148	60		
Median (in weeks)	-	-		
% of event-free patients+	76,82 [71,79; 81,85]	79,20 [69,99; 88,41]		
			1,22 [0,91; 1,65]	0,190
Region = Other				
Number of patients with event	38	14		
Median (in weeks)	-	-		
% of event-free patients+	64,47 [43,41; 85,53]	81,51 [69,39; 93,63]		
			1,41 [0,77; 2,61]	0,268
Any SAE, disease specific events excluded[1]				
Interaction test:	p=0,967			
Region = Europe				
Number of patients with event	114	41		
Median (in weeks)	-	-		
% of event-free patients+	83,47 [80,49; 86,44]	84,17 [75,09; 93,25]		
			1,37 [0,96; 1,96]	0,081
Region = Other				
Number of patients with event	32	12		
Median (in weeks)	-	-		
% of event-free patients+	69,79 [53,26; 86,33]	83,18 [71,05; 95,32]		
			1,35 [0,70; 2,63]	0,372
Any severe AE[2]				
Interaction test:	p=0,521			
Region = Europe				
Number of patients with event	107	49		
Median (in weeks)	-	-		
% of event-free patients+	84,92 [81,95; 87,90]	85,48 [81,21; 89,75]		
			1,07 [0,77; 1,51]	0,677

	Treatment groups		Comparison	
	BAF312 (N=1099)	**Placebo (N=546)**	**HR [95% CI]**	**p-value**
Region = Other				
Number of patients with event	32	12		
Median (in weeks)	-	-		
% of event-free patients+	69,69 [51,75; 87,63]	83,60 [71,97; 95,23]		
			1,37 [0,71; 2,66]	0,351
Any severe AE[2], disease specific events excluded[1]				
Interaction test:	p=0,811			
Region = Europe				
Number of patients with event	86	35		
Median (in weeks)	-	-		
% of event-free patients+	87,55 [84,73; 90,37]	89,07 [85,14; 93,00]		
			1,20 [0,81; 1,78]	0,353
Region = Other				
Number of patients with event	24	9		
Median (in weeks)	-	-		
% of event-free patients+	73,30 [56,20; 90,40]	86,43 [74,88; 97,97]		
			1,34 [0,62; 2,88]	0,456
Any AE leading to study discontinuation				
Interaction test:	p=0,834			
Region = Europe				
Number of patients with event	33	11		
Median (in weeks)	-	-		
% of event-free patients+	95,92 [94,54; 97,30]	97,21 [95,58; 98,84]		
			1,49 [0,75; 2,95]	0,251
Region = Other				
Number of patients with event	13	5		
Median (in weeks)	-	-		
% of event-free patients+	93,81 [90,45; 97,17]	90,49 [79,59; 100,00]		
			1,31 [0,47; 3,67]	0,611

	Treatment groups		Comparison	
	BAF312 (N=1099)	**Placebo (N=546)**	**HR [95% CI]**	**p-value**
Any AE leading to study drug discontinuation				
Interaction test:	p=0,599			
Region = Europe				
Number of patients with event	62	22		
Median (in weeks)	-	-		
% of event-free patients+	92,23 [90,35; 94,11]	94,03 [91,52; 96,53]		
			1,40 [0,86; 2,28]	0,175
Region = Other				
Number of patients with event	22	6		
Median (in weeks)	-	-		
% of event-free patients+	89,79 [85,66; 93,92]	89,66 [78,74; 100,00]		
			1,84 [0,75; 4,54]	0,185

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 total population

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

	Treatment groups		Comparison	
	BAF312 (N=1099)	**Placebo (N=546)**	**HR [95% CI]**	**p-value**
N'	1099	546		
N' Region = Europe	860	427		
N' Region = Other	239	119		
BLOOD AND LYMPHATIC SYSTEM DISORDERS				
Interaction test:	p=0,238			
Region = Europe				
Number of patients with event	33	9		
Median (in weeks)	-	-		
% of event-free patients+	95,35 [93,71; 96,98]	97,77 [96,32; 99,22]		
			1,81 [0,86; 3,78]	0,115
Region = Other				
Number of patients with event	13	1		
Median (in weeks)	-	-		
% of event-free patients+	89,94 [82,64; 97,25]	99,15 [97,48; 100,00]		
			6,65 [0,87; 50,84]	0,068
EAR AND LABYRINTH DISORDERS				
VERTIGO				
Interaction test:	p=0,519			
Region = Europe				
Number of patients with event	23	25		
Median (in weeks)	-	-		
% of event-free patients+	96,84 [95,41; 98,26]	93,36 [90,79; 95,92]		
			0,45 [0,25; 0,79]	0,005 *
Region = Other				
Number of patients with event	2	1		
Median (in weeks)	-	-		
% of event-free patients+	99,06 [97,76; 100,00]	99,09 [97,32; 100,00]		
			1,01 [0,09; 11,11]	0,995

	Treatment groups		Comparison	
	BAF312 (N=1099)	**Placebo (N=546)**	**HR [95% CI]**	**p-value**
EYE DISORDERS				
MACULAR OEDEMA				
Interaction test:	p=0,991			
Region = Europe				
Number of patients with event	15	1		
Median (in weeks)	-	-		
% of event-free patients+	97,94 [96,86; 99,03]	99,55 [98,67; 100,00]		
			7,39 [0,98; 55,96]	0,053
Region = Other				
Number of patients with event	3	0		
Median (in weeks)	-	-		
% of event-free patients+	98,69 [97,22; 100,00]	100,00 [100,00; 100,00]		
			-	-
GASTROINTESTINAL DISORDERS				
NAUSEA				
Interaction test:	p=0,692			
Region = Europe				
Number of patients with event	47	11		
Median (in weeks)	-	-		
% of event-free patients+	94,22 [92,57; 95,87]	97,38 [95,85; 98,91]		
			2,14 [1,11; 4,12]	0,023 *
Region = Other				
Number of patients with event	27	8		
Median (in weeks)	-	-		
% of event-free patients+	84,87 [77,41; 92,33]	87,01 [75,73; 98,29]		
			1,74 [0,79; 3,83]	0,170
GENERAL DISORDERS AND ADMINISTRATION SITE CONDITIONS				
GAIT DISTURBANCE				
Interaction test:	p=0,100			
Region = Europe				
Number of patients with event	16	19		
Median (in weeks)	-	-		
% of event-free patients+	91,53 [79,12; 100,00]	93,70 [90,65; 96,74]		
			0,40 [0,20; 0,78]	0,007 *

	Treatment groups		Comparison	
	BAF312 (N=1099)	**Placebo (N=546)**	**HR [95% CI]**	**p-value**
Region = Other				
Number of patients with event	8	3		
Median (in weeks)	-	-		
% of event-free patients+	96,27 [93,72; 98,82]	96,54 [92,55; 100,00]		
			1,39 [0,37; 5,24]	0,627
OEDEMA PERIPHERAL				
Interaction test:	p=0,051			
Region = Europe				
Number of patients with event	38	6		
Median (in weeks)	-	-		
% of event-free patients+	88,89 [77,53; 100,00]	98,30 [96,87; 99,73]		
			3,13 [1,32; 7,41]	0,009 *
Region = Other				
Number of patients with event	12	7		
Median (in weeks)	-	-		
% of event-free patients+	93,90 [90,30; 97,49]	93,28 [88,41; 98,15]		
			0,89 [0,35; 2,25]	0,799
HEPATOBILIARY DISORDERS				
Interaction test:	p=0,988			
Region = Europe				
Number of patients with event	24	4		
Median (in weeks)	-	-		
% of event-free patients+	96,36 [94,80; 97,91]	98,65 [97,32; 99,99]		
			2,97 [1,03; 8,56]	0,044 *
Region = Other				
Number of patients with event	3	0		
Median (in weeks)	-	-		
% of event-free patients+	98,60 [97,02; 100,00]	100,00 [100,00; 100,00]		
			-	-

	Treatment groups		Comparison	
	BAF312 (N=1099)	**Placebo (N=546)**	**HR [95% CI]**	**p-value**
INFECTIONS AND INFESTATIONS				
HERPES ZOSTER				
Interaction test:	p=0,987			
Region = Europe				
Number of patients with event	19	4		
Median (in weeks)	-	-		
% of event-free patients+	97,28 [96,02; 98,53]	98,74 [97,48; 100,00]		
			2,36 [0,80; 6,95]	0,118
Region = Other				
Number of patients with event	6	0		
Median (in weeks)	-	-		
% of event-free patients+	96,86 [94,33; 99,40]	100,00 [100,00; 100,00]		
			-	-
INVESTIGATIONS				
Interaction test:	p=0,682			
Region = Europe				
Number of patients with event	213	66		
Median (in weeks)	-	-		
% of event-free patients+	68,25 [64,08; 72,41]	75,48 [68,38; 82,58]		
			1,68 [1,27; 2,21]	<0,001 *
Region = Other				
Number of patients with event	50	14		
Median (in weeks)	-	-		
% of event-free patients+	60,08 [44,12; 76,05]	74,61 [59,13; 90,09]		
			1,92 [1,06; 3,47]	0,031 *
ALANINE AMINOTRANSFERASE INCREASED				
Interaction test:	p=0,777			
Region = Europe				
Number of patients with event	59	7		
Median (in weeks)	-	-		
% of event-free patients+	91,27 [88,94; 93,59]	98,29 [97,03; 99,55]		
			4,24 [1,93; 9,27]	<0,001 *

	Treatment groups		Comparison	
	BAF312 (N=1099)	**Placebo (N=546)**	**HR [95% CI]**	**p-value**
Region = Other				
Number of patients with event	6	1		
Median (in weeks)	-	-		
% of event-free patients+	97,04 [94,61; 99,46]	99,12 [97,41; 100,00]		
			3,06 [0,37; 25,39]	0,301
GAMMA-GLUTAMYLTRANSFERASE INCREASED				
Interaction test:	p=0,041 *			
Region = Europe				
Number of patients with event	41	4		
Median (in weeks)	-	-		
% of event-free patients+	93,59 [91,24; 95,93]	98,27 [96,40; 100,00]		
			5,09 [1,82; 14,21]	0,002 *
Region = Other				
Number of patients with event	2	2		
Median (in weeks)	-	-		
% of event-free patients+	99,11 [97,88; 100,00]	97,00 [92,53; 100,00]		
			0,51 [0,07; 3,59]	0,495
HEPATIC ENZYME INCREASED				
Interaction test:	p=0,991			
Region = Europe				
Number of patients with event	13	1		
Median (in weeks)	-	-		
% of event-free patients+	98,28 [97,33; 99,22]	99,67 [99,03; 100,00]		
			6,47 [0,85; 49,47]	0,072
Region = Other				
Number of patients with event	3	0		
Median (in weeks)	-	-		
% of event-free patients+	98,53 [96,87; 100,00]	100,00 [100,00; 100,00]		
			-	-

	Treatment groups		Comparison	
	BAF312 (N=1099)	**Placebo (N=546)**	**HR [95% CI]**	**p-value**
NERVOUS SYSTEM DISORDERS				
Interaction test:	p=0,172			
Region = Europe				
Number of patients with event	312	138		
Median (in weeks)	-	-		
% of event-free patients+	53,36 [44,52; 62,20]	62,74 [57,02; 68,46]		
			1,14 [0,93; 1,39]	0,197
Region = Other				
Number of patients with event	104	37		
Median (in weeks)	-	-		
% of event-free patients+	51,53 [44,07; 58,99]	66,11 [56,92; 75,29]		
			1,53 [1,05; 2,23]	0,025 *
PARAESTHESIA				
Interaction test:	p=0,304			
Region = Europe				
Number of patients with event	16	15		
Median (in weeks)	-	-		
% of event-free patients+	97,01 [95,07; 98,96]	95,89 [93,70; 98,08]		
			0,51 [0,25; 1,04]	0,063
Region = Other				
Number of patients with event	2	5		
Median (in weeks)	-	-		
% of event-free patients+	99,12 [97,90; 100,00]	91,55 [81,76; 100,00]		
			0,20 [0,04; 1,03]	0,055

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 total population

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

	Treatment groups		Comparison	
	BAF312 (N=1099)	**Placebo (N=546)**	**HR [95% CI]**	**p-value**
N'	1099	546		
N' Region = Europe	860	427		
N' Region = Other	239	119		
INVESTIGATIONS				
Interaction test:	p=0,425			
Region = Europe				
Number of patients with event	18	2		
Median (in weeks)	-	-		
% of event-free patients+	97,55 [96,40; 98,69]	99,53 [98,87; 100,00]		
			4,45 [1,03; 19,19]	0,045 *
Region = Other				
Number of patients with event	3	1		
Median (in weeks)	-	-		
% of event-free patients+	98,74 [97,33; 100,00]	98,78 [96,40; 100,00]		
			1,49 [0,15; 14,31]	0,730

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 total population

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=1099)	**Placebo (N=546)**	**HR [95% CI]**	**p-value**
N'	1099	546		
N' Region = Europe	860	427		
N' Region = Other	239	119		
Infections and infestations				
Interaction test:	p=0,579			
Region = Europe				
Number of patients with event	426	215		
Median (in weeks)	77,0 [66,7; 98,3]	73,4 [61,0; 95,4]		
% of event-free patients+	40,70 [36,14; 45,25]	42,65 [36,97; 48,33]		
			0,97 [0,82; 1,14]	0,695
Region = Other				
Number of patients with event	113	53		
Median (in weeks)	73,0 [54,1; 86,1]	105,0 [41,9; -]		
% of event-free patients+	32,44 [21,42; 43,47]	40,22 [20,77; 59,67]		
			1,07 [0,77; 1,49]	0,672
Herpes simplex virus infections				
Interaction test:	p=0,391			
Region = Europe				
Number of patients with event	23	9		
Median (in weeks)	-	-		
% of event-free patients+	96,67 [95,18; 98,16]	96,54 [93,79; 99,30]		
			1,26 [0,58; 2,71]	0,562
Region = Other				
Number of patients with event	2	2		
Median (in weeks)	-	-		
% of event-free patients+	98,24 [95,58; 100,00]	98,32 [96,01; 100,00]		
			0,50 [0,07; 3,55]	0,488
Varicella-zoster virus infections				
Interaction test:	p=0,986			
Region = Europe				
Number of patients with event	27	4		
Median (in weeks)	-	-		
% of event-free patients+	95,75 [94,02; 97,49]	98,74 [97,48; 100,00]		
			3,35 [1,17; 9,57]	0,024 *

	Treatment groups		Comparison	
	BAF312 (N=1099)	**Placebo (N=546)**	**HR [95% CI]**	**p-value**
Region = Other				
Number of patients with event	6	0		
Median (in weeks)	-	-		
% of event-free patients+	96,86 [94,33; 99,40]	100,00 [100,00; 100,00]		
			-	-
Lymphopenia				
Interaction test:	p=1,000			
Region = Europe				
Number of patients with event	10	0		
Median (in weeks)	-	-		
% of event-free patients+	98,71 [97,91; 99,51]	100,00 [100,00; 100,00]		
			-	-
Region = Other				
Number of patients with event	4	0		
Median (in weeks)	-	-		
% of event-free patients+	98,01 [96,07; 99,96]	100,00 [100,00; 100,00]		
			-	-
Macular edema				
Interaction test:	p=0,990			
Region = Europe				
Number of patients with event	16	1		
Median (in weeks)	-	-		
% of event-free patients+	97,81 [96,70; 98,92]	99,55 [98,67; 100,00]		
			7,89 [1,05; 59,50]	0,045 *
Region = Other				
Number of patients with event	4	0		
Median (in weeks)	-	-		
% of event-free patients+	98,12 [96,29; 99,96]	100,00 [100,00; 100,00]		
			-	-

	Treatment groups		Comparison	
	BAF312 (N=1099)	**Placebo (N=546)**	**HR [95% CI]**	**p-value**
Abnormal hepatic enzymes				
Interaction test:	p=0,918			
Region = Europe				
Number of patients with event	117	18		
Median (in weeks)	-	-		
% of event-free patients+	82,23 [78,61; 85,85]	94,11 [91,15; 97,07]		
			3,34 [2,03; 5,49]	<0,001 *
Region = Other				
Number of patients with event	18	3		
Median (in weeks)	-	-		
% of event-free patients+	91,79 [88,14; 95,45]	96,15 [91,40; 100,00]		
			3,12 [0,92; 10,58]	0,068
Malignancies				
Interaction test:	p=0,973			
Region = Europe				
Number of patients with event	13	9		
Median (in weeks)	-	-		
% of event-free patients+	98,17 [97,16; 99,18]	92,68 [83,21; 100,00]		
			0,69 [0,29; 1,61]	0,390
Region = Other				
Number of patients with event	7	5		
Median (in weeks)	-	-		
% of event-free patients+	93,29 [86,81; 99,77]	89,69 [78,16; 100,00]		
			0,71 [0,22; 2,23]	0,552
Hypertension				
Interaction test:	p=0,942			
Region = Europe				
Number of patients with event	118	43		
Median (in weeks)	-	-		
% of event-free patients+	81,65 [77,03; 86,28]	82,79 [72,77; 92,82]		
			1,35 [0,95; 1,91]	0,093

	Treatment groups		Comparison	
	BAF312 (N=1099)	**Placebo (N=546)**	**HR [95% CI]**	**p-value**
Region = Other				
Number of patients with event	19	7		
Median (in weeks)	-	-		
% of event-free patients+	87,76 [80,53; 95,00]	89,52 [81,44; 97,60]		
			1,40 [0,59; 3,32]	0,450
Seizures				
Interaction test:	p=0,989			
Region = Europe				
Number of patients with event	15	2		
Median (in weeks)	-	-		
% of event-free patients+	97,12 [95,20; 99,04]	99,52 [98,85; 100,00]		
			3,64 [0,83; 15,94]	0,086
Region = Other				
Number of patients with event	4	0		
Median (in weeks)	-	-		
% of event-free patients+	98,20 [96,45; 99,95]	100,00 [100,00; 100,00]		
			-	-
Thromboembolic events				
Interaction test:	p=0,567			
Region = Europe				
Number of patients with event	21	8		
Median (in weeks)	-	-		
% of event-free patients+	96,69 [94,82; 98,57]	97,64 [95,94; 99,35]		
			1,27 [0,56; 2,86]	0,571
Region = Other				
Number of patients with event	12	7		
Median (in weeks)	-	-		
% of event-free patients+	86,18 [69,84; 100,00]	82,30 [60,34; 100,00]		
			0,88 [0,35; 2,24]	0,790

	Treatment groups		Comparison	
	BAF312 (N=1099)	**Placebo (N=546)**	**HR [95% CI]**	**p-value**
Respiratory disorders				
Interaction test:	p=0,598			
Region = Europe				
Number of patients with event	89	56		
Median (in weeks)	-	-		
% of event-free patients+	88,24 [85,90; 90,58]	75,73 [63,65; 87,82]		
			0,77 [0,55; 1,07]	0,121
Region = Other				
Number of patients with event	28	15		
Median (in weeks)	-	-		
% of event-free patients+	79,50 [69,64; 89,35]	81,88 [69,46; 94,31]		
			0,93 [0,50; 1,74]	0,818
Peripheral edema/swelling				
Interaction test:	p=0,077			
Region = Europe				
Number of patients with event	54	9		
Median (in weeks)	-	-		
% of event-free patients+	86,57 [75,43; 97,71]	97,32 [95,48; 99,16]		
			2,99 [1,47; 6,05]	0,002 *
Region = Other				
Number of patients with event	20	9		
Median (in weeks)	-	-		
% of event-free patients+	89,01 [84,07; 93,96]	90,90 [85,08; 96,72]		
			1,15 [0,52; 2,53]	0,728

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 total population

	Treatment groups		Comparison	
	BAF312 (N=1099)	**Placebo (N=546)**	**HR [95% CI]**	**p-value**
N'	1099	546		
N' Region = Europe	860	427		
N' Region = Other	239	119		
Asthma/bronchospasm				
Interaction test:	p=0,992			
Region = Europe				
Number of patients with event	5	2		
Median (in weeks)	-	-		
% of event-free patients+	99,34 [98,77; 99,92]	99,38 [98,50; 100,00]		
			1,24 [0,24; 6,40]	0,795
Region = Other				
Number of patients with event	3	0		
Median (in weeks)	-	-		
% of event-free patients+	98,60 [97,02; 100,00]	100,00 [100,00; 100,00]		
			-	-
Pregnancy and neonatal topics				
Interaction test:	p=1,000			
Region = Europe				
Number of patients with event	5	0		
Median (in weeks)	-	-		
% of event-free patients+	99,35 [98,78; 99,92]	100,00 [100,00; 100,00]		
			-	-
Region = Other				
Number of patients with event	1	0		
Median (in weeks)	-	-		
% of event-free patients+	99,50 [98,53; 100,00]	100,00 [100,00; 100,00]		
			-	-

	Treatment groups		Comparison	
	BAF312 (N=1099)	**Placebo (N=546)**	**HR [95% CI]**	**p-value**
Bradyarrhythmias and bradycardia				
Interaction test:	p=0,520			
Region = Europe				
Number of patients with event	85	27		
Median (in weeks)	-	-		
% of event-free patients+	87,15 [83,25; 91,04]	93,20 [90,68; 95,71]		
			1,57 [1,02; 2,42]	0,041 *
Region = Other				
Number of patients with event	18	4		
Median (in weeks)	-	-		
% of event-free patients+	89,73 [82,98; 96,49]	87,32 [73,18; 100,00]		
			2,31 [0,78; 6,81]	0,131

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 total population

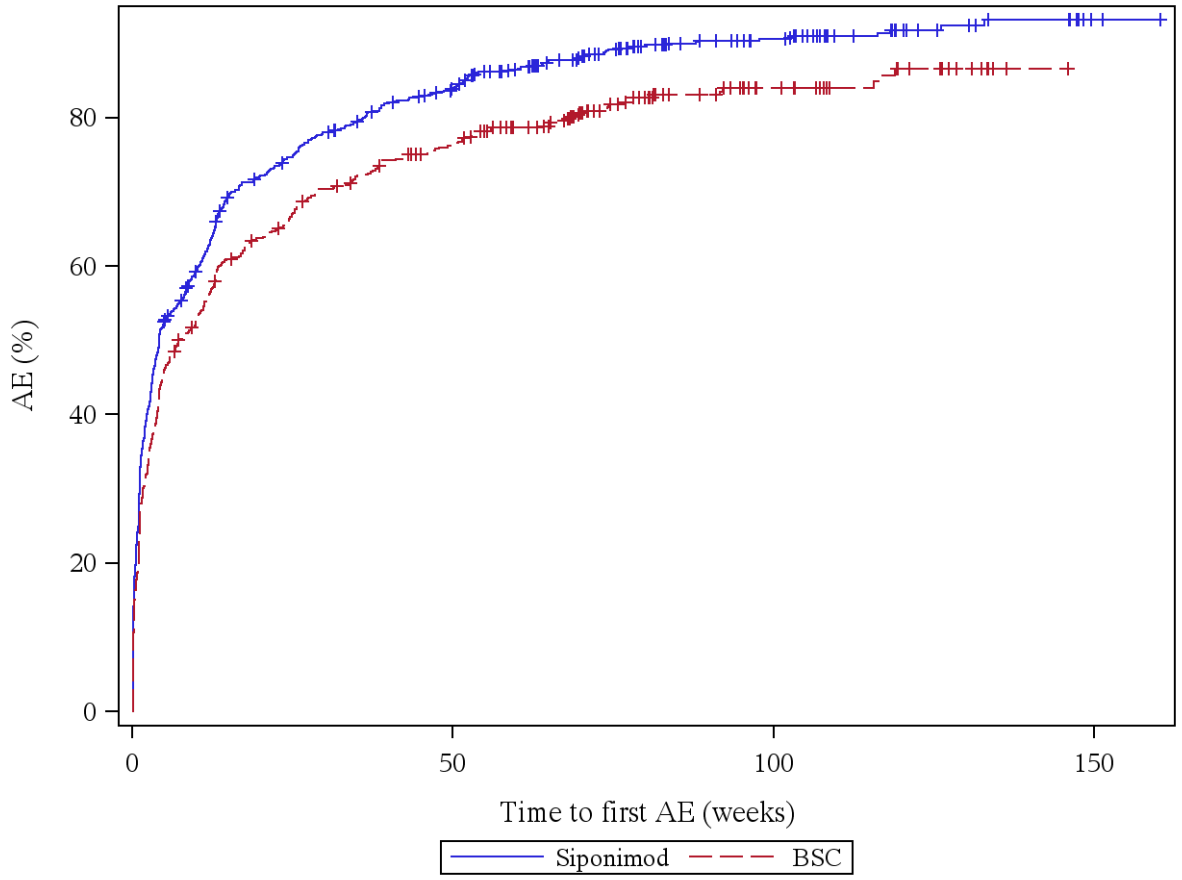
Safety Figures

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

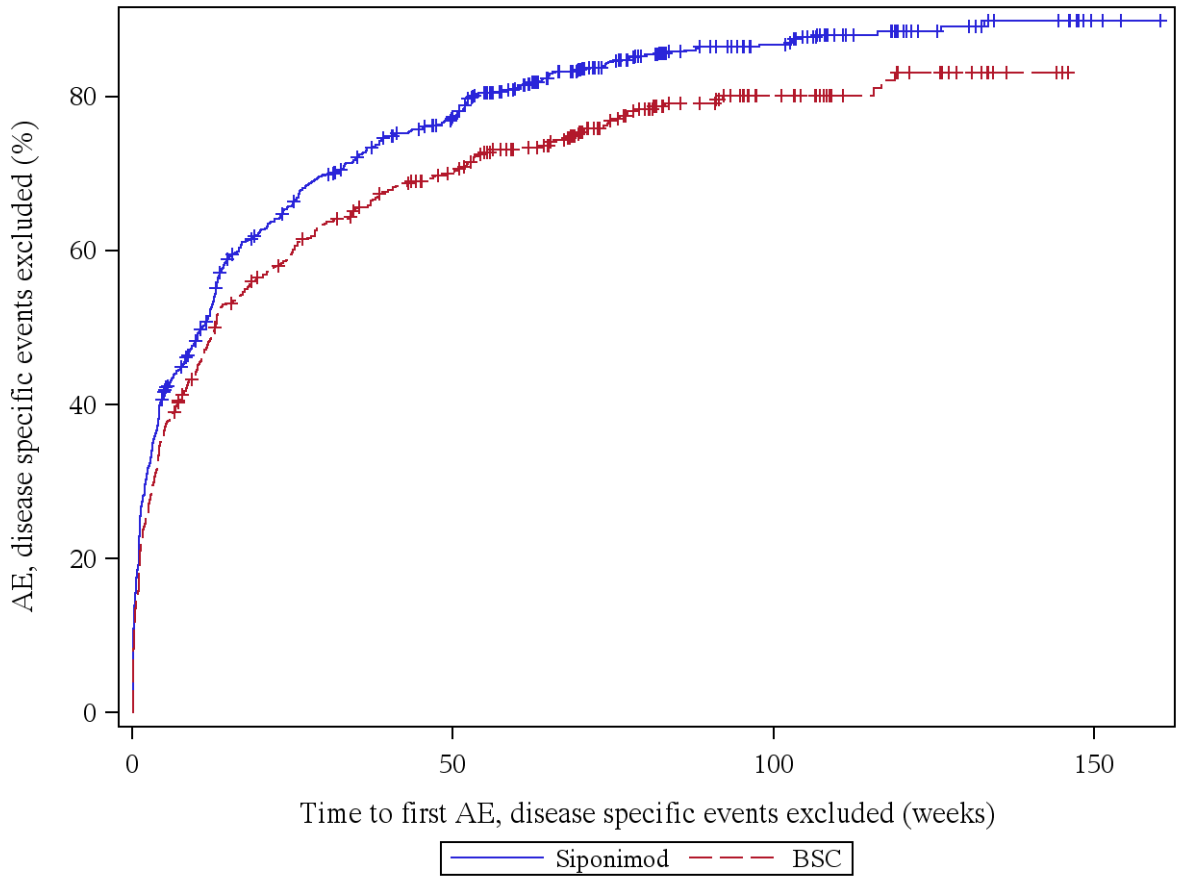


Patients at risk (Siponimod/BSC): Week 0: 1099/546, Week 4: 560/319, Week 12: 402/236, Week 24: 273/182, Week 36: 210/144, Week 48: 169/120, Week 60: 125/96, Week 72: 85/65, Week 84: 56/40, Week 96: 46/31, Week 108: 28/21, Week 120: 17/13, Week 132: 10/6, Week 144: 8/1, Week 156: 1/0, Week 168: 0/0

Log rank test: p-value = <0,001 *
*: p < 0,05

Analysis population: A2304 SAF total population

Figure 12.1.1.2: Any AE, disease specific events excluded

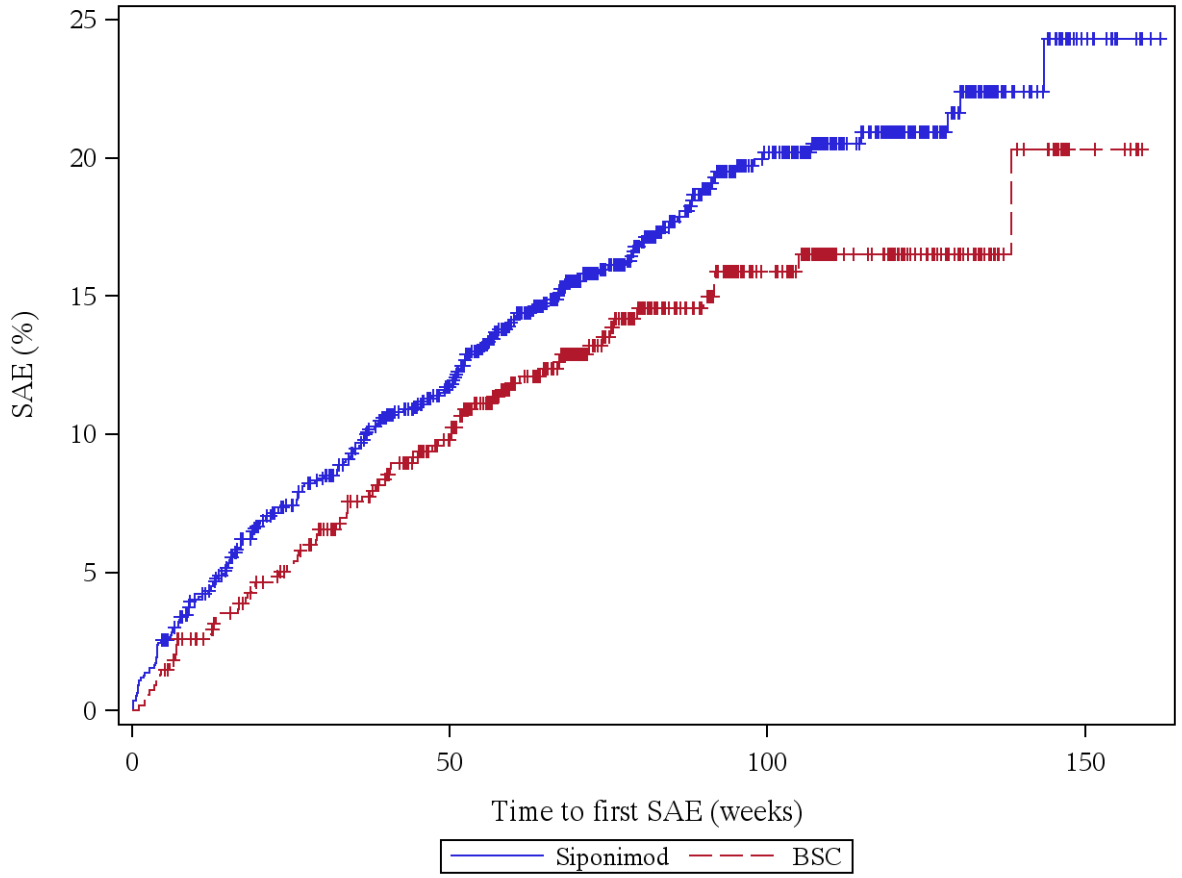


Patients at risk (Siponimod/BSC): Week 0: 1099/546, Week 4: 680/364, Week 12: 521/278, Week 24: 366/217, Week 36: 281/176, Week 48: 232/148, Week 60: 165/118, Week 72: 111/82, Week 84: 72/50, Week 96: 58/37, Week 108: 36/25, Week 120: 23/15, Week 132: 15/8, Week 144: 10/3, Week 156: 1/0, Week 168: 0/0

Log rank test: p-value = 0,001 *
*: p < 0,05

Analysis population: A2304 SAF total population

Figure 12.1.1.3: Any SAE

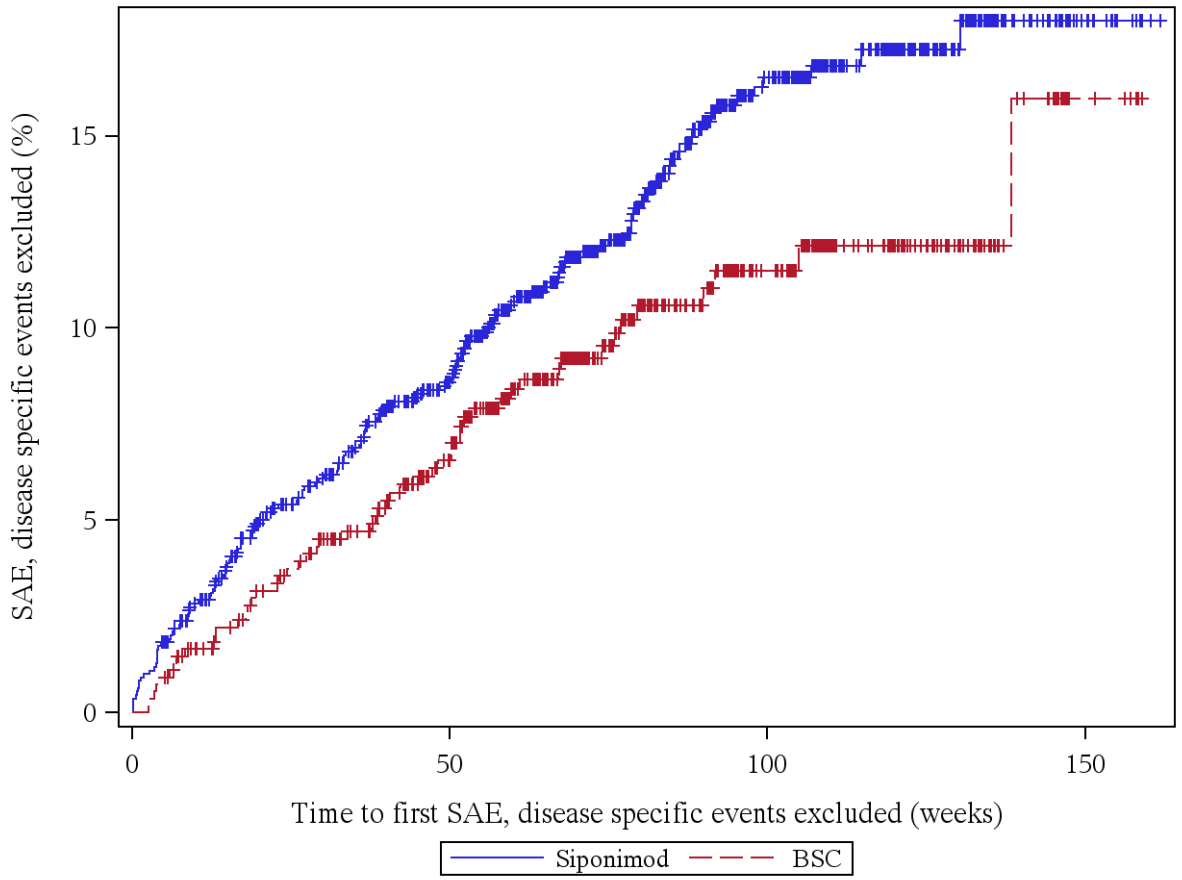


Patients at risk (Siponimod/BSC): Week 0: 1099/546, Week 4: 1073/540, Week 12: 1024/522, Week 24: 959/496, Week 36: 912/465, Week 48: 845/423, Week 60: 730/354, Week 72: 564/277, Week 84: 437/211, Week 96: 337/157, Week 108: 242/112, Week 120: 164/72, Week 132: 88/38, Week 144: 40/19, Week 156: 7/5, Week 168: 0/0

Log rank test: p-value = 0,095
*: p < 0,05

Analysis population: A2304 SAF total population

Figure 12.1.1.4: Any SAE, disease specific events excluded

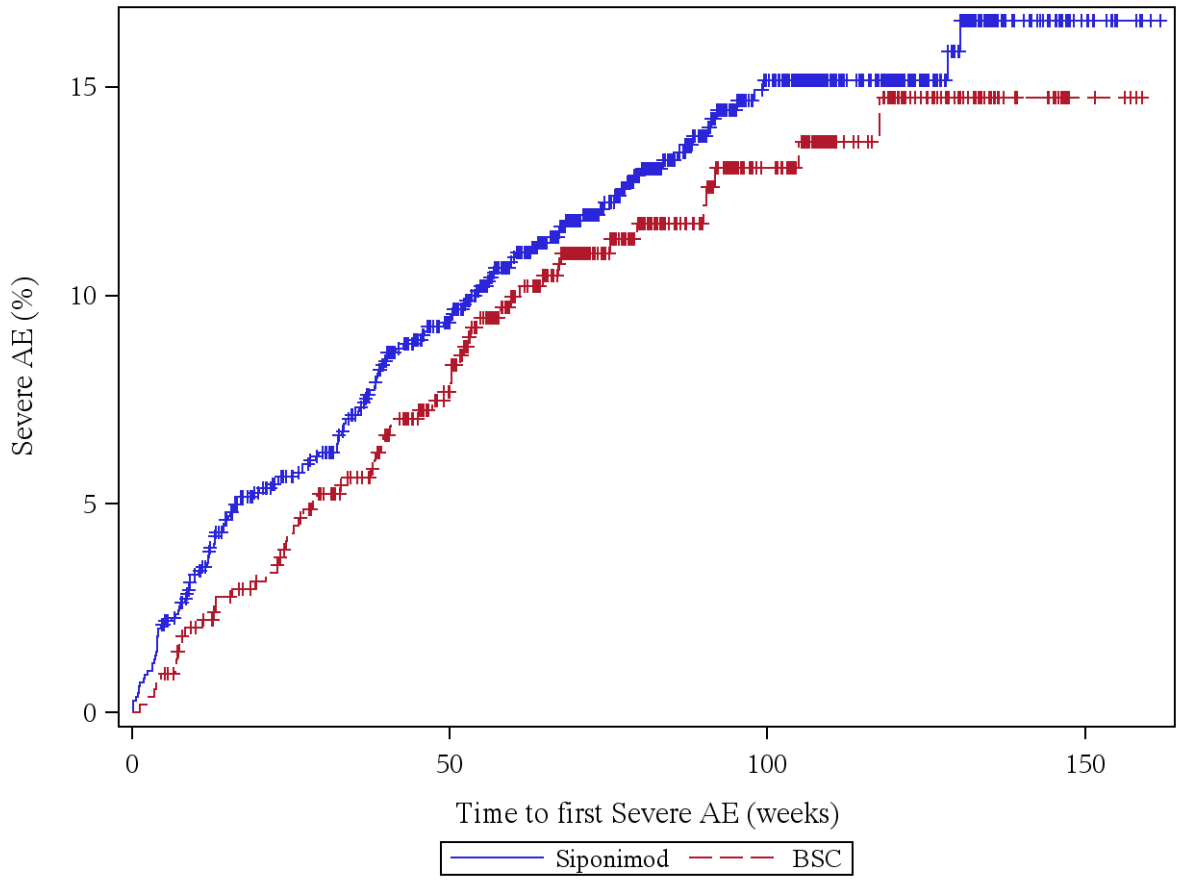


Patients at risk (Siponimod/BSC): Week 0: 1099/546, Week 4: 1081/542, Week 12: 1036/526, Week 24: 975/503, Week 36: 935/477, Week 48: 870/435, Week 60: 755/363, Week 72: 588/283, Week 84: 455/217, Week 96: 352/162, Week 108: 252/114, Week 120: 171/73, Week 132: 95/39, Week 144: 44/20, Week 156: 8/5, Week 168: 0/0

Log rank test: p-value = 0,049 *
*: p < 0,05

Analysis population: A2304 SAF total population

Figure 12.1.1.5: Any severe AE

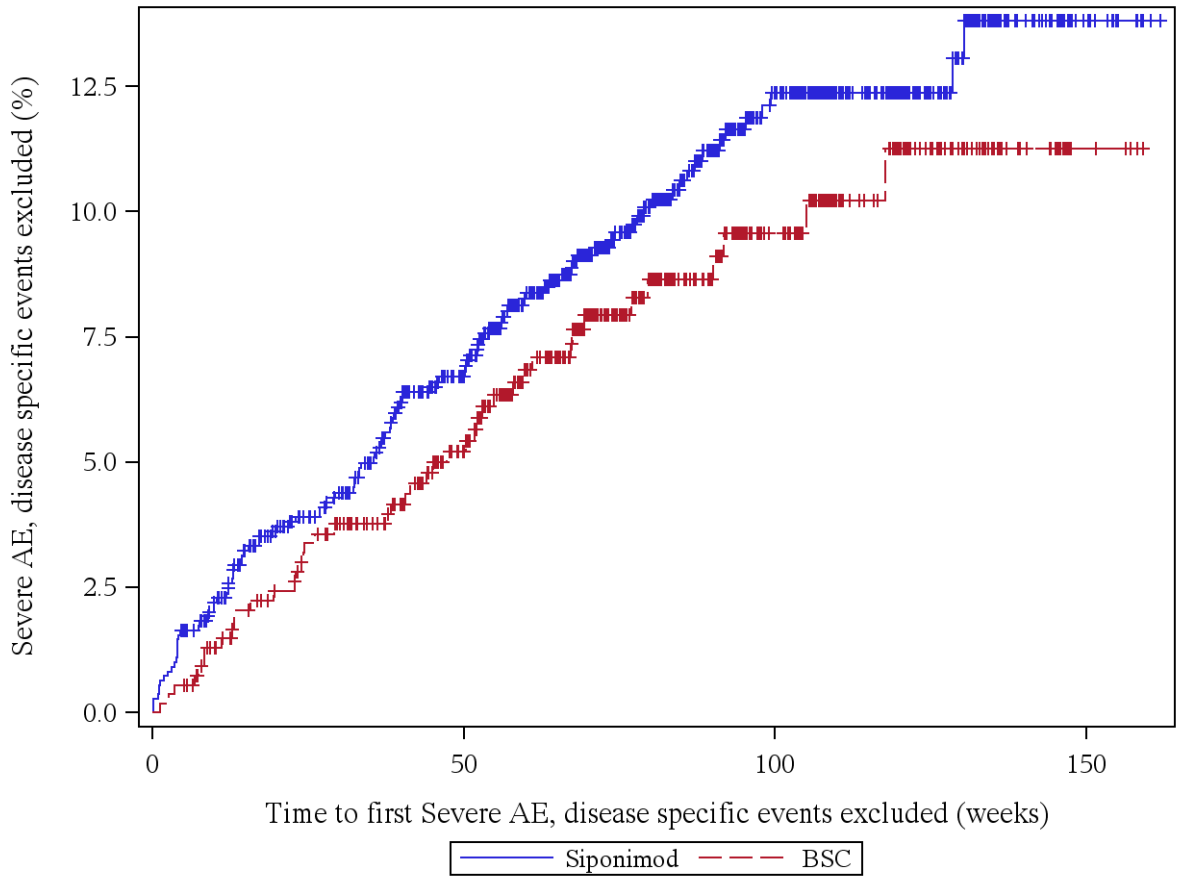


Patients at risk (Siponimod/BSC): Week 0: 1099/546, Week 4: 1079/542, Week 12: 1028/525, Week 24: 974/504, Week 36: 934/476, Week 48: 863/433, Week 60: 753/361, Week 72: 594/281, Week 84: 462/216, Week 96: 356/161, Week 108: 258/112, Week 120: 179/70, Week 132: 99/35, Week 144: 45/17, Week 156: 8/4, Week 168: 0/0

Log rank test: p-value = 0,423
*: p < 0,05

Analysis population: A2304 SAF total population

Figure 12.1.1.6: Any severe AE, disease specific events excluded

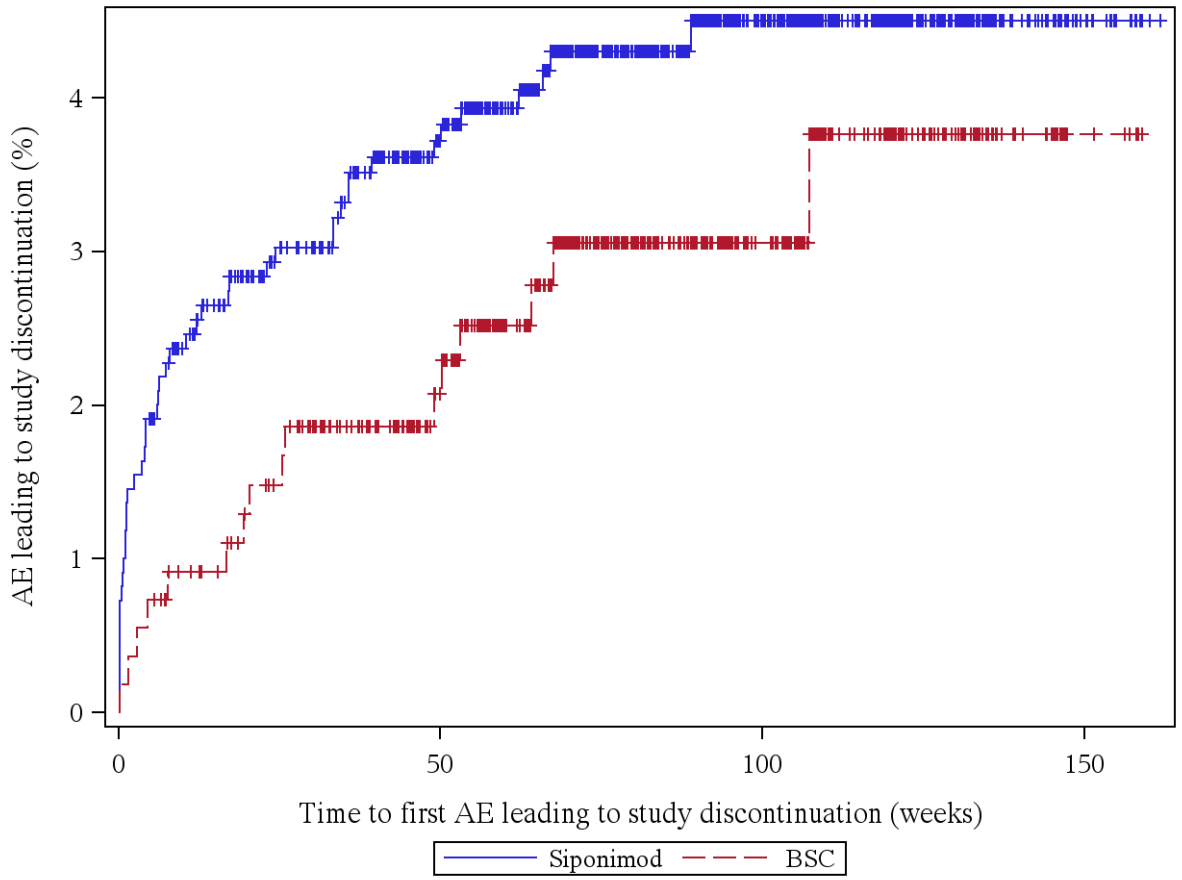


Patients at risk (Siponimod/BSC): Week 0: 1099/546, Week 4: 1083/543, Week 12: 1041/527, Week 24: 989/507, Week 36: 952/482, Week 48: 883/440, Week 60: 770/370, Week 72: 608/287, Week 84: 475/222, Week 96: 365/164, Week 108: 265/115, Week 120: 183/73, Week 132: 101/38, Week 144: 45/19, Week 156: 8/4, Week 168: 0/0

Log rank test: p-value = 0,243
*: p < 0,05

Analysis population: A2304 SAF total population

Figure 12.1.1.7: Any AE leading to study discontinuation

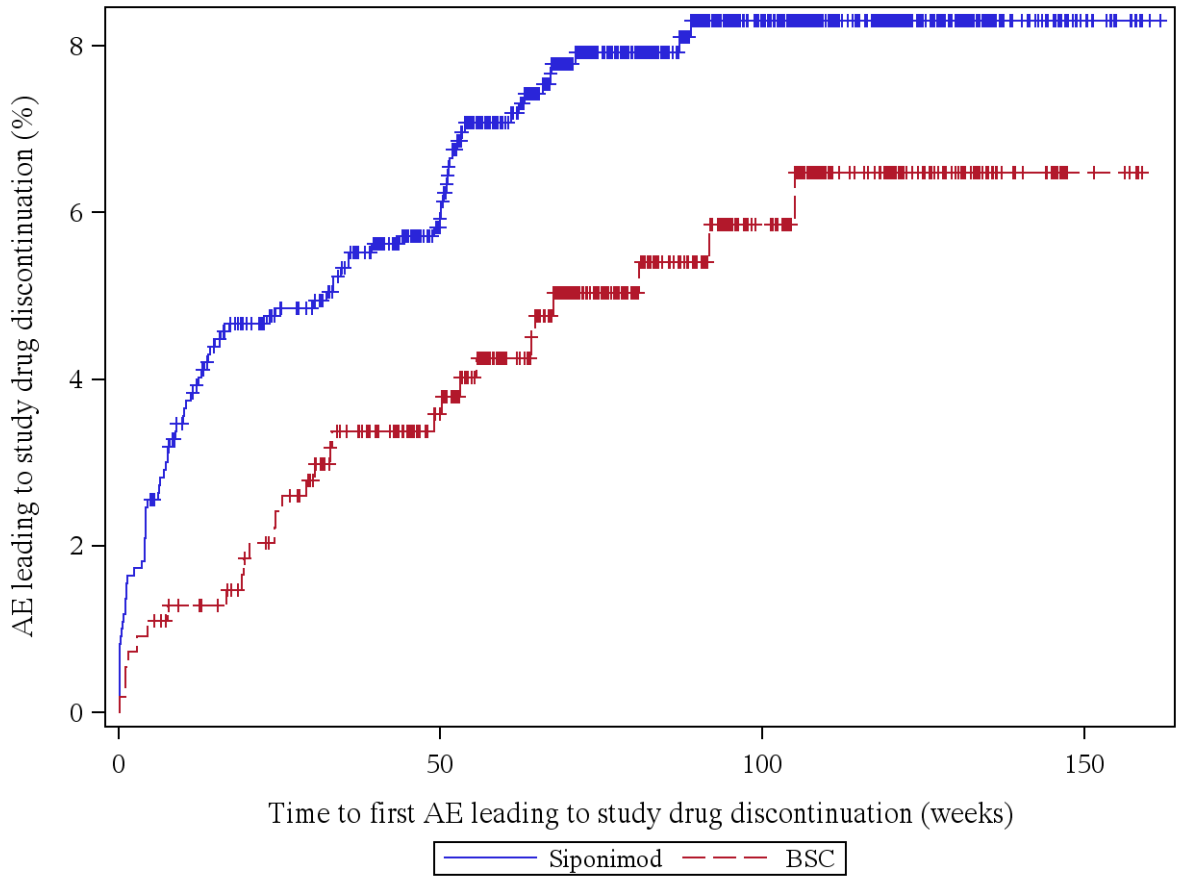


Patients at risk (Siponimod/BSC): Week 0: 1099/546, Week 4: 1080/543, Week 12: 1051/534, Week 24: 1012/519, Week 36: 982/497, Week 48: 922/461, Week 60: 816/387, Week 72: 650/304, Week 84: 515/237, Week 96: 400/176, Week 108: 291/125, Week 120: 200/80, Week 132: 113/40, Week 144: 51/20, Week 156: 10/5, Week 168: 0/0

Log rank test: p-value = 0,213
*: p < 0,05

Analysis population: A2304 SAF total population

Figure 12.1.1.8: Any AE leading to study drug discontinuation



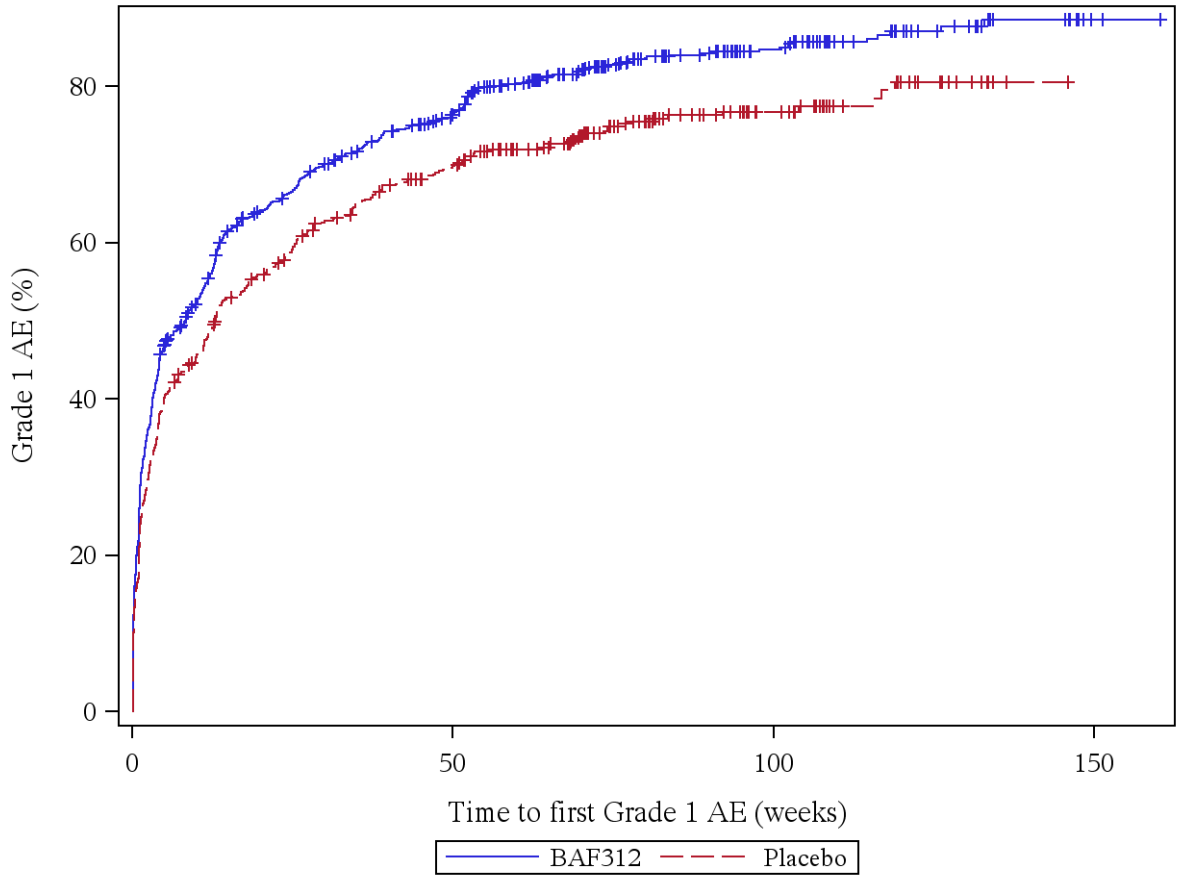
Patients at risk (Siponimod/BSC): Week 0: 1099/546, Week 4: 1076/541, Week 12: 1044/534, Week 24: 1008/519, Week 36: 980/493, Week 48: 921/459, Week 60: 813/386, Week 72: 646/304, Week 84: 514/236, Week 96: 400/175, Week 108: 291/125, Week 120: 200/80, Week 132: 113/40, Week 144: 51/20, Week 156: 10/5, Week 168: 0/0

Log rank test: p-value = 0,064
*: p < 0,05

Analysis population: A2304 SAF total population

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

Figure 12.1.2.1: Grade 1

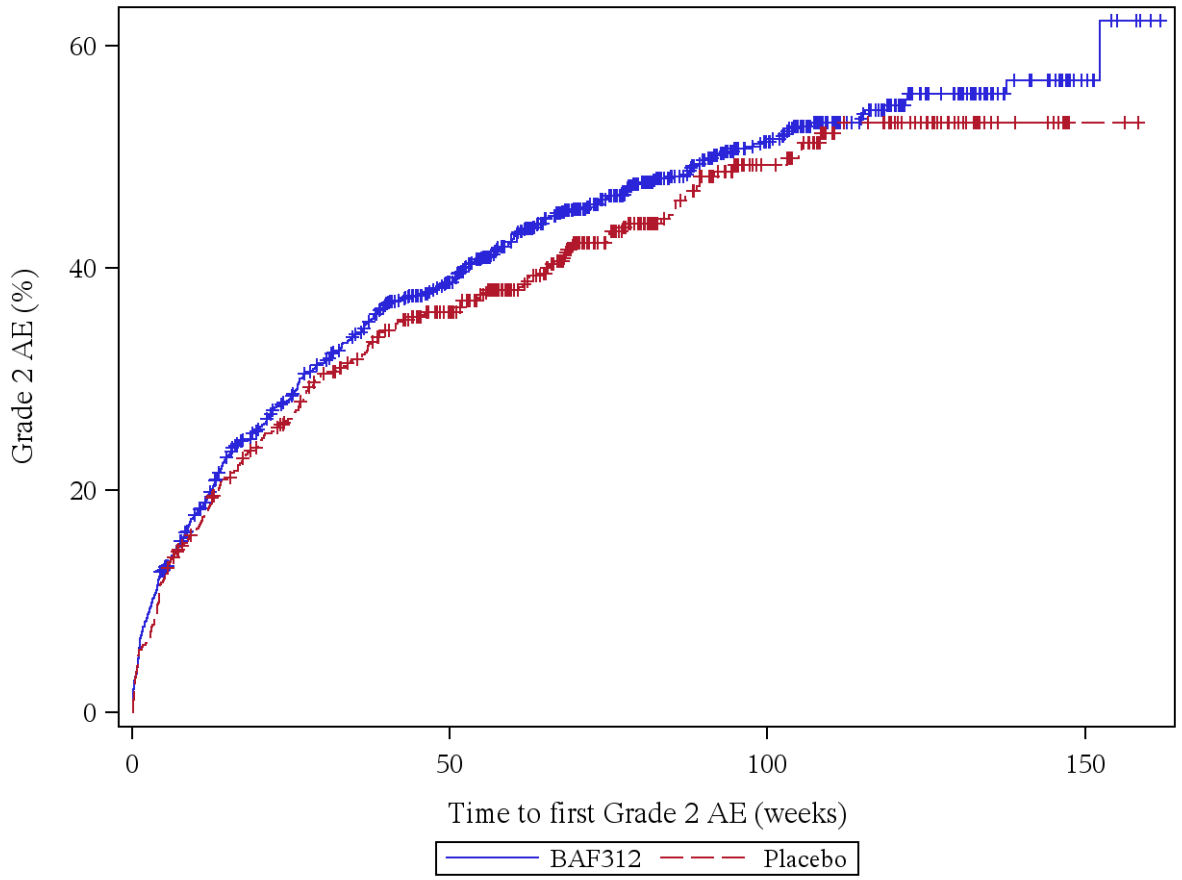


Patients at risk (BAF312/Placebo): Week 0: 1099/546, Week 4: 618/345, Week 12: 476/278, Week 24: 353/219, Week 36: 281/176, Week 48: 236/149, Week 60: 170/120, Week 72: 122/86, Week 84: 85/57, Week 96: 65/42, Week 108: 42/27, Week 120: 26/16, Week 132: 15/6, Week 144: 10/1, Week 156: 1/0, Week 168: 0/0

Log rank test: p-value = <0,001 *
*: p < 0,05

Analysis population: A2304 SAF total population

Figure 12.1.2.2: Grade 2

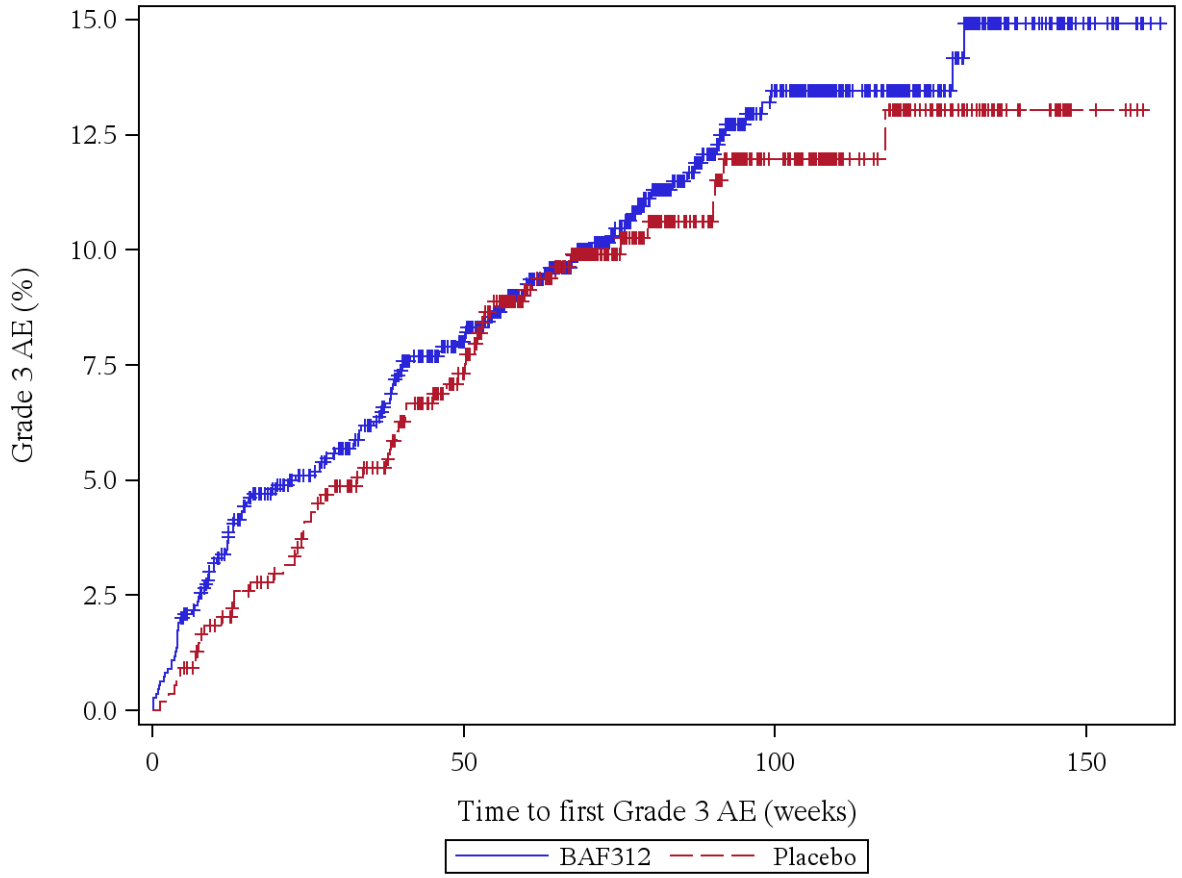


Patients at risk (BAF312/Placebo): Week 0: 1099/546, Week 4: 973/493, Week 12: 864/440, Week 24: 753/388, Week 36: 673/346, Week 48: 593/303, Week 60: 491/249, Week 72: 378/179, Week 84: 290/132, Week 96: 228/90, Week 108: 155/61, Week 120: 100/38, Week 132: 59/19, Week 144: 32/9, Week 156: 5/2, Week 168: 0/0

Log rank test: p-value = 0,279
*: p < 0,05

Analysis population: A2304 SAF total population

Figure 12.1.2.3: Grade 3

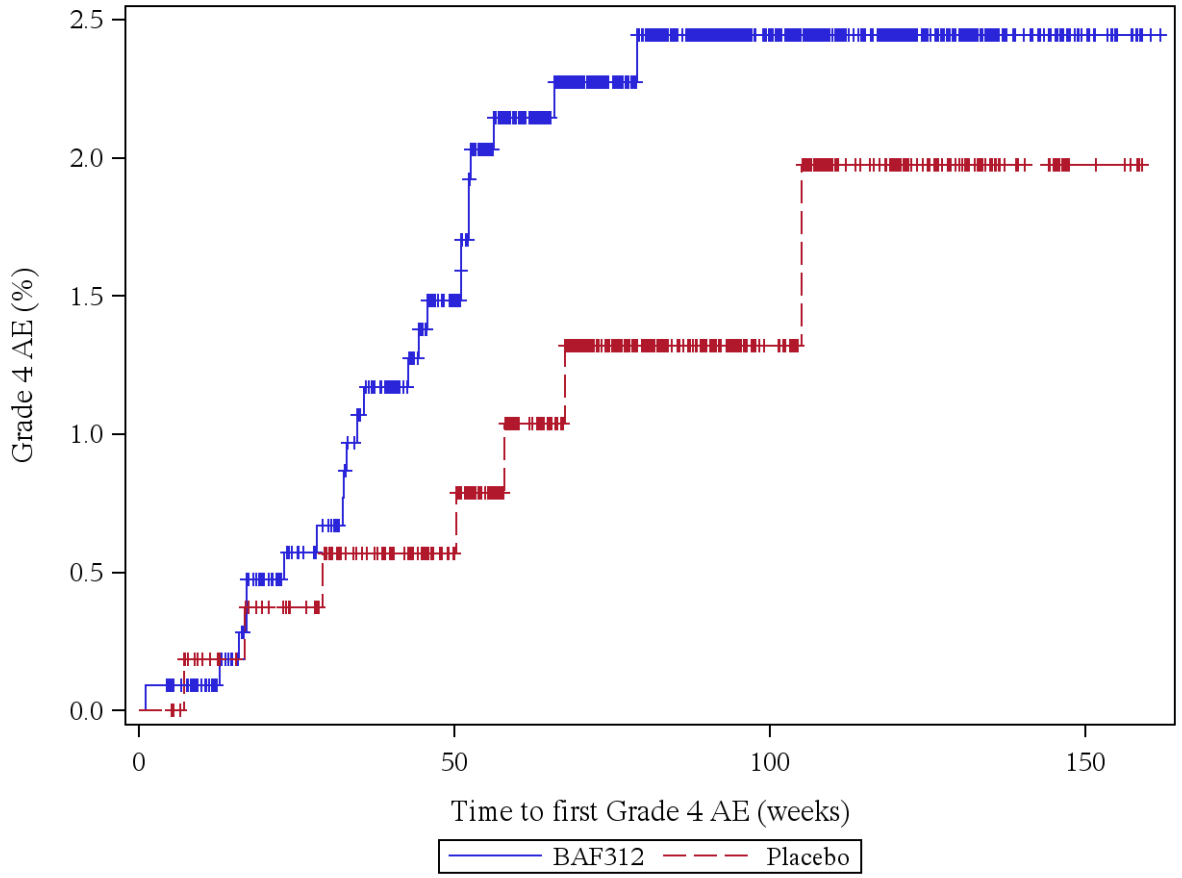


Patients at risk (BAF312/Placebo): Week 0: 1099/546, Week 4: 1080/542, Week 12: 1028/526, Week 24: 978/505, Week 36: 941/478, Week 48: 867/435, Week 60: 757/364, Week 72: 594/281, Week 84: 462/216, Week 96: 356/161, Week 108: 258/113, Week 120: 179/70, Week 132: 99/35, Week 144: 45/17, Week 156: 8/4, Week 168: 0/0

Log rank test: p-value = 0,592
*: p < 0,05

Analysis population: A2304 SAF total population

Figure 12.1.2.4: Grade 4

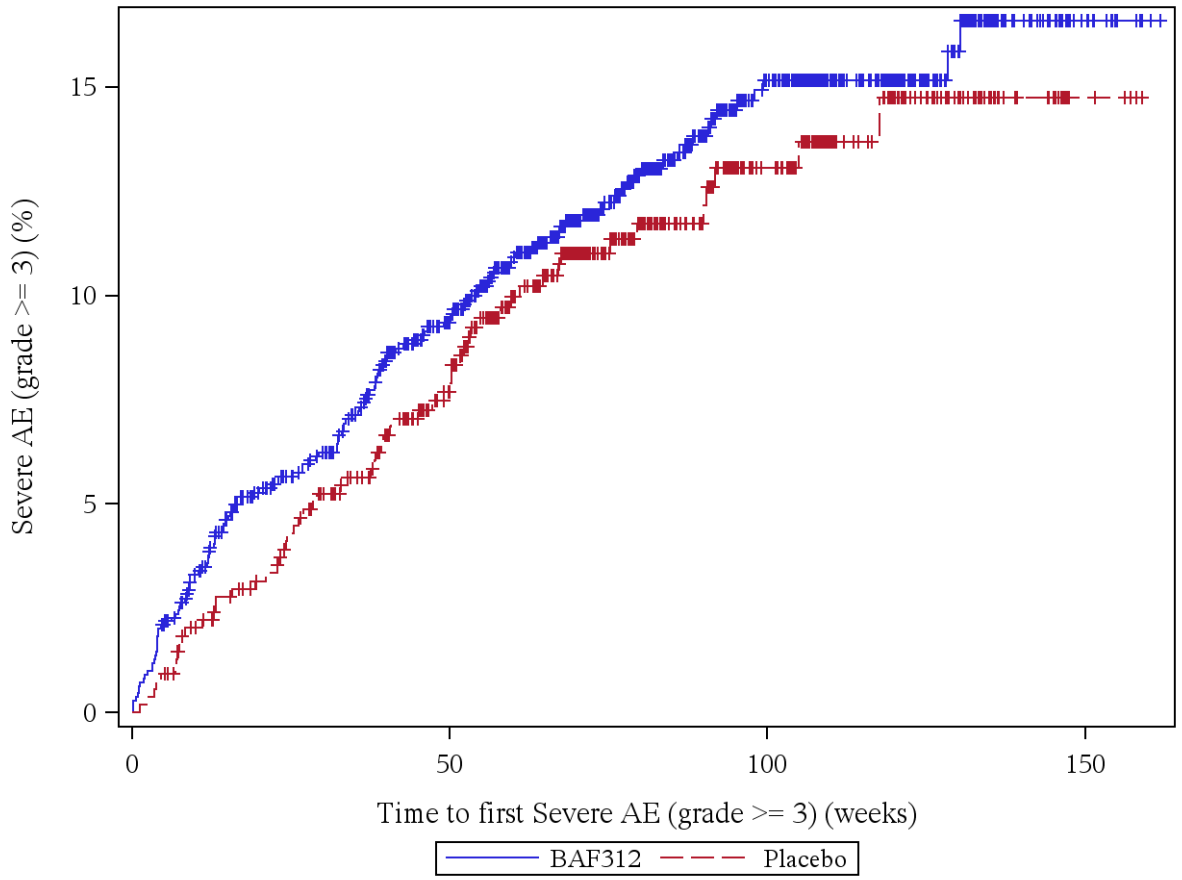


Patients at risk (BAF312/Placebo): Week 0: 1099/546, Week 4: 1098/546, Week 12: 1059/534, Week 24: 1013/519, Week 36: 982/494, Week 48: 920/458, Week 60: 810/385, Week 72: 650/305, Week 84: 513/237, Week 96: 397/176, Week 108: 288/125, Week 120: 198/80, Week 132: 111/40, Week 144: 51/20, Week 156: 10/5, Week 168: 0/0

Log rank test: p-value = 0,258
*: p < 0,05

Analysis population: A2304 SAF total population

Figure 12.1.2.5: Severe (Grade ≥ 3)

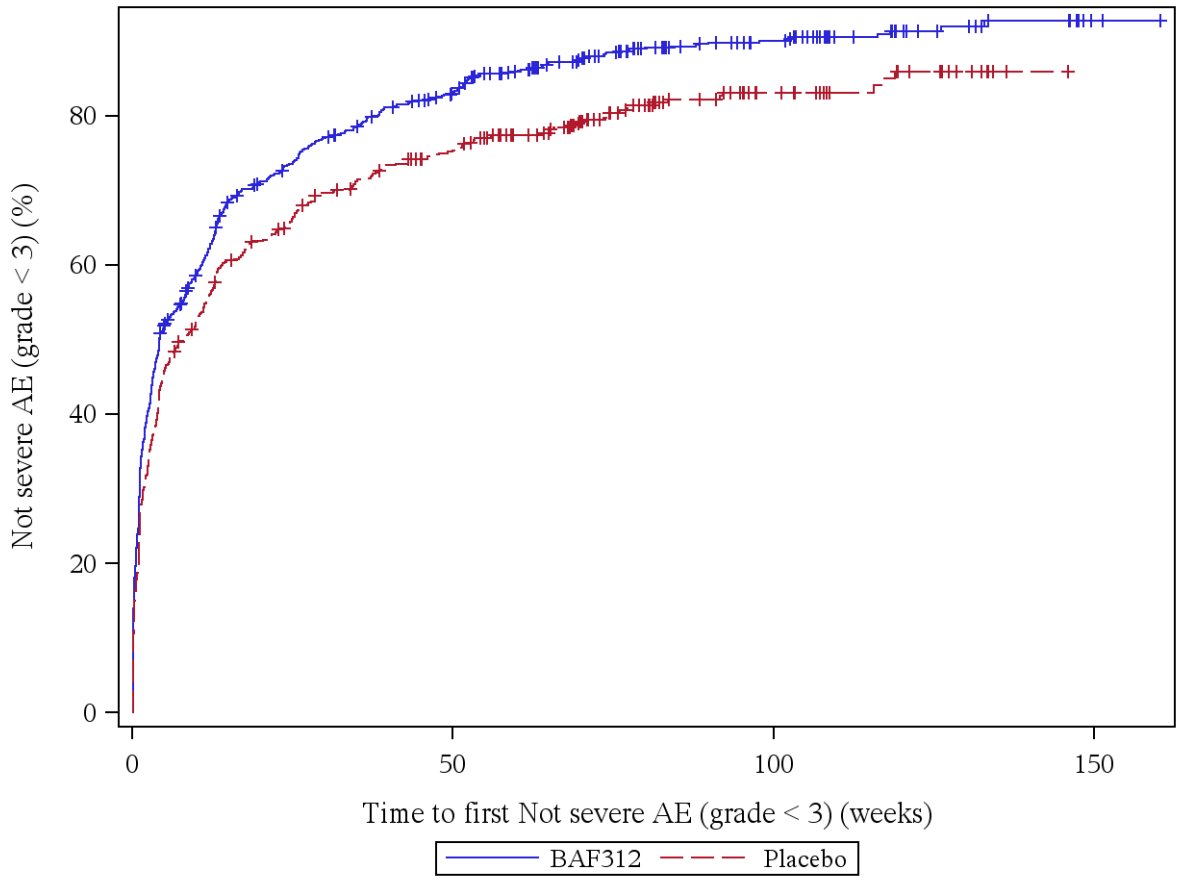


Patients at risk (BAF312/Placebo): Week 0: 1099/546, Week 4: 1079/542, Week 12: 1028/525, Week 24: 974/504, Week 36: 934/476, Week 48: 863/433, Week 60: 753/361, Week 72: 594/281, Week 84: 462/216, Week 96: 356/161, Week 108: 258/112, Week 120: 179/70, Week 132: 99/35, Week 144: 45/17, Week 156: 8/4, Week 168: 0/0

Log rank test: p-value = 0,423
*: p < 0,05

Analysis population: A2304 SAF total population

Figure 12.1.2.6: Not severe (Grade < 3)



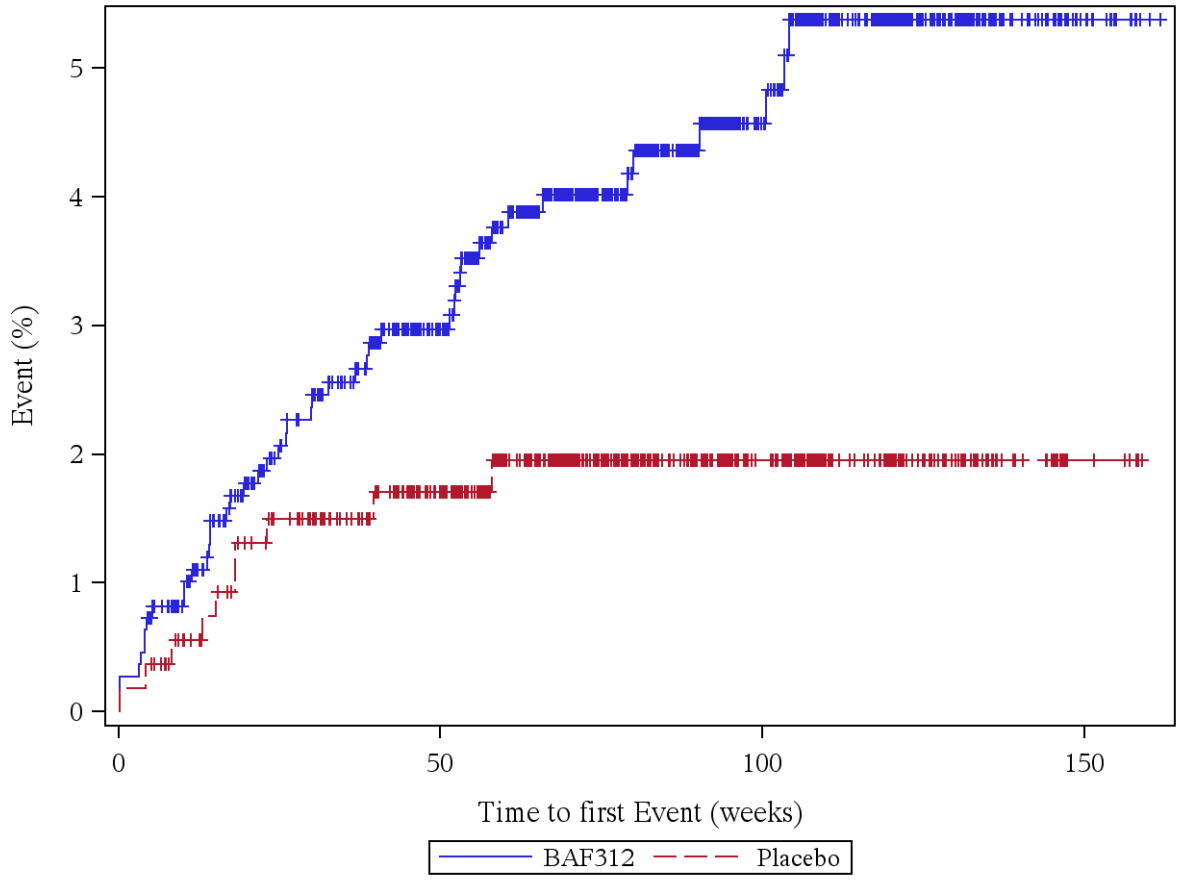
Patients at risk (BAF312/Placebo): Week 0: 1099/546, Week 4: 566/320, Week 12: 408/238, Week 24: 282/184, Week 36: 216/147, Week 48: 174/123, Week 60: 128/99, Week 72: 88/68, Week 84: 60/40, Week 96: 49/31, Week 108: 30/21, Week 120: 18/13, Week 132: 11/6, Week 144: 8/1, Week 156: 1/0, Week 168: 0/0

Log rank test: p-value = <0,001 *
*: p < 0,05

Analysis population: A2304 SAF total population

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

Figure 12.1.3.1: BLOOD AND LYMPHATIC SYSTEM DISORDERS (SOC)

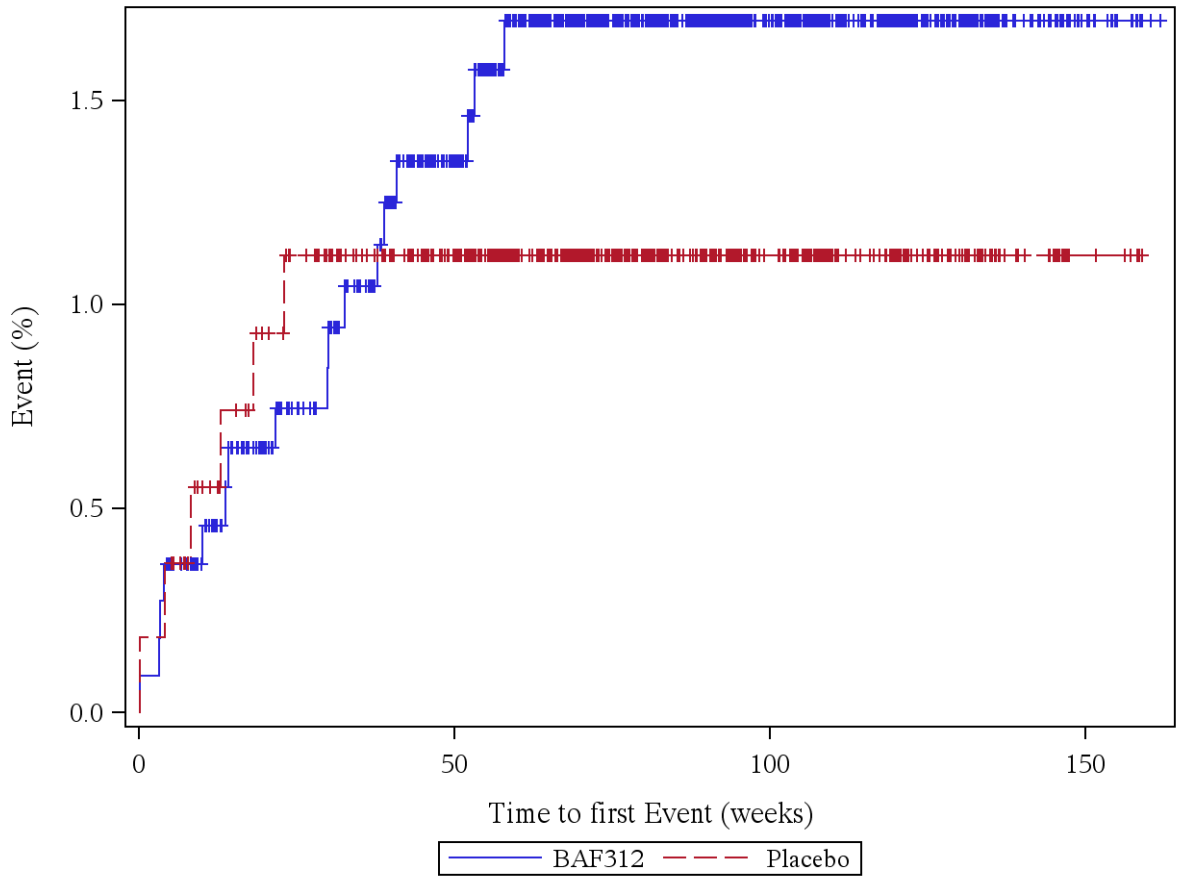


Patients at risk (BAF312/Placebo): Week 0: 1099/546, Week 4: 1092/545, Week 12: 1047/532, Week 24: 996/513, Week 36: 965/489, Week 48: 898/452, Week 60: 789/379, Week 72: 632/297, Week 84: 499/231, Week 96: 385/172, Week 108: 279/122, Week 120: 191/77, Week 132: 108/39, Week 144: 50/20, Week 156: 9/5, Week 168: 0/0

Log rank test: p-value = 0,015 *
*: p < 0,05

Analysis population: A2304 SAF total population

Figure 12.1.3.2: ANAEMIA (PT)

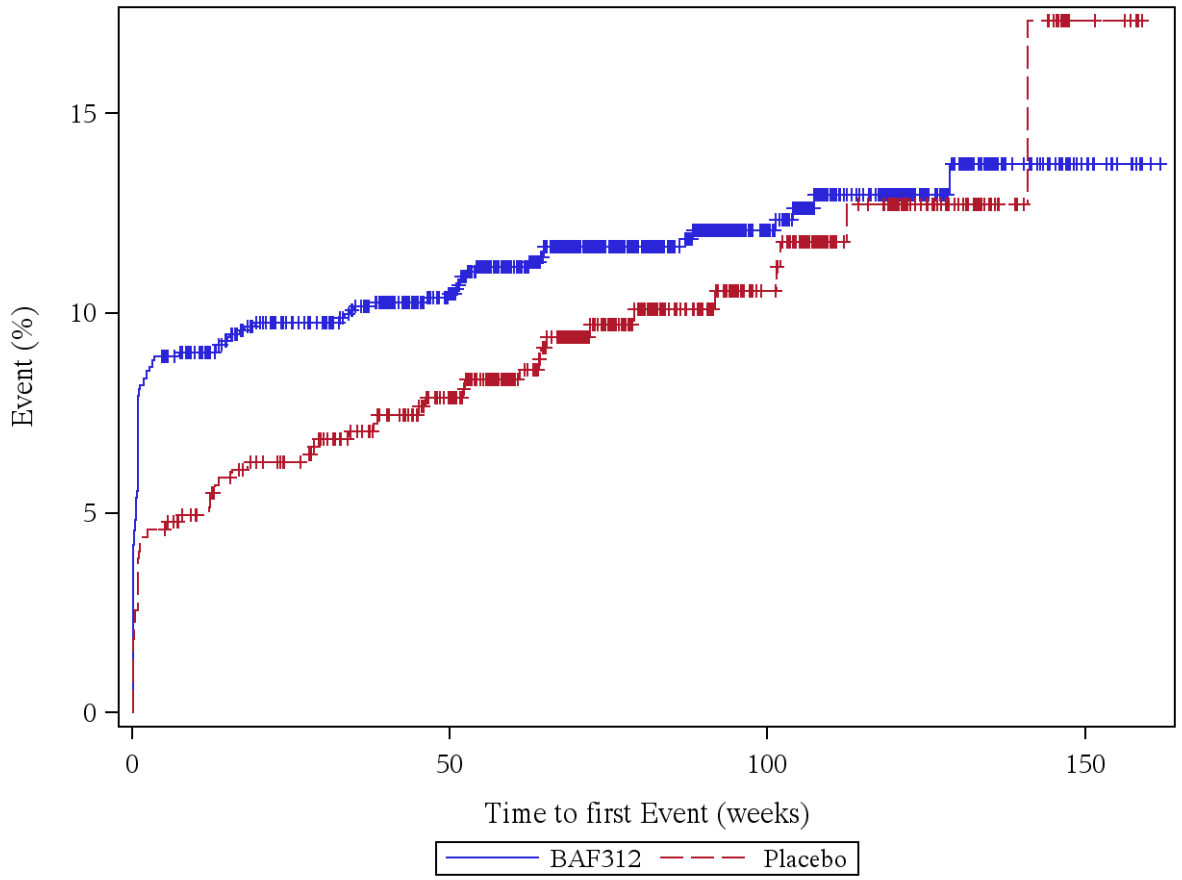


Patients at risk (BAF312/Placebo): Week 0: 1099/546, Week 4: 1095/545, Week 12: 1054/532, Week 24: 1009/515, Week 36: 980/491, Week 48: 913/455, Week 60: 806/382, Week 72: 643/299, Week 84: 509/233, Week 96: 395/174, Week 108: 288/124, Week 120: 198/79, Week 132: 113/40, Week 144: 51/20, Week 156: 10/5, Week 168: 0/0

Log rank test: p-value = 0,463
*: p < 0,05

Analysis population: A2304 SAF total population

Figure 12.1.3.3: CARDIAC DISORDERS (SOC)

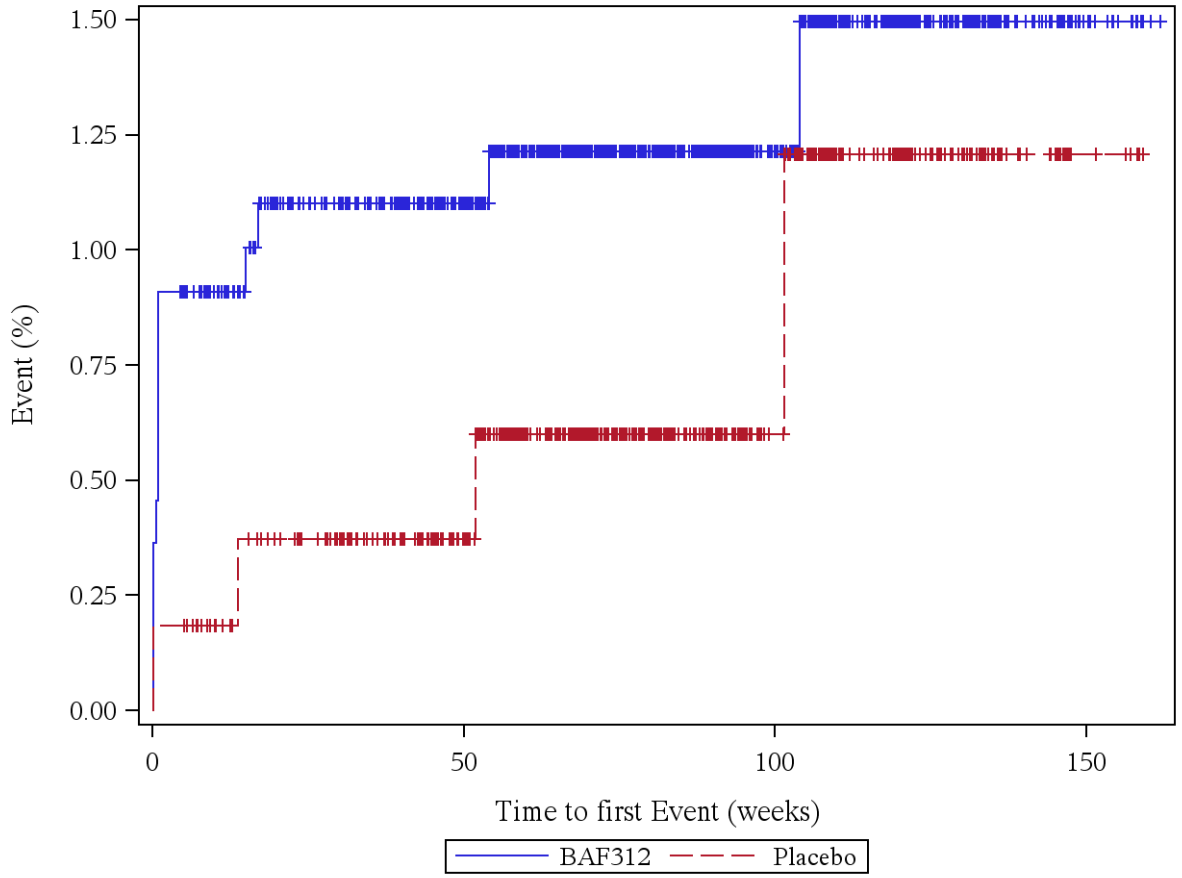


Patients at risk (BAF312/Placebo): Week 0: 1099/546, Week 4: 1001/521, Week 12: 970/510, Week 24: 927/489, Week 36: 897/463, Week 48: 833/426, Week 60: 730/356, Week 72: 574/280, Week 84: 449/214, Week 96: 345/159, Week 108: 250/112, Week 120: 169/75, Week 132: 93/37, Week 144: 43/18, Week 156: 9/5, Week 168: 0/0

Log rank test: p-value = 0,277
*: p < 0,05

Analysis population: A2304 SAF total population

Figure 12.1.3.4: ATRIOVENTRICULAR BLOCK FIRST DEGREE (PT)

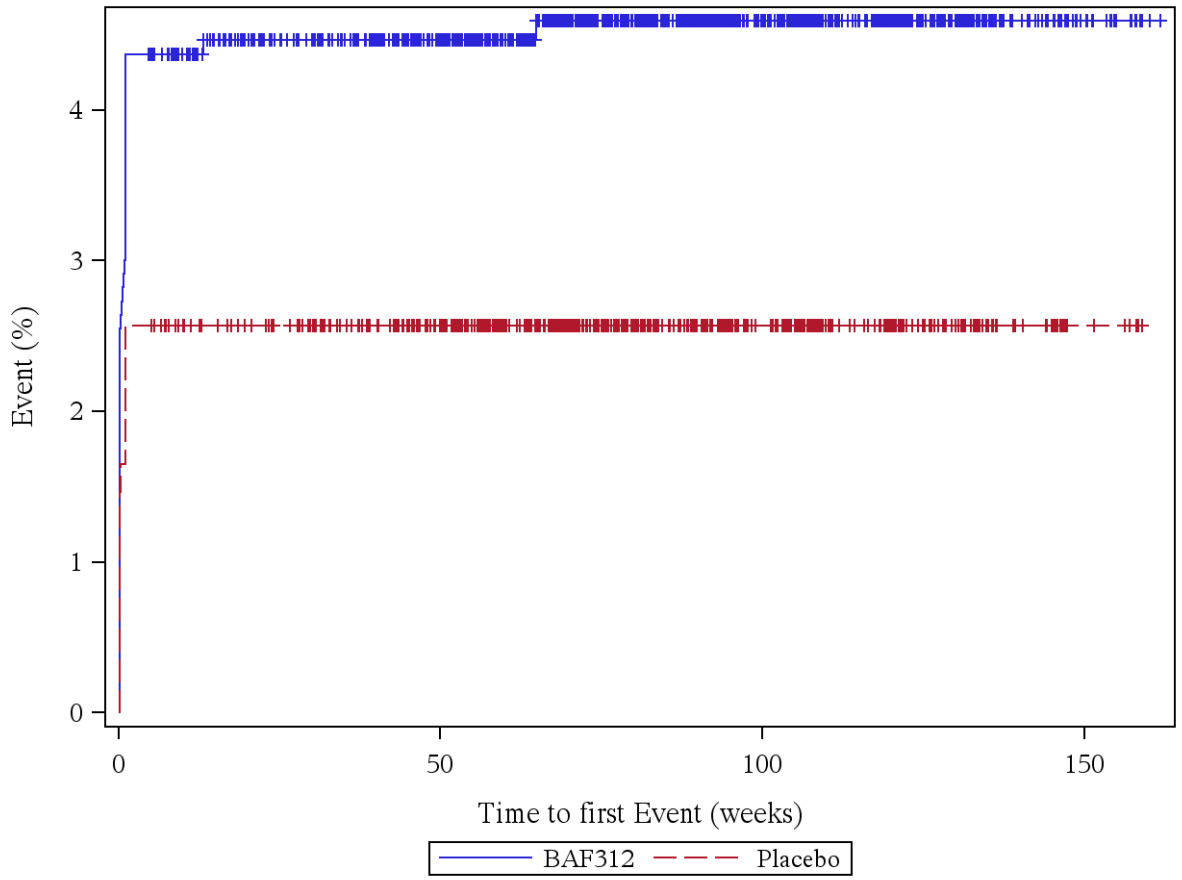


Patients at risk (BAF312/Placebo): Week 0: 1099/546, Week 4: 1089/545, Week 12: 1050/534, Week 24: 1007/519, Week 36: 980/495, Week 48: 915/459, Week 60: 807/387, Week 72: 641/304, Week 84: 505/236, Week 96: 390/176, Week 108: 283/125, Week 120: 194/80, Week 132: 111/40, Week 144: 50/20, Week 156: 10/5, Week 168: 0/0

Log rank test: p-value = 0,333
*: p < 0,05

Analysis population: A2304 SAF total population

Figure 12.1.3.5: BRADYCARDIA (PT)

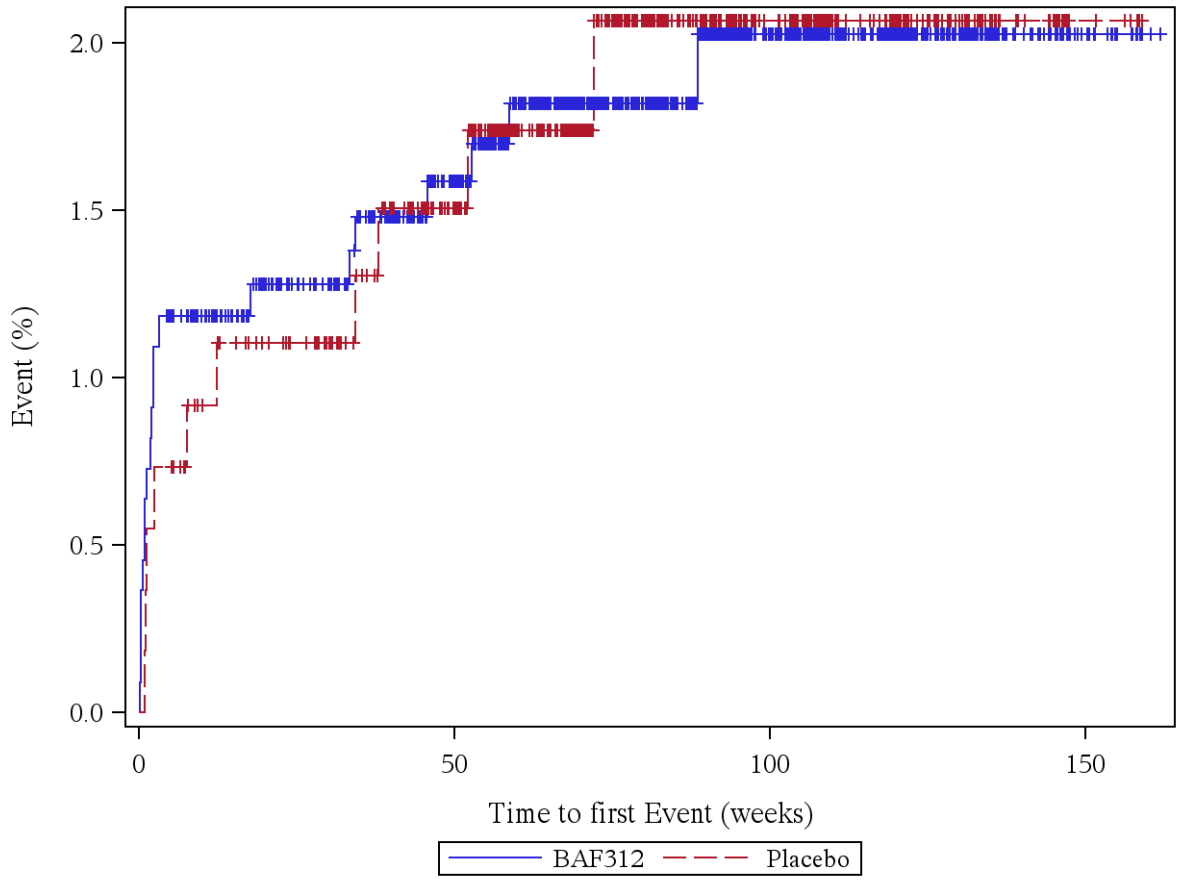


Patients at risk (BAF312/Placebo): Week 0: 1099/546, Week 4: 1051/532, Week 12: 1015/521, Week 24: 973/507, Week 36: 947/483, Week 48: 883/449, Week 60: 780/378, Week 72: 619/298, Week 84: 487/232, Week 96: 375/172, Week 108: 275/122, Week 120: 192/79, Week 132: 106/39, Week 144: 48/20, Week 156: 10/5, Week 168: 0/0

Log rank test: p-value = 0,050
*: p < 0,05

Analysis population: A2304 SAF total population

Figure 12.1.3.6: PALPITATIONS (PT)

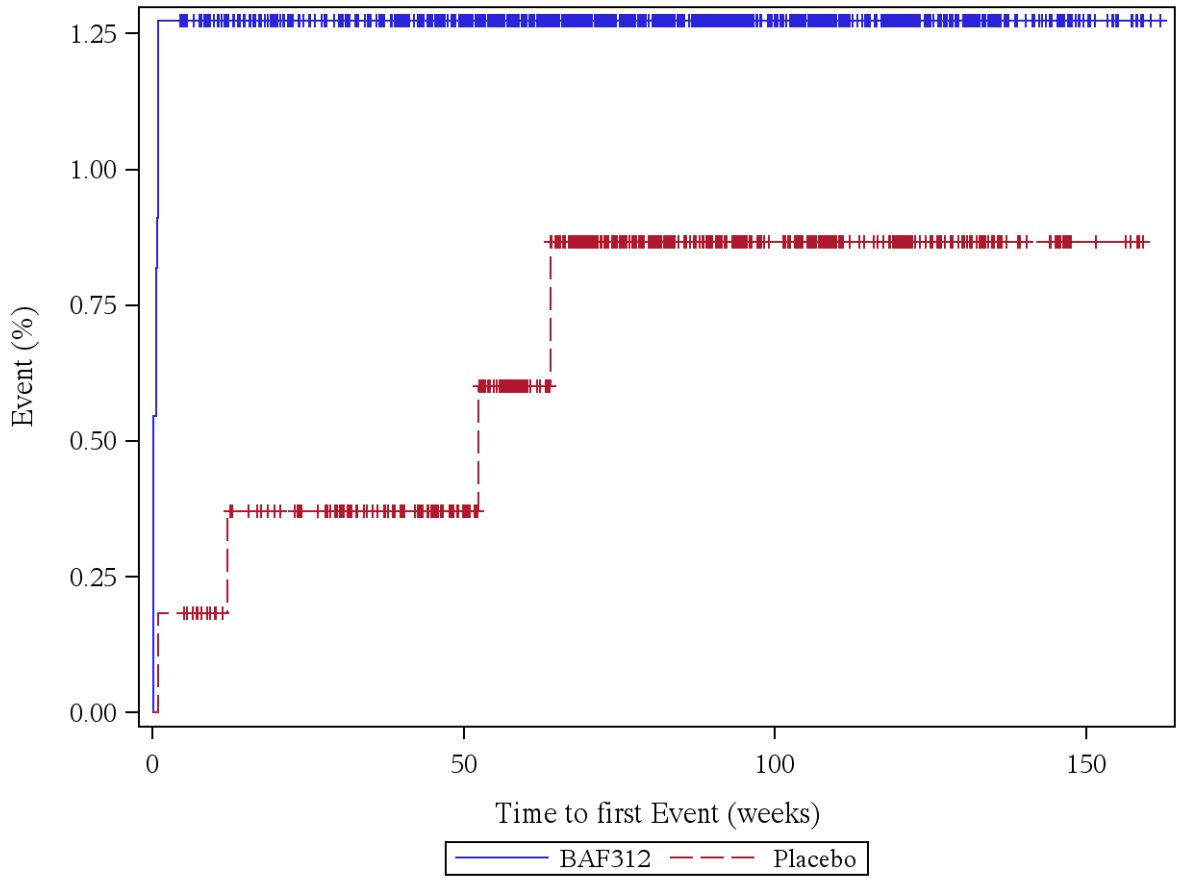


Patients at risk (BAF312/Placebo): Week 0: 1099/546, Week 4: 1086/542, Week 12: 1047/531, Week 24: 1004/516, Week 36: 975/491, Week 48: 909/454, Week 60: 804/381, Week 72: 642/299, Week 84: 510/231, Week 96: 396/171, Week 108: 287/123, Week 120: 196/79, Week 132: 112/39, Week 144: 50/20, Week 156: 10/5, Week 168: 0/0

Log rank test: p-value = 0,982
*: p < 0,05

Analysis population: A2304 SAF total population

Figure 12.1.3.7: SINUS BRADYCARDIA (PT)

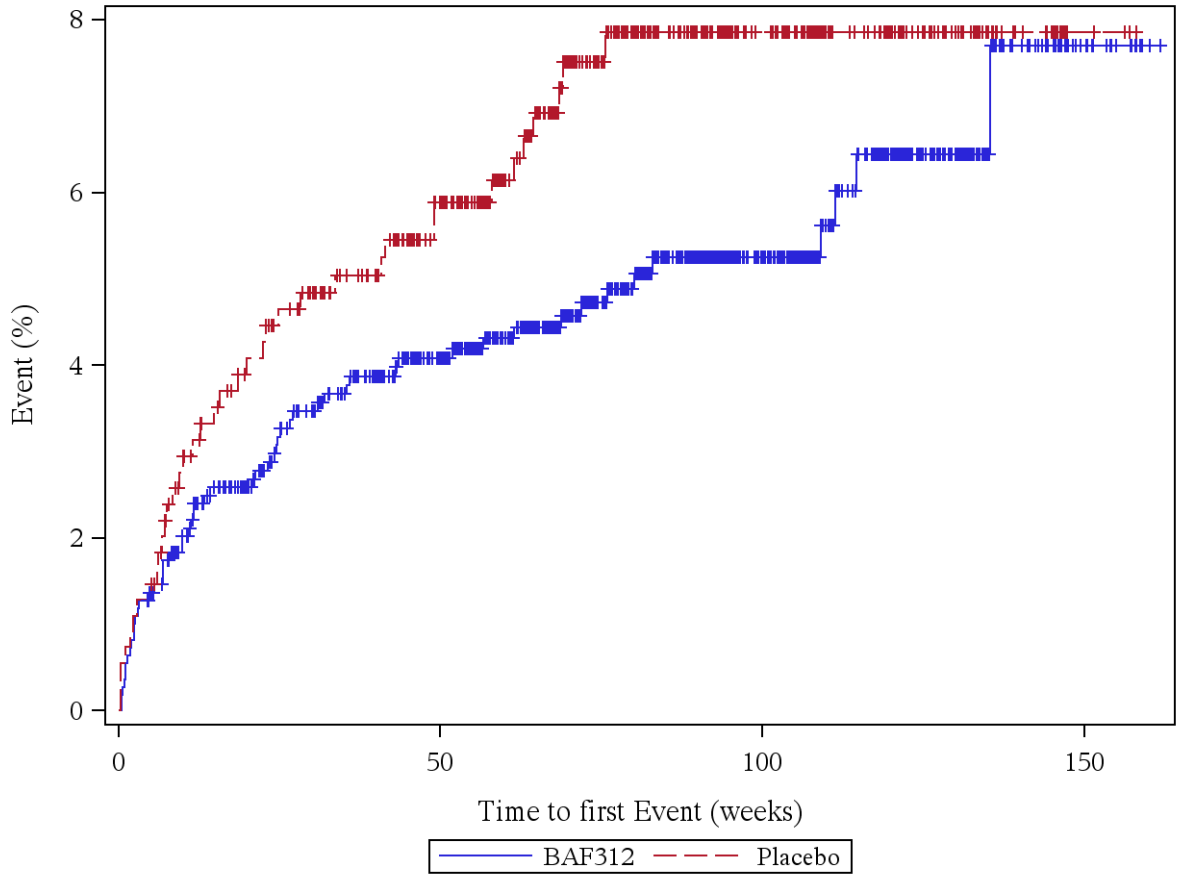


Patients at risk (BAF312/Placebo): Week 0: 1099/546, Week 4: 1085/545, Week 12: 1047/533, Week 24: 1006/519, Week 36: 979/495, Week 48: 914/459, Week 60: 808/385, Week 72: 642/303, Week 84: 508/235, Week 96: 394/175, Week 108: 286/125, Week 120: 195/80, Week 132: 111/40, Week 144: 51/20, Week 156: 10/5, Week 168: 0/0

Log rank test: p-value = 0,321
*: p < 0,05

Analysis population: A2304 SAF total population

Figure 12.1.3.8: EAR AND LABYRINTH DISORDERS (SOC)

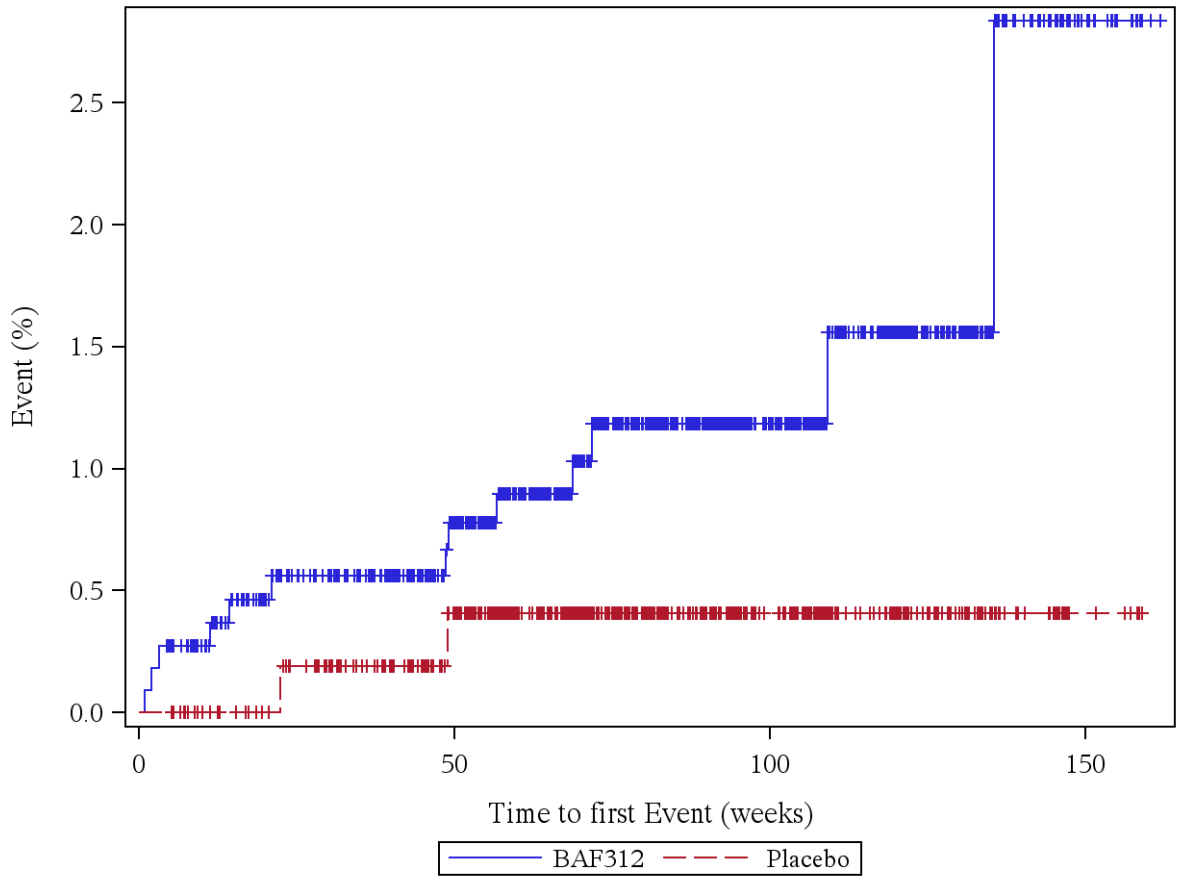


Patients at risk (BAF312/Placebo): Week 0: 1099/546, Week 4: 1085/539, Week 12: 1033/518, Week 24: 987/498, Week 36: 951/471, Week 48: 886/437, Week 60: 784/364, Week 72: 621/281, Week 84: 490/216, Week 96: 382/158, Week 108: 278/114, Week 120: 188/71, Week 132: 107/37, Week 144: 48/17, Week 156: 10/3, Week 168: 0/0

Log rank test: p-value = 0,095
*: p < 0,05

Analysis population: A2304 SAF total population

Figure 12.1.3.9: TINNITUS (PT)

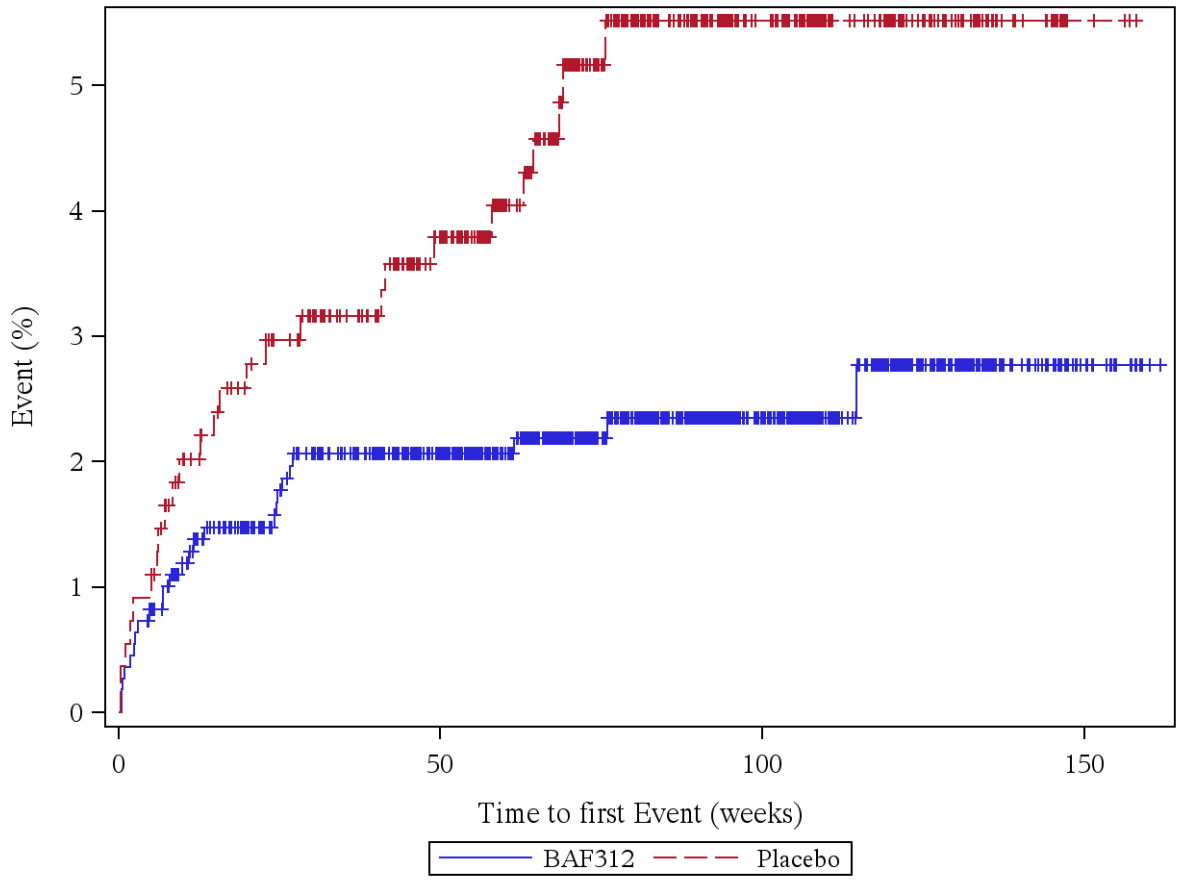


Patients at risk (BAF312/Placebo): Week 0: 1099/546, Week 4: 1096/546, Week 12: 1055/535, Week 24: 1011/520, Week 36: 984/496, Week 48: 920/460, Week 60: 811/386, Week 72: 643/304, Week 84: 509/236, Week 96: 396/175, Week 108: 288/126, Week 120: 197/80, Week 132: 113/40, Week 144: 51/20, Week 156: 10/5, Week 168: 0/0

Log rank test: p-value = 0,113
*: p < 0,05

Analysis population: A2304 SAF total population

Figure 12.1.3.10: VERTIGO (PT)

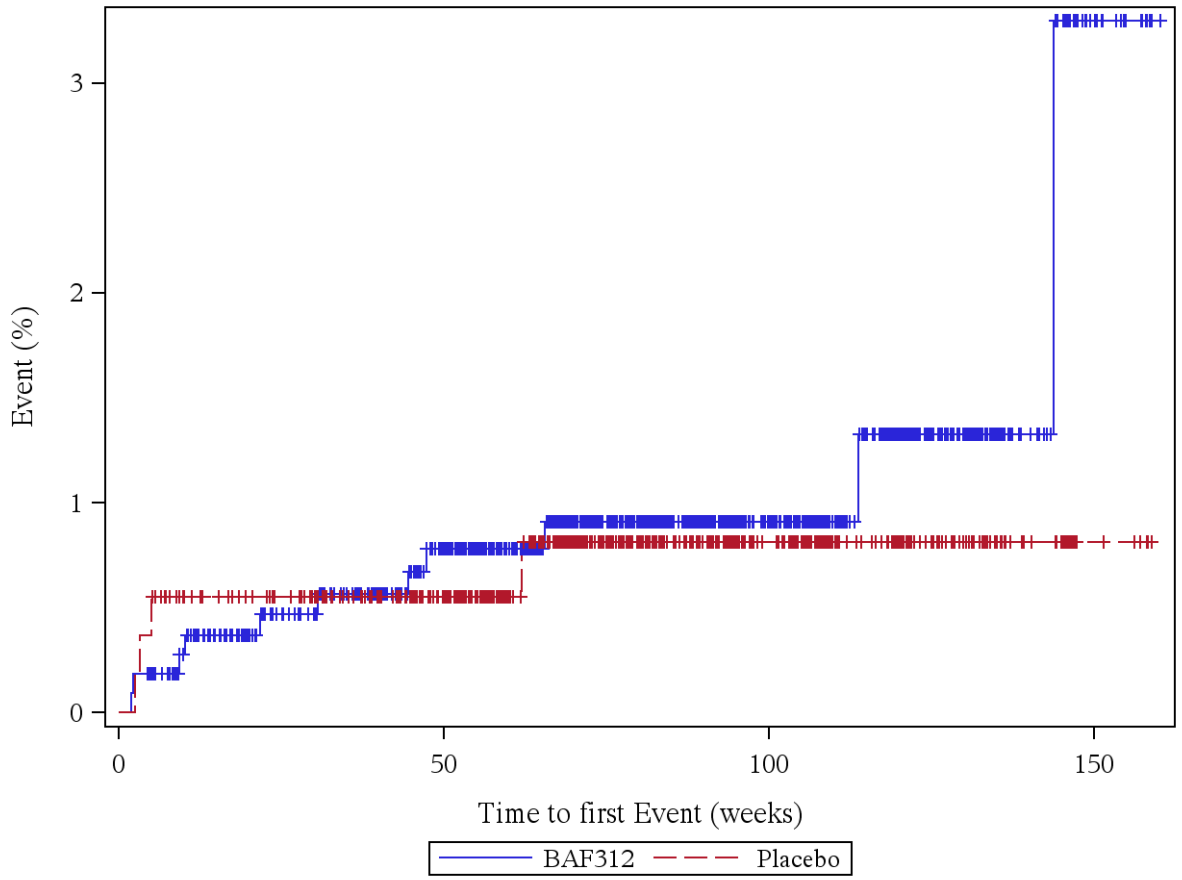


Patients at risk (BAF312/Placebo): Week 0: 1099/546, Week 4: 1091/541, Week 12: 1044/524, Week 24: 1002/505, Week 36: 970/480, Week 48: 906/445, Week 60: 801/371, Week 72: 636/286, Week 84: 504/220, Week 96: 393/161, Week 108: 287/116, Week 120: 196/72, Week 132: 111/37, Week 144: 51/17, Week 156: 10/3, Week 168: 0/0

Log rank test: p-value = 0,006 *
*: p < 0,05

Analysis population: A2304 SAF total population

Figure 12.1.3.11: ENDOCRINE DISORDERS (SOC)

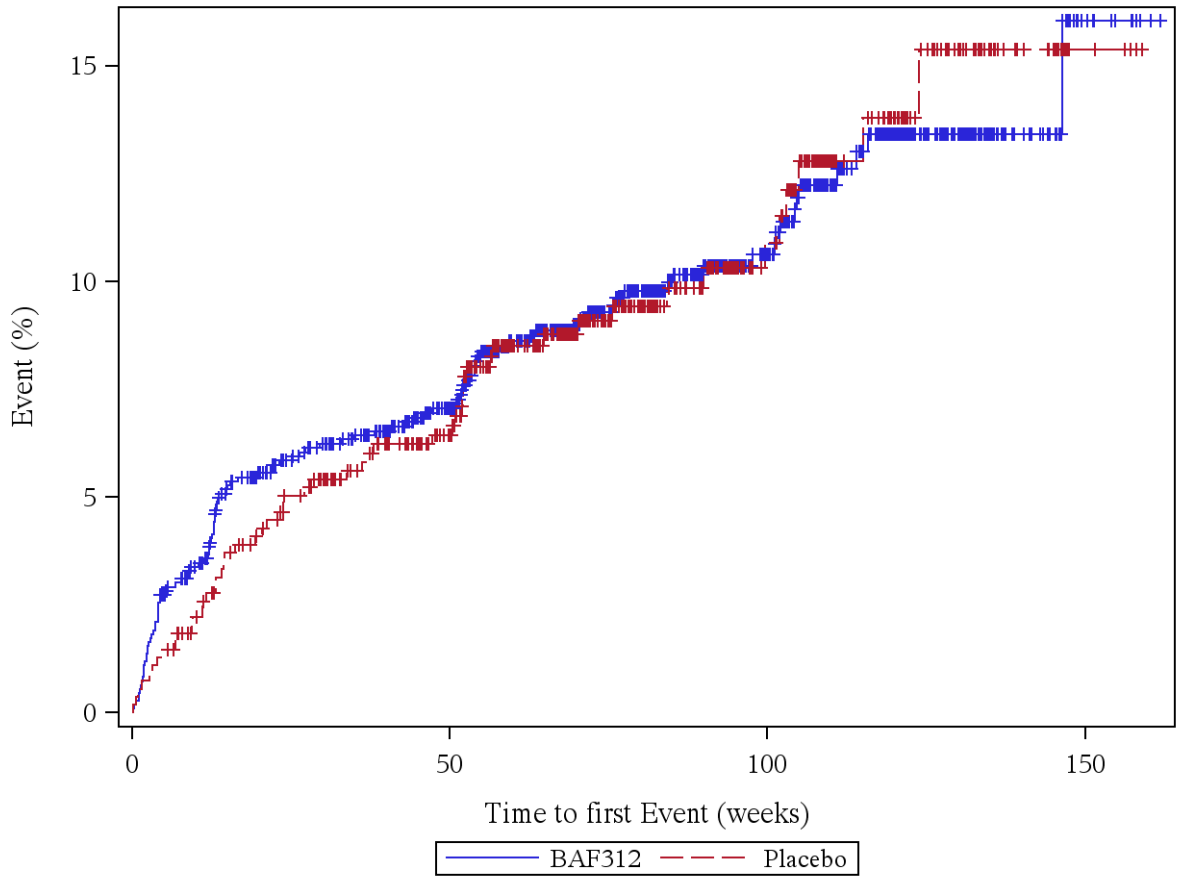


Patients at risk (BAF312/Placebo): Week 0: 1099/546, Week 4: 1097/544, Week 12: 1056/532, Week 24: 1013/518, Week 36: 985/494, Week 48: 918/458, Week 60: 811/385, Week 72: 645/301, Week 84: 510/234, Week 96: 397/174, Week 108: 289/125, Week 120: 197/79, Week 132: 111/40, Week 144: 49/20, Week 156: 9/5, Week 168: 0/0

Log rank test: p-value = 0,625
*: p < 0,05

Analysis population: A2304 SAF total population

Figure 12.1.3.12: EYE DISORDERS (SOC)

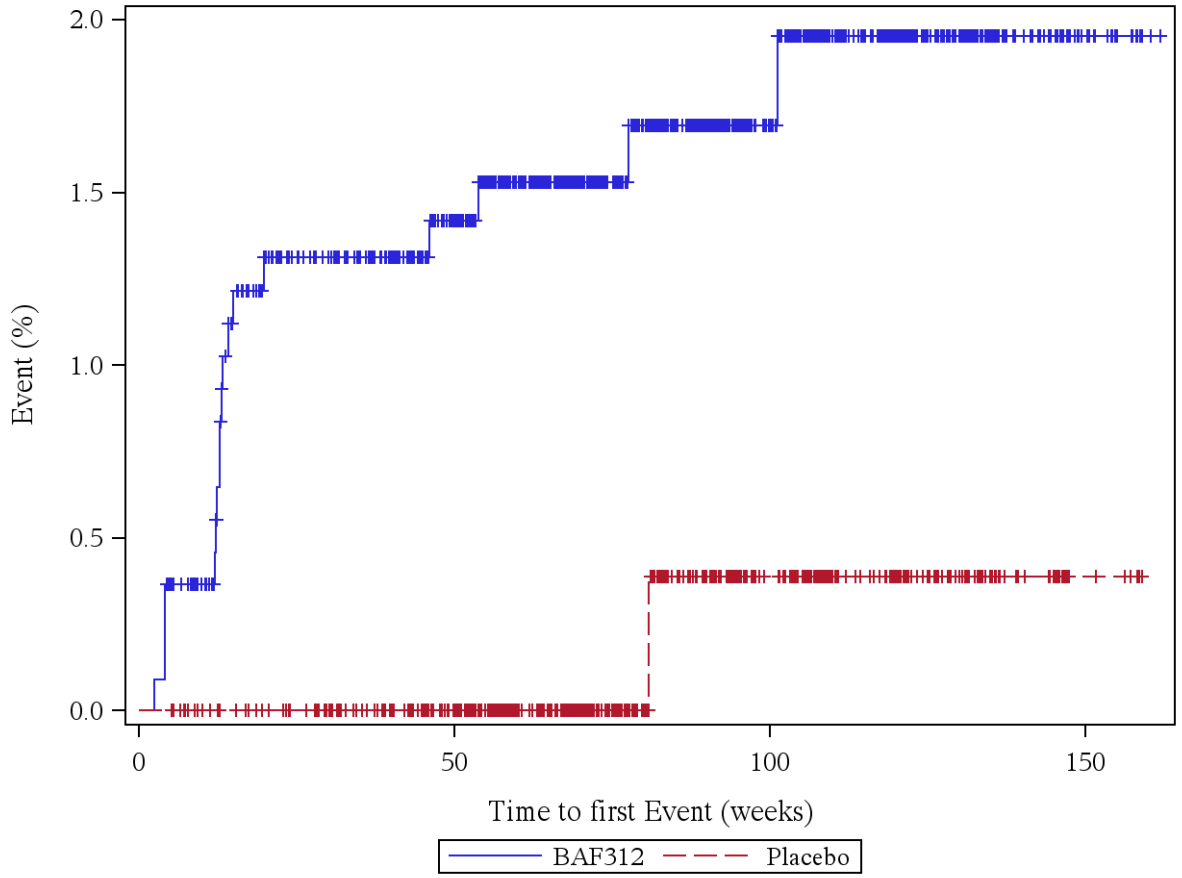


Patients at risk (BAF312/Placebo): Week 0: 1099/546, Week 4: 1076/539, Week 12: 1024/522, Week 24: 970/496, Week 36: 940/469, Week 48: 873/436, Week 60: 762/357, Week 72: 602/277, Week 84: 473/215, Week 96: 370/159, Week 108: 265/110, Week 120: 175/69, Week 132: 99/34, Week 144: 44/16, Week 156: 8/4, Week 168: 0/0

Log rank test: p-value = 0,993
*: p < 0,05

Analysis population: A2304 SAF total population

Figure 12.1.3.13: MACULAR OEDEMA (PT)

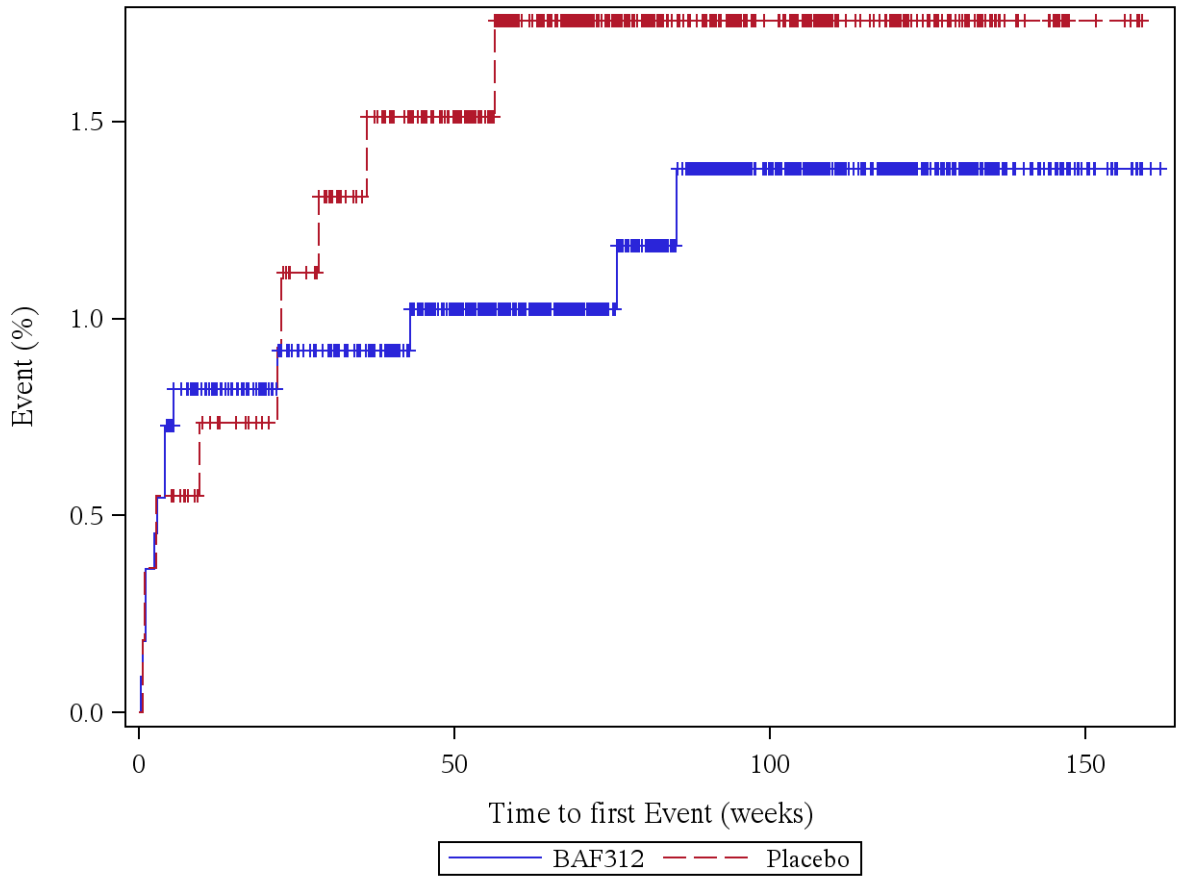


Patients at risk (BAF312/Placebo): Week 0: 1099/546, Week 4: 1098/546, Week 12: 1057/535, Week 24: 1012/521, Week 36: 986/497, Week 48: 921/461, Week 60: 815/388, Week 72: 650/305, Week 84: 514/236, Week 96: 400/176, Week 108: 291/126, Week 120: 200/80, Week 132: 113/40, Week 144: 51/20, Week 156: 10/5, Week 168: 0/0

Log rank test: p-value = 0,010 *
*: p < 0,05

Analysis population: A2304 SAF total population

Figure 12.1.3.14: VISION BLURRED (PT)

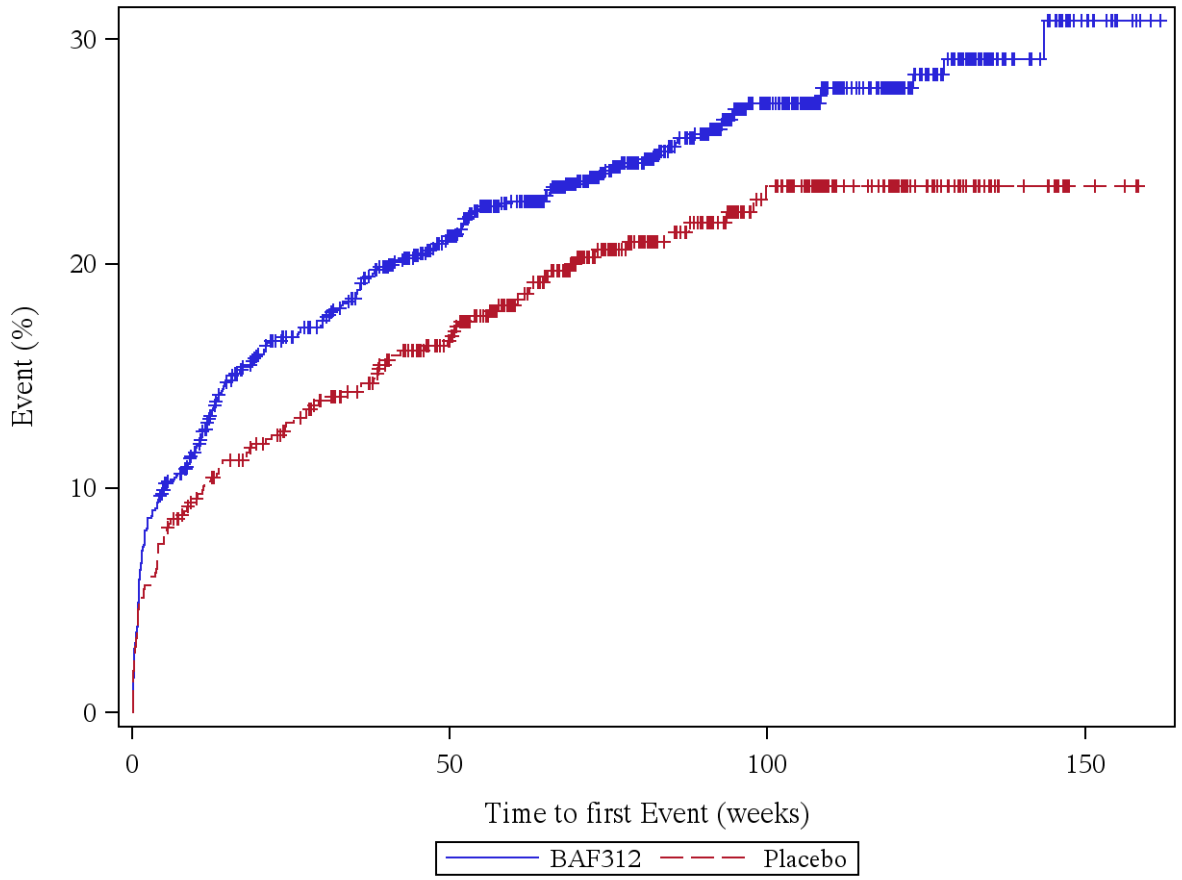


Patients at risk (BAF312/Placebo): Week 0: 1099/546, Week 4: 1093/543, Week 12: 1050/531, Week 24: 1007/515, Week 36: 980/490, Week 48: 915/454, Week 60: 809/381, Week 72: 645/298, Week 84: 510/233, Week 96: 394/175, Week 108: 288/126, Week 120: 197/80, Week 132: 112/40, Week 144: 51/20, Week 156: 10/5, Week 168: 0/0

Log rank test: p-value = 0,441
*: p < 0,05

Analysis population: A2304 SAF total population

Figure 12.1.3.15: GASTROINTESTINAL DISORDERS (SOC)

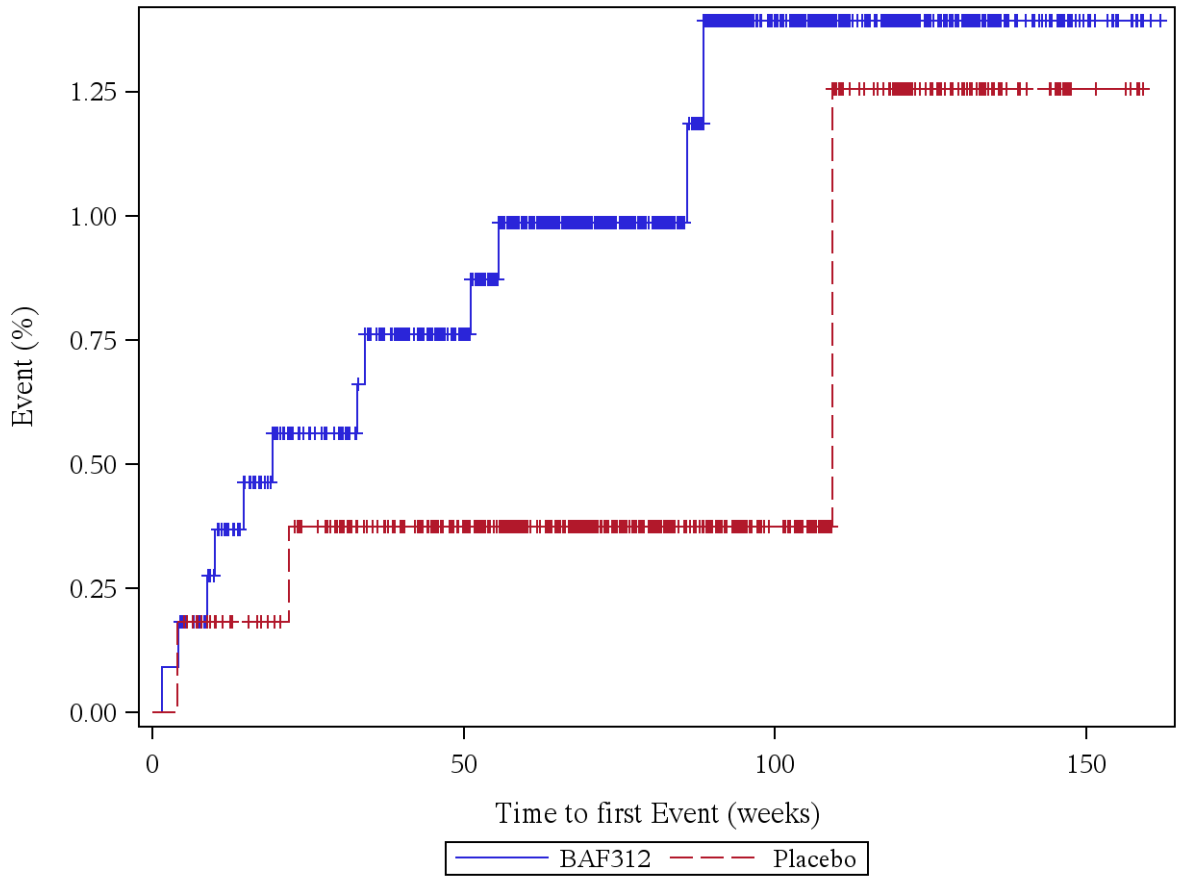


Patients at risk (BAF312/Placebo): Week 0: 1099/546, Week 4: 996/507, Week 12: 921/482, Week 24: 847/456, Week 36: 803/427, Week 48: 737/389, Week 60: 646/324, Week 72: 508/246, Week 84: 394/190, Week 96: 307/143, Week 108: 223/101, Week 120: 151/63, Week 132: 82/27, Week 144: 40/15, Week 156: 6/3, Week 168: 0/0

Log rank test: p-value = 0,051
*: p < 0,05

Analysis population: A2304 SAF total population

Figure 12.1.3.16: ABDOMINAL PAIN (PT)

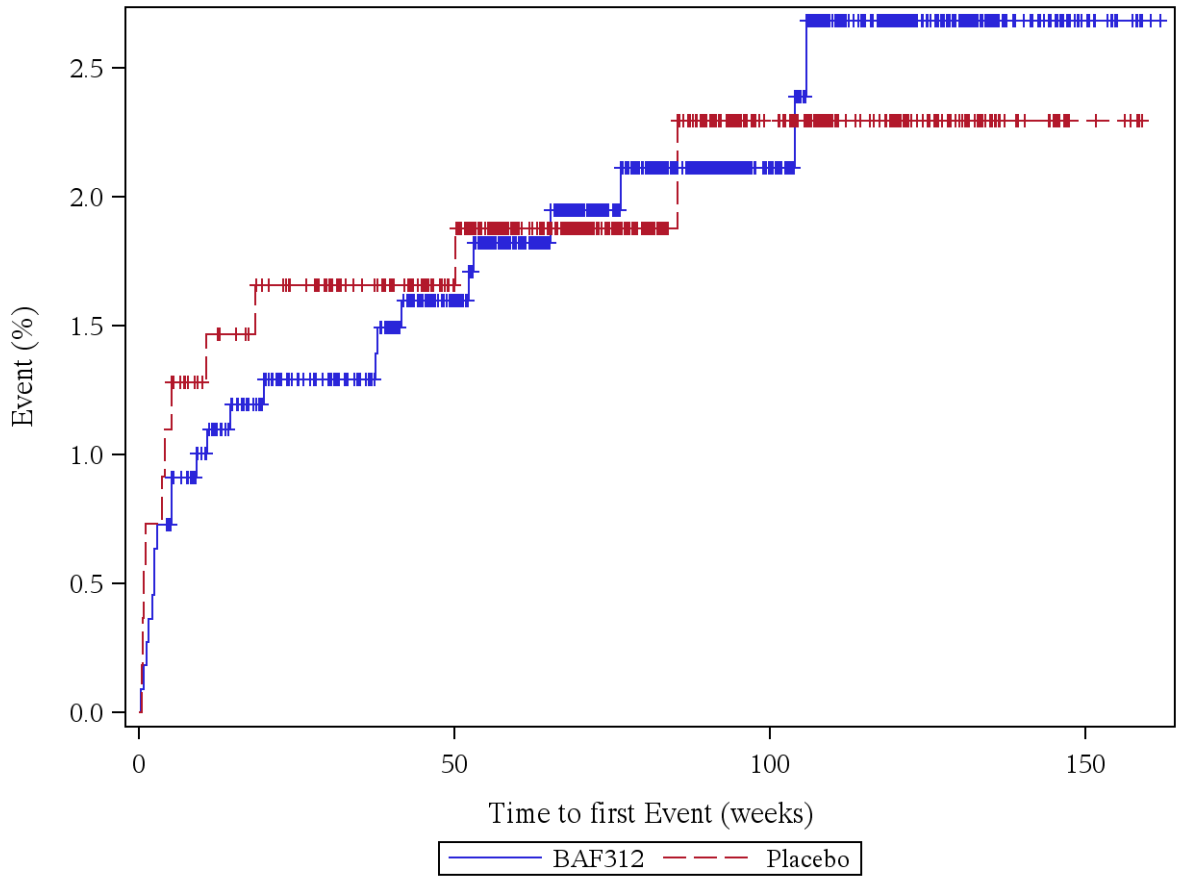


Patients at risk (BAF312/Placebo): Week 0: 1099/546, Week 4: 1098/545, Week 12: 1055/534, Week 24: 1011/519, Week 36: 982/495, Week 48: 918/459, Week 60: 809/387, Week 72: 644/304, Week 84: 509/236, Week 96: 392/175, Week 108: 285/125, Week 120: 195/79, Week 132: 110/39, Week 144: 50/20, Week 156: 10/5, Week 168: 0/0

Log rank test: p-value = 0,286
*: p < 0,05

Analysis population: A2304 SAF total population

Figure 12.1.3.17: ABDOMINAL PAIN UPPER (PT)

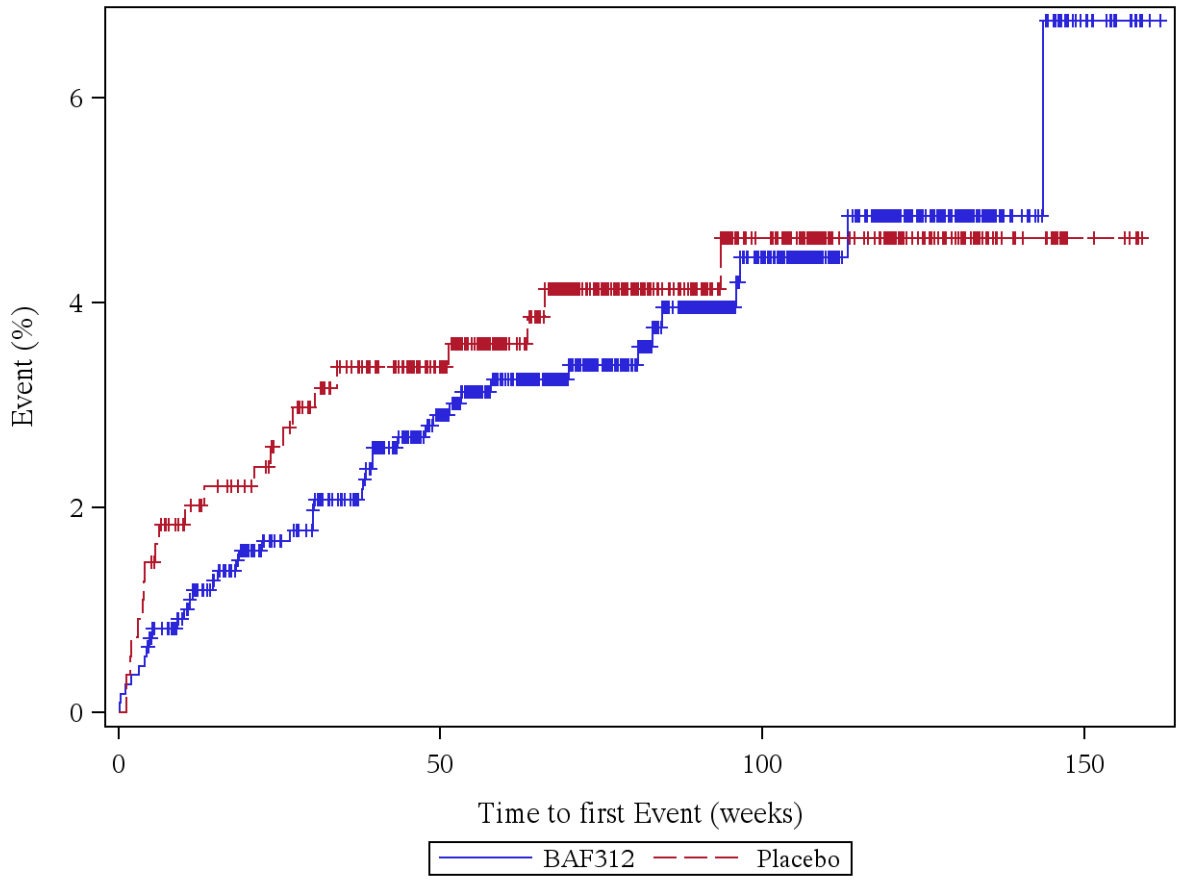


Patients at risk (BAF312/Placebo): Week 0: 1099/546, Week 4: 1091/541, Week 12: 1047/528, Week 24: 1003/513, Week 36: 976/490, Week 48: 911/455, Week 60: 804/382, Week 72: 643/301, Week 84: 508/235, Week 96: 395/174, Week 108: 285/125, Week 120: 194/79, Week 132: 110/39, Week 144: 49/19, Week 156: 9/5, Week 168: 0/0

Log rank test: p-value = 0,940
*: p < 0,05

Analysis population: A2304 SAF total population

Figure 12.1.3.18: CONSTIPATION (PT)

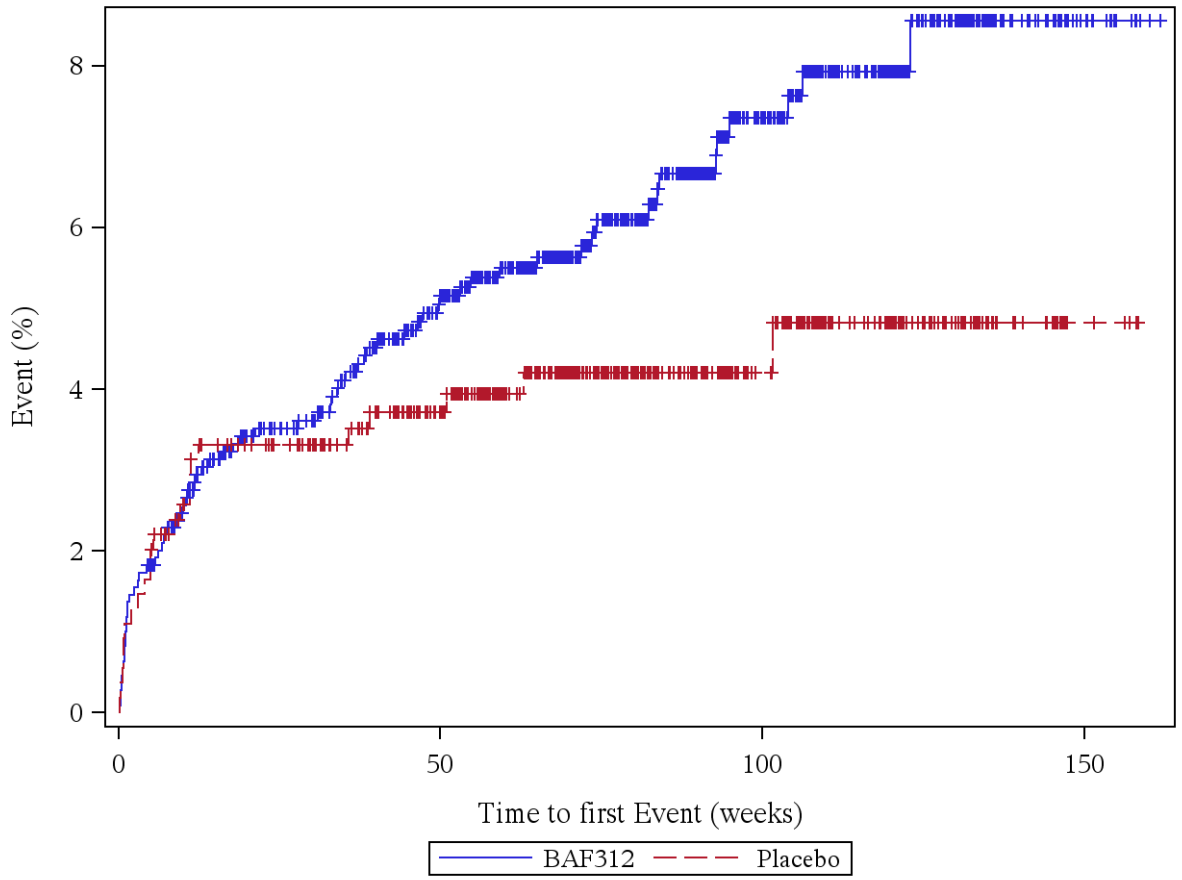


Patients at risk (BAF312/Placebo): Week 0: 1099/546, Week 4: 1093/538, Week 12: 1046/524, Week 24: 999/507, Week 36: 969/483, Week 48: 899/449, Week 60: 792/376, Week 72: 631/295, Week 84: 500/229, Week 96: 389/170, Week 108: 284/125, Week 120: 195/79, Week 132: 110/39, Week 144: 49/20, Week 156: 10/5, Week 168: 0/0

Log rank test: p-value = 0,728
*: p < 0,05

Analysis population: A2304 SAF total population

Figure 12.1.3.19: DIARRHOEA (PT)

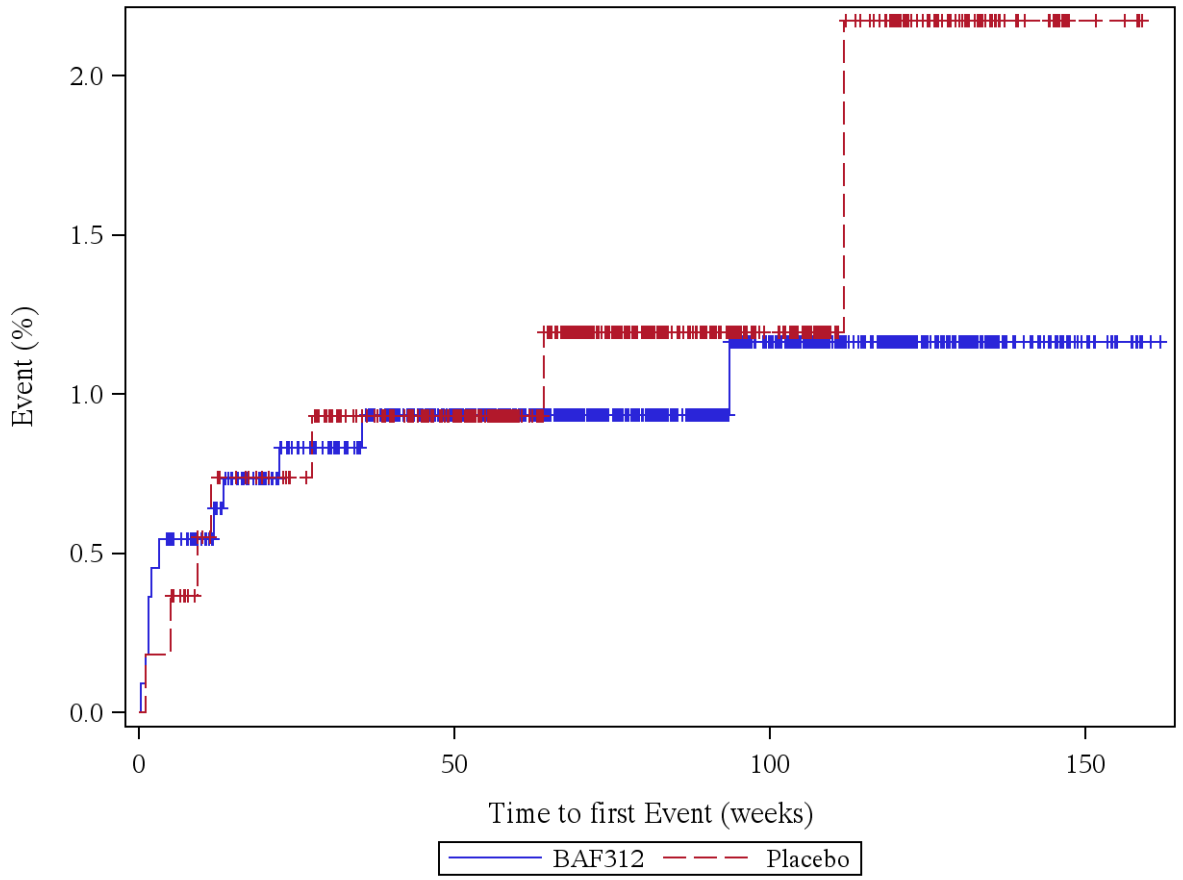


Patients at risk (BAF312/Placebo): Week 0: 1099/546, Week 4: 1080/537, Week 12: 1029/518, Week 24: 985/503, Week 36: 953/480, Week 48: 885/446, Week 60: 778/374, Week 72: 619/292, Week 84: 481/225, Week 96: 374/169, Week 108: 275/121, Week 120: 186/77, Week 132: 106/37, Week 144: 48/18, Week 156: 8/4, Week 168: 0/0

Log rank test: p-value = 0,088
*: p < 0,05

Analysis population: A2304 SAF total population

Figure 12.1.3.20: DYSPEPSIA (PT)

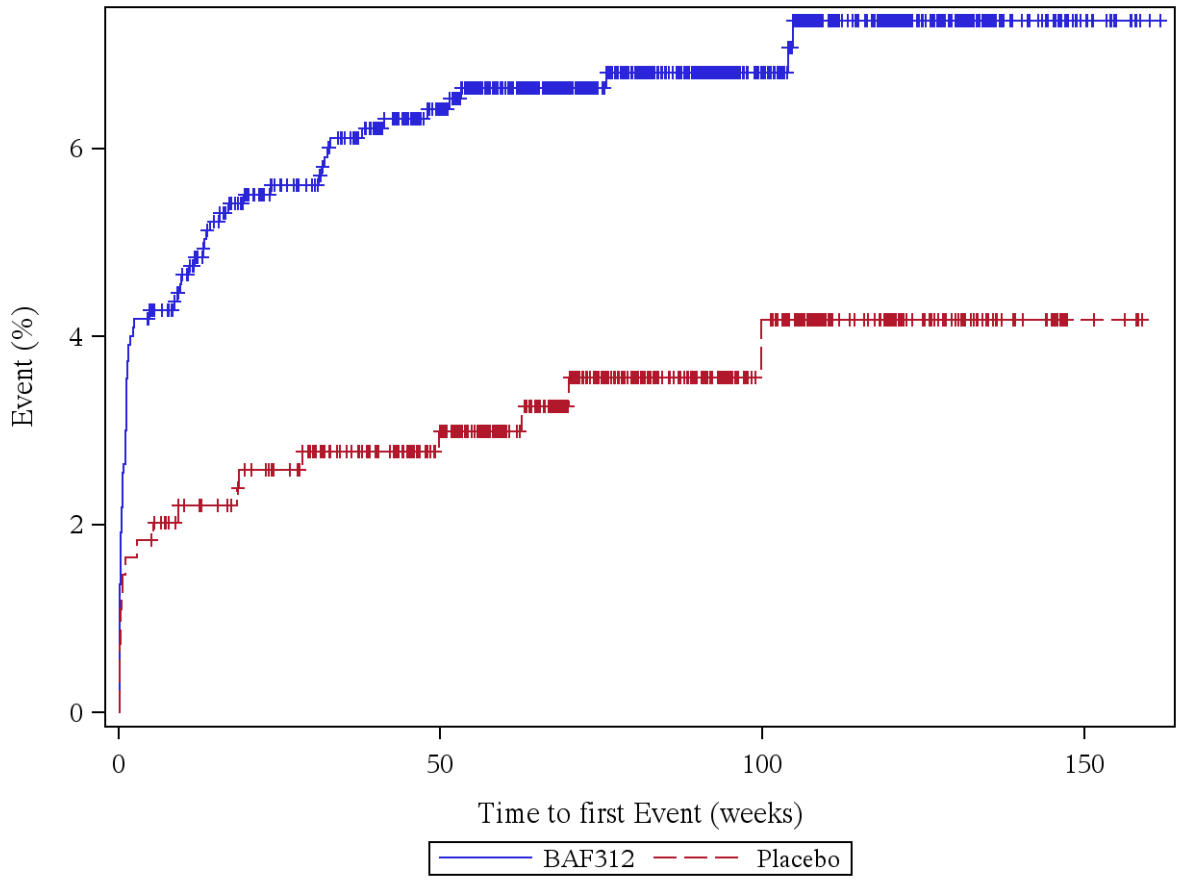


Patients at risk (BAF312/Placebo): Week 0: 1099/546, Week 4: 1093/545, Week 12: 1052/531, Week 24: 1008/517, Week 36: 980/492, Week 48: 916/457, Week 60: 809/386, Week 72: 643/302, Week 84: 511/235, Week 96: 394/174, Week 108: 287/125, Week 120: 197/79, Week 132: 112/39, Week 144: 50/19, Week 156: 10/4, Week 168: 0/0

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

Analysis population: A2304 SAF total population

Figure 12.1.3.21: NAUSEA (PT)

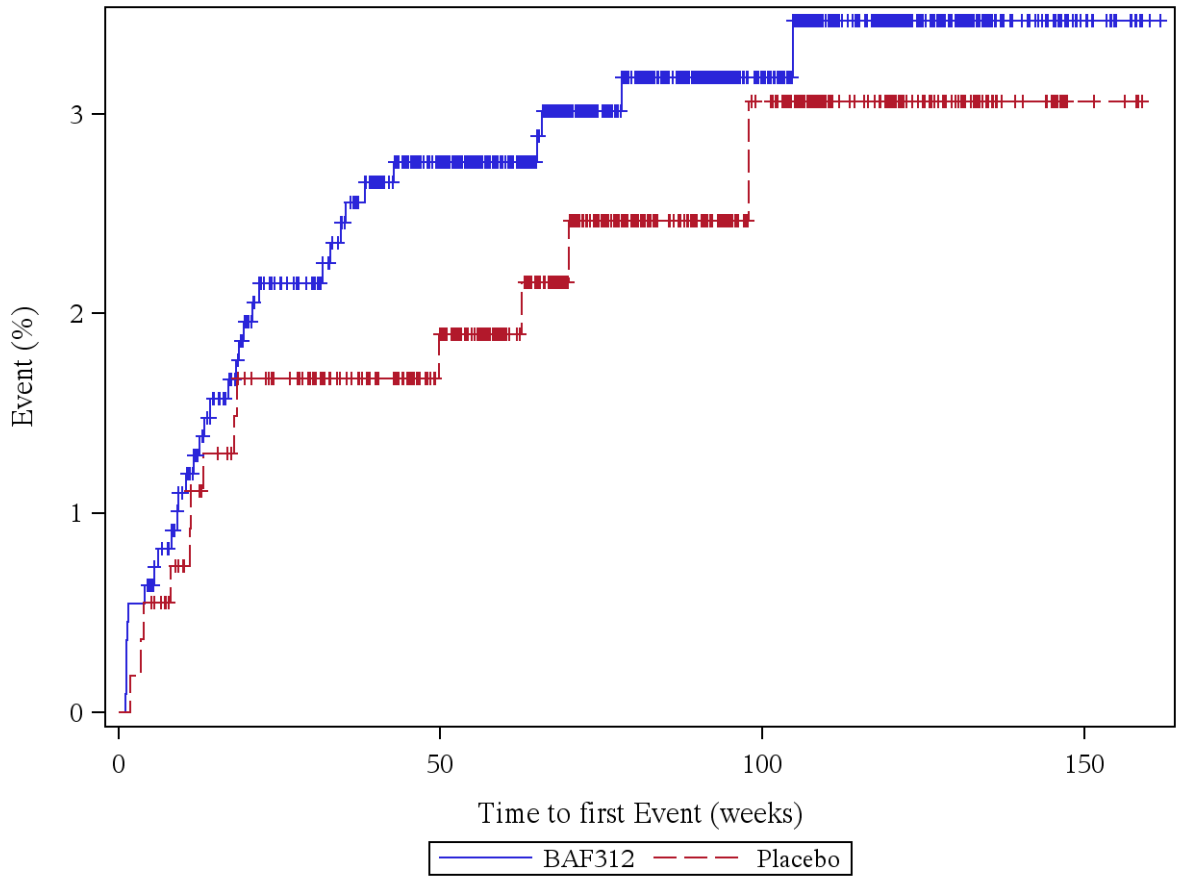


Patients at risk (BAF312/Placebo): Week 0: 1099/546, Week 4: 1053/536, Week 12: 1007/525, Week 24: 960/509, Week 36: 932/484, Week 48: 870/448, Week 60: 770/375, Week 72: 610/291, Week 84: 483/226, Week 96: 379/167, Week 108: 272/117, Week 120: 187/73, Week 132: 105/35, Week 144: 49/19, Week 156: 9/4, Week 168: 0/0

Log rank test: p-value = 0,007 *
*: p < 0,05

Analysis population: A2304 SAF total population

Figure 12.1.3.22: VOMITING (PT)

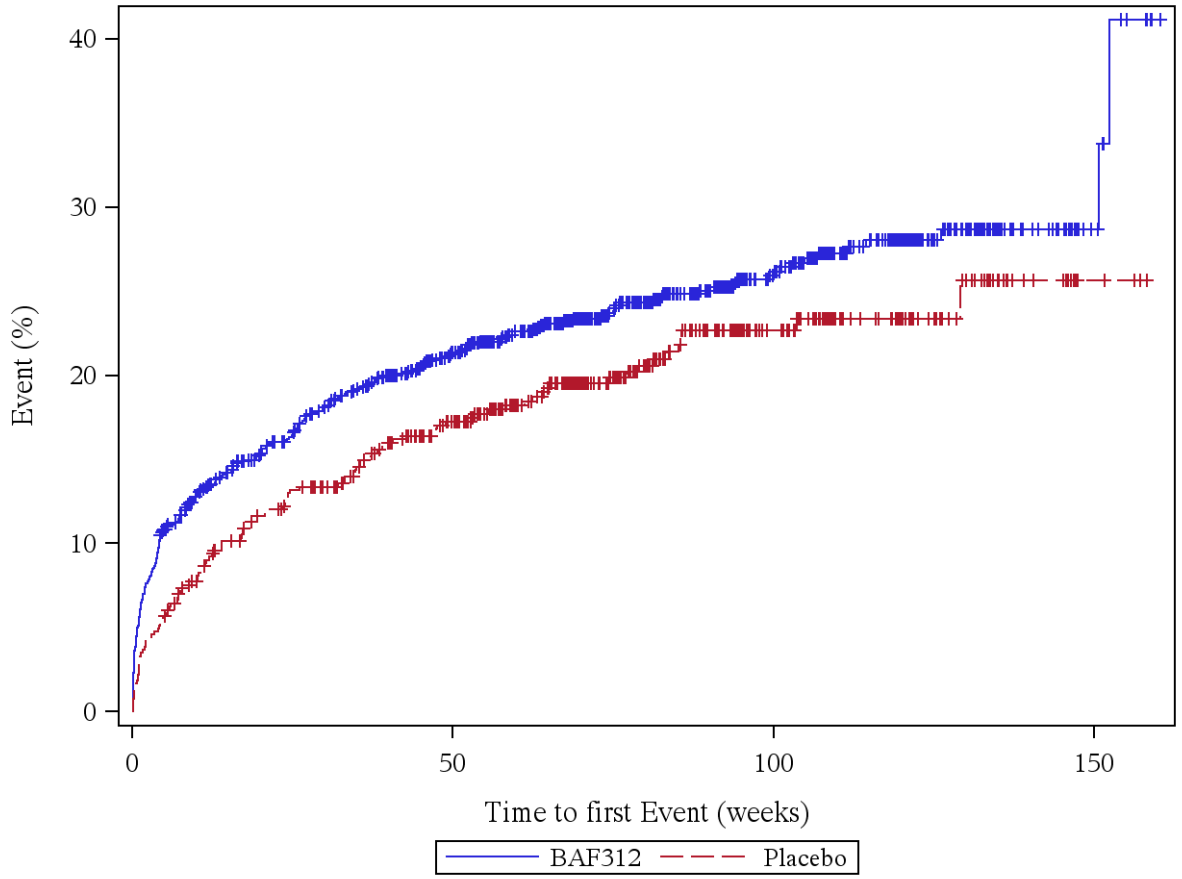


Patients at risk (BAF312/Placebo): Week 0: 1099/546, Week 4: 1092/543, Week 12: 1047/529, Week 24: 997/512, Week 36: 967/489, Week 48: 902/454, Week 60: 798/381, Week 72: 635/296, Week 84: 503/230, Week 96: 393/171, Week 108: 285/120, Week 120: 195/77, Week 132: 108/38, Week 144: 51/19, Week 156: 10/4, Week 168: 0/0

Log rank test: p-value = 0,477
*: p < 0,05

Analysis population: A2304 SAF total population

Figure 12.1.3.23: GENERAL DISORDERS AND ADMINISTRATION SITE CONDITIONS (SOC)

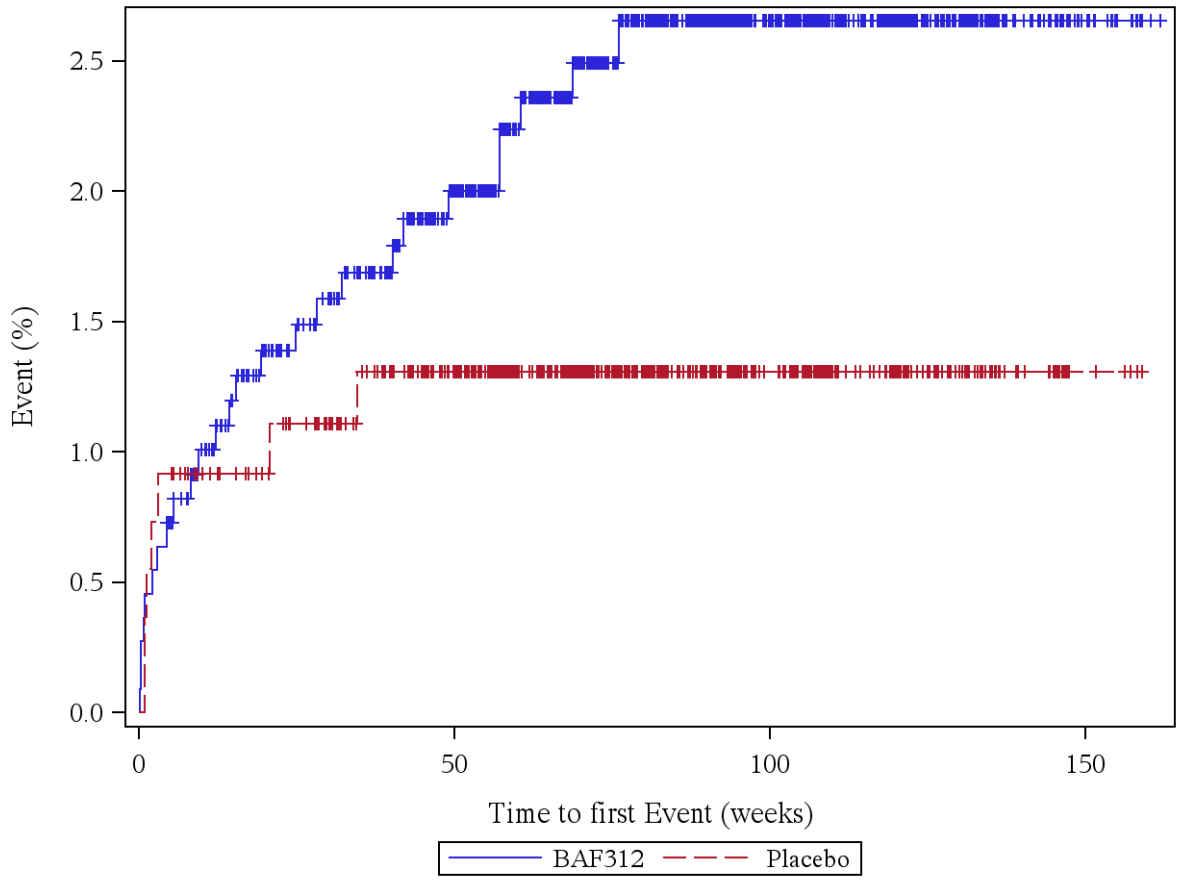


Patients at risk (BAF312/Placebo): Week 0: 1099/546, Week 4: 992/519, Week 12: 917/487, Week 24: 857/458, Week 36: 807/424, Week 48: 741/385, Week 60: 647/318, Week 72: 512/245, Week 84: 400/184, Week 96: 315/135, Week 108: 225/93, Week 120: 150/55, Week 132: 83/28, Week 144: 40/12, Week 156: 6/3, Week 168: 0/0

Log rank test: p-value = 0,052
*: p < 0,05

Analysis population: A2304 SAF total population

Figure 12.1.3.24: ASTHENIA (PT)

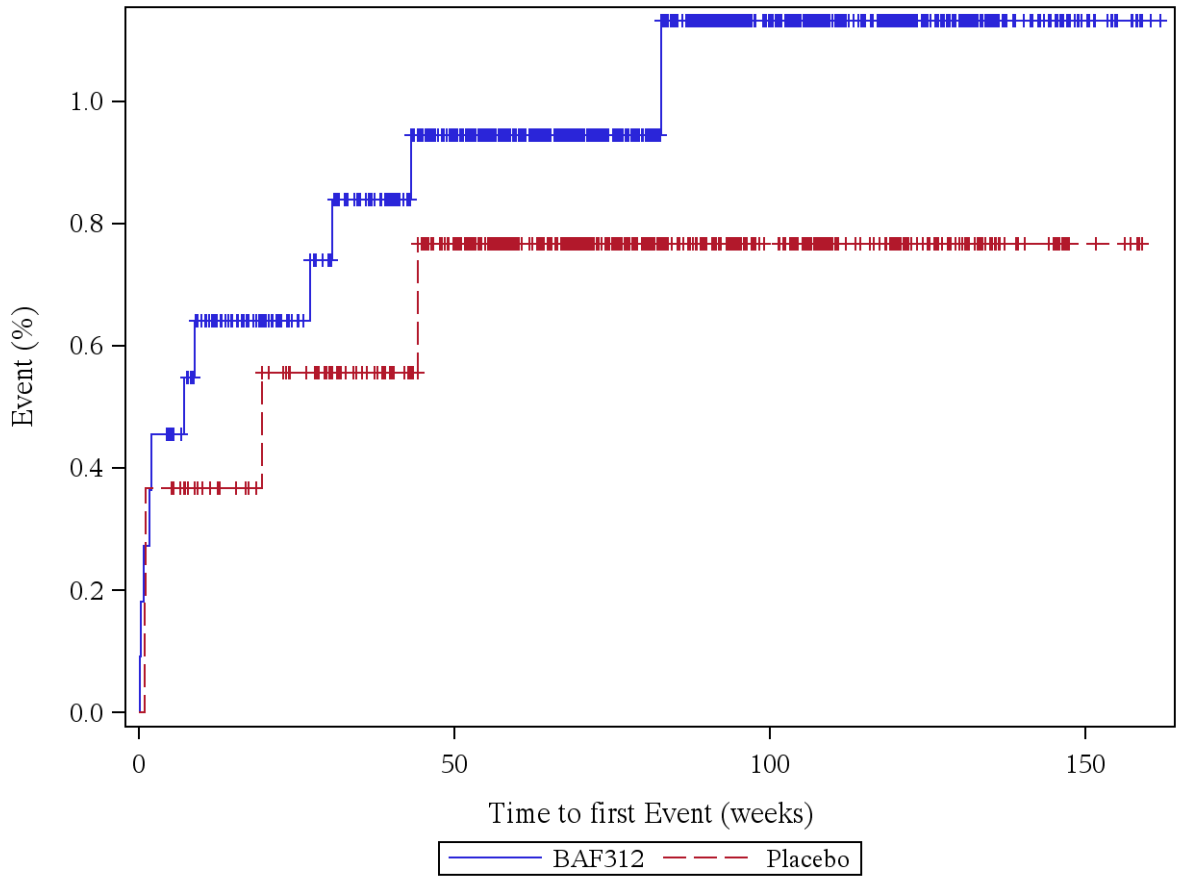


Patients at risk (BAF312/Placebo): Week 0: 1099/546, Week 4: 1092/541, Week 12: 1048/531, Week 24: 1003/516, Week 36: 976/491, Week 48: 913/455, Week 60: 807/384, Week 72: 641/301, Week 84: 508/233, Week 96: 392/173, Week 108: 285/124, Week 120: 197/78, Week 132: 112/38, Week 144: 51/19, Week 156: 10/4, Week 168: 0/0

Log rank test: p-value = 0,143
*: p < 0,05

Analysis population: A2304 SAF total population

Figure 12.1.3.25: CHEST DISCOMFORT (PT)

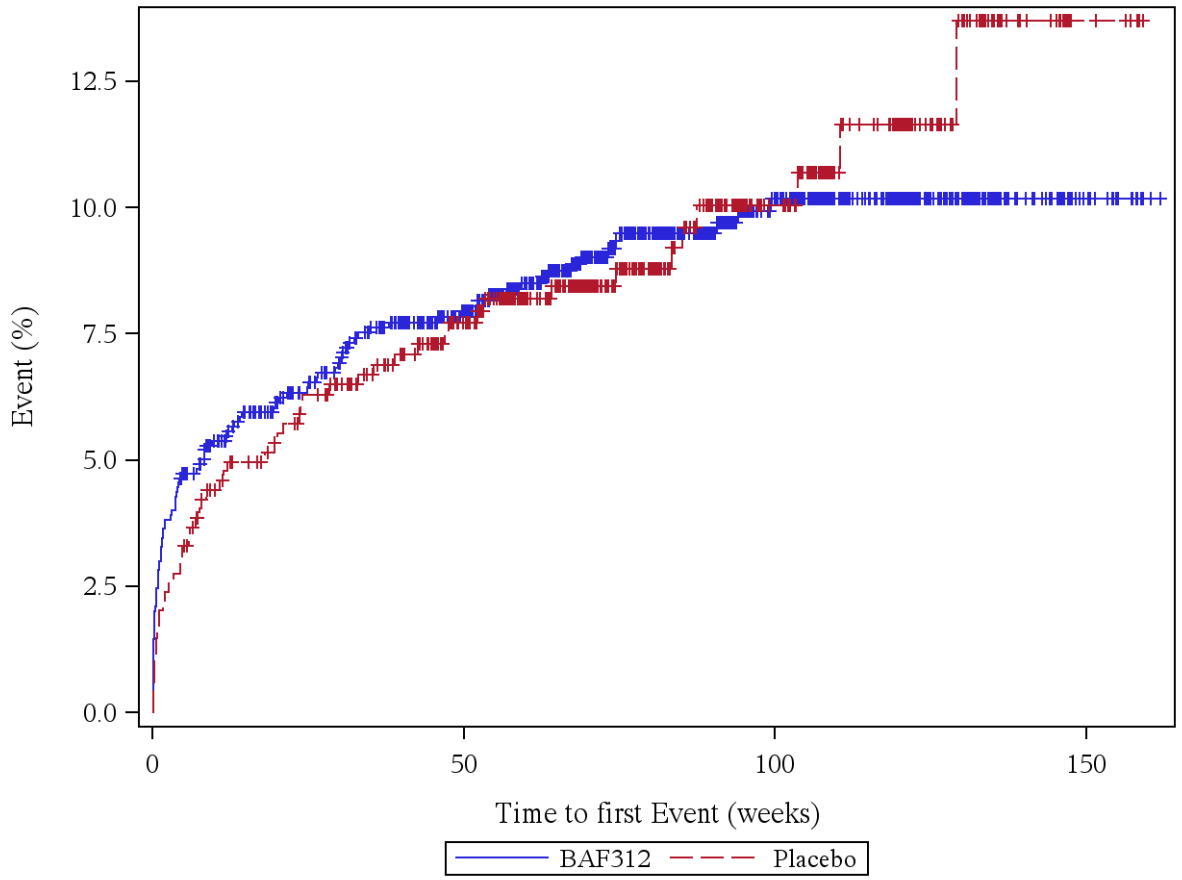


Patients at risk (BAF312/Placebo): Week 0: 1099/546, Week 4: 1094/544, Week 12: 1052/533, Week 24: 1010/518, Week 36: 981/494, Week 48: 918/457, Week 60: 812/385, Week 72: 648/302, Week 84: 511/234, Week 96: 397/174, Week 108: 289/124, Week 120: 198/78, Week 132: 112/38, Week 144: 50/18, Week 156: 10/5, Week 168: 0/0

Log rank test: p-value = 0,586
*: p < 0,05

Analysis population: A2304 SAF total population

Figure 12.1.3.26: FATIGUE (PT)

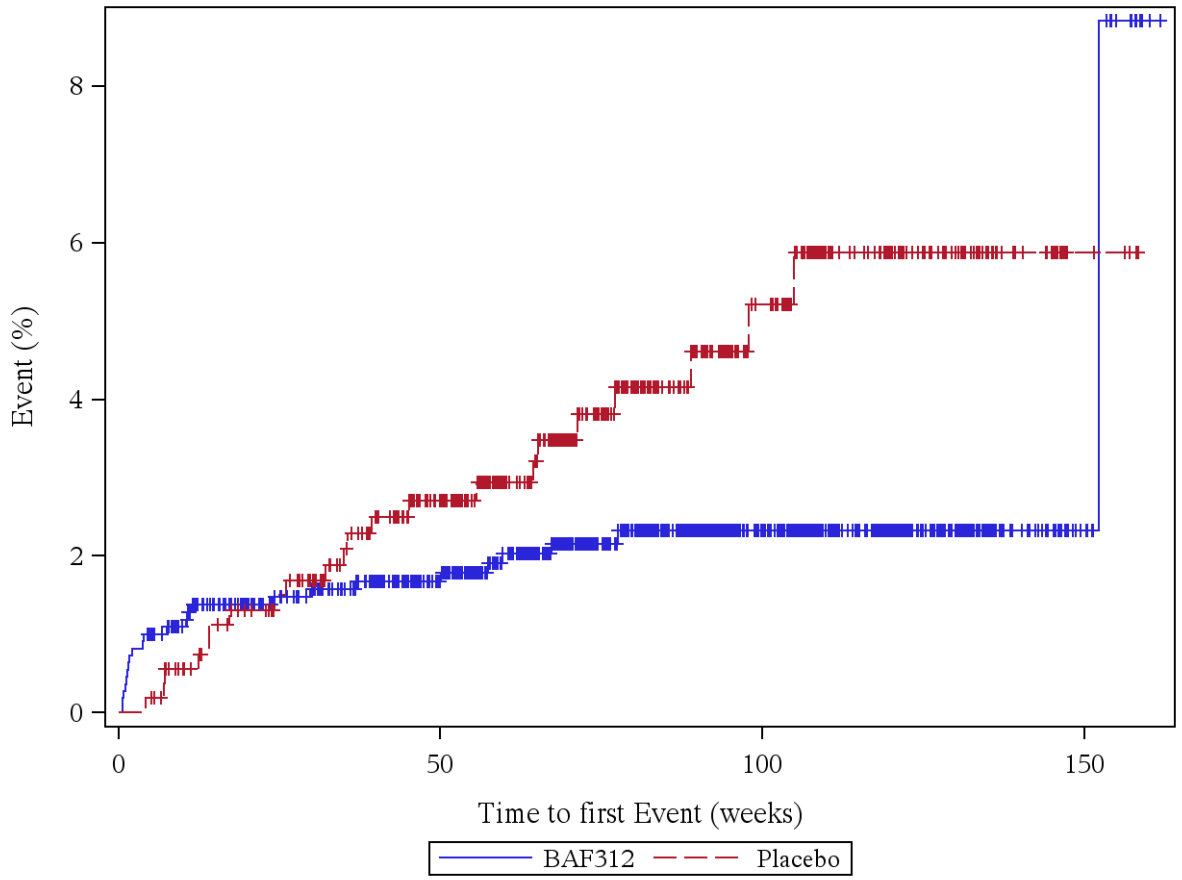


Patients at risk (BAF312/Placebo): Week 0: 1099/546, Week 4: 1050/531, Week 12: 1002/509, Week 24: 957/491, Week 36: 920/465, Week 48: 858/428, Week 60: 759/359, Week 72: 605/282, Week 84: 477/217, Week 96: 370/161, Week 108: 269/112, Week 120: 186/73, Week 132: 104/37, Week 144: 50/17, Week 156: 10/5, Week 168: 0/0

Log rank test: p-value = 0,879
*: p < 0,05

Analysis population: A2304 SAF total population

Figure 12.1.3.27: GAIT DISTURBANCE (PT)

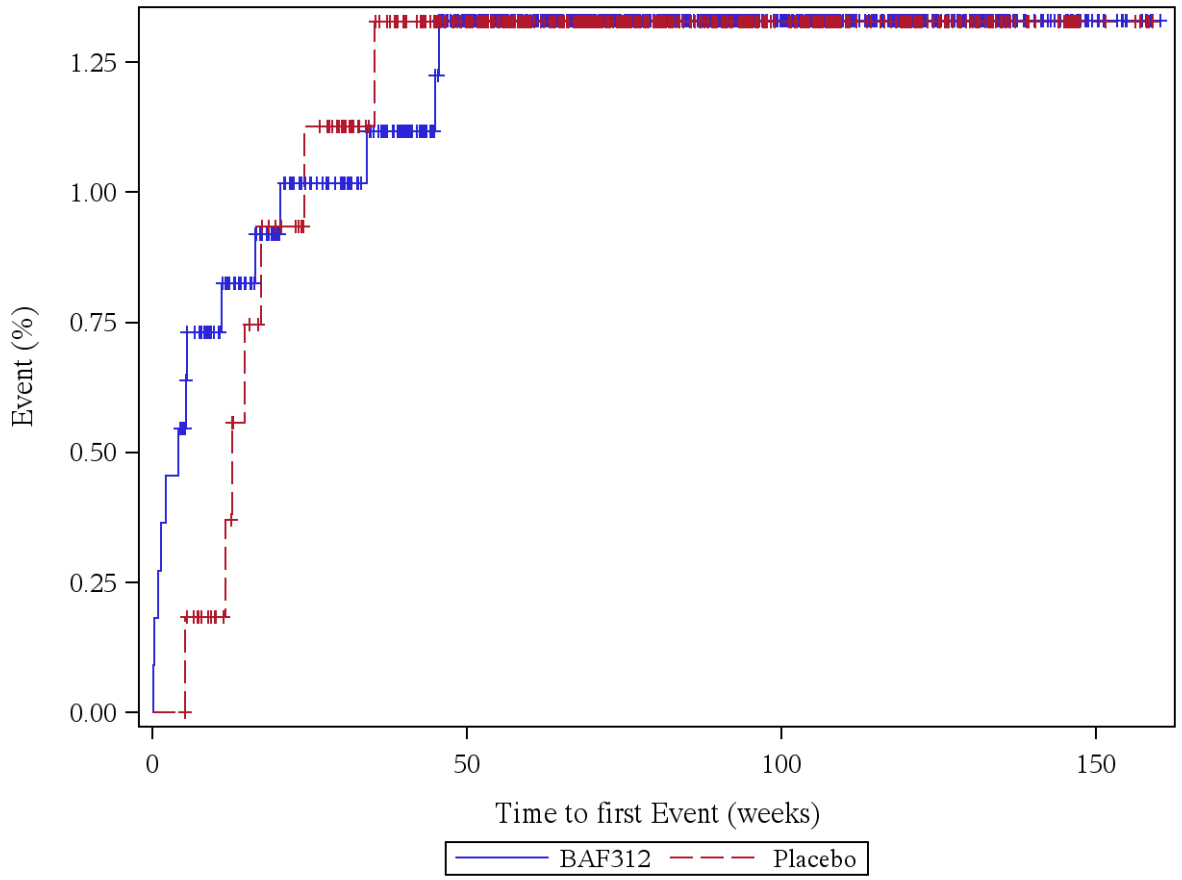


Patients at risk (BAF312/Placebo): Week 0: 1099/546, Week 4: 1088/546, Week 12: 1045/532, Week 24: 1003/514, Week 36: 975/486, Week 48: 910/449, Week 60: 803/376, Week 72: 641/293, Week 84: 508/227, Week 96: 393/167, Week 108: 289/118, Week 120: 198/72, Week 132: 112/37, Week 144: 50/18, Week 156: 10/4, Week 168: 0/0

Log rank test: p-value = 0,028 *
*: p < 0,05

Analysis population: A2304 SAF total population

Figure 12.1.3.28: INFLUENZA LIKE ILLNESS (PT)

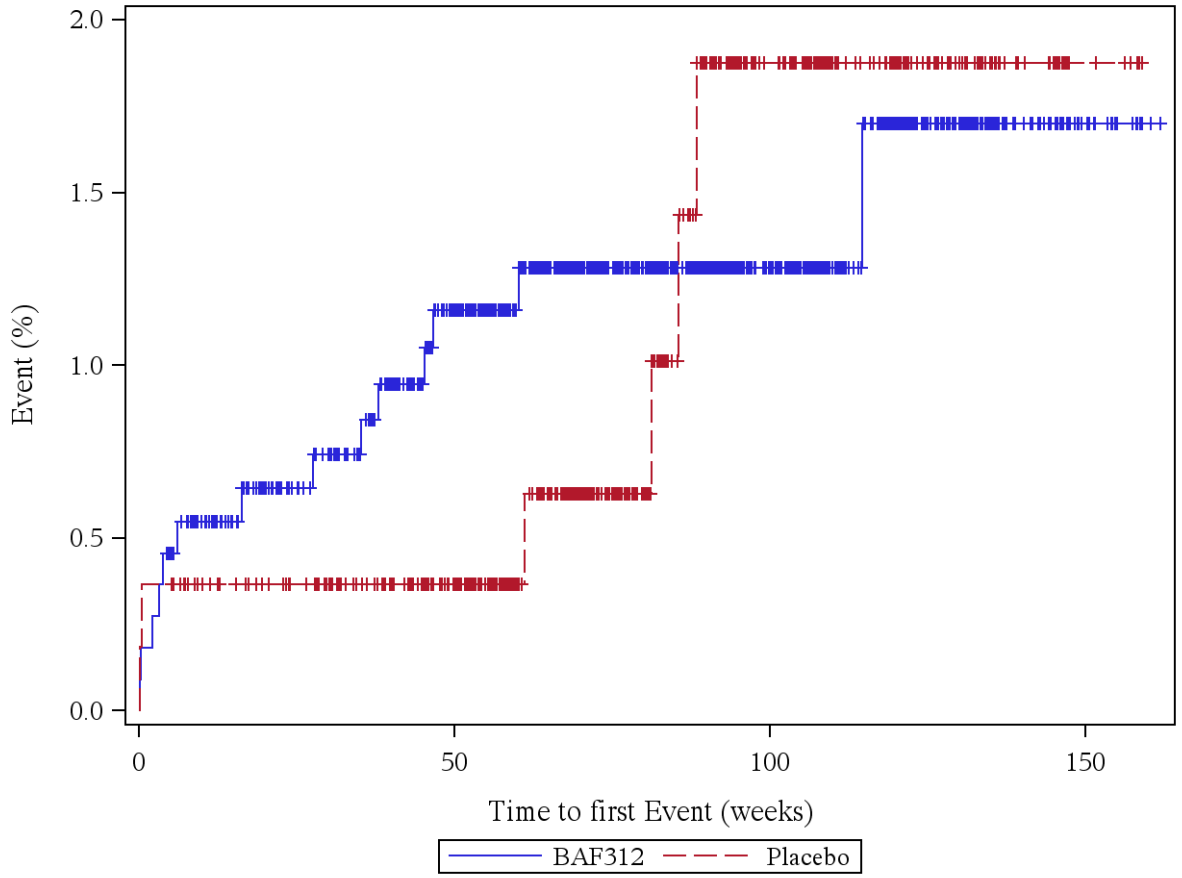


Patients at risk (BAF312/Placebo): Week 0: 1099/546, Week 4: 1094/546, Week 12: 1050/533, Week 24: 1008/516, Week 36: 980/490, Week 48: 914/455, Week 60: 807/382, Week 72: 644/302, Week 84: 511/235, Week 96: 396/175, Week 108: 287/125, Week 120: 198/80, Week 132: 111/40, Week 144: 50/20, Week 156: 9/5, Week 168: 0/0

Log rank test: p-value = 0,989
*: p < 0,05

Analysis population: A2304 SAF total population

Figure 12.1.3.29: NON-CARDIAC CHEST PAIN (PT)

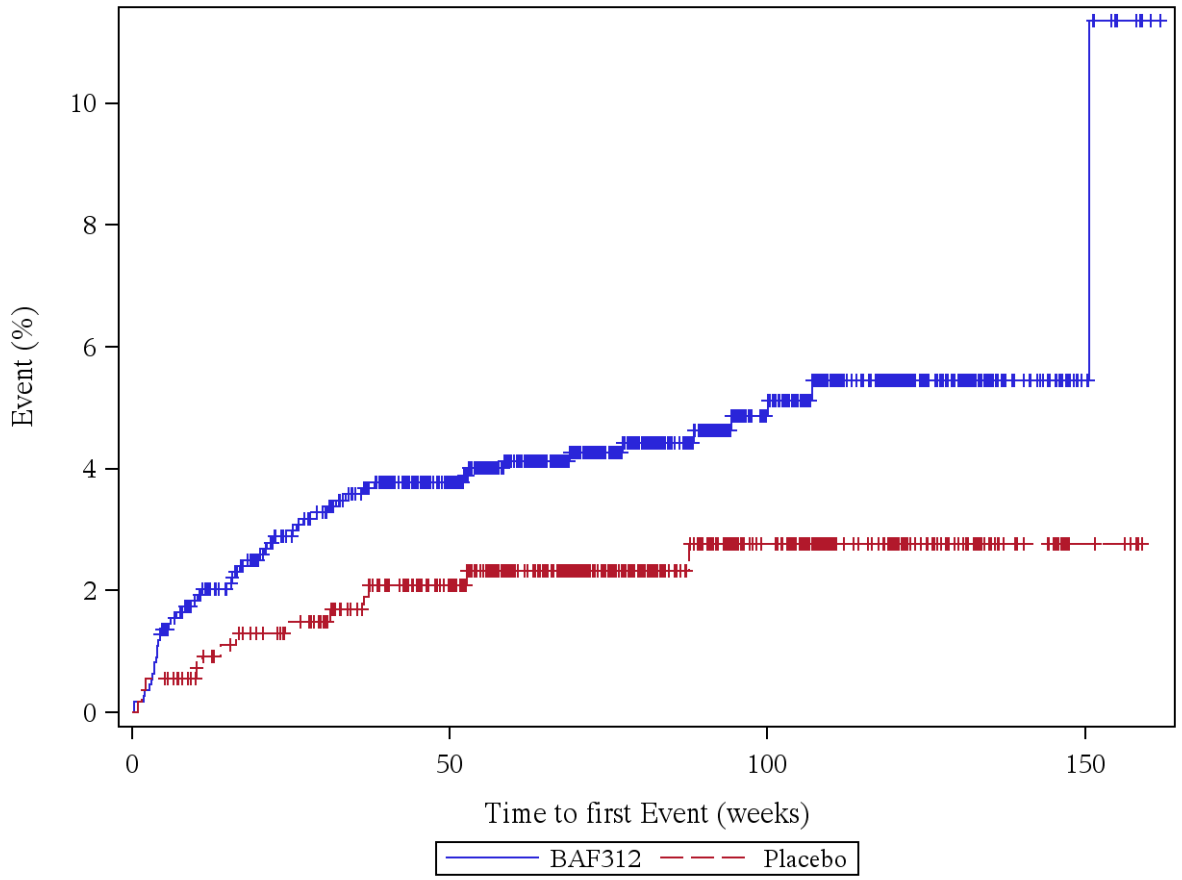


Patients at risk (BAF312/Placebo): Week 0: 1099/546, Week 4: 1094/544, Week 12: 1053/533, Week 24: 1011/519, Week 36: 982/495, Week 48: 914/459, Week 60: 808/387, Week 72: 642/305, Week 84: 508/236, Week 96: 394/173, Week 108: 286/124, Week 120: 197/78, Week 132: 112/40, Week 144: 50/20, Week 156: 9/5, Week 168: 0/0

Log rank test: p-value = 0,786
*: p < 0,05

Analysis population: A2304 SAF total population

Figure 12.1.3.30: OEDEMA PERIPHERAL (PT)

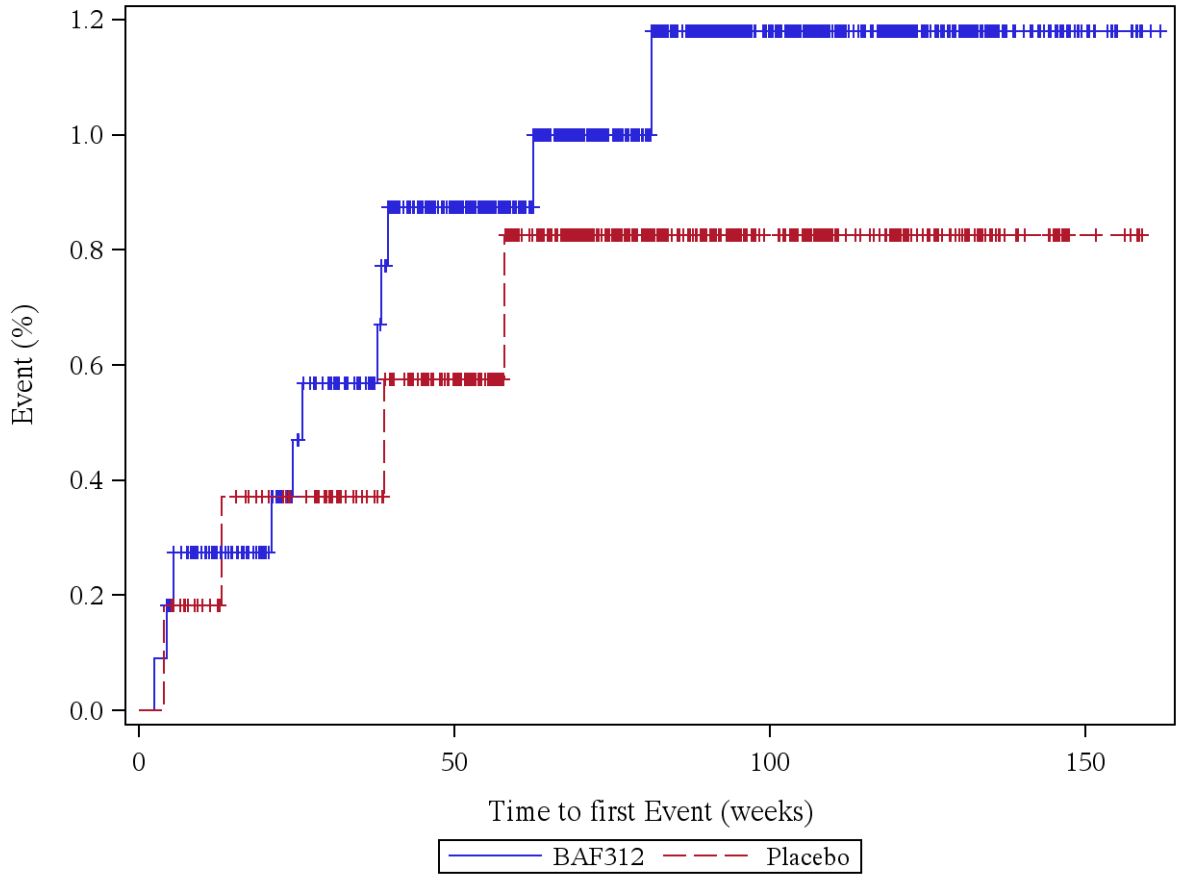


Patients at risk (BAF312/Placebo): Week 0: 1099/546, Week 4: 1087/543, Week 12: 1037/530, Week 24: 988/514, Week 36: 957/488, Week 48: 891/451, Week 60: 785/379, Week 72: 627/297, Week 84: 494/231, Week 96: 381/171, Week 108: 275/122, Week 120: 187/76, Week 132: 105/39, Week 144: 47/20, Week 156: 8/5, Week 168: 0/0

Log rank test: p-value = 0,033 *
*: p < 0,05

Analysis population: A2304 SAF total population

Figure 12.1.3.31: PAIN (PT)

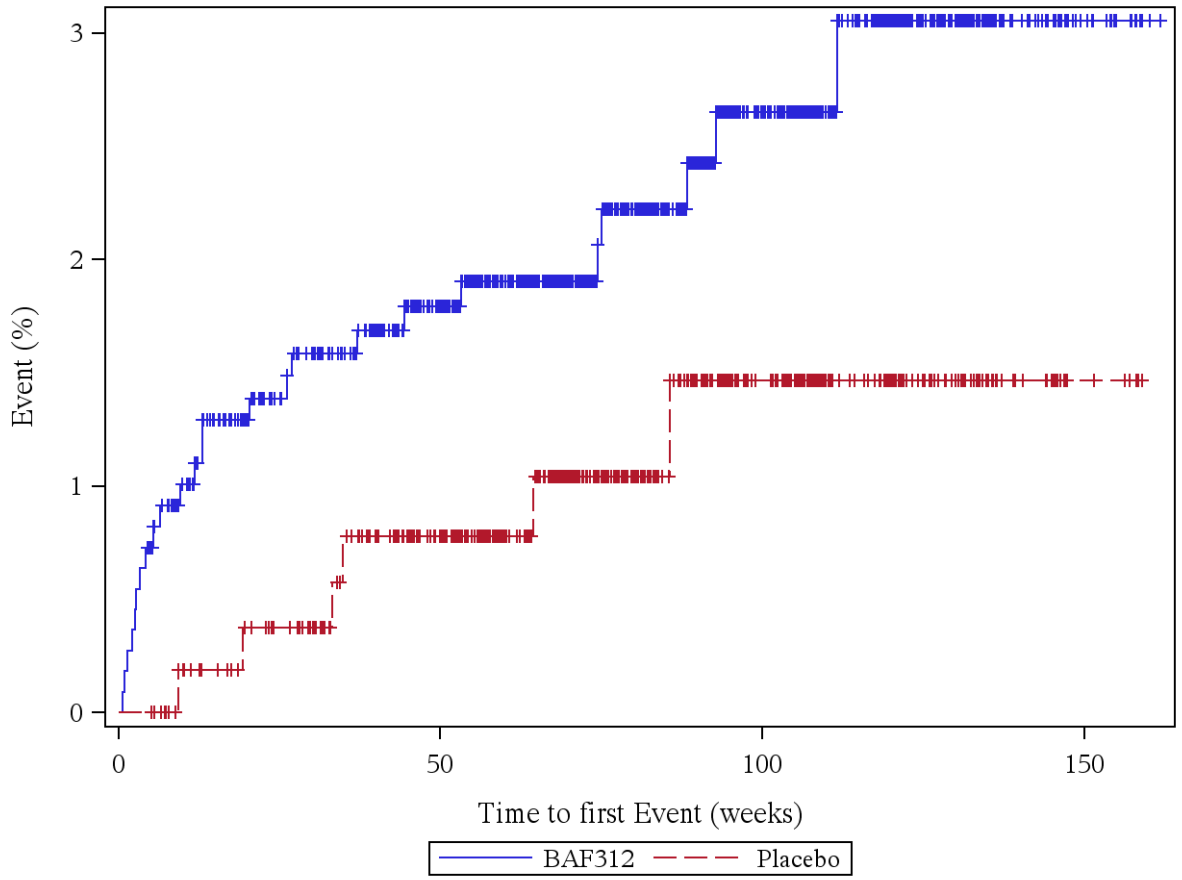


Patients at risk (BAF312/Placebo): Week 0: 1099/546, Week 4: 1098/545, Week 12: 1057/534, Week 24: 1014/519, Week 36: 986/495, Week 48: 920/458, Week 60: 813/385, Week 72: 647/302, Week 84: 511/235, Week 96: 396/174, Week 108: 288/124, Week 120: 197/78, Week 132: 113/39, Week 144: 51/20, Week 156: 10/5, Week 168: 0/0

Log rank test: p-value = 0,589
*: p < 0,05

Analysis population: A2304 SAF total population

Figure 12.1.3.32: PERIPHERAL SWELLING (PT)

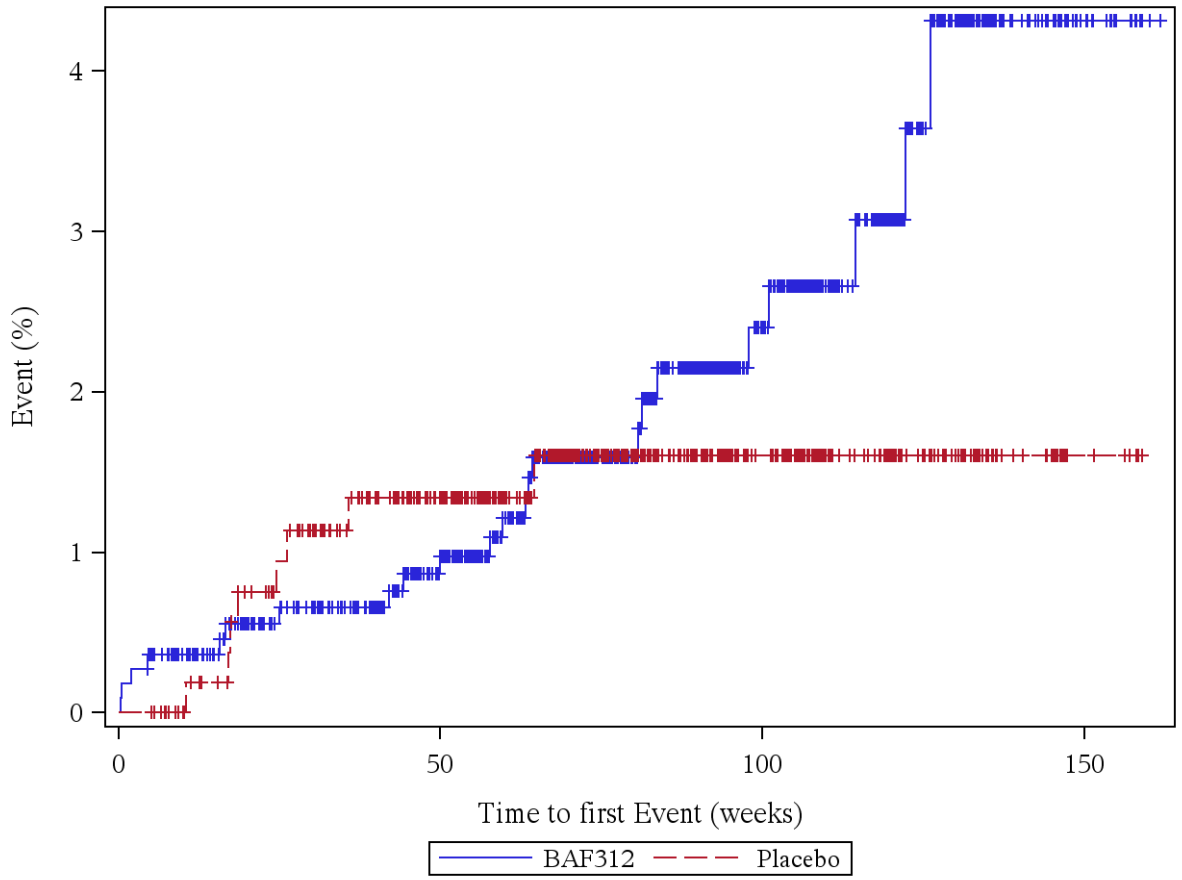


Patients at risk (BAF312/Placebo): Week 0: 1099/546, Week 4: 1092/546, Week 12: 1048/534, Week 24: 1003/519, Week 36: 975/493, Week 48: 909/458, Week 60: 803/387, Week 72: 641/303, Week 84: 505/235, Week 96: 391/173, Week 108: 285/123, Week 120: 194/77, Week 132: 110/38, Week 144: 49/19, Week 156: 10/5, Week 168: 0/0

Log rank test: p-value = 0,103
*: p < 0,05

Analysis population: A2304 SAF total population

Figure 12.1.3.33: PYREXIA (PT)

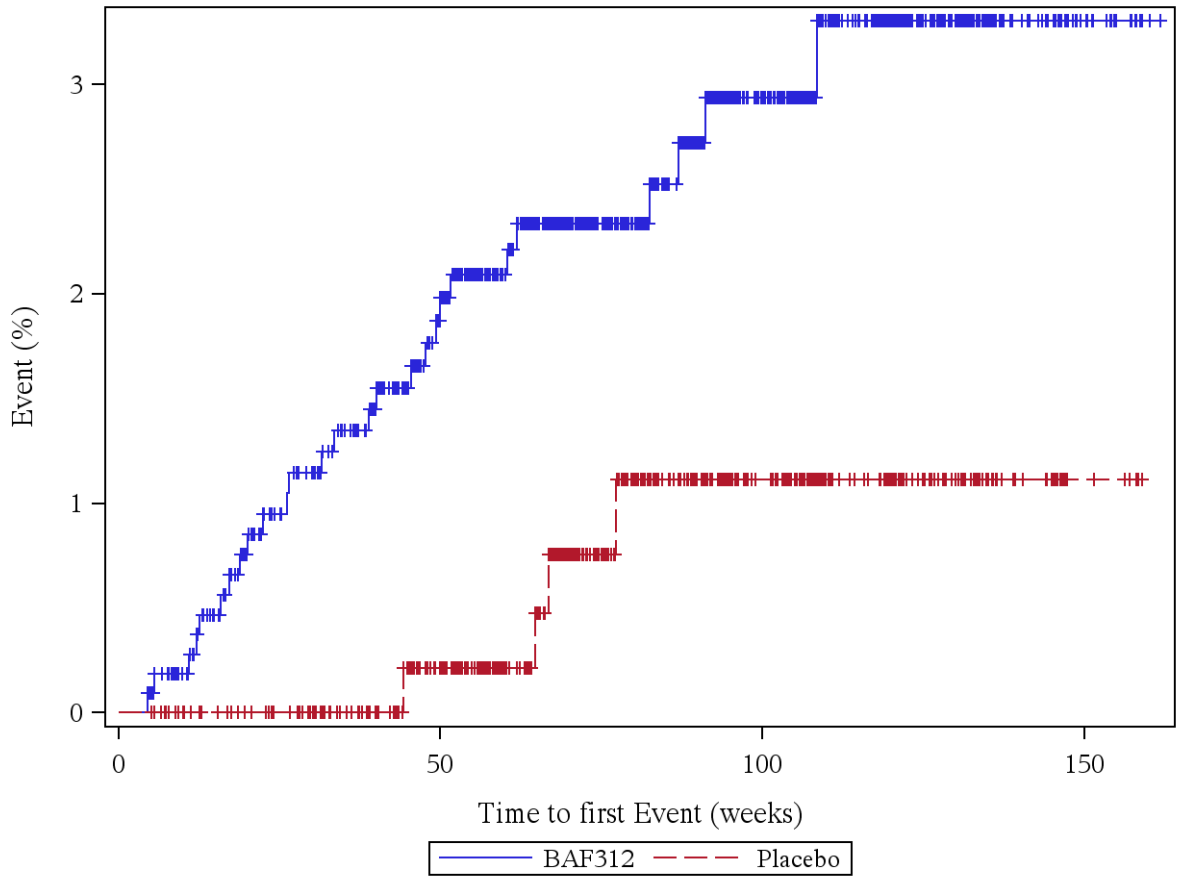


Patients at risk (BAF312/Placebo): Week 0: 1099/546, Week 4: 1096/546, Week 12: 1055/534, Week 24: 1011/517, Week 36: 983/490, Week 48: 917/455, Week 60: 807/383, Week 72: 640/299, Week 84: 504/232, Week 96: 395/172, Week 108: 289/123, Week 120: 197/77, Week 132: 108/39, Week 144: 48/20, Week 156: 9/5, Week 168: 0/0

Log rank test: p-value = 0,437
*: p < 0,05

Analysis population: A2304 SAF total population

Figure 12.1.3.34: HEPATOBILIARY DISORDERS (SOC)

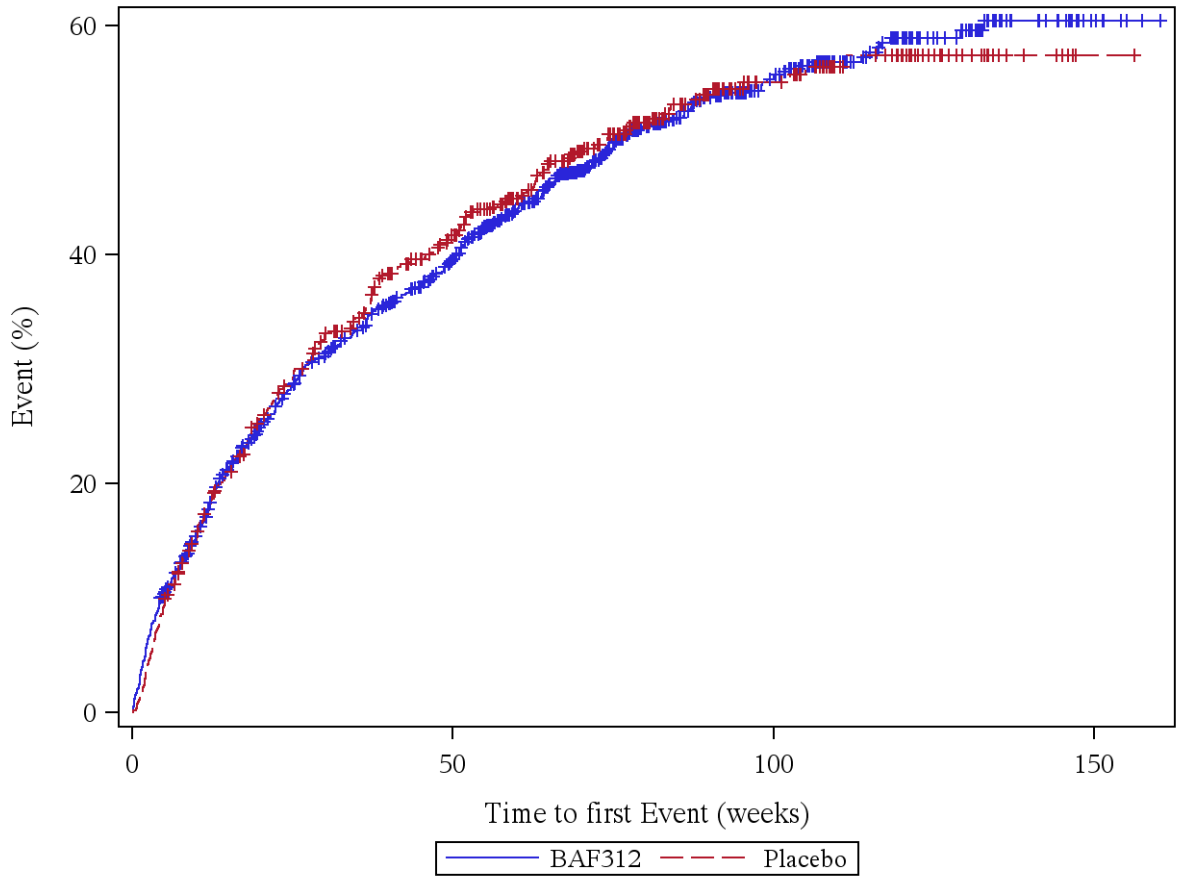


Patients at risk (BAF312/Placebo): Week 0: 1099/546, Week 4: 1099/546, Week 12: 1057/535, Week 24: 1008/521, Week 36: 979/497, Week 48: 912/460, Week 60: 802/387, Week 72: 637/302, Week 84: 503/233, Week 96: 388/172, Week 108: 281/123, Week 120: 191/79, Week 132: 109/40, Week 144: 49/20, Week 156: 10/5, Week 168: 0/0

Log rank test: p-value = 0,017 *
*: p < 0,05

Analysis population: A2304 SAF total population

Figure 12.1.3.35: INFECTIONS AND INFESTATIONS (SOC)

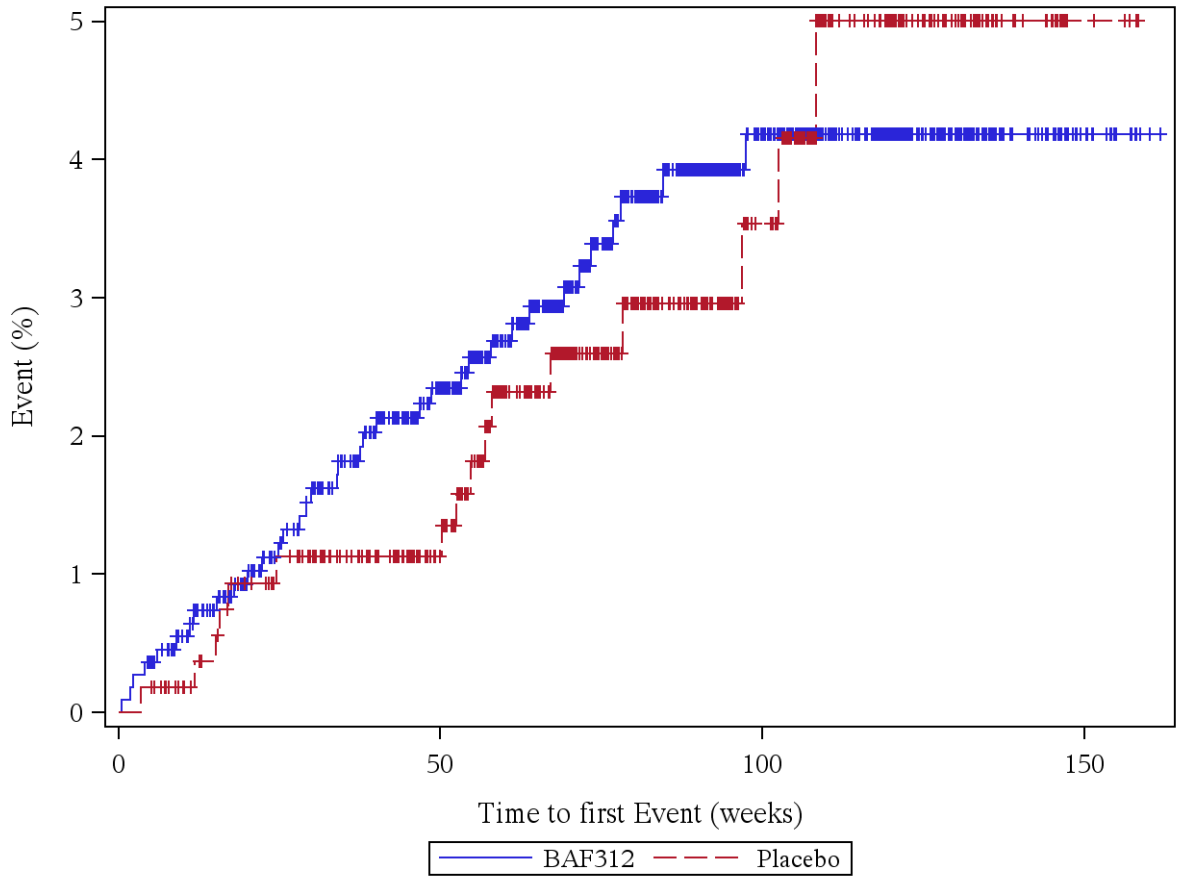


Patients at risk (BAF312/Placebo): Week 0: 1099/546, Week 4: 999/505, Week 12: 873/438, Week 24: 737/371, Week 36: 663/325, Week 48: 581/277, Week 60: 466/223, Week 72: 347/166, Week 84: 260/114, Week 96: 198/74, Week 108: 134/53, Week 120: 85/34, Week 132: 50/17, Week 144: 24/7, Week 156: 2/1, Week 168: 0/0

Log rank test: p-value = 0,874
*: p < 0,05

Analysis population: A2304 SAF total population

Figure 12.1.3.36: BRONCHITIS (PT)

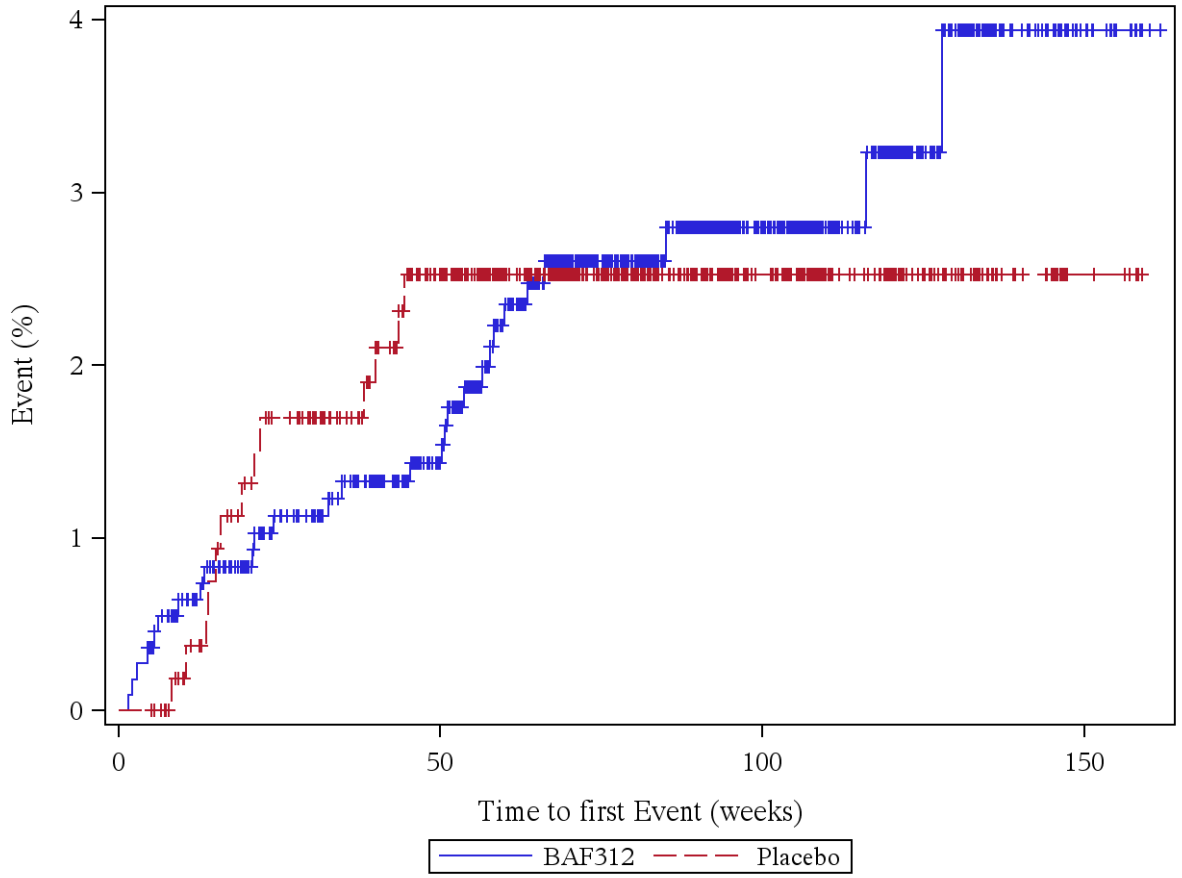


Patients at risk (BAF312/Placebo): Week 0: 1099/546, Week 4: 1095/545, Week 12: 1051/533, Week 24: 1005/516, Week 36: 972/491, Week 48: 904/455, Week 60: 794/378, Week 72: 626/299, Week 84: 494/233, Week 96: 381/172, Week 108: 278/121, Week 120: 188/77, Week 132: 107/38, Week 144: 50/18, Week 156: 9/4, Week 168: 0/0

Log rank test: p-value = 0,734
*: p < 0,05

Analysis population: A2304 SAF total population

Figure 12.1.3.37: CYSTITIS (PT)

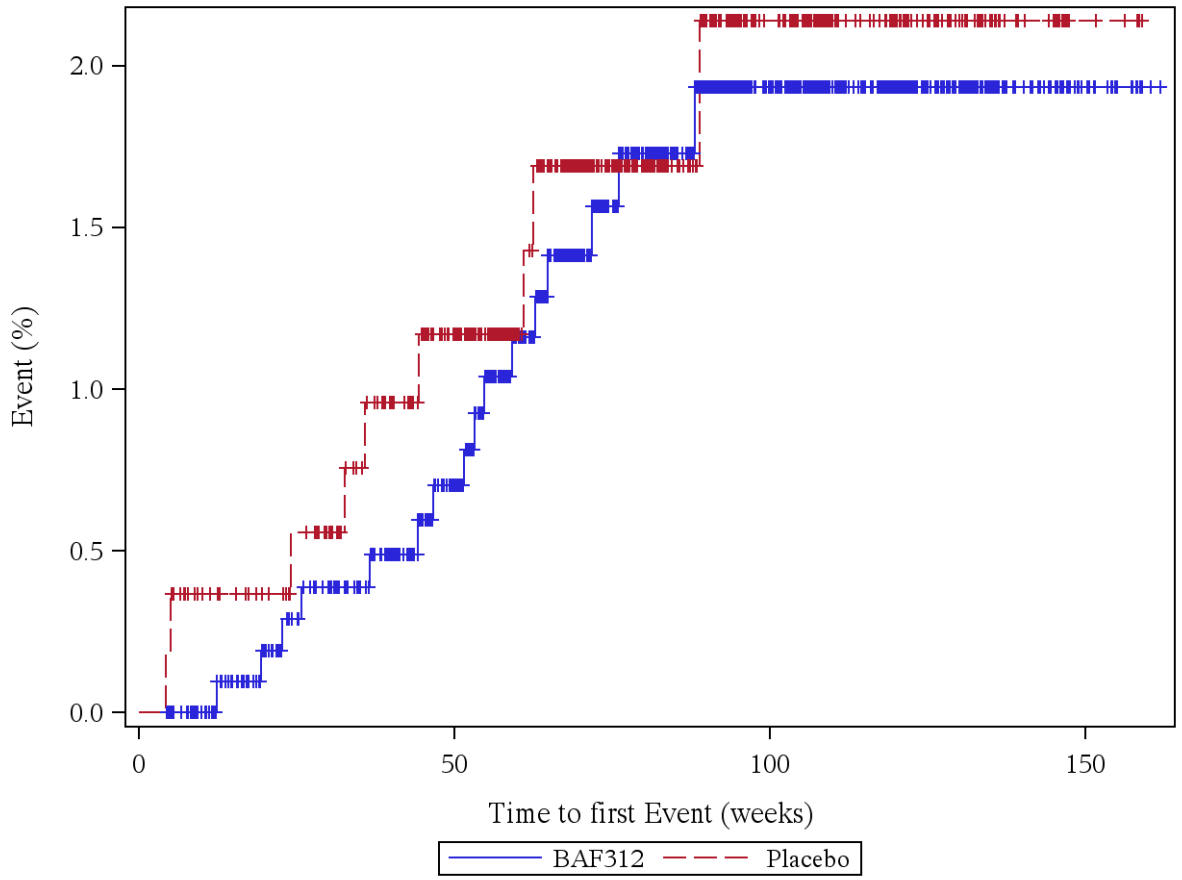


Patients at risk (BAF312/Placebo): Week 0: 1099/546, Week 4: 1096/546, Week 12: 1053/533, Week 24: 1008/513, Week 36: 979/489, Week 48: 916/451, Week 60: 801/380, Week 72: 635/298, Week 84: 504/233, Week 96: 390/172, Week 108: 283/123, Week 120: 194/78, Week 132: 110/39, Week 144: 51/20, Week 156: 10/5, Week 168: 0/0

Log rank test: p-value = 0,874
*: p < 0,05

Analysis population: A2304 SAF total population

Figure 12.1.3.38: GASTROENTERITIS (PT)

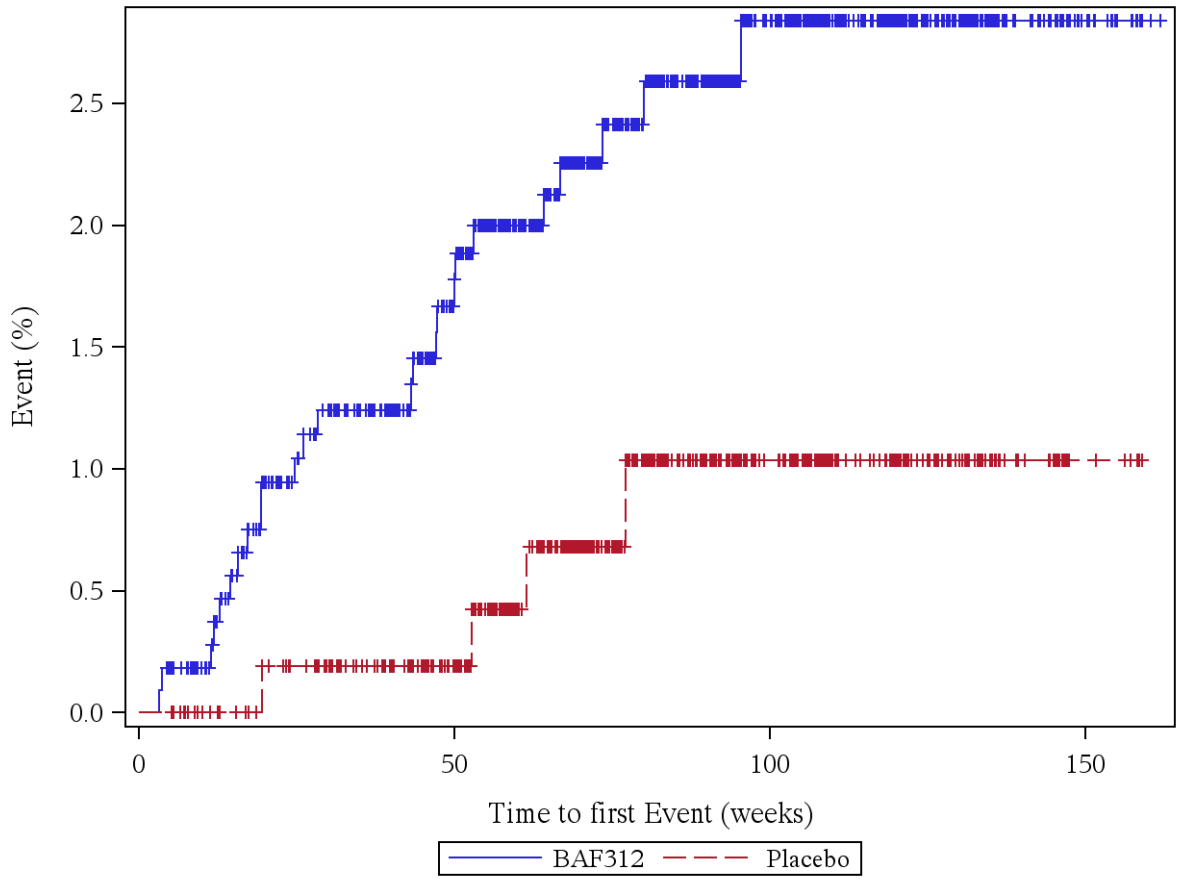


Patients at risk (BAF312/Placebo): Week 0: 1099/546, Week 4: 1099/546, Week 12: 1059/533, Week 24: 1014/519, Week 36: 986/492, Week 48: 919/455, Week 60: 809/383, Week 72: 642/299, Week 84: 506/231, Week 96: 392/170, Week 108: 284/122, Week 120: 195/76, Week 132: 110/38, Week 144: 49/18, Week 156: 10/4, Week 168: 0/0

Log rank test: p-value = 0,733
*: p < 0,05

Analysis population: A2304 SAF total population

Figure 12.1.3.39: HERPES ZOSTER (PT)

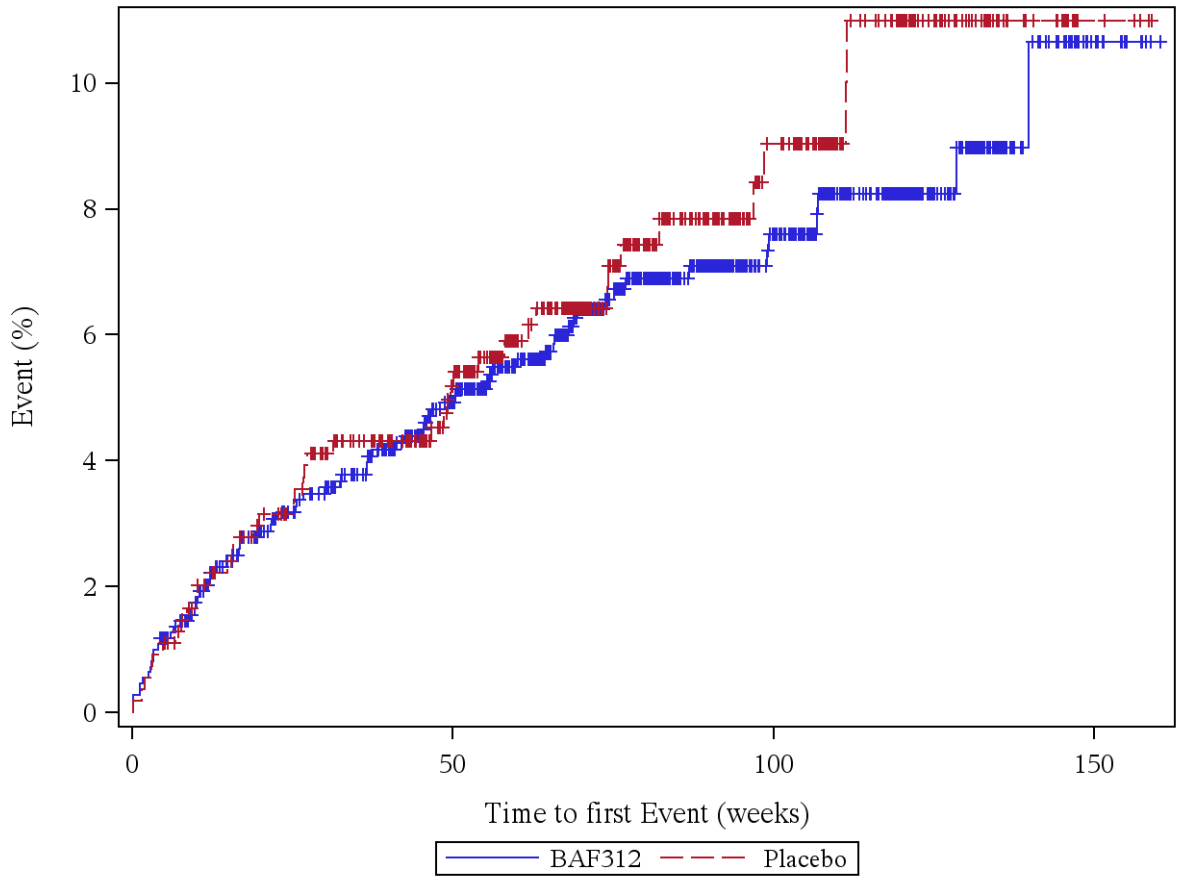


Patients at risk (BAF312/Placebo): Week 0: 1099/546, Week 4: 1097/546, Week 12: 1055/535, Week 24: 1008/520, Week 36: 978/496, Week 48: 909/460, Week 60: 802/387, Week 72: 636/303, Week 84: 500/234, Week 96: 386/174, Week 108: 279/126, Week 120: 191/80, Week 132: 109/40, Week 144: 50/20, Week 156: 9/5, Week 168: 0/0

Log rank test: p-value = 0,026 *
*: p < 0,05

Analysis population: A2304 SAF total population

Figure 12.1.3.40: INFLUENZA (PT)

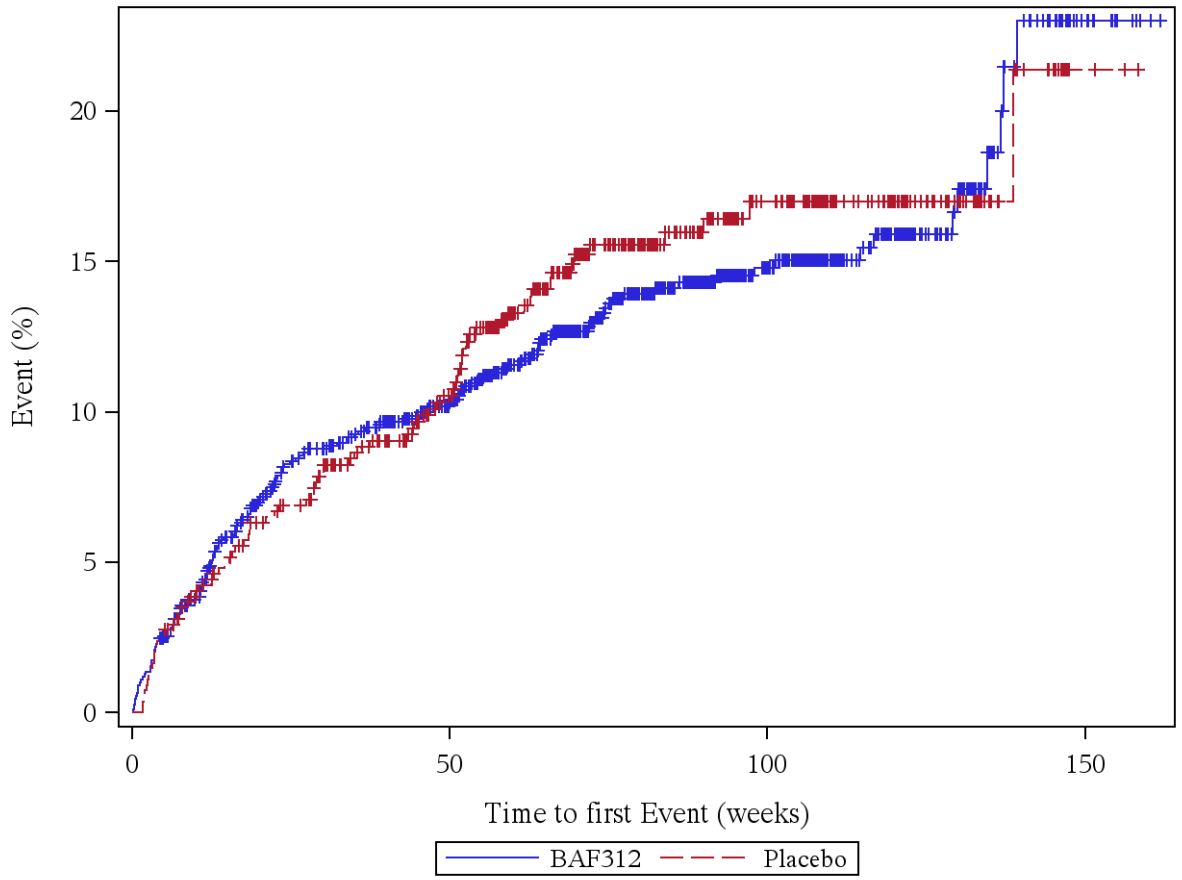


Patients at risk (BAF312/Placebo): Week 0: 1099/546, Week 4: 1087/541, Week 12: 1037/525, Week 24: 986/505, Week 36: 954/476, Week 48: 882/439, Week 60: 772/364, Week 72: 611/286, Week 84: 479/220, Week 96: 373/161, Week 108: 270/116, Week 120: 186/72, Week 132: 103/36, Week 144: 45/18, Week 156: 6/4, Week 168: 0/0

Log rank test: p-value = 0,548
*: p < 0,05

Analysis population: A2304 SAF total population

Figure 12.1.3.41: NASOPHARYNGITIS (PT)

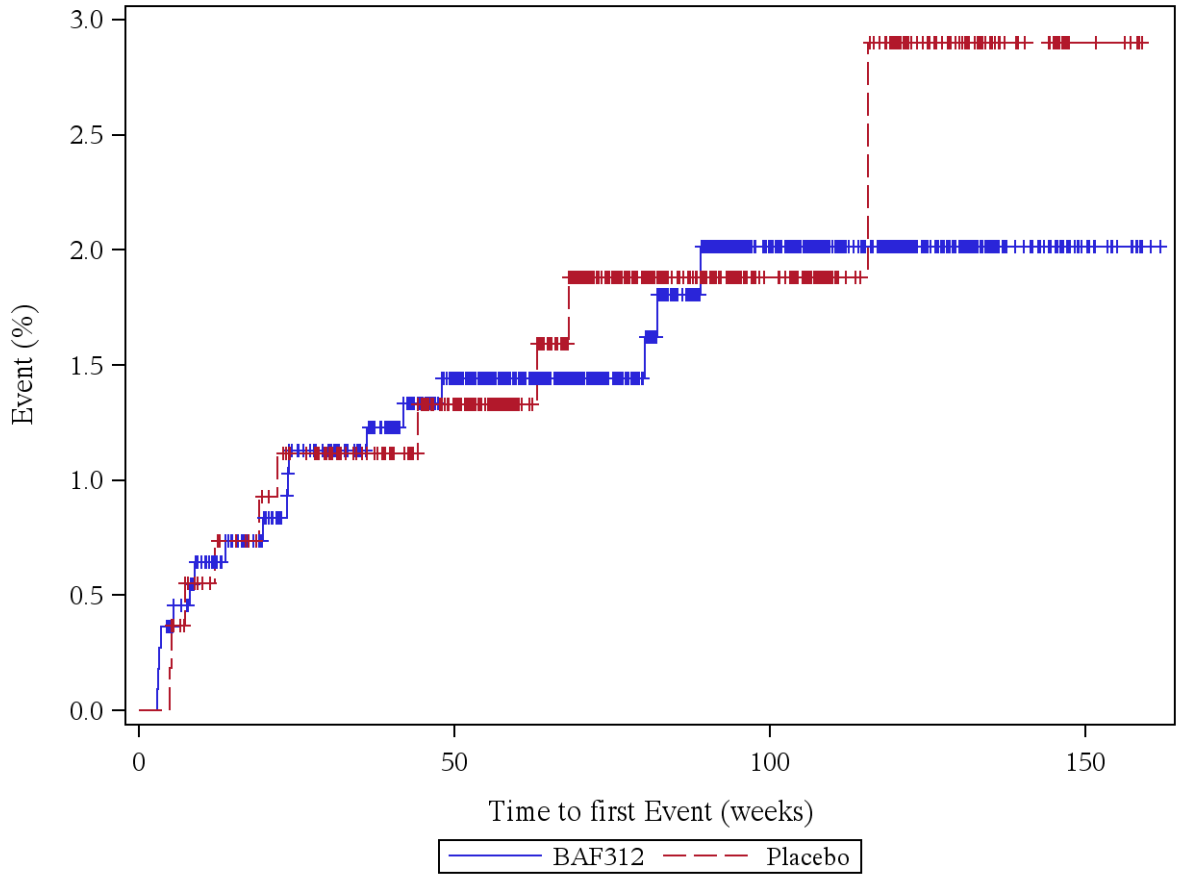


Patients at risk (BAF312/Placebo): Week 0: 1099/546, Week 4: 1073/533, Week 12: 1008/512, Week 24: 932/485, Week 36: 898/454, Week 48: 835/415, Week 60: 728/340, Week 72: 576/259, Week 84: 454/201, Week 96: 346/148, Week 108: 247/105, Week 120: 163/65, Week 132: 92/33, Week 144: 42/15, Week 156: 7/2, Week 168: 0/0

Log rank test: p-value = 0,562
*: p < 0,05

Analysis population: A2304 SAF total population

Figure 12.1.3.42: ORAL HERPES (PT)

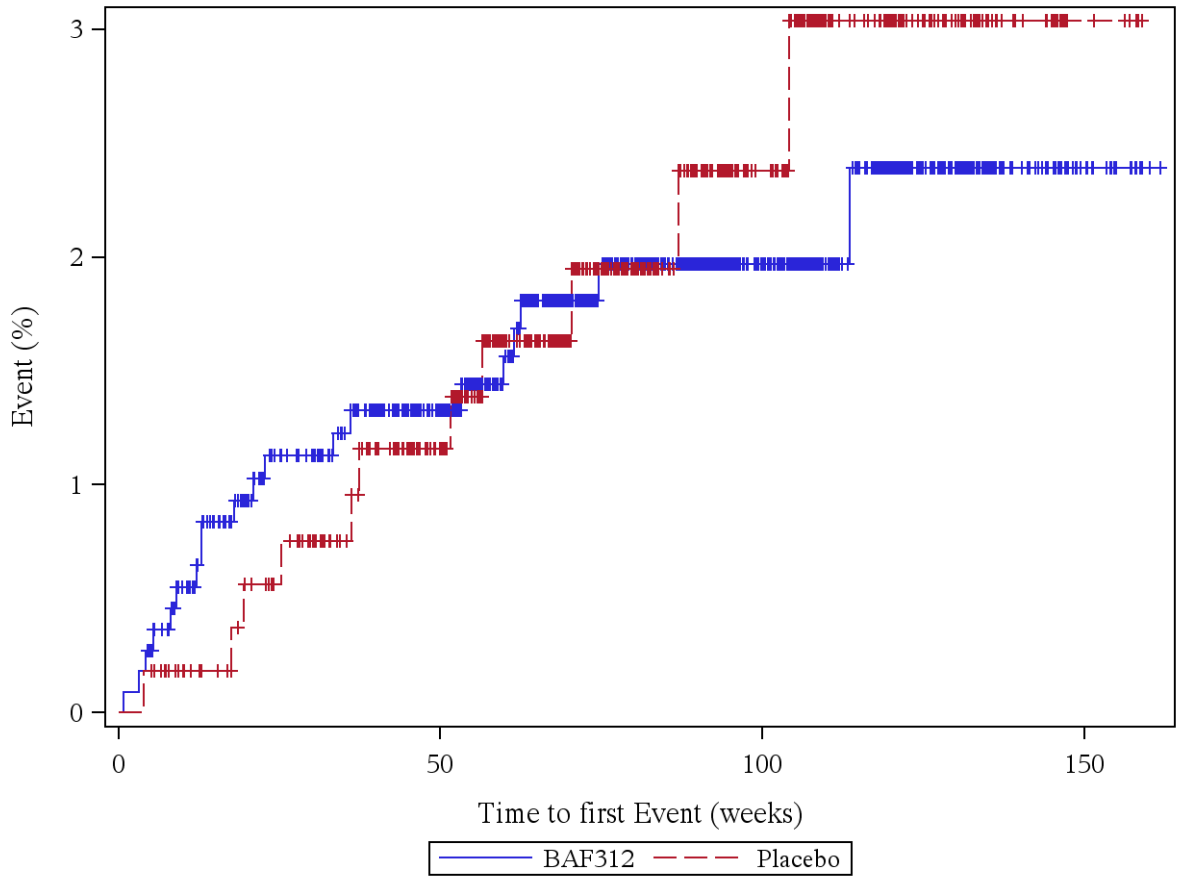


Patients at risk (BAF312/Placebo): Week 0: 1099/546, Week 4: 1095/546, Week 12: 1052/531, Week 24: 1005/515, Week 36: 978/491, Week 48: 910/454, Week 60: 803/381, Week 72: 639/299, Week 84: 506/232, Week 96: 393/171, Week 108: 287/122, Week 120: 197/78, Week 132: 110/39, Week 144: 50/20, Week 156: 10/5, Week 168: 0/0

Log rank test: p-value = 0,765
*: p < 0,05

Analysis population: A2304 SAF total population

Figure 12.1.3.43: PHARYNGITIS (PT)

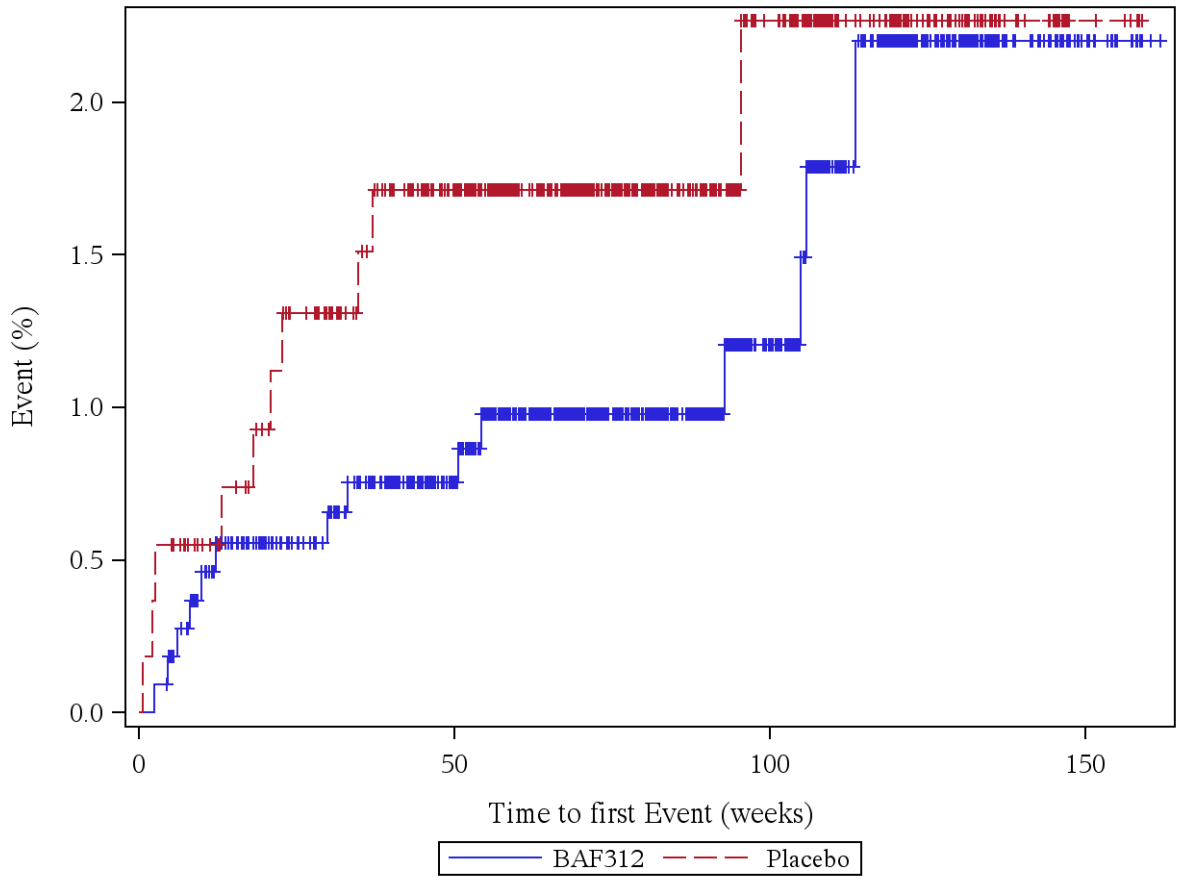


Patients at risk (BAF312/Placebo): Week 0: 1099/546, Week 4: 1097/545, Week 12: 1053/534, Week 24: 1006/518, Week 36: 978/493, Week 48: 913/455, Week 60: 806/381, Week 72: 640/300, Week 84: 503/233, Week 96: 390/171, Week 108: 281/121, Week 120: 192/78, Week 132: 110/39, Week 144: 50/20, Week 156: 10/5, Week 168: 0/0

Log rank test: p-value = 0,762
*: p < 0,05

Analysis population: A2304 SAF total population

Figure 12.1.3.44: RHINITIS (PT)

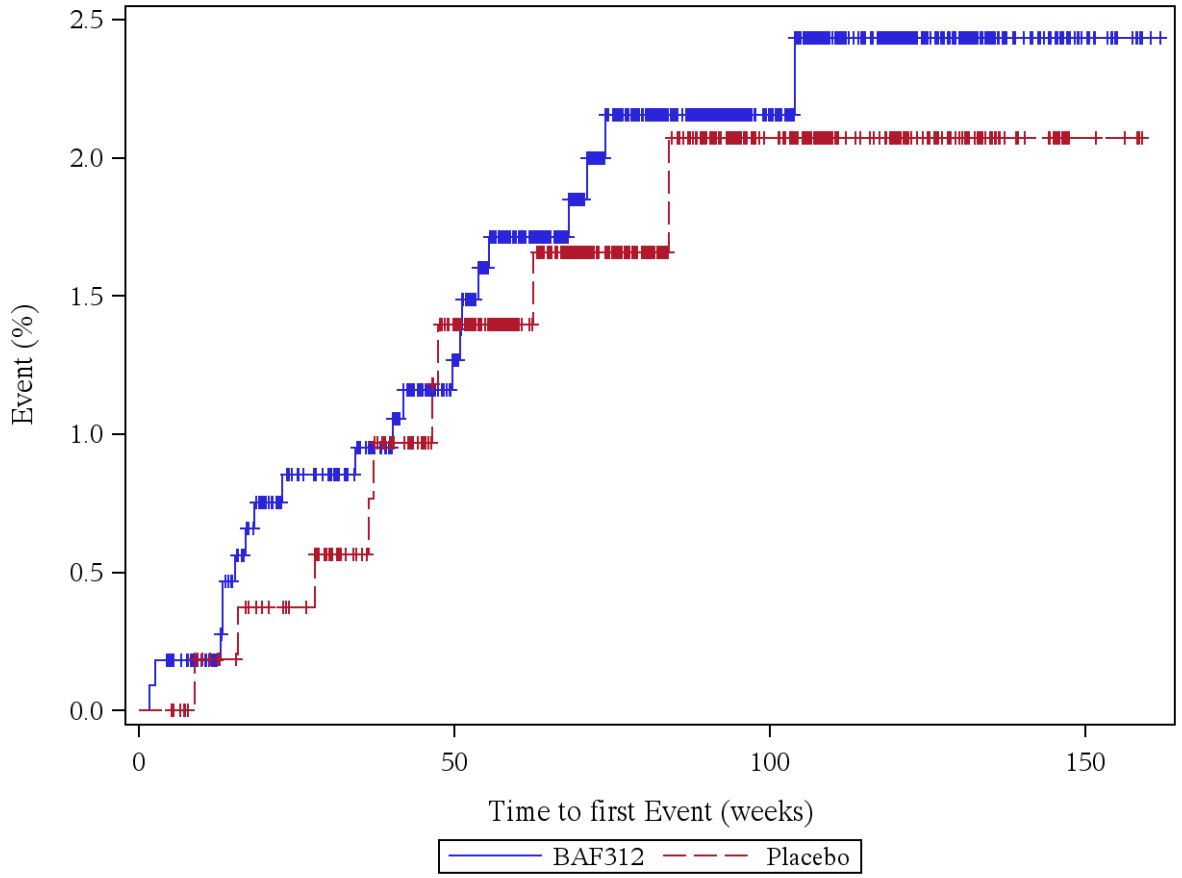


Patients at risk (BAF312/Placebo): Week 0: 1099/546, Week 4: 1098/543, Week 12: 1054/532, Week 24: 1012/514, Week 36: 983/489, Week 48: 918/453, Week 60: 809/381, Week 72: 646/299, Week 84: 511/233, Week 96: 395/172, Week 108: 287/123, Week 120: 198/78, Week 132: 112/39, Week 144: 51/20, Week 156: 10/5, Week 168: 0/0

Log rank test: p-value = 0,346
*: p < 0,05

Analysis population: A2304 SAF total population

Figure 12.1.3.45: SINUSITIS (PT)

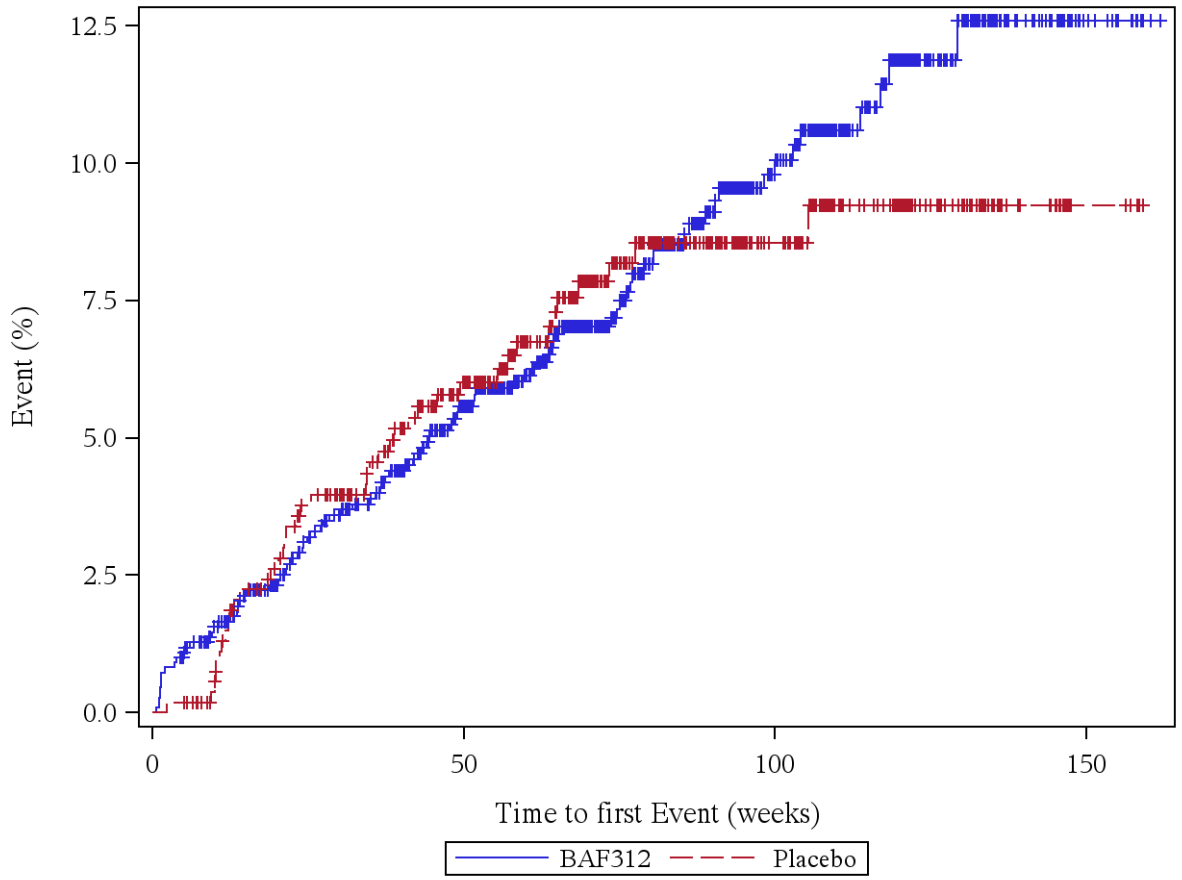


Patients at risk (BAF312/Placebo): Week 0: 1099/546, Week 4: 1097/546, Week 12: 1057/534, Week 24: 1008/520, Week 36: 981/495, Week 48: 916/457, Week 60: 806/385, Week 72: 640/303, Week 84: 506/235, Week 96: 392/175, Week 108: 282/125, Week 120: 195/79, Week 132: 110/39, Week 144: 50/19, Week 156: 9/4, Week 168: 0/0

Log rank test: p-value = 0,719
*: p < 0,05

Analysis population: A2304 SAF total population

Figure 12.1.3.46: UPPER RESPIRATORY TRACT INFECTION (PT)

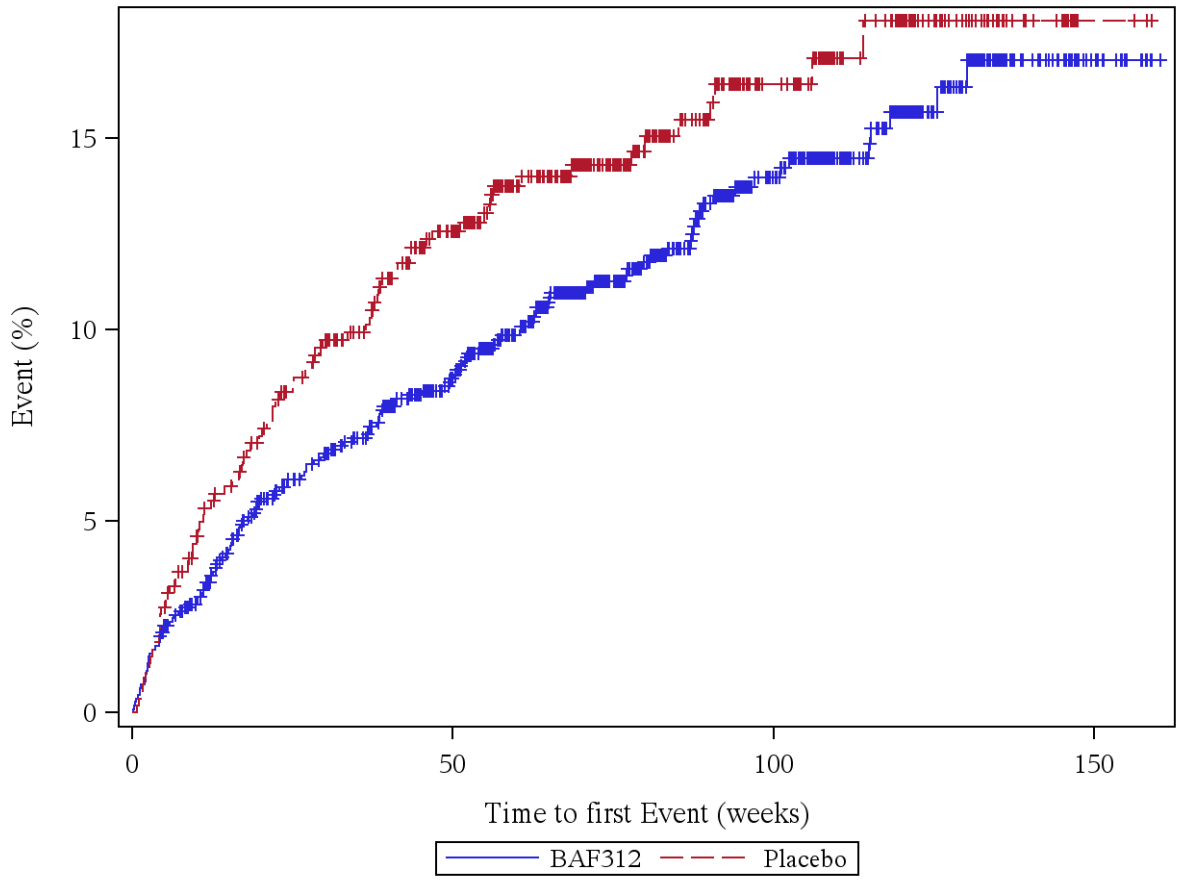


Patients at risk (BAF312/Placebo): Week 0: 1099/546, Week 4: 1088/545, Week 12: 1042/527, Week 24: 988/501, Week 36: 951/475, Week 48: 877/435, Week 60: 771/360, Week 72: 609/281, Week 84: 474/214, Week 96: 363/157, Week 108: 265/109, Week 120: 181/69, Week 132: 101/36, Week 144: 47/17, Week 156: 10/5, Week 168: 0/0

Log rank test: p-value = 0,682
*: p < 0,05

Analysis population: A2304 SAF total population

Figure 12.1.3.47: URINARY TRACT INFECTION (PT)

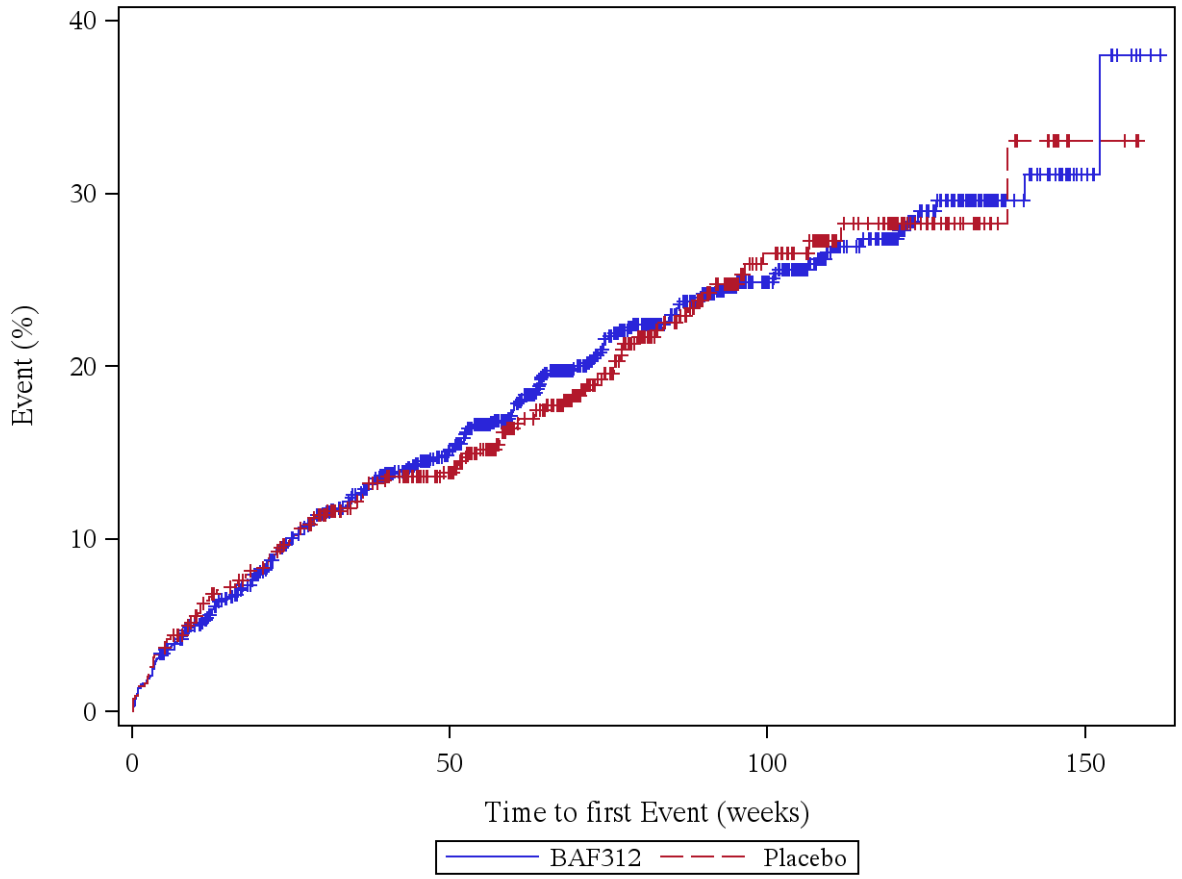


Patients at risk (BAF312/Placebo): Week 0: 1099/546, Week 4: 1080/536, Week 12: 1024/506, Week 24: 958/477, Week 36: 921/451, Week 48: 852/406, Week 60: 744/340, Week 72: 595/263, Week 84: 467/198, Week 96: 362/144, Week 108: 264/106, Week 120: 180/67, Week 132: 99/32, Week 144: 42/15, Week 156: 8/3, Week 168: 0/0

Log rank test: p-value = 0,106
*: p < 0,05

Analysis population: A2304 SAF total population

Figure 12.1.3.48: INJURY, POISONING AND PROCEDURAL COMPLICATIONS (SOC)

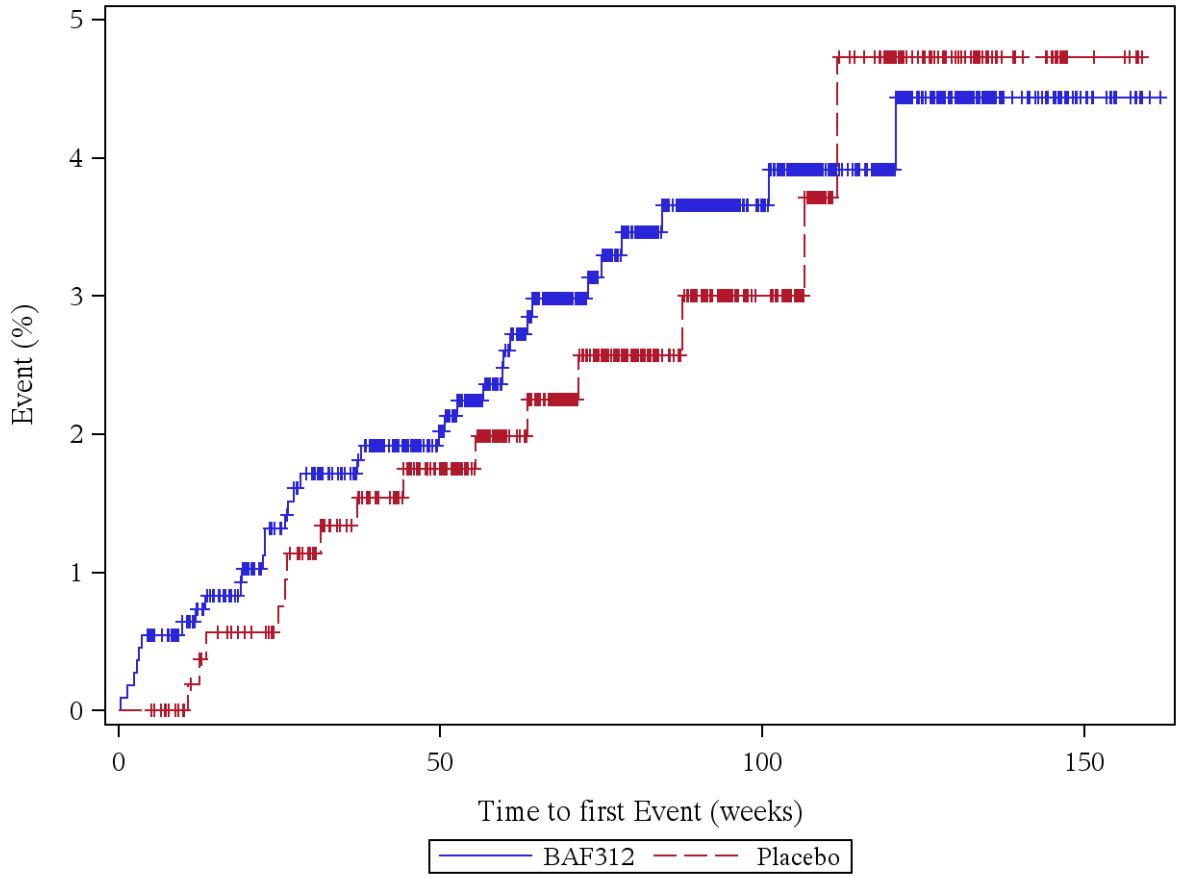


Patients at risk (BAF312/Placebo): Week 0: 1099/546, Week 4: 1065/528, Week 12: 999/501, Week 24: 919/472, Week 36: 863/435, Week 48: 787/401, Week 60: 676/329, Week 72: 520/251, Week 84: 402/185, Week 96: 315/130, Week 108: 225/88, Week 120: 151/53, Week 132: 86/26, Week 144: 39/12, Week 156: 6/3, Week 168: 0/0

Log rank test: p-value = 0,844
*: p < 0,05

Analysis population: A2304 SAF total population

Figure 12.1.3.49: CONTUSION (PT)

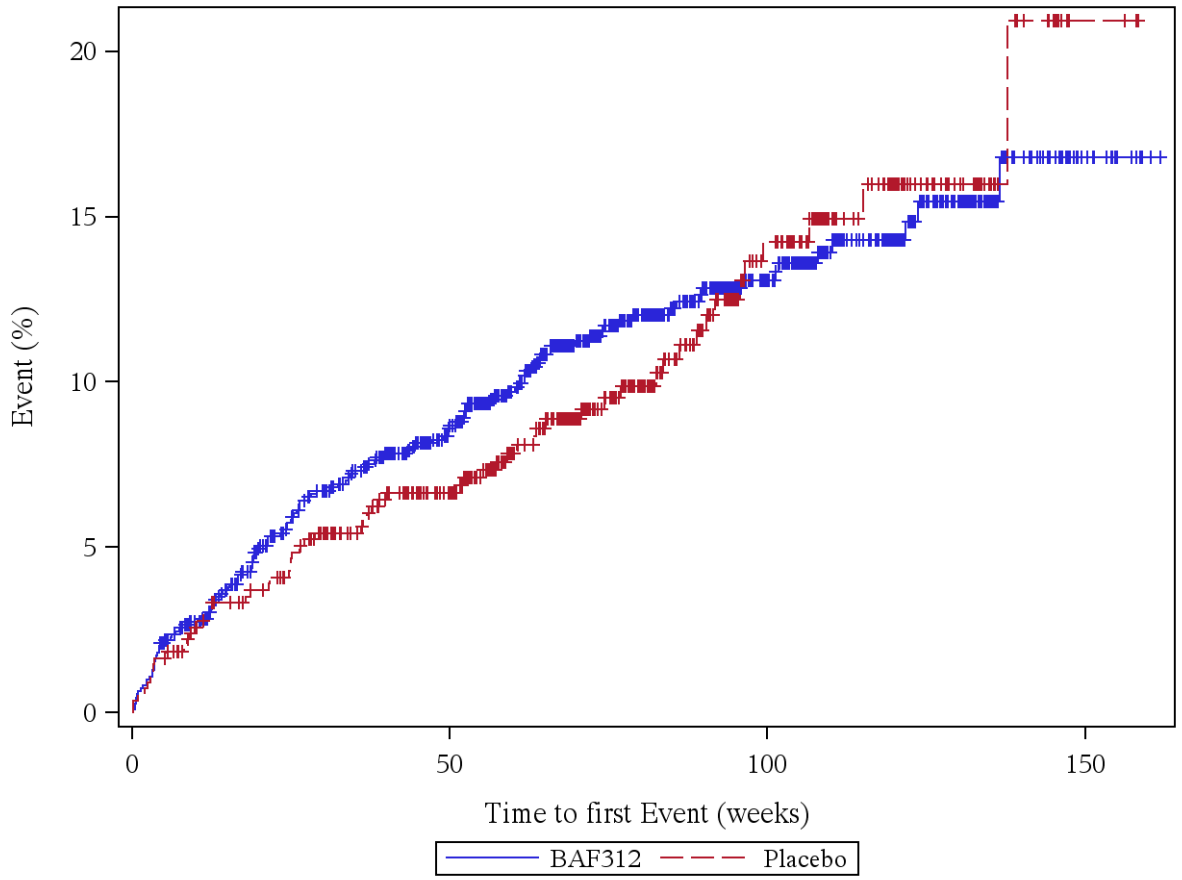


Patients at risk (BAF312/Placebo): Week 0: 1099/546, Week 4: 1093/546, Week 12: 1051/534, Week 24: 1005/518, Week 36: 975/490, Week 48: 910/454, Week 60: 800/383, Week 72: 635/300, Week 84: 501/232, Week 96: 390/170, Week 108: 282/120, Week 120: 193/74, Week 132: 109/38, Week 144: 50/19, Week 156: 9/5, Week 168: 0/0

Log rank test: p-value = 0,663
*: p < 0,05

Analysis population: A2304 SAF total population

Figure 12.1.3.50: FALL (PT)

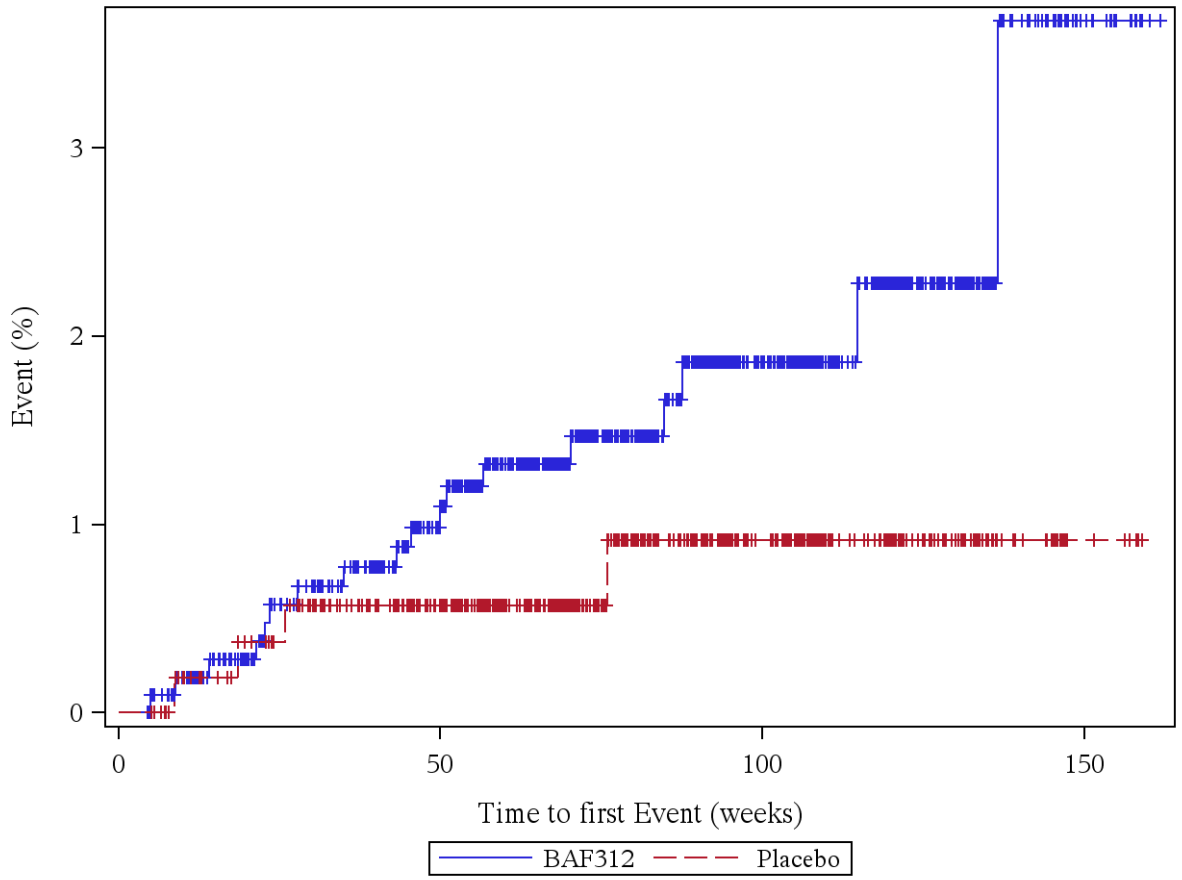


Patients at risk (BAF312/Placebo): Week 0: 1099/546, Week 4: 1079/537, Week 12: 1027/519, Week 24: 962/500, Week 36: 917/469, Week 48: 848/433, Week 60: 740/361, Week 72: 580/280, Week 84: 458/212, Week 96: 359/153, Week 108: 259/106, Week 120: 177/63, Week 132: 100/32, Week 144: 44/13, Week 156: 8/3, Week 168: 0/0

Log rank test: p-value = 0,674
*: p < 0,05

Analysis population: A2304 SAF total population

Figure 12.1.3.51: LACERATION (PT)

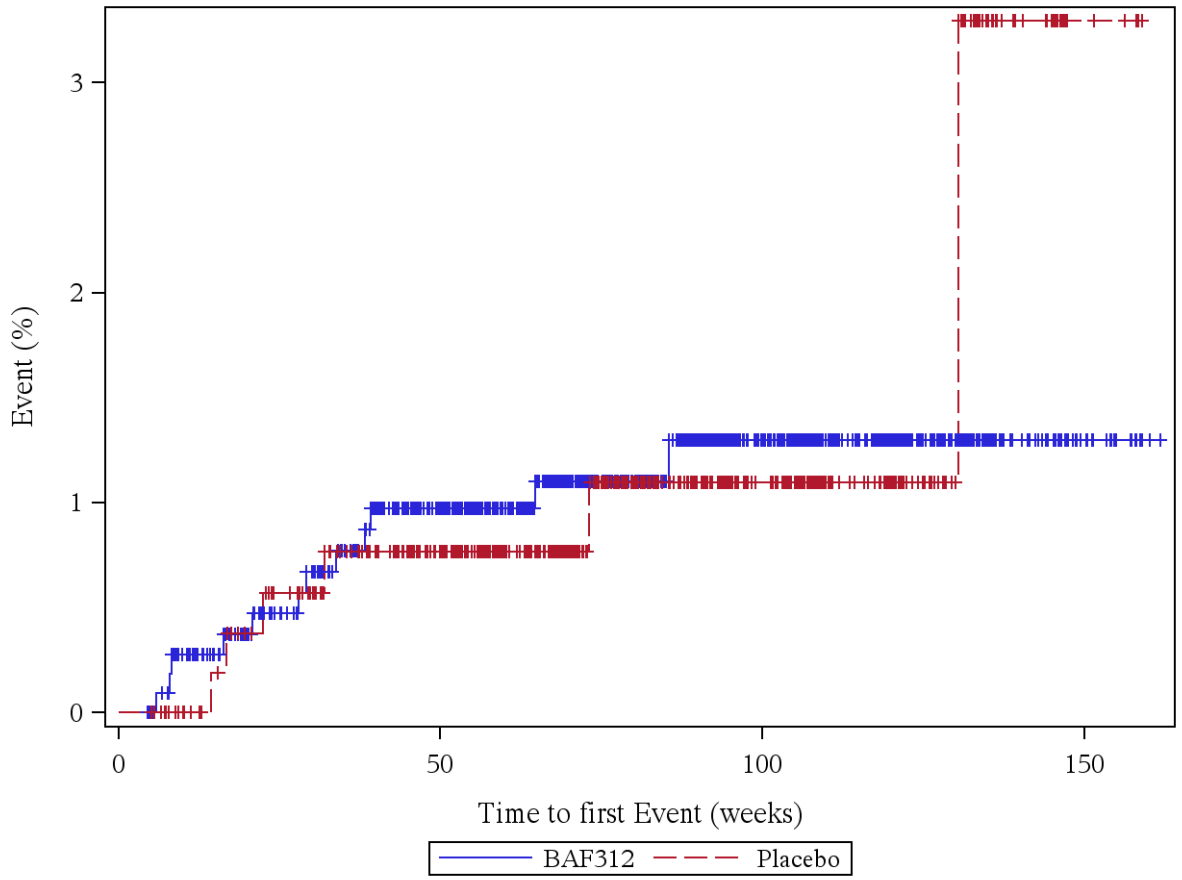


Patients at risk (BAF312/Placebo): Week 0: 1099/546, Week 4: 1099/546, Week 12: 1057/534, Week 24: 1011/519, Week 36: 982/494, Week 48: 915/458, Week 60: 806/386, Week 72: 642/304, Week 84: 507/236, Week 96: 394/176, Week 108: 287/126, Week 120: 195/80, Week 132: 110/40, Week 144: 49/20, Week 156: 9/5, Week 168: 0/0

Log rank test: p-value = 0,147
*: p < 0,05

Analysis population: A2304 SAF total population

Figure 12.1.3.52: LIGAMENT SPRAIN (PT)

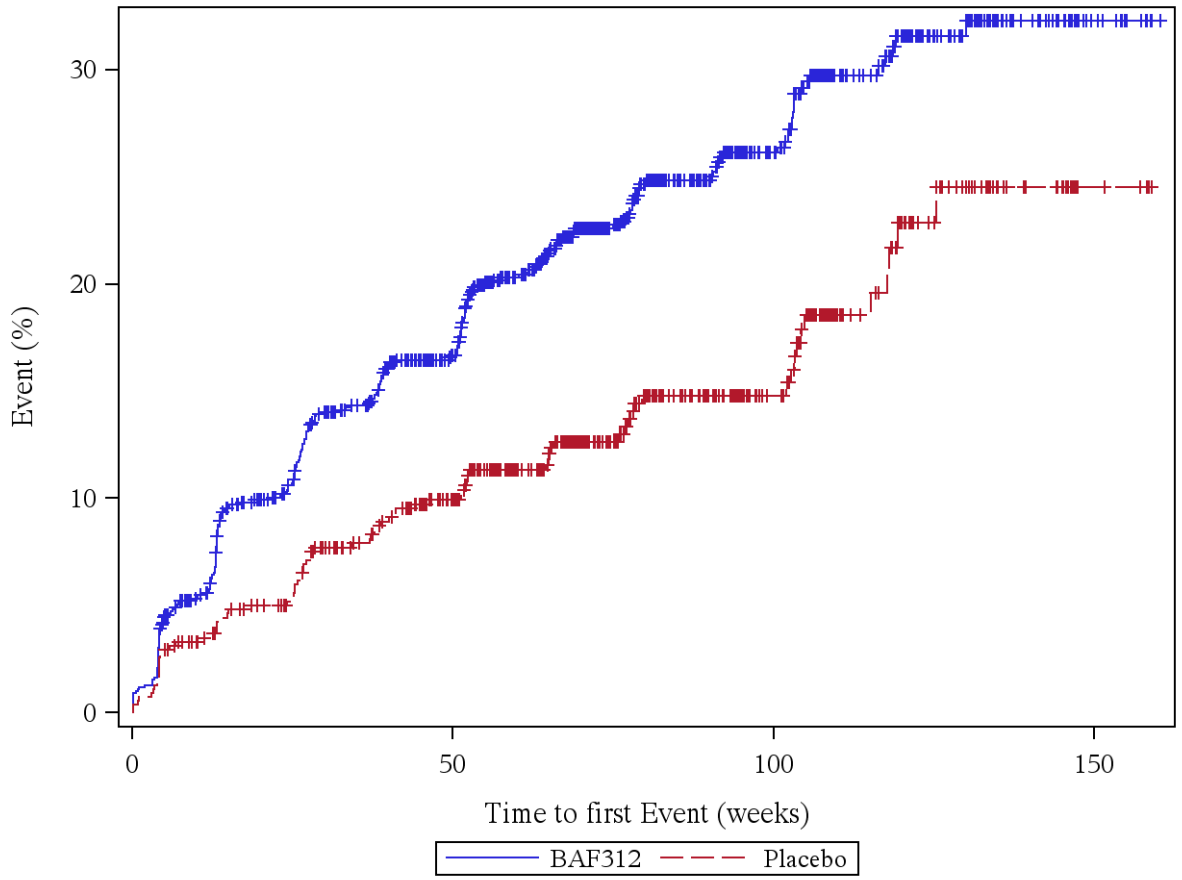


Patients at risk (BAF312/Placebo): Week 0: 1099/546, Week 4: 1099/546, Week 12: 1056/535, Week 24: 1012/518, Week 36: 982/493, Week 48: 916/457, Week 60: 810/384, Week 72: 644/303, Week 84: 510/234, Week 96: 395/173, Week 108: 289/123, Week 120: 198/78, Week 132: 112/39, Week 144: 50/19, Week 156: 9/4, Week 168: 0/0

Log rank test: p-value = 0,972
*: p < 0,05

Analysis population: A2304 SAF total population

Figure 12.1.3.53: INVESTIGATIONS (SOC)

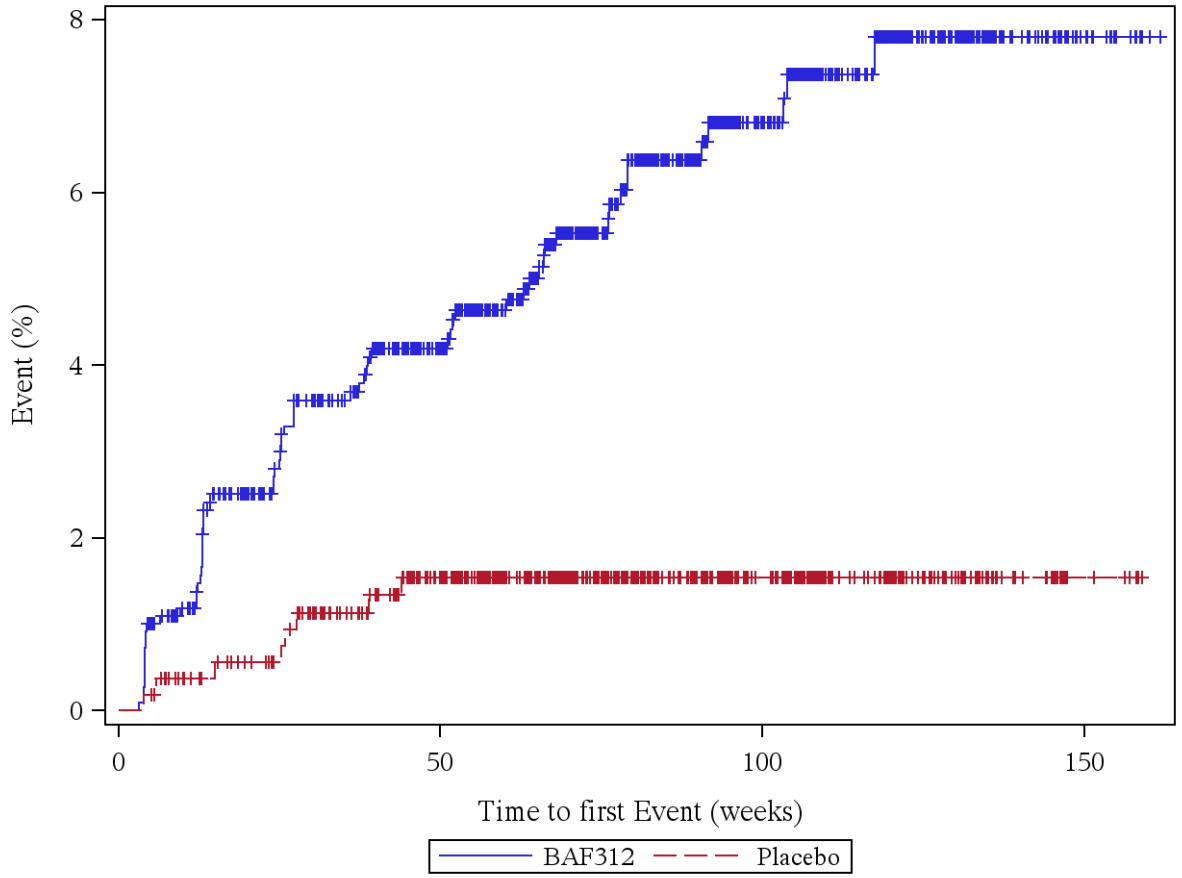


Patients at risk (BAF312/Placebo): Week 0: 1099/546, Week 4: 1066/538, Week 12: 1003/515, Week 24: 920/494, Week 36: 857/458, Week 48: 781/418, Week 60: 657/348, Week 72: 498/269, Week 84: 381/203, Week 96: 291/155, Week 108: 200/105, Week 120: 135/59, Week 132: 79/31, Week 144: 35/17, Week 156: 8/4, Week 168: 0/0

Log rank test: p-value = <0,001 *
*: p < 0,05

Analysis population: A2304 SAF total population

Figure 12.1.3.54: ALANINE AMINOTRANSFERASE INCREASED (PT)

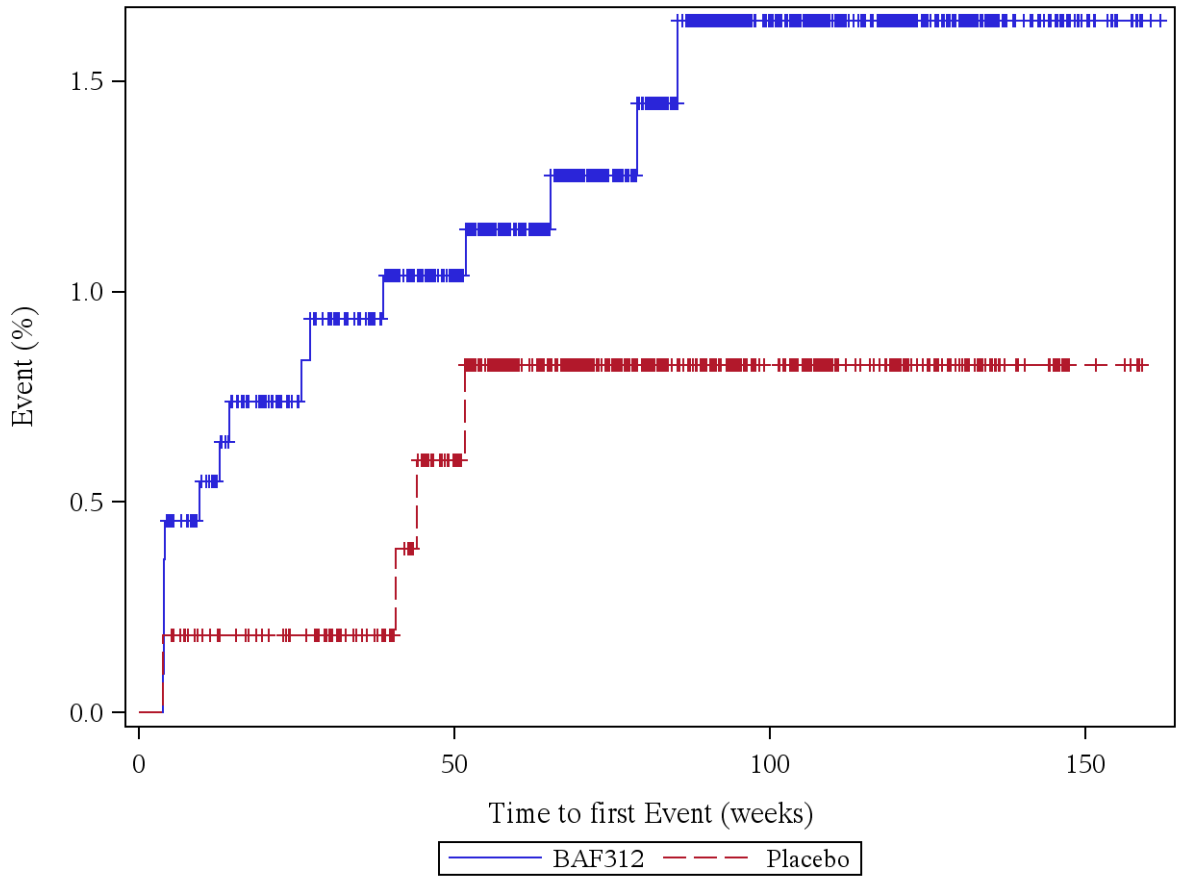


Patients at risk (BAF312/Placebo): Week 0: 1099/546, Week 4: 1091/545, Week 12: 1049/533, Week 24: 995/518, Week 36: 959/492, Week 48: 889/454, Week 60: 783/382, Week 72: 617/301, Week 84: 481/233, Week 96: 370/175, Week 108: 266/125, Week 120: 186/79, Week 132: 107/39, Week 144: 47/20, Week 156: 9/5, Week 168: 0/0

Log rank test: p-value = <0,001 *
*: p < 0,05

Analysis population: A2304 SAF total population

Figure 12.1.3.55: ASPARTATE AMINOTRANSFERASE INCREASED (PT)

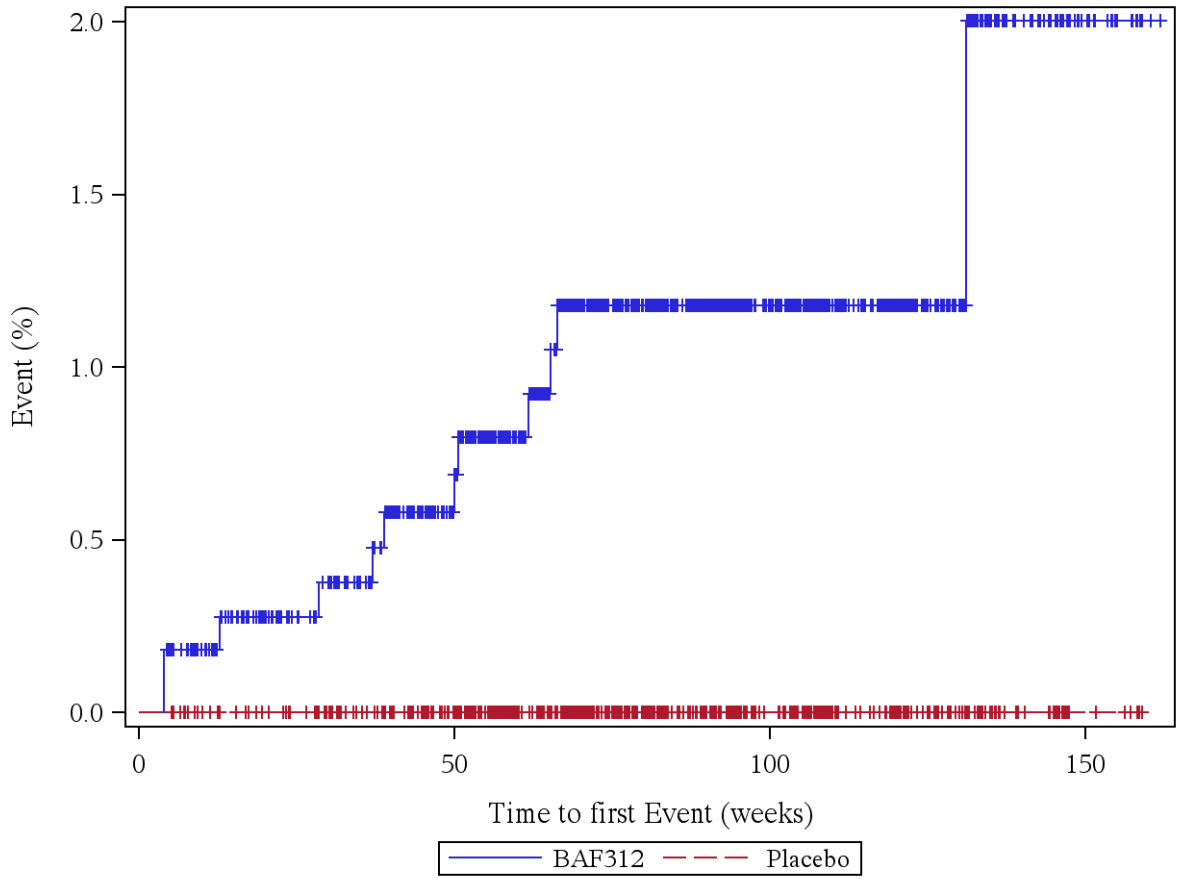


Patients at risk (BAF312/Placebo): Week 0: 1099/546, Week 4: 1095/545, Week 12: 1055/534, Week 24: 1012/520, Week 36: 985/497, Week 48: 919/459, Week 60: 812/386, Week 72: 646/304, Week 84: 509/236, Week 96: 394/175, Week 108: 287/125, Week 120: 197/79, Week 132: 113/40, Week 144: 51/20, Week 156: 10/5, Week 168: 0/0

Log rank test: p-value = 0,263
*: p < 0,05

Analysis population: A2304 SAF total population

Figure 12.1.3.56: BLOOD ALKALINE PHOSPHATASE INCREASED (PT)

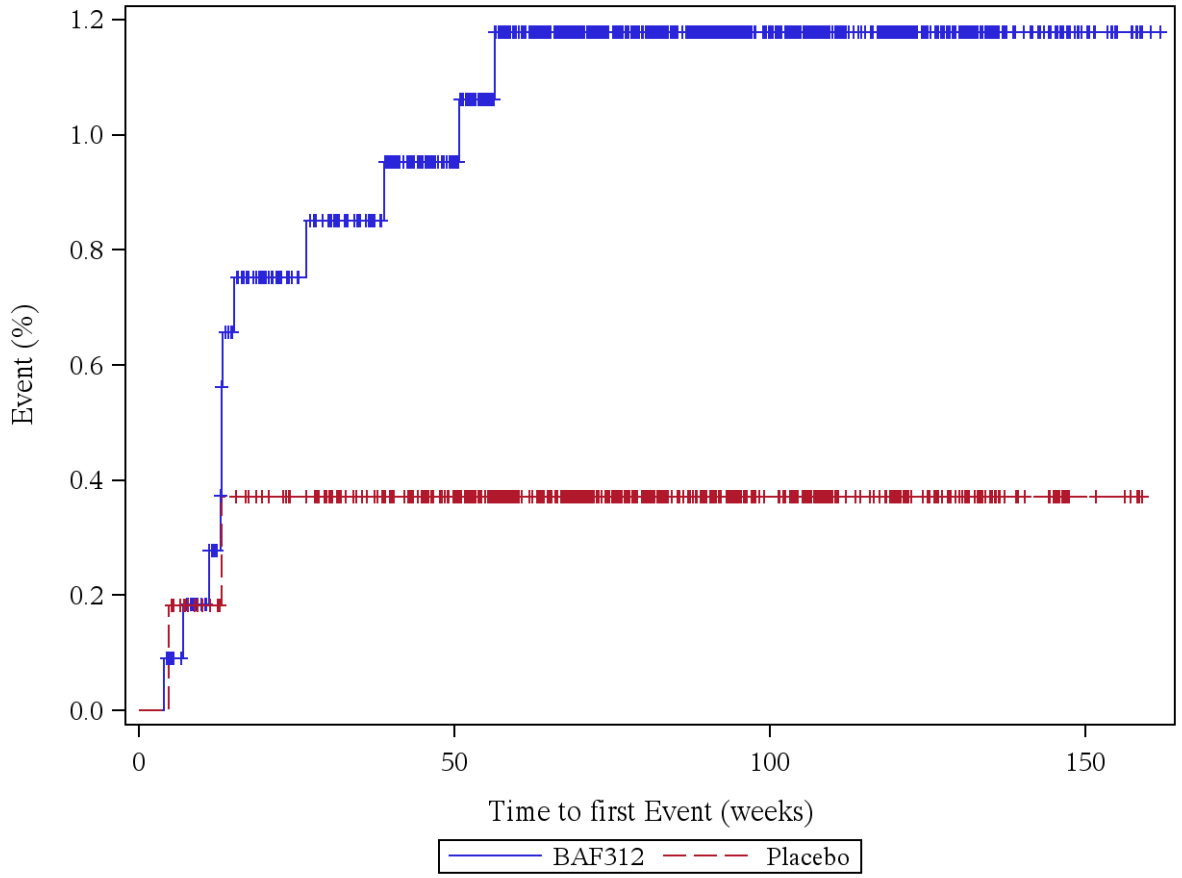


Patients at risk (BAF312/Placebo): Week 0: 1099/546, Week 4: 1097/546, Week 12: 1057/535, Week 24: 1014/521, Week 36: 987/497, Week 48: 920/461, Week 60: 812/388, Week 72: 645/305, Week 84: 511/237, Week 96: 395/176, Week 108: 289/126, Week 120: 198/80, Week 132: 111/40, Week 144: 50/20, Week 156: 10/5, Week 168: 0/0

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

Analysis population: A2304 SAF total population

Figure 12.1.3.57: BLOOD BILIRUBIN INCREASED (PT)

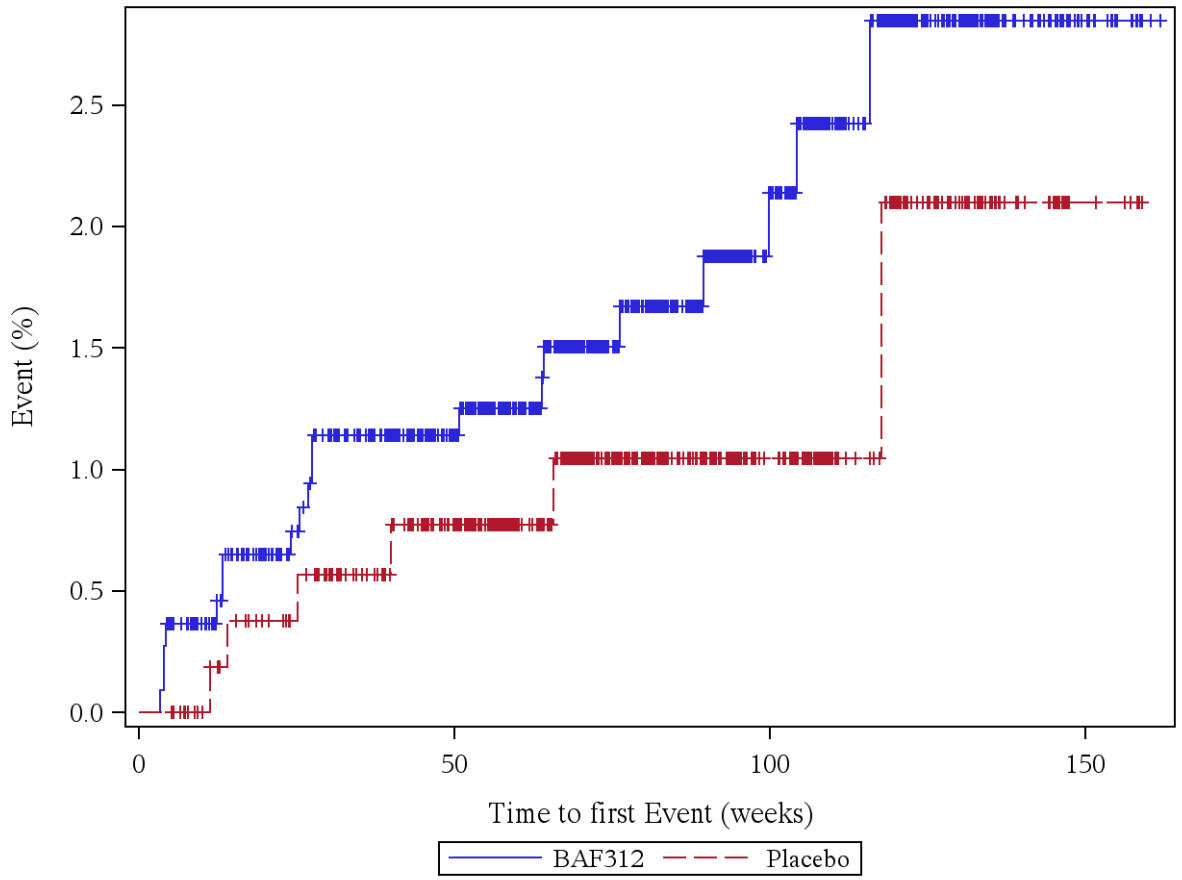


Patients at risk (BAF312/Placebo): Week 0: 1099/546, Week 4: 1098/546, Week 12: 1056/534, Week 24: 1010/519, Week 36: 983/495, Week 48: 918/459, Week 60: 810/386, Week 72: 646/303, Week 84: 511/235, Week 96: 396/174, Week 108: 287/125, Week 120: 198/79, Week 132: 111/40, Week 144: 50/20, Week 156: 10/5, Week 168: 0/0

Log rank test: p-value = 0,129
*: p < 0,05

Analysis population: A2304 SAF total population

Figure 12.1.3.58: BLOOD CHOLESTEROL INCREASED (PT)

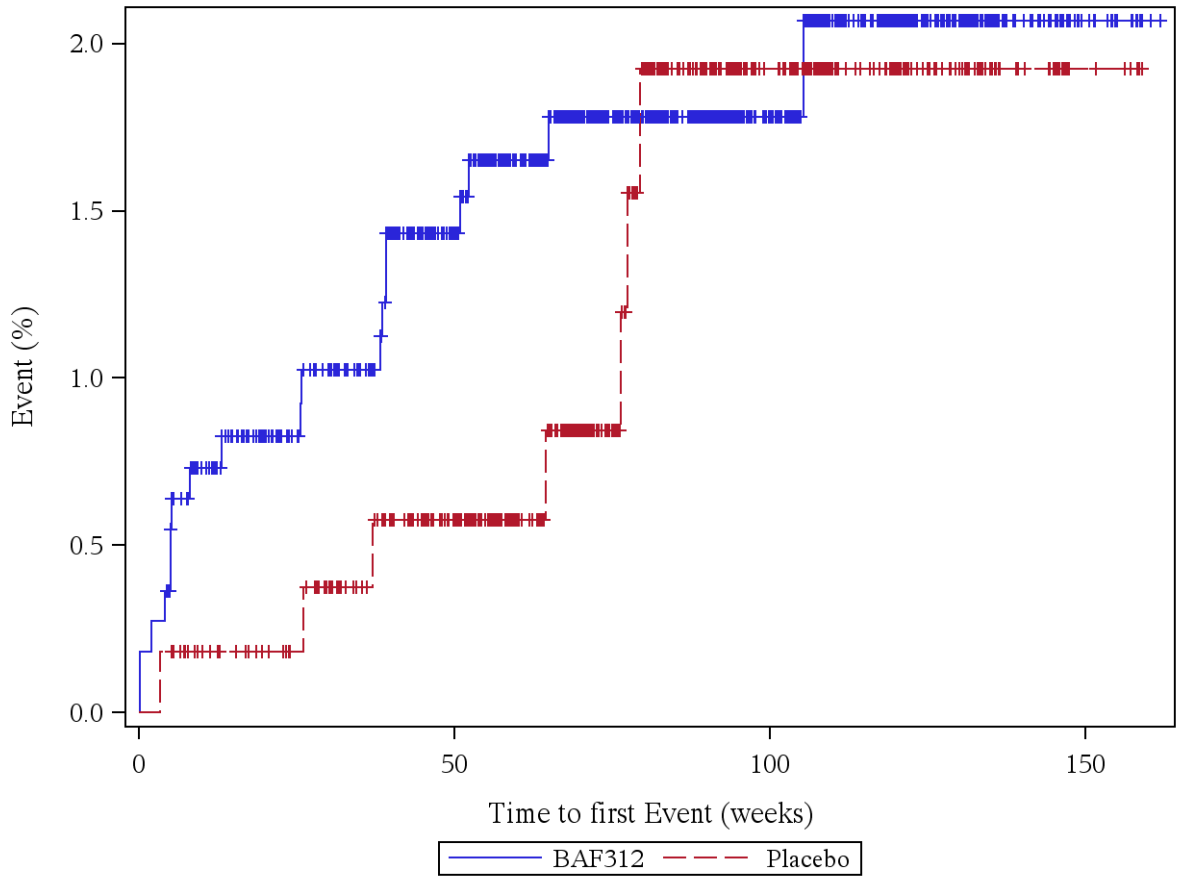


Patients at risk (BAF312/Placebo): Week 0: 1099/546, Week 4: 1096/546, Week 12: 1055/534, Week 24: 1010/519, Week 36: 978/494, Week 48: 914/457, Week 60: 807/385, Week 72: 639/301, Week 84: 506/234, Week 96: 391/175, Week 108: 283/125, Week 120: 193/79, Week 132: 111/40, Week 144: 50/20, Week 156: 10/5, Week 168: 0/0

Log rank test: p-value = 0,290
*: p < 0,05

Analysis population: A2304 SAF total population

Figure 12.1.3.59: BLOOD PRESSURE INCREASED (PT)

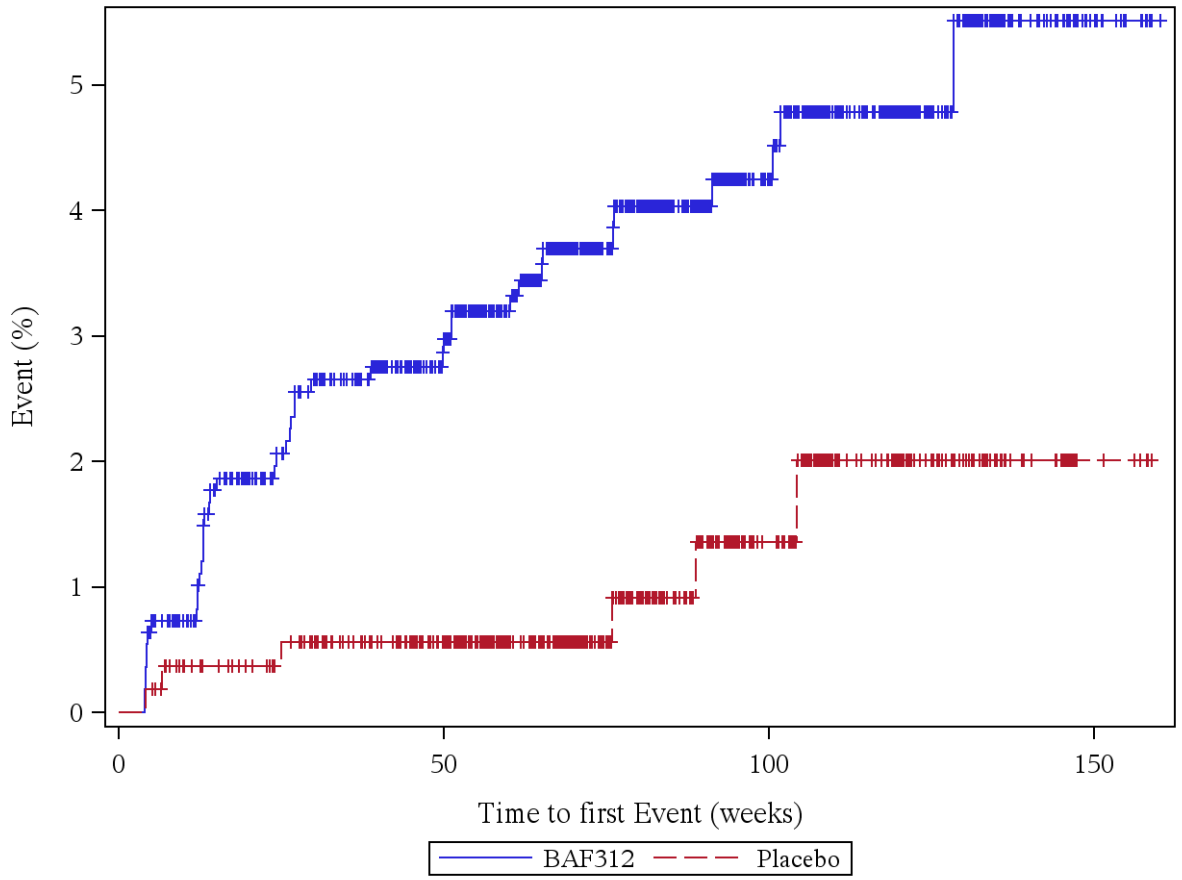


Patients at risk (BAF312/Placebo): Week 0: 1099/546, Week 4: 1096/545, Week 12: 1053/534, Week 24: 1010/520, Week 36: 981/495, Week 48: 912/458, Week 60: 804/386, Week 72: 639/303, Week 84: 506/232, Week 96: 396/171, Week 108: 286/122, Week 120: 197/76, Week 132: 110/39, Week 144: 50/20, Week 156: 10/5, Week 168: 0/0

Log rank test: p-value = 0,503
*: p < 0,05

Analysis population: A2304 SAF total population

Figure 12.1.3.60: GAMMA-GLUTAMYLTRANSFERASE INCREASED (PT)

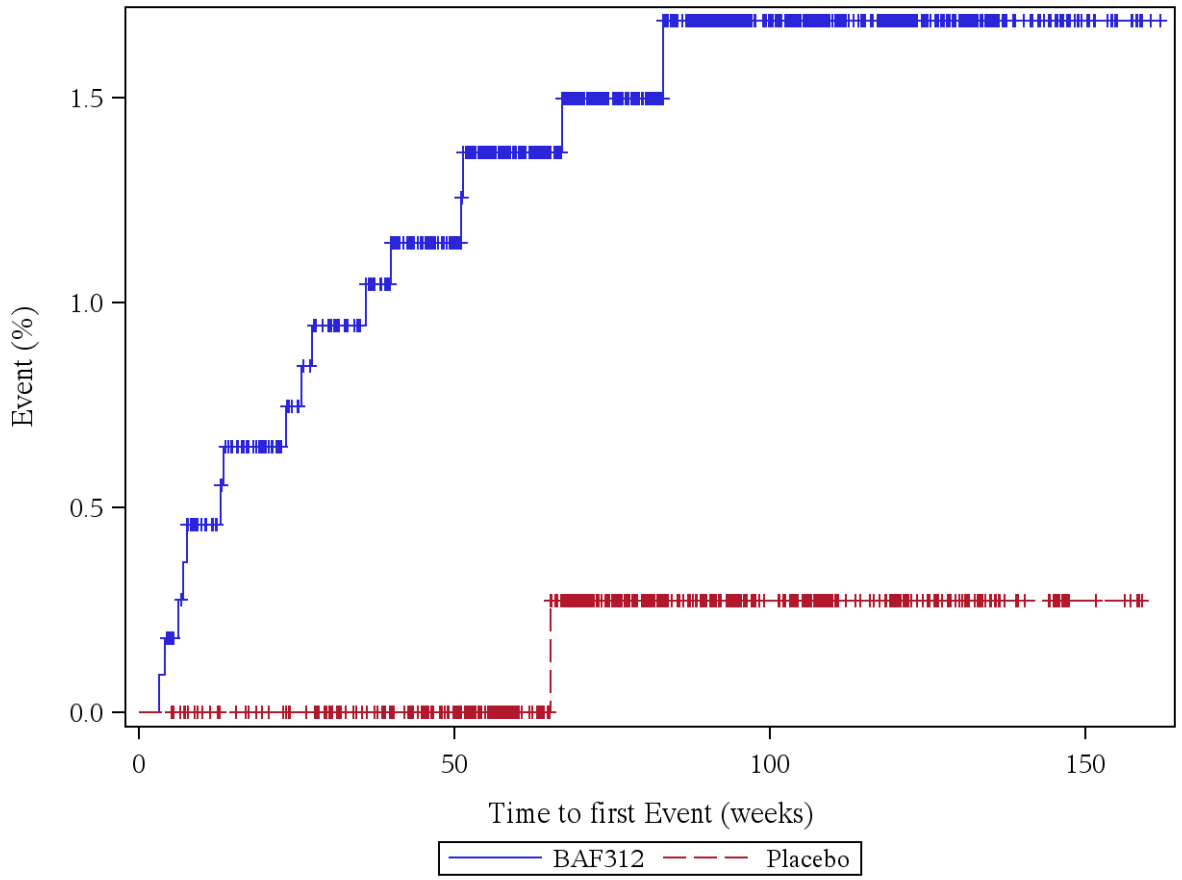


Patients at risk (BAF312/Placebo): Week 0: 1099/546, Week 4: 1097/546, Week 12: 1050/533, Week 24: 997/519, Week 36: 965/494, Week 48: 900/459, Week 60: 791/386, Week 72: 625/303, Week 84: 488/234, Week 96: 379/175, Week 108: 274/125, Week 120: 187/79, Week 132: 106/40, Week 144: 46/20, Week 156: 9/5, Week 168: 0/0

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

Analysis population: A2304 SAF total population

Figure 12.1.3.61: HEPATIC ENZYME INCREASED (PT)

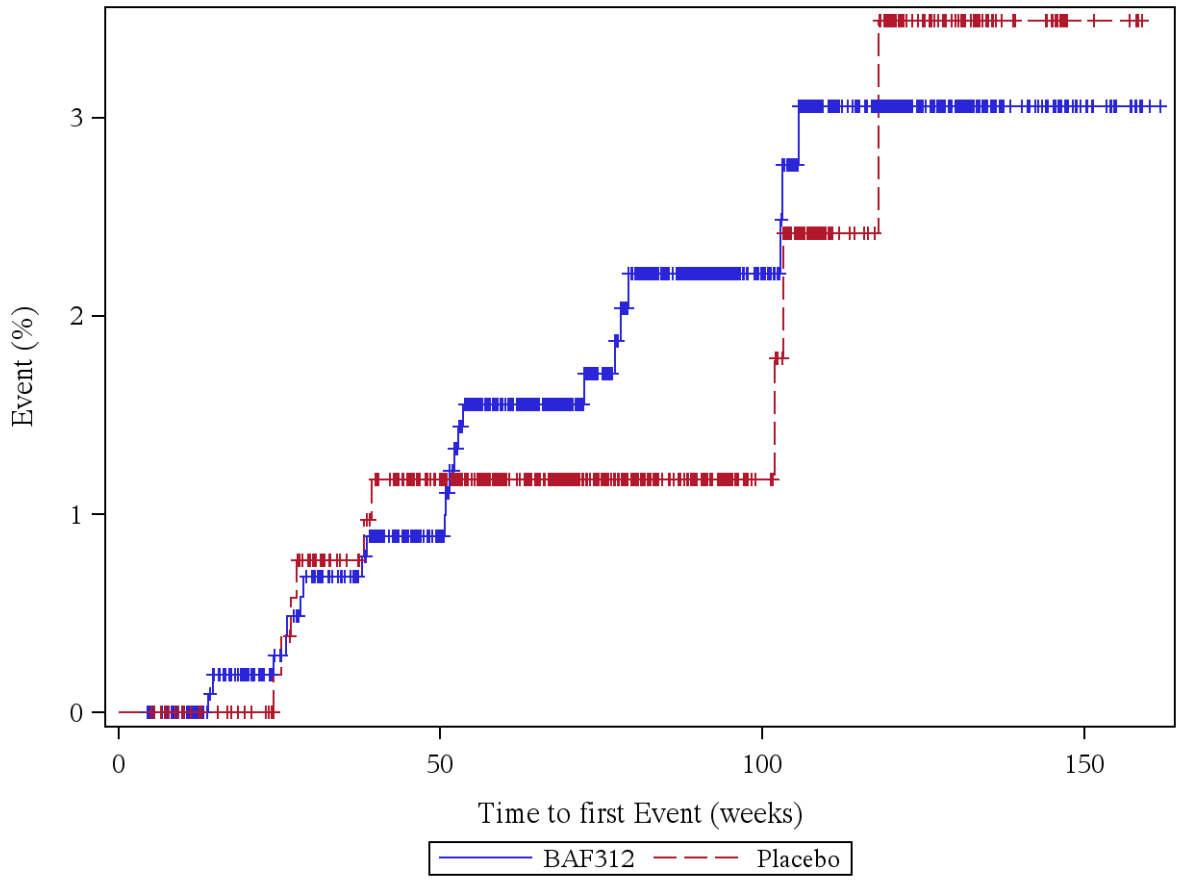


Patients at risk (BAF312/Placebo): Week 0: 1099/546, Week 4: 1098/546, Week 12: 1056/535, Week 24: 1011/521, Week 36: 981/497, Week 48: 916/461, Week 60: 809/388, Week 72: 642/304, Week 84: 506/236, Week 96: 393/175, Week 108: 285/125, Week 120: 196/79, Week 132: 112/39, Week 144: 51/20, Week 156: 10/5, Week 168: 0/0

Log rank test: p-value = 0,017 *
*: p < 0,05

Analysis population: A2304 SAF total population

Figure 12.1.3.62: WEIGHT DECREASED (PT)

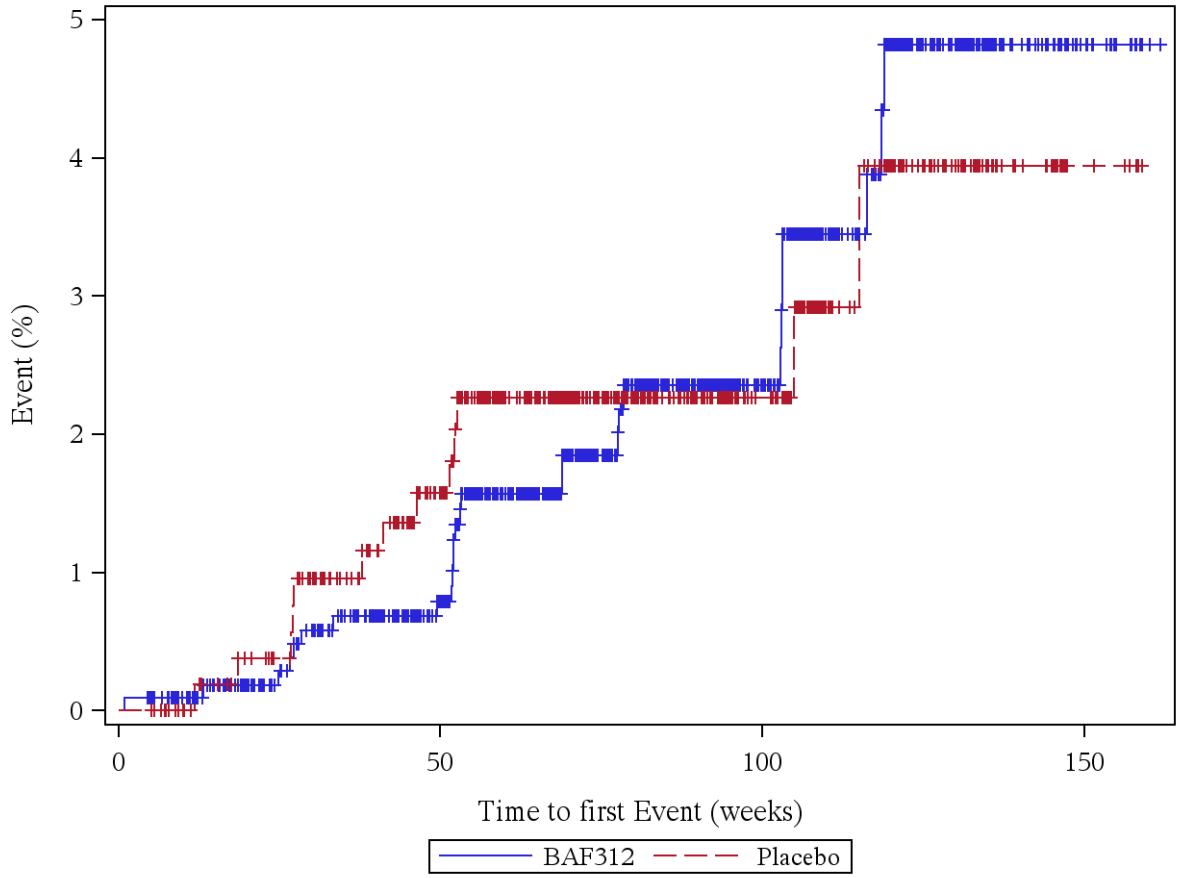


Patients at risk (BAF312/Placebo): Week 0: 1099/546, Week 4: 1099/546, Week 12: 1059/535, Week 24: 1015/521, Week 36: 984/493, Week 48: 918/458, Week 60: 805/386, Week 72: 642/303, Week 84: 505/236, Week 96: 391/175, Week 108: 280/123, Week 120: 191/76, Week 132: 109/36, Week 144: 50/18, Week 156: 10/4, Week 168: 0/0

Log rank test: p-value = 0,661
*: p < 0,05

Analysis population: A2304 SAF total population

Figure 12.1.3.63: WEIGHT INCREASED (PT)

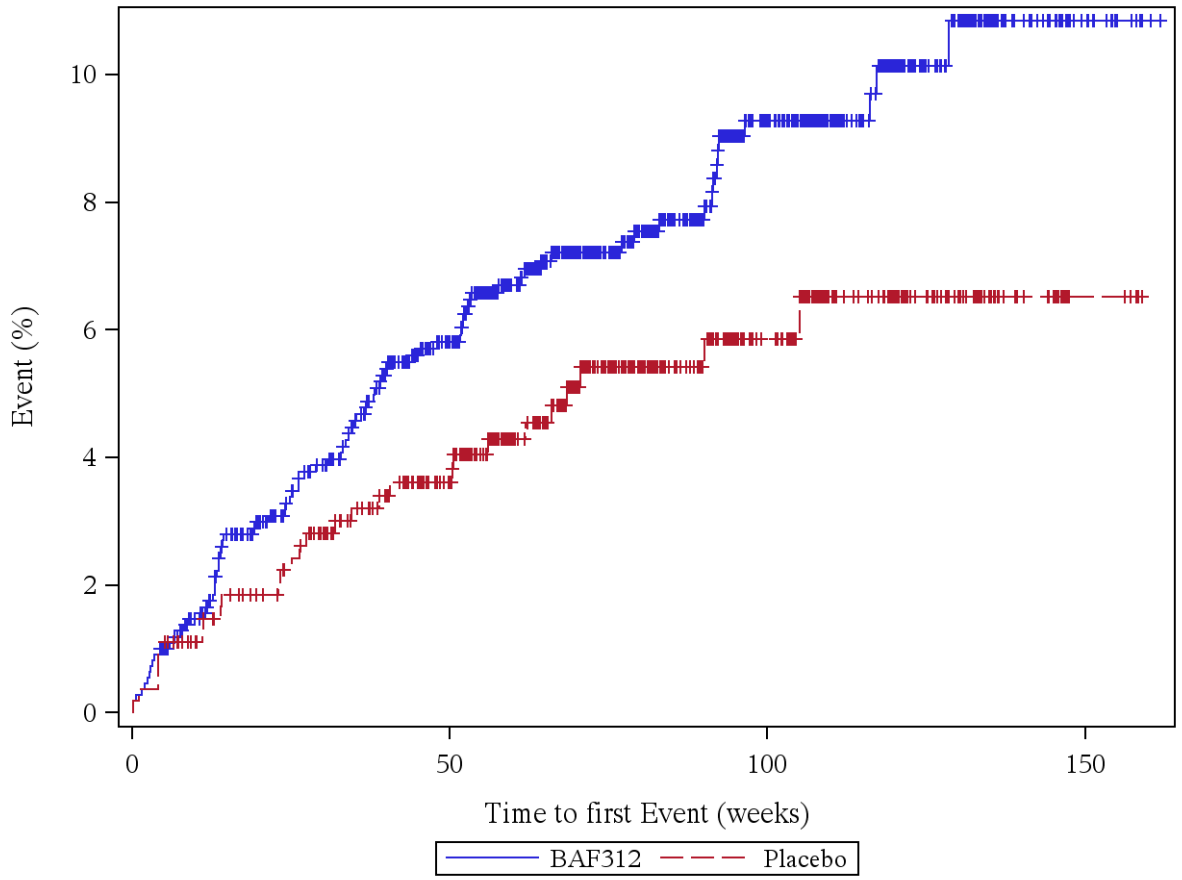


Patients at risk (BAF312/Placebo): Week 0: 1099/546, Week 4: 1098/546, Week 12: 1058/534, Week 24: 1015/519, Week 36: 983/492, Week 48: 918/454, Week 60: 805/380, Week 72: 637/299, Week 84: 502/233, Week 96: 389/173, Week 108: 279/123, Week 120: 188/77, Week 132: 107/40, Week 144: 49/20, Week 156: 10/5, Week 168: 0/0

Log rank test: p-value = 0,982
*: p < 0,05

Analysis population: A2304 SAF total population

Figure 12.1.3.64: METABOLISM AND NUTRITION DISORDERS (SOC)

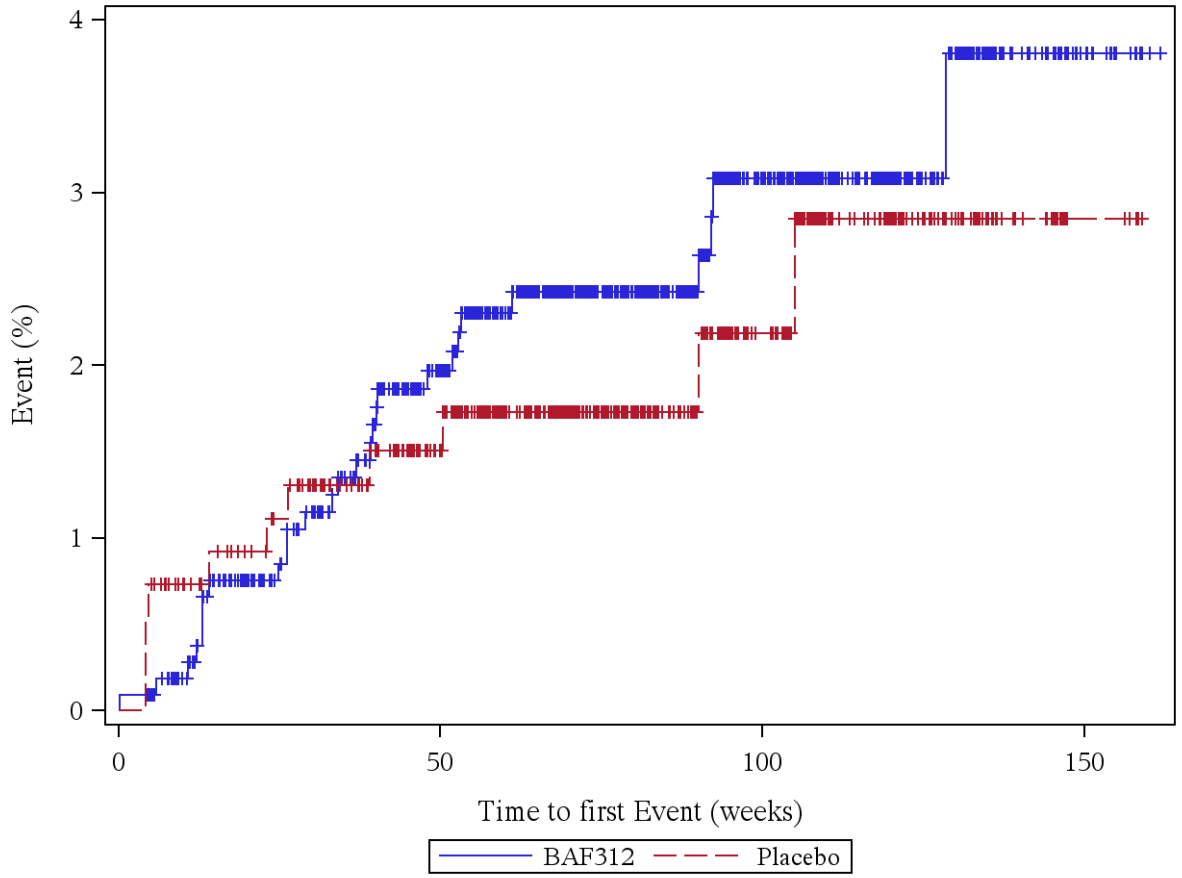


Patients at risk (BAF312/Placebo): Week 0: 1099/546, Week 4: 1089/544, Week 12: 1041/527, Week 24: 986/511, Week 36: 944/484, Week 48: 875/450, Week 60: 765/377, Week 72: 605/293, Week 84: 477/227, Week 96: 365/168, Week 108: 268/120, Week 120: 179/75, Week 132: 102/39, Week 144: 45/19, Week 156: 9/5, Week 168: 0/0

Log rank test: p-value = 0,054
*: p < 0,05

Analysis population: A2304 SAF total population

Figure 12.1.3.65: HYPERCHOLESTEROLAEMIA (PT)

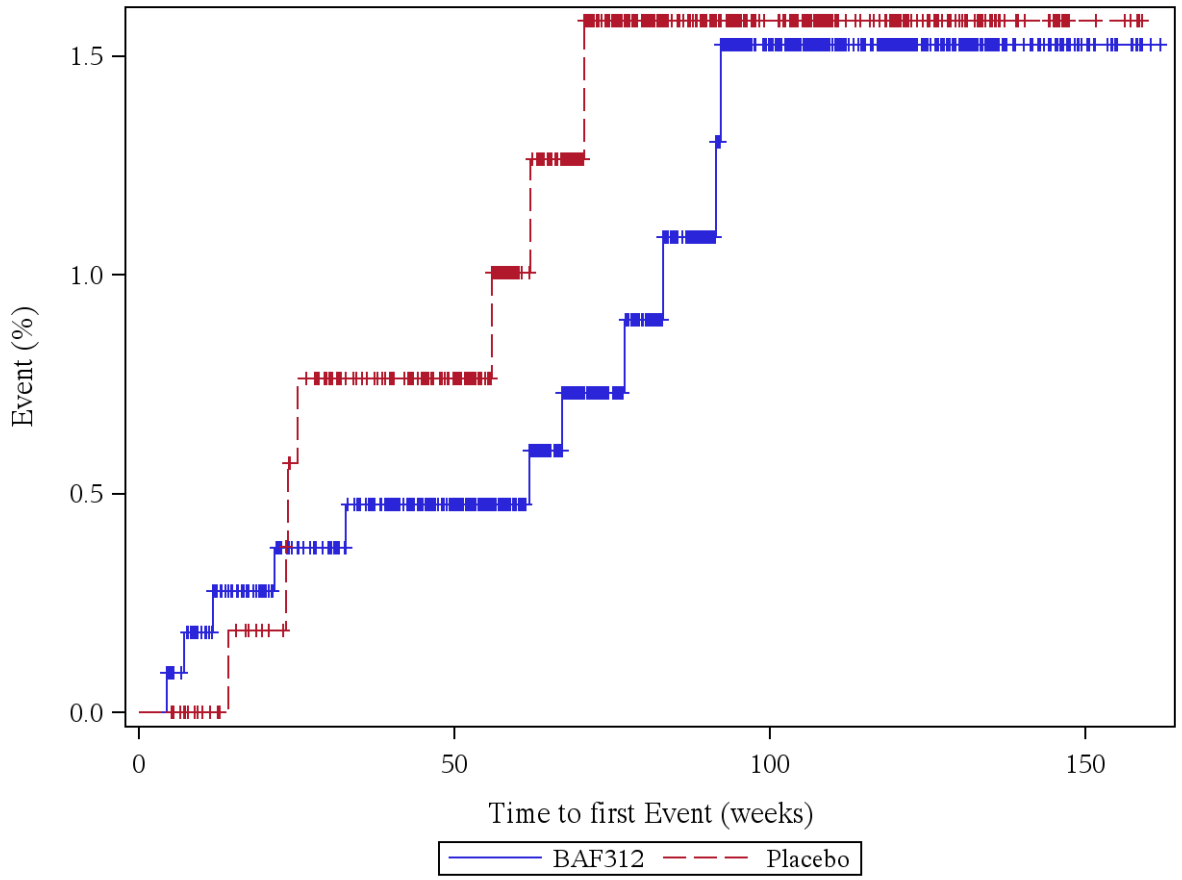


Patients at risk (BAF312/Placebo): Week 0: 1099/546, Week 4: 1098/546, Week 12: 1056/531, Week 24: 1009/516, Week 36: 976/493, Week 48: 906/457, Week 60: 797/384, Week 72: 635/301, Week 84: 502/233, Week 96: 387/172, Week 108: 280/124, Week 120: 190/78, Week 132: 109/39, Week 144: 50/19, Week 156: 9/5, Week 168: 0/0

Log rank test: p-value = 0,527
*: p < 0,05

Analysis population: A2304 SAF total population

Figure 12.1.3.66: VITAMIN D DEFICIENCY (PT)

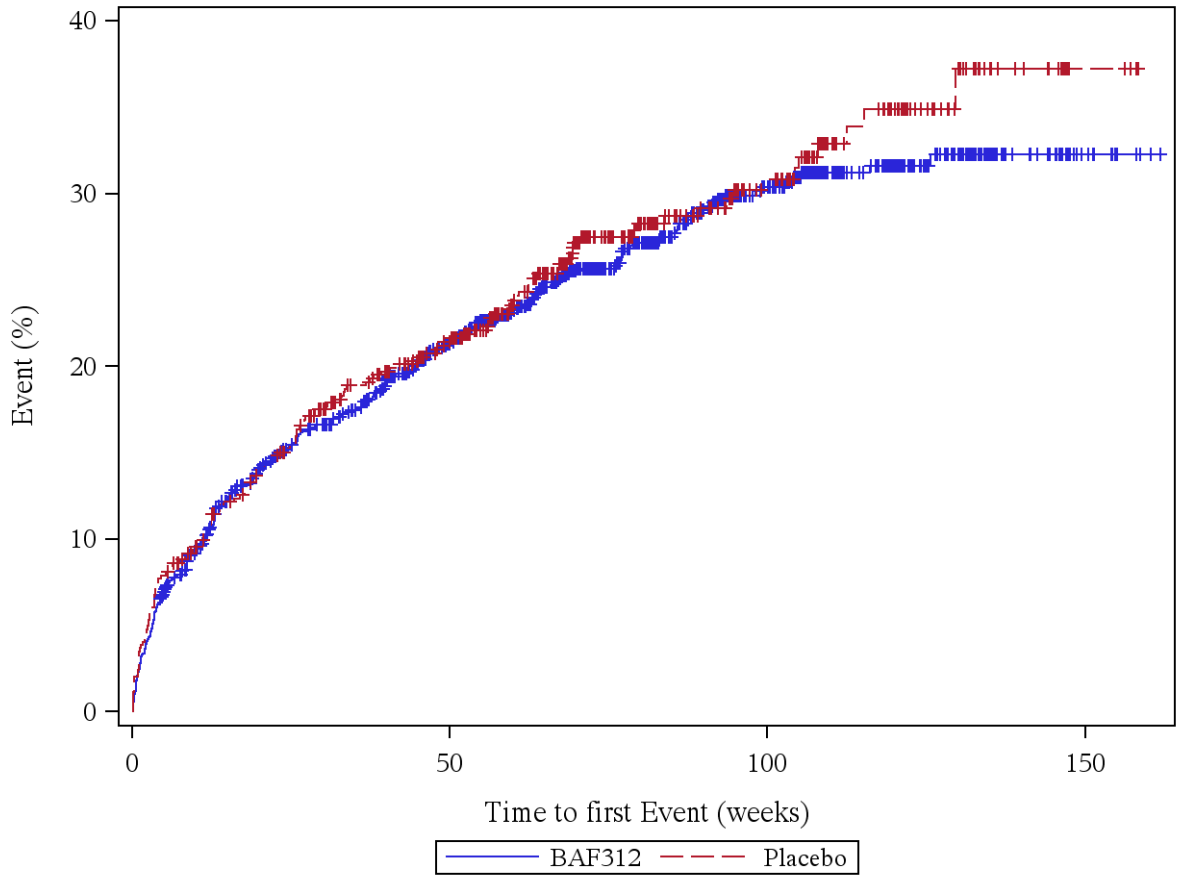


Patients at risk (BAF312/Placebo): Week 0: 1099/546, Week 4: 1099/546, Week 12: 1056/535, Week 24: 1013/518, Week 36: 985/493, Week 48: 921/458, Week 60: 814/385, Week 72: 646/301, Week 84: 511/235, Week 96: 393/174, Week 108: 289/124, Week 120: 199/78, Week 132: 112/40, Week 144: 51/20, Week 156: 10/5, Week 168: 0/0

Log rank test: p-value = 0,579
*: p < 0,05

Analysis population: A2304 SAF total population

Figure 12.1.3.67: MUSCULOSKELETAL AND CONNECTIVE TISSUE DISORDERS (SOC)

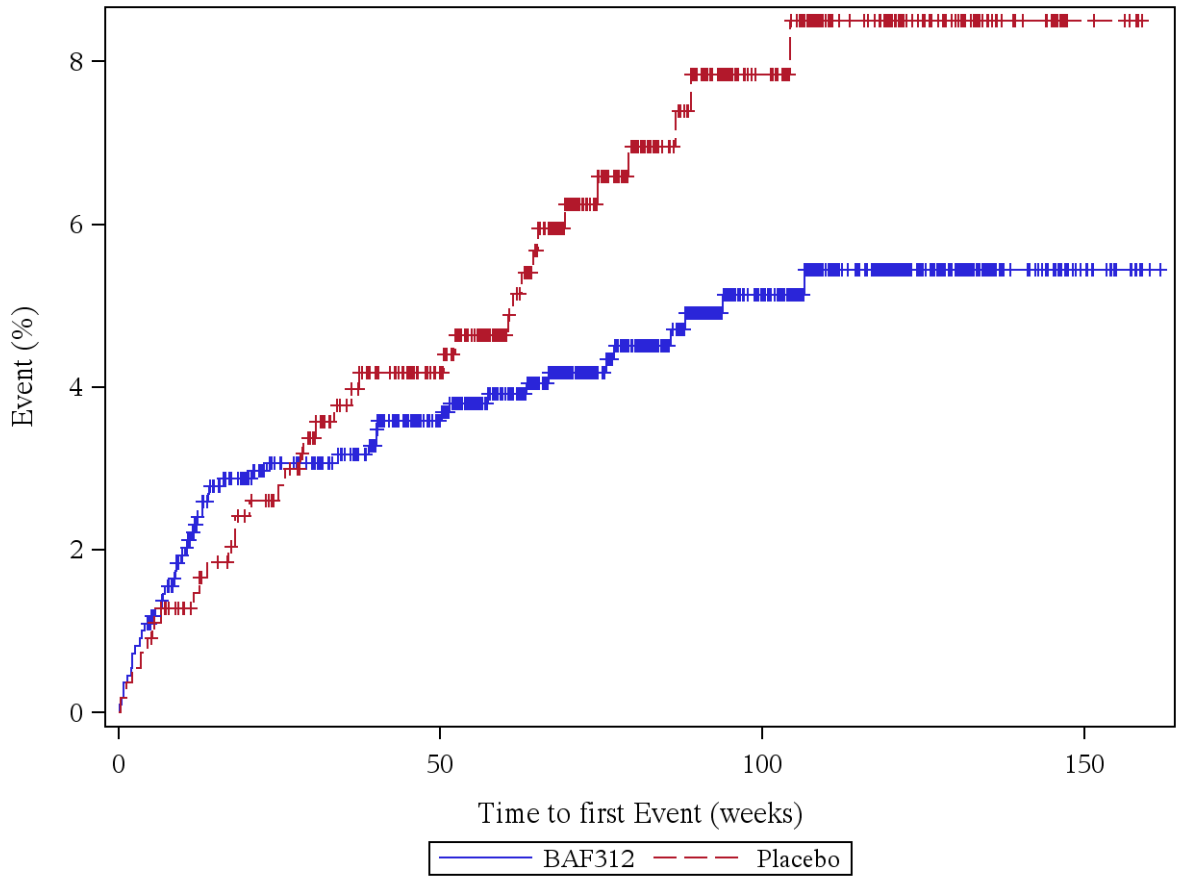


Patients at risk (BAF312/Placebo): Week 0: 1099/546, Week 4: 1031/506, Week 12: 952/479, Week 24: 864/444, Week 36: 818/404, Week 48: 732/367, Week 60: 634/297, Week 72: 486/211, Week 84: 386/162, Week 96: 294/125, Week 108: 209/87, Week 120: 142/53, Week 132: 82/23, Week 144: 39/12, Week 156: 7/4, Week 168: 0/0

Log rank test: p-value = 0,581
*: p < 0,05

Analysis population: A2304 SAF total population

Figure 12.1.3.68: ARTHRALGIA (PT)

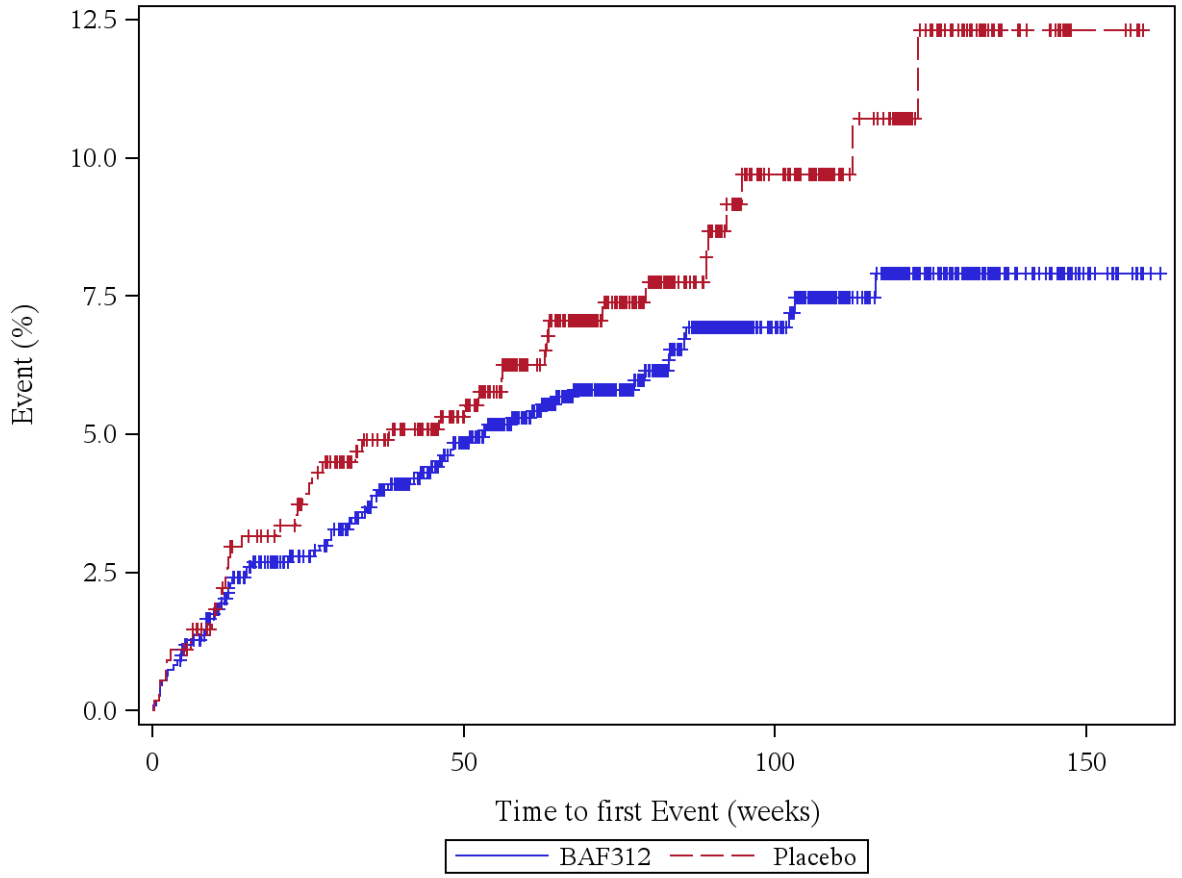


Patients at risk (BAF312/Placebo): Week 0: 1099/546, Week 4: 1087/542, Week 12: 1034/527, Week 24: 986/507, Week 36: 959/477, Week 48: 894/442, Week 60: 786/371, Week 72: 625/285, Week 84: 494/220, Week 96: 381/161, Week 108: 277/114, Week 120: 190/73, Week 132: 108/37, Week 144: 49/20, Week 156: 10/5, Week 168: 0/0

Log rank test: p-value = 0,088
*: p < 0,05

Analysis population: A2304 SAF total population

Figure 12.1.3.69: BACK PAIN (PT)

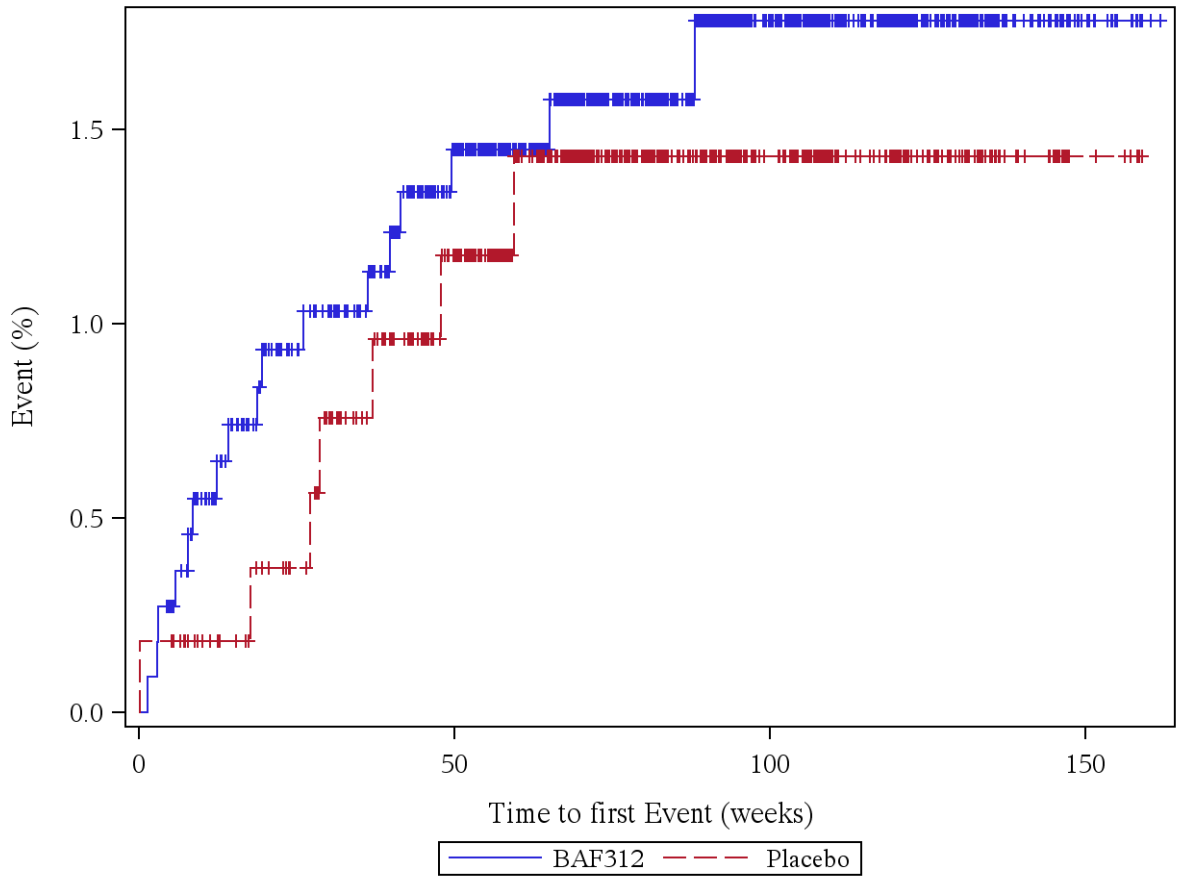


Patients at risk (BAF312/Placebo): Week 0: 1099/546, Week 4: 1089/540, Week 12: 1037/521, Week 24: 988/501, Week 36: 951/473, Week 48: 879/435, Week 60: 771/361, Week 72: 605/280, Week 84: 480/213, Week 96: 373/156, Week 108: 269/113, Week 120: 184/72, Week 132: 105/34, Week 144: 48/16, Week 156: 9/5, Week 168: 0/0

Log rank test: p-value = 0,155
*: p < 0,05

Analysis population: A2304 SAF total population

Figure 12.1.3.70: JOINT SWELLING (PT)

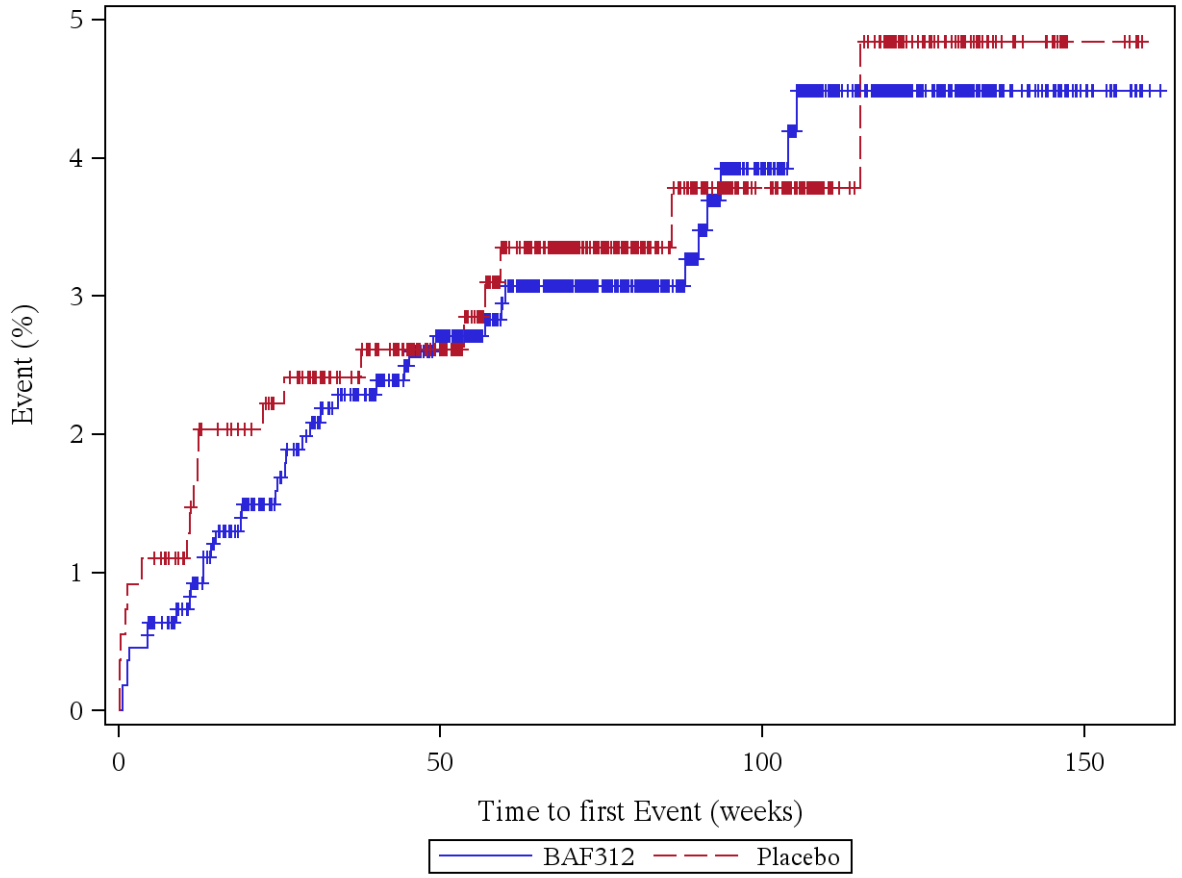


Patients at risk (BAF312/Placebo): Week 0: 1099/546, Week 4: 1096/545, Week 12: 1053/534, Week 24: 1008/519, Week 36: 981/493, Week 48: 914/456, Week 60: 806/383, Week 72: 642/300, Week 84: 508/234, Week 96: 396/173, Week 108: 291/124, Week 120: 200/79, Week 132: 113/40, Week 144: 51/20, Week 156: 10/5, Week 168: 0/0

Log rank test: p-value = 0,662
*: p < 0,05

Analysis population: A2304 SAF total population

Figure 12.1.3.71: MUSCLE SPASMS (PT)

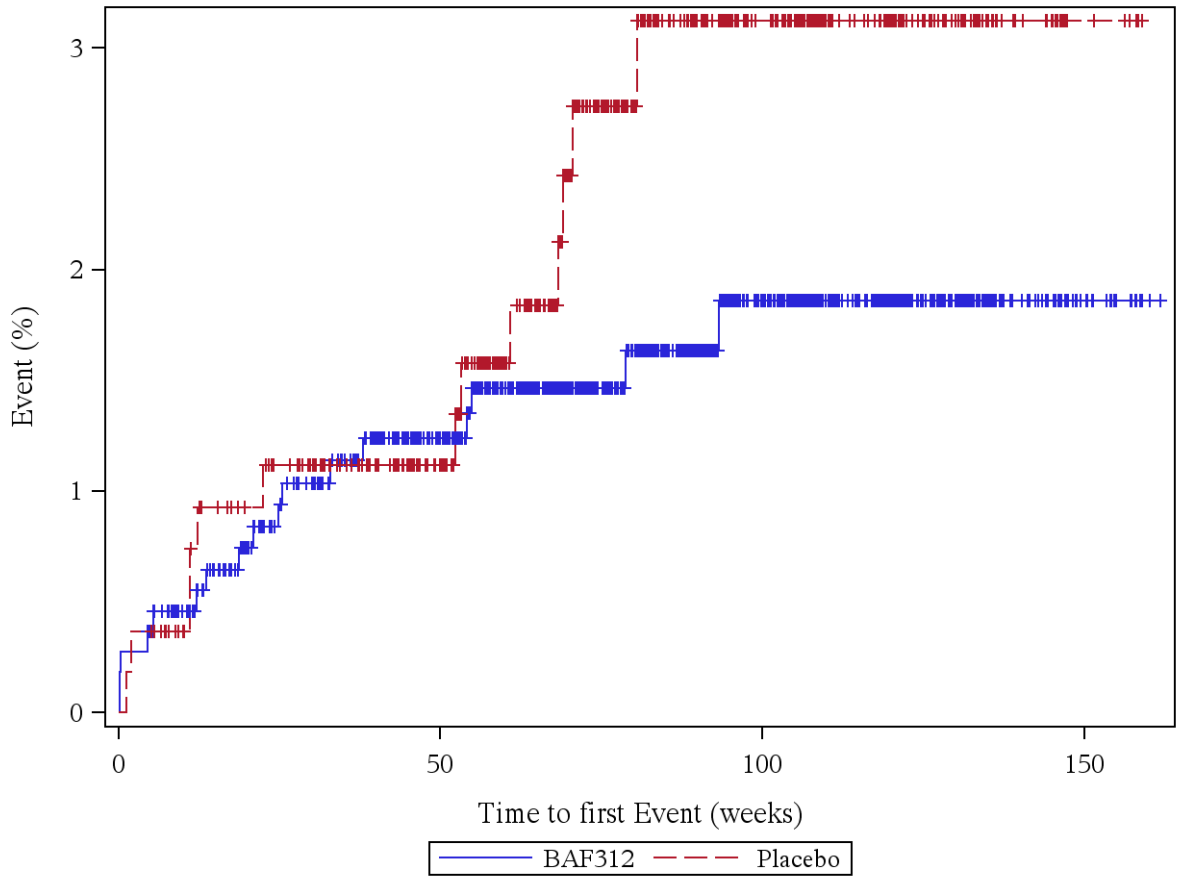


Patients at risk (BAF312/Placebo): Week 0: 1099/546, Week 4: 1094/540, Week 12: 1049/527, Week 24: 1001/510, Week 36: 967/486, Week 48: 903/449, Week 60: 798/375, Week 72: 641/293, Week 84: 507/228, Week 96: 391/167, Week 108: 282/118, Week 120: 193/72, Week 132: 111/33, Week 144: 51/17, Week 156: 10/5, Week 168: 0/0

Log rank test: p-value = 0,860
*: p < 0,05

Analysis population: A2304 SAF total population

Figure 12.1.3.72: MUSCULAR WEAKNESS (PT)

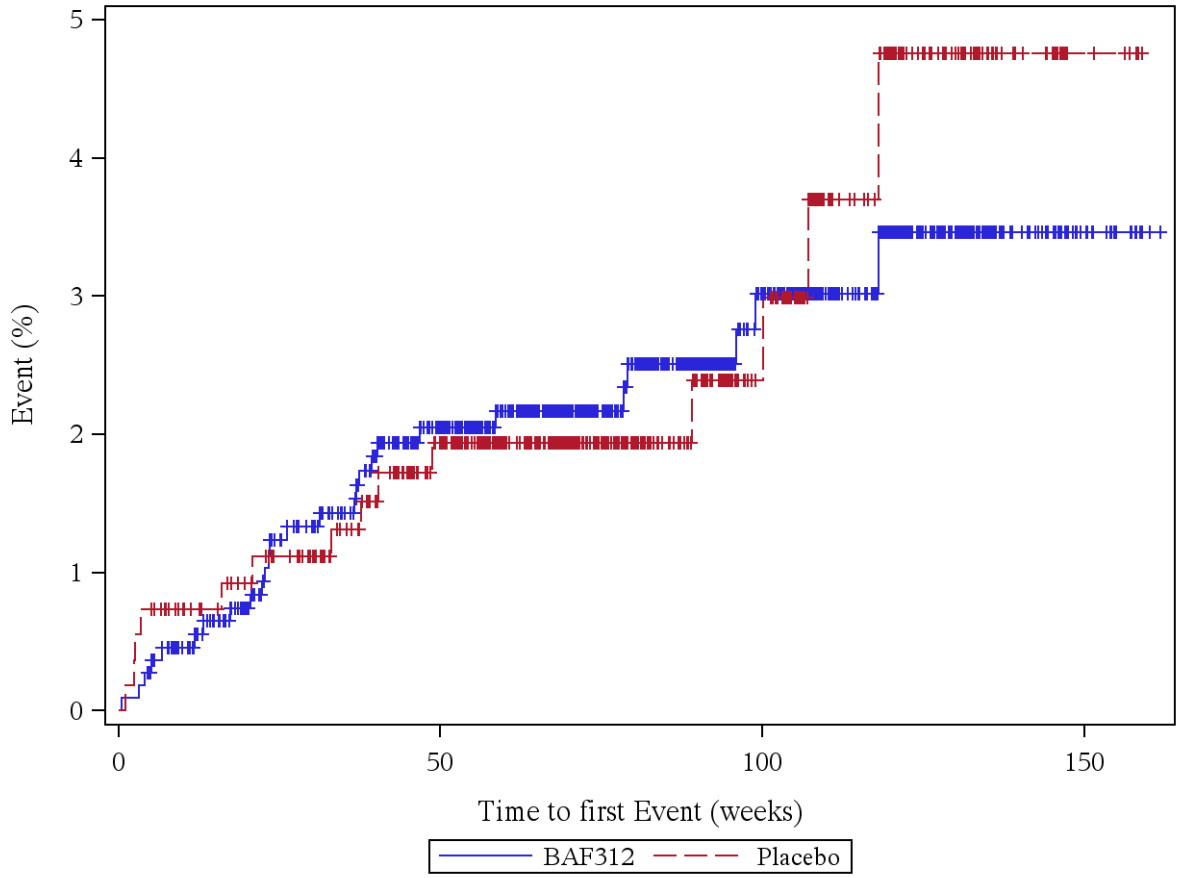


Patients at risk (BAF312/Placebo): Week 0: 1099/546, Week 4: 1096/544, Week 12: 1055/531, Week 24: 1009/516, Week 36: 980/492, Week 48: 915/457, Week 60: 809/384, Week 72: 647/297, Week 84: 512/229, Week 96: 396/173, Week 108: 287/124, Week 120: 198/78, Week 132: 113/38, Week 144: 51/18, Week 156: 10/5, Week 168: 0/0

Log rank test: p-value = 0,223
*: p < 0,05

Analysis population: A2304 SAF total population

Figure 12.1.3.73: MUSCULOSKELETAL PAIN (PT)

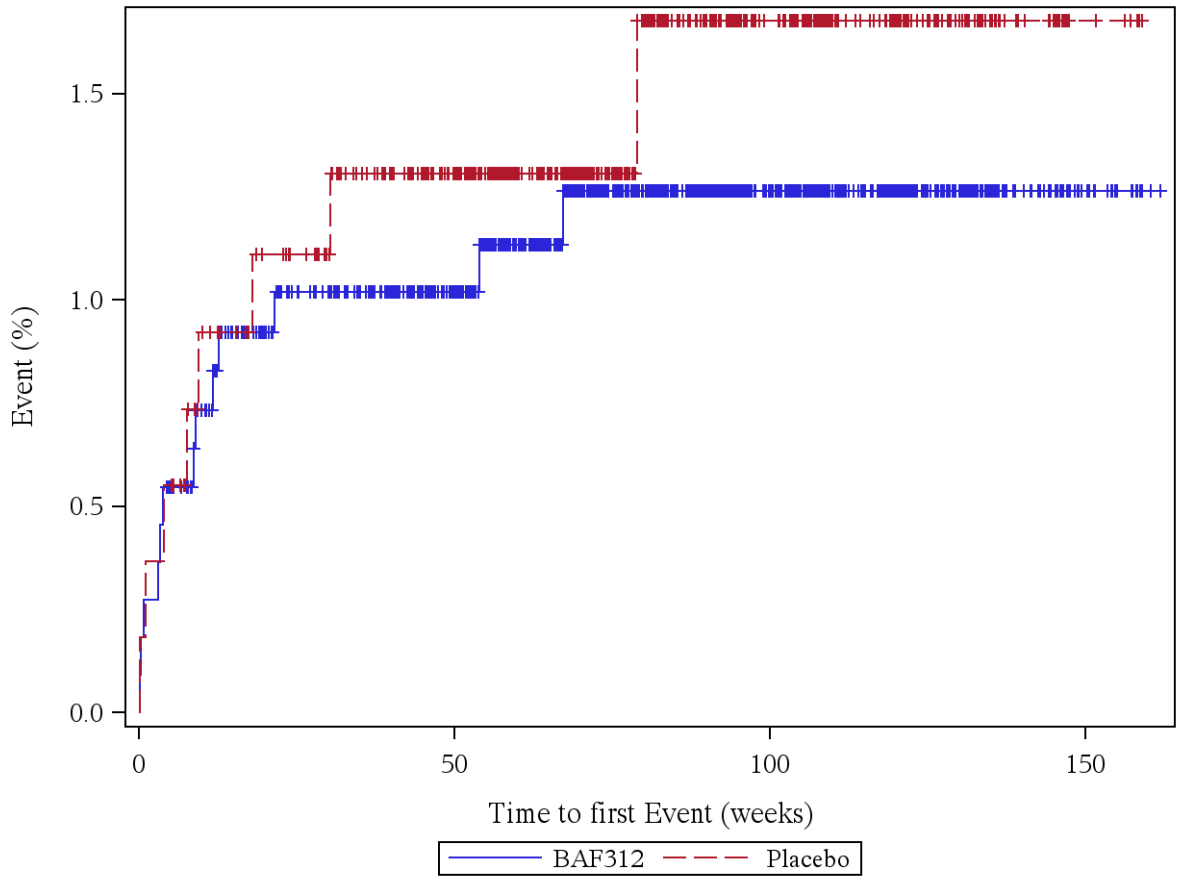


Patients at risk (BAF312/Placebo): Week 0: 1099/546, Week 4: 1096/542, Week 12: 1054/531, Week 24: 1005/515, Week 36: 976/490, Week 48: 906/453, Week 60: 800/379, Week 72: 638/296, Week 84: 503/231, Week 96: 389/172, Week 108: 283/122, Week 120: 194/76, Week 132: 111/37, Week 144: 49/18, Week 156: 10/5, Week 168: 0/0

Log rank test: p-value = 0,860
*: p < 0,05

Analysis population: A2304 SAF total population

Figure 12.1.3.74: MYALGIA (PT)

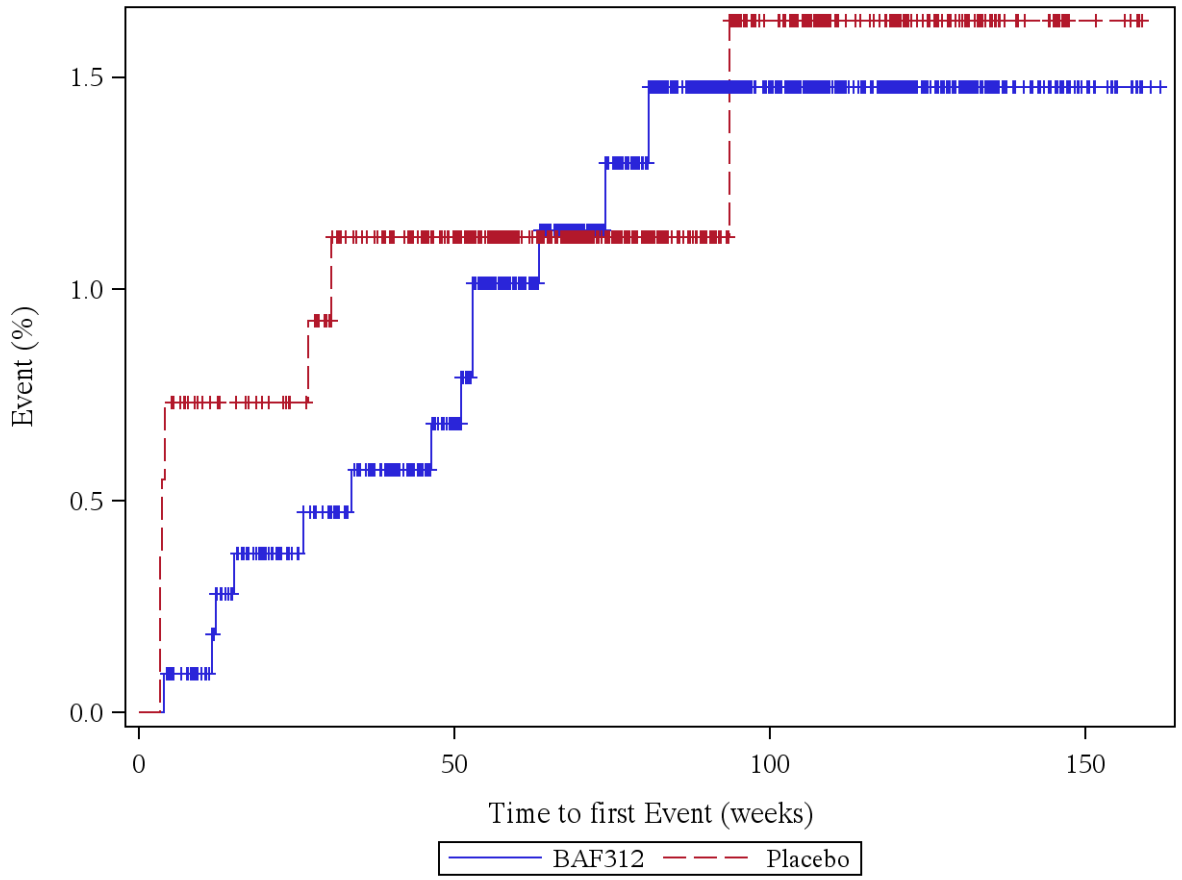


Patients at risk (BAF312/Placebo): Week 0: 1099/546, Week 4: 1093/543, Week 12: 1050/530, Week 24: 1006/516, Week 36: 980/491, Week 48: 915/457, Week 60: 809/384, Week 72: 643/301, Week 84: 513/232, Week 96: 398/174, Week 108: 289/126, Week 120: 198/80, Week 132: 112/40, Week 144: 51/20, Week 156: 10/5, Week 168: 0/0

Log rank test: p-value = 0,632
*: p < 0,05

Analysis population: A2304 SAF total population

Figure 12.1.3.75: NECK PAIN (PT)

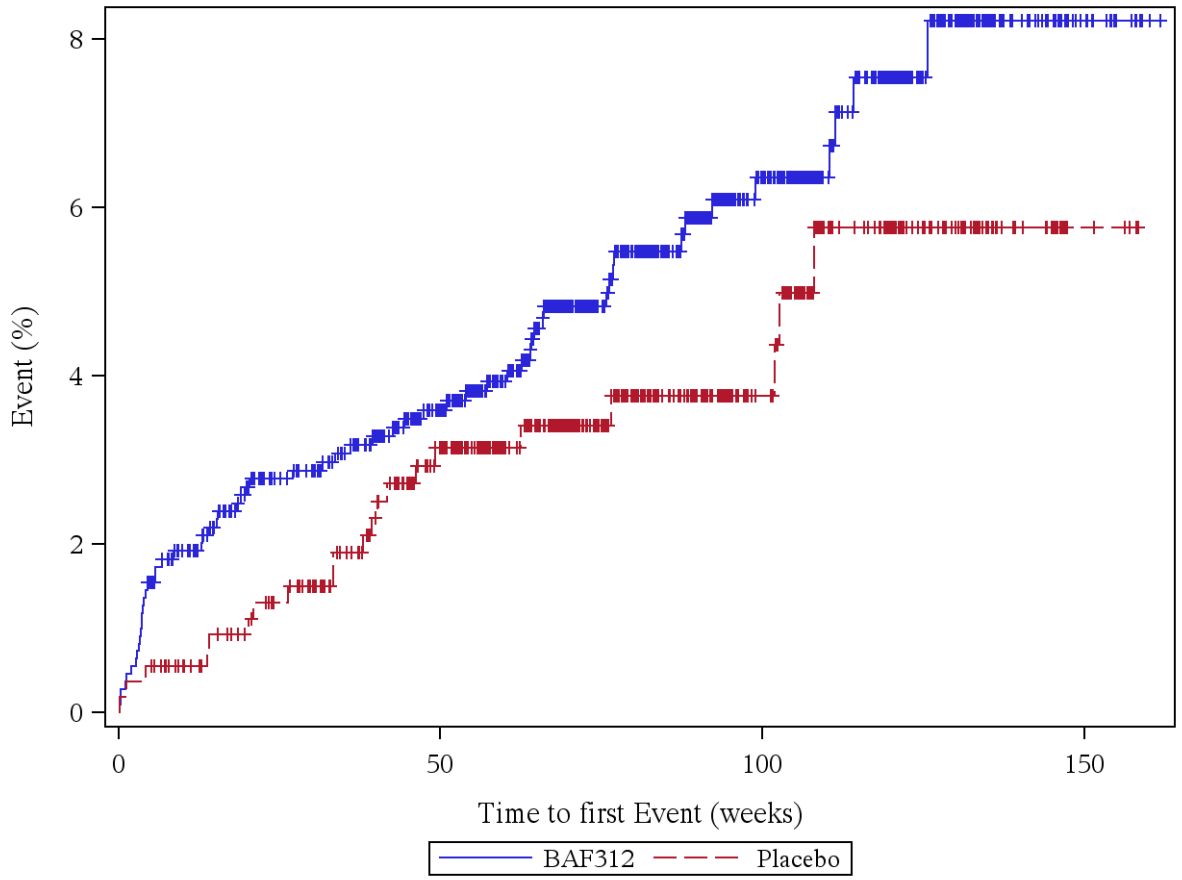


Patients at risk (BAF312/Placebo): Week 0: 1099/546, Week 4: 1098/543, Week 12: 1057/531, Week 24: 1013/517, Week 36: 985/491, Week 48: 920/456, Week 60: 811/383, Week 72: 645/301, Week 84: 511/233, Week 96: 397/171, Week 108: 289/122, Week 120: 199/79, Week 132: 112/40, Week 144: 51/20, Week 156: 10/5, Week 168: 0/0

Log rank test: p-value = 0,840
*: p < 0,05

Analysis population: A2304 SAF total population

Figure 12.1.3.76: PAIN IN EXTREMITY (PT)

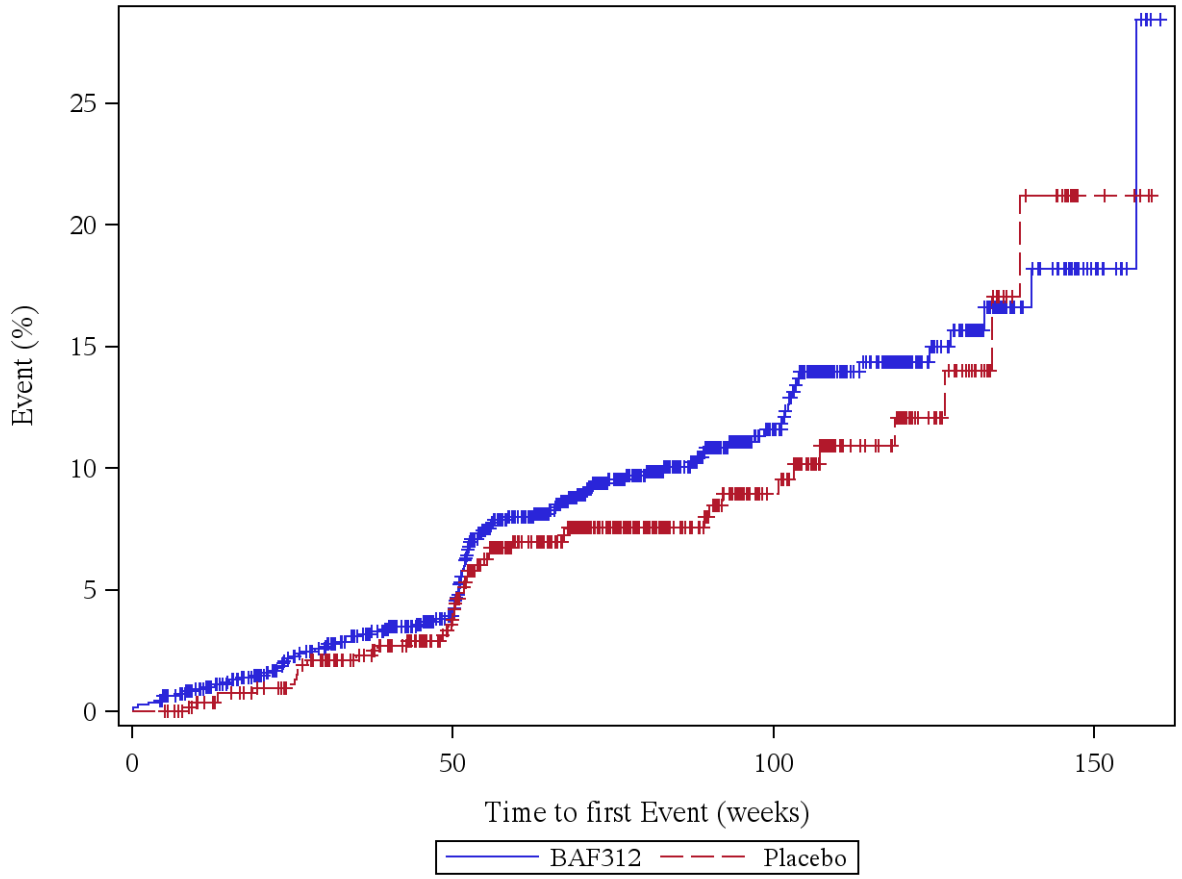


Patients at risk (BAF312/Placebo): Week 0: 1099/546, Week 4: 1084/544, Week 12: 1042/532, Week 24: 992/514, Week 36: 962/487, Week 48: 894/449, Week 60: 787/379, Week 72: 623/297, Week 84: 491/229, Week 96: 381/172, Week 108: 274/120, Week 120: 189/78, Week 132: 104/39, Week 144: 47/19, Week 156: 9/4, Week 168: 0/0

Log rank test: p-value = 0,178
*: p < 0,05

Analysis population: A2304 SAF total population

Figure 12.1.3.77: NEOPLASMS BENIGN, MALIGNANT AND UNSPECIFIED (INCL CYSTS AND POLYPS) (SOC)

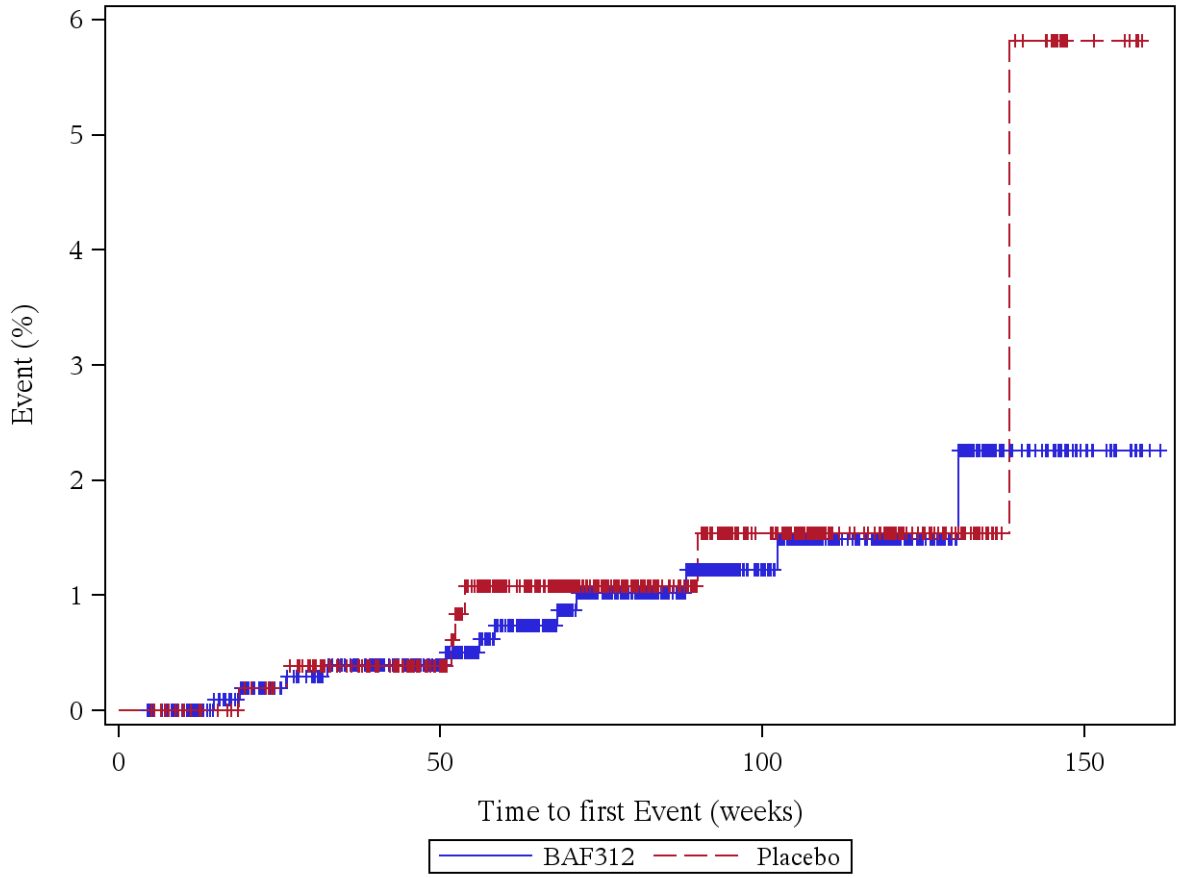


Patients at risk (BAF312/Placebo): Week 0: 1099/546, Week 4: 1094/546, Week 12: 1048/533, Week 24: 995/516, Week 36: 957/488, Week 48: 895/451, Week 60: 757/364, Week 72: 599/283, Week 84: 470/218, Week 96: 366/159, Week 108: 258/110, Week 120: 173/69, Week 132: 100/34, Week 144: 44/18, Week 156: 8/4, Week 168: 0/0

Log rank test: p-value = 0,284
*: p < 0,05

Analysis population: A2304 SAF total population

Figure 12.1.3.78: BASAL CELL CARCINOMA (PT)

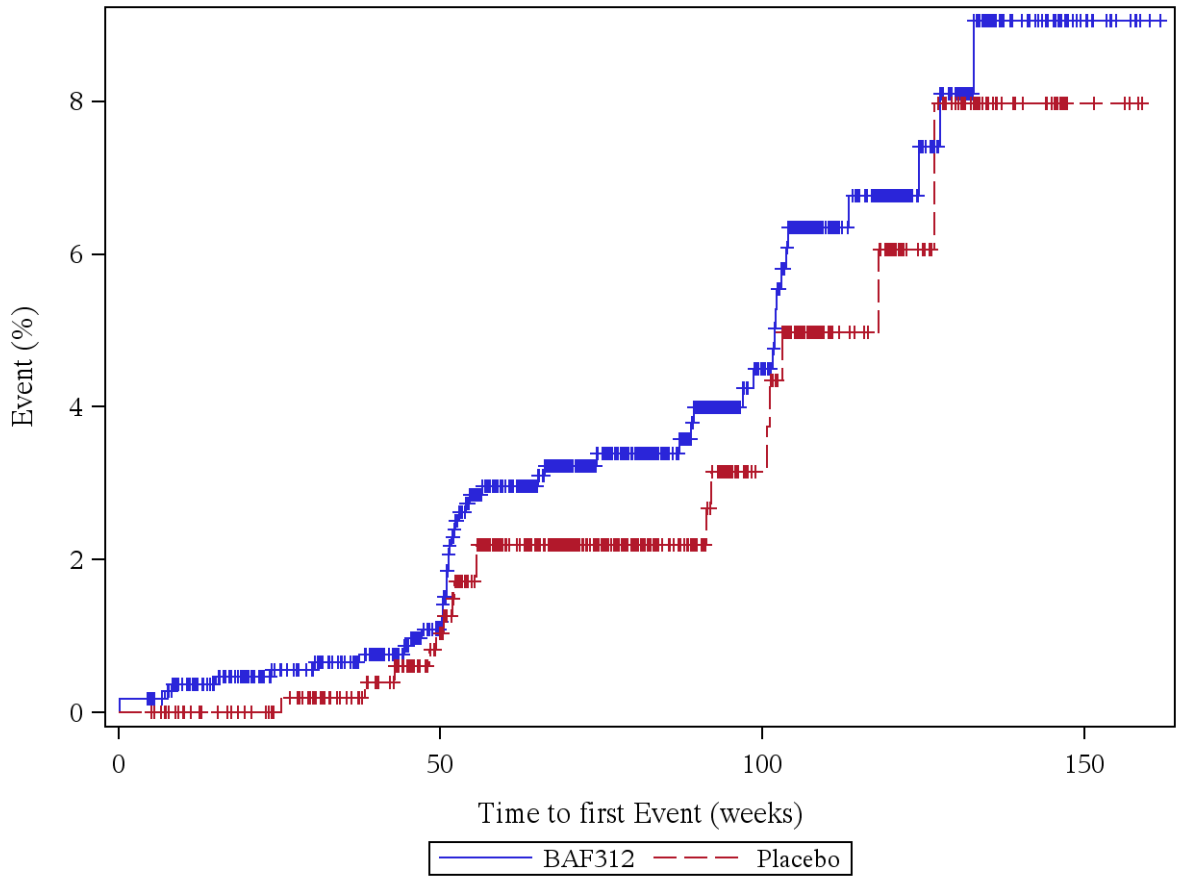


Patients at risk (BAF312/Placebo): Week 0: 1099/546, Week 4: 1099/546, Week 12: 1059/535, Week 24: 1015/520, Week 36: 986/495, Week 48: 921/459, Week 60: 812/383, Week 72: 645/302, Week 84: 510/235, Week 96: 397/173, Week 108: 288/123, Week 120: 197/79, Week 132: 111/40, Week 144: 51/20, Week 156: 10/5, Week 168: 0/0

Log rank test: p-value = 0,646
*: p < 0,05

Analysis population: A2304 SAF total population

Figure 12.1.3.79: MELANOCYTIC NAEVUS (PT)

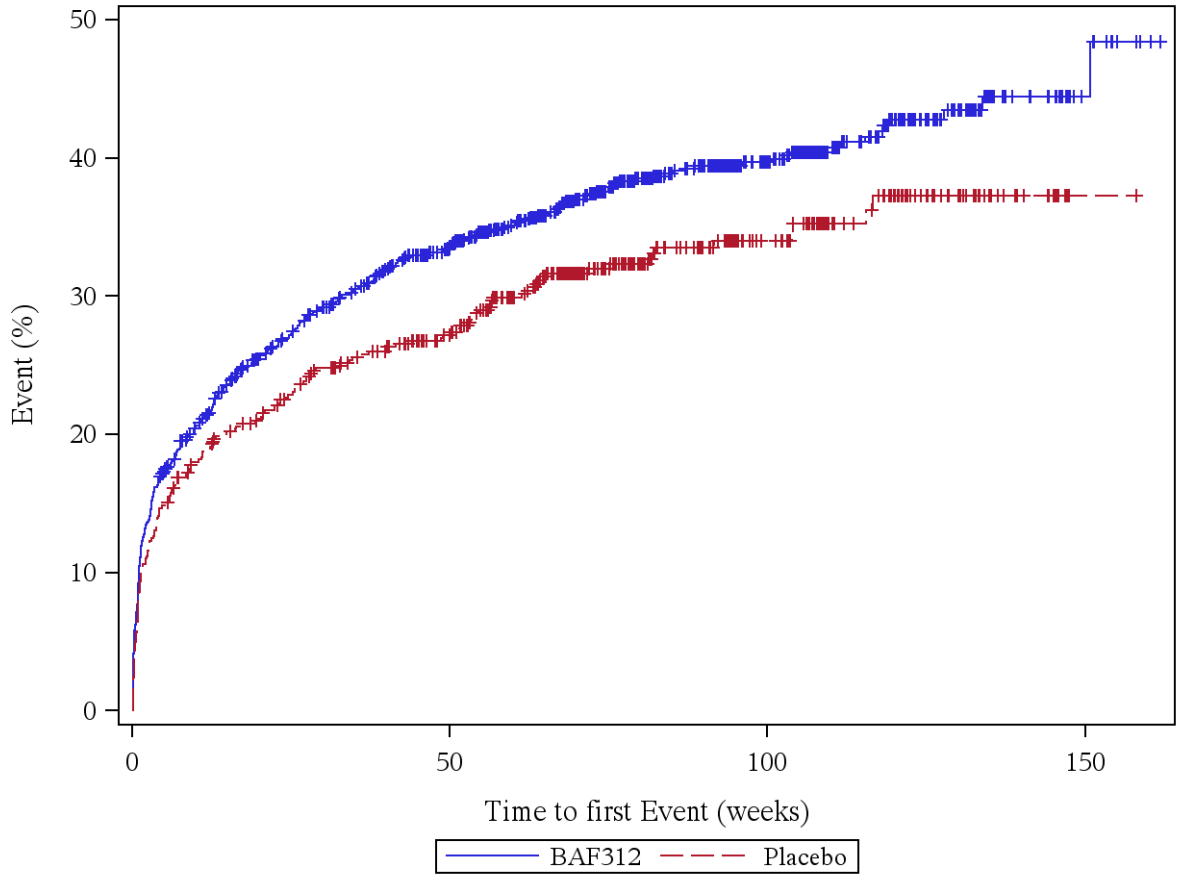


Patients at risk (BAF312/Placebo): Week 0: 1099/546, Week 4: 1097/546, Week 12: 1055/535, Week 24: 1011/521, Week 36: 983/496, Week 48: 916/460, Week 60: 793/382, Week 72: 635/299, Week 84: 501/232, Week 96: 392/170, Week 108: 278/118, Week 120: 190/74, Week 132: 106/37, Week 144: 46/18, Week 156: 8/4, Week 168: 0/0

Log rank test: p-value = 0,359
*: p < 0,05

Analysis population: A2304 SAF total population

Figure 12.1.3.80: NERVOUS SYSTEM DISORDERS (SOC)

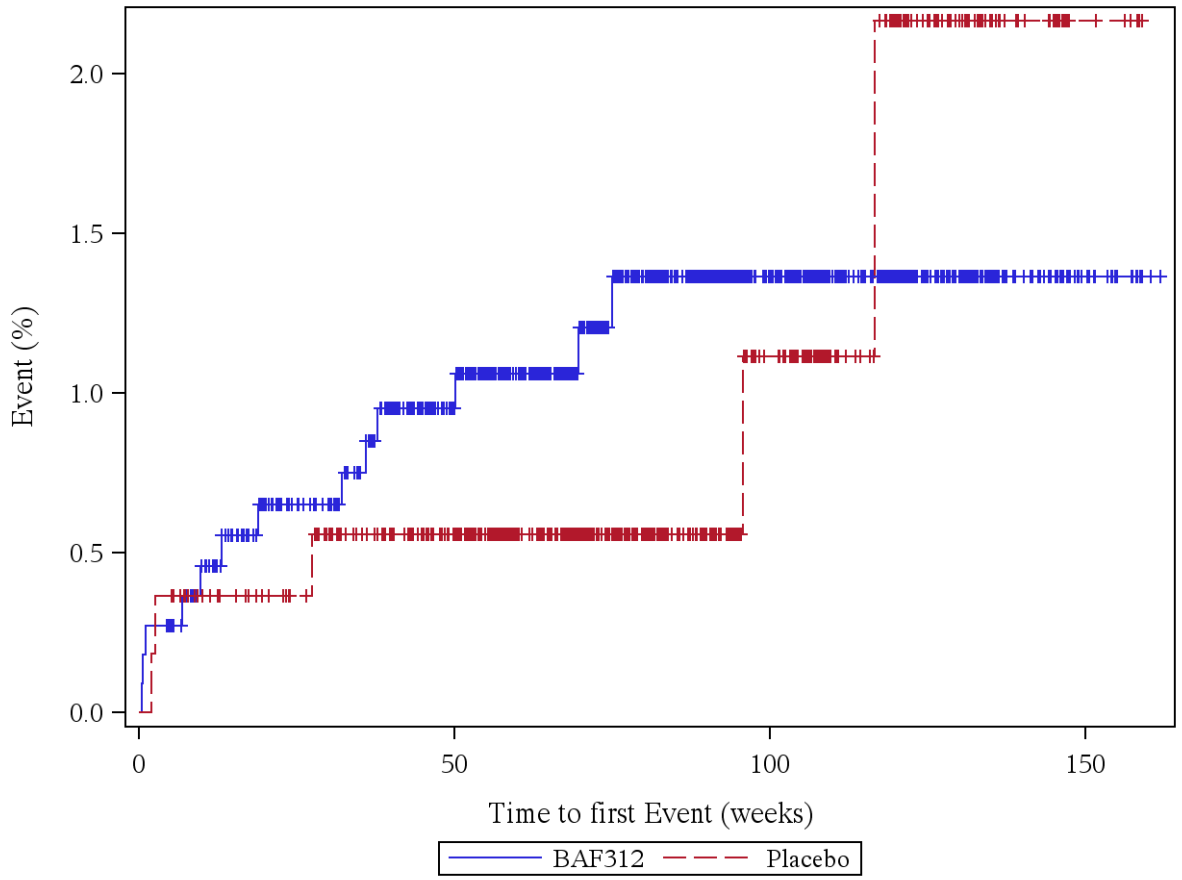


Patients at risk (BAF312/Placebo): Week 0: 1099/546, Week 4: 920/470, Week 12: 836/438, Week 24: 754/406, Week 36: 698/374, Week 48: 633/344, Week 60: 551/286, Week 72: 424/212, Week 84: 326/156, Week 96: 265/120, Week 108: 187/85, Week 120: 126/52, Week 132: 68/24, Week 144: 35/11, Week 156: 6/1, Week 168: 0/0

Log rank test: p-value = 0,027 *
*: p < 0,05

Analysis population: A2304 SAF total population

Figure 12.1.3.81: BALANCE DISORDER (PT)

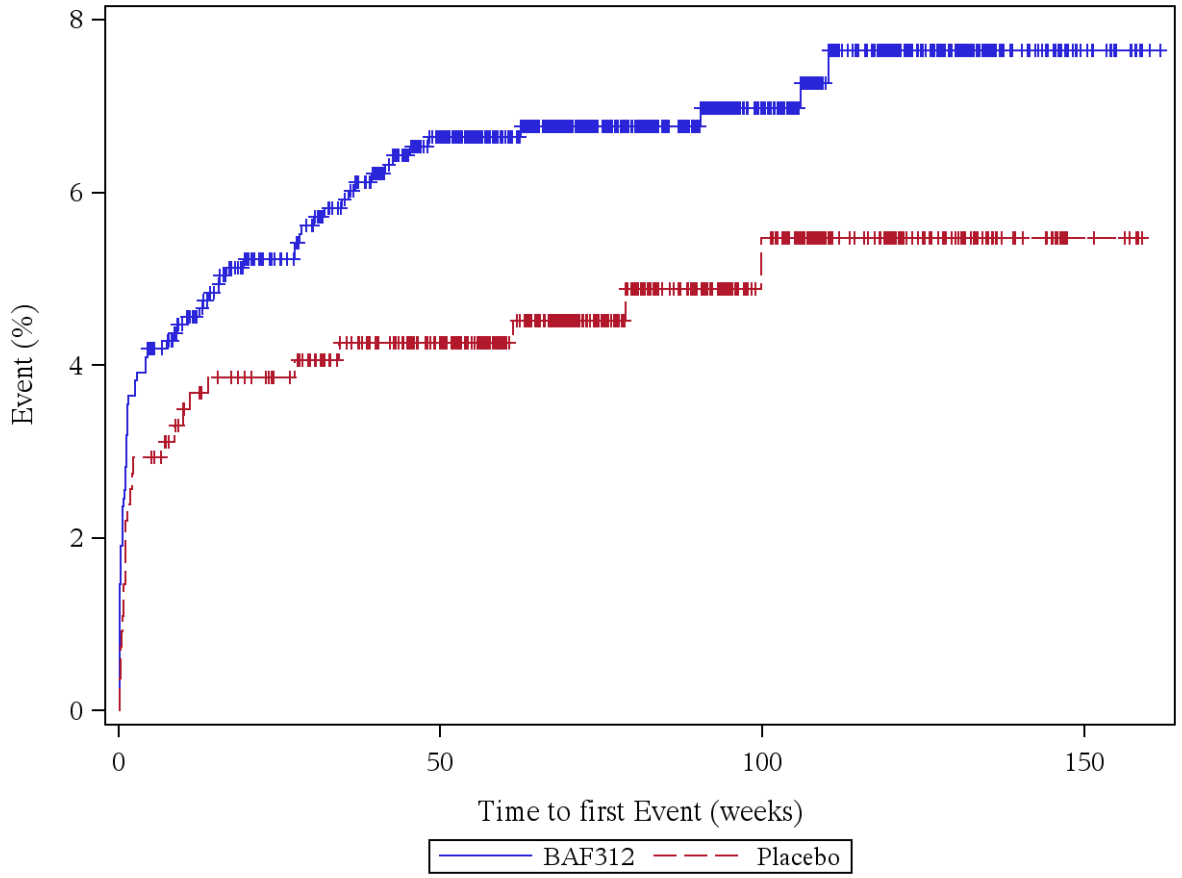


Patients at risk (BAF312/Placebo): Week 0: 1099/546, Week 4: 1096/544, Week 12: 1055/533, Week 24: 1012/519, Week 36: 983/494, Week 48: 917/459, Week 60: 811/386, Week 72: 645/303, Week 84: 512/236, Week 96: 398/174, Week 108: 290/124, Week 120: 199/78, Week 132: 113/38, Week 144: 51/19, Week 156: 10/5, Week 168: 0/0

Log rank test: p-value = 0,646
*: p < 0,05

Analysis population: A2304 SAF total population

Figure 12.1.3.82: DIZZINESS (PT)

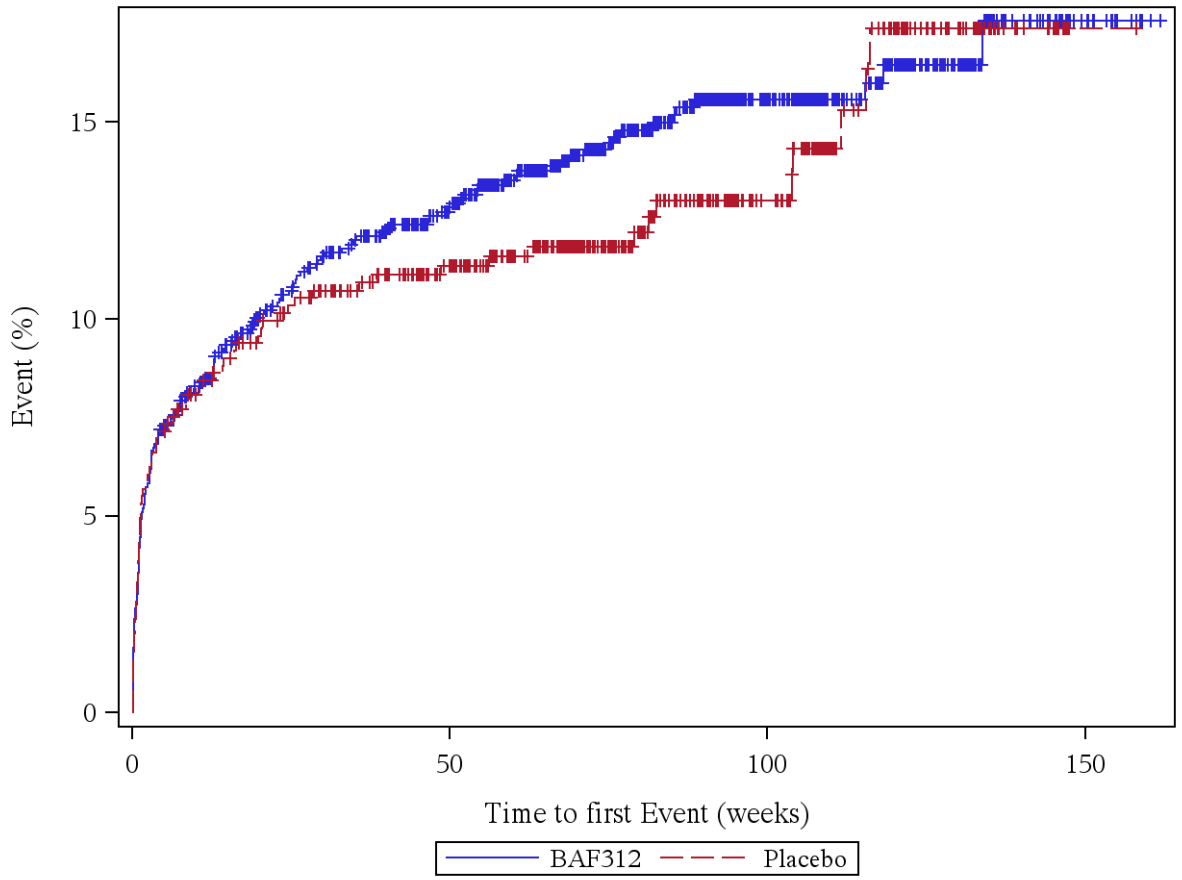


Patients at risk (BAF312/Placebo): Week 0: 1099/546, Week 4: 1056/530, Week 12: 1012/516, Week 24: 969/502, Week 36: 936/477, Week 48: 869/443, Week 60: 770/375, Week 72: 614/295, Week 84: 490/227, Week 96: 382/171, Week 108: 277/121, Week 120: 191/75, Week 132: 108/37, Week 144: 49/19, Week 156: 10/5, Week 168: 0/0

Log rank test: p-value = 0,103
*: p < 0,05

Analysis population: A2304 SAF total population

Figure 12.1.3.83: HEADACHE (PT)

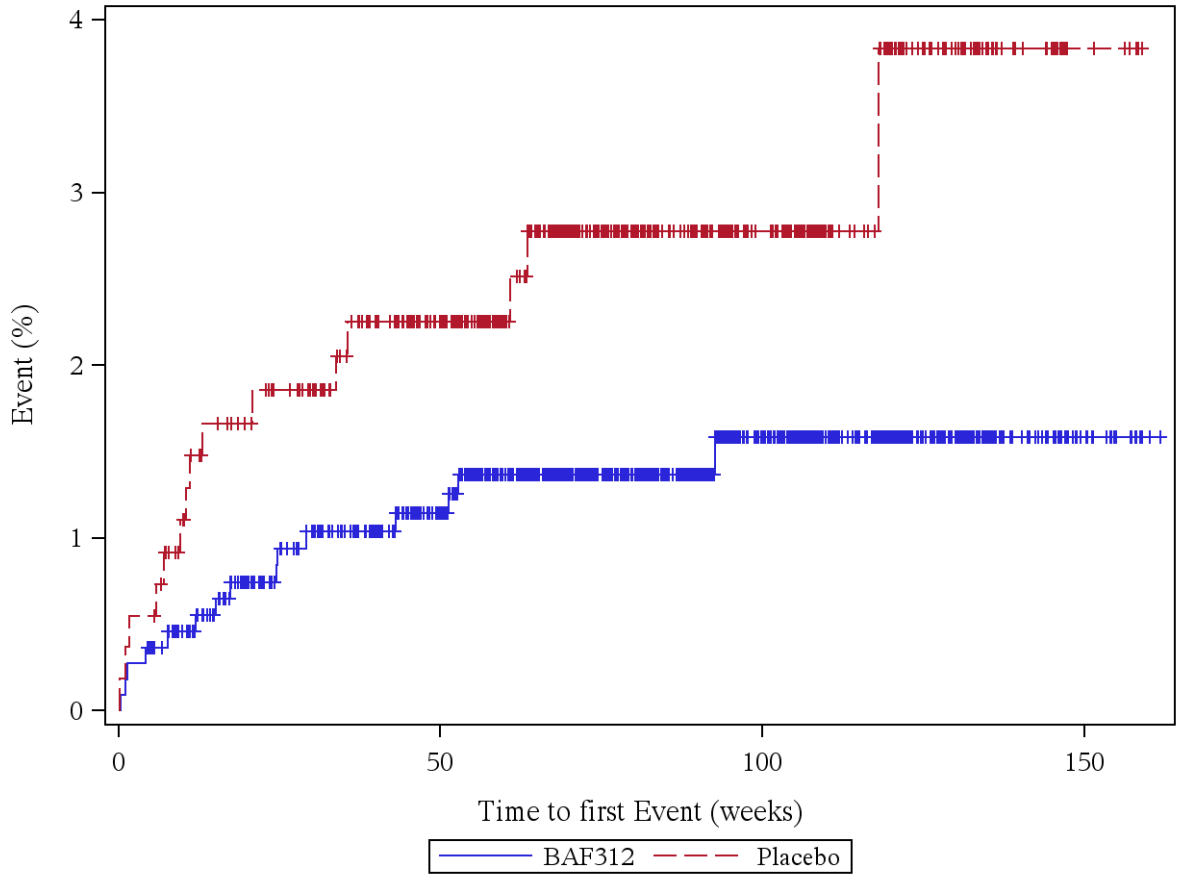


Patients at risk (BAF312/Placebo): Week 0: 1099/546, Week 4: 1024/508, Week 12: 967/490, Week 24: 909/467, Week 36: 873/444, Week 48: 810/410, Week 60: 712/349, Week 72: 560/273, Week 84: 437/205, Week 96: 340/152, Week 108: 247/107, Week 120: 168/66, Week 132: 91/33, Week 144: 44/13, Week 156: 9/1, Week 168: 0/0

Log rank test: p-value = 0,460
*: p < 0,05

Analysis population: A2304 SAF total population

Figure 12.1.3.84: HYPOAESTHESIA (PT)

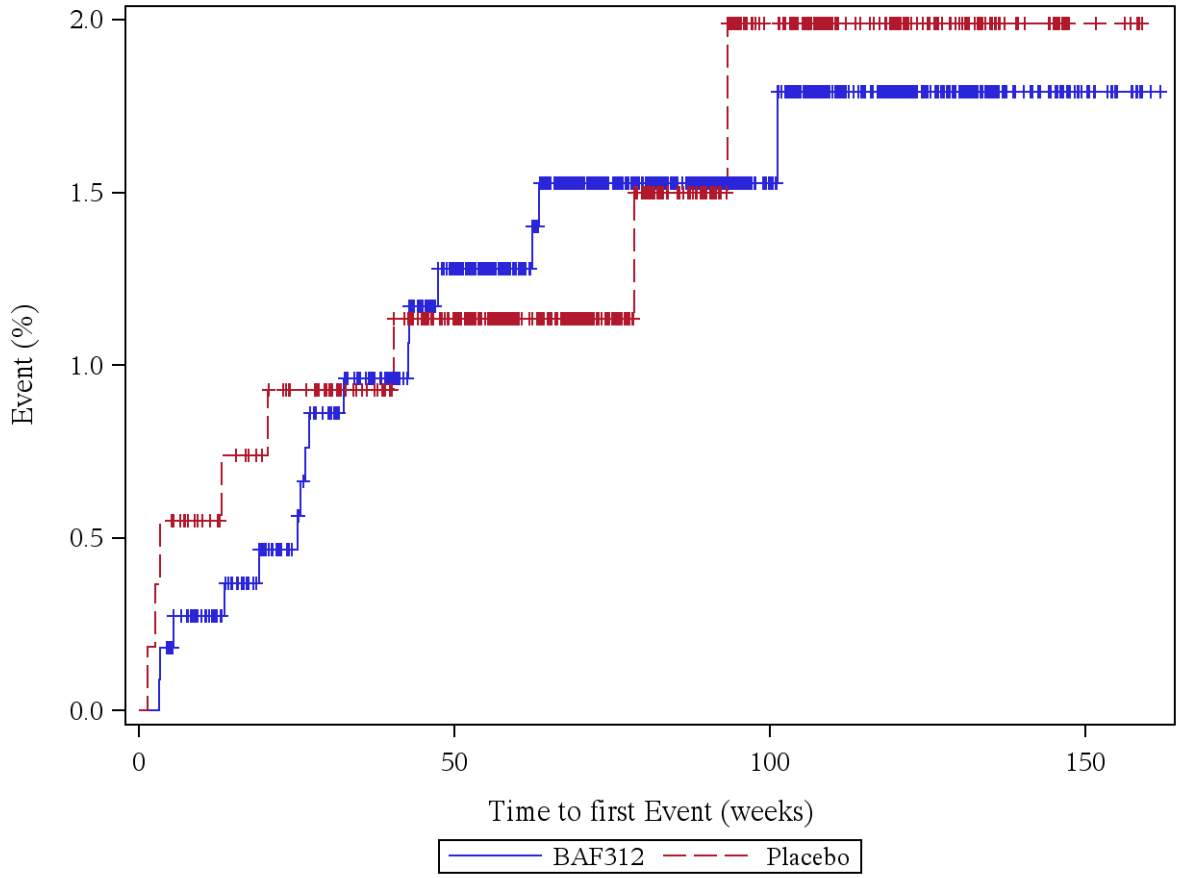


Patients at risk (BAF312/Placebo): Week 0: 1099/546, Week 4: 1096/543, Week 12: 1054/528, Week 24: 1010/512, Week 36: 981/486, Week 48: 917/451, Week 60: 809/380, Week 72: 646/296, Week 84: 513/230, Week 96: 398/174, Week 108: 290/124, Week 120: 199/77, Week 132: 113/40, Week 144: 51/20, Week 156: 10/5, Week 168: 0/0

Log rank test: p-value = 0,047 *
*: p < 0,05

Analysis population: A2304 SAF total population

Figure 12.1.3.85: MIGRAINE (PT)

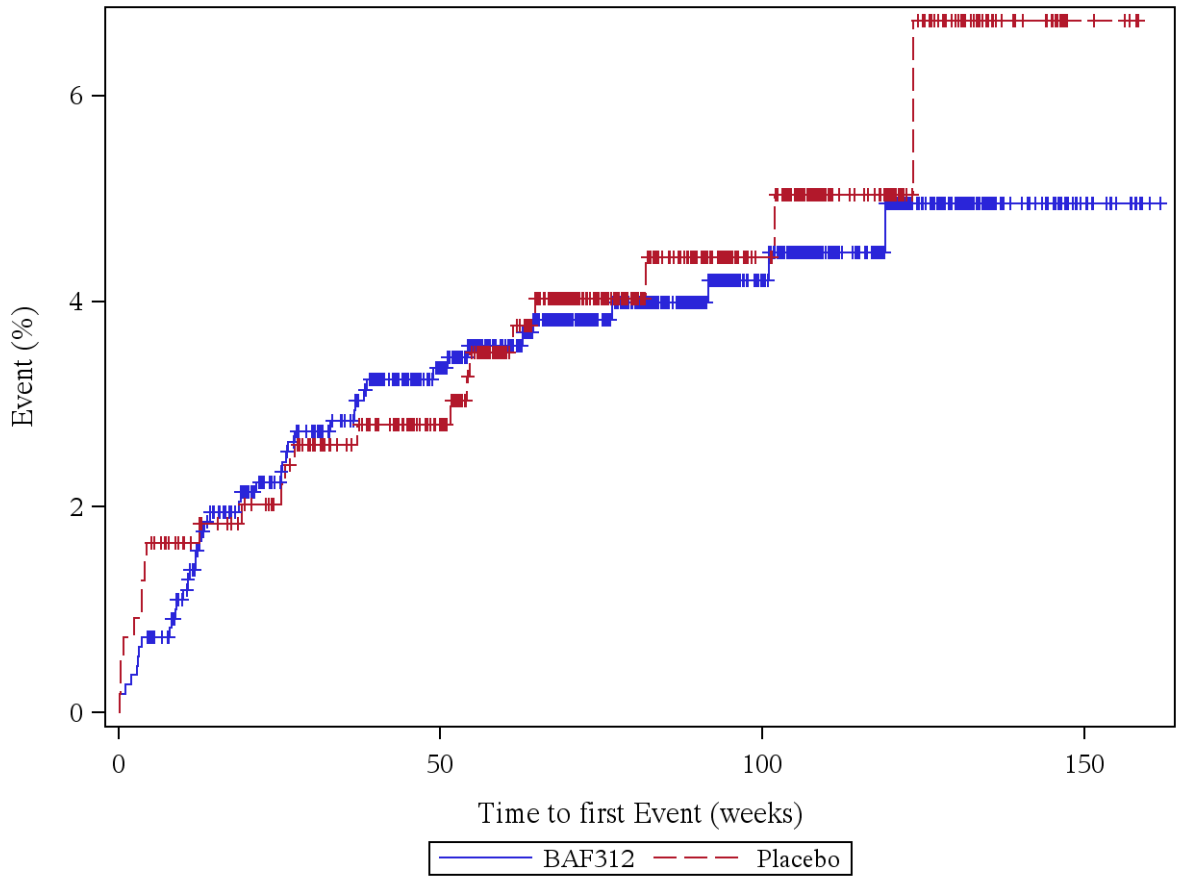


Patients at risk (BAF312/Placebo): Week 0: 1099/546, Week 4: 1097/543, Week 12: 1056/532, Week 24: 1012/516, Week 36: 980/493, Week 48: 912/456, Week 60: 805/384, Week 72: 641/302, Week 84: 507/234, Week 96: 395/173, Week 108: 286/125, Week 120: 197/79, Week 132: 111/40, Week 144: 51/20, Week 156: 10/5, Week 168: 0/0

Log rank test: p-value = 0,984
*: p < 0,05

Analysis population: A2304 SAF total population

Figure 12.1.3.86: MUSCLE SPASTICITY (PT)

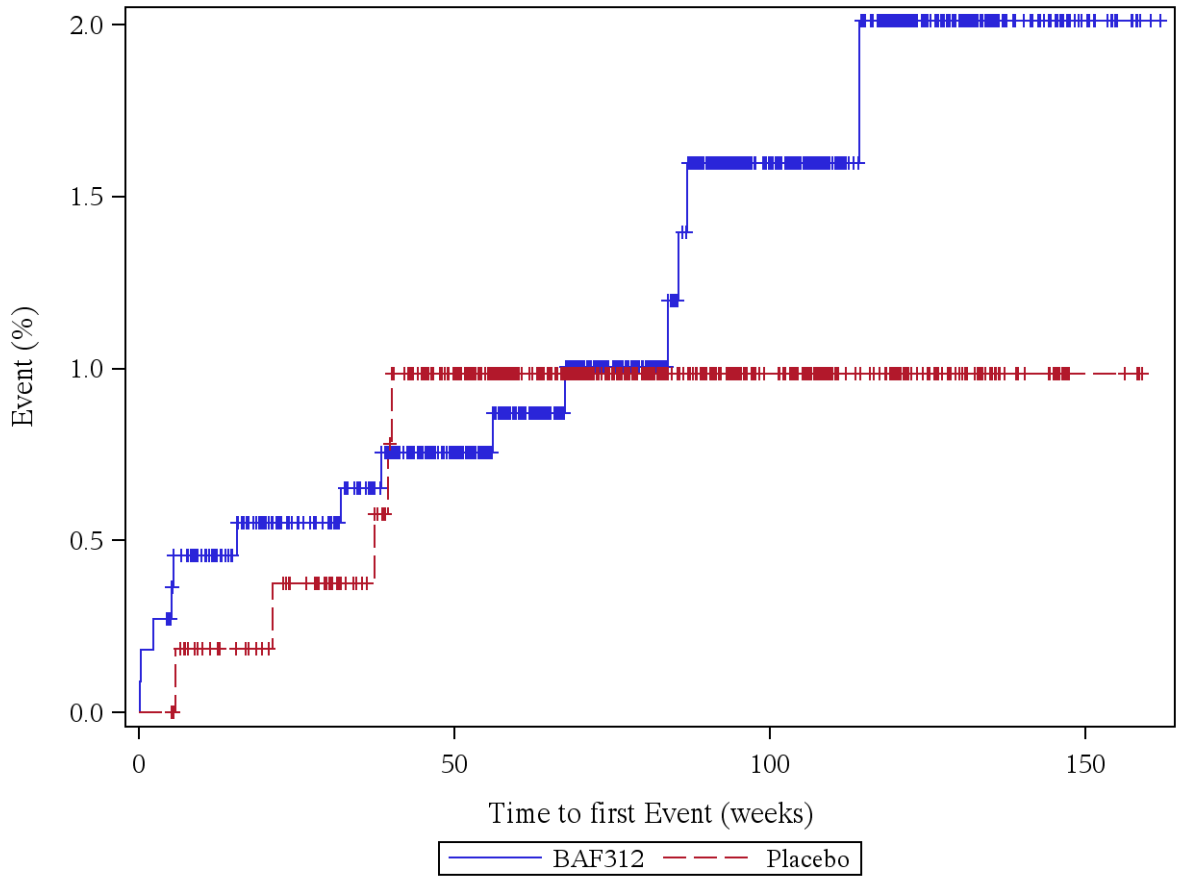


Patients at risk (BAF312/Placebo): Week 0: 1099/546, Week 4: 1091/538, Week 12: 1043/526, Week 24: 996/510, Week 36: 964/486, Week 48: 899/451, Week 60: 794/376, Week 72: 629/296, Week 84: 496/229, Week 96: 383/170, Week 108: 278/121, Week 120: 189/75, Week 132: 106/34, Week 144: 49/18, Week 156: 10/4, Week 168: 0/0

Log rank test: p-value = 0,750
*: p < 0,05

Analysis population: A2304 SAF total population

Figure 12.1.3.87: NEURALGIA (PT)

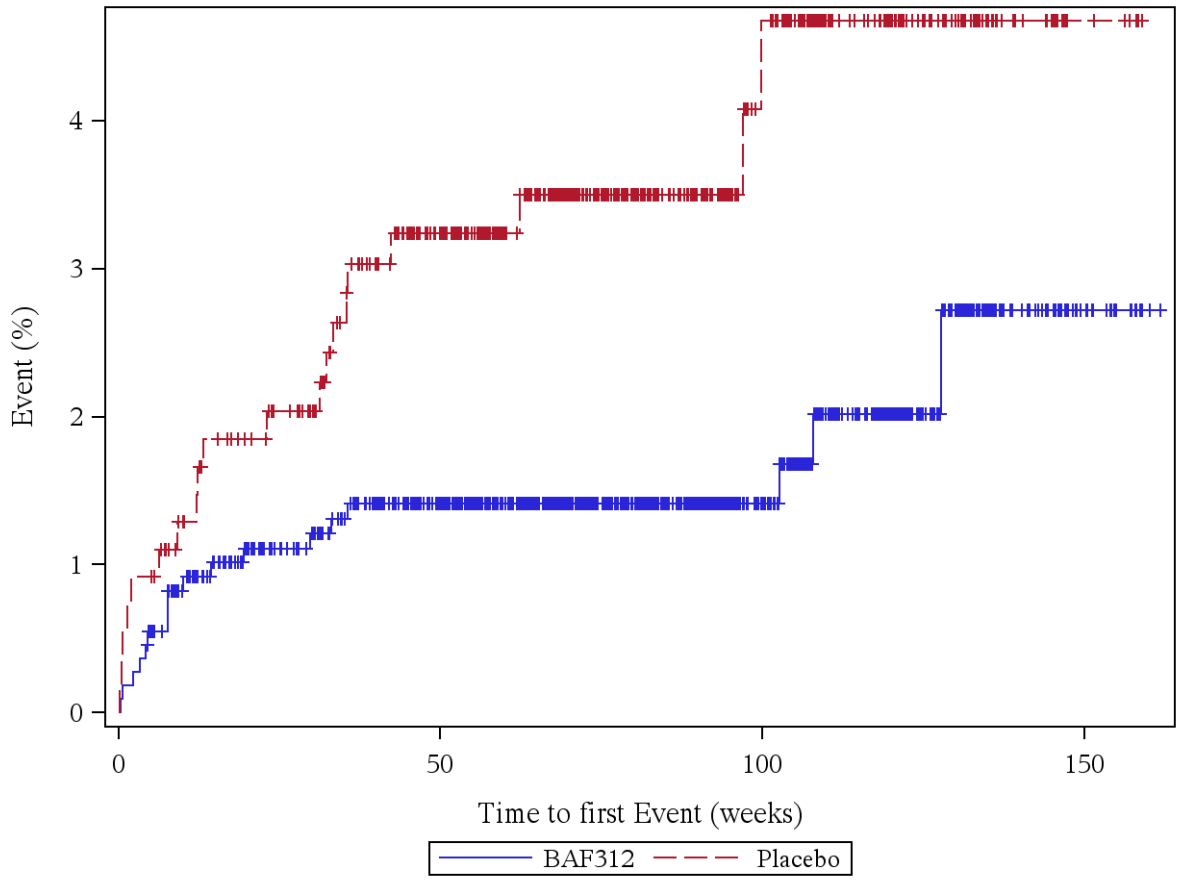


Patients at risk (BAF312/Placebo): Week 0: 1099/546, Week 4: 1096/546, Week 12: 1054/534, Week 24: 1011/519, Week 36: 983/495, Week 48: 918/456, Week 60: 810/383, Week 72: 646/300, Week 84: 509/233, Week 96: 393/173, Week 108: 286/123, Week 120: 196/77, Week 132: 111/38, Week 144: 49/18, Week 156: 9/4, Week 168: 0/0

Log rank test: p-value = 0,549
*: p < 0,05

Analysis population: A2304 SAF total population

Figure 12.1.3.88: PARAESTHESIA (PT)

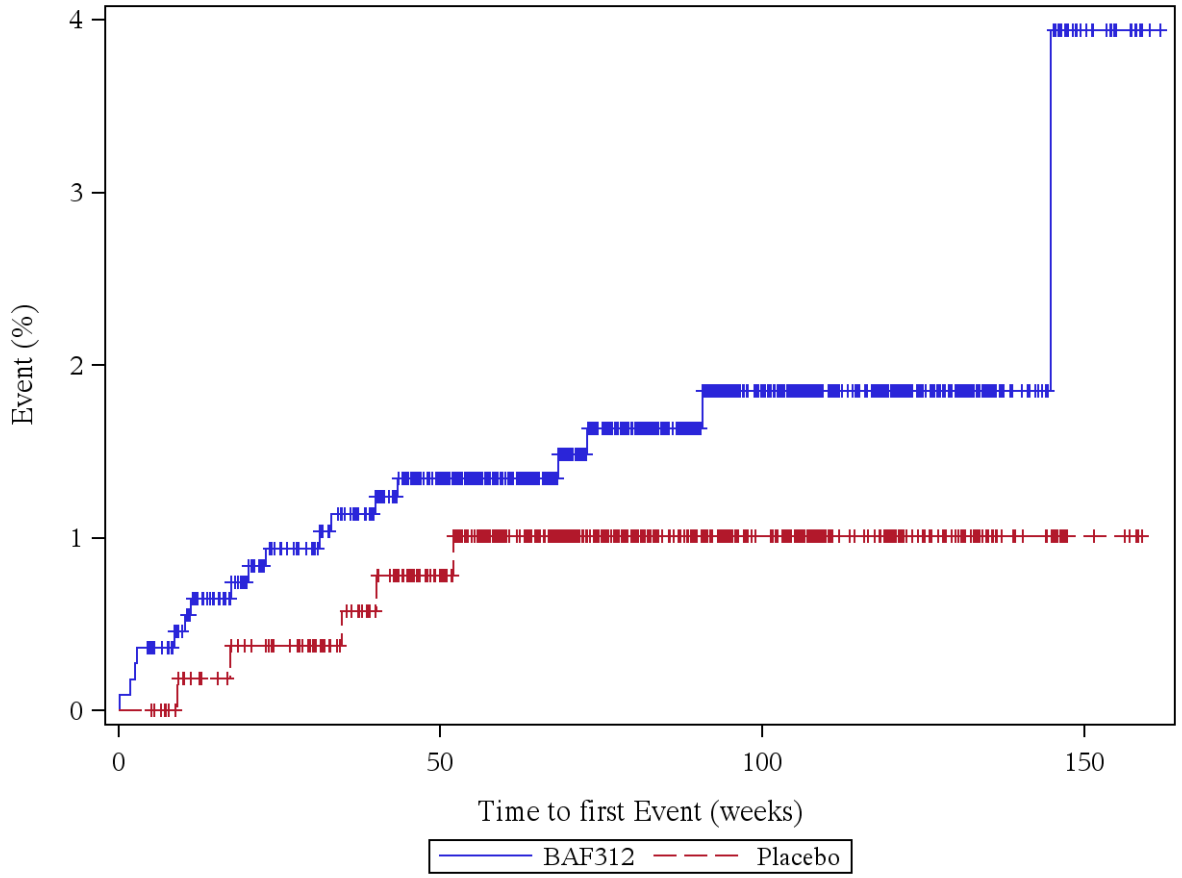


Patients at risk (BAF312/Placebo): Week 0: 1099/546, Week 4: 1095/541, Week 12: 1049/529, Week 24: 1005/511, Week 36: 975/482, Week 48: 914/447, Week 60: 808/378, Week 72: 645/295, Week 84: 511/229, Week 96: 398/171, Week 108: 288/120, Week 120: 199/75, Week 132: 111/38, Week 144: 51/19, Week 156: 10/5, Week 168: 0/0

Log rank test: p-value = 0,009 *
*: p < 0,05

Analysis population: A2304 SAF total population

Figure 12.1.3.89: SCIATICA (PT)

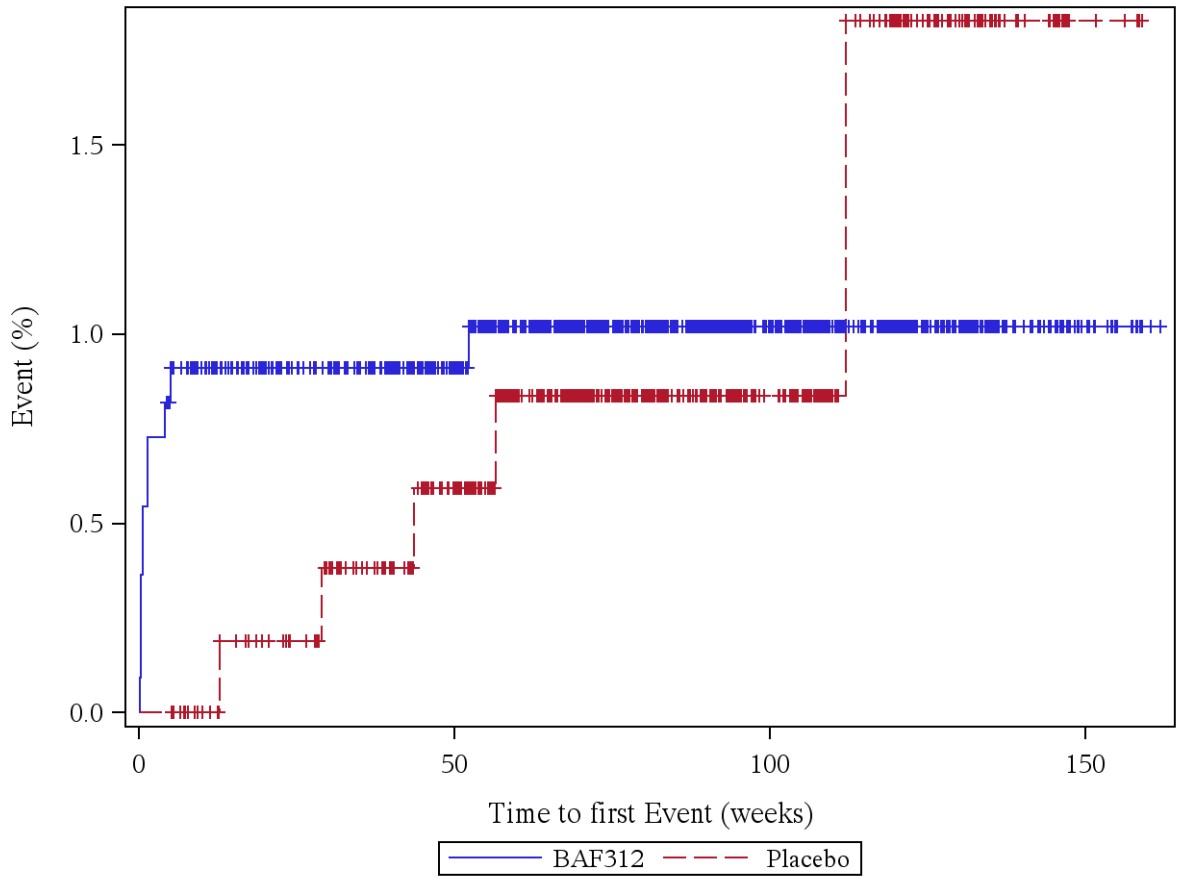


Patients at risk (BAF312/Placebo): Week 0: 1099/546, Week 4: 1095/546, Week 12: 1052/534, Week 24: 1007/519, Week 36: 979/494, Week 48: 912/457, Week 60: 808/384, Week 72: 642/303, Week 84: 508/235, Week 96: 393/174, Week 108: 286/124, Week 120: 197/78, Week 132: 112/39, Week 144: 50/19, Week 156: 10/5, Week 168: 0/0

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

Analysis population: A2304 SAF total population

Figure 12.1.3.90: SOMNOLENCE (PT)

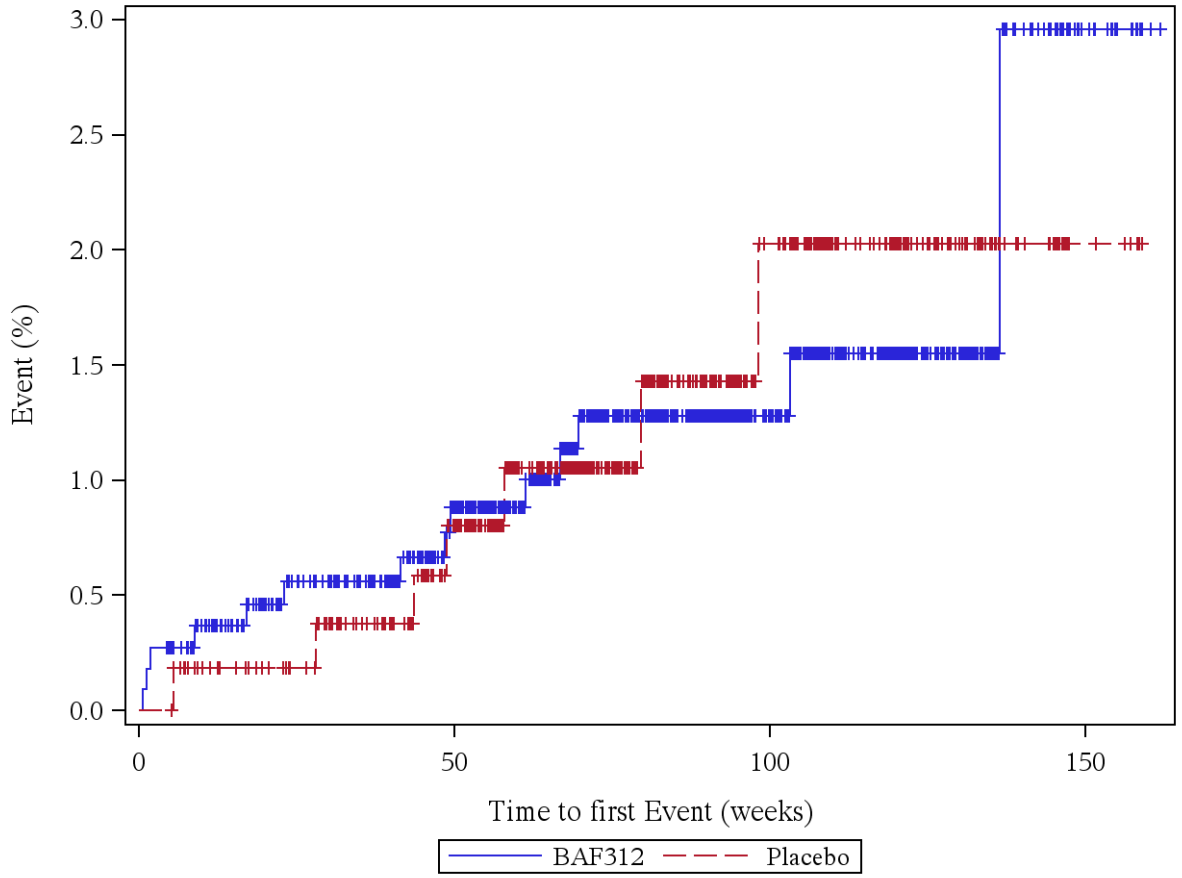


Patients at risk (BAF312/Placebo): Week 0: 1099/546, Week 4: 1091/546, Week 12: 1051/535, Week 24: 1009/520, Week 36: 982/495, Week 48: 917/458, Week 60: 812/386, Week 72: 647/303, Week 84: 513/235, Week 96: 399/174, Week 108: 290/125, Week 120: 200/79, Week 132: 113/39, Week 144: 51/19, Week 156: 10/4, Week 168: 0/0

Log rank test: p-value = 0,881
*: p < 0,05

Analysis population: A2304 SAF total population

Figure 12.1.3.91: SYNCOPE (PT)

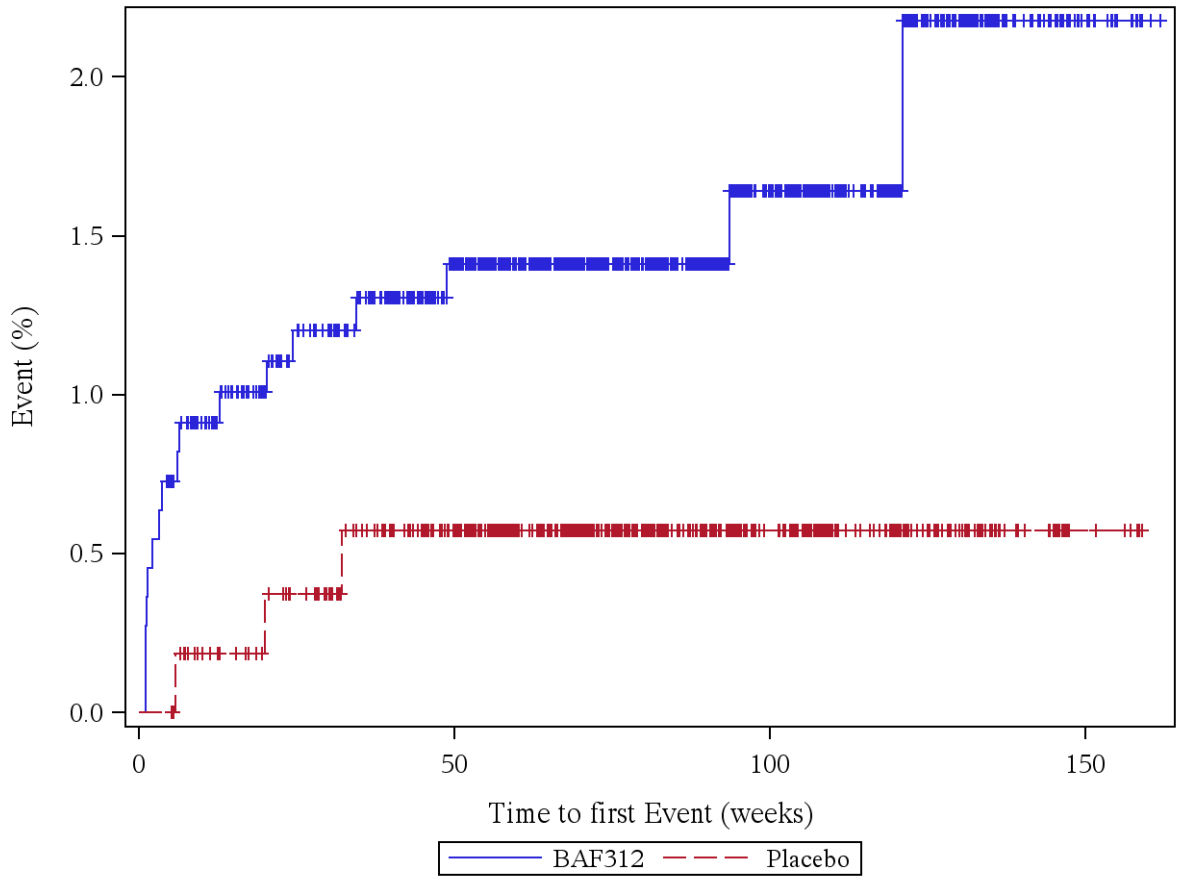


Patients at risk (BAF312/Placebo): Week 0: 1099/546, Week 4: 1096/546, Week 12: 1055/534, Week 24: 1012/520, Week 36: 985/495, Week 48: 920/458, Week 60: 811/383, Week 72: 643/301, Week 84: 509/233, Week 96: 394/173, Week 108: 285/123, Week 120: 197/78, Week 132: 112/40, Week 144: 50/20, Week 156: 10/5, Week 168: 0/0

Log rank test: p-value = 0,933
*: p < 0,05

Analysis population: A2304 SAF total population

Figure 12.1.3.92: TREMOR (PT)

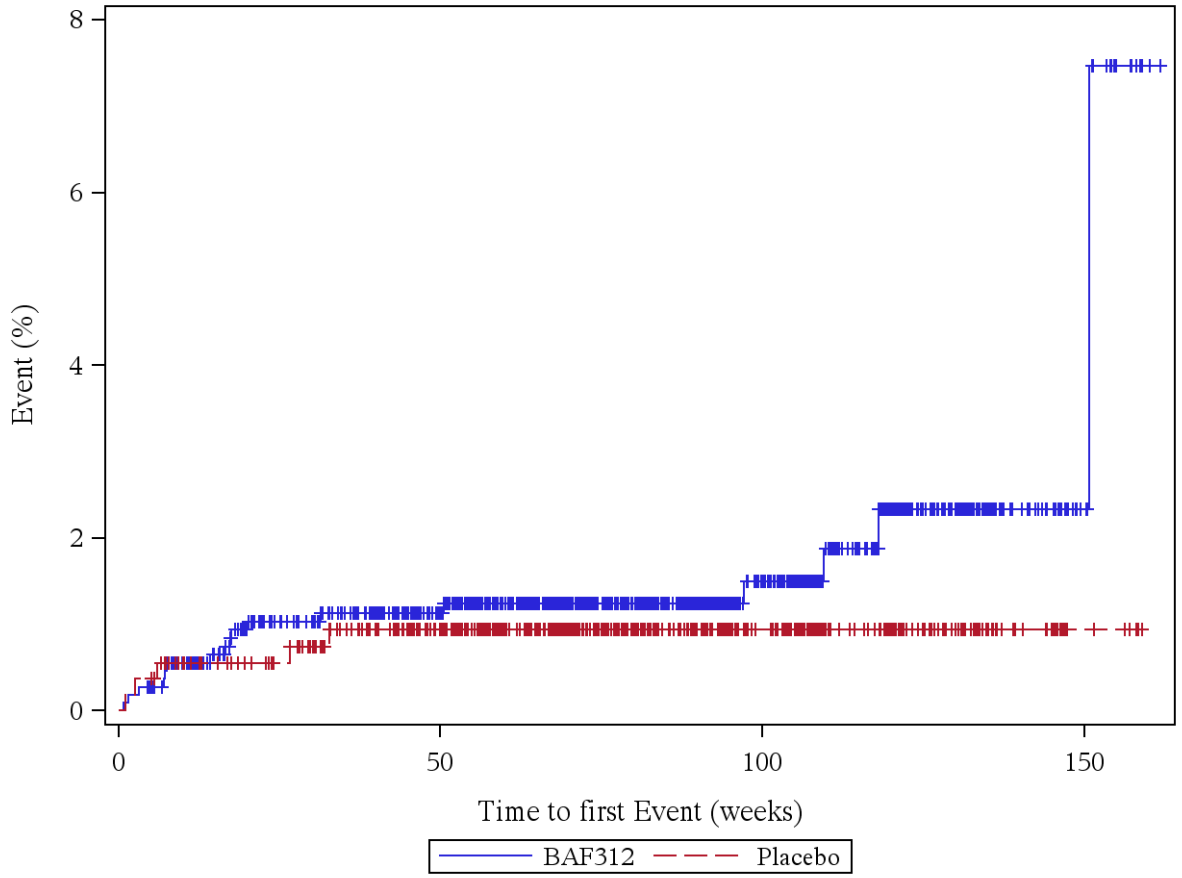


Patients at risk (BAF312/Placebo): Week 0: 1099/546, Week 4: 1091/546, Week 12: 1049/534, Week 24: 1005/519, Week 36: 977/494, Week 48: 912/459, Week 60: 806/387, Week 72: 642/305, Week 84: 509/237, Week 96: 394/176, Week 108: 287/126, Week 120: 198/80, Week 132: 110/40, Week 144: 51/20, Week 156: 10/5, Week 168: 0/0

Log rank test: p-value = 0,084
*: p < 0,05

Analysis population: A2304 SAF total population

Figure 12.1.3.93: TRIGEMINAL NEURALGIA (PT)

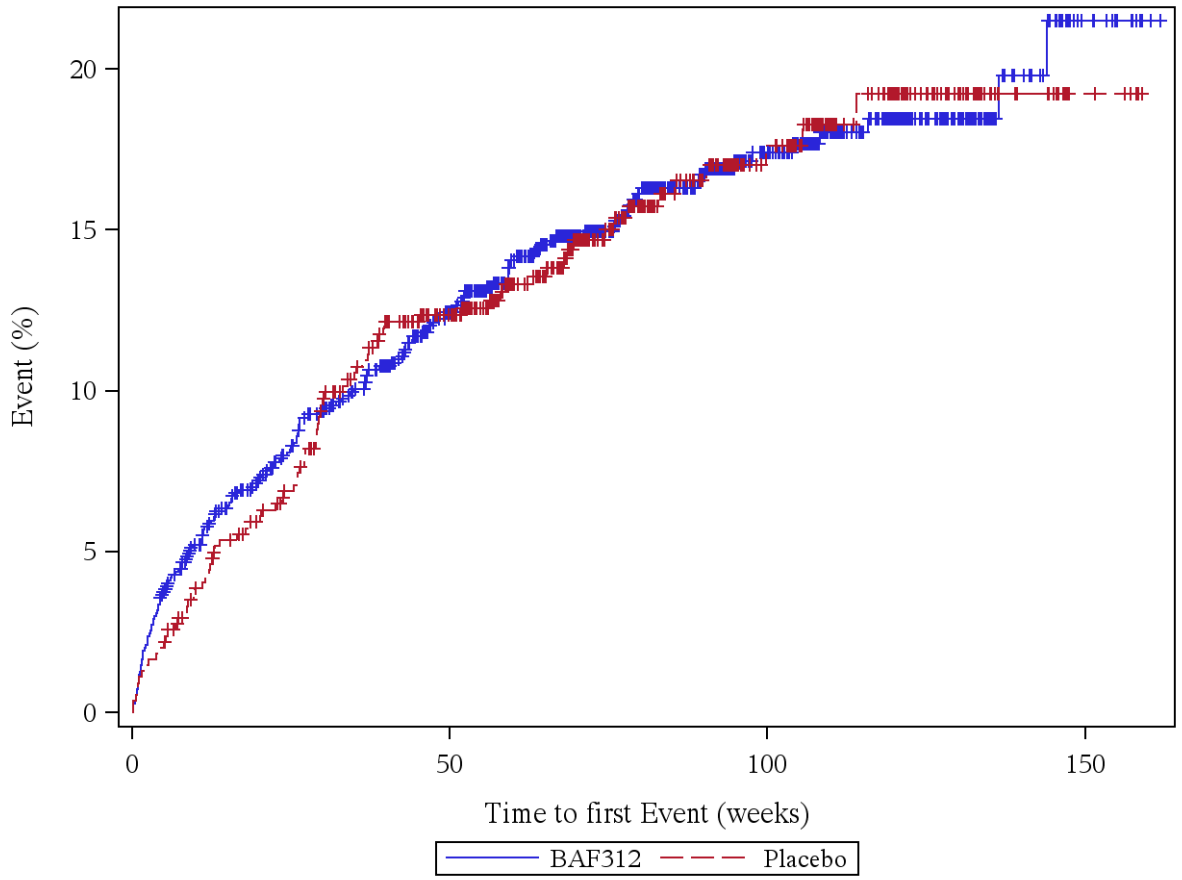


Patients at risk (BAF312/Placebo): Week 0: 1099/546, Week 4: 1096/544, Week 12: 1054/532, Week 24: 1007/518, Week 36: 980/492, Week 48: 919/456, Week 60: 811/383, Week 72: 646/300, Week 84: 512/234, Week 96: 397/173, Week 108: 288/123, Week 120: 196/78, Week 132: 111/39, Week 144: 50/19, Week 156: 9/5, Week 168: 0/0

Log rank test: p-value = 0,326
*: p < 0,05

Analysis population: A2304 SAF total population

Figure 12.1.3.94: PSYCHIATRIC DISORDERS (SOC)

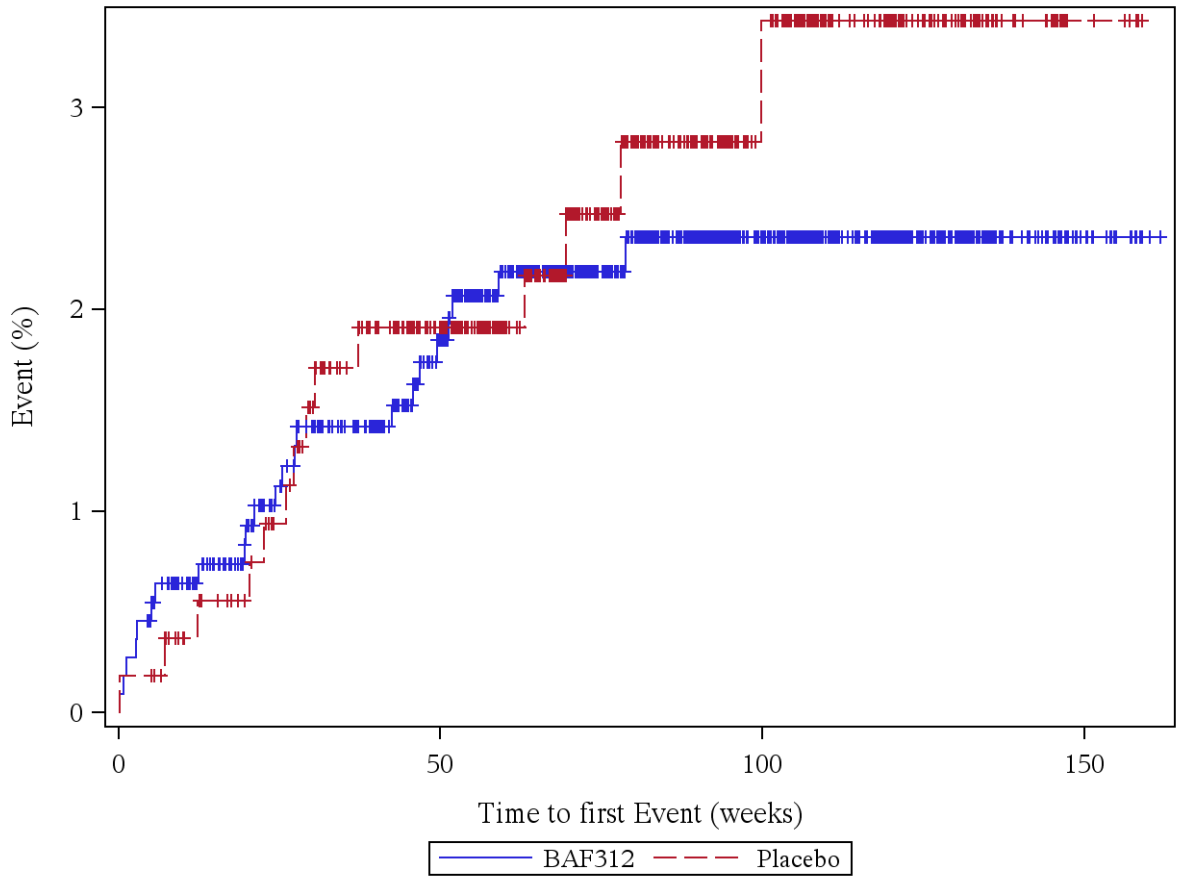


Patients at risk (BAF312/Placebo): Week 0: 1099/546, Week 4: 1064/536, Week 12: 999/515, Week 24: 941/487, Week 36: 896/449, Week 48: 821/411, Week 60: 715/344, Week 72: 556/264, Week 84: 437/201, Week 96: 336/147, Week 108: 240/106, Week 120: 158/68, Week 132: 92/31, Week 144: 46/16, Week 156: 10/5, Week 168: 0/0

Log rank test: p-value = 0,911
*: p < 0,05

Analysis population: A2304 SAF total population

Figure 12.1.3.95: ANXIETY (PT)

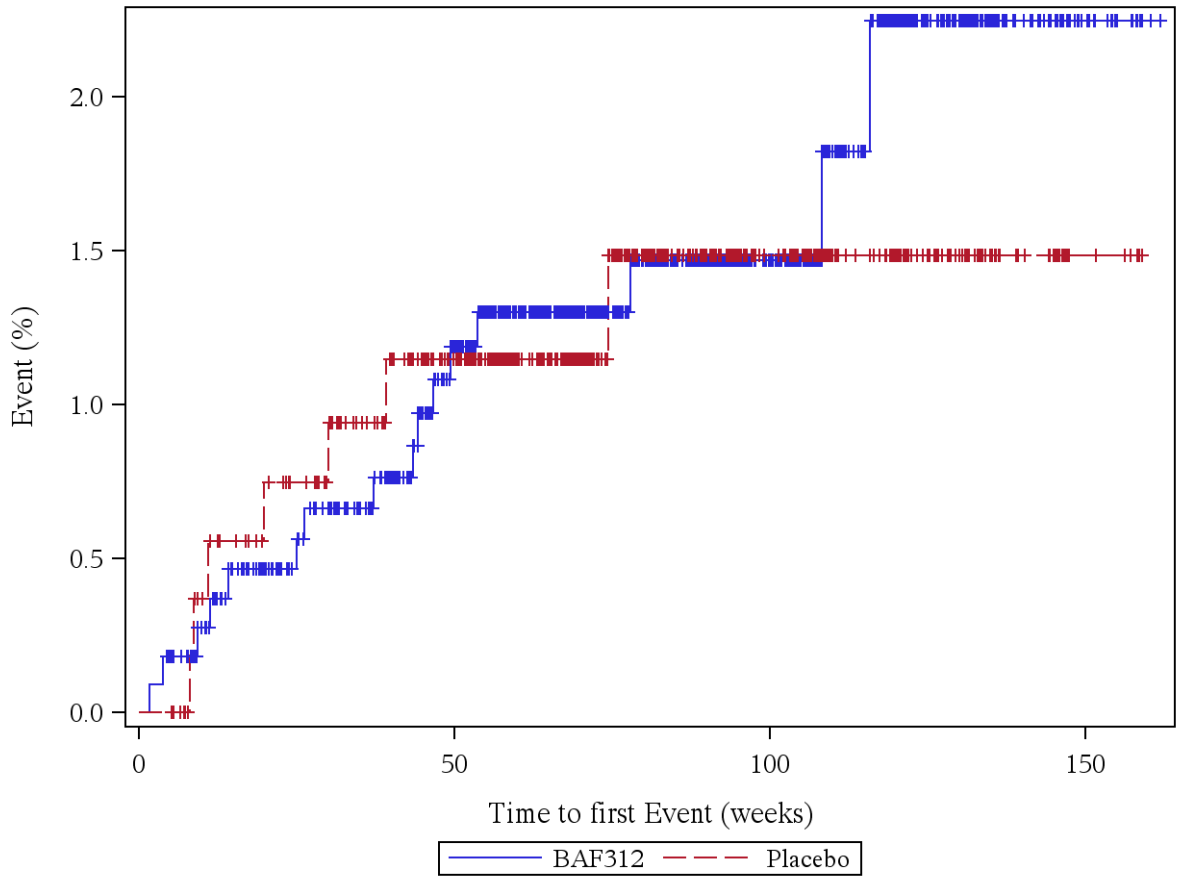


Patients at risk (BAF312/Placebo): Week 0: 1099/546, Week 4: 1094/545, Week 12: 1052/534, Week 24: 1008/517, Week 36: 978/490, Week 48: 910/455, Week 60: 800/382, Week 72: 637/298, Week 84: 506/232, Week 96: 394/172, Week 108: 287/122, Week 120: 197/79, Week 132: 111/39, Week 144: 51/20, Week 156: 10/5, Week 168: 0/0

Log rank test: p-value = 0,554
*: p < 0,05

Analysis population: A2304 SAF total population

Figure 12.1.3.96: DEPRESSED MOOD (PT)

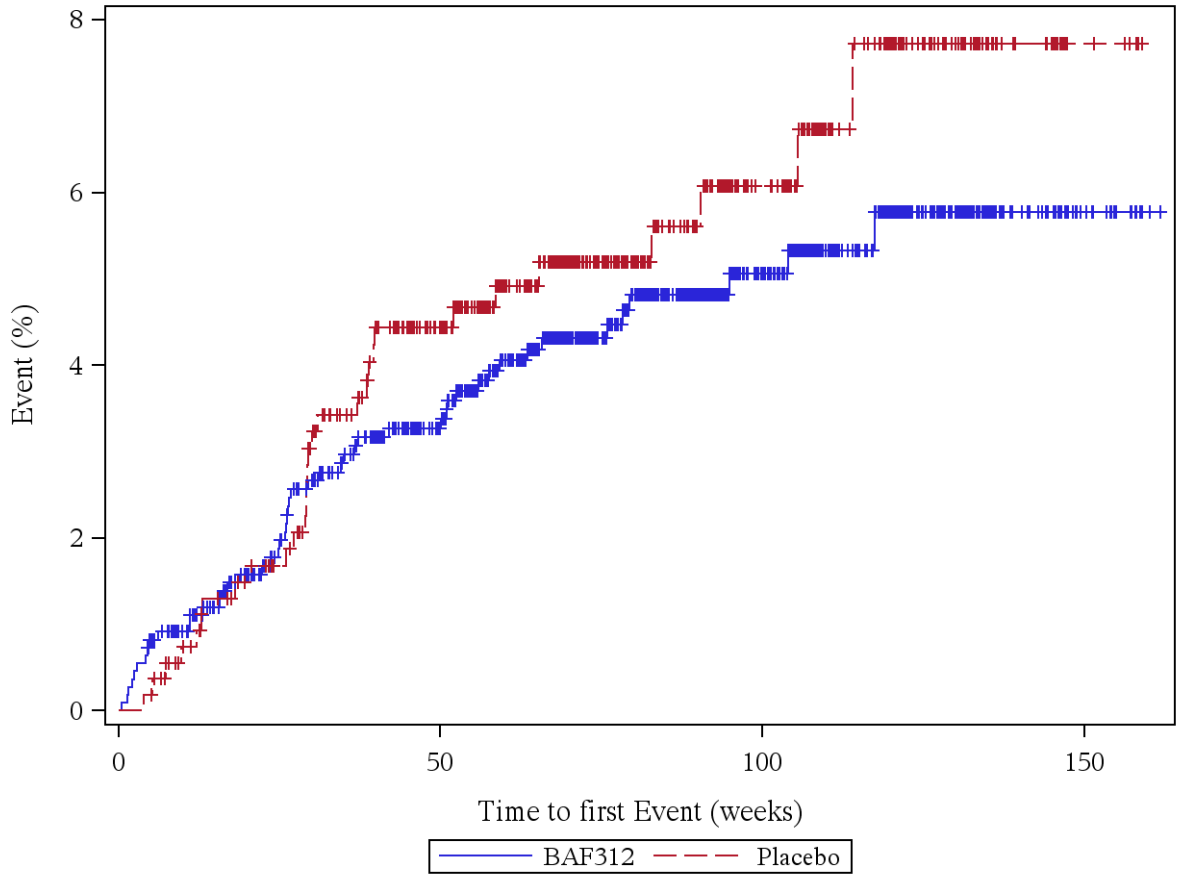


Patients at risk (BAF312/Placebo): Week 0: 1099/546, Week 4: 1097/546, Week 12: 1056/532, Week 24: 1014/517, Week 36: 985/493, Week 48: 916/456, Week 60: 809/384, Week 72: 645/302, Week 84: 510/233, Week 96: 394/172, Week 108: 287/124, Week 120: 196/79, Week 132: 111/39, Week 144: 50/20, Week 156: 10/5, Week 168: 0/0

Log rank test: p-value = 0,797
*: p < 0,05

Analysis population: A2304 SAF total population

Figure 12.1.3.97: DEPRESSION (PT)

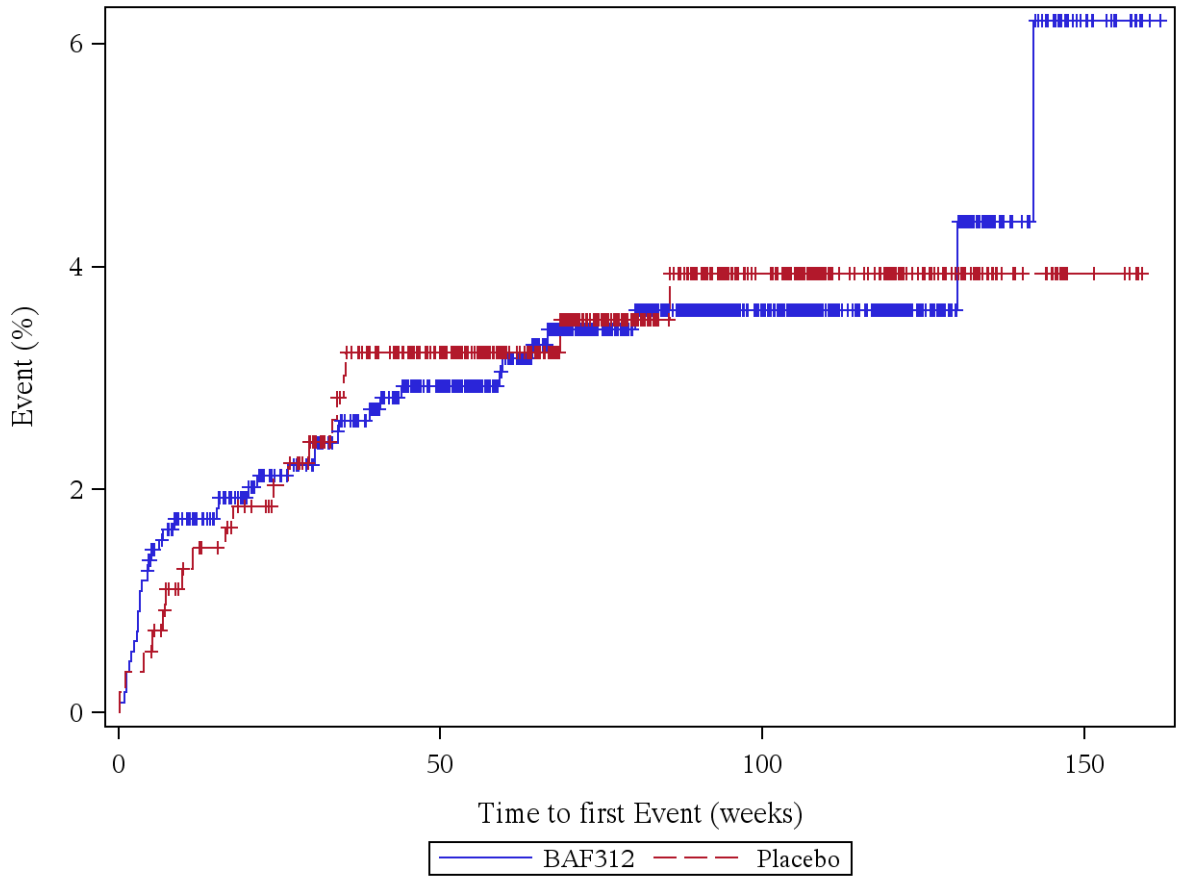


Patients at risk (BAF312/Placebo): Week 0: 1099/546, Week 4: 1093/545, Week 12: 1048/532, Week 24: 1001/513, Week 36: 963/481, Week 48: 901/441, Week 60: 794/369, Week 72: 628/289, Week 84: 492/222, Week 96: 380/166, Week 108: 273/121, Week 120: 184/76, Week 132: 107/38, Week 144: 50/19, Week 156: 10/5, Week 168: 0/0

Log rank test: p-value = 0,347
*: p < 0,05

Analysis population: A2304 SAF total population

Figure 12.1.3.98: INSOMNIA (PT)

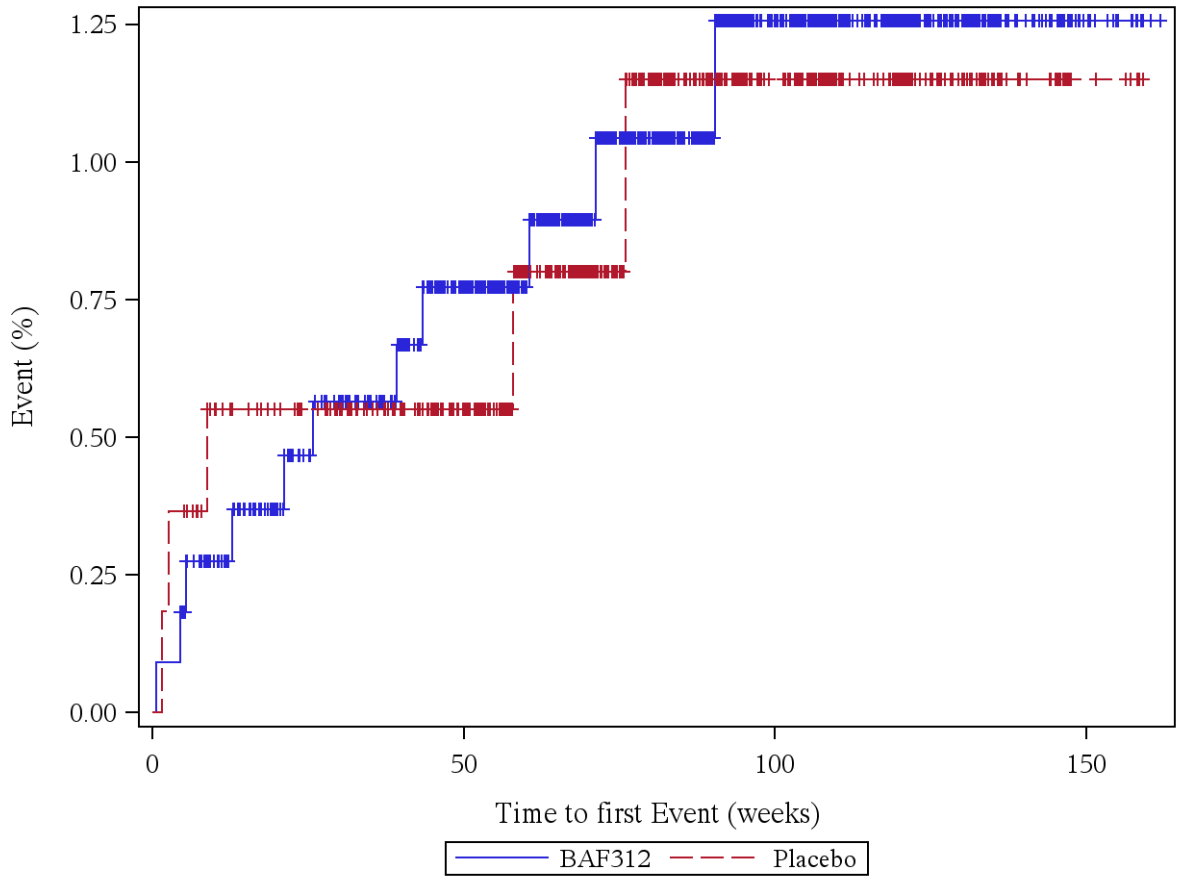


Patients at risk (BAF312/Placebo): Week 0: 1099/546, Week 4: 1086/543, Week 12: 1040/529, Week 24: 995/512, Week 36: 963/483, Week 48: 898/448, Week 60: 792/378, Week 72: 626/295, Week 84: 495/230, Week 96: 385/170, Week 108: 279/122, Week 120: 190/78, Week 132: 106/38, Week 144: 49/19, Week 156: 10/5, Week 168: 0/0

Log rank test: p-value = 0,970
*: p < 0,05

Analysis population: A2304 SAF total population

Figure 12.1.3.99: SLEEP DISORDER (PT)

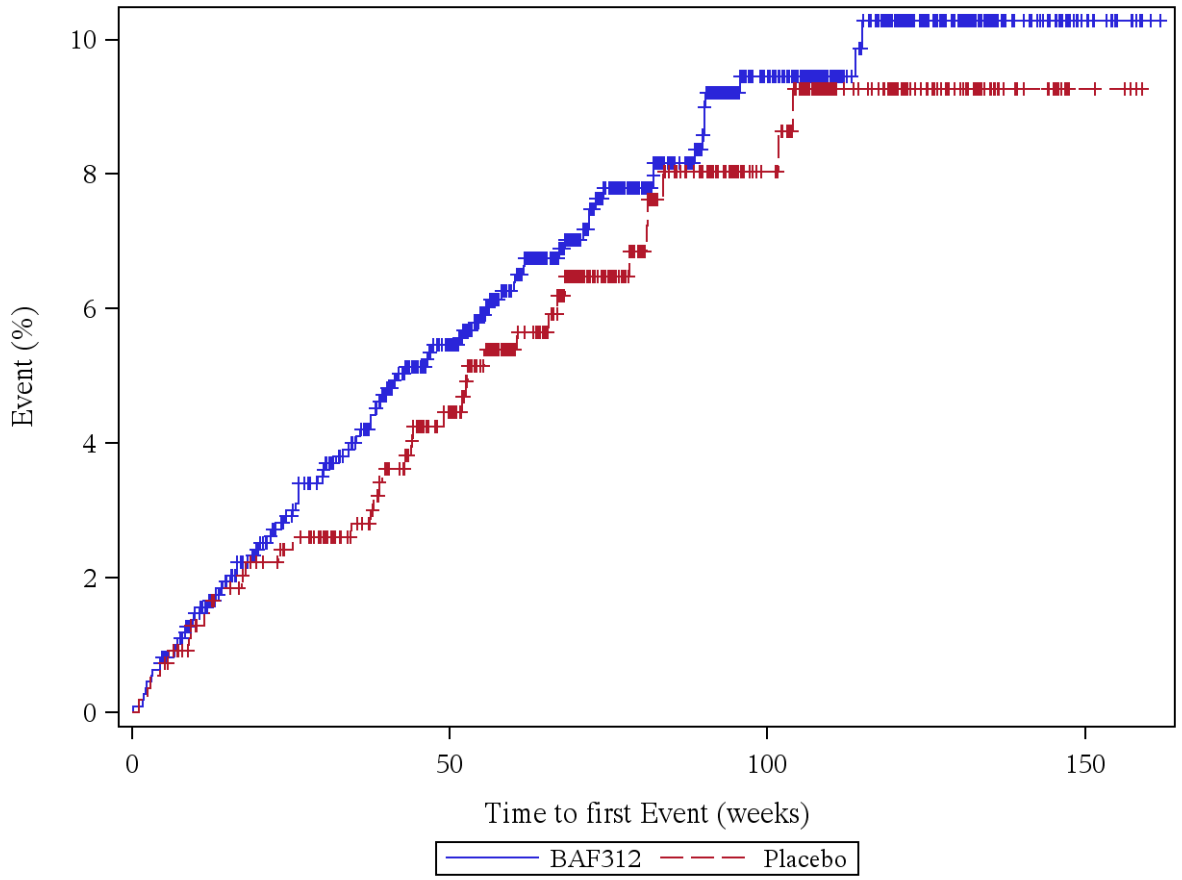


Patients at risk (BAF312/Placebo): Week 0: 1099/546, Week 4: 1098/544, Week 12: 1057/532, Week 24: 1013/518, Week 36: 985/495, Week 48: 918/460, Week 60: 812/386, Week 72: 646/304, Week 84: 512/235, Week 96: 395/174, Week 108: 288/124, Week 120: 197/79, Week 132: 110/40, Week 144: 50/20, Week 156: 10/5, Week 168: 0/0

Log rank test: p-value = 0,884
*: p < 0,05

Analysis population: A2304 SAF total population

Figure 12.1.3.100: RENAL AND URINARY DISORDERS (SOC)

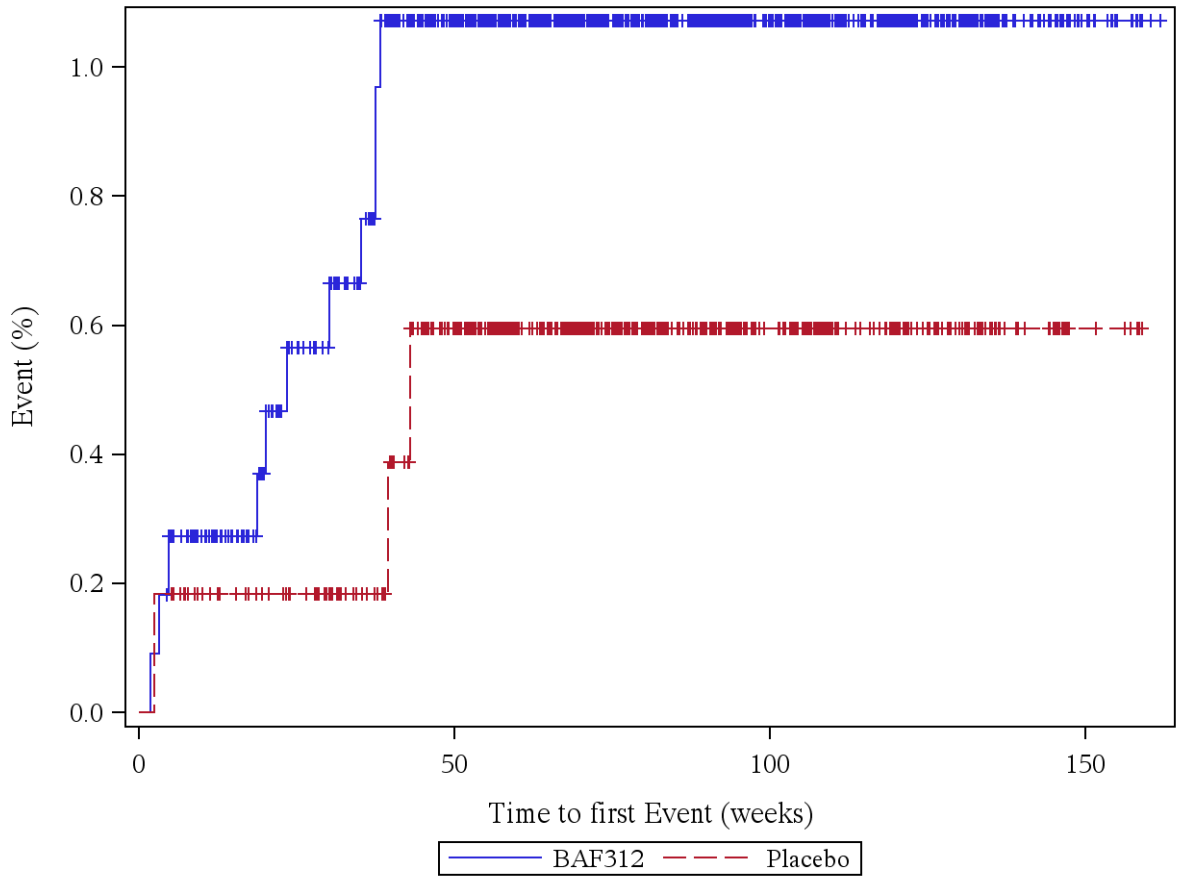


Patients at risk (BAF312/Placebo): Week 0: 1099/546, Week 4: 1092/543, Week 12: 1042/528, Week 24: 987/509, Week 36: 947/485, Week 48: 872/443, Week 60: 764/367, Week 72: 601/287, Week 84: 478/219, Week 96: 365/166, Week 108: 269/118, Week 120: 181/75, Week 132: 103/37, Week 144: 47/18, Week 156: 10/4, Week 168: 0/0

Log rank test: p-value = 0,549
*: p < 0,05

Analysis population: A2304 SAF total population

Figure 12.1.3.101: DYSURIA (PT)

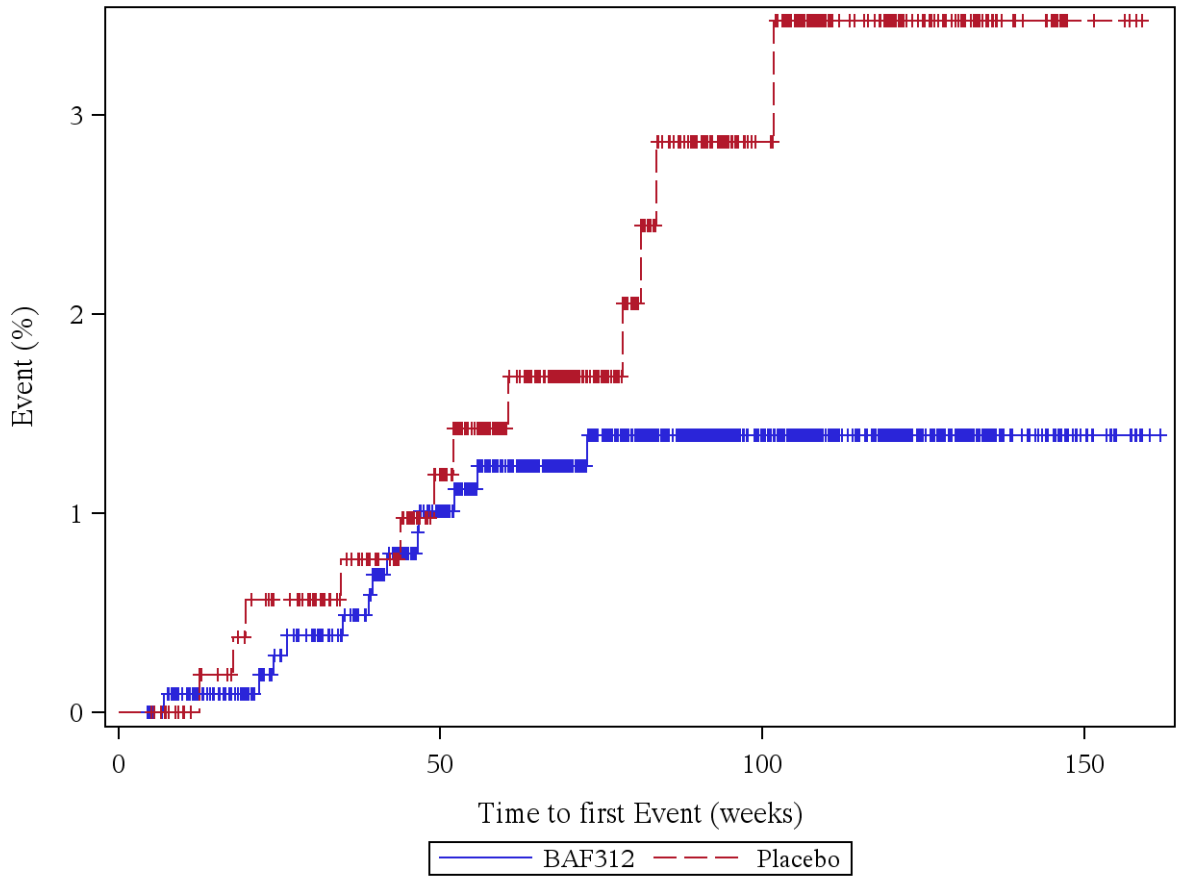


Patients at risk (BAF312/Placebo): Week 0: 1099/546, Week 4: 1097/545, Week 12: 1056/534, Week 24: 1011/520, Week 36: 982/496, Week 48: 914/458, Week 60: 808/385, Week 72: 643/303, Week 84: 510/236, Week 96: 398/175, Week 108: 289/125, Week 120: 199/79, Week 132: 113/40, Week 144: 51/20, Week 156: 10/5, Week 168: 0/0

Log rank test: p-value = 0,336
*: p < 0,05

Analysis population: A2304 SAF total population

Figure 12.1.3.102: URINARY INCONTINENCE (PT)

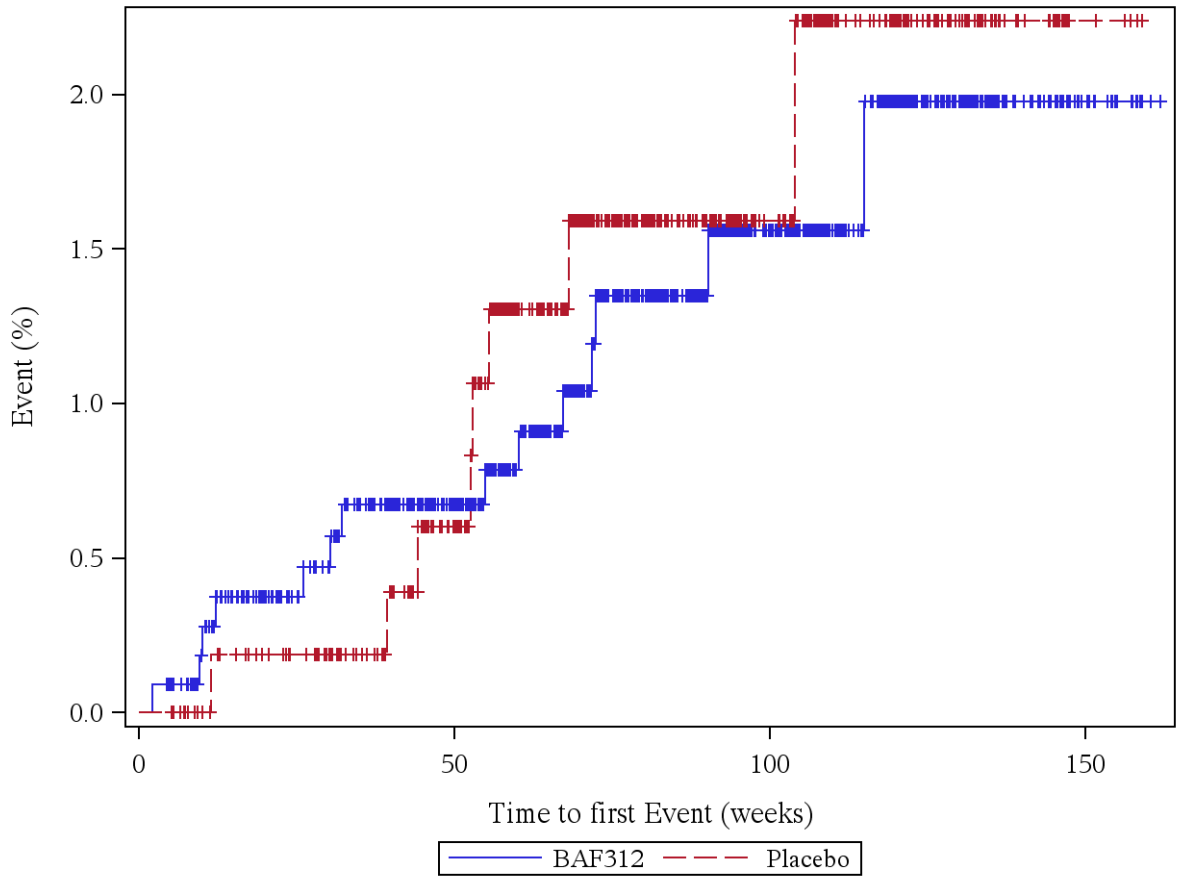


Patients at risk (BAF312/Placebo): Week 0: 1099/546, Week 4: 1099/546, Week 12: 1058/535, Week 24: 1014/518, Week 36: 985/493, Week 48: 915/456, Week 60: 807/381, Week 72: 642/298, Week 84: 506/228, Week 96: 394/172, Week 108: 288/123, Week 120: 198/79, Week 132: 112/39, Week 144: 50/19, Week 156: 10/4, Week 168: 0/0

Log rank test: p-value = 0,107
*: p < 0,05

Analysis population: A2304 SAF total population

Figure 12.1.3.103: URINARY RETENTION (PT)

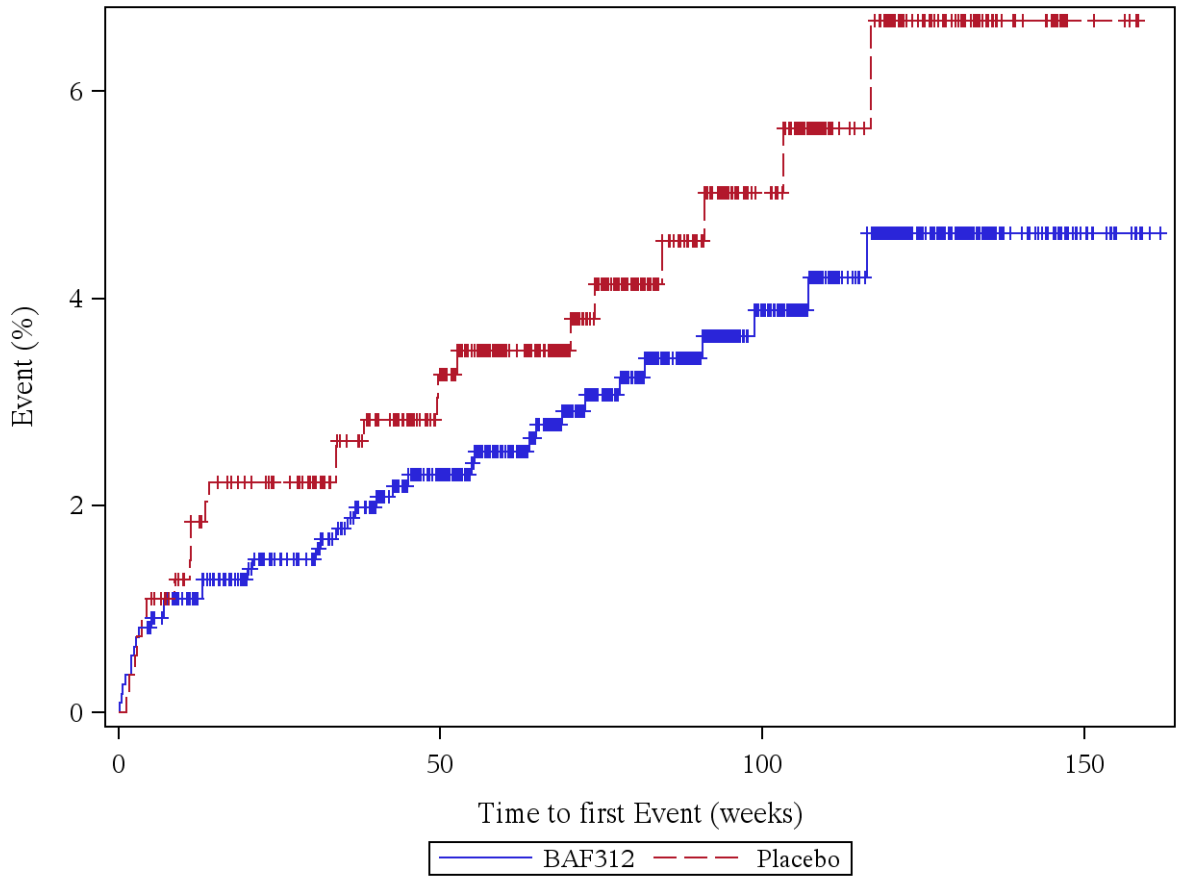


Patients at risk (BAF312/Placebo): Week 0: 1099/546, Week 4: 1098/546, Week 12: 1056/534, Week 24: 1013/520, Week 36: 983/496, Week 48: 918/458, Week 60: 810/383, Week 72: 645/300, Week 84: 511/233, Week 96: 396/173, Week 108: 289/124, Week 120: 198/78, Week 132: 111/38, Week 144: 49/19, Week 156: 10/4, Week 168: 0/0

Log rank test: p-value = 0,701
*: p < 0,05

Analysis population: A2304 SAF total population

Figure 12.1.3.104: REPRODUCTIVE SYSTEM AND BREAST DISORDERS (SOC)

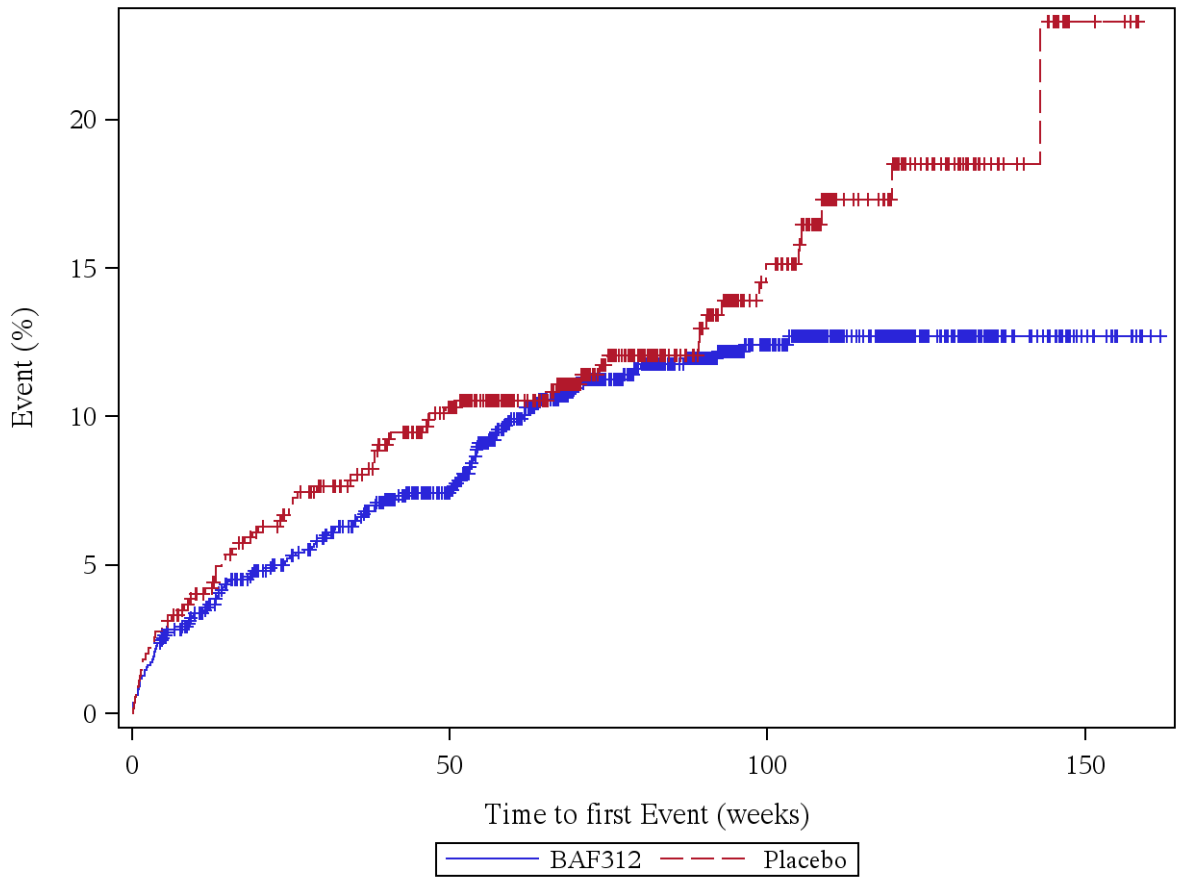


Patients at risk (BAF312/Placebo): Week 0: 1099/546, Week 4: 1090/541, Week 12: 1048/525, Week 24: 1003/509, Week 36: 972/483, Week 48: 906/448, Week 60: 798/376, Week 72: 637/295, Week 84: 501/229, Week 96: 389/168, Week 108: 281/121, Week 120: 191/75, Week 132: 107/37, Week 144: 49/18, Week 156: 9/4, Week 168: 0/0

Log rank test: p-value = 0,224
*: p < 0,05

Analysis population: A2304 SAF total population

Figure 12.1.3.105: RESPIRATORY, THORACIC AND MEDIASTINAL DISORDERS (SOC)

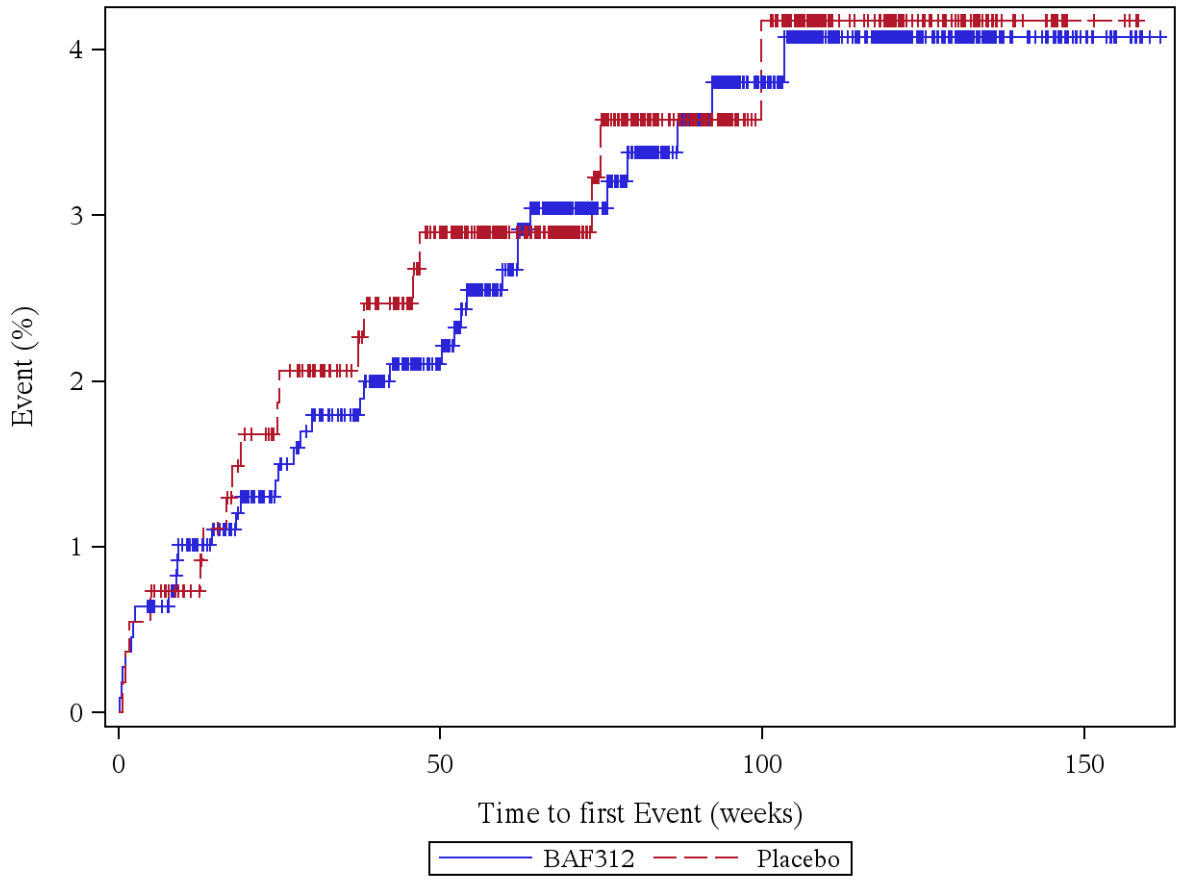


Patients at risk (BAF312/Placebo): Week 0: 1099/546, Week 4: 1073/531, Week 12: 1020/513, Week 24: 966/486, Week 36: 926/459, Week 48: 856/418, Week 60: 739/350, Week 72: 585/274, Week 84: 463/207, Week 96: 358/150, Week 108: 262/105, Week 120: 178/63, Week 132: 102/30, Week 144: 48/16, Week 156: 10/4, Week 168: 0/0

Log rank test: p-value = 0,139
*: p < 0,05

Analysis population: A2304 SAF total population

Figure 12.1.3.106: COUGH (PT)

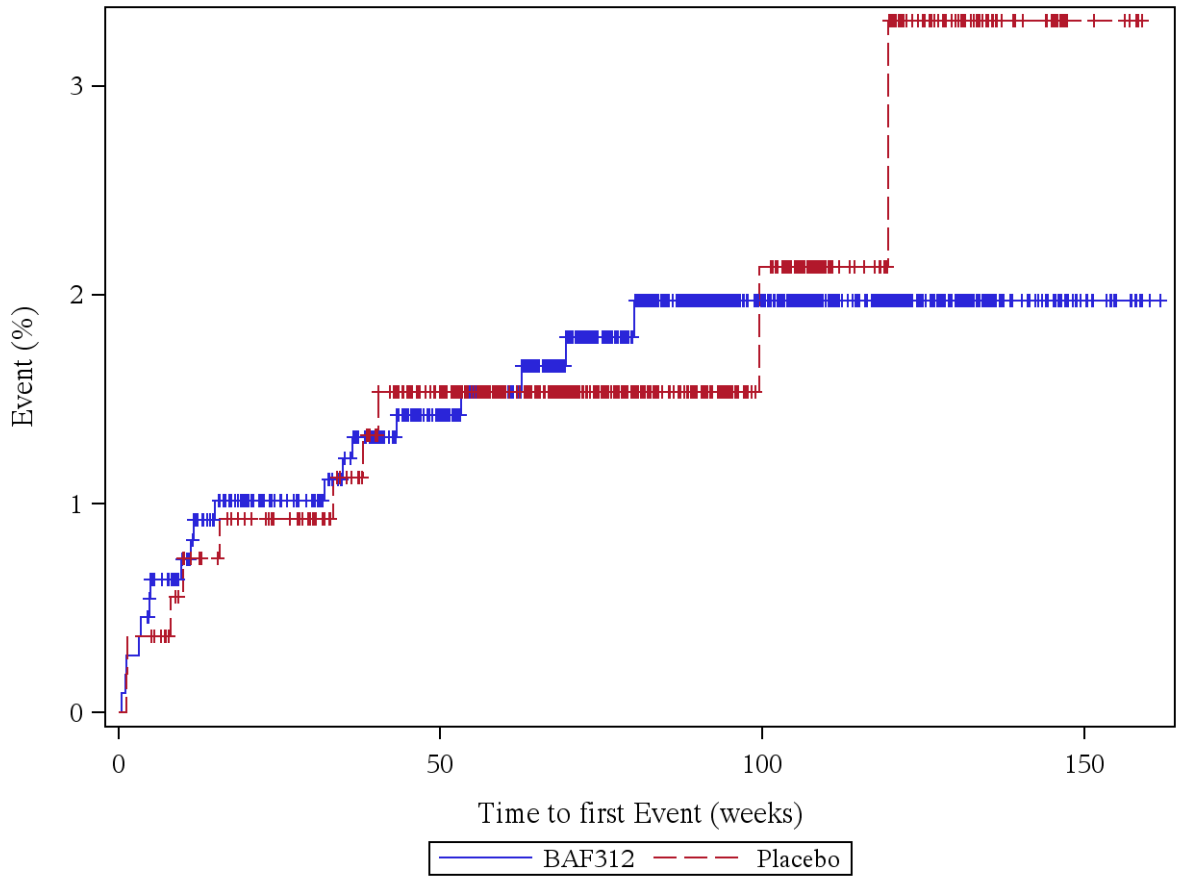


Patients at risk (BAF312/Placebo): Week 0: 1099/546, Week 4: 1092/543, Week 12: 1048/531, Week 24: 1003/512, Week 36: 973/487, Week 48: 905/447, Week 60: 797/376, Week 72: 631/296, Week 84: 497/227, Week 96: 383/170, Week 108: 281/120, Week 120: 191/76, Week 132: 107/38, Week 144: 51/18, Week 156: 10/4, Week 168: 0/0

Log rank test: p-value = 0,876
*: p < 0,05

Analysis population: A2304 SAF total population

Figure 12.1.3.107: DYSPNOEA (PT)

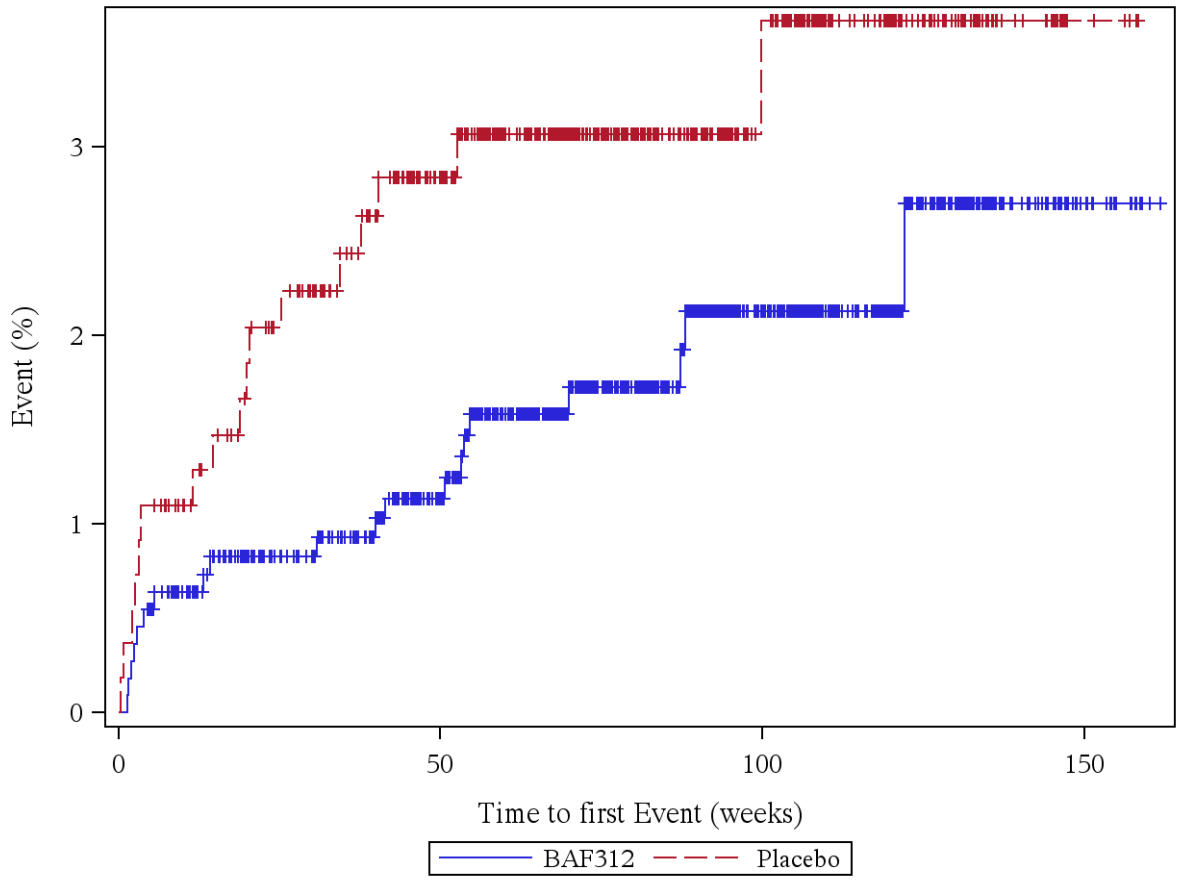


Patients at risk (BAF312/Placebo): Week 0: 1099/546, Week 4: 1094/544, Week 12: 1049/531, Week 24: 1007/516, Week 36: 978/492, Week 48: 912/456, Week 60: 807/384, Week 72: 646/303, Week 84: 512/235, Week 96: 396/174, Week 108: 289/123, Week 120: 198/77, Week 132: 112/38, Week 144: 50/19, Week 156: 10/5, Week 168: 0/0

Log rank test: p-value = 0,864
*: p < 0,05

Analysis population: A2304 SAF total population

Figure 12.1.3.108: OROPHARYNGEAL PAIN (PT)

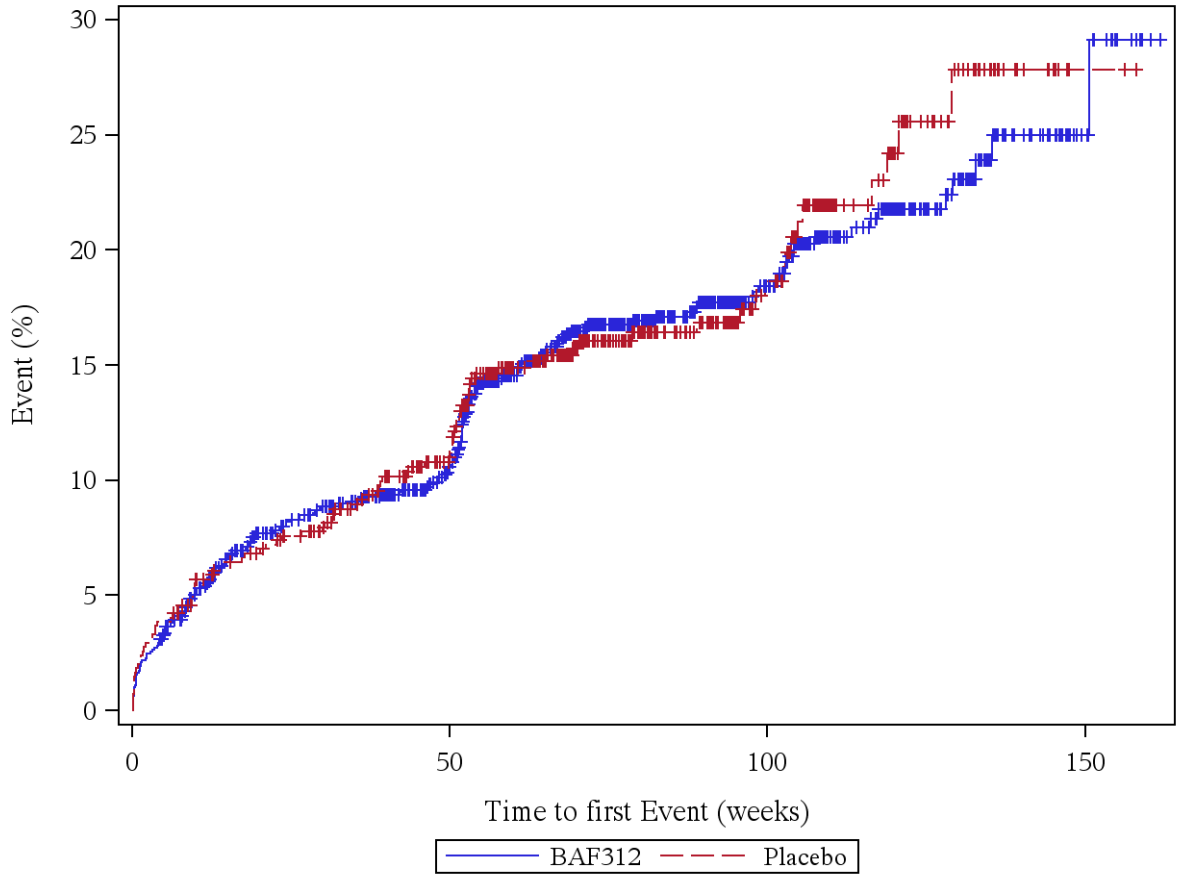


Patients at risk (BAF312/Placebo): Week 0: 1099/546, Week 4: 1093/540, Week 12: 1052/529, Week 24: 1008/511, Week 36: 980/486, Week 48: 914/450, Week 60: 805/379, Week 72: 640/297, Week 84: 508/230, Week 96: 392/171, Week 108: 287/121, Week 120: 198/76, Week 132: 112/38, Week 144: 50/19, Week 156: 10/4, Week 168: 0/0

Log rank test: p-value = 0,087
*: p < 0,05

Analysis population: A2304 SAF total population

Figure 12.1.3.109: SKIN AND SUBCUTANEOUS TISSUE DISORDERS (SOC)

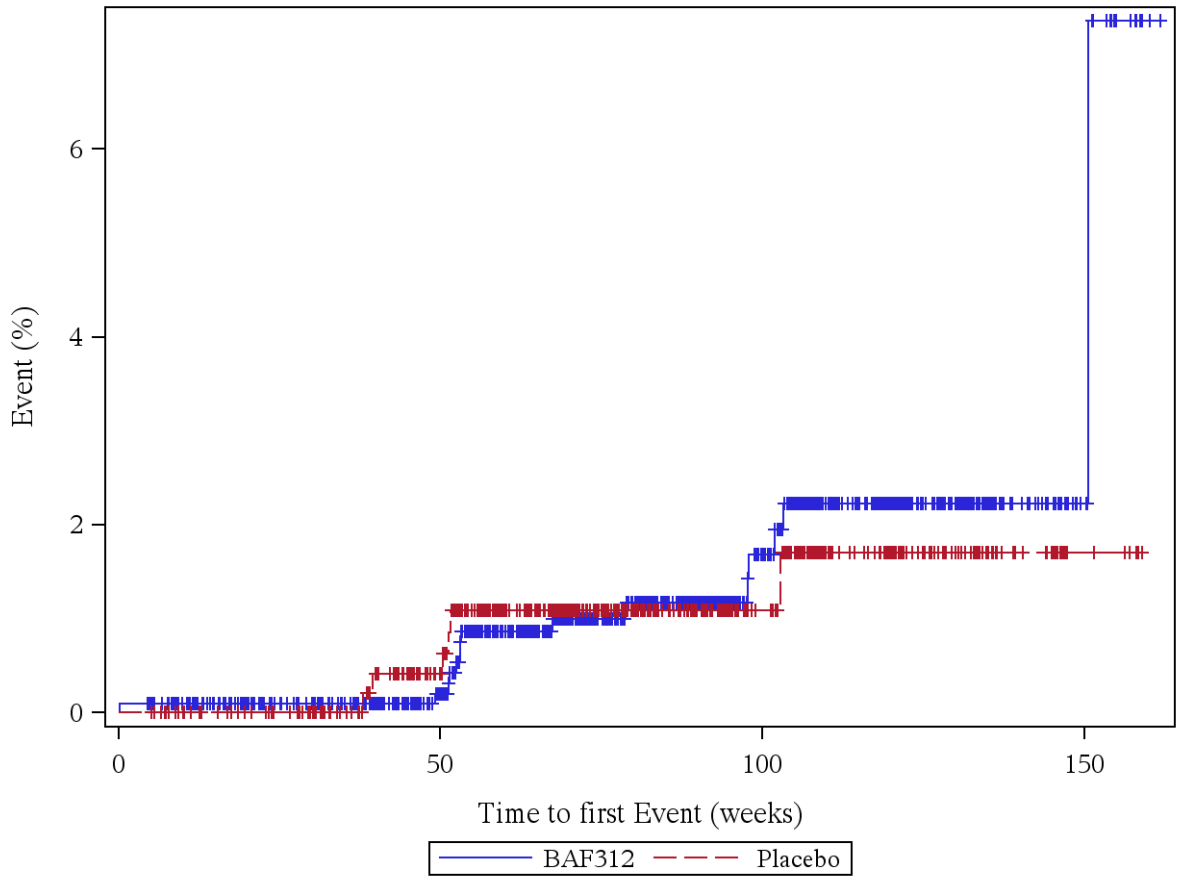


Patients at risk (BAF312/Placebo): Week 0: 1099/546, Week 4: 1068/525, Week 12: 1002/505, Week 24: 938/484, Week 36: 904/454, Week 48: 839/414, Week 60: 703/328, Week 72: 555/255, Week 84: 441/199, Week 96: 341/145, Week 108: 246/96, Week 120: 168/57, Week 132: 102/28, Week 144: 48/12, Week 156: 9/2, Week 168: 0/0

Log rank test: p-value = 0,771
*: p < 0,05

Analysis population: A2304 SAF total population

Figure 12.1.3.110: ACTINIC KERATOSIS (PT)

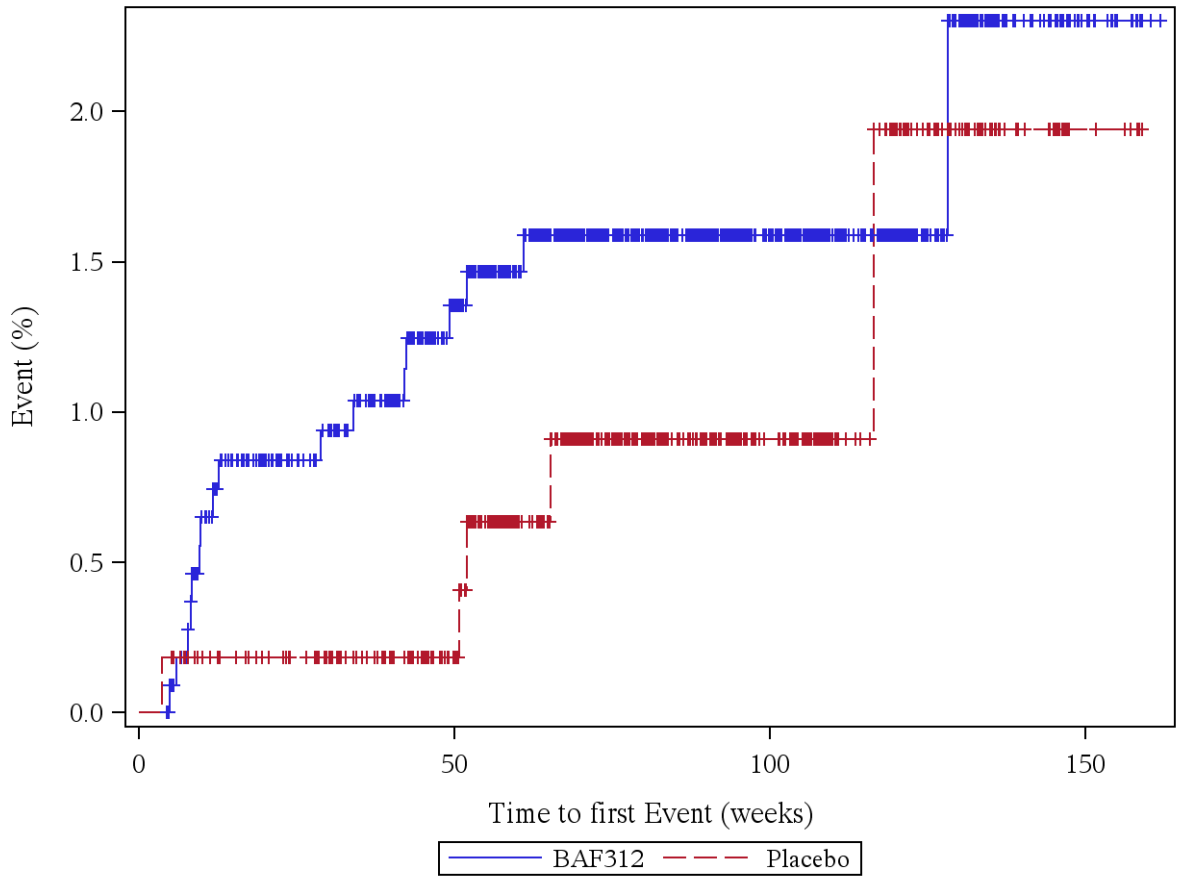


Patients at risk (BAF312/Placebo): Week 0: 1099/546, Week 4: 1098/546, Week 12: 1058/535, Week 24: 1016/521, Week 36: 989/497, Week 48: 924/460, Week 60: 810/384, Week 72: 644/303, Week 84: 509/236, Week 96: 397/175, Week 108: 287/124, Week 120: 196/78, Week 132: 111/40, Week 144: 51/20, Week 156: 9/5, Week 168: 0/0

Log rank test: p-value = 0,760
*: p < 0,05

Analysis population: A2304 SAF total population

Figure 12.1.3.111: ECZEMA (PT)

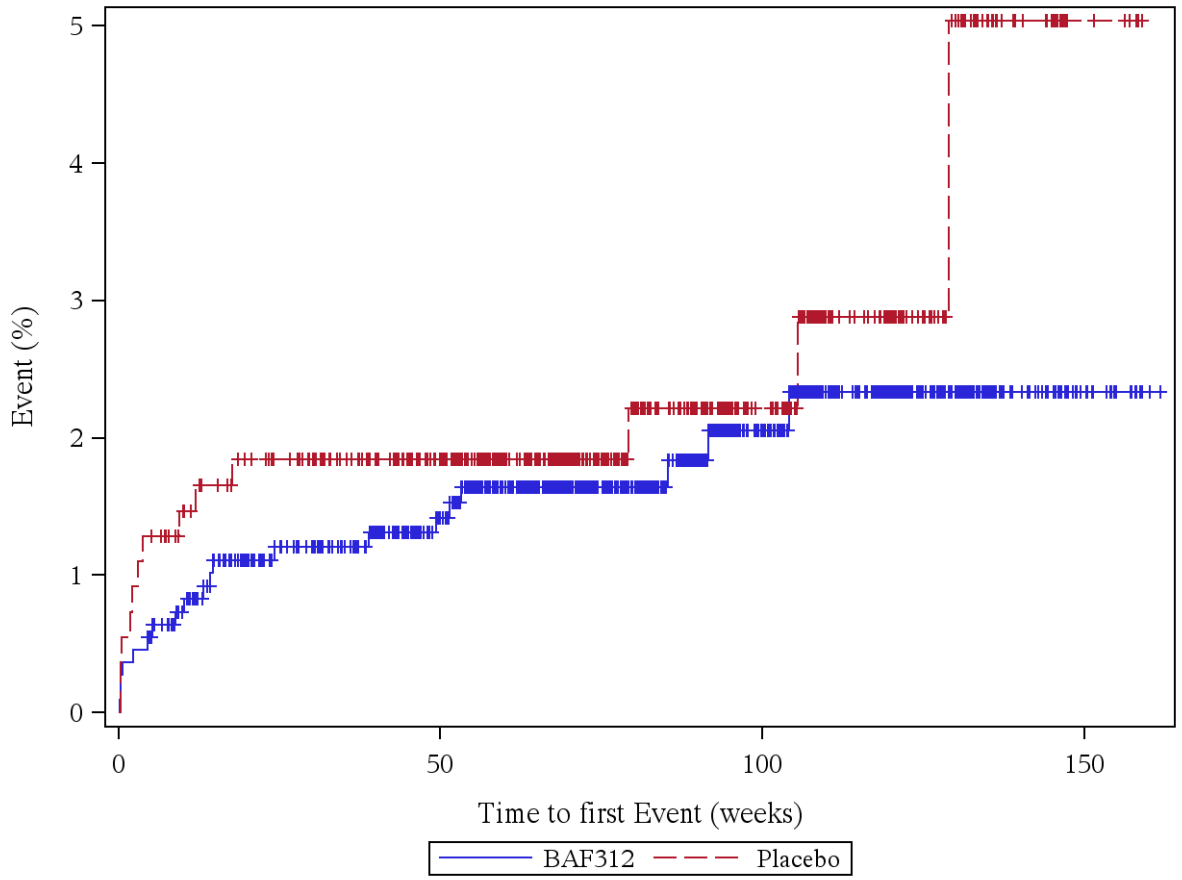


Patients at risk (BAF312/Placebo): Week 0: 1099/546, Week 4: 1099/545, Week 12: 1051/534, Week 24: 1008/520, Week 36: 979/496, Week 48: 912/460, Week 60: 803/385, Week 72: 638/304, Week 84: 505/237, Week 96: 392/176, Week 108: 286/126, Week 120: 198/79, Week 132: 111/40, Week 144: 51/20, Week 156: 10/5, Week 168: 0/0

Log rank test: p-value = 0,312
*: p < 0,05

Analysis population: A2304 SAF total population

Figure 12.1.3.112: RASH (PT)

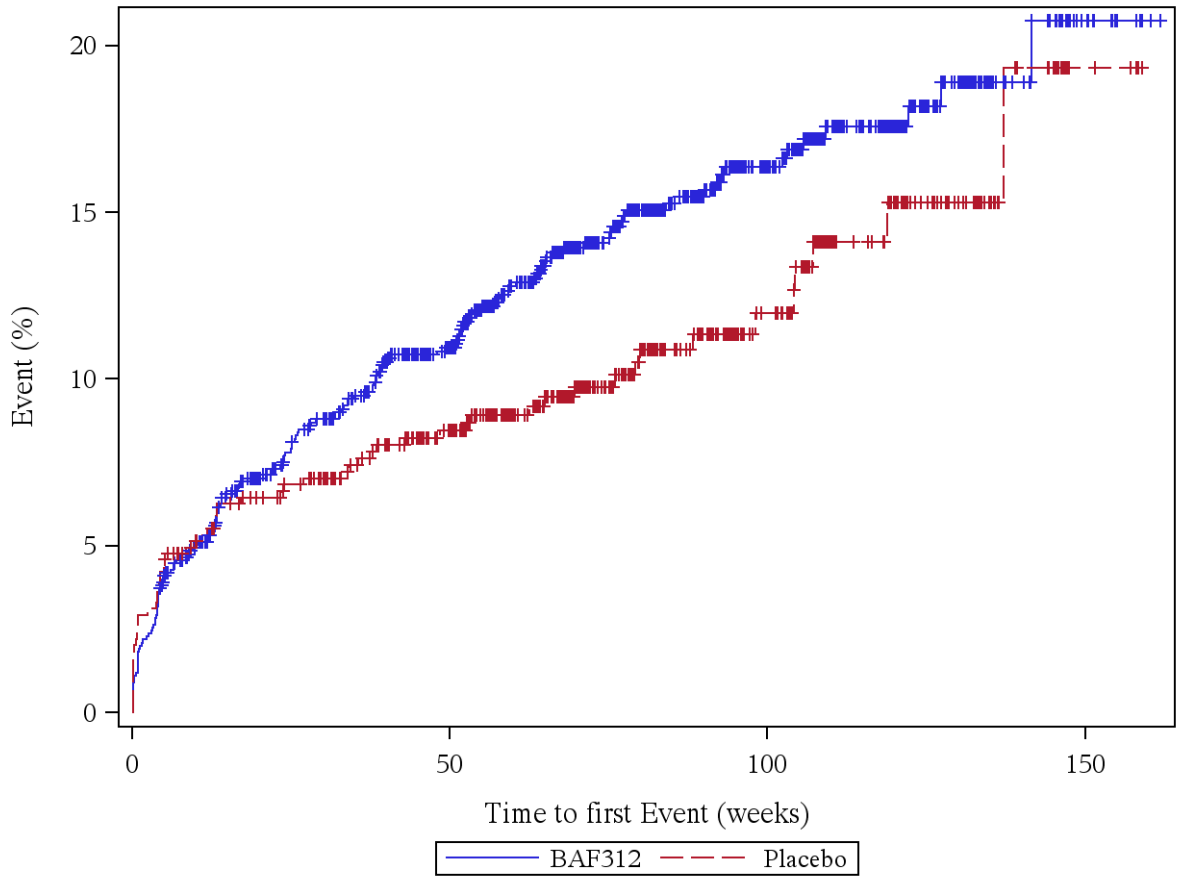


Patients at risk (BAF312/Placebo): Week 0: 1099/546, Week 4: 1094/539, Week 12: 1050/527, Week 24: 1007/512, Week 36: 979/489, Week 48: 914/454, Week 60: 809/382, Week 72: 645/300, Week 84: 511/232, Week 96: 394/174, Week 108: 286/123, Week 120: 197/78, Week 132: 111/38, Week 144: 50/20, Week 156: 10/5, Week 168: 0/0

Log rank test: p-value = 0,406
*: p < 0,05

Analysis population: A2304 SAF total population

Figure 12.1.3.113: VASCULAR DISORDERS (SOC)

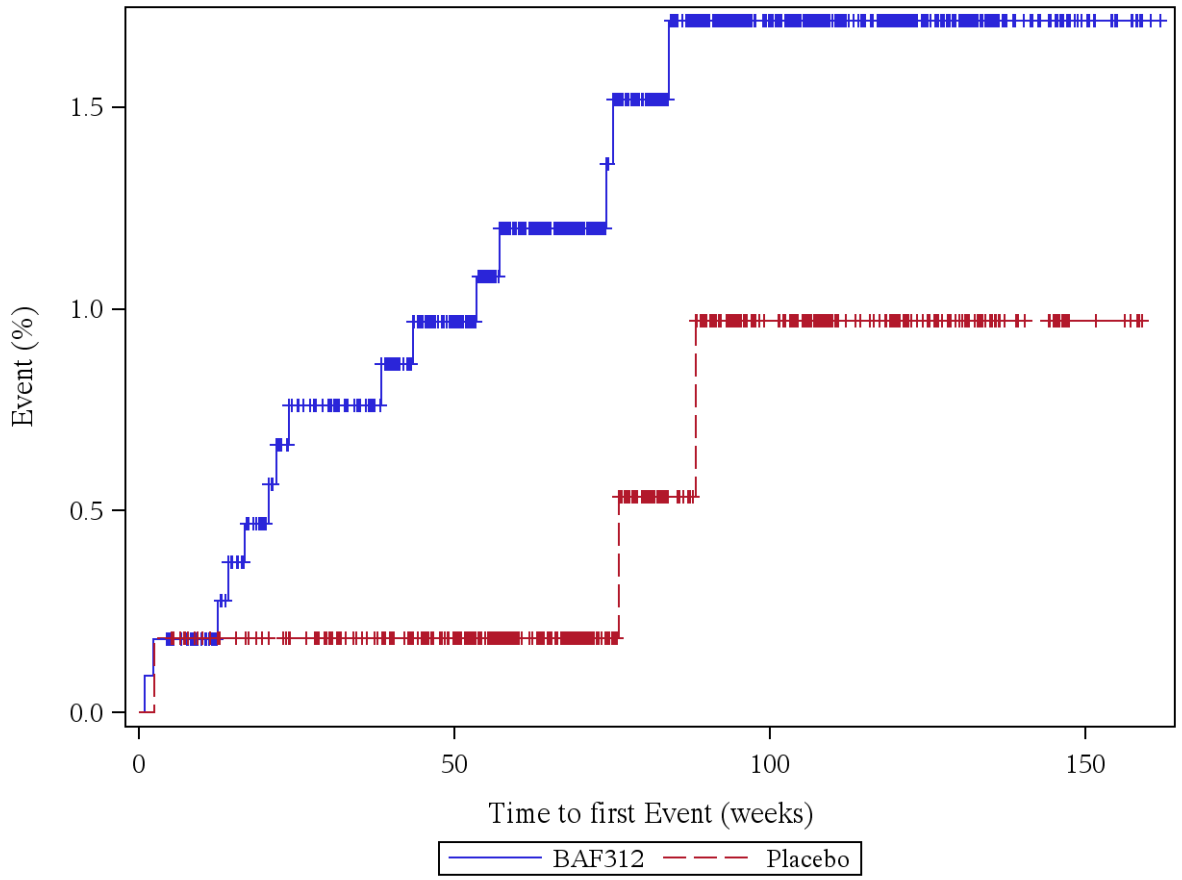


Patients at risk (BAF312/Placebo): Week 0: 1099/546, Week 4: 1064/526, Week 12: 1005/507, Week 24: 936/486, Week 36: 896/458, Week 48: 827/423, Week 60: 710/352, Week 72: 553/270, Week 84: 433/203, Week 96: 333/149, Week 108: 239/100, Week 120: 159/64, Week 132: 88/37, Week 144: 42/18, Week 156: 8/4, Week 168: 0/0

Log rank test: p-value = 0,064
*: p < 0,05

Analysis population: A2304 SAF total population

Figure 12.1.3.114: HAEMATOMA (PT)

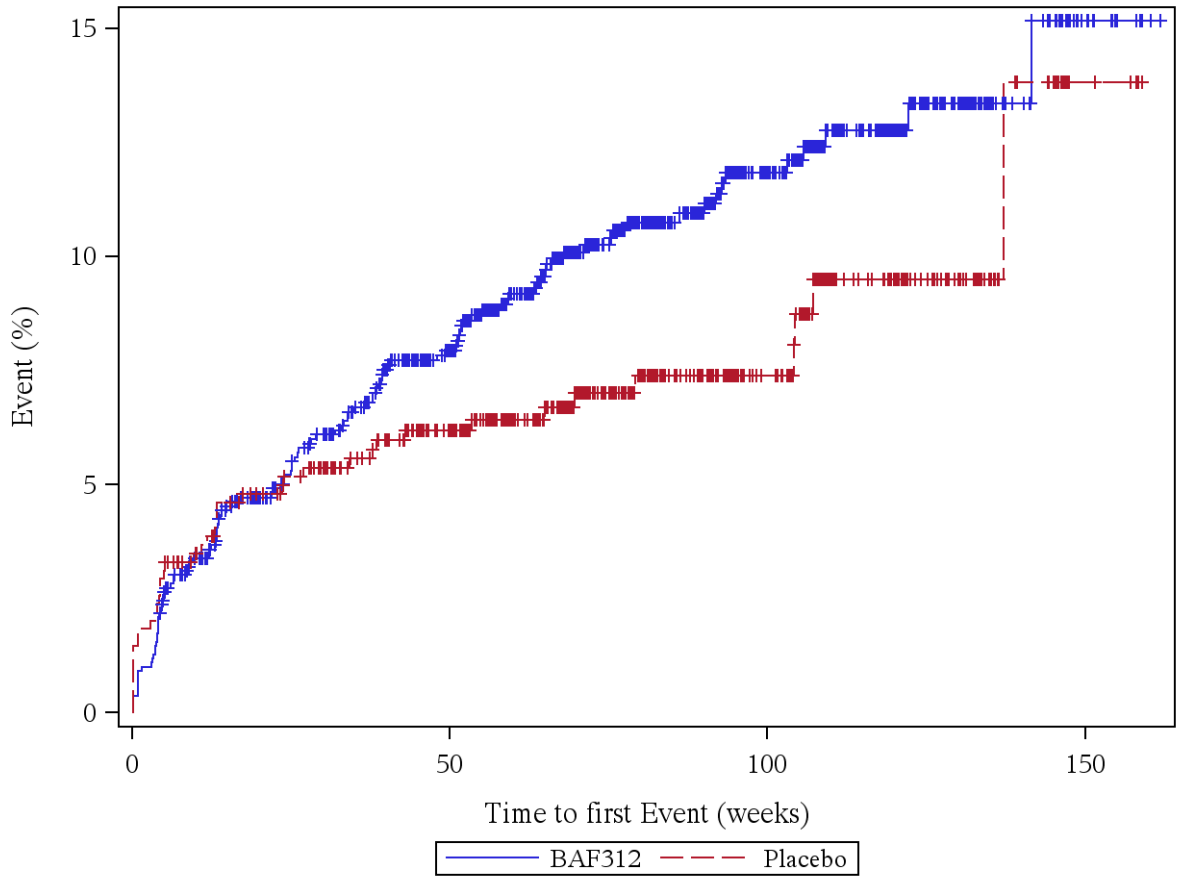


Patients at risk (BAF312/Placebo): Week 0: 1099/546, Week 4: 1097/545, Week 12: 1057/534, Week 24: 1009/520, Week 36: 982/496, Week 48: 916/460, Week 60: 807/387, Week 72: 643/304, Week 84: 505/236, Week 96: 391/175, Week 108: 284/125, Week 120: 194/79, Week 132: 109/40, Week 144: 48/20, Week 156: 10/5, Week 168: 0/0

Log rank test: p-value = 0,139
*: p < 0,05

Analysis population: A2304 SAF total population

Figure 12.1.3.115: HYPERTENSION (PT)



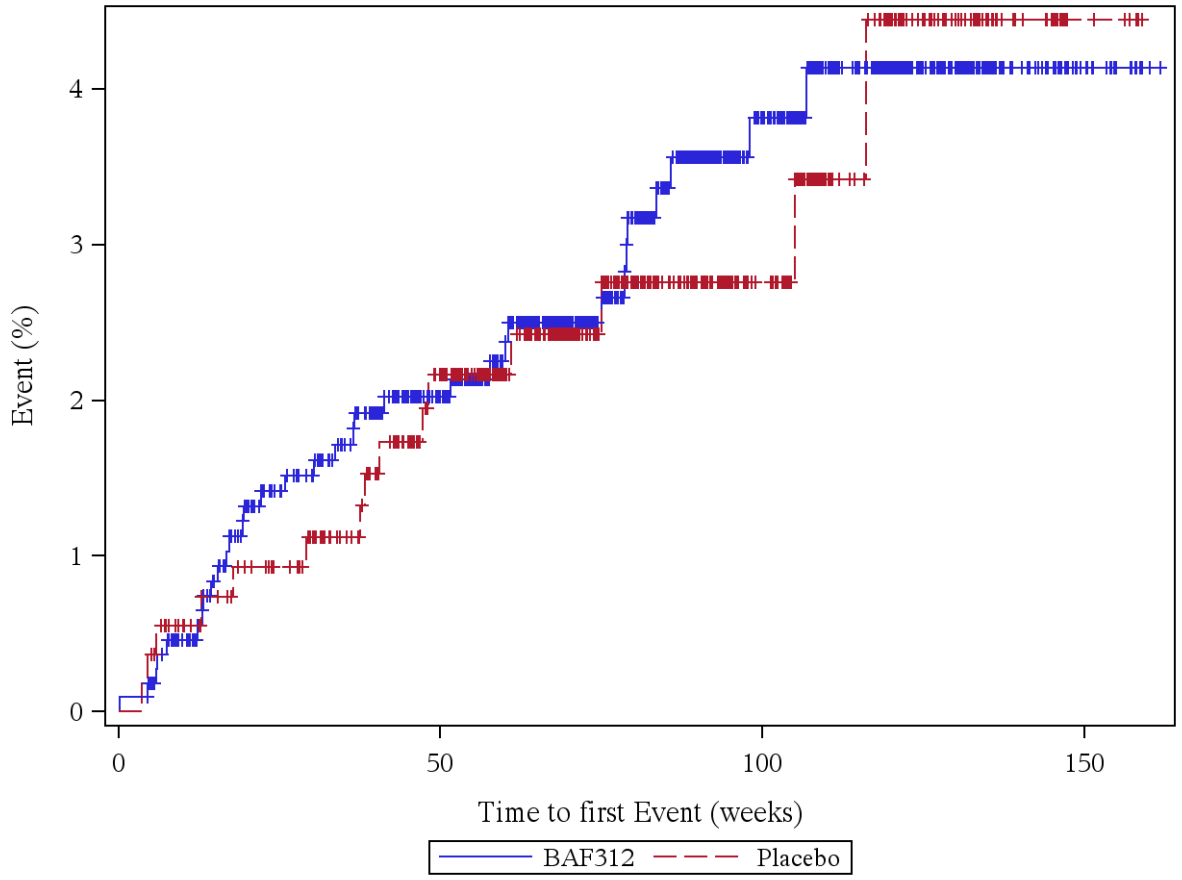
Patients at risk (BAF312/Placebo): Week 0: 1099/546, Week 4: 1080/533, Week 12: 1023/516, Week 24: 962/495, Week 36: 925/469, Week 48: 854/433, Week 60: 740/363, Week 72: 575/279, Week 84: 455/213, Week 96: 351/157, Week 108: 255/106, Week 120: 170/67, Week 132: 95/37, Week 144: 45/18, Week 156: 8/4, Week 168: 0/0

Log rank test: p-value = 0,072
*: p < 0,05

Analysis population: A2304 SAF total population

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

Figure 12.1.4.1: INFECTIONS AND INFESTATIONS (SOC)

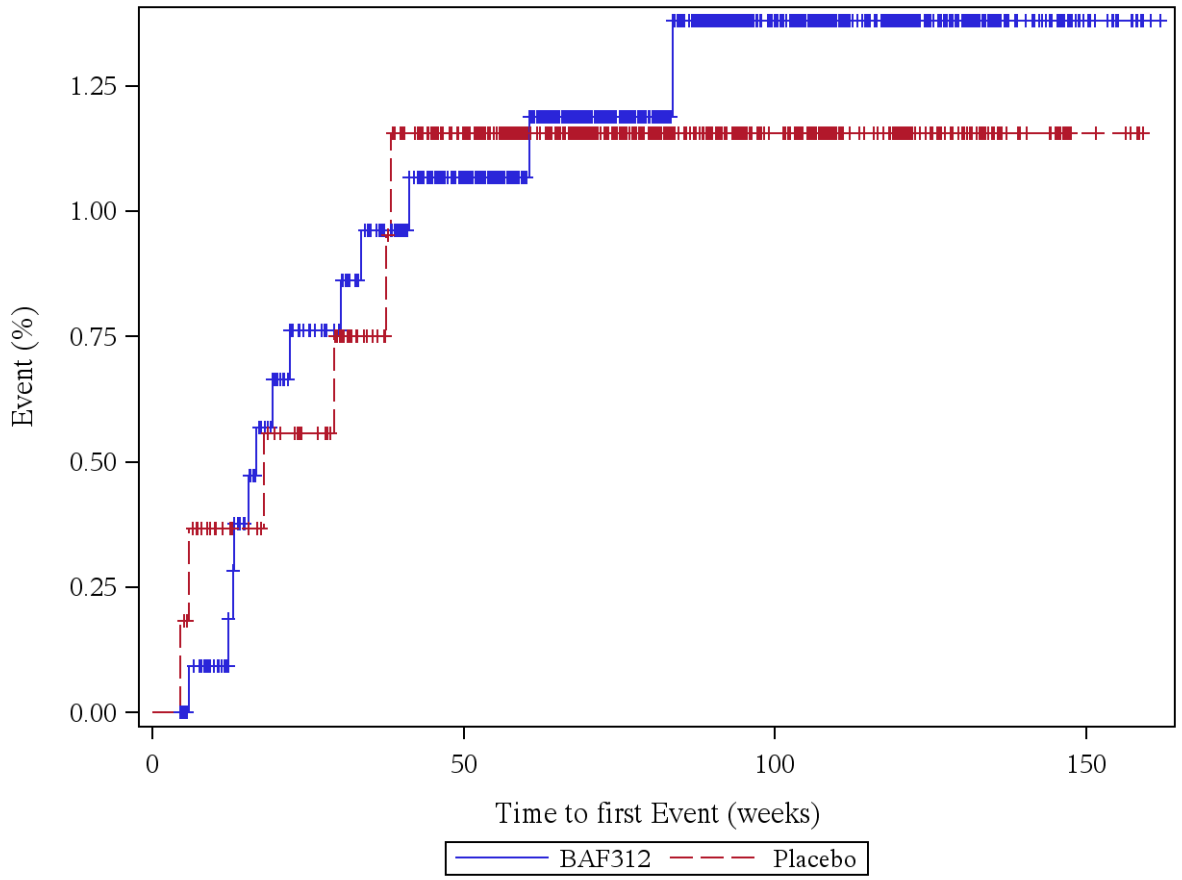


Patients at risk (BAF312/Placebo): Week 0: 1099/546, Week 4: 1098/545, Week 12: 1054/532, Week 24: 1003/516, Week 36: 973/492, Week 48: 908/453, Week 60: 801/383, Week 72: 635/301, Week 84: 499/234, Week 96: 386/173, Week 108: 277/123, Week 120: 189/78, Week 132: 104/40, Week 144: 46/20, Week 156: 9/5, Week 168: 0/0

Log rank test: p-value = 0,798
*: p < 0,05

Analysis population: A2304 SAF total population

Figure 12.1.4.2: URINARY TRACT INFECTION (PT)

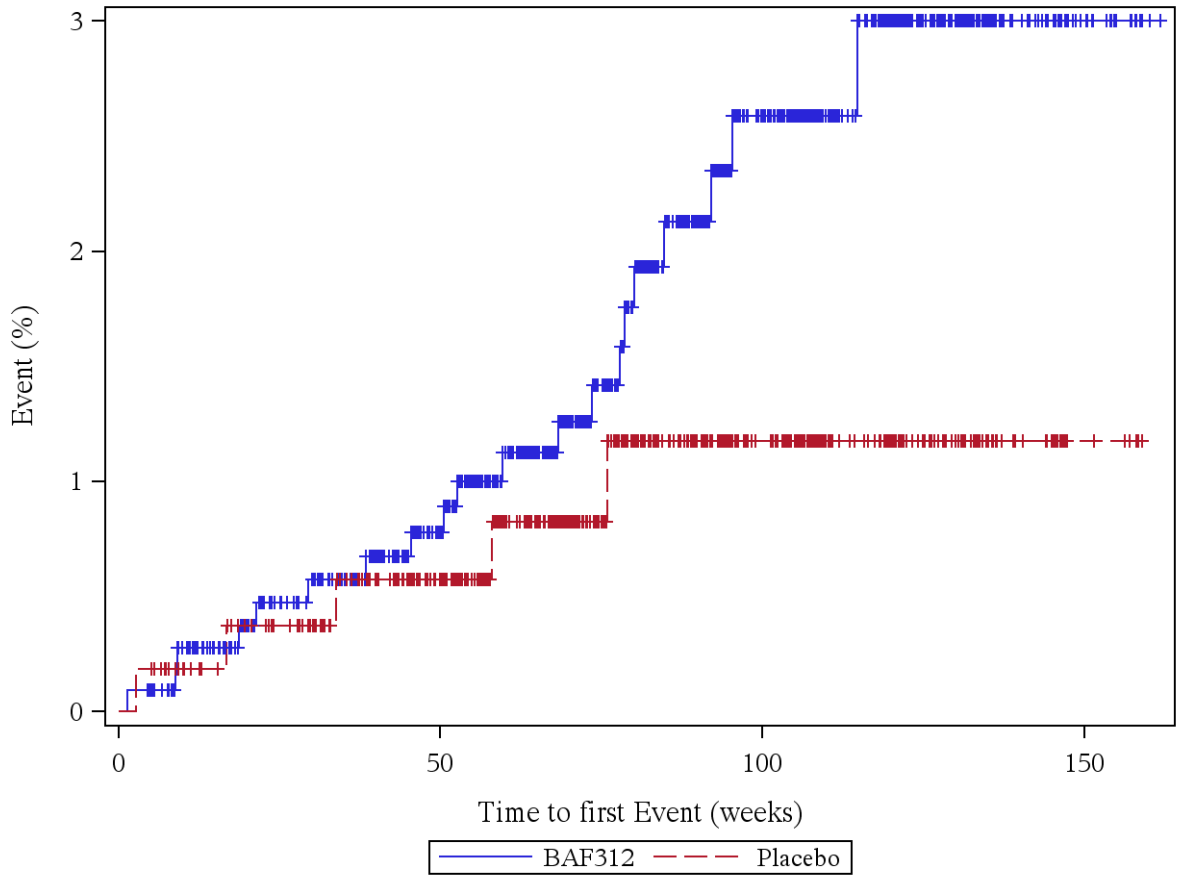


Patients at risk (BAF312/Placebo): Week 0: 1099/546, Week 4: 1099/546, Week 12: 1058/533, Week 24: 1010/518, Week 36: 981/494, Week 48: 917/456, Week 60: 812/386, Week 72: 646/304, Week 84: 511/237, Week 96: 397/176, Week 108: 288/126, Week 120: 198/80, Week 132: 111/40, Week 144: 50/20, Week 156: 10/5, Week 168: 0/0

Log rank test: p-value = 0,866
*: p < 0,05

Analysis population: A2304 SAF total population

Figure 12.1.4.3: INJURY, POISONING AND PROCEDURAL COMPLICATIONS (SOC)

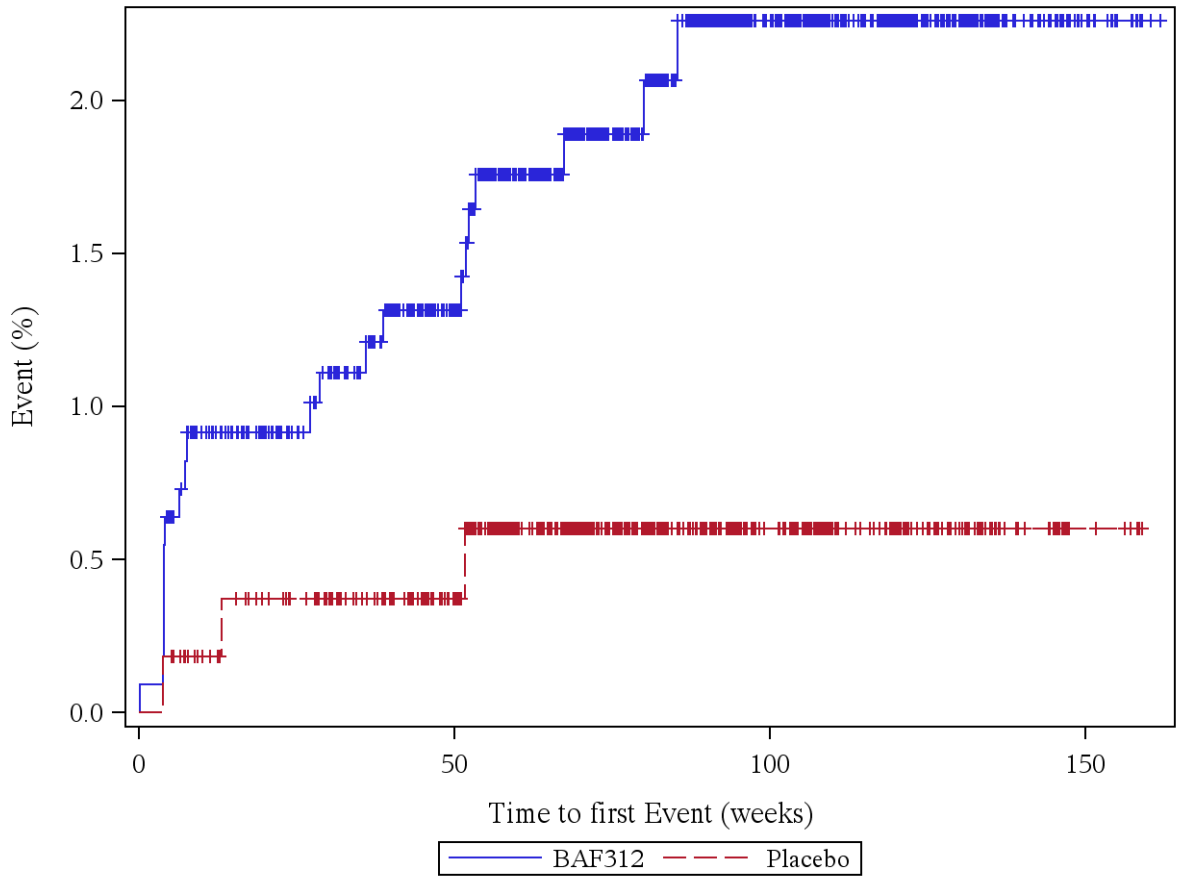


Patients at risk (BAF312/Placebo): Week 0: 1099/546, Week 4: 1098/545, Week 12: 1056/534, Week 24: 1012/519, Week 36: 984/494, Week 48: 917/458, Week 60: 809/384, Week 72: 645/303, Week 84: 505/235, Week 96: 393/176, Week 108: 288/126, Week 120: 197/80, Week 132: 112/40, Week 144: 50/20, Week 156: 10/5, Week 168: 0/0

Log rank test: p-value = 0,179
*: p < 0,05

Analysis population: A2304 SAF total population

Figure 12.1.4.4: INVESTIGATIONS (SOC)

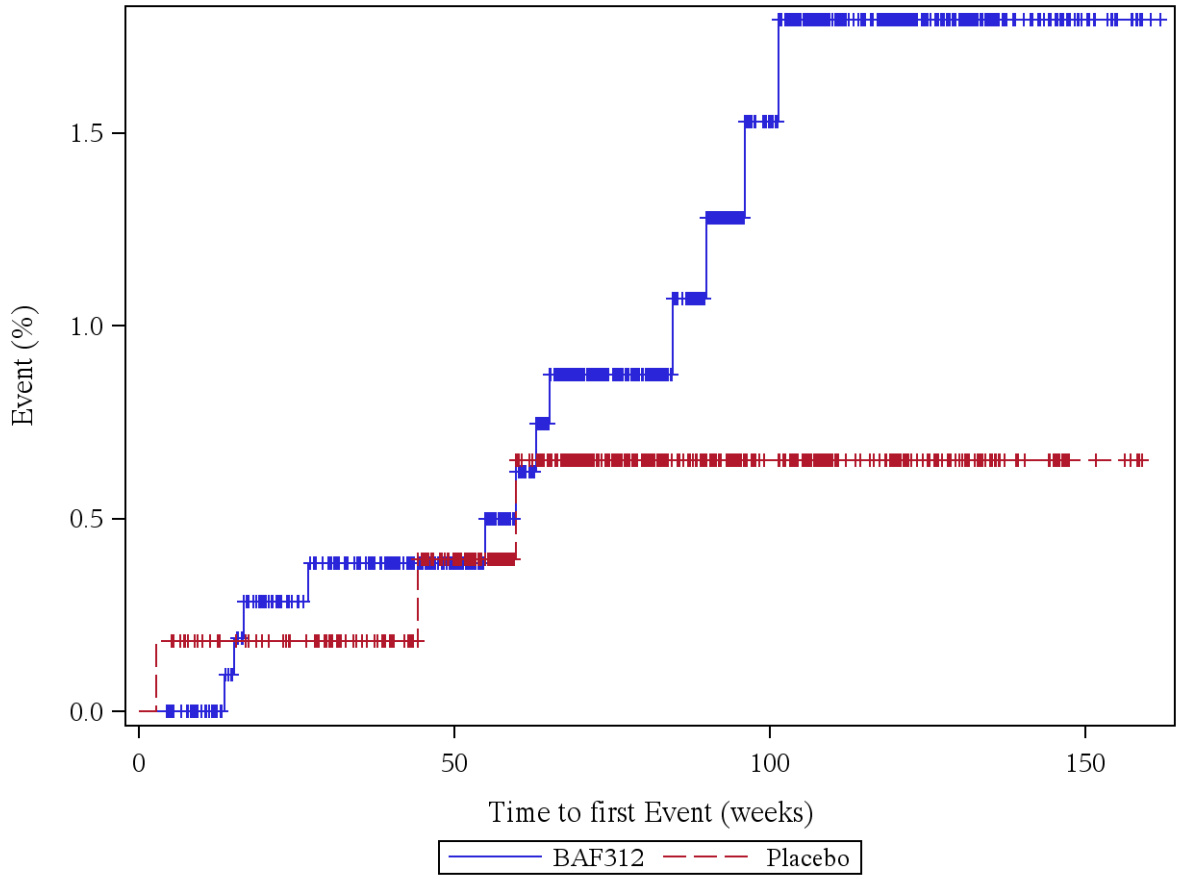


Patients at risk (BAF312/Placebo): Week 0: 1099/546, Week 4: 1093/545, Week 12: 1052/534, Week 24: 1012/519, Week 36: 982/496, Week 48: 916/460, Week 60: 809/387, Week 72: 642/304, Week 84: 507/237, Week 96: 393/176, Week 108: 286/126, Week 120: 198/80, Week 132: 113/40, Week 144: 51/20, Week 156: 10/5, Week 168: 0/0

Log rank test: p-value = 0,032 *
*: p < 0,05

Analysis population: A2304 SAF total population

Figure 12.1.4.5: MUSCULOSKELETAL AND CONNECTIVE TISSUE DISORDERS (SOC)

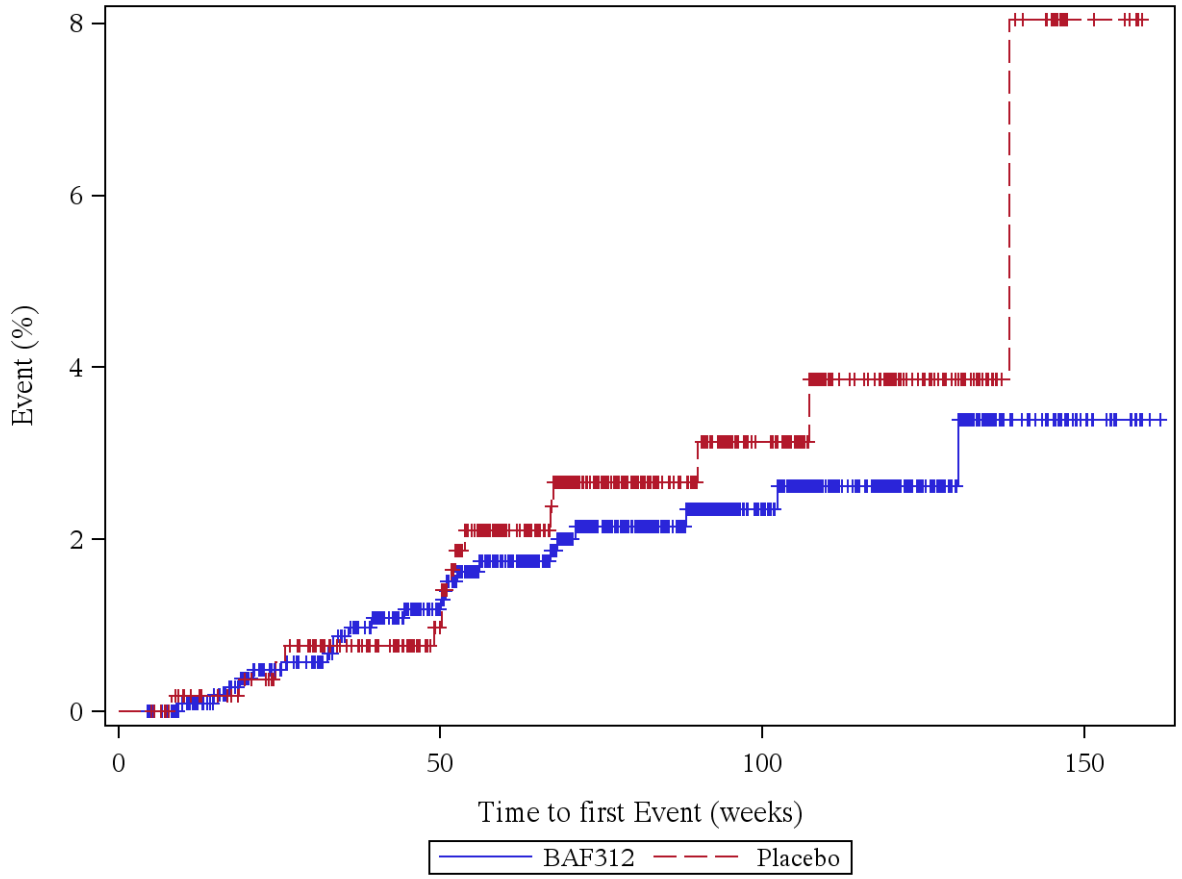


Patients at risk (BAF312/Placebo): Week 0: 1099/546, Week 4: 1099/545, Week 12: 1059/534, Week 24: 1014/520, Week 36: 986/496, Week 48: 921/459, Week 60: 813/385, Week 72: 645/302, Week 84: 510/234, Week 96: 395/175, Week 108: 287/125, Week 120: 197/80, Week 132: 111/40, Week 144: 50/20, Week 156: 10/5, Week 168: 0/0

Log rank test: p-value = 0,302
*: p < 0,05

Analysis population: A2304 SAF total population

Figure 12.1.4.6: NEOPLASMS BENIGN, MALIGNANT AND UNSPECIFIED (INCL CYSTS AND POLYPS) (SOC)

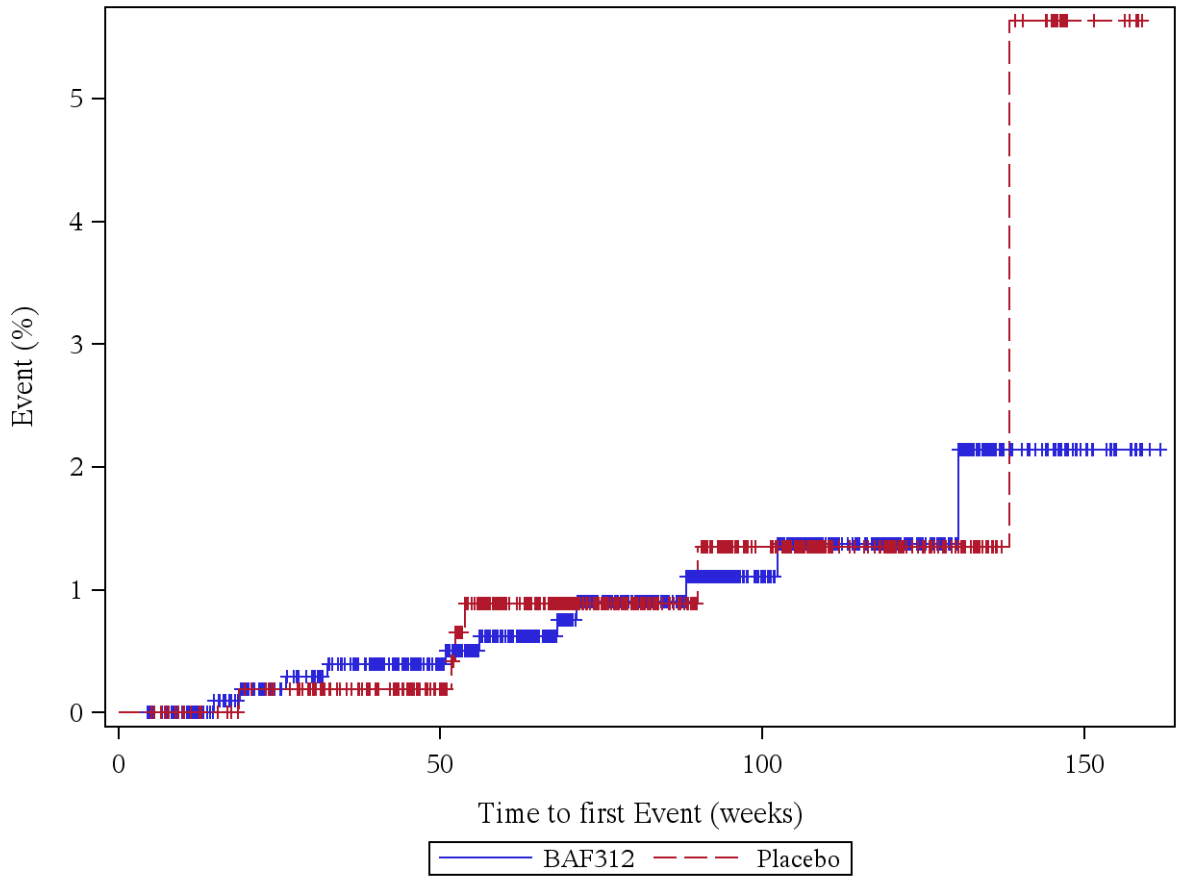


Patients at risk (BAF312/Placebo): Week 0: 1099/546, Week 4: 1099/546, Week 12: 1058/534, Week 24: 1012/519, Week 36: 980/495, Week 48: 918/459, Week 60: 809/381, Week 72: 642/298, Week 84: 509/231, Week 96: 395/171, Week 108: 286/120, Week 120: 195/77, Week 132: 109/39, Week 144: 51/20, Week 156: 10/5, Week 168: 0/0

Log rank test: p-value = 0,355
*: p < 0,05

Analysis population: A2304 SAF total population

Figure 12.1.4.7: BASAL CELL CARCINOMA (PT)

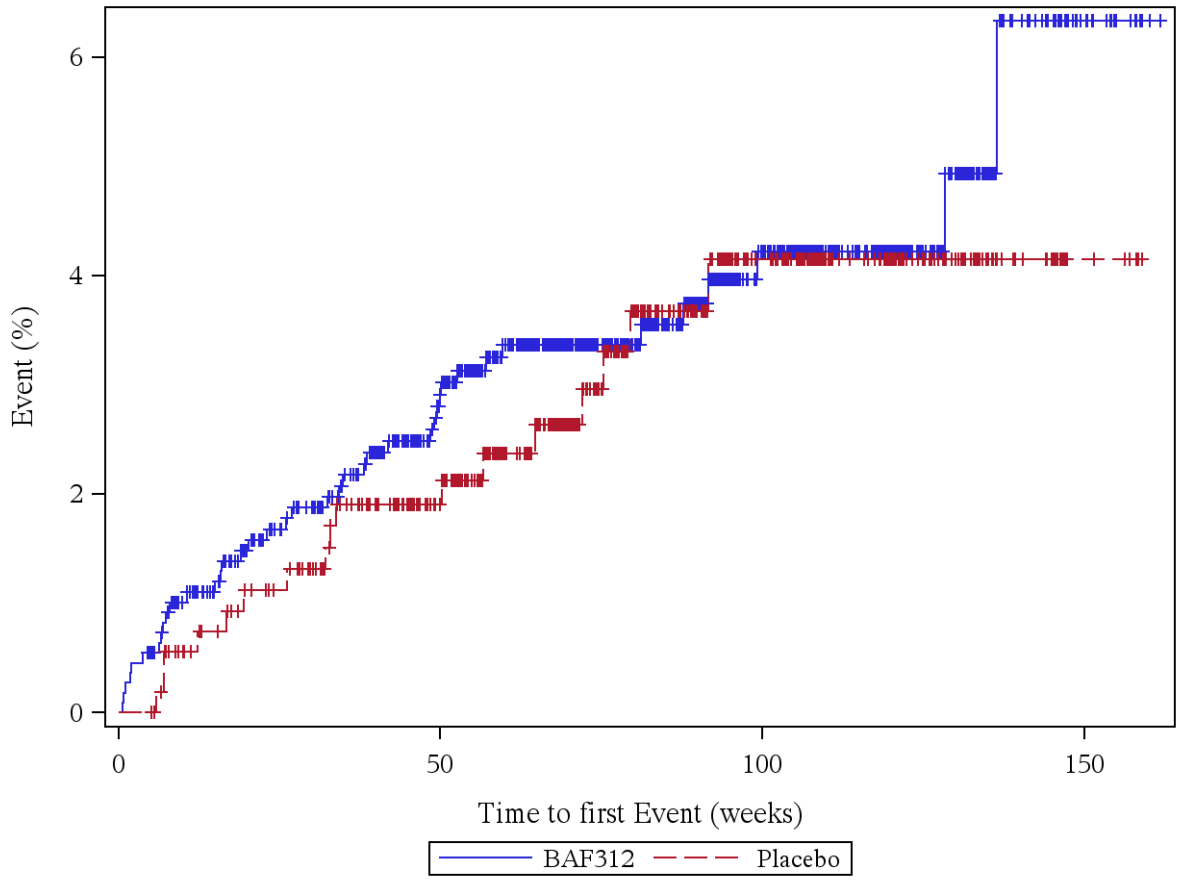


Patients at risk (BAF312/Placebo): Week 0: 1099/546, Week 4: 1099/546, Week 12: 1059/535, Week 24: 1015/520, Week 36: 986/496, Week 48: 921/460, Week 60: 813/384, Week 72: 646/302, Week 84: 511/235, Week 96: 397/173, Week 108: 288/123, Week 120: 197/79, Week 132: 111/40, Week 144: 51/20, Week 156: 10/5, Week 168: 0/0

Log rank test: p-value = 0,757
*: p < 0,05

Analysis population: A2304 SAF total population

Figure 12.1.4.8: NERVOUS SYSTEM DISORDERS (SOC)

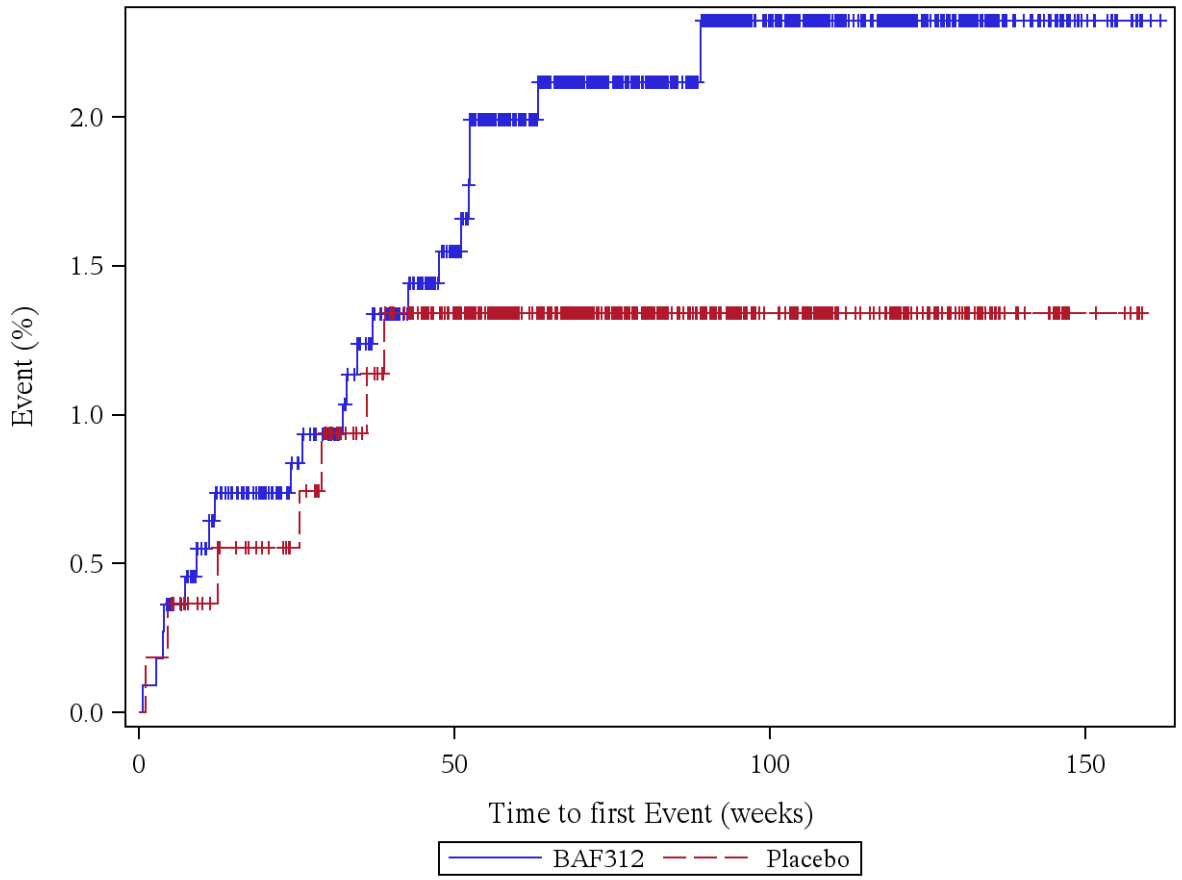


Patients at risk (BAF312/Placebo): Week 0: 1099/546, Week 4: 1093/546, Week 12: 1050/532, Week 24: 1006/516, Week 36: 974/489, Week 48: 909/454, Week 60: 797/381, Week 72: 634/299, Week 84: 500/230, Week 96: 388/169, Week 108: 282/122, Week 120: 194/77, Week 132: 109/39, Week 144: 49/19, Week 156: 9/5, Week 168: 0/0

Log rank test: p-value = 0,623
*: p < 0,05

Analysis population: A2304 SAF total population

Figure 12.1.4.9: PSYCHIATRIC DISORDERS (SOC)

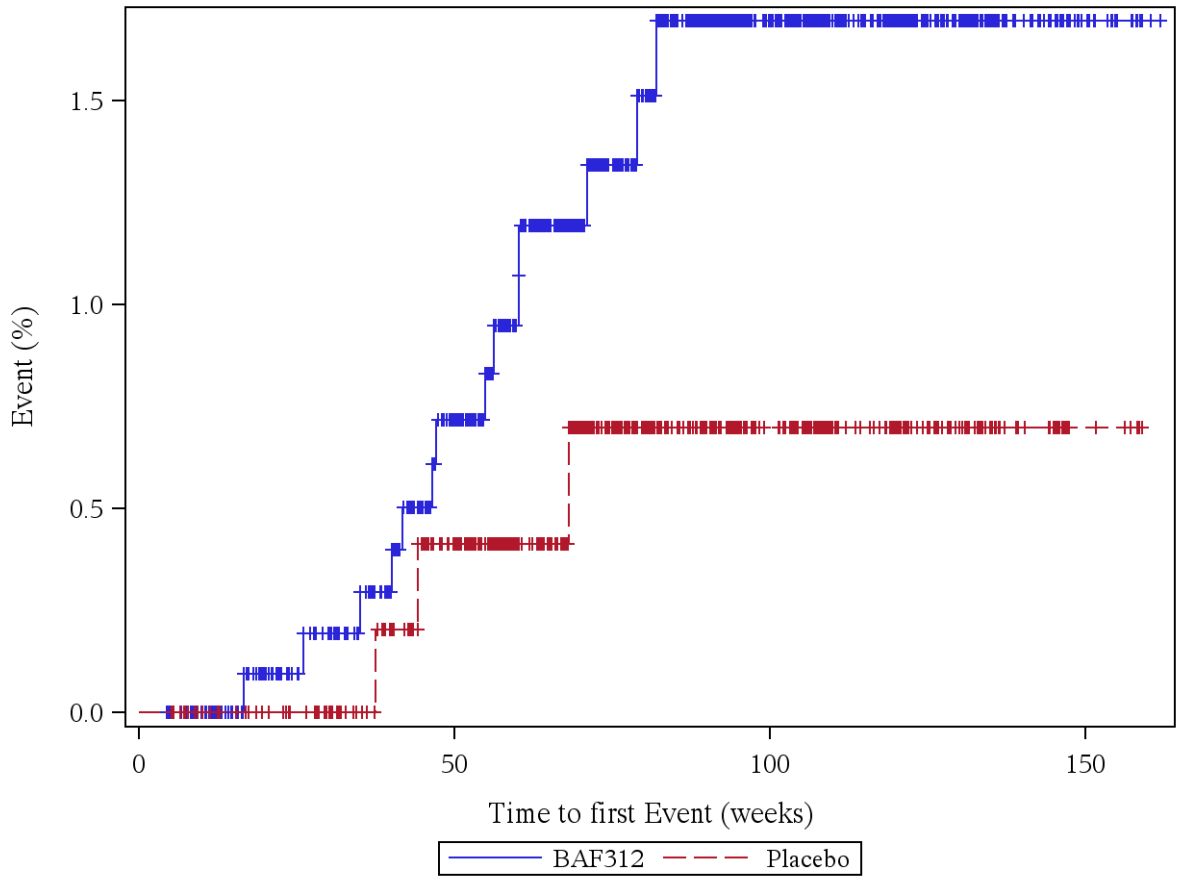


Patients at risk (BAF312/Placebo): Week 0: 1099/546, Week 4: 1095/545, Week 12: 1052/534, Week 24: 1010/519, Week 36: 978/495, Week 48: 914/457, Week 60: 805/386, Week 72: 640/303, Week 84: 505/235, Week 96: 392/175, Week 108: 285/126, Week 120: 197/80, Week 132: 110/40, Week 144: 50/20, Week 156: 10/5, Week 168: 0/0

Log rank test: p-value = 0,293
*: p < 0,05

Analysis population: A2304 SAF total population

Figure 12.1.4.10: RENAL AND URINARY DISORDERS (SOC)



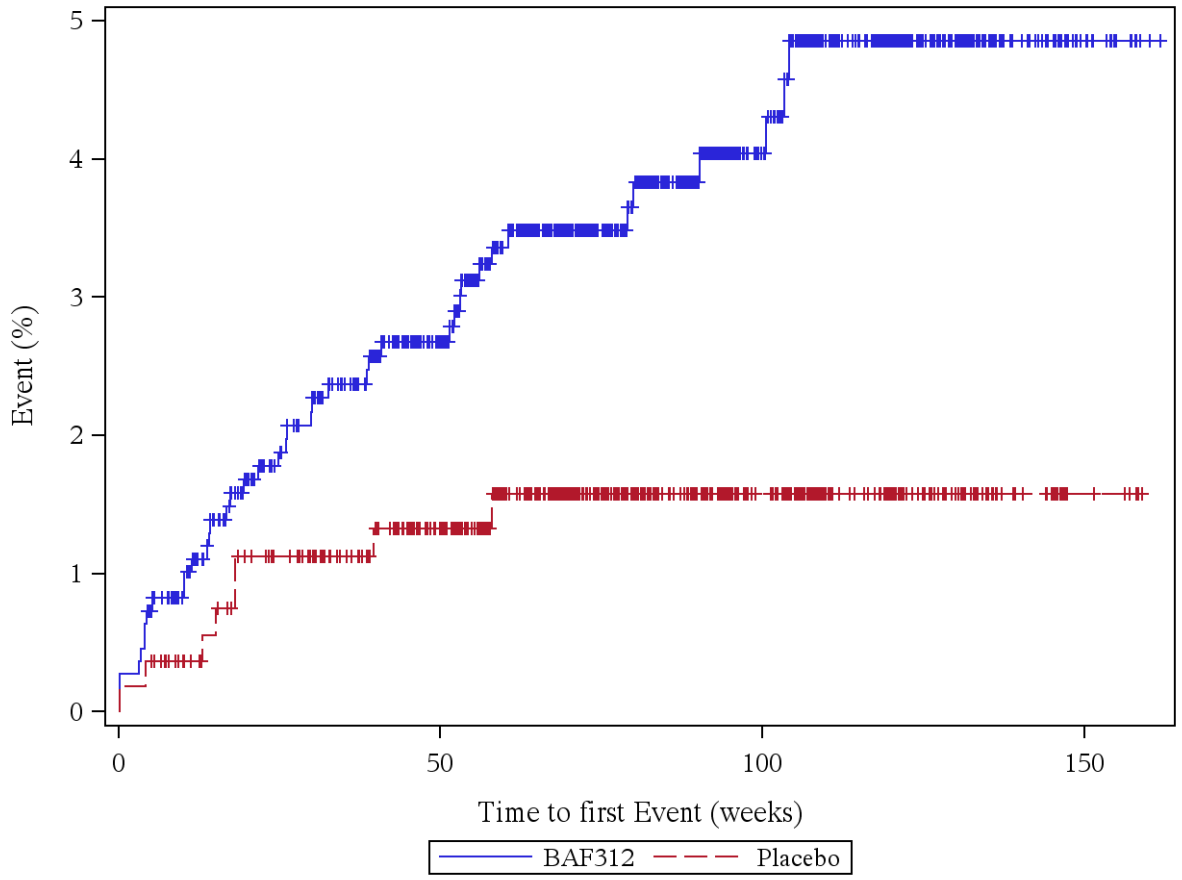
Patients at risk (BAF312/Placebo): Week 0: 1099/546, Week 4: 1099/546, Week 12: 1059/535, Week 24: 1016/521, Week 36: 987/497, Week 48: 918/459, Week 60: 811/387, Week 72: 645/304, Week 84: 512/237, Week 96: 396/176, Week 108: 287/126, Week 120: 197/80, Week 132: 111/40, Week 144: 51/20, Week 156: 10/5, Week 168: 0/0

Log rank test: p-value = 0,182
*: p < 0,05

Analysis population: A2304 SAF total population

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)

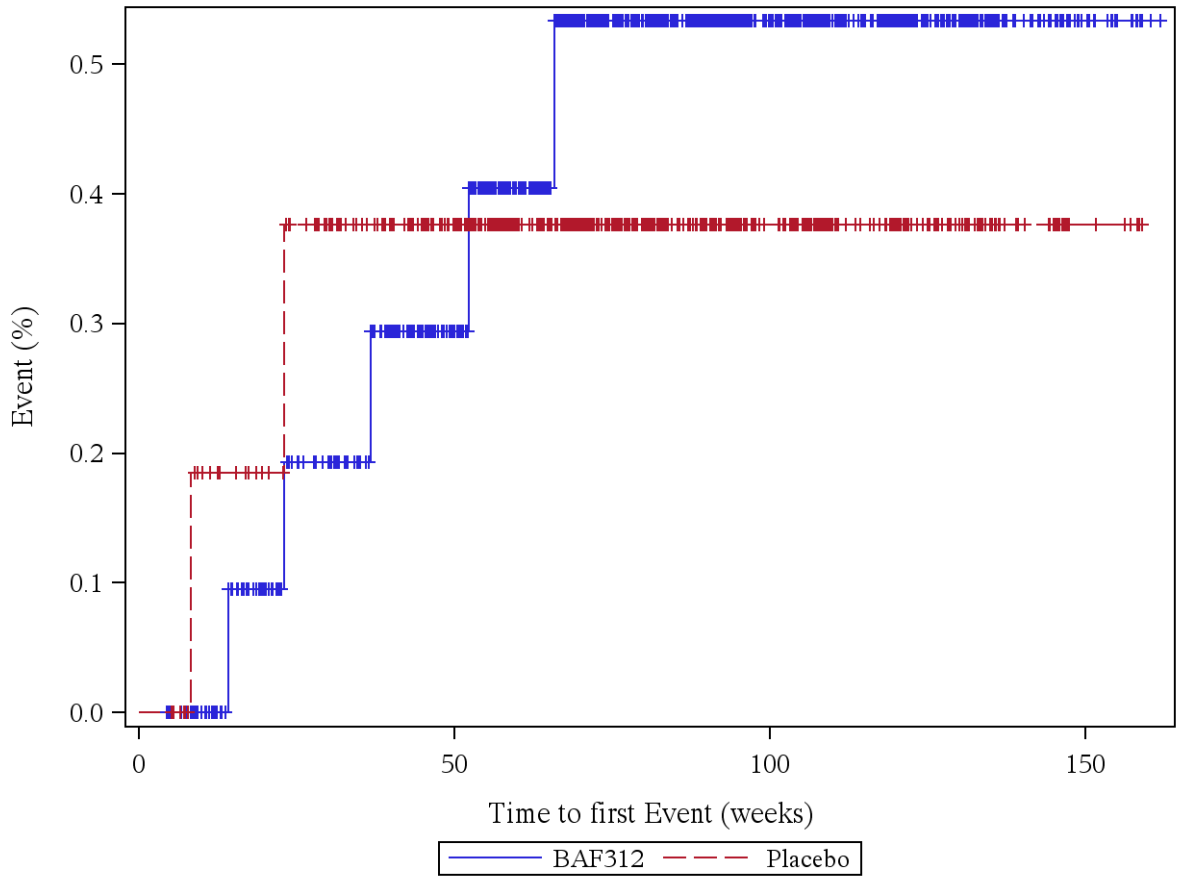


Patients at risk (BAF312/Placebo): Week 0: 1099/546, Week 4: 1092/545, Week 12: 1047/533, Week 24: 998/515, Week 36: 966/491, Week 48: 900/454, Week 60: 791/381, Week 72: 632/299, Week 84: 499/232, Week 96: 385/172, Week 108: 279/122, Week 120: 191/77, Week 132: 108/39, Week 144: 50/20, Week 156: 9/5, Week 168: 0/0

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

Analysis population: A2304 SAF total population

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

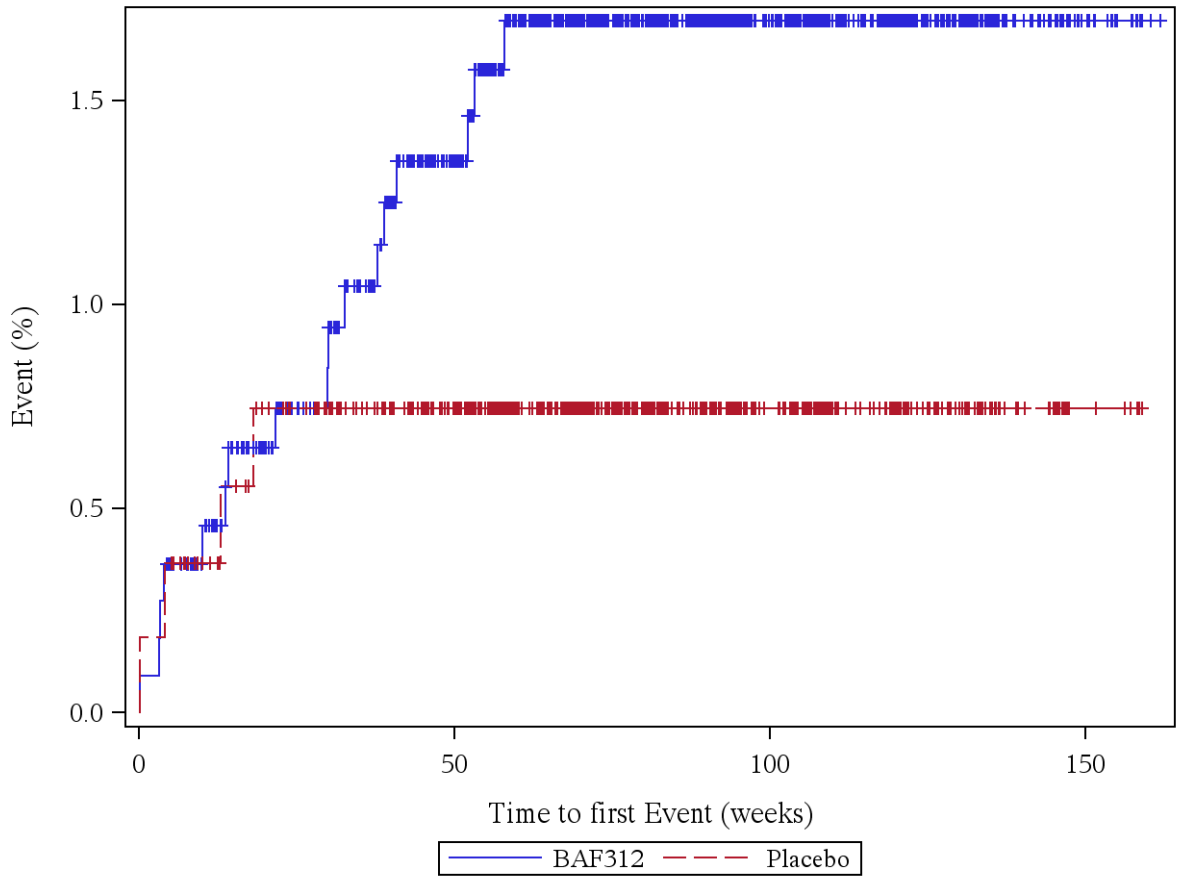


Patients at risk (BAF312/Placebo): Week 0: 1099/546, Week 4: 1099/546, Week 12: 1059/534, Week 24: 1015/519, Week 36: 989/495, Week 48: 923/459, Week 60: 816/386, Week 72: 652/303, Week 84: 516/236, Week 96: 400/176, Week 108: 291/126, Week 120: 200/80, Week 132: 113/40, Week 144: 51/20, Week 156: 10/5, Week 168: 0/0

Log rank test: p-value = 0,795
*: p < 0,05

Analysis population: A2304 SAF total population

Figure 12.1.5.3: ANAEMIA (PT, not severe)

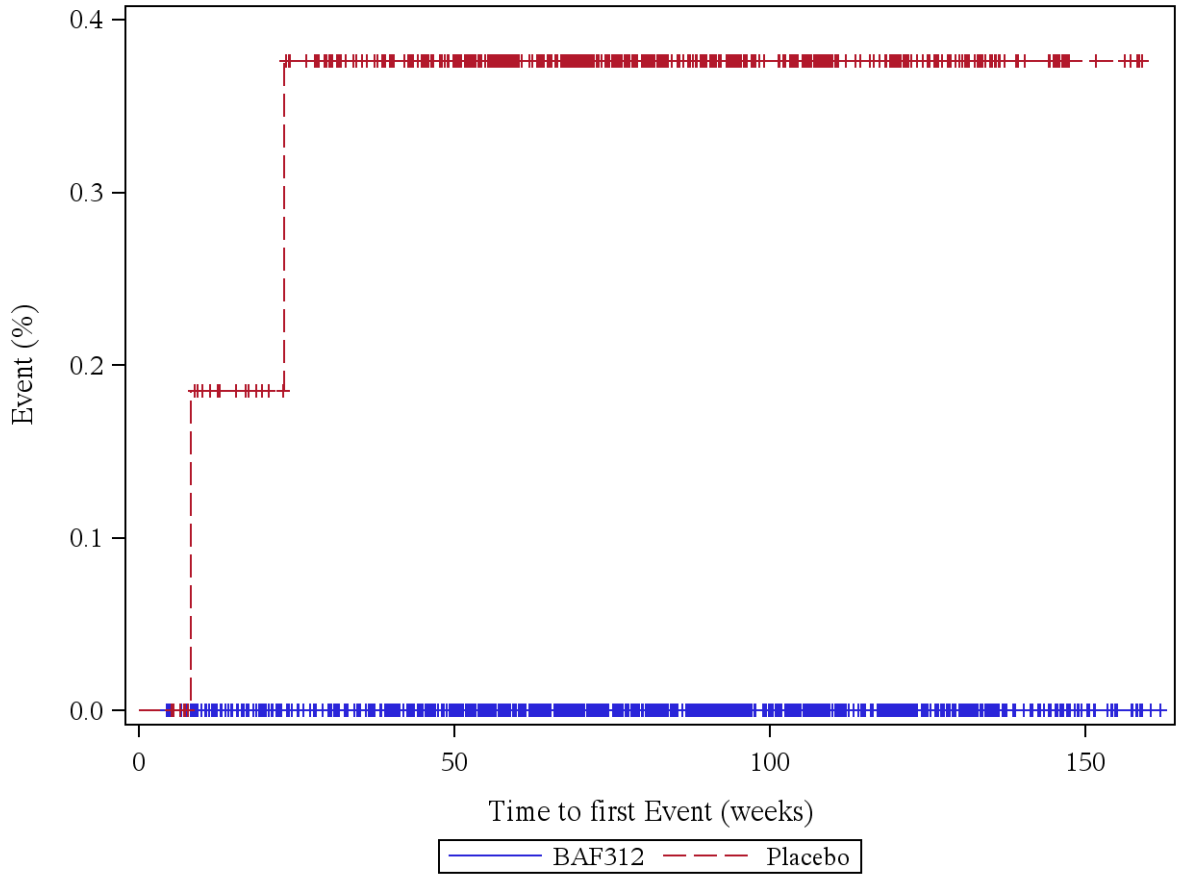


Patients at risk (BAF312/Placebo): Week 0: 1099/546, Week 4: 1095/545, Week 12: 1054/533, Week 24: 1009/517, Week 36: 980/493, Week 48: 913/457, Week 60: 806/384, Week 72: 643/301, Week 84: 509/234, Week 96: 395/174, Week 108: 288/124, Week 120: 198/79, Week 132: 113/40, Week 144: 51/20, Week 156: 10/5, Week 168: 0/0

Log rank test: p-value = 0,165
*: p < 0,05

Analysis population: A2304 SAF total population

Figure 12.1.5.4: ANAEMIA (PT, severe)

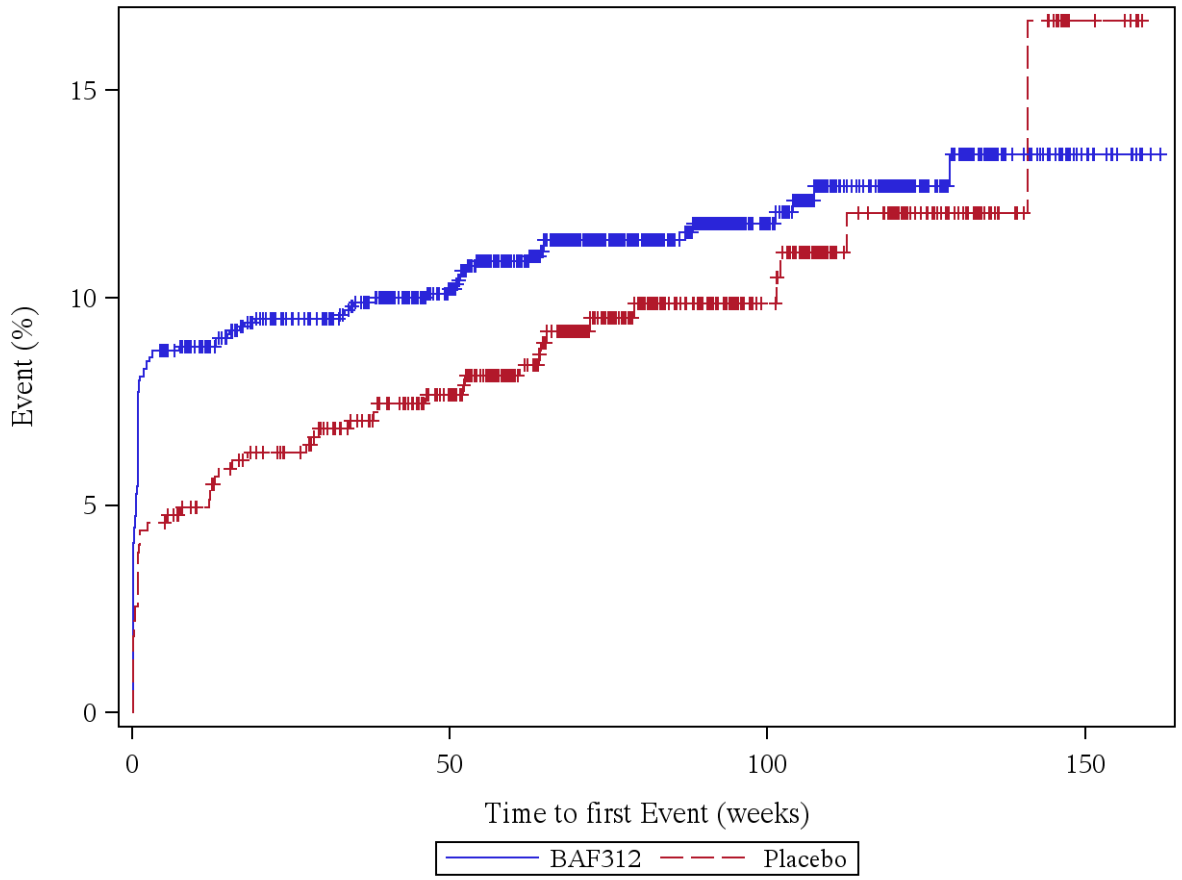


Patients at risk (BAF312/Placebo): Week 0: 1099/546, Week 4: 1099/546, Week 12: 1059/534, Week 24: 1017/519, Week 36: 990/495, Week 48: 925/459, Week 60: 818/386, Week 72: 652/303, Week 84: 516/236, Week 96: 400/176, Week 108: 291/126, Week 120: 200/80, Week 132: 113/40, Week 144: 51/20, Week 156: 10/5, Week 168: 0/0

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

Analysis population: A2304 SAF total population

Figure 12.1.5.5: CARDIAC DISORDERS (SOC, not severe)

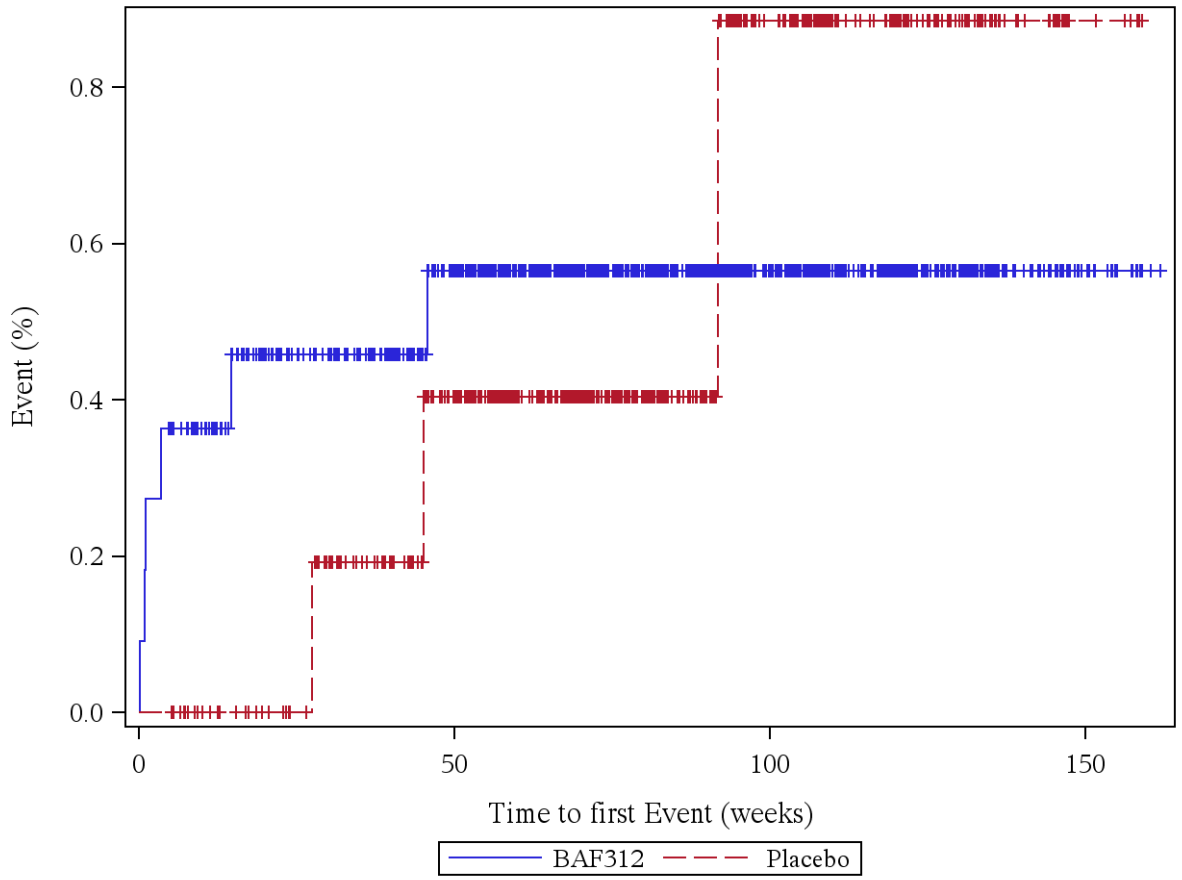


Patients at risk (BAF312/Placebo): Week 0: 1099/546, Week 4: 1003/521, Week 12: 970/510, Week 24: 928/489, Week 36: 898/463, Week 48: 833/427, Week 60: 730/357, Week 72: 574/281, Week 84: 449/215, Week 96: 345/160, Week 108: 250/112, Week 120: 169/75, Week 132: 93/37, Week 144: 43/18, Week 156: 9/5, Week 168: 0/0

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

Analysis population: A2304 SAF total population

Figure 12.1.5.6: CARDIAC DISORDERS (SOC, severe)

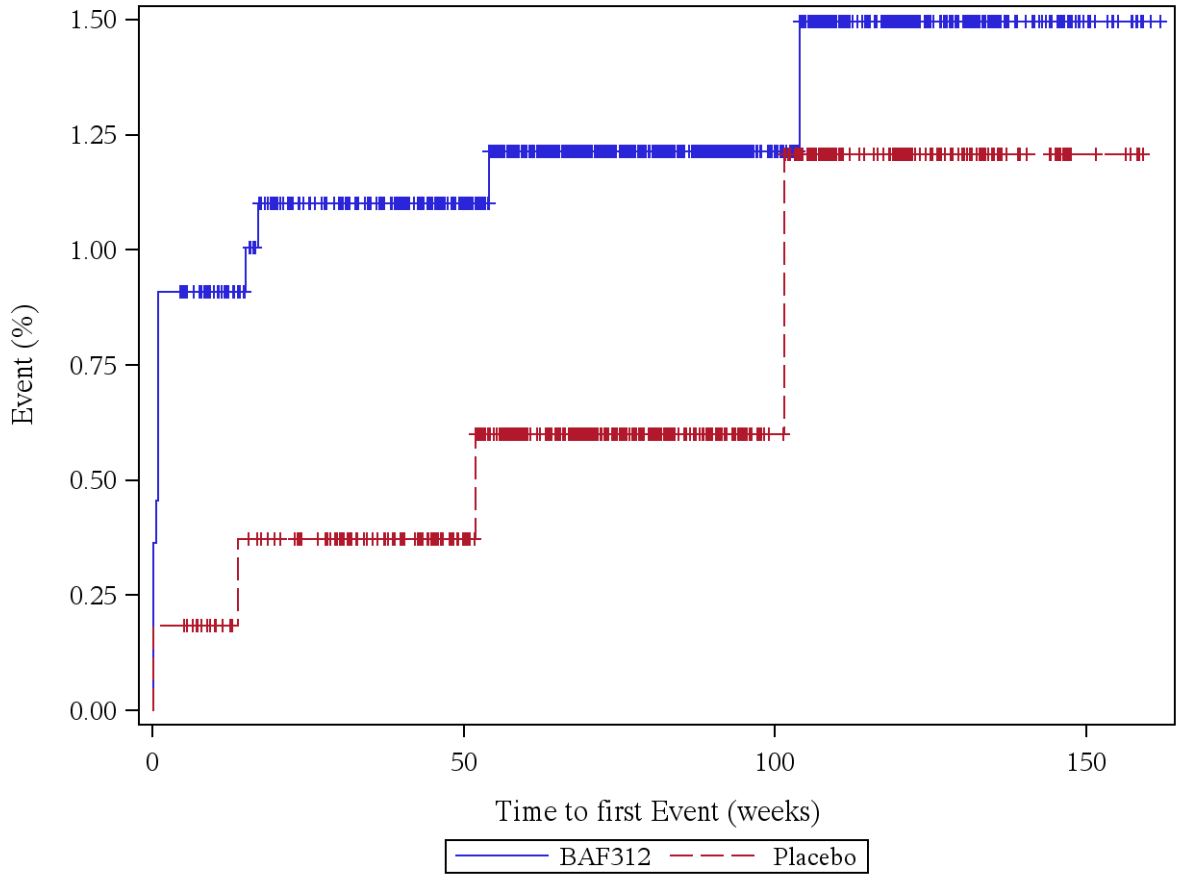


Patients at risk (BAF312/Placebo): Week 0: 1099/546, Week 4: 1095/546, Week 12: 1059/535, Week 24: 1016/521, Week 36: 989/496, Week 48: 924/459, Week 60: 818/386, Week 72: 652/303, Week 84: 516/235, Week 96: 400/174, Week 108: 291/125, Week 120: 200/80, Week 132: 113/40, Week 144: 51/20, Week 156: 10/5, Week 168: 0/0

Log rank test: p-value = 0,990
*: p < 0,05

Analysis population: A2304 SAF total population

Figure 12.1.5.7: ATRIOVENTRICULAR BLOCK FIRST DEGREE (PT, not severe)

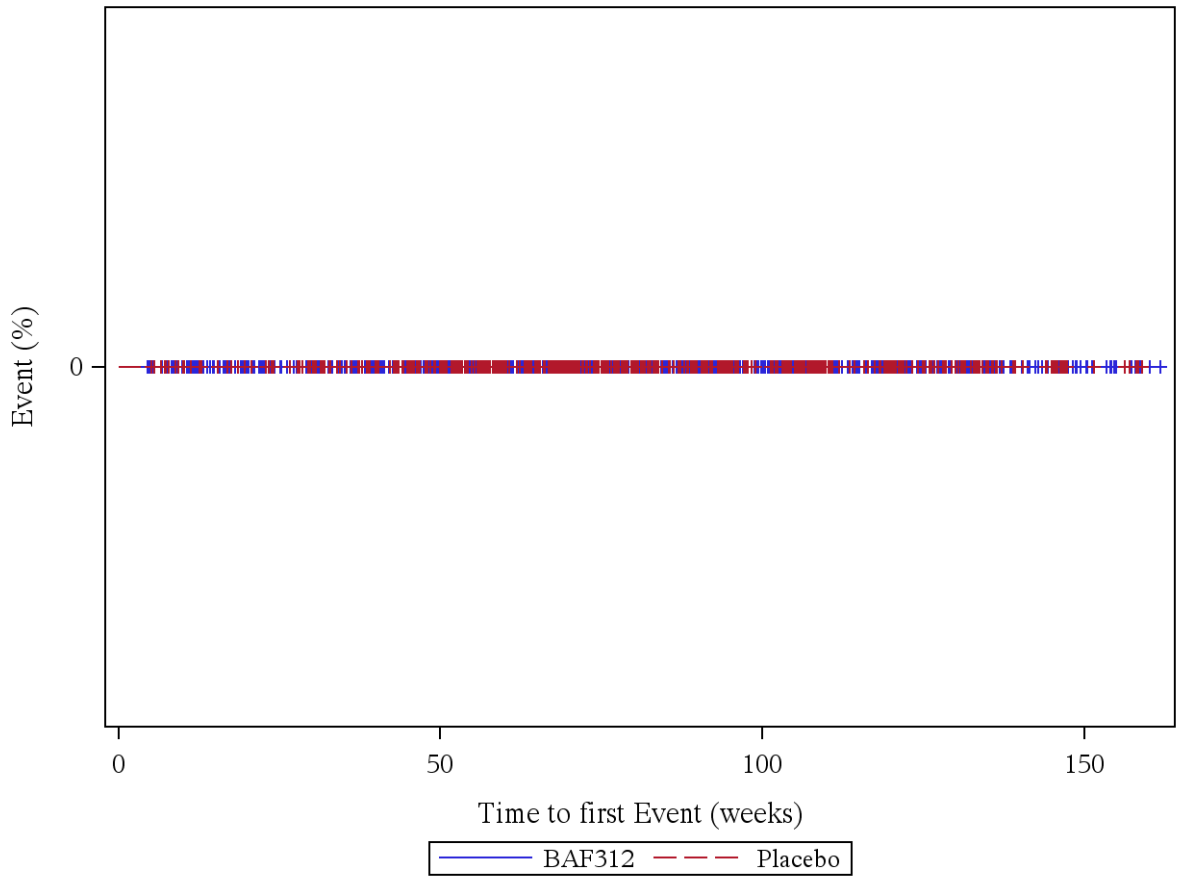


Patients at risk (BAF312/Placebo): Week 0: 1099/546, Week 4: 1089/545, Week 12: 1050/534, Week 24: 1007/519, Week 36: 980/495, Week 48: 915/459, Week 60: 807/387, Week 72: 641/304, Week 84: 505/236, Week 96: 390/176, Week 108: 283/125, Week 120: 194/80, Week 132: 111/40, Week 144: 50/20, Week 156: 10/5, Week 168: 0/0

Log rank test: p-value = 0,333
*: p < 0,05

Analysis population: A2304 SAF total population

Figure 12.1.5.8: ATRIOVENTRICULAR BLOCK FIRST DEGREE (PT, severe)

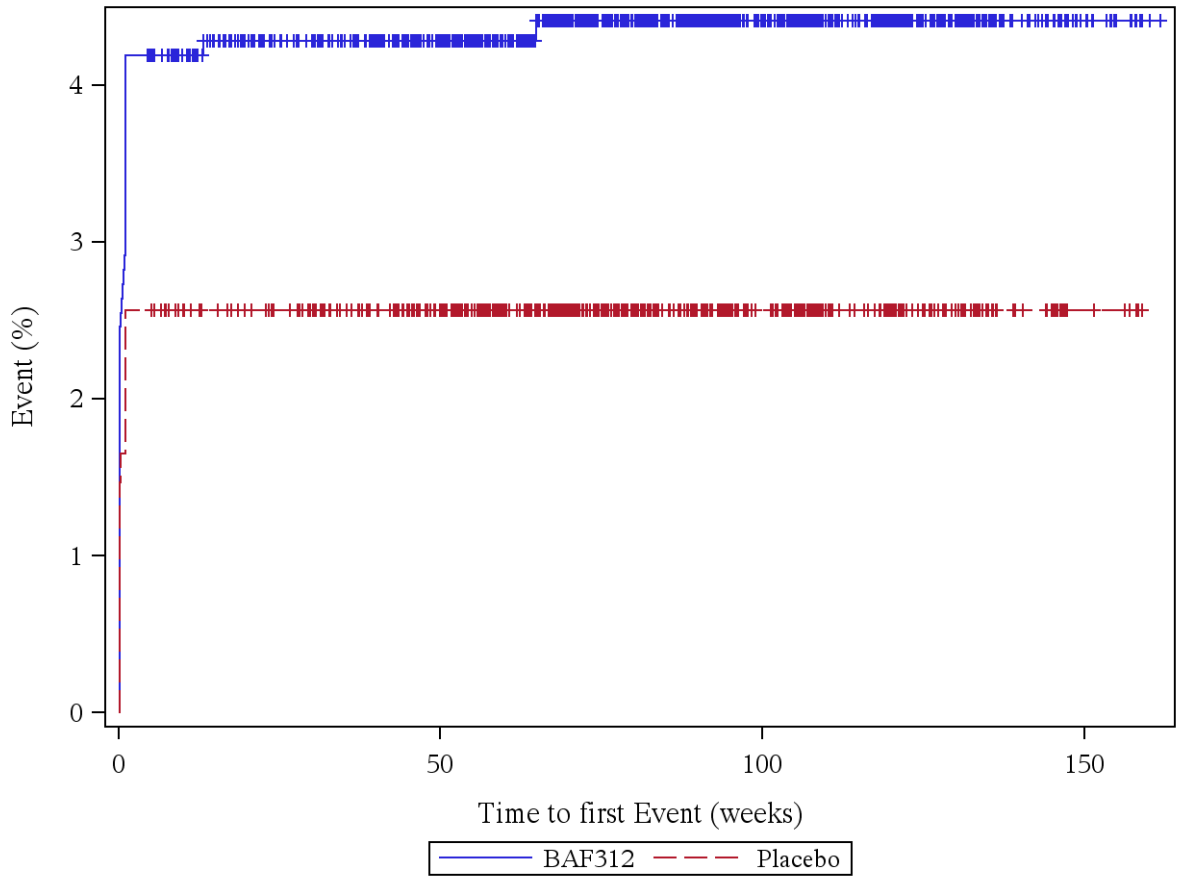


Patients at risk (BAF312/Placebo): Week 0: 1099/546, Week 4: 1099/546, Week 12: 1059/535, Week 24: 1017/521, Week 36: 990/497, Week 48: 925/461, Week 60: 818/388, Week 72: 652/305, Week 84: 516/237, Week 96: 400/176, Week 108: 291/126, Week 120: 200/80, Week 132: 113/40, Week 144: 51/20, Week 156: 10/5, Week 168: 0/0

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

Analysis population: A2304 SAF total population

Figure 12.1.5.9: BRADYCARDIA (PT, not severe)

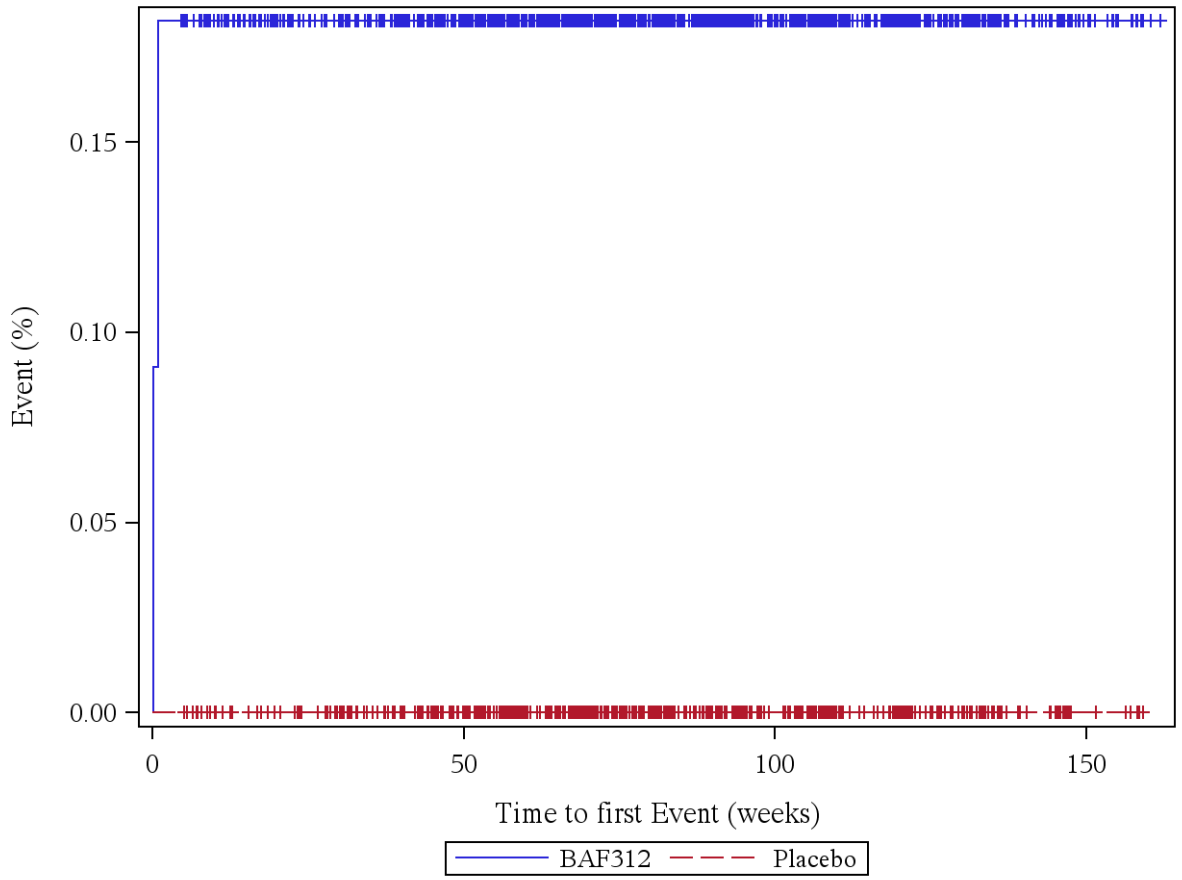


Patients at risk (BAF312/Placebo): Week 0: 1099/546, Week 4: 1053/532, Week 12: 1015/521, Week 24: 973/507, Week 36: 947/483, Week 48: 883/449, Week 60: 780/378, Week 72: 619/298, Week 84: 487/232, Week 96: 375/172, Week 108: 275/122, Week 120: 192/79, Week 132: 106/39, Week 144: 48/20, Week 156: 10/5, Week 168: 0/0

Log rank test: p-value = 0,071
*: p < 0,05

Analysis population: A2304 SAF total population

Figure 12.1.5.10: BRADYCARDIA (PT, severe)

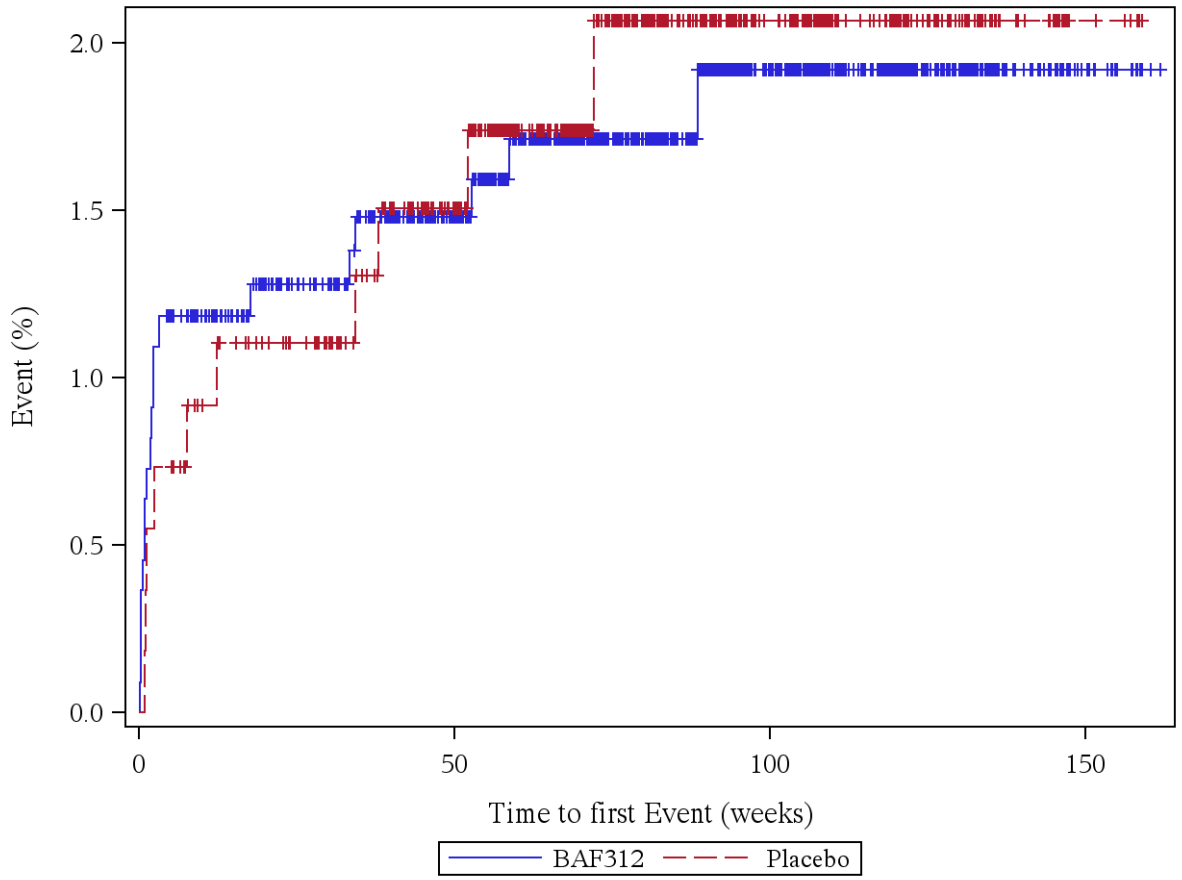


Patients at risk (BAF312/Placebo): Week 0: 1099/546, Week 4: 1097/546, Week 12: 1059/535, Week 24: 1017/521, Week 36: 990/497, Week 48: 925/461, Week 60: 818/388, Week 72: 652/305, Week 84: 516/237, Week 96: 400/176, Week 108: 291/126, Week 120: 200/80, Week 132: 113/40, Week 144: 51/20, Week 156: 10/5, Week 168: 0/0

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

Analysis population: A2304 SAF total population

Figure 12.1.5.11: PALPITATIONS (PT, not severe)

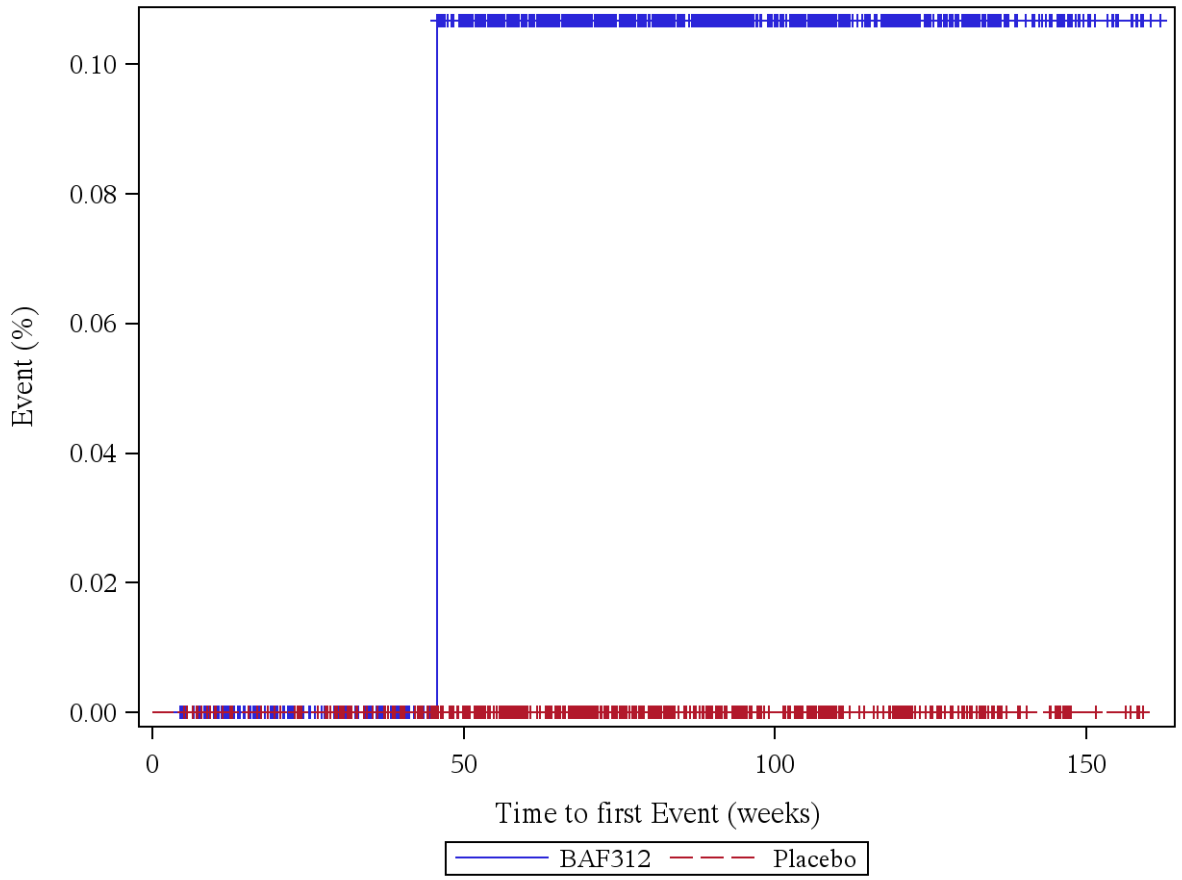


Patients at risk (BAF312/Placebo): Week 0: 1099/546, Week 4: 1086/542, Week 12: 1047/531, Week 24: 1004/516, Week 36: 975/491, Week 48: 910/454, Week 60: 804/381, Week 72: 642/299, Week 84: 510/231, Week 96: 396/171, Week 108: 287/123, Week 120: 196/79, Week 132: 112/39, Week 144: 50/20, Week 156: 10/5, Week 168: 0/0

Log rank test: p-value = 0,878
*: p < 0,05

Analysis population: A2304 SAF total population

Figure 12.1.5.12: PALPITATIONS (PT, severe)

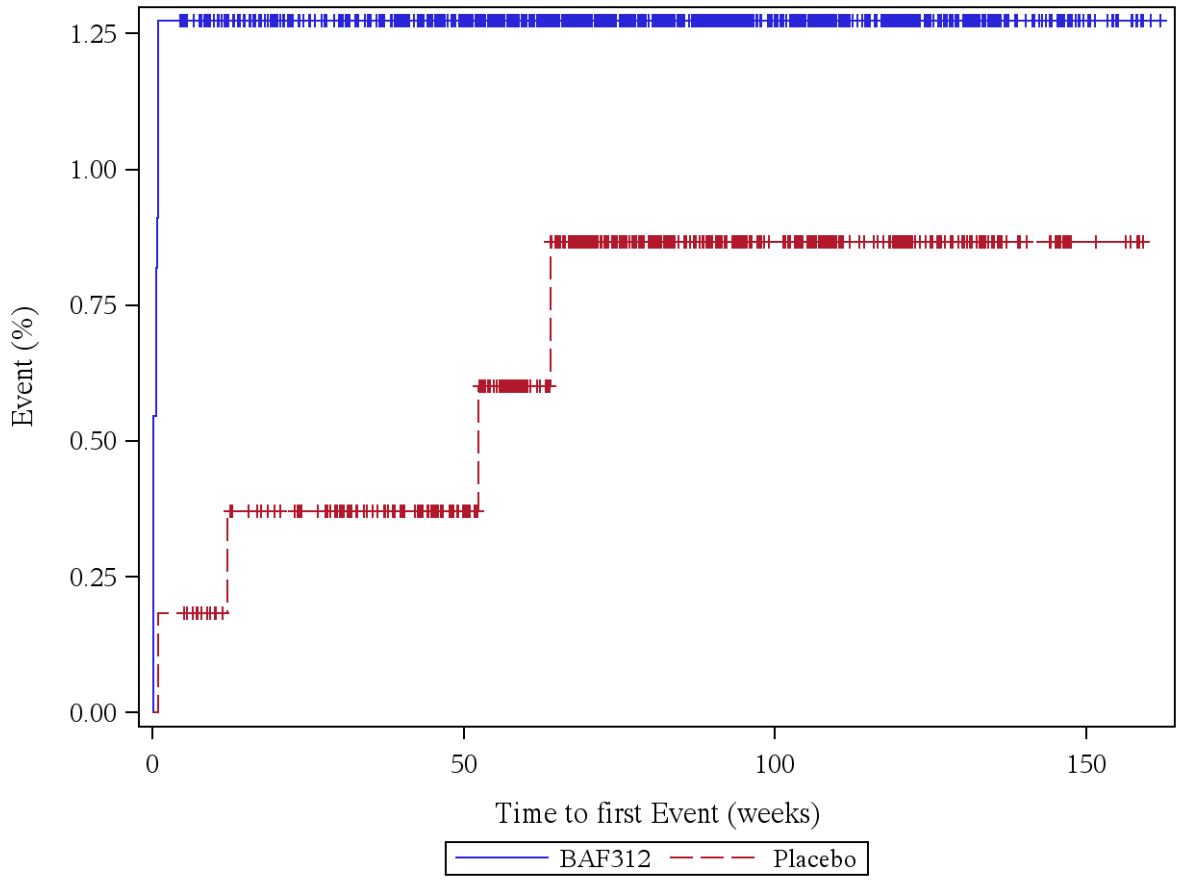


Patients at risk (BAF312/Placebo): Week 0: 1099/546, Week 4: 1099/546, Week 12: 1059/535, Week 24: 1017/521, Week 36: 990/497, Week 48: 924/461, Week 60: 818/388, Week 72: 652/305, Week 84: 516/237, Week 96: 400/176, Week 108: 291/126, Week 120: 200/80, Week 132: 113/40, Week 144: 51/20, Week 156: 10/5, Week 168: 0/0

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

Analysis population: A2304 SAF total population

Figure 12.1.5.13: SINUS BRADYCARDIA (PT, not severe)

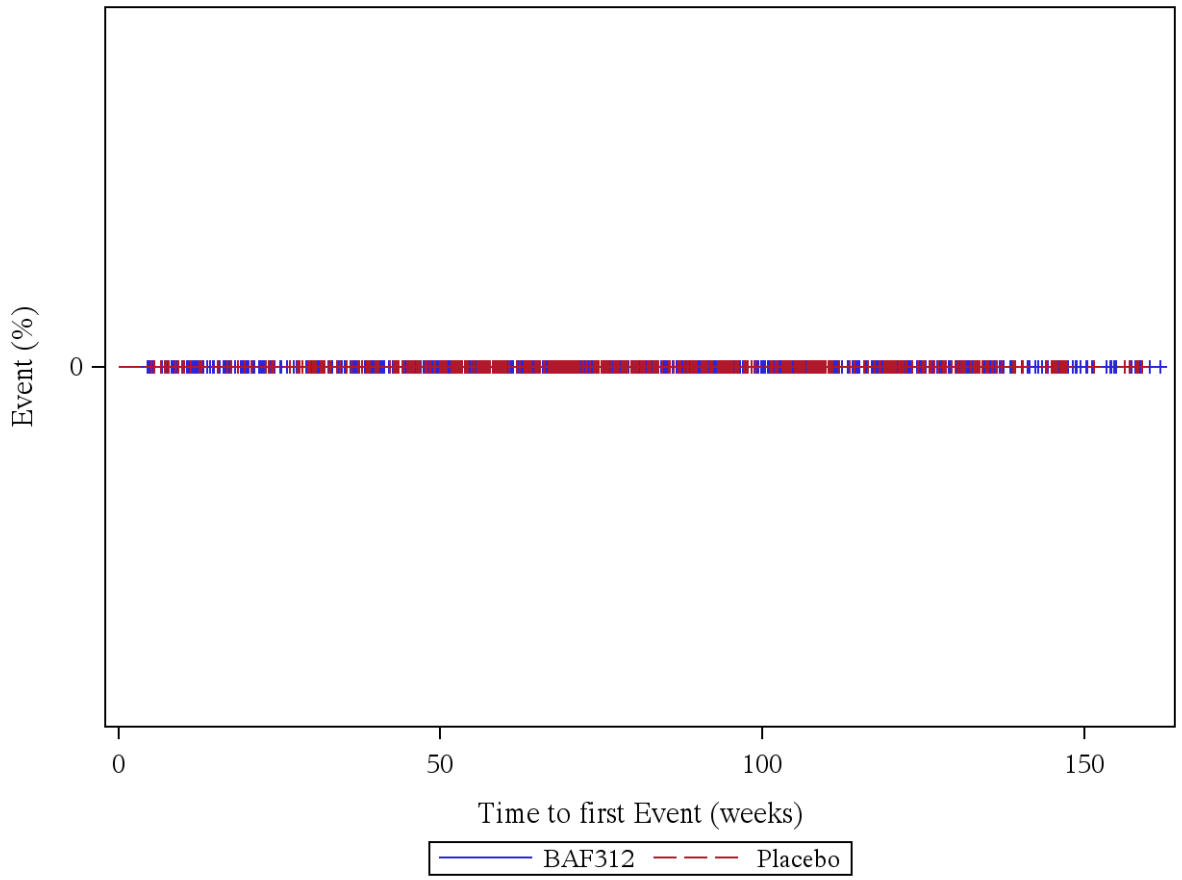


Patients at risk (BAF312/Placebo): Week 0: 1099/546, Week 4: 1085/545, Week 12: 1047/533, Week 24: 1006/519, Week 36: 979/495, Week 48: 914/459, Week 60: 808/385, Week 72: 642/303, Week 84: 508/235, Week 96: 394/175, Week 108: 286/125, Week 120: 195/80, Week 132: 111/40, Week 144: 51/20, Week 156: 10/5, Week 168: 0/0

Log rank test: p-value = 0,321
*: p < 0,05

Analysis population: A2304 SAF total population

Figure 12.1.5.14: SINUS BRADYCARDIA (PT, severe)

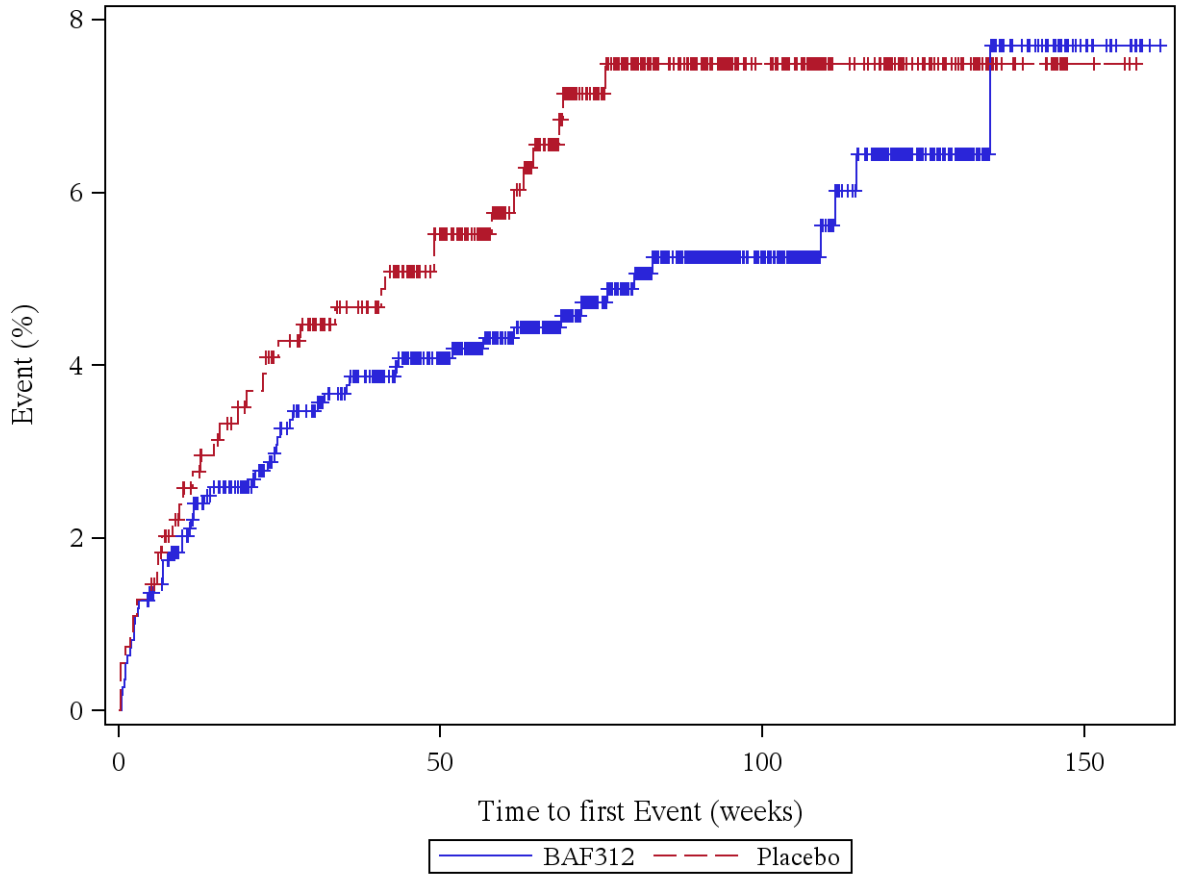


Patients at risk (BAF312/Placebo): Week 0: 1099/546, Week 4: 1099/546, Week 12: 1059/535, Week 24: 1017/521, Week 36: 990/497, Week 48: 925/461, Week 60: 818/388, Week 72: 652/305, Week 84: 516/237, Week 96: 400/176, Week 108: 291/126, Week 120: 200/80, Week 132: 113/40, Week 144: 51/20, Week 156: 10/5, Week 168: 0/0

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

Analysis population: A2304 SAF total population

Figure 12.1.5.15: EAR AND LABYRINTH DISORDERS (SOC, not severe)

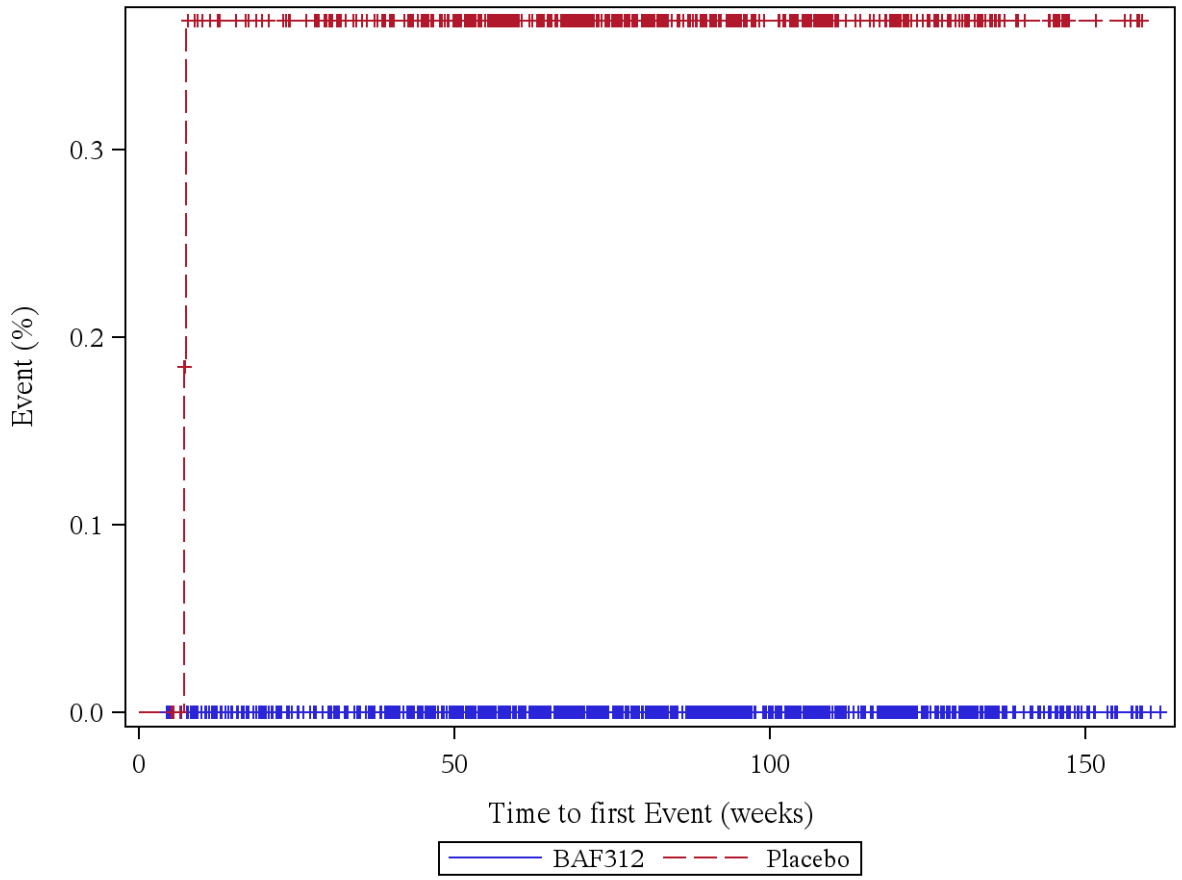


Patients at risk (BAF312/Placebo): Week 0: 1099/546, Week 4: 1085/539, Week 12: 1033/520, Week 24: 987/500, Week 36: 951/473, Week 48: 886/439, Week 60: 784/366, Week 72: 621/282, Week 84: 490/217, Week 96: 382/158, Week 108: 278/114, Week 120: 188/71, Week 132: 107/37, Week 144: 48/17, Week 156: 10/3, Week 168: 0/0

Log rank test: p-value = 0,169
*: p < 0,05

Analysis population: A2304 SAF total population

Figure 12.1.5.16: EAR AND LABYRINTH DISORDERS (SOC, severe)

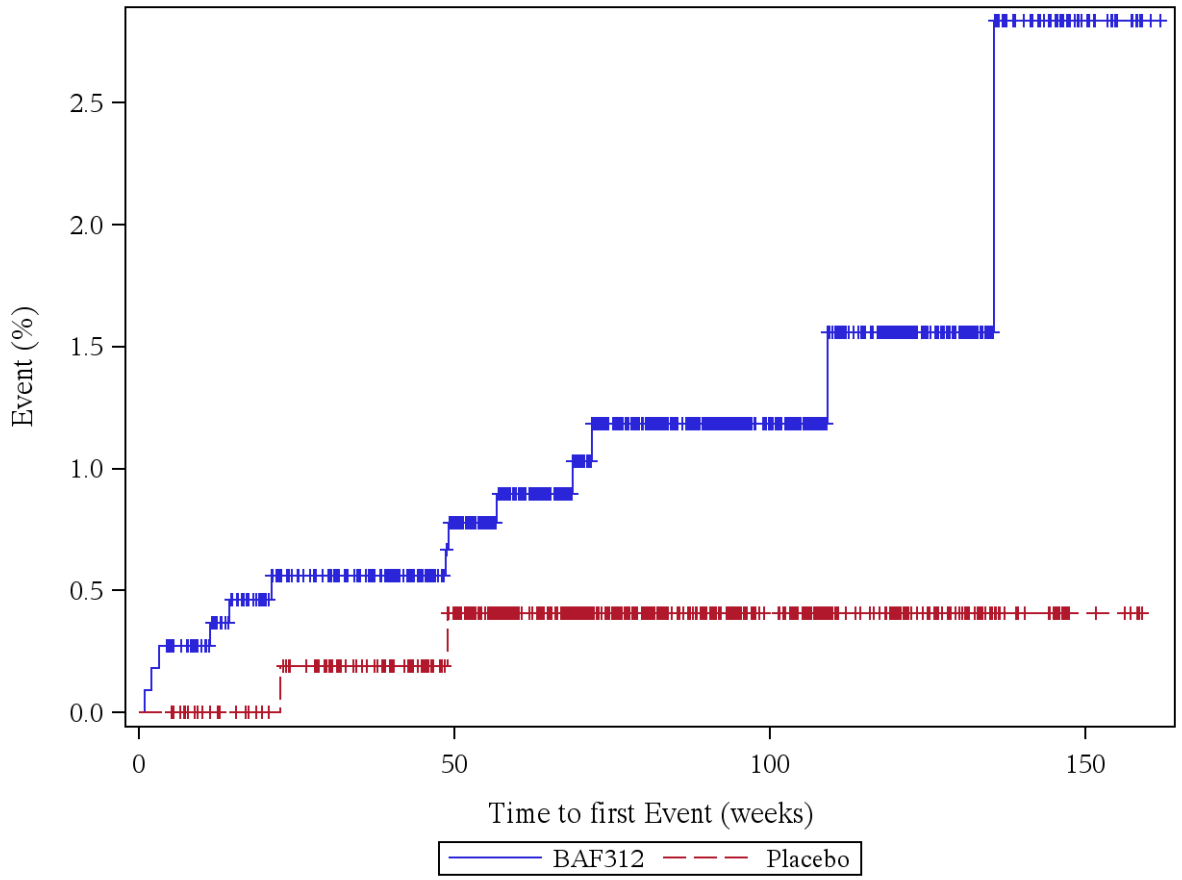


Patients at risk (BAF312/Placebo): Week 0: 1099/546, Week 4: 1099/546, Week 12: 1059/533, Week 24: 1017/519, Week 36: 990/495, Week 48: 925/459, Week 60: 818/386, Week 72: 652/304, Week 84: 516/236, Week 96: 400/176, Week 108: 291/126, Week 120: 200/80, Week 132: 113/40, Week 144: 51/20, Week 156: 10/5, Week 168: 0/0

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

Analysis population: A2304 SAF total population

Figure 12.1.5.17: TINNITUS (PT, not severe)

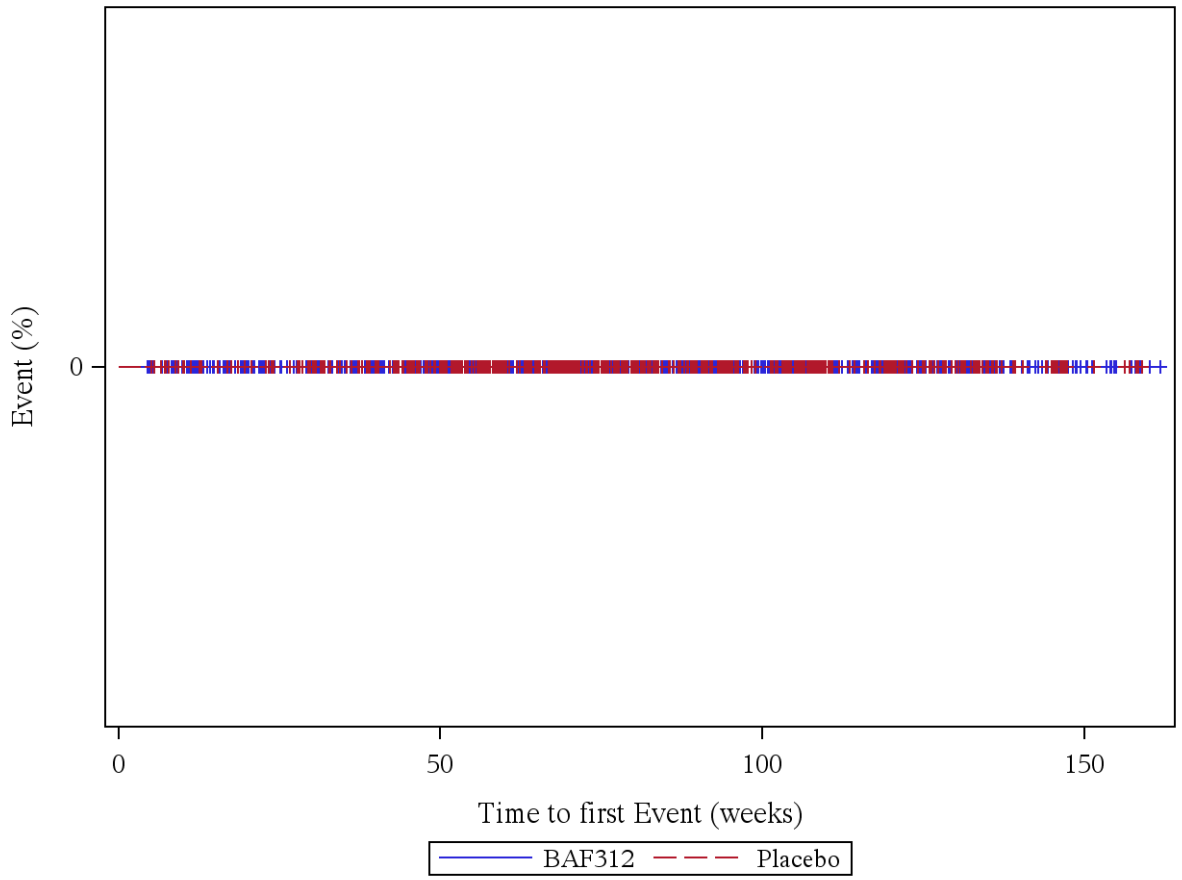


Patients at risk (BAF312/Placebo): Week 0: 1099/546, Week 4: 1096/546, Week 12: 1055/535, Week 24: 1011/520, Week 36: 984/496, Week 48: 920/460, Week 60: 811/386, Week 72: 643/304, Week 84: 509/236, Week 96: 396/175, Week 108: 288/126, Week 120: 197/80, Week 132: 113/40, Week 144: 51/20, Week 156: 10/5, Week 168: 0/0

Log rank test: p-value = 0,113
*: p < 0,05

Analysis population: A2304 SAF total population

Figure 12.1.5.18: TINNITUS (PT, severe)

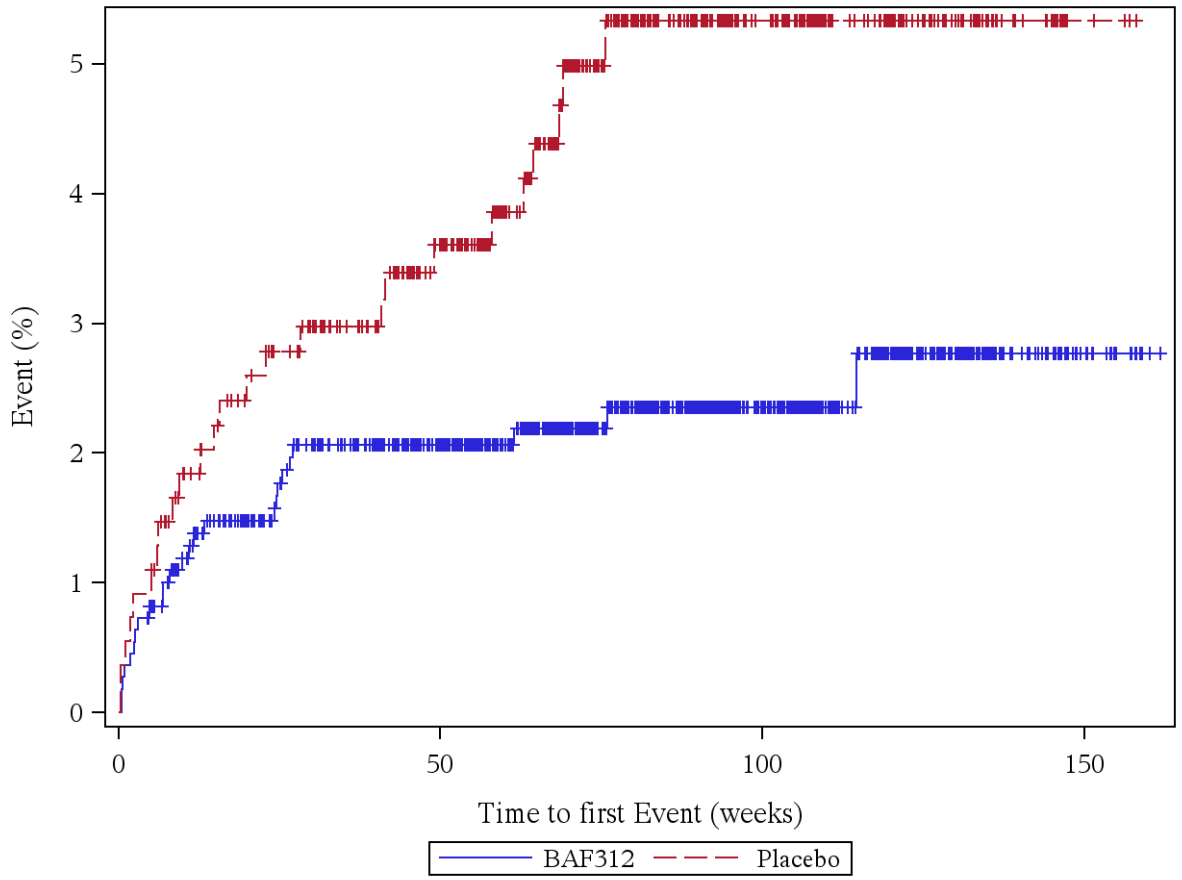


Patients at risk (BAF312/Placebo): Week 0: 1099/546, Week 4: 1099/546, Week 12: 1059/535, Week 24: 1017/521, Week 36: 990/497, Week 48: 925/461, Week 60: 818/388, Week 72: 652/305, Week 84: 516/237, Week 96: 400/176, Week 108: 291/126, Week 120: 200/80, Week 132: 113/40, Week 144: 51/20, Week 156: 10/5, Week 168: 0/0

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

Analysis population: A2304 SAF total population

Figure 12.1.5.19: VERTIGO (PT, not severe)

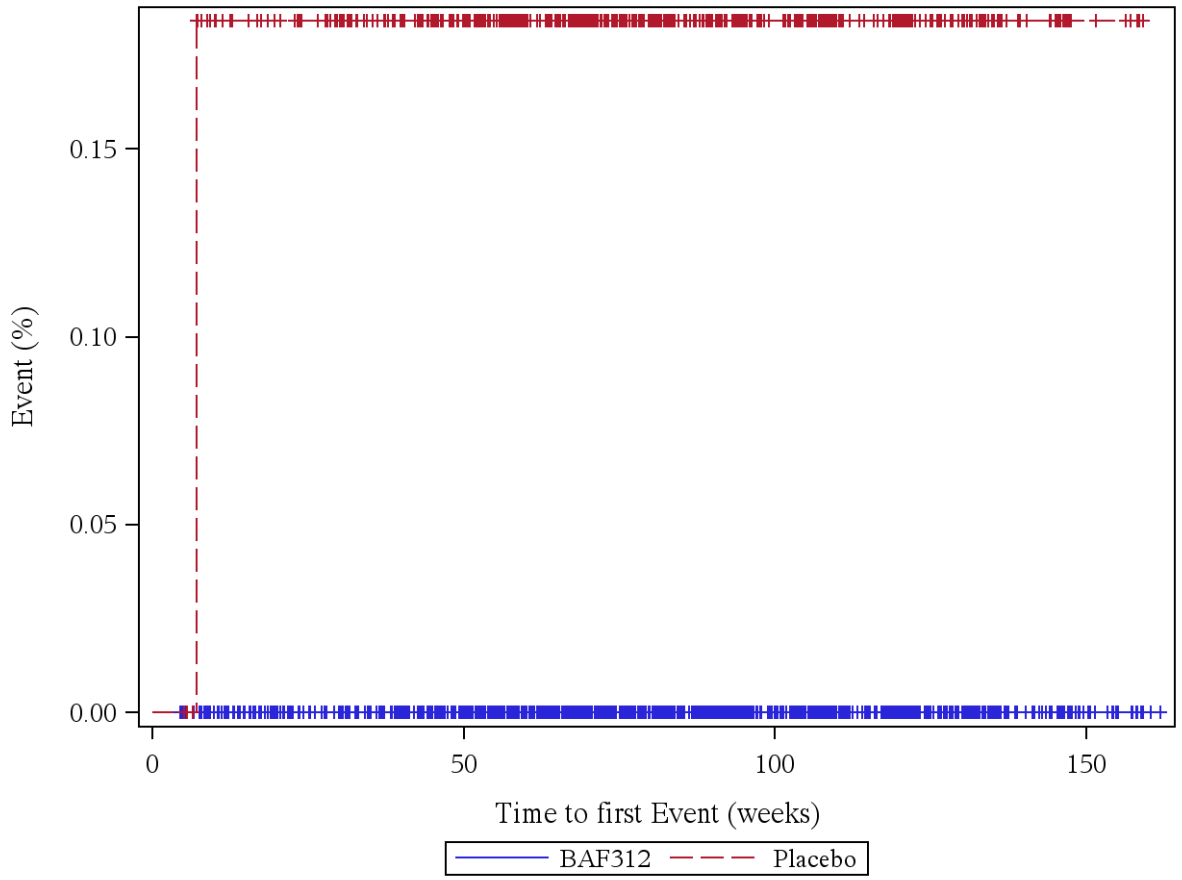


Patients at risk (BAF312/Placebo): Week 0: 1099/546, Week 4: 1091/541, Week 12: 1044/525, Week 24: 1002/506, Week 36: 970/481, Week 48: 906/446, Week 60: 801/372, Week 72: 636/286, Week 84: 504/220, Week 96: 393/161, Week 108: 287/116, Week 120: 196/72, Week 132: 111/37, Week 144: 51/17, Week 156: 10/3, Week 168: 0/0

Log rank test: p-value = 0,010 *
*: p < 0,05

Analysis population: A2304 SAF total population

Figure 12.1.5.20: VERTIGO (PT, severe)

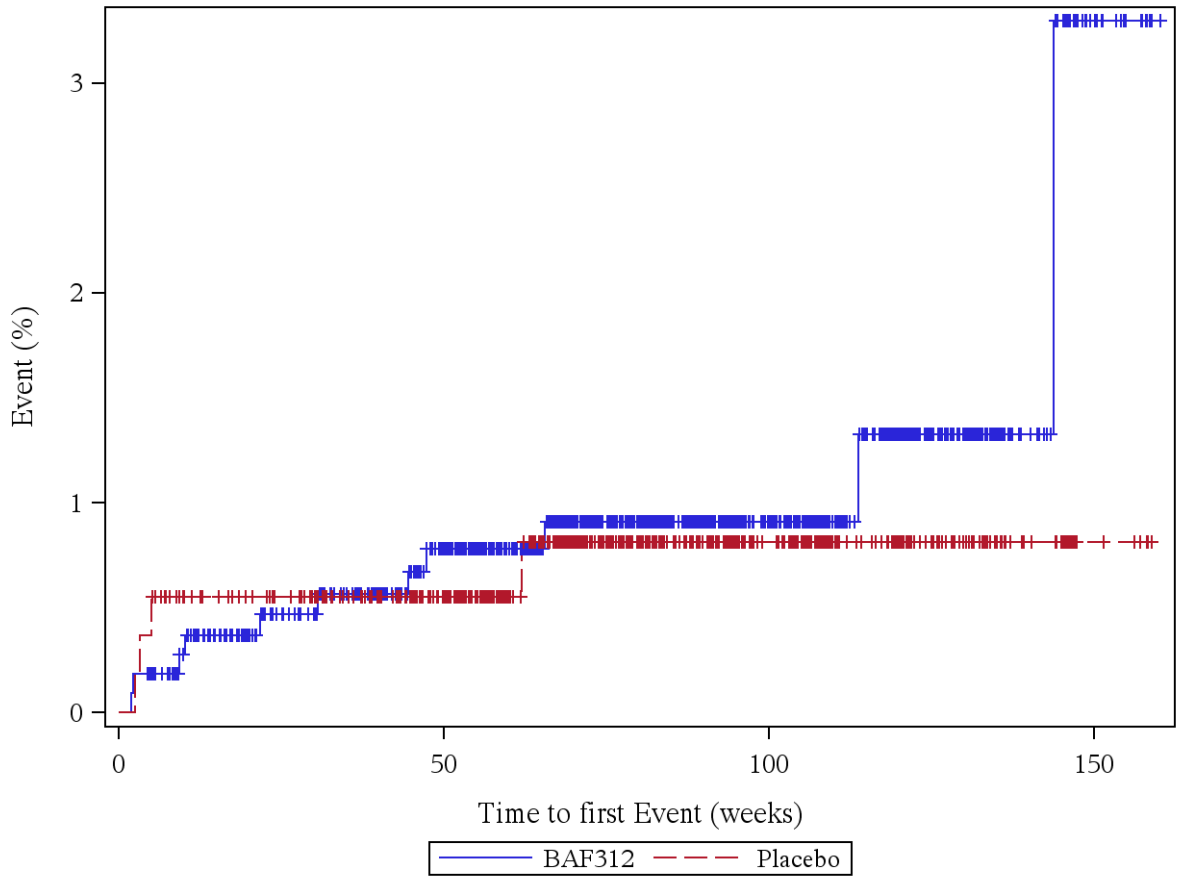


Patients at risk (BAF312/Placebo): Week 0: 1099/546, Week 4: 1099/546, Week 12: 1059/534, Week 24: 1017/520, Week 36: 990/496, Week 48: 925/460, Week 60: 818/387, Week 72: 652/305, Week 84: 516/237, Week 96: 400/176, Week 108: 291/126, Week 120: 200/80, Week 132: 113/40, Week 144: 51/20, Week 156: 10/5, Week 168: 0/0

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

Analysis population: A2304 SAF total population

Figure 12.1.5.21: ENDOCRINE DISORDERS (SOC, not severe)

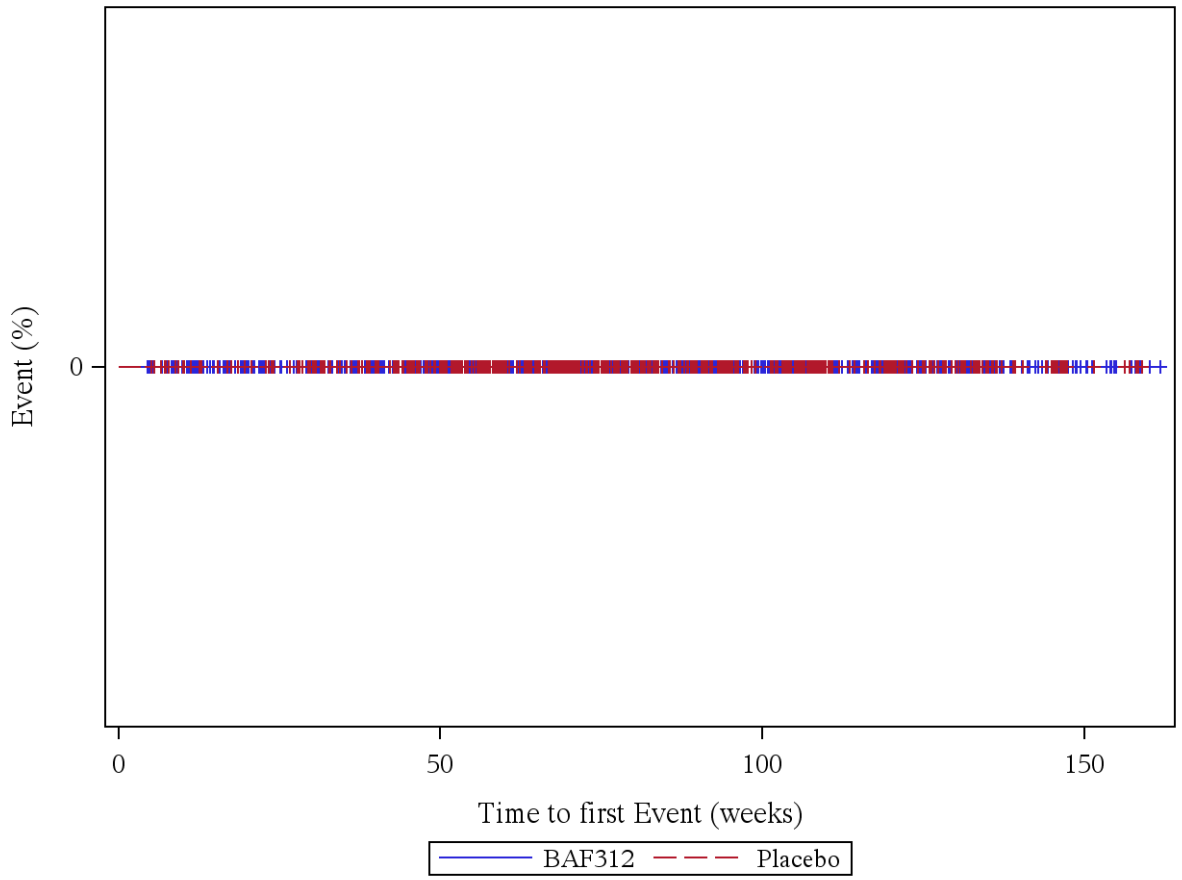


Patients at risk (BAF312/Placebo): Week 0: 1099/546, Week 4: 1097/544, Week 12: 1056/532, Week 24: 1013/518, Week 36: 985/494, Week 48: 918/458, Week 60: 811/385, Week 72: 645/301, Week 84: 510/234, Week 96: 397/174, Week 108: 289/125, Week 120: 197/79, Week 132: 111/40, Week 144: 49/20, Week 156: 9/5, Week 168: 0/0

Log rank test: p-value = 0,625
*: p < 0,05

Analysis population: A2304 SAF total population

Figure 12.1.5.22: ENDOCRINE DISORDERS (SOC, severe)

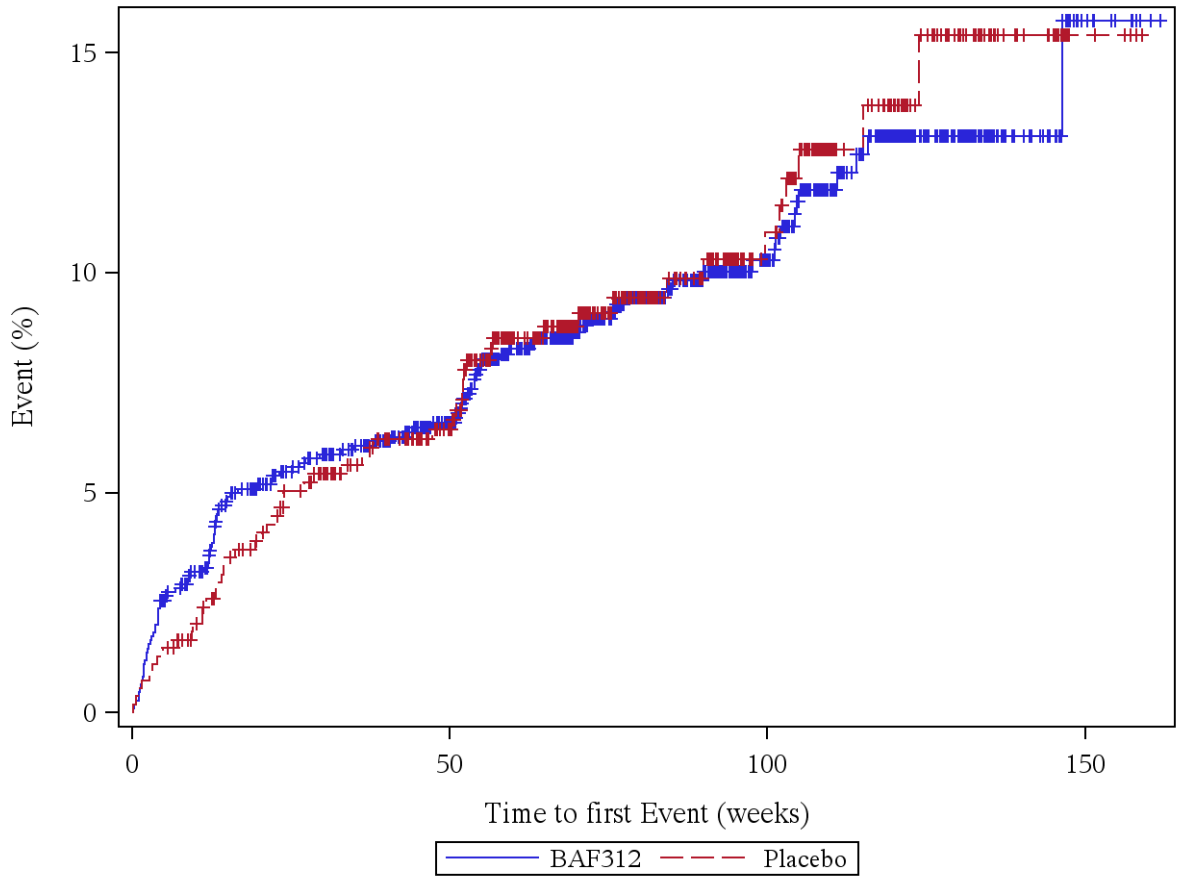


Patients at risk (BAF312/Placebo): Week 0: 1099/546, Week 4: 1099/546, Week 12: 1059/535, Week 24: 1017/521, Week 36: 990/497, Week 48: 925/461, Week 60: 818/388, Week 72: 652/305, Week 84: 516/237, Week 96: 400/176, Week 108: 291/126, Week 120: 200/80, Week 132: 113/40, Week 144: 51/20, Week 156: 10/5, Week 168: 0/0

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

Analysis population: A2304 SAF total population

Figure 12.1.5.23: EYE DISORDERS (SOC, not severe)

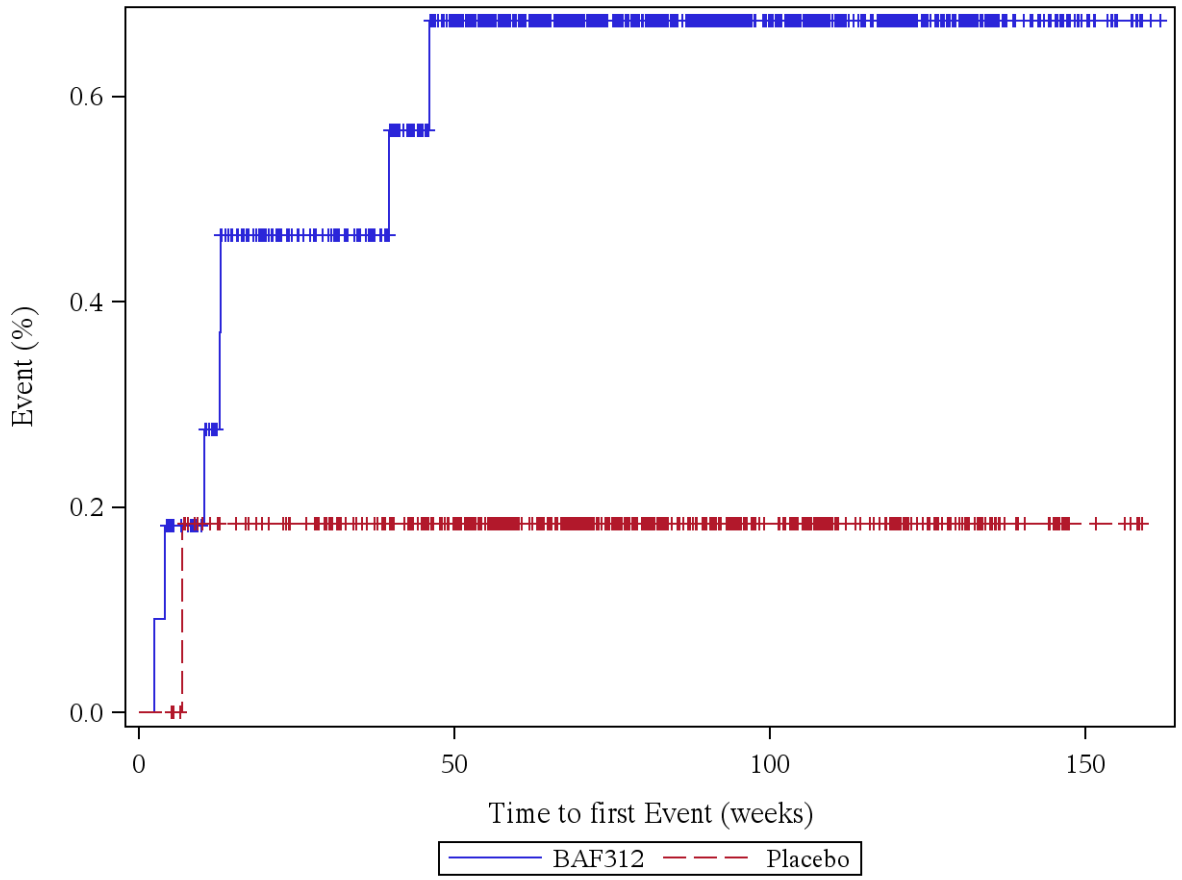


Patients at risk (BAF312/Placebo): Week 0: 1099/546, Week 4: 1077/539, Week 12: 1026/523, Week 24: 971/496, Week 36: 940/469, Week 48: 874/436, Week 60: 762/357, Week 72: 602/277, Week 84: 473/215, Week 96: 370/159, Week 108: 265/110, Week 120: 175/69, Week 132: 99/34, Week 144: 44/16, Week 156: 8/4, Week 168: 0/0

Log rank test: p-value = 0,825
*: p < 0,05

Analysis population: A2304 SAF total population

Figure 12.1.5.24: EYE DISORDERS (SOC, severe)

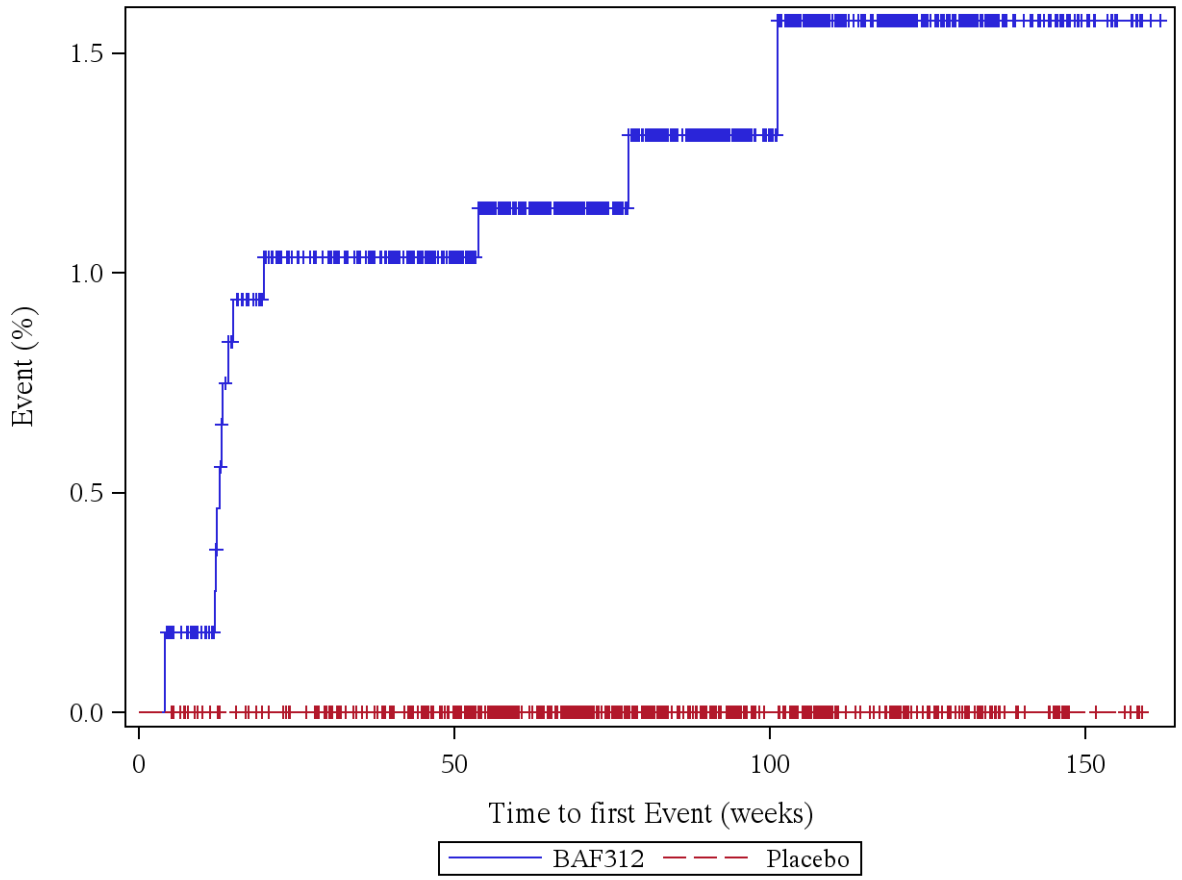


Patients at risk (BAF312/Placebo): Week 0: 1099/546, Week 4: 1098/546, Week 12: 1057/534, Week 24: 1016/520, Week 36: 990/496, Week 48: 923/460, Week 60: 816/387, Week 72: 650/304, Week 84: 516/236, Week 96: 400/176, Week 108: 291/126, Week 120: 200/80, Week 132: 113/40, Week 144: 51/20, Week 156: 10/5, Week 168: 0/0

Log rank test: p-value = 0,211
*: p < 0,05

Analysis population: A2304 SAF total population

Figure 12.1.5.25: MACULAR OEDEMA (PT, not severe)

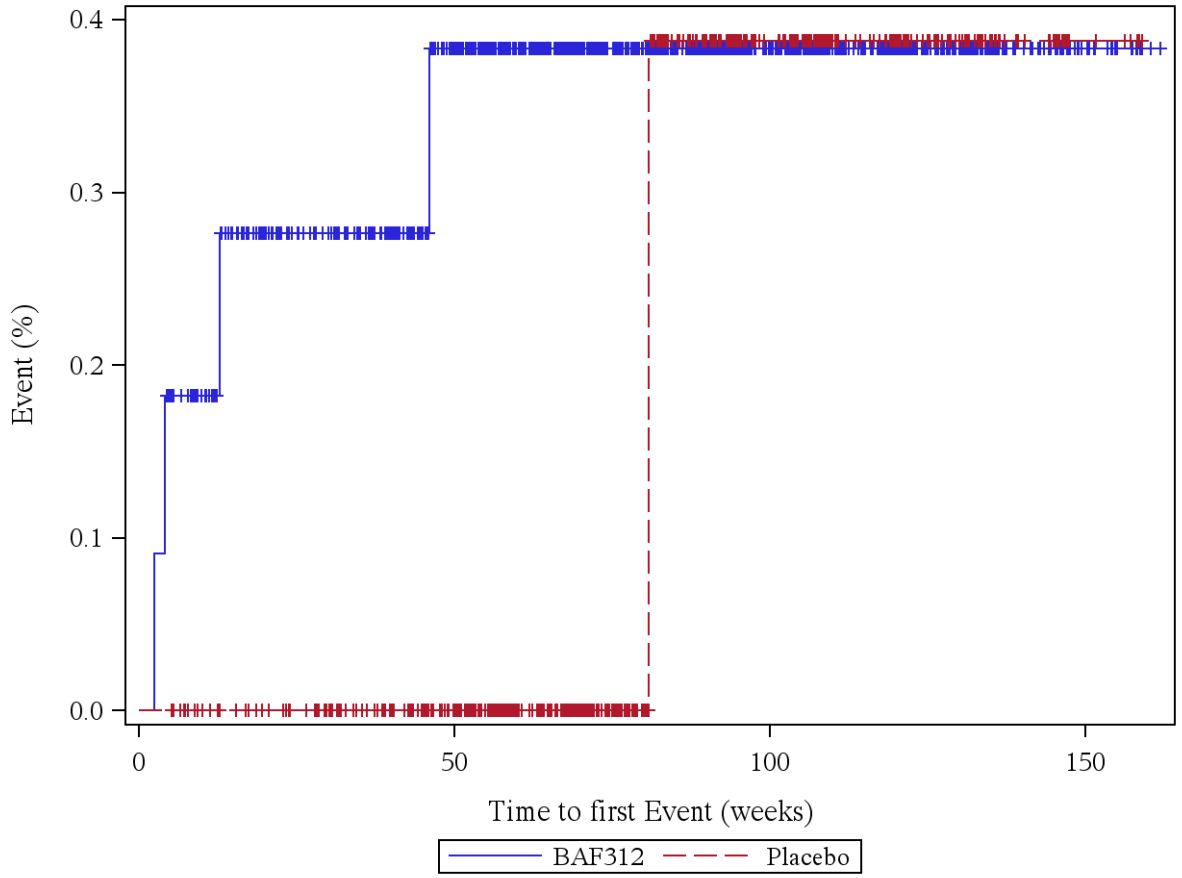


Patients at risk (BAF312/Placebo): Week 0: 1099/546, Week 4: 1099/546, Week 12: 1058/535, Week 24: 1013/521, Week 36: 986/497, Week 48: 922/461, Week 60: 816/388, Week 72: 651/305, Week 84: 514/237, Week 96: 400/176, Week 108: 291/126, Week 120: 200/80, Week 132: 113/40, Week 144: 51/20, Week 156: 10/5, Week 168: 0/0

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

Analysis population: A2304 SAF total population

Figure 12.1.5.26: MACULAR OEDEMA (PT, severe)

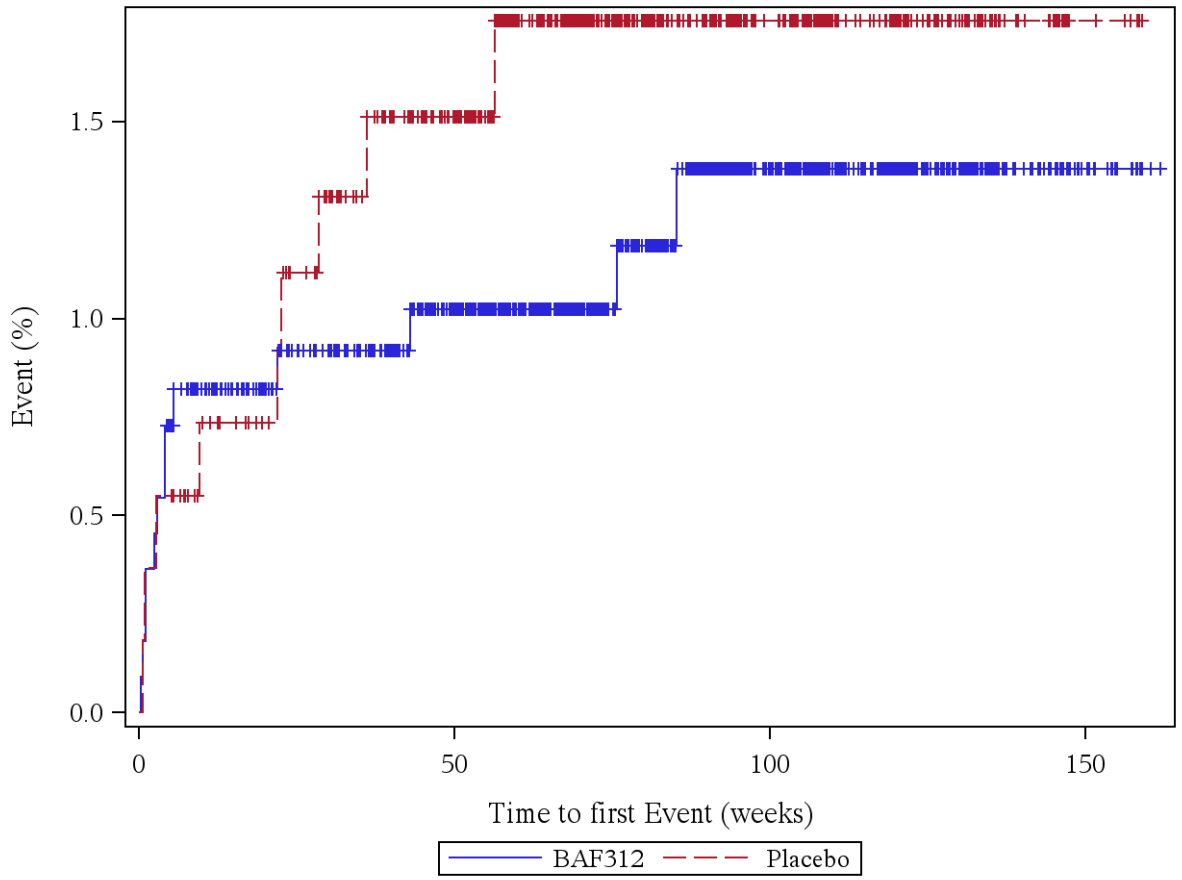


Patients at risk (BAF312/Placebo): Week 0: 1099/546, Week 4: 1098/546, Week 12: 1058/535, Week 24: 1016/521, Week 36: 990/497, Week 48: 924/461, Week 60: 817/388, Week 72: 651/305, Week 84: 516/236, Week 96: 400/176, Week 108: 291/126, Week 120: 200/80, Week 132: 113/40, Week 144: 51/20, Week 156: 10/5, Week 168: 0/0

Log rank test: p-value = 0,537
*: p < 0,05

Analysis population: A2304 SAF total population

Figure 12.1.5.27: VISION BLURRED (PT, not severe)

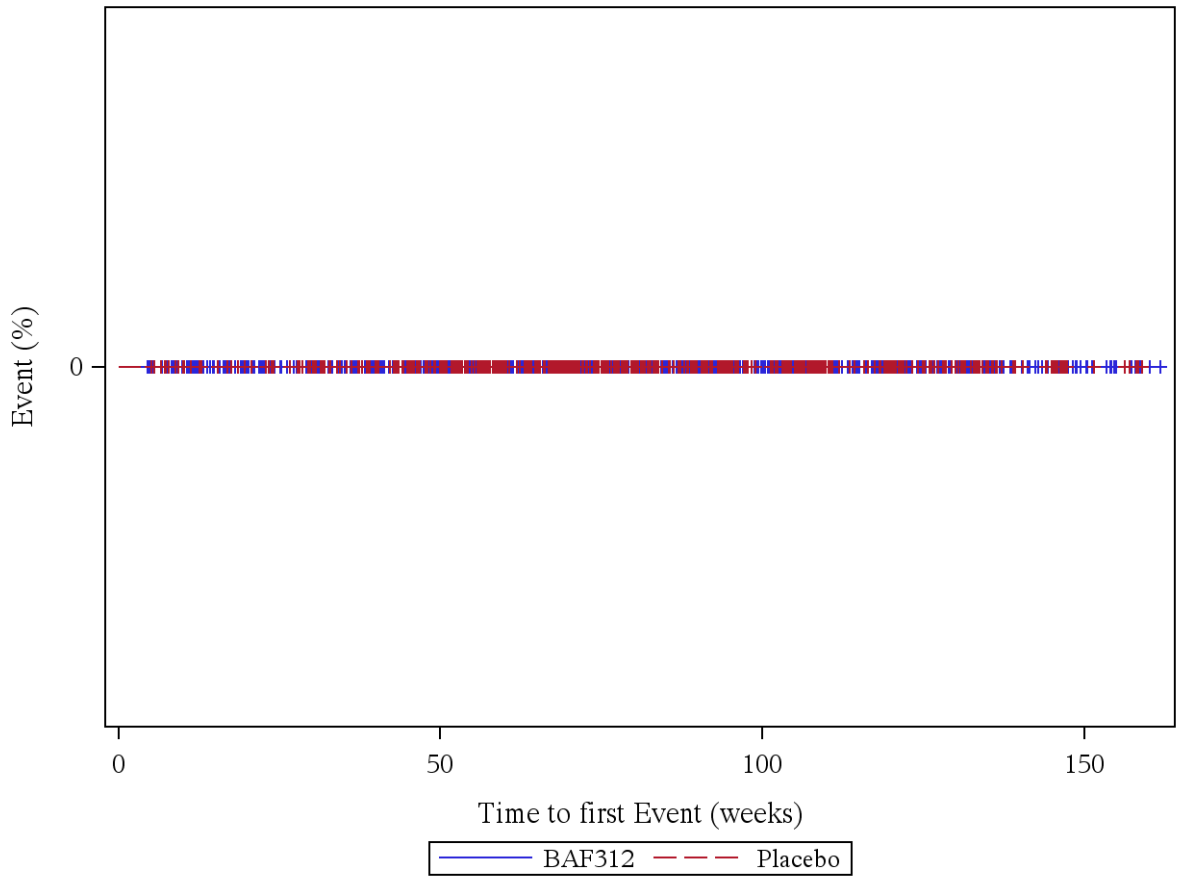


Patients at risk (BAF312/Placebo): Week 0: 1099/546, Week 4: 1093/543, Week 12: 1050/531, Week 24: 1007/515, Week 36: 980/490, Week 48: 915/454, Week 60: 809/381, Week 72: 645/298, Week 84: 510/233, Week 96: 394/175, Week 108: 288/126, Week 120: 197/80, Week 132: 112/40, Week 144: 51/20, Week 156: 10/5, Week 168: 0/0

Log rank test: p-value = 0,441
*: p < 0,05

Analysis population: A2304 SAF total population

Figure 12.1.5.28: VISION BLURRED (PT, severe)

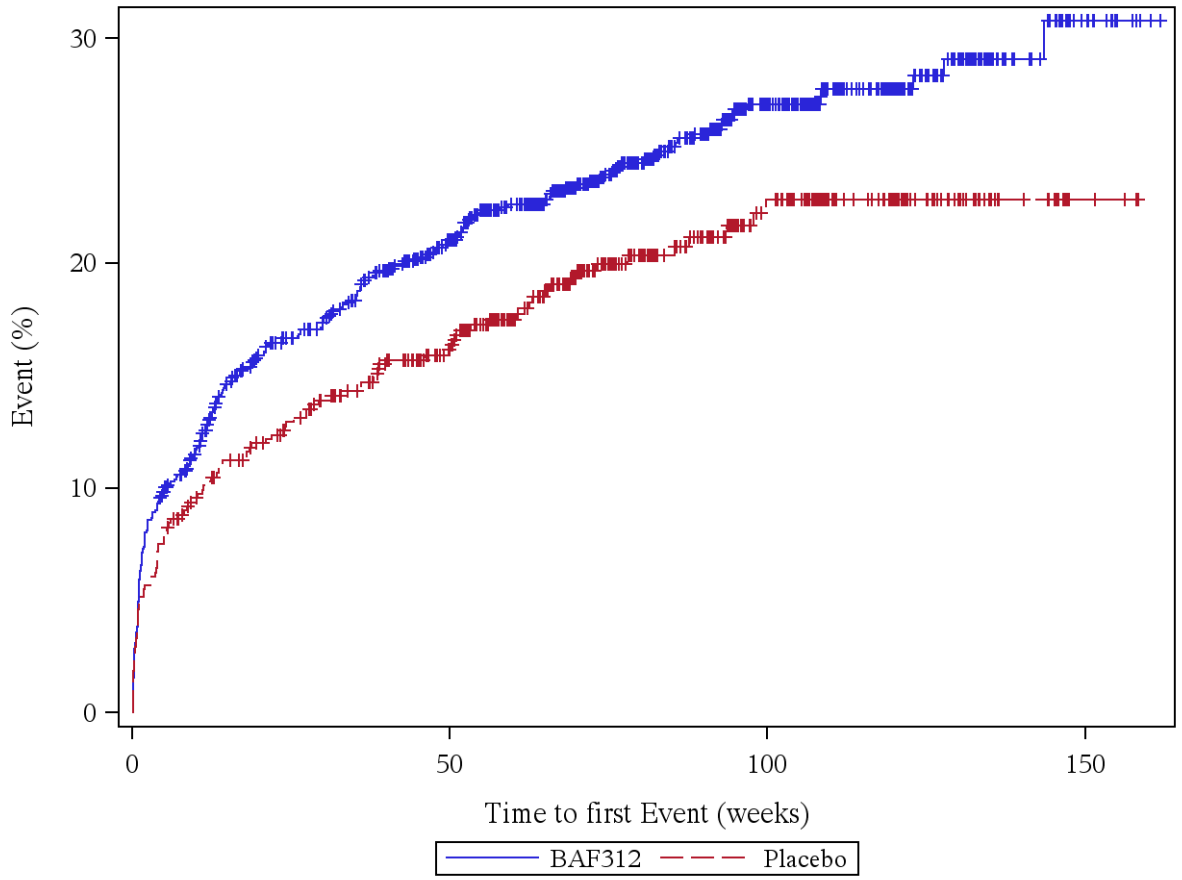


Patients at risk (BAF312/Placebo): Week 0: 1099/546, Week 4: 1099/546, Week 12: 1059/535, Week 24: 1017/521, Week 36: 990/497, Week 48: 925/461, Week 60: 818/388, Week 72: 652/305, Week 84: 516/237, Week 96: 400/176, Week 108: 291/126, Week 120: 200/80, Week 132: 113/40, Week 144: 51/20, Week 156: 10/5, Week 168: 0/0

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

Analysis population: A2304 SAF total population

Figure 12.1.5.29: GASTROINTESTINAL DISORDERS (SOC, not severe)

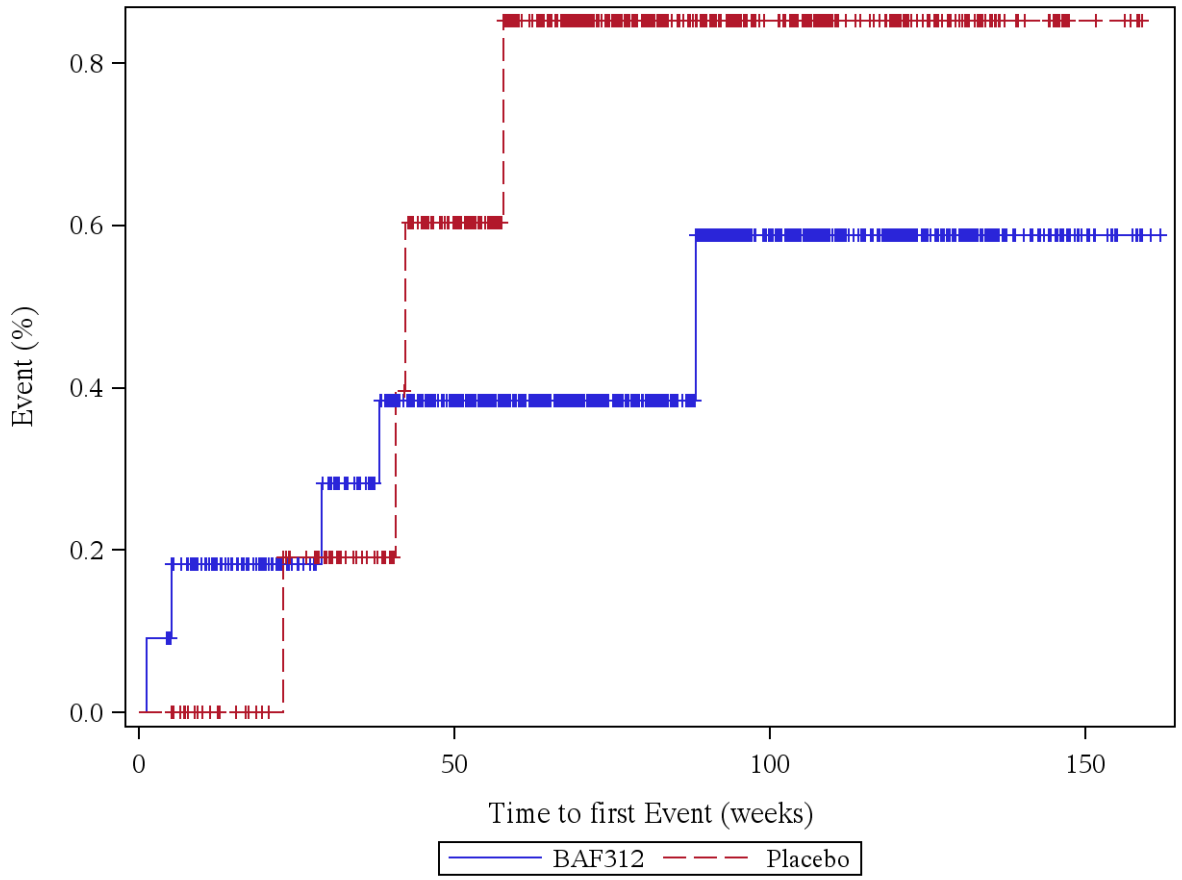


Patients at risk (BAF312/Placebo): Week 0: 1099/546, Week 4: 997/507, Week 12: 922/482, Week 24: 848/456, Week 36: 804/427, Week 48: 739/391, Week 60: 648/325, Week 72: 510/247, Week 84: 395/191, Week 96: 308/143, Week 108: 224/101, Week 120: 151/63, Week 132: 82/27, Week 144: 40/15, Week 156: 6/3, Week 168: 0/0

Log rank test: p-value = 0,033 *
*: p < 0,05

Analysis population: A2304 SAF total population

Figure 12.1.5.30: GASTROINTESTINAL DISORDERS (SOC, severe)

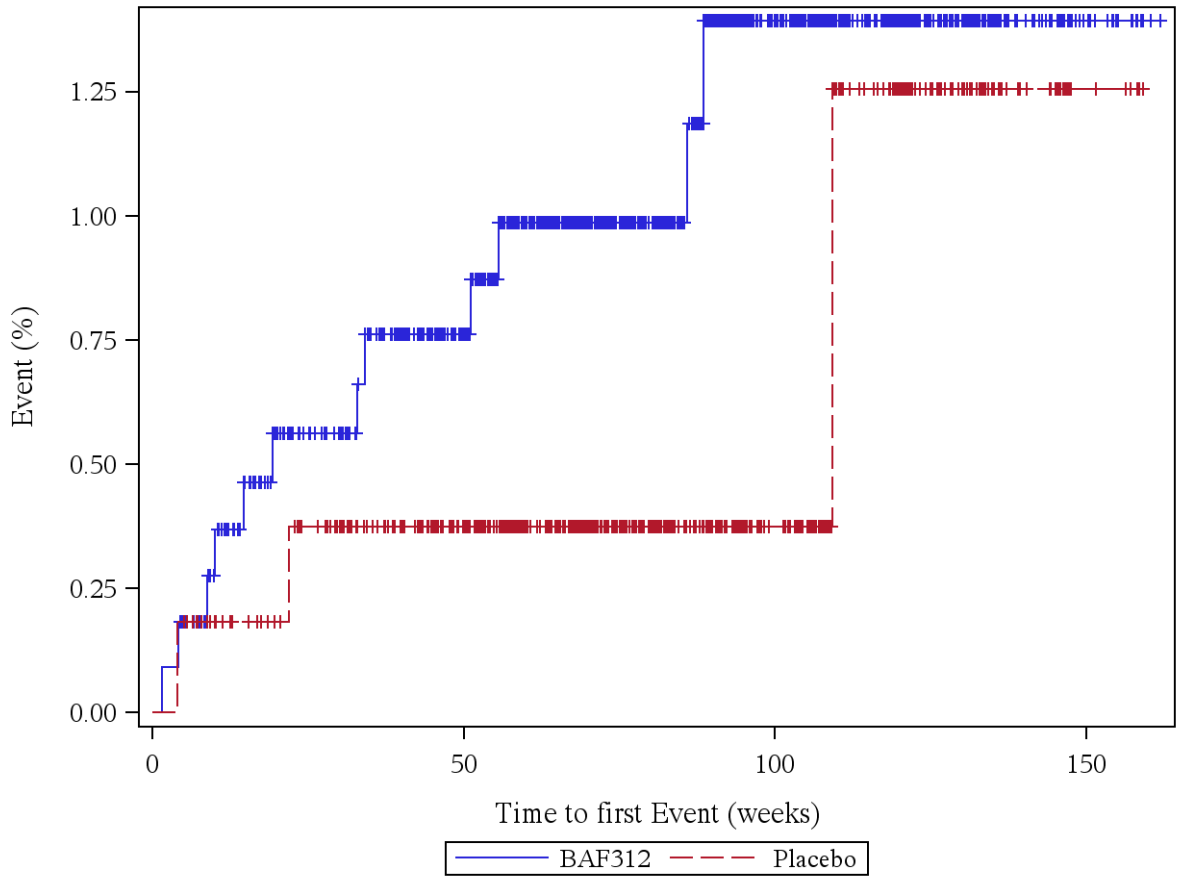


Patients at risk (BAF312/Placebo): Week 0: 1099/546, Week 4: 1098/546, Week 12: 1057/535, Week 24: 1015/520, Week 36: 987/496, Week 48: 921/458, Week 60: 814/387, Week 72: 649/304, Week 84: 513/236, Week 96: 397/176, Week 108: 288/126, Week 120: 199/80, Week 132: 112/40, Week 144: 50/20, Week 156: 9/5, Week 168: 0/0

Log rank test: p-value = 0,475
*: p < 0,05

Analysis population: A2304 SAF total population

Figure 12.1.5.31: ABDOMINAL PAIN (PT, not severe)

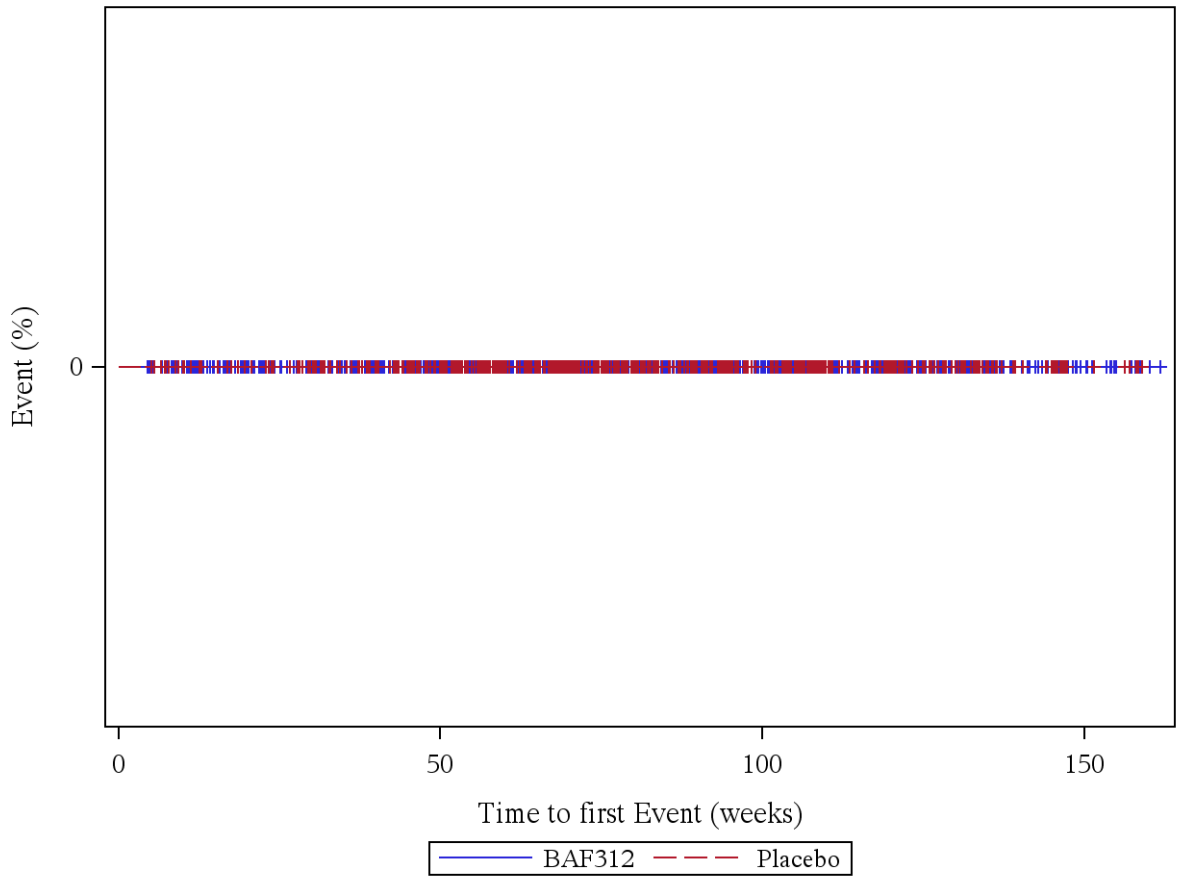


Patients at risk (BAF312/Placebo): Week 0: 1099/546, Week 4: 1098/545, Week 12: 1055/534, Week 24: 1011/519, Week 36: 982/495, Week 48: 918/459, Week 60: 809/387, Week 72: 644/304, Week 84: 509/236, Week 96: 392/175, Week 108: 285/125, Week 120: 195/79, Week 132: 110/39, Week 144: 50/20, Week 156: 10/5, Week 168: 0/0

Log rank test: p-value = 0,286
*: p < 0,05

Analysis population: A2304 SAF total population

Figure 12.1.5.32: ABDOMINAL PAIN (PT, severe)

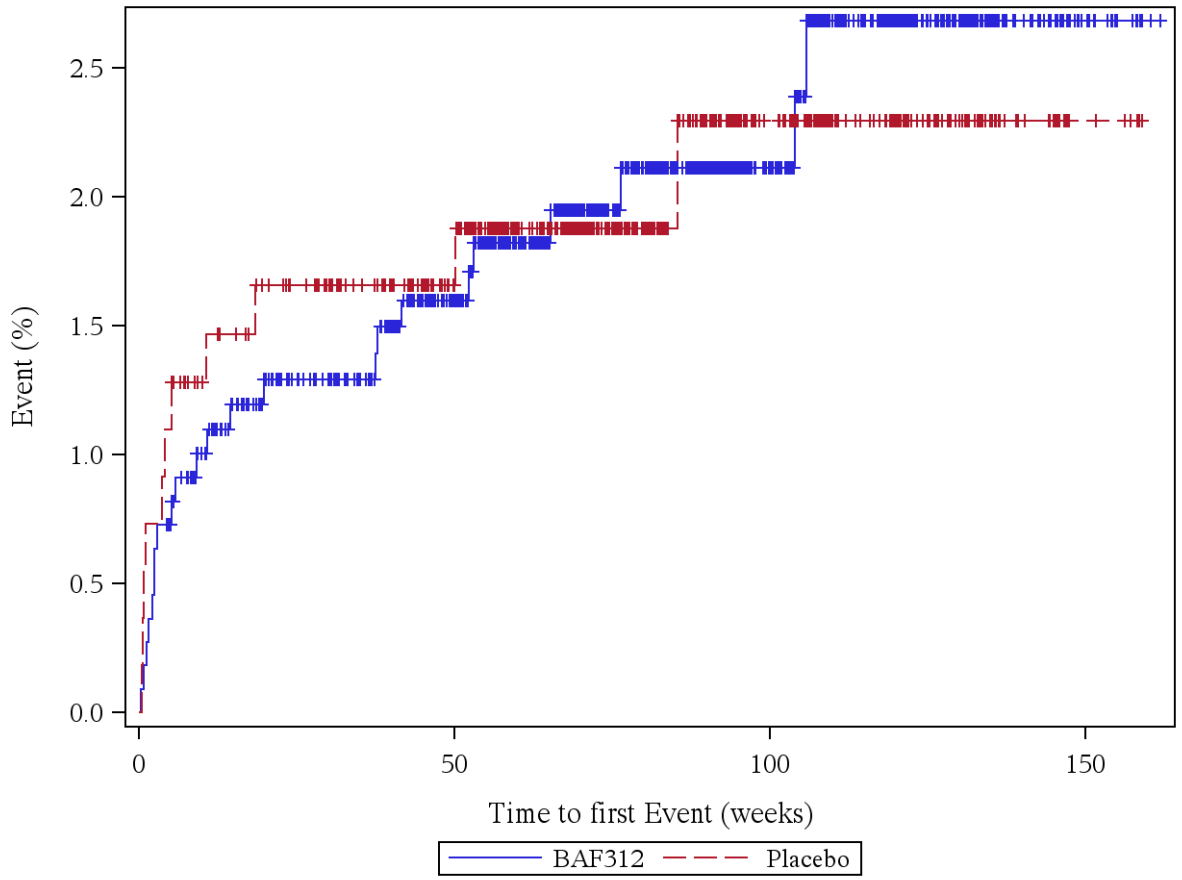


Patients at risk (BAF312/Placebo): Week 0: 1099/546, Week 4: 1099/546, Week 12: 1059/535, Week 24: 1017/521, Week 36: 990/497, Week 48: 925/461, Week 60: 818/388, Week 72: 652/305, Week 84: 516/237, Week 96: 400/176, Week 108: 291/126, Week 120: 200/80, Week 132: 113/40, Week 144: 51/20, Week 156: 10/5, Week 168: 0/0

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

Analysis population: A2304 SAF total population

Figure 12.1.5.33: ABDOMINAL PAIN UPPER (PT, not severe)

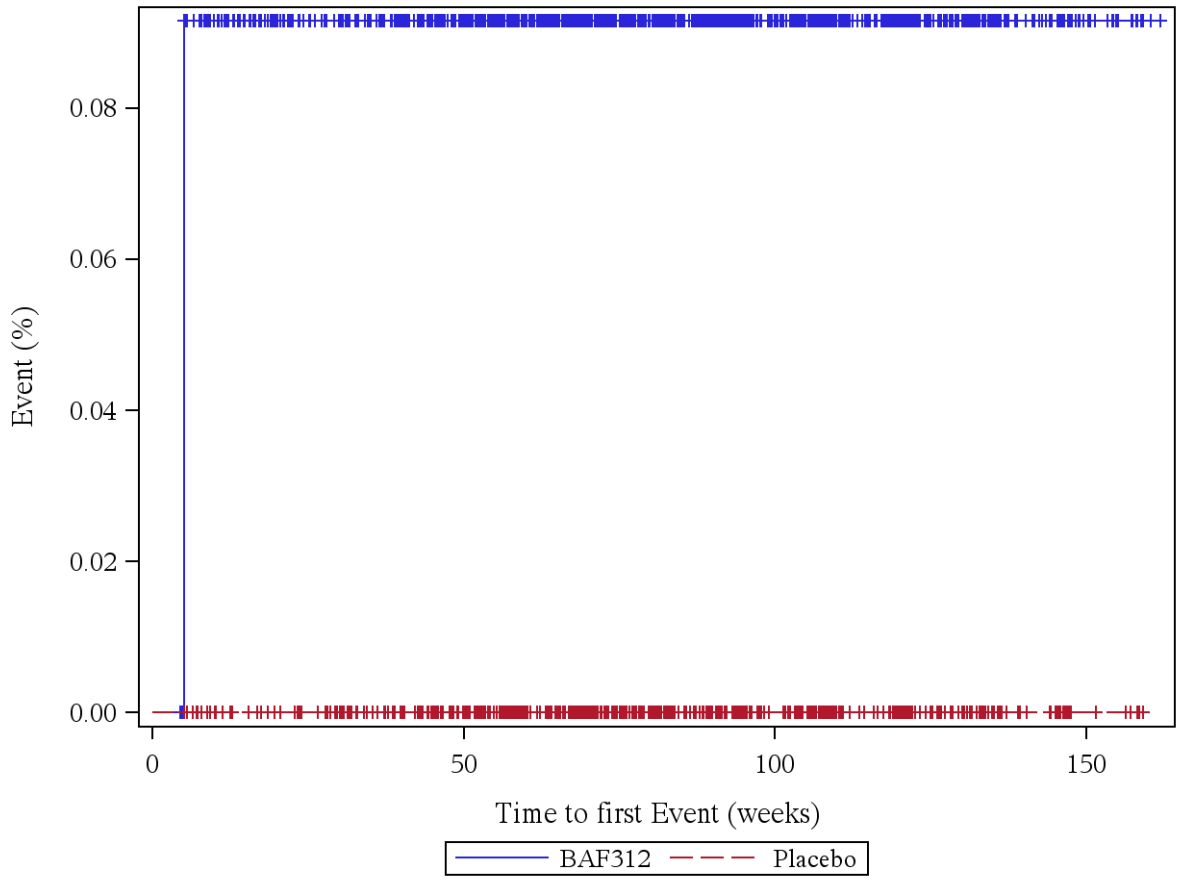


Patients at risk (BAF312/Placebo): Week 0: 1099/546, Week 4: 1091/541, Week 12: 1047/528, Week 24: 1003/513, Week 36: 976/490, Week 48: 911/455, Week 60: 804/382, Week 72: 643/301, Week 84: 508/235, Week 96: 395/174, Week 108: 285/125, Week 120: 194/79, Week 132: 110/39, Week 144: 49/19, Week 156: 9/5, Week 168: 0/0

Log rank test: p-value = 0,940
*: p < 0,05

Analysis population: A2304 SAF total population

Figure 12.1.5.34: ABDOMINAL PAIN UPPER (PT, severe)

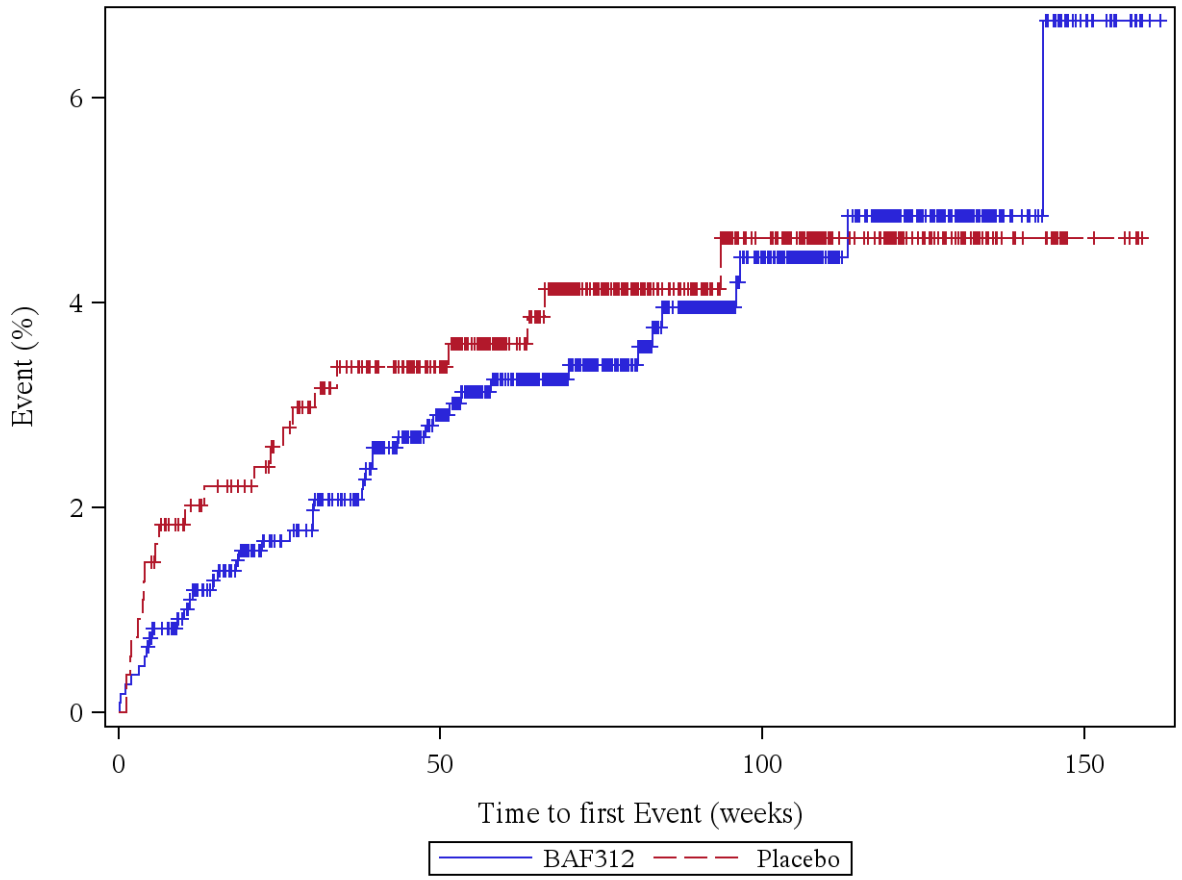


Patients at risk (BAF312/Placebo): Week 0: 1099/546, Week 4: 1099/546, Week 12: 1058/535, Week 24: 1016/521, Week 36: 989/497, Week 48: 924/461, Week 60: 817/388, Week 72: 652/305, Week 84: 516/237, Week 96: 400/176, Week 108: 291/126, Week 120: 200/80, Week 132: 113/40, Week 144: 51/20, Week 156: 10/5, Week 168: 0/0

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

Analysis population: A2304 SAF total population

Figure 12.1.5.35: CONSTIPATION (PT, not severe)

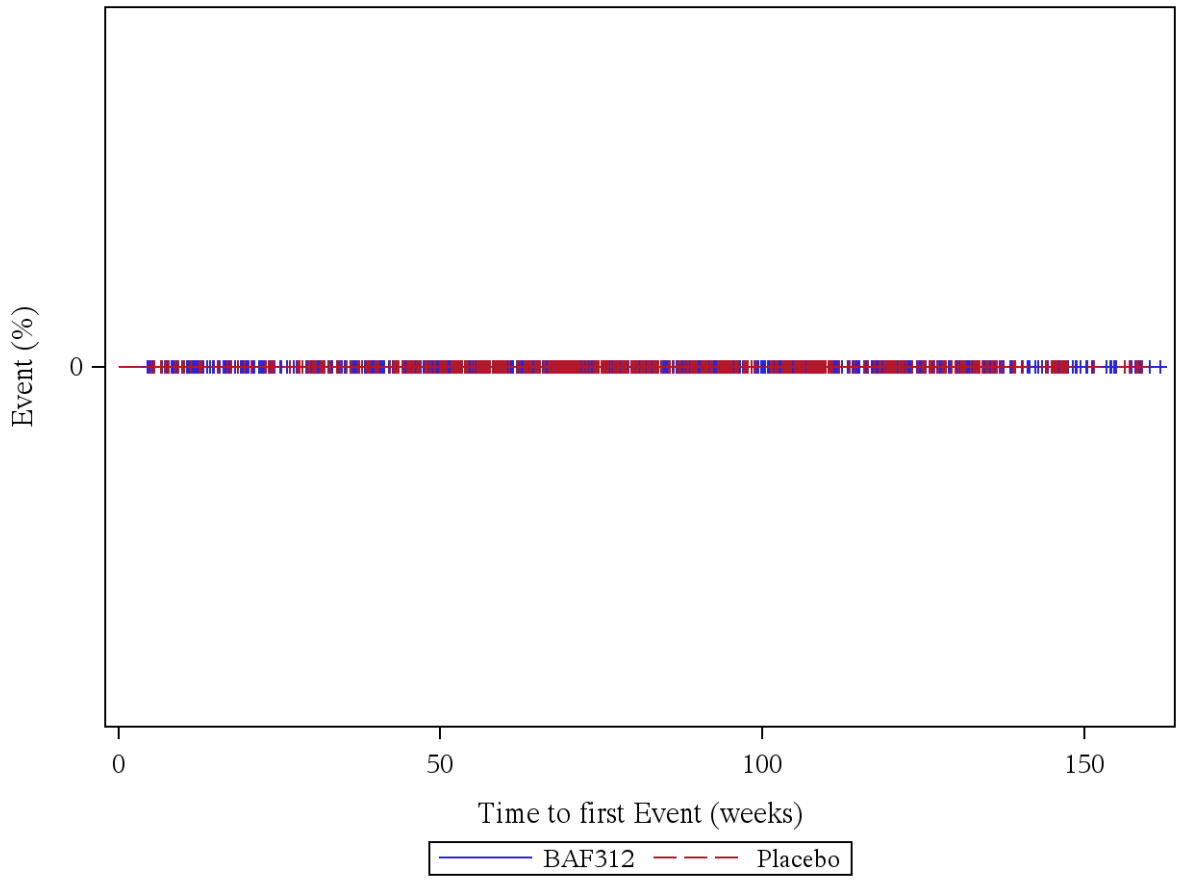


Patients at risk (BAF312/Placebo): Week 0: 1099/546, Week 4: 1093/538, Week 12: 1046/524, Week 24: 999/507, Week 36: 969/483, Week 48: 899/449, Week 60: 792/376, Week 72: 631/295, Week 84: 500/229, Week 96: 389/170, Week 108: 284/125, Week 120: 195/79, Week 132: 110/39, Week 144: 49/20, Week 156: 10/5, Week 168: 0/0

Log rank test: p-value = 0,728
*: p < 0,05

Analysis population: A2304 SAF total population

Figure 12.1.5.36: CONSTIPATION (PT, severe)

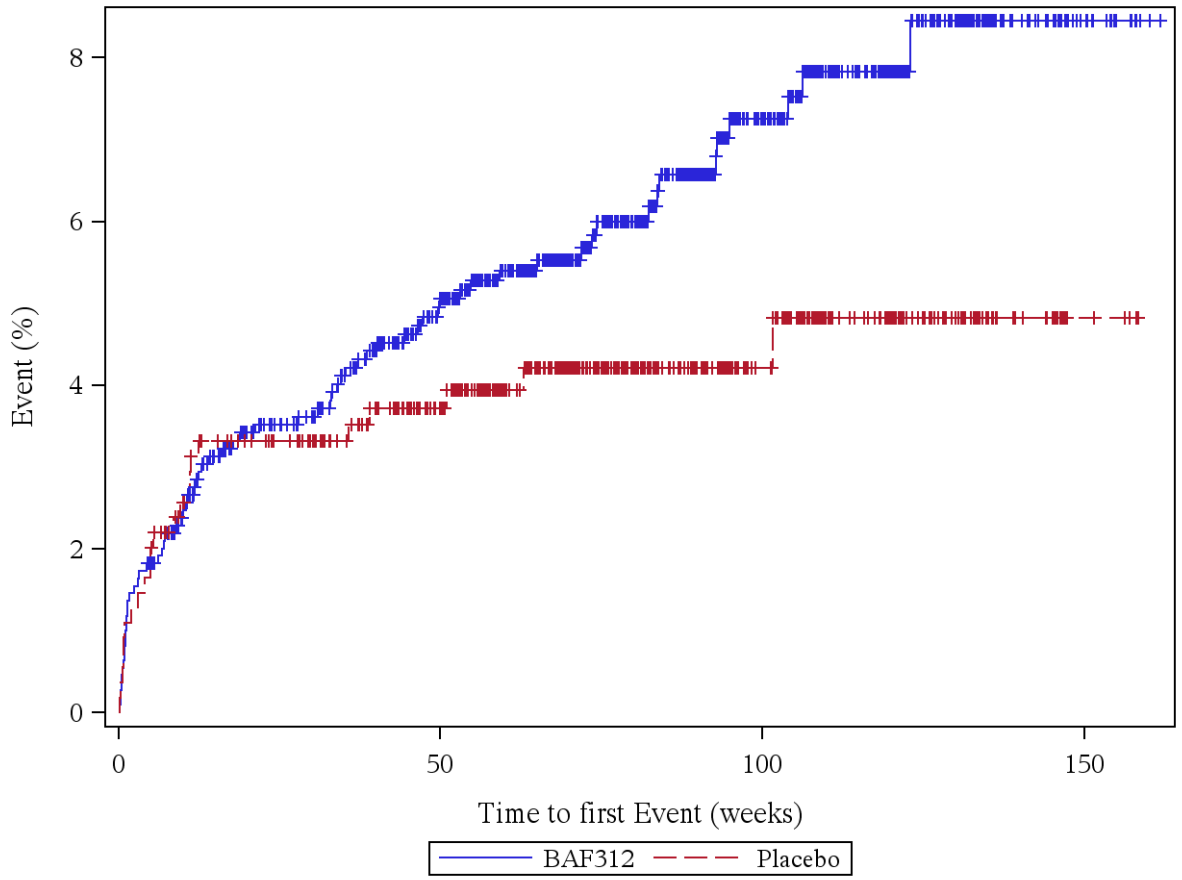


Patients at risk (BAF312/Placebo): Week 0: 1099/546, Week 4: 1099/546, Week 12: 1059/535, Week 24: 1017/521, Week 36: 990/497, Week 48: 925/461, Week 60: 818/388, Week 72: 652/305, Week 84: 516/237, Week 96: 400/176, Week 108: 291/126, Week 120: 200/80, Week 132: 113/40, Week 144: 51/20, Week 156: 10/5, Week 168: 0/0

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

Analysis population: A2304 SAF total population

Figure 12.1.5.37: DIARRHOEA (PT, not severe)

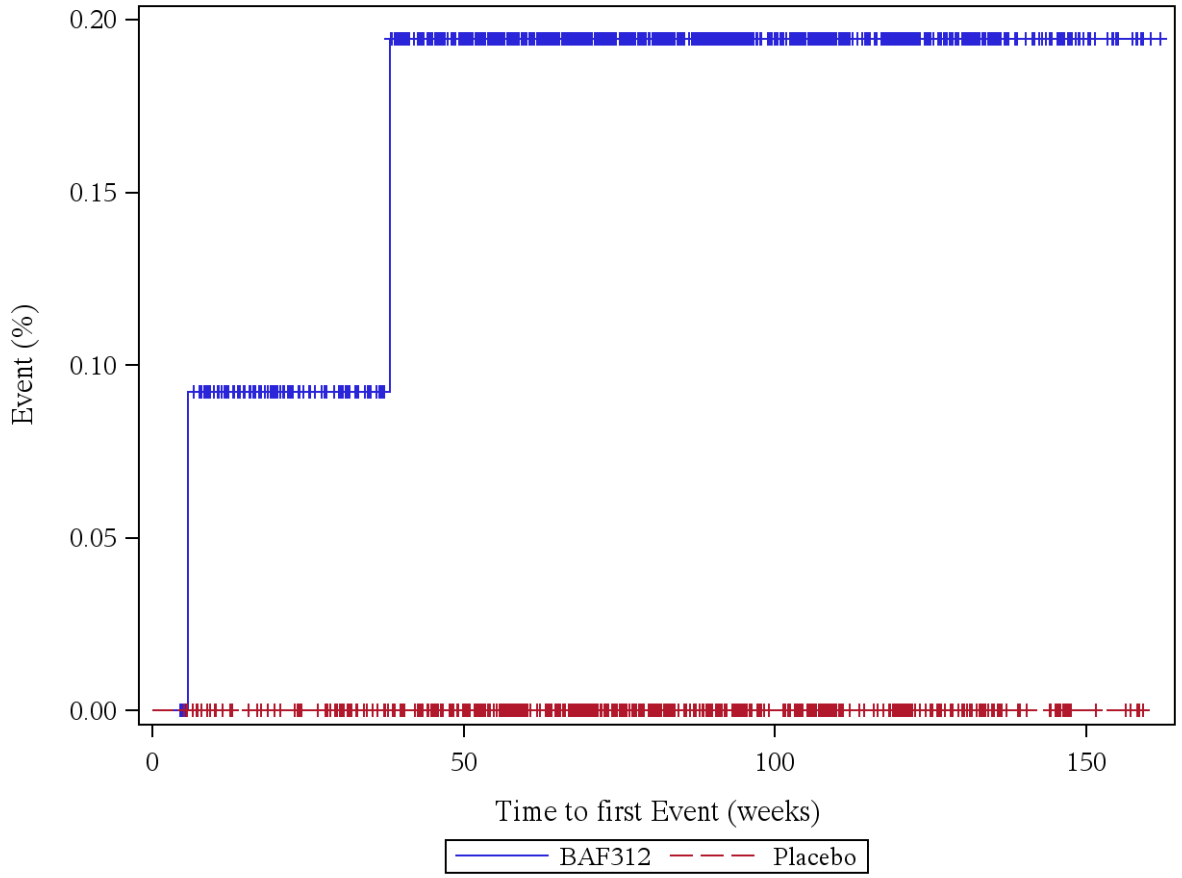


Patients at risk (BAF312/Placebo): Week 0: 1099/546, Week 4: 1080/537, Week 12: 1030/518, Week 24: 985/503, Week 36: 953/480, Week 48: 886/446, Week 60: 779/374, Week 72: 620/292, Week 84: 482/225, Week 96: 375/169, Week 108: 276/121, Week 120: 187/77, Week 132: 107/37, Week 144: 49/18, Week 156: 9/4, Week 168: 0/0

Log rank test: p-value = 0,101
*: p < 0,05

Analysis population: A2304 SAF total population

Figure 12.1.5.38: DIARRHOEA (PT, severe)

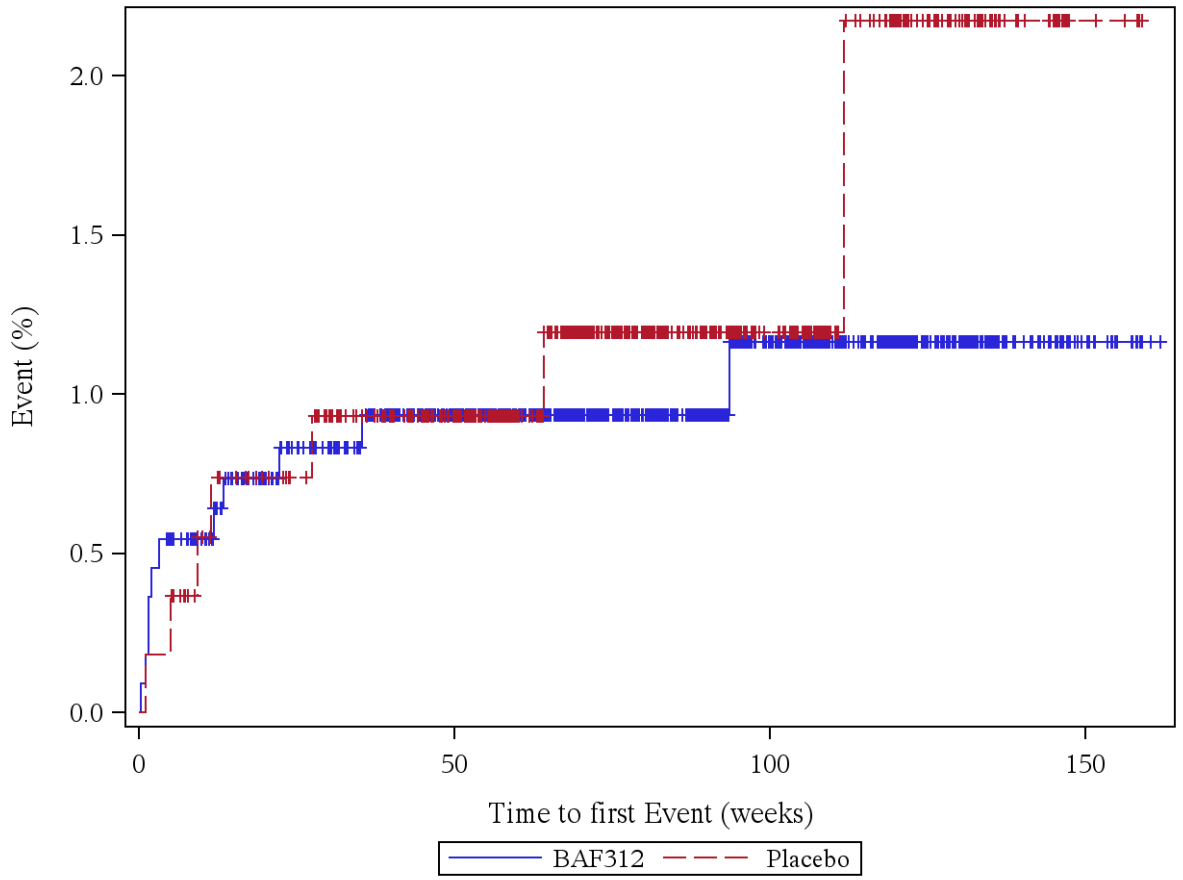


Patients at risk (BAF312/Placebo): Week 0: 1099/546, Week 4: 1099/546, Week 12: 1058/535, Week 24: 1016/521, Week 36: 989/497, Week 48: 923/461, Week 60: 816/388, Week 72: 651/305, Week 84: 515/237, Week 96: 399/176, Week 108: 290/126, Week 120: 199/80, Week 132: 112/40, Week 144: 50/20, Week 156: 9/5, Week 168: 0/0

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

Analysis population: A2304 SAF total population

Figure 12.1.5.39: DYSPEPSIA (PT, not severe)

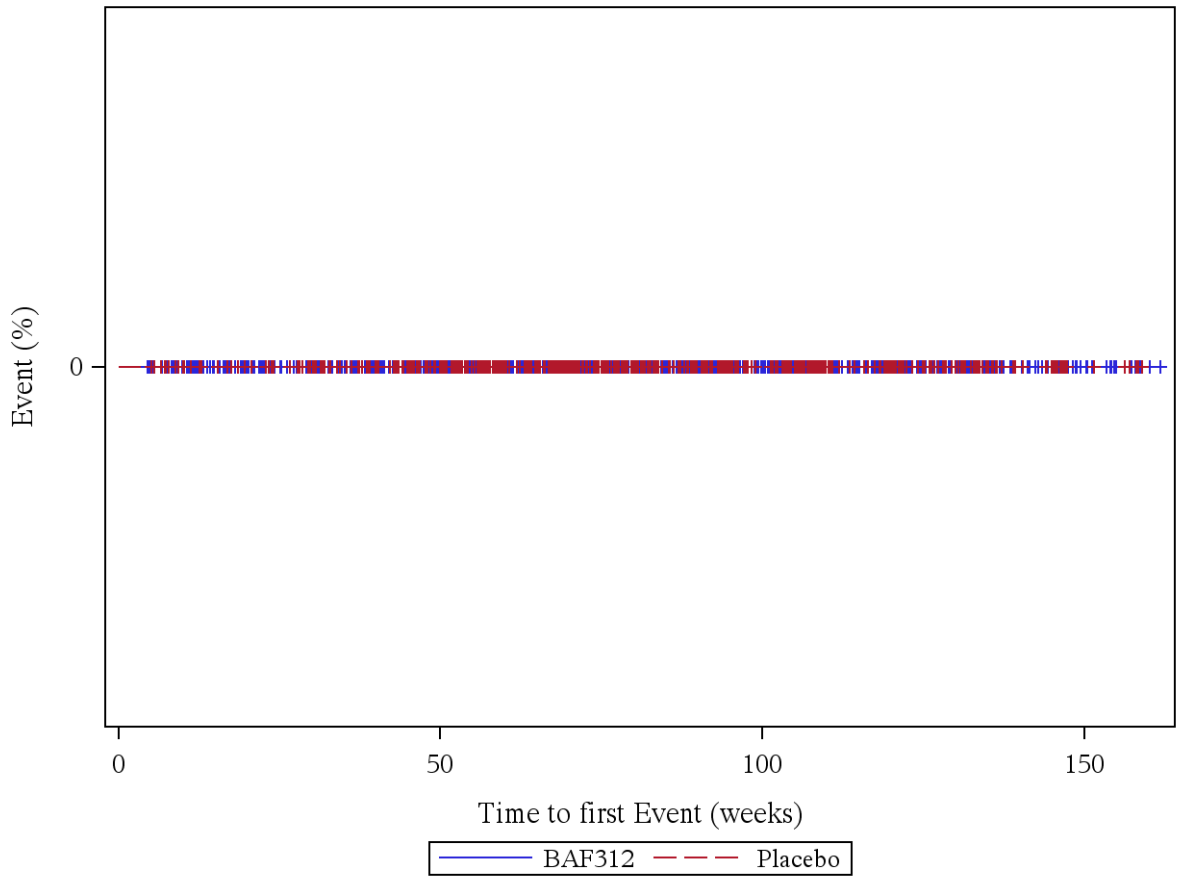


Patients at risk (BAF312/Placebo): Week 0: 1099/546, Week 4: 1093/545, Week 12: 1052/531, Week 24: 1008/517, Week 36: 980/492, Week 48: 916/457, Week 60: 809/386, Week 72: 643/302, Week 84: 511/235, Week 96: 394/174, Week 108: 287/125, Week 120: 197/79, Week 132: 112/39, Week 144: 50/19, Week 156: 10/4, Week 168: 0/0

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

Analysis population: A2304 SAF total population

Figure 12.1.5.40: DYSPEPSIA (PT, severe)

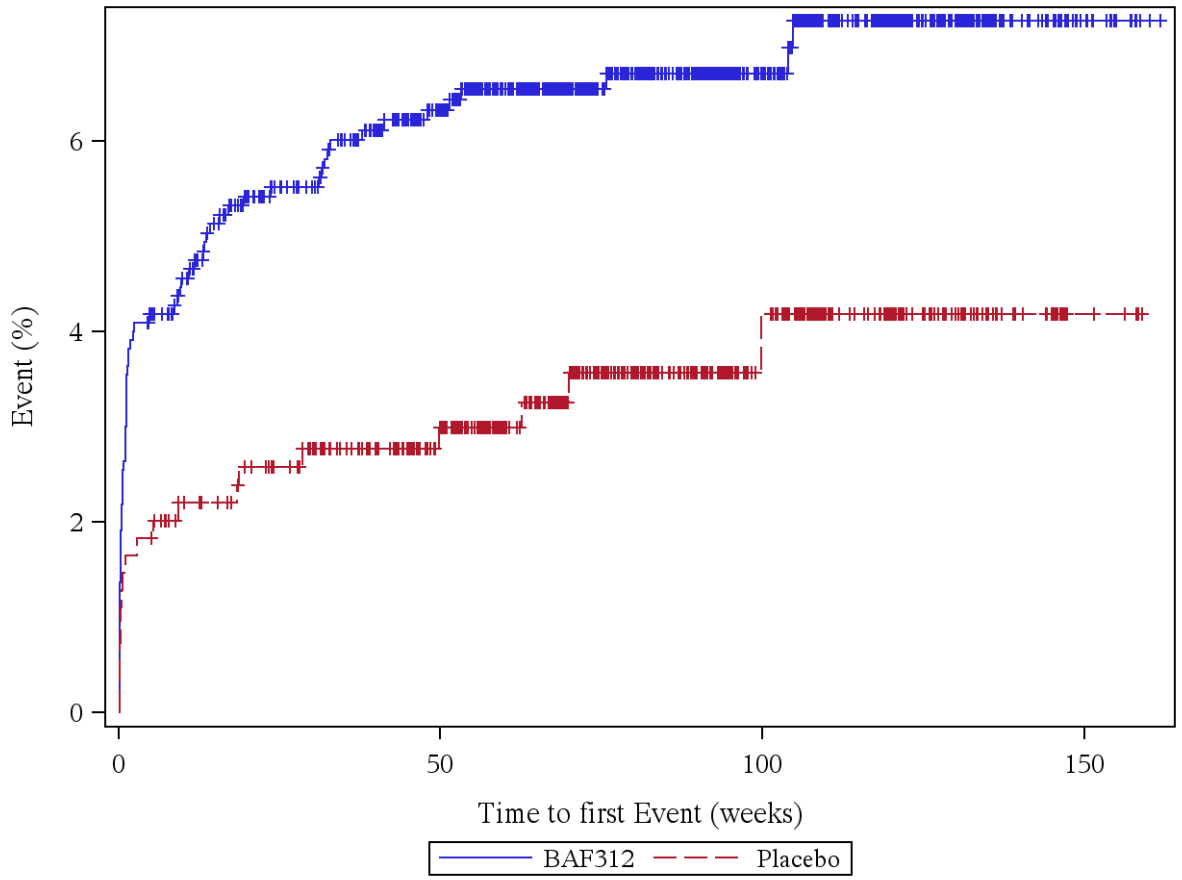


Patients at risk (BAF312/Placebo): Week 0: 1099/546, Week 4: 1099/546, Week 12: 1059/535, Week 24: 1017/521, Week 36: 990/497, Week 48: 925/461, Week 60: 818/388, Week 72: 652/305, Week 84: 516/237, Week 96: 400/176, Week 108: 291/126, Week 120: 200/80, Week 132: 113/40, Week 144: 51/20, Week 156: 10/5, Week 168: 0/0

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

Analysis population: A2304 SAF total population

Figure 12.1.5.41: NAUSEA (PT, not severe)

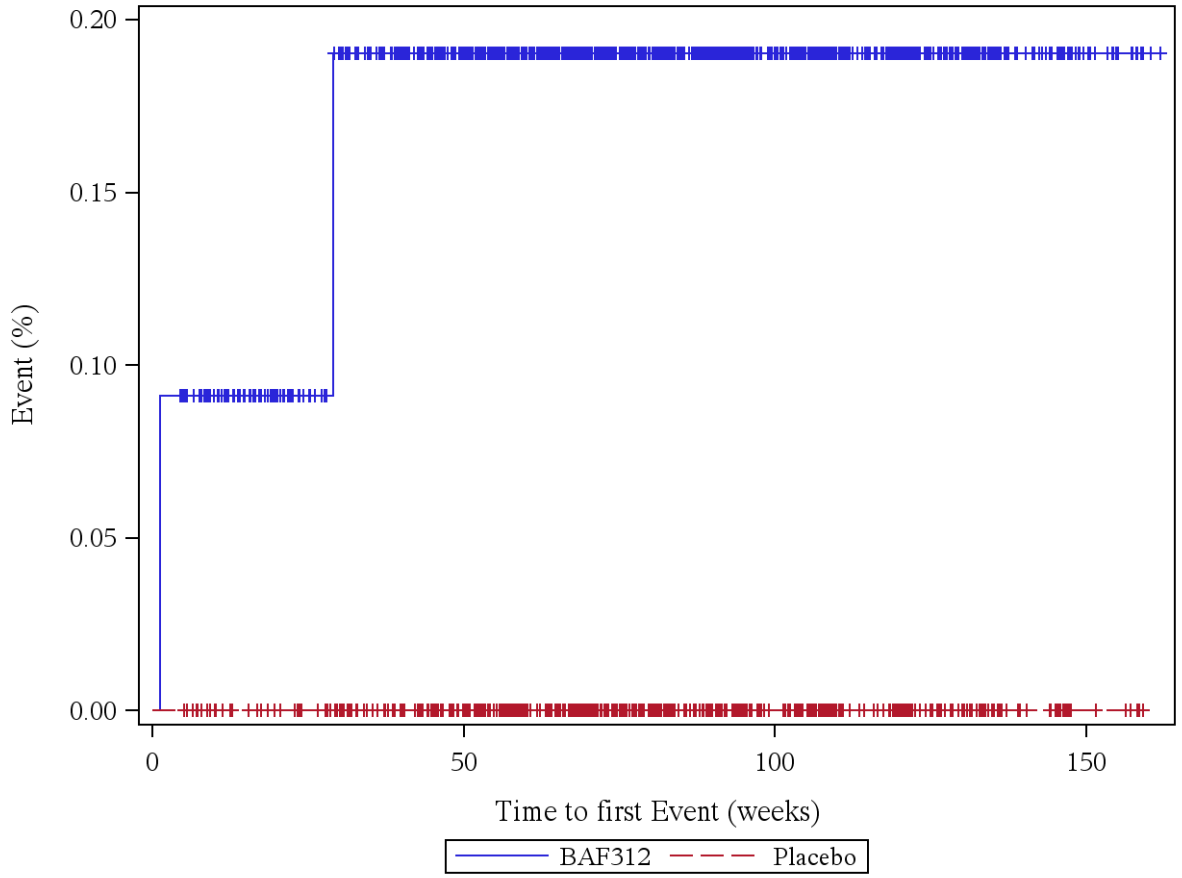


Patients at risk (BAF312/Placebo): Week 0: 1099/546, Week 4: 1054/536, Week 12: 1008/525, Week 24: 961/509, Week 36: 933/484, Week 48: 871/448, Week 60: 771/375, Week 72: 611/291, Week 84: 484/226, Week 96: 380/167, Week 108: 273/117, Week 120: 187/73, Week 132: 105/35, Week 144: 49/19, Week 156: 9/4, Week 168: 0/0

Log rank test: p-value = 0,009 *
*: p < 0,05

Analysis population: A2304 SAF total population

Figure 12.1.5.42: NAUSEA (PT, severe)

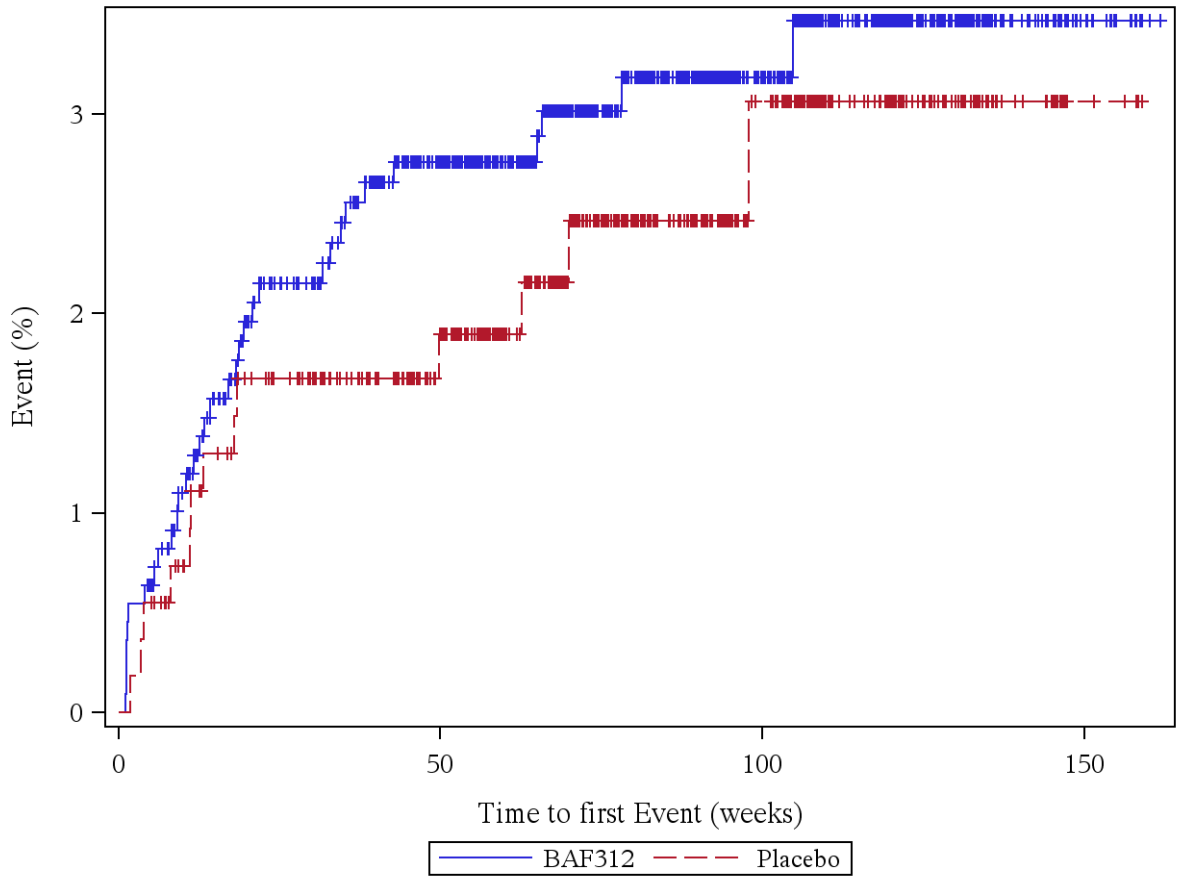


Patients at risk (BAF312/Placebo): Week 0: 1099/546, Week 4: 1098/546, Week 12: 1058/535, Week 24: 1016/521, Week 36: 988/497, Week 48: 923/461, Week 60: 816/388, Week 72: 650/305, Week 84: 514/237, Week 96: 398/176, Week 108: 289/126, Week 120: 200/80, Week 132: 113/40, Week 144: 51/20, Week 156: 10/5, Week 168: 0/0

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

Analysis population: A2304 SAF total population

Figure 12.1.5.43: VOMITING (PT, not severe)

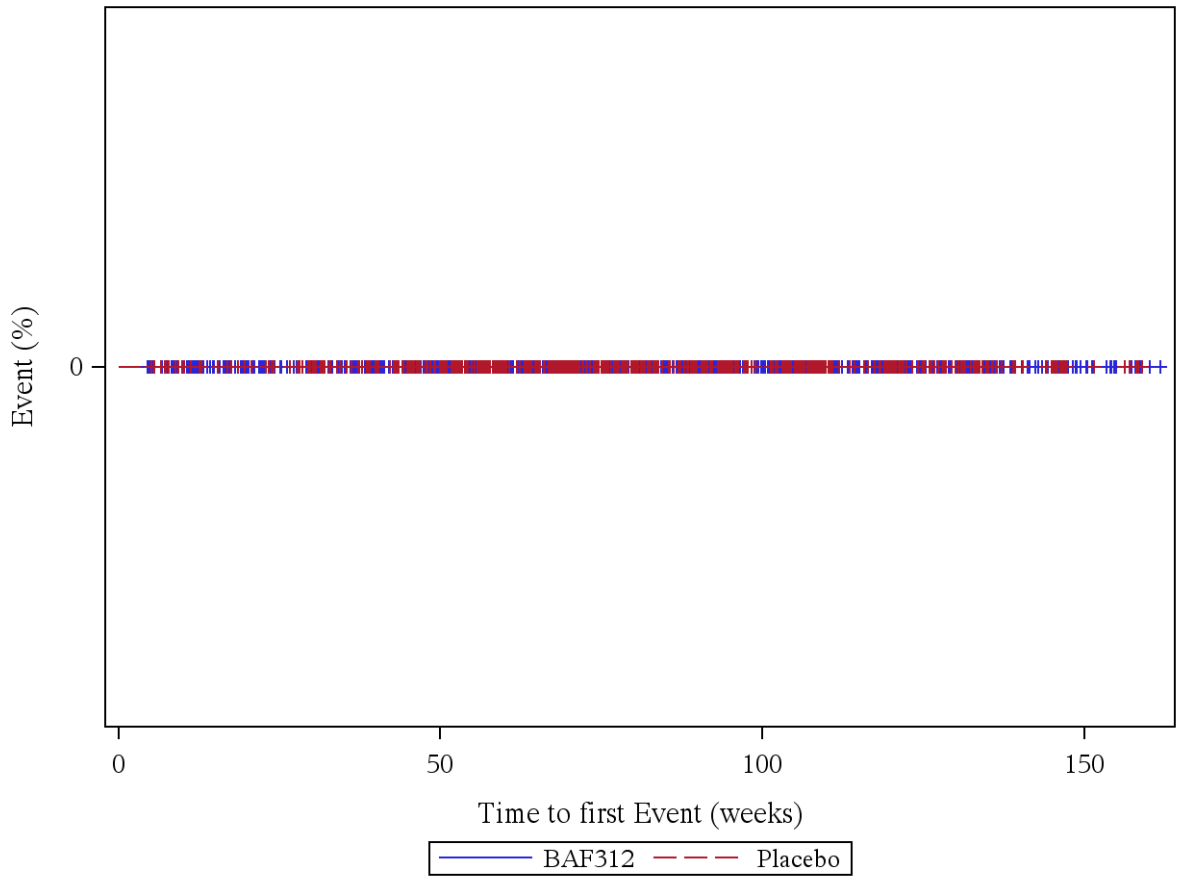


Patients at risk (BAF312/Placebo): Week 0: 1099/546, Week 4: 1092/543, Week 12: 1047/529, Week 24: 997/512, Week 36: 967/489, Week 48: 902/454, Week 60: 798/381, Week 72: 635/296, Week 84: 503/230, Week 96: 393/171, Week 108: 285/120, Week 120: 195/77, Week 132: 108/38, Week 144: 51/19, Week 156: 10/4, Week 168: 0/0

Log rank test: p-value = 0,477
*: p < 0,05

Analysis population: A2304 SAF total population

Figure 12.1.5.44: VOMITING (PT, severe)

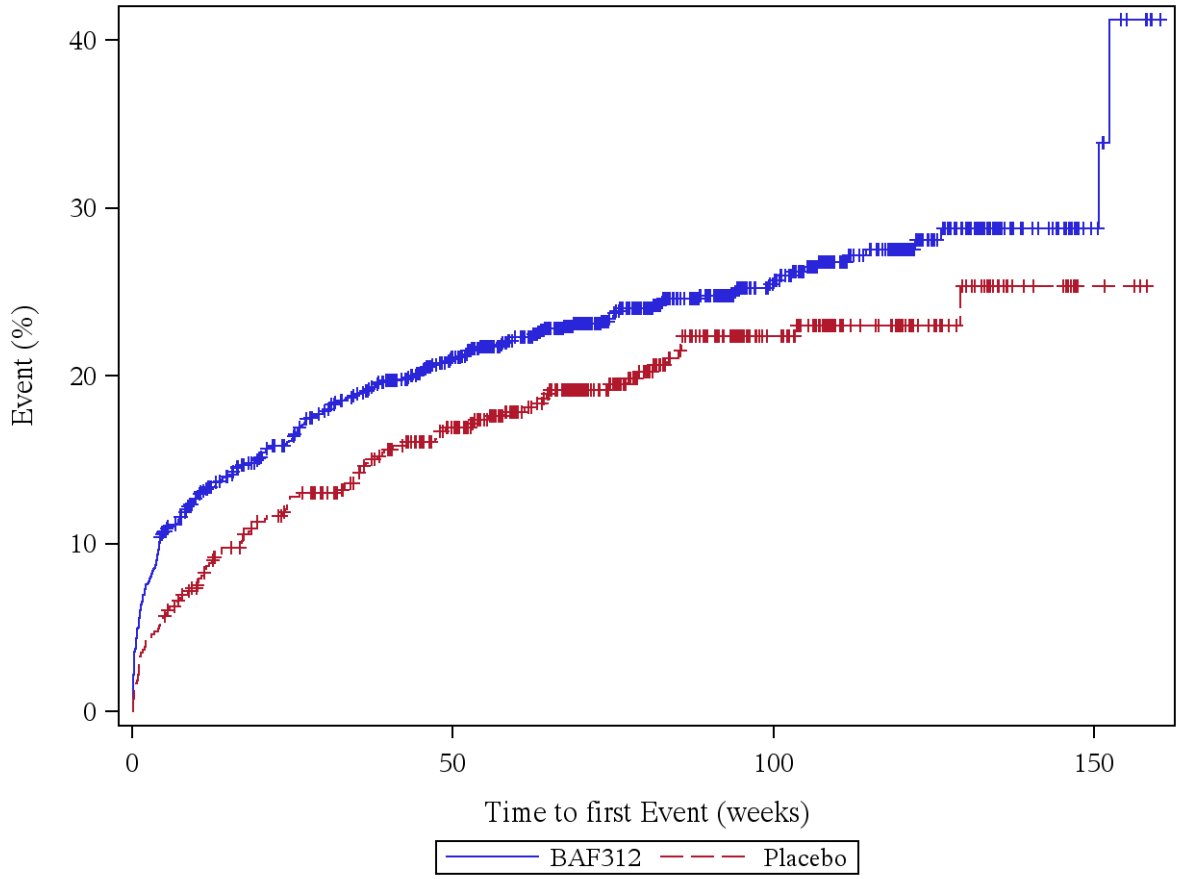


Patients at risk (BAF312/Placebo): Week 0: 1099/546, Week 4: 1099/546, Week 12: 1059/535, Week 24: 1017/521, Week 36: 990/497, Week 48: 925/461, Week 60: 818/388, Week 72: 652/305, Week 84: 516/237, Week 96: 400/176, Week 108: 291/126, Week 120: 200/80, Week 132: 113/40, Week 144: 51/20, Week 156: 10/5, Week 168: 0/0

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

Analysis population: A2304 SAF total population

Figure 12.1.5.45: GENERAL DISORDERS AND ADMINISTRATION SITE CONDITIONS (SOC, not severe)

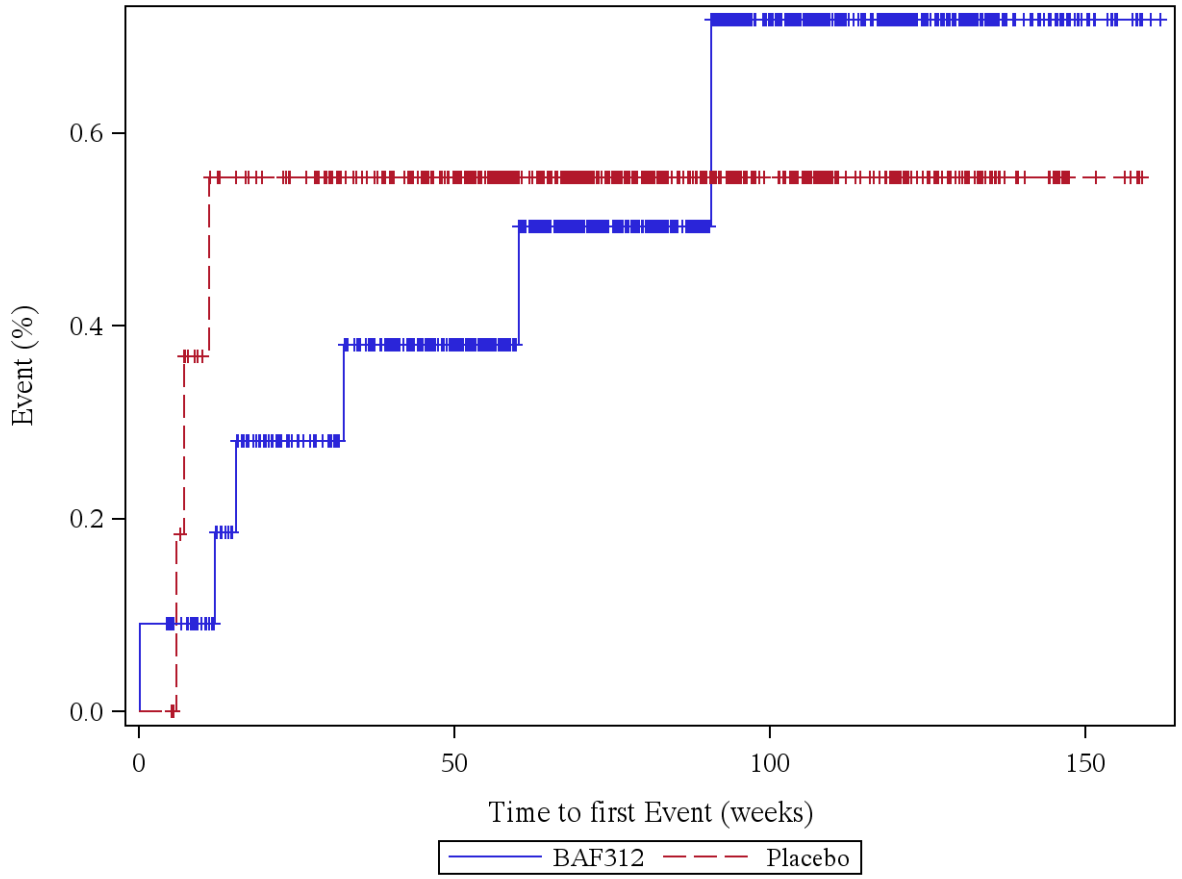


Patients at risk (BAF312/Placebo): Week 0: 1099/546, Week 4: 993/519, Week 12: 919/488, Week 24: 858/459, Week 36: 809/425, Week 48: 742/386, Week 60: 648/319, Week 72: 513/245, Week 84: 401/184, Week 96: 317/135, Week 108: 227/93, Week 120: 152/55, Week 132: 83/28, Week 144: 40/12, Week 156: 6/3, Week 168: 0/0

Log rank test: p-value = 0,048 *
*: p < 0,05

Analysis population: A2304 SAF total population

Figure 12.1.5.46: GENERAL DISORDERS AND ADMINISTRATION SITE CONDITIONS (SOC, severe)

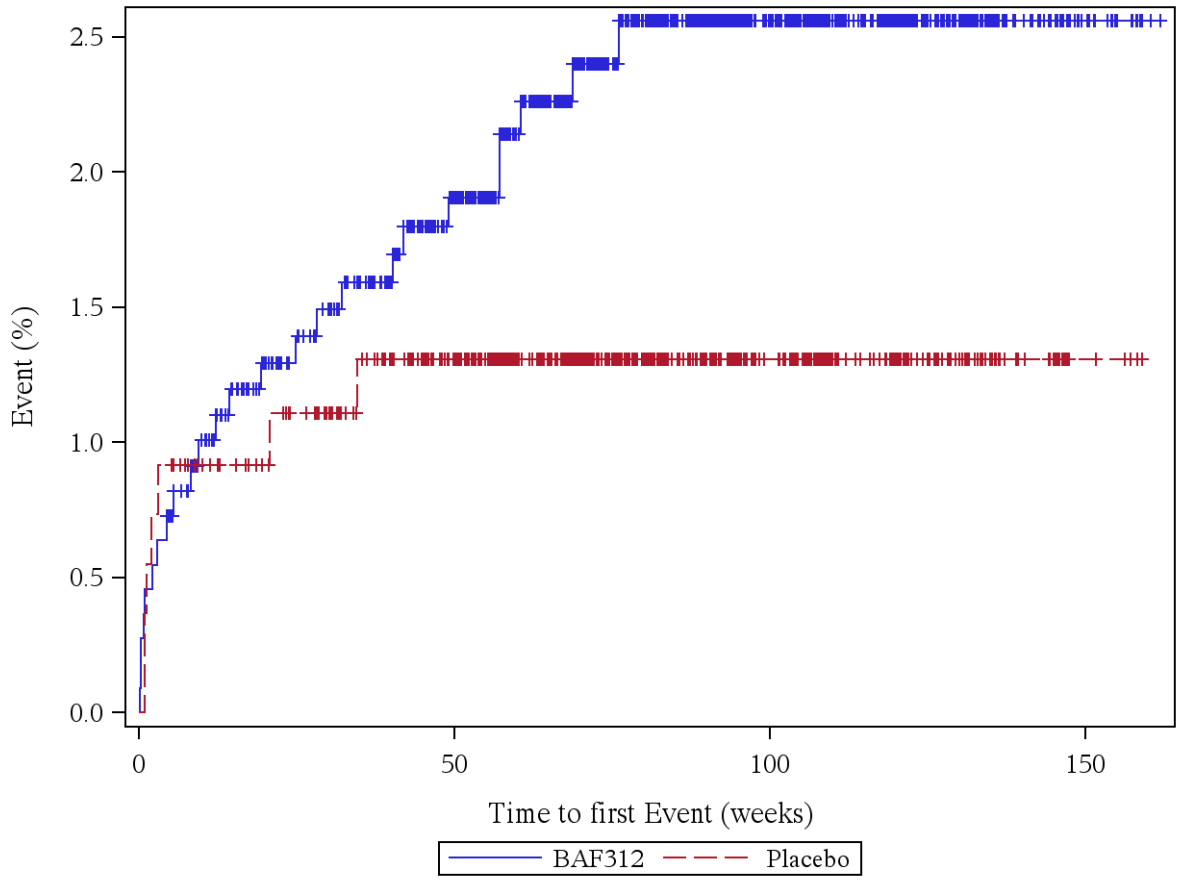


Patients at risk (BAF312/Placebo): Week 0: 1099/546, Week 4: 1098/546, Week 12: 1057/533, Week 24: 1015/520, Week 36: 987/496, Week 48: 923/460, Week 60: 817/387, Week 72: 650/305, Week 84: 514/237, Week 96: 397/176, Week 108: 288/126, Week 120: 197/80, Week 132: 112/40, Week 144: 50/20, Week 156: 9/5, Week 168: 0/0

Log rank test: p-value = 0,989
*: p < 0,05

Analysis population: A2304 SAF total population

Figure 12.1.5.47: ASTHENIA (PT, not severe)

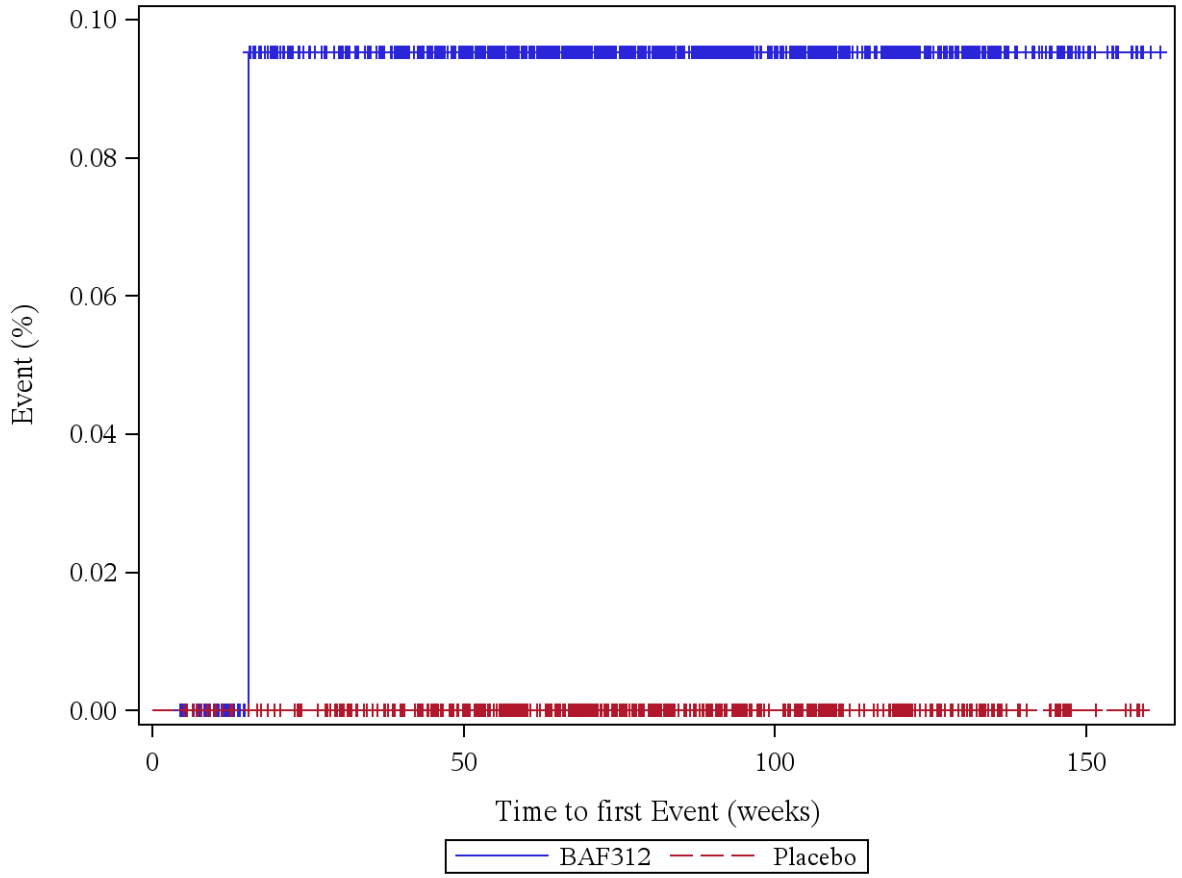


Patients at risk (BAF312/Placebo): Week 0: 1099/546, Week 4: 1092/541, Week 12: 1048/531, Week 24: 1004/516, Week 36: 977/491, Week 48: 913/455, Week 60: 807/384, Week 72: 641/301, Week 84: 508/233, Week 96: 392/173, Week 108: 285/124, Week 120: 197/78, Week 132: 112/38, Week 144: 51/19, Week 156: 10/4, Week 168: 0/0

Log rank test: p-value = 0,173
*: p < 0,05

Analysis population: A2304 SAF total population

Figure 12.1.5.48: ASTHENIA (PT, severe)

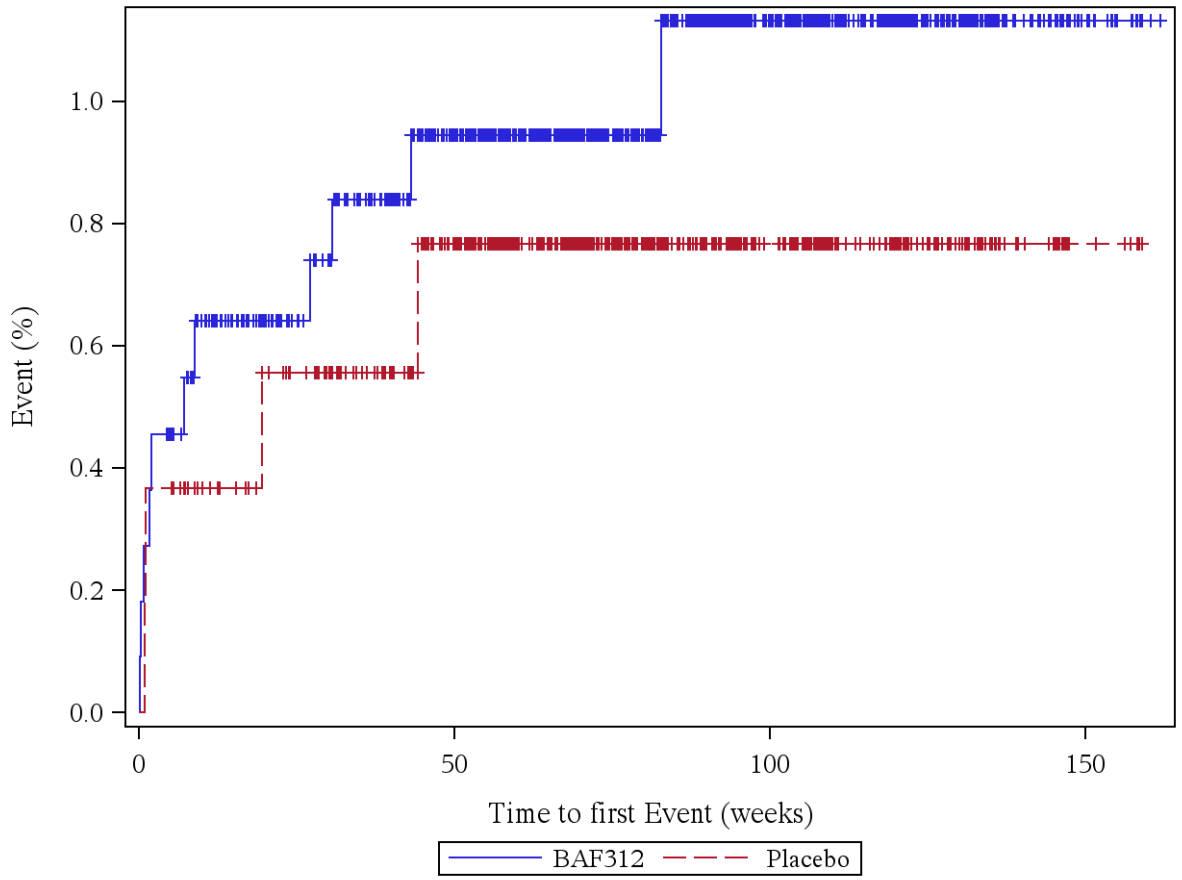


Patients at risk (BAF312/Placebo): Week 0: 1099/546, Week 4: 1099/546, Week 12: 1059/535, Week 24: 1016/521, Week 36: 989/497, Week 48: 925/461, Week 60: 818/388, Week 72: 652/305, Week 84: 516/237, Week 96: 400/176, Week 108: 291/126, Week 120: 200/80, Week 132: 113/40, Week 144: 51/20, Week 156: 10/5, Week 168: 0/0

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

Analysis population: A2304 SAF total population

Figure 12.1.5.49: CHEST DISCOMFORT (PT, not severe)

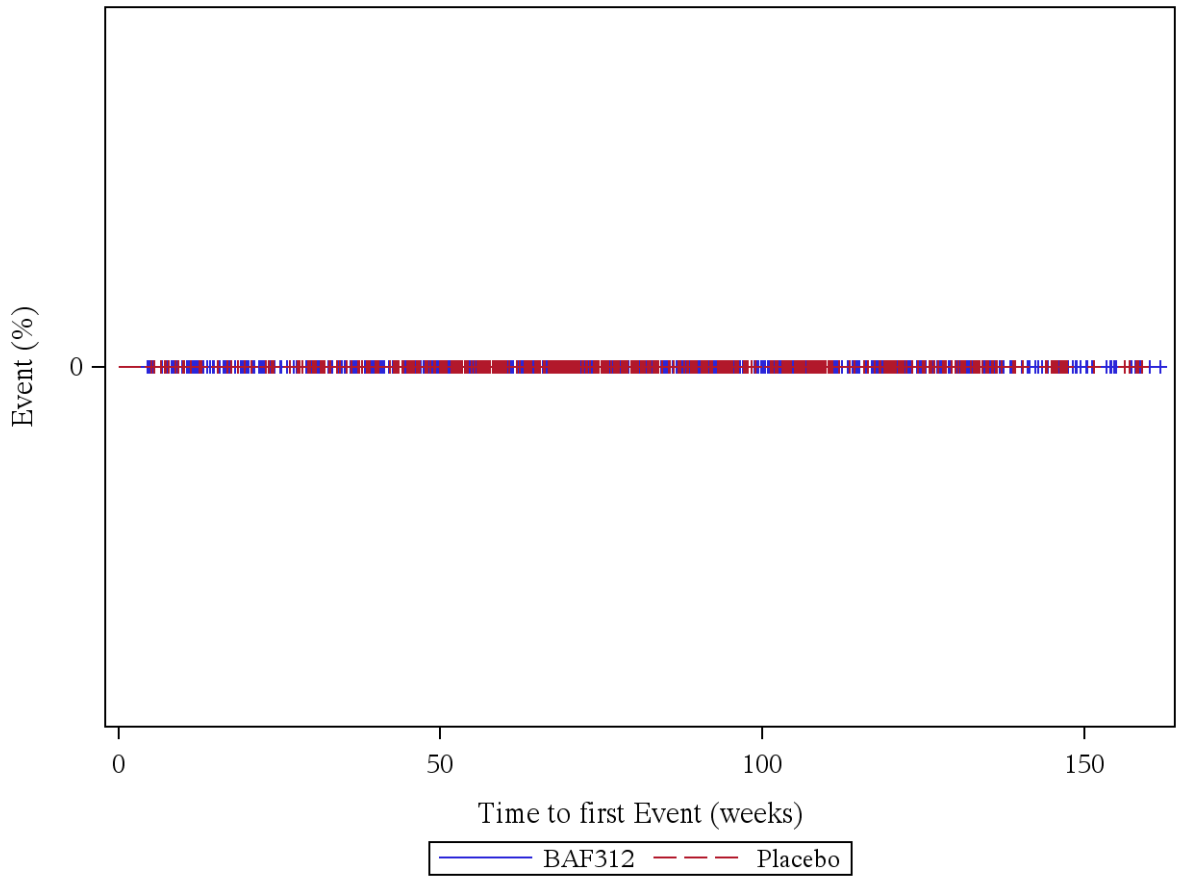


Patients at risk (BAF312/Placebo): Week 0: 1099/546, Week 4: 1094/544, Week 12: 1052/533, Week 24: 1010/518, Week 36: 981/494, Week 48: 918/457, Week 60: 812/385, Week 72: 648/302, Week 84: 511/234, Week 96: 397/174, Week 108: 289/124, Week 120: 198/78, Week 132: 112/38, Week 144: 50/18, Week 156: 10/5, Week 168: 0/0

Log rank test: p-value = 0,586
*: p < 0,05

Analysis population: A2304 SAF total population

Figure 12.1.5.50: CHEST DISCOMFORT (PT, severe)

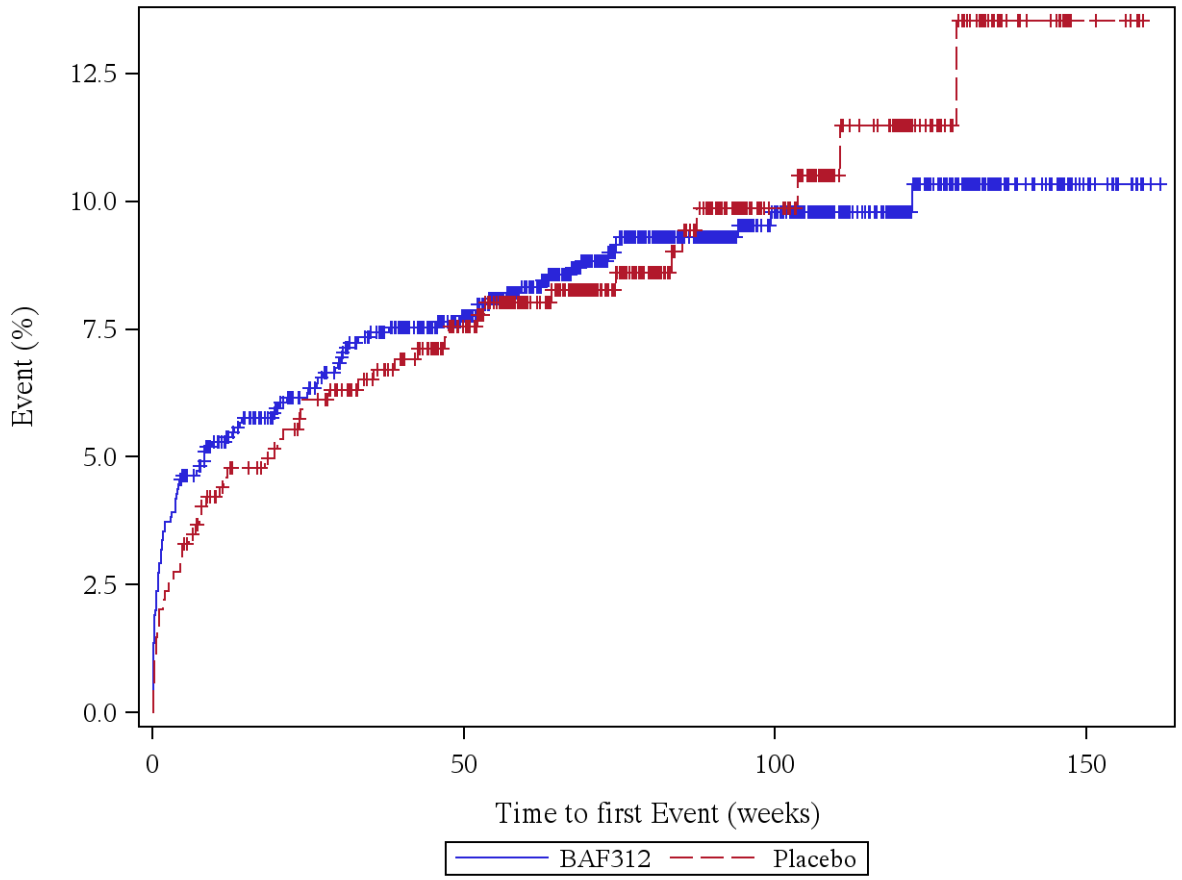


Patients at risk (BAF312/Placebo): Week 0: 1099/546, Week 4: 1099/546, Week 12: 1059/535, Week 24: 1017/521, Week 36: 990/497, Week 48: 925/461, Week 60: 818/388, Week 72: 652/305, Week 84: 516/237, Week 96: 400/176, Week 108: 291/126, Week 120: 200/80, Week 132: 113/40, Week 144: 51/20, Week 156: 10/5, Week 168: 0/0

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

Analysis population: A2304 SAF total population

Figure 12.1.5.51: FATIGUE (PT, not severe)

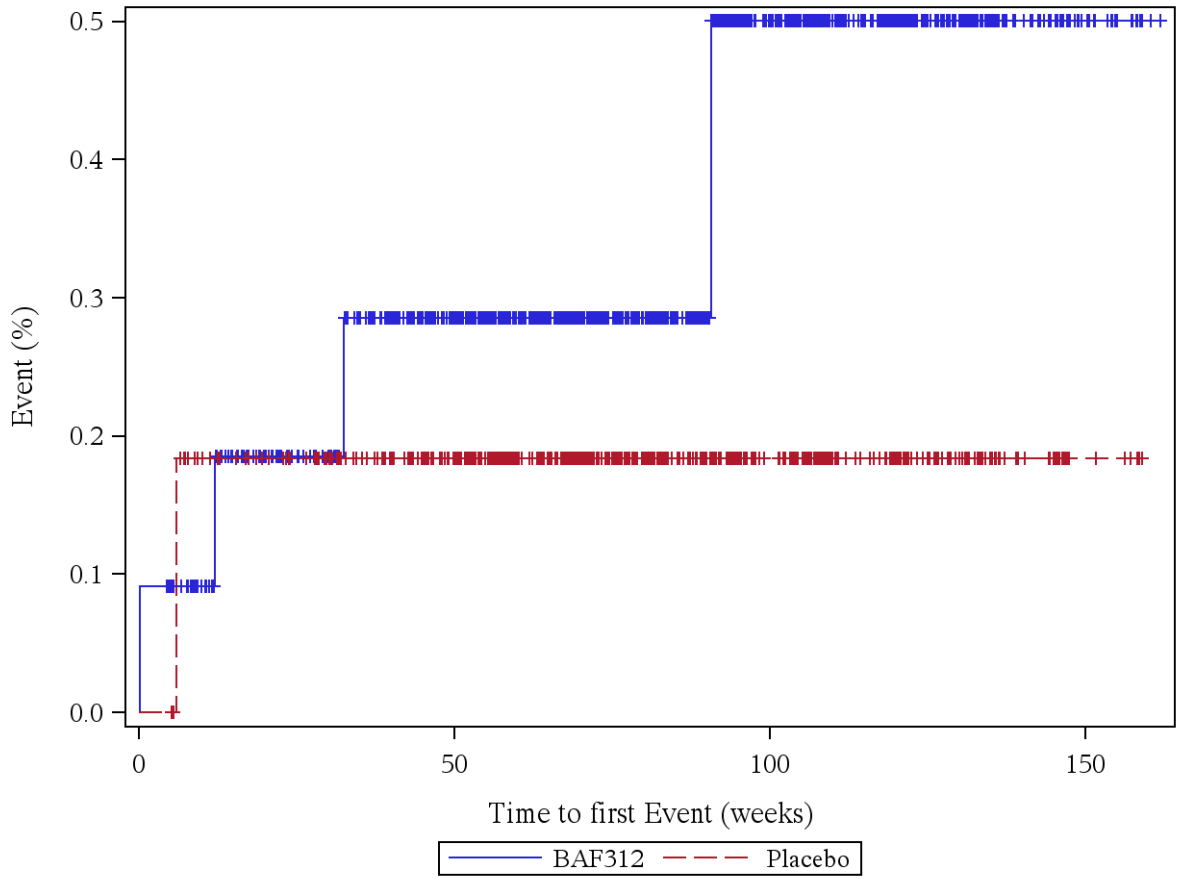


Patients at risk (BAF312/Placebo): Week 0: 1099/546, Week 4: 1051/531, Week 12: 1004/509, Week 24: 958/491, Week 36: 921/465, Week 48: 859/428, Week 60: 760/359, Week 72: 606/282, Week 84: 478/217, Week 96: 372/161, Week 108: 271/112, Week 120: 188/73, Week 132: 104/37, Week 144: 50/17, Week 156: 10/5, Week 168: 0/0

Log rank test: p-value = 0,866
*: p < 0,05

Analysis population: A2304 SAF total population

Figure 12.1.5.52: FATIGUE (PT, severe)

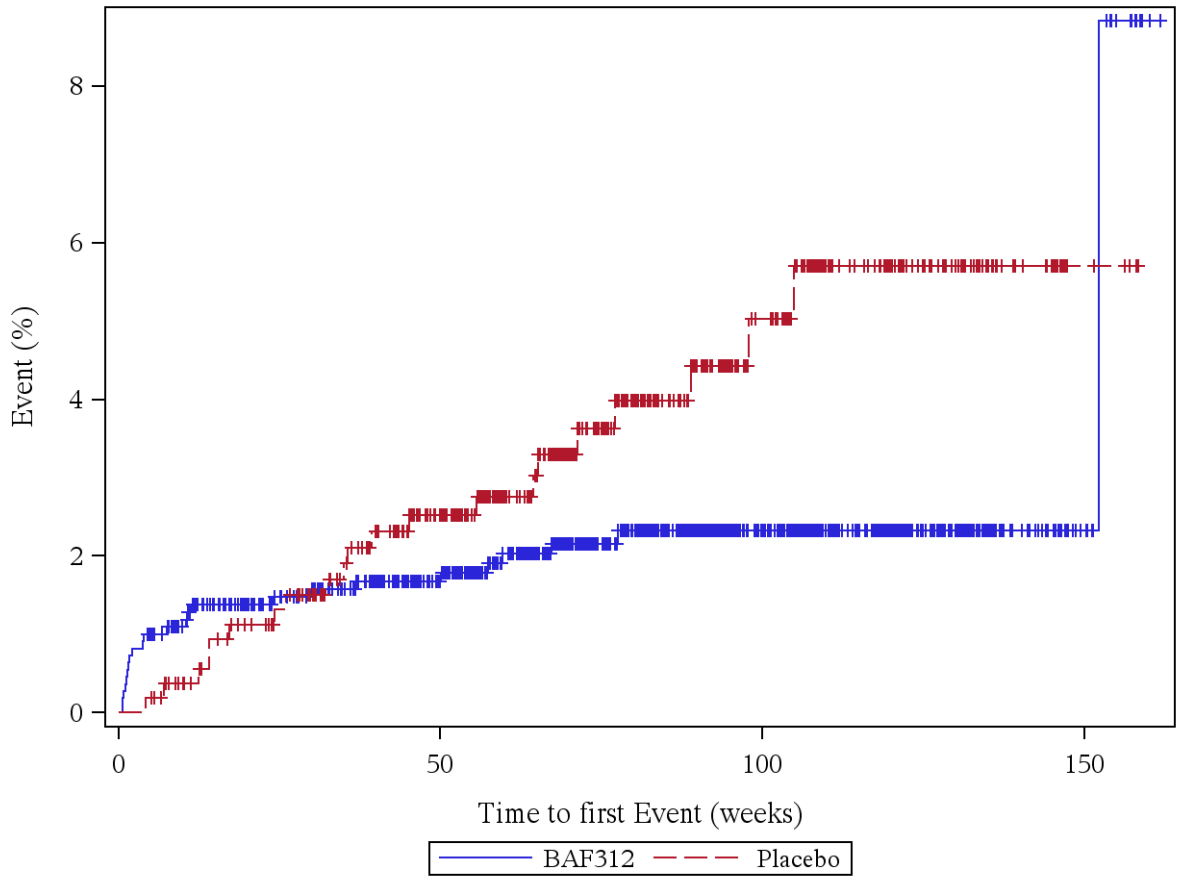


Patients at risk (BAF312/Placebo): Week 0: 1099/546, Week 4: 1098/546, Week 12: 1057/535, Week 24: 1016/521, Week 36: 988/497, Week 48: 923/461, Week 60: 817/388, Week 72: 651/305, Week 84: 515/237, Week 96: 398/176, Week 108: 289/126, Week 120: 198/80, Week 132: 113/40, Week 144: 51/20, Week 156: 10/5, Week 168: 0/0

Log rank test: p-value = 0,533
*: p < 0,05

Analysis population: A2304 SAF total population

Figure 12.1.5.53: GAIT DISTURBANCE (PT, not severe)

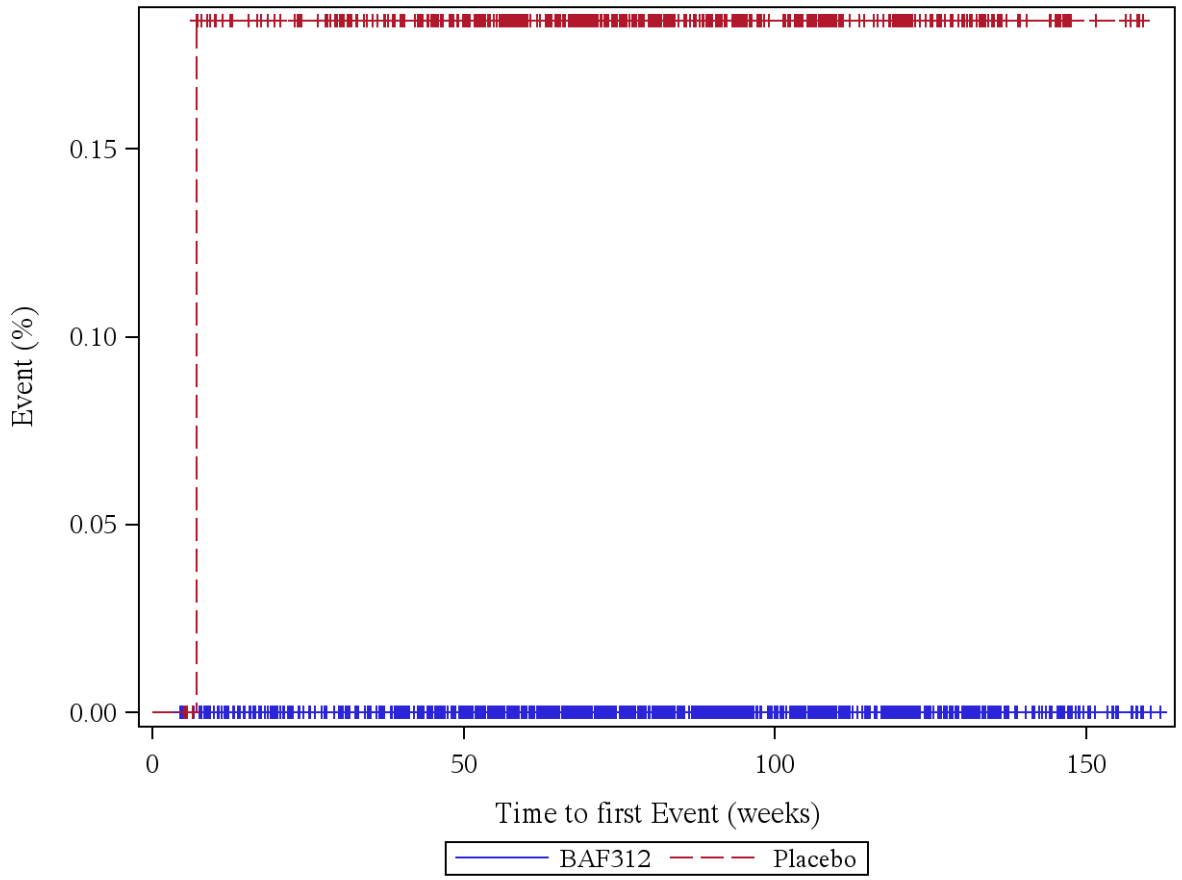


Patients at risk (BAF312/Placebo): Week 0: 1099/546, Week 4: 1088/546, Week 12: 1045/533, Week 24: 1003/515, Week 36: 975/487, Week 48: 910/450, Week 60: 803/377, Week 72: 641/293, Week 84: 508/227, Week 96: 393/167, Week 108: 289/118, Week 120: 198/72, Week 132: 112/37, Week 144: 50/18, Week 156: 10/4, Week 168: 0/0

Log rank test: p-value = 0,044 *
*: p < 0,05

Analysis population: A2304 SAF total population

Figure 12.1.5.54: GAIT DISTURBANCE (PT, severe)

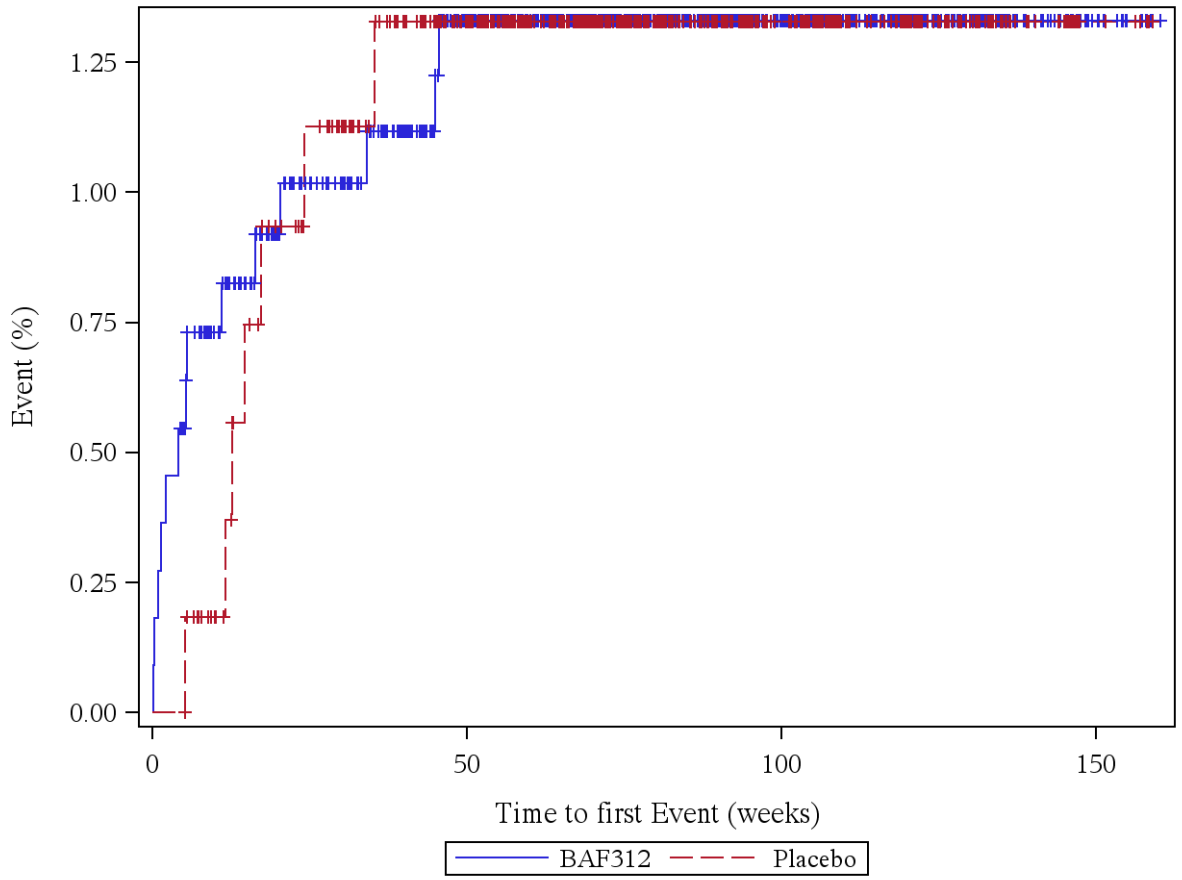


Patients at risk (BAF312/Placebo): Week 0: 1099/546, Week 4: 1099/546, Week 12: 1059/534, Week 24: 1017/520, Week 36: 990/496, Week 48: 925/460, Week 60: 818/387, Week 72: 652/305, Week 84: 516/237, Week 96: 400/176, Week 108: 291/126, Week 120: 200/80, Week 132: 113/40, Week 144: 51/20, Week 156: 10/5, Week 168: 0/0

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

Analysis population: A2304 SAF total population

Figure 12.1.5.55: INFLUENZA LIKE ILLNESS (PT, not severe)

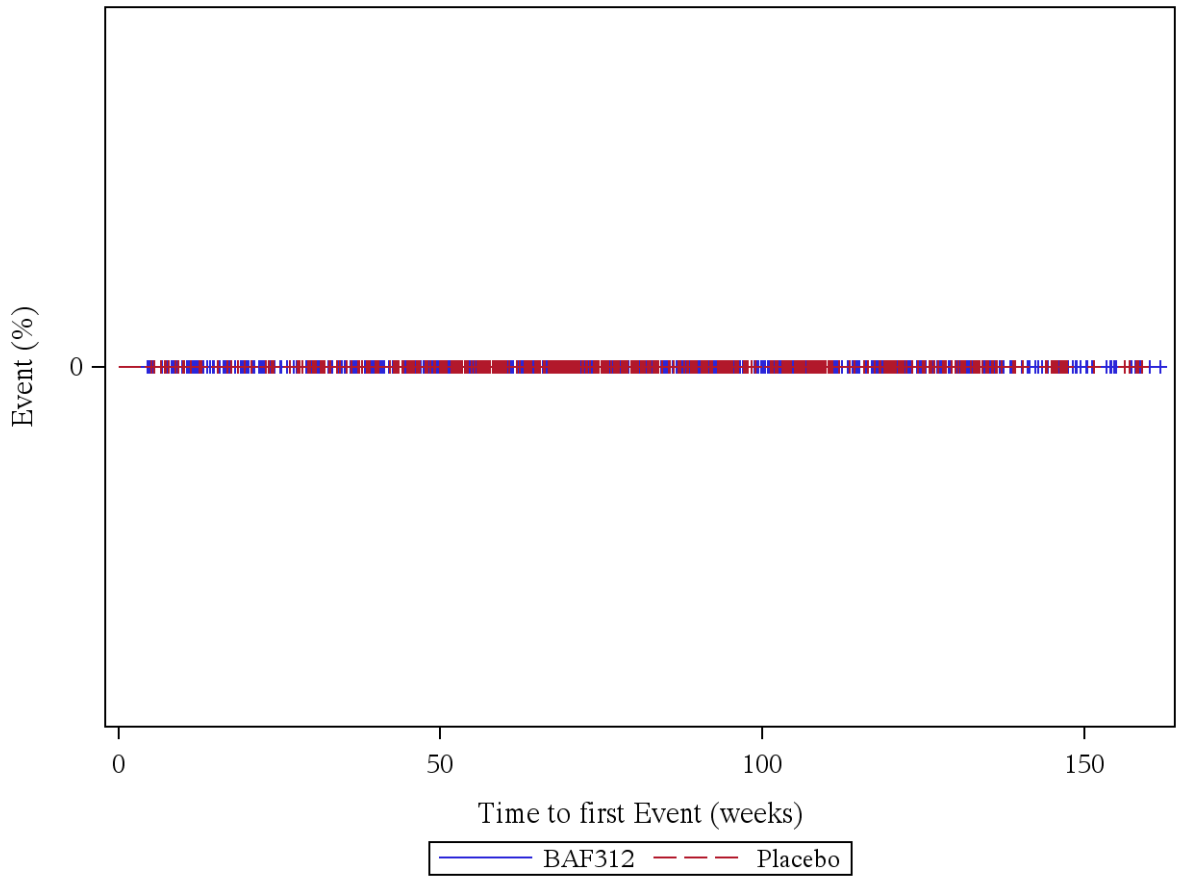


Patients at risk (BAF312/Placebo): Week 0: 1099/546, Week 4: 1094/546, Week 12: 1050/533, Week 24: 1008/516, Week 36: 980/490, Week 48: 914/455, Week 60: 807/382, Week 72: 644/302, Week 84: 511/235, Week 96: 396/175, Week 108: 287/125, Week 120: 198/80, Week 132: 111/40, Week 144: 50/20, Week 156: 9/5, Week 168: 0/0

Log rank test: p-value = 0,989
*: p < 0,05

Analysis population: A2304 SAF total population

Figure 12.1.5.56: INFLUENZA LIKE ILLNESS (PT, severe)

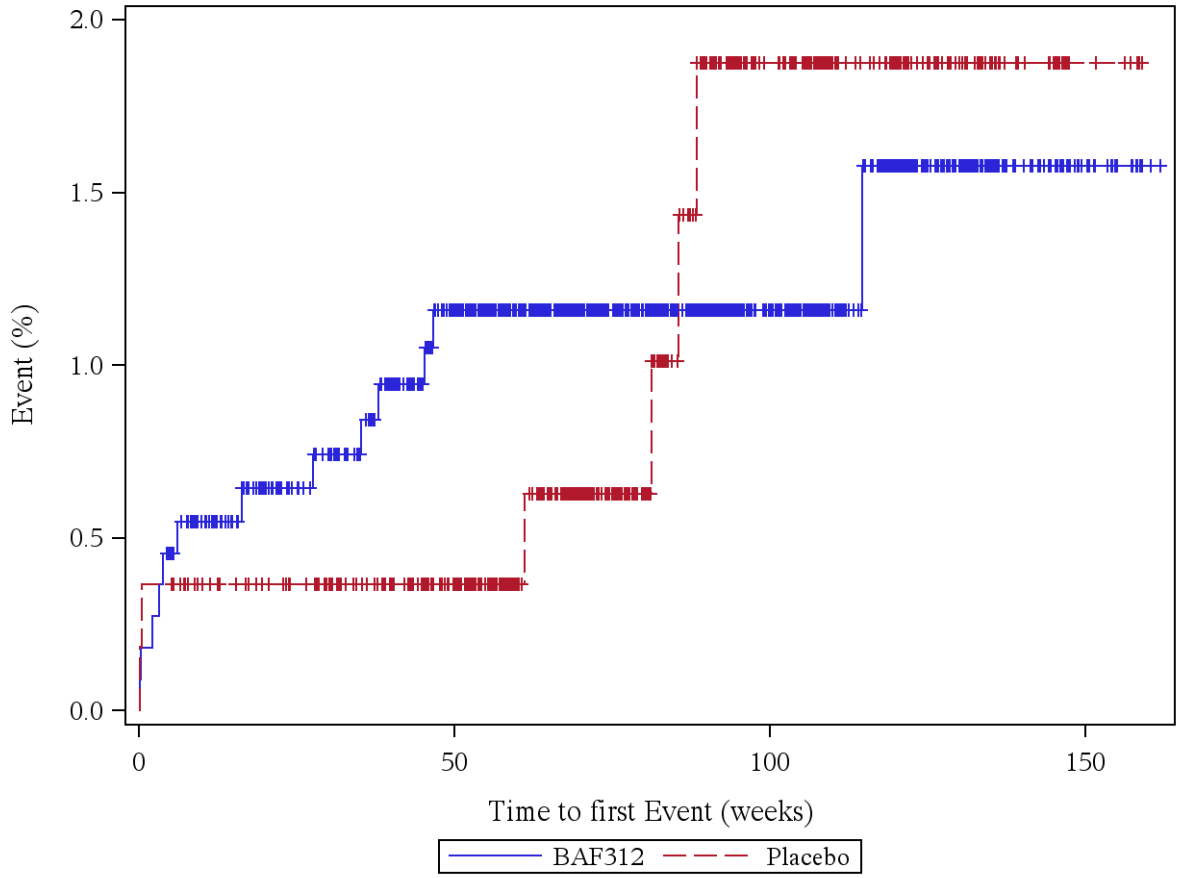


Patients at risk (BAF312/Placebo): Week 0: 1099/546, Week 4: 1099/546, Week 12: 1059/535, Week 24: 1017/521, Week 36: 990/497, Week 48: 925/461, Week 60: 818/388, Week 72: 652/305, Week 84: 516/237, Week 96: 400/176, Week 108: 291/126, Week 120: 200/80, Week 132: 113/40, Week 144: 51/20, Week 156: 10/5, Week 168: 0/0

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

Analysis population: A2304 SAF total population

Figure 12.1.5.57: NON-CARDIAC CHEST PAIN (PT, not severe)

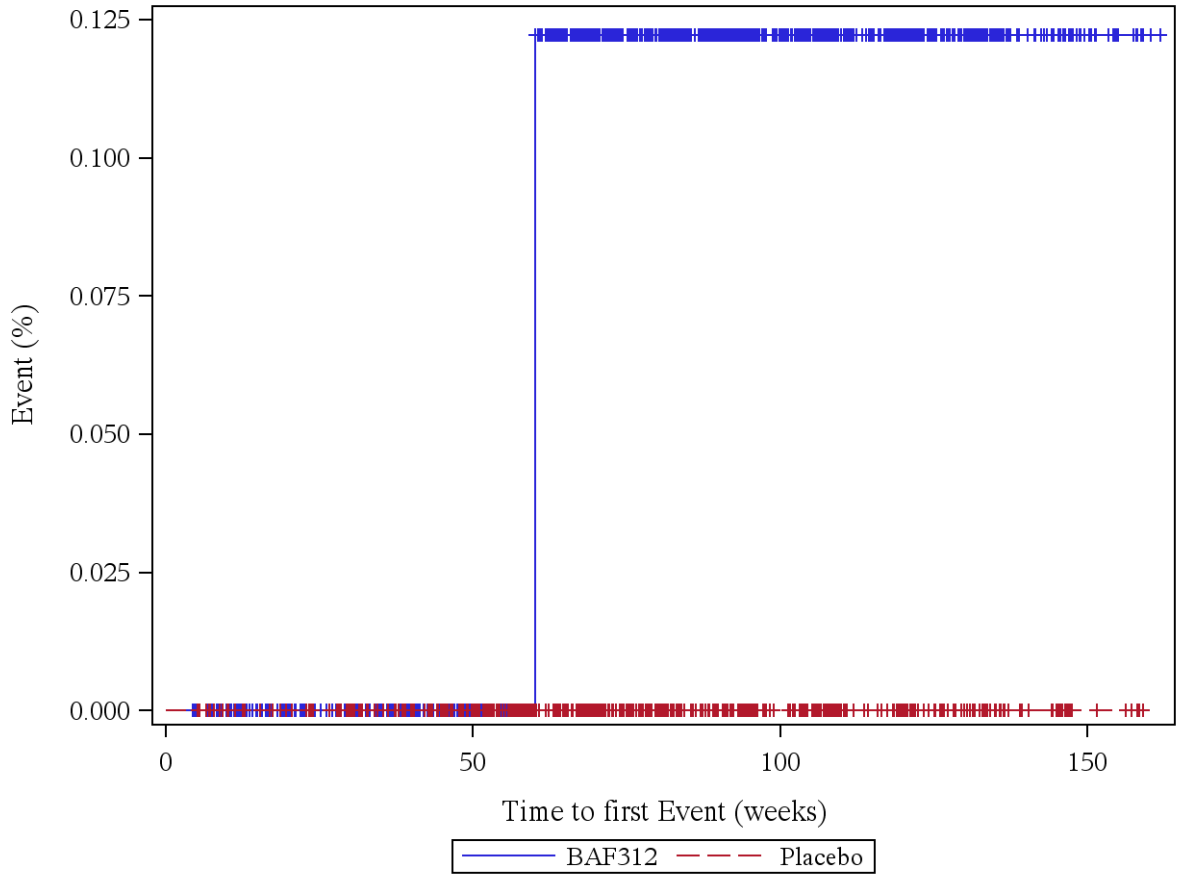


Patients at risk (BAF312/Placebo): Week 0: 1099/546, Week 4: 1094/544, Week 12: 1053/533, Week 24: 1011/519, Week 36: 982/495, Week 48: 914/459, Week 60: 808/387, Week 72: 643/305, Week 84: 509/236, Week 96: 395/173, Week 108: 287/124, Week 120: 198/78, Week 132: 113/40, Week 144: 51/20, Week 156: 10/5, Week 168: 0/0

Log rank test: p-value = 0,905
*: p < 0,05

Analysis population: A2304 SAF total population

Figure 12.1.5.58: NON-CARDIAC CHEST PAIN (PT, severe)

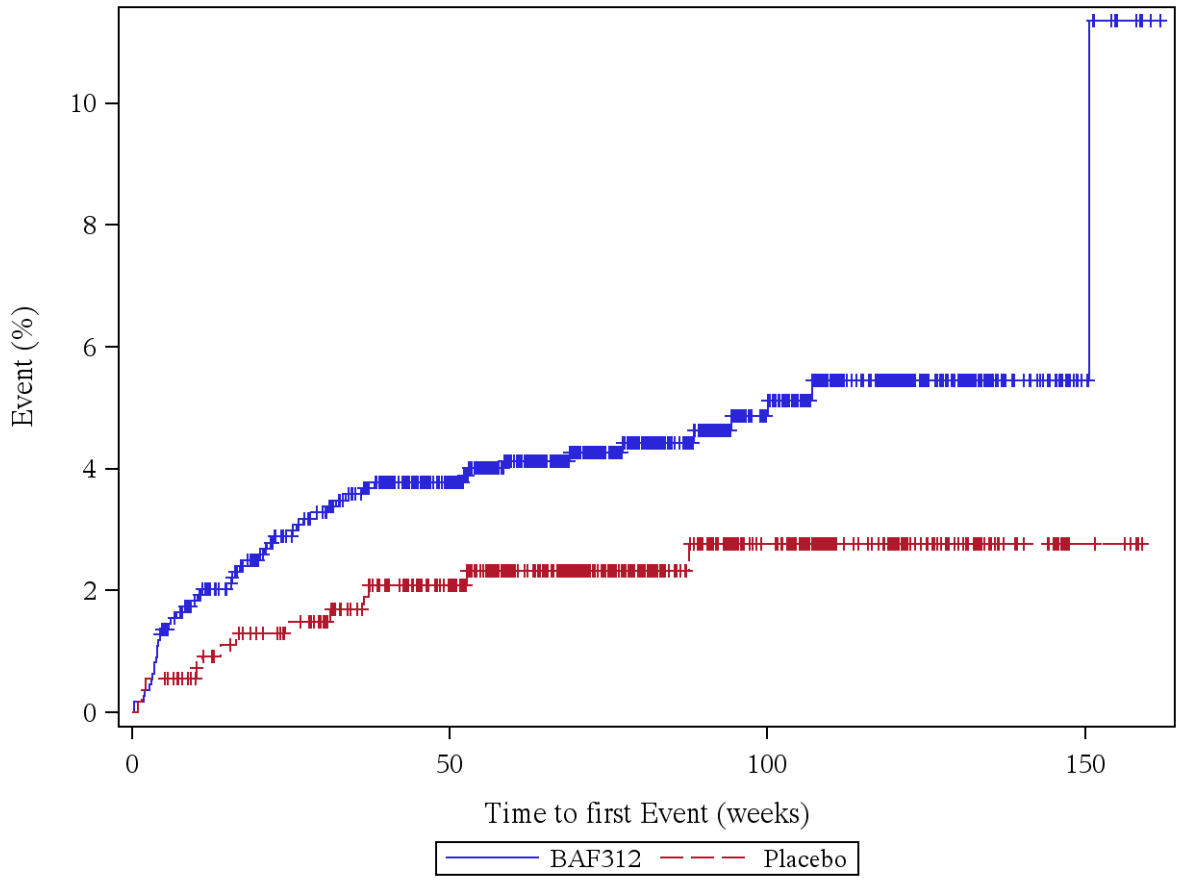


Patients at risk (BAF312/Placebo): Week 0: 1099/546, Week 4: 1099/546, Week 12: 1059/535, Week 24: 1017/521, Week 36: 990/497, Week 48: 925/461, Week 60: 818/388, Week 72: 651/305, Week 84: 515/237, Week 96: 399/176, Week 108: 290/126, Week 120: 199/80, Week 132: 112/40, Week 144: 50/20, Week 156: 9/5, Week 168: 0/0

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

Analysis population: A2304 SAF total population

Figure 12.1.5.59: OEDEMA PERIPHERAL (PT, not severe)

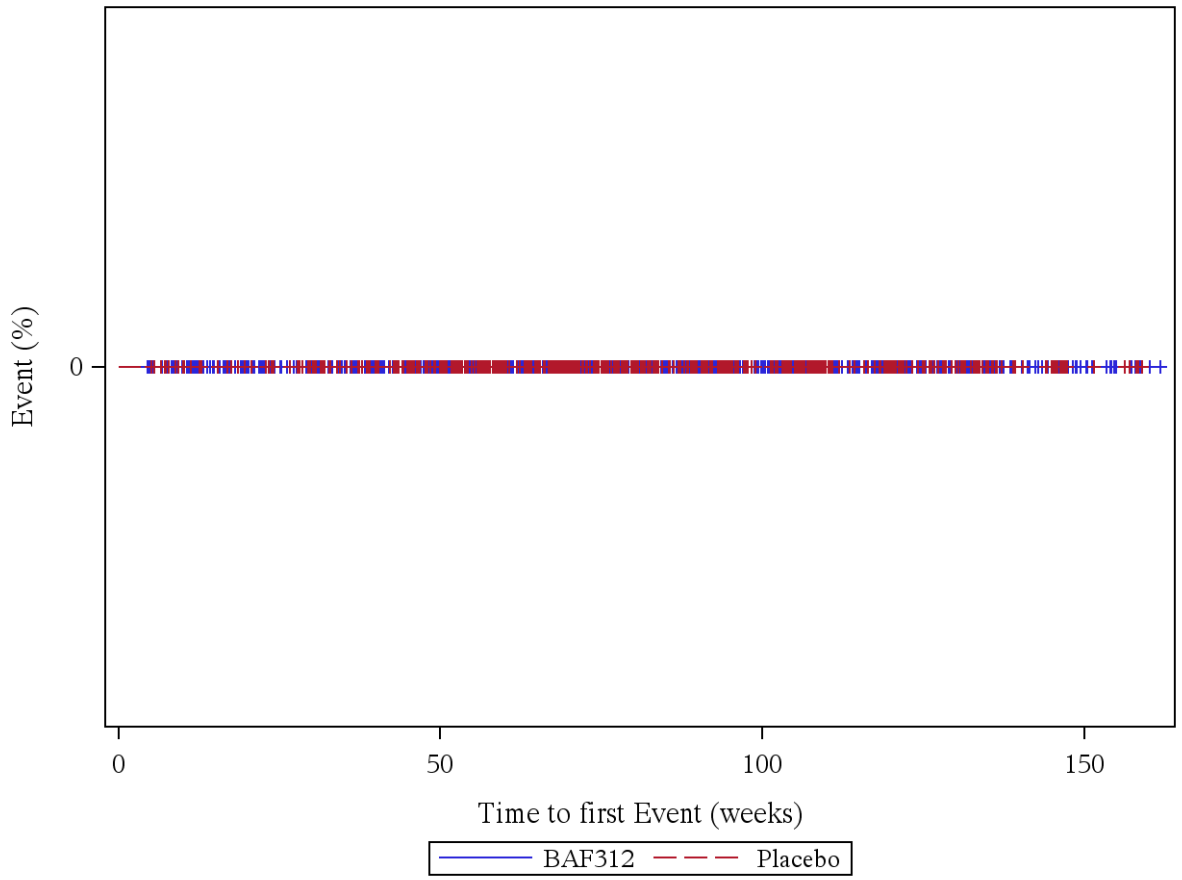


Patients at risk (BAF312/Placebo): Week 0: 1099/546, Week 4: 1087/543, Week 12: 1037/530, Week 24: 988/514, Week 36: 957/488, Week 48: 891/451, Week 60: 785/379, Week 72: 627/297, Week 84: 494/231, Week 96: 381/171, Week 108: 275/122, Week 120: 187/76, Week 132: 105/39, Week 144: 47/20, Week 156: 8/5, Week 168: 0/0

Log rank test: p-value = 0,033 *
*: p < 0,05

Analysis population: A2304 SAF total population

Figure 12.1.5.60: OEDEMA PERIPHERAL (PT, severe)

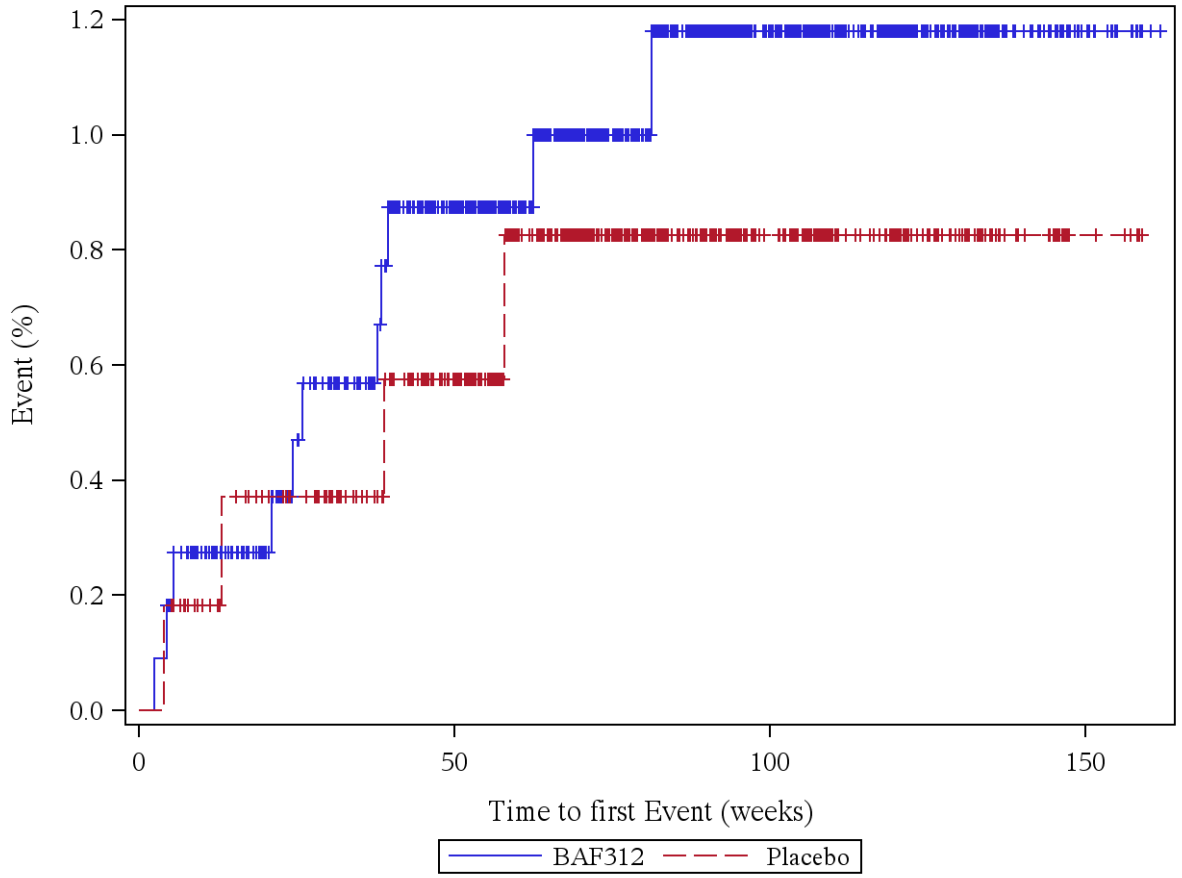


Patients at risk (BAF312/Placebo): Week 0: 1099/546, Week 4: 1099/546, Week 12: 1059/535, Week 24: 1017/521, Week 36: 990/497, Week 48: 925/461, Week 60: 818/388, Week 72: 652/305, Week 84: 516/237, Week 96: 400/176, Week 108: 291/126, Week 120: 200/80, Week 132: 113/40, Week 144: 51/20, Week 156: 10/5, Week 168: 0/0

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

Analysis population: A2304 SAF total population

Figure 12.1.5.61: PAIN (PT, not severe)

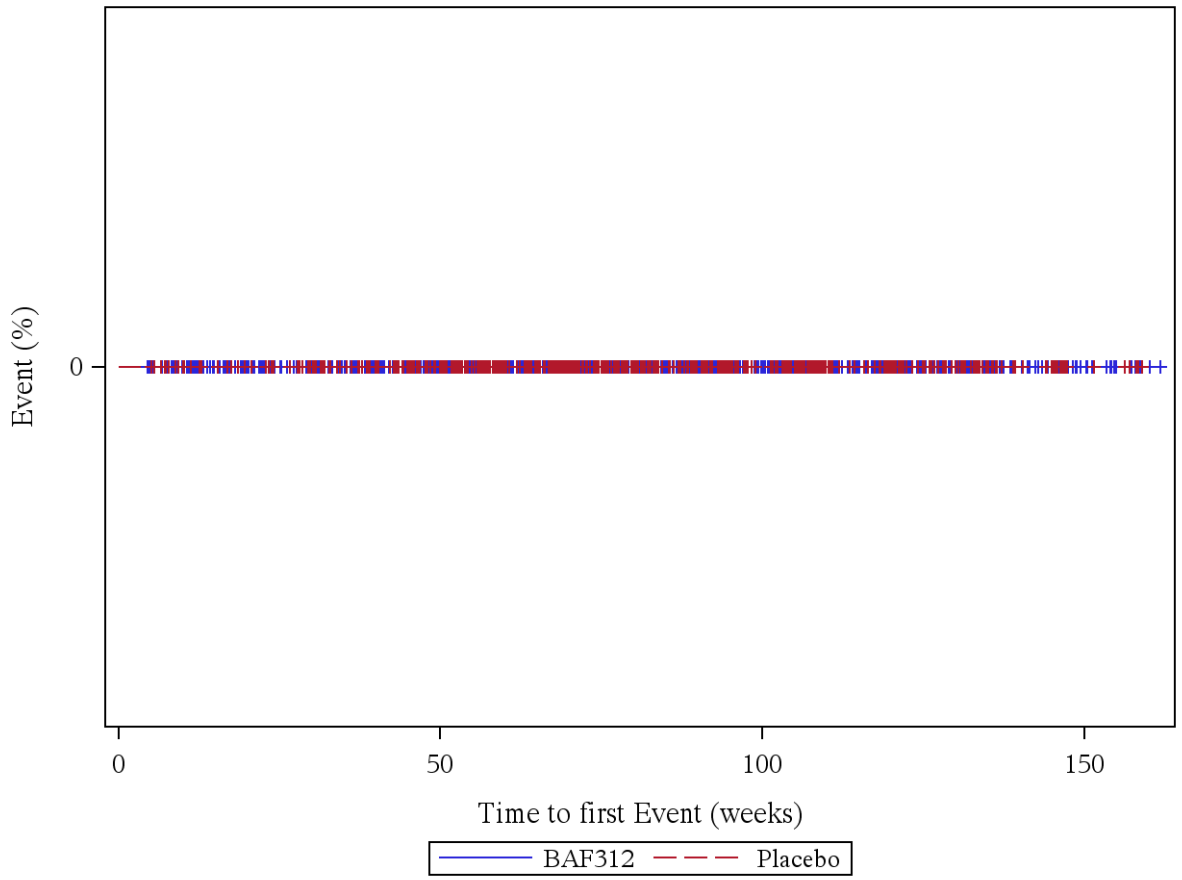


Patients at risk (BAF312/Placebo): Week 0: 1099/546, Week 4: 1098/545, Week 12: 1057/534, Week 24: 1014/519, Week 36: 986/495, Week 48: 920/458, Week 60: 813/385, Week 72: 647/302, Week 84: 511/235, Week 96: 396/174, Week 108: 288/124, Week 120: 197/78, Week 132: 113/39, Week 144: 51/20, Week 156: 10/5, Week 168: 0/0

Log rank test: p-value = 0,589
*: p < 0,05

Analysis population: A2304 SAF total population

Figure 12.1.5.62: PAIN (PT, severe)

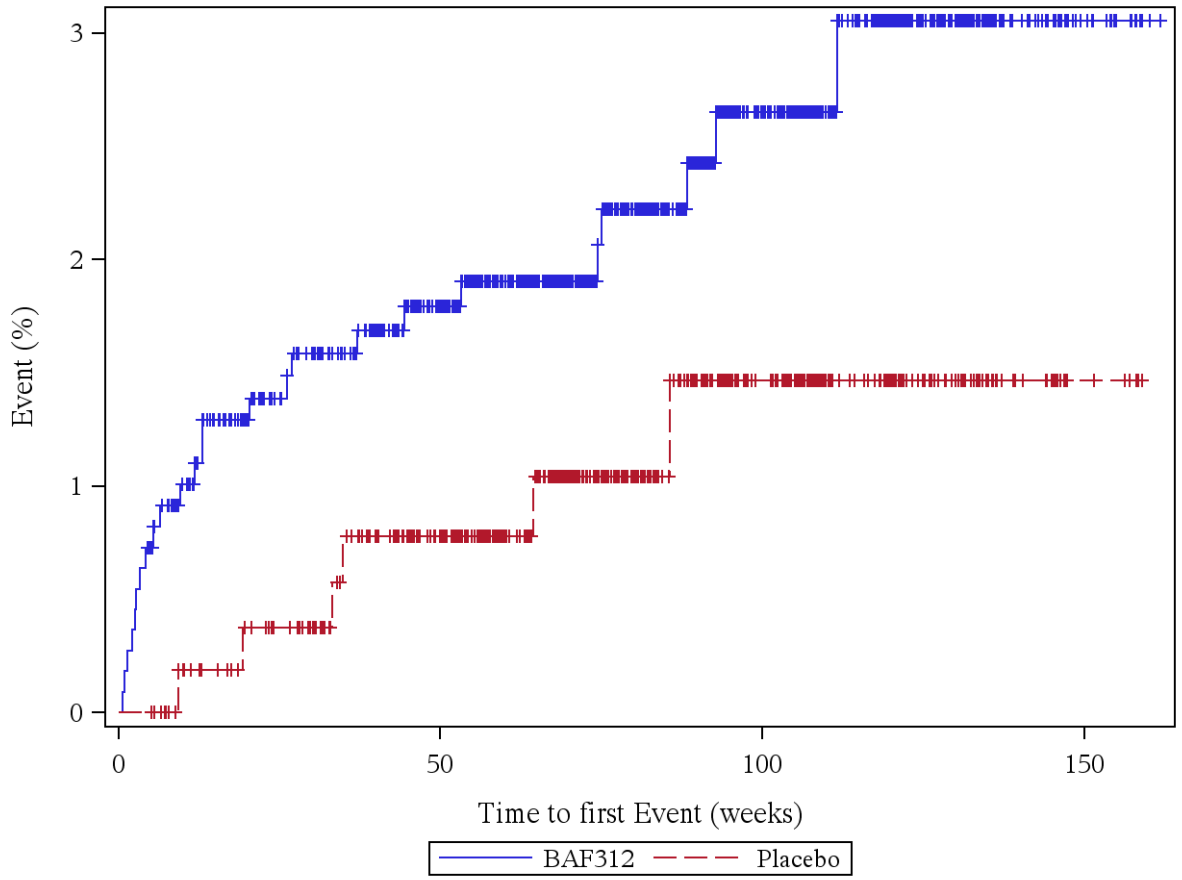


Patients at risk (BAF312/Placebo): Week 0: 1099/546, Week 4: 1099/546, Week 12: 1059/535, Week 24: 1017/521, Week 36: 990/497, Week 48: 925/461, Week 60: 818/388, Week 72: 652/305, Week 84: 516/237, Week 96: 400/176, Week 108: 291/126, Week 120: 200/80, Week 132: 113/40, Week 144: 51/20, Week 156: 10/5, Week 168: 0/0

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

Analysis population: A2304 SAF total population

Figure 12.1.5.63: PERIPHERAL SWELLING (PT, not severe)

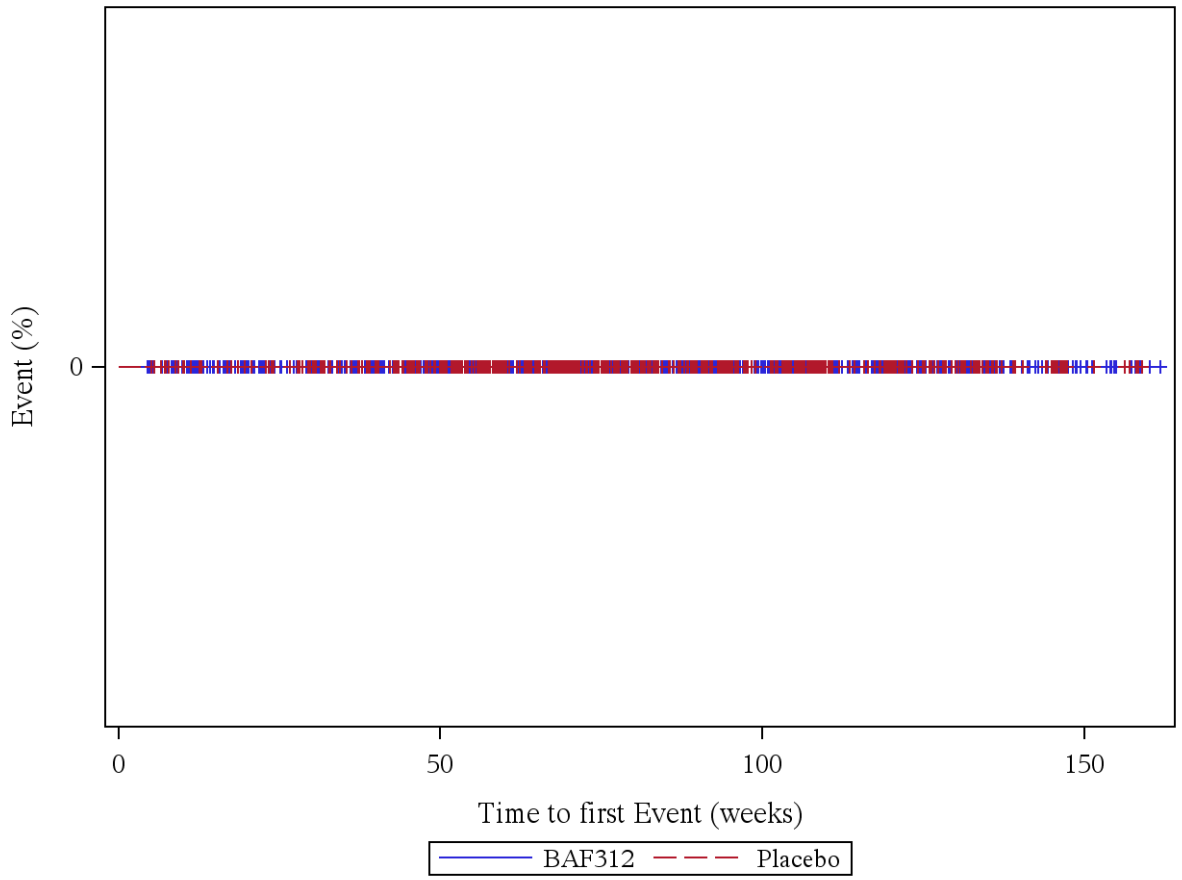


Patients at risk (BAF312/Placebo): Week 0: 1099/546, Week 4: 1092/546, Week 12: 1048/534, Week 24: 1003/519, Week 36: 975/493, Week 48: 909/458, Week 60: 803/387, Week 72: 641/303, Week 84: 505/235, Week 96: 391/173, Week 108: 285/123, Week 120: 194/77, Week 132: 110/38, Week 144: 49/19, Week 156: 10/5, Week 168: 0/0

Log rank test: p-value = 0,103
*: p < 0,05

Analysis population: A2304 SAF total population

Figure 12.1.5.64: PERIPHERAL SWELLING (PT, severe)

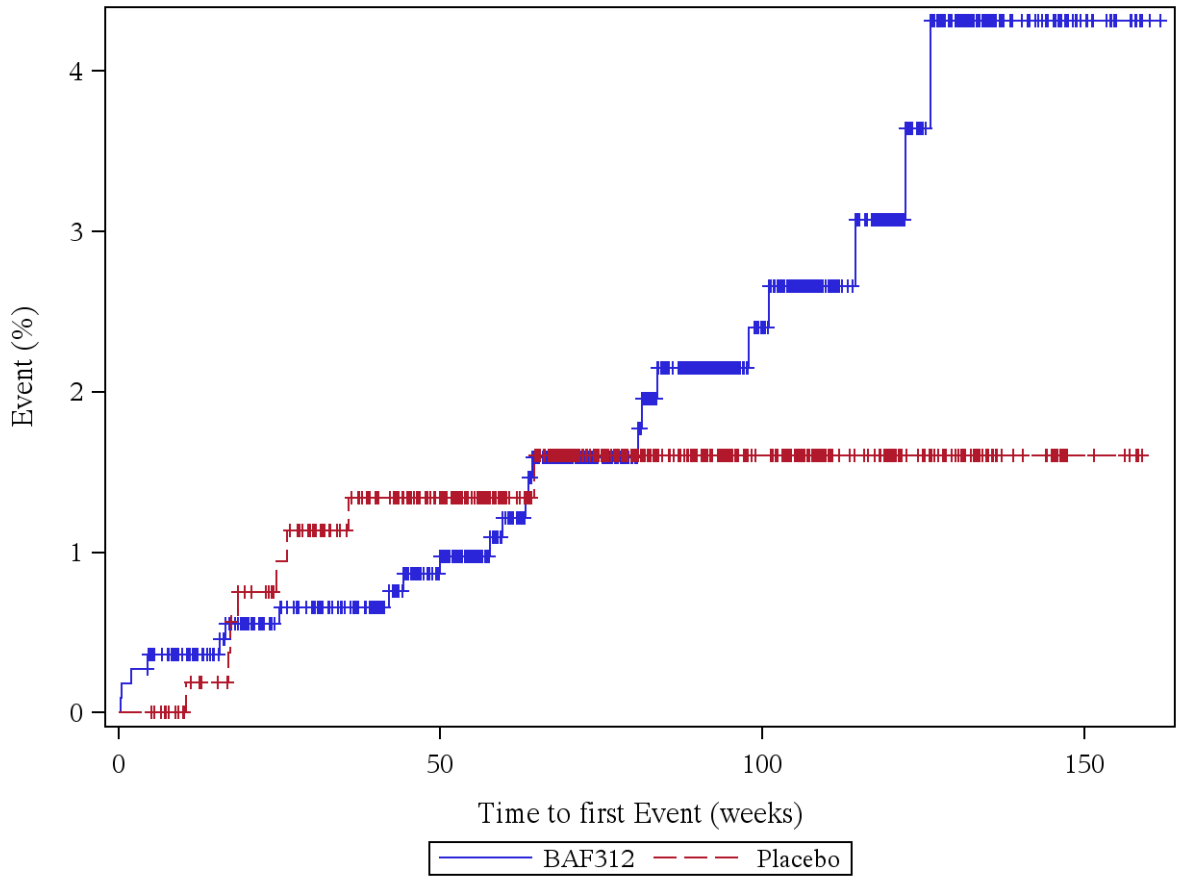


Patients at risk (BAF312/Placebo): Week 0: 1099/546, Week 4: 1099/546, Week 12: 1059/535, Week 24: 1017/521, Week 36: 990/497, Week 48: 925/461, Week 60: 818/388, Week 72: 652/305, Week 84: 516/237, Week 96: 400/176, Week 108: 291/126, Week 120: 200/80, Week 132: 113/40, Week 144: 51/20, Week 156: 10/5, Week 168: 0/0

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

Analysis population: A2304 SAF total population

Figure 12.1.5.65: PYREXIA (PT, not severe)

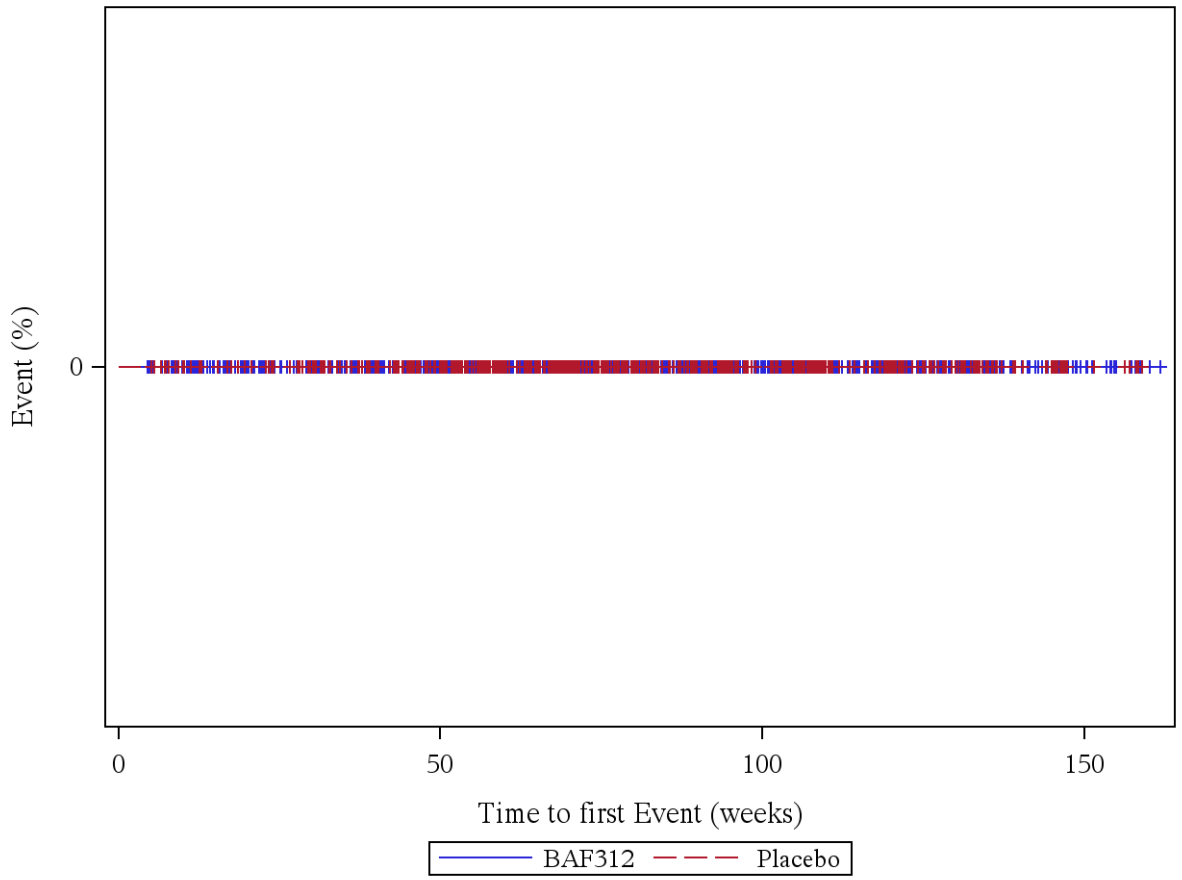


Patients at risk (BAF312/Placebo): Week 0: 1099/546, Week 4: 1096/546, Week 12: 1055/534, Week 24: 1011/517, Week 36: 983/490, Week 48: 917/455, Week 60: 807/383, Week 72: 640/299, Week 84: 504/232, Week 96: 395/172, Week 108: 289/123, Week 120: 197/77, Week 132: 108/39, Week 144: 48/20, Week 156: 9/5, Week 168: 0/0

Log rank test: p-value = 0,437
*: p < 0,05

Analysis population: A2304 SAF total population

Figure 12.1.5.66: PYREXIA (PT, severe)

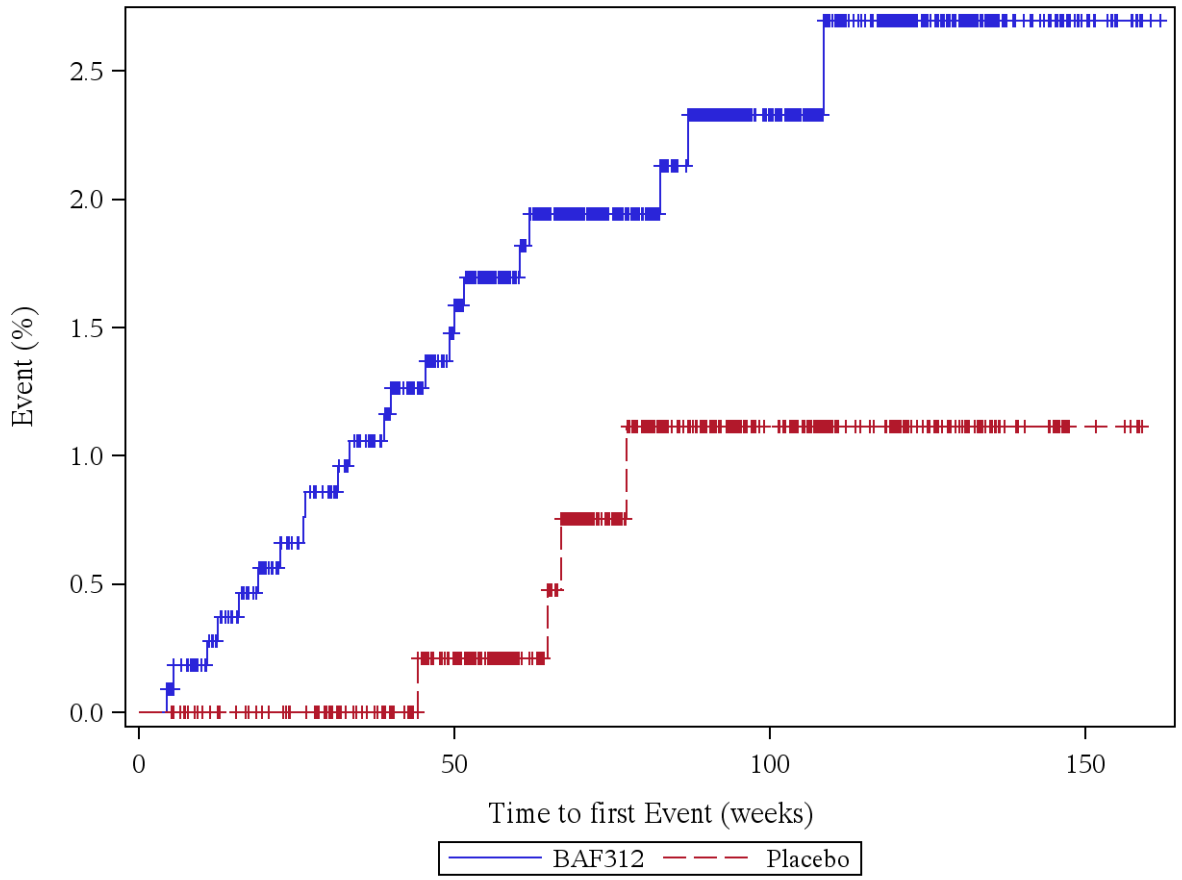


Patients at risk (BAF312/Placebo): Week 0: 1099/546, Week 4: 1099/546, Week 12: 1059/535, Week 24: 1017/521, Week 36: 990/497, Week 48: 925/461, Week 60: 818/388, Week 72: 652/305, Week 84: 516/237, Week 96: 400/176, Week 108: 291/126, Week 120: 200/80, Week 132: 113/40, Week 144: 51/20, Week 156: 10/5, Week 168: 0/0

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

Analysis population: A2304 SAF total population

Figure 12.1.5.67: HEPATOBILIARY DISORDERS (SOC, not severe)

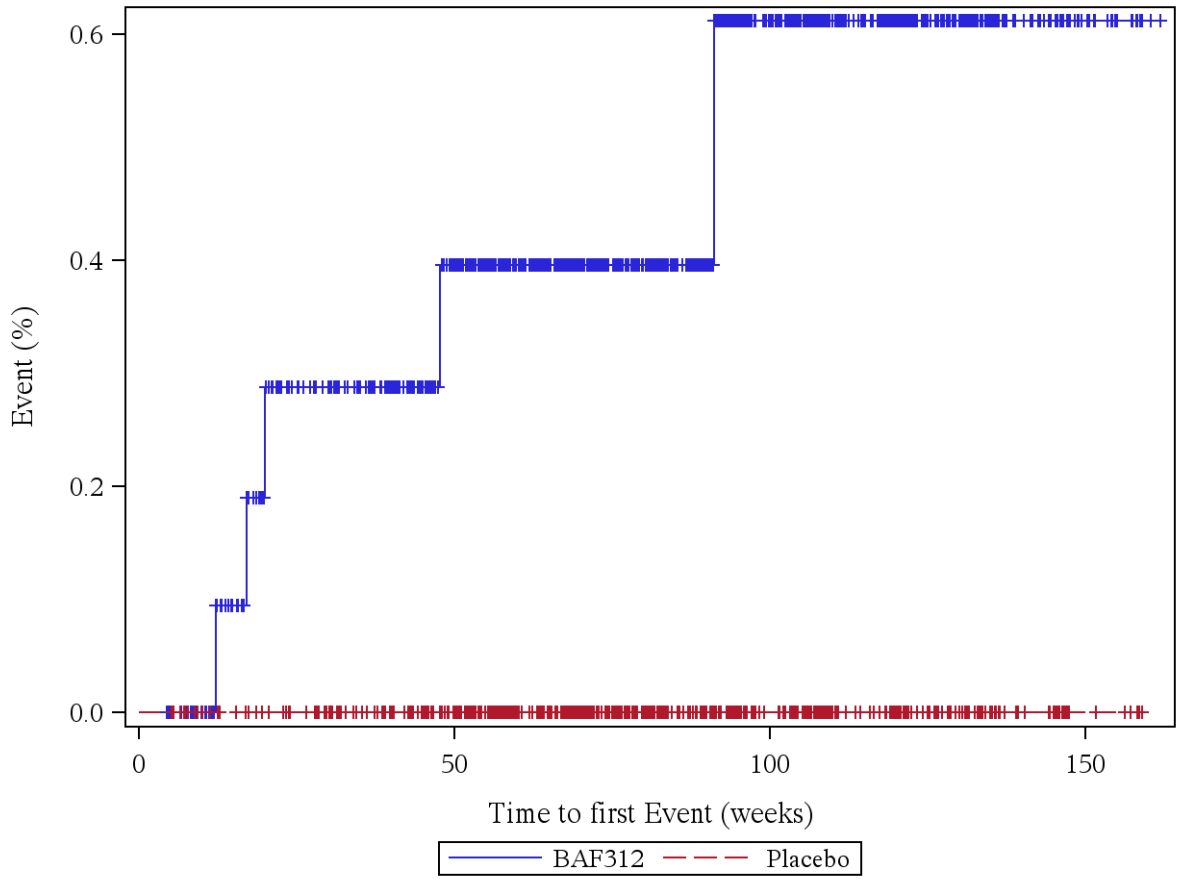


Patients at risk (BAF312/Placebo): Week 0: 1099/546, Week 4: 1099/546, Week 12: 1057/535, Week 24: 1011/521, Week 36: 981/497, Week 48: 915/460, Week 60: 805/387, Week 72: 639/302, Week 84: 504/233, Week 96: 390/172, Week 108: 282/123, Week 120: 192/79, Week 132: 110/40, Week 144: 49/20, Week 156: 10/5, Week 168: 0/0

Log rank test: p-value = 0,055
*: p < 0,05

Analysis population: A2304 SAF total population

Figure 12.1.5.68: HEPATOBILIARY DISORDERS (SOC, severe)

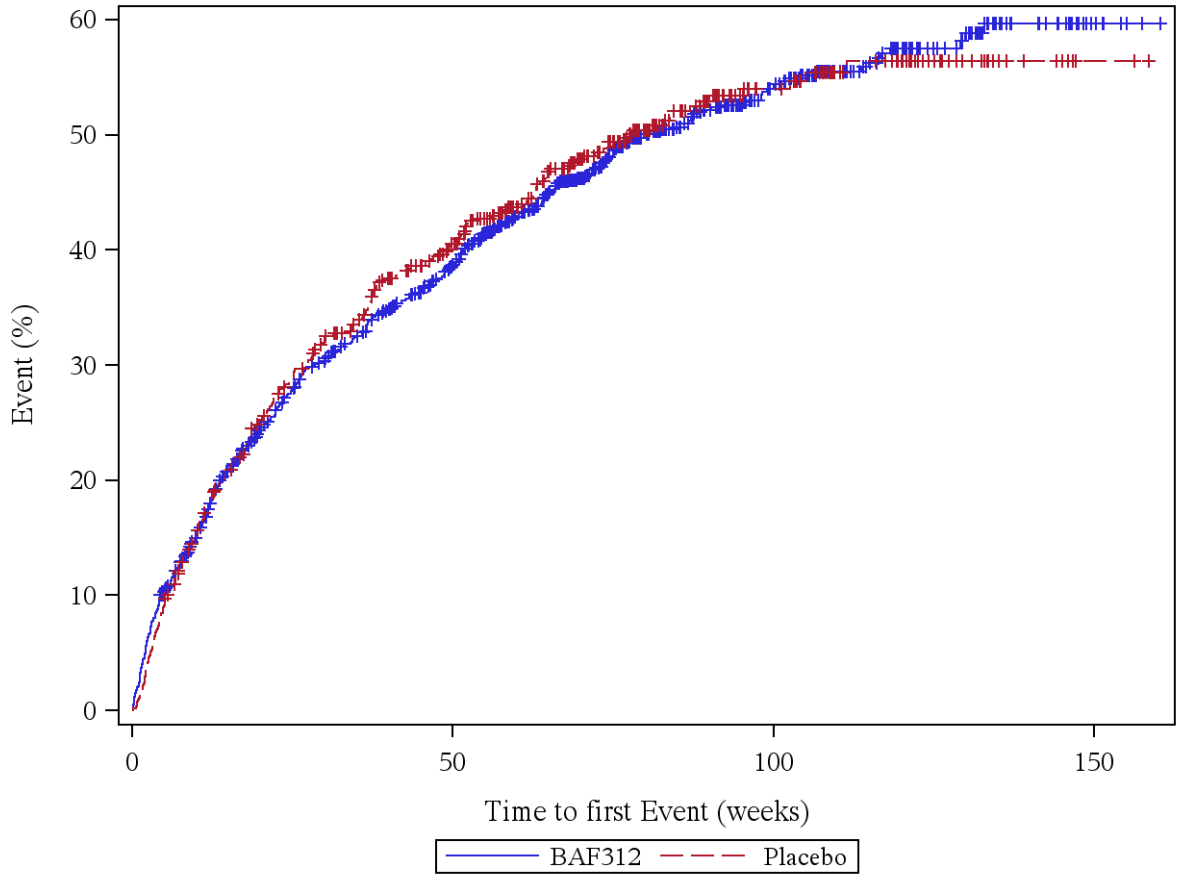


Patients at risk (BAF312/Placebo): Week 0: 1099/546, Week 4: 1099/546, Week 12: 1059/535, Week 24: 1014/521, Week 36: 988/497, Week 48: 922/461, Week 60: 815/388, Week 72: 650/305, Week 84: 515/237, Week 96: 398/176, Week 108: 290/126, Week 120: 199/80, Week 132: 112/40, Week 144: 51/20, Week 156: 10/5, Week 168: 0/0

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

Analysis population: A2304 SAF total population

Figure 12.1.5.69: INFECTIONS AND INFESTATIONS (SOC, not severe)

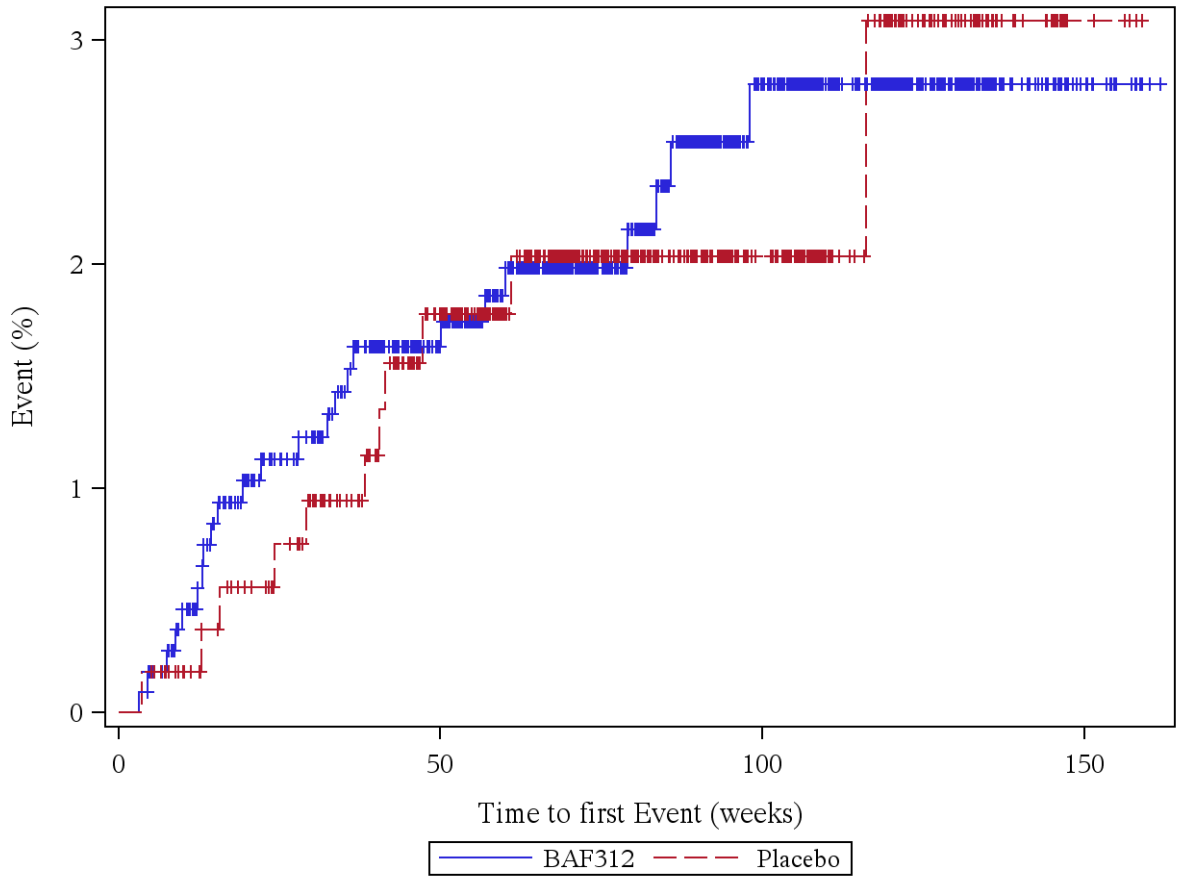


Patients at risk (BAF312/Placebo): Week 0: 1099/546, Week 4: 999/506, Week 12: 876/439, Week 24: 744/373, Week 36: 671/328, Week 48: 590/283, Week 60: 476/225, Week 72: 356/168, Week 84: 269/115, Week 96: 206/75, Week 108: 141/54, Week 120: 90/35, Week 132: 52/18, Week 144: 26/8, Week 156: 2/2, Week 168: 0/0

Log rank test: p-value = 0,844
*: p < 0,05

Analysis population: A2304 SAF total population

Figure 12.1.5.70: INFECTIONS AND INFESTATIONS (SOC, severe)

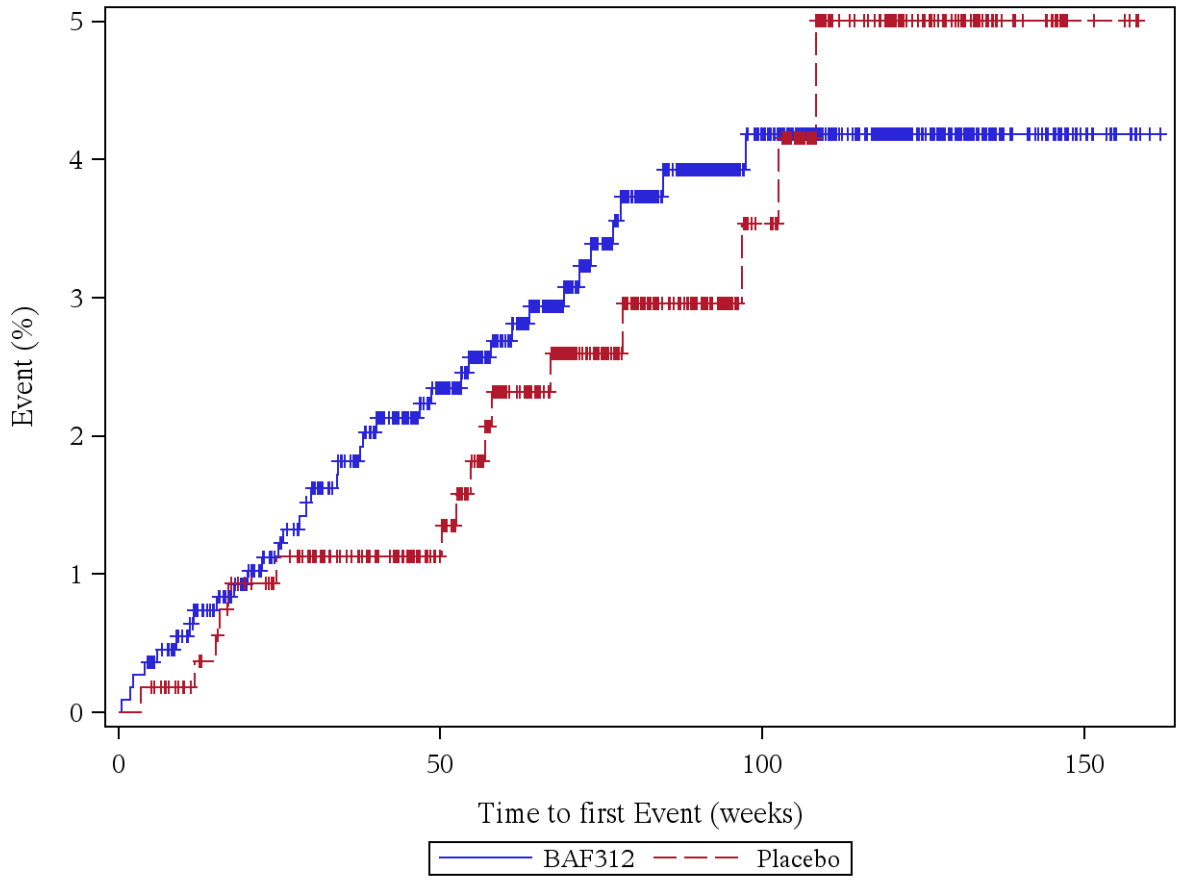


Patients at risk (BAF312/Placebo): Week 0: 1099/546, Week 4: 1098/545, Week 12: 1054/534, Week 24: 1006/518, Week 36: 975/493, Week 48: 911/454, Week 60: 803/385, Week 72: 638/301, Week 84: 503/234, Week 96: 388/173, Week 108: 280/123, Week 120: 191/77, Week 132: 108/39, Week 144: 48/19, Week 156: 9/4, Week 168: 0/0

Log rank test: p-value = 0,831
*: p < 0,05

Analysis population: A2304 SAF total population

Figure 12.1.5.71: BRONCHITIS (PT, not severe)

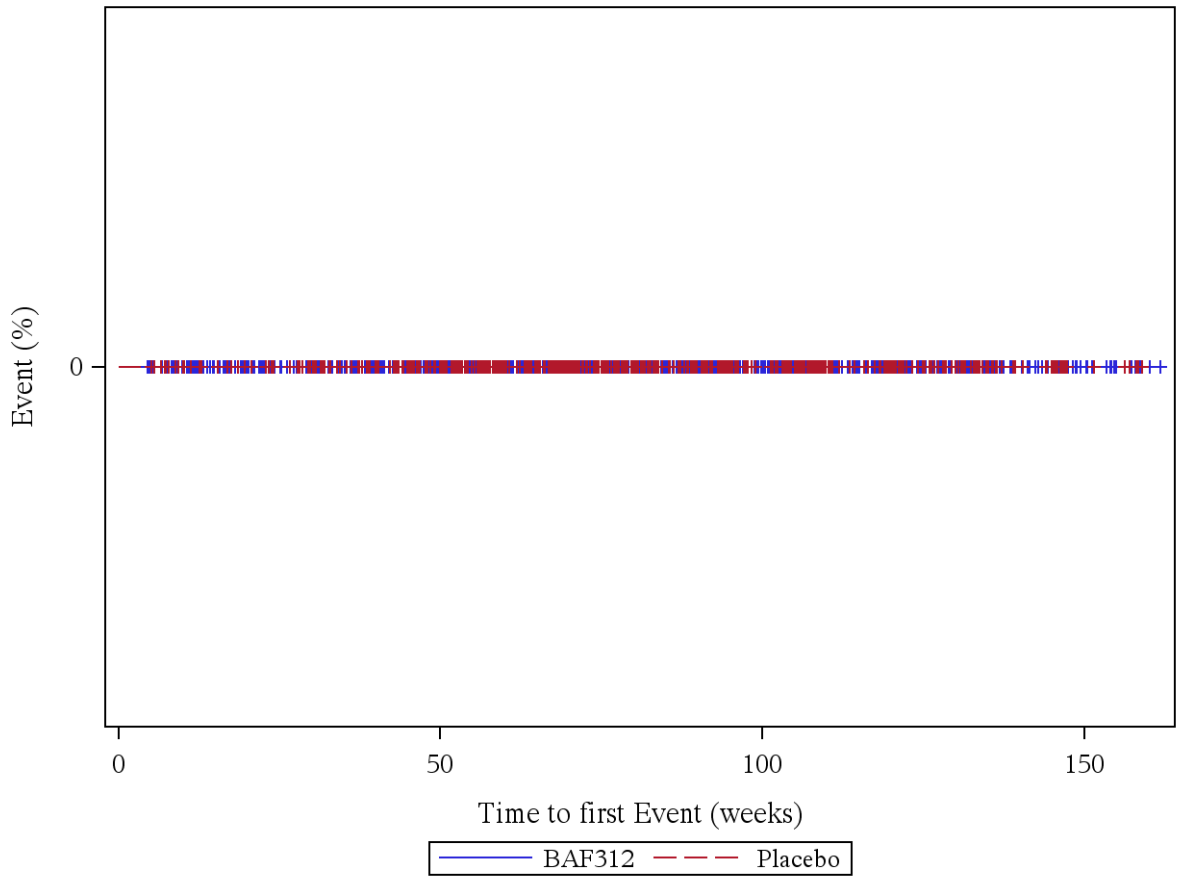


Patients at risk (BAF312/Placebo): Week 0: 1099/546, Week 4: 1095/545, Week 12: 1051/533, Week 24: 1005/516, Week 36: 972/491, Week 48: 904/455, Week 60: 794/378, Week 72: 626/299, Week 84: 494/233, Week 96: 381/172, Week 108: 278/121, Week 120: 188/77, Week 132: 107/38, Week 144: 50/18, Week 156: 9/4, Week 168: 0/0

Log rank test: p-value = 0,734
*: p < 0,05

Analysis population: A2304 SAF total population

Figure 12.1.5.72: BRONCHITIS (PT, severe)

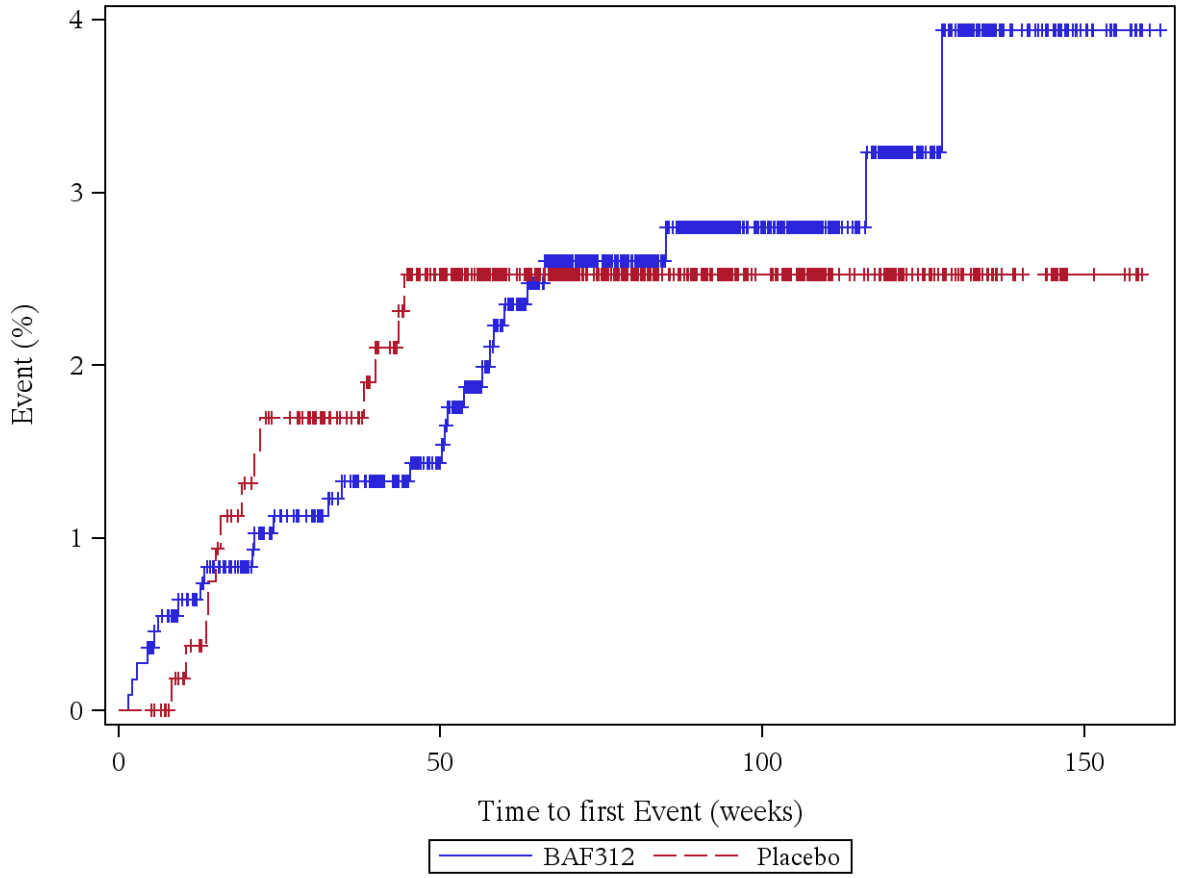


Patients at risk (BAF312/Placebo): Week 0: 1099/546, Week 4: 1099/546, Week 12: 1059/535, Week 24: 1017/521, Week 36: 990/497, Week 48: 925/461, Week 60: 818/388, Week 72: 652/305, Week 84: 516/237, Week 96: 400/176, Week 108: 291/126, Week 120: 200/80, Week 132: 113/40, Week 144: 51/20, Week 156: 10/5, Week 168: 0/0

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

Analysis population: A2304 SAF total population

Figure 12.1.5.73: CYSTITIS (PT, not severe)

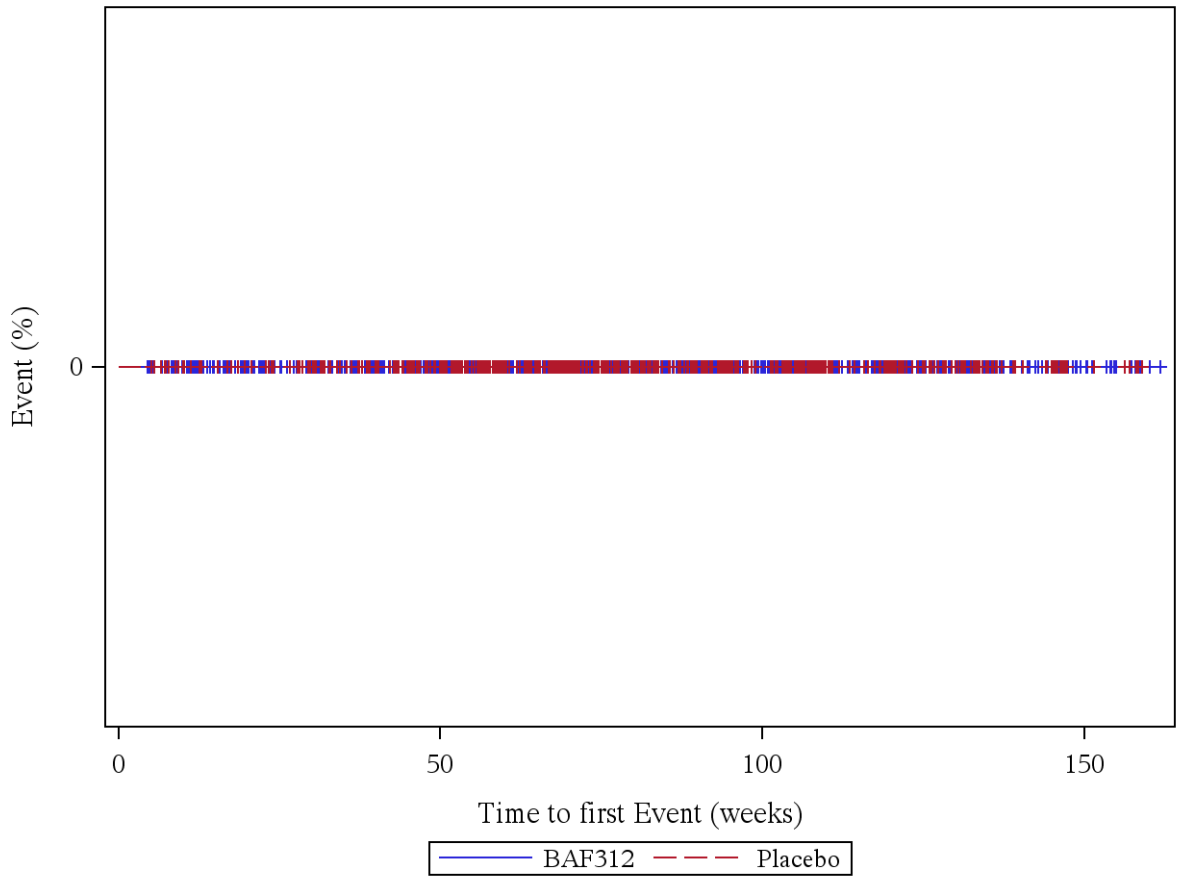


Patients at risk (BAF312/Placebo): Week 0: 1099/546, Week 4: 1096/546, Week 12: 1053/533, Week 24: 1008/513, Week 36: 979/489, Week 48: 916/451, Week 60: 801/380, Week 72: 635/298, Week 84: 504/233, Week 96: 390/172, Week 108: 283/123, Week 120: 194/78, Week 132: 110/39, Week 144: 51/20, Week 156: 10/5, Week 168: 0/0

Log rank test: p-value = 0,874
*: p < 0,05

Analysis population: A2304 SAF total population

Figure 12.1.5.74: CYSTITIS (PT, severe)

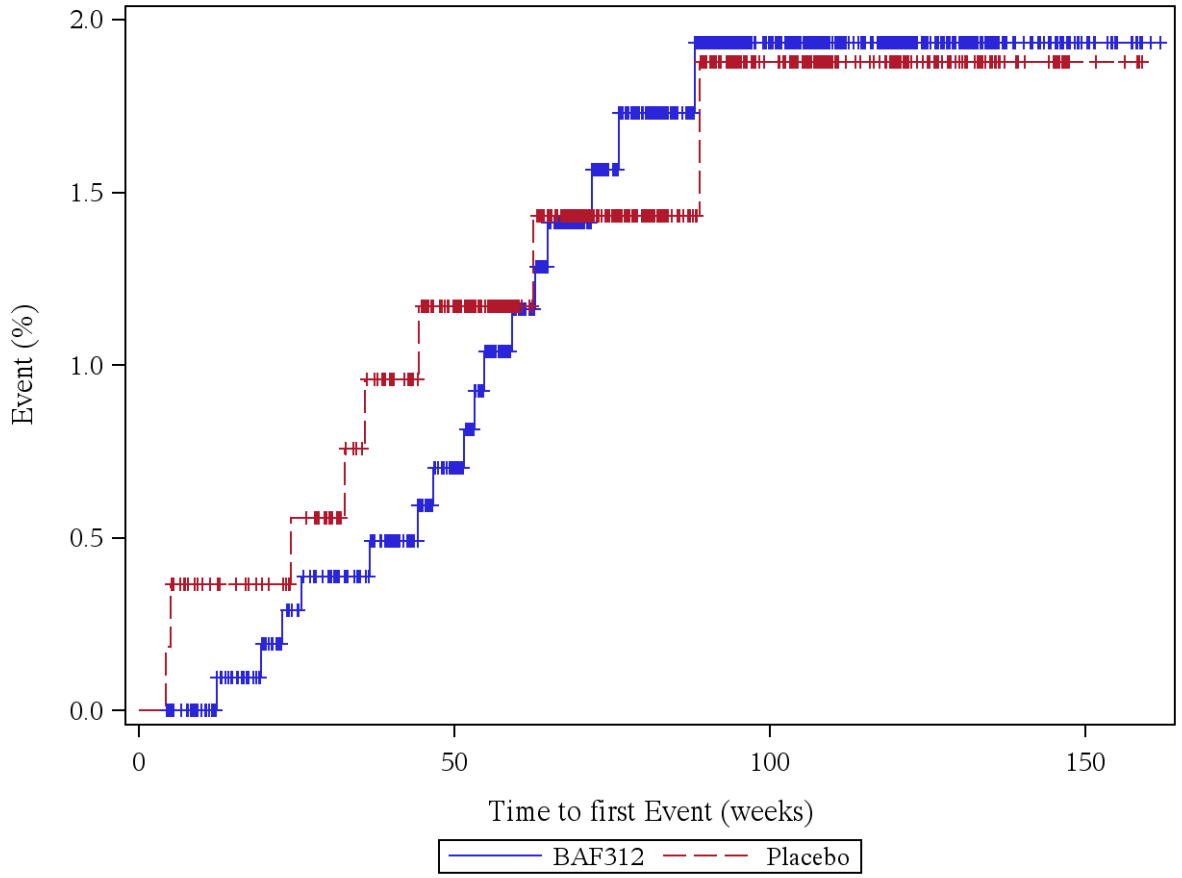


Patients at risk (BAF312/Placebo): Week 0: 1099/546, Week 4: 1099/546, Week 12: 1059/535, Week 24: 1017/521, Week 36: 990/497, Week 48: 925/461, Week 60: 818/388, Week 72: 652/305, Week 84: 516/237, Week 96: 400/176, Week 108: 291/126, Week 120: 200/80, Week 132: 113/40, Week 144: 51/20, Week 156: 10/5, Week 168: 0/0

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

Analysis population: A2304 SAF total population

Figure 12.1.5.75: GASTROENTERITIS (PT, not severe)

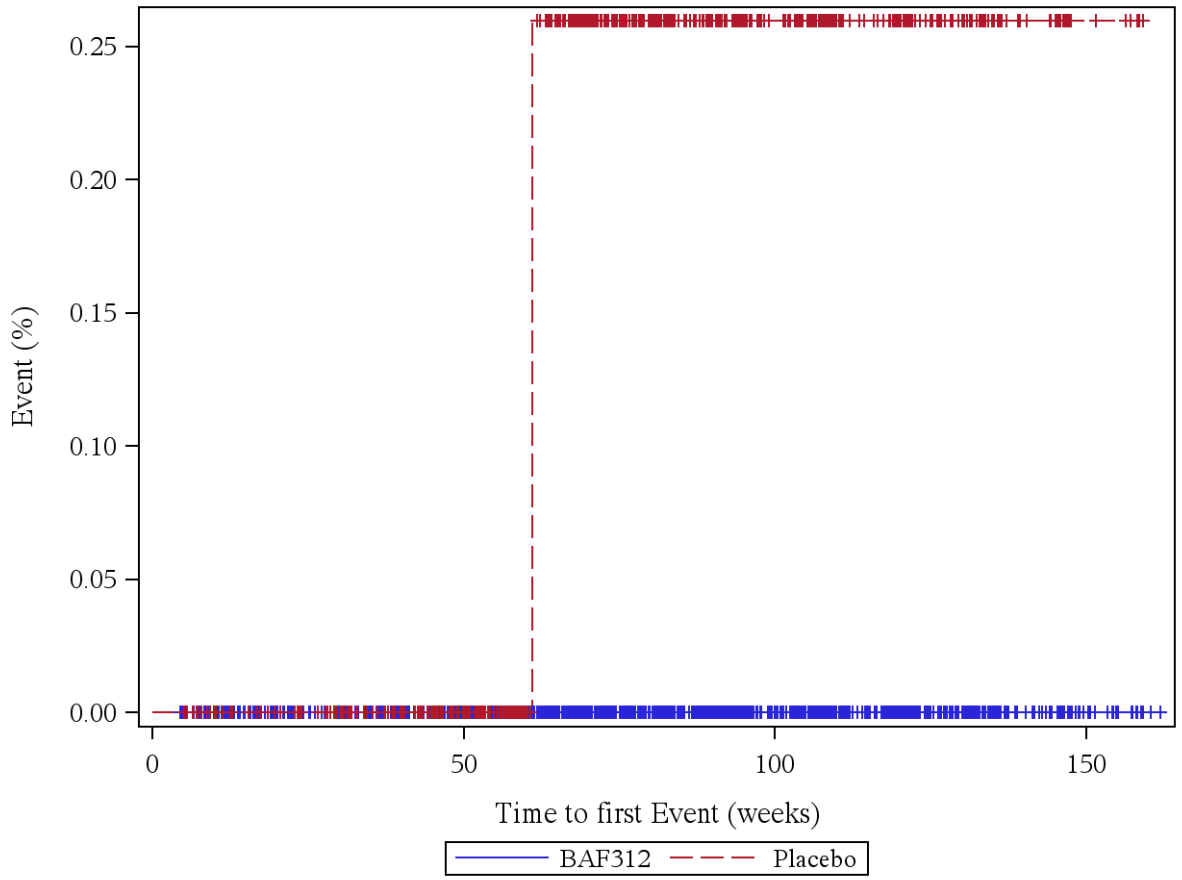


Patients at risk (BAF312/Placebo): Week 0: 1099/546, Week 4: 1099/546, Week 12: 1059/533, Week 24: 1014/519, Week 36: 986/492, Week 48: 919/455, Week 60: 809/383, Week 72: 642/300, Week 84: 506/232, Week 96: 392/171, Week 108: 284/123, Week 120: 195/77, Week 132: 110/38, Week 144: 49/18, Week 156: 10/4, Week 168: 0/0

Log rank test: p-value = 0,960
*: p < 0,05

Analysis population: A2304 SAF total population

Figure 12.1.5.76: GASTROENTERITIS (PT, severe)

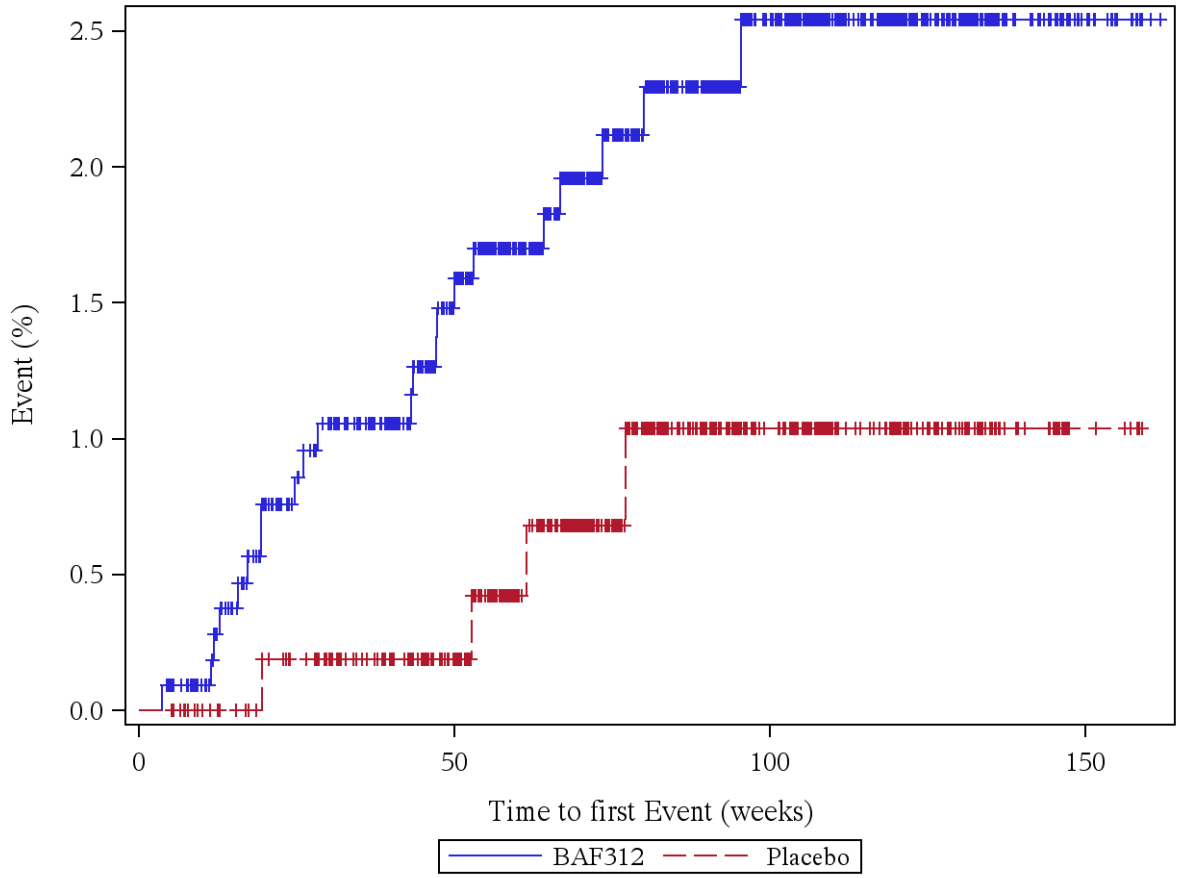


Patients at risk (BAF312/Placebo): Week 0: 1099/546, Week 4: 1099/546, Week 12: 1059/535, Week 24: 1017/521, Week 36: 990/497, Week 48: 925/461, Week 60: 818/388, Week 72: 652/304, Week 84: 516/236, Week 96: 400/175, Week 108: 291/125, Week 120: 200/79, Week 132: 113/40, Week 144: 51/20, Week 156: 10/5, Week 168: 0/0

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

Analysis population: A2304 SAF total population

Figure 12.1.5.77: HERPES ZOSTER (PT, not severe)

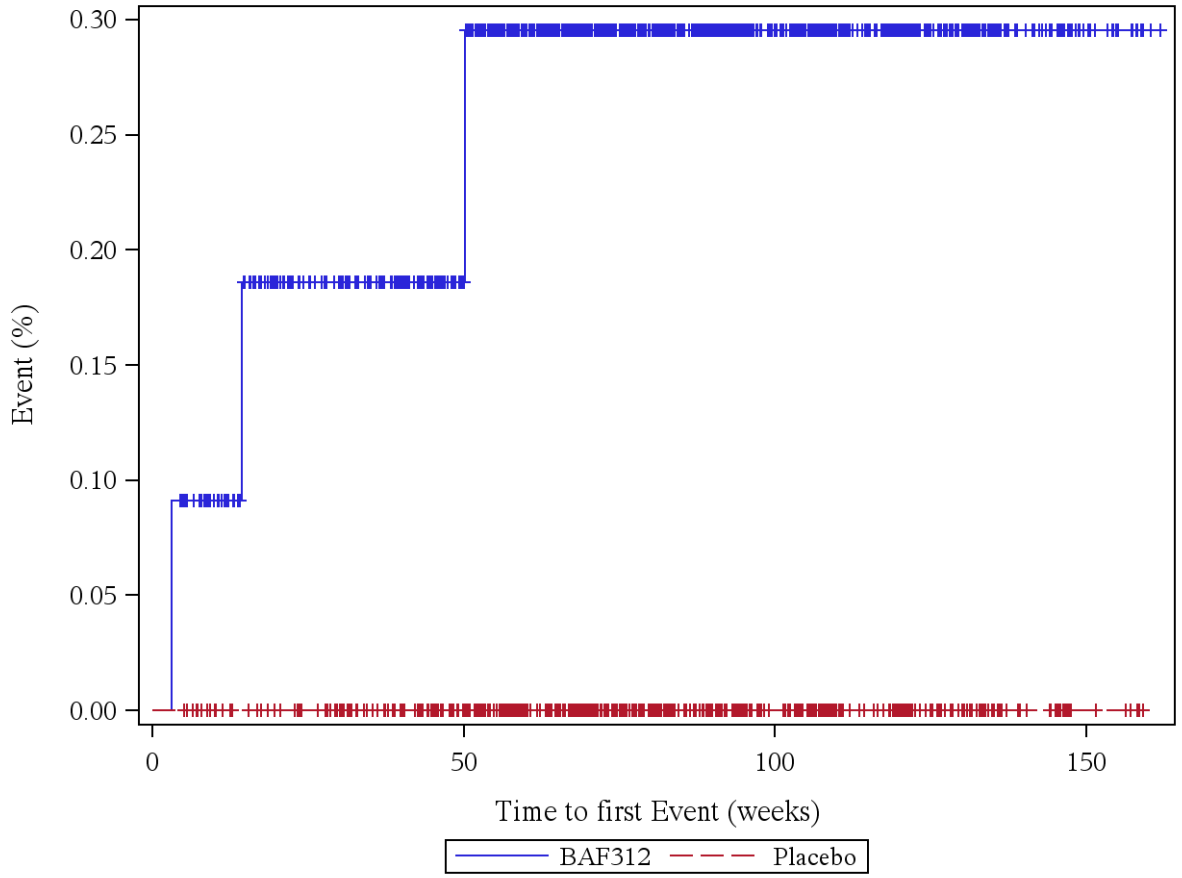


Patients at risk (BAF312/Placebo): Week 0: 1099/546, Week 4: 1098/546, Week 12: 1056/535, Week 24: 1010/520, Week 36: 980/496, Week 48: 911/460, Week 60: 805/387, Week 72: 638/303, Week 84: 502/234, Week 96: 388/174, Week 108: 280/126, Week 120: 192/80, Week 132: 109/40, Week 144: 50/20, Week 156: 9/5, Week 168: 0/0

Log rank test: p-value = 0,053
*: p < 0,05

Analysis population: A2304 SAF total population

Figure 12.1.5.78: HERPES ZOSTER (PT, severe)

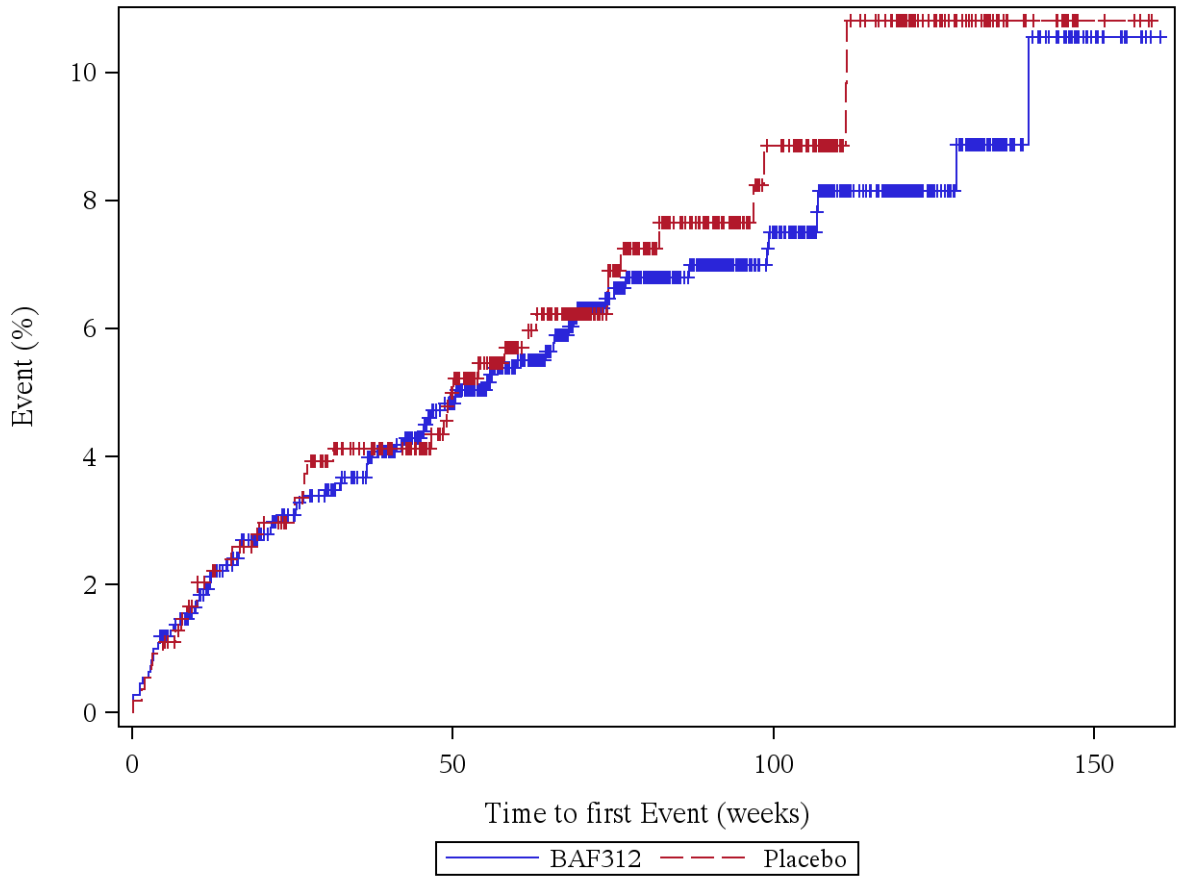


Patients at risk (BAF312/Placebo): Week 0: 1099/546, Week 4: 1098/546, Week 12: 1058/535, Week 24: 1015/521, Week 36: 988/497, Week 48: 923/461, Week 60: 815/388, Week 72: 650/305, Week 84: 514/237, Week 96: 398/176, Week 108: 290/126, Week 120: 199/80, Week 132: 113/40, Week 144: 51/20, Week 156: 10/5, Week 168: 0/0

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

Analysis population: A2304 SAF total population

Figure 12.1.5.79: INFLUENZA (PT, not severe)

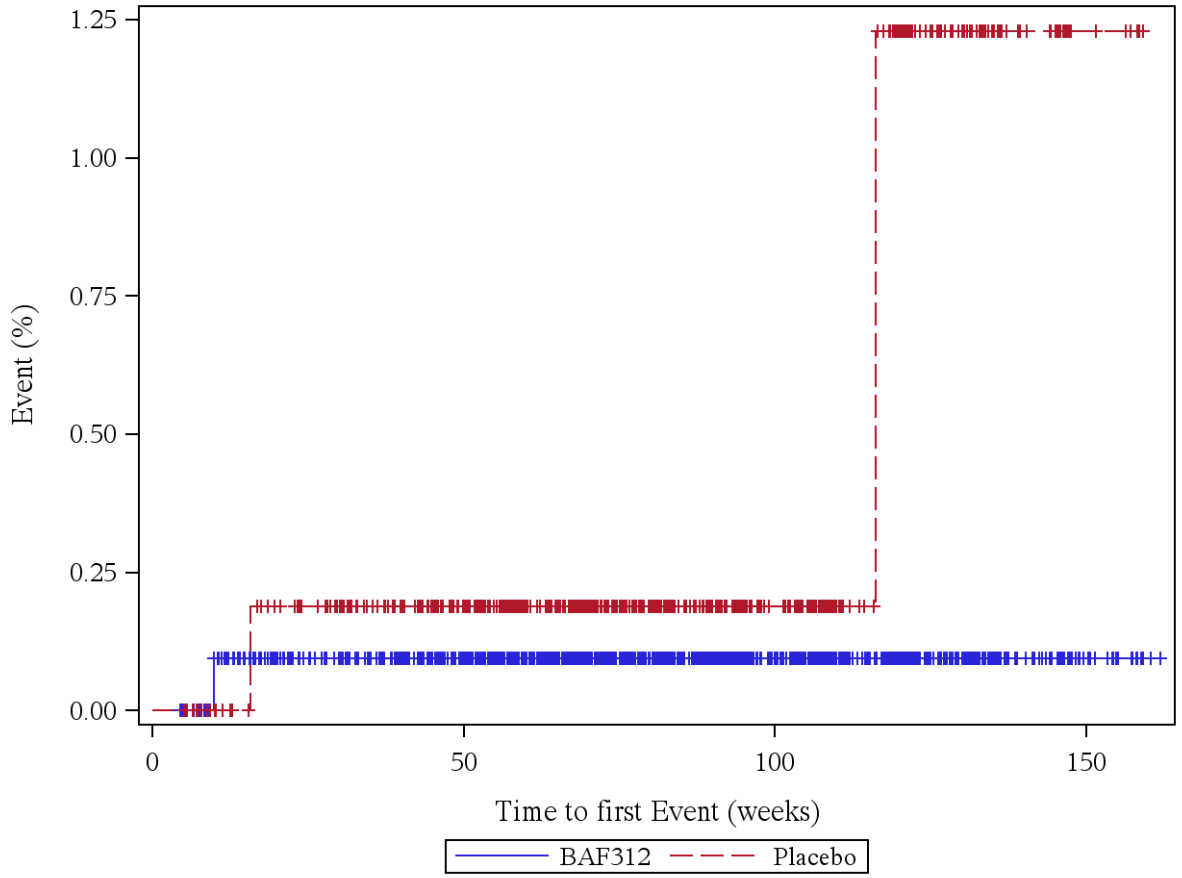


Patients at risk (BAF312/Placebo): Week 0: 1099/546, Week 4: 1087/541, Week 12: 1038/525, Week 24: 987/506, Week 36: 955/477, Week 48: 883/440, Week 60: 773/364, Week 72: 611/286, Week 84: 479/220, Week 96: 373/161, Week 108: 270/116, Week 120: 186/72, Week 132: 103/36, Week 144: 45/18, Week 156: 6/4, Week 168: 0/0

Log rank test: p-value = 0,589
*: p < 0,05

Analysis population: A2304 SAF total population

Figure 12.1.5.80: INFLUENZA (PT, severe)

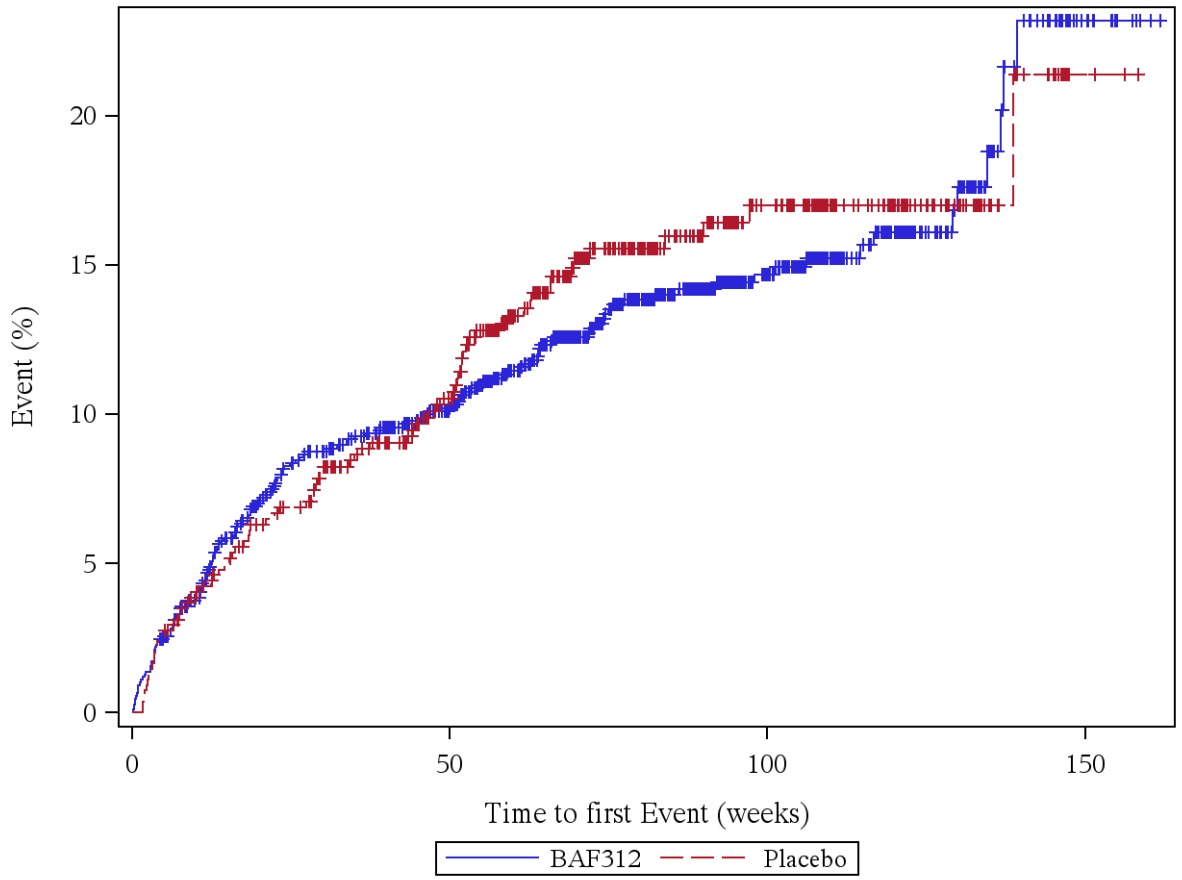


Patients at risk (BAF312/Placebo): Week 0: 1099/546, Week 4: 1099/546, Week 12: 1058/535, Week 24: 1016/520, Week 36: 989/496, Week 48: 924/460, Week 60: 817/388, Week 72: 652/305, Week 84: 516/237, Week 96: 400/176, Week 108: 291/126, Week 120: 200/80, Week 132: 113/40, Week 144: 51/20, Week 156: 10/5, Week 168: 0/0

Log rank test: p-value = 0,199
*: p < 0,05

Analysis population: A2304 SAF total population

Figure 12.1.5.81: NASOPHARYNGITIS (PT, not severe)

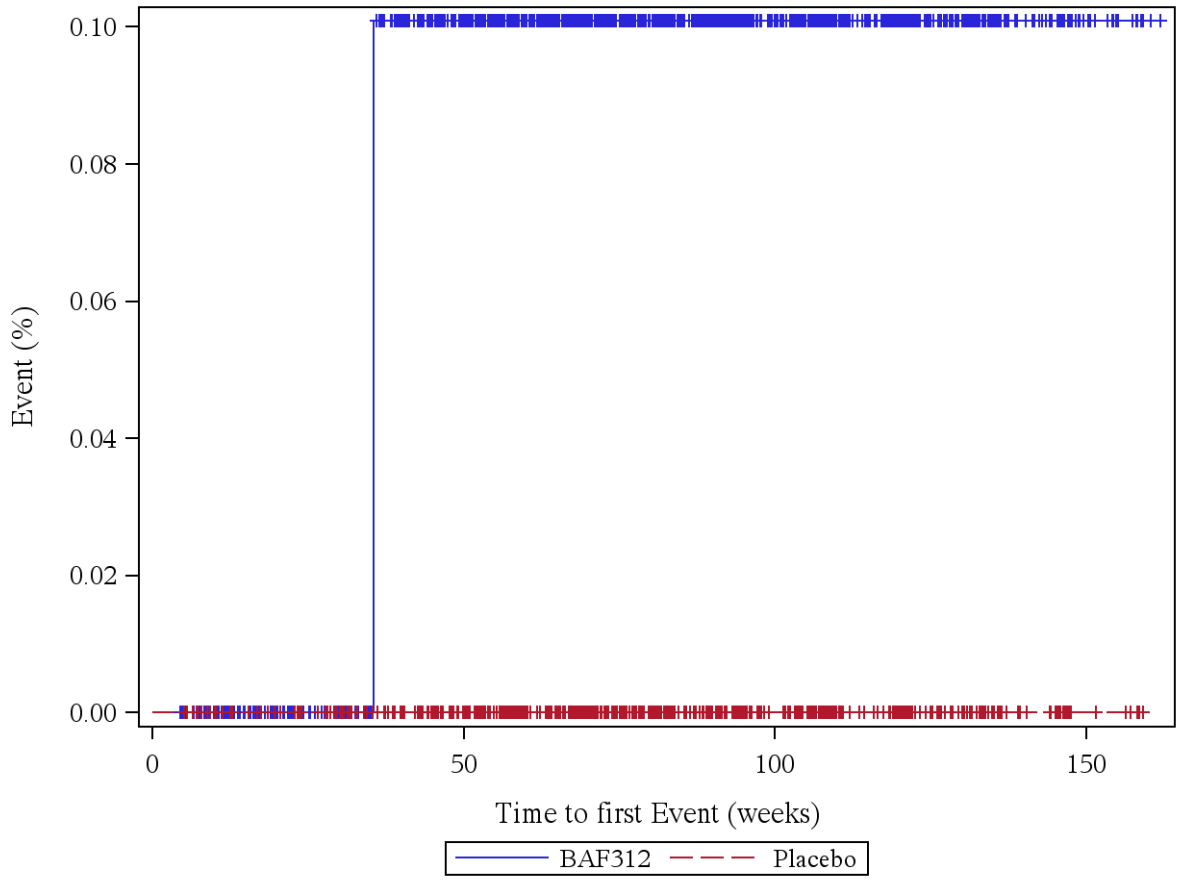


Patients at risk (BAF312/Placebo): Week 0: 1099/546, Week 4: 1073/533, Week 12: 1008/512, Week 24: 932/485, Week 36: 899/454, Week 48: 836/415, Week 60: 729/340, Week 72: 577/259, Week 84: 455/201, Week 96: 347/148, Week 108: 247/105, Week 120: 163/65, Week 132: 92/33, Week 144: 42/15, Week 156: 7/2, Week 168: 0/0

Log rank test: p-value = 0,557
*: p < 0,05

Analysis population: A2304 SAF total population

Figure 12.1.5.82: NASOPHARYNGITIS (PT, severe)

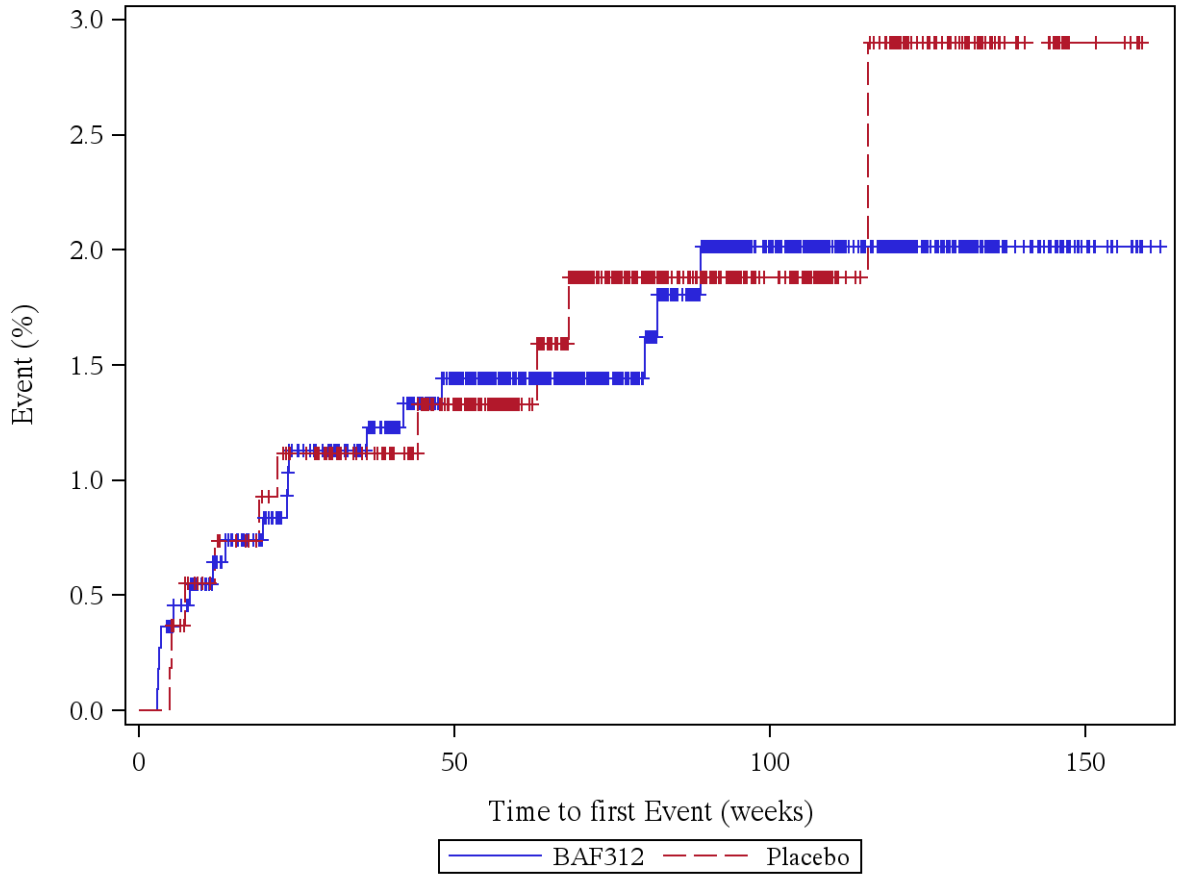


Patients at risk (BAF312/Placebo): Week 0: 1099/546, Week 4: 1099/546, Week 12: 1059/535, Week 24: 1017/521, Week 36: 989/497, Week 48: 924/461, Week 60: 817/388, Week 72: 651/305, Week 84: 515/237, Week 96: 399/176, Week 108: 290/126, Week 120: 199/80, Week 132: 112/40, Week 144: 50/20, Week 156: 9/5, Week 168: 0/0

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

Analysis population: A2304 SAF total population

Figure 12.1.5.83: ORAL HERPES (PT, not severe)

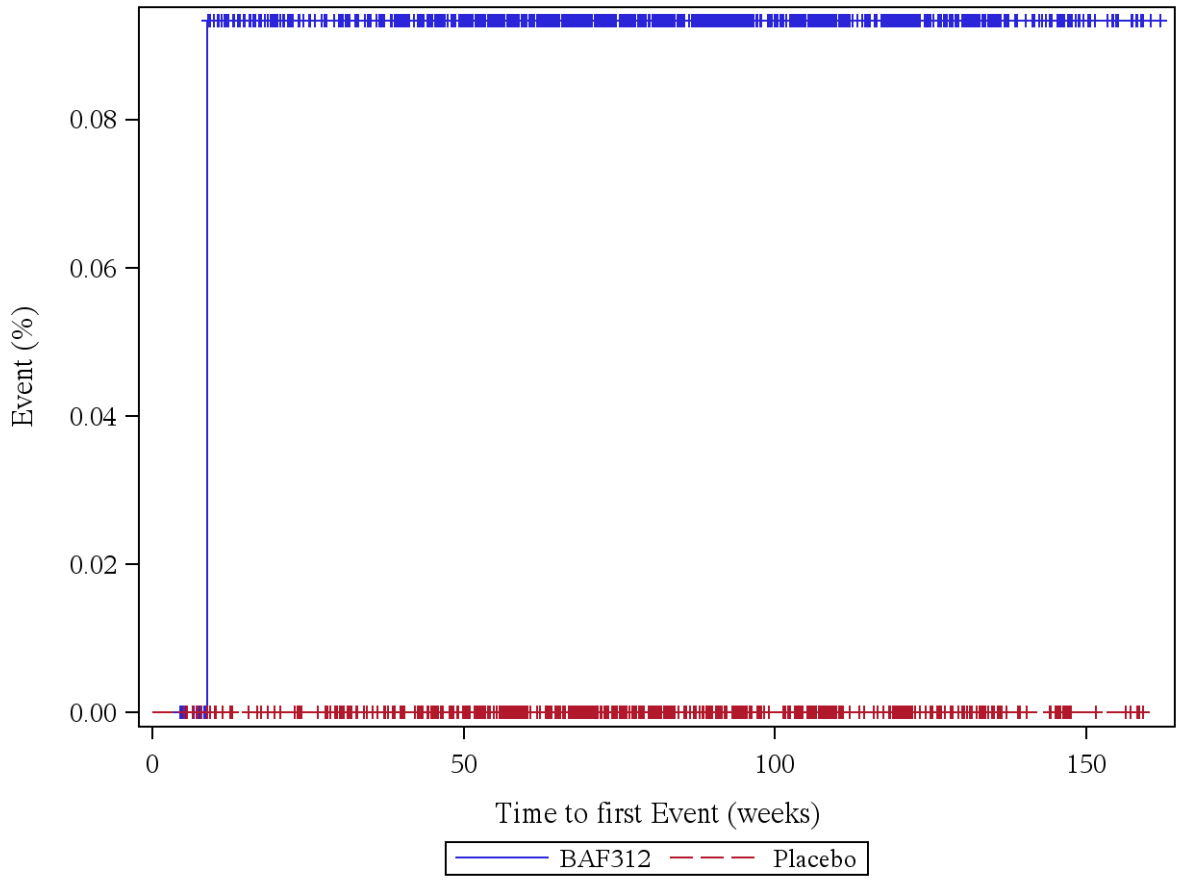


Patients at risk (BAF312/Placebo): Week 0: 1099/546, Week 4: 1095/546, Week 12: 1052/531, Week 24: 1005/515, Week 36: 978/491, Week 48: 910/454, Week 60: 803/381, Week 72: 639/299, Week 84: 506/232, Week 96: 393/171, Week 108: 287/122, Week 120: 197/78, Week 132: 110/39, Week 144: 50/20, Week 156: 10/5, Week 168: 0/0

Log rank test: p-value = 0,765
*: p < 0,05

Analysis population: A2304 SAF total population

Figure 12.1.5.84: ORAL HERPES (PT, severe)

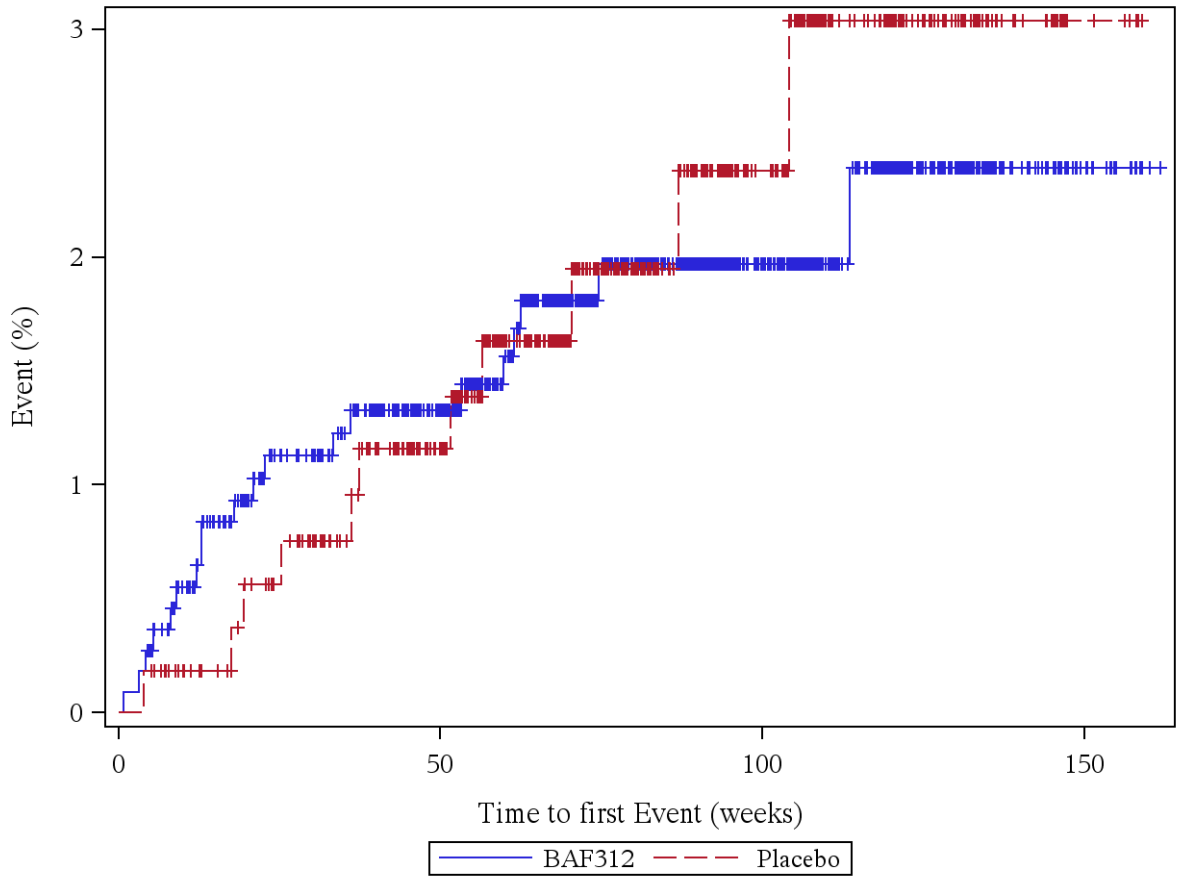


Patients at risk (BAF312/Placebo): Week 0: 1099/546, Week 4: 1099/546, Week 12: 1058/535, Week 24: 1016/521, Week 36: 989/497, Week 48: 924/461, Week 60: 817/388, Week 72: 651/305, Week 84: 516/237, Week 96: 400/176, Week 108: 291/126, Week 120: 200/80, Week 132: 113/40, Week 144: 51/20, Week 156: 10/5, Week 168: 0/0

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

Analysis population: A2304 SAF total population

Figure 12.1.5.85: PHARYNGITIS (PT, not severe)

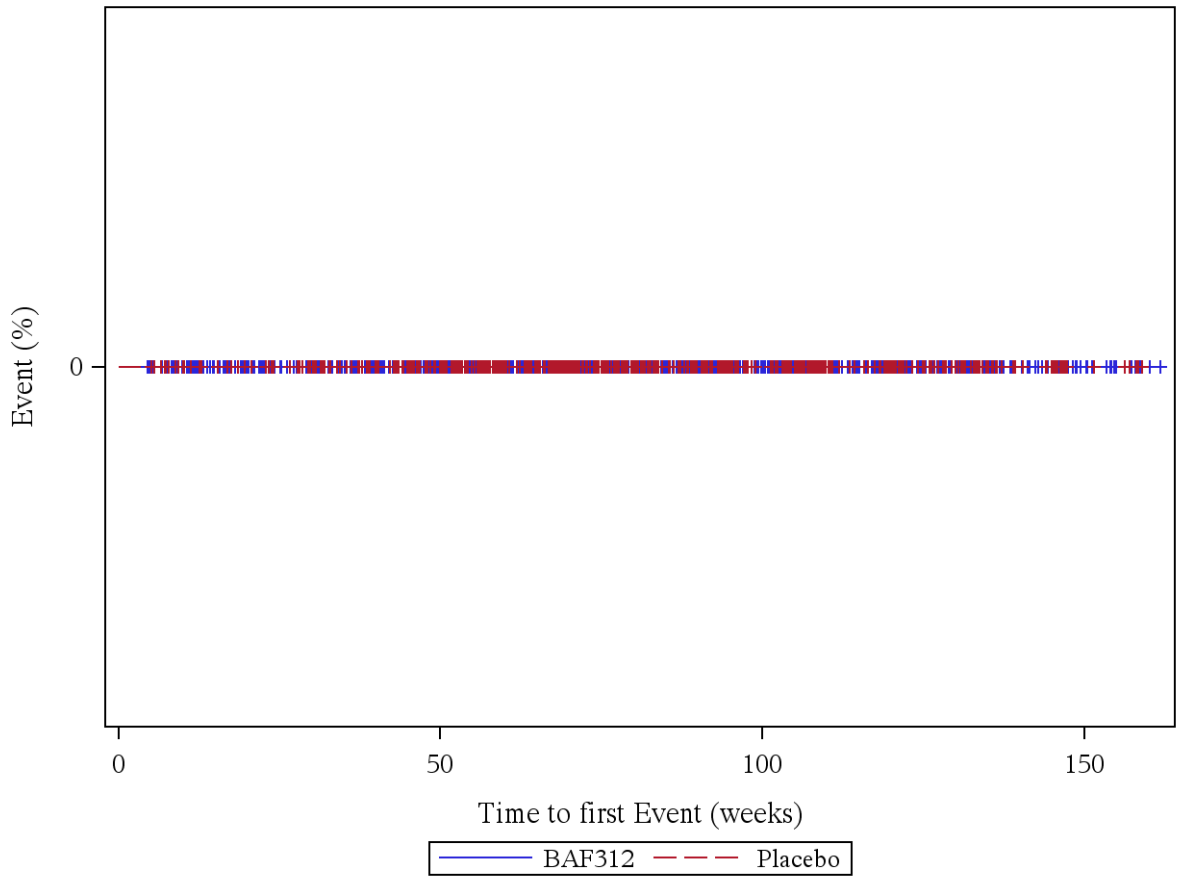


Patients at risk (BAF312/Placebo): Week 0: 1099/546, Week 4: 1097/545, Week 12: 1053/534, Week 24: 1006/518, Week 36: 978/493, Week 48: 913/455, Week 60: 806/381, Week 72: 640/300, Week 84: 503/233, Week 96: 390/171, Week 108: 281/121, Week 120: 192/78, Week 132: 110/39, Week 144: 50/20, Week 156: 10/5, Week 168: 0/0

Log rank test: p-value = 0,762
*: p < 0,05

Analysis population: A2304 SAF total population

Figure 12.1.5.86: PHARYNGITIS (PT, severe)

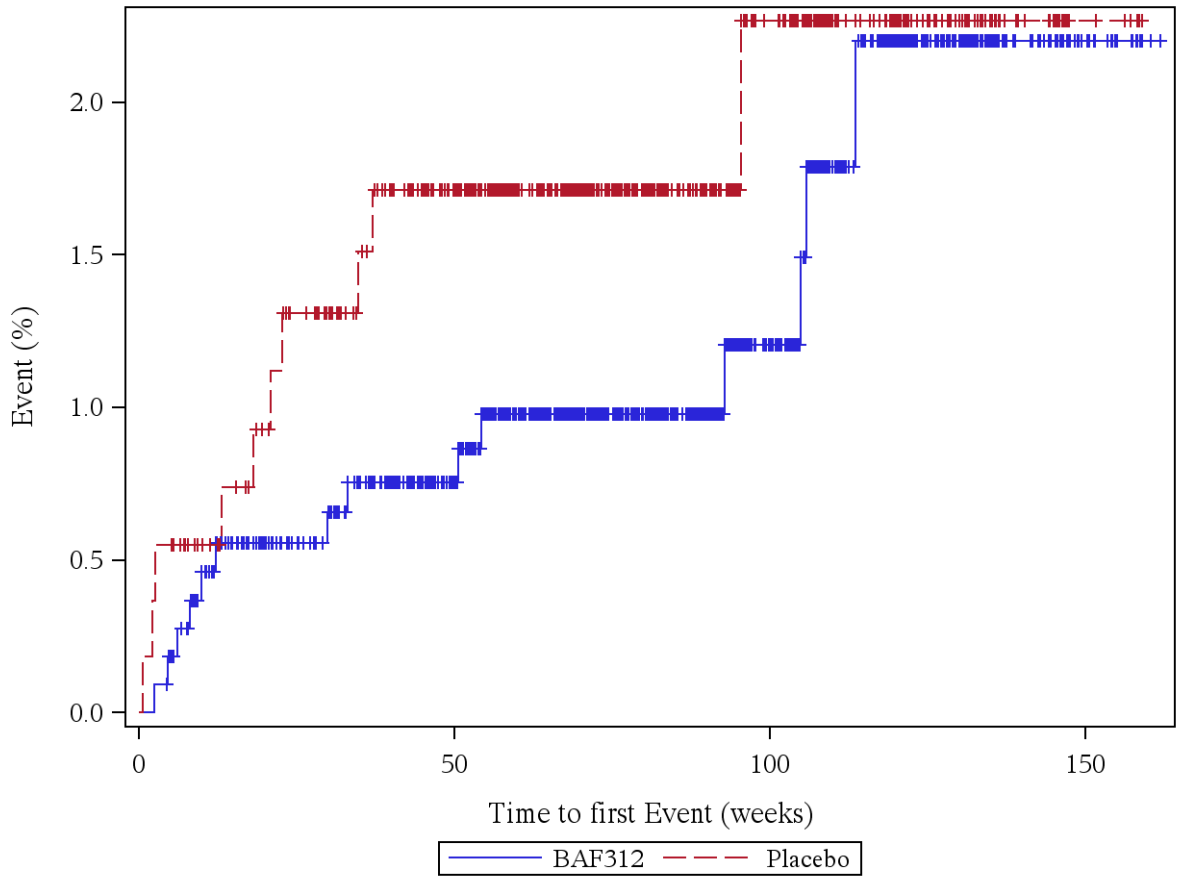


Patients at risk (BAF312/Placebo): Week 0: 1099/546, Week 4: 1099/546, Week 12: 1059/535, Week 24: 1017/521, Week 36: 990/497, Week 48: 925/461, Week 60: 818/388, Week 72: 652/305, Week 84: 516/237, Week 96: 400/176, Week 108: 291/126, Week 120: 200/80, Week 132: 113/40, Week 144: 51/20, Week 156: 10/5, Week 168: 0/0

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

Analysis population: A2304 SAF total population

Figure 12.1.5.87: RHINITIS (PT, not severe)

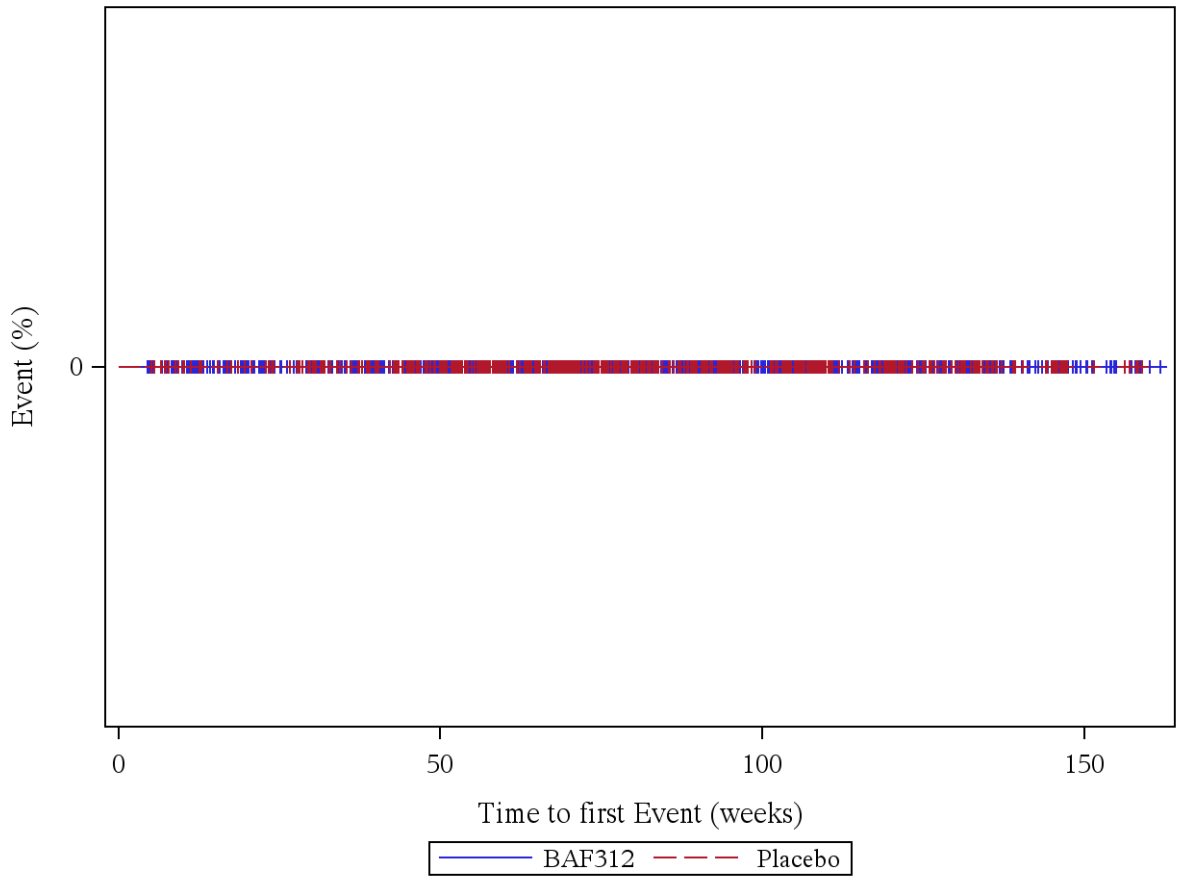


Patients at risk (BAF312/Placebo): Week 0: 1099/546, Week 4: 1098/543, Week 12: 1054/532, Week 24: 1012/514, Week 36: 983/489, Week 48: 918/453, Week 60: 809/381, Week 72: 646/299, Week 84: 511/233, Week 96: 395/172, Week 108: 287/123, Week 120: 198/78, Week 132: 112/39, Week 144: 51/20, Week 156: 10/5, Week 168: 0/0

Log rank test: p-value = 0,346
*: p < 0,05

Analysis population: A2304 SAF total population

Figure 12.1.5.88: RHINITIS (PT, severe)

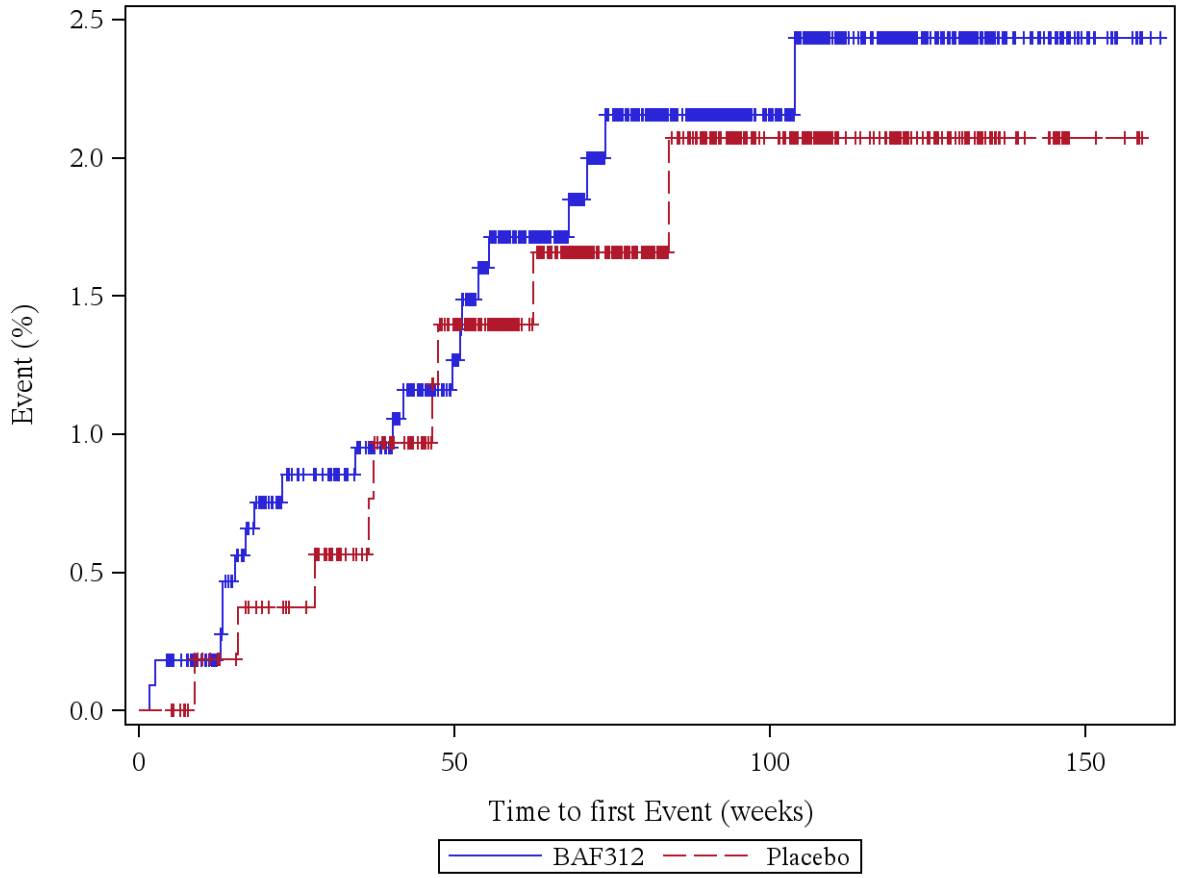


Patients at risk (BAF312/Placebo): Week 0: 1099/546, Week 4: 1099/546, Week 12: 1059/535, Week 24: 1017/521, Week 36: 990/497, Week 48: 925/461, Week 60: 818/388, Week 72: 652/305, Week 84: 516/237, Week 96: 400/176, Week 108: 291/126, Week 120: 200/80, Week 132: 113/40, Week 144: 51/20, Week 156: 10/5, Week 168: 0/0

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

Analysis population: A2304 SAF total population

Figure 12.1.5.89: SINUSITIS (PT, not severe)

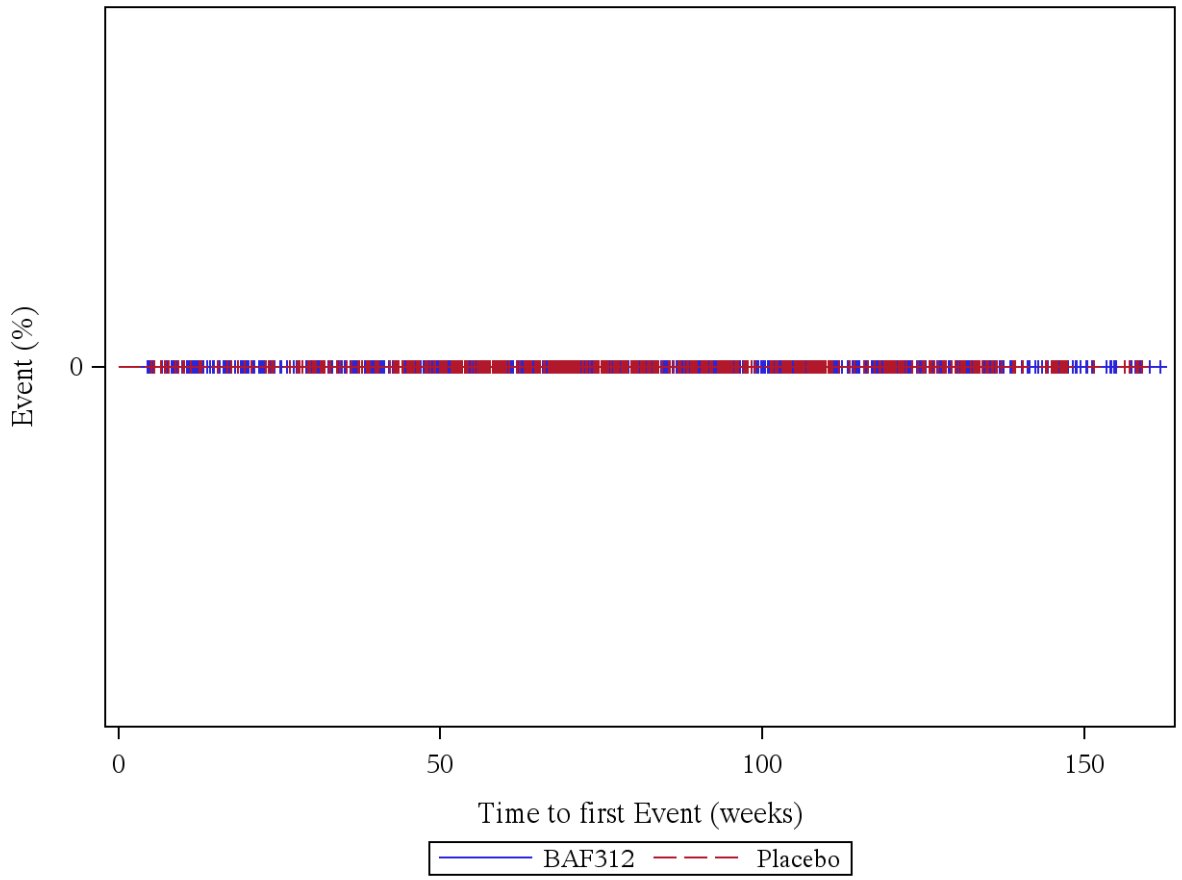


Patients at risk (BAF312/Placebo): Week 0: 1099/546, Week 4: 1097/546, Week 12: 1057/534, Week 24: 1008/520, Week 36: 981/495, Week 48: 916/457, Week 60: 806/385, Week 72: 640/303, Week 84: 506/235, Week 96: 392/175, Week 108: 282/125, Week 120: 195/79, Week 132: 110/39, Week 144: 50/19, Week 156: 9/4, Week 168: 0/0

Log rank test: p-value = 0,719
*: p < 0,05

Analysis population: A2304 SAF total population

Figure 12.1.5.90: SINUSITIS (PT, severe)

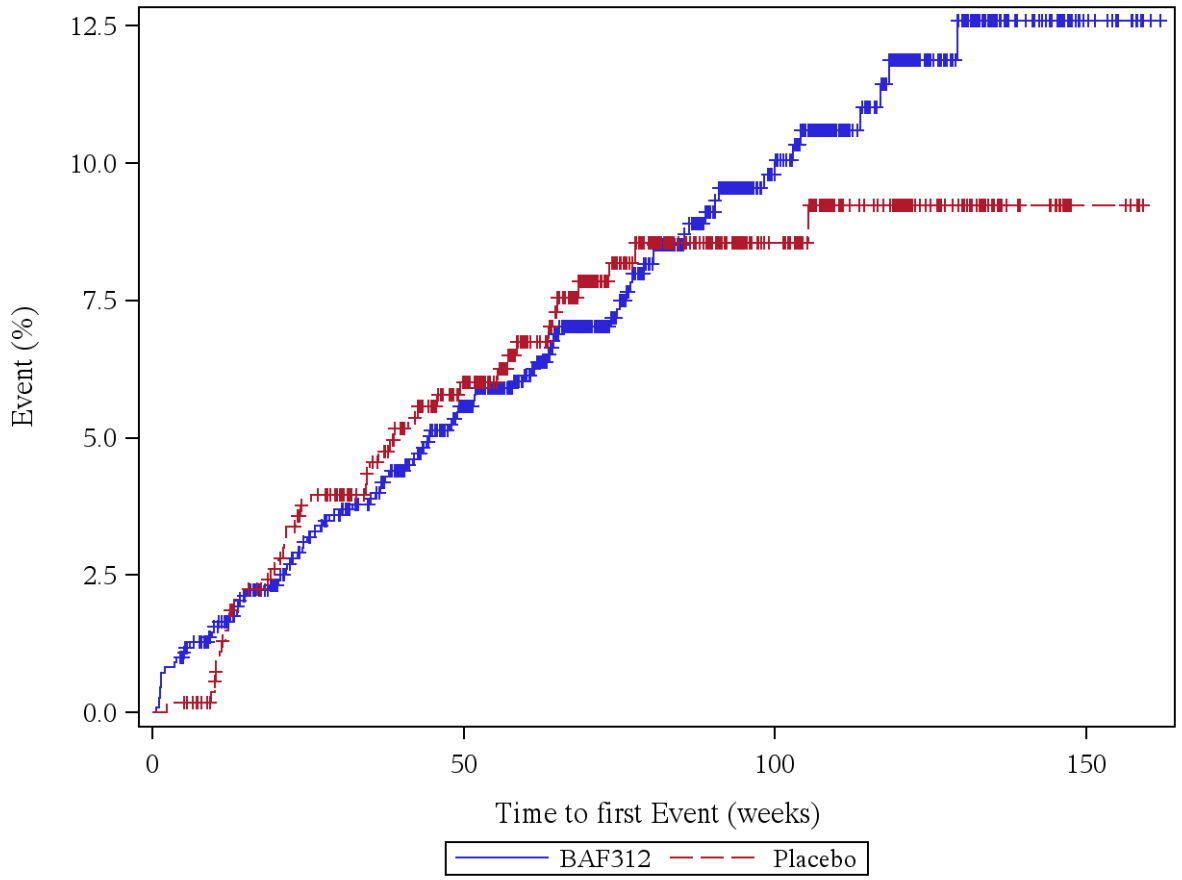


Patients at risk (BAF312/Placebo): Week 0: 1099/546, Week 4: 1099/546, Week 12: 1059/535, Week 24: 1017/521, Week 36: 990/497, Week 48: 925/461, Week 60: 818/388, Week 72: 652/305, Week 84: 516/237, Week 96: 400/176, Week 108: 291/126, Week 120: 200/80, Week 132: 113/40, Week 144: 51/20, Week 156: 10/5, Week 168: 0/0

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

Analysis population: A2304 SAF total population

Figure 12.1.5.91: UPPER RESPIRATORY TRACT INFECTION (PT, not severe)

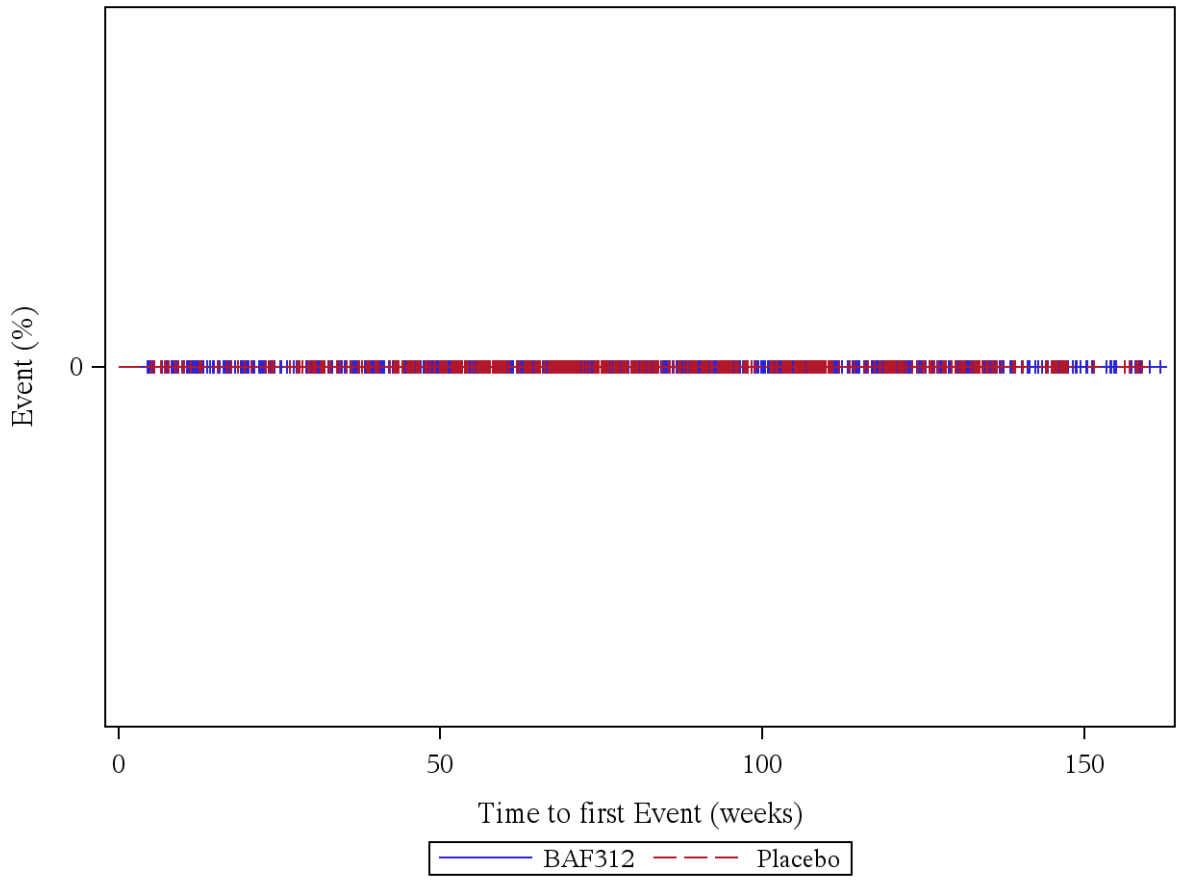


Patients at risk (BAF312/Placebo): Week 0: 1099/546, Week 4: 1088/545, Week 12: 1042/527, Week 24: 988/501, Week 36: 951/475, Week 48: 877/435, Week 60: 771/360, Week 72: 609/281, Week 84: 474/214, Week 96: 363/157, Week 108: 265/109, Week 120: 181/69, Week 132: 101/36, Week 144: 47/17, Week 156: 10/5, Week 168: 0/0

Log rank test: p-value = 0,682
*: p < 0,05

Analysis population: A2304 SAF total population

Figure 12.1.5.92: UPPER RESPIRATORY TRACT INFECTION (PT, severe)

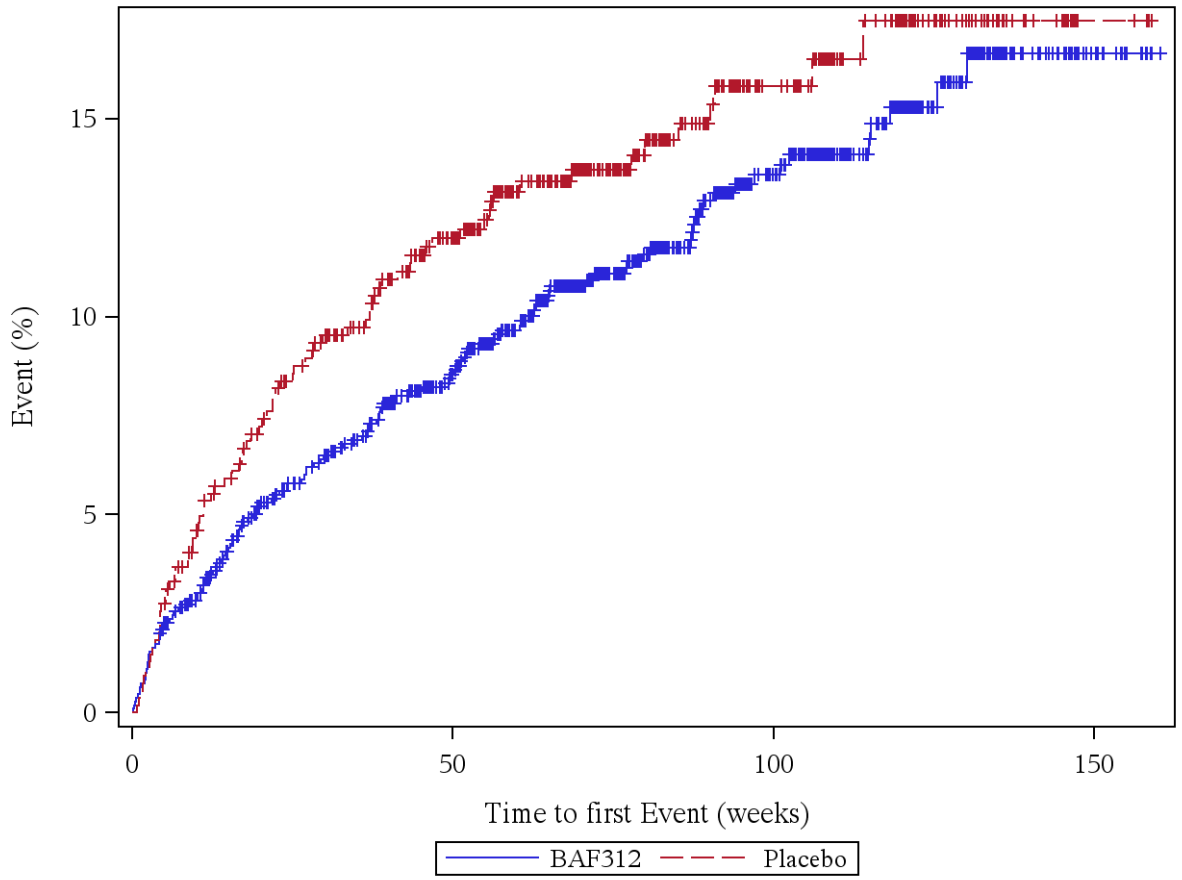


Patients at risk (BAF312/Placebo): Week 0: 1099/546, Week 4: 1099/546, Week 12: 1059/535, Week 24: 1017/521, Week 36: 990/497, Week 48: 925/461, Week 60: 818/388, Week 72: 652/305, Week 84: 516/237, Week 96: 400/176, Week 108: 291/126, Week 120: 200/80, Week 132: 113/40, Week 144: 51/20, Week 156: 10/5, Week 168: 0/0

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

Analysis population: A2304 SAF total population

Figure 12.1.5.93: URINARY TRACT INFECTION (PT, not severe)

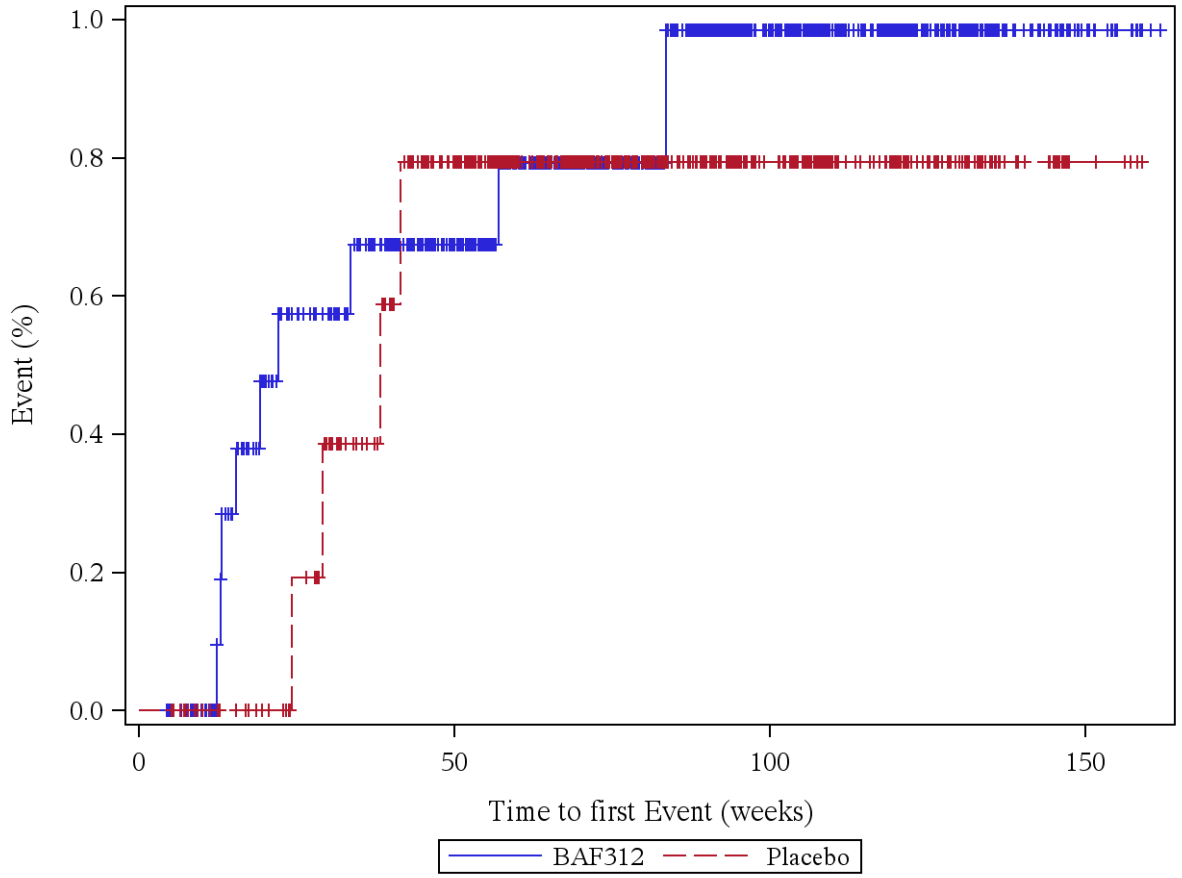


Patients at risk (BAF312/Placebo): Week 0: 1099/546, Week 4: 1080/536, Week 12: 1024/506, Week 24: 961/477, Week 36: 923/452, Week 48: 854/409, Week 60: 746/341, Week 72: 597/264, Week 84: 470/199, Week 96: 365/145, Week 108: 267/107, Week 120: 182/68, Week 132: 101/33, Week 144: 43/16, Week 156: 8/4, Week 168: 0/0

Log rank test: p-value = 0,137
*: p < 0,05

Analysis population: A2304 SAF total population

Figure 12.1.5.94: URINARY TRACT INFECTION (PT, severe)

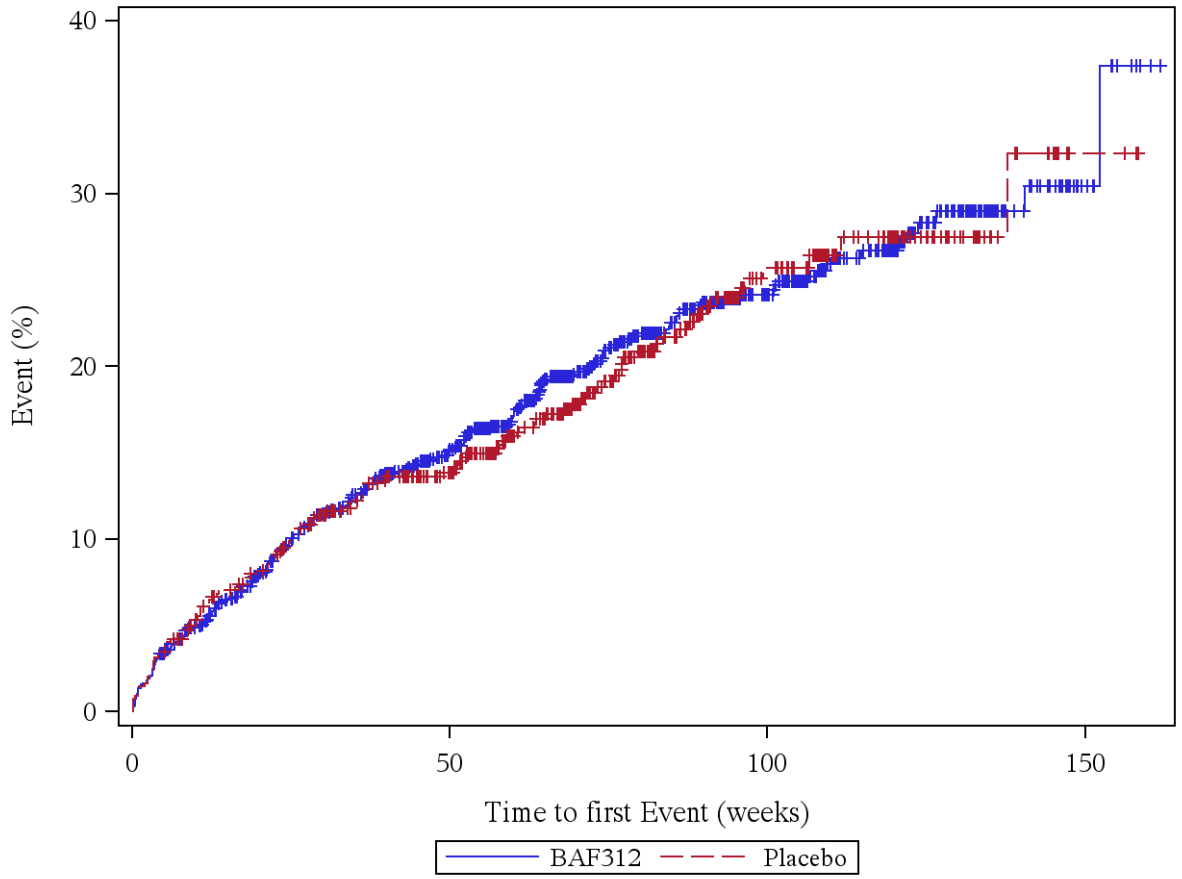


Patients at risk (BAF312/Placebo): Week 0: 1099/546, Week 4: 1099/546, Week 12: 1059/535, Week 24: 1012/521, Week 36: 984/496, Week 48: 921/458, Week 60: 814/387, Week 72: 648/304, Week 84: 512/236, Week 96: 397/175, Week 108: 288/125, Week 120: 198/79, Week 132: 111/39, Week 144: 50/19, Week 156: 10/4, Week 168: 0/0

Log rank test: p-value = 0,838
*: p < 0,05

Analysis population: A2304 SAF total population

Figure 12.1.5.95: INJURY, POISONING AND PROCEDURAL COMPLICATIONS (SOC, not severe)

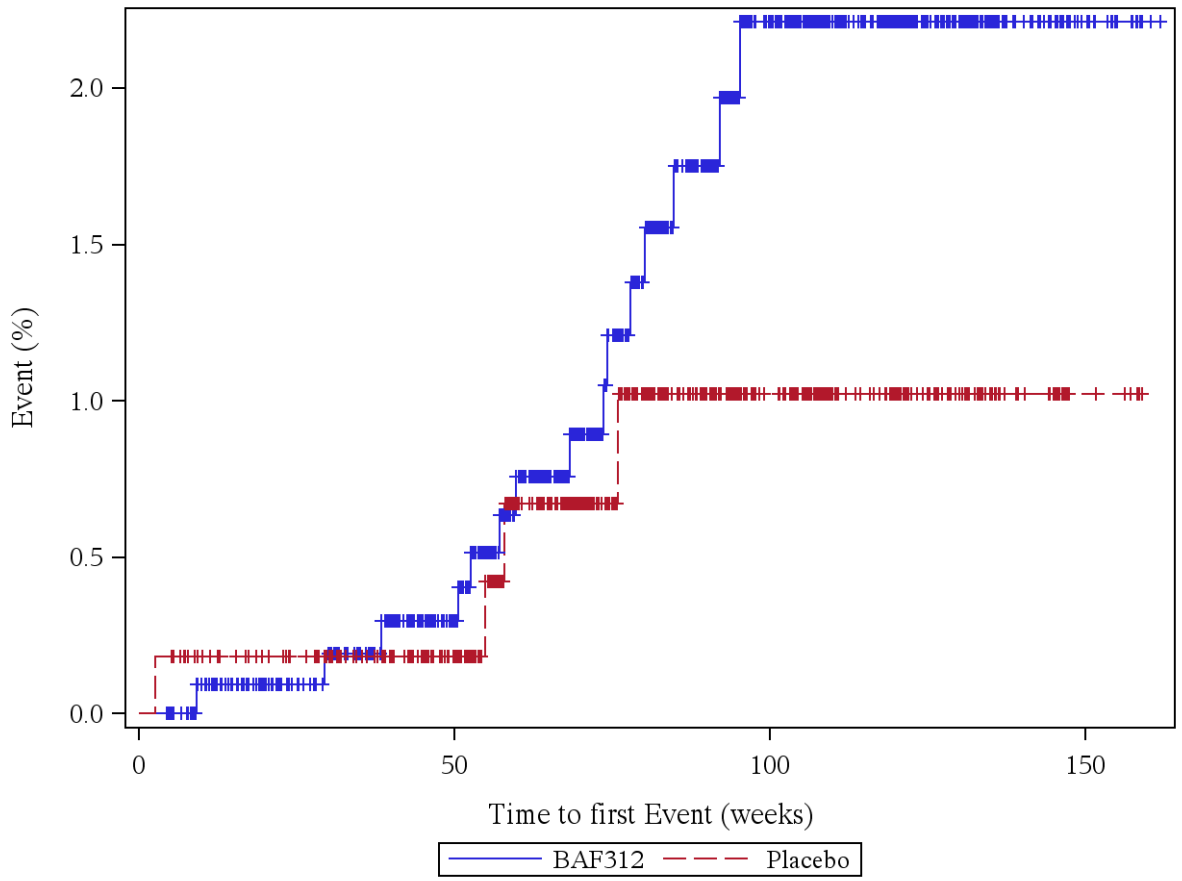


Patients at risk (BAF312/Placebo): Week 0: 1099/546, Week 4: 1065/529, Week 12: 1000/502, Week 24: 920/473, Week 36: 863/435, Week 48: 787/401, Week 60: 678/331, Week 72: 521/252, Week 84: 404/186, Week 96: 317/131, Week 108: 227/89, Week 120: 152/53, Week 132: 87/26, Week 144: 40/12, Week 156: 6/3, Week 168: 0/0

Log rank test: p-value = 0,803
*: p < 0,05

Analysis population: A2304 SAF total population

Figure 12.1.5.96: INJURY, POISONING AND PROCEDURAL COMPLICATIONS (SOC, severe)

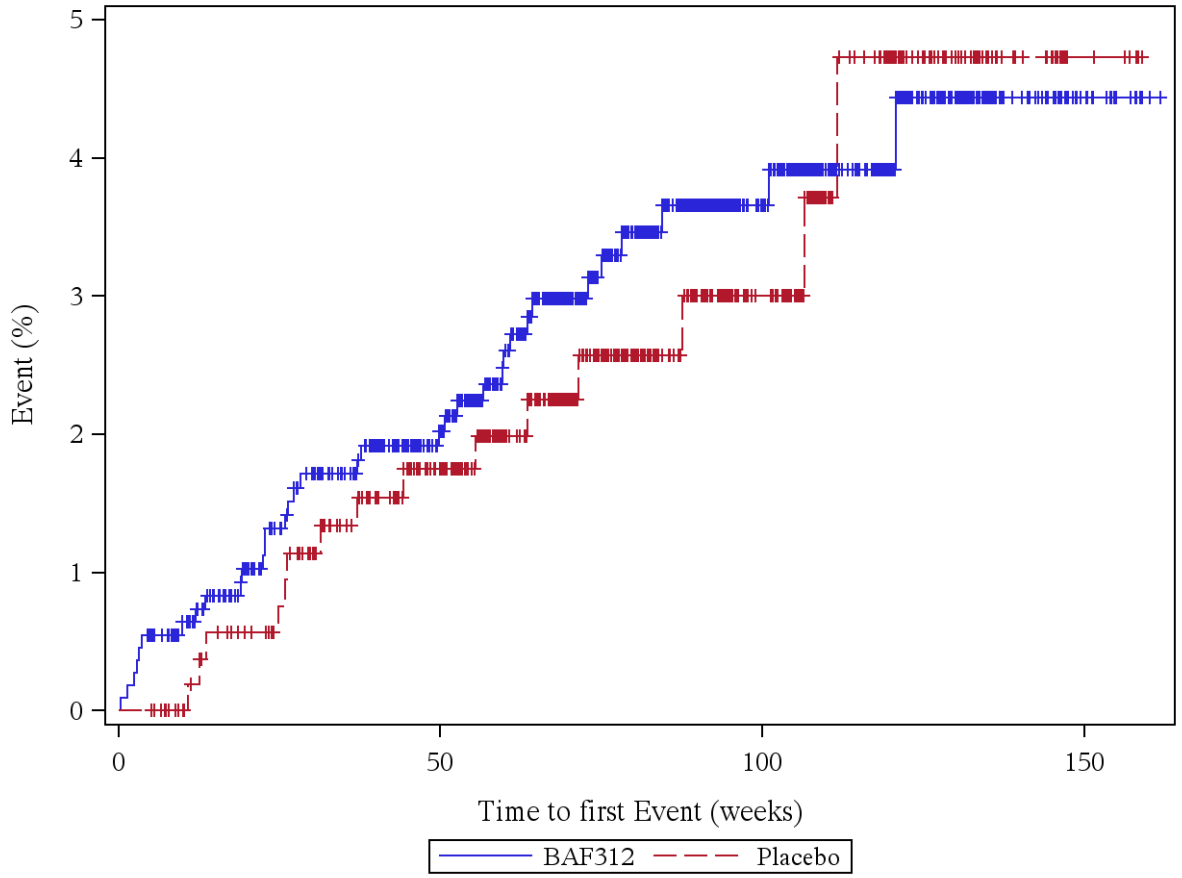


Patients at risk (BAF312/Placebo): Week 0: 1099/546, Week 4: 1099/545, Week 12: 1058/534, Week 24: 1016/520, Week 36: 988/496, Week 48: 922/460, Week 60: 812/386, Week 72: 647/304, Week 84: 507/236, Week 96: 393/175, Week 108: 288/125, Week 120: 198/80, Week 132: 112/40, Week 144: 50/20, Week 156: 10/5, Week 168: 0/0

Log rank test: p-value = 0,290
*: p < 0,05

Analysis population: A2304 SAF total population

Figure 12.1.5.97: CONTUSION (PT, not severe)

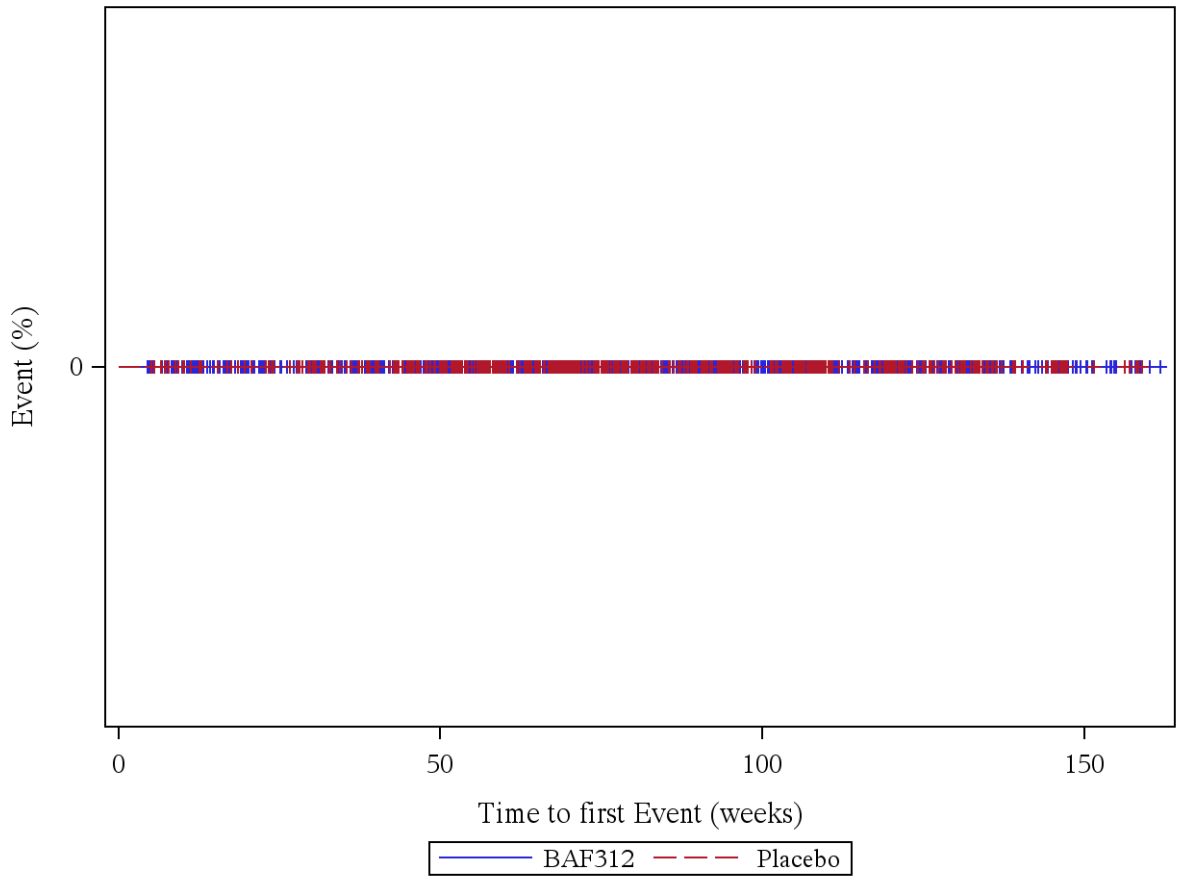


Patients at risk (BAF312/Placebo): Week 0: 1099/546, Week 4: 1093/546, Week 12: 1051/534, Week 24: 1005/518, Week 36: 975/490, Week 48: 910/454, Week 60: 800/383, Week 72: 635/300, Week 84: 501/232, Week 96: 390/170, Week 108: 282/120, Week 120: 193/74, Week 132: 109/38, Week 144: 50/19, Week 156: 9/5, Week 168: 0/0

Log rank test: p-value = 0,663
*: p < 0,05

Analysis population: A2304 SAF total population

Figure 12.1.5.98: CONTUSION (PT, severe)

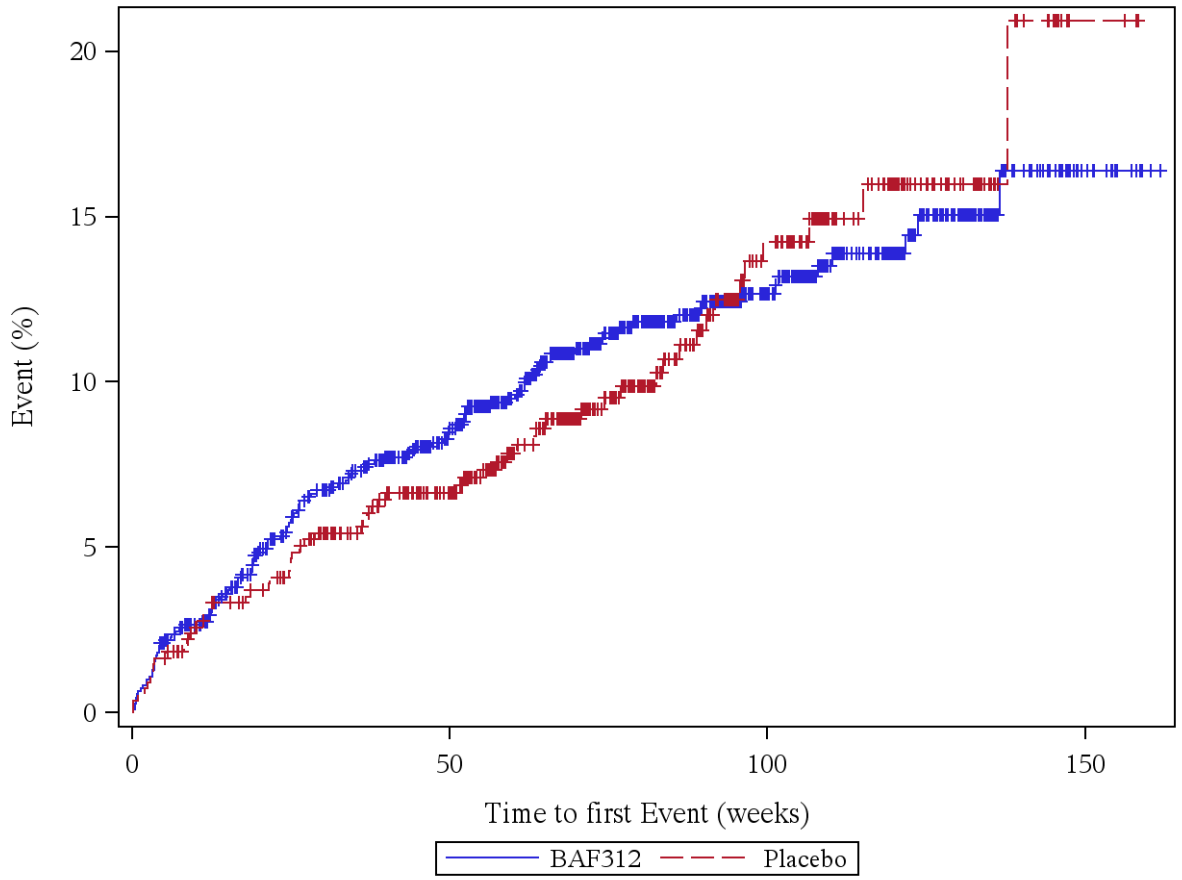


Patients at risk (BAF312/Placebo): Week 0: 1099/546, Week 4: 1099/546, Week 12: 1059/535, Week 24: 1017/521, Week 36: 990/497, Week 48: 925/461, Week 60: 818/388, Week 72: 652/305, Week 84: 516/237, Week 96: 400/176, Week 108: 291/126, Week 120: 200/80, Week 132: 113/40, Week 144: 51/20, Week 156: 10/5, Week 168: 0/0

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

Analysis population: A2304 SAF total population

Figure 12.1.5.99: FALL (PT, not severe)

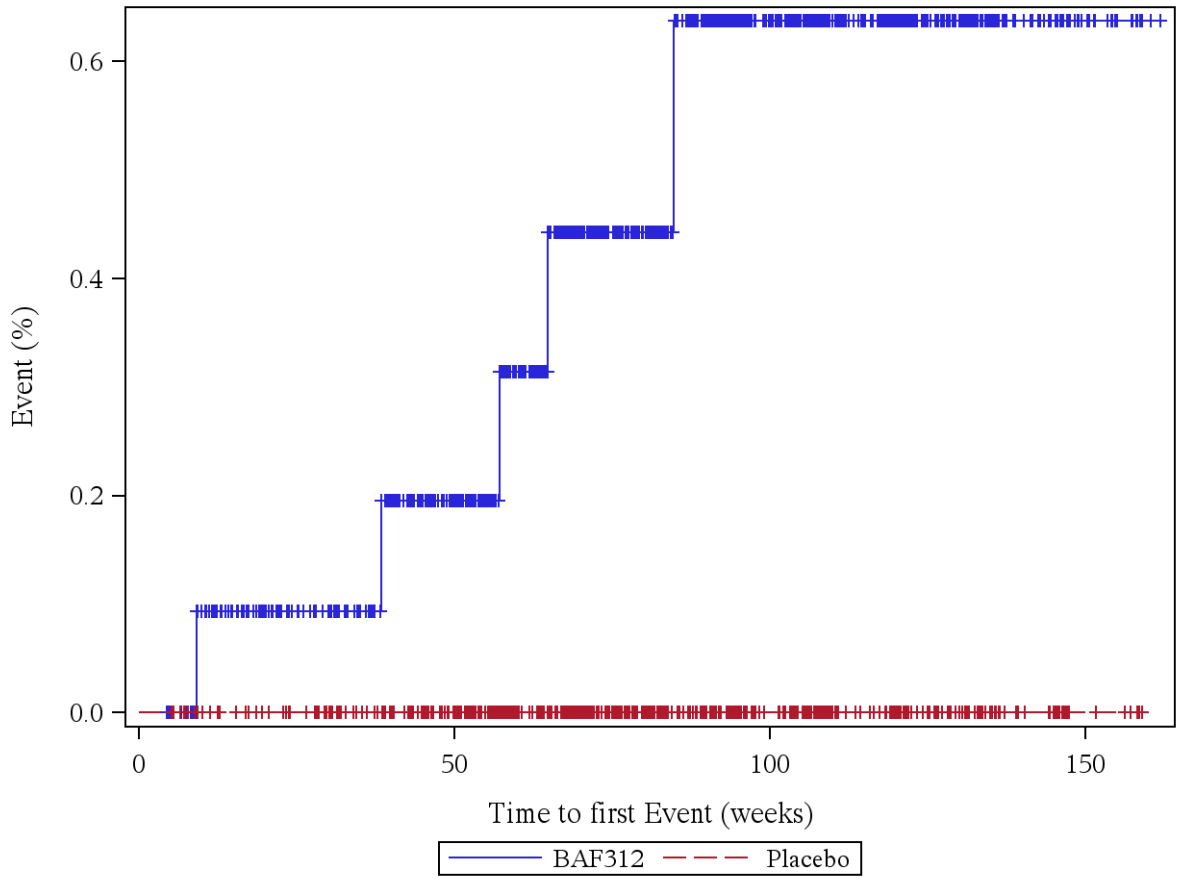


Patients at risk (BAF312/Placebo): Week 0: 1099/546, Week 4: 1079/537, Week 12: 1028/519, Week 24: 963/500, Week 36: 917/469, Week 48: 849/433, Week 60: 742/361, Week 72: 581/280, Week 84: 459/212, Week 96: 360/153, Week 108: 260/106, Week 120: 178/63, Week 132: 100/32, Week 144: 44/13, Week 156: 8/3, Week 168: 0/0

Log rank test: p-value = 0,792
*: p < 0,05

Analysis population: A2304 SAF total population

Figure 12.1.5.100: FALL (PT, severe)

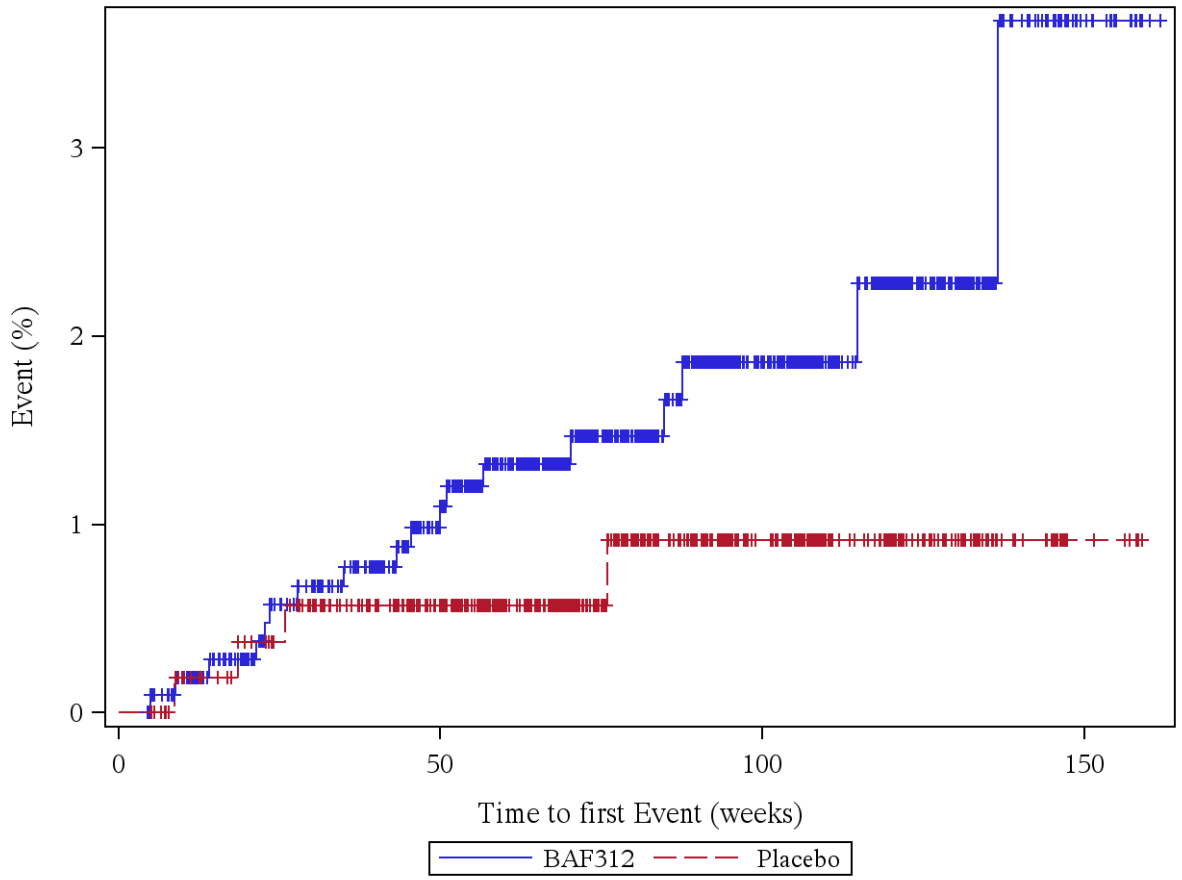


Patients at risk (BAF312/Placebo): Week 0: 1099/546, Week 4: 1099/546, Week 12: 1058/535, Week 24: 1016/521, Week 36: 989/497, Week 48: 923/461, Week 60: 815/388, Week 72: 649/305, Week 84: 513/237, Week 96: 398/176, Week 108: 290/126, Week 120: 199/80, Week 132: 113/40, Week 144: 51/20, Week 156: 10/5, Week 168: 0/0

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

Analysis population: A2304 SAF total population

Figure 12.1.5.101: LACERATION (PT, not severe)

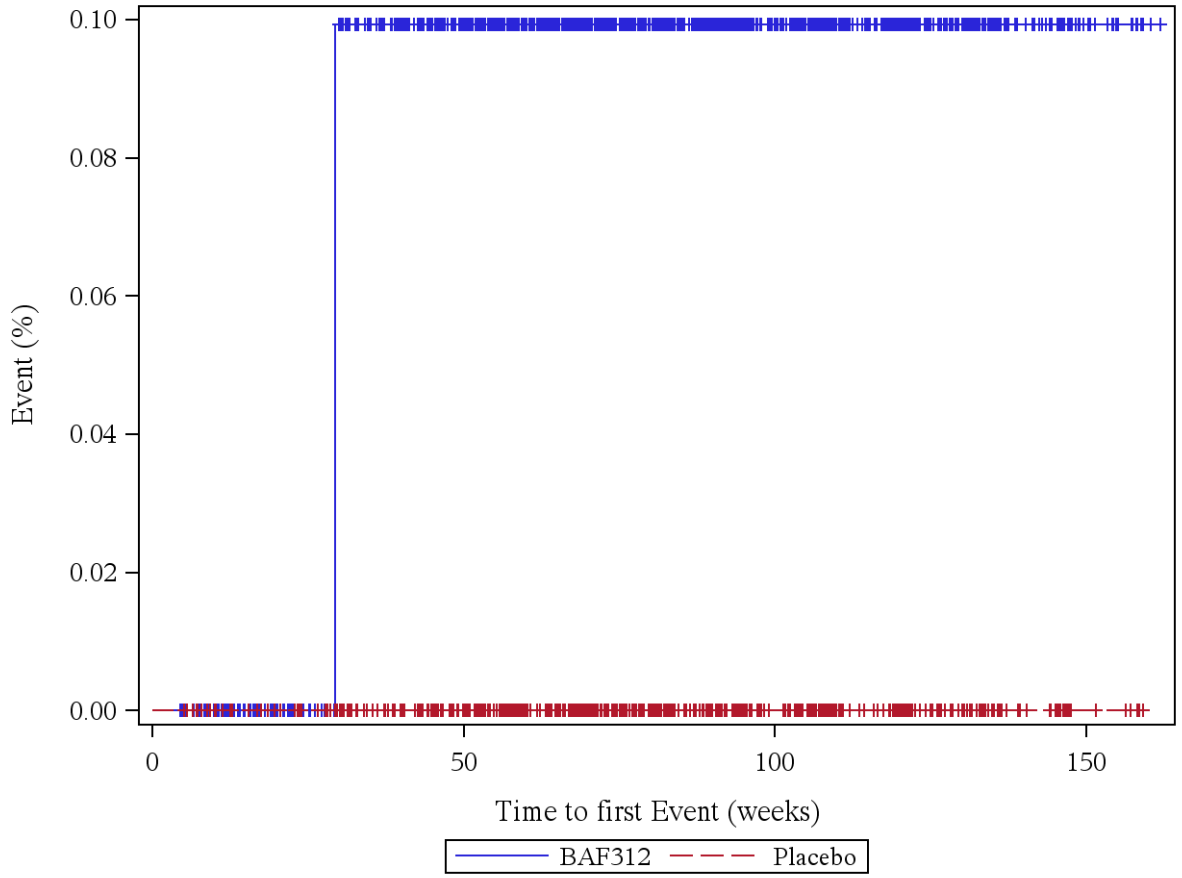


Patients at risk (BAF312/Placebo): Week 0: 1099/546, Week 4: 1099/546, Week 12: 1057/534, Week 24: 1011/519, Week 36: 982/494, Week 48: 915/458, Week 60: 806/386, Week 72: 642/304, Week 84: 507/236, Week 96: 394/176, Week 108: 287/126, Week 120: 195/80, Week 132: 110/40, Week 144: 49/20, Week 156: 9/5, Week 168: 0/0

Log rank test: p-value = 0,147
*: p < 0,05

Analysis population: A2304 SAF total population

Figure 12.1.5.102: LACERATION (PT, severe)

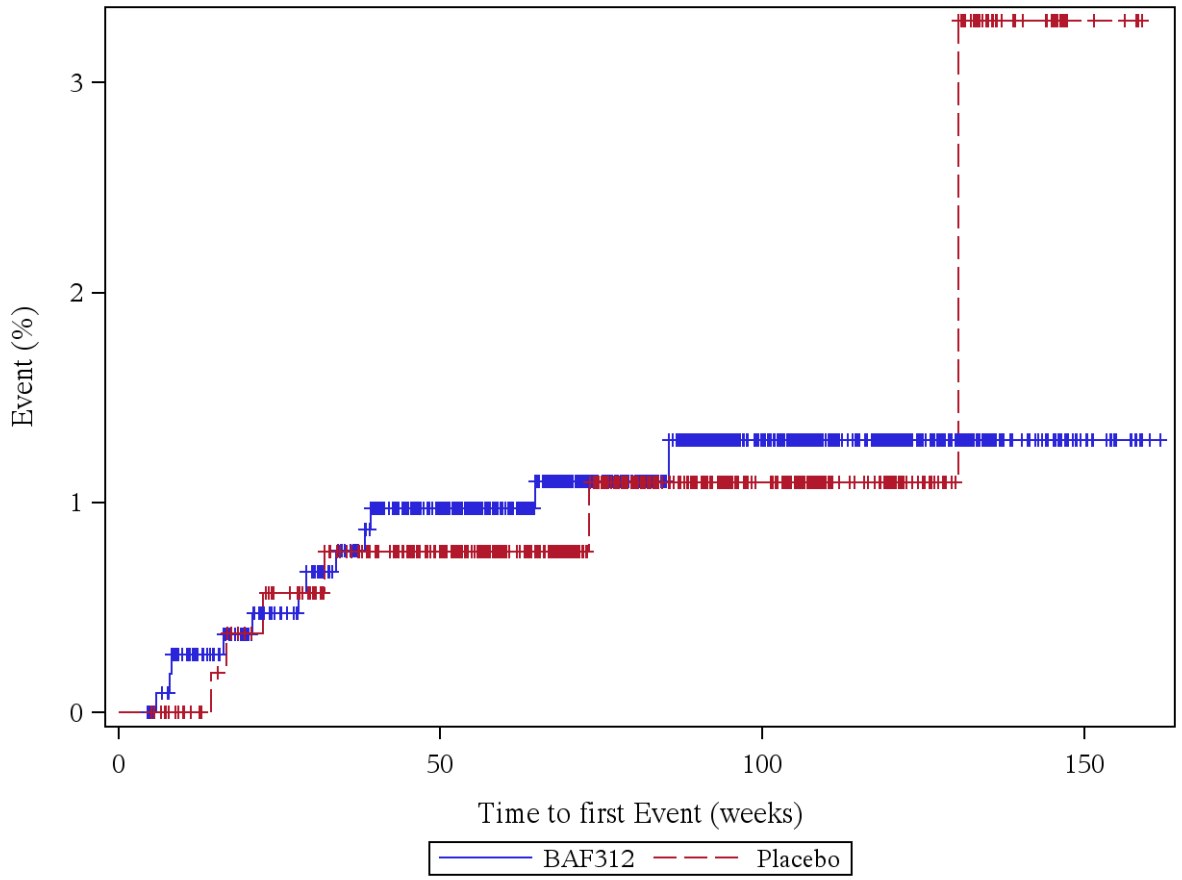


Patients at risk (BAF312/Placebo): Week 0: 1099/546, Week 4: 1099/546, Week 12: 1059/535, Week 24: 1017/521, Week 36: 989/497, Week 48: 924/461, Week 60: 817/388, Week 72: 651/305, Week 84: 515/237, Week 96: 400/176, Week 108: 291/126, Week 120: 200/80, Week 132: 113/40, Week 144: 51/20, Week 156: 10/5, Week 168: 0/0

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

Analysis population: A2304 SAF total population

Figure 12.1.5.103: LIGAMENT SPRAIN (PT, not severe)

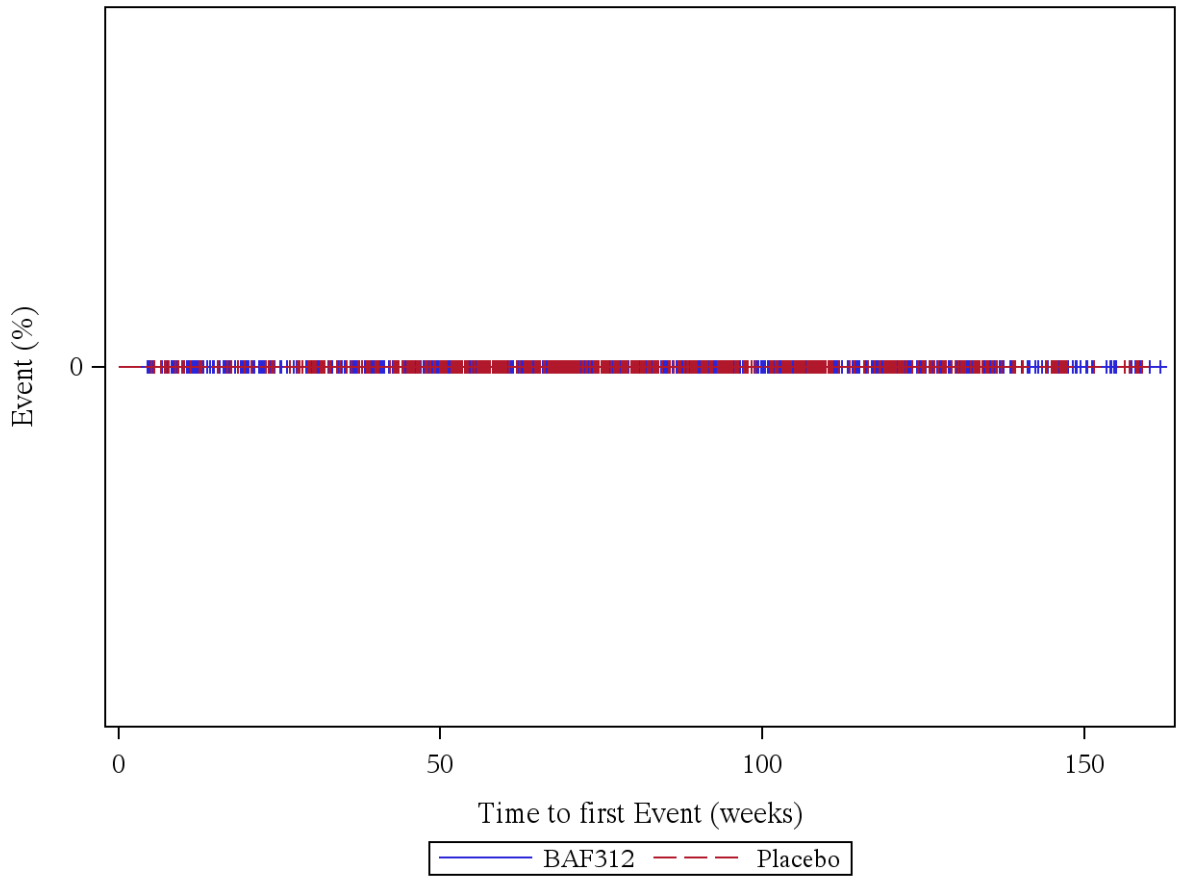


Patients at risk (BAF312/Placebo): Week 0: 1099/546, Week 4: 1099/546, Week 12: 1056/535, Week 24: 1012/518, Week 36: 982/493, Week 48: 916/457, Week 60: 810/384, Week 72: 644/303, Week 84: 510/234, Week 96: 395/173, Week 108: 289/123, Week 120: 198/78, Week 132: 112/39, Week 144: 50/19, Week 156: 9/4, Week 168: 0/0

Log rank test: p-value = 0,972
*: p < 0,05

Analysis population: A2304 SAF total population

Figure 12.1.5.104: LIGAMENT SPRAIN (PT, severe)

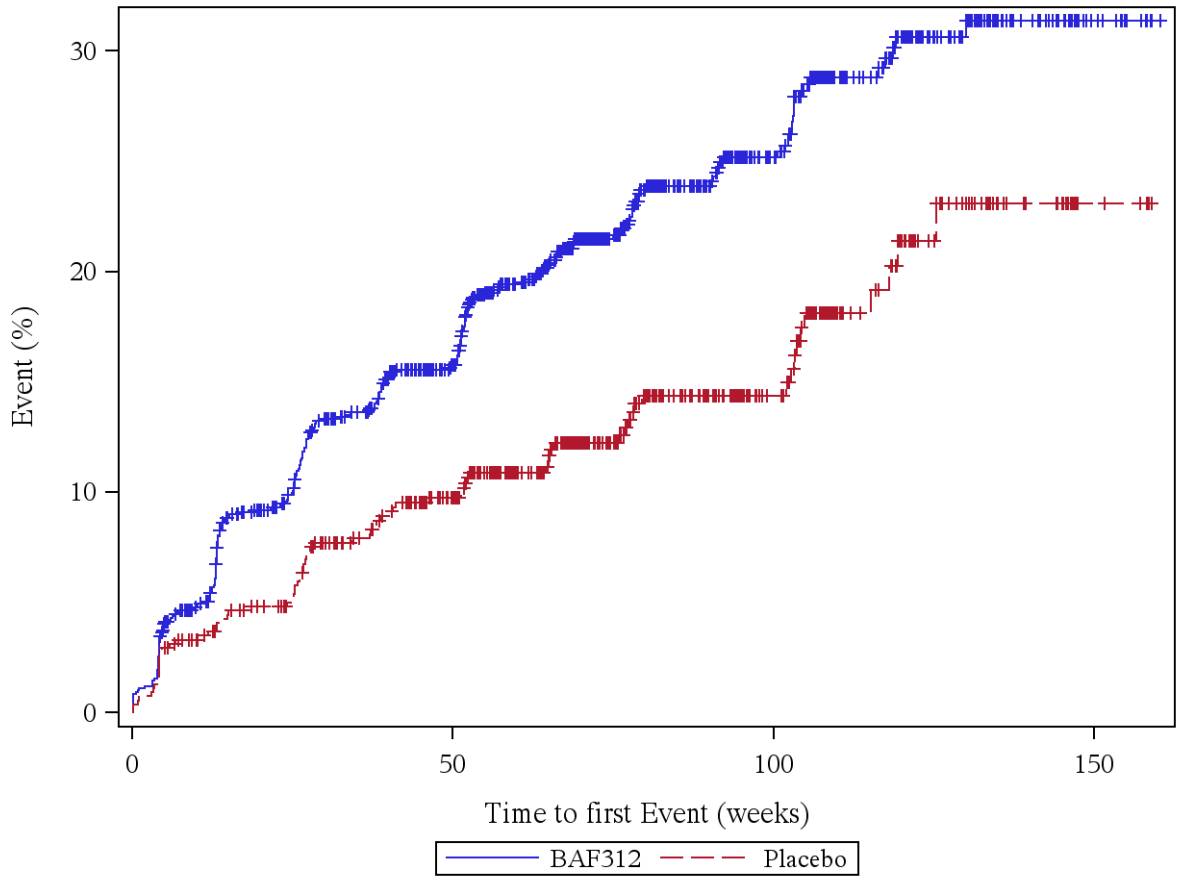


Patients at risk (BAF312/Placebo): Week 0: 1099/546, Week 4: 1099/546, Week 12: 1059/535, Week 24: 1017/521, Week 36: 990/497, Week 48: 925/461, Week 60: 818/388, Week 72: 652/305, Week 84: 516/237, Week 96: 400/176, Week 108: 291/126, Week 120: 200/80, Week 132: 113/40, Week 144: 51/20, Week 156: 10/5, Week 168: 0/0

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

Analysis population: A2304 SAF total population

Figure 12.1.5.105: INVESTIGATIONS (SOC, not severe)

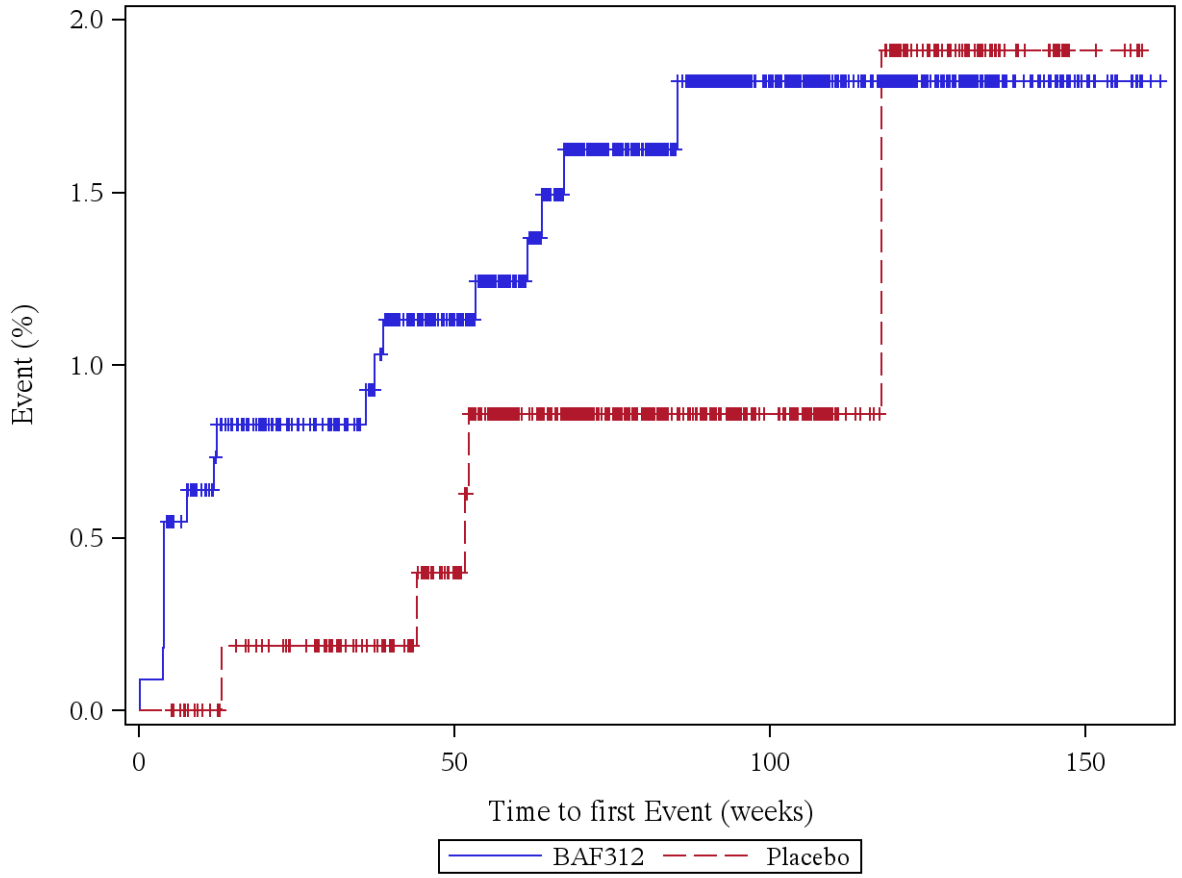


Patients at risk (BAF312/Placebo): Week 0: 1099/546, Week 4: 1071/538, Week 12: 1008/515, Week 24: 925/495, Week 36: 862/458, Week 48: 788/419, Week 60: 660/349, Week 72: 503/269, Week 84: 385/203, Week 96: 294/155, Week 108: 202/105, Week 120: 135/60, Week 132: 79/31, Week 144: 35/17, Week 156: 8/4, Week 168: 0/0

Log rank test: p-value = <0,001 *
*: p < 0,05

Analysis population: A2304 SAF total population

Figure 12.1.5.106: INVESTIGATIONS (SOC, severe)

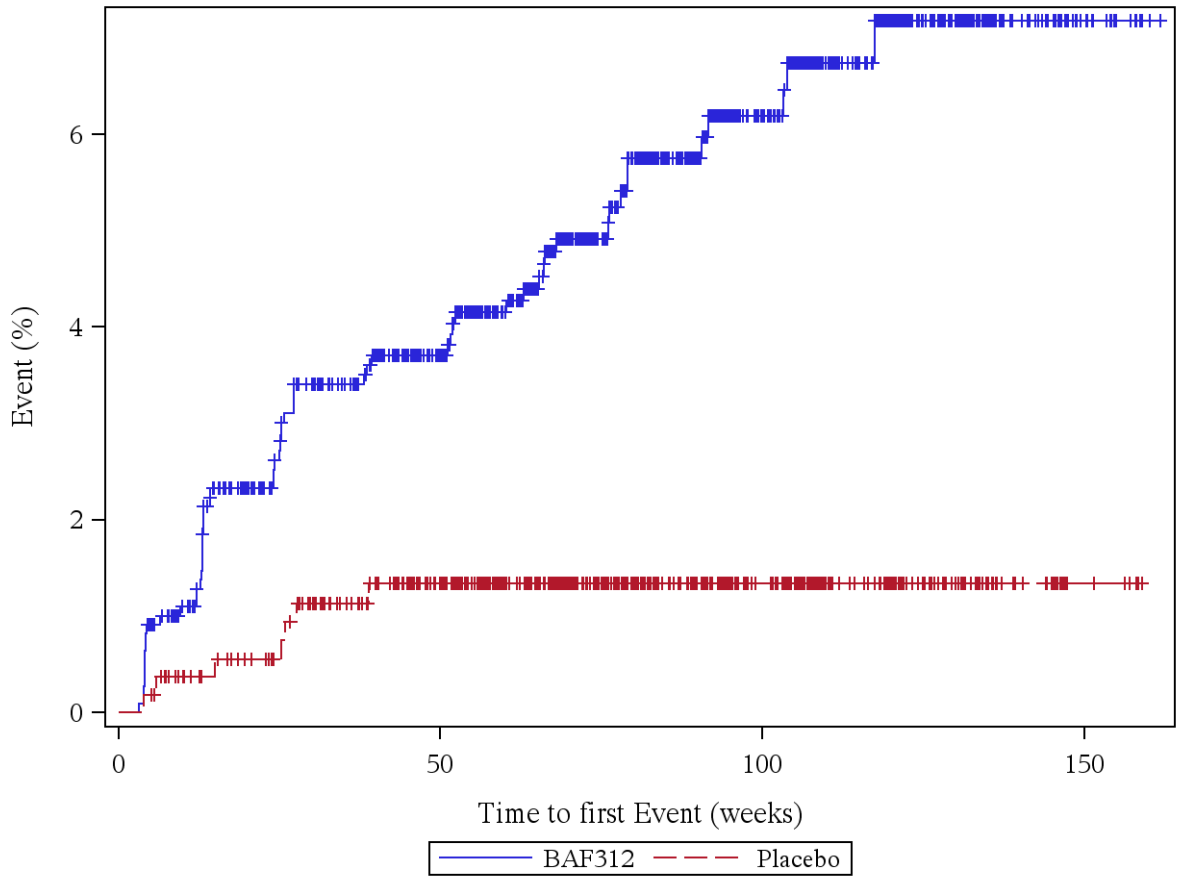


Patients at risk (BAF312/Placebo): Week 0: 1099/546, Week 4: 1093/546, Week 12: 1053/535, Week 24: 1011/520, Week 36: 983/496, Week 48: 916/459, Week 60: 812/386, Week 72: 644/304, Week 84: 509/237, Week 96: 395/176, Week 108: 288/126, Week 120: 200/79, Week 132: 113/40, Week 144: 51/20, Week 156: 10/5, Week 168: 0/0

Log rank test: p-value = 0,309
*: p < 0,05

Analysis population: A2304 SAF total population

Figure 12.1.5.107: ALANINE AMINOTRANSFERASE INCREASED (PT, not severe)

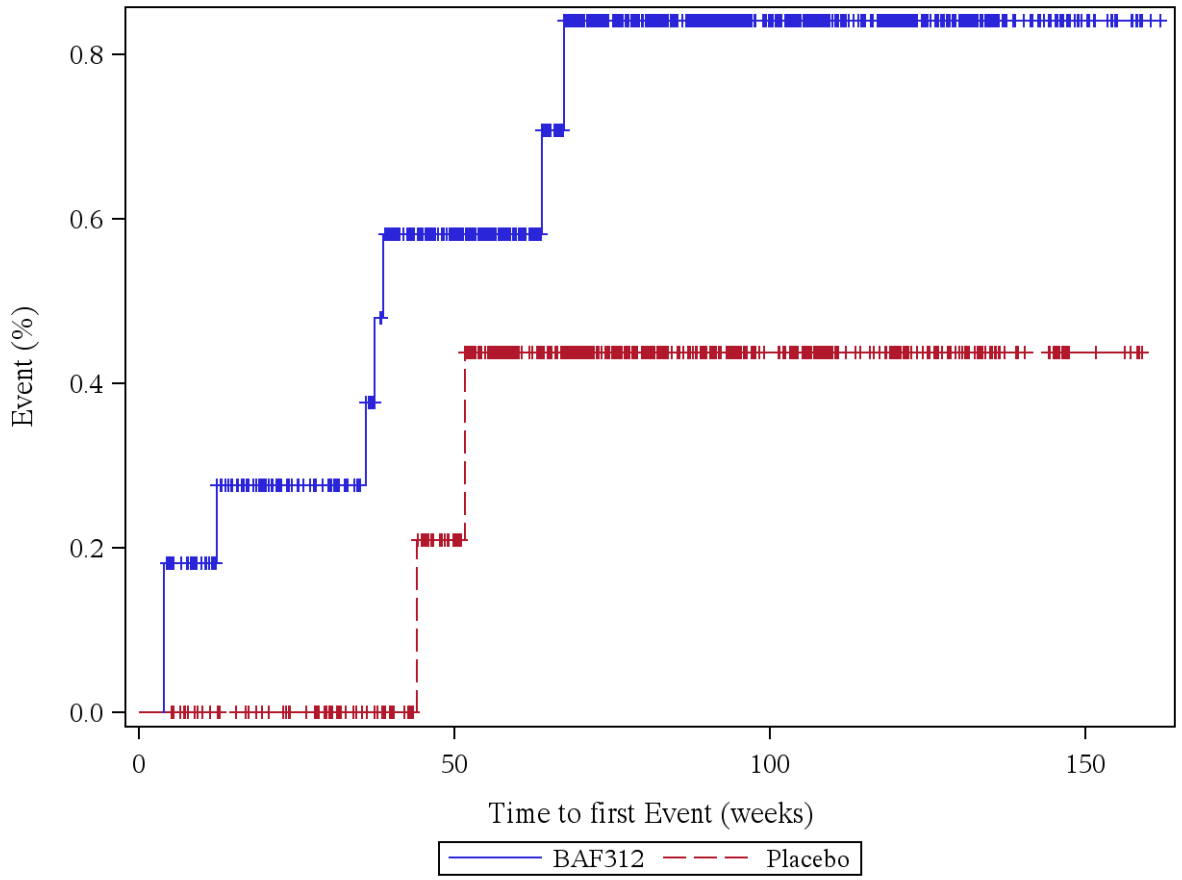


Patients at risk (BAF312/Placebo): Week 0: 1099/546, Week 4: 1092/545, Week 12: 1049/533, Week 24: 996/518, Week 36: 961/492, Week 48: 893/455, Week 60: 787/383, Week 72: 622/301, Week 84: 486/233, Week 96: 375/175, Week 108: 269/125, Week 120: 186/79, Week 132: 107/39, Week 144: 47/20, Week 156: 9/5, Week 168: 0/0

Log rank test: p-value = <0,001 *
*: p < 0,05

Analysis population: A2304 SAF total population

Figure 12.1.5.108: ALANINE AMINOTRANSFERASE INCREASED (PT, severe)

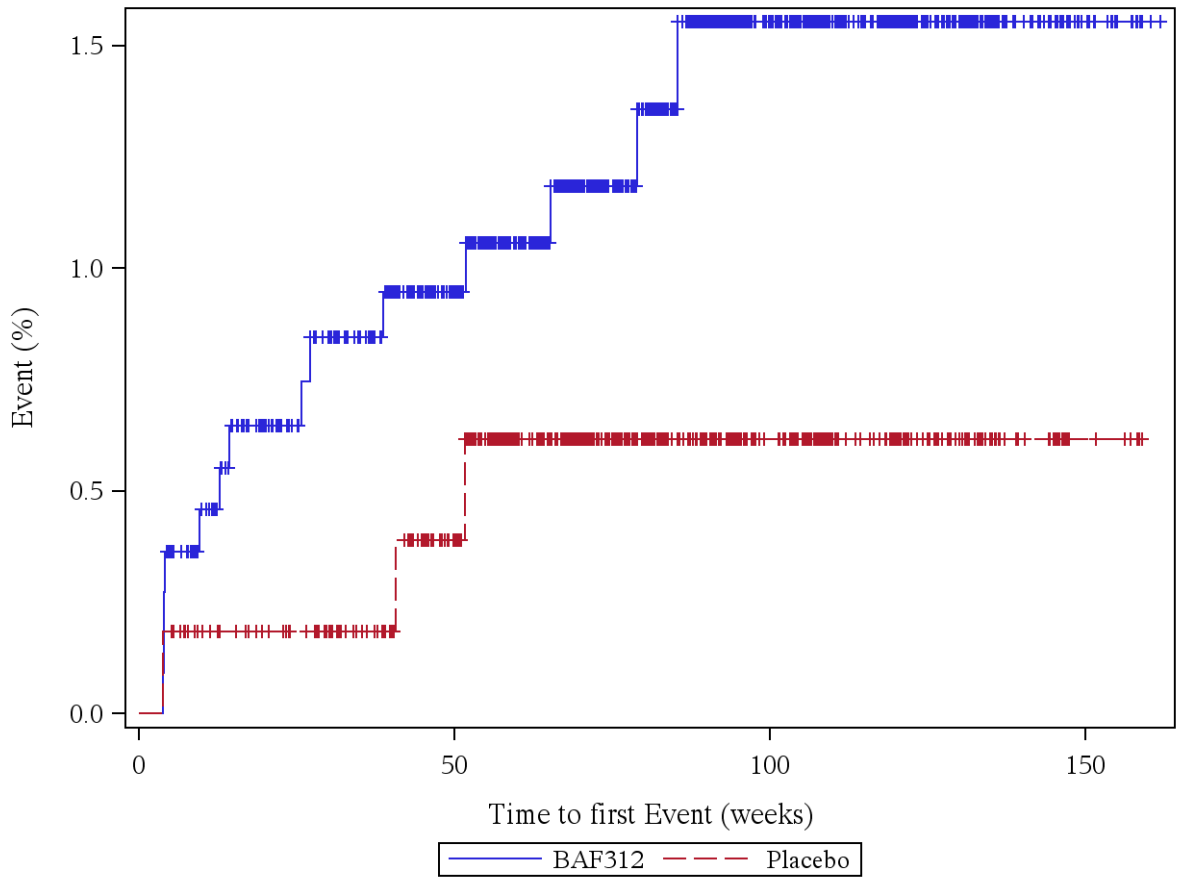


Patients at risk (BAF312/Placebo): Week 0: 1099/546, Week 4: 1097/546, Week 12: 1058/535, Week 24: 1015/521, Week 36: 987/497, Week 48: 920/460, Week 60: 813/387, Week 72: 645/305, Week 84: 510/237, Week 96: 395/176, Week 108: 288/126, Week 120: 200/80, Week 132: 113/40, Week 144: 51/20, Week 156: 10/5, Week 168: 0/0

Log rank test: p-value = 0,377
*: p < 0,05

Analysis population: A2304 SAF total population

Figure 12.1.5.109: ASPARTATE AMINOTRANSFERASE INCREASED (PT, not severe)

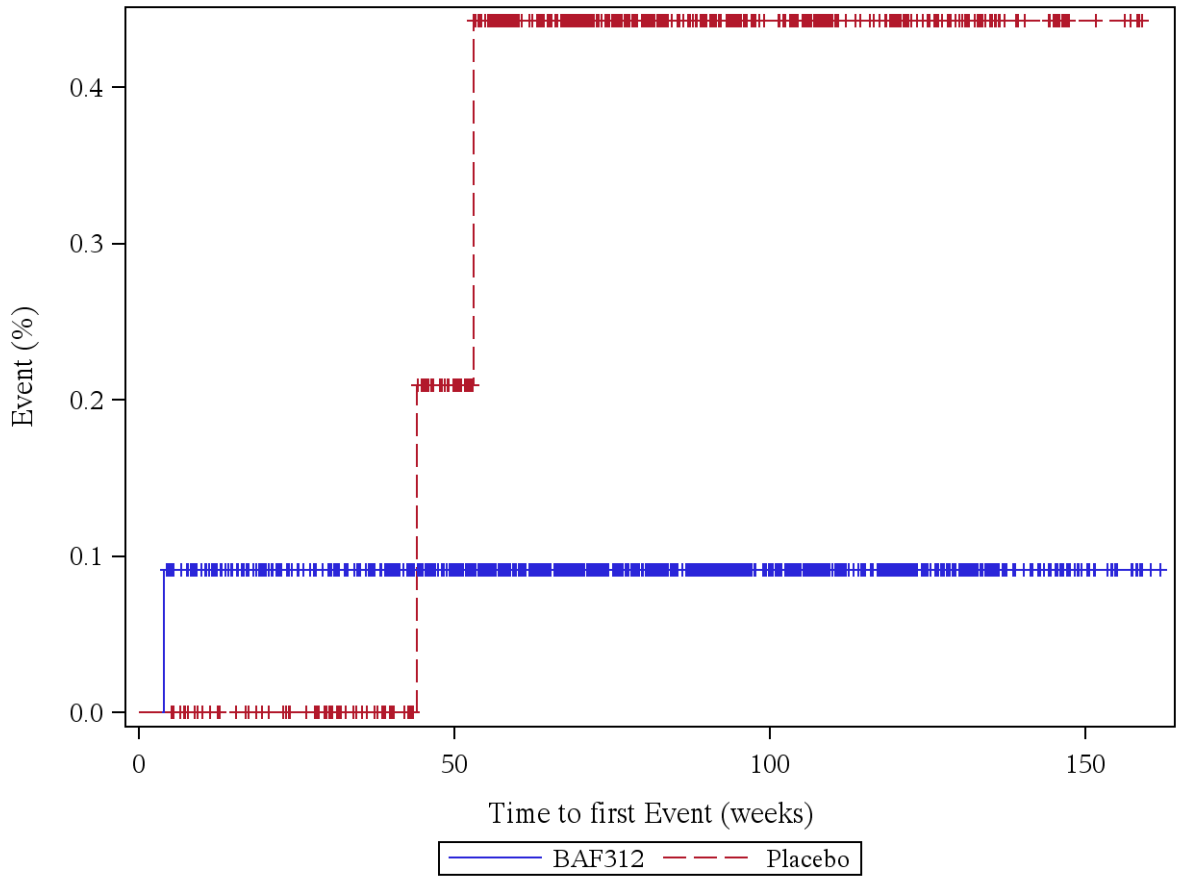


Patients at risk (BAF312/Placebo): Week 0: 1099/546, Week 4: 1096/545, Week 12: 1055/534, Week 24: 1012/520, Week 36: 985/497, Week 48: 919/460, Week 60: 812/387, Week 72: 646/304, Week 84: 509/236, Week 96: 394/175, Week 108: 287/125, Week 120: 197/79, Week 132: 113/40, Week 144: 51/20, Week 156: 10/5, Week 168: 0/0

Log rank test: p-value = 0,175
*: p < 0,05

Analysis population: A2304 SAF total population

Figure 12.1.5.110: ASPARTATE AMINOTRANSFERASE INCREASED (PT, severe)

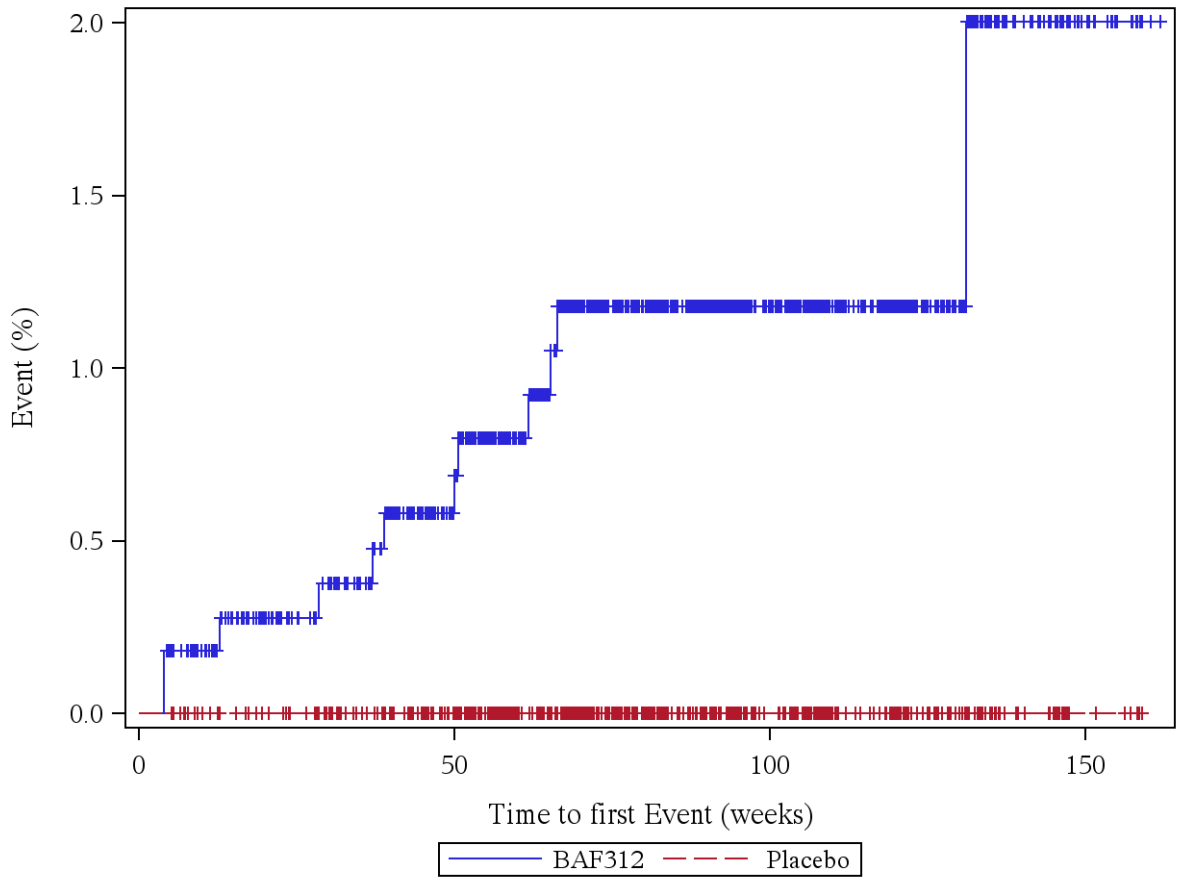


Patients at risk (BAF312/Placebo): Week 0: 1099/546, Week 4: 1098/546, Week 12: 1059/535, Week 24: 1017/521, Week 36: 990/497, Week 48: 925/460, Week 60: 818/387, Week 72: 652/305, Week 84: 516/237, Week 96: 400/176, Week 108: 291/126, Week 120: 200/80, Week 132: 113/40, Week 144: 51/20, Week 156: 10/5, Week 168: 0/0

Log rank test: p-value = 0,215
*: p < 0,05

Analysis population: A2304 SAF total population

Figure 12.1.5.111: BLOOD ALKALINE PHOSPHATASE INCREASED (PT, not severe)

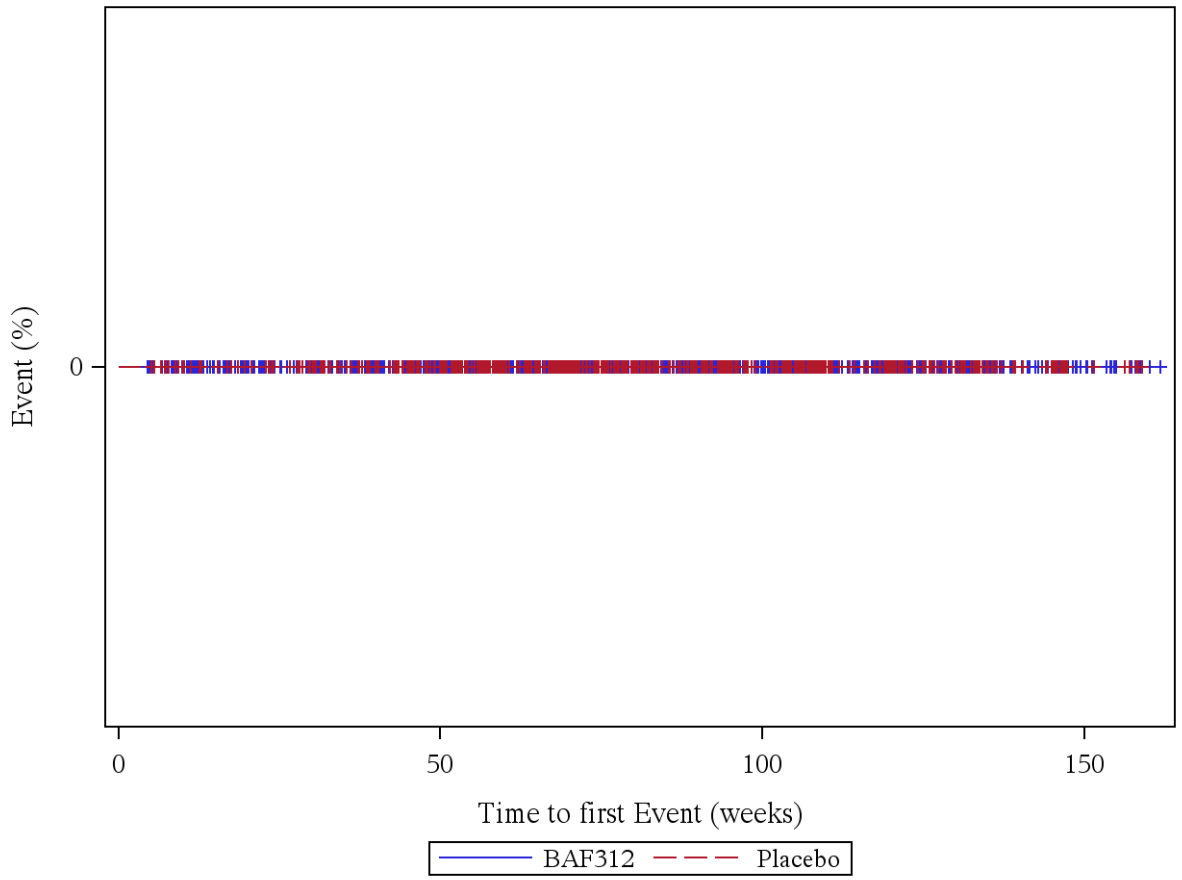


Patients at risk (BAF312/Placebo): Week 0: 1099/546, Week 4: 1097/546, Week 12: 1057/535, Week 24: 1014/521, Week 36: 987/497, Week 48: 920/461, Week 60: 812/388, Week 72: 645/305, Week 84: 511/237, Week 96: 395/176, Week 108: 289/126, Week 120: 198/80, Week 132: 111/40, Week 144: 50/20, Week 156: 10/5, Week 168: 0/0

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

Analysis population: A2304 SAF total population

Figure 12.1.5.112: BLOOD ALKALINE PHOSPHATASE INCREASED (PT, severe)

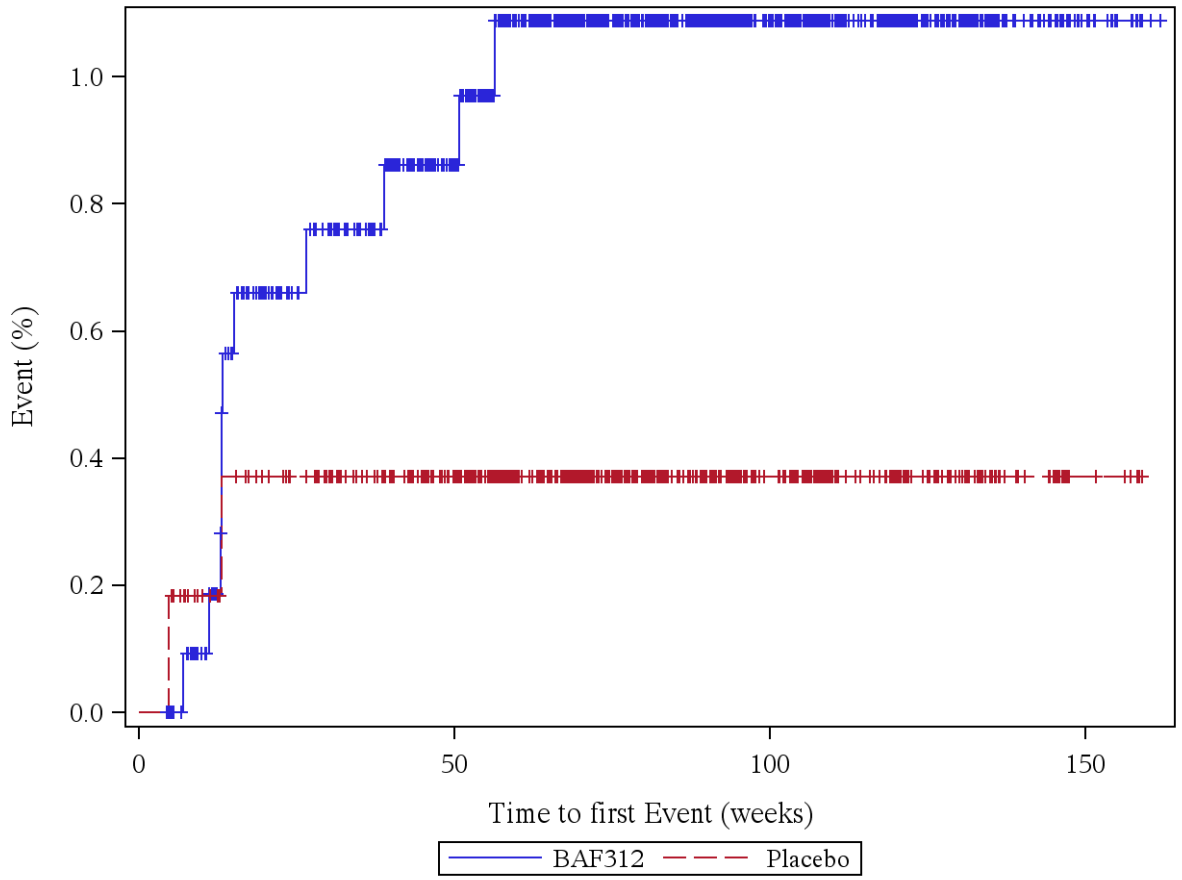


Patients at risk (BAF312/Placebo): Week 0: 1099/546, Week 4: 1099/546, Week 12: 1059/535, Week 24: 1017/521, Week 36: 990/497, Week 48: 925/461, Week 60: 818/388, Week 72: 652/305, Week 84: 516/237, Week 96: 400/176, Week 108: 291/126, Week 120: 200/80, Week 132: 113/40, Week 144: 51/20, Week 156: 10/5, Week 168: 0/0

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

Analysis population: A2304 SAF total population

Figure 12.1.5.113: BLOOD BILIRUBIN INCREASED (PT, not severe)

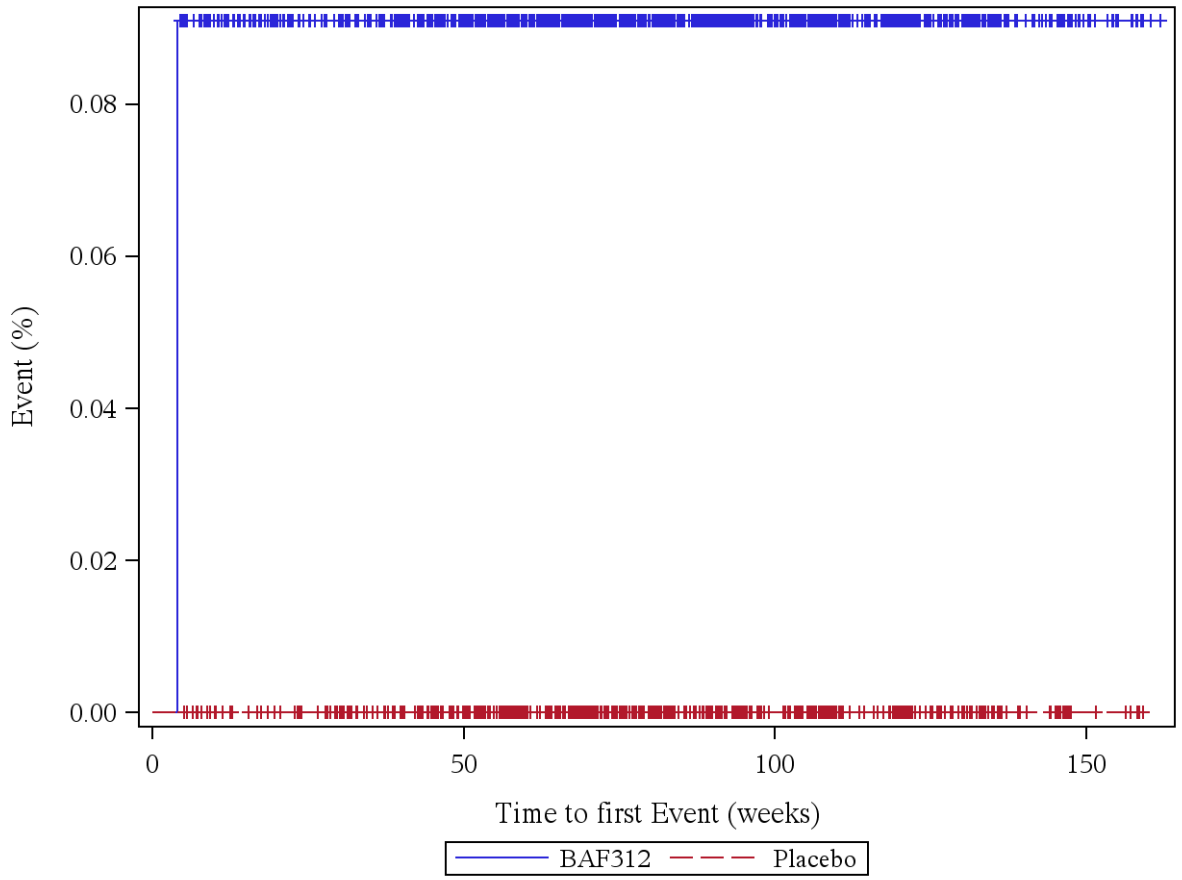


Patients at risk (BAF312/Placebo): Week 0: 1099/546, Week 4: 1099/546, Week 12: 1057/534, Week 24: 1011/519, Week 36: 984/495, Week 48: 919/459, Week 60: 810/386, Week 72: 646/303, Week 84: 511/235, Week 96: 396/174, Week 108: 287/125, Week 120: 198/79, Week 132: 111/40, Week 144: 50/20, Week 156: 10/5, Week 168: 0/0

Log rank test: p-value = 0,169
*: p < 0,05

Analysis population: A2304 SAF total population

Figure 12.1.5.114: BLOOD BILIRUBIN INCREASED (PT, severe)

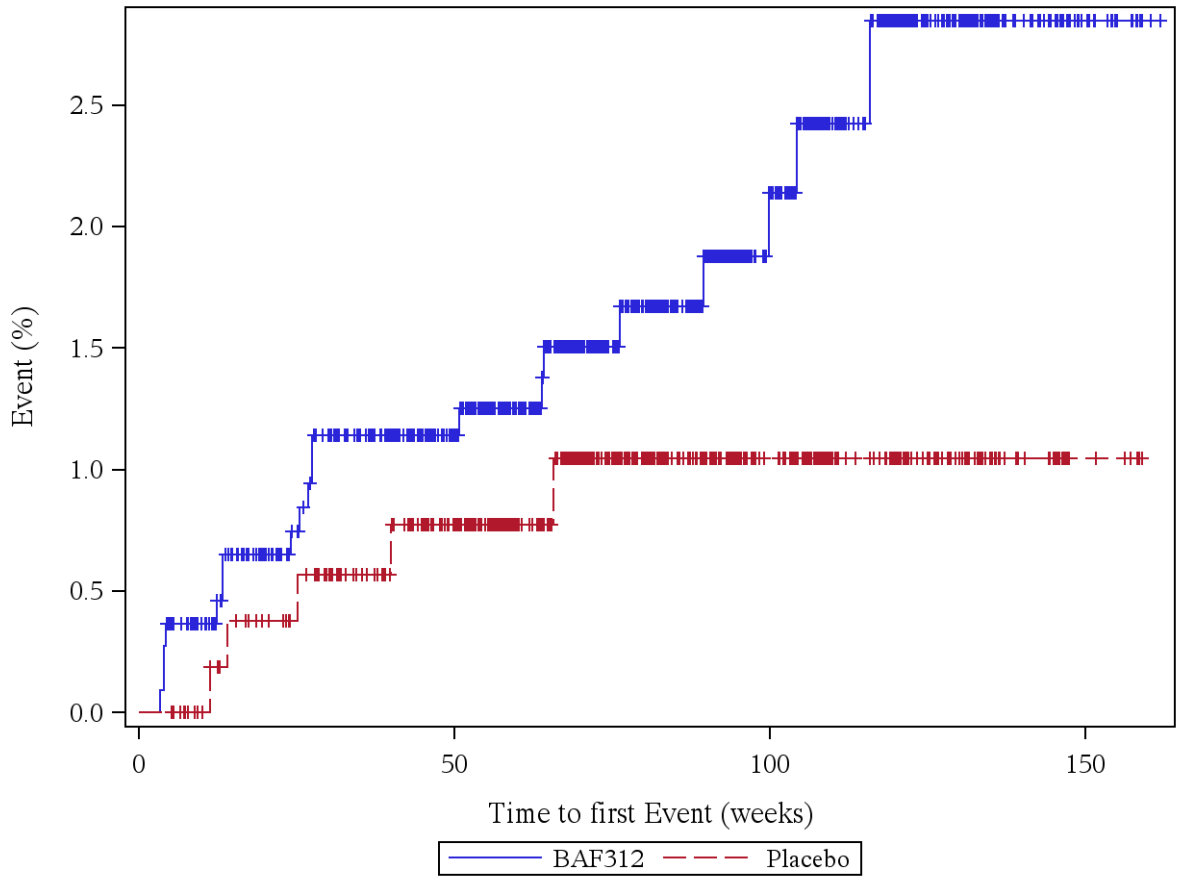


Patients at risk (BAF312/Placebo): Week 0: 1099/546, Week 4: 1098/546, Week 12: 1058/535, Week 24: 1016/521, Week 36: 989/497, Week 48: 924/461, Week 60: 818/388, Week 72: 652/305, Week 84: 516/237, Week 96: 400/176, Week 108: 291/126, Week 120: 200/80, Week 132: 113/40, Week 144: 51/20, Week 156: 10/5, Week 168: 0/0

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

Analysis population: A2304 SAF total population

Figure 12.1.5.115: BLOOD CHOLESTEROL INCREASED (PT, not severe)

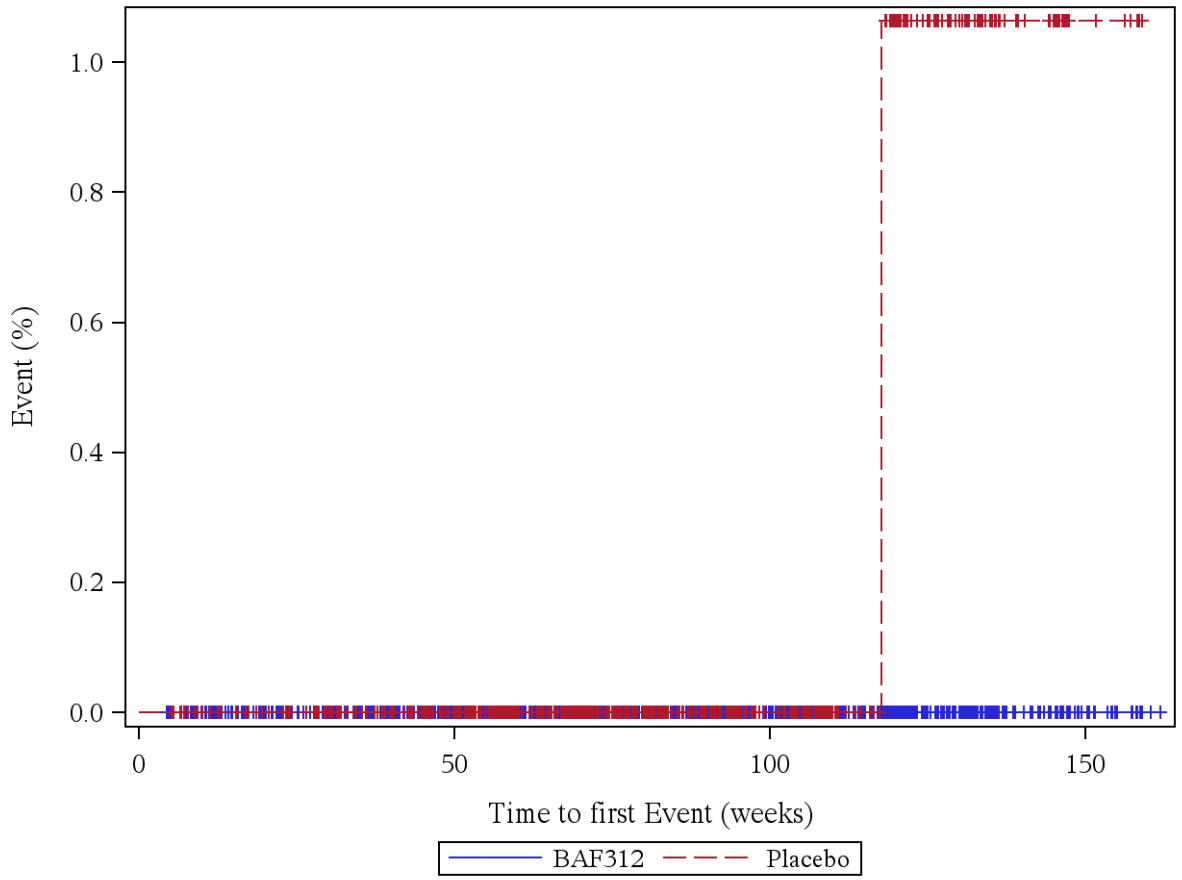


Patients at risk (BAF312/Placebo): Week 0: 1099/546, Week 4: 1096/546, Week 12: 1055/534, Week 24: 1010/519, Week 36: 978/494, Week 48: 914/457, Week 60: 807/385, Week 72: 639/301, Week 84: 506/234, Week 96: 391/175, Week 108: 283/125, Week 120: 193/80, Week 132: 111/40, Week 144: 50/20, Week 156: 10/5, Week 168: 0/0

Log rank test: p-value = 0,169
*: p < 0,05

Analysis population: A2304 SAF total population

Figure 12.1.5.116: BLOOD CHOLESTEROL INCREASED (PT, severe)

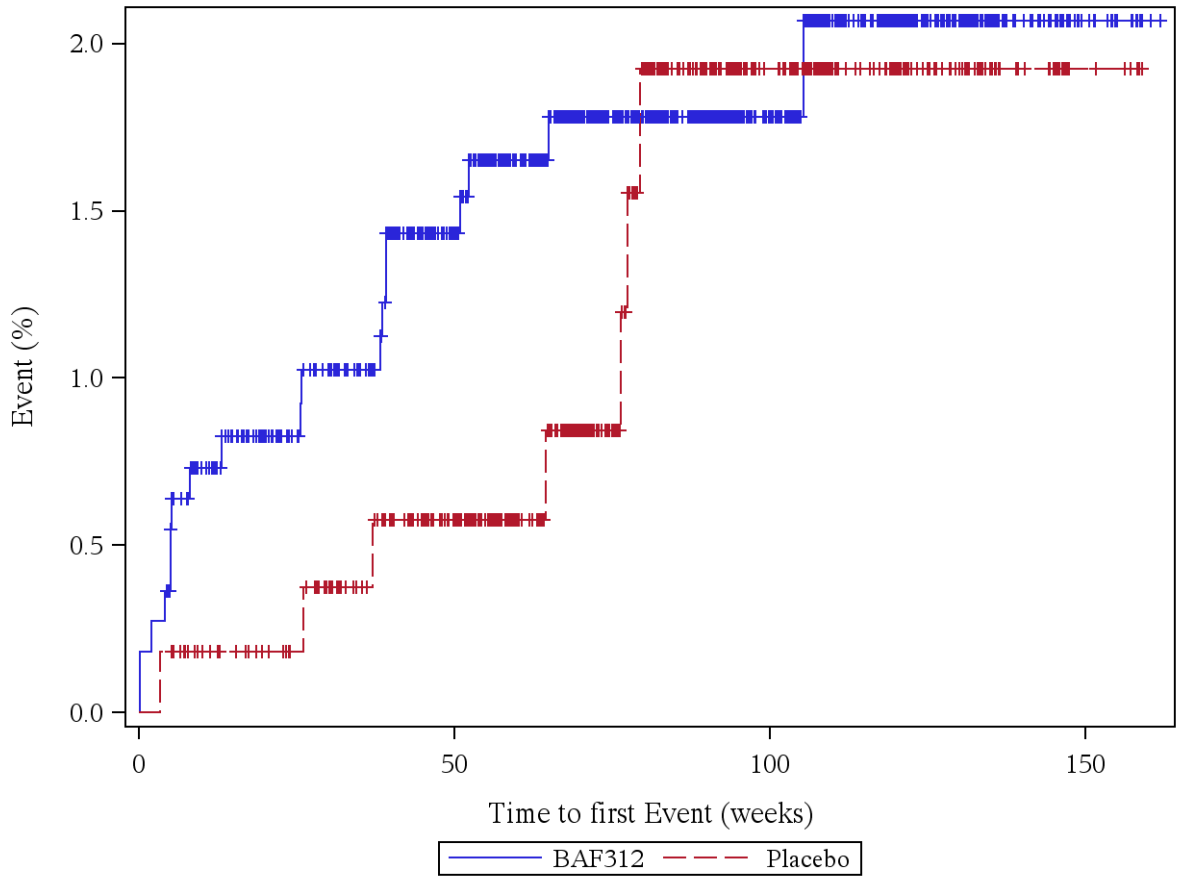


Patients at risk (BAF312/Placebo): Week 0: 1099/546, Week 4: 1099/546, Week 12: 1059/535, Week 24: 1017/521, Week 36: 990/497, Week 48: 925/461, Week 60: 818/388, Week 72: 652/305, Week 84: 516/237, Week 96: 400/176, Week 108: 291/126, Week 120: 200/79, Week 132: 113/40, Week 144: 51/20, Week 156: 10/5, Week 168: 0/0

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

Analysis population: A2304 SAF total population

Figure 12.1.5.117: BLOOD PRESSURE INCREASED (PT, not severe)

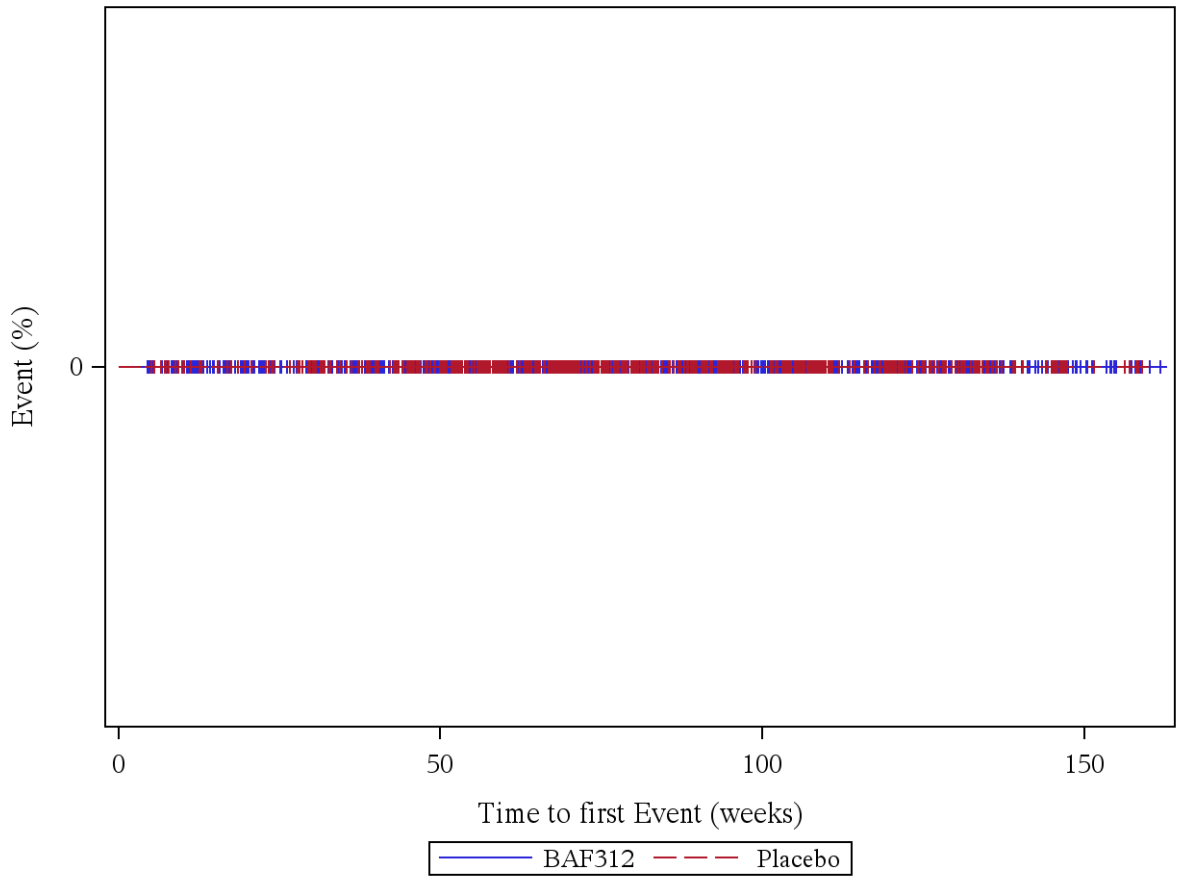


Patients at risk (BAF312/Placebo): Week 0: 1099/546, Week 4: 1096/545, Week 12: 1053/534, Week 24: 1010/520, Week 36: 981/495, Week 48: 912/458, Week 60: 804/386, Week 72: 639/303, Week 84: 506/232, Week 96: 396/171, Week 108: 286/122, Week 120: 197/76, Week 132: 110/39, Week 144: 50/20, Week 156: 10/5, Week 168: 0/0

Log rank test: p-value = 0,503
*: p < 0,05

Analysis population: A2304 SAF total population

Figure 12.1.5.118: BLOOD PRESSURE INCREASED (PT, severe)

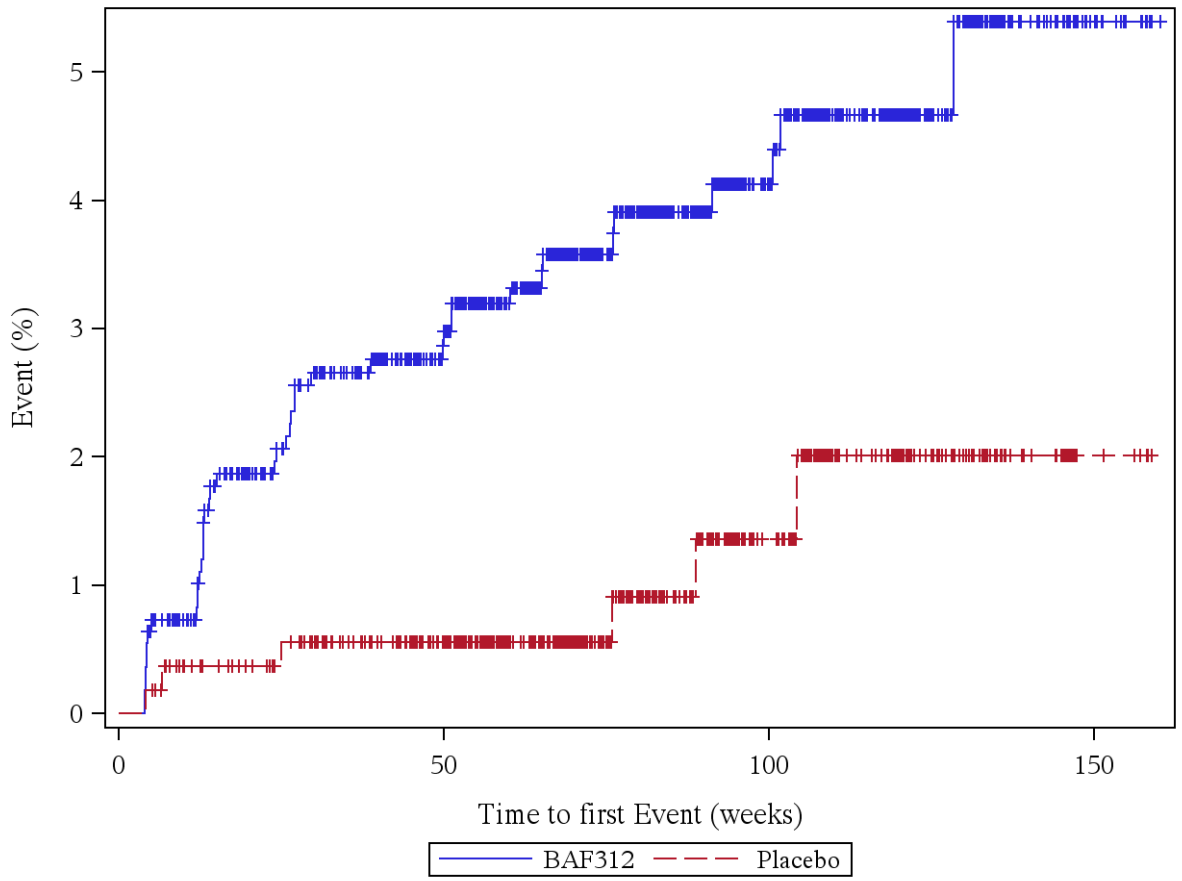


Patients at risk (BAF312/Placebo): Week 0: 1099/546, Week 4: 1099/546, Week 12: 1059/535, Week 24: 1017/521, Week 36: 990/497, Week 48: 925/461, Week 60: 818/388, Week 72: 652/305, Week 84: 516/237, Week 96: 400/176, Week 108: 291/126, Week 120: 200/80, Week 132: 113/40, Week 144: 51/20, Week 156: 10/5, Week 168: 0/0

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

Analysis population: A2304 SAF total population

Figure 12.1.5.119: GAMMA-GLUTAMYLTRANSFERASE INCREASED (PT, not severe)

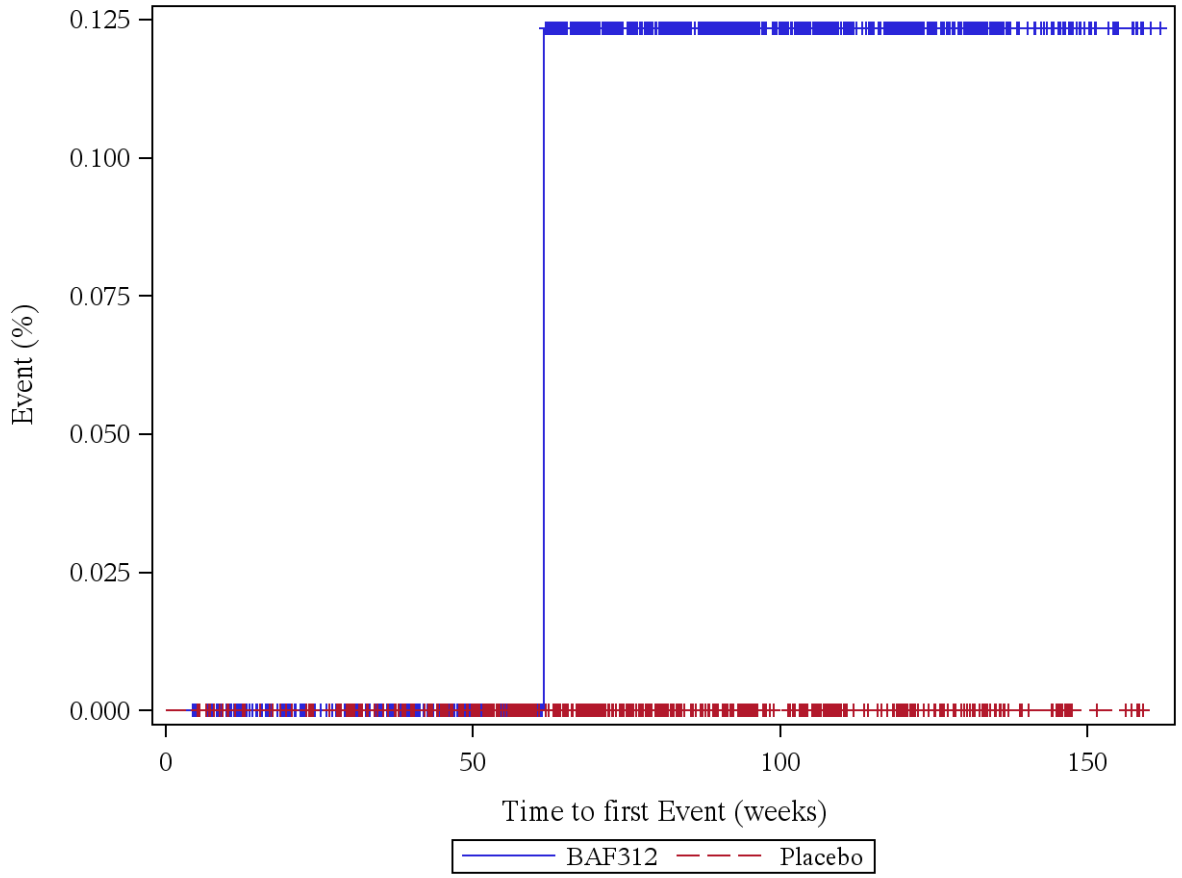


Patients at risk (BAF312/Placebo): Week 0: 1099/546, Week 4: 1097/546, Week 12: 1050/533, Week 24: 997/519, Week 36: 965/494, Week 48: 900/459, Week 60: 791/386, Week 72: 626/303, Week 84: 489/234, Week 96: 379/175, Week 108: 274/125, Week 120: 187/79, Week 132: 106/40, Week 144: 46/20, Week 156: 9/5, Week 168: 0/0

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

Analysis population: A2304 SAF total population

Figure 12.1.5.120: GAMMA-GLUTAMYLTRANSFERASE INCREASED (PT, severe)

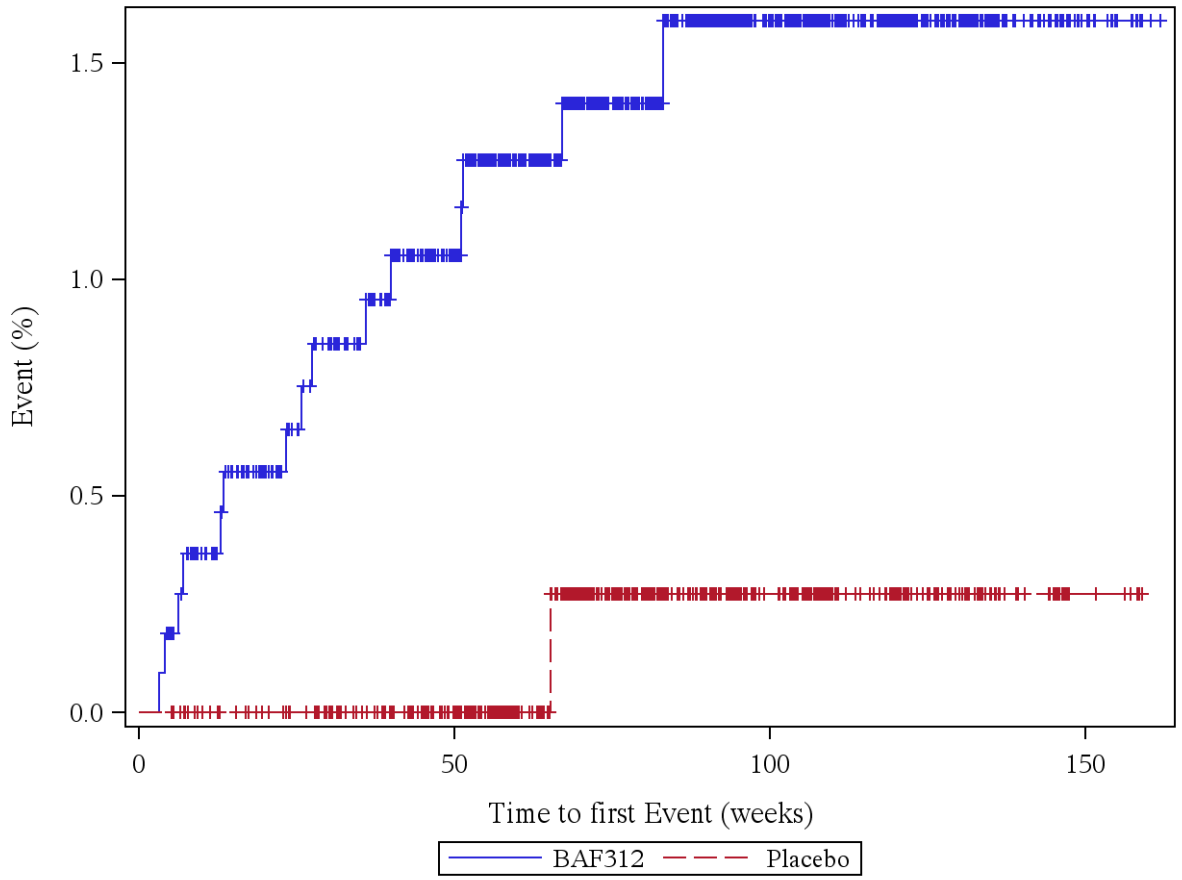


Patients at risk (BAF312/Placebo): Week 0: 1099/546, Week 4: 1099/546, Week 12: 1059/535, Week 24: 1017/521, Week 36: 990/497, Week 48: 925/461, Week 60: 818/388, Week 72: 651/305, Week 84: 515/237, Week 96: 400/176, Week 108: 291/126, Week 120: 200/80, Week 132: 113/40, Week 144: 51/20, Week 156: 10/5, Week 168: 0/0

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

Analysis population: A2304 SAF total population

Figure 12.1.5.121: HEPATIC ENZYME INCREASED (PT, not severe)

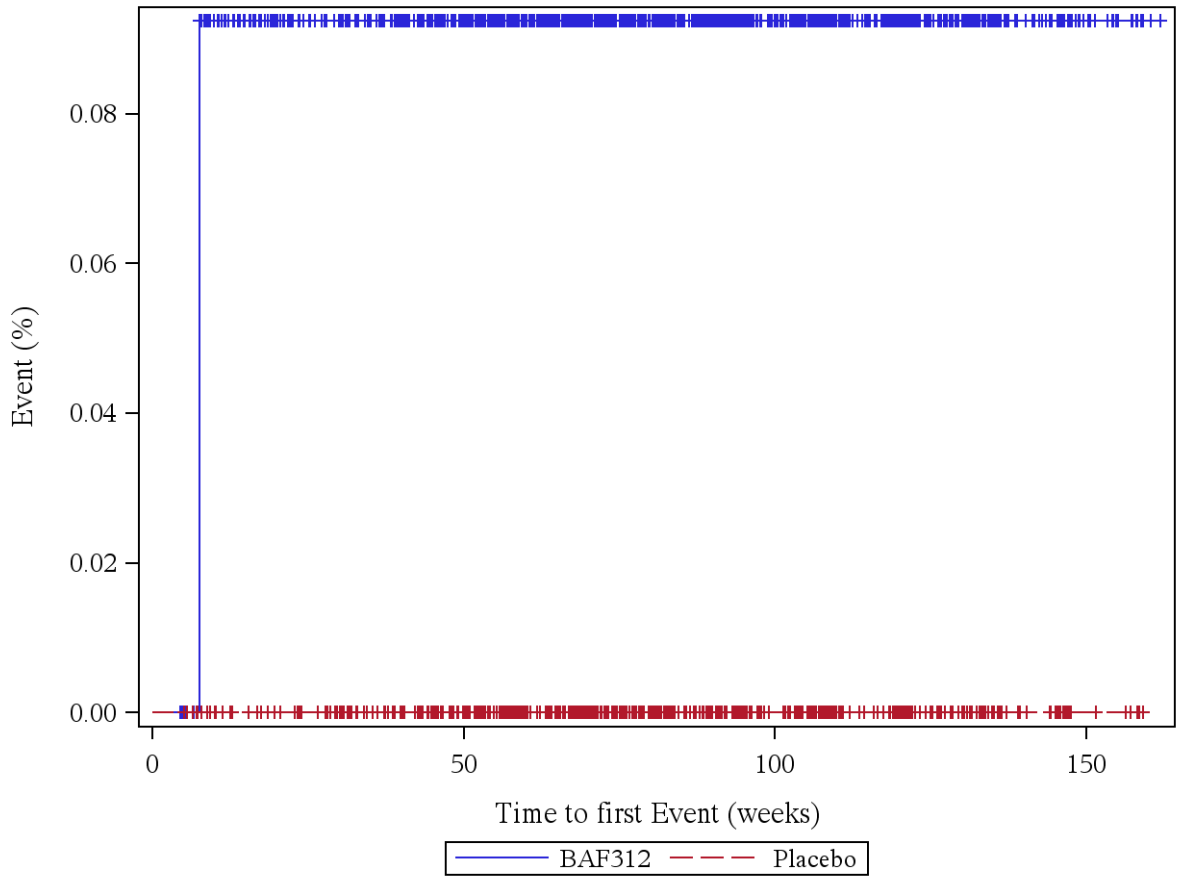


Patients at risk (BAF312/Placebo): Week 0: 1099/546, Week 4: 1098/546, Week 12: 1056/535, Week 24: 1011/521, Week 36: 981/497, Week 48: 916/461, Week 60: 809/388, Week 72: 642/304, Week 84: 506/236, Week 96: 393/175, Week 108: 285/125, Week 120: 196/79, Week 132: 112/39, Week 144: 51/20, Week 156: 10/5, Week 168: 0/0

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

Analysis population: A2304 SAF total population

Figure 12.1.5.122: HEPATIC ENZYME INCREASED (PT, severe)

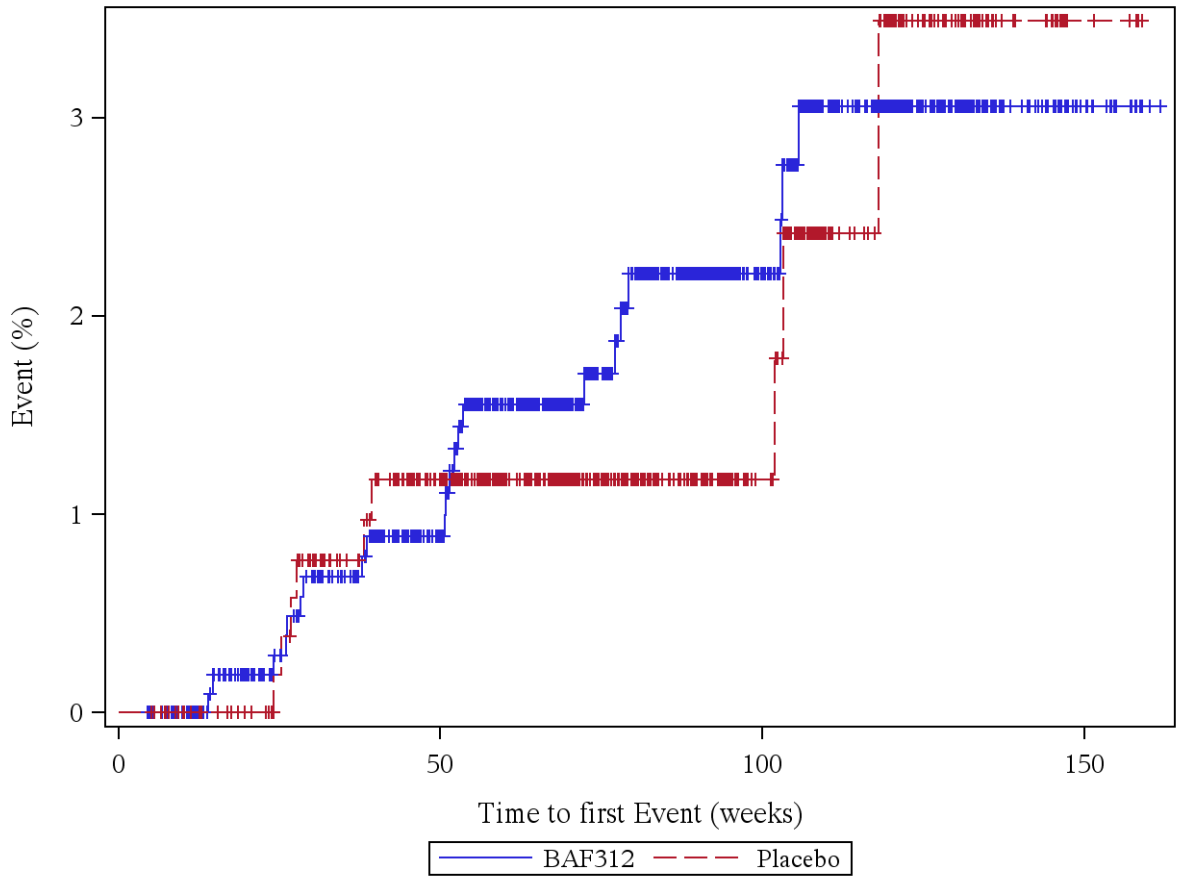


Patients at risk (BAF312/Placebo): Week 0: 1099/546, Week 4: 1099/546, Week 12: 1059/535, Week 24: 1017/521, Week 36: 990/497, Week 48: 925/461, Week 60: 818/388, Week 72: 652/305, Week 84: 516/237, Week 96: 400/176, Week 108: 291/126, Week 120: 200/80, Week 132: 113/40, Week 144: 51/20, Week 156: 10/5, Week 168: 0/0

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

Analysis population: A2304 SAF total population

Figure 12.1.5.123: WEIGHT DECREASED (PT, not severe)

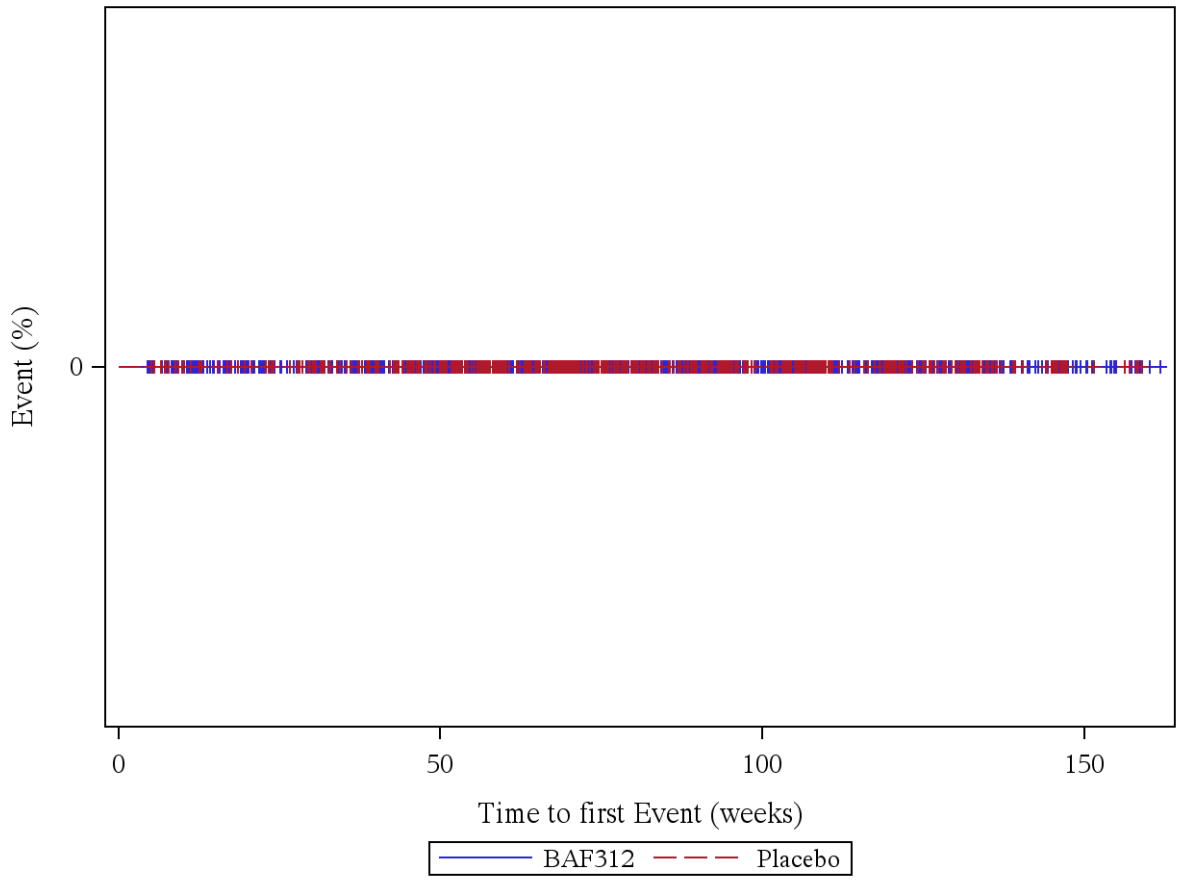


Patients at risk (BAF312/Placebo): Week 0: 1099/546, Week 4: 1099/546, Week 12: 1059/535, Week 24: 1015/521, Week 36: 984/493, Week 48: 918/458, Week 60: 805/386, Week 72: 642/303, Week 84: 505/236, Week 96: 391/175, Week 108: 280/123, Week 120: 191/76, Week 132: 109/36, Week 144: 50/18, Week 156: 10/4, Week 168: 0/0

Log rank test: p-value = 0,661
*: p < 0,05

Analysis population: A2304 SAF total population

Figure 12.1.5.124: WEIGHT DECREASED (PT, severe)

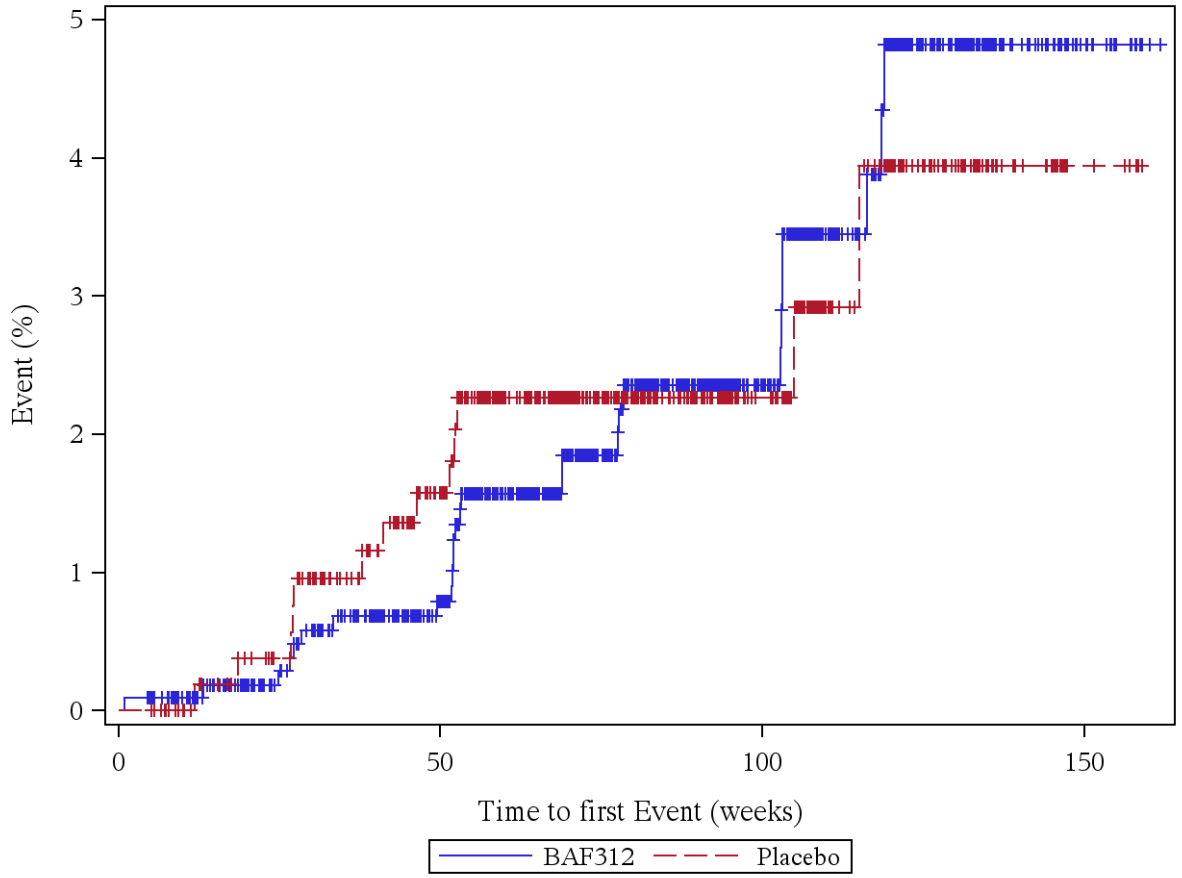


Patients at risk (BAF312/Placebo): Week 0: 1099/546, Week 4: 1099/546, Week 12: 1059/535, Week 24: 1017/521, Week 36: 990/497, Week 48: 925/461, Week 60: 818/388, Week 72: 652/305, Week 84: 516/237, Week 96: 400/176, Week 108: 291/126, Week 120: 200/80, Week 132: 113/40, Week 144: 51/20, Week 156: 10/5, Week 168: 0/0

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

Analysis population: A2304 SAF total population

Figure 12.1.5.125: WEIGHT INCREASED (PT, not severe)

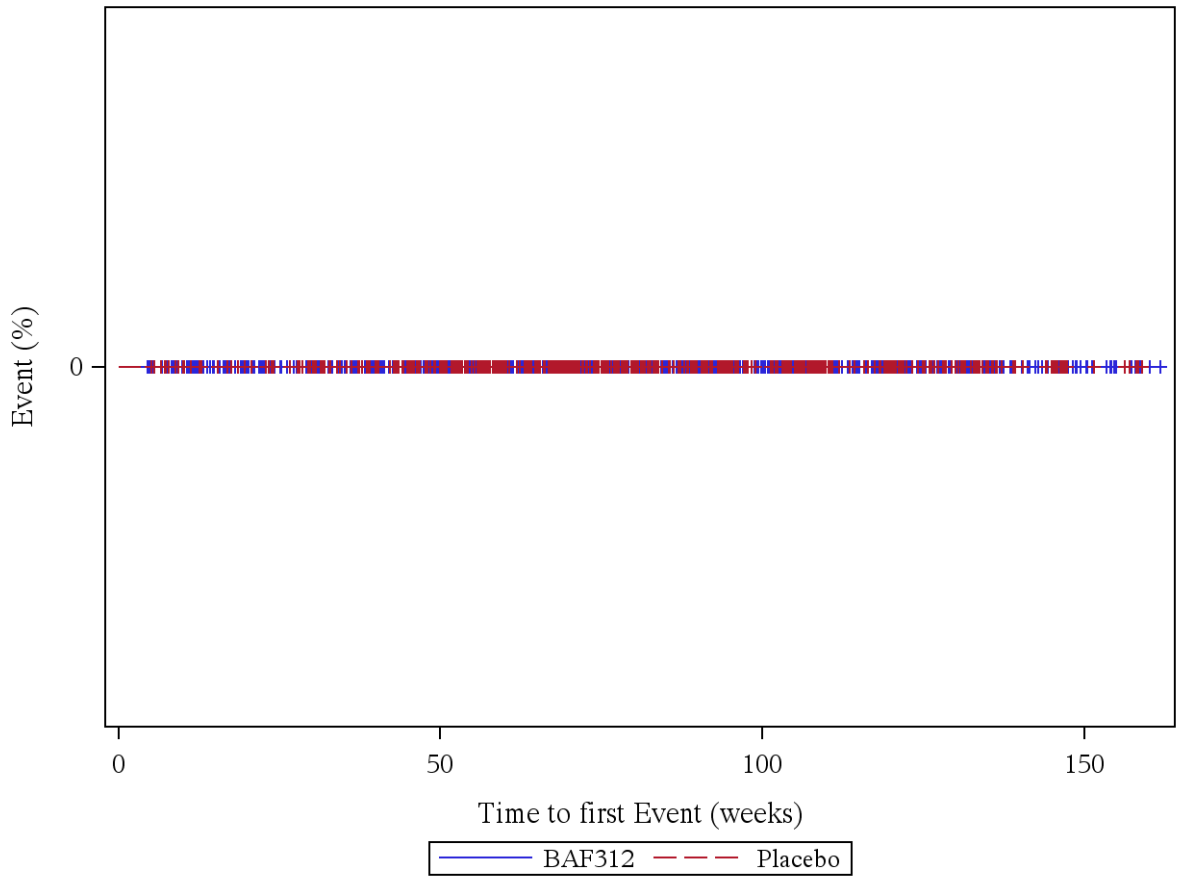


Patients at risk (BAF312/Placebo): Week 0: 1099/546, Week 4: 1098/546, Week 12: 1058/534, Week 24: 1015/519, Week 36: 983/492, Week 48: 918/454, Week 60: 805/380, Week 72: 637/299, Week 84: 502/233, Week 96: 389/173, Week 108: 279/123, Week 120: 188/77, Week 132: 107/40, Week 144: 49/20, Week 156: 10/5, Week 168: 0/0

Log rank test: p-value = 0,982
*: p < 0,05

Analysis population: A2304 SAF total population

Figure 12.1.5.126: WEIGHT INCREASED (PT, severe)

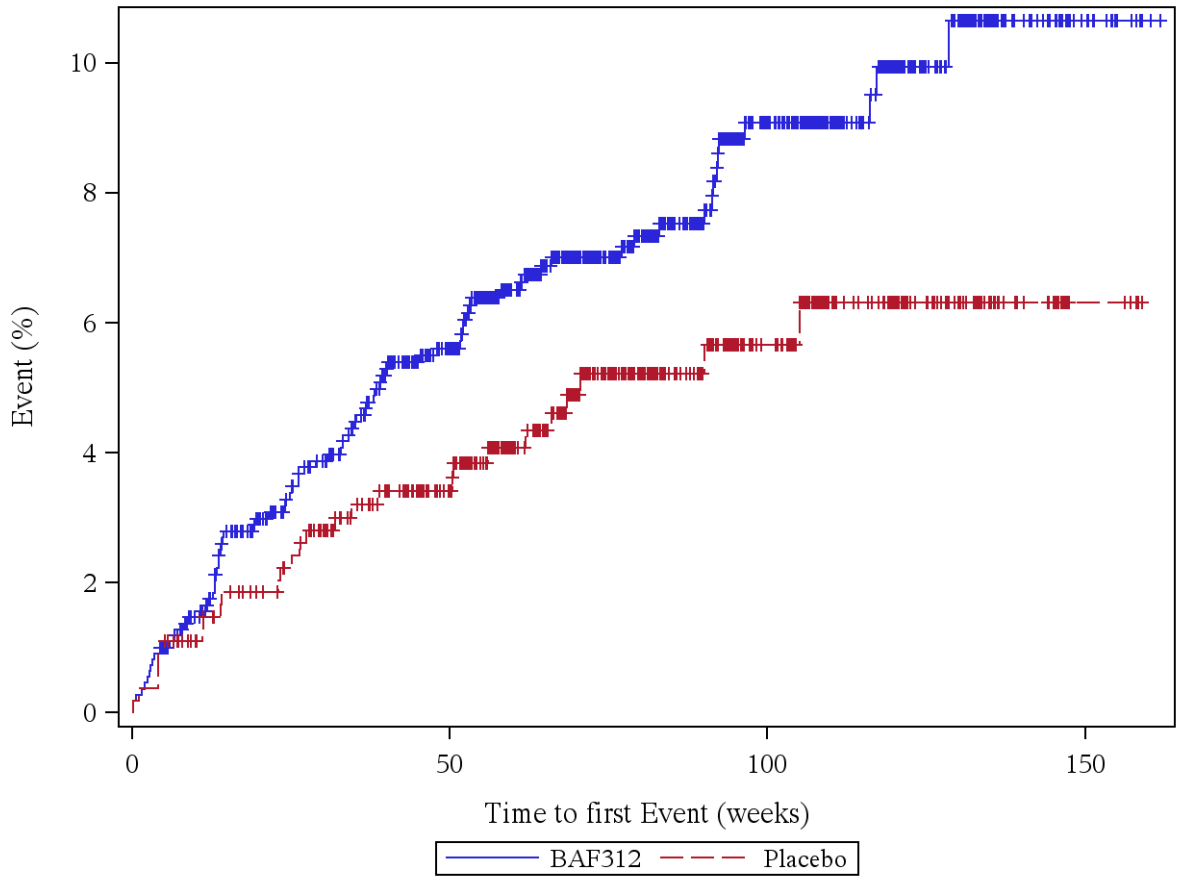


Patients at risk (BAF312/Placebo): Week 0: 1099/546, Week 4: 1099/546, Week 12: 1059/535, Week 24: 1017/521, Week 36: 990/497, Week 48: 925/461, Week 60: 818/388, Week 72: 652/305, Week 84: 516/237, Week 96: 400/176, Week 108: 291/126, Week 120: 200/80, Week 132: 113/40, Week 144: 51/20, Week 156: 10/5, Week 168: 0/0

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

Analysis population: A2304 SAF total population

Figure 12.1.5.127: METABOLISM AND NUTRITION DISORDERS (SOC, not severe)

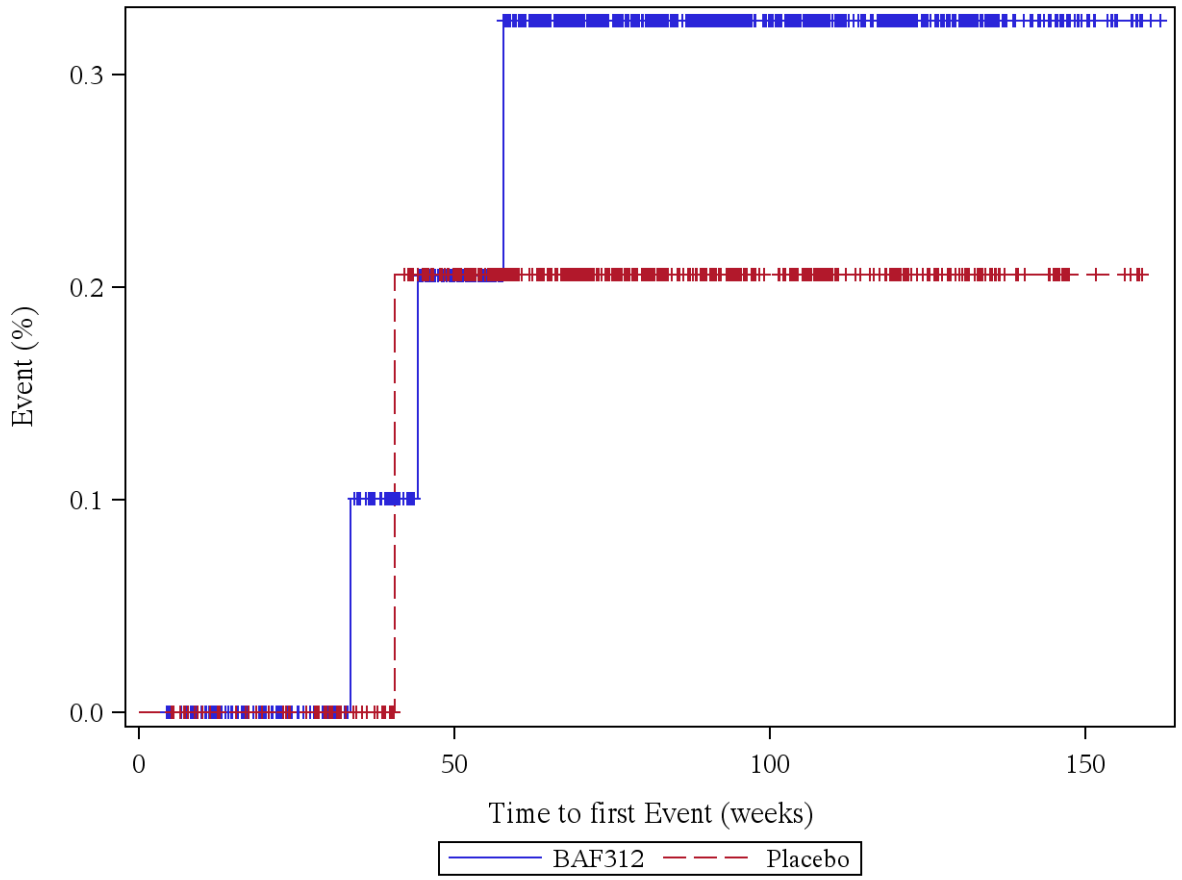


Patients at risk (BAF312/Placebo): Week 0: 1099/546, Week 4: 1089/544, Week 12: 1041/527, Week 24: 986/511, Week 36: 945/484, Week 48: 876/450, Week 60: 765/377, Week 72: 605/293, Week 84: 477/227, Week 96: 365/168, Week 108: 268/120, Week 120: 179/75, Week 132: 102/39, Week 144: 45/19, Week 156: 9/5, Week 168: 0/0

Log rank test: p-value = 0,051
*: p < 0,05

Analysis population: A2304 SAF total population

Figure 12.1.5.128: METABOLISM AND NUTRITION DISORDERS (SOC, severe)

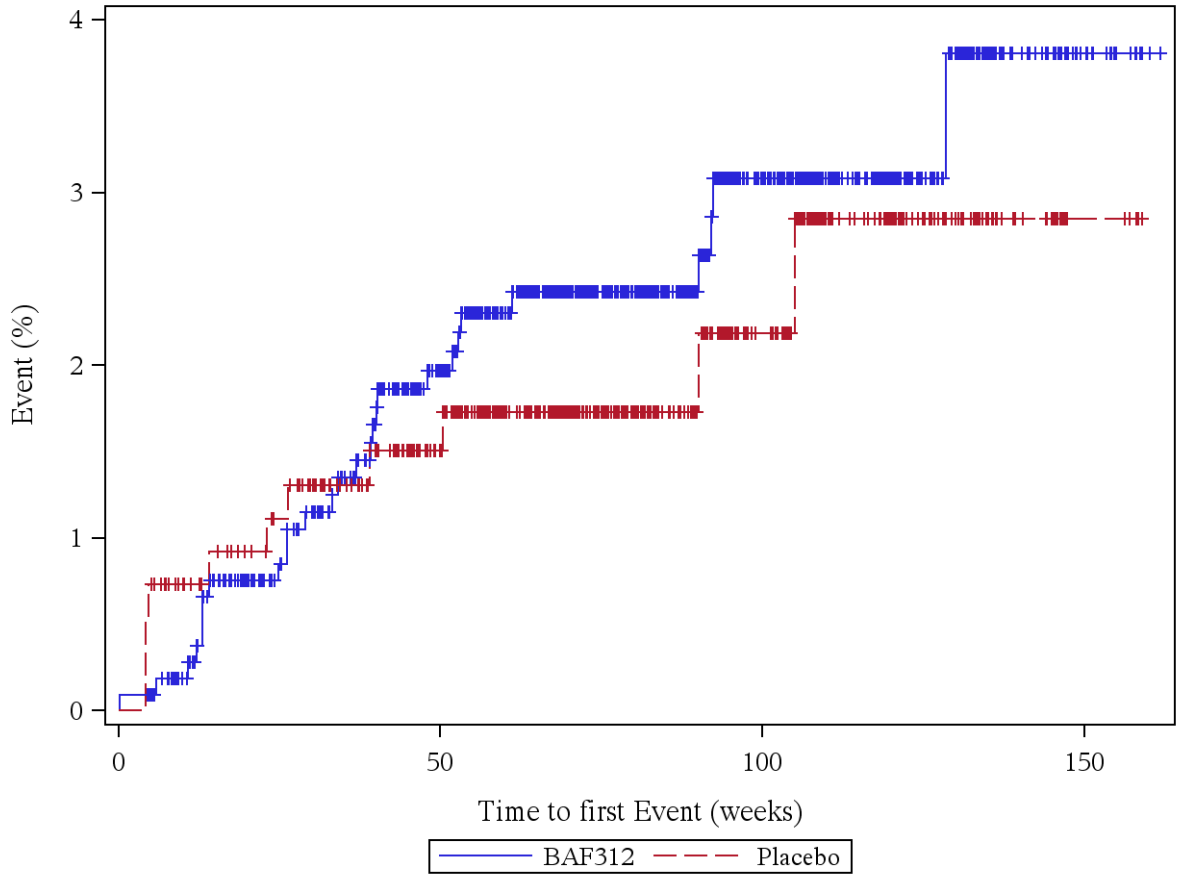


Patients at risk (BAF312/Placebo): Week 0: 1099/546, Week 4: 1099/546, Week 12: 1059/535, Week 24: 1017/521, Week 36: 989/497, Week 48: 924/461, Week 60: 817/388, Week 72: 651/305, Week 84: 516/237, Week 96: 400/176, Week 108: 291/126, Week 120: 200/80, Week 132: 113/40, Week 144: 51/20, Week 156: 10/5, Week 168: 0/0

Log rank test: p-value = 0,728
*: p < 0,05

Analysis population: A2304 SAF total population

Figure 12.1.5.129: HYPERCHOLESTEROLAEMIA (PT, not severe)

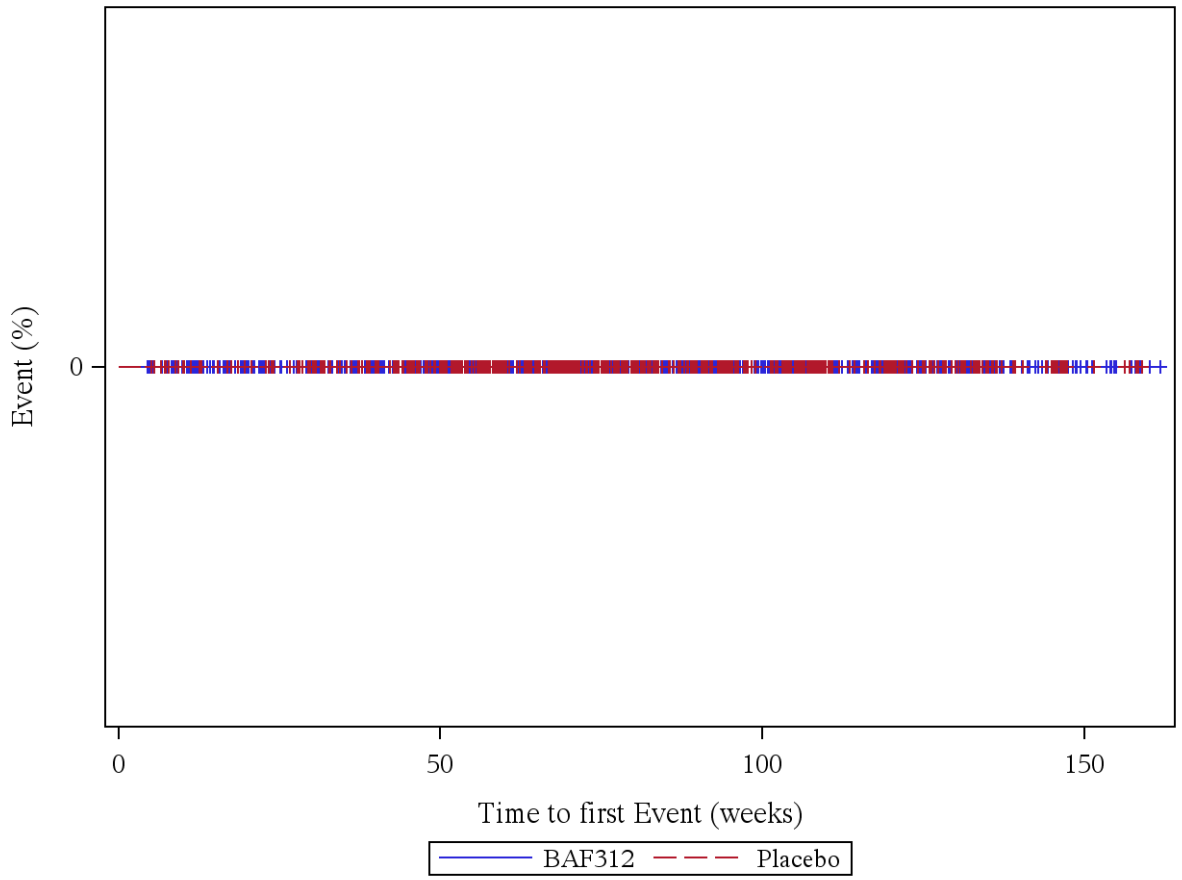


Patients at risk (BAF312/Placebo): Week 0: 1099/546, Week 4: 1098/546, Week 12: 1056/531, Week 24: 1009/516, Week 36: 976/493, Week 48: 906/457, Week 60: 797/384, Week 72: 635/301, Week 84: 502/233, Week 96: 387/172, Week 108: 280/124, Week 120: 190/78, Week 132: 109/39, Week 144: 50/19, Week 156: 9/5, Week 168: 0/0

Log rank test: p-value = 0,527
*: p < 0,05

Analysis population: A2304 SAF total population

Figure 12.1.5.130: HYPERCHOLESTEROLAEMIA (PT, severe)

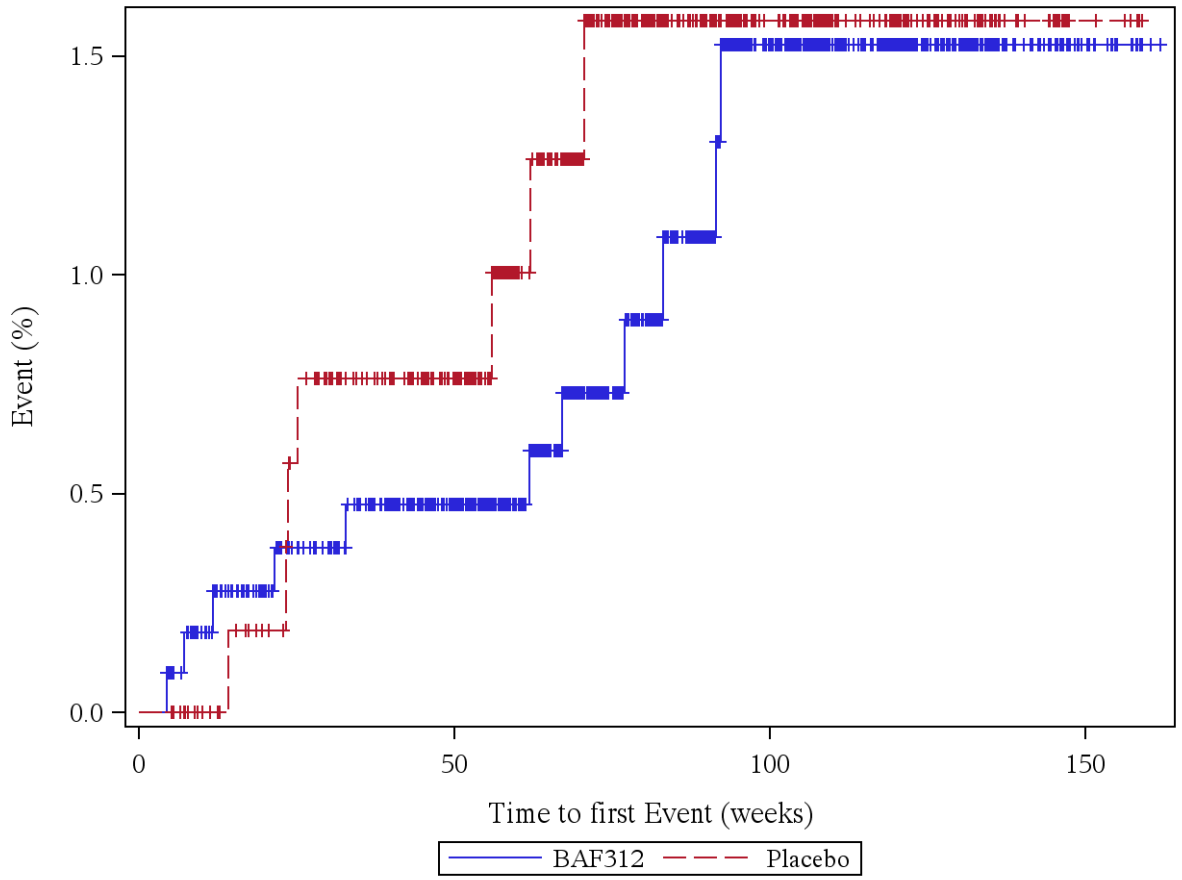


Patients at risk (BAF312/Placebo): Week 0: 1099/546, Week 4: 1099/546, Week 12: 1059/535, Week 24: 1017/521, Week 36: 990/497, Week 48: 925/461, Week 60: 818/388, Week 72: 652/305, Week 84: 516/237, Week 96: 400/176, Week 108: 291/126, Week 120: 200/80, Week 132: 113/40, Week 144: 51/20, Week 156: 10/5, Week 168: 0/0

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

Analysis population: A2304 SAF total population

Figure 12.1.5.131: VITAMIN D DEFICIENCY (PT, not severe)

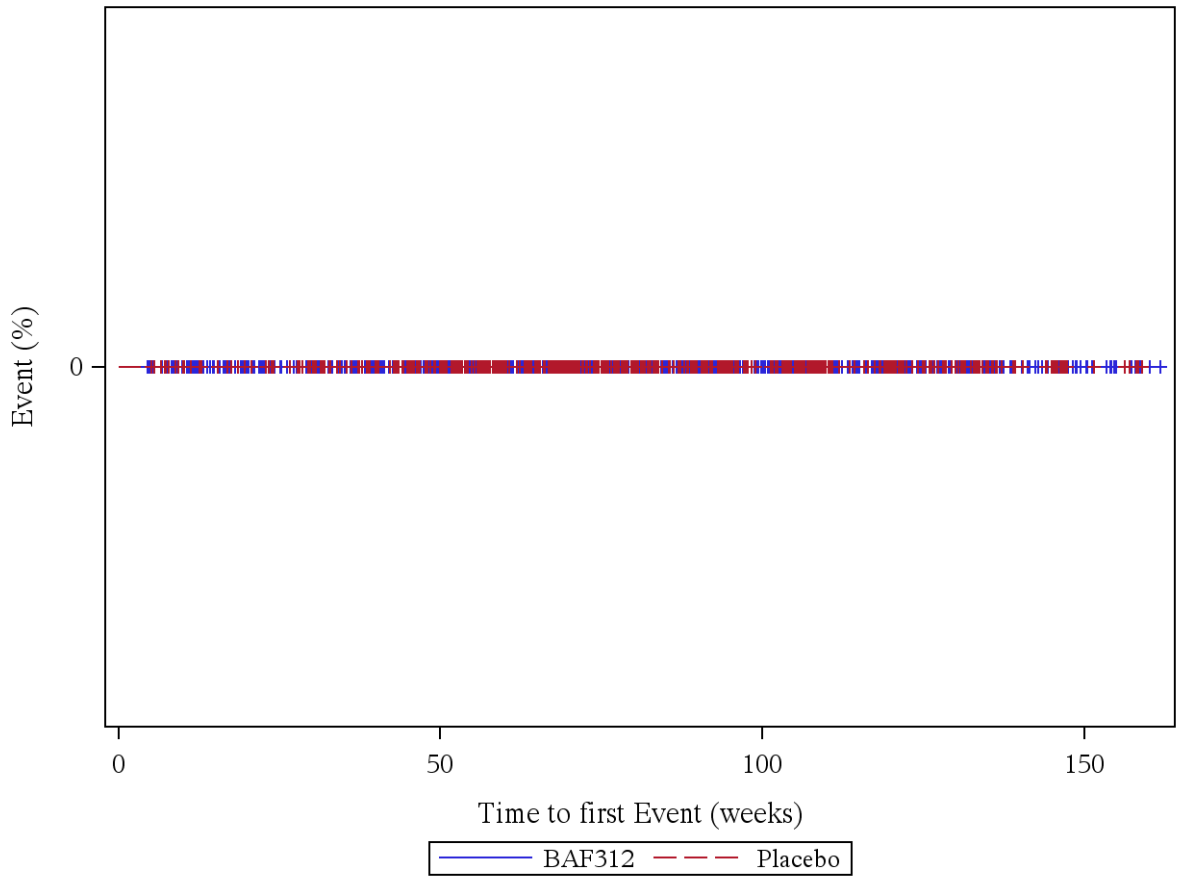


Patients at risk (BAF312/Placebo): Week 0: 1099/546, Week 4: 1099/546, Week 12: 1056/535, Week 24: 1013/518, Week 36: 985/493, Week 48: 921/458, Week 60: 814/385, Week 72: 646/301, Week 84: 511/235, Week 96: 393/174, Week 108: 289/124, Week 120: 199/78, Week 132: 112/40, Week 144: 51/20, Week 156: 10/5, Week 168: 0/0

Log rank test: p-value = 0,579
*: p < 0,05

Analysis population: A2304 SAF total population

Figure 12.1.5.132: VITAMIN D DEFICIENCY (PT, severe)

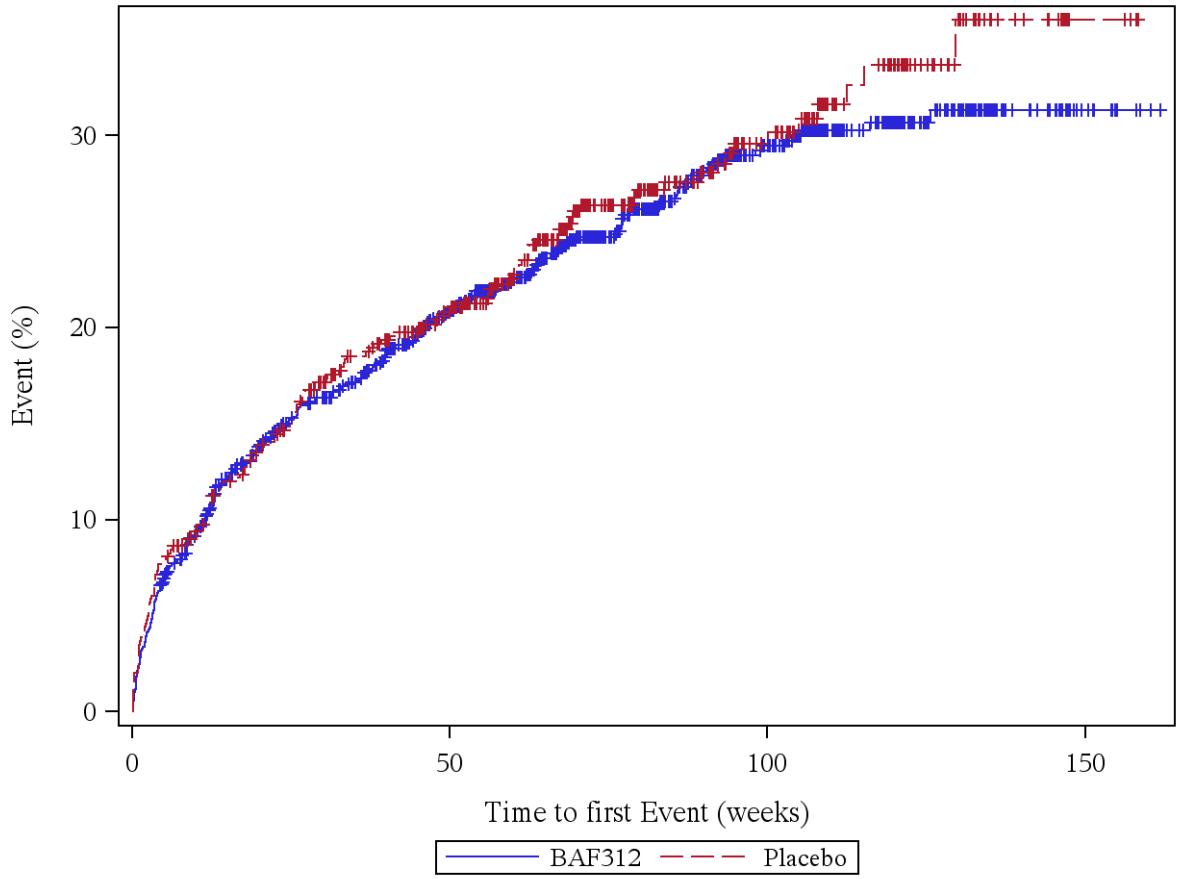


Patients at risk (BAF312/Placebo): Week 0: 1099/546, Week 4: 1099/546, Week 12: 1059/535, Week 24: 1017/521, Week 36: 990/497, Week 48: 925/461, Week 60: 818/388, Week 72: 652/305, Week 84: 516/237, Week 96: 400/176, Week 108: 291/126, Week 120: 200/80, Week 132: 113/40, Week 144: 51/20, Week 156: 10/5, Week 168: 0/0

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

Analysis population: A2304 SAF total population

Figure 12.1.5.133: MUSCULOSKELETAL AND CONNECTIVE TISSUE DISORDERS (SOC, not severe)

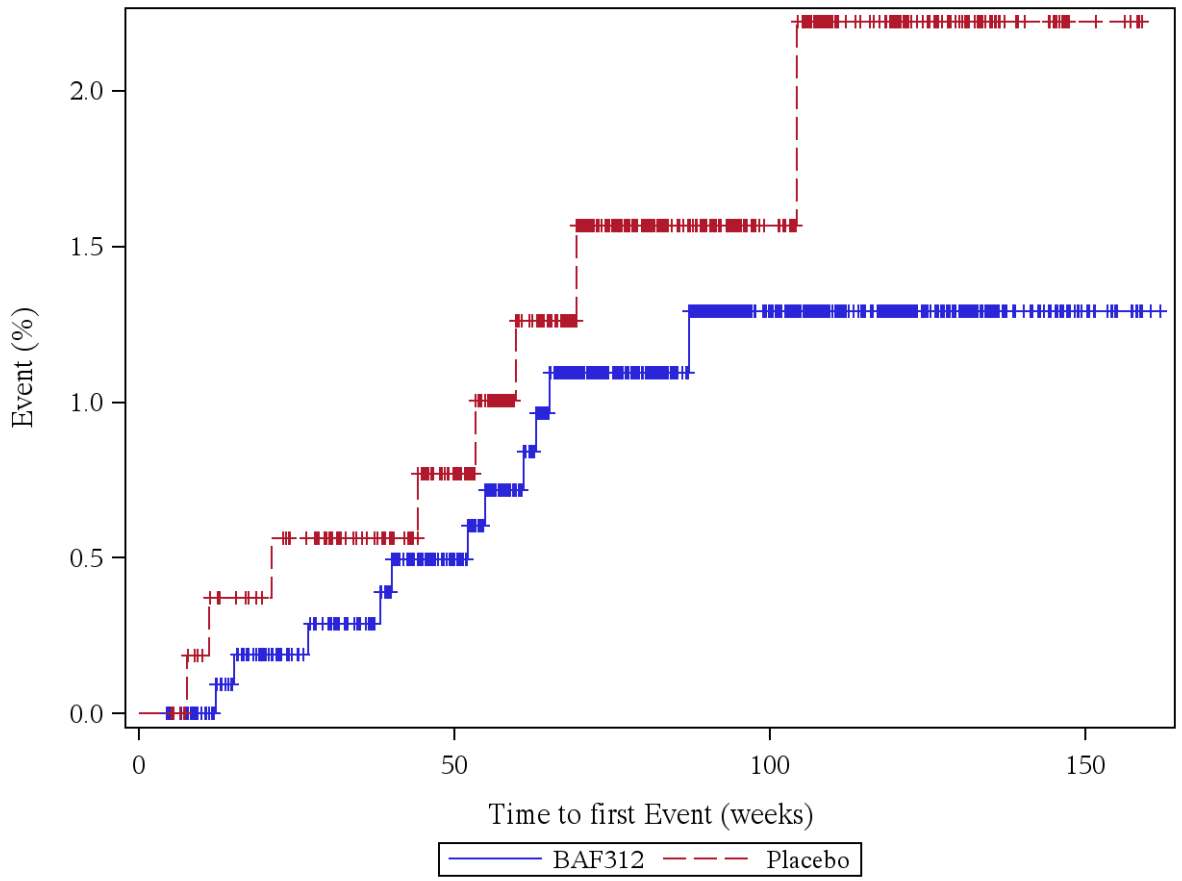


Patients at risk (BAF312/Placebo): Week 0: 1099/546, Week 4: 1031/506, Week 12: 952/480, Week 24: 866/445, Week 36: 821/405, Week 48: 737/369, Week 60: 638/301, Week 72: 492/215, Week 84: 389/165, Week 96: 296/125, Week 108: 211/88, Week 120: 143/53, Week 132: 83/23, Week 144: 39/12, Week 156: 7/4, Week 168: 0/0

Log rank test: p-value = 0,609
*: p < 0,05

Analysis population: A2304 SAF total population

Figure 12.1.5.134: MUSCULOSKELETAL AND CONNECTIVE TISSUE DISORDERS (SOC, severe)

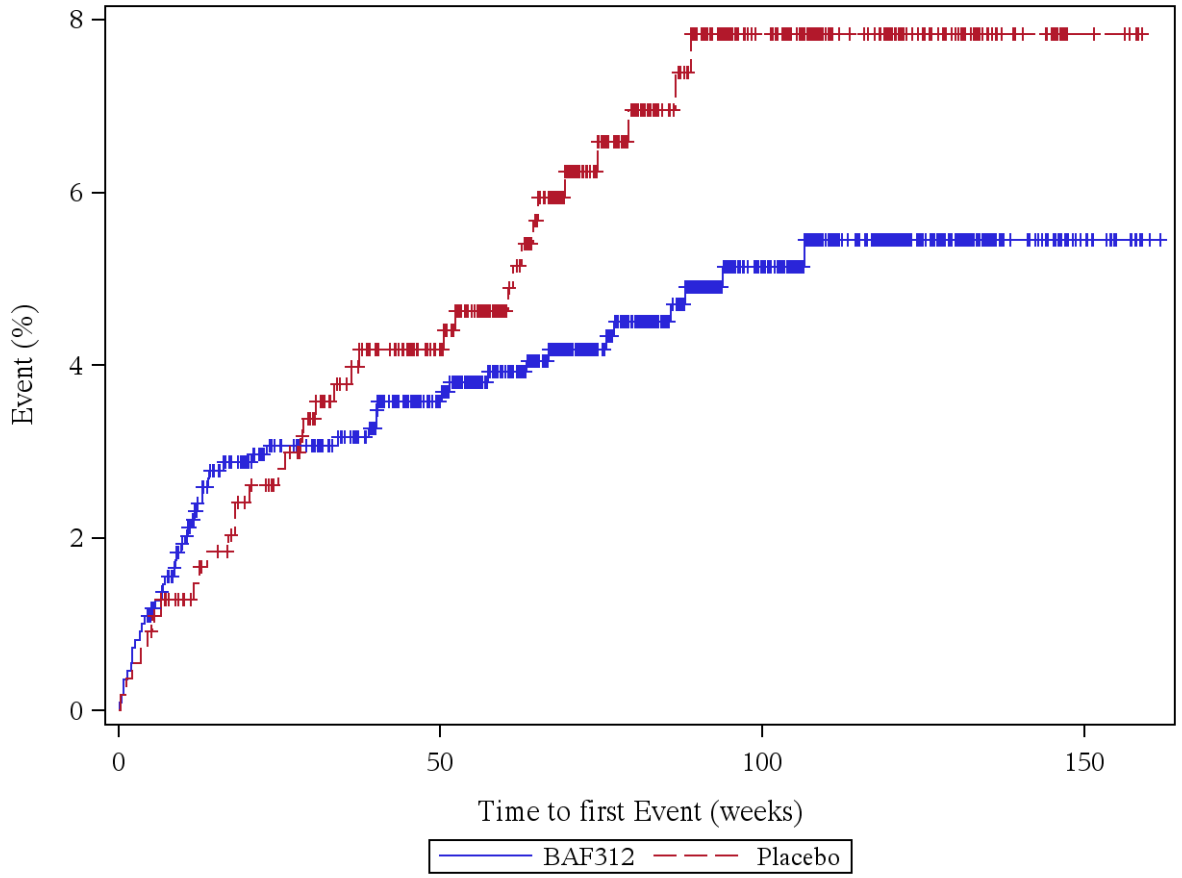


Patients at risk (BAF312/Placebo): Week 0: 1099/546, Week 4: 1099/546, Week 12: 1059/533, Week 24: 1015/519, Week 36: 987/495, Week 48: 920/458, Week 60: 814/383, Week 72: 645/299, Week 84: 512/232, Week 96: 397/174, Week 108: 288/123, Week 120: 198/79, Week 132: 111/39, Week 144: 51/19, Week 156: 10/5, Week 168: 0/0

Log rank test: p-value = 0,378
*: p < 0,05

Analysis population: A2304 SAF total population

Figure 12.1.5.135: ARTHRALGIA (PT, not severe)

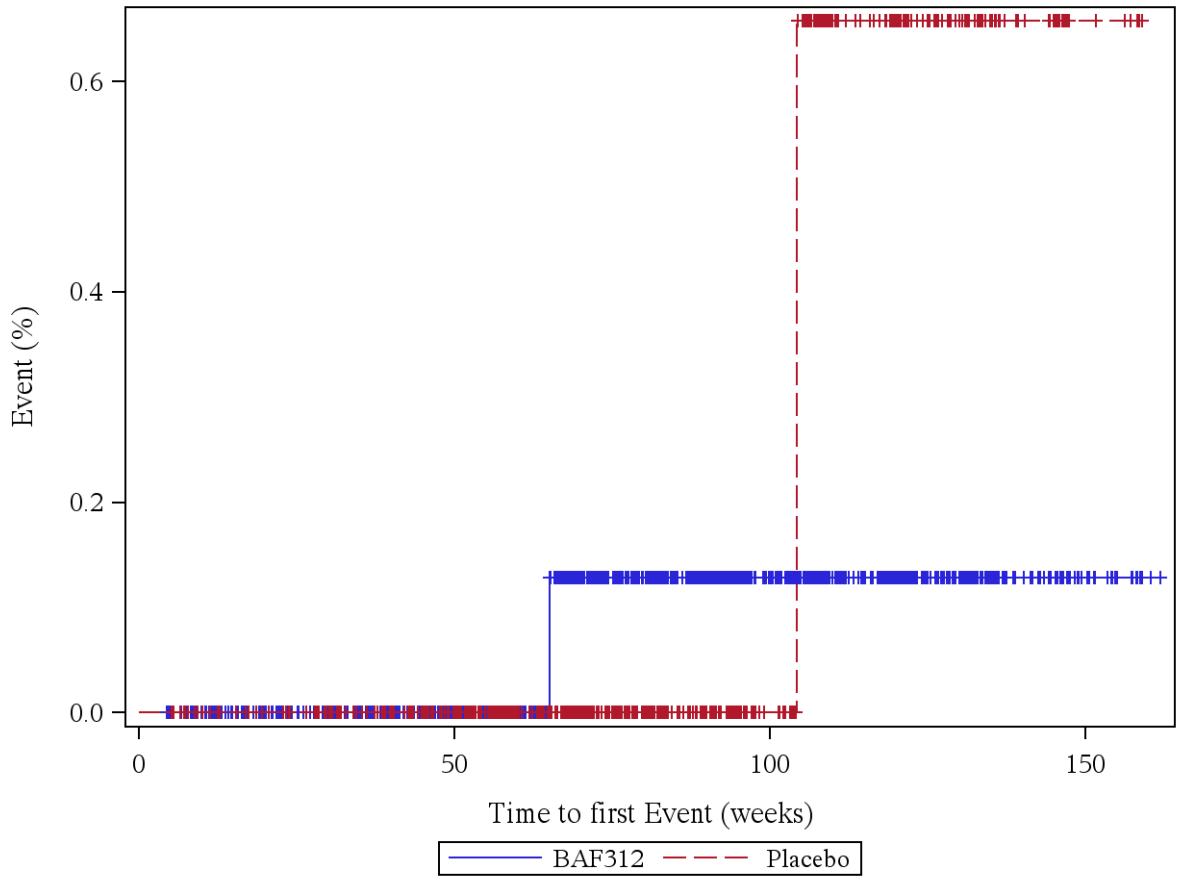


Patients at risk (BAF312/Placebo): Week 0: 1099/546, Week 4: 1087/542, Week 12: 1034/527, Week 24: 986/507, Week 36: 959/477, Week 48: 894/442, Week 60: 786/371, Week 72: 625/285, Week 84: 494/220, Week 96: 381/161, Week 108: 277/115, Week 120: 190/73, Week 132: 108/37, Week 144: 49/20, Week 156: 10/5, Week 168: 0/0

Log rank test: p-value = 0,122
*: p < 0,05

Analysis population: A2304 SAF total population

Figure 12.1.5.136: ARTHRALGIA (PT, severe)

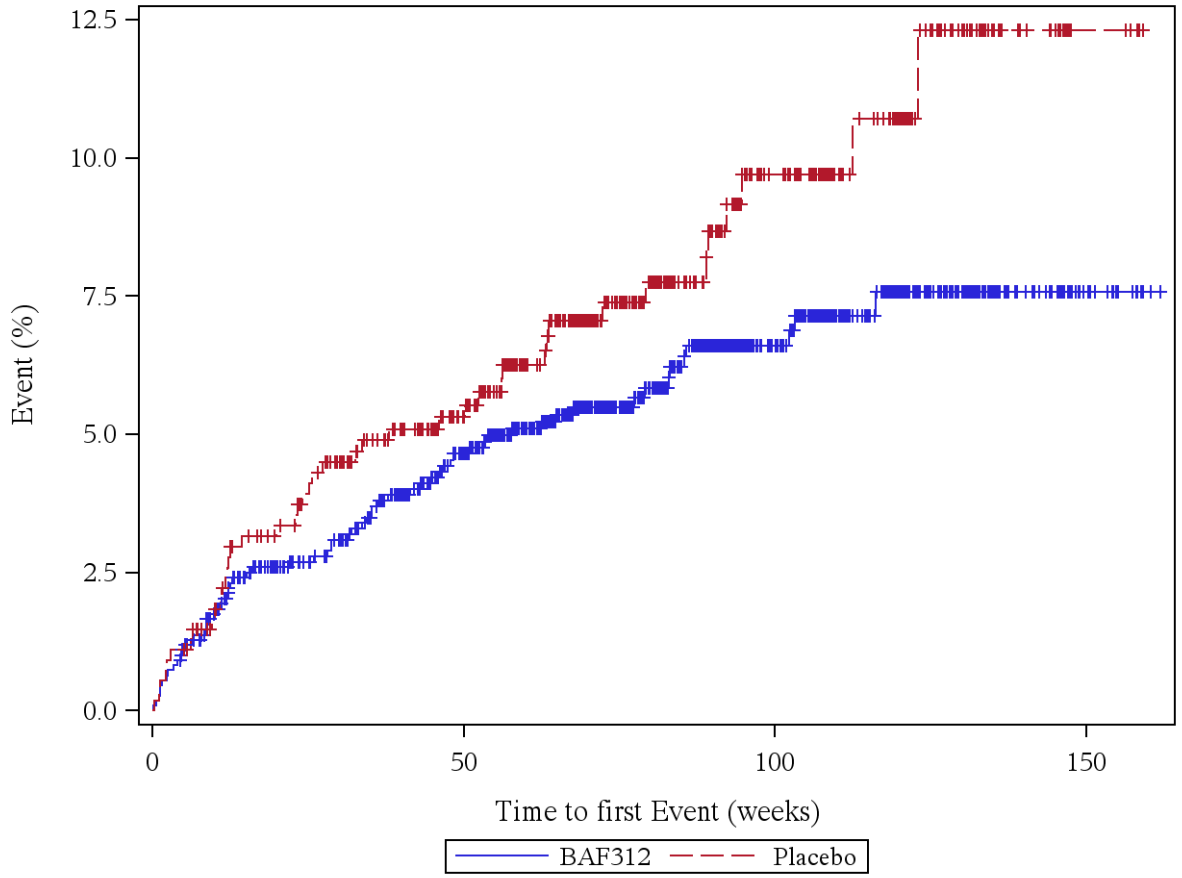


Patients at risk (BAF312/Placebo): Week 0: 1099/546, Week 4: 1099/546, Week 12: 1059/535, Week 24: 1017/521, Week 36: 990/497, Week 48: 925/461, Week 60: 818/388, Week 72: 651/305, Week 84: 515/237, Week 96: 400/176, Week 108: 291/125, Week 120: 200/80, Week 132: 113/40, Week 144: 51/20, Week 156: 10/5, Week 168: 0/0

Log rank test: p-value = 0,561
*: p < 0,05

Analysis population: A2304 SAF total population

Figure 12.1.5.137: BACK PAIN (PT, not severe)

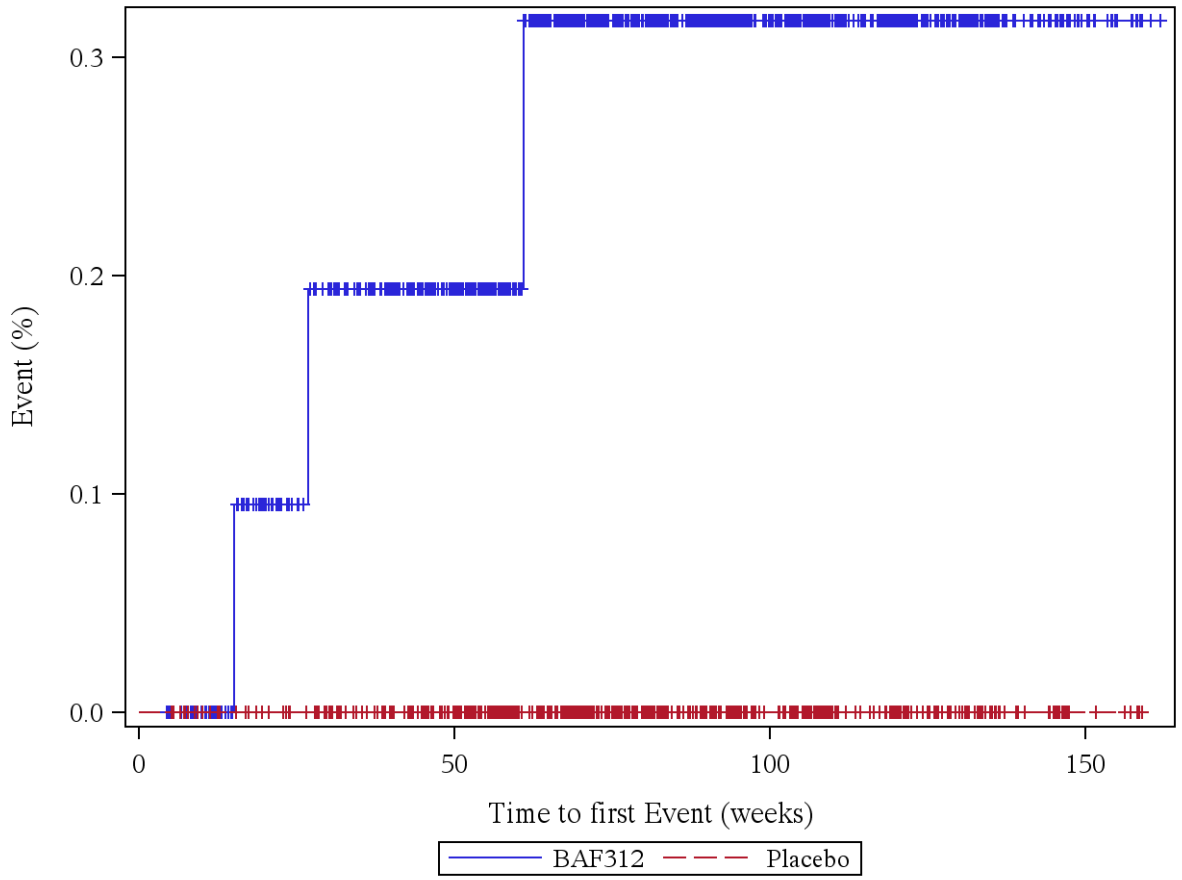


Patients at risk (BAF312/Placebo): Week 0: 1099/546, Week 4: 1089/540, Week 12: 1037/521, Week 24: 989/501, Week 36: 953/473, Week 48: 881/435, Week 60: 773/361, Week 72: 608/280, Week 84: 482/213, Week 96: 375/156, Week 108: 271/113, Week 120: 185/72, Week 132: 106/34, Week 144: 48/16, Week 156: 9/5, Week 168: 0/0

Log rank test: p-value = 0,098
*: p < 0,05

Analysis population: A2304 SAF total population

Figure 12.1.5.138: BACK PAIN (PT, severe)

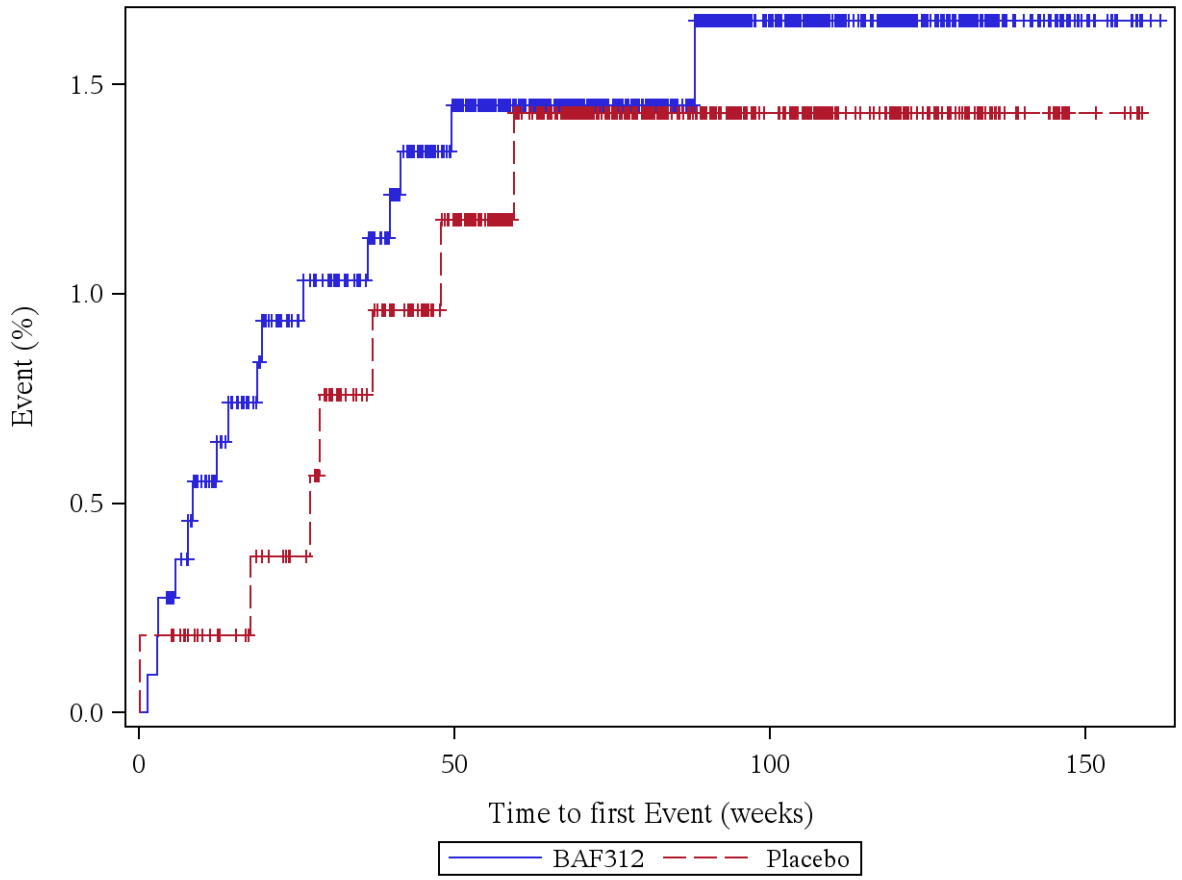


Patients at risk (BAF312/Placebo): Week 0: 1099/546, Week 4: 1099/546, Week 12: 1059/535, Week 24: 1016/521, Week 36: 988/497, Week 48: 923/461, Week 60: 816/388, Week 72: 649/305, Week 84: 514/237, Week 96: 398/176, Week 108: 289/126, Week 120: 199/80, Week 132: 112/40, Week 144: 51/20, Week 156: 10/5, Week 168: 0/0

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

Analysis population: A2304 SAF total population

Figure 12.1.5.139: JOINT SWELLING (PT, not severe)

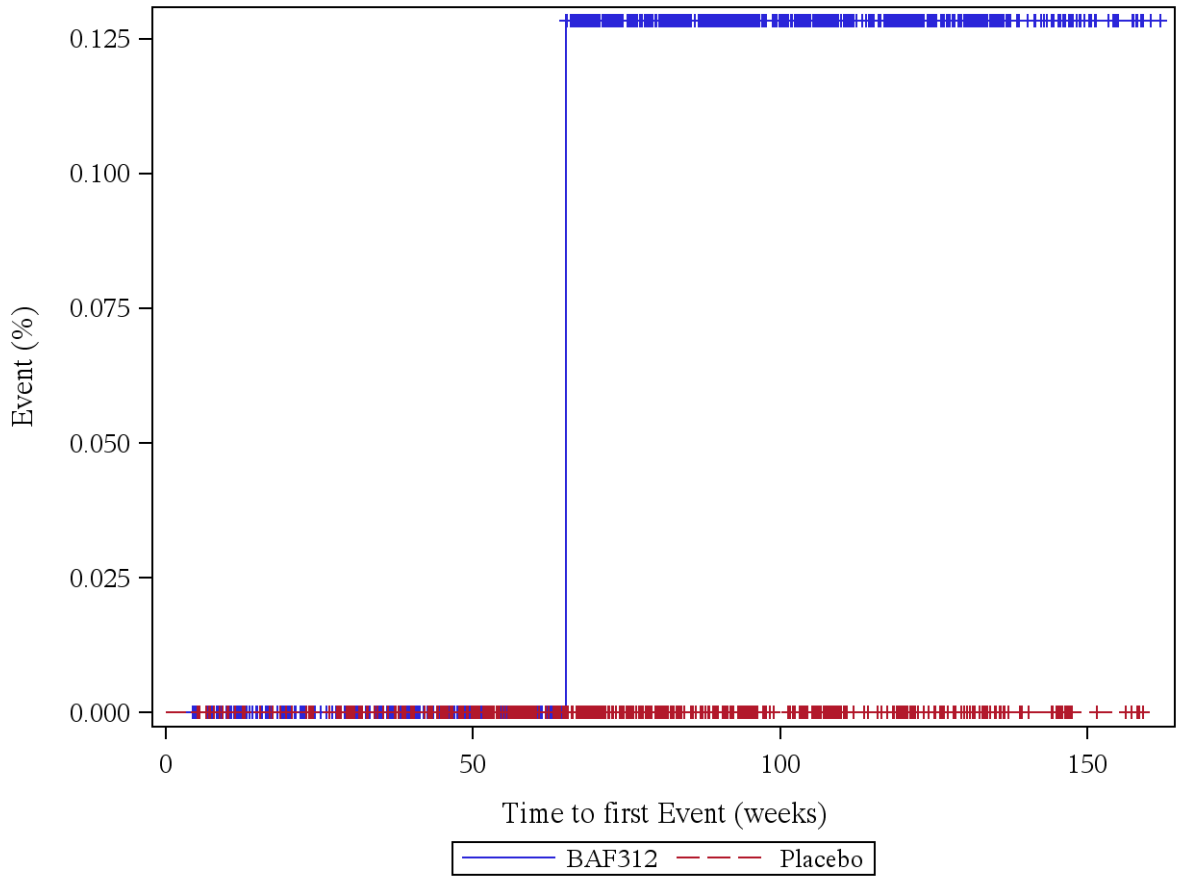


Patients at risk (BAF312/Placebo): Week 0: 1099/546, Week 4: 1096/545, Week 12: 1053/534, Week 24: 1008/519, Week 36: 981/493, Week 48: 914/456, Week 60: 806/383, Week 72: 643/300, Week 84: 509/234, Week 96: 396/173, Week 108: 291/124, Week 120: 200/79, Week 132: 113/40, Week 144: 51/20, Week 156: 10/5, Week 168: 0/0

Log rank test: p-value = 0,761
*: p < 0,05

Analysis population: A2304 SAF total population

Figure 12.1.5.140: JOINT SWELLING (PT, severe)

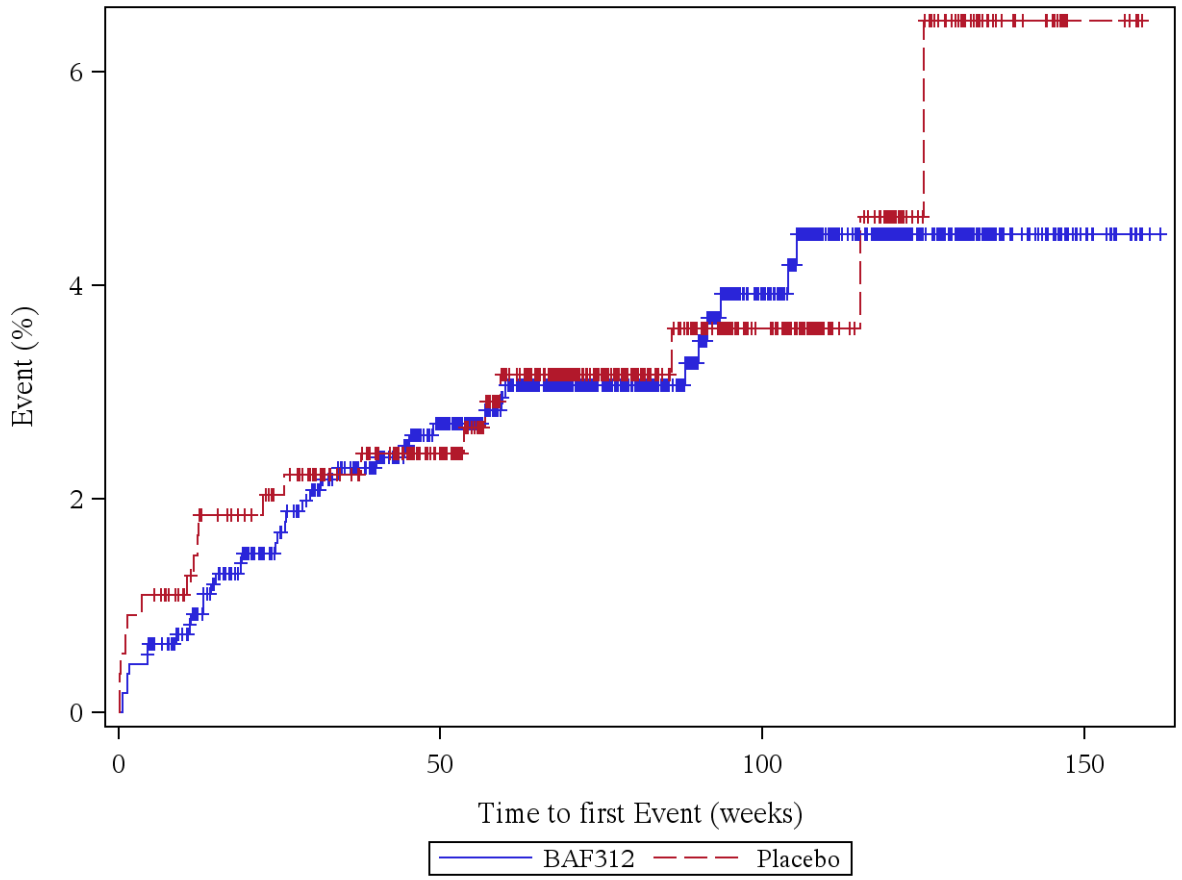


Patients at risk (BAF312/Placebo): Week 0: 1099/546, Week 4: 1099/546, Week 12: 1059/535, Week 24: 1017/521, Week 36: 990/497, Week 48: 925/461, Week 60: 818/388, Week 72: 651/305, Week 84: 515/237, Week 96: 400/176, Week 108: 291/126, Week 120: 200/80, Week 132: 113/40, Week 144: 51/20, Week 156: 10/5, Week 168: 0/0

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

Analysis population: A2304 SAF total population

Figure 12.1.5.141: MUSCLE SPASMS (PT, not severe)

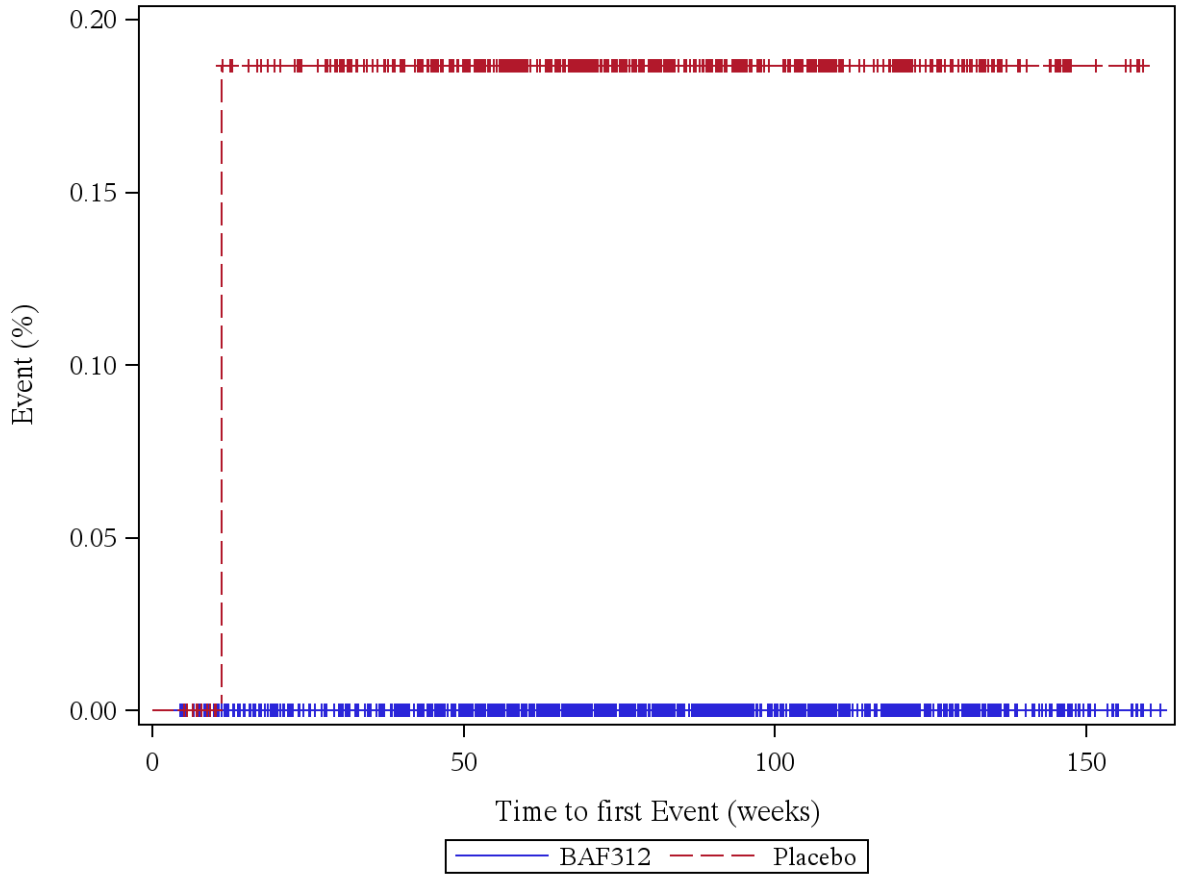


Patients at risk (BAF312/Placebo): Week 0: 1099/546, Week 4: 1094/540, Week 12: 1049/528, Week 24: 1001/511, Week 36: 967/487, Week 48: 903/450, Week 60: 798/376, Week 72: 641/294, Week 84: 507/229, Week 96: 391/168, Week 108: 282/119, Week 120: 193/73, Week 132: 111/33, Week 144: 51/17, Week 156: 10/5, Week 168: 0/0

Log rank test: p-value = 0,850
*: p < 0,05

Analysis population: A2304 SAF total population

Figure 12.1.5.142: MUSCLE SPASMS (PT, severe)

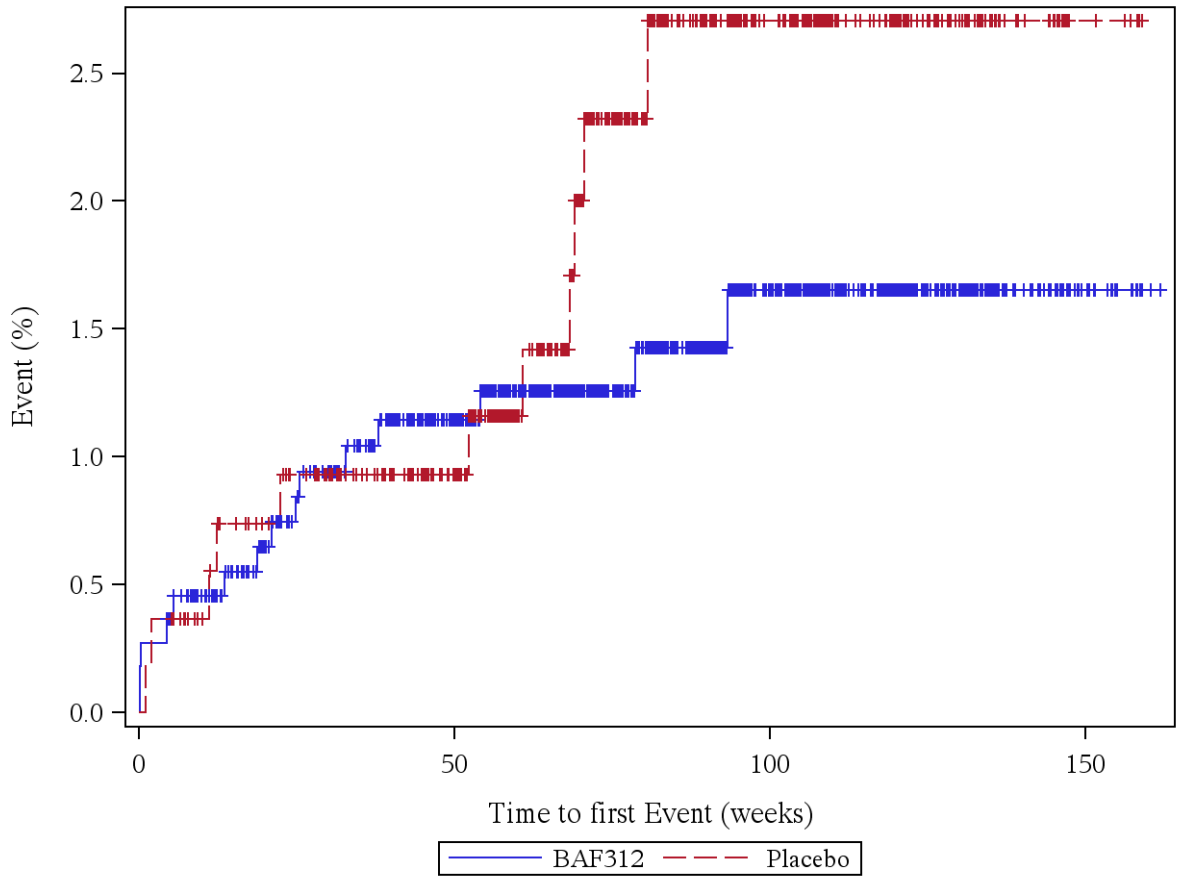


Patients at risk (BAF312/Placebo): Week 0: 1099/546, Week 4: 1099/546, Week 12: 1059/534, Week 24: 1017/520, Week 36: 990/496, Week 48: 925/460, Week 60: 818/387, Week 72: 652/304, Week 84: 516/236, Week 96: 400/175, Week 108: 291/125, Week 120: 200/79, Week 132: 113/39, Week 144: 51/19, Week 156: 10/5, Week 168: 0/0

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

Analysis population: A2304 SAF total population

Figure 12.1.5.143: MUSCULAR WEAKNESS (PT, not severe)

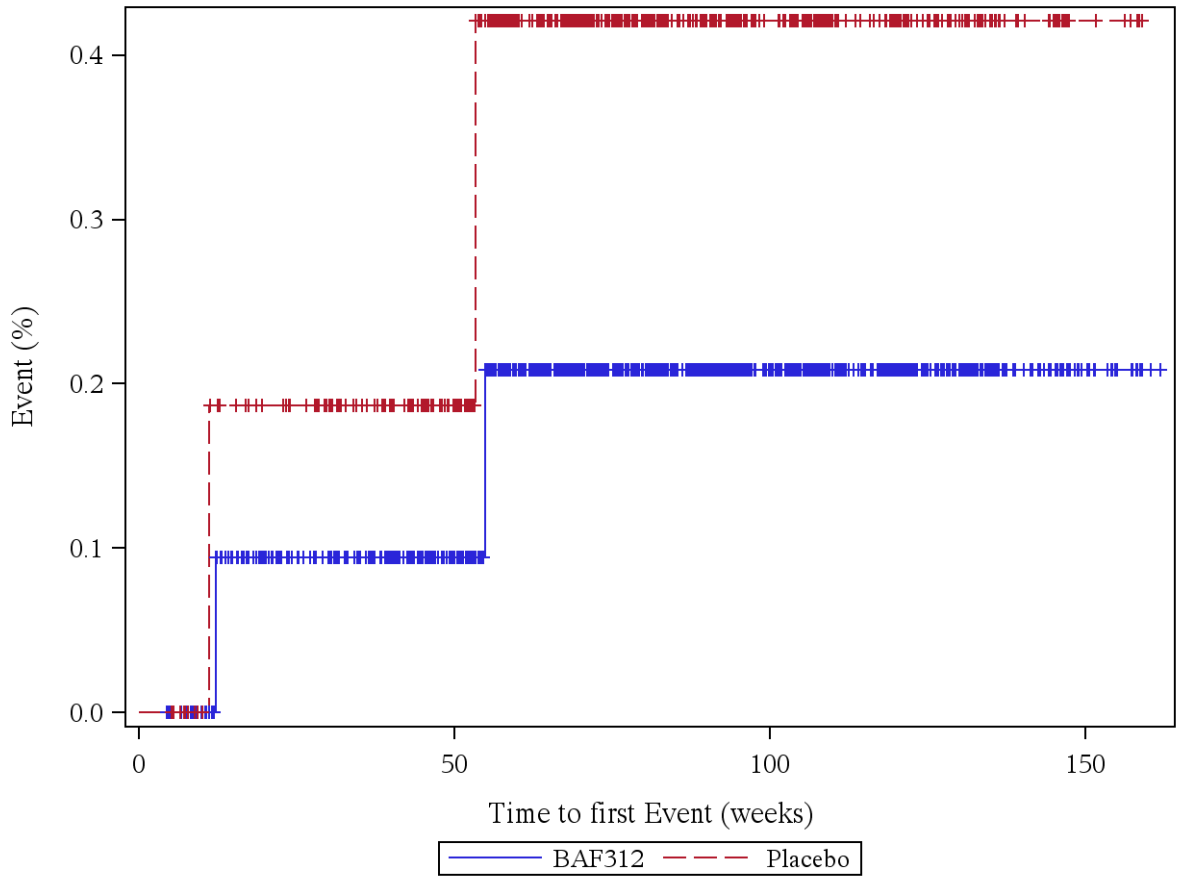


Patients at risk (BAF312/Placebo): Week 0: 1099/546, Week 4: 1096/544, Week 12: 1055/532, Week 24: 1010/516, Week 36: 981/492, Week 48: 916/457, Week 60: 810/385, Week 72: 648/298, Week 84: 512/230, Week 96: 396/173, Week 108: 287/124, Week 120: 198/78, Week 132: 113/38, Week 144: 51/18, Week 156: 10/5, Week 168: 0/0

Log rank test: p-value = 0,307
*: p < 0,05

Analysis population: A2304 SAF total population

Figure 12.1.5.144: MUSCULAR WEAKNESS (PT, severe)

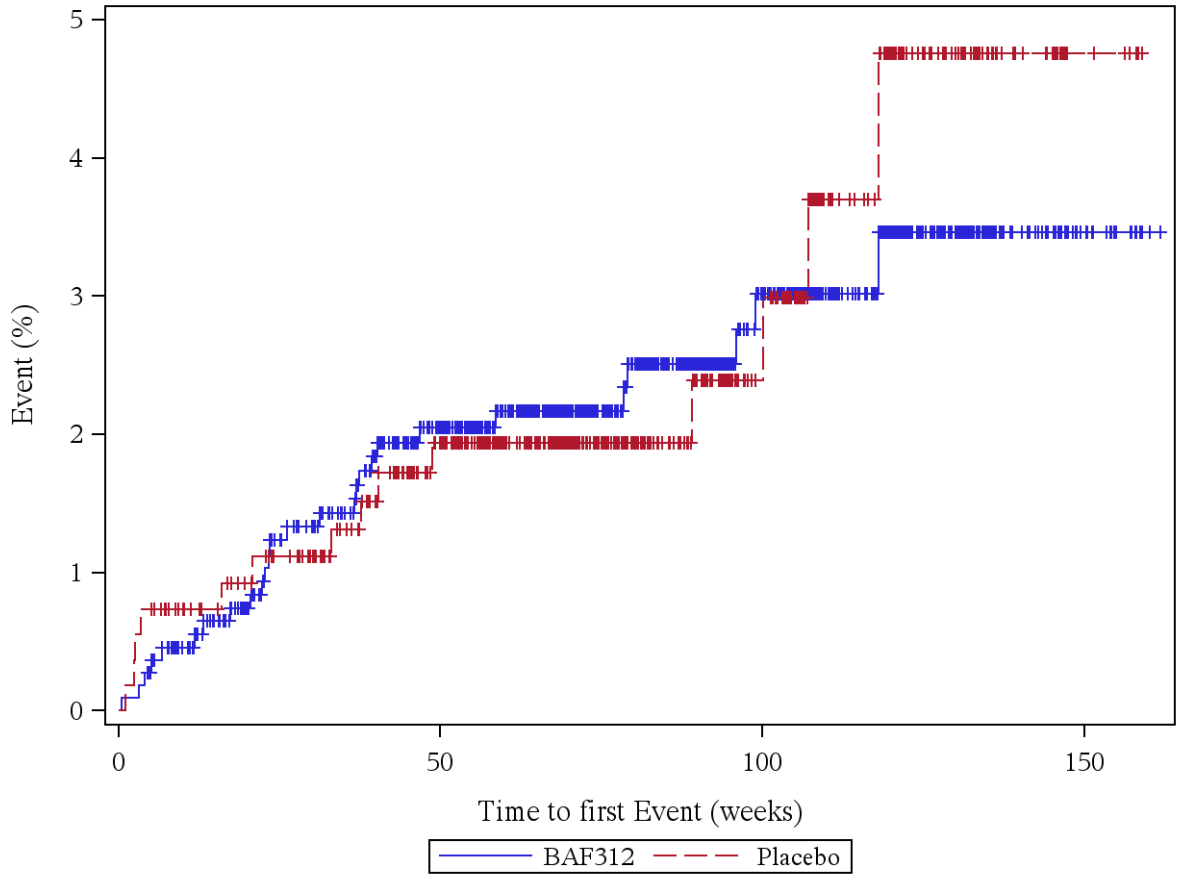


Patients at risk (BAF312/Placebo): Week 0: 1099/546, Week 4: 1099/546, Week 12: 1059/534, Week 24: 1016/521, Week 36: 989/497, Week 48: 924/461, Week 60: 817/387, Week 72: 651/304, Week 84: 516/236, Week 96: 400/176, Week 108: 291/126, Week 120: 200/80, Week 132: 113/40, Week 144: 51/20, Week 156: 10/5, Week 168: 0/0

Log rank test: p-value = 0,468
*: p < 0,05

Analysis population: A2304 SAF total population

Figure 12.1.5.145: MUSCULOSKELETAL PAIN (PT, not severe)

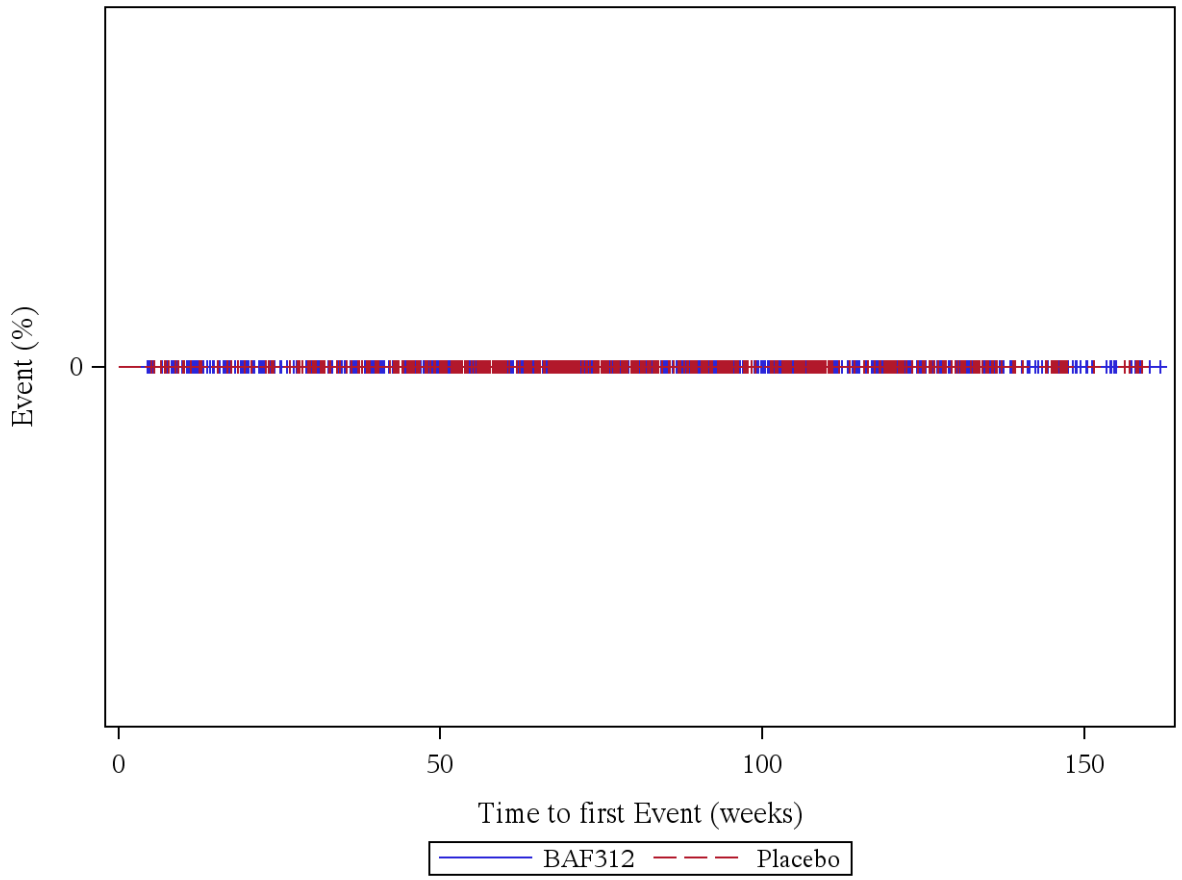


Patients at risk (BAF312/Placebo): Week 0: 1099/546, Week 4: 1096/542, Week 12: 1054/531, Week 24: 1005/515, Week 36: 976/490, Week 48: 906/453, Week 60: 800/379, Week 72: 638/296, Week 84: 503/231, Week 96: 389/172, Week 108: 283/122, Week 120: 194/76, Week 132: 111/37, Week 144: 49/18, Week 156: 10/5, Week 168: 0/0

Log rank test: p-value = 0,860
*: p < 0,05

Analysis population: A2304 SAF total population

Figure 12.1.5.146: MUSCULOSKELETAL PAIN (PT, severe)

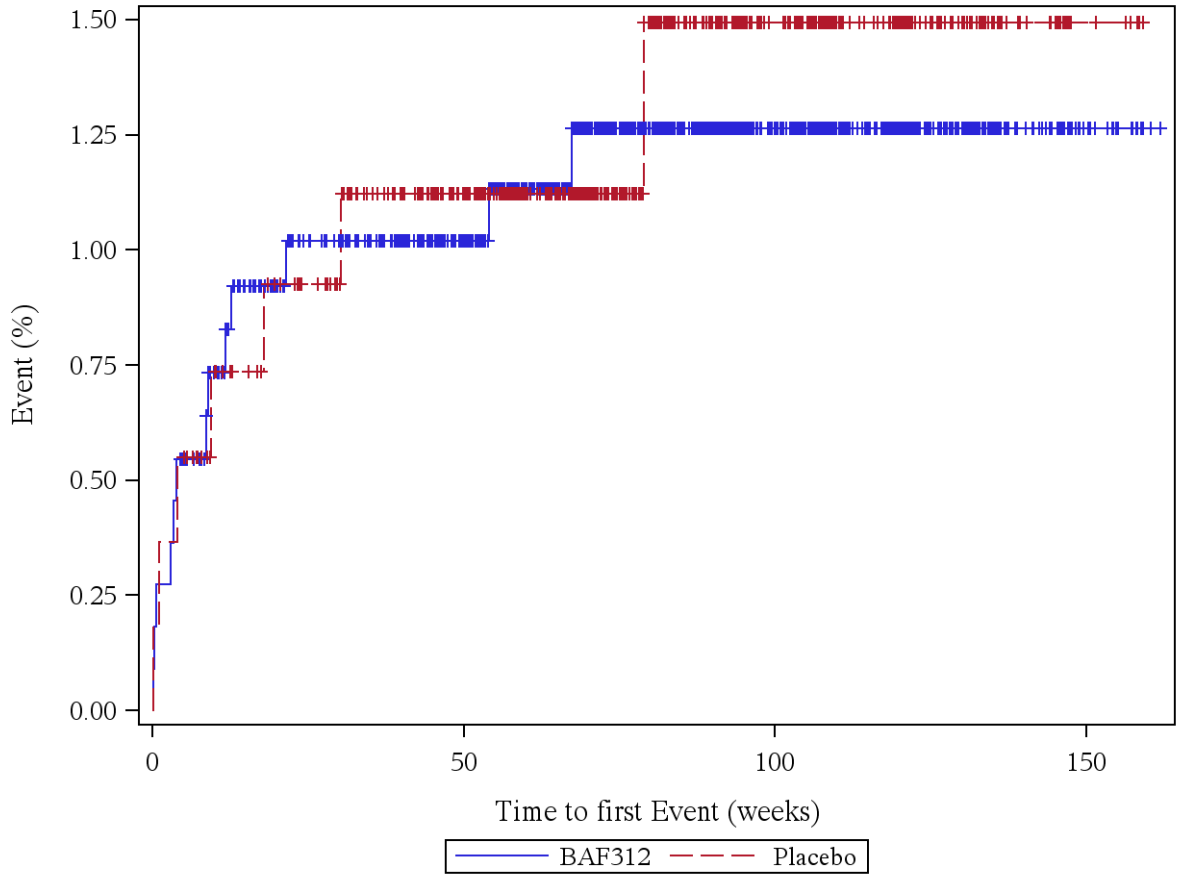


Patients at risk (BAF312/Placebo): Week 0: 1099/546, Week 4: 1099/546, Week 12: 1059/535, Week 24: 1017/521, Week 36: 990/497, Week 48: 925/461, Week 60: 818/388, Week 72: 652/305, Week 84: 516/237, Week 96: 400/176, Week 108: 291/126, Week 120: 200/80, Week 132: 113/40, Week 144: 51/20, Week 156: 10/5, Week 168: 0/0

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

Analysis population: A2304 SAF total population

Figure 12.1.5.147: MYALGIA (PT, not severe)

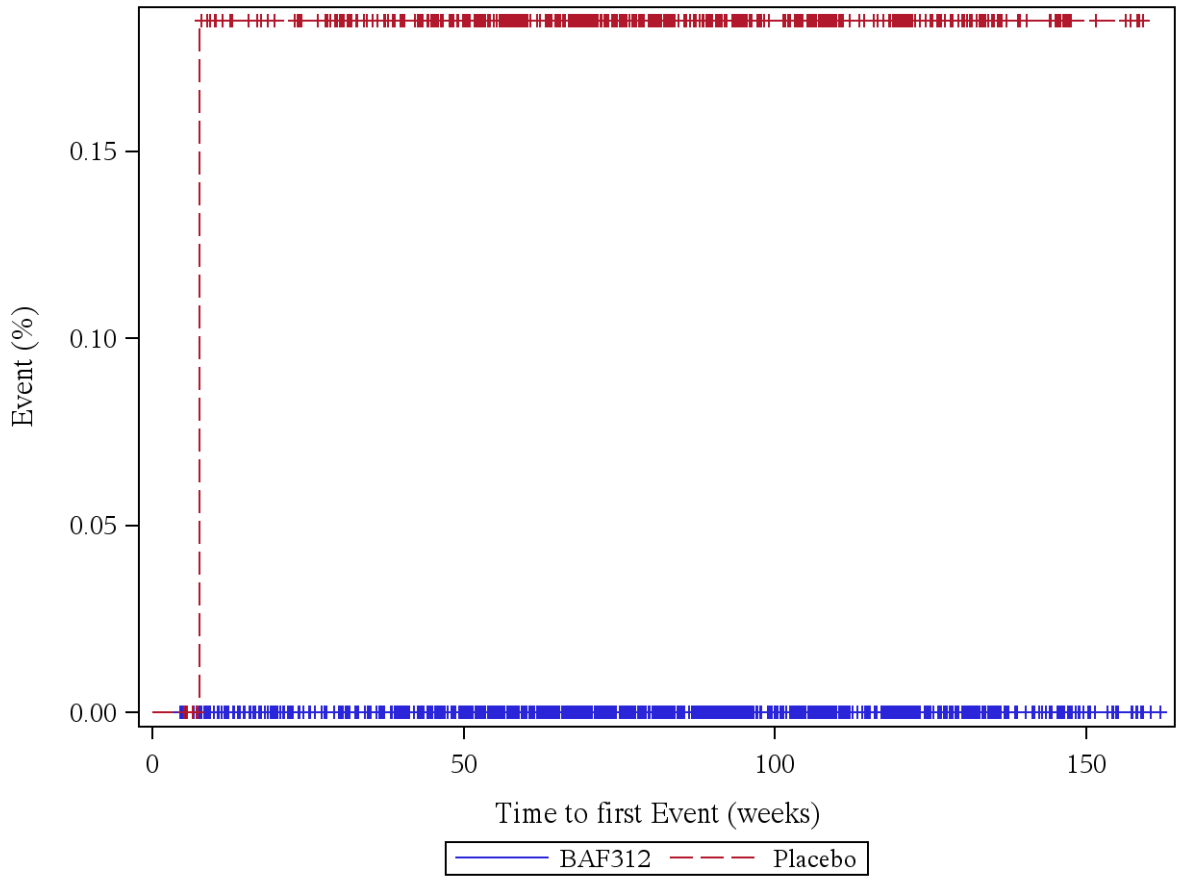


Patients at risk (BAF312/Placebo): Week 0: 1099/546, Week 4: 1093/543, Week 12: 1050/531, Week 24: 1006/516, Week 36: 980/491, Week 48: 915/457, Week 60: 809/384, Week 72: 643/301, Week 84: 513/232, Week 96: 398/174, Week 108: 289/126, Week 120: 198/80, Week 132: 112/40, Week 144: 51/20, Week 156: 10/5, Week 168: 0/0

Log rank test: p-value = 0,863
*: p < 0,05

Analysis population: A2304 SAF total population

Figure 12.1.5.148: MYALGIA (PT, severe)

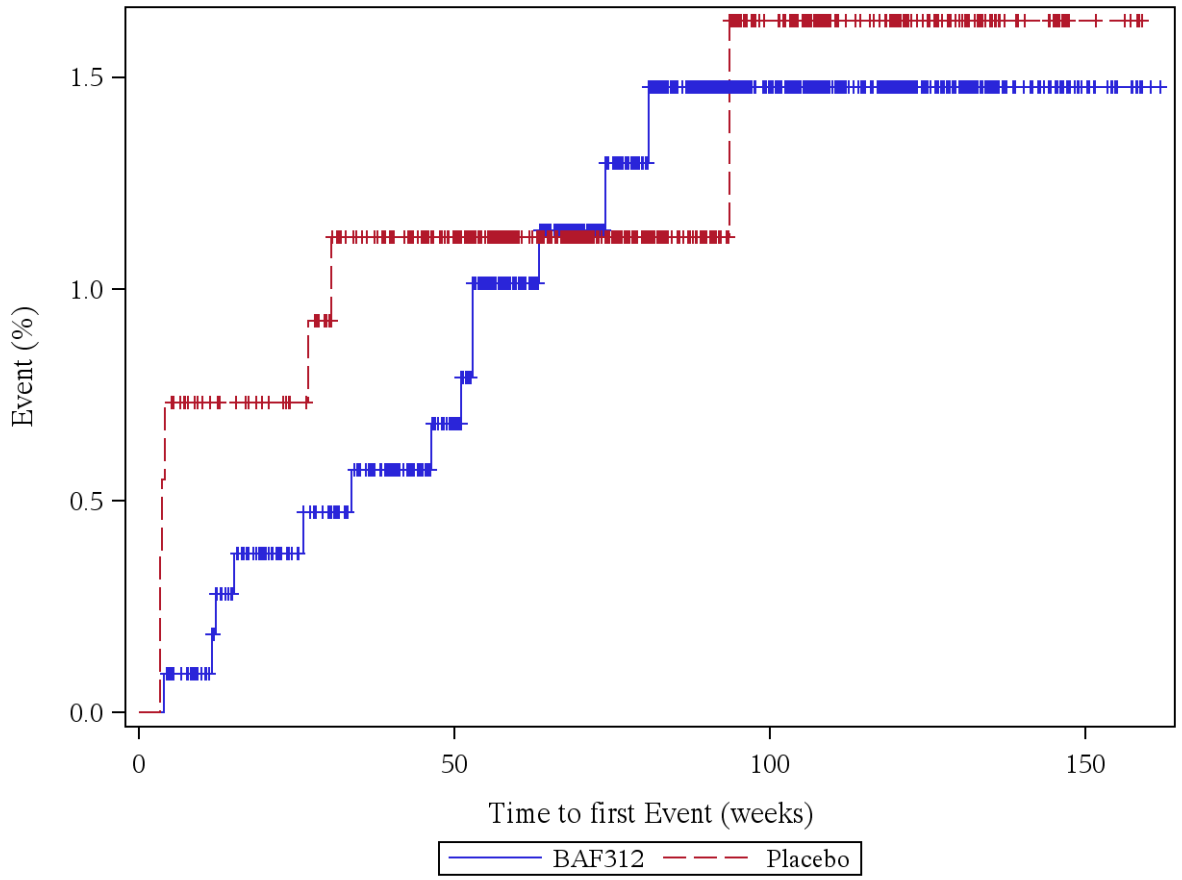


Patients at risk (BAF312/Placebo): Week 0: 1099/546, Week 4: 1099/546, Week 12: 1059/534, Week 24: 1017/521, Week 36: 990/497, Week 48: 925/461, Week 60: 818/388, Week 72: 652/305, Week 84: 516/237, Week 96: 400/176, Week 108: 291/126, Week 120: 200/80, Week 132: 113/40, Week 144: 51/20, Week 156: 10/5, Week 168: 0/0

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

Analysis population: A2304 SAF total population

Figure 12.1.5.149: NECK PAIN (PT, not severe)

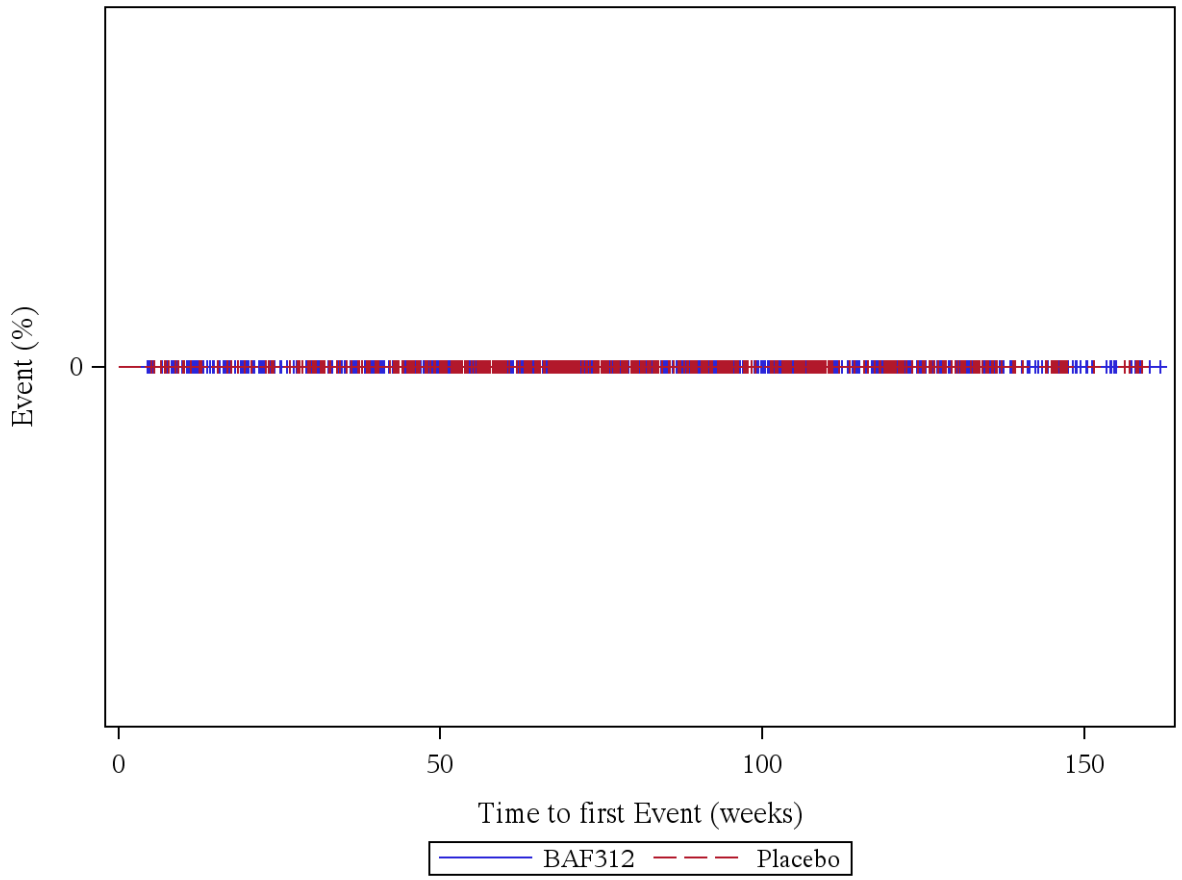


Patients at risk (BAF312/Placebo): Week 0: 1099/546, Week 4: 1098/543, Week 12: 1057/531, Week 24: 1013/517, Week 36: 985/491, Week 48: 920/456, Week 60: 811/383, Week 72: 645/301, Week 84: 511/233, Week 96: 397/171, Week 108: 289/122, Week 120: 199/79, Week 132: 112/40, Week 144: 51/20, Week 156: 10/5, Week 168: 0/0

Log rank test: p-value = 0,840
*: p < 0,05

Analysis population: A2304 SAF total population

Figure 12.1.5.150: NECK PAIN (PT, severe)

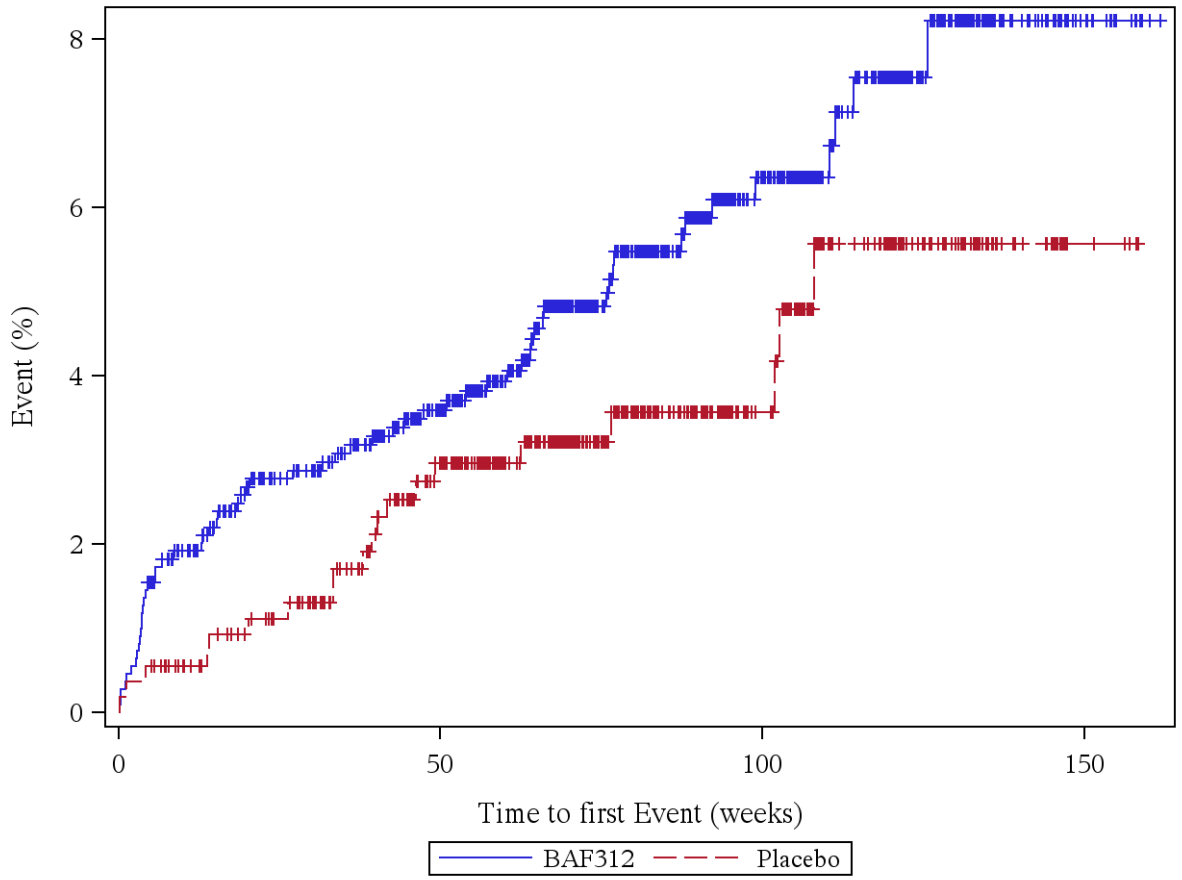


Patients at risk (BAF312/Placebo): Week 0: 1099/546, Week 4: 1099/546, Week 12: 1059/535, Week 24: 1017/521, Week 36: 990/497, Week 48: 925/461, Week 60: 818/388, Week 72: 652/305, Week 84: 516/237, Week 96: 400/176, Week 108: 291/126, Week 120: 200/80, Week 132: 113/40, Week 144: 51/20, Week 156: 10/5, Week 168: 0/0

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

Analysis population: A2304 SAF total population

Figure 12.1.5.151: PAIN IN EXTREMITY (PT, not severe)

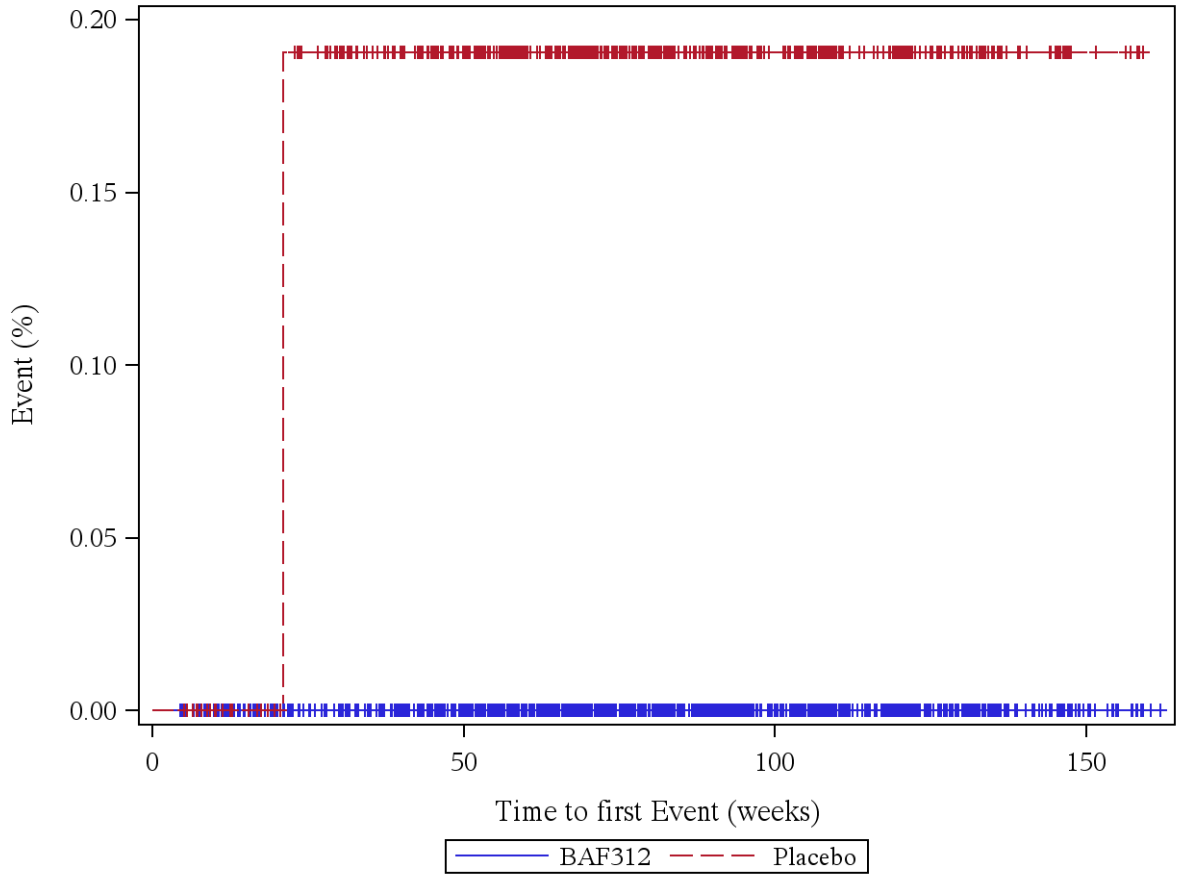


Patients at risk (BAF312/Placebo): Week 0: 1099/546, Week 4: 1084/544, Week 12: 1042/532, Week 24: 992/515, Week 36: 962/488, Week 48: 894/450, Week 60: 787/380, Week 72: 623/298, Week 84: 491/230, Week 96: 381/172, Week 108: 274/120, Week 120: 189/78, Week 132: 104/39, Week 144: 47/19, Week 156: 9/4, Week 168: 0/0

Log rank test: p-value = 0,129
*: p < 0,05

Analysis population: A2304 SAF total population

Figure 12.1.5.152: PAIN IN EXTREMITY (PT, severe)

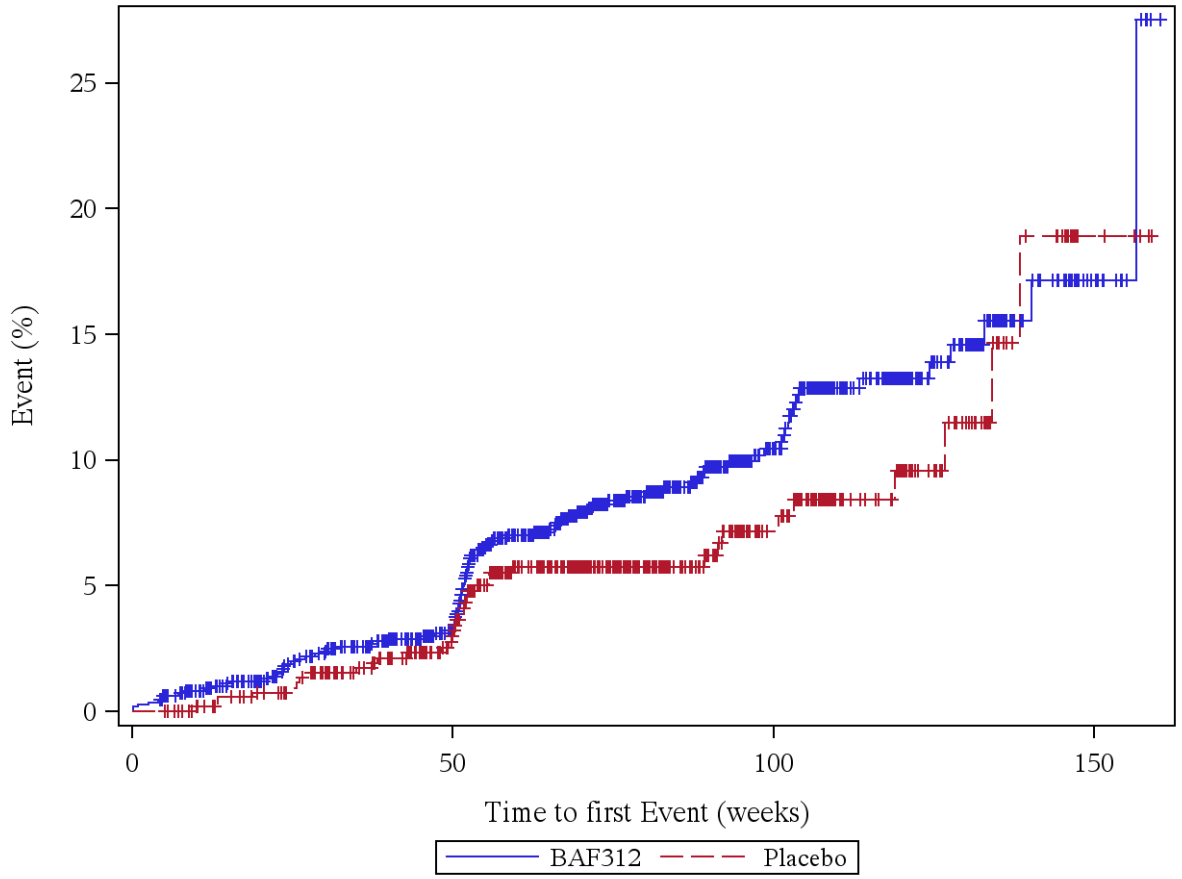


Patients at risk (BAF312/Placebo): Week 0: 1099/546, Week 4: 1099/546, Week 12: 1059/535, Week 24: 1017/520, Week 36: 990/496, Week 48: 925/460, Week 60: 818/387, Week 72: 652/304, Week 84: 516/236, Week 96: 400/176, Week 108: 291/126, Week 120: 200/80, Week 132: 113/40, Week 144: 51/20, Week 156: 10/5, Week 168: 0/0

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

Analysis population: A2304 SAF total population

Figure 12.1.5.153: NEOPLASMS BENIGN, MALIGNANT AND UNSPECIFIED (INCL CYSTS AND POLYPS) (SOC, not severe)

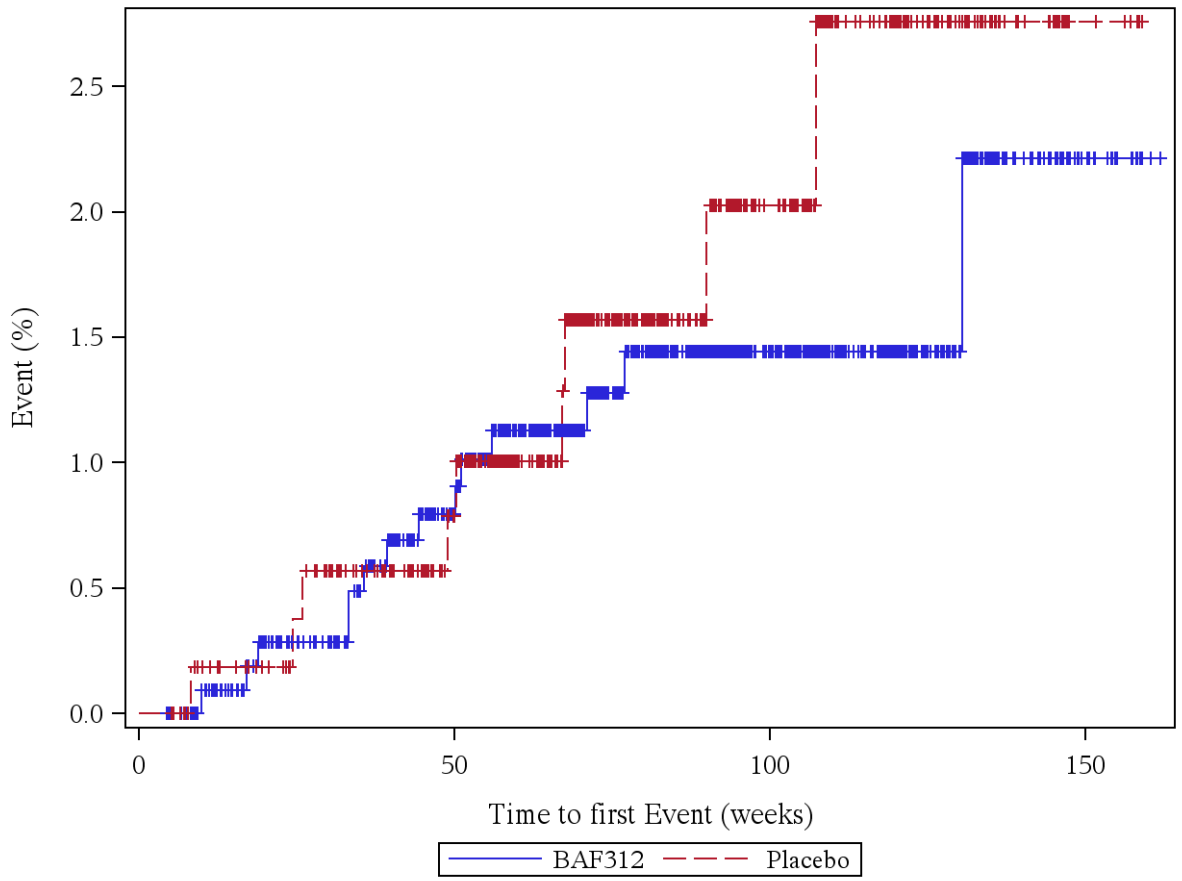


Patients at risk (BAF312/Placebo): Week 0: 1099/546, Week 4: 1094/546, Week 12: 1049/534, Week 24: 998/517, Week 36: 963/489, Week 48: 897/452, Week 60: 761/367, Week 72: 602/287, Week 84: 471/222, Week 96: 367/162, Week 108: 259/113, Week 120: 174/70, Week 132: 100/35, Week 144: 44/18, Week 156: 8/4, Week 168: 0/0

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

Analysis population: A2304 SAF total population

Figure 12.1.5.154: NEOPLASMS BENIGN, MALIGNANT AND UNSPECIFIED (INCL CYSTS AND POLYPS) (SOC, severe)

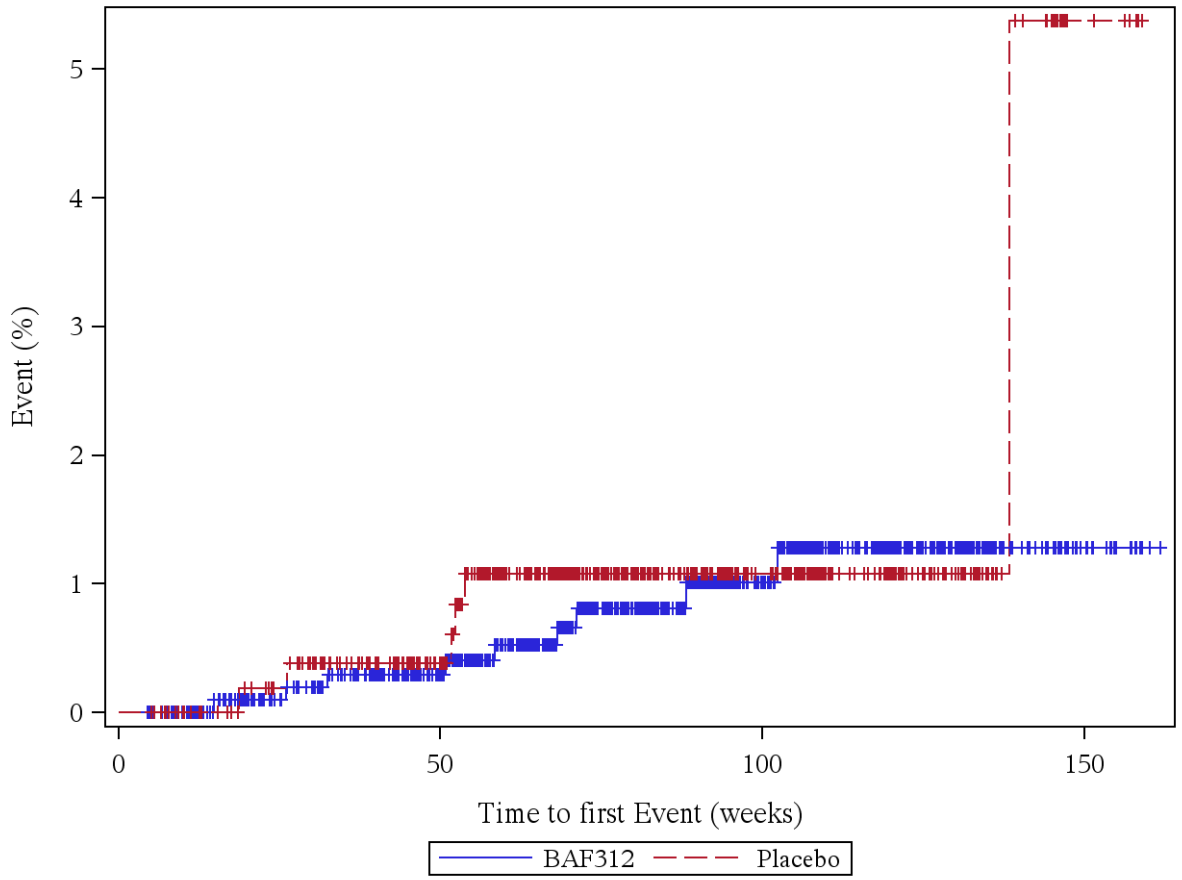


Patients at risk (BAF312/Placebo): Week 0: 1099/546, Week 4: 1099/546, Week 12: 1058/534, Week 24: 1014/520, Week 36: 984/496, Week 48: 922/460, Week 60: 813/386, Week 72: 648/302, Week 84: 513/234, Week 96: 397/173, Week 108: 288/122, Week 120: 197/78, Week 132: 111/39, Week 144: 51/20, Week 156: 10/5, Week 168: 0/0

Log rank test: p-value = 0,500
*: p < 0,05

Analysis population: A2304 SAF total population

Figure 12.1.5.155: BASAL CELL CARCINOMA (PT, not severe)

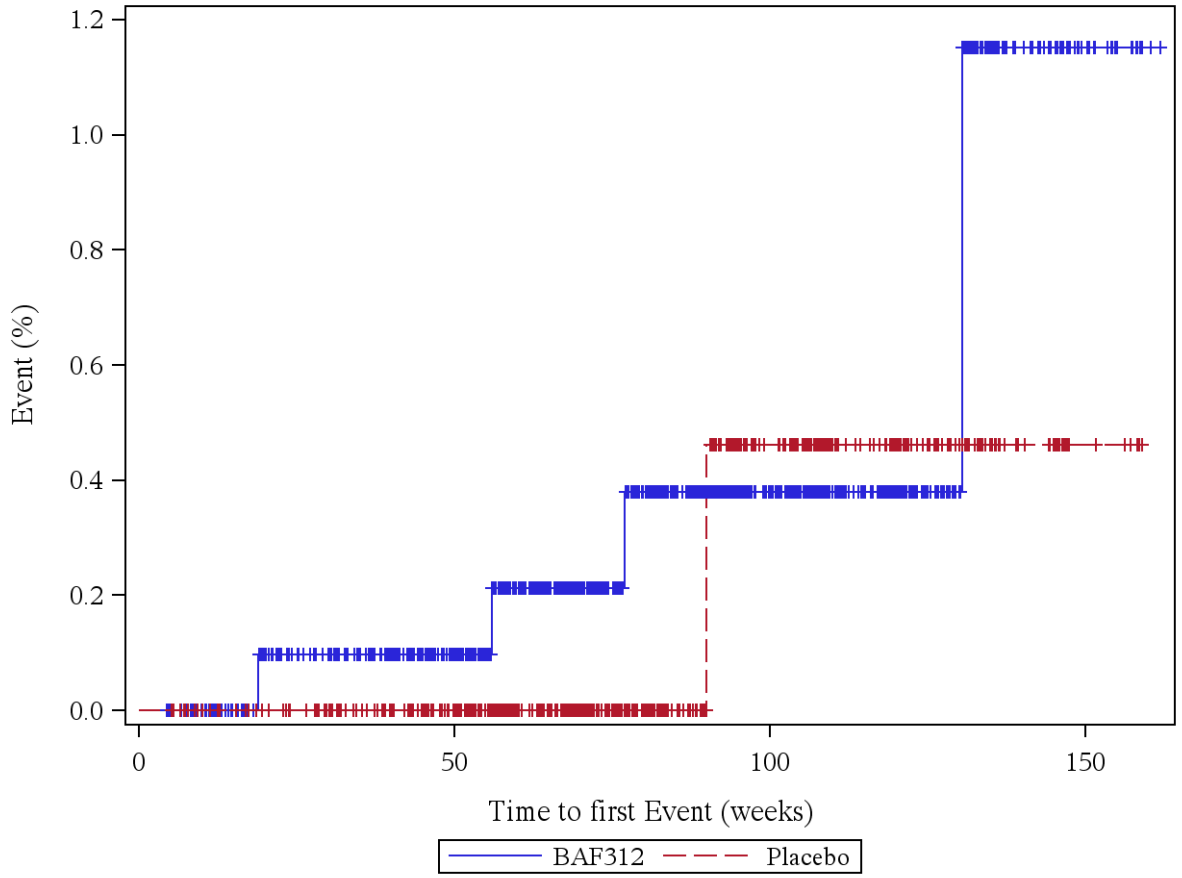


Patients at risk (BAF312/Placebo): Week 0: 1099/546, Week 4: 1099/546, Week 12: 1059/535, Week 24: 1016/520, Week 36: 987/495, Week 48: 922/459, Week 60: 814/383, Week 72: 646/302, Week 84: 511/235, Week 96: 398/174, Week 108: 289/124, Week 120: 198/79, Week 132: 112/40, Week 144: 51/20, Week 156: 10/5, Week 168: 0/0

Log rank test: p-value = 0,517
*: p < 0,05

Analysis population: A2304 SAF total population

Figure 12.1.5.156: BASAL CELL CARCINOMA (PT, severe)

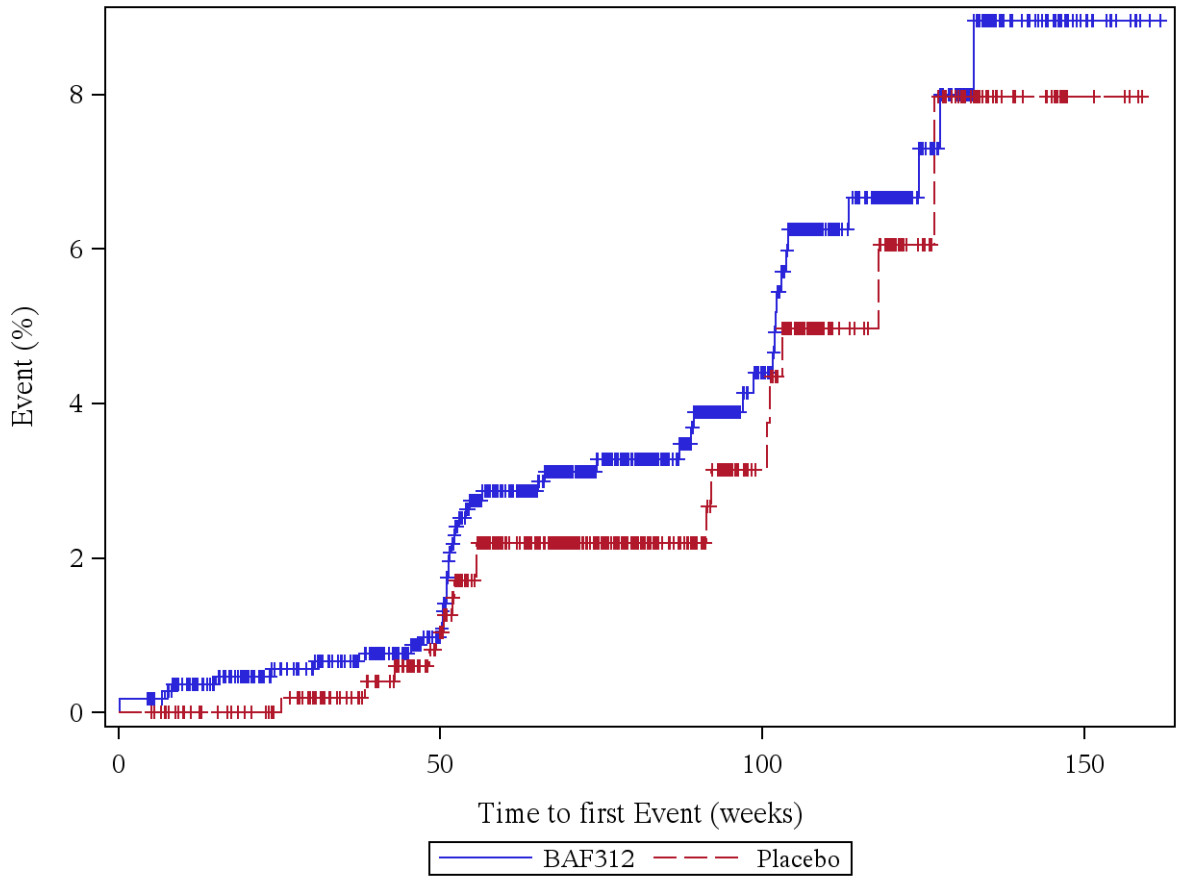


Patients at risk (BAF312/Placebo): Week 0: 1099/546, Week 4: 1099/546, Week 12: 1059/535, Week 24: 1016/521, Week 36: 989/497, Week 48: 924/461, Week 60: 816/388, Week 72: 651/305, Week 84: 514/237, Week 96: 398/175, Week 108: 289/125, Week 120: 198/80, Week 132: 112/40, Week 144: 51/20, Week 156: 10/5, Week 168: 0/0

Log rank test: p-value = 0,591
*: p < 0,05

Analysis population: A2304 SAF total population

Figure 12.1.5.157: MELANOCYTIC NAEVUS (PT, not severe)

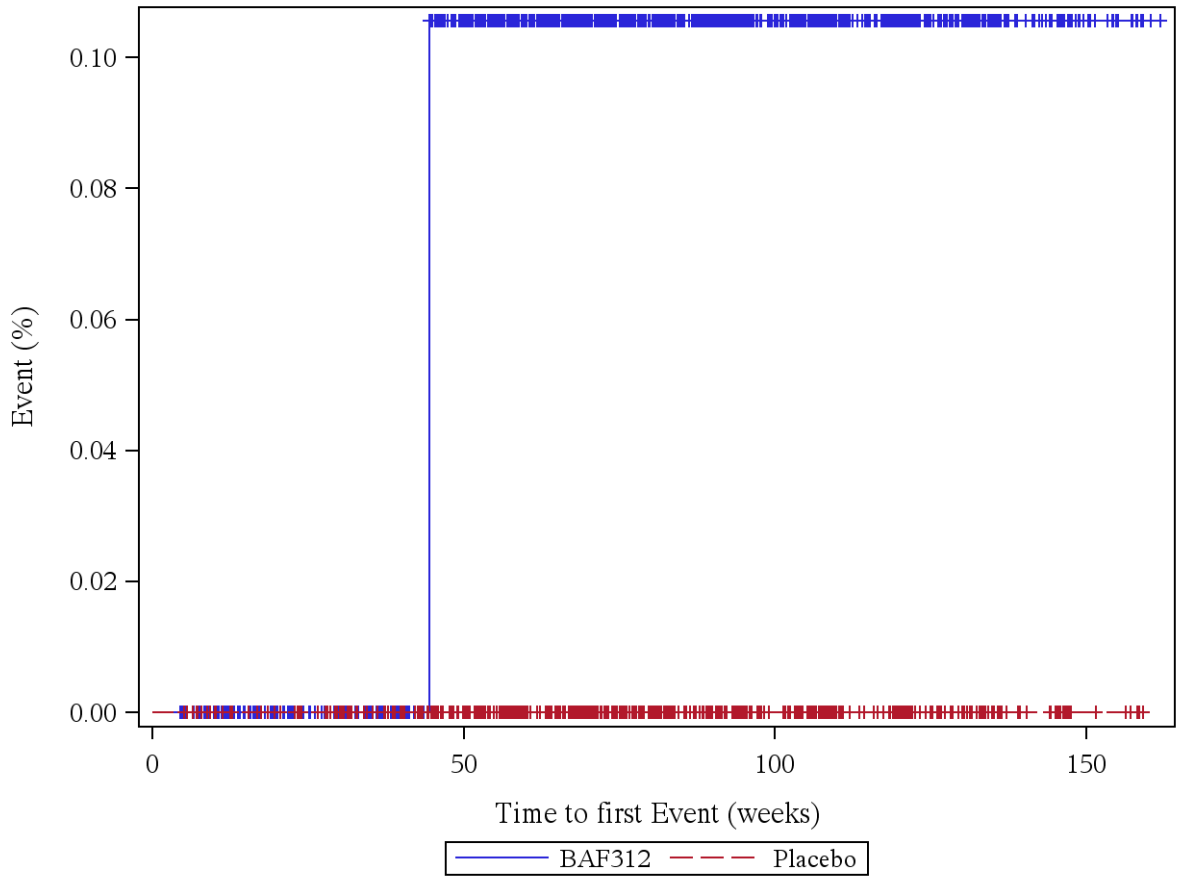


Patients at risk (BAF312/Placebo): Week 0: 1099/546, Week 4: 1097/546, Week 12: 1055/535, Week 24: 1011/521, Week 36: 983/496, Week 48: 916/460, Week 60: 793/382, Week 72: 635/299, Week 84: 501/232, Week 96: 392/170, Week 108: 278/118, Week 120: 190/74, Week 132: 106/37, Week 144: 46/18, Week 156: 8/4, Week 168: 0/0

Log rank test: p-value = 0,404
*: p < 0,05

Analysis population: A2304 SAF total population

Figure 12.1.5.158: MELANOCYTIC NAEVUS (PT, severe)

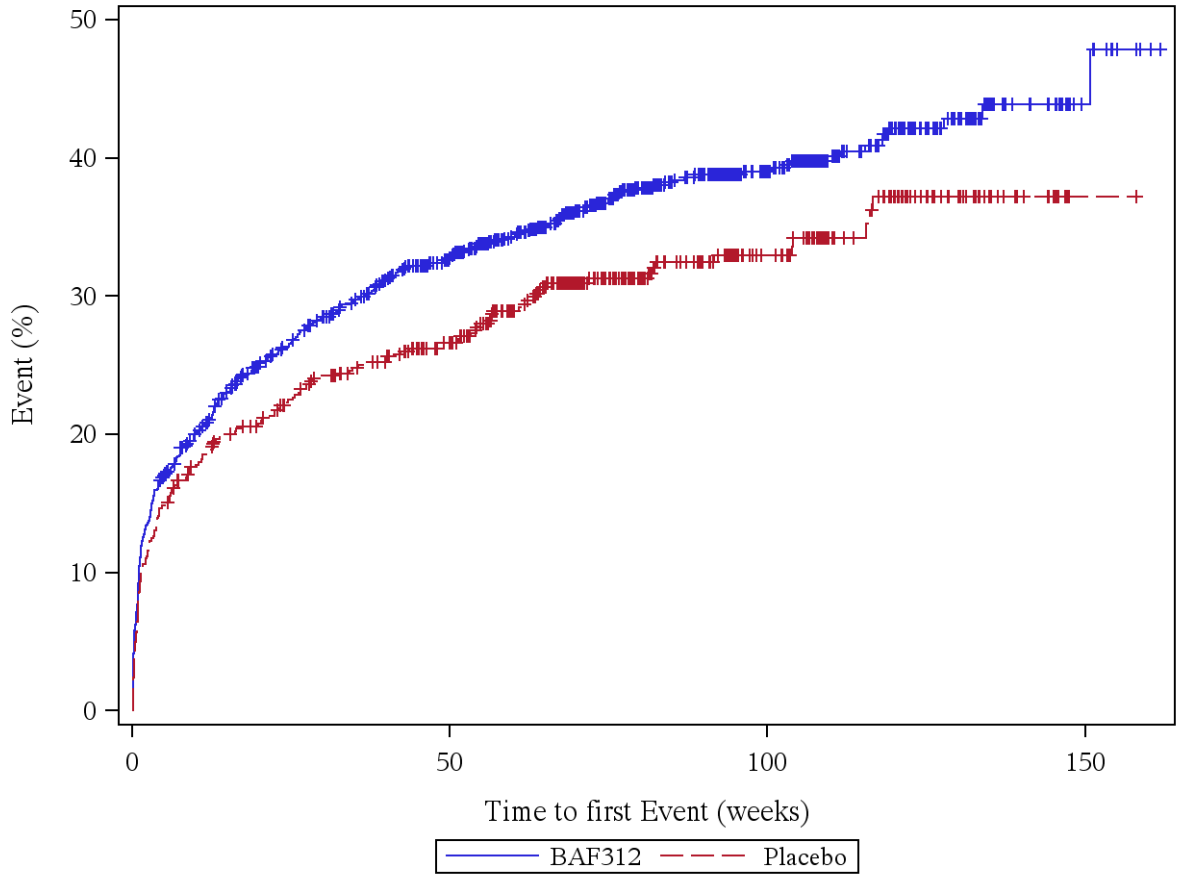


Patients at risk (BAF312/Placebo): Week 0: 1099/546, Week 4: 1099/546, Week 12: 1059/535, Week 24: 1017/521, Week 36: 990/497, Week 48: 925/461, Week 60: 818/388, Week 72: 652/305, Week 84: 516/237, Week 96: 400/176, Week 108: 291/126, Week 120: 200/80, Week 132: 113/40, Week 144: 51/20, Week 156: 10/5, Week 168: 0/0

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

Analysis population: A2304 SAF total population

Figure 12.1.5.159: NERVOUS SYSTEM DISORDERS (SOC, not severe)

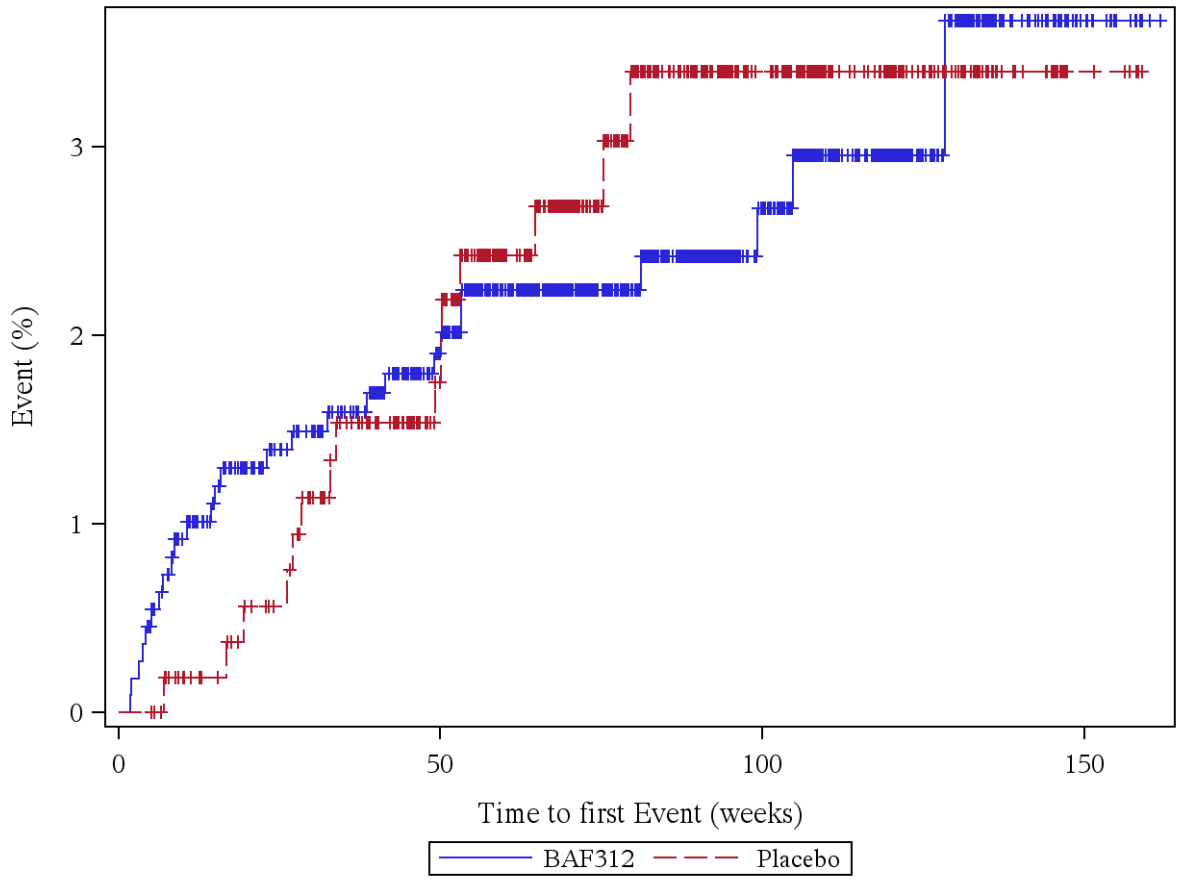


Patients at risk (BAF312/Placebo): Week 0: 1099/546, Week 4: 923/470, Week 12: 842/439, Week 24: 759/407, Week 36: 704/377, Week 48: 639/345, Week 60: 557/288, Week 72: 429/213, Week 84: 329/158, Week 96: 266/121, Week 108: 187/86, Week 120: 126/52, Week 132: 68/24, Week 144: 35/11, Week 156: 6/1, Week 168: 0/0

Log rank test: p-value = 0,028 *
*: p < 0,05

Analysis population: A2304 SAF total population

Figure 12.1.5.160: NERVOUS SYSTEM DISORDERS (SOC, severe)

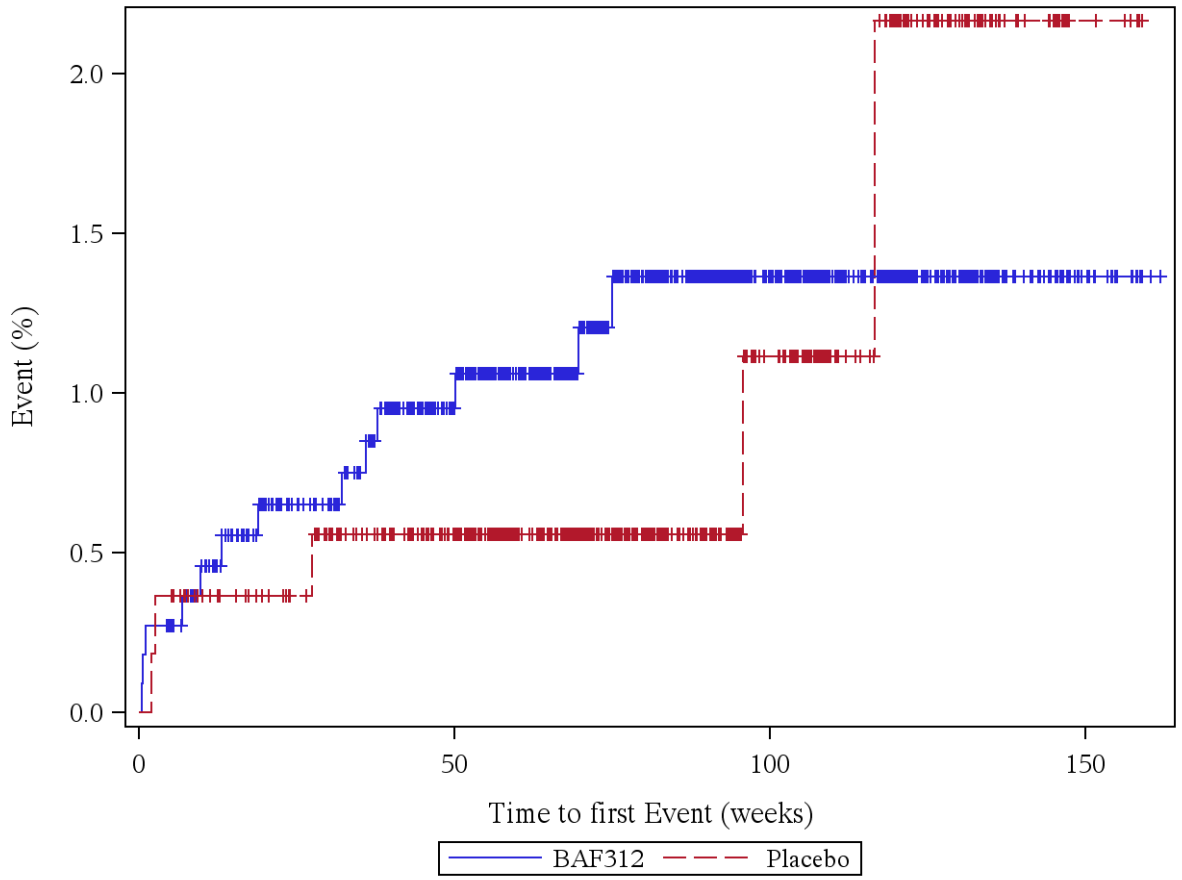


Patients at risk (BAF312/Placebo): Week 0: 1099/546, Week 4: 1095/546, Week 12: 1049/534, Week 24: 1007/519, Week 36: 978/492, Week 48: 913/457, Week 60: 805/382, Week 72: 642/300, Week 84: 507/231, Week 96: 394/172, Week 108: 286/123, Week 120: 196/77, Week 132: 110/39, Week 144: 49/19, Week 156: 9/5, Week 168: 0/0

Log rank test: p-value = 0,705
*: p < 0,05

Analysis population: A2304 SAF total population

Figure 12.1.5.161: BALANCE DISORDER (PT, not severe)

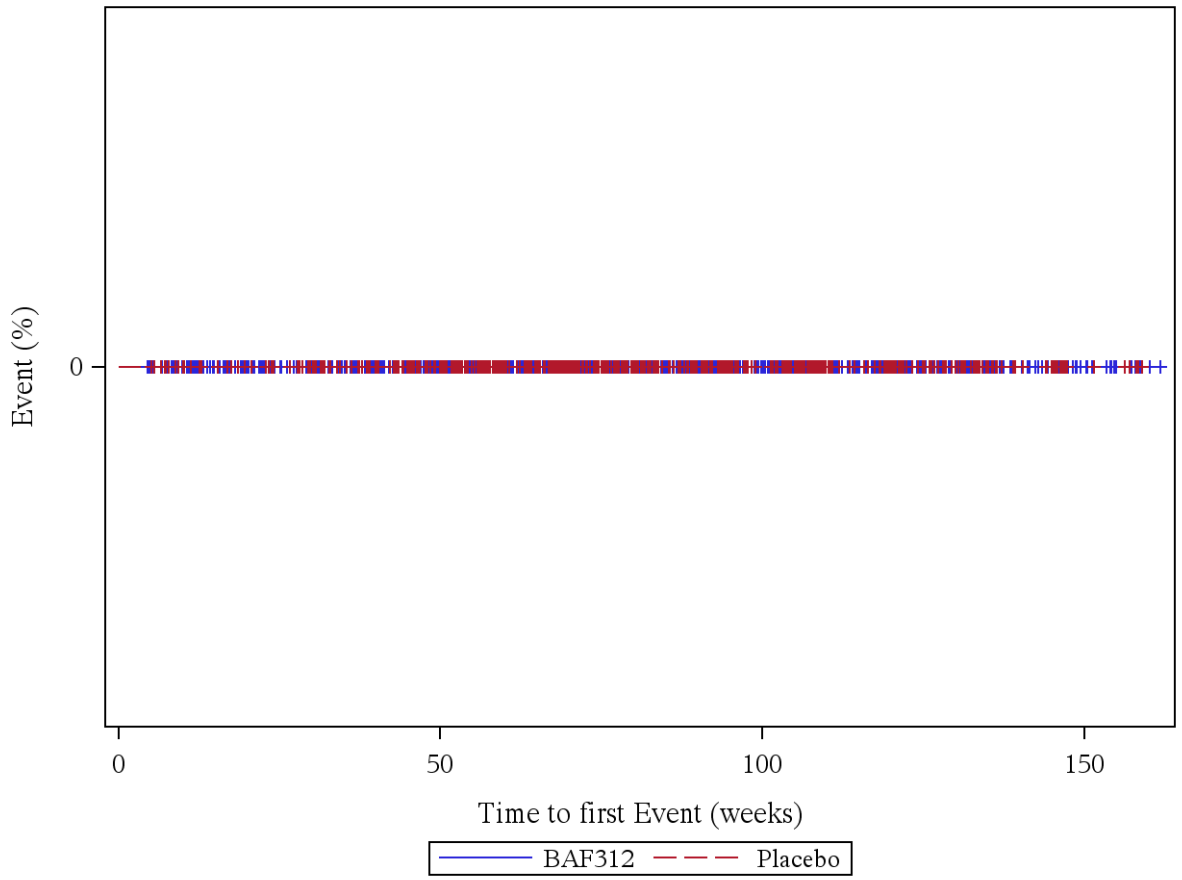


Patients at risk (BAF312/Placebo): Week 0: 1099/546, Week 4: 1096/544, Week 12: 1055/533, Week 24: 1012/519, Week 36: 983/494, Week 48: 917/459, Week 60: 811/386, Week 72: 645/303, Week 84: 512/236, Week 96: 398/174, Week 108: 290/124, Week 120: 199/78, Week 132: 113/38, Week 144: 51/19, Week 156: 10/5, Week 168: 0/0

Log rank test: p-value = 0,646
*: p < 0,05

Analysis population: A2304 SAF total population

Figure 12.1.5.162: BALANCE DISORDER (PT, severe)

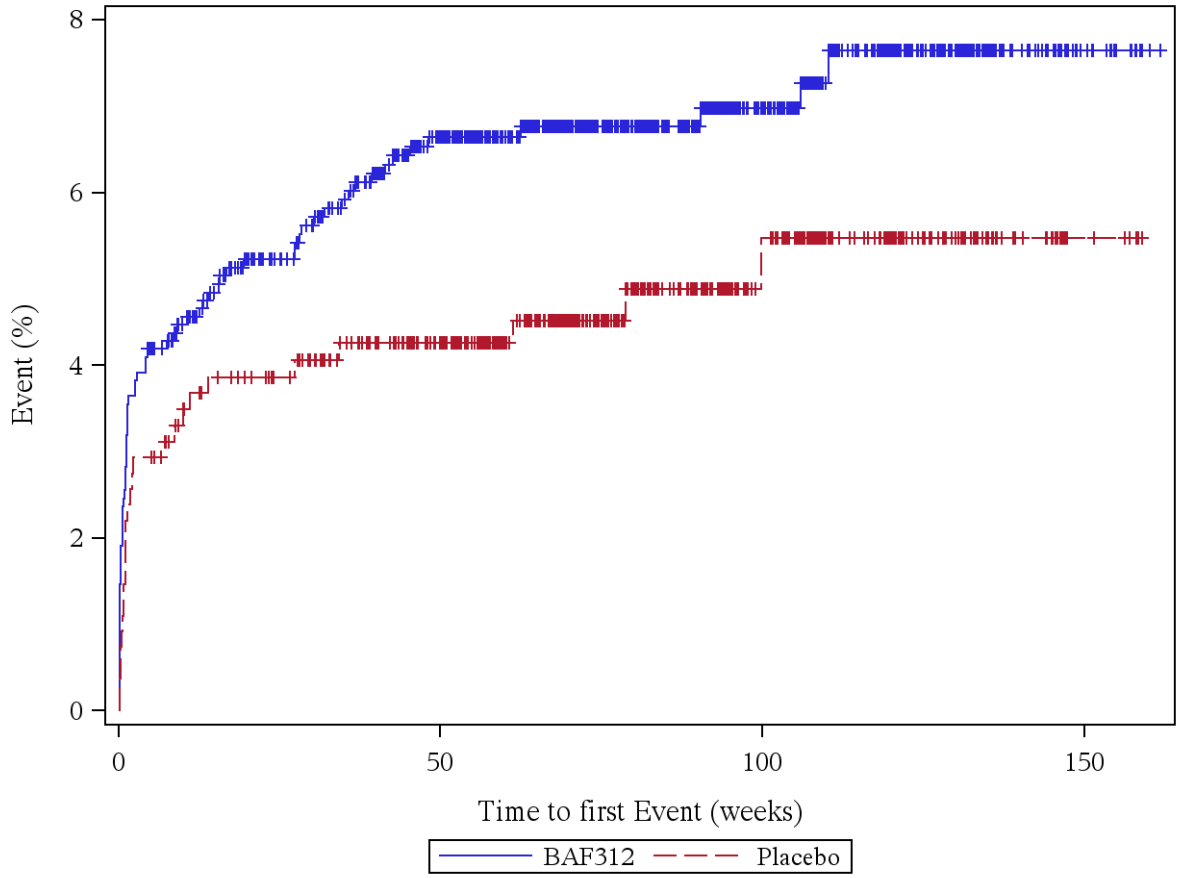


Patients at risk (BAF312/Placebo): Week 0: 1099/546, Week 4: 1099/546, Week 12: 1059/535, Week 24: 1017/521, Week 36: 990/497, Week 48: 925/461, Week 60: 818/388, Week 72: 652/305, Week 84: 516/237, Week 96: 400/176, Week 108: 291/126, Week 120: 200/80, Week 132: 113/40, Week 144: 51/20, Week 156: 10/5, Week 168: 0/0

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

Analysis population: A2304 SAF total population

Figure 12.1.5.163: DIZZINESS (PT, not severe)

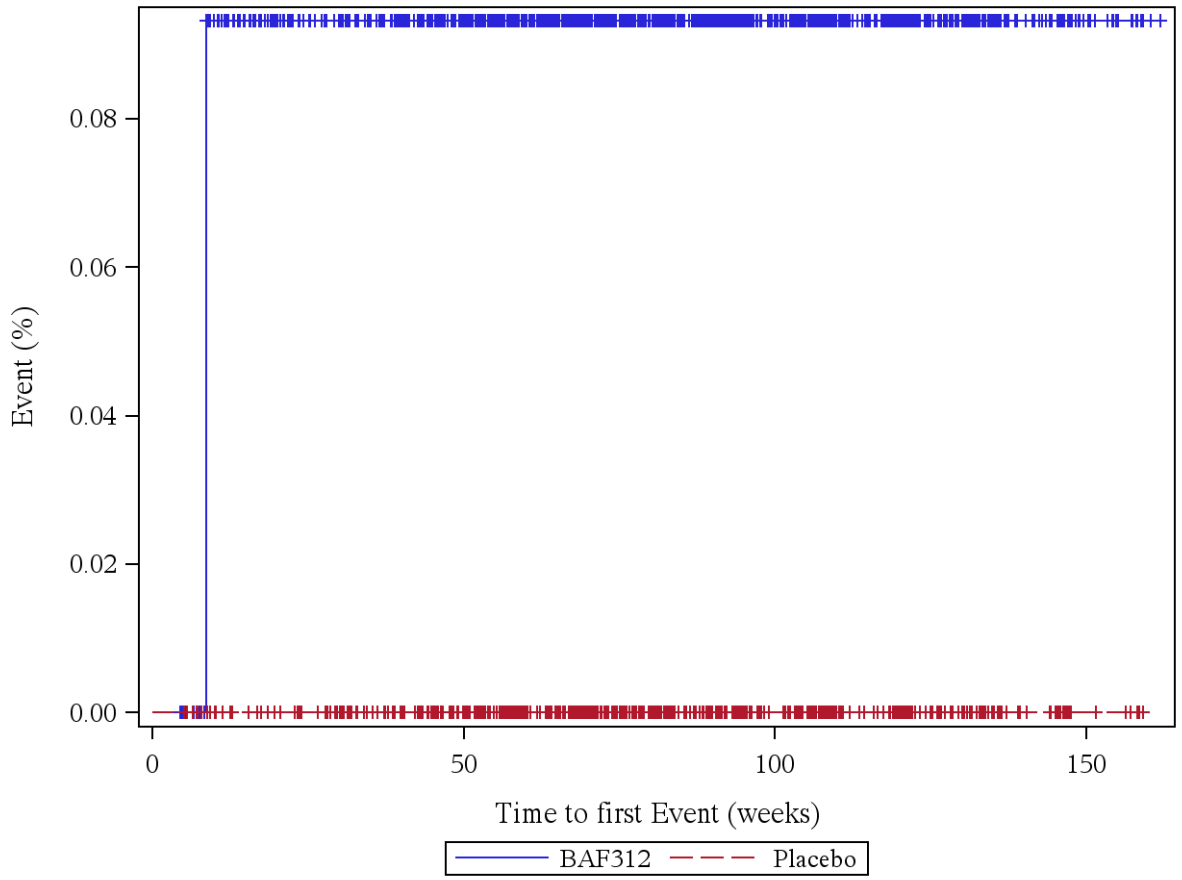


Patients at risk (BAF312/Placebo): Week 0: 1099/546, Week 4: 1056/530, Week 12: 1012/516, Week 24: 969/502, Week 36: 936/477, Week 48: 869/443, Week 60: 770/375, Week 72: 614/295, Week 84: 490/227, Week 96: 382/171, Week 108: 277/121, Week 120: 191/75, Week 132: 108/37, Week 144: 49/19, Week 156: 10/5, Week 168: 0/0

Log rank test: p-value = 0,103
*: p < 0,05

Analysis population: A2304 SAF total population

Figure 12.1.5.164: DIZZINESS (PT, severe)

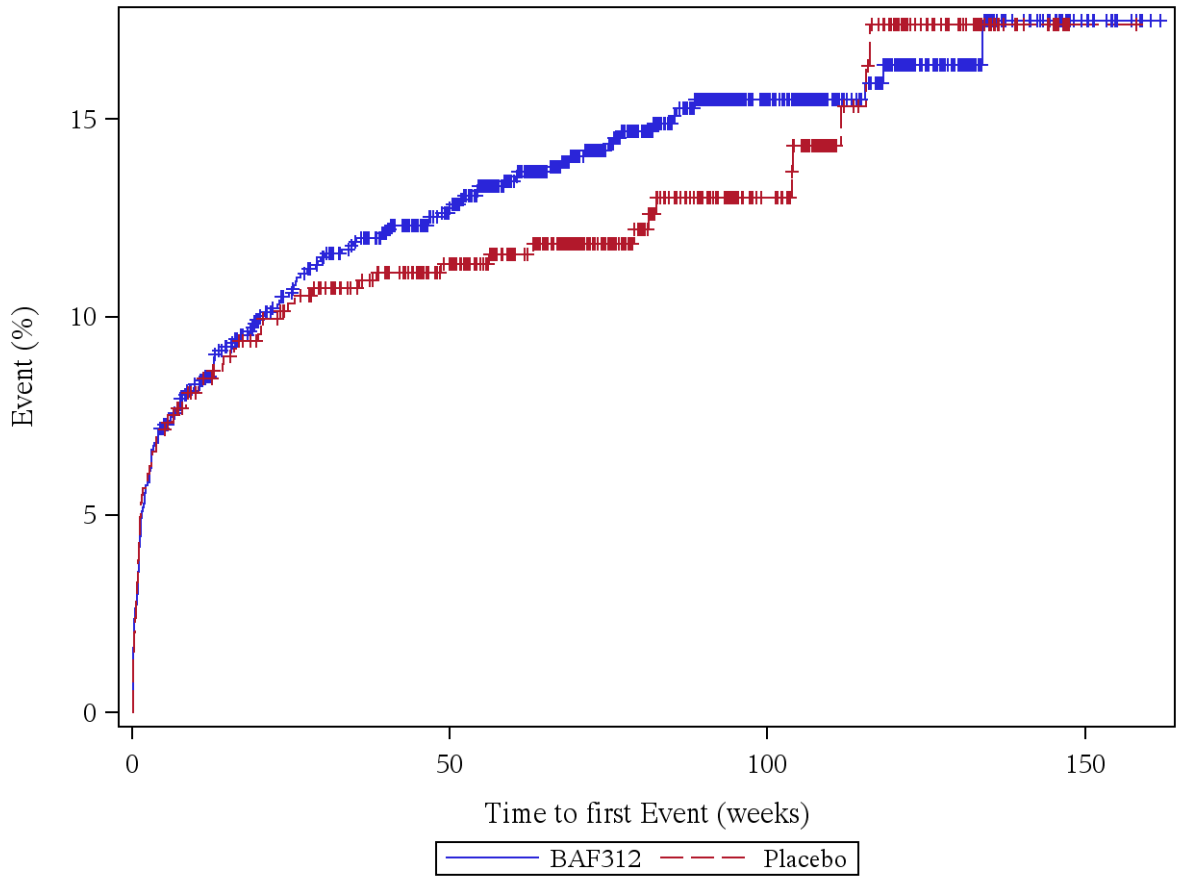


Patients at risk (BAF312/Placebo): Week 0: 1099/546, Week 4: 1099/546, Week 12: 1058/535, Week 24: 1016/521, Week 36: 989/497, Week 48: 924/461, Week 60: 817/388, Week 72: 651/305, Week 84: 516/237, Week 96: 400/176, Week 108: 291/126, Week 120: 200/80, Week 132: 113/40, Week 144: 51/20, Week 156: 10/5, Week 168: 0/0

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

Analysis population: A2304 SAF total population

Figure 12.1.5.165: HEADACHE (PT, not severe)

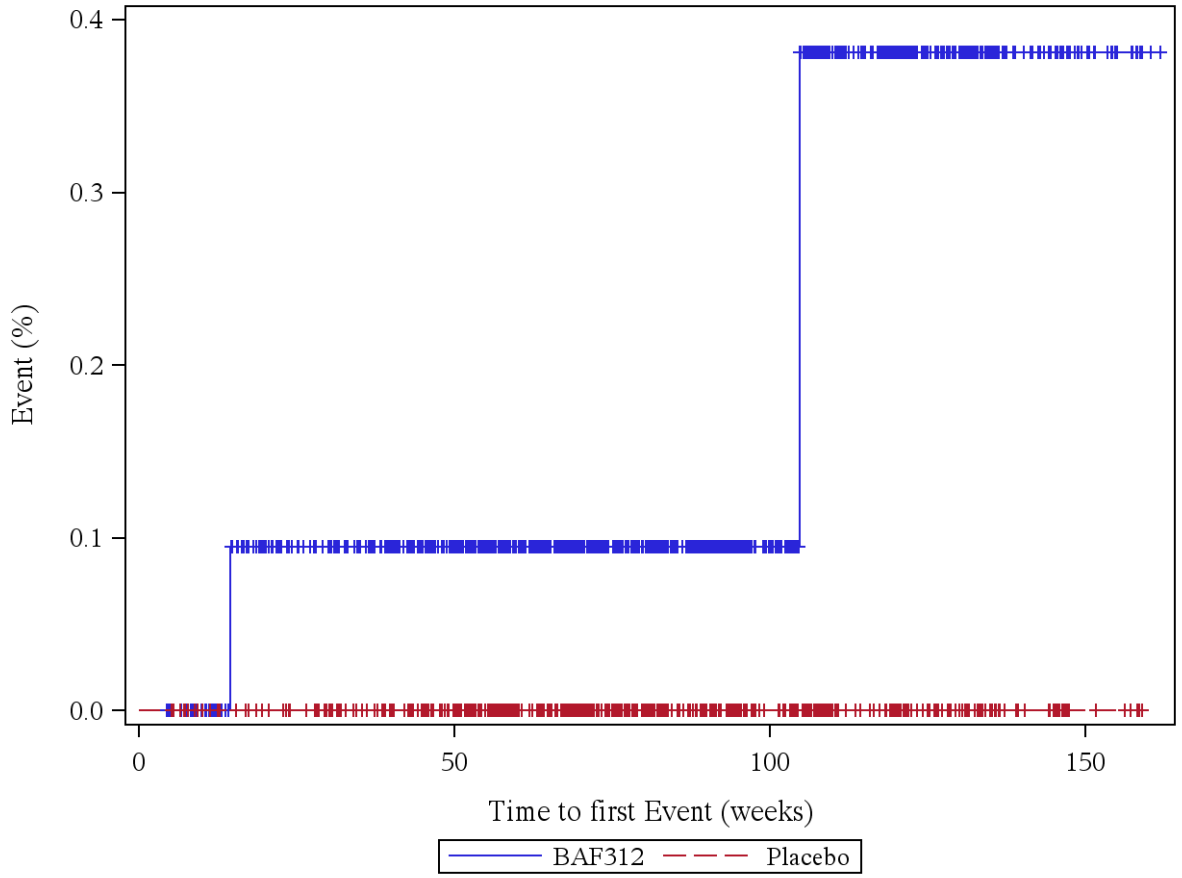


Patients at risk (BAF312/Placebo): Week 0: 1099/546, Week 4: 1024/508, Week 12: 967/490, Week 24: 910/467, Week 36: 874/444, Week 48: 811/410, Week 60: 713/349, Week 72: 560/273, Week 84: 437/205, Week 96: 340/152, Week 108: 247/107, Week 120: 168/66, Week 132: 91/33, Week 144: 44/13, Week 156: 9/1, Week 168: 0/0

Log rank test: p-value = 0,489
*: p < 0,05

Analysis population: A2304 SAF total population

Figure 12.1.5.166: HEADACHE (PT, severe)

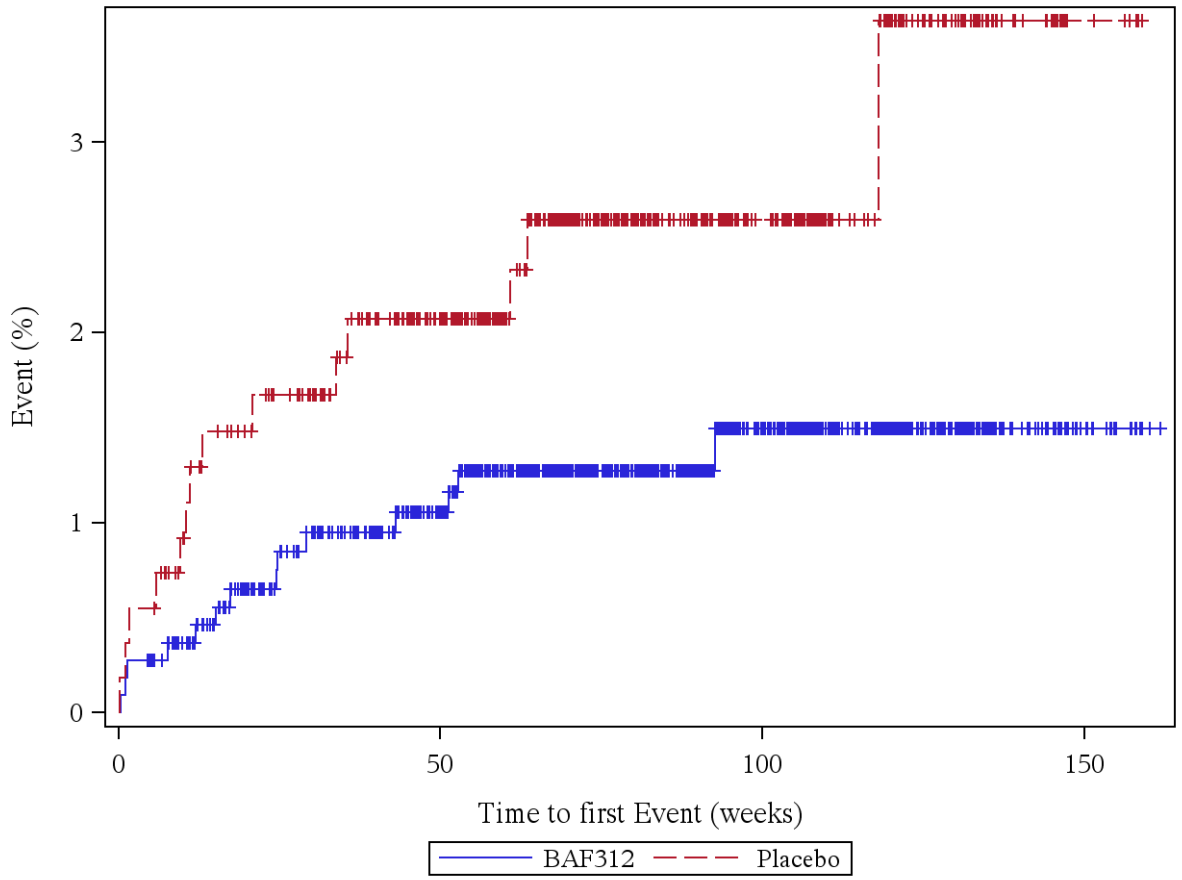


Patients at risk (BAF312/Placebo): Week 0: 1099/546, Week 4: 1099/546, Week 12: 1059/535, Week 24: 1016/521, Week 36: 989/497, Week 48: 924/461, Week 60: 817/388, Week 72: 652/305, Week 84: 516/237, Week 96: 400/176, Week 108: 290/126, Week 120: 199/80, Week 132: 112/40, Week 144: 51/20, Week 156: 10/5, Week 168: 0/0

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

Analysis population: A2304 SAF total population

Figure 12.1.5.167: HYPOAESTHESIA (PT, not severe)

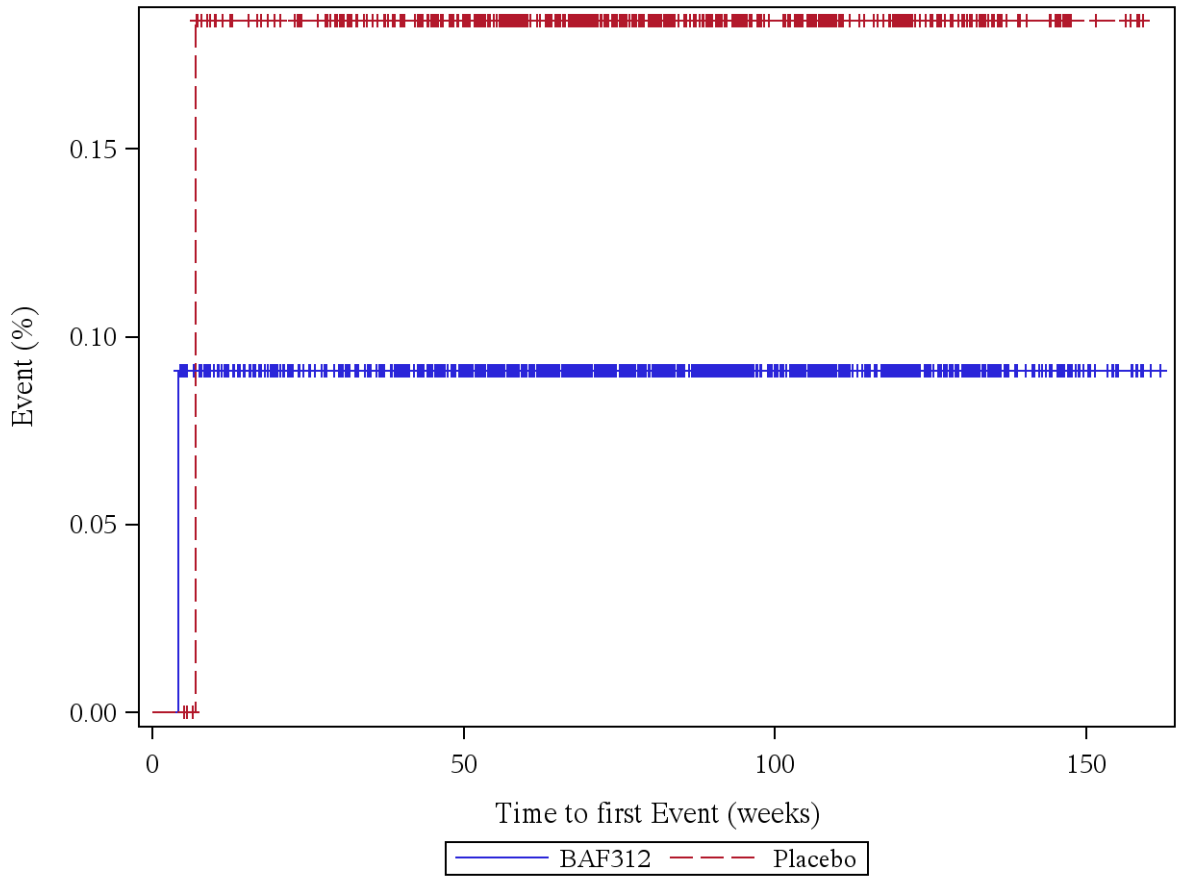


Patients at risk (BAF312/Placebo): Week 0: 1099/546, Week 4: 1096/543, Week 12: 1055/529, Week 24: 1011/513, Week 36: 982/487, Week 48: 918/452, Week 60: 809/381, Week 72: 646/297, Week 84: 513/231, Week 96: 398/175, Week 108: 290/125, Week 120: 199/78, Week 132: 113/40, Week 144: 51/20, Week 156: 10/5, Week 168: 0/0

Log rank test: p-value = 0,055
*: p < 0,05

Analysis population: A2304 SAF total population

Figure 12.1.5.168: HYPOAESTHESIA (PT, severe)

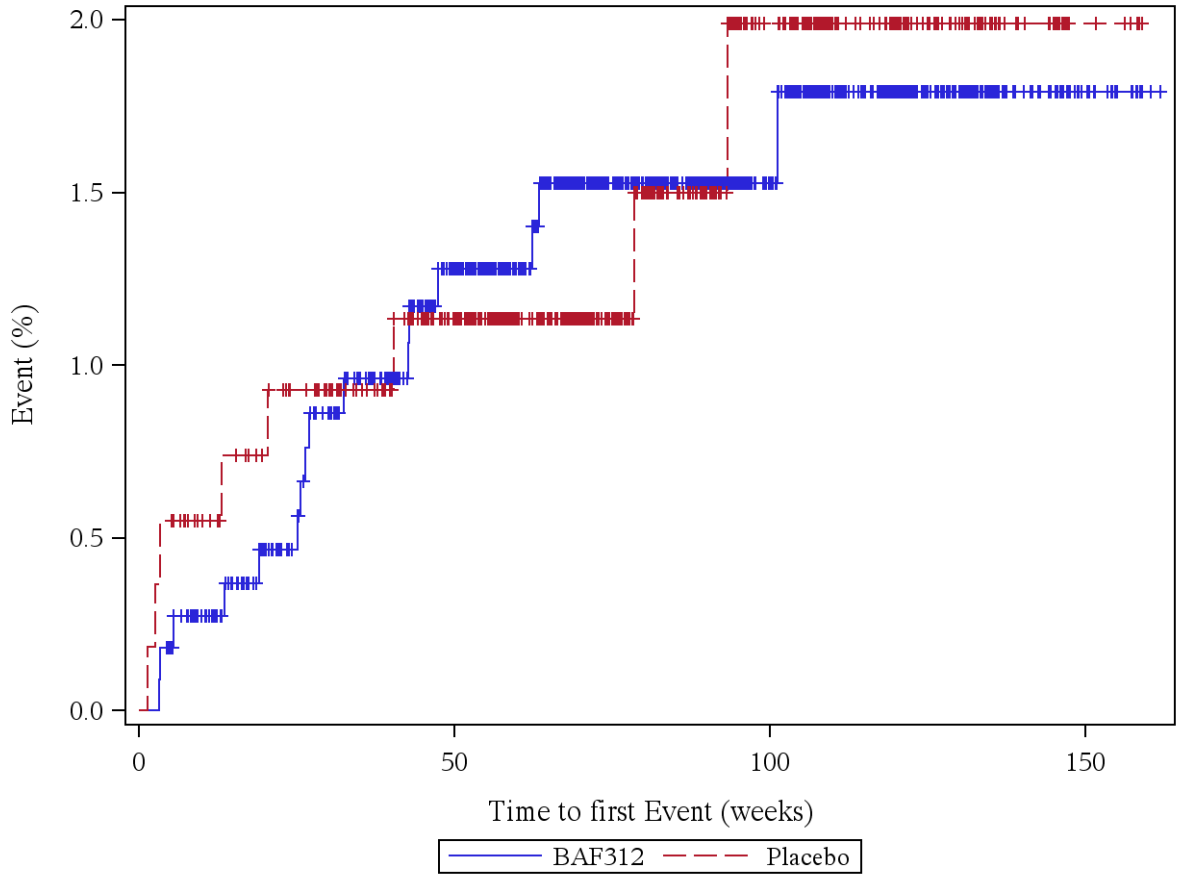


Patients at risk (BAF312/Placebo): Week 0: 1099/546, Week 4: 1099/546, Week 12: 1058/534, Week 24: 1016/520, Week 36: 989/496, Week 48: 924/460, Week 60: 818/387, Week 72: 652/304, Week 84: 516/236, Week 96: 400/175, Week 108: 291/125, Week 120: 200/79, Week 132: 113/40, Week 144: 51/20, Week 156: 10/5, Week 168: 0/0

Log rank test: p-value = 0,617
*: p < 0,05

Analysis population: A2304 SAF total population

Figure 12.1.5.169: MIGRAINE (PT, not severe)

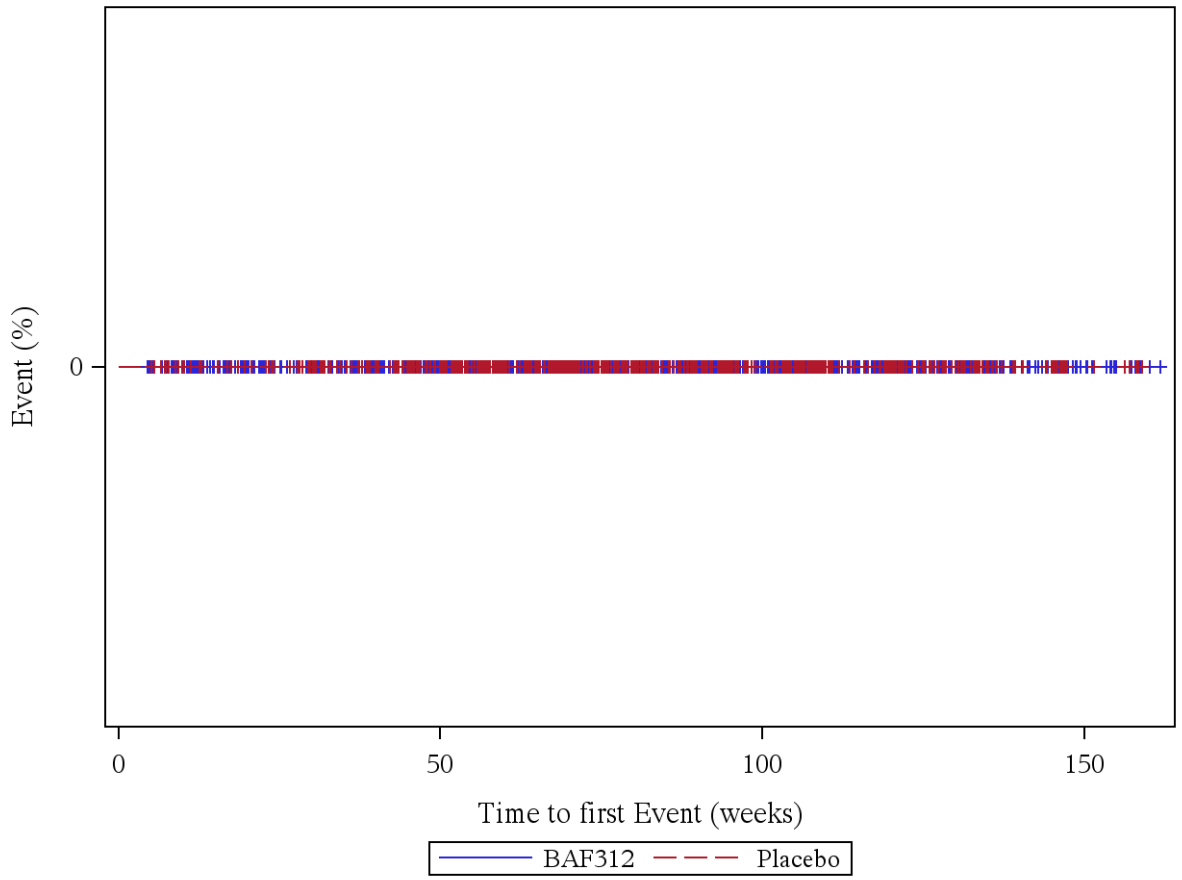


Patients at risk (BAF312/Placebo): Week 0: 1099/546, Week 4: 1097/543, Week 12: 1056/532, Week 24: 1012/516, Week 36: 980/493, Week 48: 912/456, Week 60: 805/384, Week 72: 641/302, Week 84: 507/234, Week 96: 395/173, Week 108: 286/125, Week 120: 197/79, Week 132: 111/40, Week 144: 51/20, Week 156: 10/5, Week 168: 0/0

Log rank test: p-value = 0,984
*: p < 0,05

Analysis population: A2304 SAF total population

Figure 12.1.5.170: MIGRAINE (PT, severe)

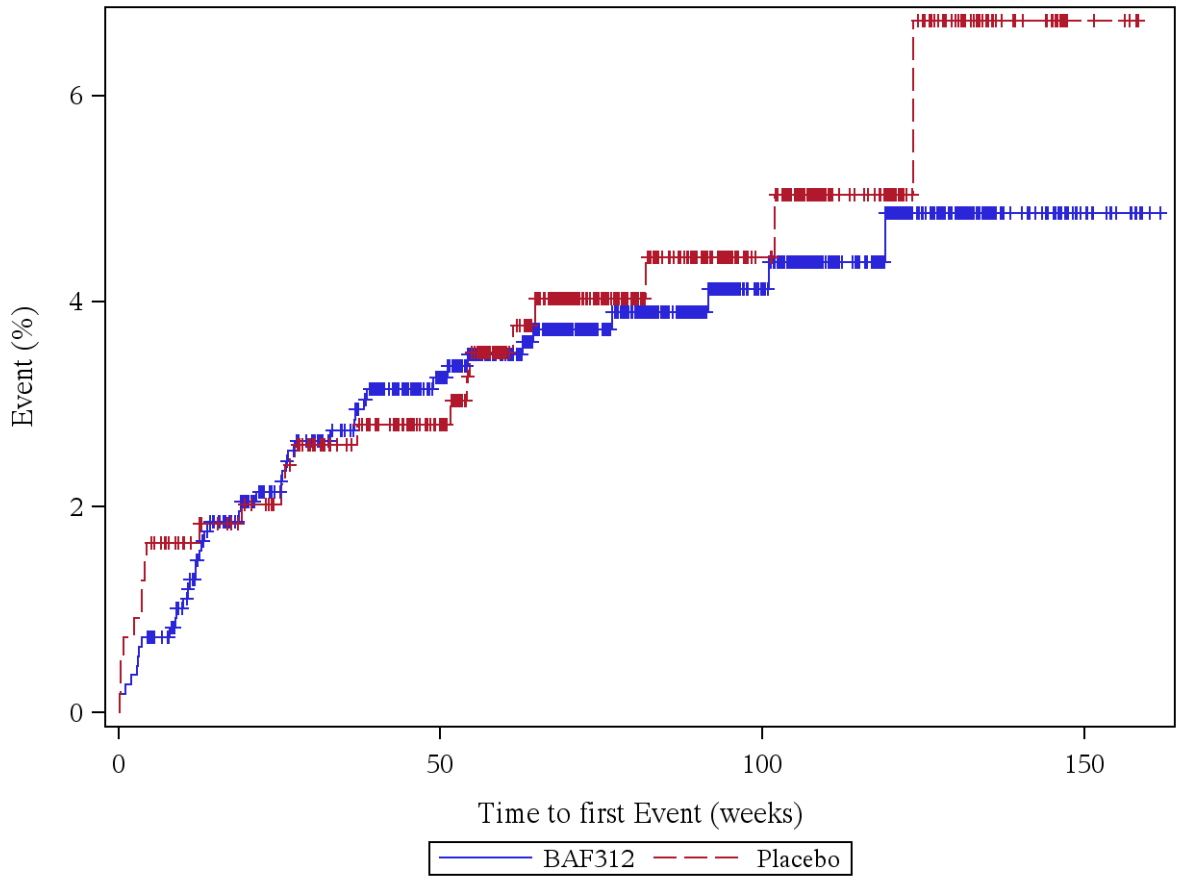


Patients at risk (BAF312/Placebo): Week 0: 1099/546, Week 4: 1099/546, Week 12: 1059/535, Week 24: 1017/521, Week 36: 990/497, Week 48: 925/461, Week 60: 818/388, Week 72: 652/305, Week 84: 516/237, Week 96: 400/176, Week 108: 291/126, Week 120: 200/80, Week 132: 113/40, Week 144: 51/20, Week 156: 10/5, Week 168: 0/0

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

Analysis population: A2304 SAF total population

Figure 12.1.5.171: MUSCLE SPASTICITY (PT, not severe)

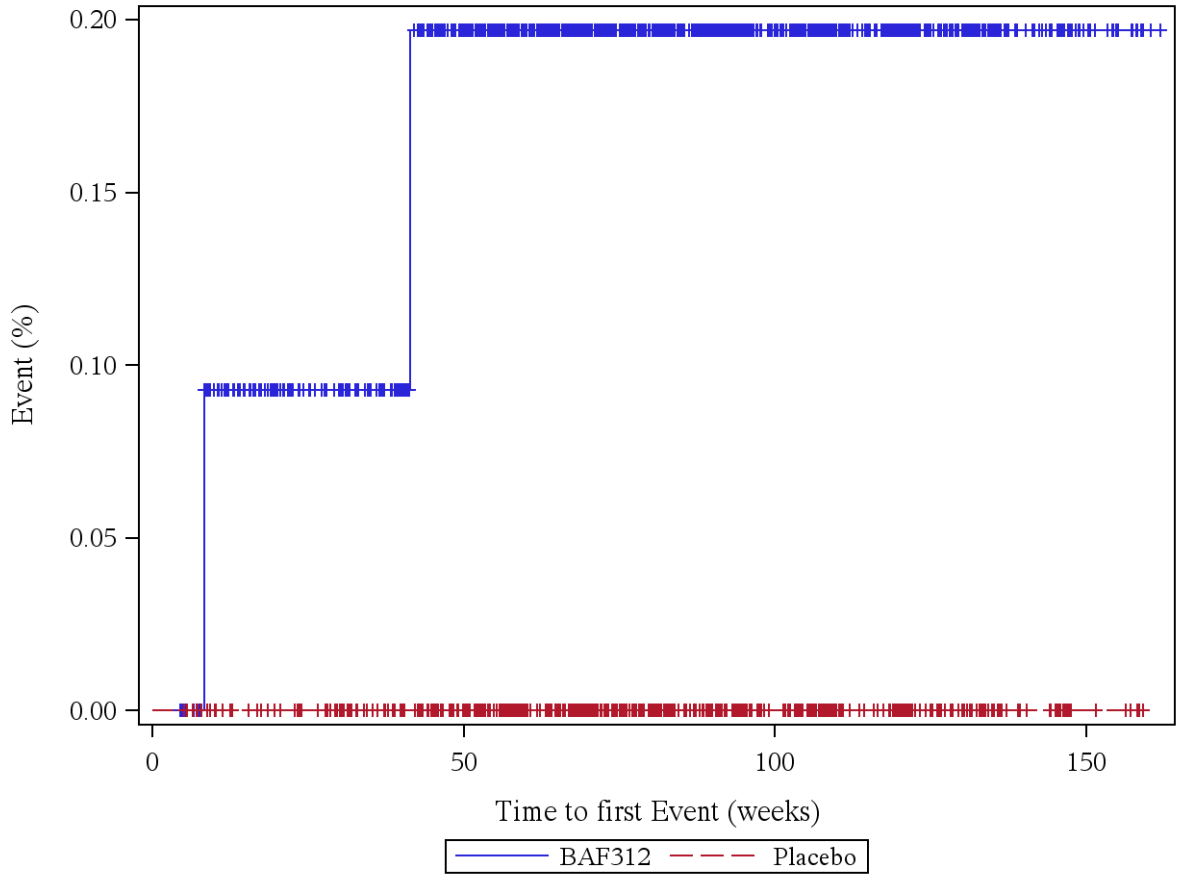


Patients at risk (BAF312/Placebo): Week 0: 1099/546, Week 4: 1091/538, Week 12: 1044/526, Week 24: 996/510, Week 36: 964/486, Week 48: 899/451, Week 60: 794/376, Week 72: 629/296, Week 84: 496/229, Week 96: 383/170, Week 108: 278/121, Week 120: 189/75, Week 132: 106/34, Week 144: 49/18, Week 156: 10/4, Week 168: 0/0

Log rank test: p-value = 0,682
*: p < 0,05

Analysis population: A2304 SAF total population

Figure 12.1.5.172: MUSCLE SPASTICITY (PT, severe)

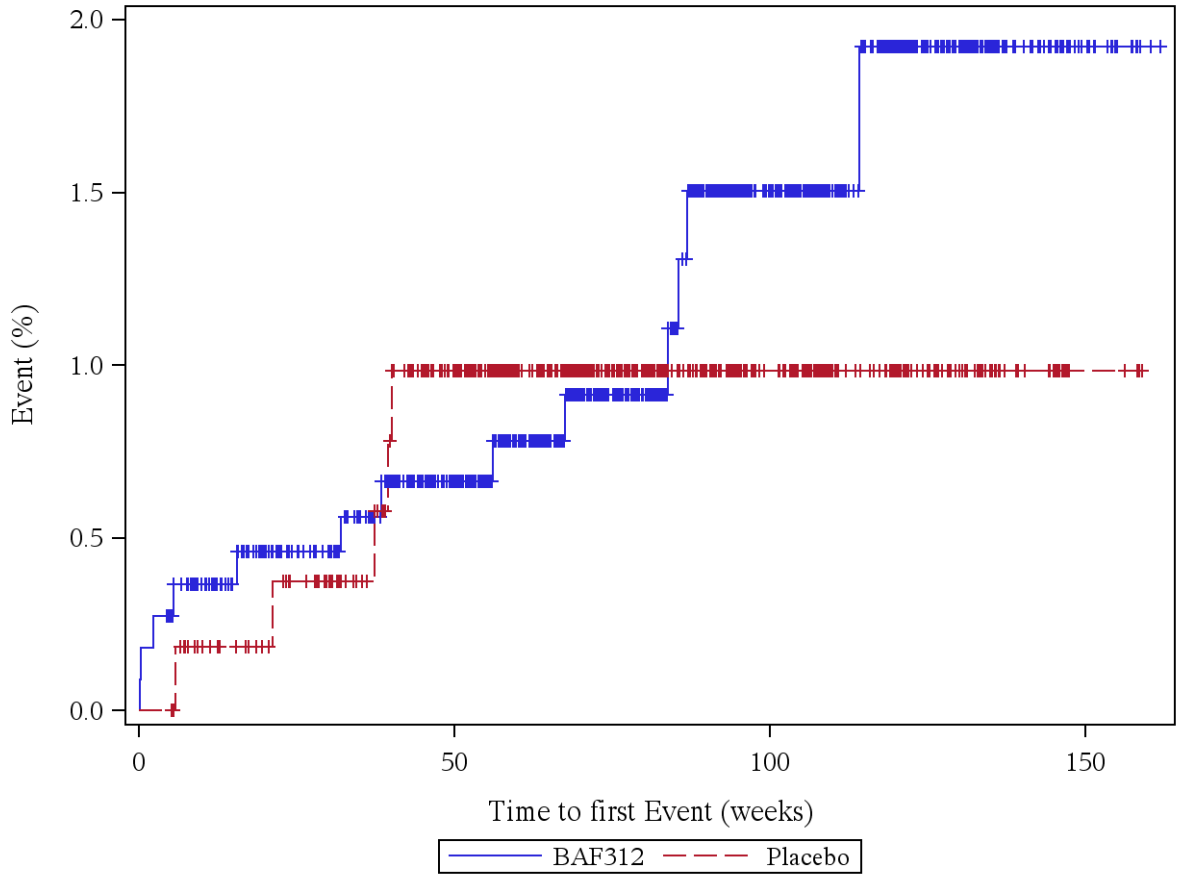


Patients at risk (BAF312/Placebo): Week 0: 1099/546, Week 4: 1099/546, Week 12: 1058/535, Week 24: 1017/521, Week 36: 990/497, Week 48: 924/461, Week 60: 817/388, Week 72: 651/305, Week 84: 515/237, Week 96: 399/176, Week 108: 291/126, Week 120: 200/80, Week 132: 113/40, Week 144: 51/20, Week 156: 10/5, Week 168: 0/0

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

Analysis population: A2304 SAF total population

Figure 12.1.5.173: NEURALGIA (PT, not severe)

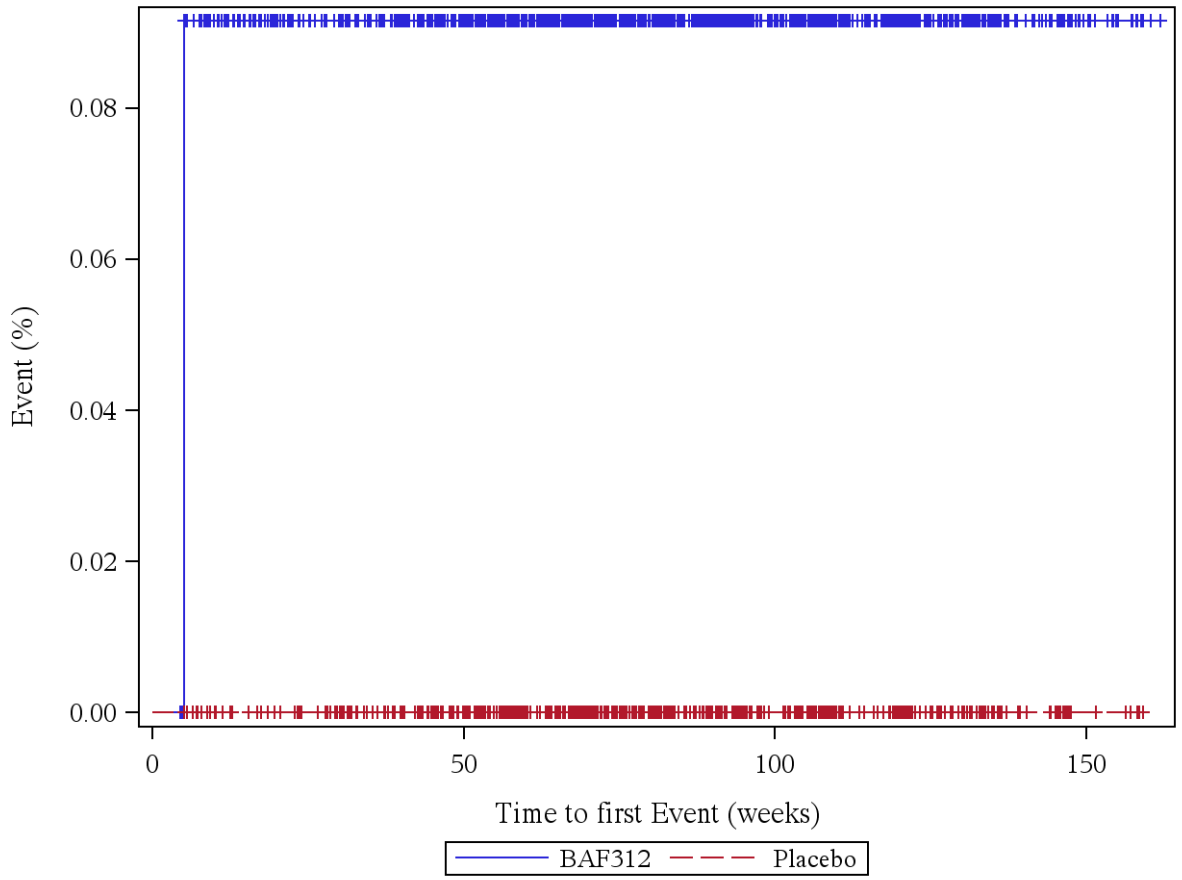


Patients at risk (BAF312/Placebo): Week 0: 1099/546, Week 4: 1096/546, Week 12: 1055/534, Week 24: 1012/519, Week 36: 984/495, Week 48: 919/456, Week 60: 811/383, Week 72: 646/300, Week 84: 509/233, Week 96: 393/173, Week 108: 286/123, Week 120: 196/77, Week 132: 111/38, Week 144: 49/18, Week 156: 9/4, Week 168: 0/0

Log rank test: p-value = 0,654
*: p < 0,05

Analysis population: A2304 SAF total population

Figure 12.1.5.174: NEURALGIA (PT, severe)

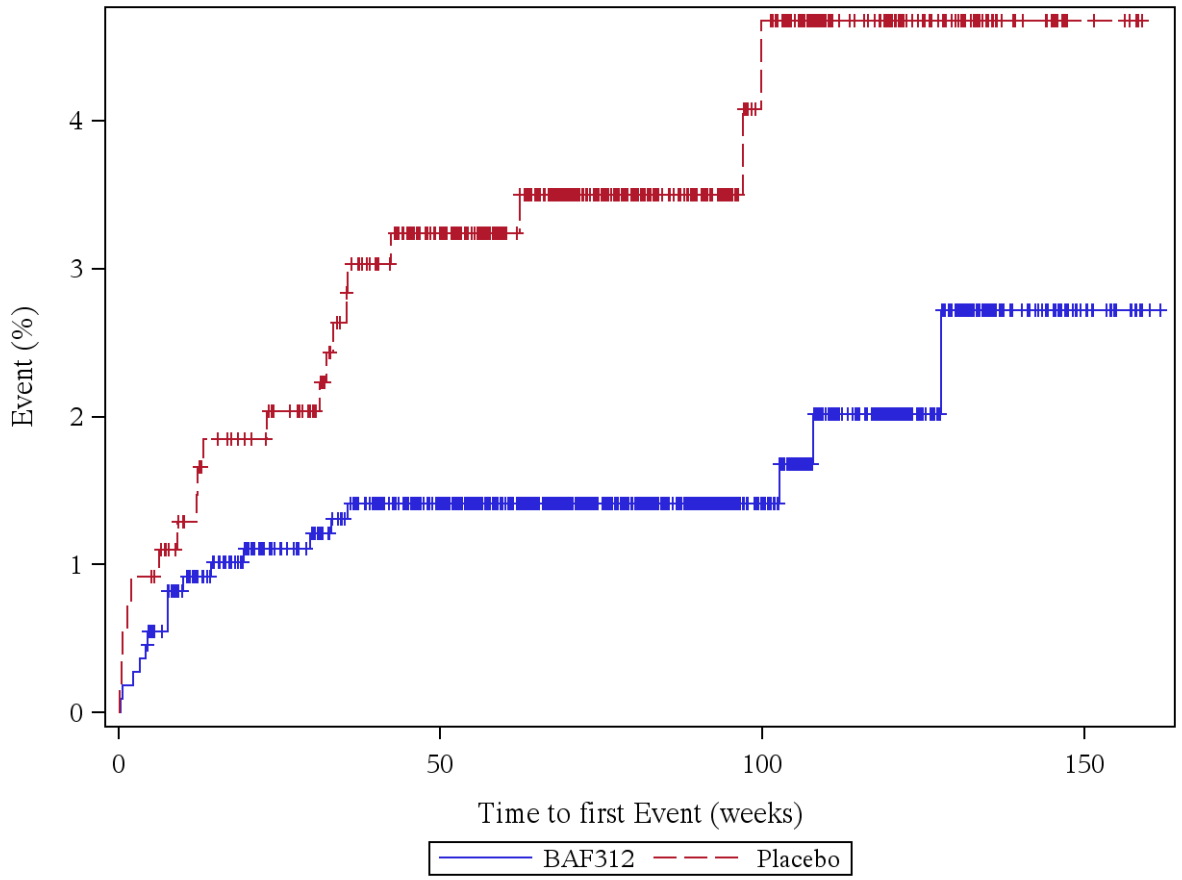


Patients at risk (BAF312/Placebo): Week 0: 1099/546, Week 4: 1099/546, Week 12: 1058/535, Week 24: 1016/521, Week 36: 989/497, Week 48: 924/461, Week 60: 817/388, Week 72: 652/305, Week 84: 516/237, Week 96: 400/176, Week 108: 291/126, Week 120: 200/80, Week 132: 113/40, Week 144: 51/20, Week 156: 10/5, Week 168: 0/0

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

Analysis population: A2304 SAF total population

Figure 12.1.5.175: PARAESTHESIA (PT, not severe)

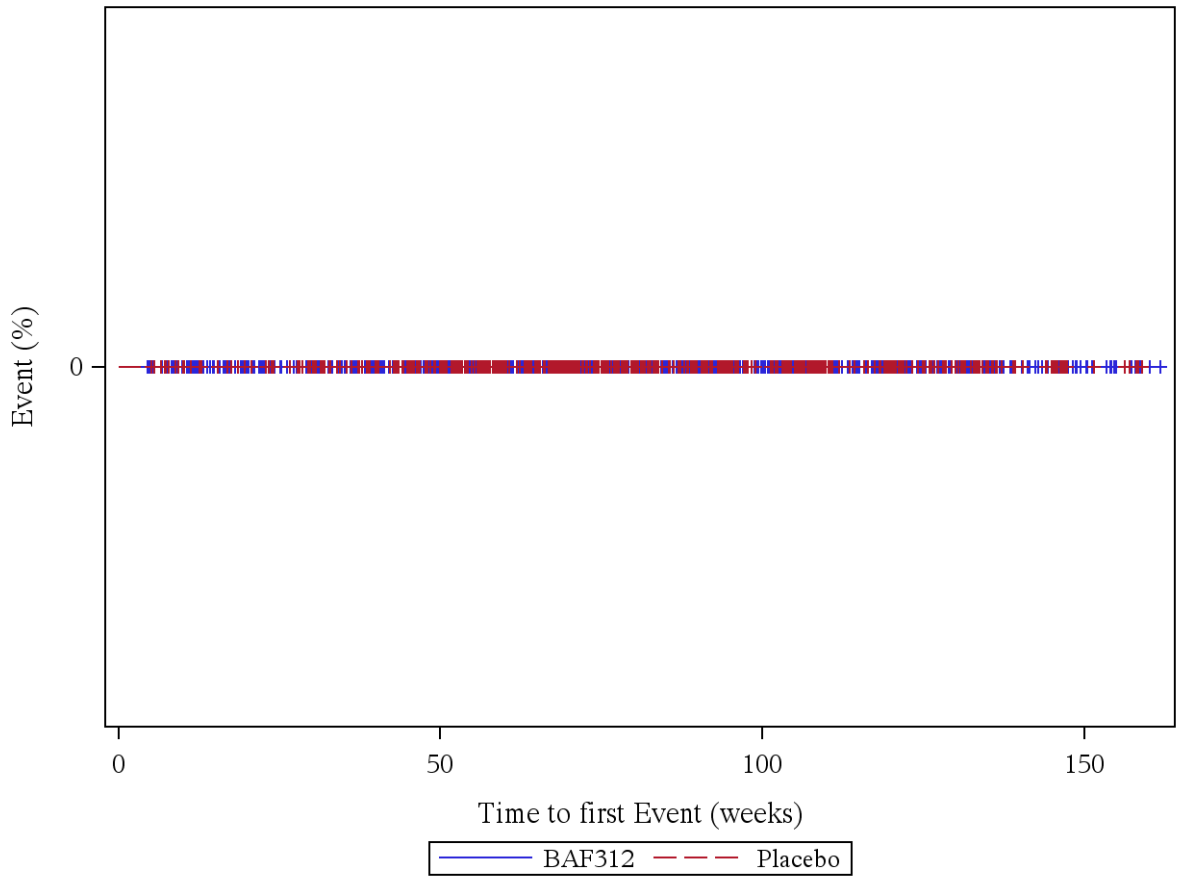


Patients at risk (BAF312/Placebo): Week 0: 1099/546, Week 4: 1095/541, Week 12: 1049/529, Week 24: 1005/511, Week 36: 975/482, Week 48: 914/447, Week 60: 808/378, Week 72: 645/295, Week 84: 511/229, Week 96: 398/171, Week 108: 288/120, Week 120: 199/75, Week 132: 111/38, Week 144: 51/19, Week 156: 10/5, Week 168: 0/0

Log rank test: p-value = 0,009 *
*: p < 0,05

Analysis population: A2304 SAF total population

Figure 12.1.5.176: PARAESTHESIA (PT, severe)

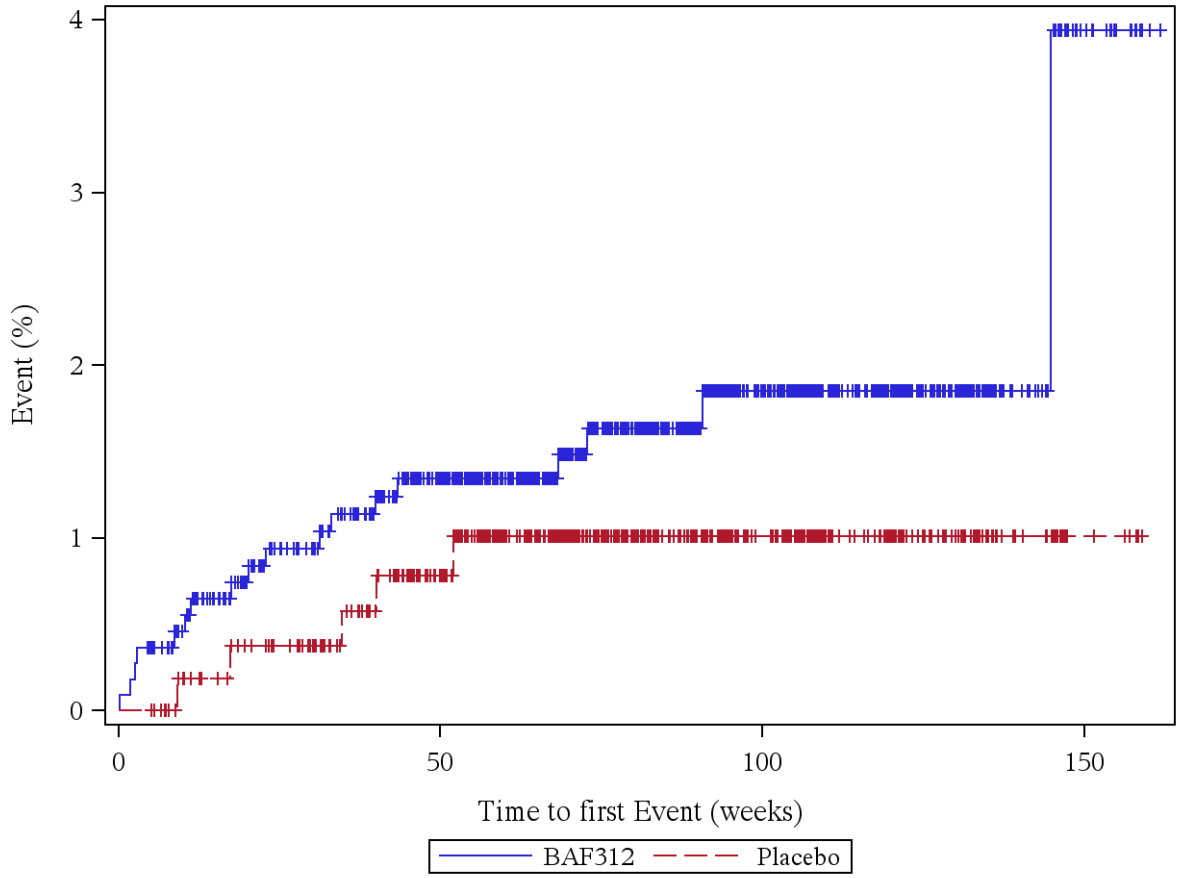


Patients at risk (BAF312/Placebo): Week 0: 1099/546, Week 4: 1099/546, Week 12: 1059/535, Week 24: 1017/521, Week 36: 990/497, Week 48: 925/461, Week 60: 818/388, Week 72: 652/305, Week 84: 516/237, Week 96: 400/176, Week 108: 291/126, Week 120: 200/80, Week 132: 113/40, Week 144: 51/20, Week 156: 10/5, Week 168: 0/0

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

Analysis population: A2304 SAF total population

Figure 12.1.5.177: SCIATICA (PT, not severe)

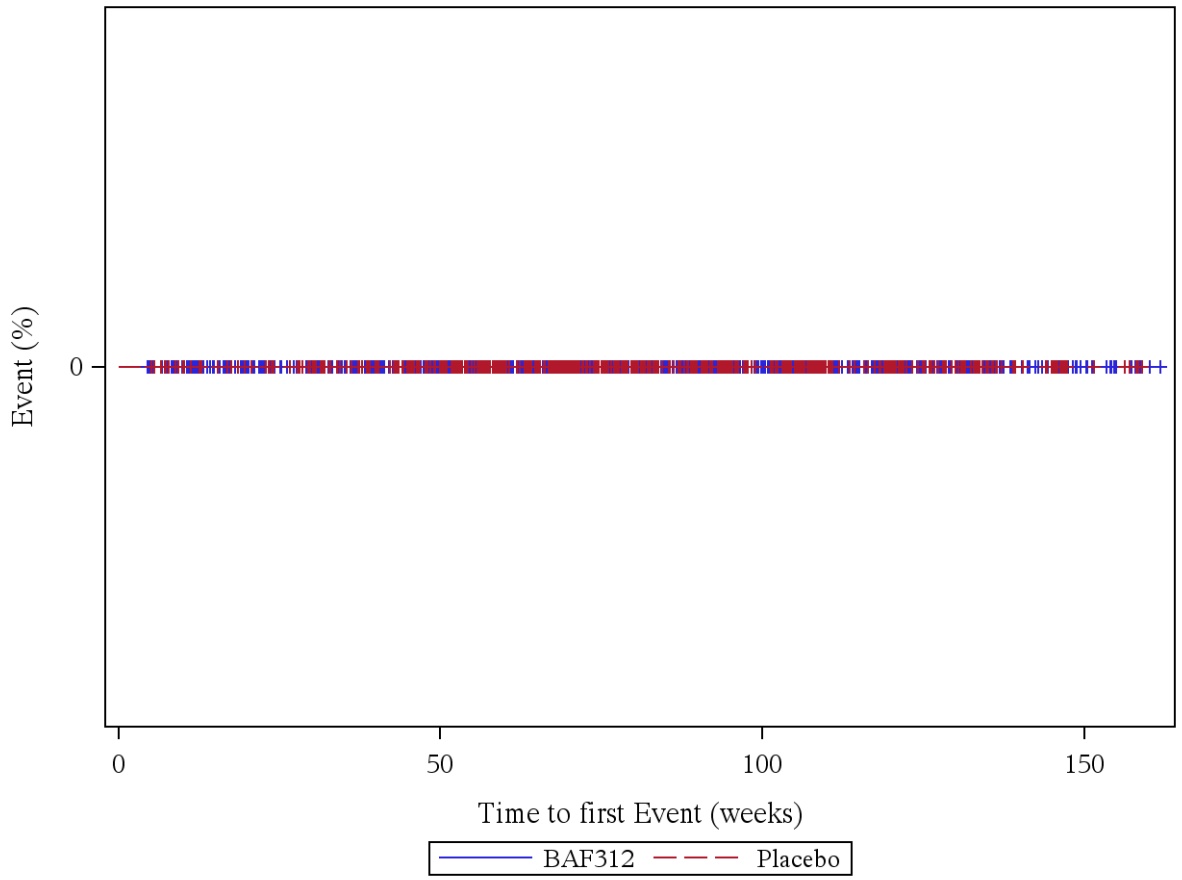


Patients at risk (BAF312/Placebo): Week 0: 1099/546, Week 4: 1095/546, Week 12: 1052/534, Week 24: 1007/519, Week 36: 979/494, Week 48: 912/457, Week 60: 808/384, Week 72: 642/303, Week 84: 508/235, Week 96: 393/174, Week 108: 286/124, Week 120: 197/78, Week 132: 112/39, Week 144: 50/19, Week 156: 10/5, Week 168: 0/0

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

Analysis population: A2304 SAF total population

Figure 12.1.5.178: SCIATICA (PT, severe)

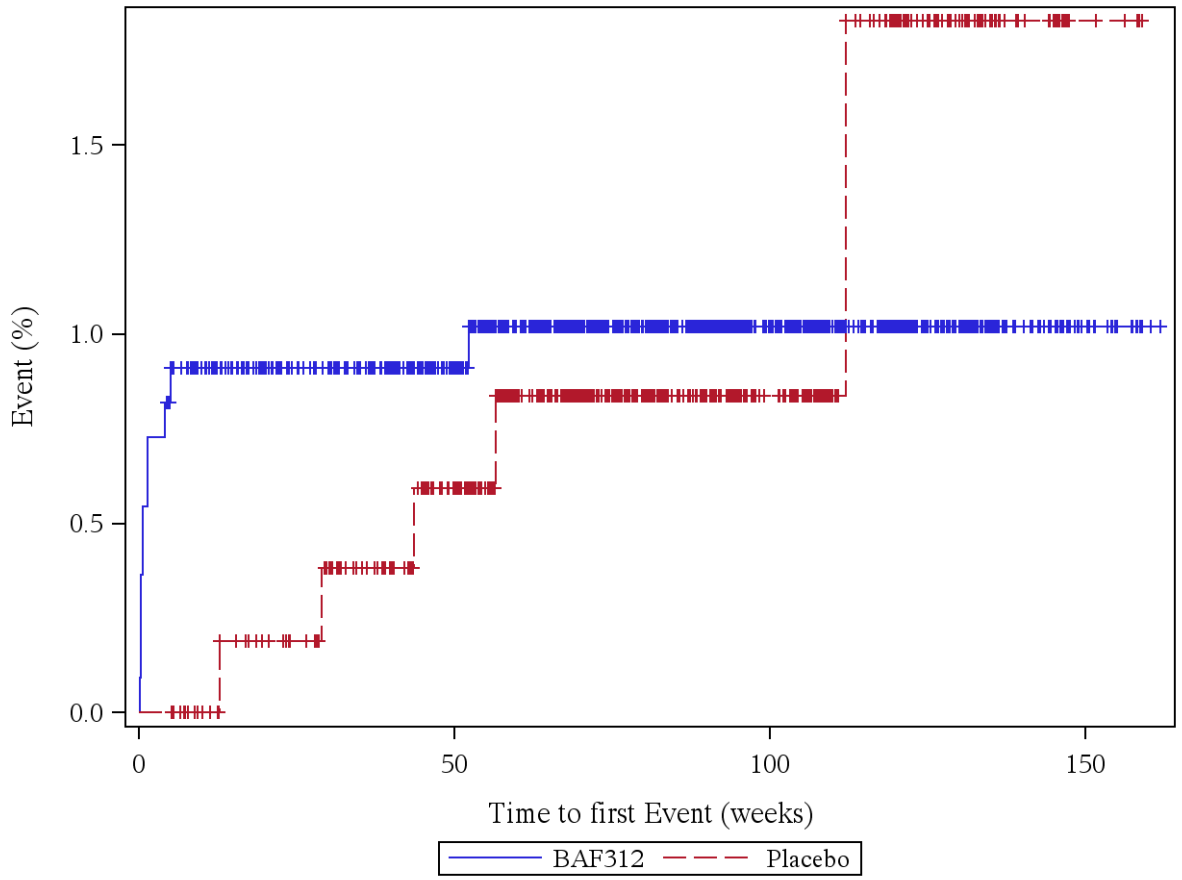


Patients at risk (BAF312/Placebo): Week 0: 1099/546, Week 4: 1099/546, Week 12: 1059/535, Week 24: 1017/521, Week 36: 990/497, Week 48: 925/461, Week 60: 818/388, Week 72: 652/305, Week 84: 516/237, Week 96: 400/176, Week 108: 291/126, Week 120: 200/80, Week 132: 113/40, Week 144: 51/20, Week 156: 10/5, Week 168: 0/0

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

Analysis population: A2304 SAF total population

Figure 12.1.5.179: SOMNOLENCE (PT, not severe)

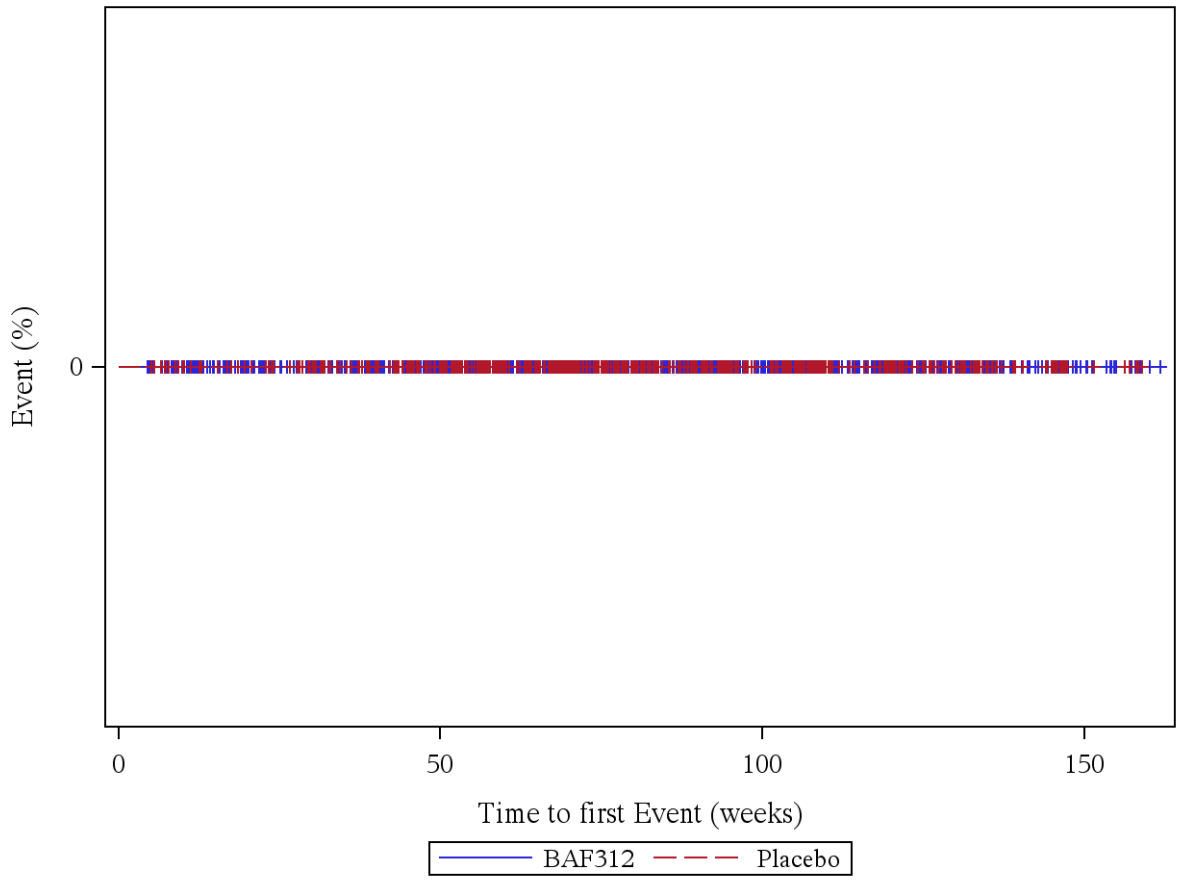


Patients at risk (BAF312/Placebo): Week 0: 1099/546, Week 4: 1091/546, Week 12: 1051/535, Week 24: 1009/520, Week 36: 982/495, Week 48: 917/458, Week 60: 812/386, Week 72: 647/303, Week 84: 513/235, Week 96: 399/174, Week 108: 290/125, Week 120: 200/79, Week 132: 113/39, Week 144: 51/19, Week 156: 10/4, Week 168: 0/0

Log rank test: p-value = 0,881
*: p < 0,05

Analysis population: A2304 SAF total population

Figure 12.1.5.180: SOMNOLENCE (PT, severe)

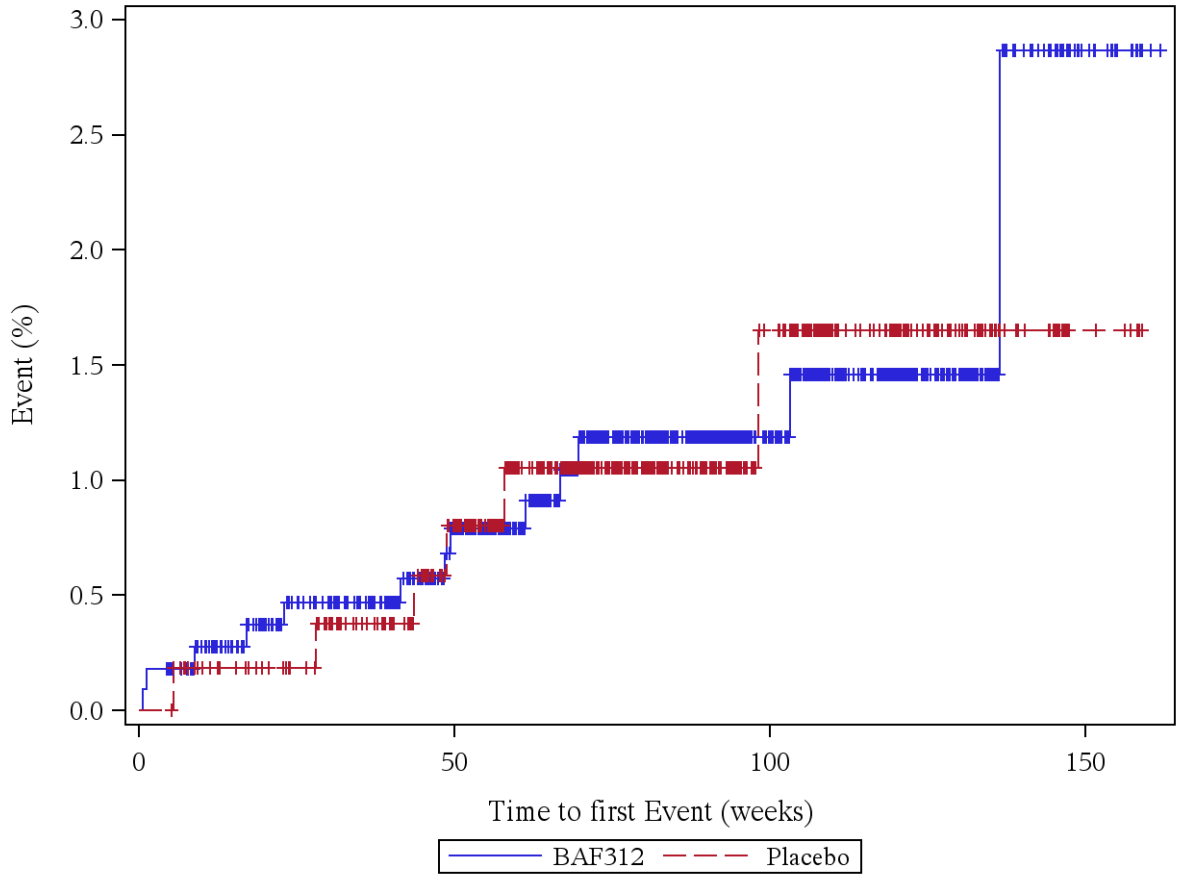


Patients at risk (BAF312/Placebo): Week 0: 1099/546, Week 4: 1099/546, Week 12: 1059/535, Week 24: 1017/521, Week 36: 990/497, Week 48: 925/461, Week 60: 818/388, Week 72: 652/305, Week 84: 516/237, Week 96: 400/176, Week 108: 291/126, Week 120: 200/80, Week 132: 113/40, Week 144: 51/20, Week 156: 10/5, Week 168: 0/0

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

Analysis population: A2304 SAF total population

Figure 12.1.5.181: SYNCOPE (PT, not severe)

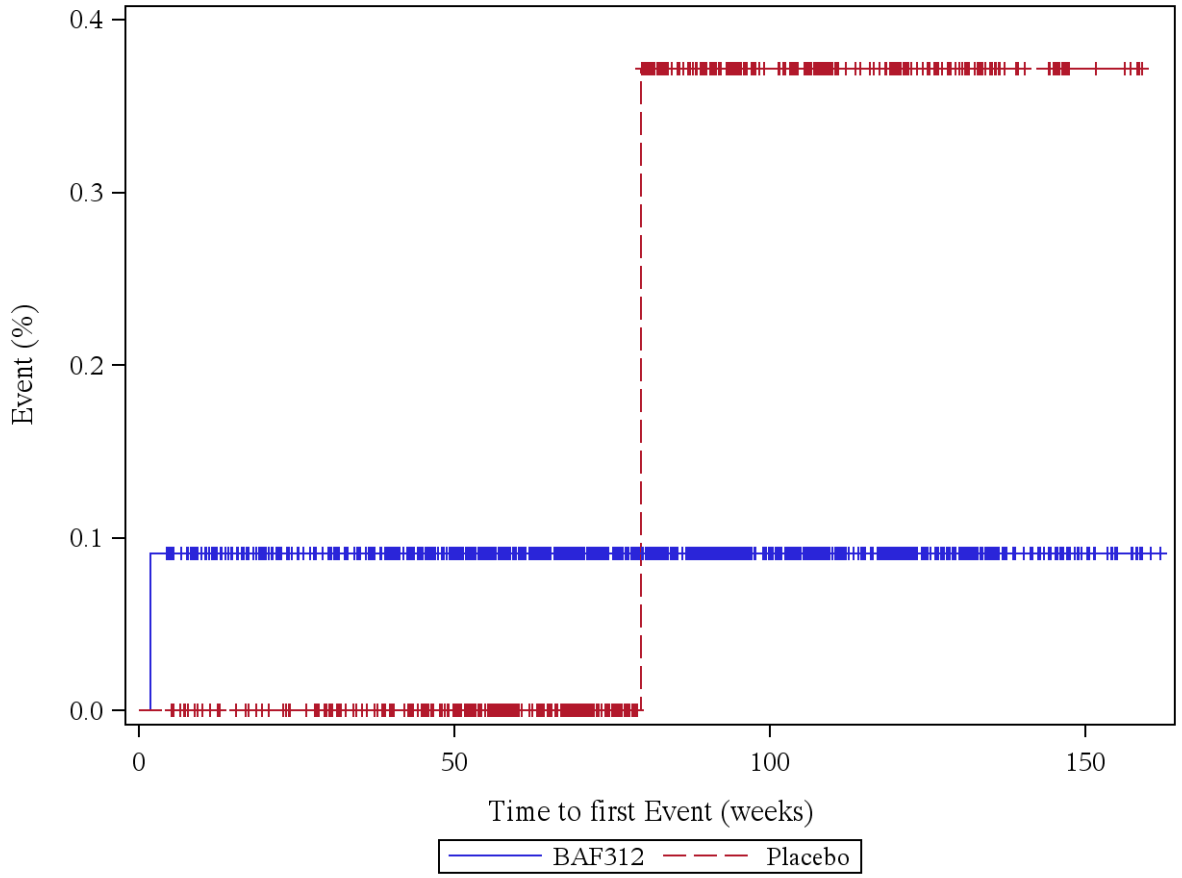


Patients at risk (BAF312/Placebo): Week 0: 1099/546, Week 4: 1097/546, Week 12: 1056/534, Week 24: 1013/520, Week 36: 986/495, Week 48: 921/458, Week 60: 812/383, Week 72: 644/301, Week 84: 510/234, Week 96: 395/174, Week 108: 286/123, Week 120: 198/78, Week 132: 112/40, Week 144: 50/20, Week 156: 10/5, Week 168: 0/0

Log rank test: p-value = 0,936
*: p < 0,05

Analysis population: A2304 SAF total population

Figure 12.1.5.182: SYNCOPE (PT, severe)

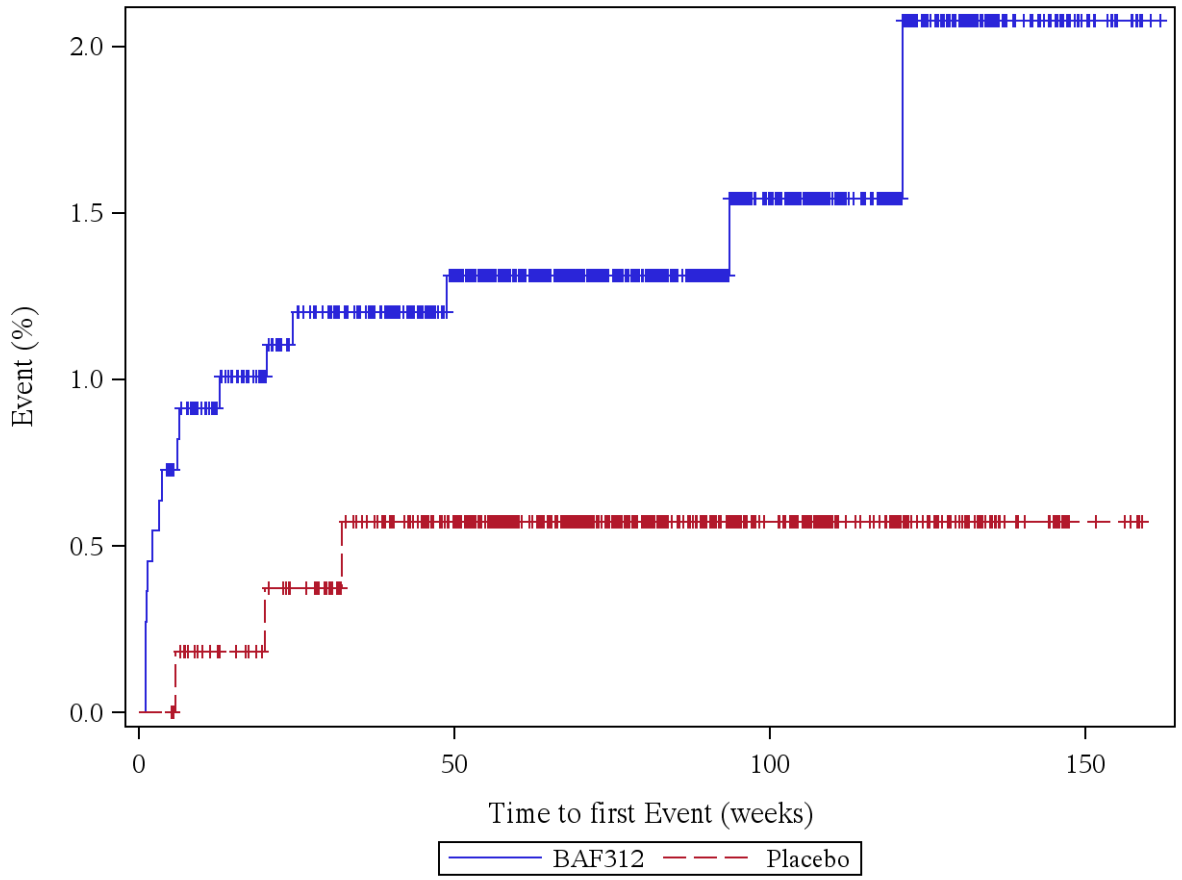


Patients at risk (BAF312/Placebo): Week 0: 1099/546, Week 4: 1098/546, Week 12: 1058/535, Week 24: 1016/521, Week 36: 989/497, Week 48: 924/461, Week 60: 817/388, Week 72: 651/305, Week 84: 515/236, Week 96: 399/175, Week 108: 290/126, Week 120: 199/80, Week 132: 113/40, Week 144: 51/20, Week 156: 10/5, Week 168: 0/0

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

Analysis population: A2304 SAF total population

Figure 12.1.5.183: TREMOR (PT, not severe)

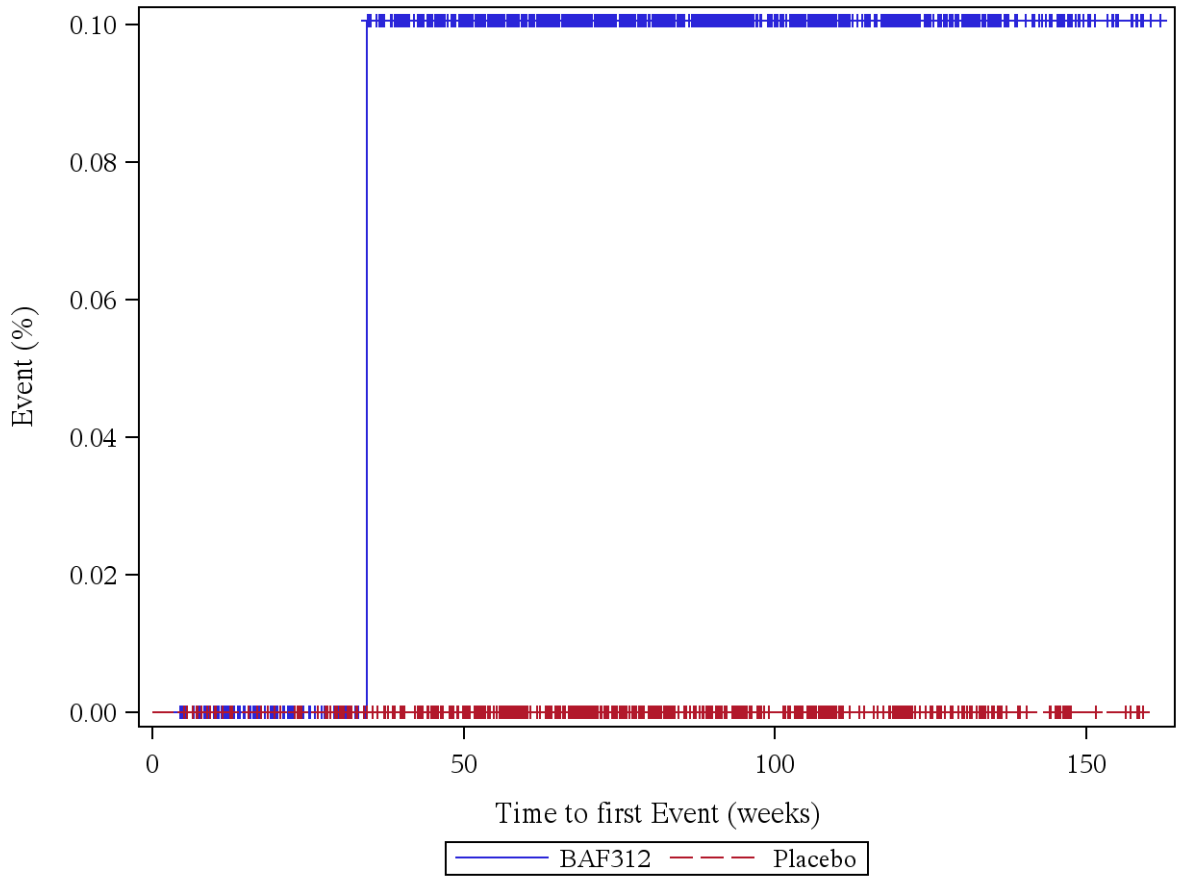


Patients at risk (BAF312/Placebo): Week 0: 1099/546, Week 4: 1091/546, Week 12: 1049/534, Week 24: 1005/519, Week 36: 978/494, Week 48: 913/459, Week 60: 807/387, Week 72: 642/305, Week 84: 509/237, Week 96: 394/176, Week 108: 287/126, Week 120: 198/80, Week 132: 110/40, Week 144: 51/20, Week 156: 10/5, Week 168: 0/0

Log rank test: p-value = 0,108
*: p < 0,05

Analysis population: A2304 SAF total population

Figure 12.1.5.184: TREMOR (PT, severe)

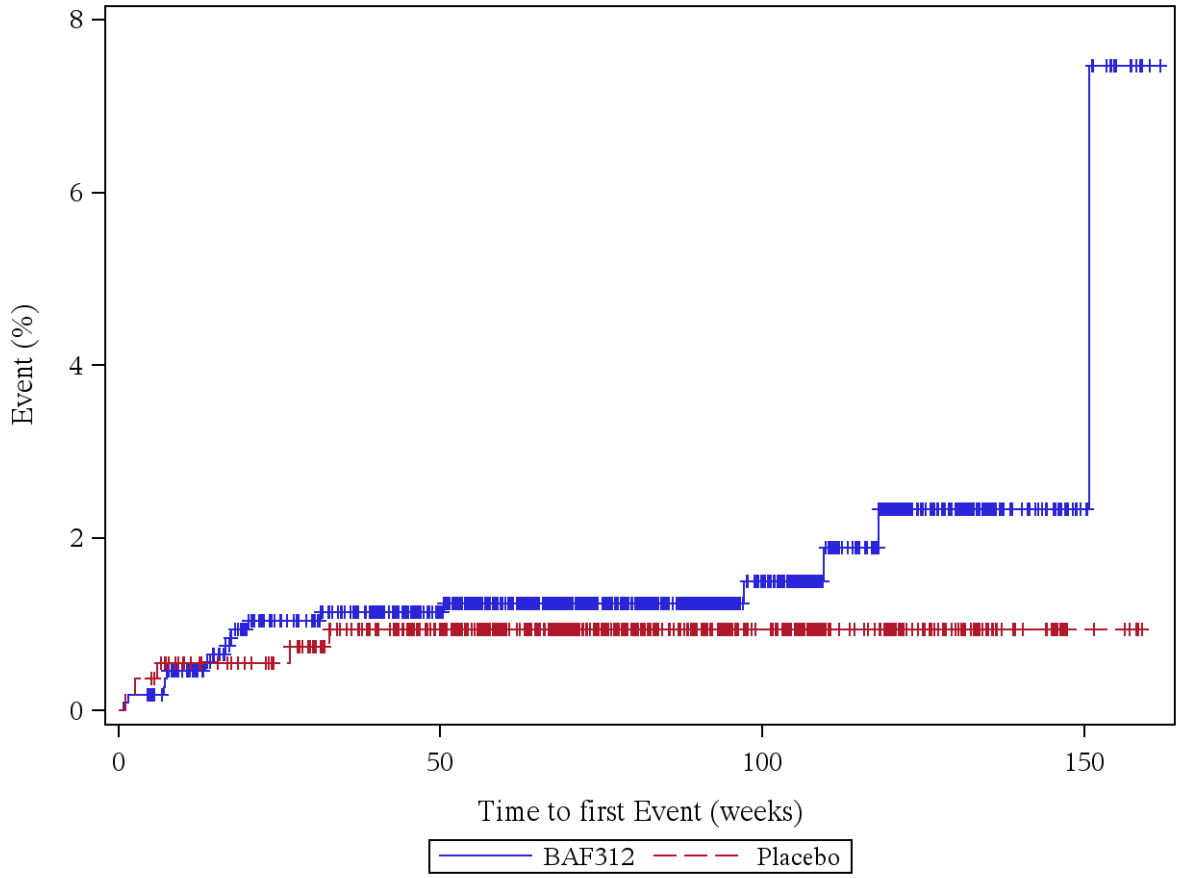


Patients at risk (BAF312/Placebo): Week 0: 1099/546, Week 4: 1099/546, Week 12: 1059/535, Week 24: 1017/521, Week 36: 989/497, Week 48: 924/461, Week 60: 817/388, Week 72: 652/305, Week 84: 516/237, Week 96: 400/176, Week 108: 291/126, Week 120: 200/80, Week 132: 113/40, Week 144: 51/20, Week 156: 10/5, Week 168: 0/0

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

Analysis population: A2304 SAF total population

Figure 12.1.5.185: TRIGEMINAL NEURALGIA (PT, not severe)

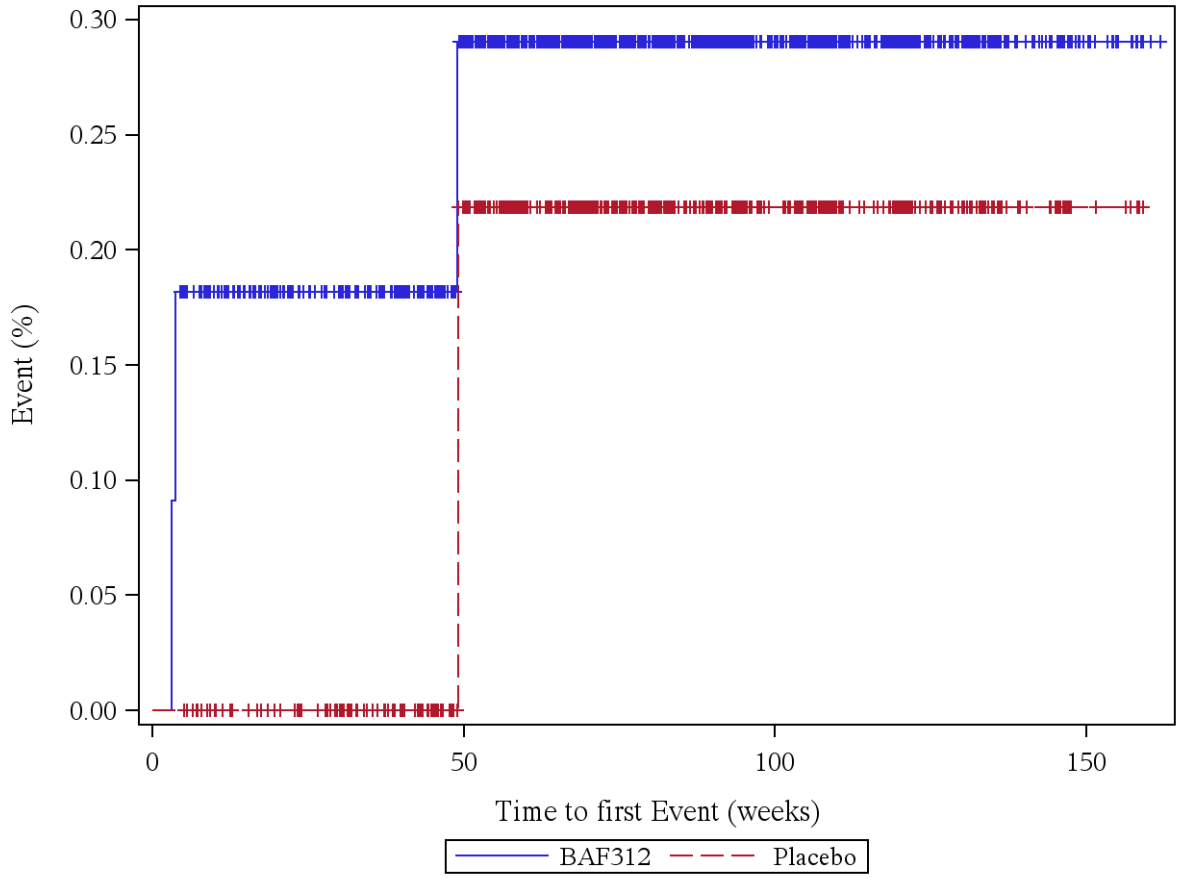


Patients at risk (BAF312/Placebo): Week 0: 1099/546, Week 4: 1097/544, Week 12: 1055/532, Week 24: 1007/518, Week 36: 980/492, Week 48: 919/456, Week 60: 811/383, Week 72: 646/300, Week 84: 512/234, Week 96: 397/173, Week 108: 288/123, Week 120: 196/78, Week 132: 111/39, Week 144: 50/19, Week 156: 9/5, Week 168: 0/0

Log rank test: p-value = 0,326
*: p < 0,05

Analysis population: A2304 SAF total population

Figure 12.1.5.186: TRIGEMINAL NEURALGIA (PT, severe)

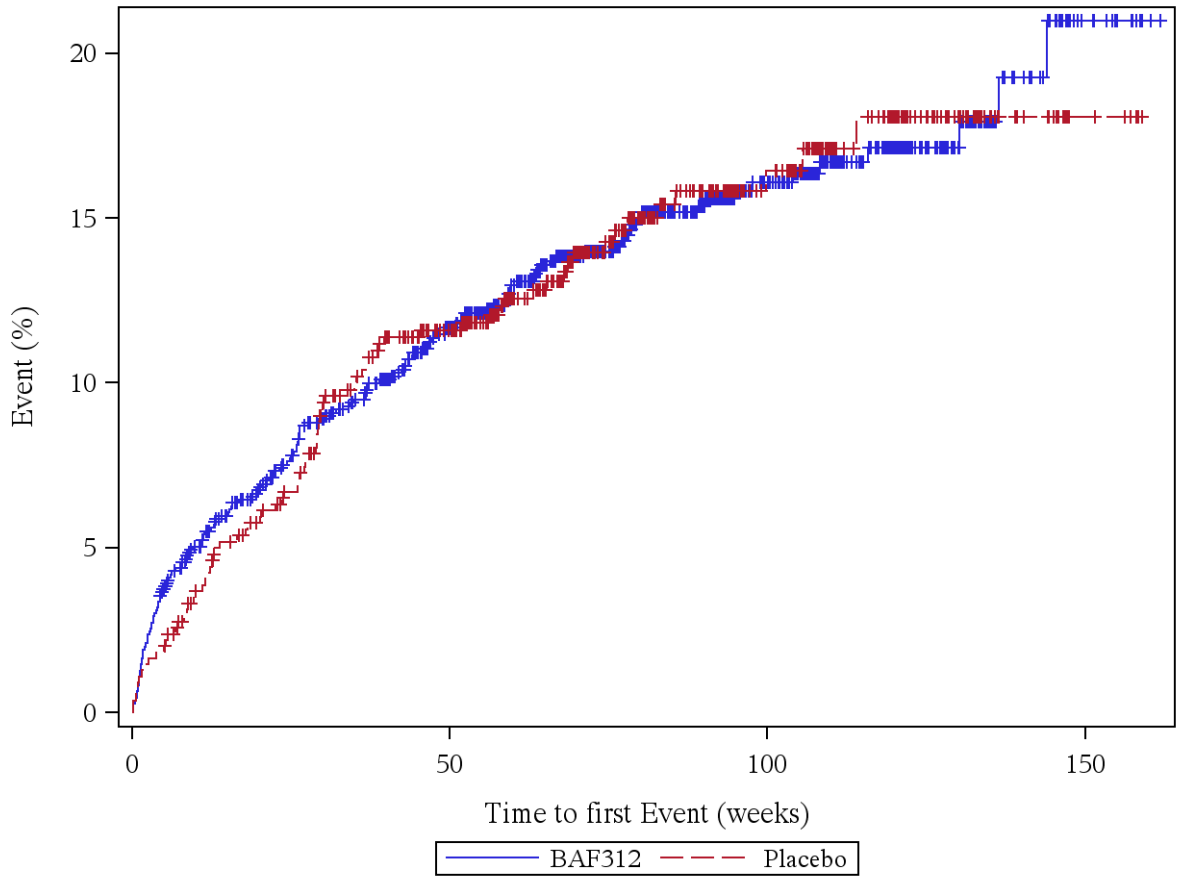


Patients at risk (BAF312/Placebo): Week 0: 1099/546, Week 4: 1097/546, Week 12: 1058/535, Week 24: 1016/521, Week 36: 989/497, Week 48: 924/461, Week 60: 816/387, Week 72: 650/304, Week 84: 514/237, Week 96: 398/176, Week 108: 290/126, Week 120: 199/80, Week 132: 113/40, Week 144: 51/20, Week 156: 10/5, Week 168: 0/0

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

Analysis population: A2304 SAF total population

Figure 12.1.5.187: PSYCHIATRIC DISORDERS (SOC, not severe)

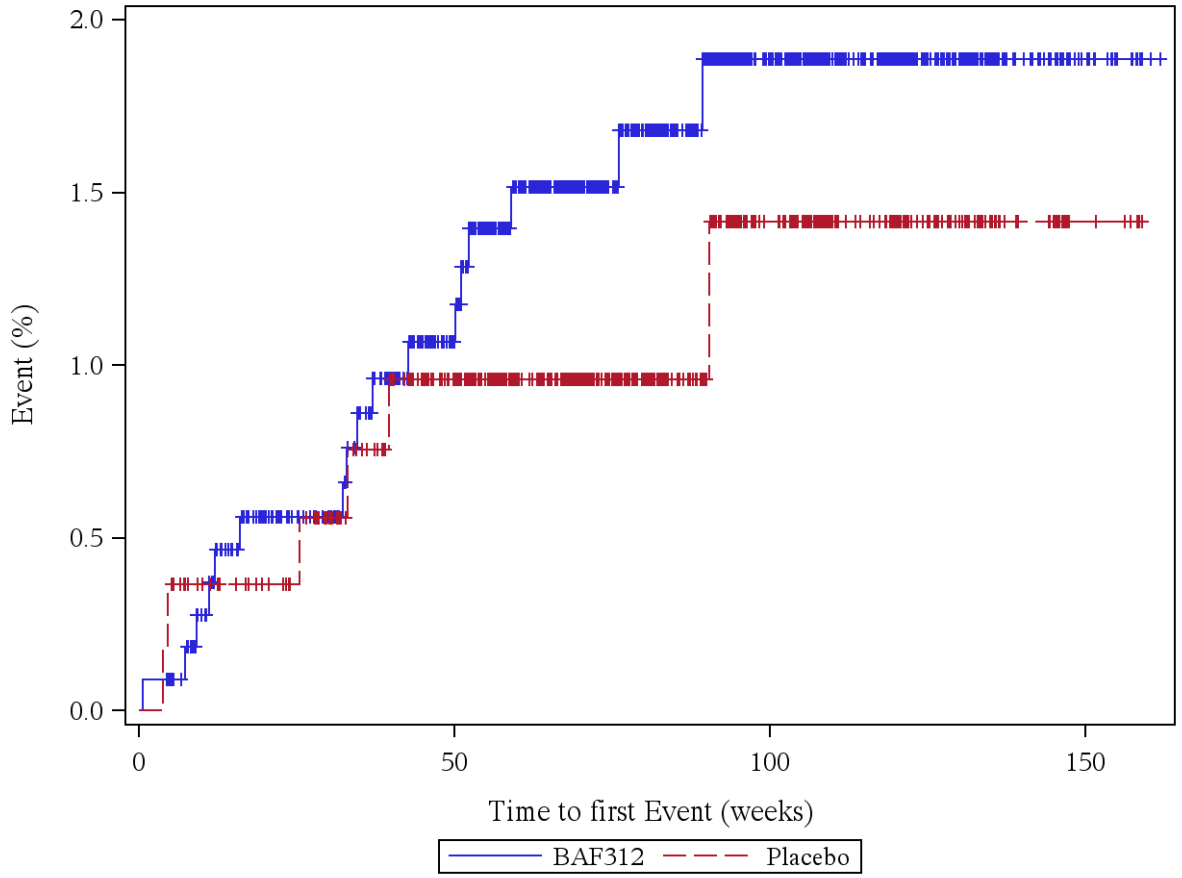


Patients at risk (BAF312/Placebo): Week 0: 1099/546, Week 4: 1064/536, Week 12: 1002/515, Week 24: 945/487, Week 36: 900/450, Week 48: 826/413, Week 60: 722/345, Week 72: 561/264, Week 84: 443/201, Week 96: 340/148, Week 108: 244/107, Week 120: 159/69, Week 132: 92/32, Week 144: 46/16, Week 156: 10/5, Week 168: 0/0

Log rank test: p-value = 0,966
*: p < 0,05

Analysis population: A2304 SAF total population

Figure 12.1.5.188: PSYCHIATRIC DISORDERS (SOC, severe)

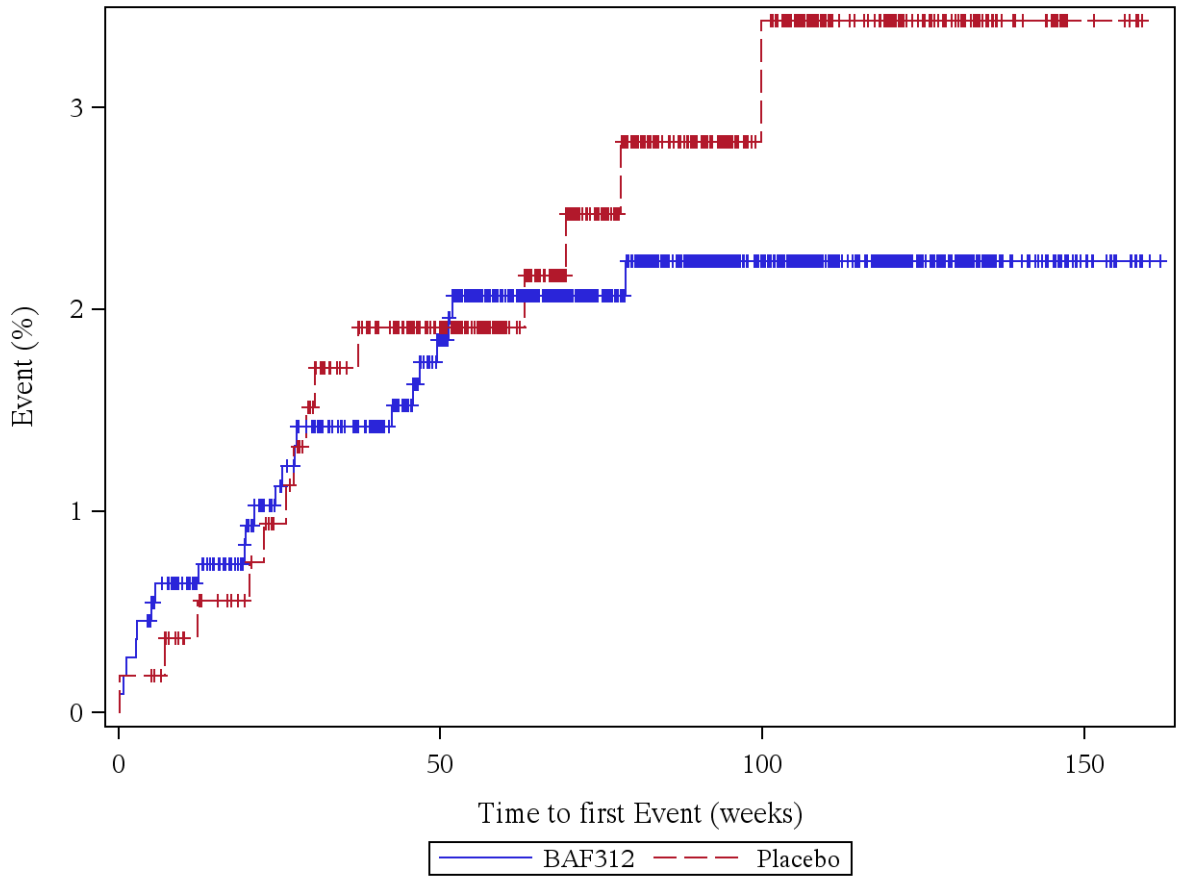


Patients at risk (BAF312/Placebo): Week 0: 1099/546, Week 4: 1098/545, Week 12: 1055/535, Week 24: 1012/521, Week 36: 983/496, Week 48: 919/459, Week 60: 810/387, Week 72: 645/305, Week 84: 508/237, Week 96: 395/175, Week 108: 286/125, Week 120: 198/79, Week 132: 111/39, Week 144: 50/20, Week 156: 10/5, Week 168: 0/0

Log rank test: p-value = 0,469
*: p < 0,05

Analysis population: A2304 SAF total population

Figure 12.1.5.189: ANXIETY (PT, not severe)

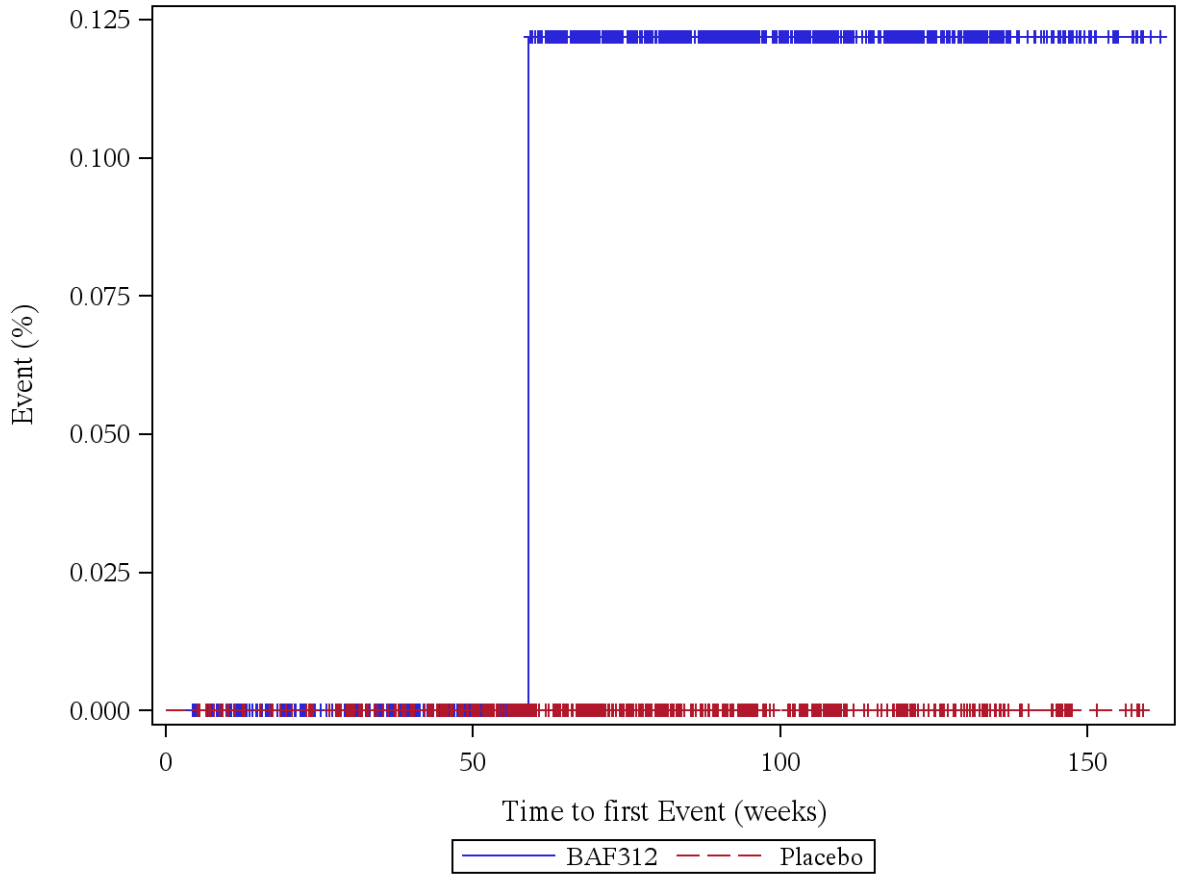


Patients at risk (BAF312/Placebo): Week 0: 1099/546, Week 4: 1094/545, Week 12: 1052/534, Week 24: 1008/517, Week 36: 978/490, Week 48: 910/455, Week 60: 801/382, Week 72: 638/298, Week 84: 507/232, Week 96: 394/172, Week 108: 287/122, Week 120: 197/79, Week 132: 111/39, Week 144: 51/20, Week 156: 10/5, Week 168: 0/0

Log rank test: p-value = 0,475
*: p < 0,05

Analysis population: A2304 SAF total population

Figure 12.1.5.190: ANXIETY (PT, severe)

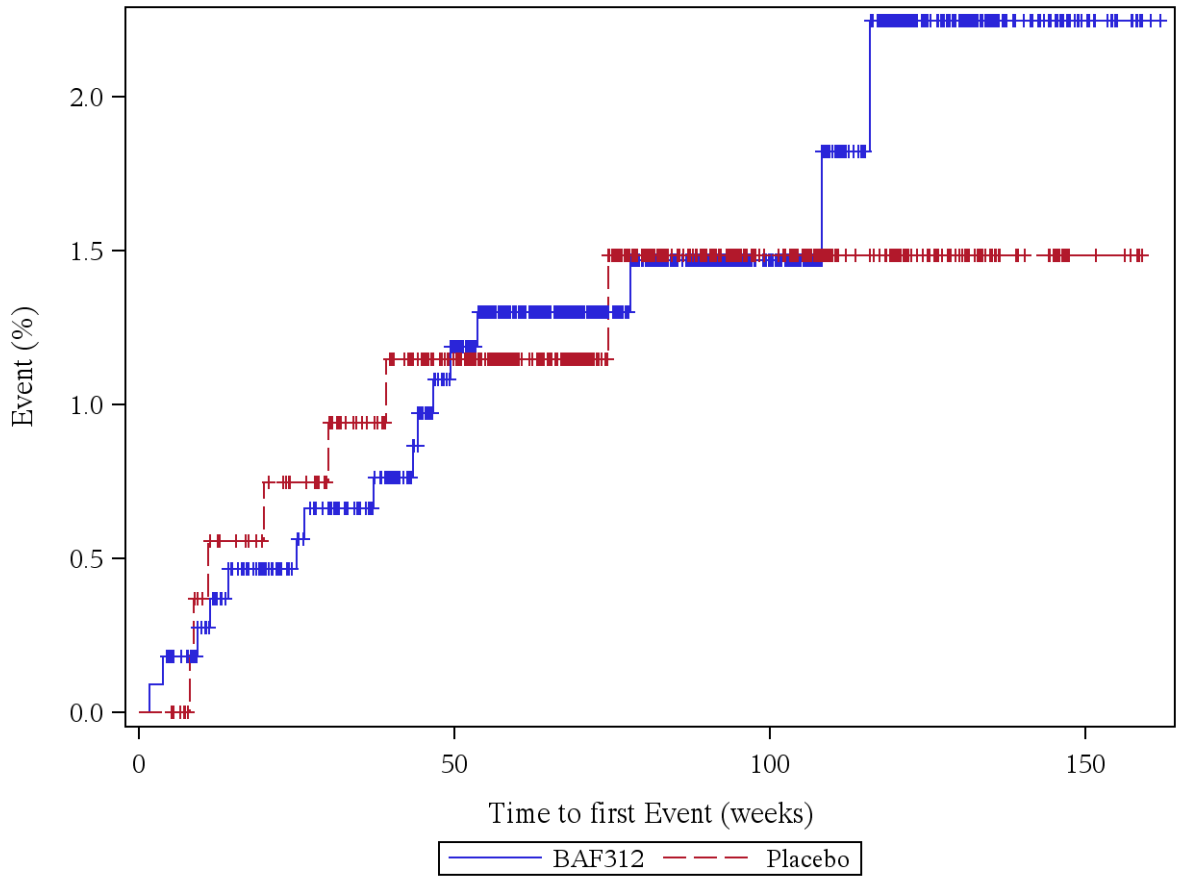


Patients at risk (BAF312/Placebo): Week 0: 1099/546, Week 4: 1099/546, Week 12: 1059/535, Week 24: 1017/521, Week 36: 990/497, Week 48: 925/461, Week 60: 817/388, Week 72: 651/305, Week 84: 515/237, Week 96: 400/176, Week 108: 291/126, Week 120: 200/80, Week 132: 113/40, Week 144: 51/20, Week 156: 10/5, Week 168: 0/0

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

Analysis population: A2304 SAF total population

Figure 12.1.5.191: DEPRESSED MOOD (PT, not severe)

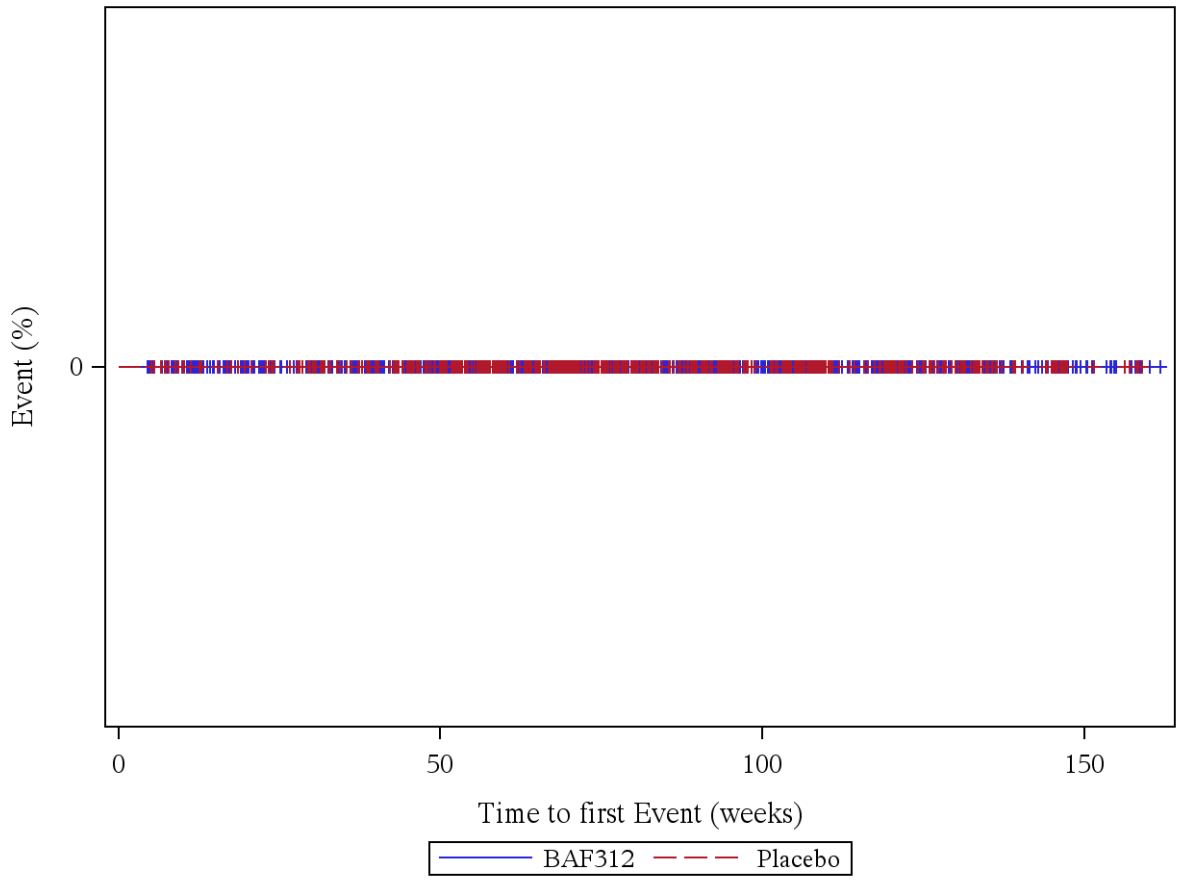


Patients at risk (BAF312/Placebo): Week 0: 1099/546, Week 4: 1097/546, Week 12: 1056/532, Week 24: 1014/517, Week 36: 985/493, Week 48: 916/456, Week 60: 809/384, Week 72: 645/302, Week 84: 510/233, Week 96: 394/172, Week 108: 287/124, Week 120: 196/79, Week 132: 111/39, Week 144: 50/20, Week 156: 10/5, Week 168: 0/0

Log rank test: p-value = 0,797
*: p < 0,05

Analysis population: A2304 SAF total population

Figure 12.1.5.192: DEPRESSED MOOD (PT, severe)

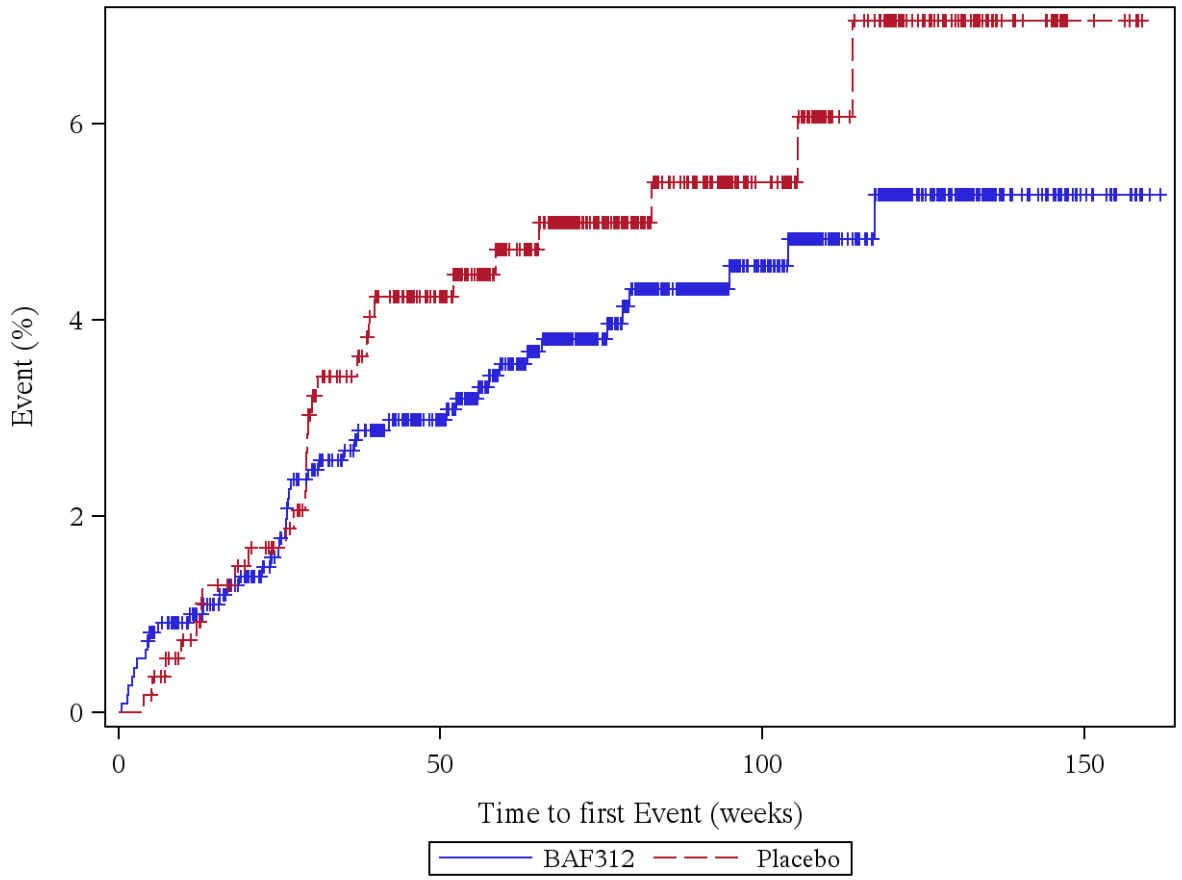


Patients at risk (BAF312/Placebo): Week 0: 1099/546, Week 4: 1099/546, Week 12: 1059/535, Week 24: 1017/521, Week 36: 990/497, Week 48: 925/461, Week 60: 818/388, Week 72: 652/305, Week 84: 516/237, Week 96: 400/176, Week 108: 291/126, Week 120: 200/80, Week 132: 113/40, Week 144: 51/20, Week 156: 10/5, Week 168: 0/0

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

Analysis population: A2304 SAF total population

Figure 12.1.5.193: DEPRESSION (PT, not severe)

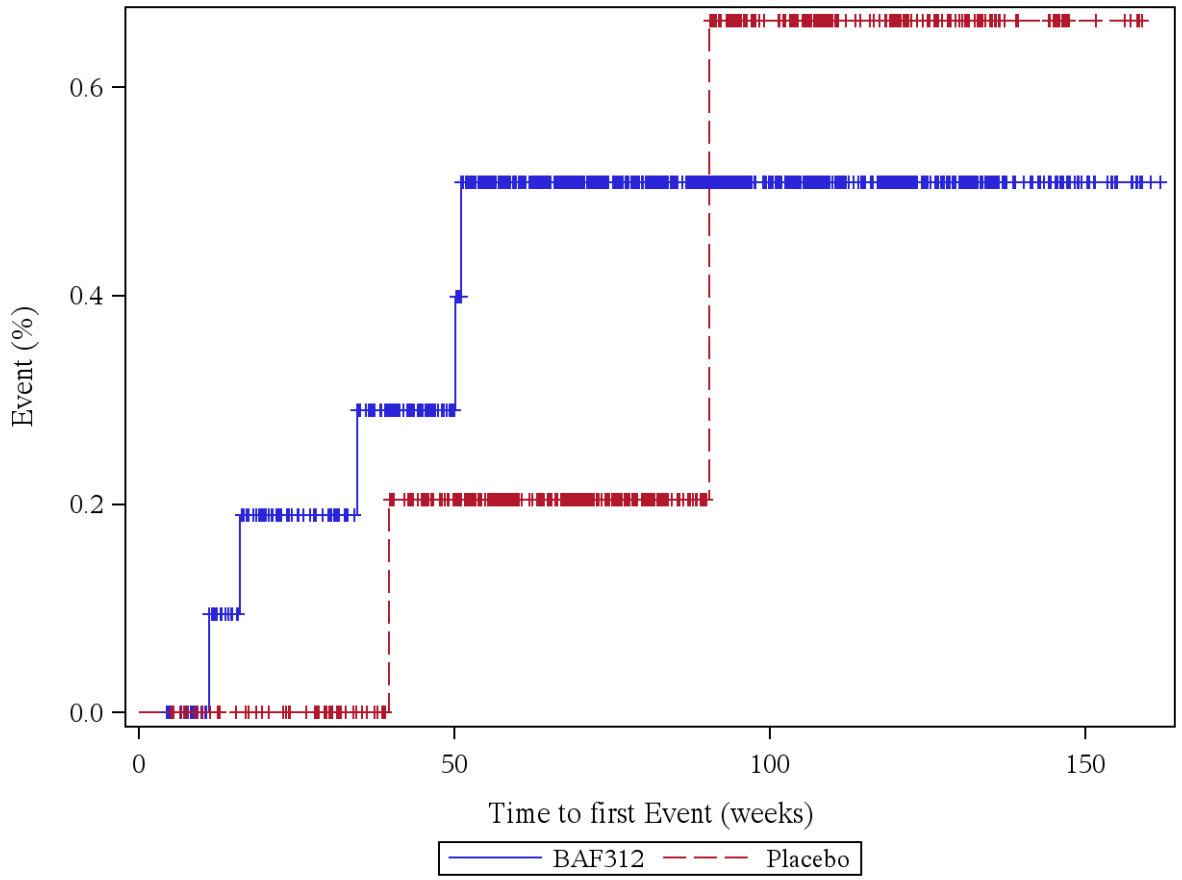


Patients at risk (BAF312/Placebo): Week 0: 1099/546, Week 4: 1093/545, Week 12: 1049/532, Week 24: 1003/513, Week 36: 965/481, Week 48: 902/442, Week 60: 796/370, Week 72: 630/289, Week 84: 494/222, Week 96: 382/167, Week 108: 275/122, Week 120: 185/77, Week 132: 108/39, Week 144: 50/19, Week 156: 10/5, Week 168: 0/0

Log rank test: p-value = 0,288
*: p < 0,05

Analysis population: A2304 SAF total population

Figure 12.1.5.194: DEPRESSION (PT, severe)

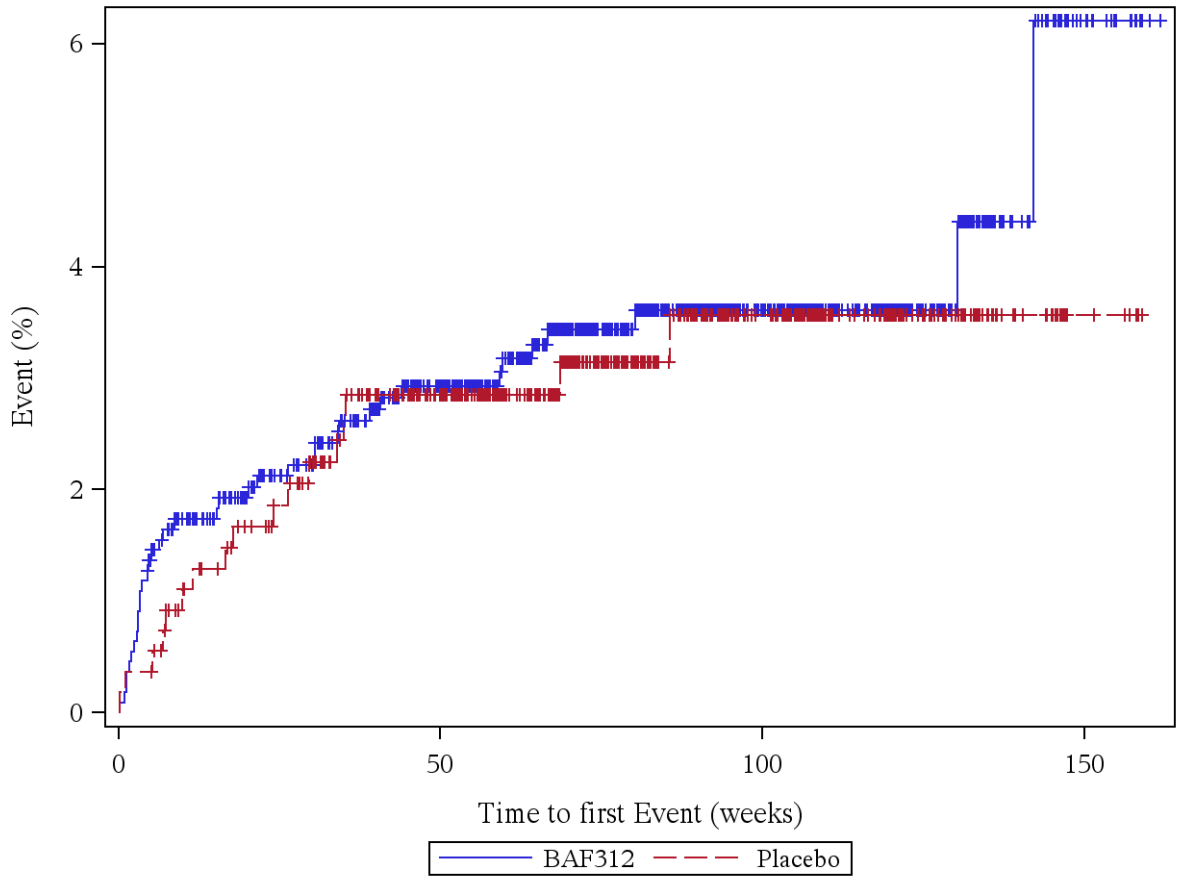


Patients at risk (BAF312/Placebo): Week 0: 1099/546, Week 4: 1099/546, Week 12: 1058/535, Week 24: 1015/521, Week 36: 988/497, Week 48: 924/460, Week 60: 816/387, Week 72: 650/305, Week 84: 514/237, Week 96: 398/175, Week 108: 289/125, Week 120: 199/79, Week 132: 112/39, Week 144: 51/20, Week 156: 10/5, Week 168: 0/0

Log rank test: p-value = 0,800
*: p < 0,05

Analysis population: A2304 SAF total population

Figure 12.1.5.195: INSOMNIA (PT, not severe)

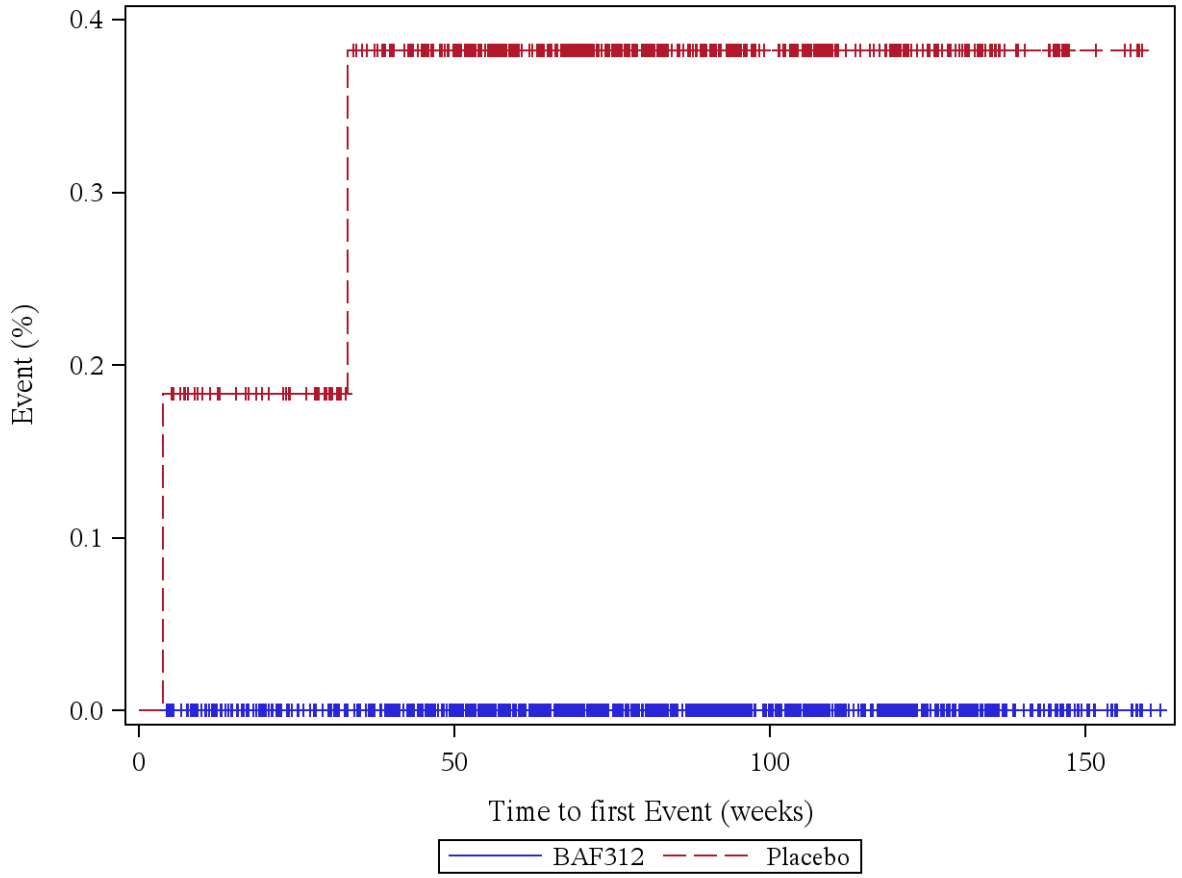


Patients at risk (BAF312/Placebo): Week 0: 1099/546, Week 4: 1086/544, Week 12: 1040/529, Week 24: 995/512, Week 36: 963/484, Week 48: 898/449, Week 60: 792/378, Week 72: 626/295, Week 84: 495/230, Week 96: 385/170, Week 108: 279/122, Week 120: 190/78, Week 132: 106/38, Week 144: 49/19, Week 156: 10/5, Week 168: 0/0

Log rank test: p-value = 0,730
*: p < 0,05

Analysis population: A2304 SAF total population

Figure 12.1.5.196: INSOMNIA (PT, severe)

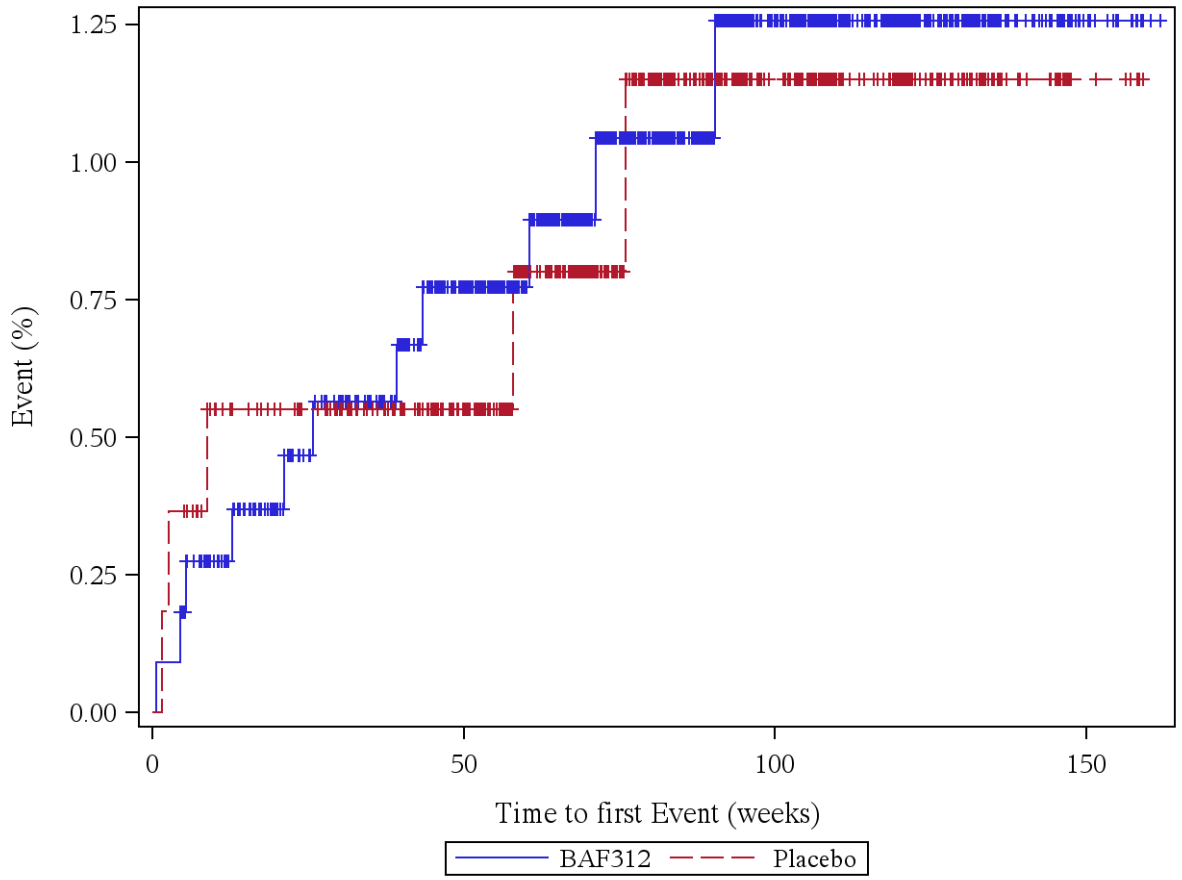


Patients at risk (BAF312/Placebo): Week 0: 1099/546, Week 4: 1099/545, Week 12: 1059/535, Week 24: 1017/521, Week 36: 990/496, Week 48: 925/460, Week 60: 818/388, Week 72: 652/305, Week 84: 516/237, Week 96: 400/176, Week 108: 291/126, Week 120: 200/80, Week 132: 113/40, Week 144: 51/20, Week 156: 10/5, Week 168: 0/0

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

Analysis population: A2304 SAF total population

Figure 12.1.5.197: SLEEP DISORDER (PT, not severe)

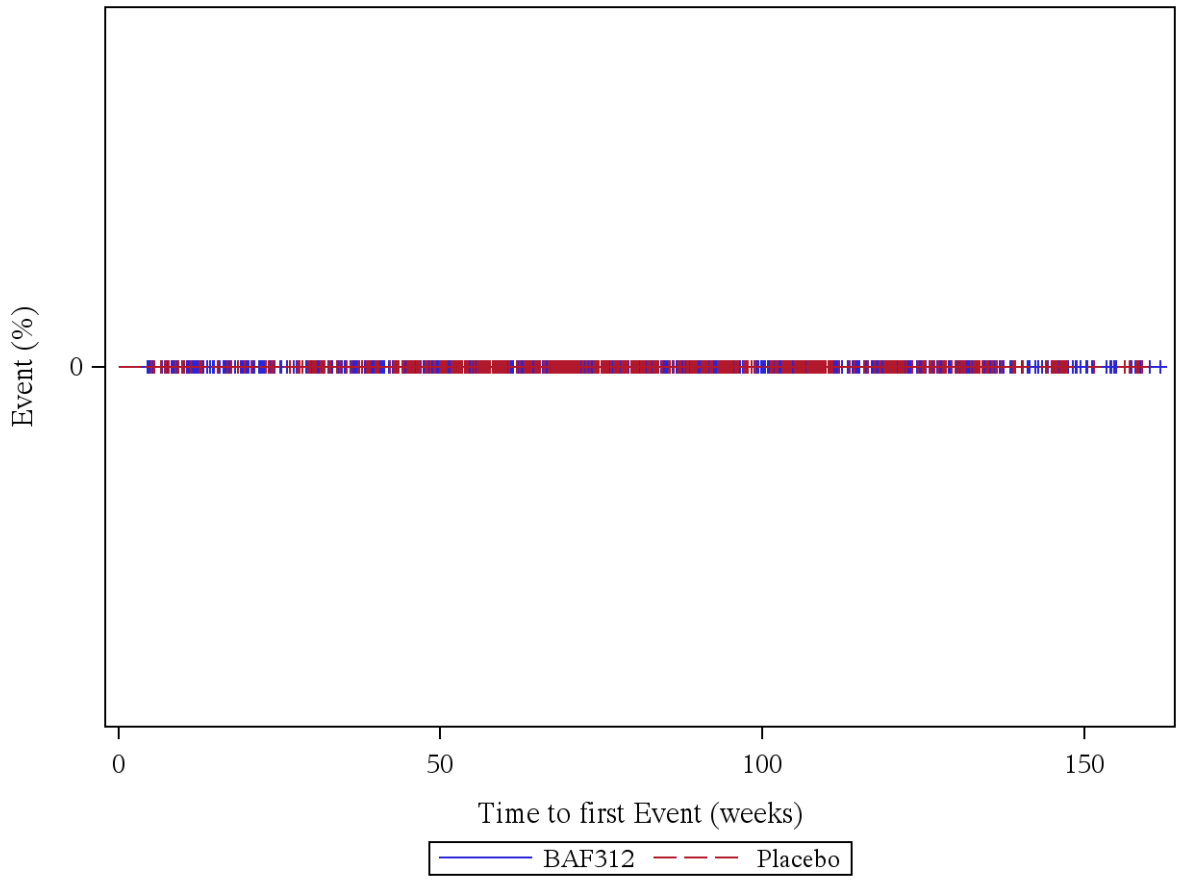


Patients at risk (BAF312/Placebo): Week 0: 1099/546, Week 4: 1098/544, Week 12: 1057/532, Week 24: 1013/518, Week 36: 985/495, Week 48: 918/460, Week 60: 812/386, Week 72: 646/304, Week 84: 512/235, Week 96: 395/174, Week 108: 288/124, Week 120: 197/79, Week 132: 110/40, Week 144: 50/20, Week 156: 10/5, Week 168: 0/0

Log rank test: p-value = 0,884
*: p < 0,05

Analysis population: A2304 SAF total population

Figure 12.1.5.198: SLEEP DISORDER (PT, severe)

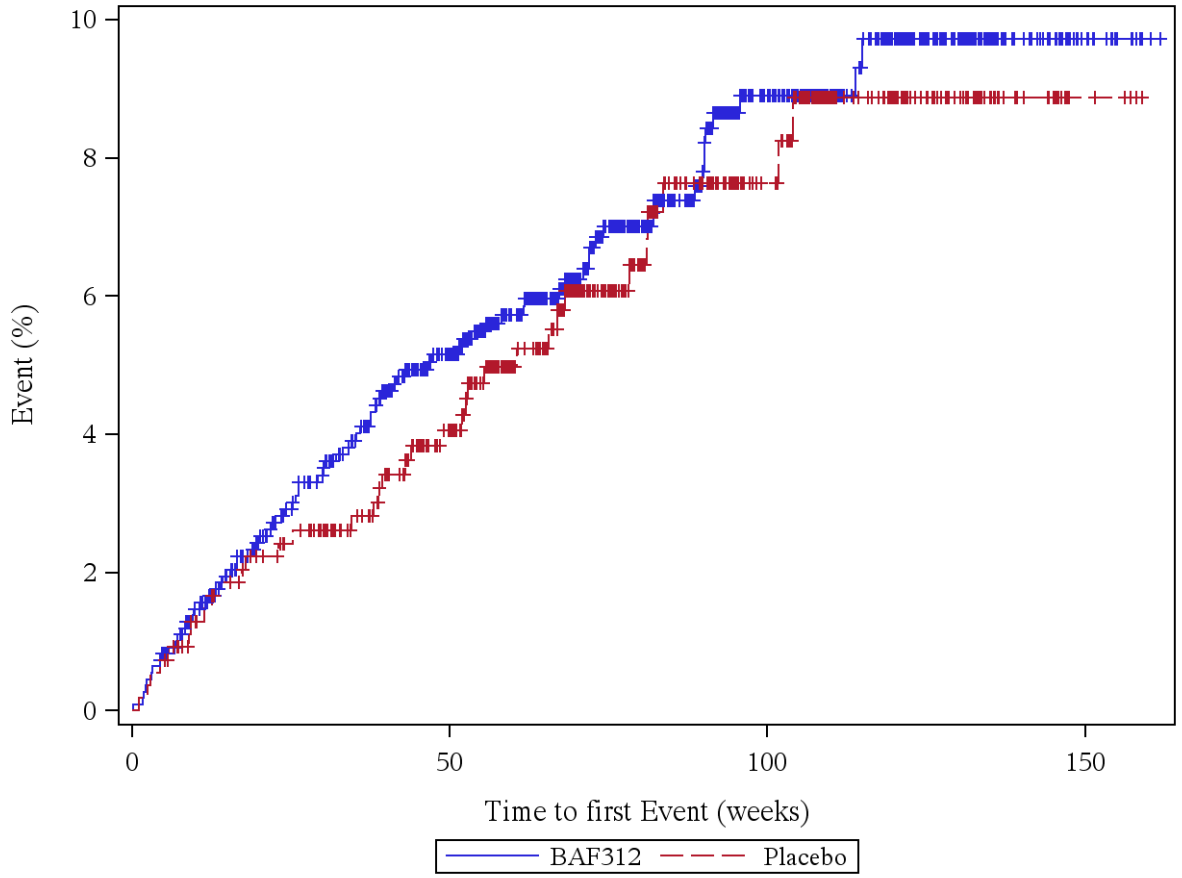


Patients at risk (BAF312/Placebo): Week 0: 1099/546, Week 4: 1099/546, Week 12: 1059/535, Week 24: 1017/521, Week 36: 990/497, Week 48: 925/461, Week 60: 818/388, Week 72: 652/305, Week 84: 516/237, Week 96: 400/176, Week 108: 291/126, Week 120: 200/80, Week 132: 113/40, Week 144: 51/20, Week 156: 10/5, Week 168: 0/0

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

Analysis population: A2304 SAF total population

Figure 12.1.5.199: RENAL AND URINARY DISORDERS (SOC, not severe)

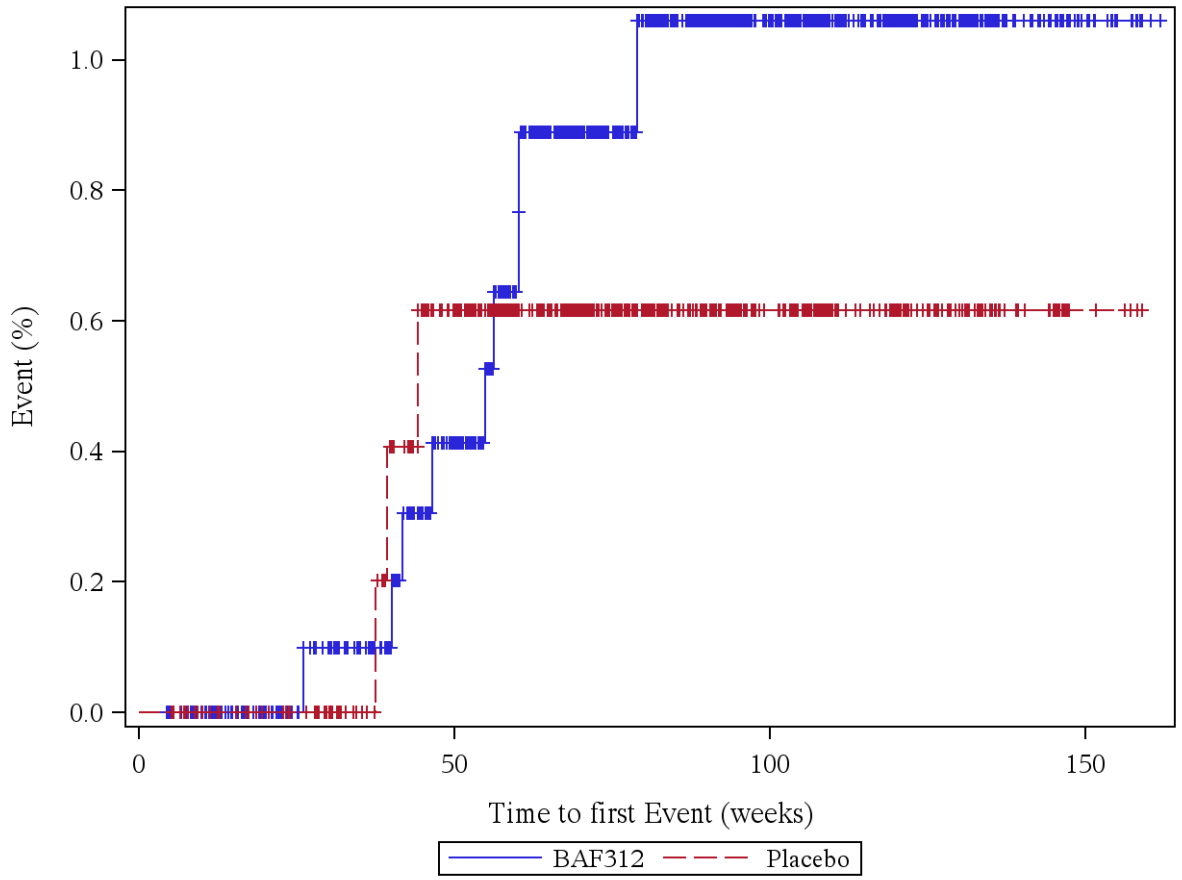


Patients at risk (BAF312/Placebo): Week 0: 1099/546, Week 4: 1092/543, Week 12: 1042/528, Week 24: 987/509, Week 36: 948/485, Week 48: 875/445, Week 60: 769/368, Week 72: 605/287, Week 84: 480/219, Week 96: 366/166, Week 108: 270/118, Week 120: 182/75, Week 132: 104/37, Week 144: 47/18, Week 156: 10/4, Week 168: 0/0

Log rank test: p-value = 0,632
*: p < 0,05

Analysis population: A2304 SAF total population

Figure 12.1.5.200: RENAL AND URINARY DISORDERS (SOC, severe)

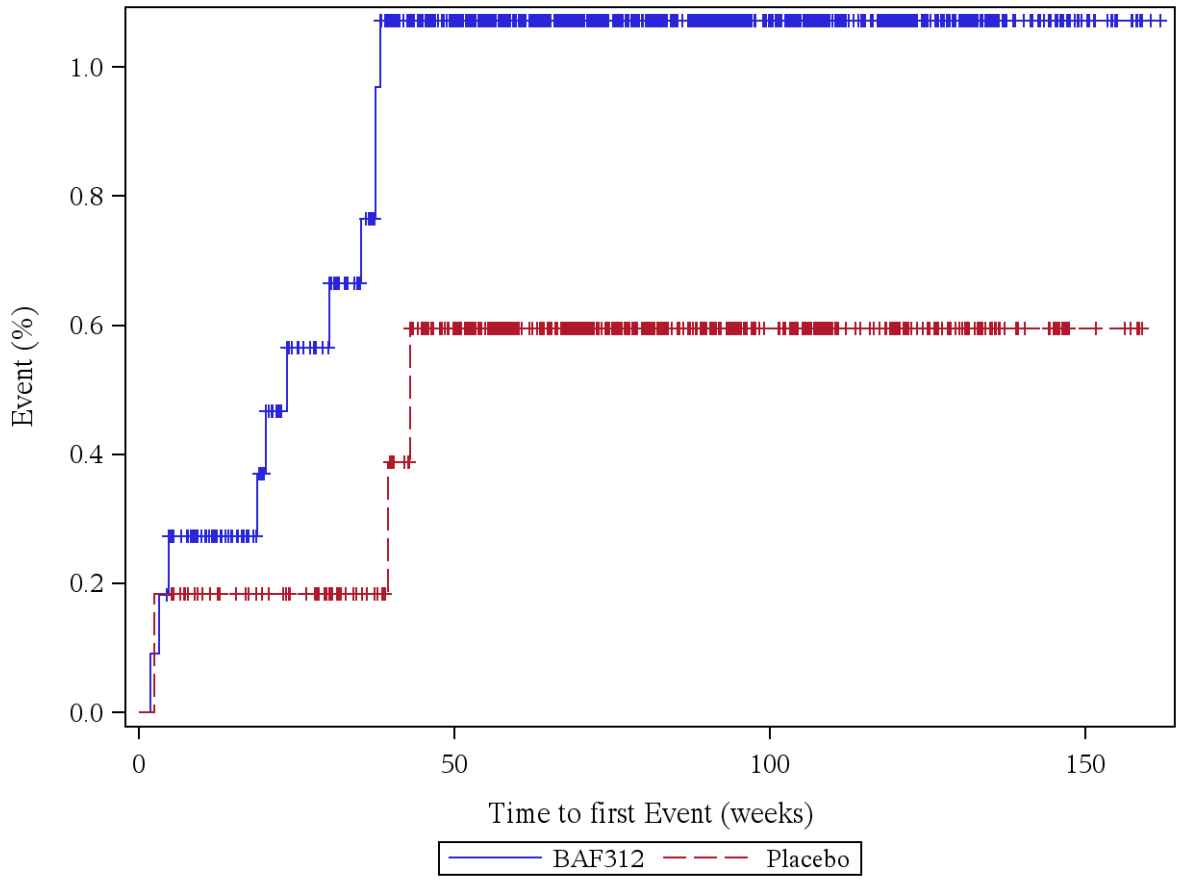


Patients at risk (BAF312/Placebo): Week 0: 1099/546, Week 4: 1099/546, Week 12: 1059/535, Week 24: 1017/521, Week 36: 989/497, Week 48: 921/458, Week 60: 813/386, Week 72: 648/304, Week 84: 513/236, Week 96: 397/175, Week 108: 288/125, Week 120: 198/79, Week 132: 111/39, Week 144: 51/19, Week 156: 10/4, Week 168: 0/0

Log rank test: p-value = 0,558
*: p < 0,05

Analysis population: A2304 SAF total population

Figure 12.1.5.201: DYSURIA (PT, not severe)

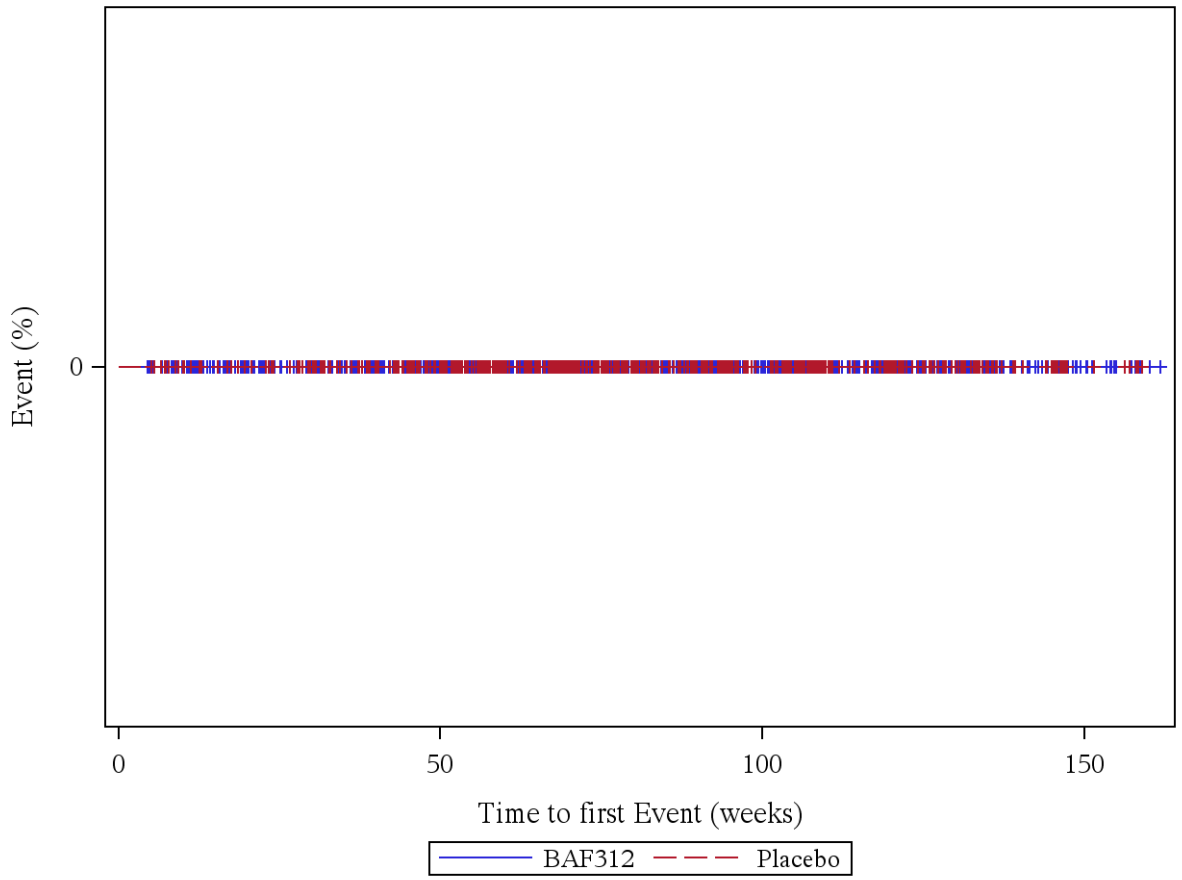


Patients at risk (BAF312/Placebo): Week 0: 1099/546, Week 4: 1097/545, Week 12: 1056/534, Week 24: 1011/520, Week 36: 982/496, Week 48: 914/458, Week 60: 808/385, Week 72: 643/303, Week 84: 510/236, Week 96: 398/175, Week 108: 289/125, Week 120: 199/79, Week 132: 113/40, Week 144: 51/20, Week 156: 10/5, Week 168: 0/0

Log rank test: p-value = 0,336
*: p < 0,05

Analysis population: A2304 SAF total population

Figure 12.1.5.202: DYSURIA (PT, severe)

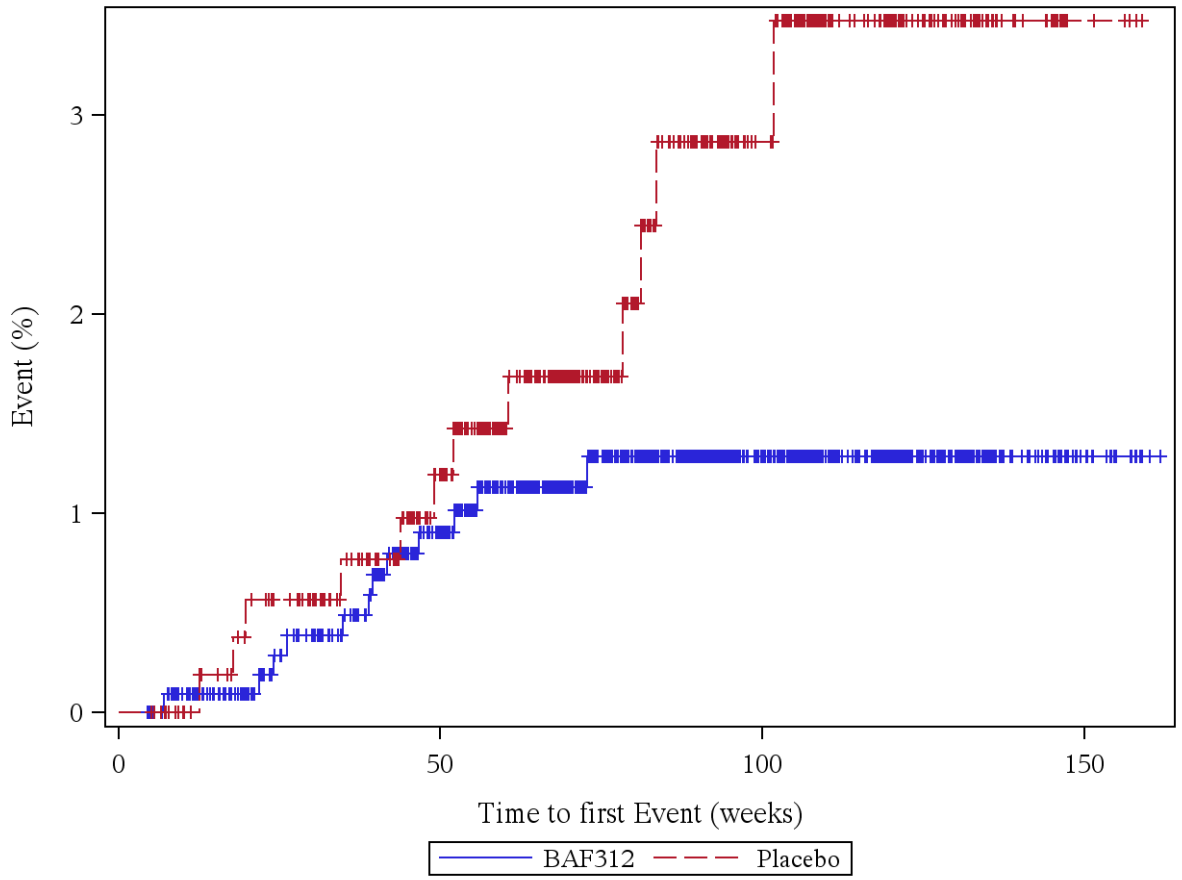


Patients at risk (BAF312/Placebo): Week 0: 1099/546, Week 4: 1099/546, Week 12: 1059/535, Week 24: 1017/521, Week 36: 990/497, Week 48: 925/461, Week 60: 818/388, Week 72: 652/305, Week 84: 516/237, Week 96: 400/176, Week 108: 291/126, Week 120: 200/80, Week 132: 113/40, Week 144: 51/20, Week 156: 10/5, Week 168: 0/0

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

Analysis population: A2304 SAF total population

Figure 12.1.5.203: URINARY INCONTINENCE (PT, not severe)

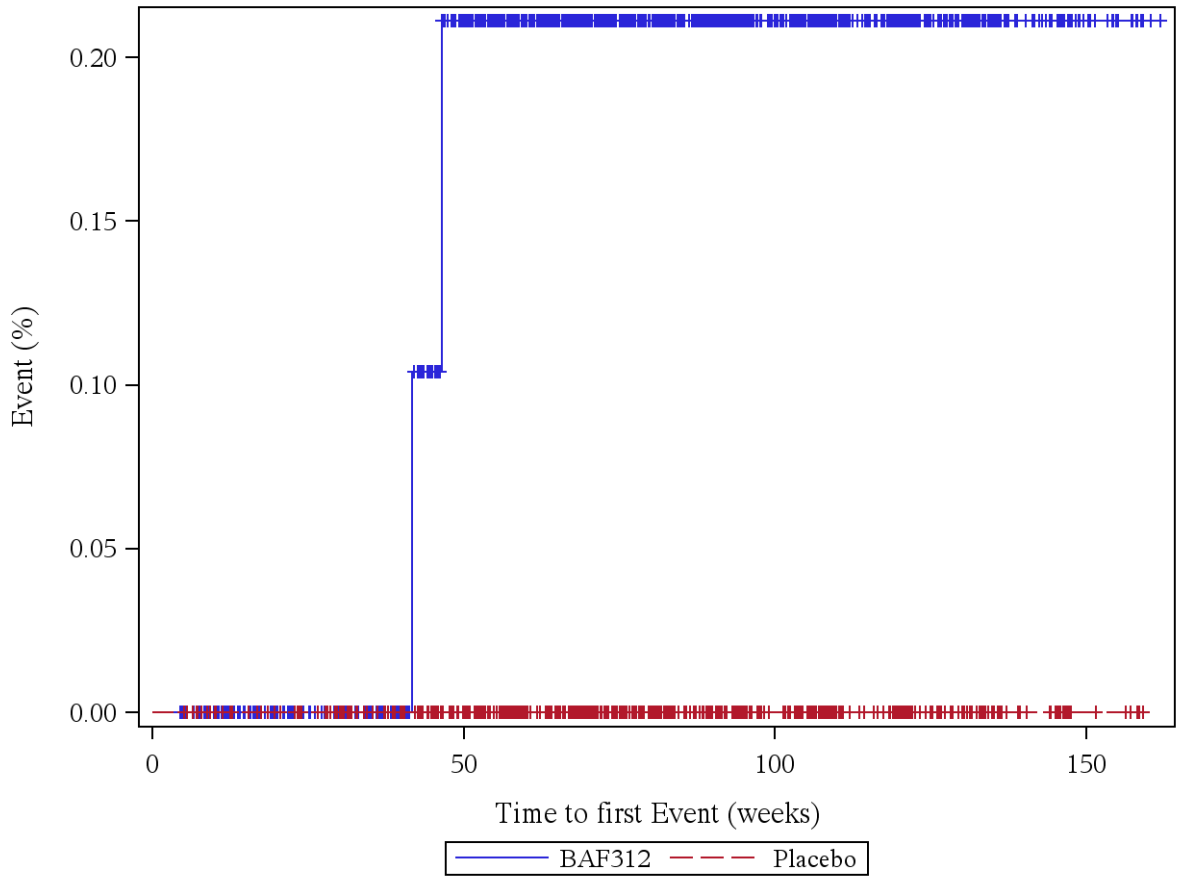


Patients at risk (BAF312/Placebo): Week 0: 1099/546, Week 4: 1099/546, Week 12: 1058/535, Week 24: 1014/518, Week 36: 985/493, Week 48: 916/456, Week 60: 808/381, Week 72: 643/298, Week 84: 507/228, Week 96: 395/172, Week 108: 289/123, Week 120: 198/79, Week 132: 112/39, Week 144: 50/19, Week 156: 10/4, Week 168: 0/0

Log rank test: p-value = 0,073
*: p < 0,05

Analysis population: A2304 SAF total population

Figure 12.1.5.204: URINARY INCONTINENCE (PT, severe)

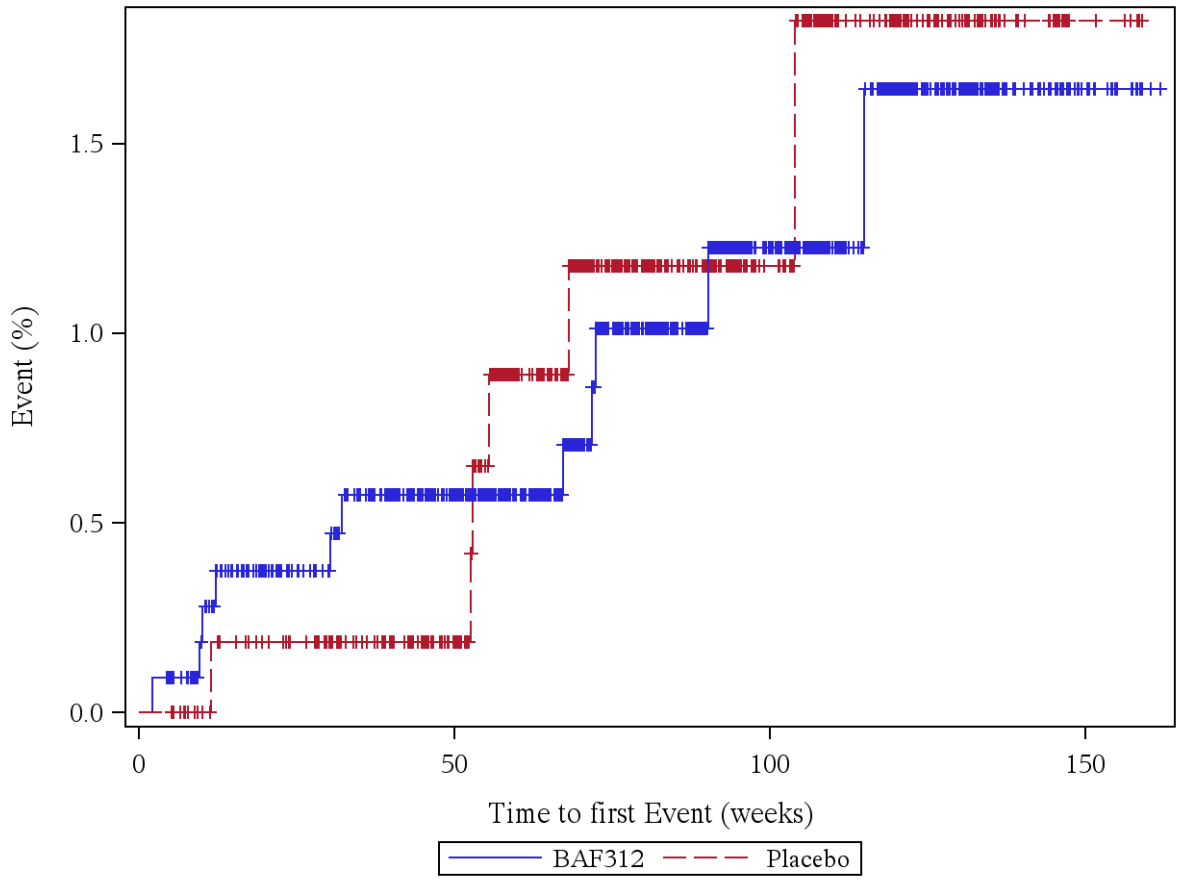


Patients at risk (BAF312/Placebo): Week 0: 1099/546, Week 4: 1099/546, Week 12: 1059/535, Week 24: 1017/521, Week 36: 990/497, Week 48: 923/461, Week 60: 817/388, Week 72: 651/305, Week 84: 515/237, Week 96: 399/176, Week 108: 290/126, Week 120: 200/80, Week 132: 113/40, Week 144: 51/20, Week 156: 10/5, Week 168: 0/0

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

Analysis population: A2304 SAF total population

Figure 12.1.5.205: URINARY RETENTION (PT, not severe)

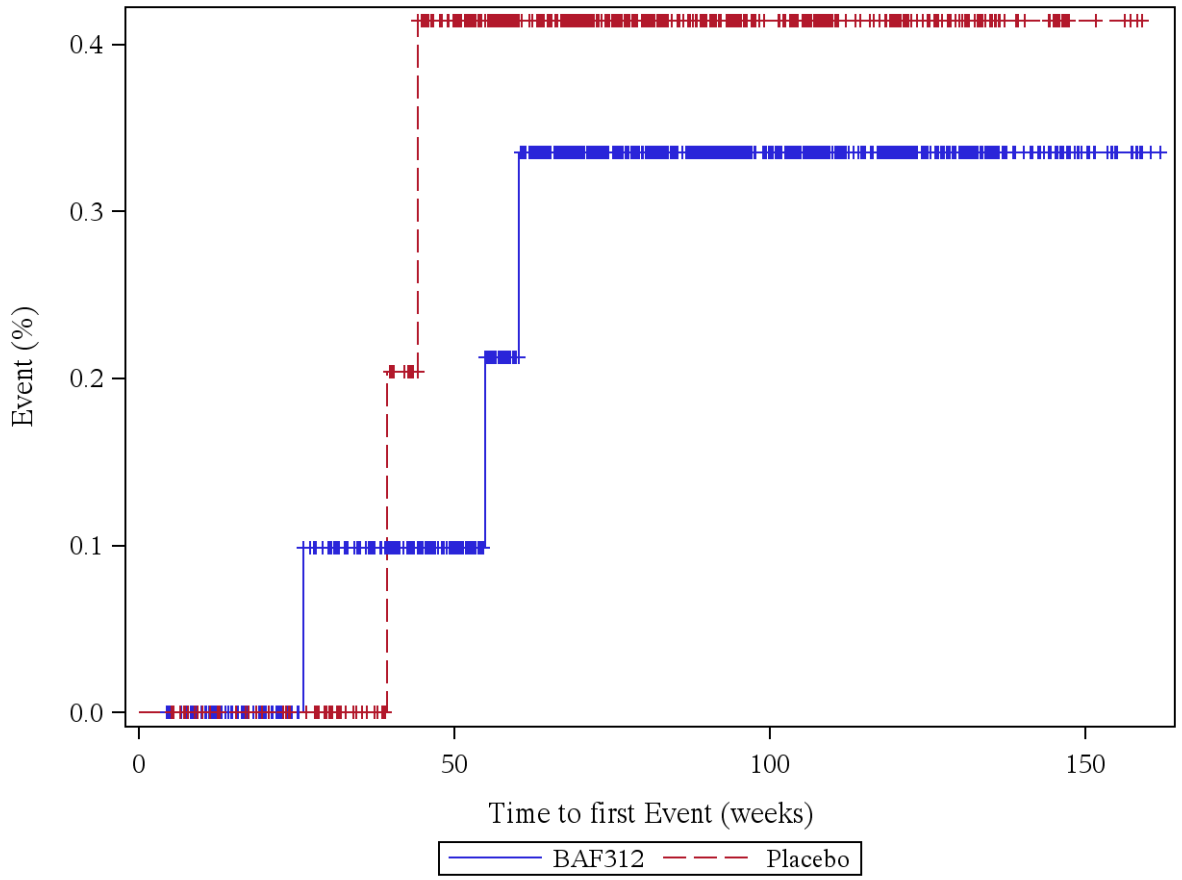


Patients at risk (BAF312/Placebo): Week 0: 1099/546, Week 4: 1098/546, Week 12: 1056/534, Week 24: 1013/520, Week 36: 984/496, Week 48: 919/460, Week 60: 812/384, Week 72: 646/301, Week 84: 511/234, Week 96: 396/174, Week 108: 289/125, Week 120: 198/79, Week 132: 111/39, Week 144: 49/20, Week 156: 10/5, Week 168: 0/0

Log rank test: p-value = 0,798
*: p < 0,05

Analysis population: A2304 SAF total population

Figure 12.1.5.206: URINARY RETENTION (PT, severe)

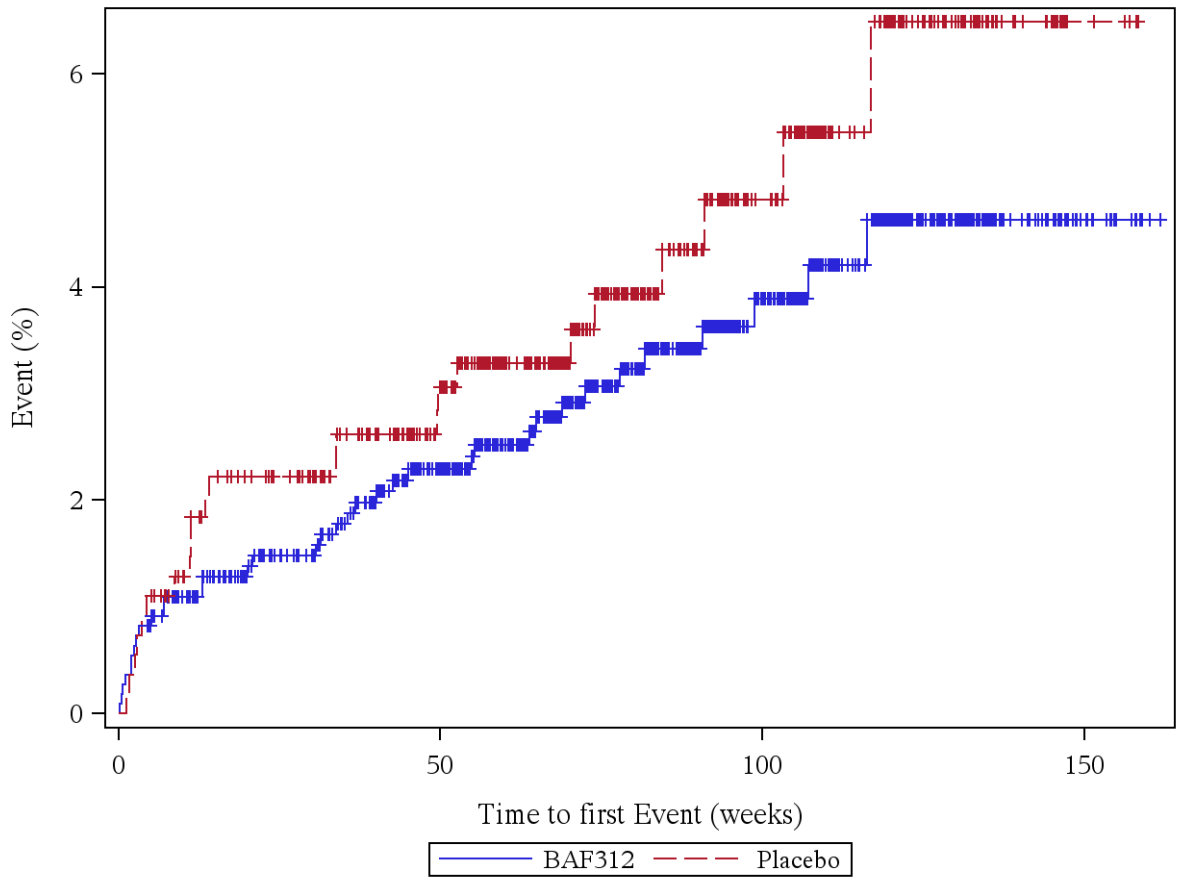


Patients at risk (BAF312/Placebo): Week 0: 1099/546, Week 4: 1099/546, Week 12: 1059/535, Week 24: 1017/521, Week 36: 989/497, Week 48: 924/459, Week 60: 816/387, Week 72: 651/304, Week 84: 516/236, Week 96: 400/175, Week 108: 291/125, Week 120: 200/79, Week 132: 113/39, Week 144: 51/19, Week 156: 10/4, Week 168: 0/0

Log rank test: p-value = 0,741
*: p < 0,05

Analysis population: A2304 SAF total population

Figure 12.1.5.207: REPRODUCTIVE SYSTEM AND BREAST DISORDERS (SOC, not severe)

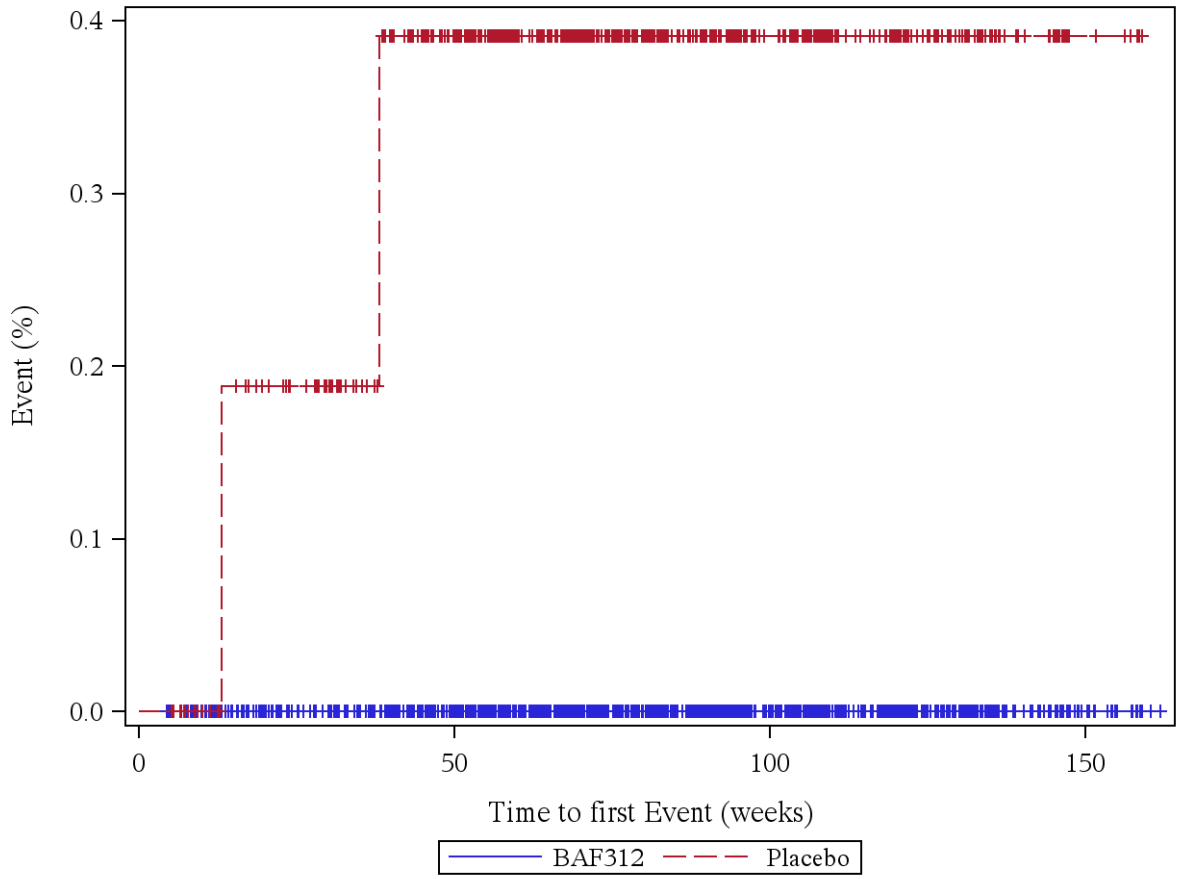


Patients at risk (BAF312/Placebo): Week 0: 1099/546, Week 4: 1090/541, Week 12: 1048/525, Week 24: 1003/509, Week 36: 972/483, Week 48: 906/449, Week 60: 798/376, Week 72: 637/295, Week 84: 501/229, Week 96: 389/168, Week 108: 281/121, Week 120: 191/75, Week 132: 107/37, Week 144: 49/18, Week 156: 9/4, Week 168: 0/0

Log rank test: p-value = 0,298
*: p < 0,05

Analysis population: A2304 SAF total population

Figure 12.1.5.208: REPRODUCTIVE SYSTEM AND BREAST DISORDERS (SOC, severe)

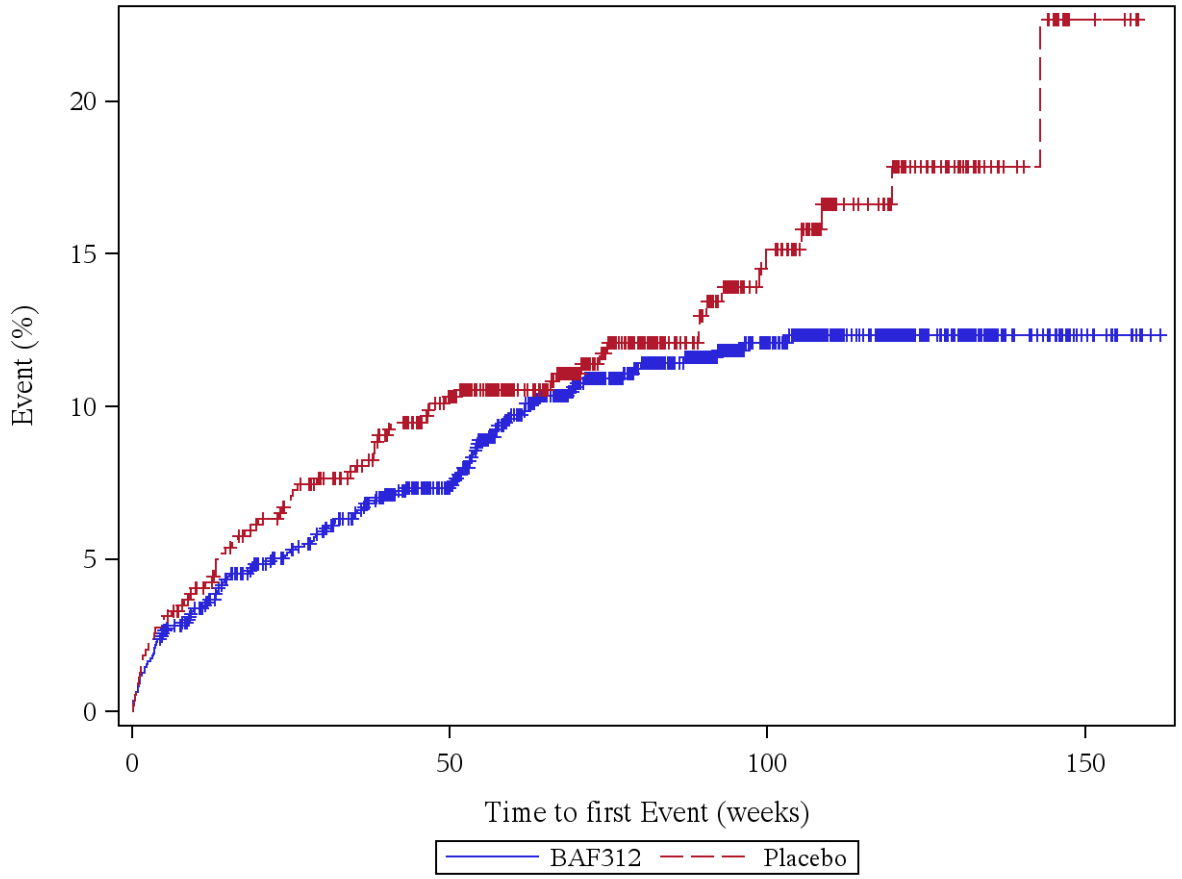


Patients at risk (BAF312/Placebo): Week 0: 1099/546, Week 4: 1099/546, Week 12: 1059/535, Week 24: 1017/520, Week 36: 990/496, Week 48: 925/459, Week 60: 818/388, Week 72: 652/305, Week 84: 516/237, Week 96: 400/176, Week 108: 291/126, Week 120: 200/80, Week 132: 113/40, Week 144: 51/20, Week 156: 10/5, Week 168: 0/0

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

Analysis population: A2304 SAF total population

Figure 12.1.5.209: RESPIRATORY, THORACIC AND MEDIASTINAL DISORDERS (SOC, not severe)

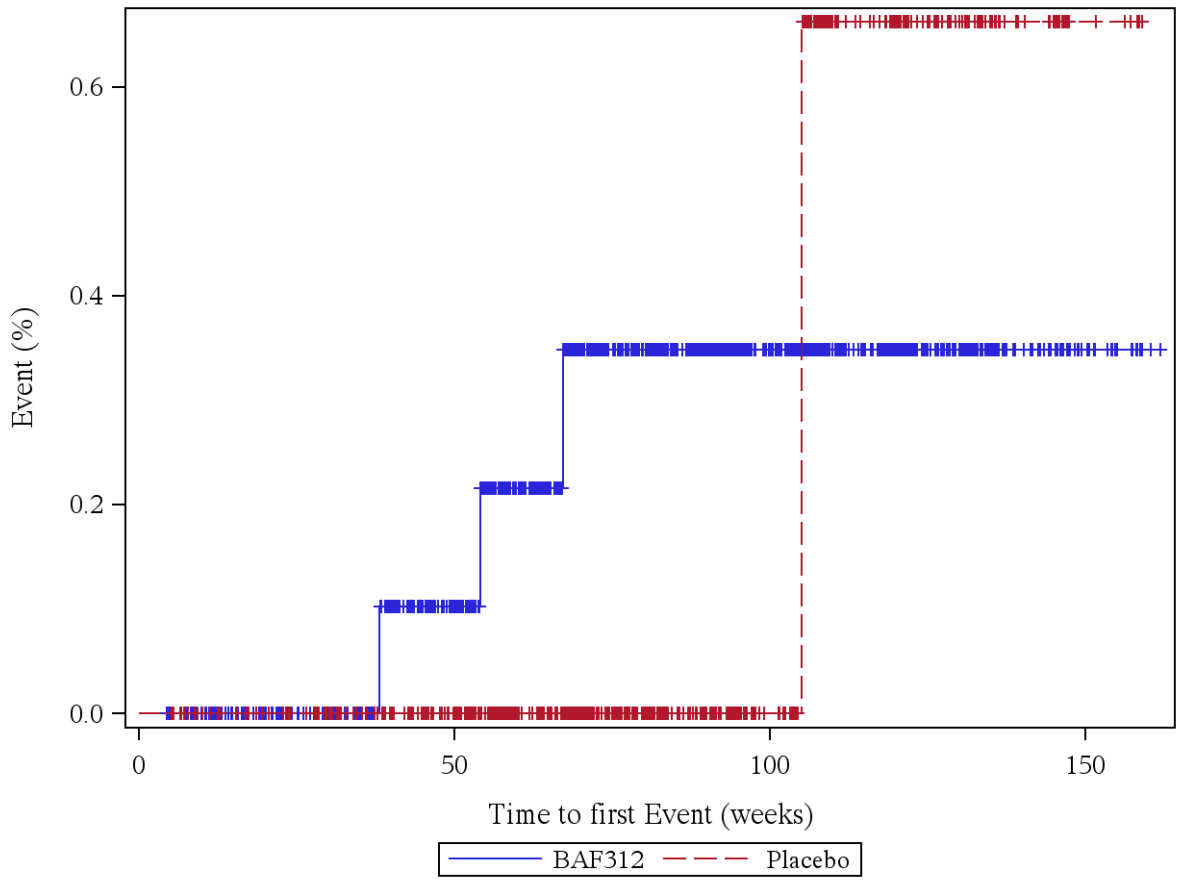


Patients at risk (BAF312/Placebo): Week 0: 1099/546, Week 4: 1073/531, Week 12: 1020/513, Week 24: 966/486, Week 36: 926/459, Week 48: 857/418, Week 60: 741/350, Week 72: 588/274, Week 84: 465/207, Week 96: 359/150, Week 108: 262/106, Week 120: 178/63, Week 132: 102/30, Week 144: 48/16, Week 156: 10/4, Week 168: 0/0

Log rank test: p-value = 0,123
*: p < 0,05

Analysis population: A2304 SAF total population

Figure 12.1.5.210: RESPIRATORY, THORACIC AND MEDIASTINAL DISORDERS (SOC, severe)

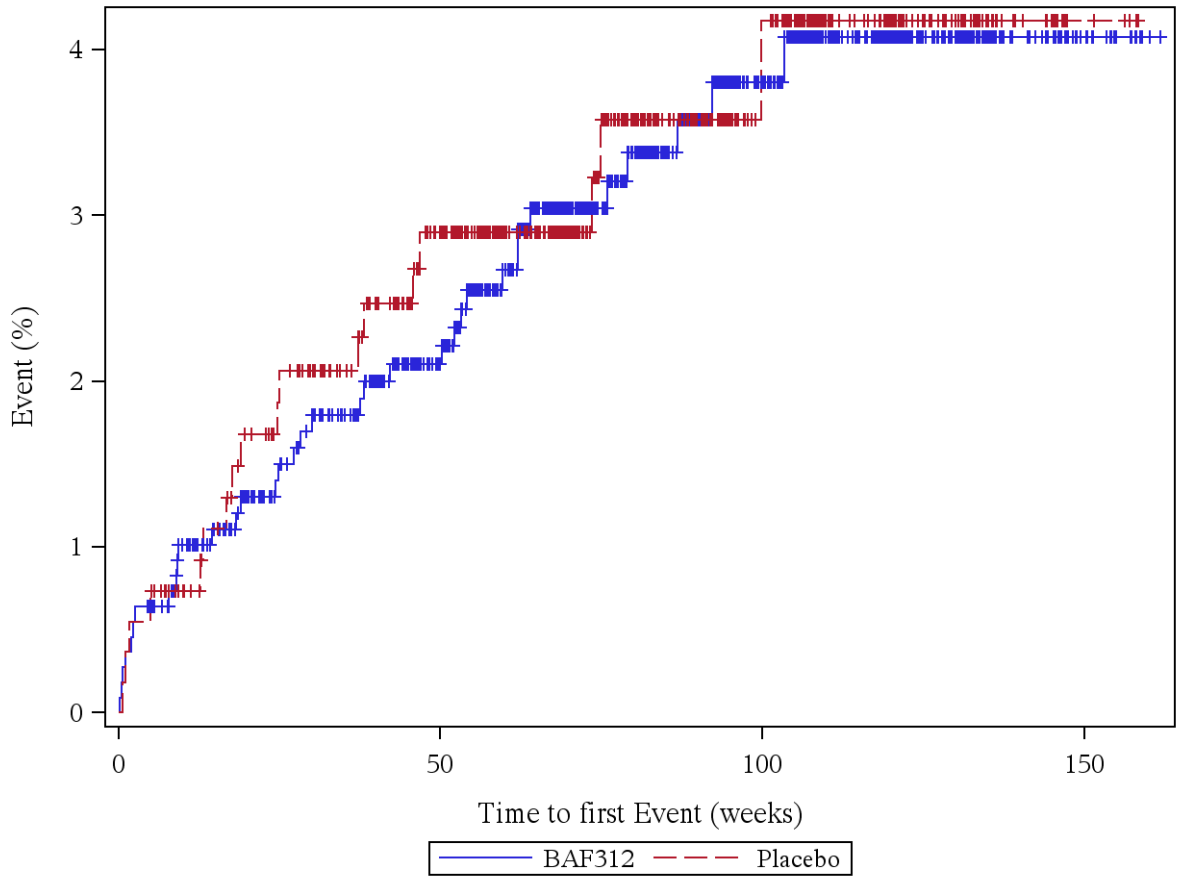


Patients at risk (BAF312/Placebo): Week 0: 1099/546, Week 4: 1099/546, Week 12: 1059/535, Week 24: 1017/521, Week 36: 990/497, Week 48: 924/461, Week 60: 816/388, Week 72: 649/305, Week 84: 514/237, Week 96: 399/176, Week 108: 291/125, Week 120: 200/80, Week 132: 113/40, Week 144: 51/20, Week 156: 10/5, Week 168: 0/0

Log rank test: p-value = 0,762
*: p < 0,05

Analysis population: A2304 SAF total population

Figure 12.1.5.211: COUGH (PT, not severe)

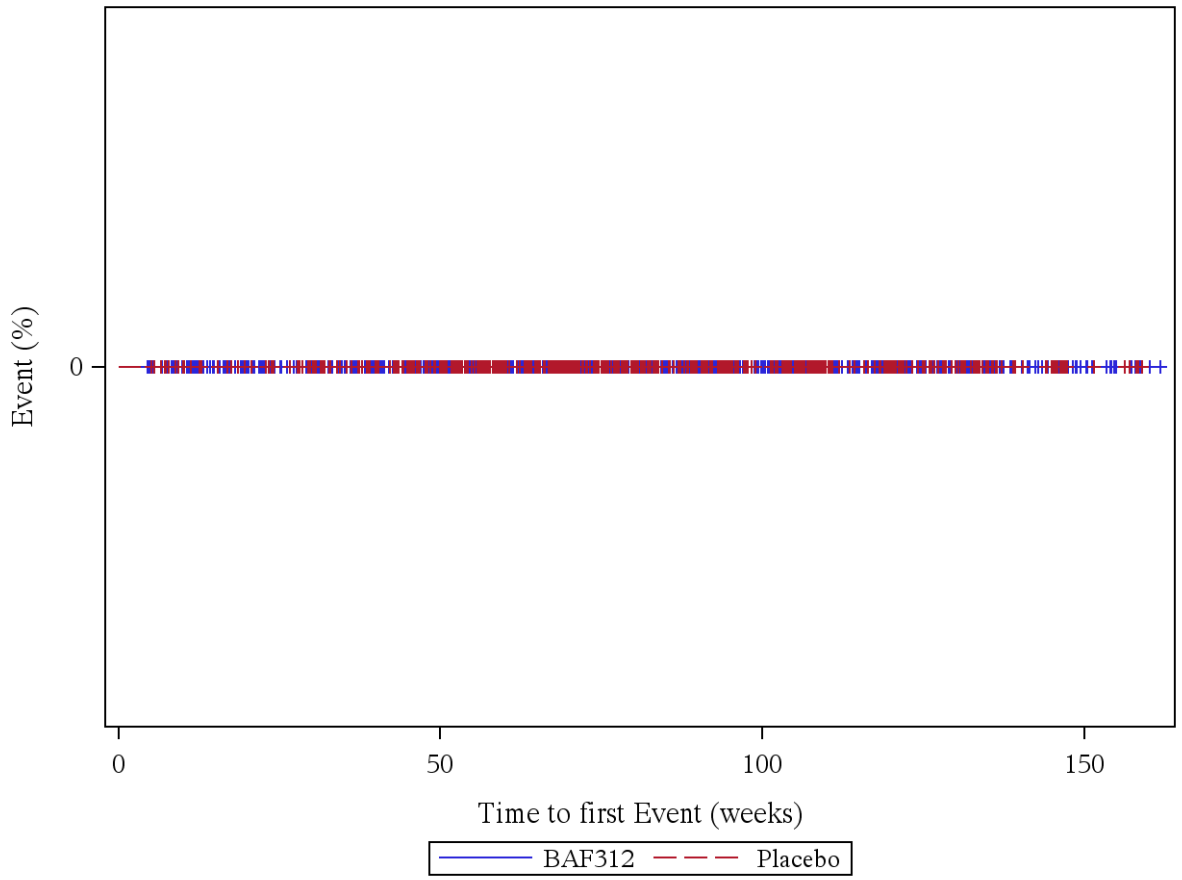


Patients at risk (BAF312/Placebo): Week 0: 1099/546, Week 4: 1092/543, Week 12: 1048/531, Week 24: 1003/512, Week 36: 973/487, Week 48: 905/447, Week 60: 797/376, Week 72: 631/296, Week 84: 497/227, Week 96: 383/170, Week 108: 281/120, Week 120: 191/76, Week 132: 107/38, Week 144: 51/18, Week 156: 10/4, Week 168: 0/0

Log rank test: p-value = 0,876
*: p < 0,05

Analysis population: A2304 SAF total population

Figure 12.1.5.212: COUGH (PT, severe)

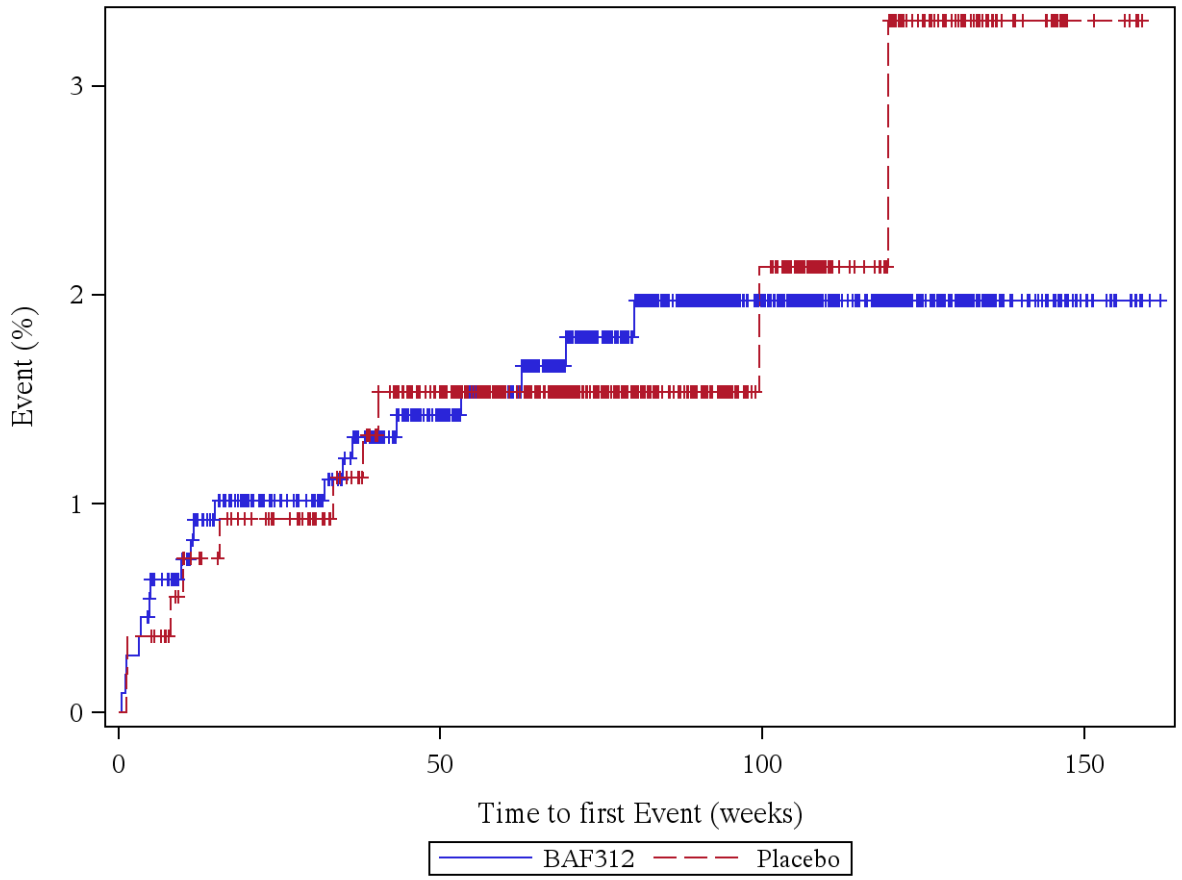


Patients at risk (BAF312/Placebo): Week 0: 1099/546, Week 4: 1099/546, Week 12: 1059/535, Week 24: 1017/521, Week 36: 990/497, Week 48: 925/461, Week 60: 818/388, Week 72: 652/305, Week 84: 516/237, Week 96: 400/176, Week 108: 291/126, Week 120: 200/80, Week 132: 113/40, Week 144: 51/20, Week 156: 10/5, Week 168: 0/0

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

Analysis population: A2304 SAF total population

Figure 12.1.5.213: DYSPNOEA (PT, not severe)

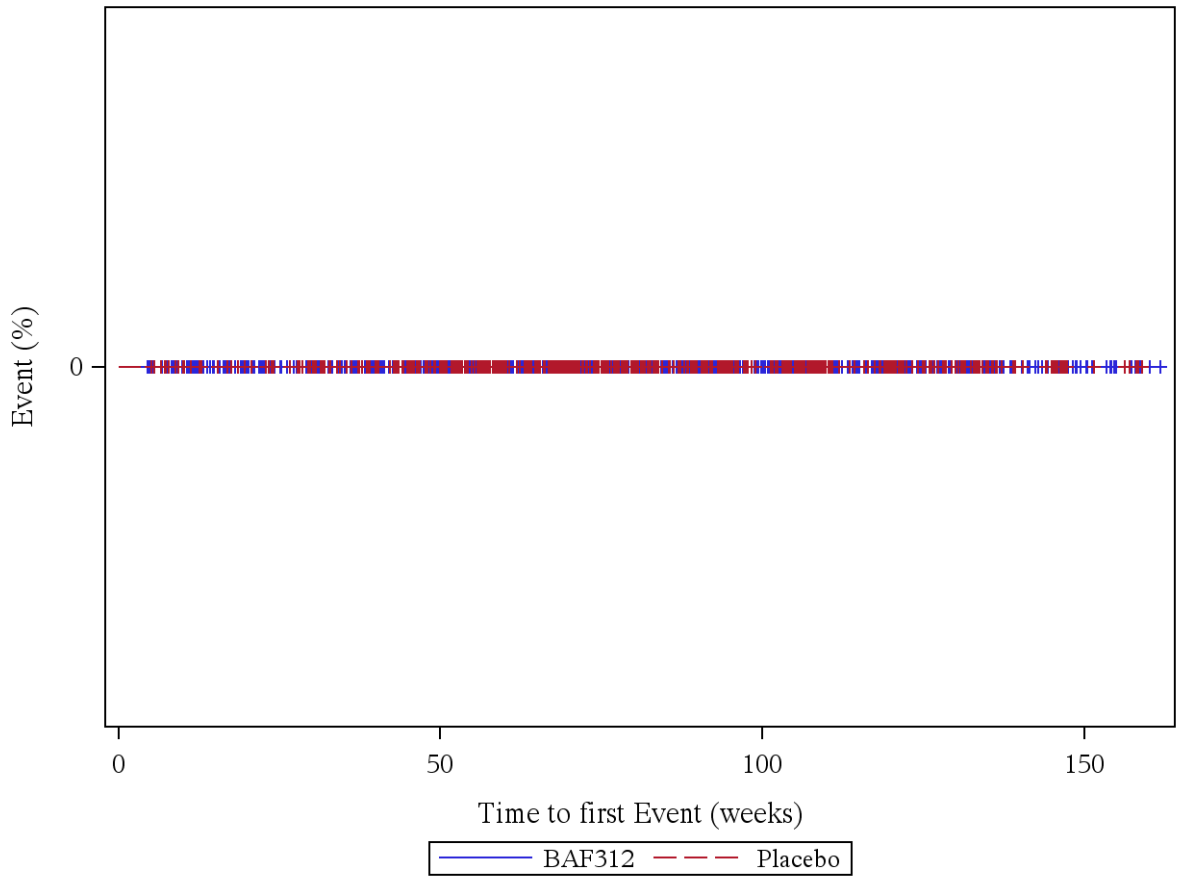


Patients at risk (BAF312/Placebo): Week 0: 1099/546, Week 4: 1094/544, Week 12: 1049/531, Week 24: 1007/516, Week 36: 978/492, Week 48: 912/456, Week 60: 807/384, Week 72: 646/303, Week 84: 512/235, Week 96: 396/174, Week 108: 289/123, Week 120: 198/77, Week 132: 112/38, Week 144: 50/19, Week 156: 10/5, Week 168: 0/0

Log rank test: p-value = 0,864
*: p < 0,05

Analysis population: A2304 SAF total population

Figure 12.1.5.214: DYSPNOEA (PT, severe)

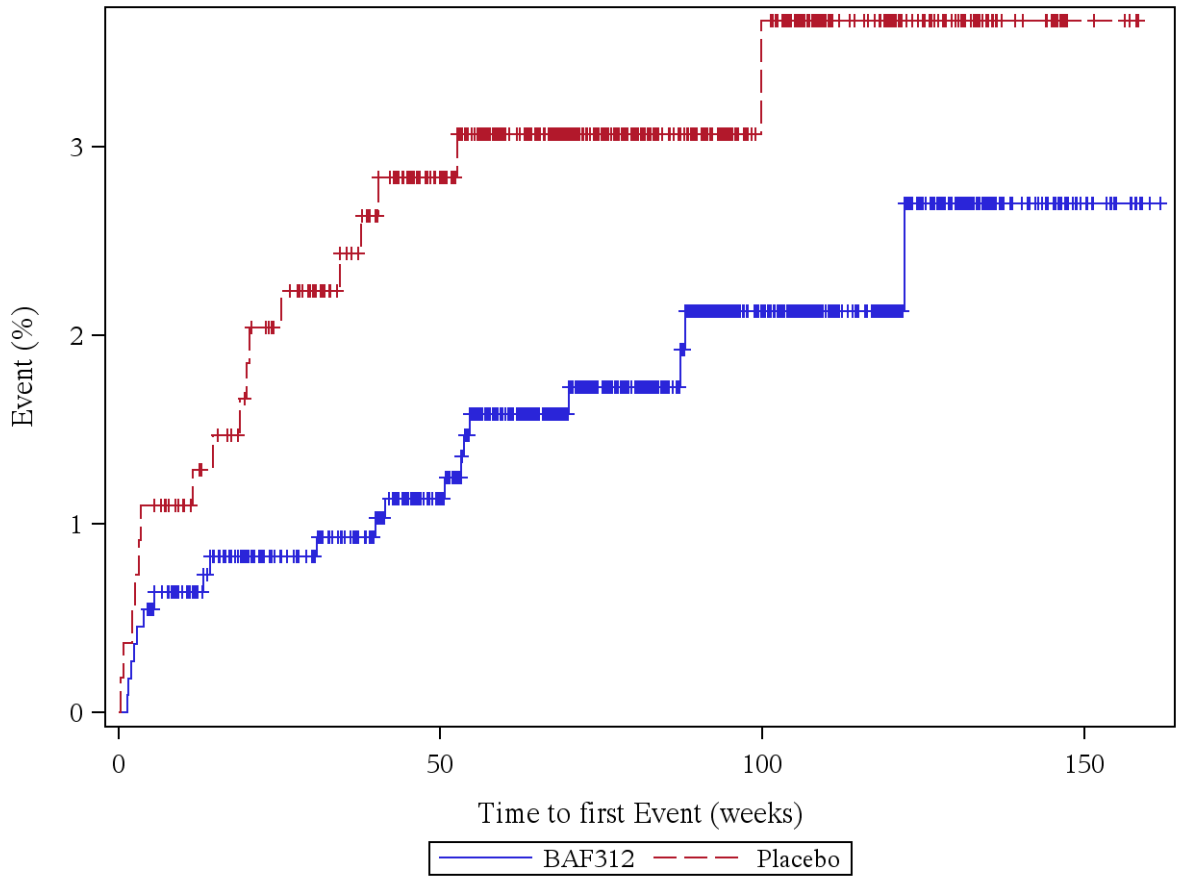


Patients at risk (BAF312/Placebo): Week 0: 1099/546, Week 4: 1099/546, Week 12: 1059/535, Week 24: 1017/521, Week 36: 990/497, Week 48: 925/461, Week 60: 818/388, Week 72: 652/305, Week 84: 516/237, Week 96: 400/176, Week 108: 291/126, Week 120: 200/80, Week 132: 113/40, Week 144: 51/20, Week 156: 10/5, Week 168: 0/0

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

Analysis population: A2304 SAF total population

Figure 12.1.5.215: OROPHARYNGEAL PAIN (PT, not severe)

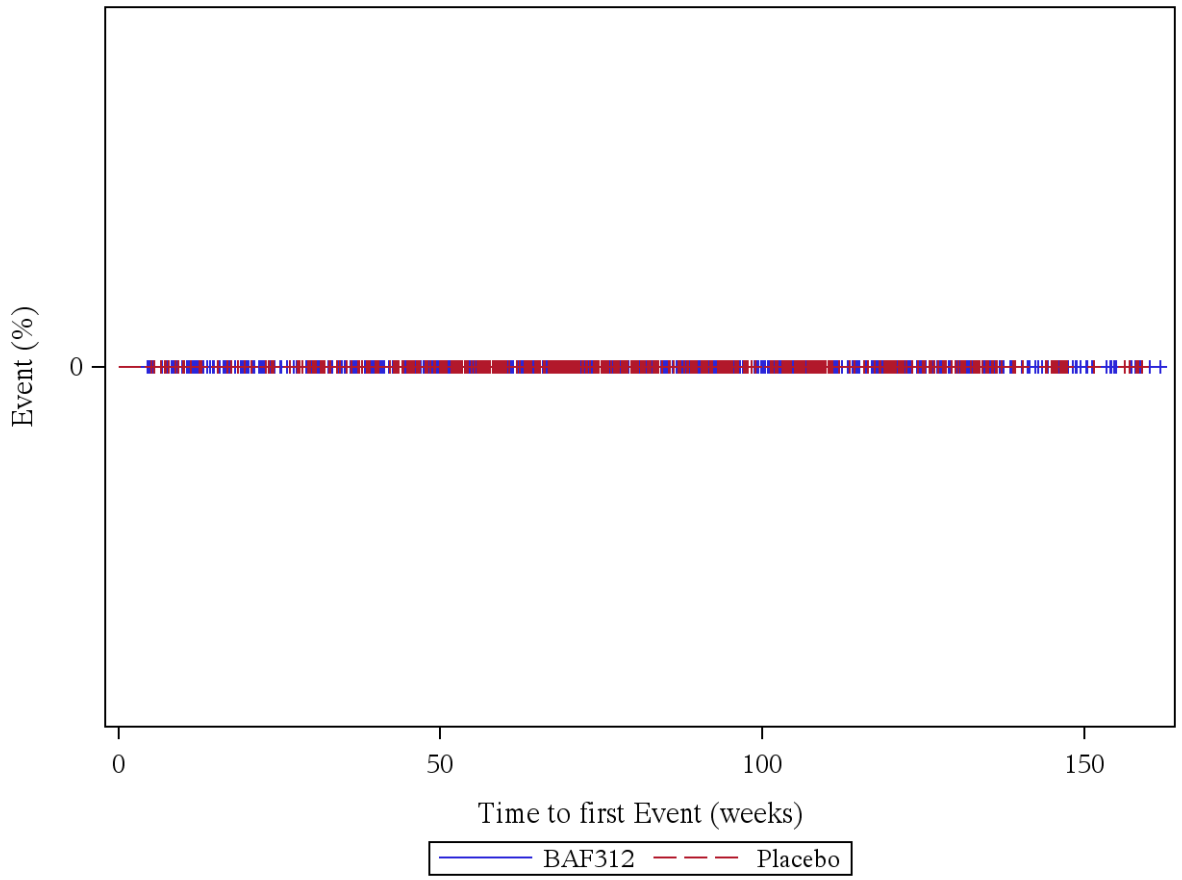


Patients at risk (BAF312/Placebo): Week 0: 1099/546, Week 4: 1093/540, Week 12: 1052/529, Week 24: 1008/511, Week 36: 980/486, Week 48: 914/450, Week 60: 805/379, Week 72: 640/297, Week 84: 508/230, Week 96: 392/171, Week 108: 287/121, Week 120: 198/76, Week 132: 112/38, Week 144: 50/19, Week 156: 10/4, Week 168: 0/0

Log rank test: p-value = 0,087
*: p < 0,05

Analysis population: A2304 SAF total population

Figure 12.1.5.216: OROPHARYNGEAL PAIN (PT, severe)

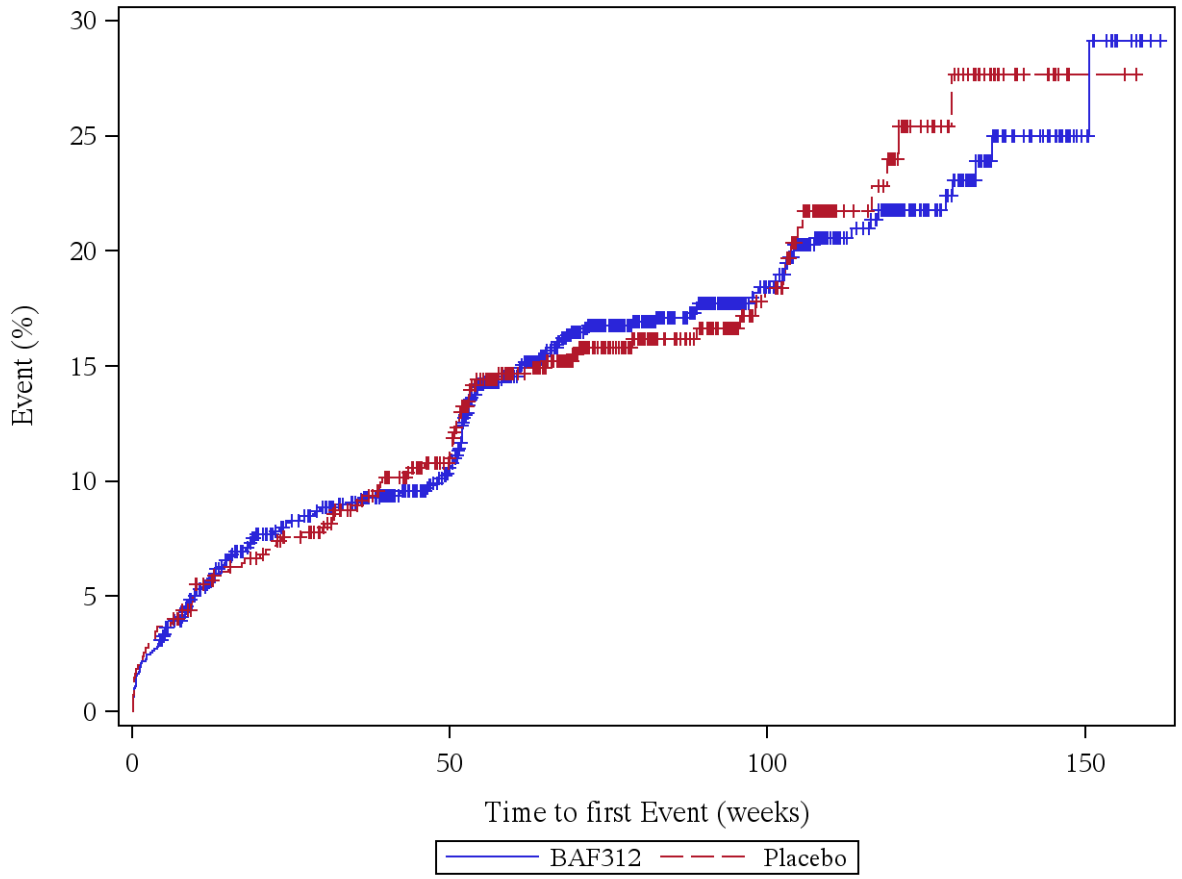


Patients at risk (BAF312/Placebo): Week 0: 1099/546, Week 4: 1099/546, Week 12: 1059/535, Week 24: 1017/521, Week 36: 990/497, Week 48: 925/461, Week 60: 818/388, Week 72: 652/305, Week 84: 516/237, Week 96: 400/176, Week 108: 291/126, Week 120: 200/80, Week 132: 113/40, Week 144: 51/20, Week 156: 10/5, Week 168: 0/0

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

Analysis population: A2304 SAF total population

Figure 12.1.5.217: SKIN AND SUBCUTANEOUS TISSUE DISORDERS (SOC, not severe)

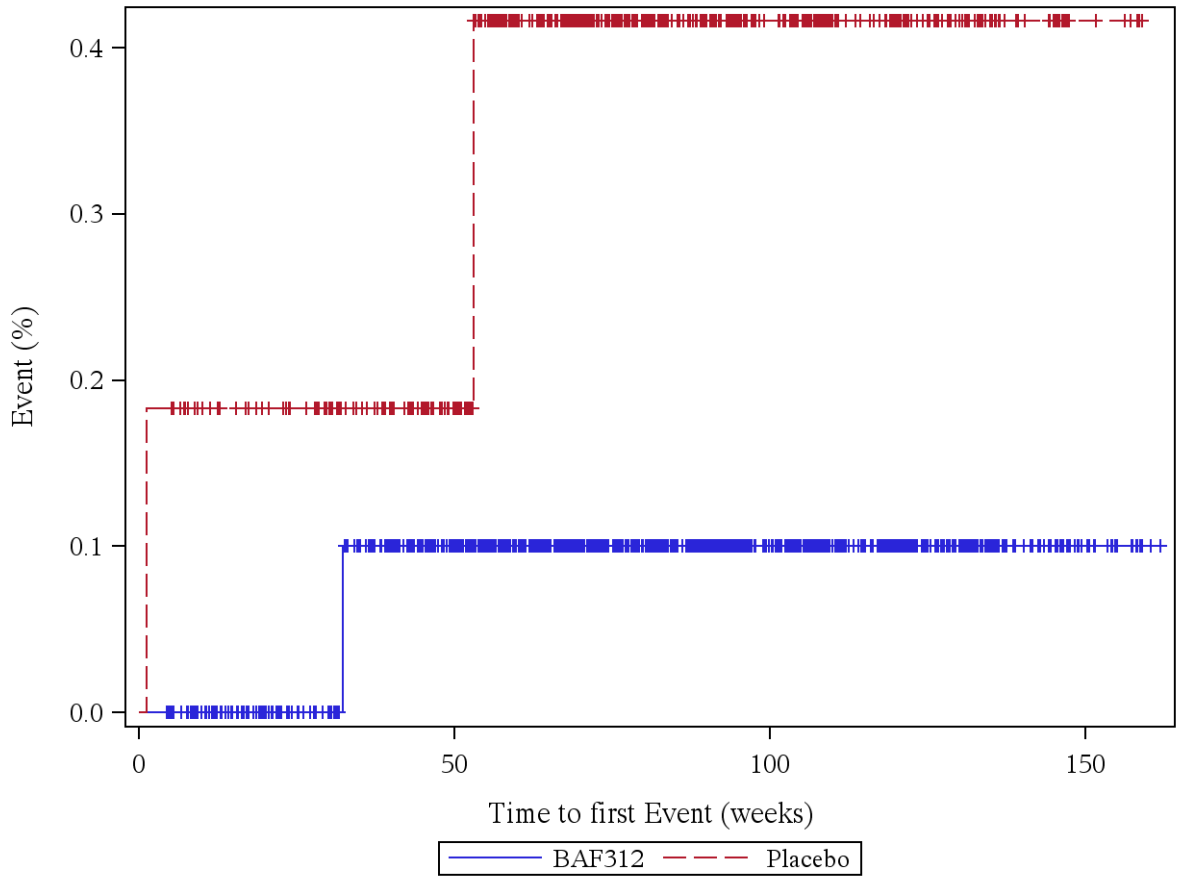


Patients at risk (BAF312/Placebo): Week 0: 1099/546, Week 4: 1068/526, Week 12: 1002/506, Week 24: 938/484, Week 36: 904/454, Week 48: 839/414, Week 60: 703/329, Week 72: 555/256, Week 84: 441/199, Week 96: 341/145, Week 108: 246/96, Week 120: 168/57, Week 132: 102/28, Week 144: 48/12, Week 156: 9/2, Week 168: 0/0

Log rank test: p-value = 0,845
*: p < 0,05

Analysis population: A2304 SAF total population

Figure 12.1.5.218: SKIN AND SUBCUTANEOUS TISSUE DISORDERS (SOC, severe)

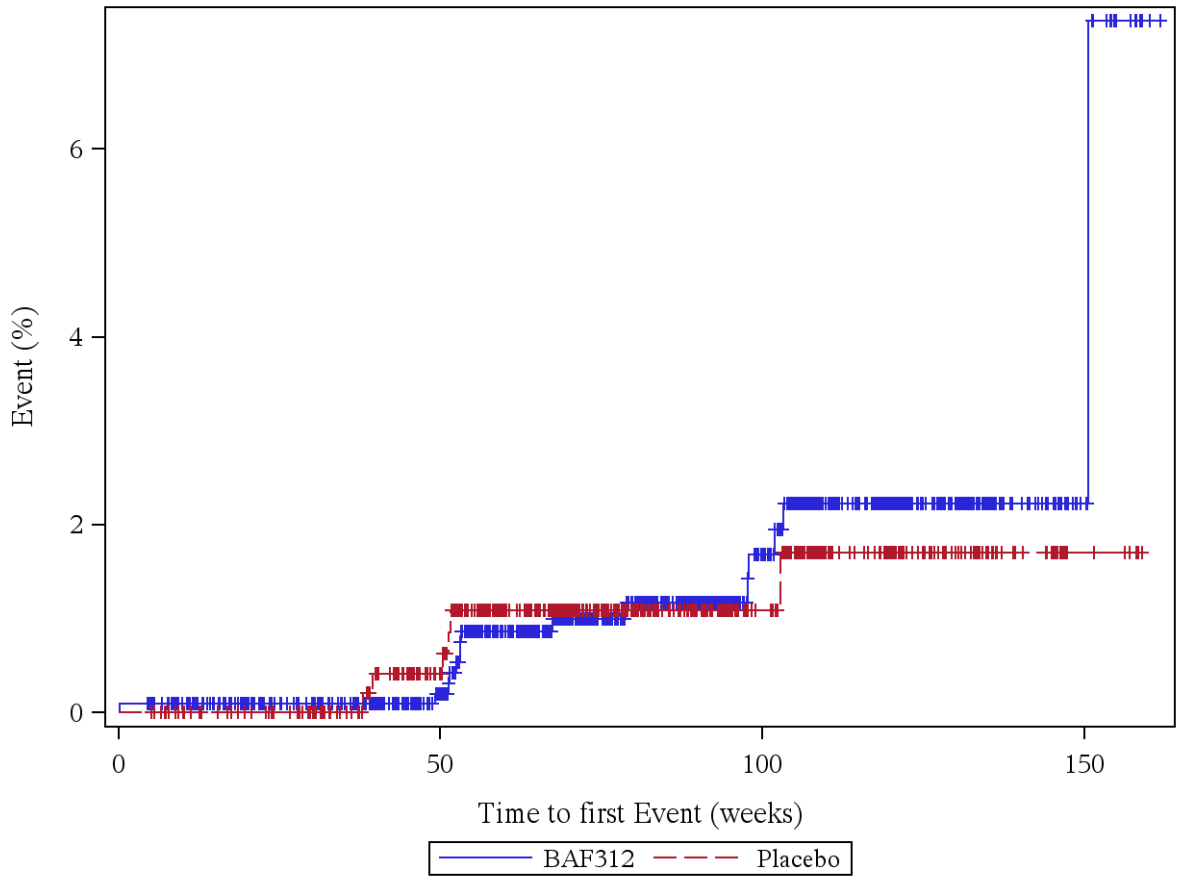


Patients at risk (BAF312/Placebo): Week 0: 1099/546, Week 4: 1099/545, Week 12: 1059/534, Week 24: 1017/520, Week 36: 989/496, Week 48: 924/460, Week 60: 817/387, Week 72: 651/304, Week 84: 515/237, Week 96: 399/176, Week 108: 291/126, Week 120: 200/80, Week 132: 113/40, Week 144: 51/20, Week 156: 10/5, Week 168: 0/0

Log rank test: p-value = 0,215
*: p < 0,05

Analysis population: A2304 SAF total population

Figure 12.1.5.219: ACTINIC KERATOSIS (PT, not severe)

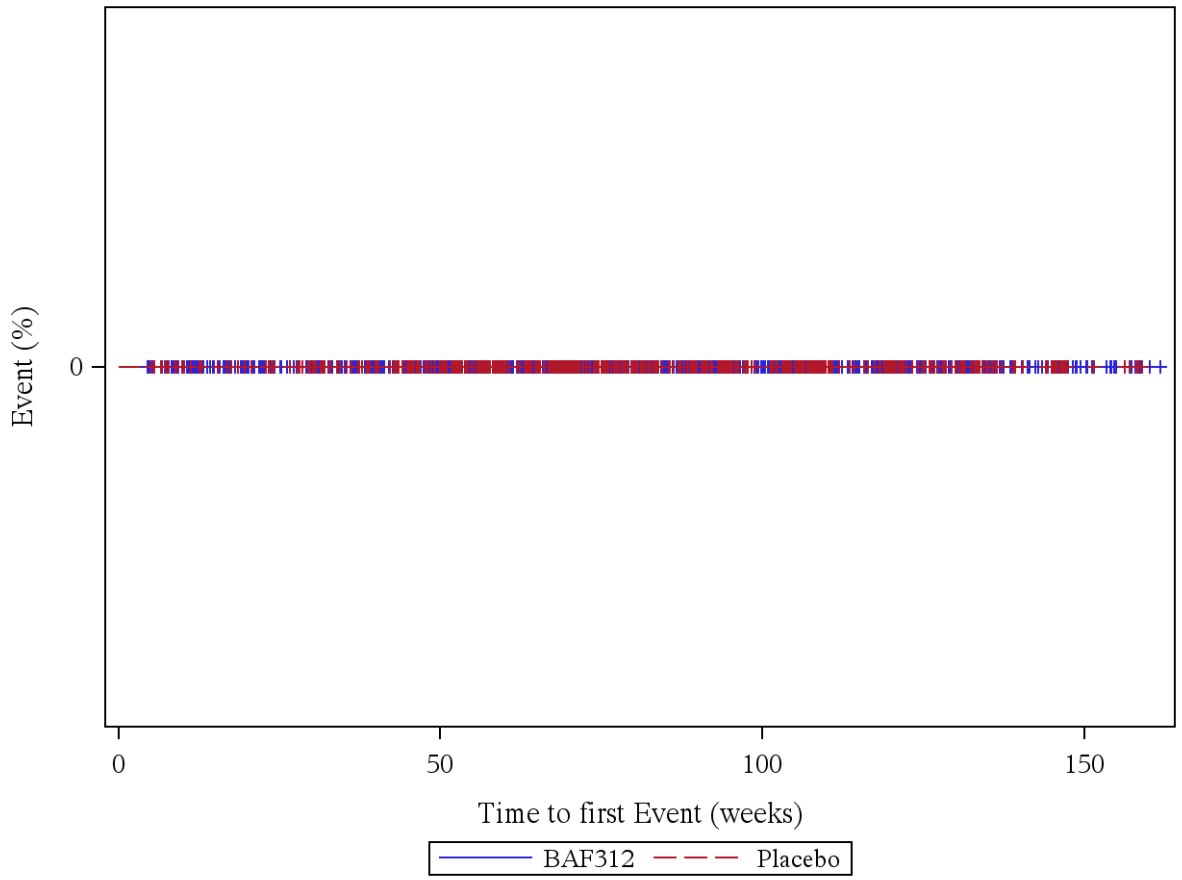


Patients at risk (BAF312/Placebo): Week 0: 1099/546, Week 4: 1098/546, Week 12: 1058/535, Week 24: 1016/521, Week 36: 989/497, Week 48: 924/460, Week 60: 810/384, Week 72: 644/303, Week 84: 509/236, Week 96: 397/175, Week 108: 287/124, Week 120: 196/78, Week 132: 111/40, Week 144: 51/20, Week 156: 9/5, Week 168: 0/0

Log rank test: p-value = 0,760
*: p < 0,05

Analysis population: A2304 SAF total population

Figure 12.1.5.220: ACTINIC KERATOSIS (PT, severe)

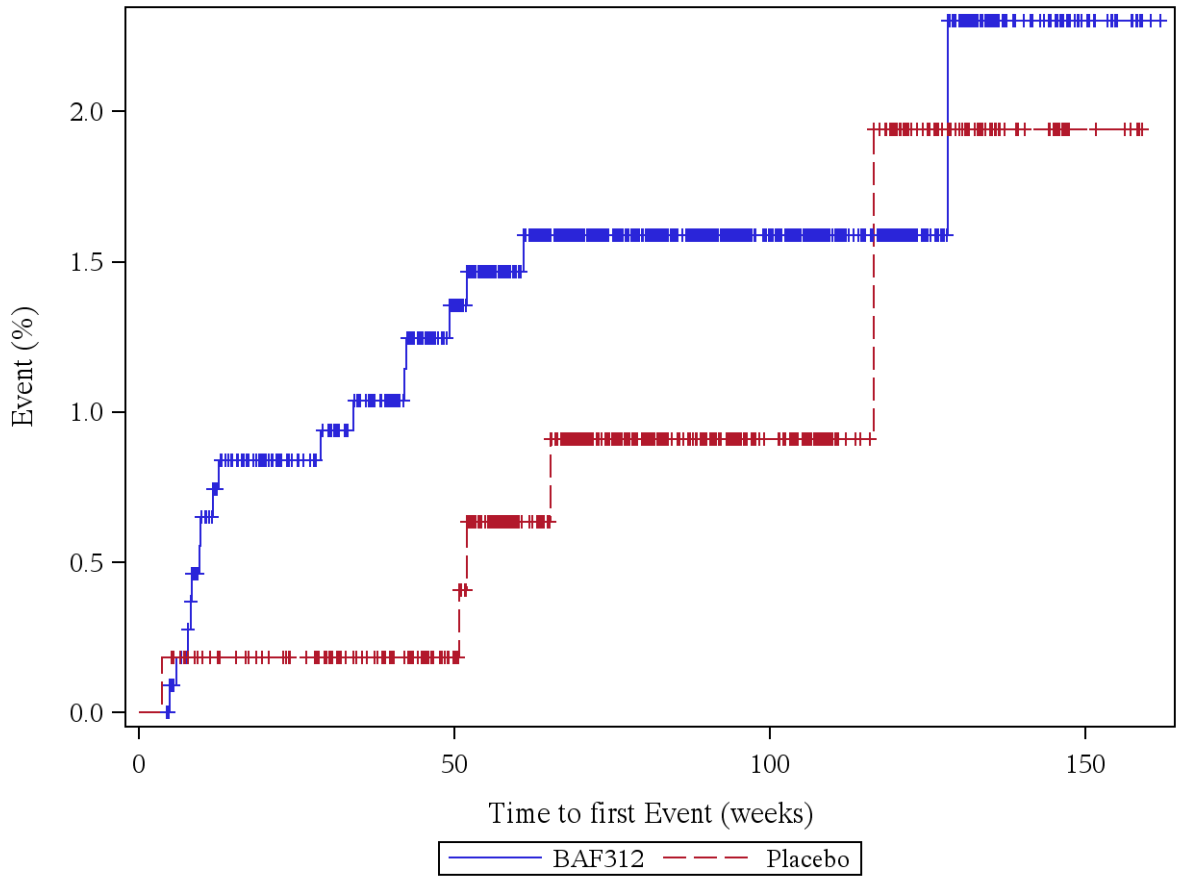


Patients at risk (BAF312/Placebo): Week 0: 1099/546, Week 4: 1099/546, Week 12: 1059/535, Week 24: 1017/521, Week 36: 990/497, Week 48: 925/461, Week 60: 818/388, Week 72: 652/305, Week 84: 516/237, Week 96: 400/176, Week 108: 291/126, Week 120: 200/80, Week 132: 113/40, Week 144: 51/20, Week 156: 10/5, Week 168: 0/0

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

Analysis population: A2304 SAF total population

Figure 12.1.5.221: ECZEMA (PT, not severe)

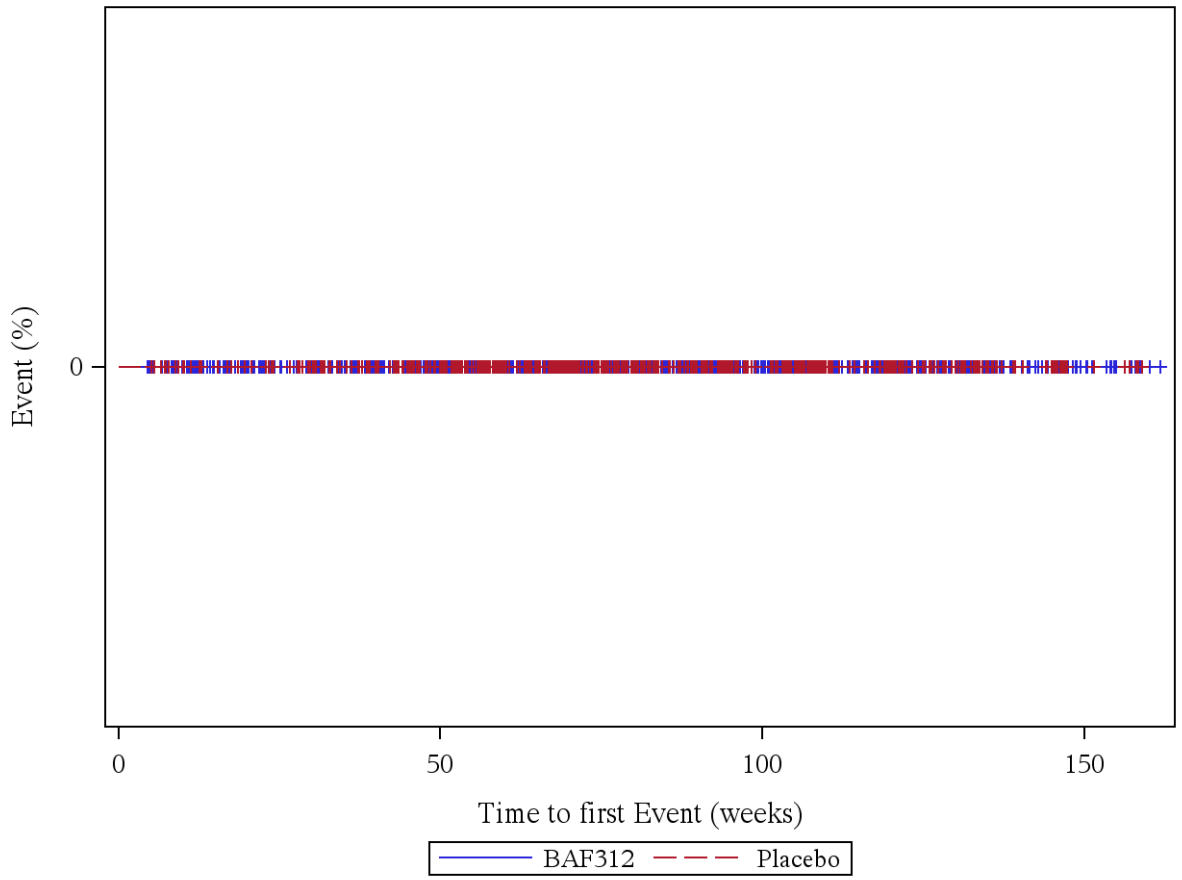


Patients at risk (BAF312/Placebo): Week 0: 1099/546, Week 4: 1099/545, Week 12: 1051/534, Week 24: 1008/520, Week 36: 979/496, Week 48: 912/460, Week 60: 803/385, Week 72: 638/304, Week 84: 505/237, Week 96: 392/176, Week 108: 286/126, Week 120: 198/79, Week 132: 111/40, Week 144: 51/20, Week 156: 10/5, Week 168: 0/0

Log rank test: p-value = 0,312
*: p < 0,05

Analysis population: A2304 SAF total population

Figure 12.1.5.222: ECZEMA (PT, severe)

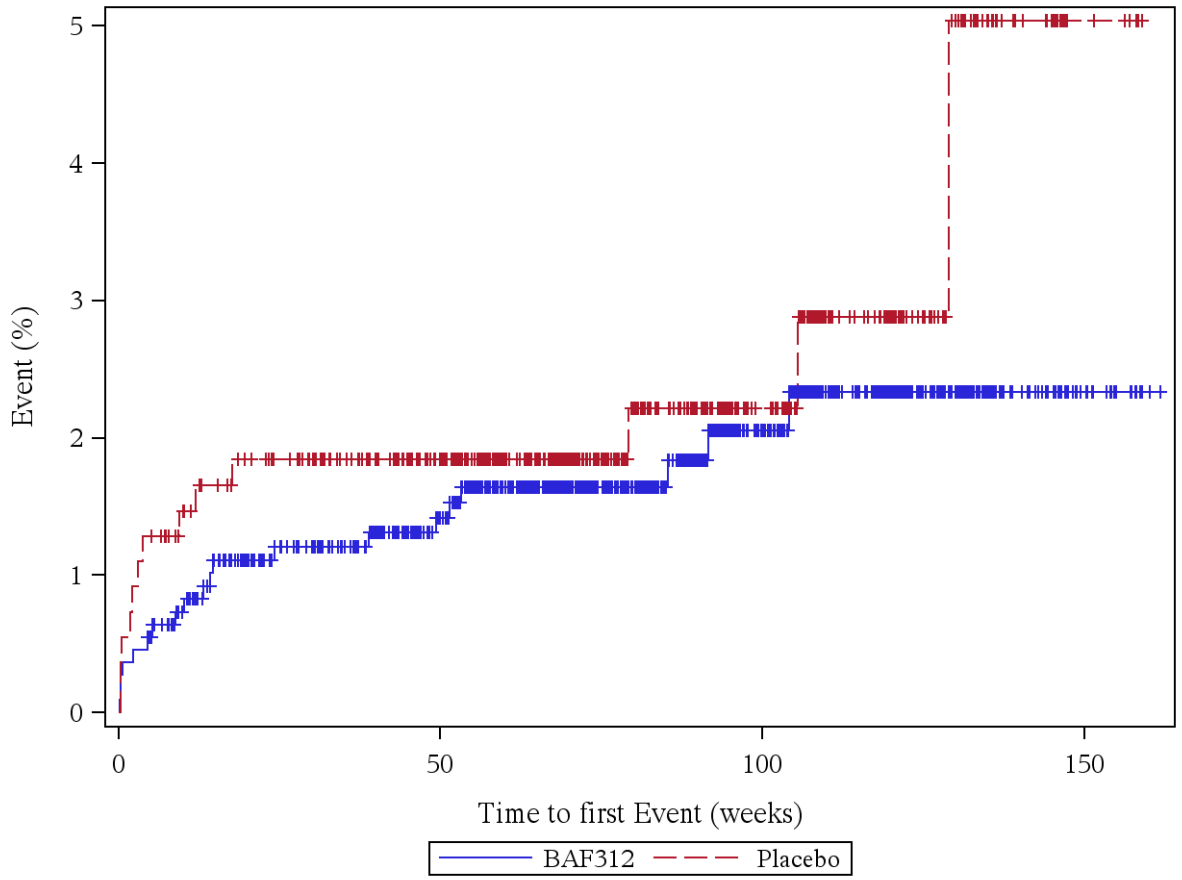


Patients at risk (BAF312/Placebo): Week 0: 1099/546, Week 4: 1099/546, Week 12: 1059/535, Week 24: 1017/521, Week 36: 990/497, Week 48: 925/461, Week 60: 818/388, Week 72: 652/305, Week 84: 516/237, Week 96: 400/176, Week 108: 291/126, Week 120: 200/80, Week 132: 113/40, Week 144: 51/20, Week 156: 10/5, Week 168: 0/0

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

Analysis population: A2304 SAF total population

Figure 12.1.5.223: RASH (PT, not severe)

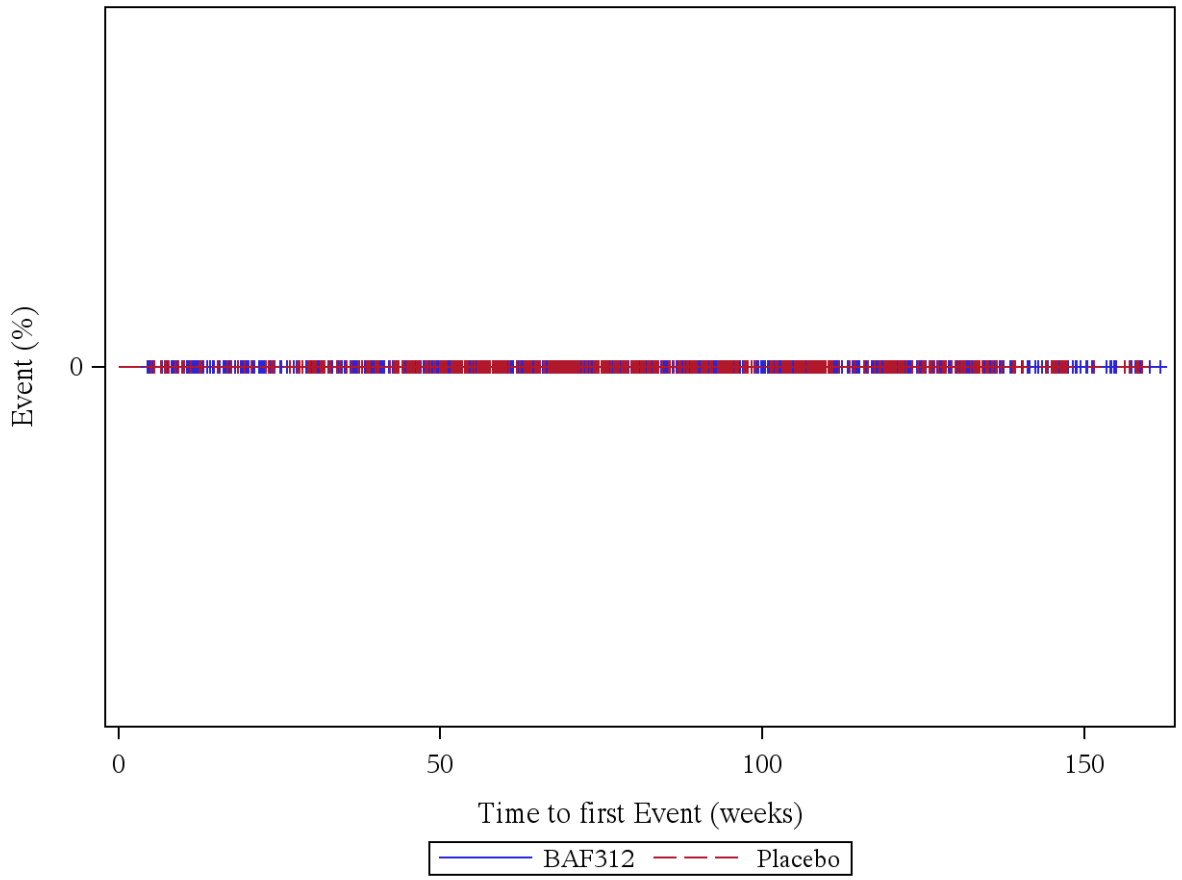


Patients at risk (BAF312/Placebo): Week 0: 1099/546, Week 4: 1094/539, Week 12: 1050/527, Week 24: 1007/512, Week 36: 979/489, Week 48: 914/454, Week 60: 809/382, Week 72: 645/300, Week 84: 511/232, Week 96: 394/174, Week 108: 286/123, Week 120: 197/78, Week 132: 111/38, Week 144: 50/20, Week 156: 10/5, Week 168: 0/0

Log rank test: p-value = 0,406
*: p < 0,05

Analysis population: A2304 SAF total population

Figure 12.1.5.224: RASH (PT, severe)

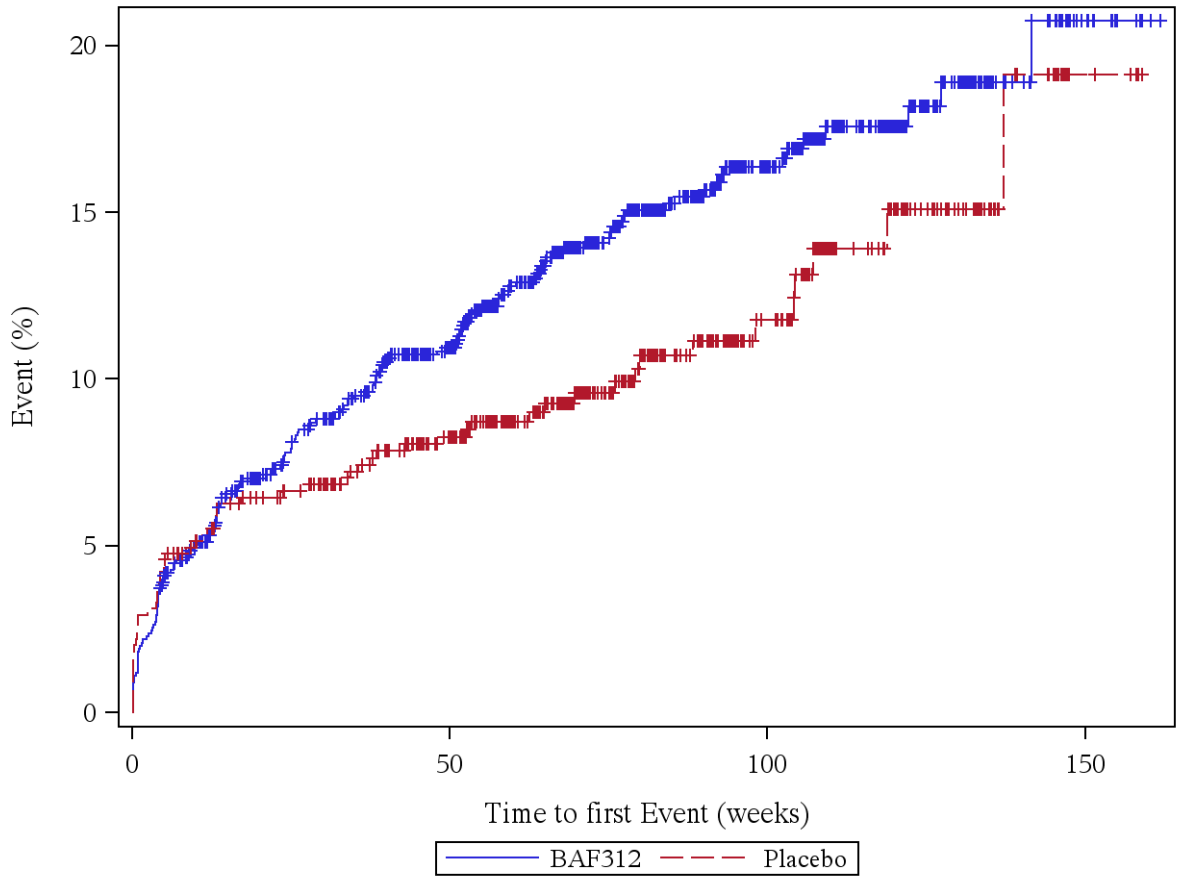


Patients at risk (BAF312/Placebo): Week 0: 1099/546, Week 4: 1099/546, Week 12: 1059/535, Week 24: 1017/521, Week 36: 990/497, Week 48: 925/461, Week 60: 818/388, Week 72: 652/305, Week 84: 516/237, Week 96: 400/176, Week 108: 291/126, Week 120: 200/80, Week 132: 113/40, Week 144: 51/20, Week 156: 10/5, Week 168: 0/0

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

Analysis population: A2304 SAF total population

Figure 12.1.5.225: VASCULAR DISORDERS (SOC, not severe)

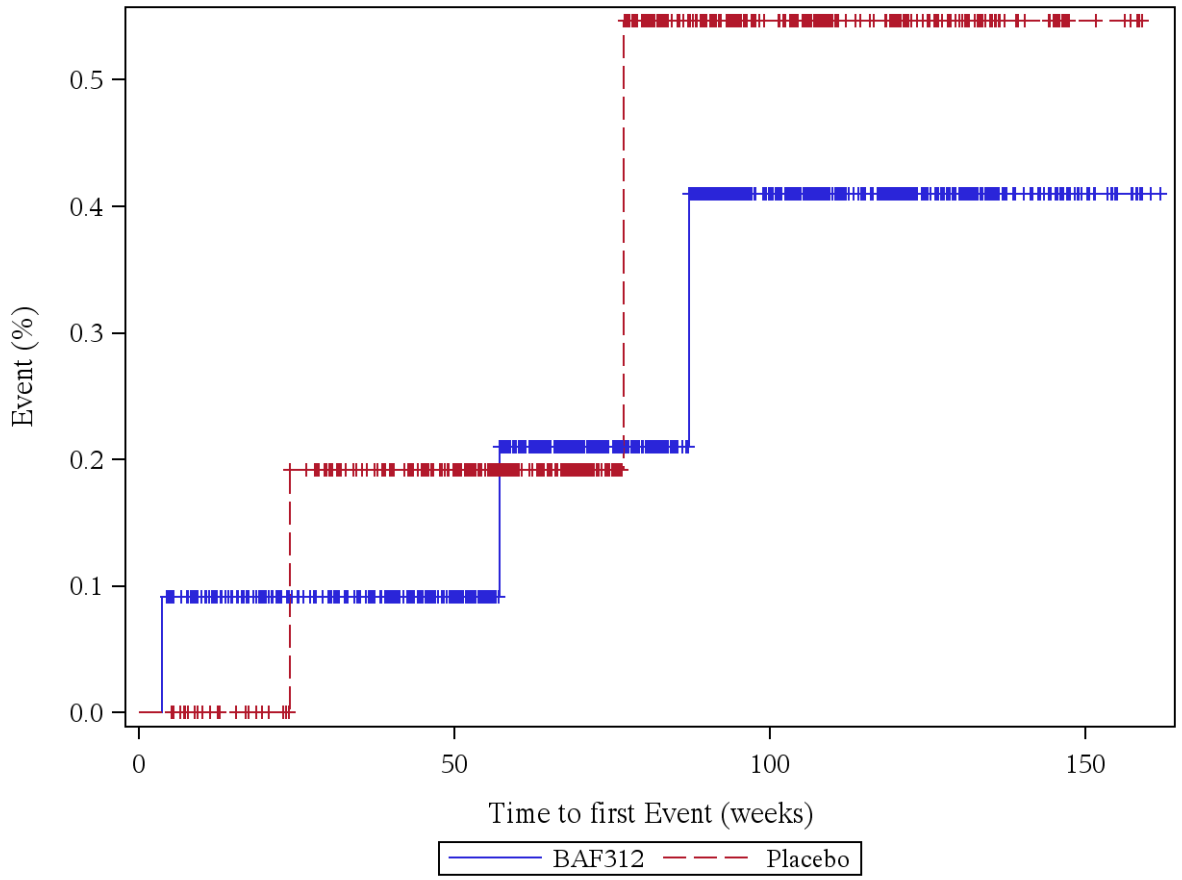


Patients at risk (BAF312/Placebo): Week 0: 1099/546, Week 4: 1064/526, Week 12: 1005/507, Week 24: 936/487, Week 36: 896/459, Week 48: 827/424, Week 60: 710/353, Week 72: 553/271, Week 84: 433/204, Week 96: 333/150, Week 108: 239/101, Week 120: 159/64, Week 132: 88/37, Week 144: 42/18, Week 156: 8/4, Week 168: 0/0

Log rank test: p-value = 0,050
*: p < 0,05

Analysis population: A2304 SAF total population

Figure 12.1.5.226: VASCULAR DISORDERS (SOC, severe)

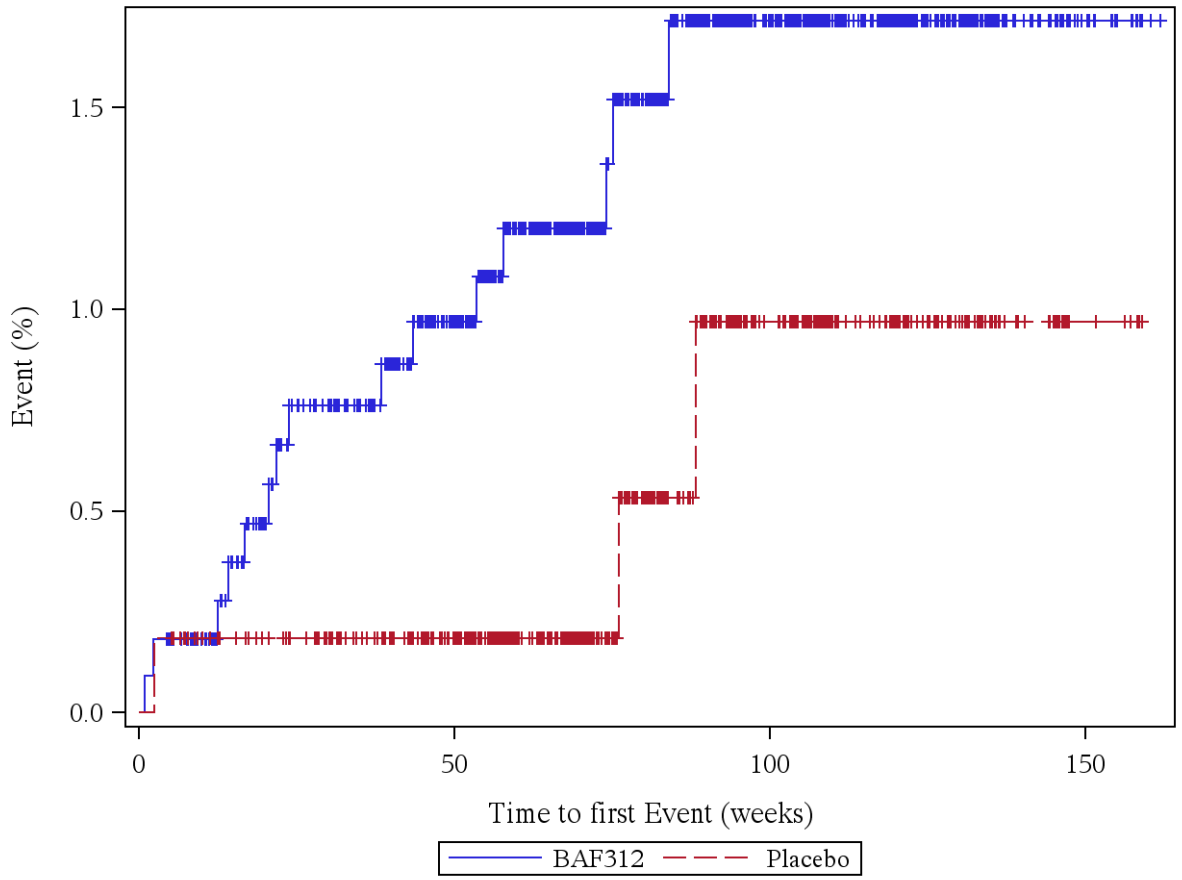


Patients at risk (BAF312/Placebo): Week 0: 1099/546, Week 4: 1098/546, Week 12: 1058/535, Week 24: 1016/520, Week 36: 989/496, Week 48: 924/460, Week 60: 816/387, Week 72: 650/304, Week 84: 514/235, Week 96: 398/174, Week 108: 289/124, Week 120: 198/79, Week 132: 113/40, Week 144: 51/20, Week 156: 10/5, Week 168: 0/0

Log rank test: p-value = 0,722
*: p < 0,05

Analysis population: A2304 SAF total population

Figure 12.1.5.227: HAEMATOMA (PT, not severe)

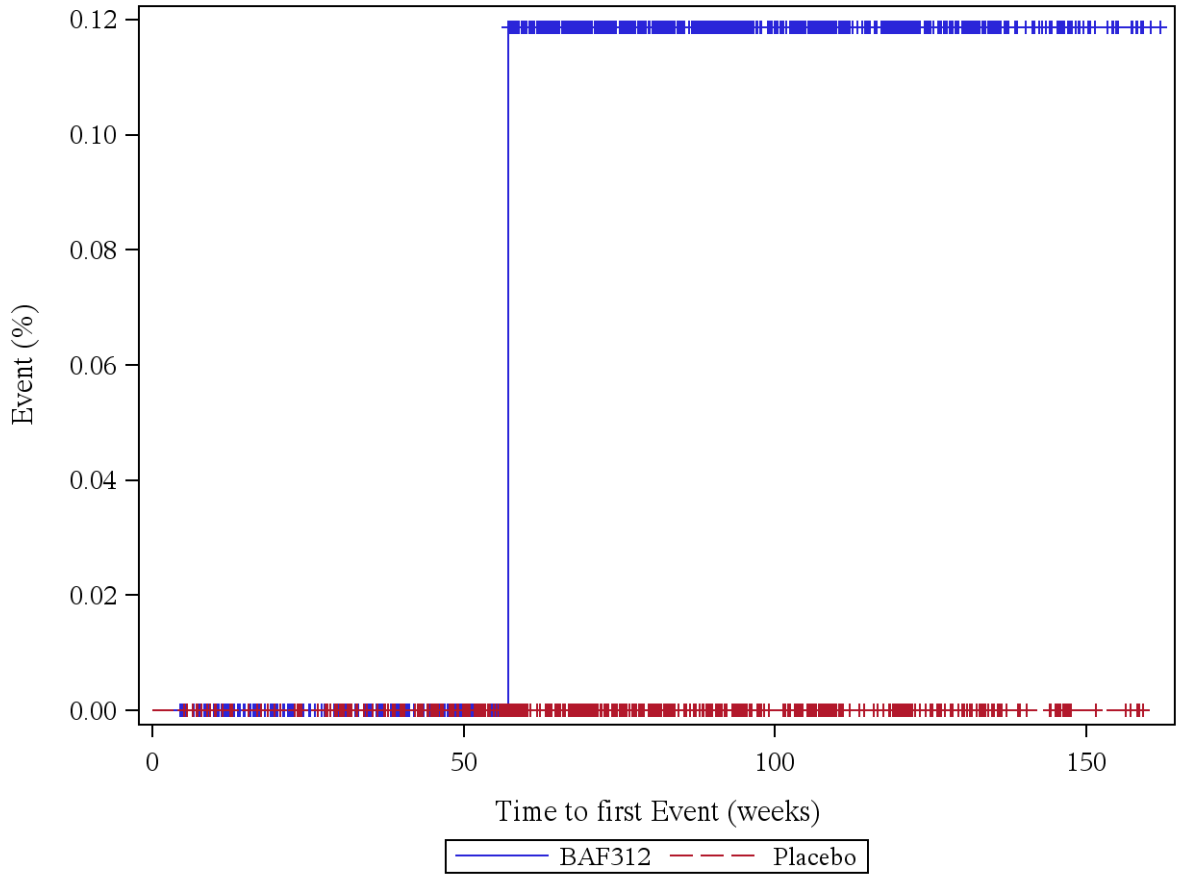


Patients at risk (BAF312/Placebo): Week 0: 1099/546, Week 4: 1097/545, Week 12: 1057/534, Week 24: 1009/520, Week 36: 982/496, Week 48: 916/460, Week 60: 807/387, Week 72: 643/304, Week 84: 505/236, Week 96: 391/175, Week 108: 284/125, Week 120: 194/79, Week 132: 109/40, Week 144: 48/20, Week 156: 10/5, Week 168: 0/0

Log rank test: p-value = 0,139
*: p < 0,05

Analysis population: A2304 SAF total population

Figure 12.1.5.228: HAEMATOMA (PT, severe)

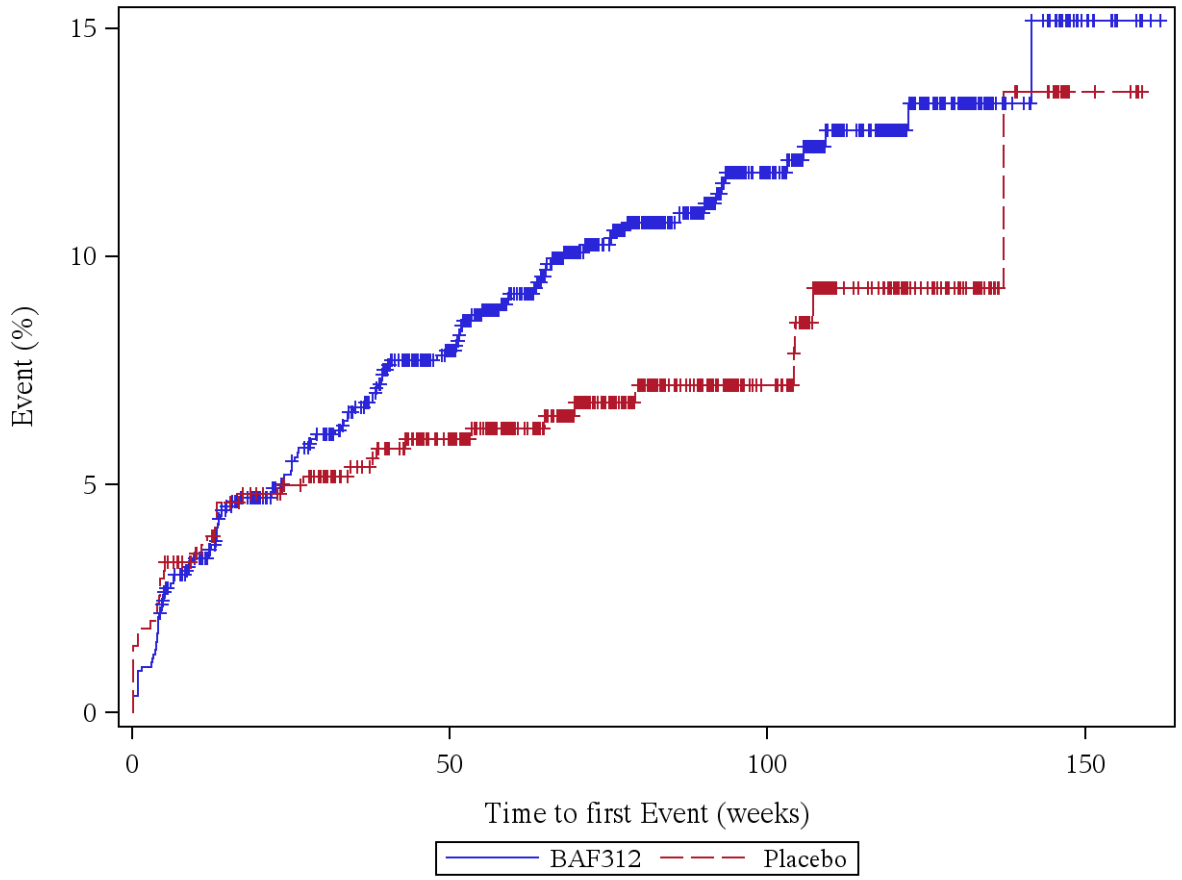


Patients at risk (BAF312/Placebo): Week 0: 1099/546, Week 4: 1099/546, Week 12: 1059/535, Week 24: 1017/521, Week 36: 990/497, Week 48: 925/461, Week 60: 817/388, Week 72: 651/305, Week 84: 515/237, Week 96: 399/176, Week 108: 290/126, Week 120: 199/80, Week 132: 113/40, Week 144: 51/20, Week 156: 10/5, Week 168: 0/0

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

Analysis population: A2304 SAF total population

Figure 12.1.5.229: HYPERTENSION (PT, not severe)

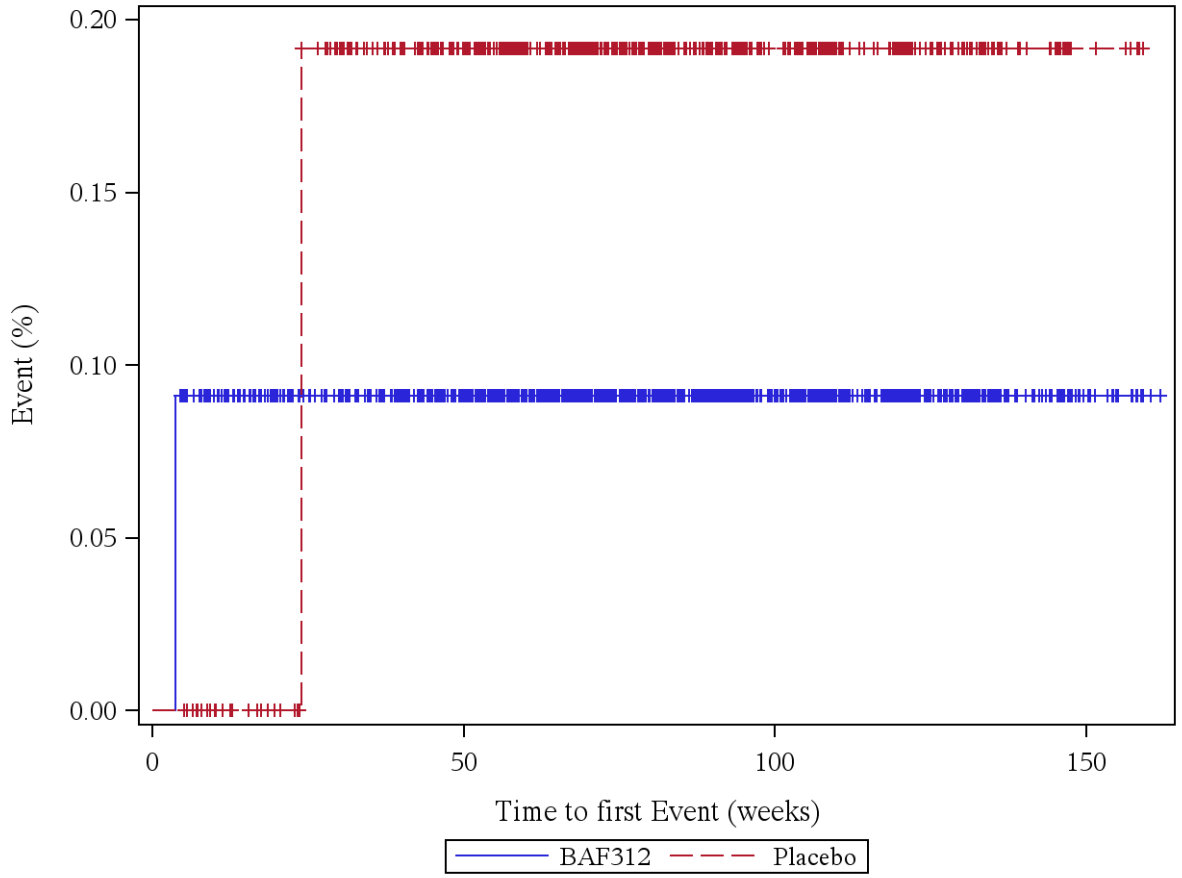


Patients at risk (BAF312/Placebo): Week 0: 1099/546, Week 4: 1080/533, Week 12: 1023/516, Week 24: 962/496, Week 36: 925/470, Week 48: 854/434, Week 60: 740/364, Week 72: 575/280, Week 84: 455/214, Week 96: 351/158, Week 108: 255/107, Week 120: 170/67, Week 132: 95/37, Week 144: 45/18, Week 156: 8/4, Week 168: 0/0

Log rank test: p-value = 0,054
*: p < 0,05

Analysis population: A2304 SAF total population

Figure 12.1.5.230: HYPERTENSION (PT, severe)



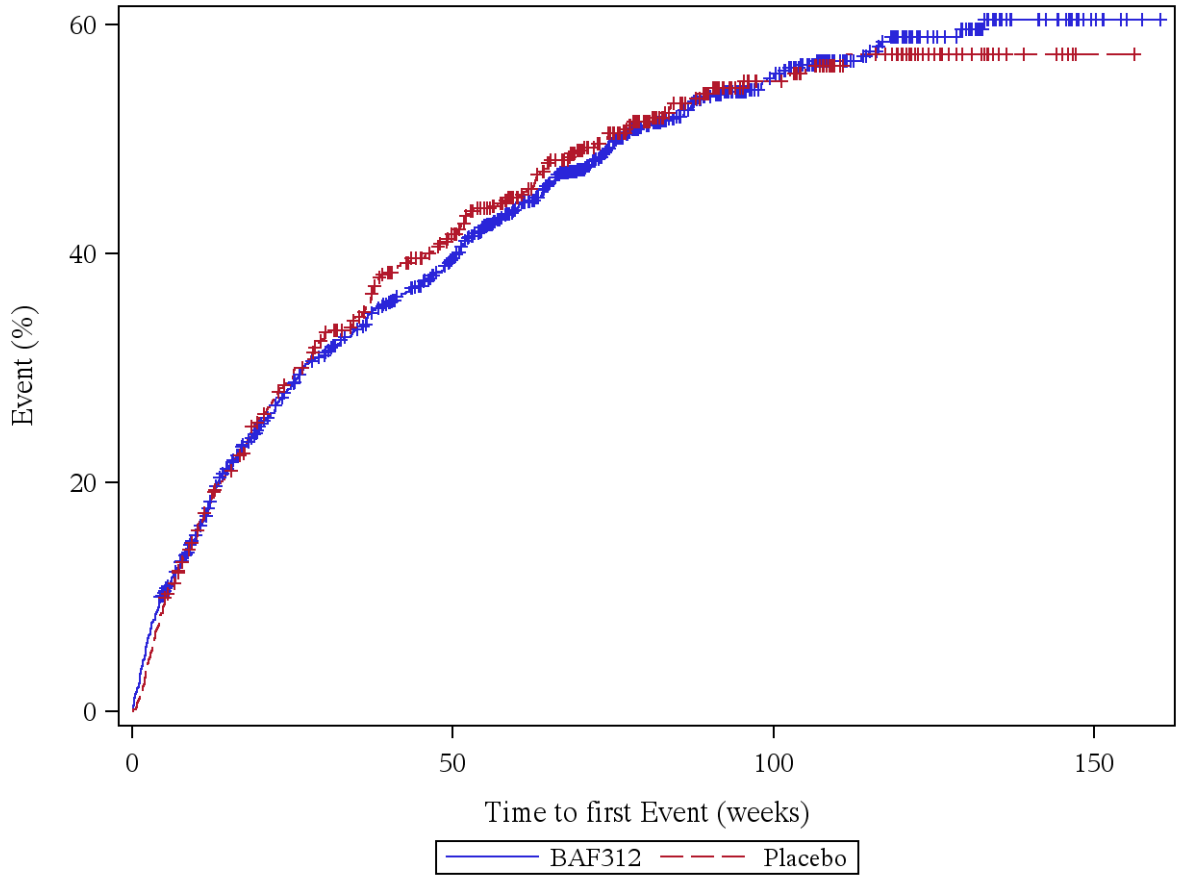
Patients at risk (BAF312/Placebo): Week 0: 1099/546, Week 4: 1098/546, Week 12: 1058/535, Week 24: 1016/520, Week 36: 989/496, Week 48: 924/460, Week 60: 817/387, Week 72: 651/304, Week 84: 515/236, Week 96: 399/175, Week 108: 290/125, Week 120: 199/80, Week 132: 113/40, Week 144: 51/20, Week 156: 10/5, Week 168: 0/0

Log rank test: p-value = 0,623
*: p < 0,05

Analysis population: A2304 SAF total population

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

Figure 12.1.6.1: Infections and infestations (AESI, all)

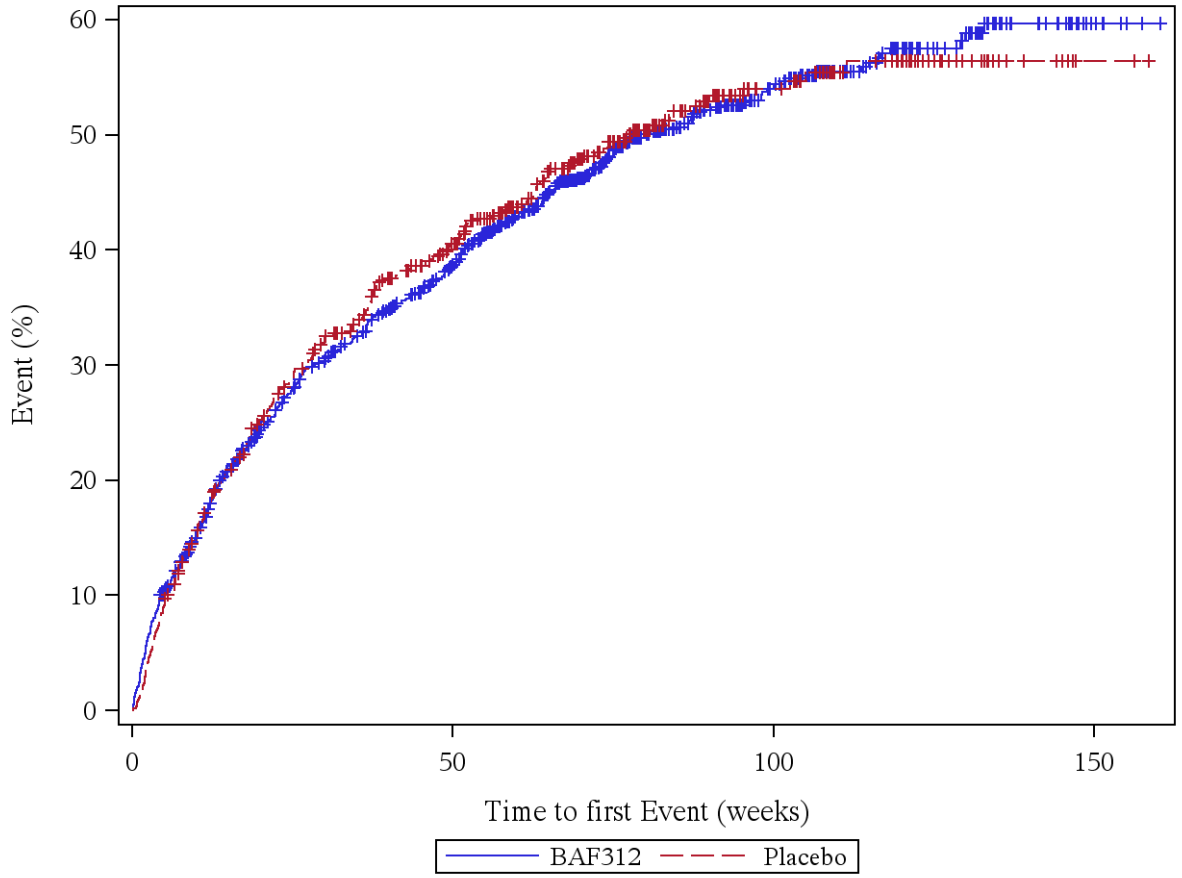


Patients at risk (BAF312/Placebo): Week 0: 1099/546, Week 4: 999/505, Week 12: 873/438, Week 24: 737/371, Week 36: 663/325, Week 48: 581/277, Week 60: 466/223, Week 72: 347/166, Week 84: 260/114, Week 96: 198/74, Week 108: 134/53, Week 120: 85/34, Week 132: 50/17, Week 144: 24/7, Week 156: 2/1, Week 168: 0/0

Log rank test: p-value = 0,874
*: p < 0,05

Analysis population: A2304 SAF total population

Figure 12.1.6.2: Infections and infestations (AESI, not severe)

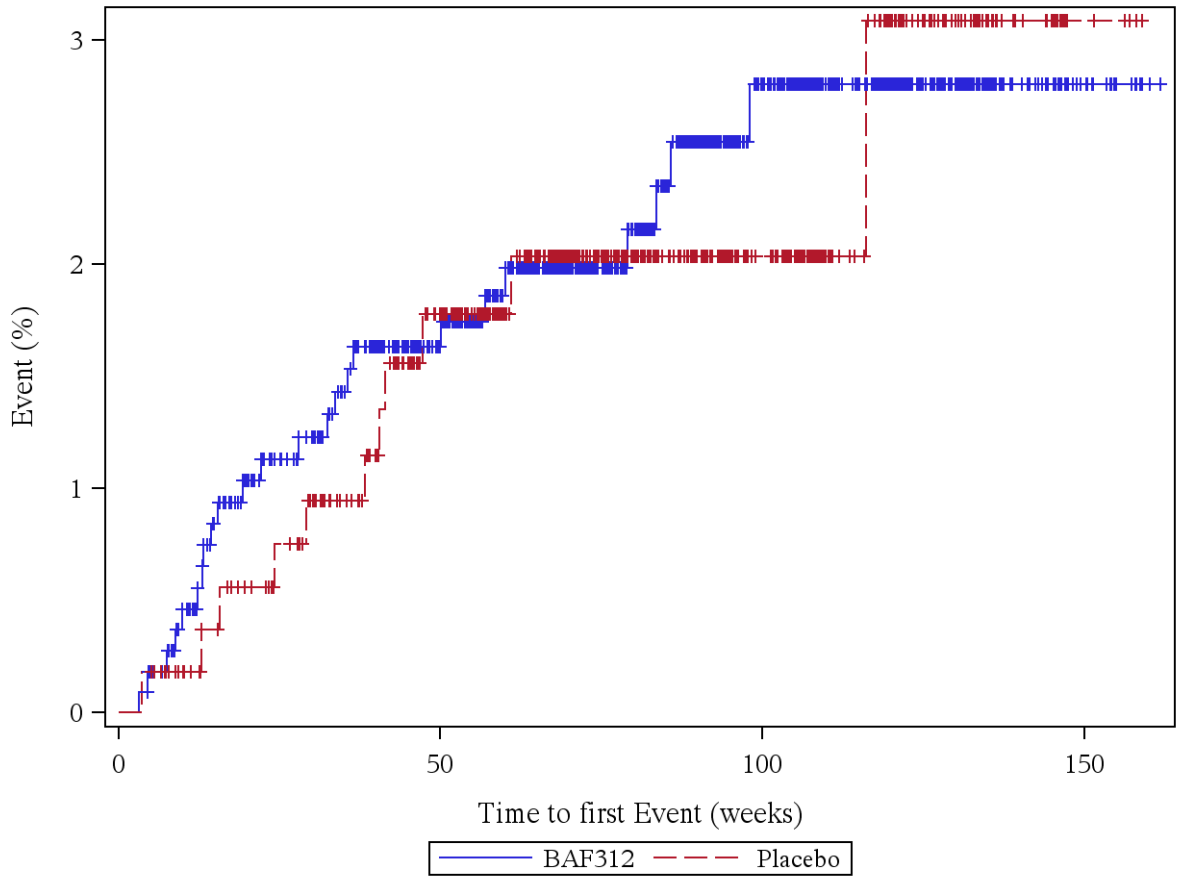


Patients at risk (BAF312/Placebo): Week 0: 1099/546, Week 4: 999/506, Week 12: 876/439, Week 24: 744/373, Week 36: 671/328, Week 48: 590/283, Week 60: 476/225, Week 72: 356/168, Week 84: 269/115, Week 96: 206/75, Week 108: 141/54, Week 120: 90/35, Week 132: 52/18, Week 144: 26/8, Week 156: 2/2, Week 168: 0/0

Log rank test: p-value = 0,844
*: p < 0,05

Analysis population: A2304 SAF total population

Figure 12.1.6.3: Infections and infestations (AESI, severe)

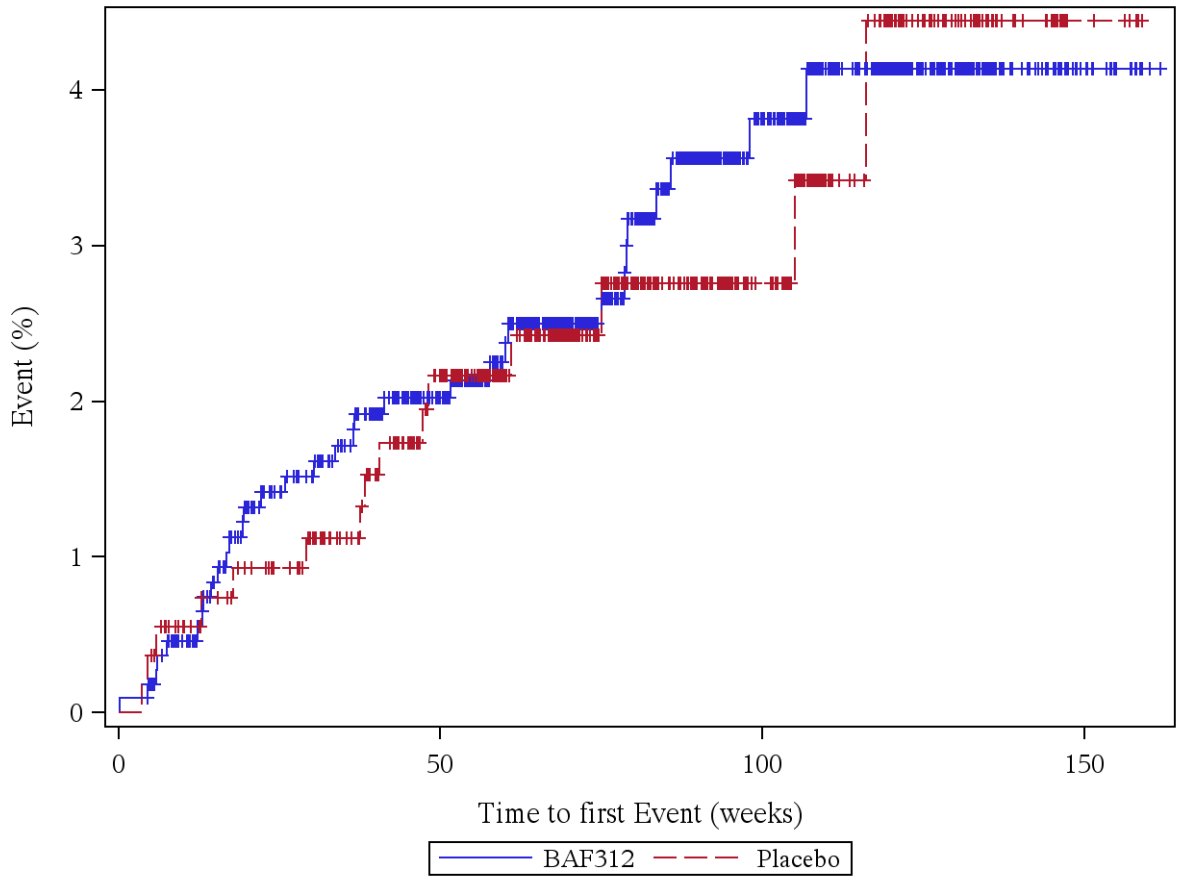


Patients at risk (BAF312/Placebo): Week 0: 1099/546, Week 4: 1098/545, Week 12: 1054/534, Week 24: 1006/518, Week 36: 975/493, Week 48: 911/454, Week 60: 803/385, Week 72: 638/301, Week 84: 503/234, Week 96: 388/173, Week 108: 280/123, Week 120: 191/77, Week 132: 108/39, Week 144: 48/19, Week 156: 9/4, Week 168: 0/0

Log rank test: p-value = 0,831
*: p < 0,05

Analysis population: A2304 SAF total population

Figure 12.1.6.4: Infections and infestations (AESI, serious)

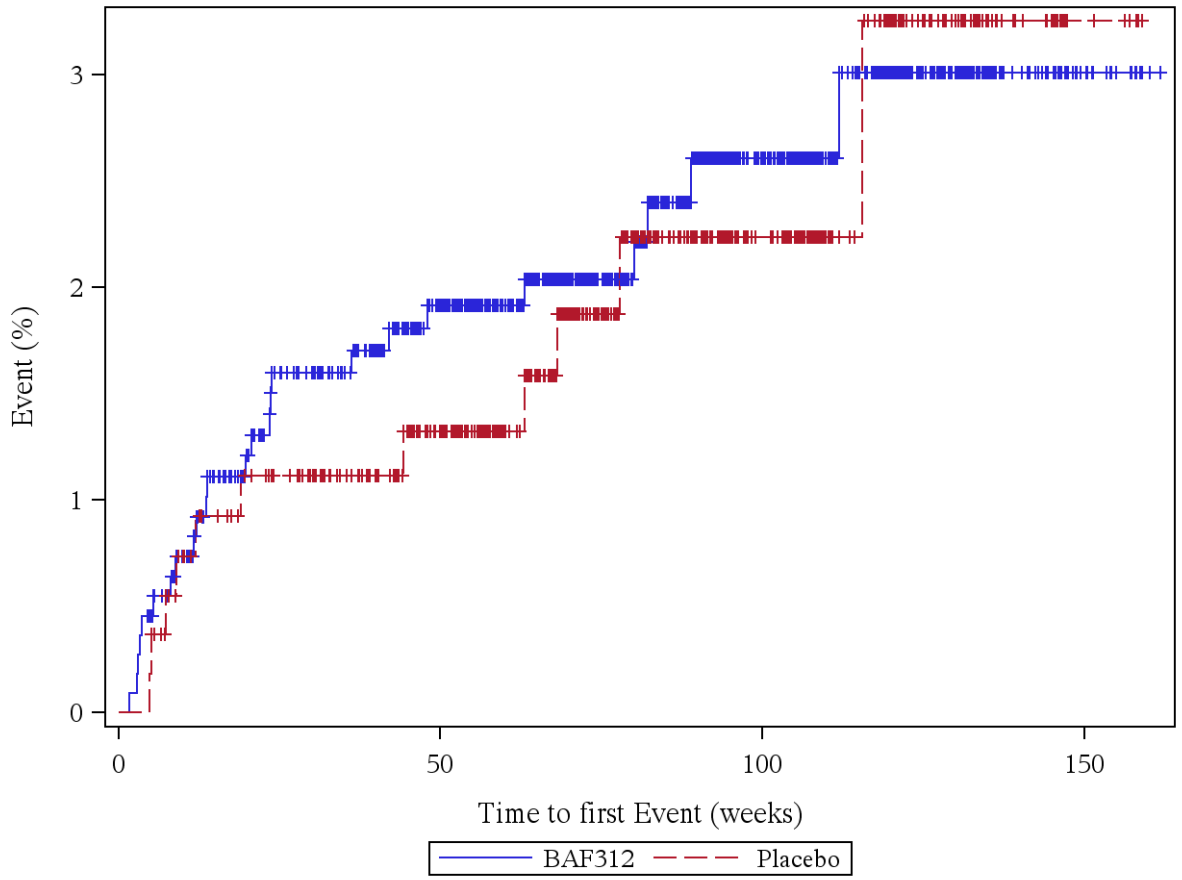


Patients at risk (BAF312/Placebo): Week 0: 1099/546, Week 4: 1098/545, Week 12: 1054/532, Week 24: 1003/516, Week 36: 973/492, Week 48: 908/453, Week 60: 801/383, Week 72: 635/301, Week 84: 499/234, Week 96: 386/173, Week 108: 277/123, Week 120: 189/78, Week 132: 104/40, Week 144: 46/20, Week 156: 9/5, Week 168: 0/0

Log rank test: p-value = 0,798
*: p < 0,05

Analysis population: A2304 SAF total population

Figure 12.1.6.5: Herpes simplex virus infections (AESI, all)

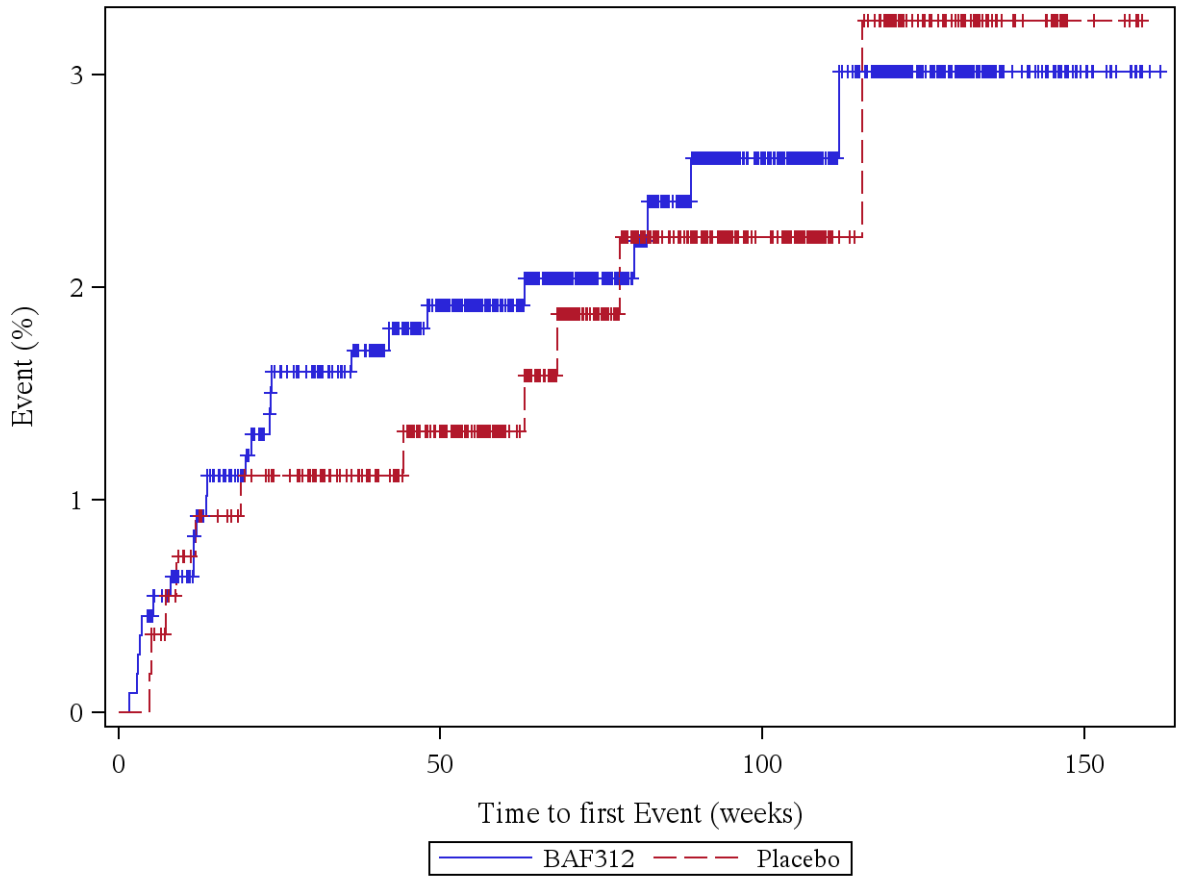


Patients at risk (BAF312/Placebo): Week 0: 1099/546, Week 4: 1094/546, Week 12: 1050/530, Week 24: 1000/515, Week 36: 974/491, Week 48: 906/454, Week 60: 799/381, Week 72: 636/299, Week 84: 504/231, Week 96: 392/170, Week 108: 286/121, Week 120: 195/78, Week 132: 110/39, Week 144: 50/20, Week 156: 10/5, Week 168: 0/0

Log rank test: p-value = 0,755
*: p < 0,05

Analysis population: A2304 SAF total population

Figure 12.1.6.6: Herpes simplex virus infections (AESI, not severe)

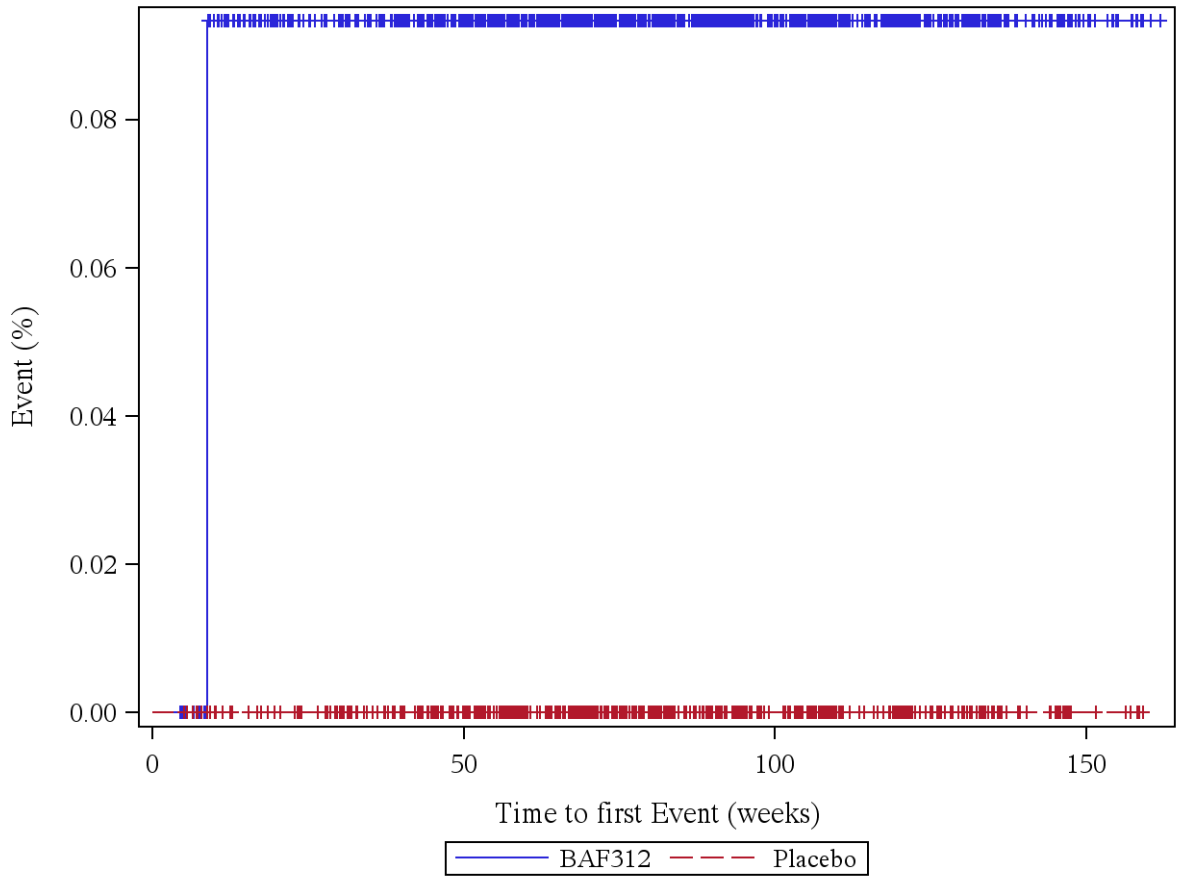


Patients at risk (BAF312/Placebo): Week 0: 1099/546, Week 4: 1094/546, Week 12: 1050/530, Week 24: 1000/515, Week 36: 974/491, Week 48: 906/454, Week 60: 799/381, Week 72: 636/299, Week 84: 504/231, Week 96: 392/170, Week 108: 286/121, Week 120: 195/78, Week 132: 110/39, Week 144: 50/20, Week 156: 10/5, Week 168: 0/0

Log rank test: p-value = 0,755
*: p < 0,05

Analysis population: A2304 SAF total population

Figure 12.1.6.7: Herpes simplex virus infections (AESI, severe)

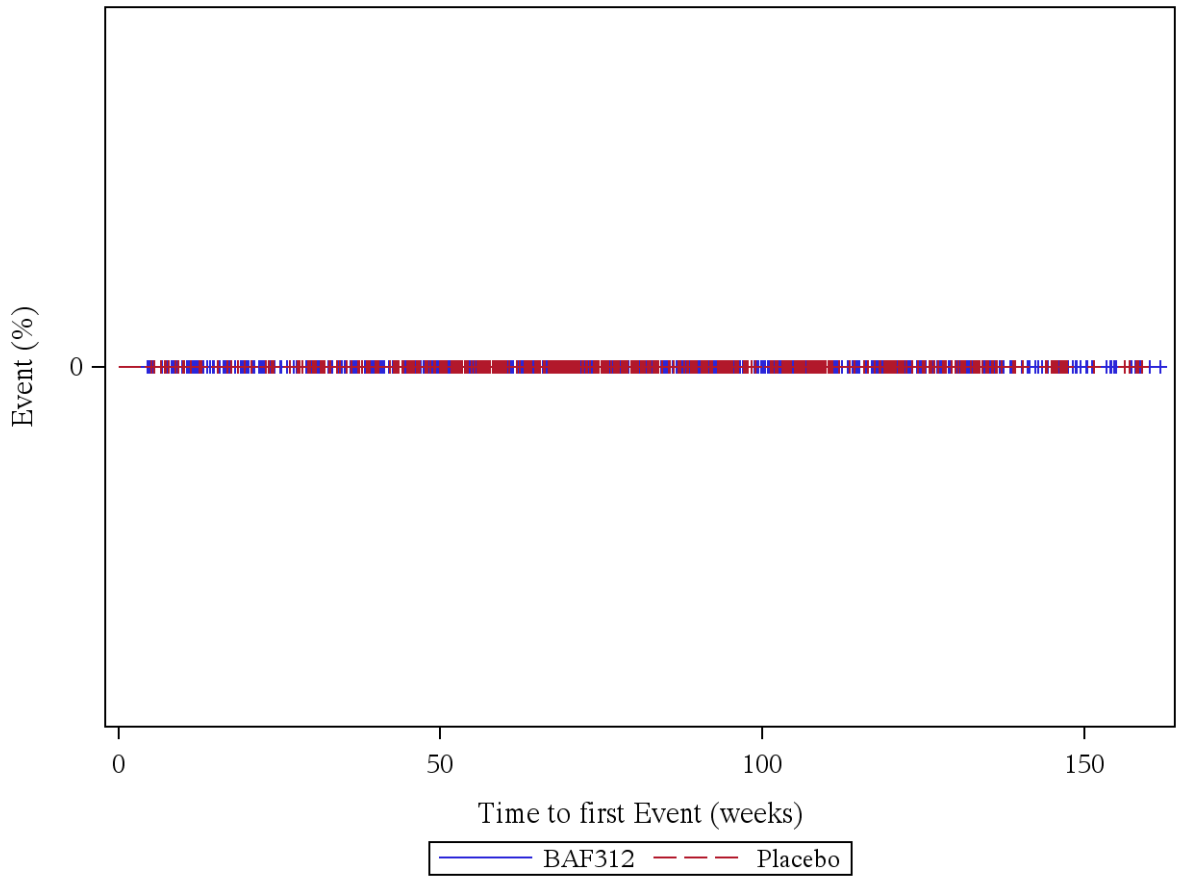


Patients at risk (BAF312/Placebo): Week 0: 1099/546, Week 4: 1099/546, Week 12: 1058/535, Week 24: 1016/521, Week 36: 989/497, Week 48: 924/461, Week 60: 817/388, Week 72: 651/305, Week 84: 516/237, Week 96: 400/176, Week 108: 291/126, Week 120: 200/80, Week 132: 113/40, Week 144: 51/20, Week 156: 10/5, Week 168: 0/0

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

Analysis population: A2304 SAF total population

Figure 12.1.6.8: Herpes simplex virus infections (AESI, serious)

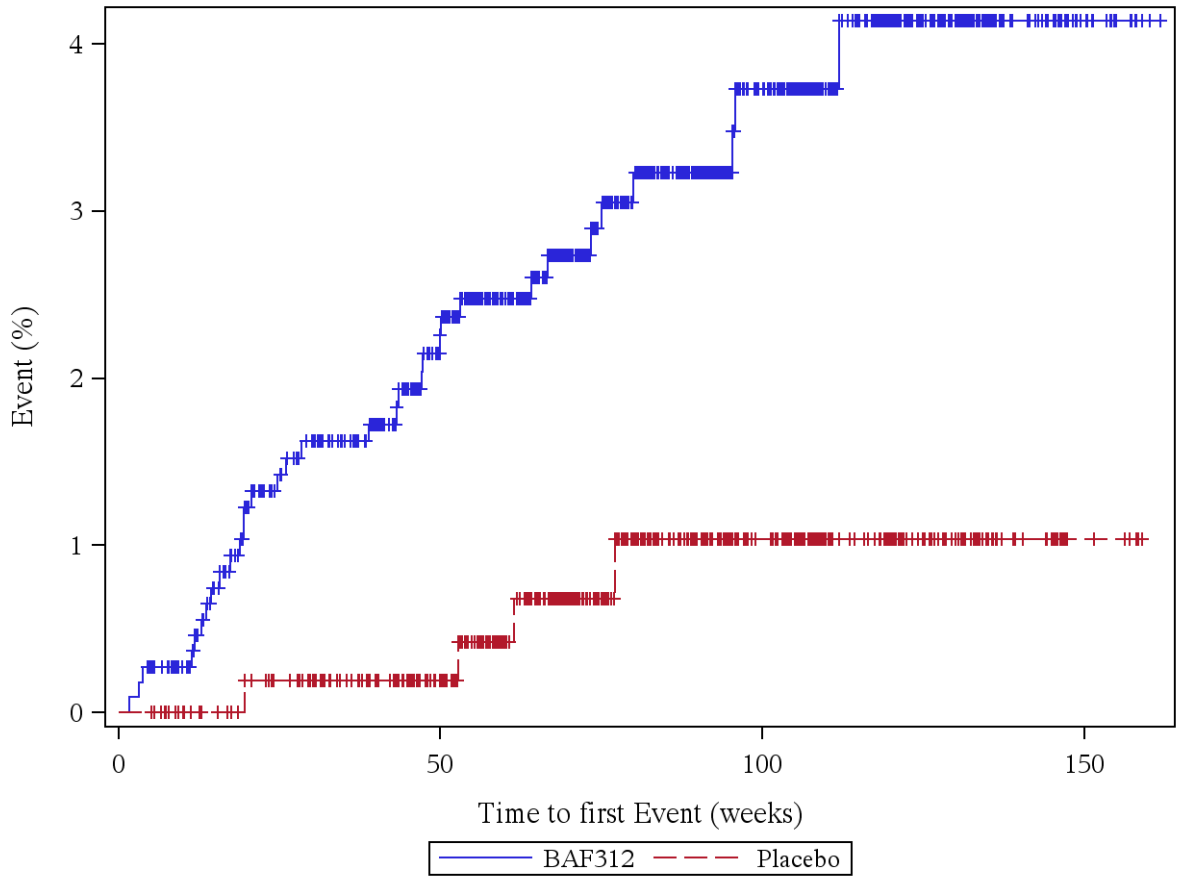


Patients at risk (BAF312/Placebo): Week 0: 1099/546, Week 4: 1099/546, Week 12: 1059/535, Week 24: 1017/521, Week 36: 990/497, Week 48: 925/461, Week 60: 818/388, Week 72: 652/305, Week 84: 516/237, Week 96: 400/176, Week 108: 291/126, Week 120: 200/80, Week 132: 113/40, Week 144: 51/20, Week 156: 10/5, Week 168: 0/0

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

Analysis population: A2304 SAF total population

Figure 12.1.6.9: Varicella-zoster virus infections (AESI, all)

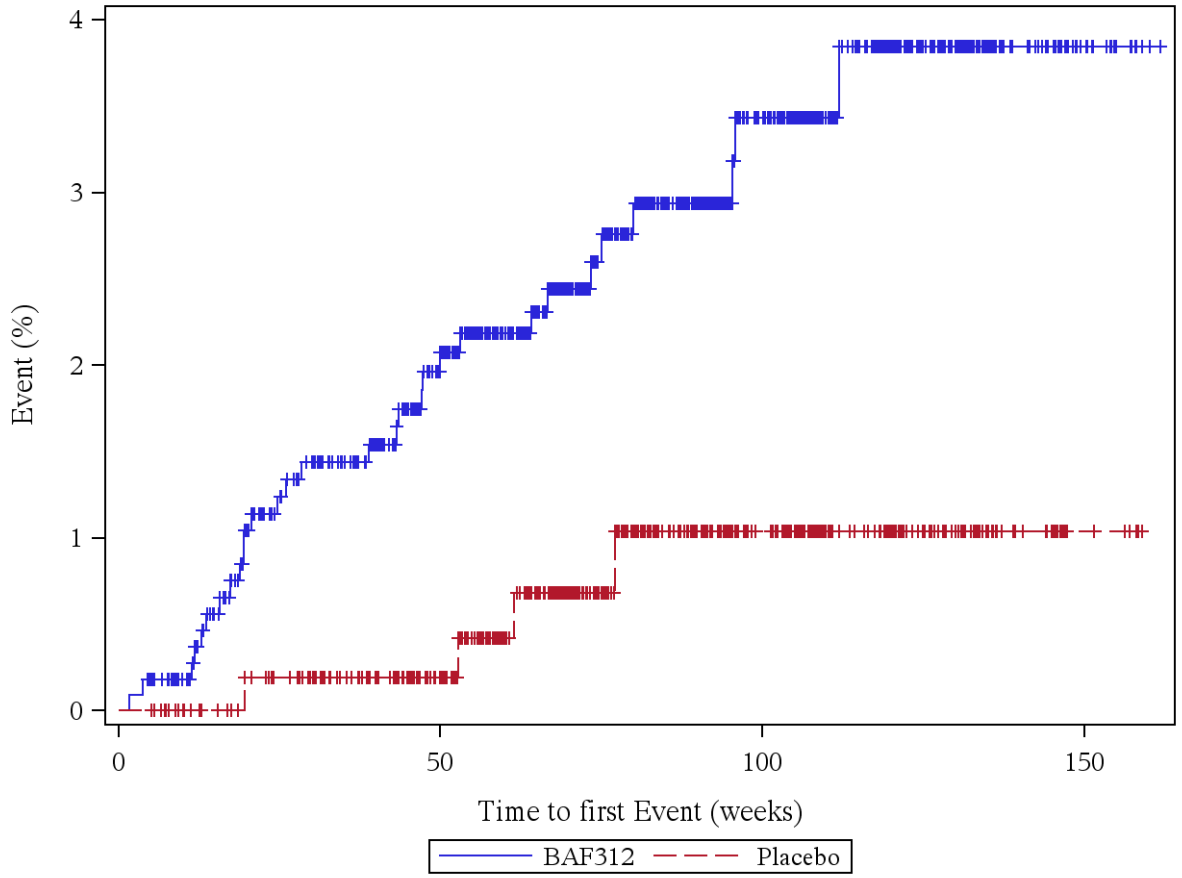


Patients at risk (BAF312/Placebo): Week 0: 1099/546, Week 4: 1096/546, Week 12: 1054/535, Week 24: 1004/520, Week 36: 975/496, Week 48: 906/460, Week 60: 800/387, Week 72: 634/303, Week 84: 497/234, Week 96: 383/174, Week 108: 277/126, Week 120: 188/80, Week 132: 108/40, Week 144: 49/20, Week 156: 8/5, Week 168: 0/0

Log rank test: p-value = 0,004 *
*: p < 0,05

Analysis population: A2304 SAF total population

Figure 12.1.6.10: Varicella-zoster virus infections (AESI, not severe)

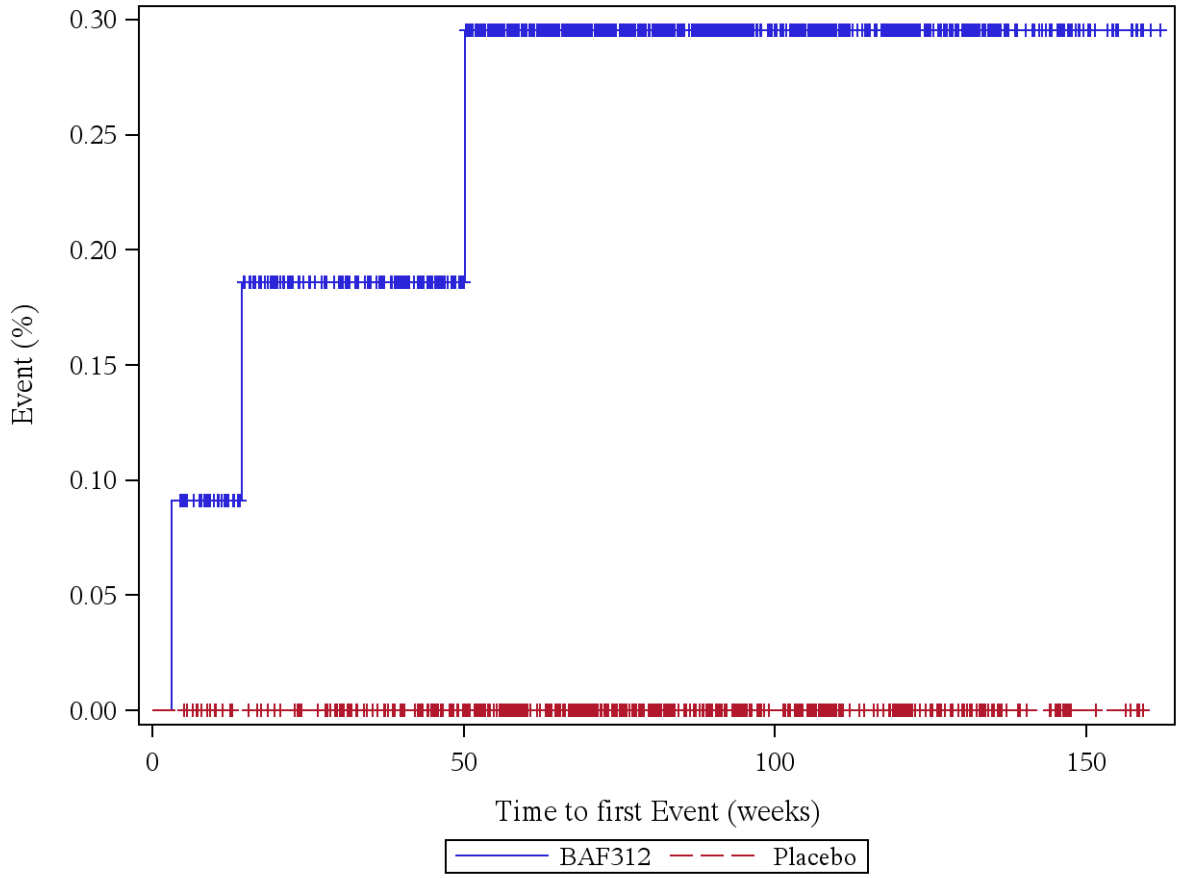


Patients at risk (BAF312/Placebo): Week 0: 1099/546, Week 4: 1097/546, Week 12: 1055/535, Week 24: 1006/520, Week 36: 977/496, Week 48: 908/460, Week 60: 803/387, Week 72: 636/303, Week 84: 499/234, Week 96: 385/174, Week 108: 278/126, Week 120: 189/80, Week 132: 108/40, Week 144: 49/20, Week 156: 8/5, Week 168: 0/0

Log rank test: p-value = 0,008 *
*: p < 0,05

Analysis population: A2304 SAF total population

Figure 12.1.6.11: Varicella-zoster virus infections (AESI, severe)

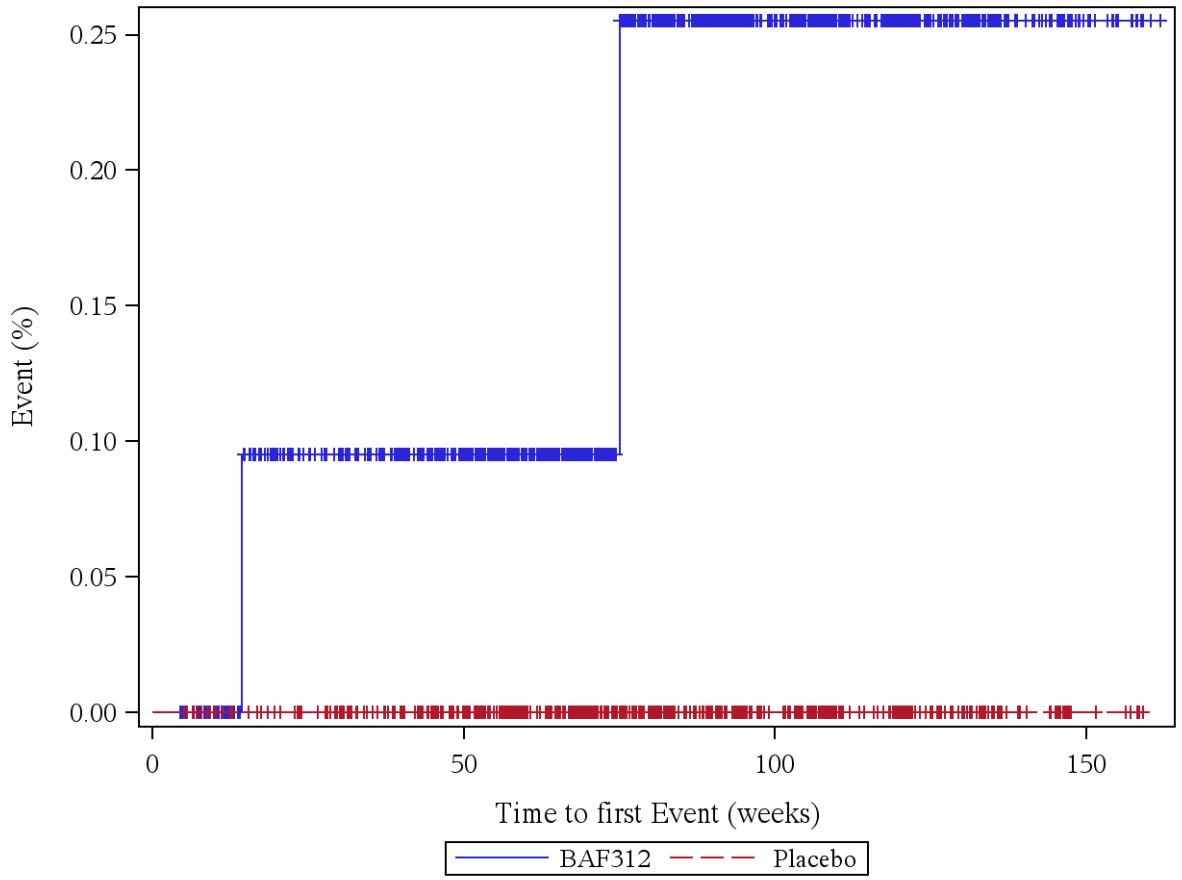


Patients at risk (BAF312/Placebo): Week 0: 1099/546, Week 4: 1098/546, Week 12: 1058/535, Week 24: 1015/521, Week 36: 988/497, Week 48: 923/461, Week 60: 815/388, Week 72: 650/305, Week 84: 514/237, Week 96: 398/176, Week 108: 290/126, Week 120: 199/80, Week 132: 113/40, Week 144: 51/20, Week 156: 10/5, Week 168: 0/0

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

Analysis population: A2304 SAF total population

Figure 12.1.6.12: Varicella-zoster virus infections (AESI, serious)

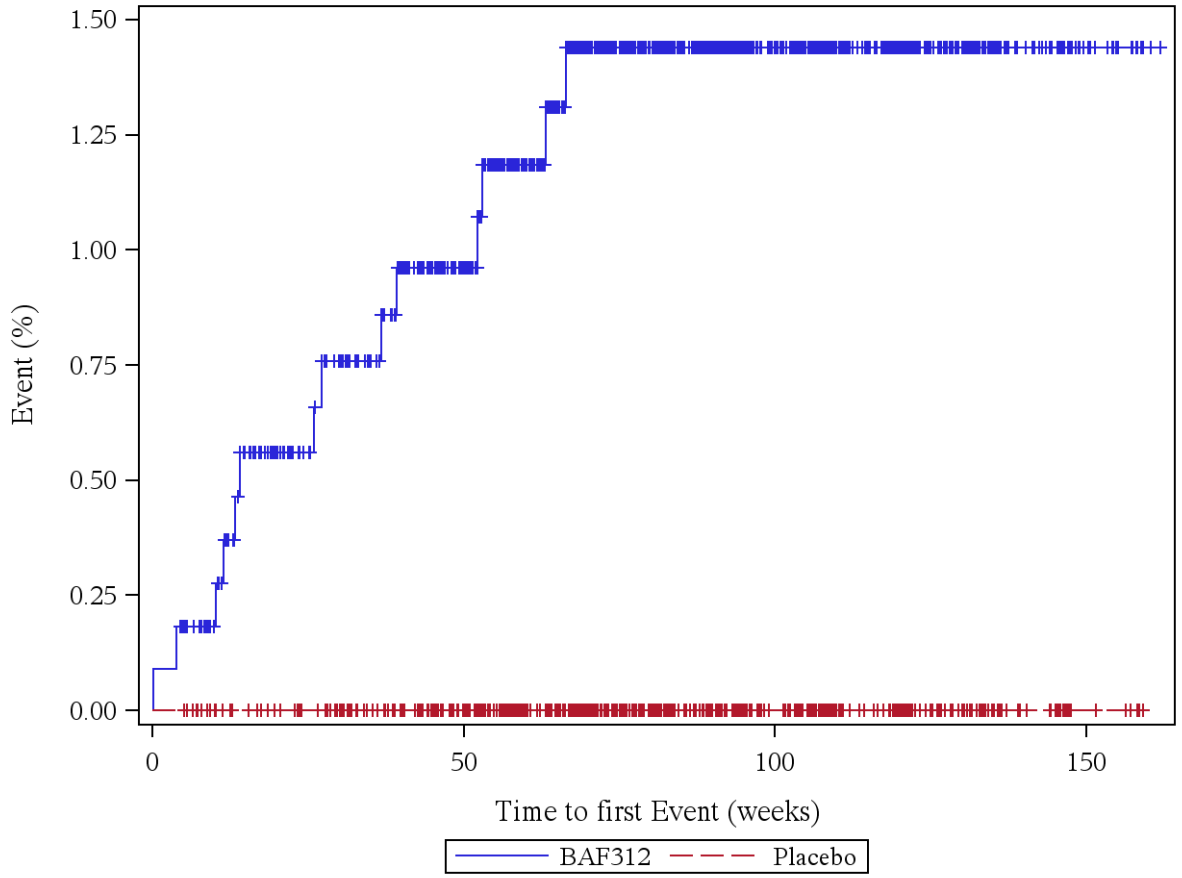


Patients at risk (BAF312/Placebo): Week 0: 1099/546, Week 4: 1099/546, Week 12: 1059/535, Week 24: 1016/521, Week 36: 989/497, Week 48: 924/461, Week 60: 817/388, Week 72: 651/305, Week 84: 514/237, Week 96: 398/176, Week 108: 290/126, Week 120: 199/80, Week 132: 112/40, Week 144: 50/20, Week 156: 9/5, Week 168: 0/0

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

Analysis population: A2304 SAF total population

Figure 12.1.6.13: Lymphopenia (AESI, all)

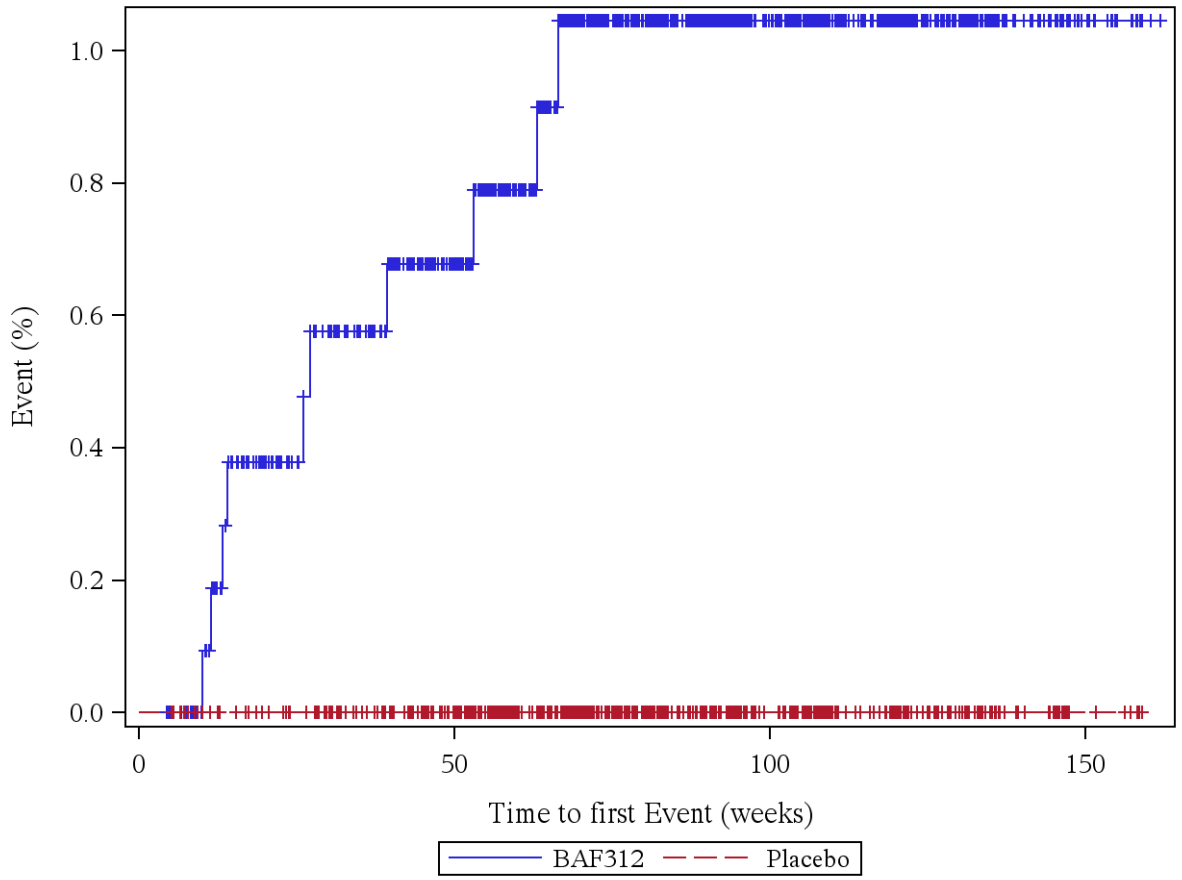


Patients at risk (BAF312/Placebo): Week 0: 1099/546, Week 4: 1097/546, Week 12: 1055/535, Week 24: 1011/521, Week 36: 982/497, Week 48: 915/461, Week 60: 807/388, Week 72: 645/305, Week 84: 510/237, Week 96: 395/176, Week 108: 290/126, Week 120: 199/80, Week 132: 113/40, Week 144: 51/20, Week 156: 10/5, Week 168: 0/0

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

Analysis population: A2304 SAF total population

Figure 12.1.6.14: Lymphopenia (AESI, not severe)

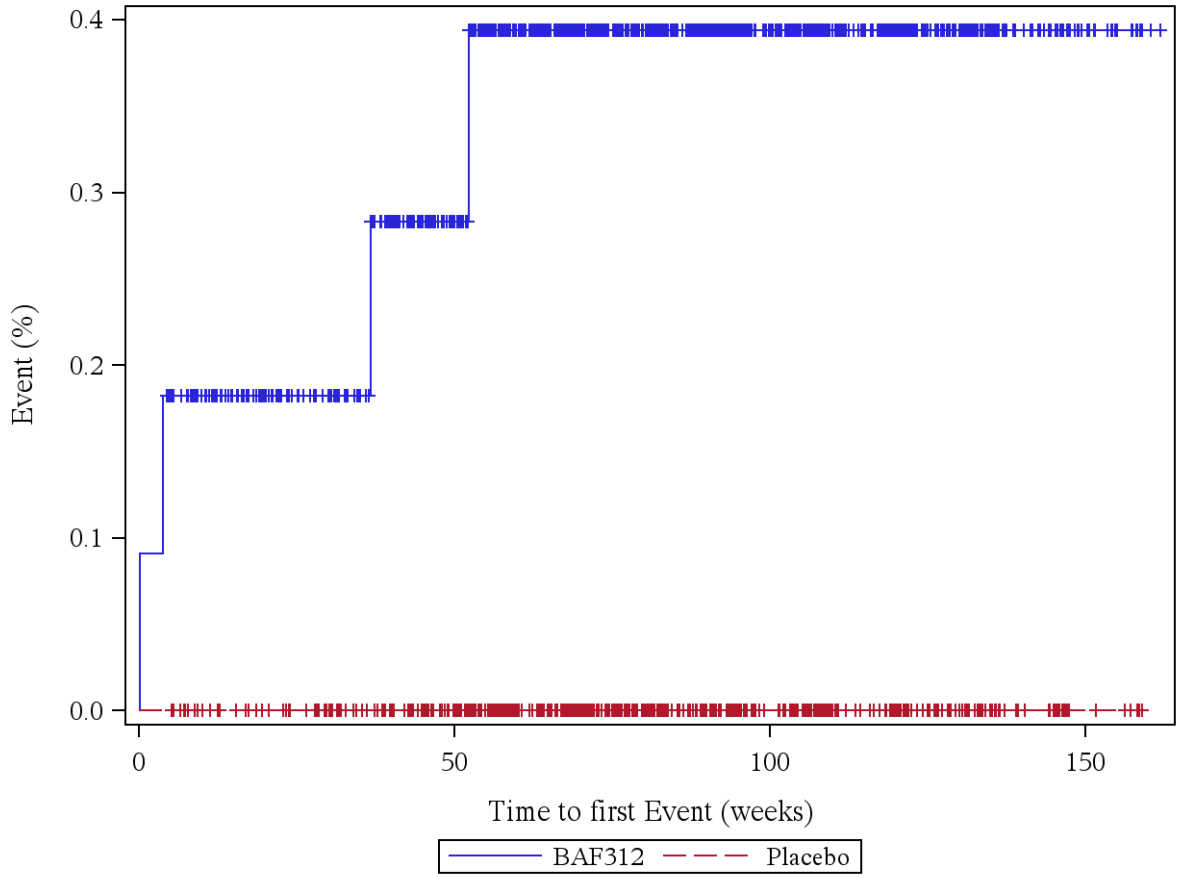


Patients at risk (BAF312/Placebo): Week 0: 1099/546, Week 4: 1099/546, Week 12: 1057/535, Week 24: 1013/521, Week 36: 984/497, Week 48: 918/461, Week 60: 810/388, Week 72: 645/305, Week 84: 510/237, Week 96: 395/176, Week 108: 290/126, Week 120: 199/80, Week 132: 113/40, Week 144: 51/20, Week 156: 10/5, Week 168: 0/0

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

Analysis population: A2304 SAF total population

Figure 12.1.6.15: Lymphopenia (AESI, severe)

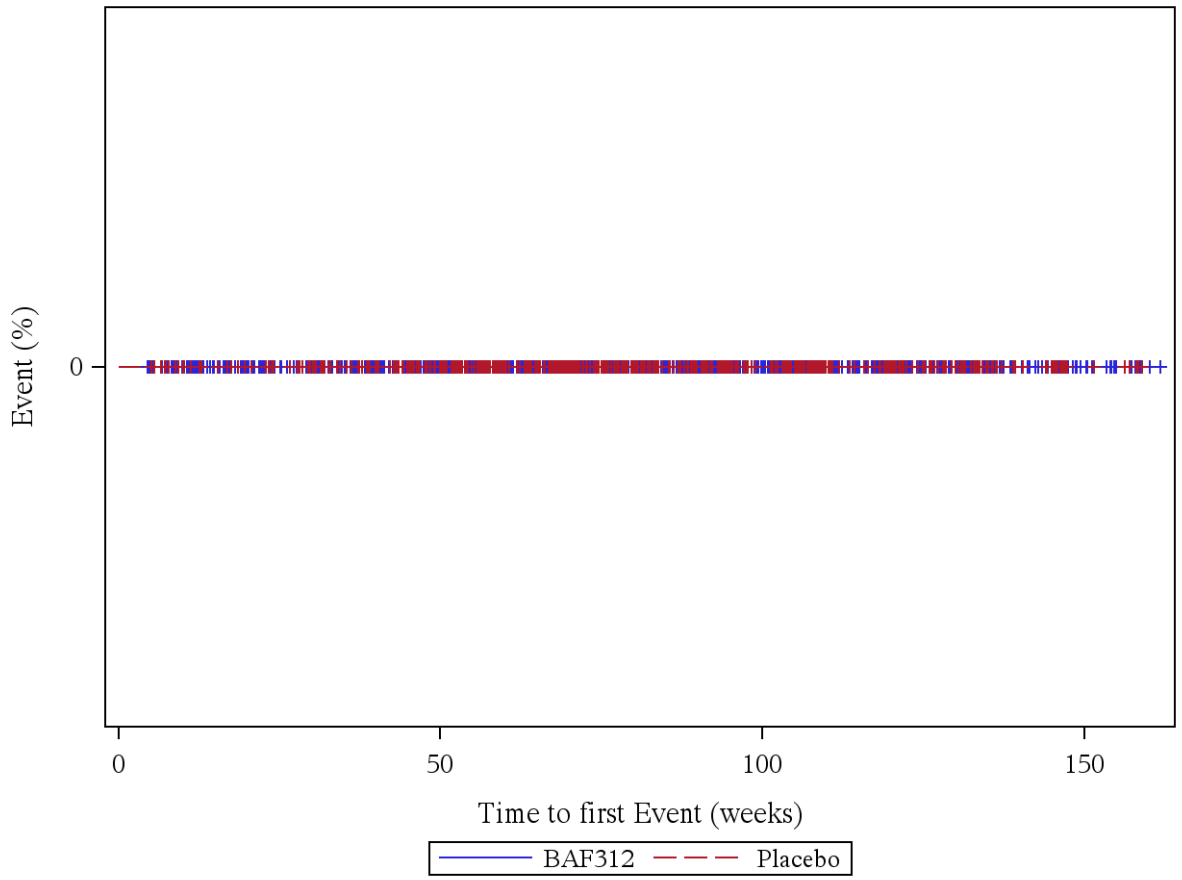


Patients at risk (BAF312/Placebo): Week 0: 1099/546, Week 4: 1097/546, Week 12: 1057/535, Week 24: 1015/521, Week 36: 988/497, Week 48: 922/461, Week 60: 815/388, Week 72: 652/305, Week 84: 516/237, Week 96: 400/176, Week 108: 291/126, Week 120: 200/80, Week 132: 113/40, Week 144: 51/20, Week 156: 10/5, Week 168: 0/0

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

Analysis population: A2304 SAF total population

Figure 12.1.6.16: Lymphopenia (AESI, serious)

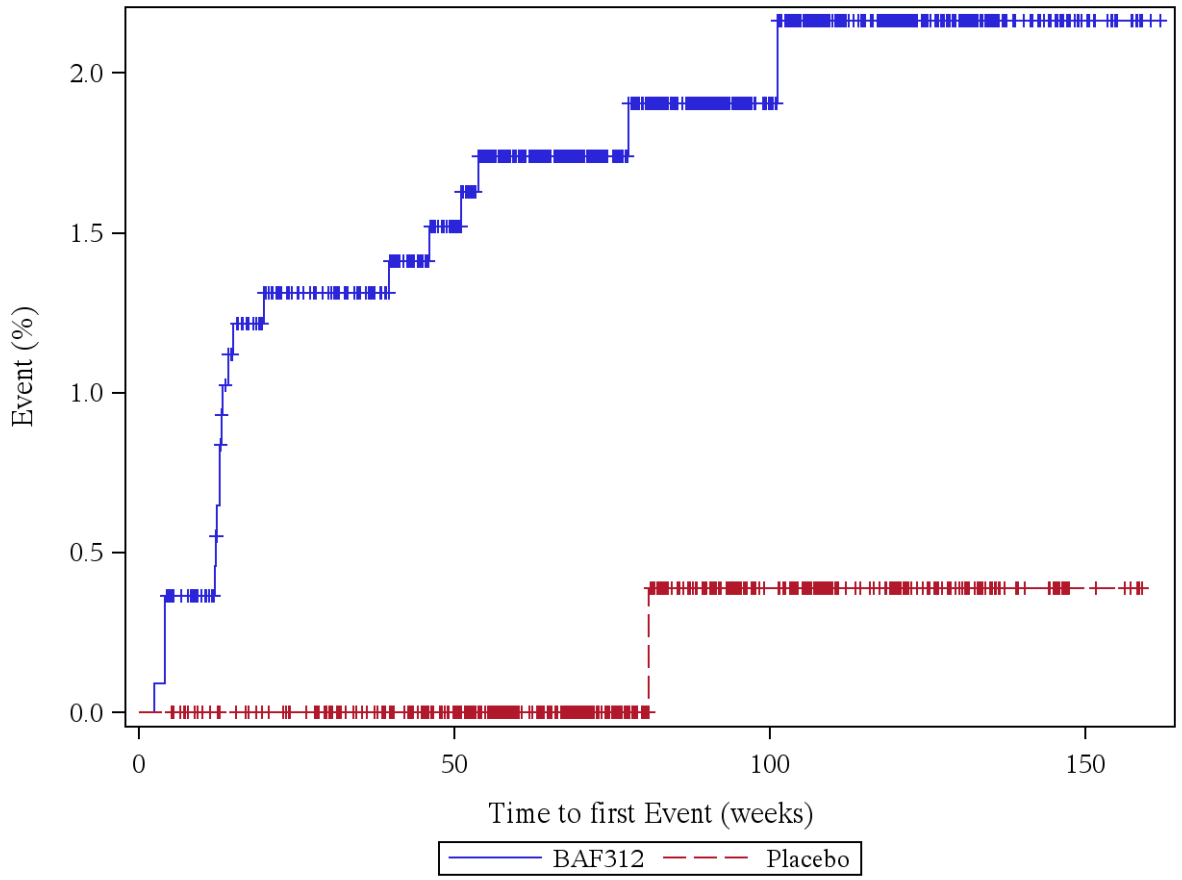


Patients at risk (BAF312/Placebo): Week 0: 1099/546, Week 4: 1099/546, Week 12: 1059/535, Week 24: 1017/521, Week 36: 990/497, Week 48: 925/461, Week 60: 818/388, Week 72: 652/305, Week 84: 516/237, Week 96: 400/176, Week 108: 291/126, Week 120: 200/80, Week 132: 113/40, Week 144: 51/20, Week 156: 10/5, Week 168: 0/0

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

Analysis population: A2304 SAF total population

Figure 12.1.6.17: Macular edema (AESI, all)

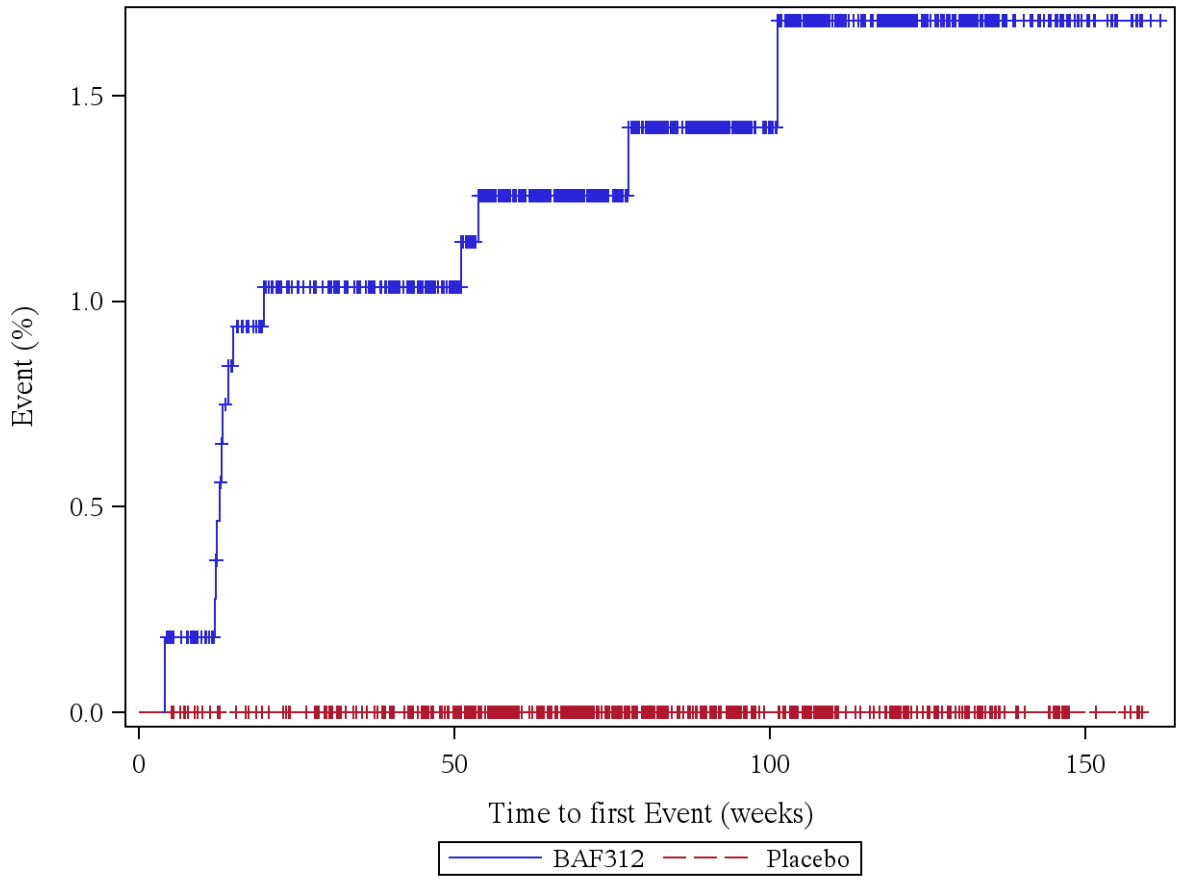


Patients at risk (BAF312/Placebo): Week 0: 1099/546, Week 4: 1098/546, Week 12: 1057/535, Week 24: 1012/521, Week 36: 986/497, Week 48: 920/461, Week 60: 814/388, Week 72: 649/305, Week 84: 514/236, Week 96: 400/176, Week 108: 291/126, Week 120: 200/80, Week 132: 113/40, Week 144: 51/20, Week 156: 10/5, Week 168: 0/0

Log rank test: p-value = 0,006 *
*: p < 0,05

Analysis population: A2304 SAF total population

Figure 12.1.6.18: Macular edema (AESI, not severe)

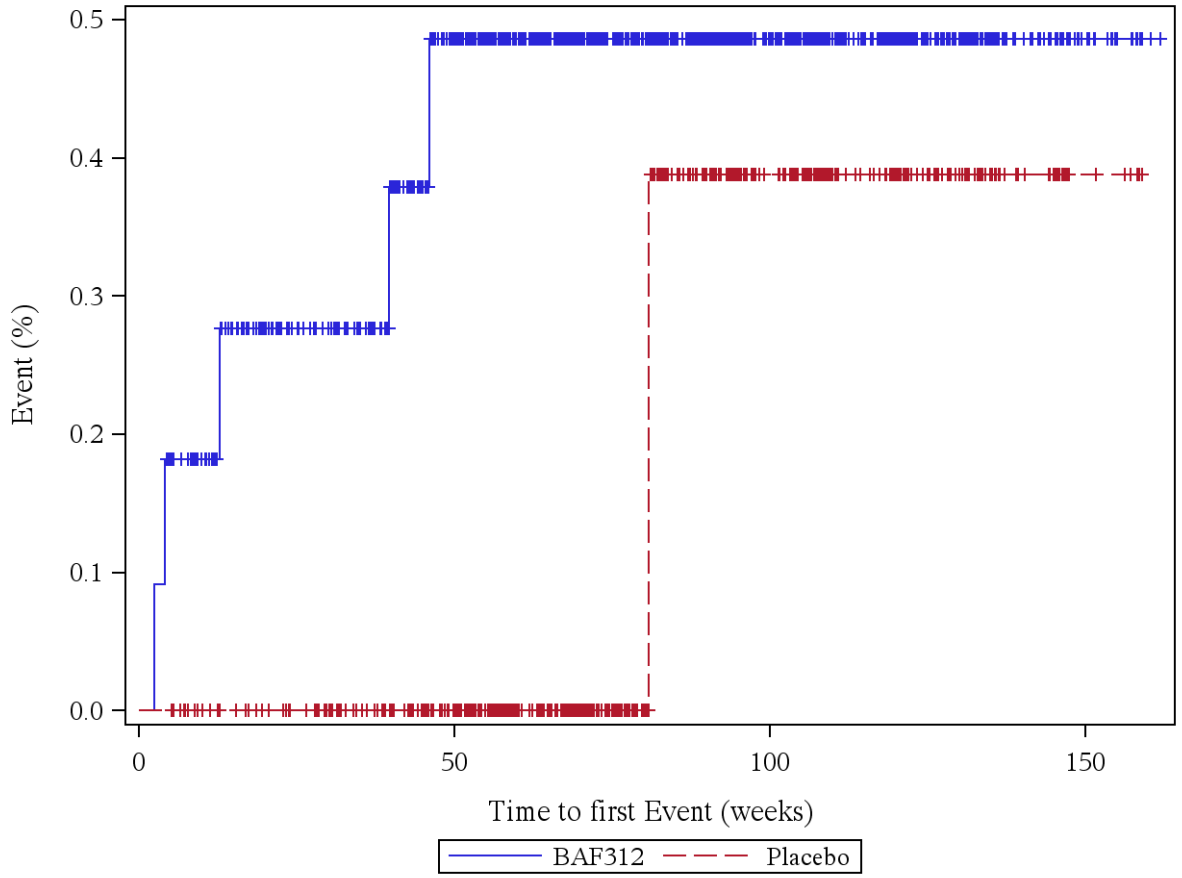


Patients at risk (BAF312/Placebo): Week 0: 1099/546, Week 4: 1099/546, Week 12: 1058/535, Week 24: 1013/521, Week 36: 986/497, Week 48: 922/461, Week 60: 816/388, Week 72: 651/305, Week 84: 514/237, Week 96: 400/176, Week 108: 291/126, Week 120: 200/80, Week 132: 113/40, Week 144: 51/20, Week 156: 10/5, Week 168: 0/0

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

Analysis population: A2304 SAF total population

Figure 12.1.6.19: Macular edema (AESI, severe)

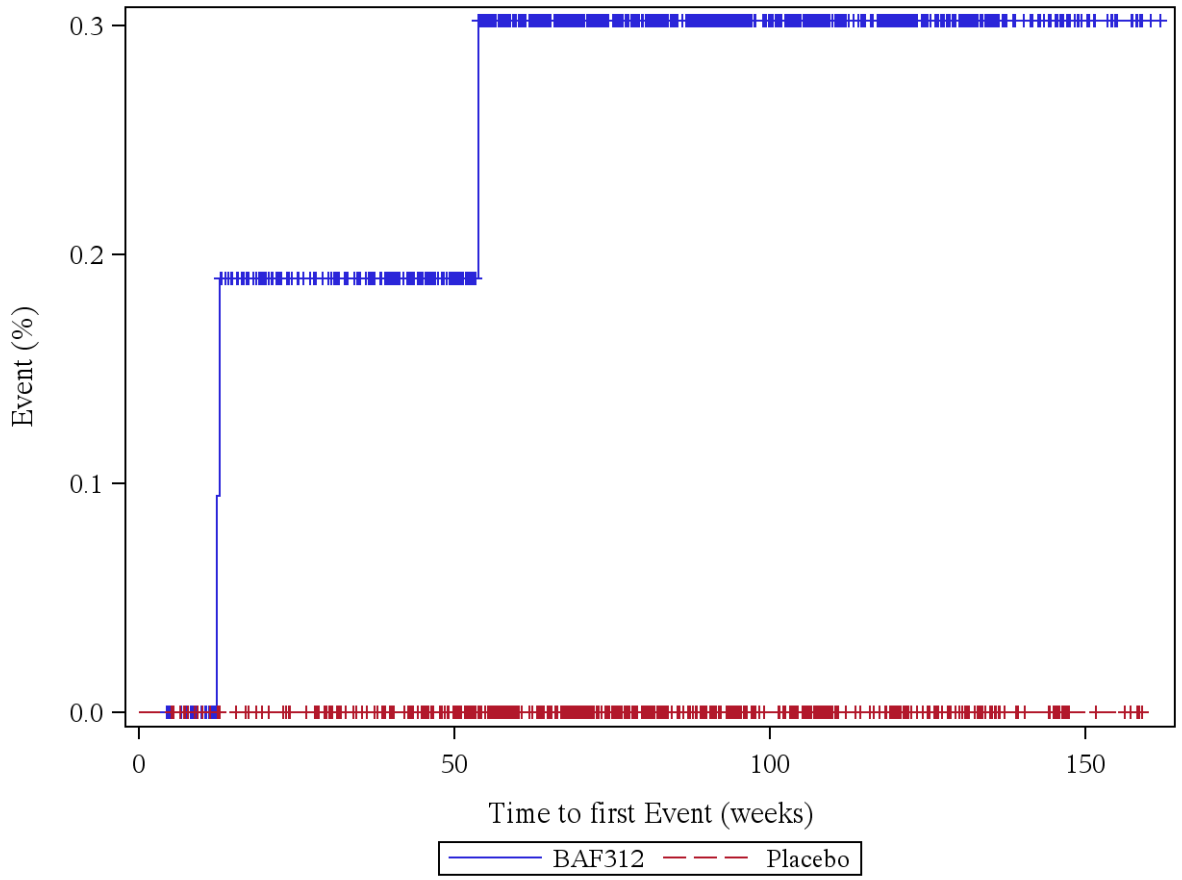


Patients at risk (BAF312/Placebo): Week 0: 1099/546, Week 4: 1098/546, Week 12: 1058/535, Week 24: 1016/521, Week 36: 990/497, Week 48: 923/461, Week 60: 816/388, Week 72: 650/305, Week 84: 516/236, Week 96: 400/176, Week 108: 291/126, Week 120: 200/80, Week 132: 113/40, Week 144: 51/20, Week 156: 10/5, Week 168: 0/0

Log rank test: p-value = 0,393
*: p < 0,05

Analysis population: A2304 SAF total population

Figure 12.1.6.20: Macular edema (AESI, serious)

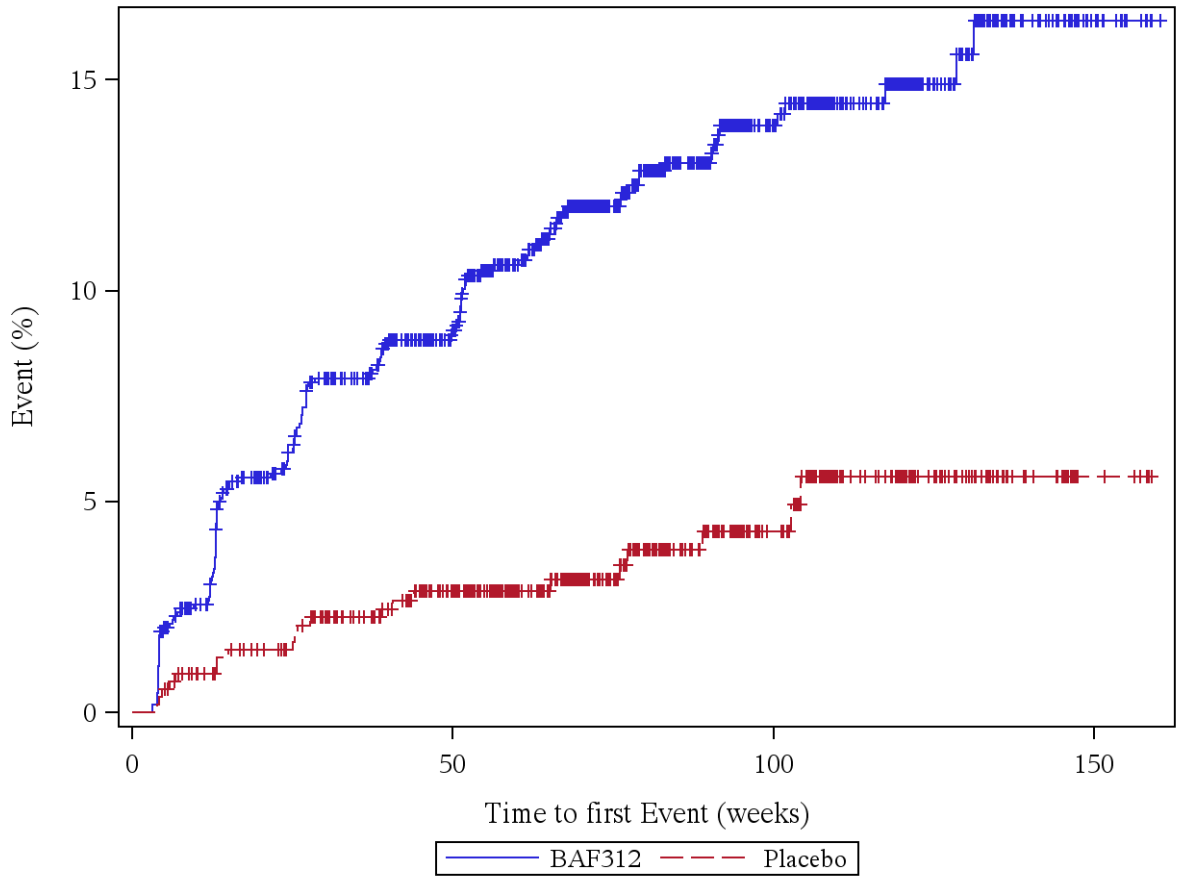


Patients at risk (BAF312/Placebo): Week 0: 1099/546, Week 4: 1099/546, Week 12: 1059/535, Week 24: 1015/521, Week 36: 989/497, Week 48: 924/461, Week 60: 817/388, Week 72: 651/305, Week 84: 515/237, Week 96: 400/176, Week 108: 291/126, Week 120: 200/80, Week 132: 113/40, Week 144: 51/20, Week 156: 10/5, Week 168: 0/0

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

Analysis population: A2304 SAF total population

Figure 12.1.6.21: Abnormal hepatic enzymes (AESI, all)

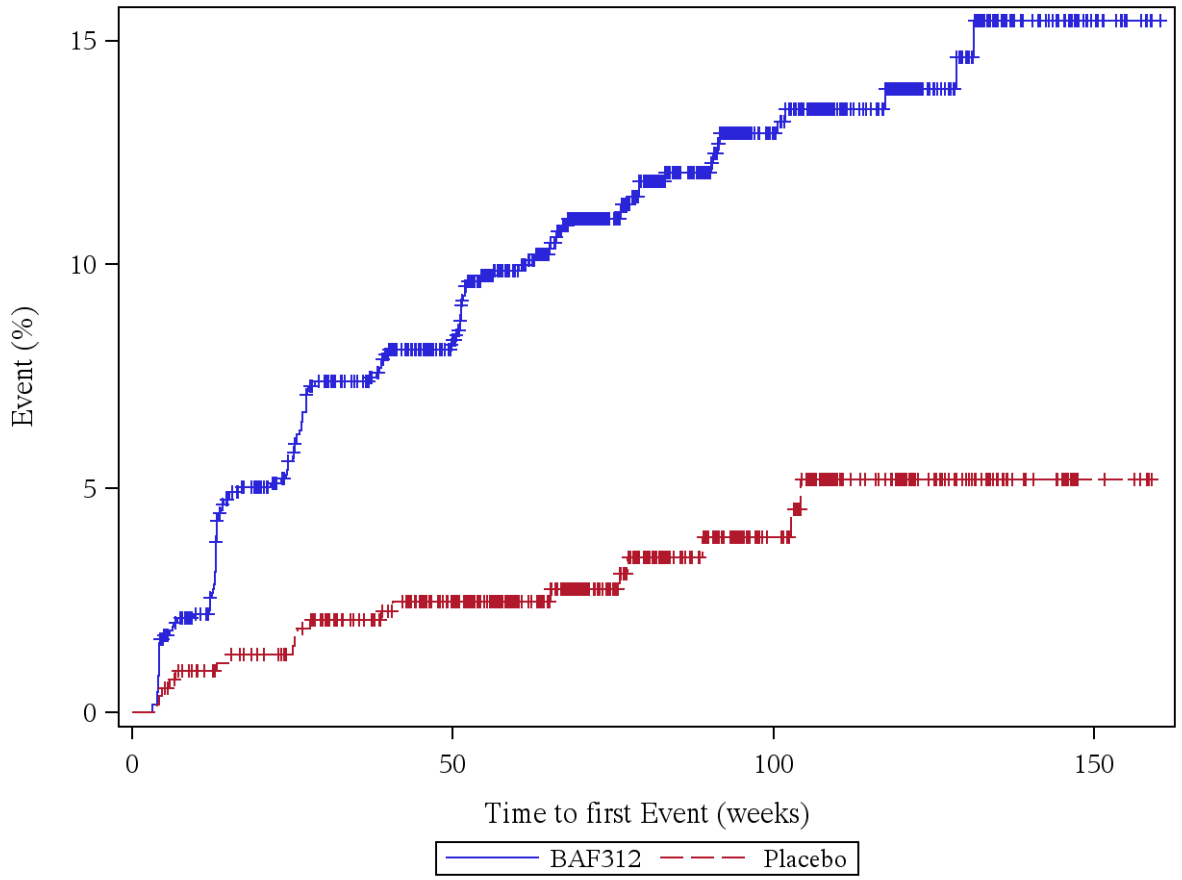


Patients at risk (BAF312/Placebo): Week 0: 1099/546, Week 4: 1087/545, Week 12: 1034/530, Week 24: 964/513, Week 36: 918/486, Week 48: 849/448, Week 60: 736/376, Week 72: 572/294, Week 84: 441/225, Week 96: 336/169, Week 108: 241/120, Week 120: 168/75, Week 132: 97/38, Week 144: 42/20, Week 156: 8/5, Week 168: 0/0

Log rank test: p-value = <0,001 *
*: p < 0,05

Analysis population: A2304 SAF total population

Figure 12.1.6.22: Abnormal hepatic enzymes (AESI, not severe)

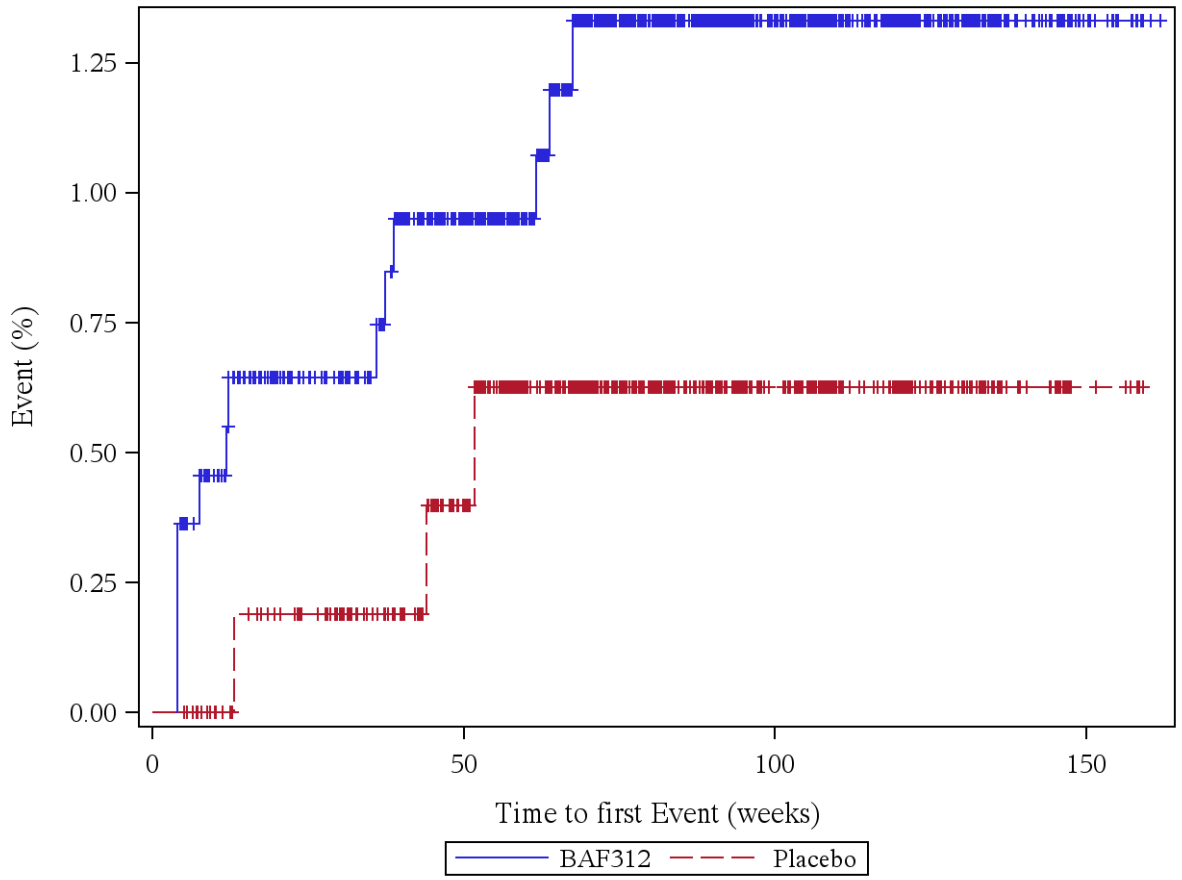


Patients at risk (BAF312/Placebo): Week 0: 1099/546, Week 4: 1090/545, Week 12: 1037/530, Week 24: 967/514, Week 36: 921/487, Week 48: 854/450, Week 60: 739/378, Week 72: 577/295, Week 84: 446/225, Week 96: 340/169, Week 108: 243/120, Week 120: 168/75, Week 132: 97/38, Week 144: 42/20, Week 156: 8/5, Week 168: 0/0

Log rank test: p-value = <0,001 *
*: p < 0,05

Analysis population: A2304 SAF total population

Figure 12.1.6.23: Abnormal hepatic enzymes (AESI, severe)

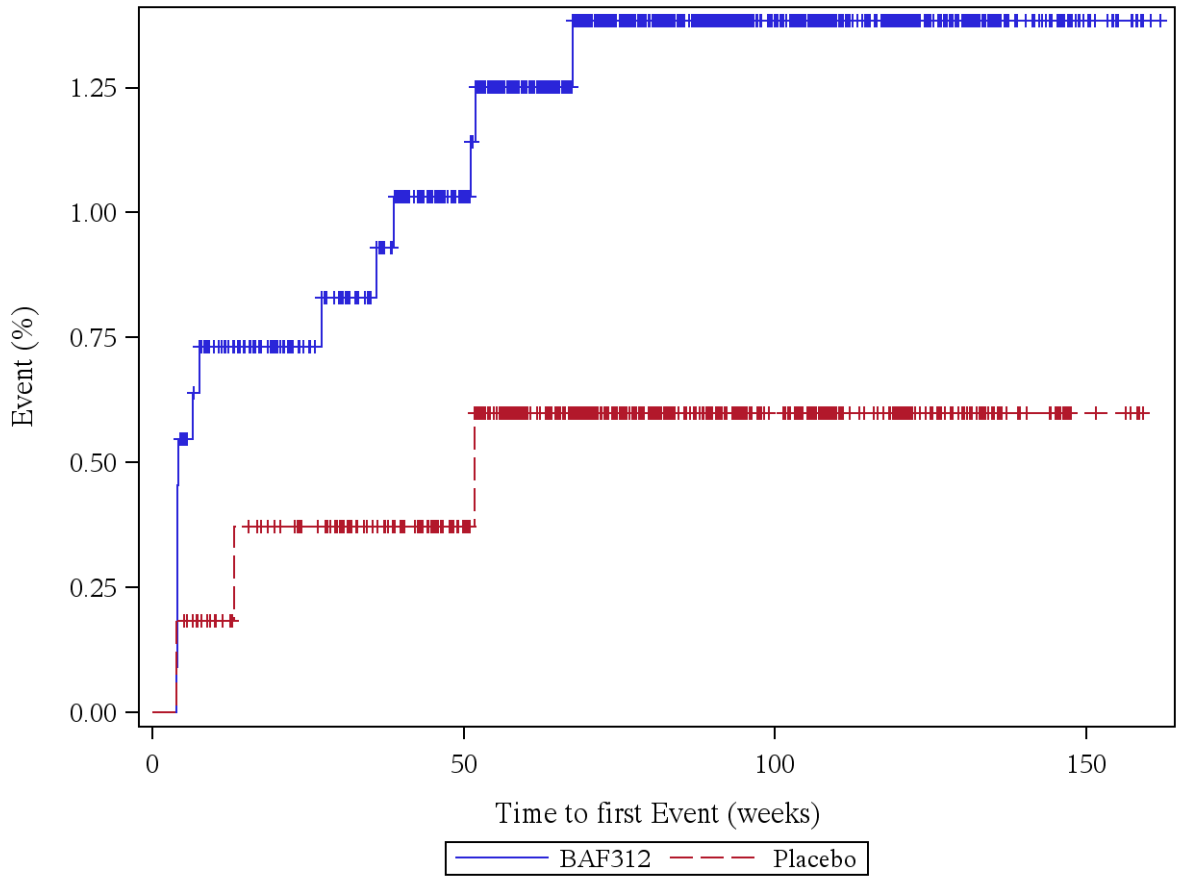


Patients at risk (BAF312/Placebo): Week 0: 1099/546, Week 4: 1095/546, Week 12: 1055/535, Week 24: 1013/520, Week 36: 985/496, Week 48: 918/459, Week 60: 813/386, Week 72: 644/304, Week 84: 509/237, Week 96: 395/176, Week 108: 288/126, Week 120: 200/80, Week 132: 113/40, Week 144: 51/20, Week 156: 10/5, Week 168: 0/0

Log rank test: p-value = 0,221
*: p < 0,05

Analysis population: A2304 SAF total population

Figure 12.1.6.24: Abnormal hepatic enzymes (AESI, serious)

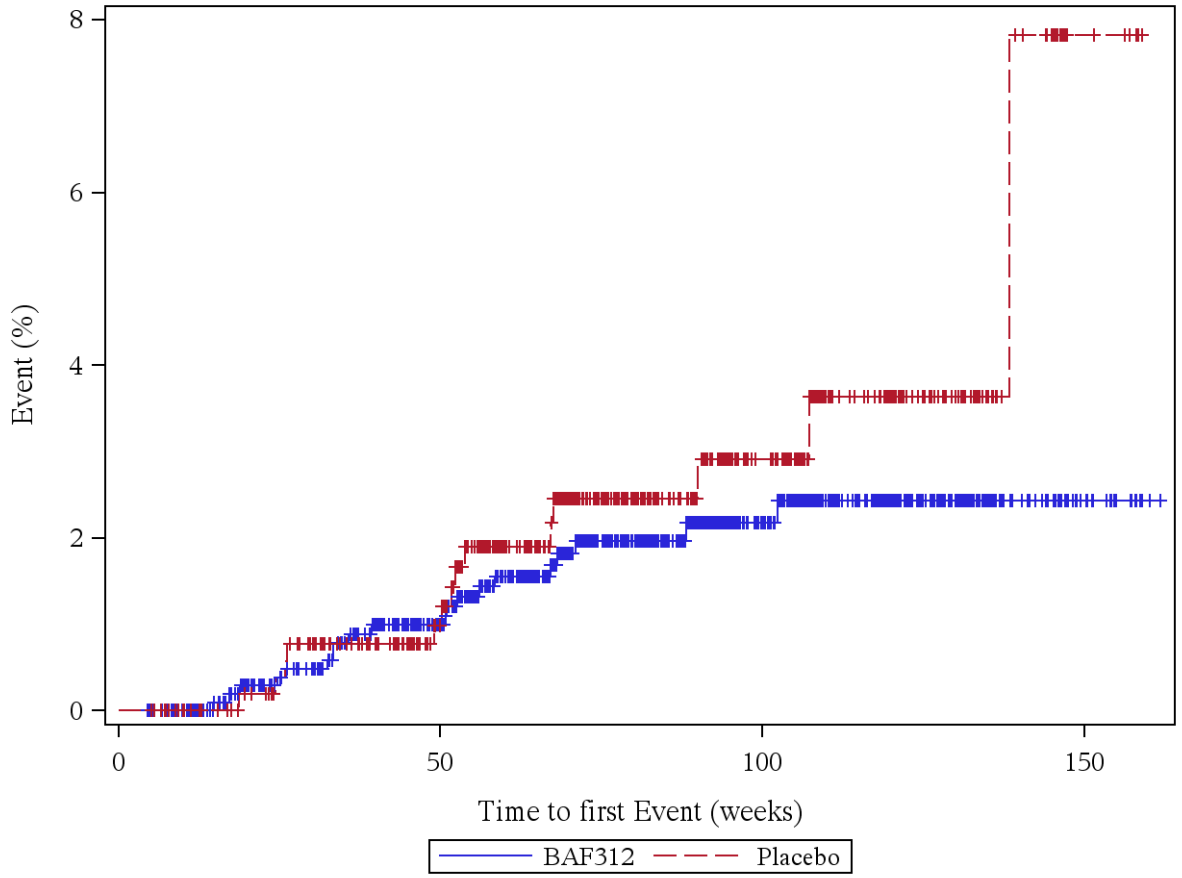


Patients at risk (BAF312/Placebo): Week 0: 1099/546, Week 4: 1094/545, Week 12: 1054/534, Week 24: 1014/519, Week 36: 985/496, Week 48: 919/460, Week 60: 812/387, Week 72: 645/304, Week 84: 511/237, Week 96: 396/176, Week 108: 287/126, Week 120: 199/80, Week 132: 113/40, Week 144: 51/20, Week 156: 10/5, Week 168: 0/0

Log rank test: p-value = 0,174
*: p < 0,05

Analysis population: A2304 SAF total population

Figure 12.1.6.25: Malignancies (AESI, all)

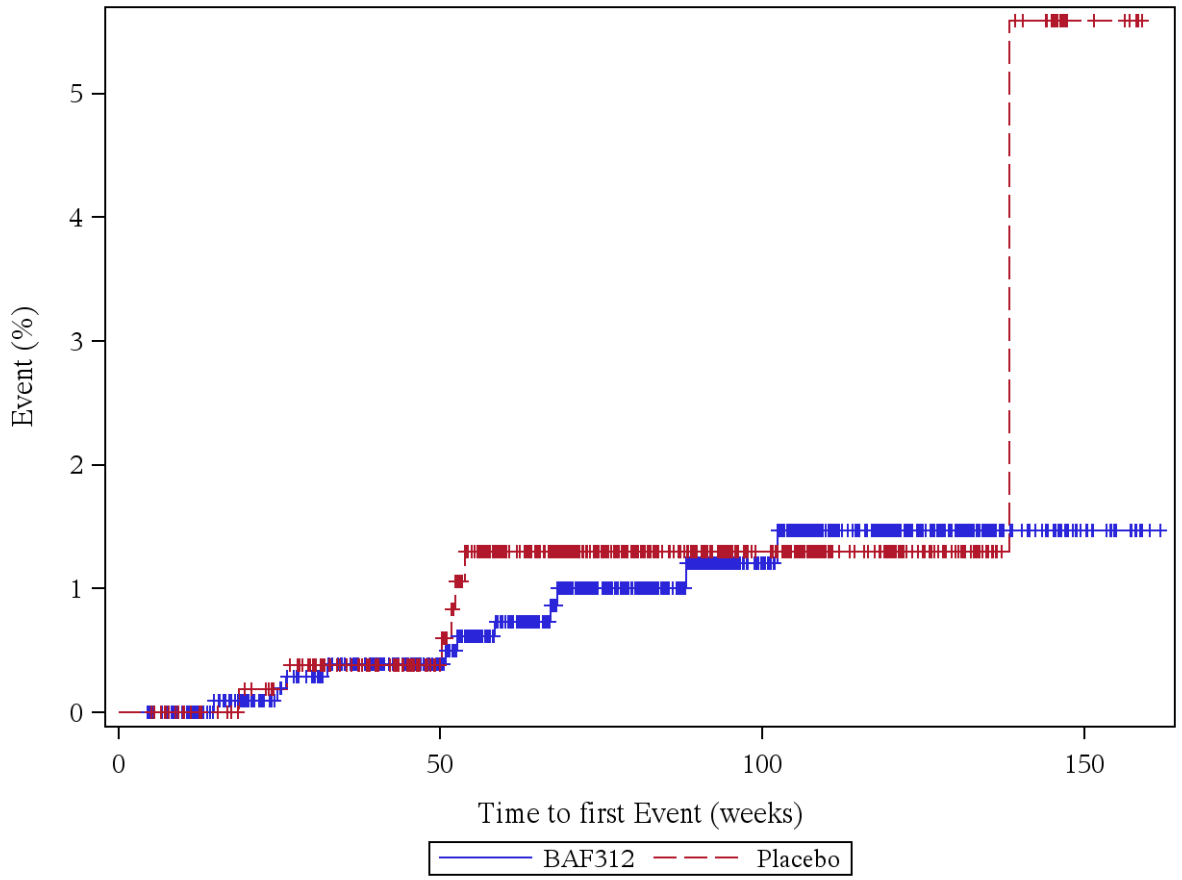


Patients at risk (BAF312/Placebo): Week 0: 1099/546, Week 4: 1099/546, Week 12: 1059/535, Week 24: 1014/520, Week 36: 981/495, Week 48: 919/459, Week 60: 810/382, Week 72: 643/300, Week 84: 509/233, Week 96: 396/173, Week 108: 287/122, Week 120: 196/79, Week 132: 111/40, Week 144: 51/20, Week 156: 10/5, Week 168: 0/0

Log rank test: p-value = 0,284
*: p < 0,05

Analysis population: A2304 SAF total population

Figure 12.1.6.26: Malignancies (AESI, not severe)

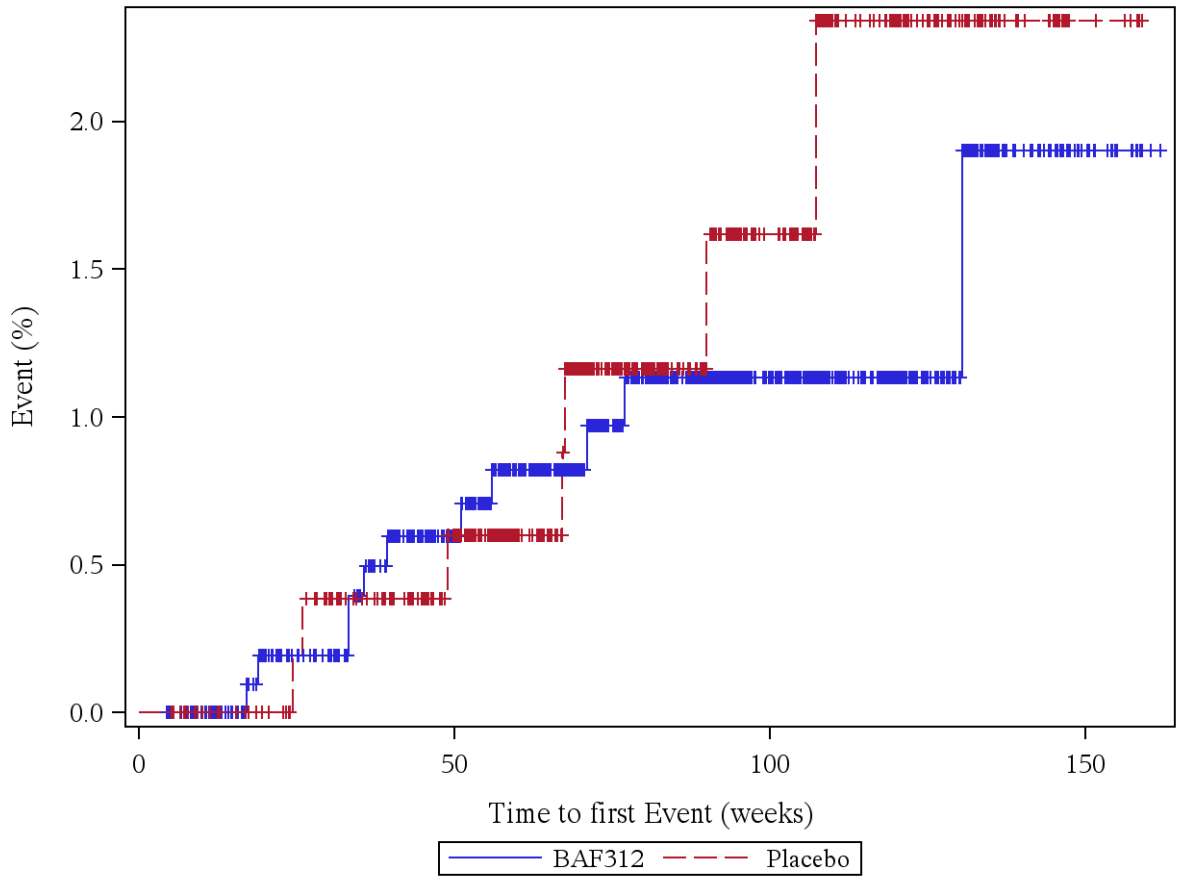


Patients at risk (BAF312/Placebo): Week 0: 1099/546, Week 4: 1099/546, Week 12: 1059/535, Week 24: 1016/520, Week 36: 986/495, Week 48: 921/459, Week 60: 813/382, Week 72: 645/301, Week 84: 510/234, Week 96: 397/174, Week 108: 288/124, Week 120: 197/79, Week 132: 111/40, Week 144: 51/20, Week 156: 10/5, Week 168: 0/0

Log rank test: p-value = 0,553
*: p < 0,05

Analysis population: A2304 SAF total population

Figure 12.1.6.27: Malignancies (AESI, severe)

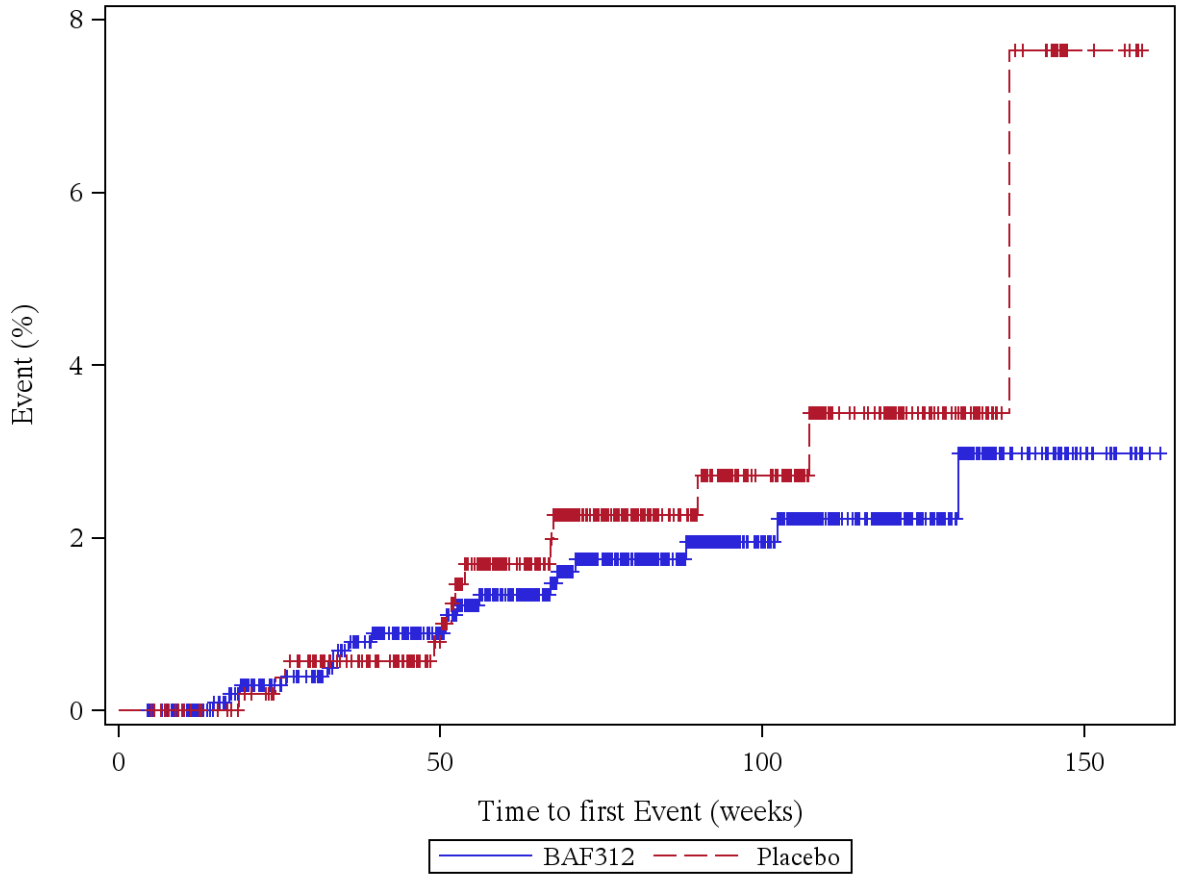


Patients at risk (BAF312/Placebo): Week 0: 1099/546, Week 4: 1099/546, Week 12: 1059/535, Week 24: 1015/521, Week 36: 985/497, Week 48: 923/461, Week 60: 815/388, Week 72: 650/304, Week 84: 514/236, Week 96: 398/175, Week 108: 289/124, Week 120: 198/80, Week 132: 112/40, Week 144: 51/20, Week 156: 10/5, Week 168: 0/0

Log rank test: p-value = 0,557
*: p < 0,05

Analysis population: A2304 SAF total population

Figure 12.1.6.28: Malignancies (AESI, serious)

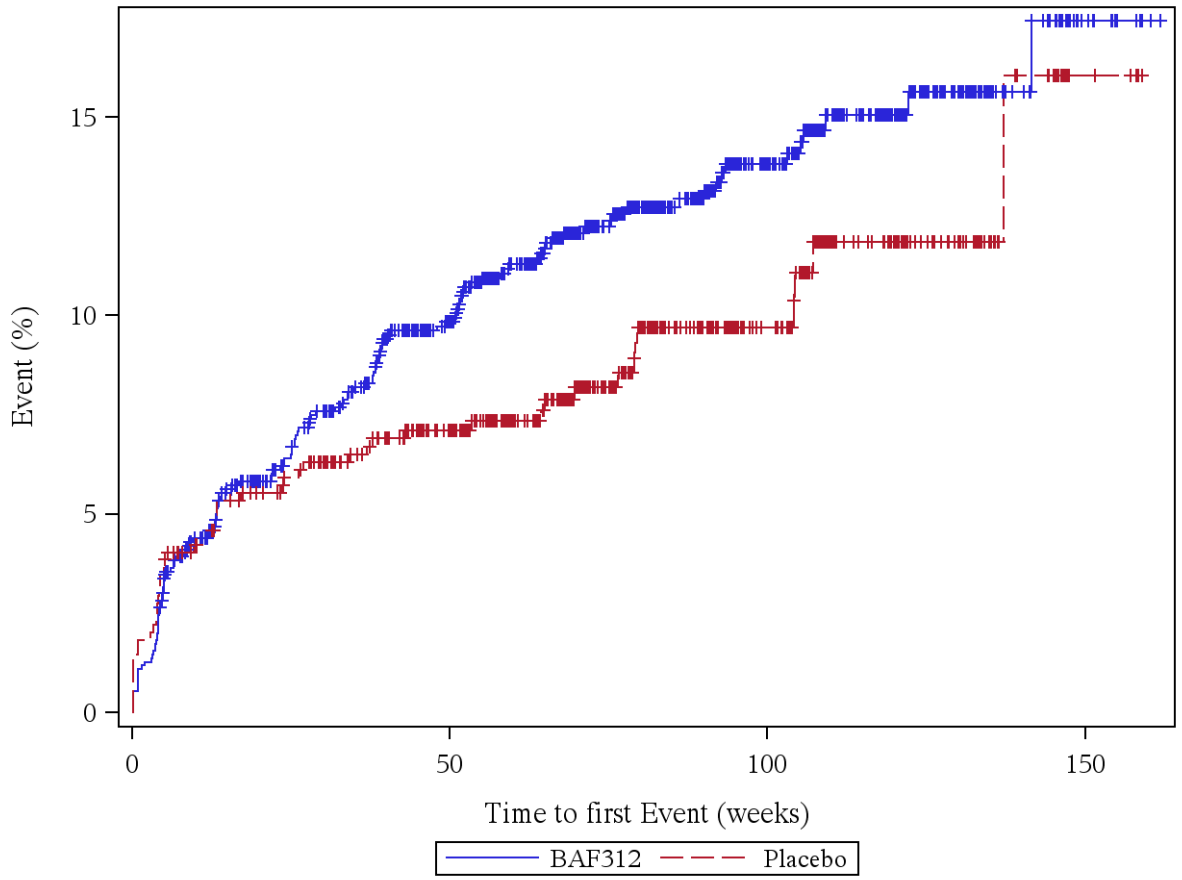


Patients at risk (BAF312/Placebo): Week 0: 1099/546, Week 4: 1099/546, Week 12: 1059/535, Week 24: 1014/520, Week 36: 982/496, Week 48: 920/460, Week 60: 812/383, Week 72: 645/300, Week 84: 511/233, Week 96: 397/173, Week 108: 288/122, Week 120: 197/79, Week 132: 111/40, Week 144: 51/20, Week 156: 10/5, Week 168: 0/0

Log rank test: p-value = 0,313
*: p < 0,05

Analysis population: A2304 SAF total population

Figure 12.1.6.29: Hypertension (AESI, all)

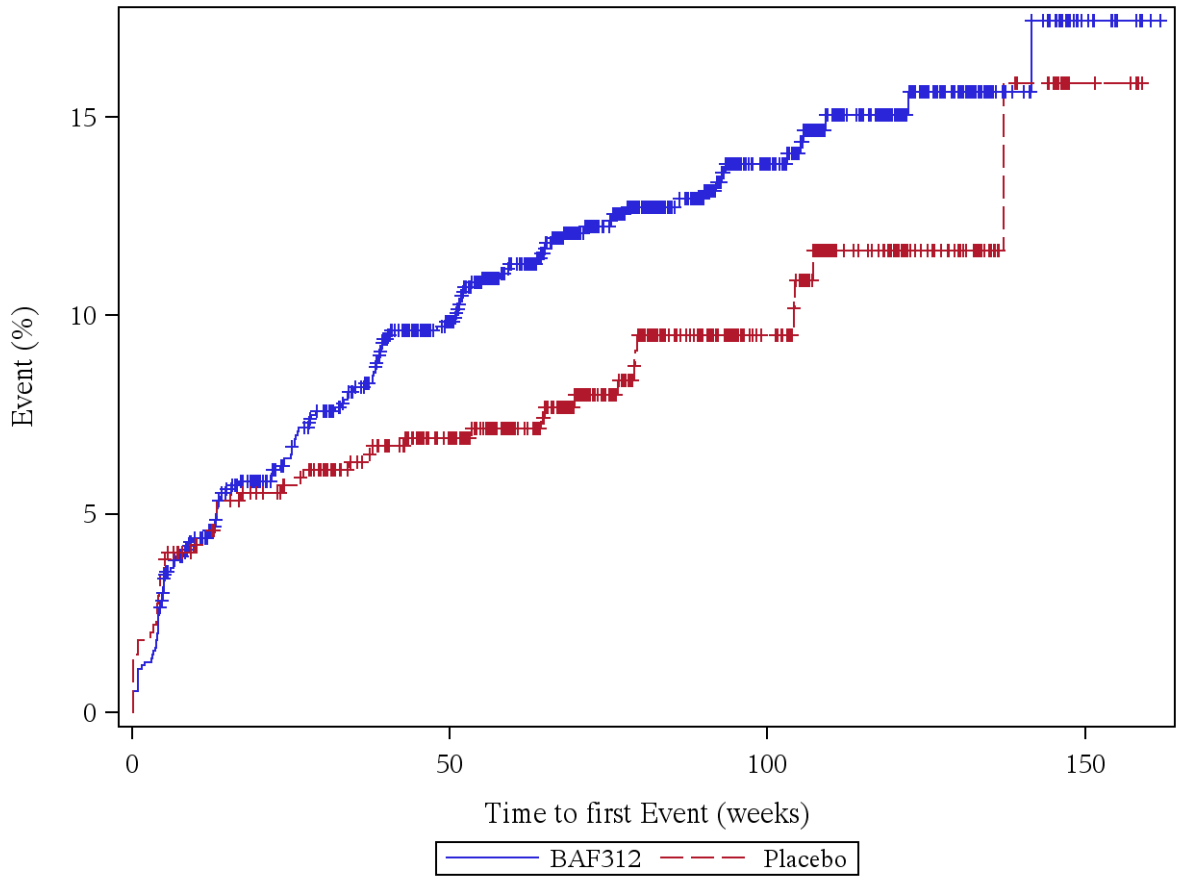


Patients at risk (BAF312/Placebo): Week 0: 1099/546, Week 4: 1077/531, Week 12: 1014/512, Week 24: 951/491, Week 36: 911/464, Week 48: 836/429, Week 60: 723/359, Week 72: 562/275, Week 84: 445/206, Week 96: 346/151, Week 108: 249/103, Week 120: 166/65, Week 132: 92/37, Week 144: 44/18, Week 156: 8/4, Week 168: 0/0

Log rank test: p-value = 0,063
*: p < 0,05

Analysis population: A2304 SAF total population

Figure 12.1.6.30: Hypertension (AESI, not severe)

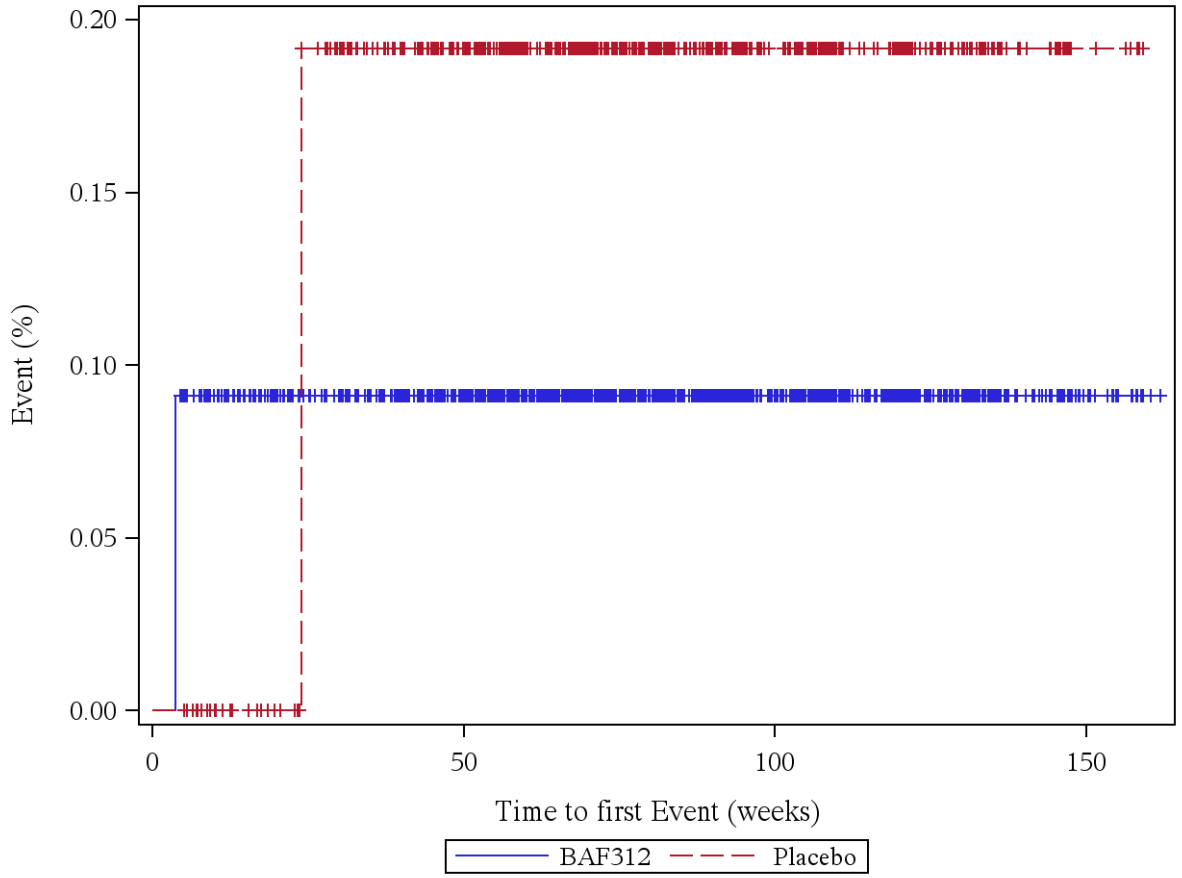


Patients at risk (BAF312/Placebo): Week 0: 1099/546, Week 4: 1077/531, Week 12: 1014/512, Week 24: 951/492, Week 36: 911/465, Week 48: 836/430, Week 60: 723/360, Week 72: 562/276, Week 84: 445/207, Week 96: 346/152, Week 108: 249/104, Week 120: 166/65, Week 132: 92/37, Week 144: 44/18, Week 156: 8/4, Week 168: 0/0

Log rank test: p-value = 0,048 *
*: p < 0,05

Analysis population: A2304 SAF total population

Figure 12.1.6.31: Hypertension (AESI, severe)

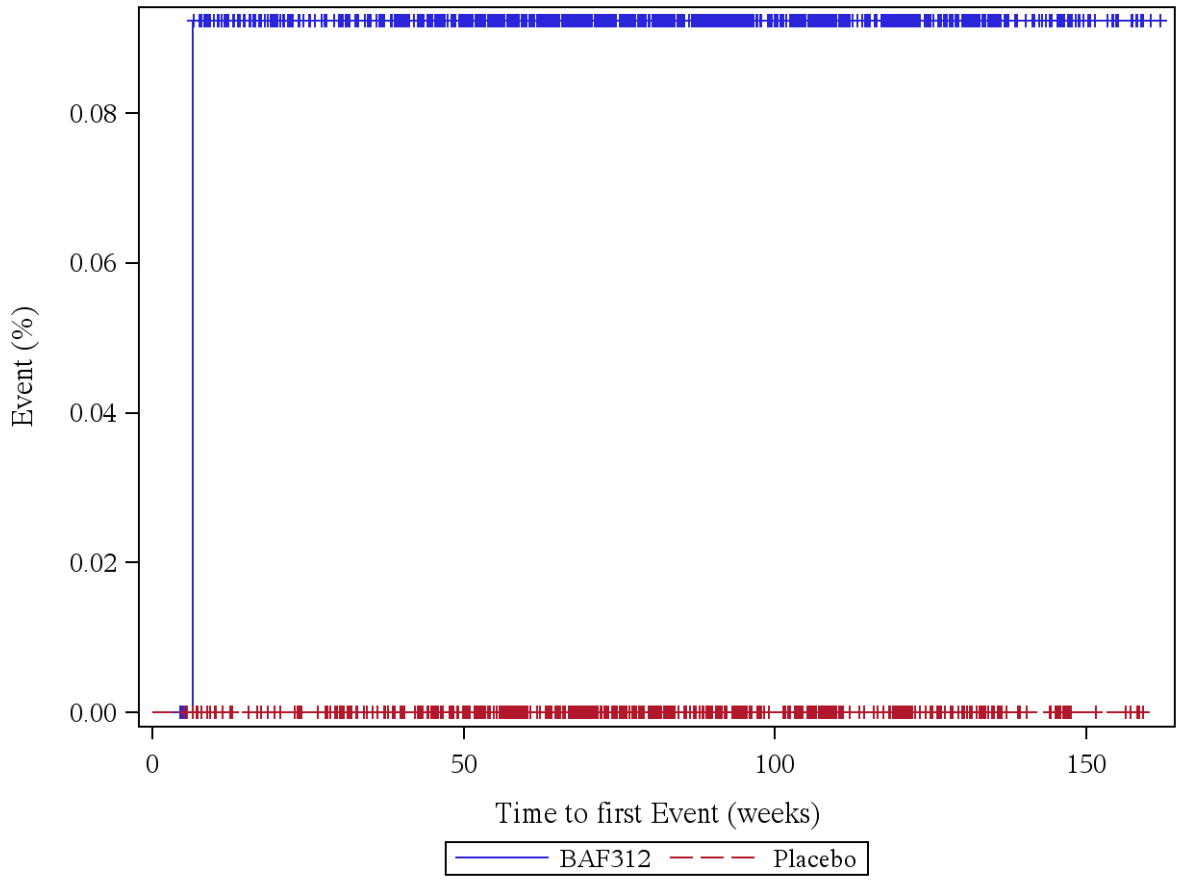


Patients at risk (BAF312/Placebo): Week 0: 1099/546, Week 4: 1098/546, Week 12: 1058/535, Week 24: 1016/520, Week 36: 989/496, Week 48: 924/460, Week 60: 817/387, Week 72: 651/304, Week 84: 515/236, Week 96: 399/175, Week 108: 290/125, Week 120: 199/80, Week 132: 113/40, Week 144: 51/20, Week 156: 10/5, Week 168: 0/0

Log rank test: p-value = 0,623
*: p < 0,05

Analysis population: A2304 SAF total population

Figure 12.1.6.32: Hypertension (AESI, serious)

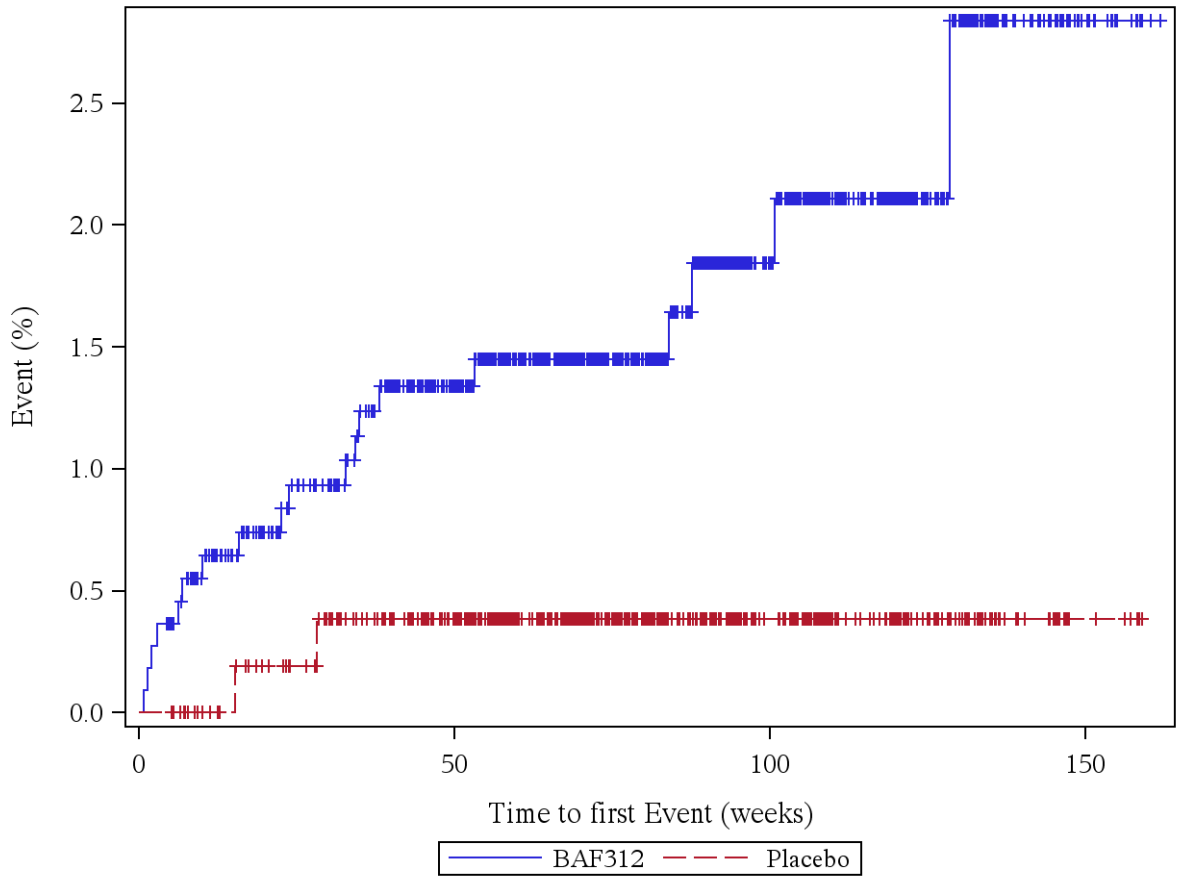


Patients at risk (BAF312/Placebo): Week 0: 1099/546, Week 4: 1099/546, Week 12: 1058/535, Week 24: 1016/521, Week 36: 989/497, Week 48: 924/461, Week 60: 817/388, Week 72: 651/305, Week 84: 515/237, Week 96: 400/176, Week 108: 291/126, Week 120: 200/80, Week 132: 113/40, Week 144: 51/20, Week 156: 10/5, Week 168: 0/0

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

Analysis population: A2304 SAF total population

Figure 12.1.6.33: Seizures (AESI, all)

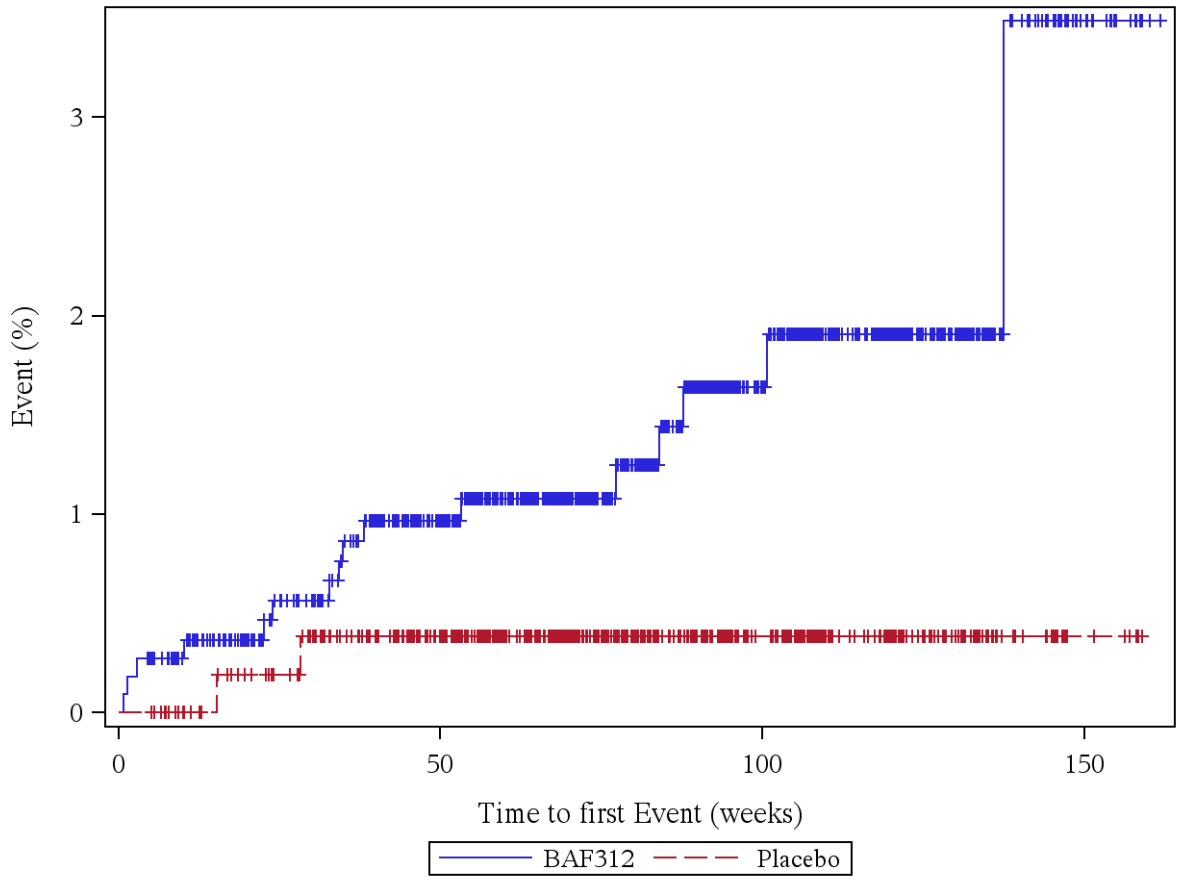


Patients at risk (BAF312/Placebo): Week 0: 1099/546, Week 4: 1095/546, Week 12: 1052/535, Week 24: 1009/520, Week 36: 979/495, Week 48: 914/459, Week 60: 806/386, Week 72: 644/304, Week 84: 507/236, Week 96: 392/175, Week 108: 283/125, Week 120: 195/79, Week 132: 108/39, Week 144: 48/19, Week 156: 9/5, Week 168: 0/0

Log rank test: p-value = 0,023 *
*: p < 0,05

Analysis population: A2304 SAF total population

Figure 12.1.6.34: Seizures (AESI, not severe)

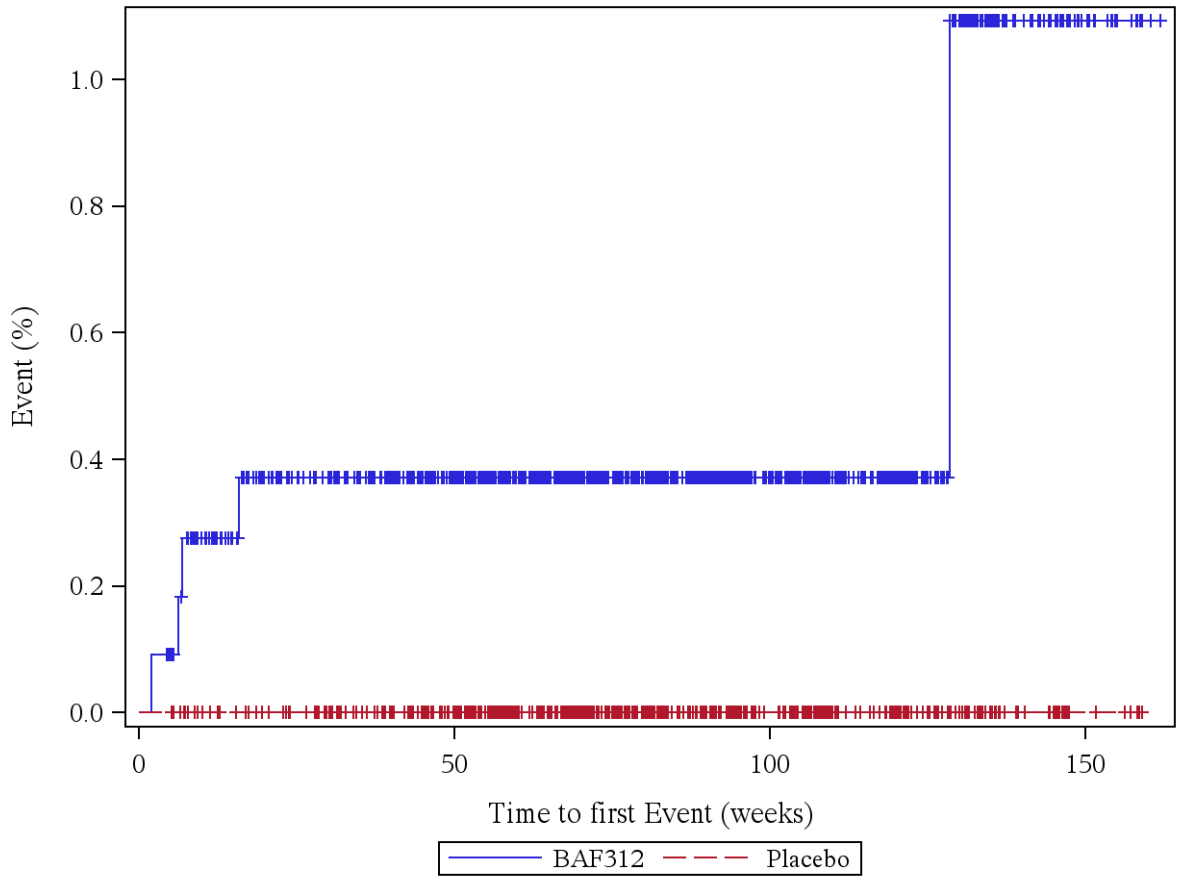


Patients at risk (BAF312/Placebo): Week 0: 1099/546, Week 4: 1096/546, Week 12: 1055/535, Week 24: 1012/520, Week 36: 982/495, Week 48: 917/459, Week 60: 809/386, Week 72: 646/304, Week 84: 508/236, Week 96: 392/175, Week 108: 283/125, Week 120: 195/79, Week 132: 109/39, Week 144: 48/19, Week 156: 9/5, Week 168: 0/0

Log rank test: p-value = 0,051
*: p < 0,05

Analysis population: A2304 SAF total population

Figure 12.1.6.35: Seizures (AESI, severe)

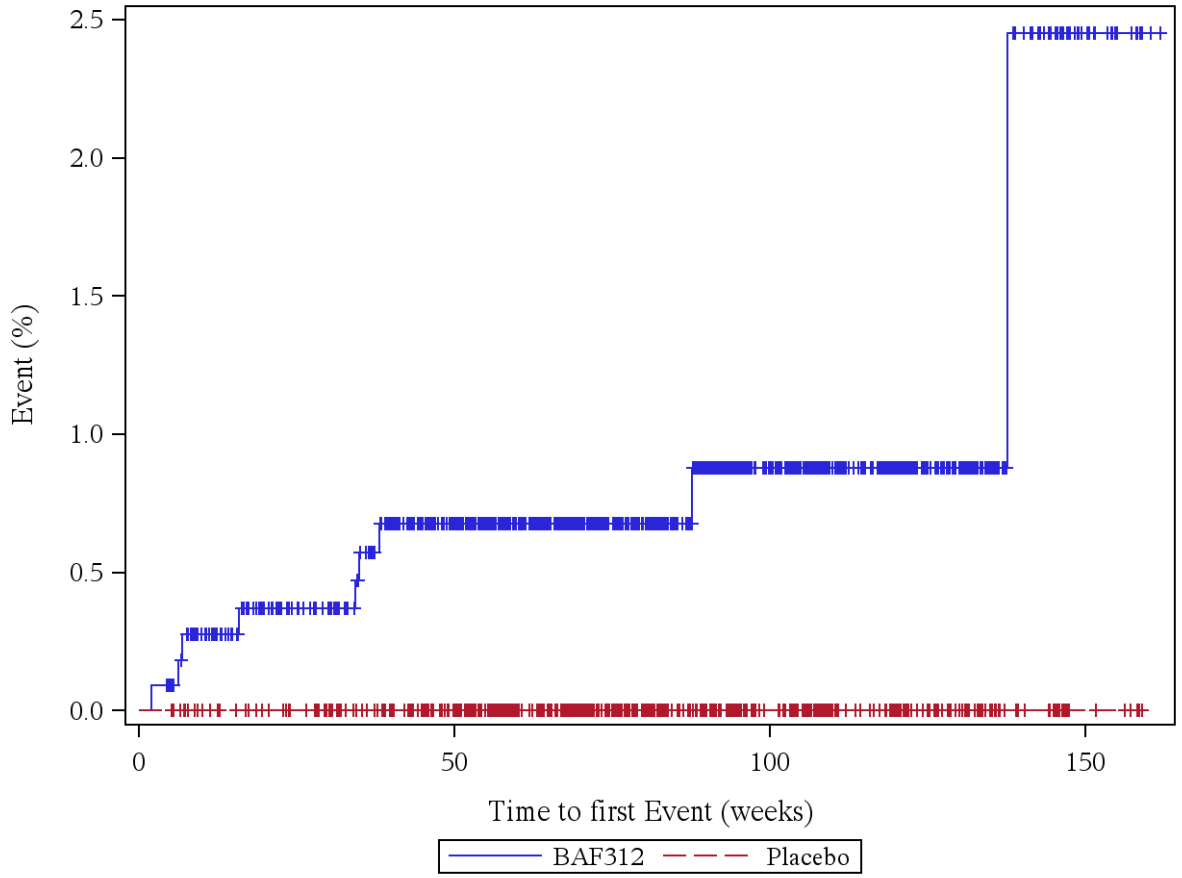


Patients at risk (BAF312/Placebo): Week 0: 1099/546, Week 4: 1098/546, Week 12: 1056/535, Week 24: 1014/521, Week 36: 987/497, Week 48: 922/461, Week 60: 815/388, Week 72: 650/305, Week 84: 514/237, Week 96: 400/176, Week 108: 291/126, Week 120: 200/80, Week 132: 112/40, Week 144: 50/20, Week 156: 9/5, Week 168: 0/0

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

Analysis population: A2304 SAF total population

Figure 12.1.6.36: Seizures (AESI, serious)

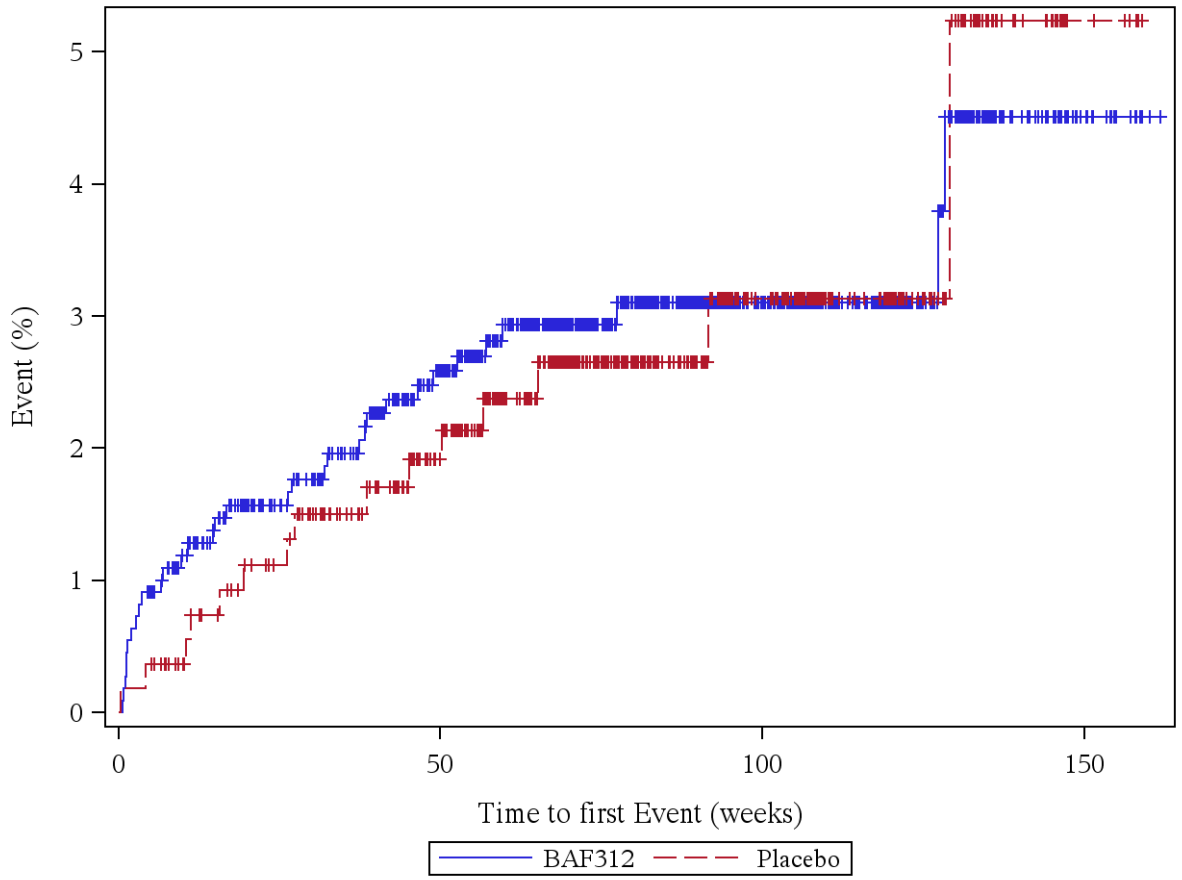


Patients at risk (BAF312/Placebo): Week 0: 1099/546, Week 4: 1098/546, Week 12: 1056/535, Week 24: 1014/521, Week 36: 985/497, Week 48: 919/461, Week 60: 812/388, Week 72: 647/305, Week 84: 511/237, Week 96: 396/176, Week 108: 287/126, Week 120: 197/80, Week 132: 111/40, Week 144: 49/20, Week 156: 9/5, Week 168: 0/0

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

Analysis population: A2304 SAF total population

Figure 12.1.6.37: Thromboembolic events (AESI, all)

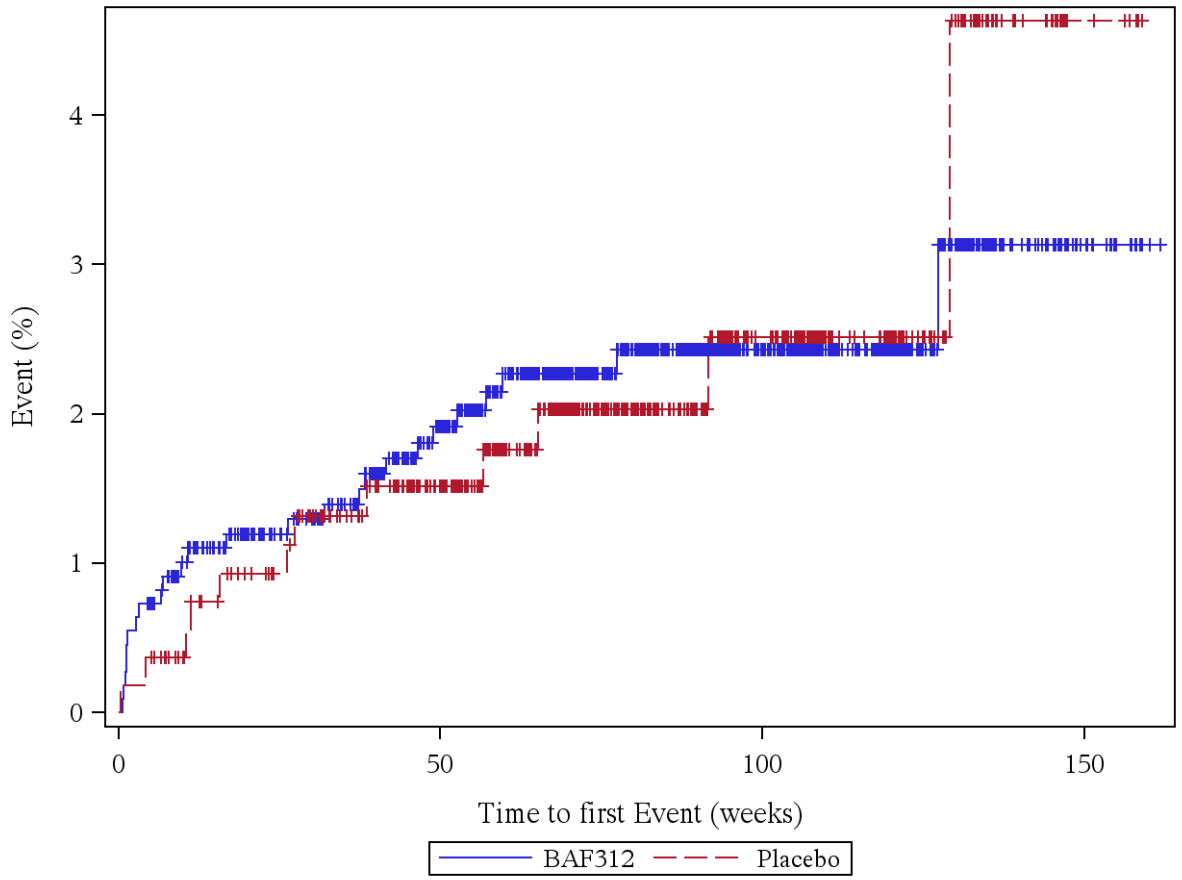


Patients at risk (BAF312/Placebo): Week 0: 1099/546, Week 4: 1089/545, Week 12: 1049/531, Week 24: 1006/516, Week 36: 975/492, Week 48: 909/455, Week 60: 801/381, Week 72: 641/298, Week 84: 505/230, Week 96: 394/170, Week 108: 286/123, Week 120: 196/79, Week 132: 109/39, Week 144: 50/19, Week 156: 9/5, Week 168: 0/0

Log rank test: p-value = 0,811
*: p < 0,05

Analysis population: A2304 SAF total population

Figure 12.1.6.38: Thromboembolic events (AESI, not severe)

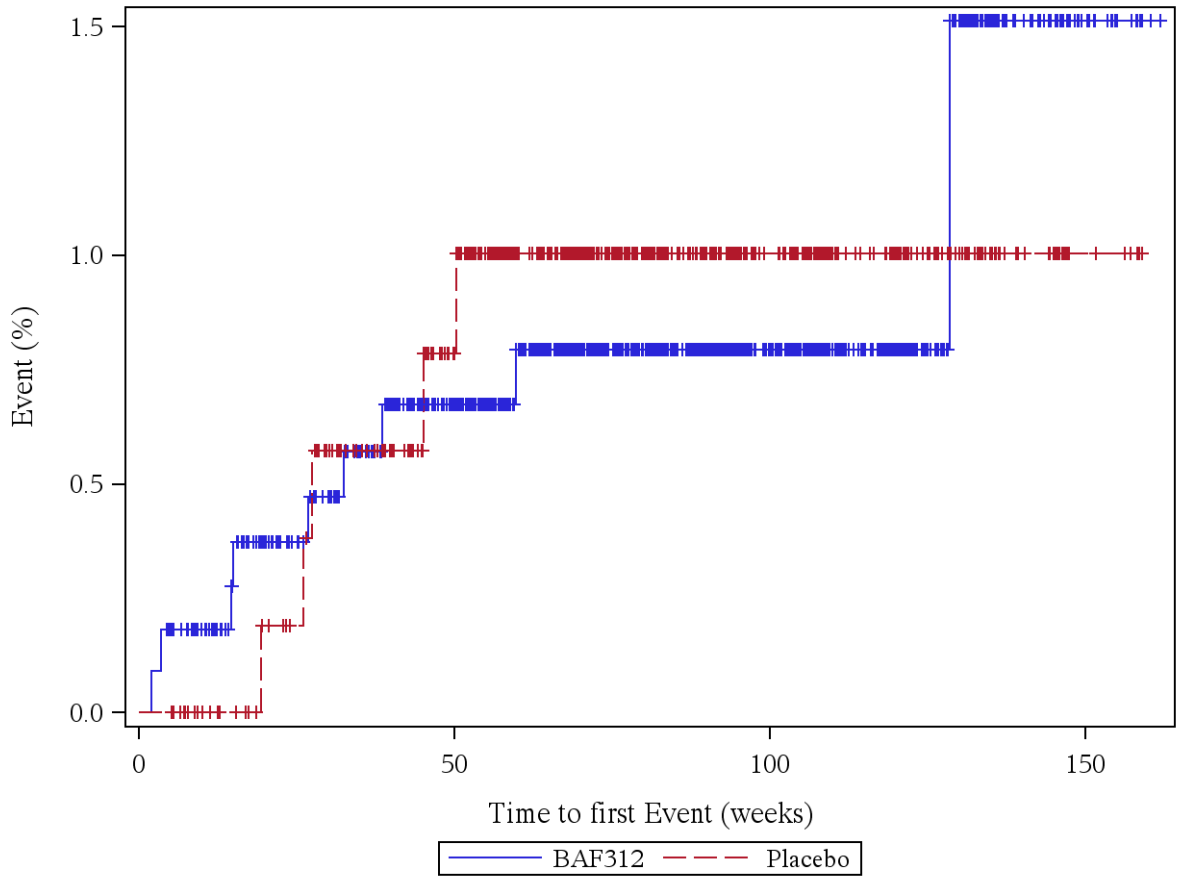


Patients at risk (BAF312/Placebo): Week 0: 1099/546, Week 4: 1091/545, Week 12: 1050/531, Week 24: 1008/516, Week 36: 979/492, Week 48: 911/456, Week 60: 803/383, Week 72: 643/299, Week 84: 507/231, Week 96: 394/170, Week 108: 286/123, Week 120: 196/79, Week 132: 110/39, Week 144: 51/19, Week 156: 10/5, Week 168: 0/0

Log rank test: p-value = 0,958
*: p < 0,05

Analysis population: A2304 SAF total population

Figure 12.1.6.39: Thromboembolic events (AESI, severe)

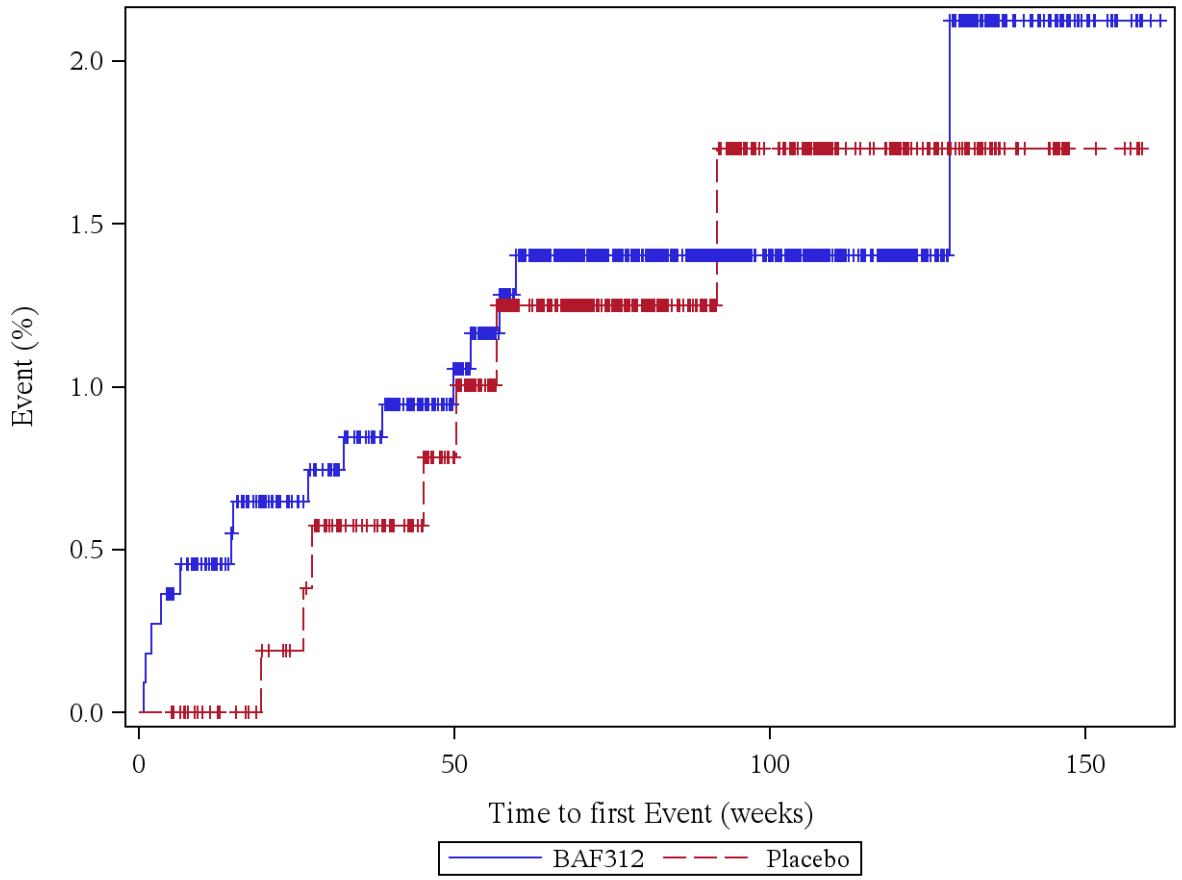


Patients at risk (BAF312/Placebo): Week 0: 1099/546, Week 4: 1097/546, Week 12: 1058/535, Week 24: 1015/521, Week 36: 986/496, Week 48: 923/459, Week 60: 815/385, Week 72: 649/303, Week 84: 513/235, Week 96: 400/175, Week 108: 291/125, Week 120: 200/80, Week 132: 112/40, Week 144: 50/20, Week 156: 9/5, Week 168: 0/0

Log rank test: p-value = 0,826
*: p < 0,05

Analysis population: A2304 SAF total population

Figure 12.1.6.40: Thromboembolic events (AESI, serious)

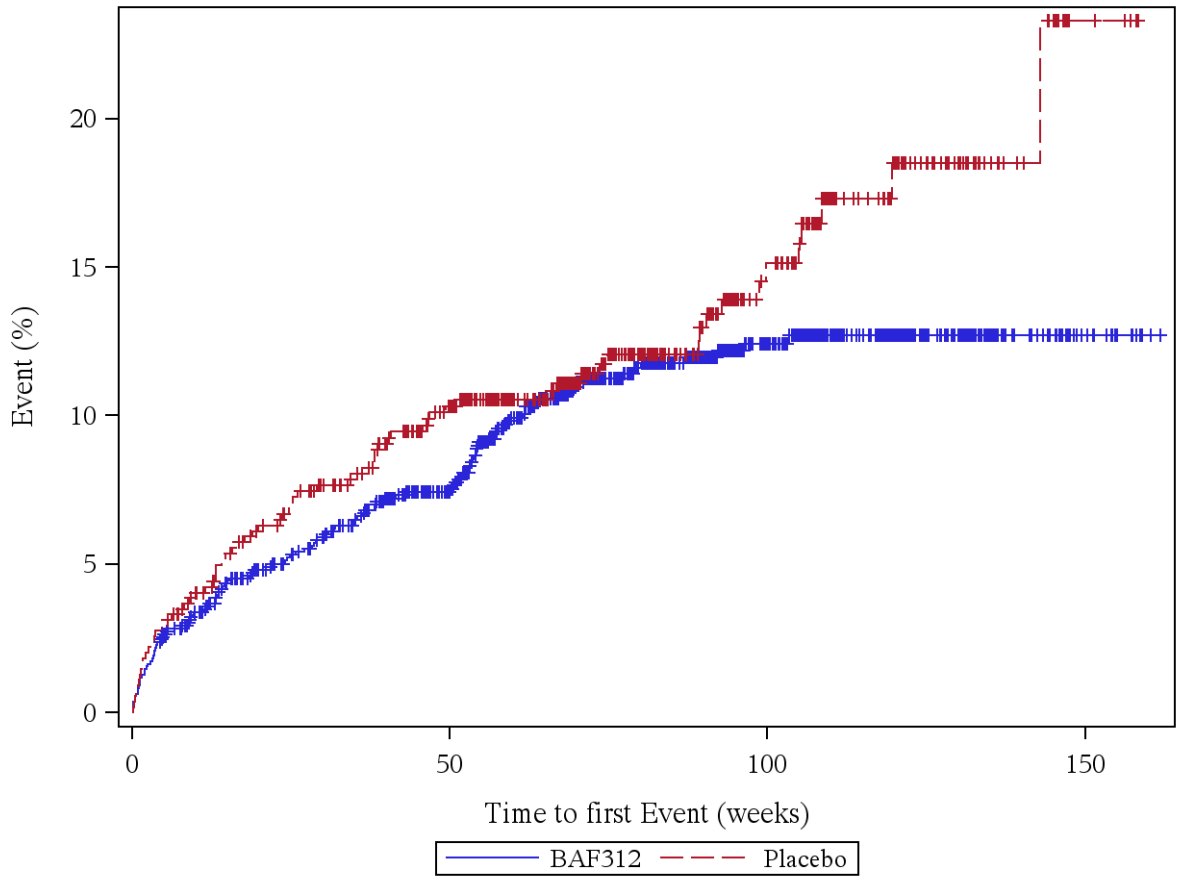


Patients at risk (BAF312/Placebo): Week 0: 1099/546, Week 4: 1095/546, Week 12: 1057/535, Week 24: 1014/521, Week 36: 985/496, Week 48: 922/459, Week 60: 812/384, Week 72: 648/302, Week 84: 512/234, Week 96: 399/173, Week 108: 290/125, Week 120: 199/80, Week 132: 112/40, Week 144: 50/20, Week 156: 9/5, Week 168: 0/0

Log rank test: p-value = 0,916
*: p < 0,05

Analysis population: A2304 SAF total population

Figure 12.1.6.41: Respiratory disorders (AESI, all)

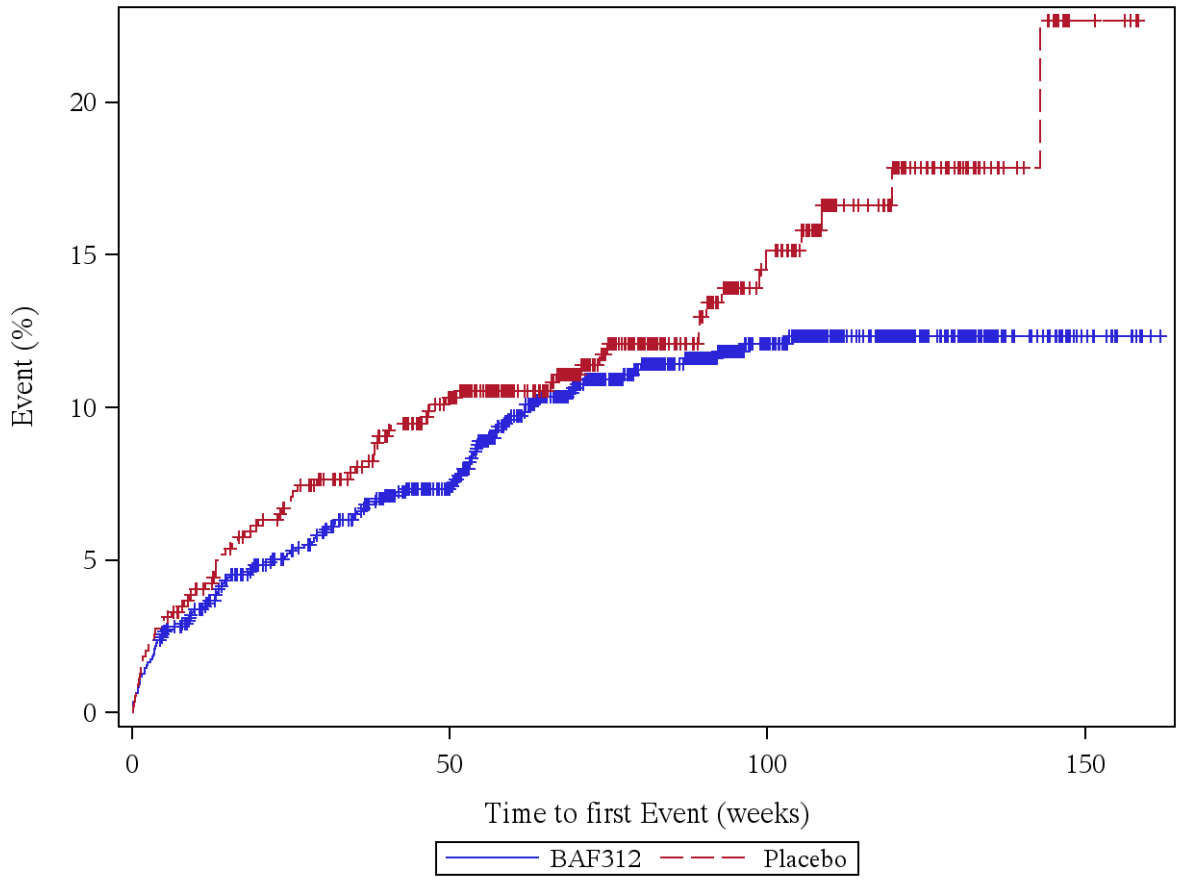


Patients at risk (BAF312/Placebo): Week 0: 1099/546, Week 4: 1073/531, Week 12: 1020/513, Week 24: 966/486, Week 36: 926/459, Week 48: 856/418, Week 60: 739/350, Week 72: 585/274, Week 84: 463/207, Week 96: 358/150, Week 108: 262/105, Week 120: 178/63, Week 132: 102/30, Week 144: 48/16, Week 156: 10/4, Week 168: 0/0

Log rank test: p-value = 0,139
*: p < 0,05

Analysis population: A2304 SAF total population

Figure 12.1.6.42: Respiratory disorders (AESI, not severe)

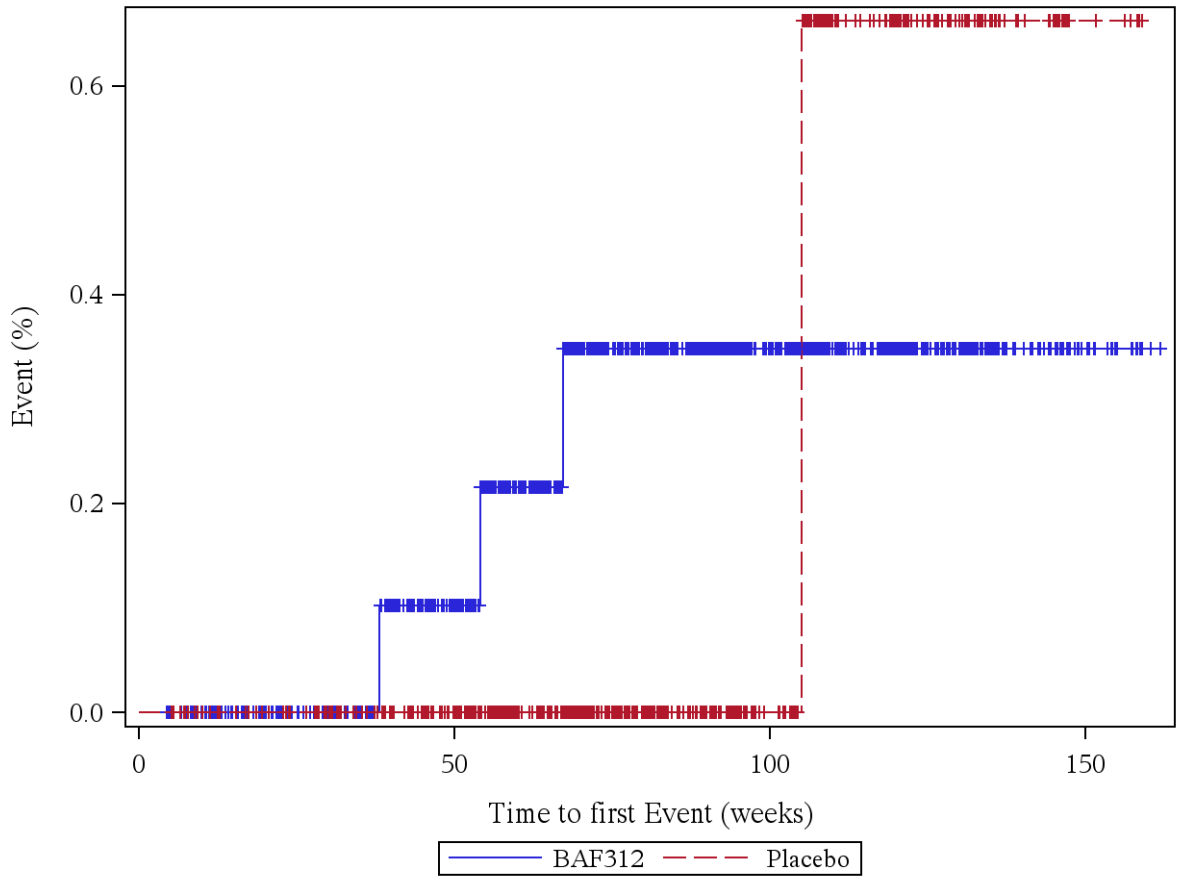


Patients at risk (BAF312/Placebo): Week 0: 1099/546, Week 4: 1073/531, Week 12: 1020/513, Week 24: 966/486, Week 36: 926/459, Week 48: 857/418, Week 60: 741/350, Week 72: 588/274, Week 84: 465/207, Week 96: 359/150, Week 108: 262/106, Week 120: 178/63, Week 132: 102/30, Week 144: 48/16, Week 156: 10/4, Week 168: 0/0

Log rank test: p-value = 0,123
*: p < 0,05

Analysis population: A2304 SAF total population

Figure 12.1.6.43: Respiratory disorders (AESI, severe)

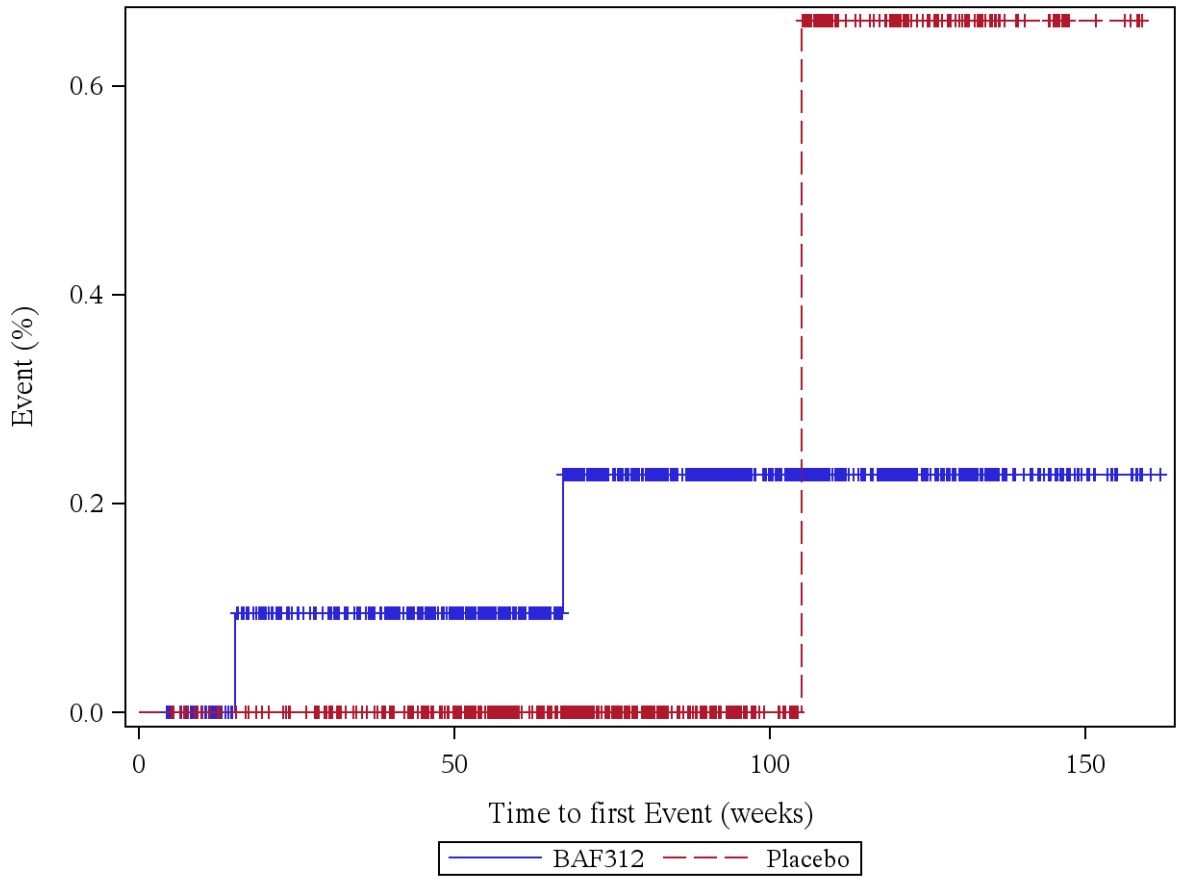


Patients at risk (BAF312/Placebo): Week 0: 1099/546, Week 4: 1099/546, Week 12: 1059/535, Week 24: 1017/521, Week 36: 990/497, Week 48: 924/461, Week 60: 816/388, Week 72: 649/305, Week 84: 514/237, Week 96: 399/176, Week 108: 291/125, Week 120: 200/80, Week 132: 113/40, Week 144: 51/20, Week 156: 10/5, Week 168: 0/0

Log rank test: p-value = 0,762
*: p < 0,05

Analysis population: A2304 SAF total population

Figure 12.1.6.44: Respiratory disorders (AESI, serious)

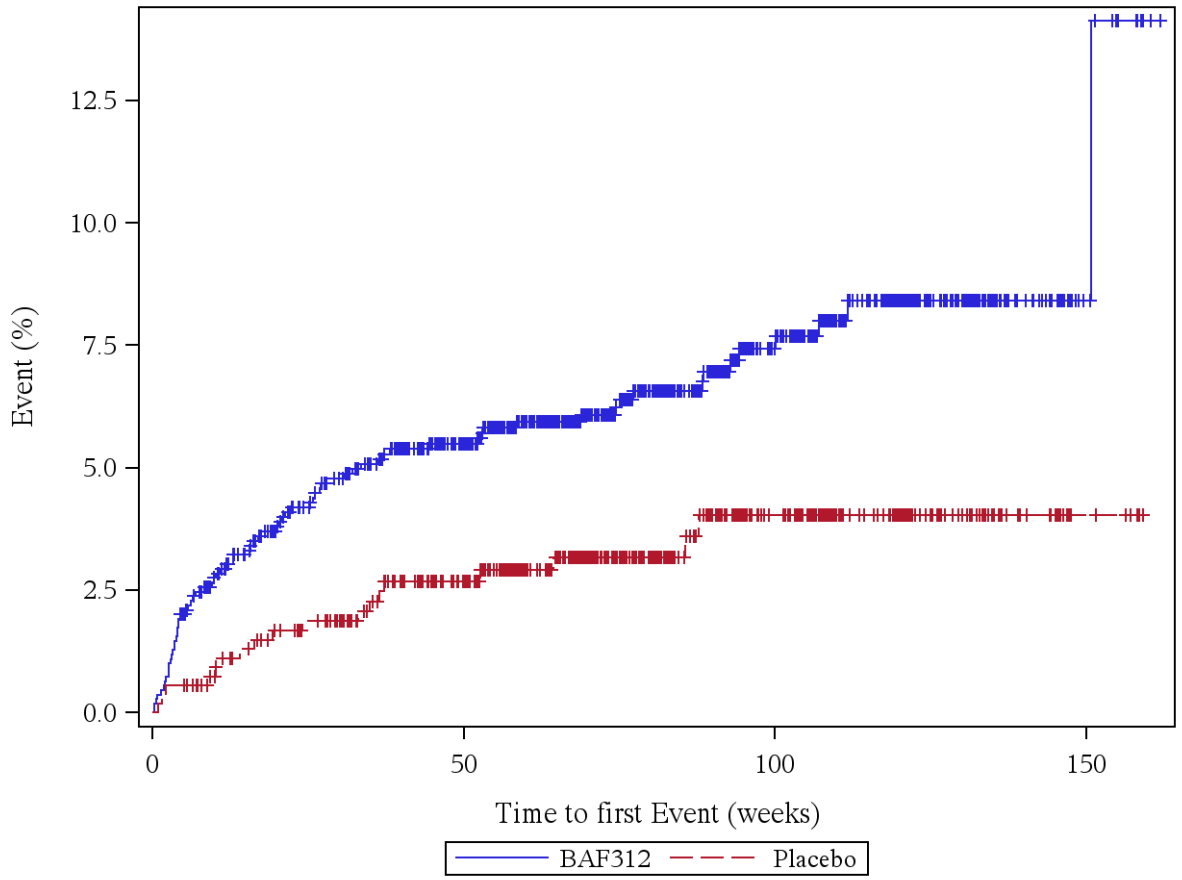


Patients at risk (BAF312/Placebo): Week 0: 1099/546, Week 4: 1099/546, Week 12: 1059/535, Week 24: 1016/521, Week 36: 989/497, Week 48: 924/461, Week 60: 817/388, Week 72: 651/305, Week 84: 516/237, Week 96: 400/176, Week 108: 291/125, Week 120: 200/80, Week 132: 113/40, Week 144: 51/20, Week 156: 10/5, Week 168: 0/0

Log rank test: p-value = 0,961
*: p < 0,05

Analysis population: A2304 SAF total population

Figure 12.1.6.45: Peripheral edema/swelling (AESI, all)

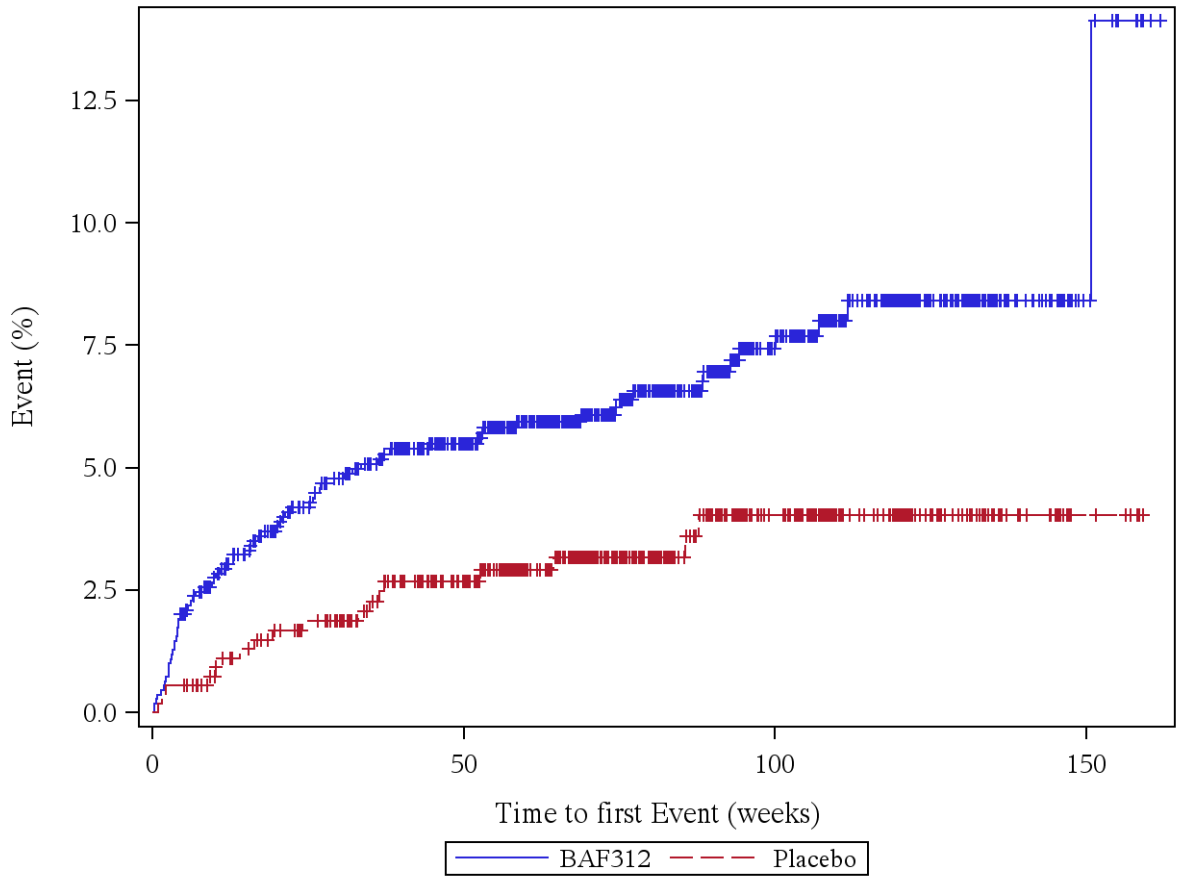


Patients at risk (BAF312/Placebo): Week 0: 1099/546, Week 4: 1080/543, Week 12: 1027/529, Week 24: 975/512, Week 36: 943/485, Week 48: 876/449, Week 60: 770/378, Week 72: 616/295, Week 84: 483/229, Week 96: 372/168, Week 108: 269/119, Week 120: 181/73, Week 132: 102/37, Week 144: 45/19, Week 156: 8/5, Week 168: 0/0

Log rank test: p-value = 0,005 *
*: p < 0,05

Analysis population: A2304 SAF total population

Figure 12.1.6.46: Peripheral edema/swelling (AESI, not severe)

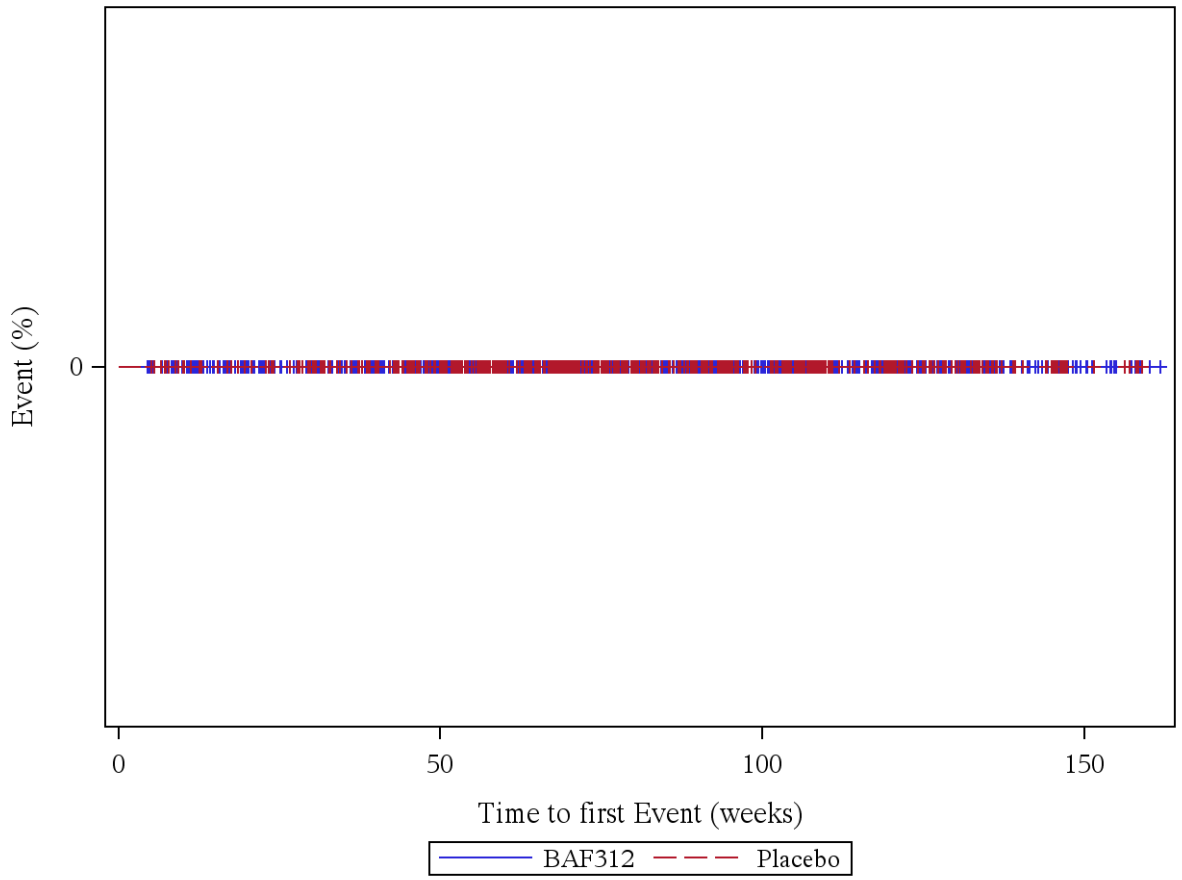


Patients at risk (BAF312/Placebo): Week 0: 1099/546, Week 4: 1080/543, Week 12: 1027/529, Week 24: 975/512, Week 36: 943/485, Week 48: 876/449, Week 60: 770/378, Week 72: 616/295, Week 84: 483/229, Week 96: 372/168, Week 108: 269/119, Week 120: 181/73, Week 132: 102/37, Week 144: 45/19, Week 156: 8/5, Week 168: 0/0

Log rank test: p-value = 0,005 *
*: p < 0,05

Analysis population: A2304 SAF total population

Figure 12.1.6.47: Peripheral edema/swelling (AESI, severe)

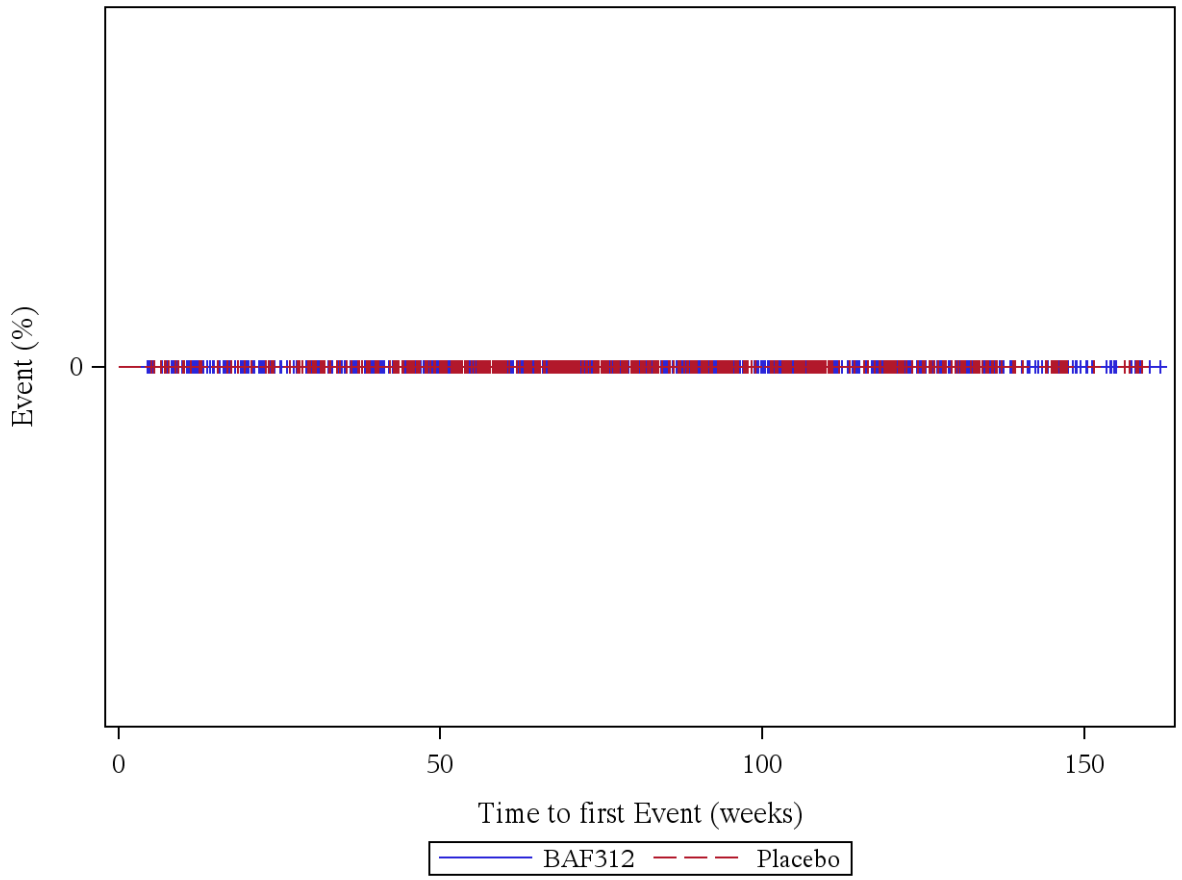


Patients at risk (BAF312/Placebo): Week 0: 1099/546, Week 4: 1099/546, Week 12: 1059/535, Week 24: 1017/521, Week 36: 990/497, Week 48: 925/461, Week 60: 818/388, Week 72: 652/305, Week 84: 516/237, Week 96: 400/176, Week 108: 291/126, Week 120: 200/80, Week 132: 113/40, Week 144: 51/20, Week 156: 10/5, Week 168: 0/0

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

Analysis population: A2304 SAF total population

Figure 12.1.6.48: Peripheral edema/swelling (AESI, serious)

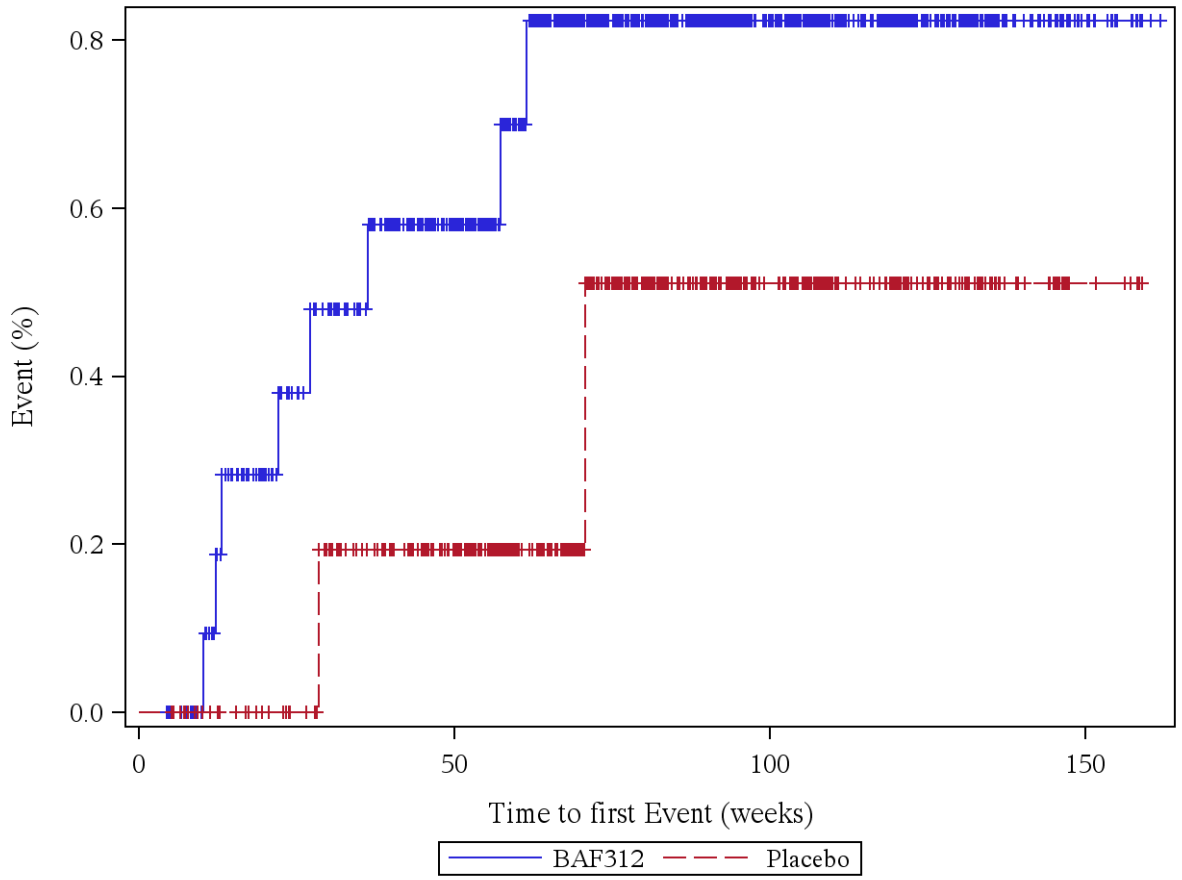


Patients at risk (BAF312/Placebo): Week 0: 1099/546, Week 4: 1099/546, Week 12: 1059/535, Week 24: 1017/521, Week 36: 990/497, Week 48: 925/461, Week 60: 818/388, Week 72: 652/305, Week 84: 516/237, Week 96: 400/176, Week 108: 291/126, Week 120: 200/80, Week 132: 113/40, Week 144: 51/20, Week 156: 10/5, Week 168: 0/0

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

Analysis population: A2304 SAF total population

Figure 12.1.6.49: Asthma/bronchospasm (AESI, all)

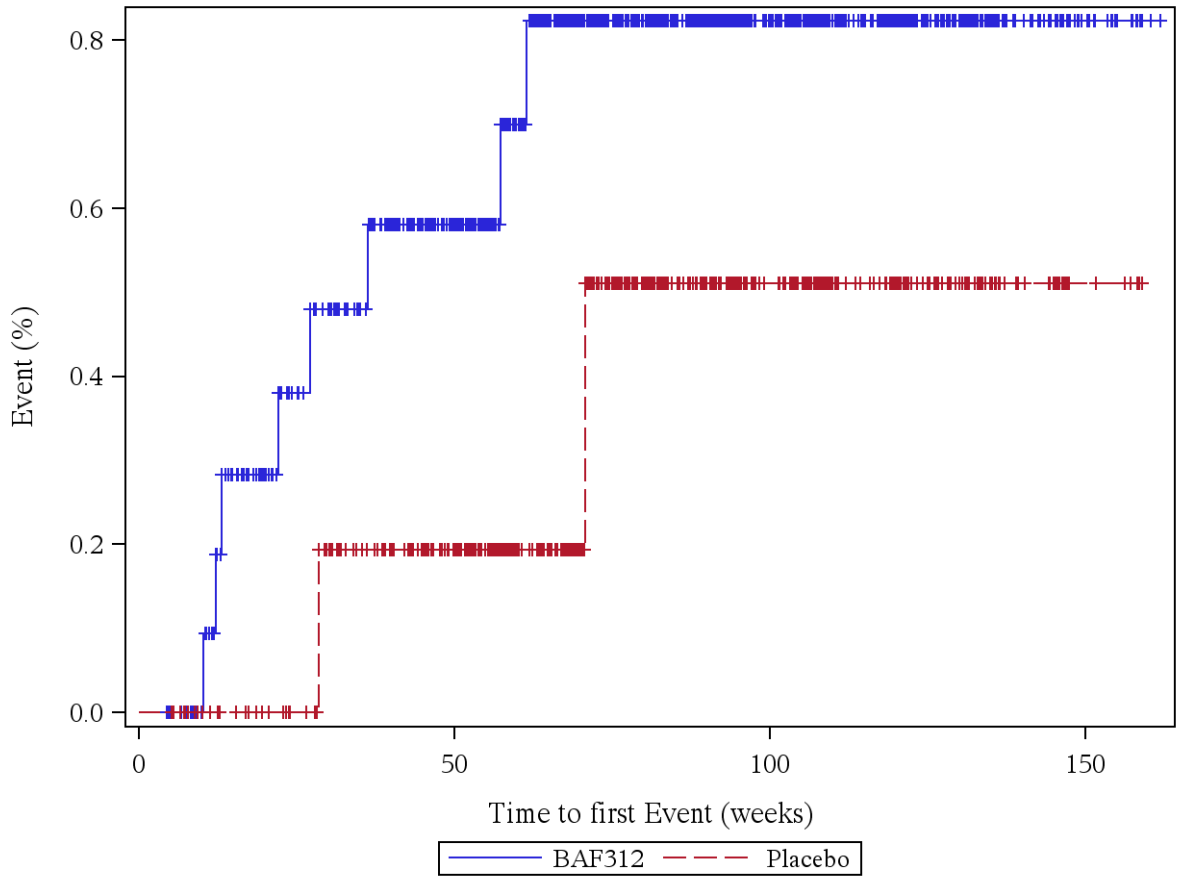


Patients at risk (BAF312/Placebo): Week 0: 1099/546, Week 4: 1099/546, Week 12: 1058/535, Week 24: 1013/521, Week 36: 985/497, Week 48: 919/461, Week 60: 811/388, Week 72: 647/304, Week 84: 511/236, Week 96: 397/175, Week 108: 288/125, Week 120: 197/79, Week 132: 112/40, Week 144: 51/20, Week 156: 10/5, Week 168: 0/0

Log rank test: p-value = 0,372
*: p < 0,05

Analysis population: A2304 SAF total population

Figure 12.1.6.50: Asthma/bronchospasm (AESI, not severe)

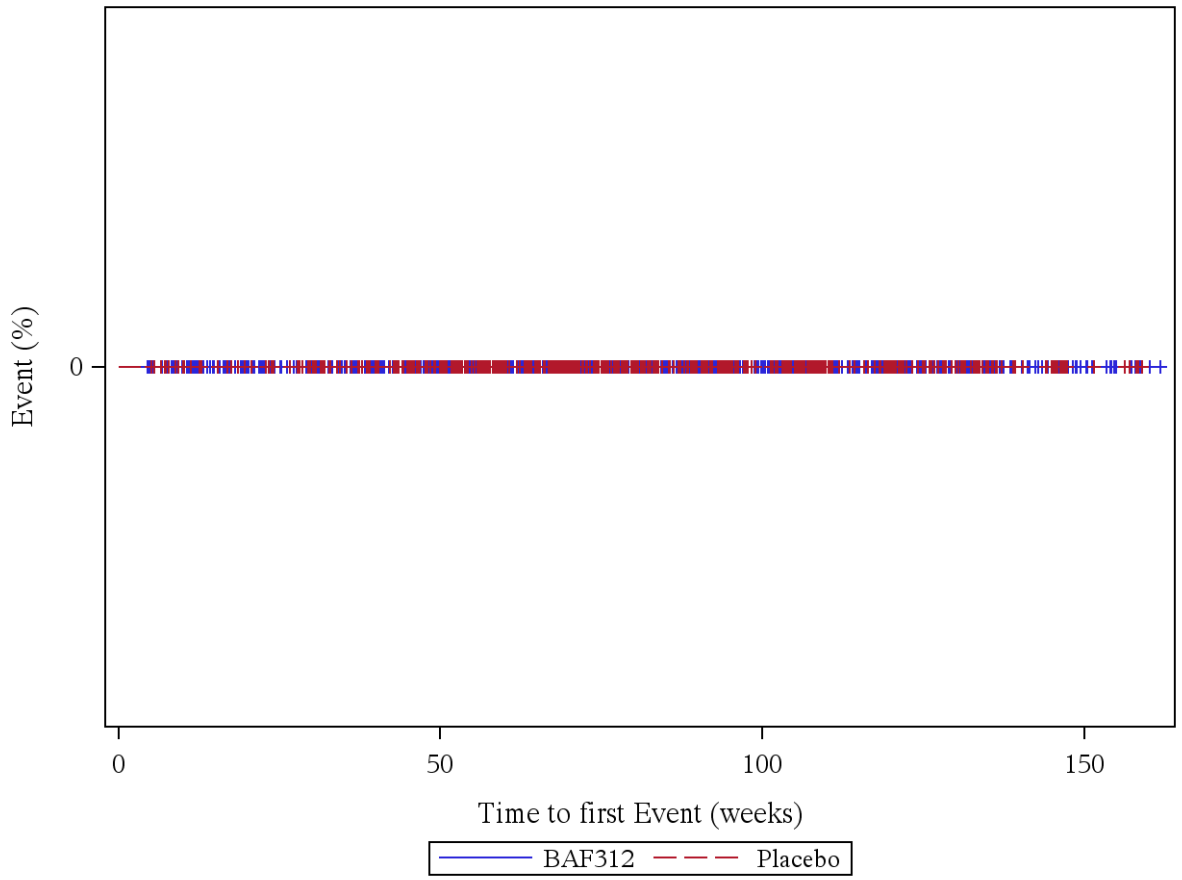


Patients at risk (BAF312/Placebo): Week 0: 1099/546, Week 4: 1099/546, Week 12: 1058/535, Week 24: 1013/521, Week 36: 985/497, Week 48: 919/461, Week 60: 811/388, Week 72: 647/304, Week 84: 511/236, Week 96: 397/175, Week 108: 288/125, Week 120: 197/79, Week 132: 112/40, Week 144: 51/20, Week 156: 10/5, Week 168: 0/0

Log rank test: p-value = 0,372
*: p < 0,05

Analysis population: A2304 SAF total population

Figure 12.1.6.51: Asthma/bronchospasm (AESI, severe)

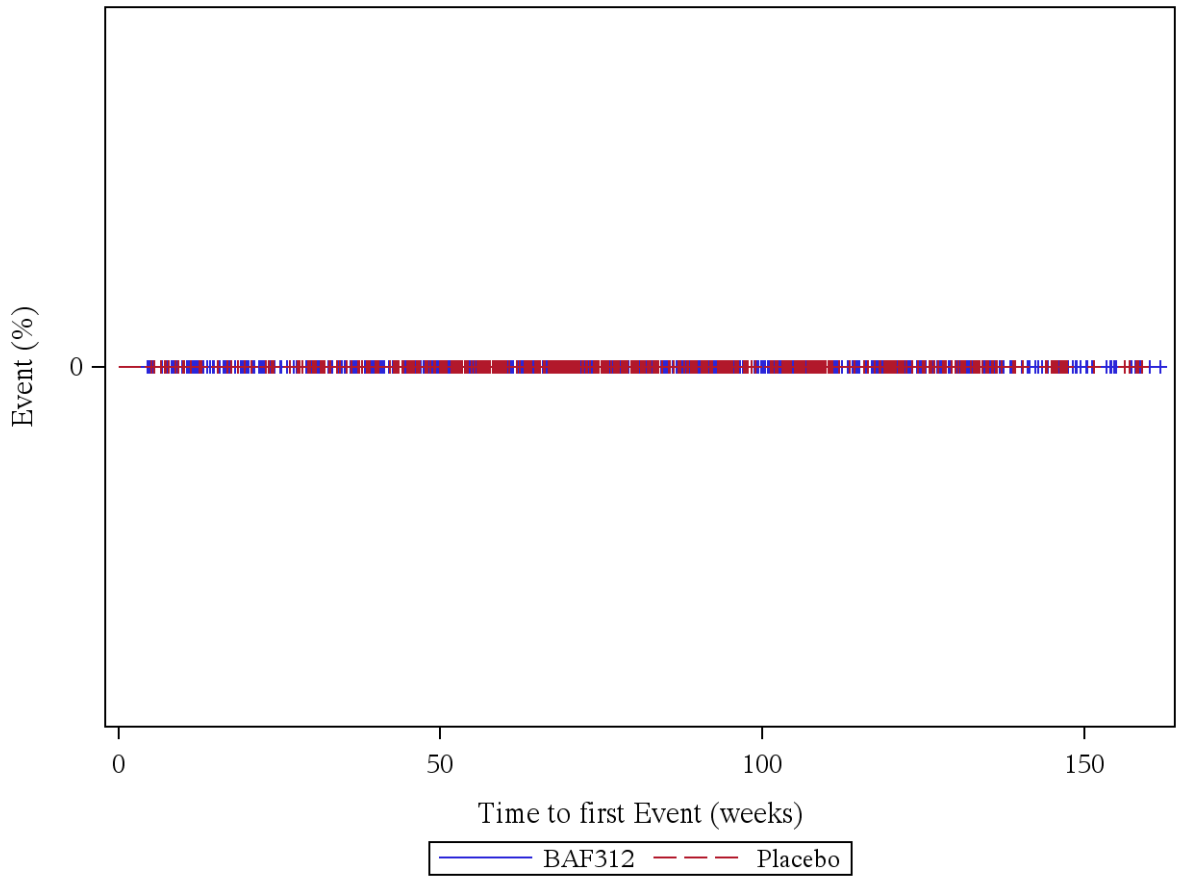


Patients at risk (BAF312/Placebo): Week 0: 1099/546, Week 4: 1099/546, Week 12: 1059/535, Week 24: 1017/521, Week 36: 990/497, Week 48: 925/461, Week 60: 818/388, Week 72: 652/305, Week 84: 516/237, Week 96: 400/176, Week 108: 291/126, Week 120: 200/80, Week 132: 113/40, Week 144: 51/20, Week 156: 10/5, Week 168: 0/0

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

Analysis population: A2304 SAF total population

Figure 12.1.6.52: Asthma/bronchospasm (AESI, serious)

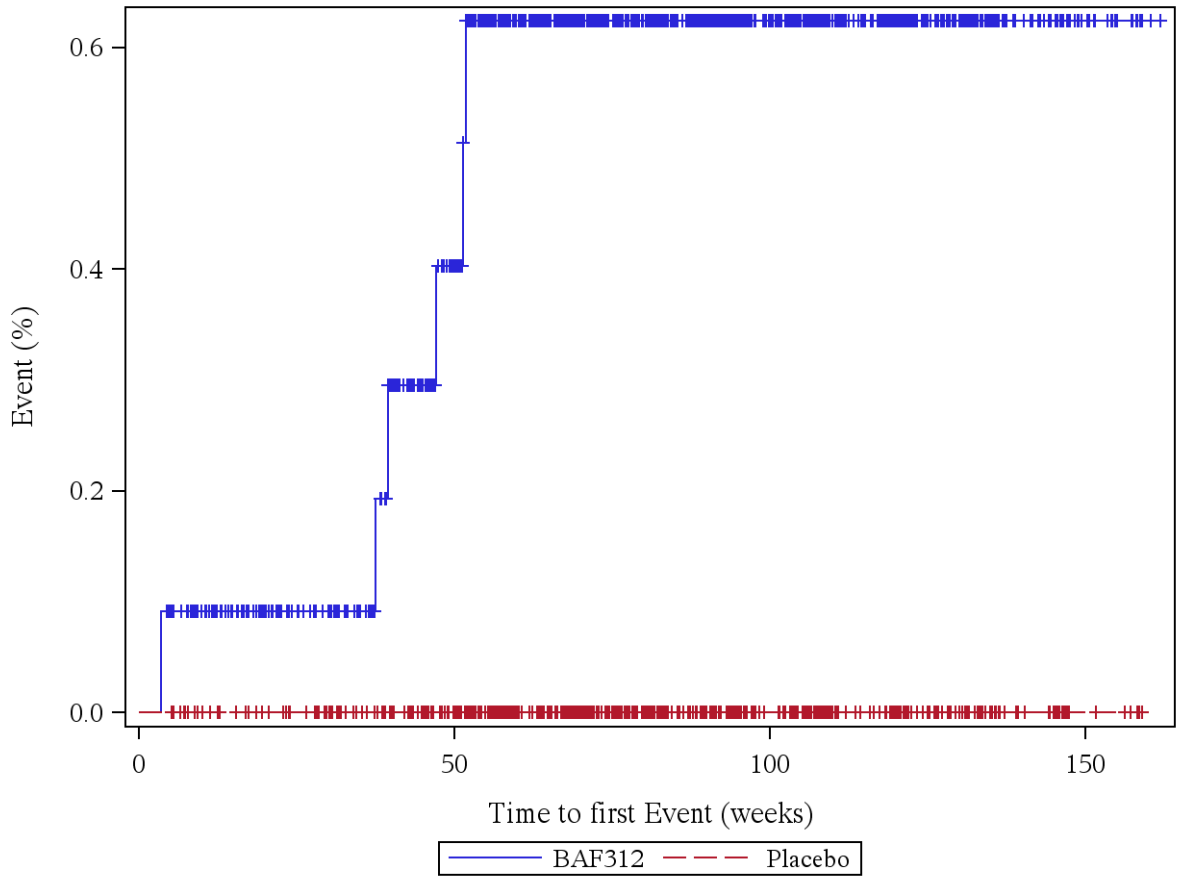


Patients at risk (BAF312/Placebo): Week 0: 1099/546, Week 4: 1099/546, Week 12: 1059/535, Week 24: 1017/521, Week 36: 990/497, Week 48: 925/461, Week 60: 818/388, Week 72: 652/305, Week 84: 516/237, Week 96: 400/176, Week 108: 291/126, Week 120: 200/80, Week 132: 113/40, Week 144: 51/20, Week 156: 10/5, Week 168: 0/0

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

Analysis population: A2304 SAF total population

Figure 12.1.6.53: Pregnancy and neonatal topics (AESI, all)

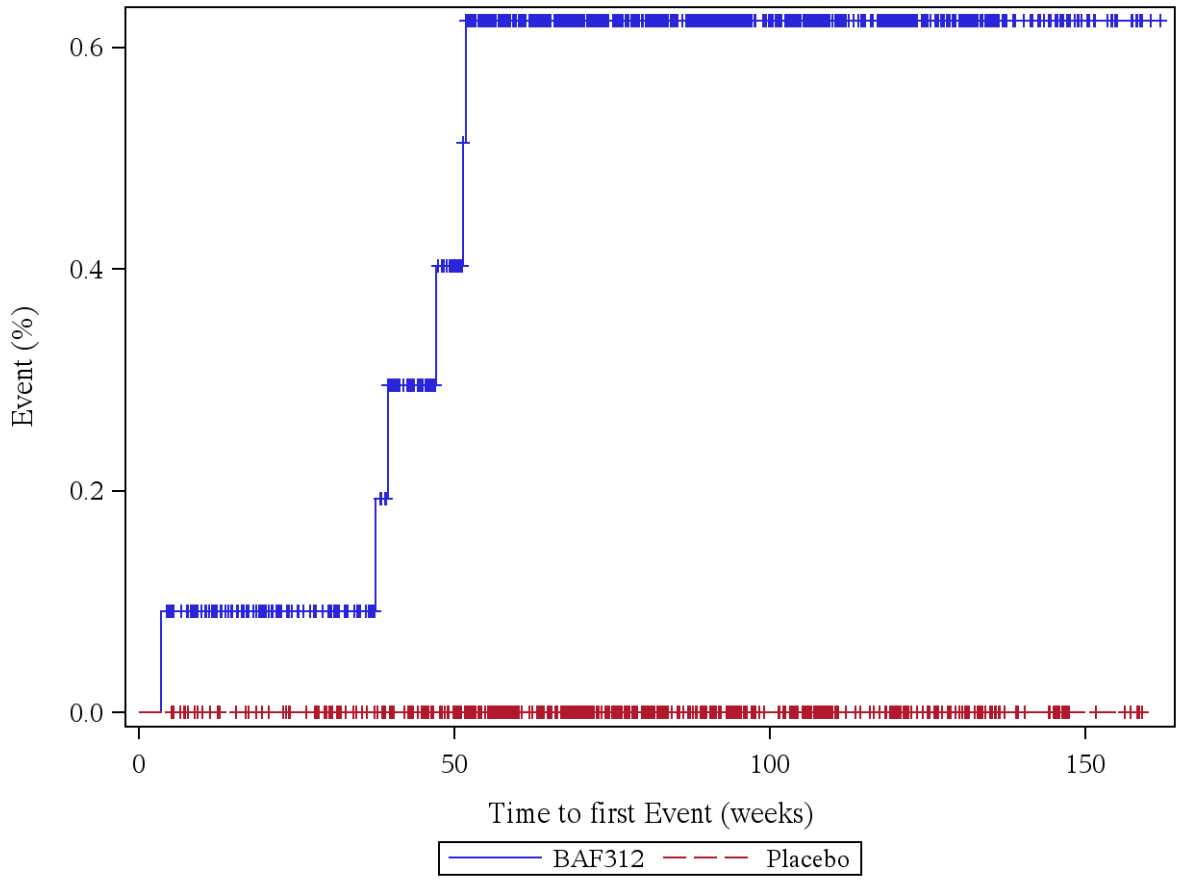


Patients at risk (BAF312/Placebo): Week 0: 1099/546, Week 4: 1098/546, Week 12: 1058/535, Week 24: 1016/521, Week 36: 989/497, Week 48: 921/461, Week 60: 812/388, Week 72: 647/305, Week 84: 513/237, Week 96: 399/176, Week 108: 290/126, Week 120: 199/80, Week 132: 113/40, Week 144: 51/20, Week 156: 10/5, Week 168: 0/0

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

Analysis population: A2304 SAF total population

Figure 12.1.6.54: Pregnancy and neonatal topics (AESI, not severe)

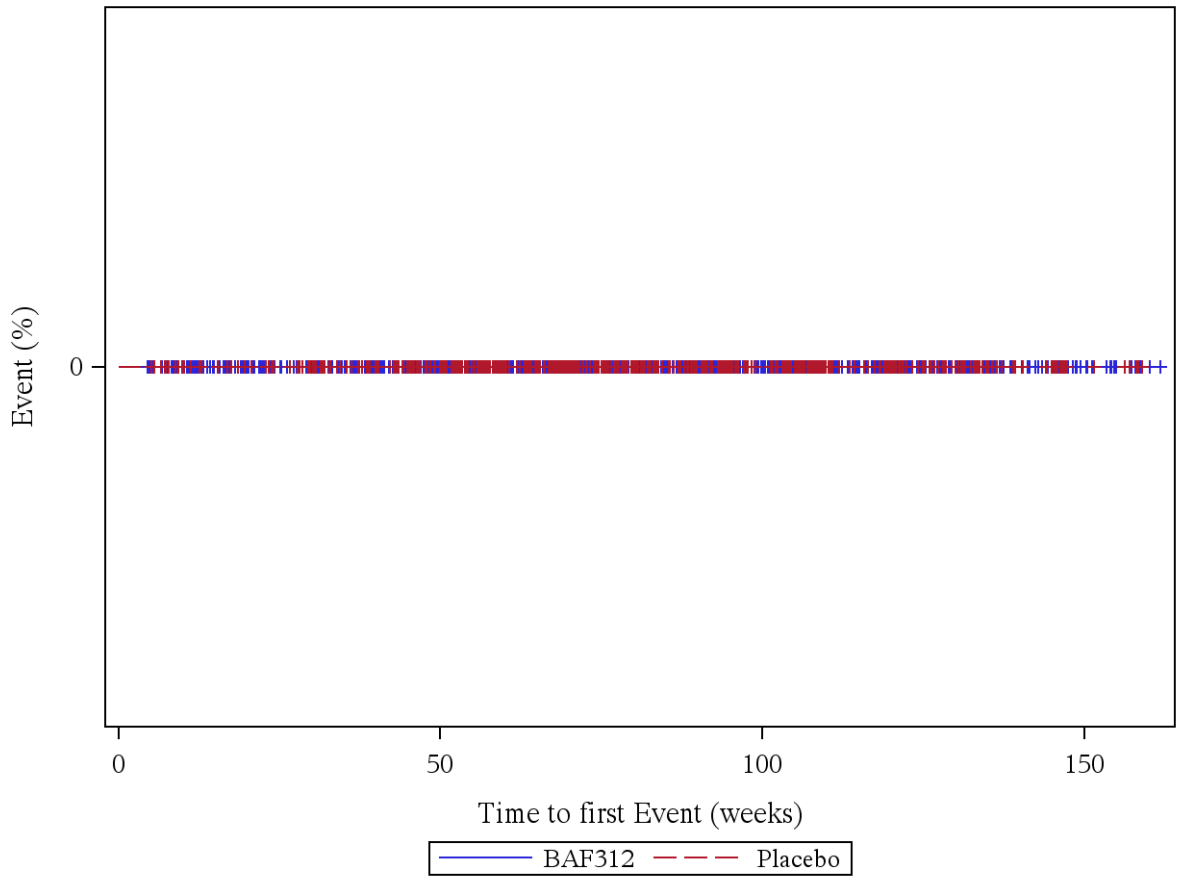


Patients at risk (BAF312/Placebo): Week 0: 1099/546, Week 4: 1098/546, Week 12: 1058/535, Week 24: 1016/521, Week 36: 989/497, Week 48: 921/461, Week 60: 812/388, Week 72: 647/305, Week 84: 513/237, Week 96: 399/176, Week 108: 290/126, Week 120: 199/80, Week 132: 113/40, Week 144: 51/20, Week 156: 10/5, Week 168: 0/0

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

Analysis population: A2304 SAF total population

Figure 12.1.6.55: Pregnancy and neonatal topics (AESI, severe)

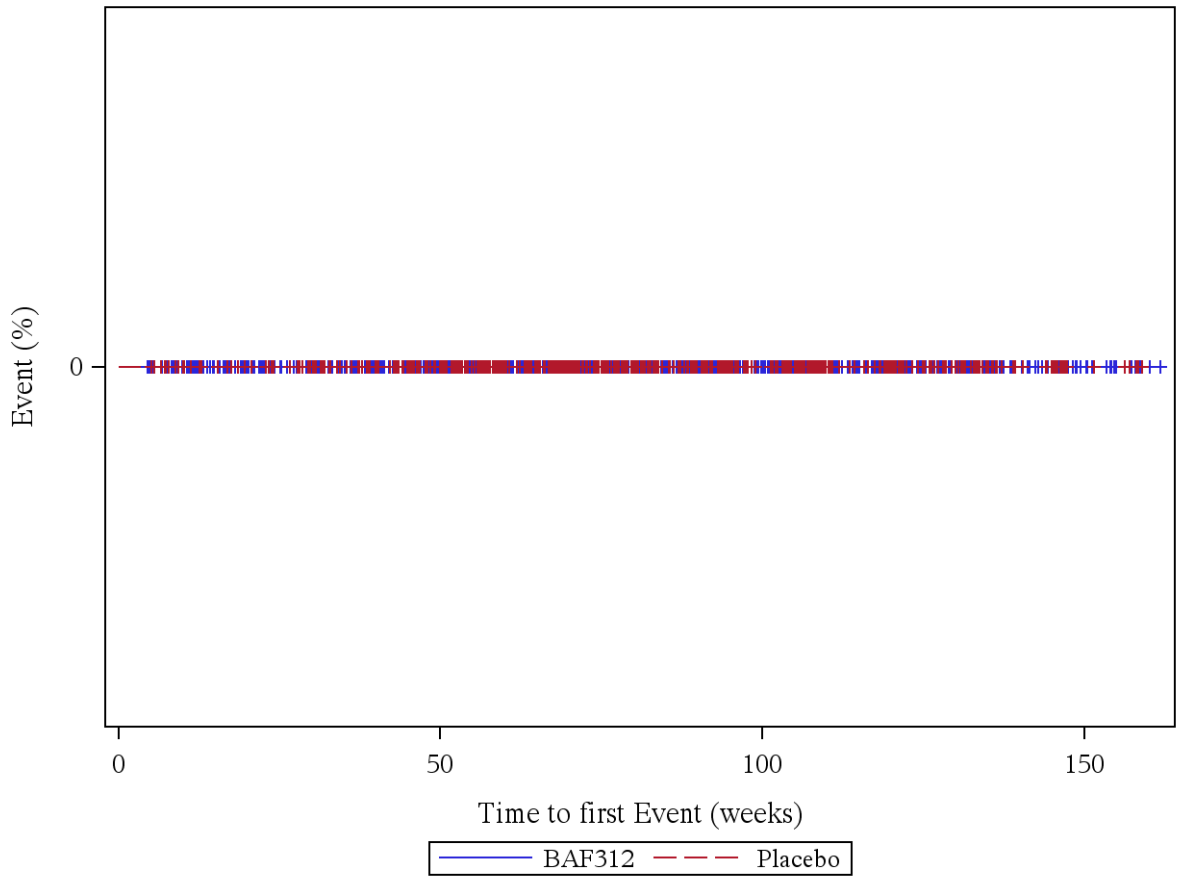


Patients at risk (BAF312/Placebo): Week 0: 1099/546, Week 4: 1099/546, Week 12: 1059/535, Week 24: 1017/521, Week 36: 990/497, Week 48: 925/461, Week 60: 818/388, Week 72: 652/305, Week 84: 516/237, Week 96: 400/176, Week 108: 291/126, Week 120: 200/80, Week 132: 113/40, Week 144: 51/20, Week 156: 10/5, Week 168: 0/0

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

Analysis population: A2304 SAF total population

Figure 12.1.6.56: Pregnancy and neonatal topics (AESI, serious)

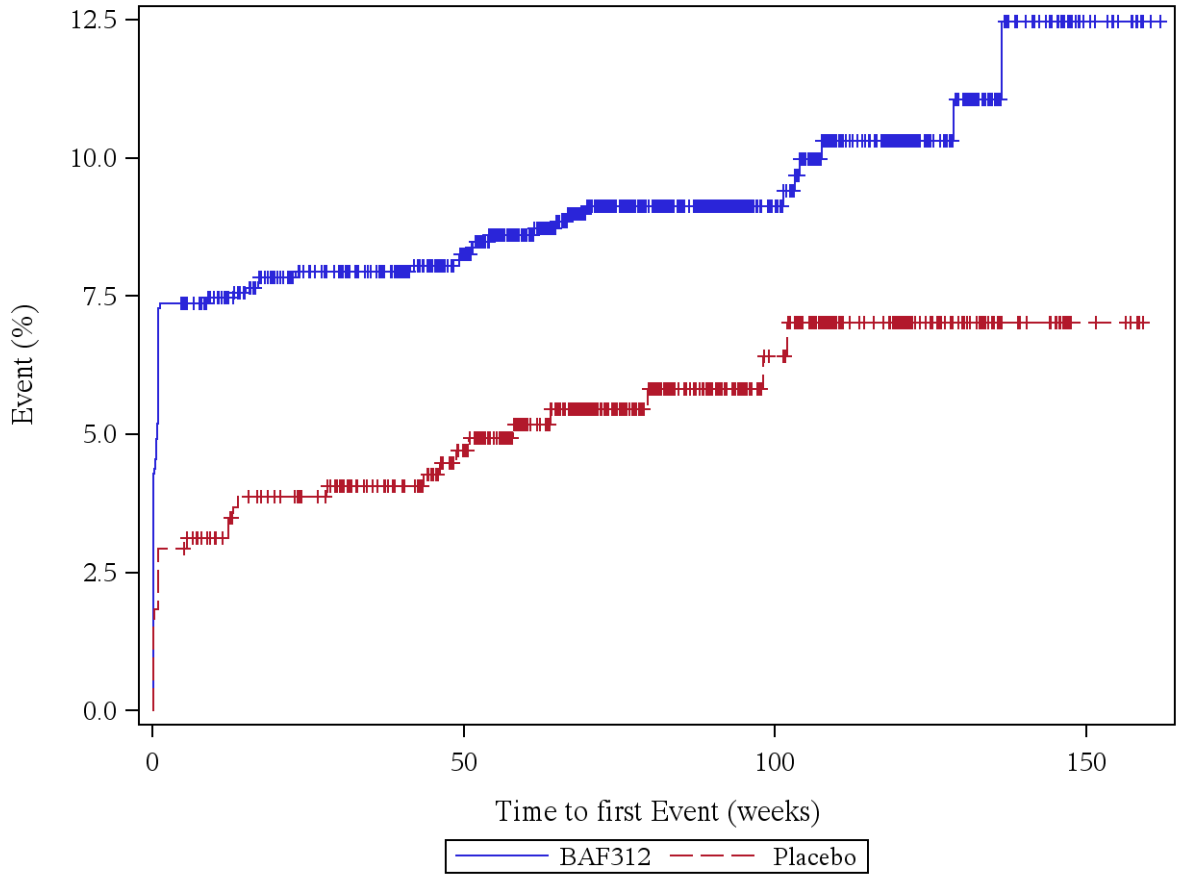


Patients at risk (BAF312/Placebo): Week 0: 1099/546, Week 4: 1099/546, Week 12: 1059/535, Week 24: 1017/521, Week 36: 990/497, Week 48: 925/461, Week 60: 818/388, Week 72: 652/305, Week 84: 516/237, Week 96: 400/176, Week 108: 291/126, Week 120: 200/80, Week 132: 113/40, Week 144: 51/20, Week 156: 10/5, Week 168: 0/0

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

Analysis population: A2304 SAF total population

Figure 12.1.6.57: Bradyarrhythmias and bradycardia (AESI, all)

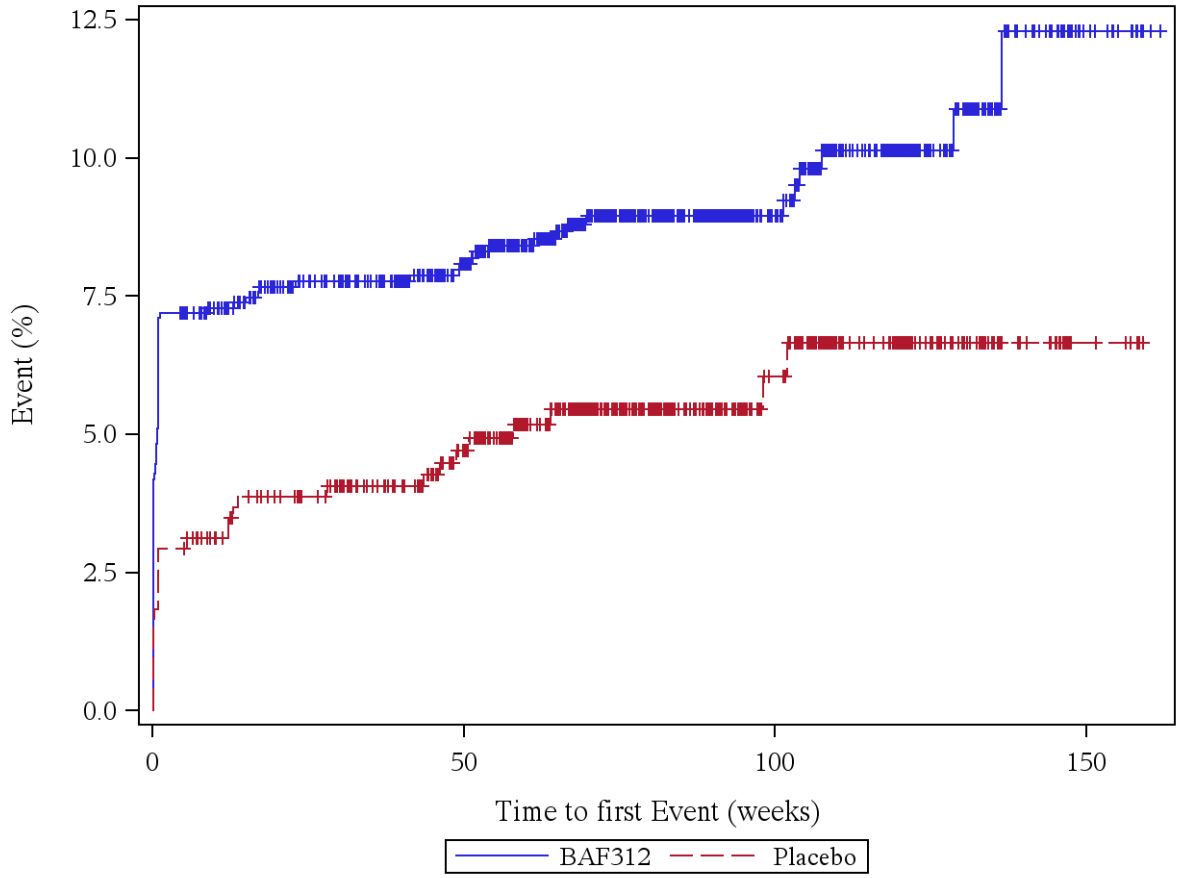


Patients at risk (BAF312/Placebo): Week 0: 1099/546, Week 4: 1018/530, Week 12: 985/518, Week 24: 942/500, Week 36: 917/475, Week 48: 853/439, Week 60: 747/367, Week 72: 586/291, Week 84: 458/225, Week 96: 350/167, Week 108: 253/116, Week 120: 176/76, Week 132: 98/38, Week 144: 43/19, Week 156: 9/5, Week 168: 0/0

Log rank test: p-value = 0,011 *
*: p < 0,05

Analysis population: A2304 SAF total population

Figure 12.1.6.58: Bradyarrhythmias and bradycardia (AESI, not severe)

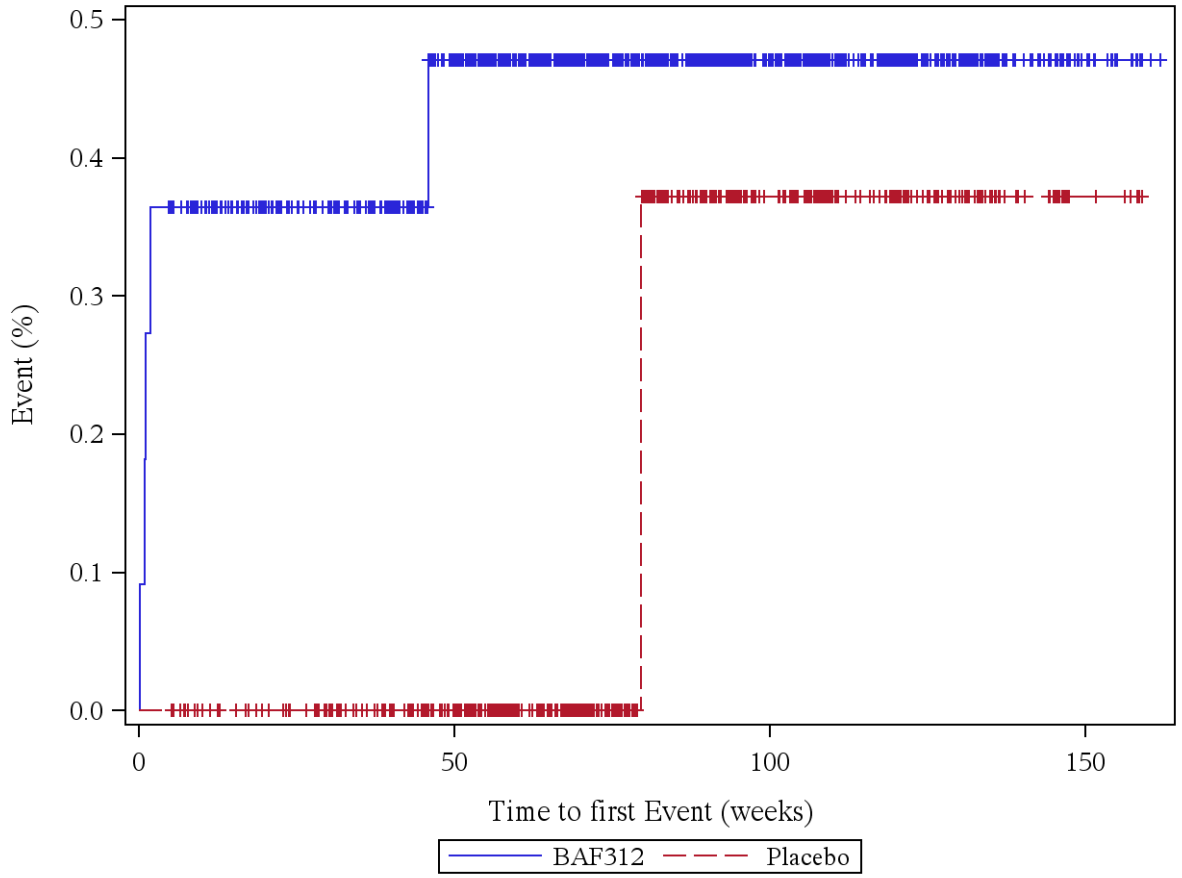


Patients at risk (BAF312/Placebo): Week 0: 1099/546, Week 4: 1020/530, Week 12: 985/518, Week 24: 942/500, Week 36: 917/475, Week 48: 853/439, Week 60: 747/367, Week 72: 586/291, Week 84: 458/226, Week 96: 350/168, Week 108: 253/116, Week 120: 176/76, Week 132: 98/38, Week 144: 43/19, Week 156: 9/5, Week 168: 0/0

Log rank test: p-value = 0,010 *
*: p < 0,05

Analysis population: A2304 SAF total population

Figure 12.1.6.59: Bradyarrhythmias and bradycardia (AESI, severe)

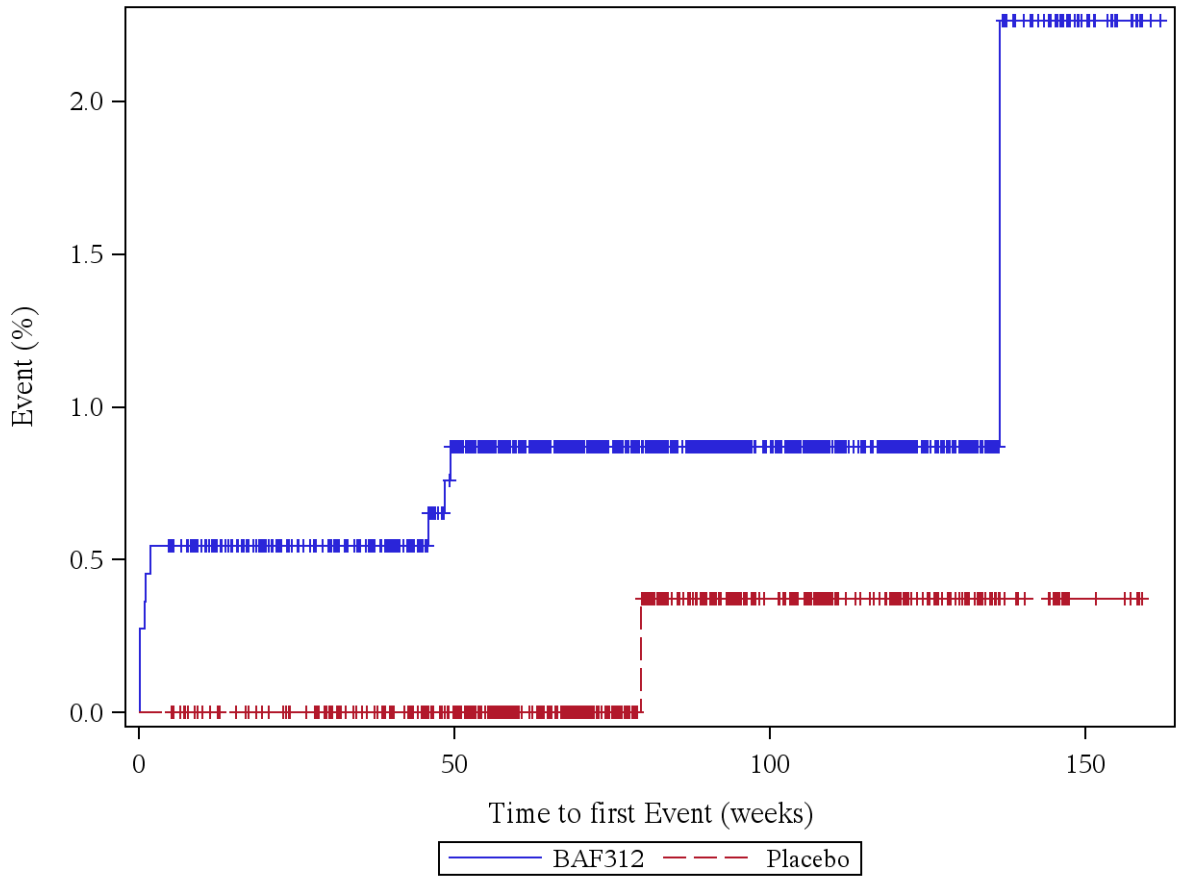


Patients at risk (BAF312/Placebo): Week 0: 1099/546, Week 4: 1095/546, Week 12: 1058/535, Week 24: 1016/521, Week 36: 989/497, Week 48: 923/461, Week 60: 817/388, Week 72: 651/305, Week 84: 515/236, Week 96: 399/175, Week 108: 290/126, Week 120: 199/80, Week 132: 113/40, Week 144: 51/20, Week 156: 10/5, Week 168: 0/0

Log rank test: p-value = 0,393
*: p < 0,05

Analysis population: A2304 SAF total population

Figure 12.1.6.60: Bradyarrhythmias and bradycardia (AESI, serious)



Patients at risk (BAF312/Placebo): Week 0: 1099/546, Week 4: 1093/546, Week 12: 1056/535, Week 24: 1014/521, Week 36: 988/497, Week 48: 922/461, Week 60: 814/388, Week 72: 648/305, Week 84: 513/236, Week 96: 397/175, Week 108: 289/126, Week 120: 199/80, Week 132: 113/40, Week 144: 51/20, Week 156: 10/5, Week 168: 0/0

Log rank test: p-value = 0,097
*: p < 0,05

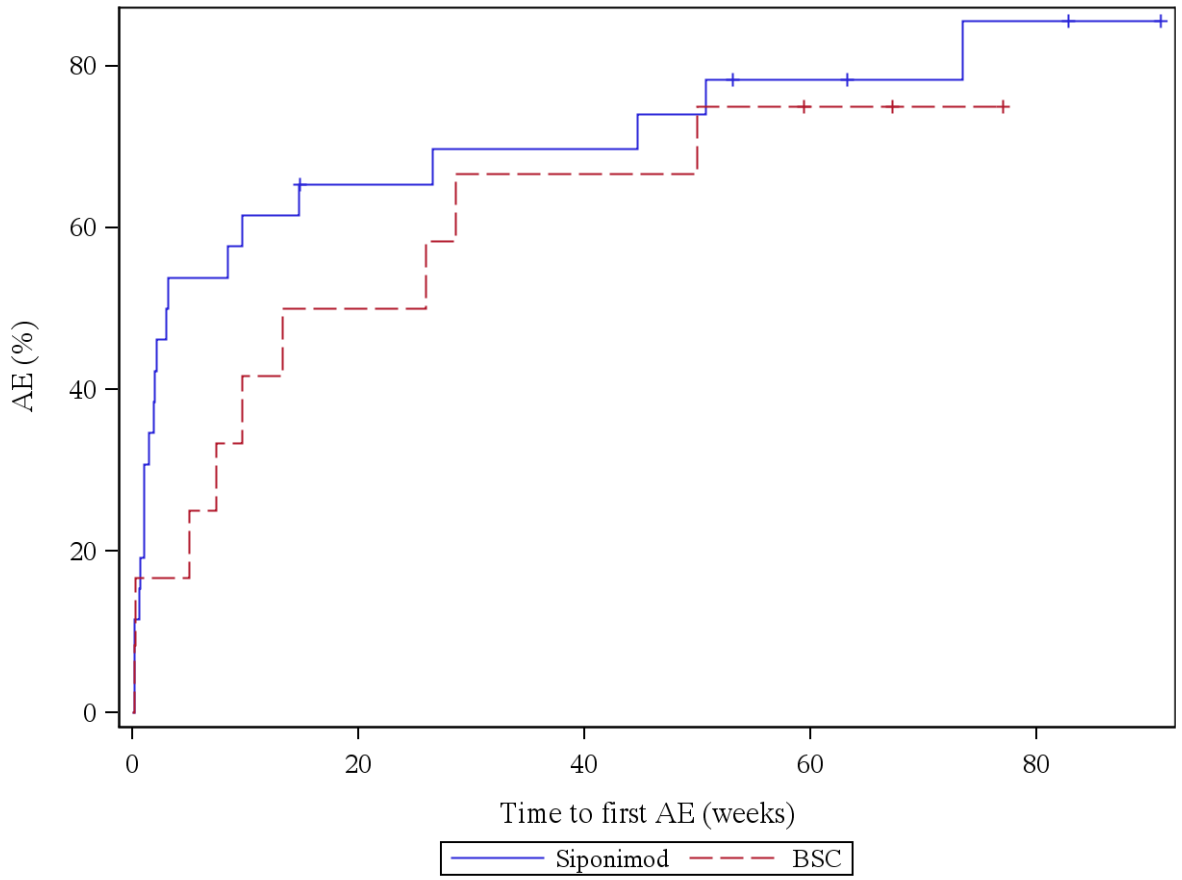
Analysis population: A2304 SAF total population

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 = 18-30 years

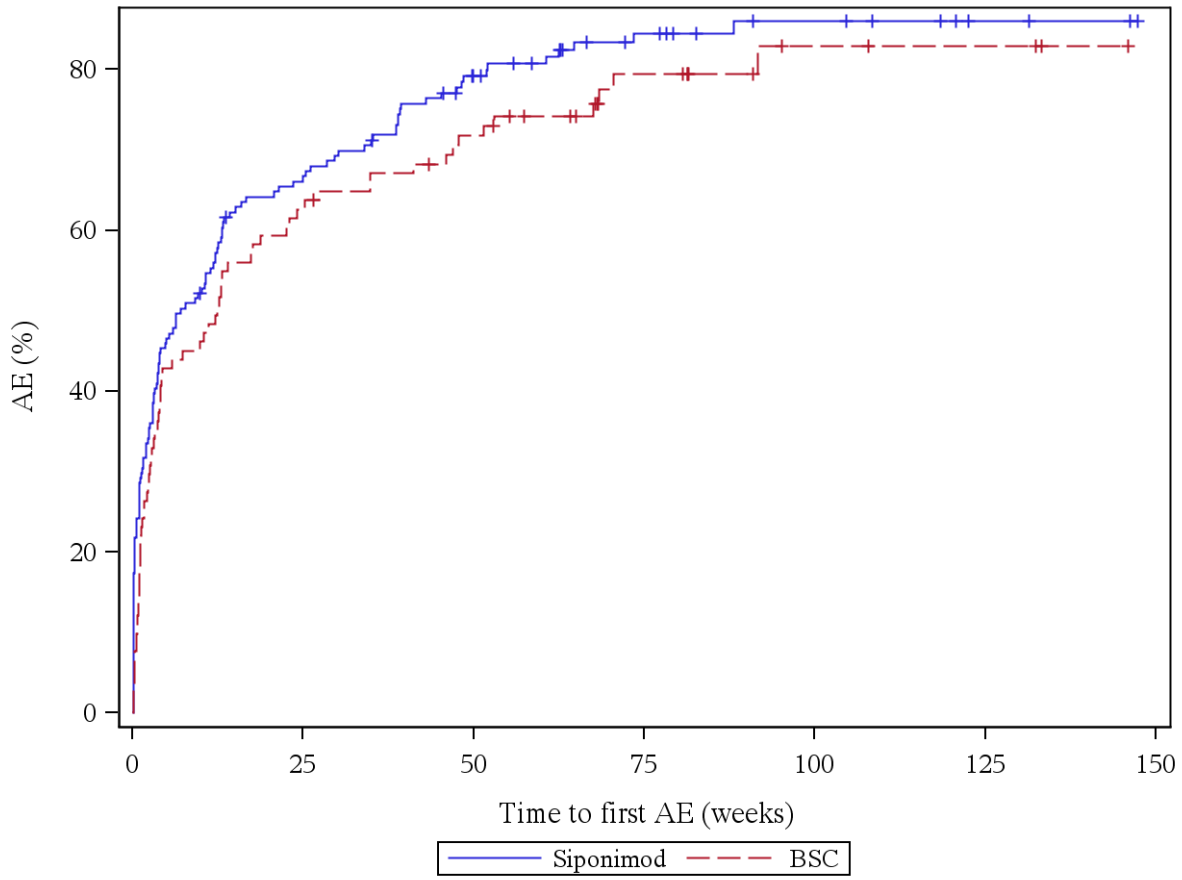


Patients at risk (Siponimod/BSC): Week 0: 26/12, Week 4: 12/10, Week 12: 10/7, Week 24: 8/6, Week 36: 7/4, Week 48: 6/4, Week 60: 4/2, Week 72: 3/1, Week 84: 1/0, Week 96: 0/0

Log rank test: p-value = 0,436
*: p < 0,05

Analysis population: A2304 SAF total population

Figure 12.2.1.1.2: AE, Age = 31-40 years

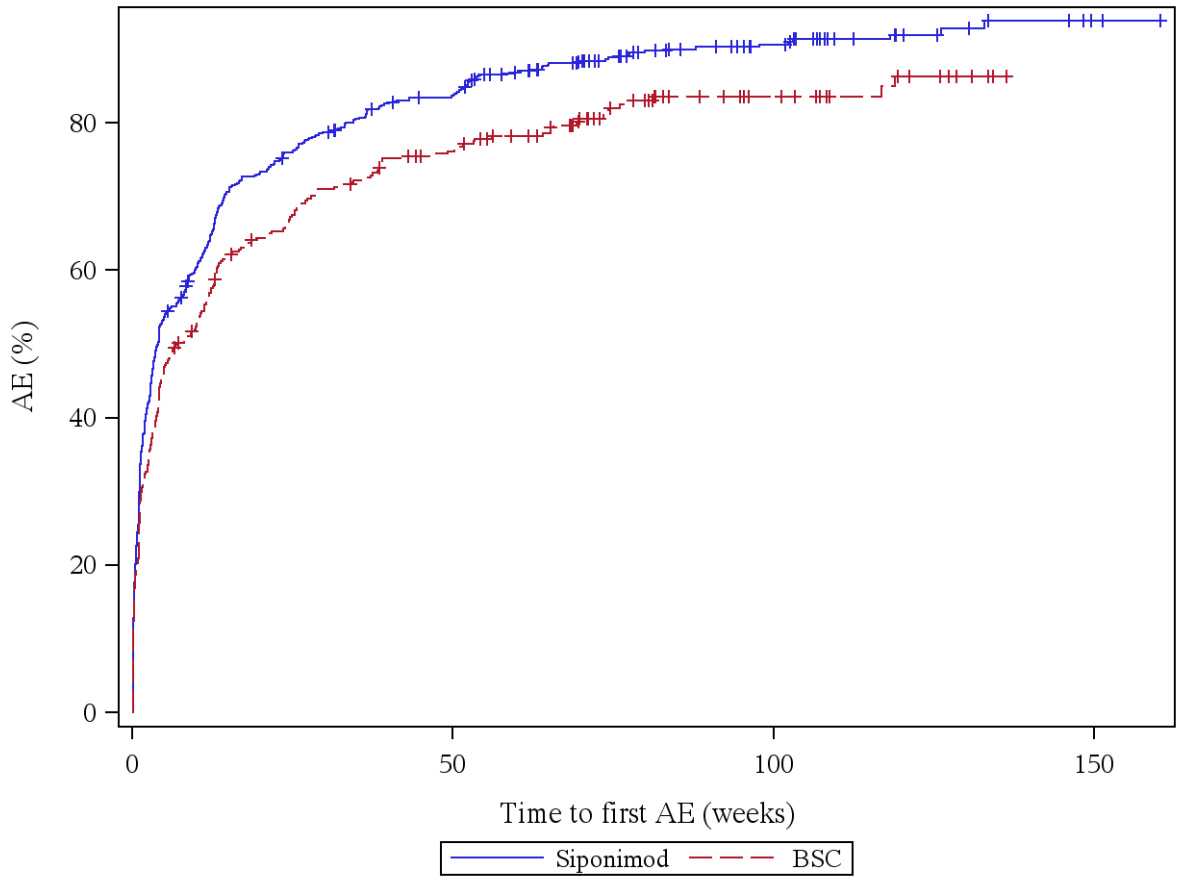


Patients at risk (Siponimod/BSC): Week 0: 161/91, Week 4: 89/56, Week 12: 70/47, Week 24: 53/35, Week 36: 43/29, Week 48: 32/24, Week 60: 23/19, Week 72: 16/11, Week 84: 10/7, Week 96: 8/4, Week 108: 7/3, Week 120: 5/3, Week 132: 2/3, Week 144: 2/1, Week 156: 0/0

Log rank test: p-value = 0,181
*: p < 0,05

Analysis population: A2304 SAF total population

Figure 12.2.1.1.3: AE, Age = 41-55 years

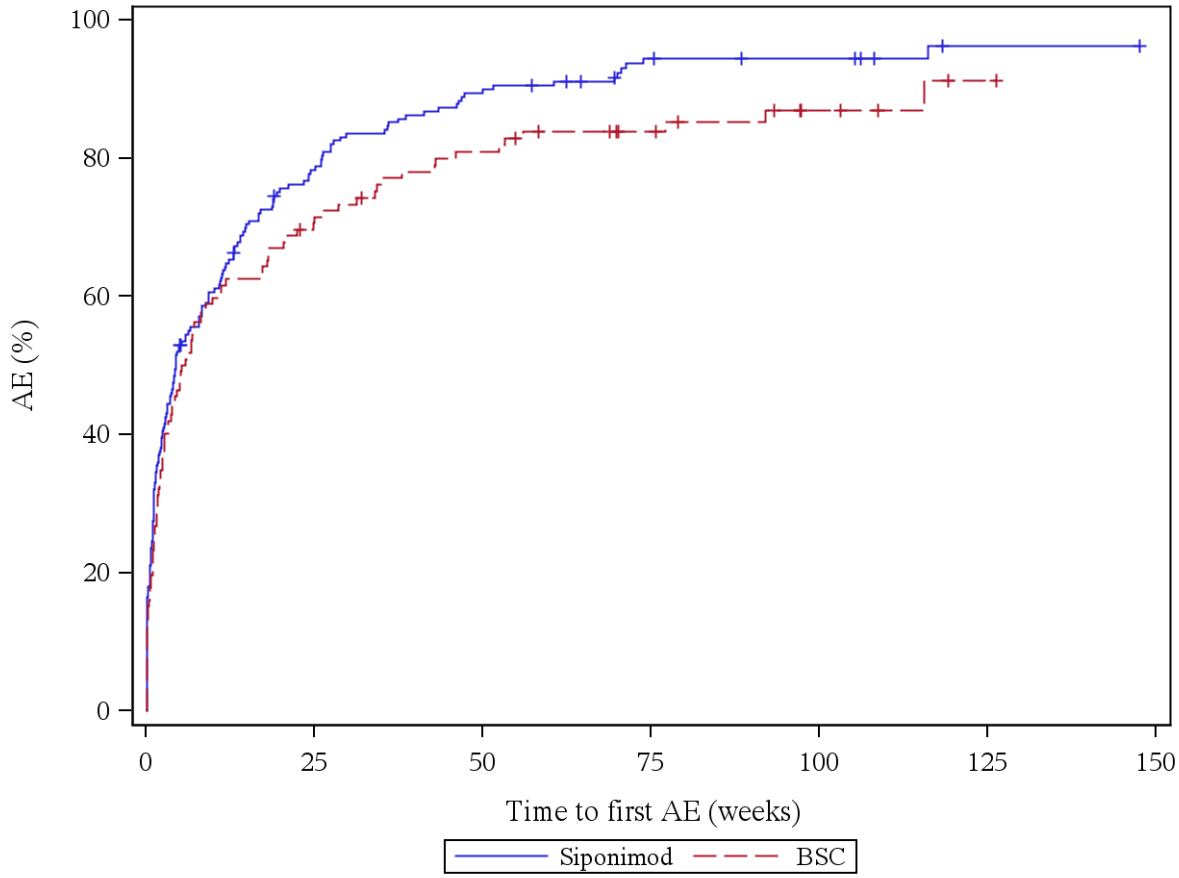


Patients at risk (Siponimod/BSC): Week 0: 712/331, Week 4: 354/191, Week 12: 253/140, Week 24: 168/108, Week 36: 132/87, Week 48: 111/72, Week 60: 81/60, Week 72: 57/41, Week 84: 38/24, Week 96: 32/20, Week 108: 17/14, Week 120: 11/9, Week 132: 7/3, Week 144: 5/0, Week 156: 1/0, Week 168: 0/0

Log rank test: p-value = 0,001 *
*: p < 0,05

Analysis population: A2304 SAF total population

Figure 12.2.1.1.4: AE, Age = >55 years



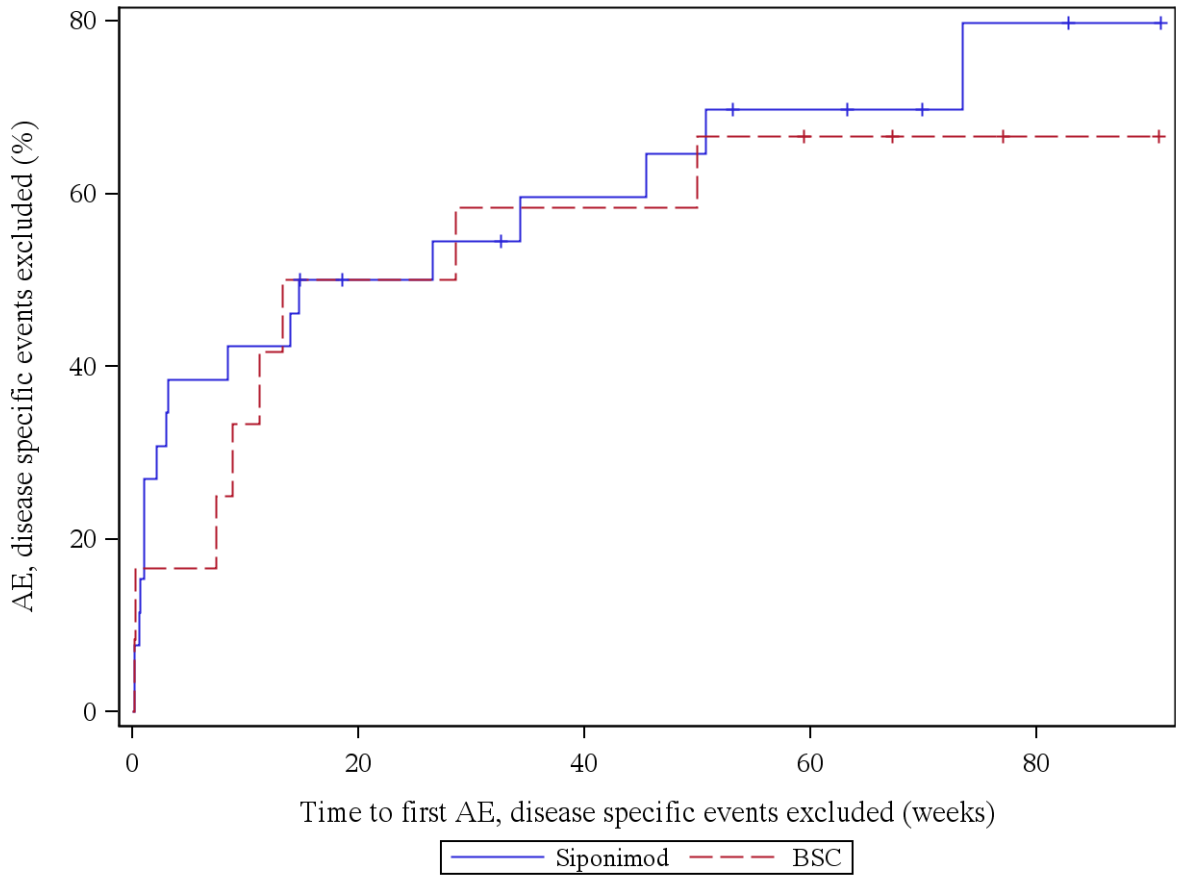
Patients at risk (Siponimod/BSC): Week 0: 200/112, Week 4: 105/62, Week 12: 69/42, Week 24: 44/33, Week 36: 28/24, Week 48: 20/20, Week 60: 17/15, Week 72: 9/12, Week 84: 7/9, Week 96: 6/7, Week 108: 4/4, Week 120: 1/1, Week 132: 1/0, Week 144: 1/0, Week 156: 0/0

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

Analysis population: A2304 SAF total population

12.2.1.2: Any AE, disease specific events excluded

Figure 12.2.1.2.1: AE, disease specific events excluded, Age = 18-30 years

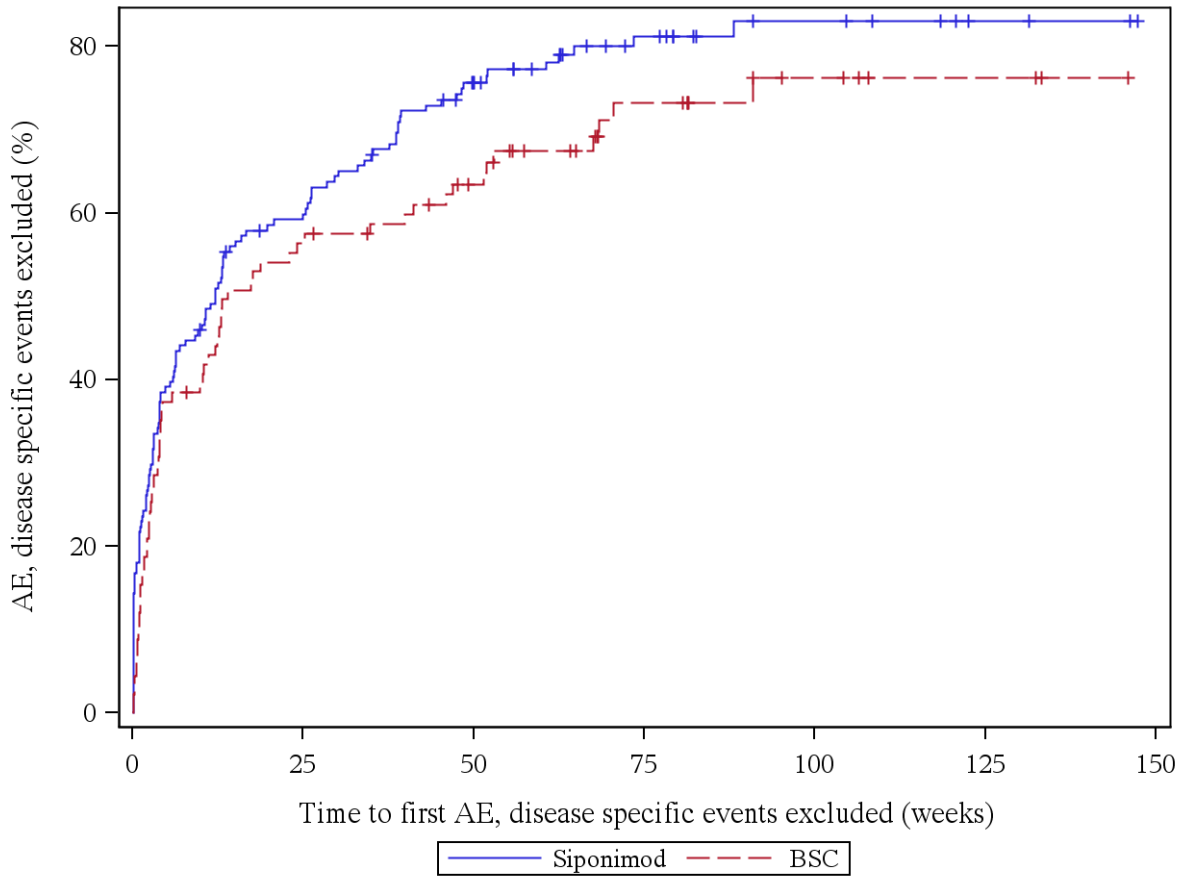


Patients at risk (Siponimod/BSC): Week 0: 26/12, Week 4: 16/10, Week 12: 15/7, Week 24: 11/6, Week 36: 8/5, Week 48: 7/5, Week 60: 5/3, Week 72: 3/2, Week 84: 1/1, Week 96: 0/0

Log rank test: p-value = 0,710
*: p < 0,05

Analysis population: A2304 SAF total population

Figure 12.2.1.2.2: AE, disease specific events excluded, Age = 31-40 years

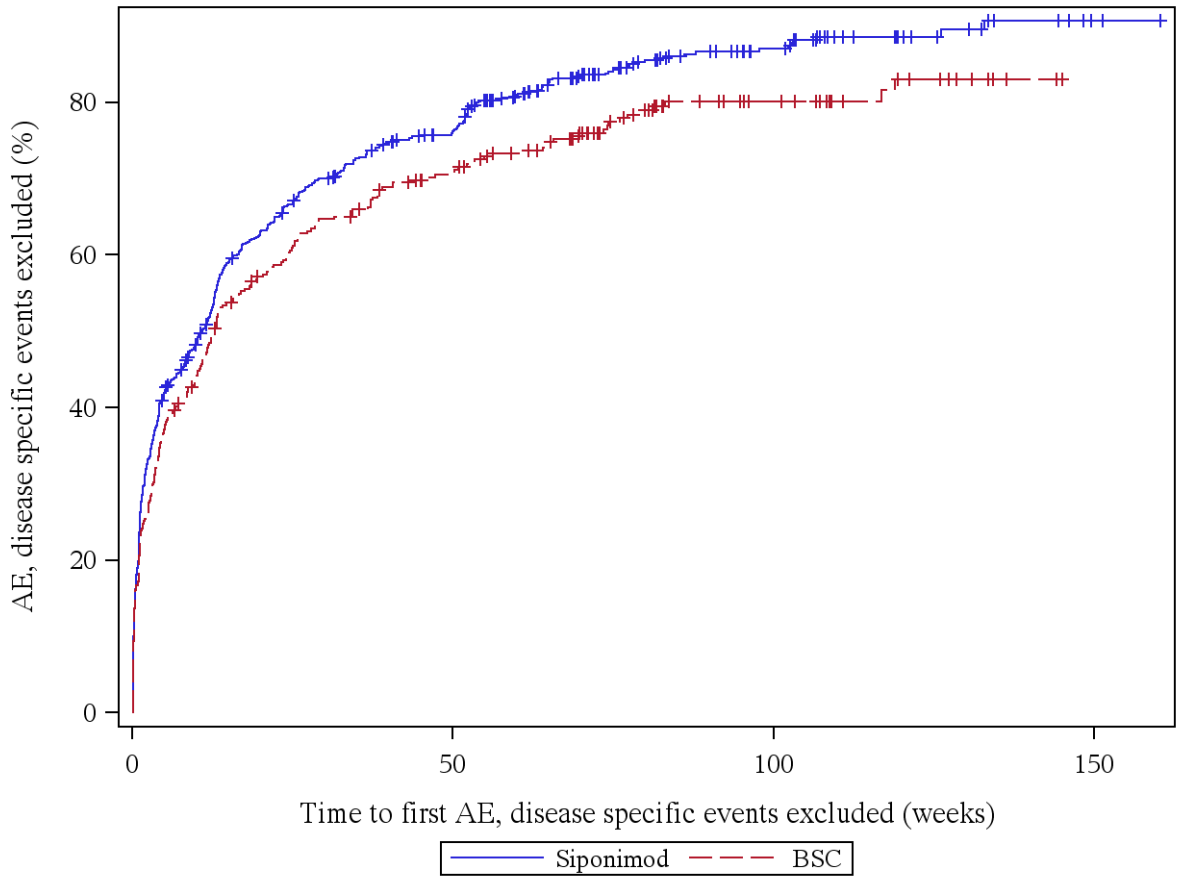


Patients at risk (Siponimod/BSC): Week 0: 161/91, Week 4: 101/61, Week 12: 81/51, Week 24: 63/40, Week 36: 49/35, Week 48: 37/29, Week 60: 26/21, Week 72: 18/13, Week 84: 10/9, Week 96: 8/6, Week 108: 7/3, Week 120: 5/3, Week 132: 2/3, Week 144: 2/1, Week 156: 0/0

Log rank test: p-value = 0,107
*: p < 0,05

Analysis population: A2304 SAF total population

Figure 12.2.1.2.3: AE, disease specific events excluded, Age = 41-55 years

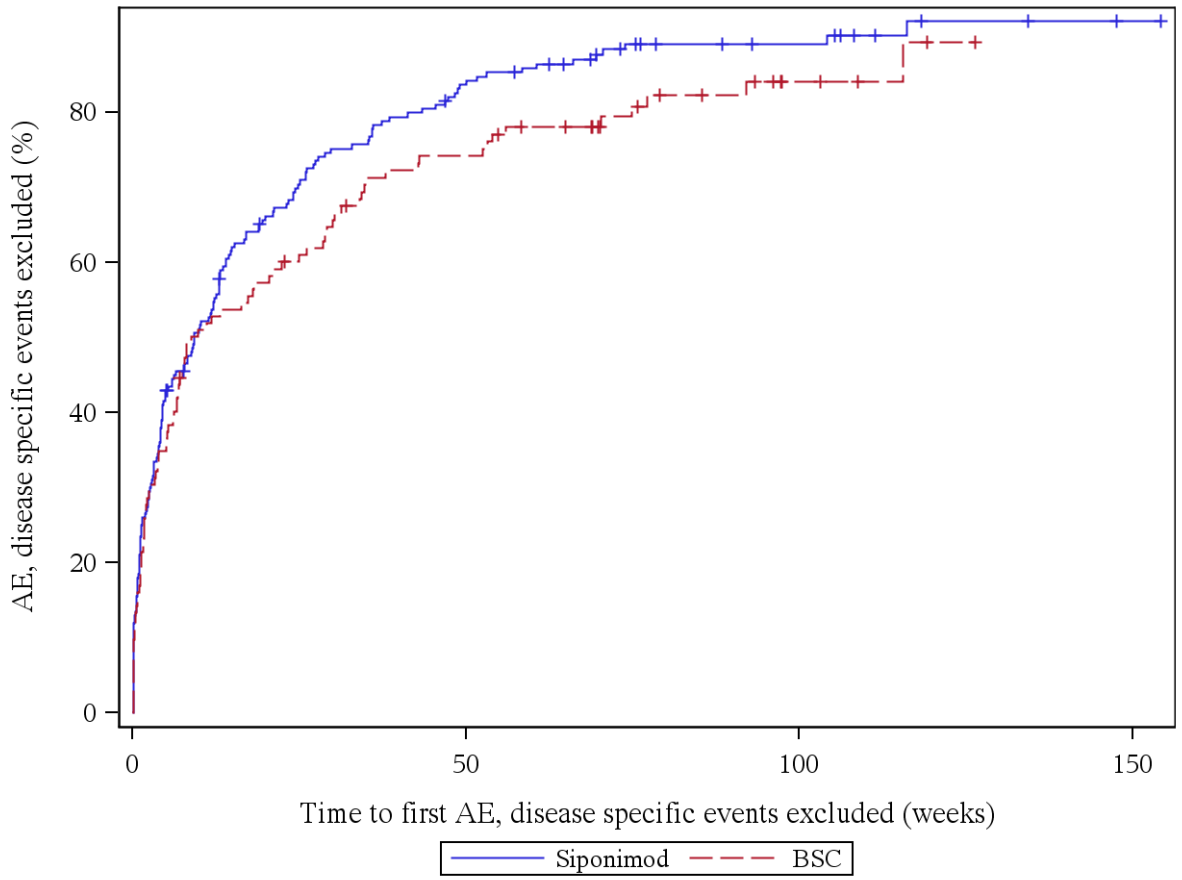


Patients at risk (Siponimod/BSC): Week 0: 712/331, Week 4: 435/220, Week 12: 335/168, Week 24: 232/128, Week 36: 183/106, Week 48: 155/87, Week 60: 109/73, Week 72: 73/52, Week 84: 49/29, Week 96: 40/24, Week 108: 22/18, Week 120: 15/11, Week 132: 10/5, Week 144: 6/2, Week 156: 1/0, Week 168: 0/0

Log rank test: p-value = 0,009 *
*: p < 0,05

Analysis population: A2304 SAF total population

Figure 12.2.1.2.4: AE, disease specific events excluded, Age = >55 years



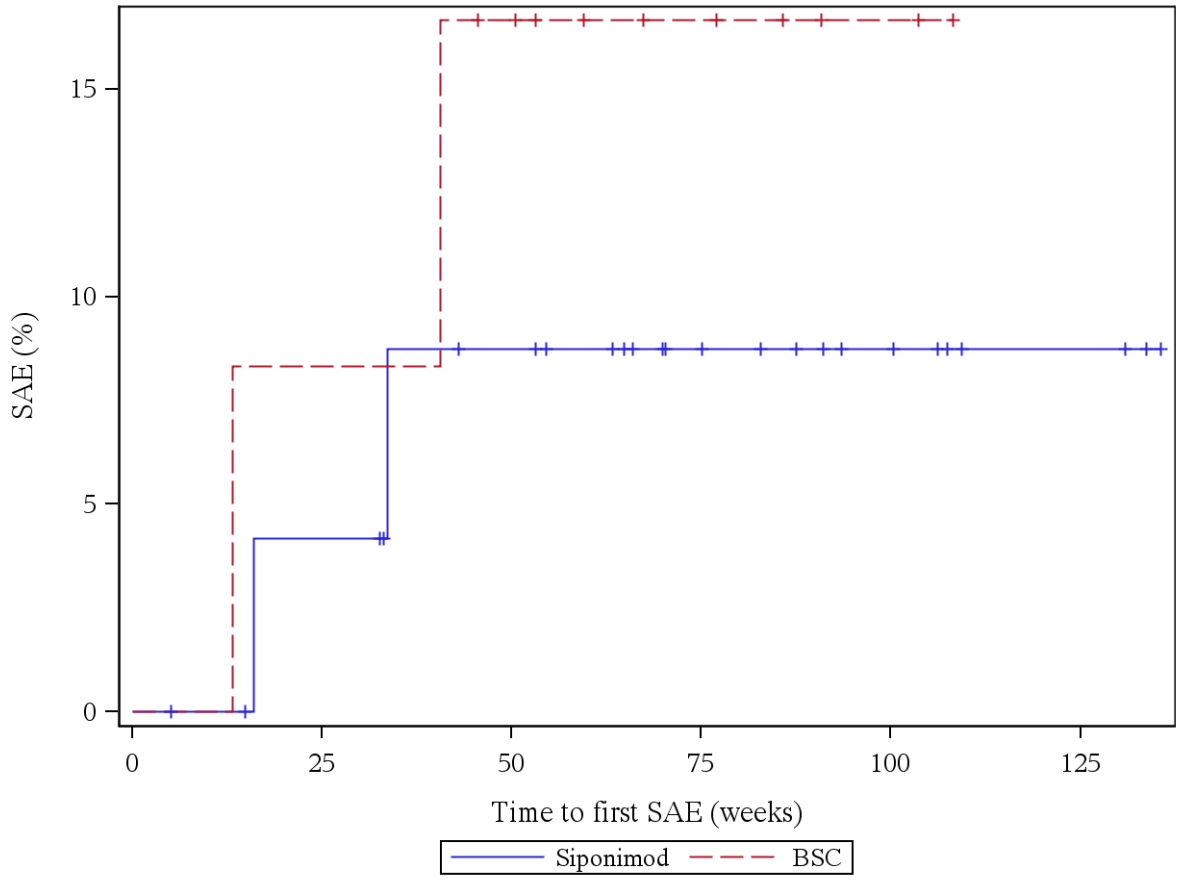
Patients at risk (Siponimod/BSC): Week 0: 200/112, Week 4: 128/73, Week 12: 90/52, Week 24: 60/43, Week 36: 41/30, Week 48: 33/27, Week 60: 25/21, Week 72: 17/15, Week 84: 12/11, Week 96: 10/7, Week 108: 7/4, Week 120: 3/1, Week 132: 3/0, Week 144: 2/0, Week 156: 0/0

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

Analysis population: A2304 SAF total population

12.2.1.3: Any SAE

Figure 12.2.1.3.1: SAE, Age = 18-30 years

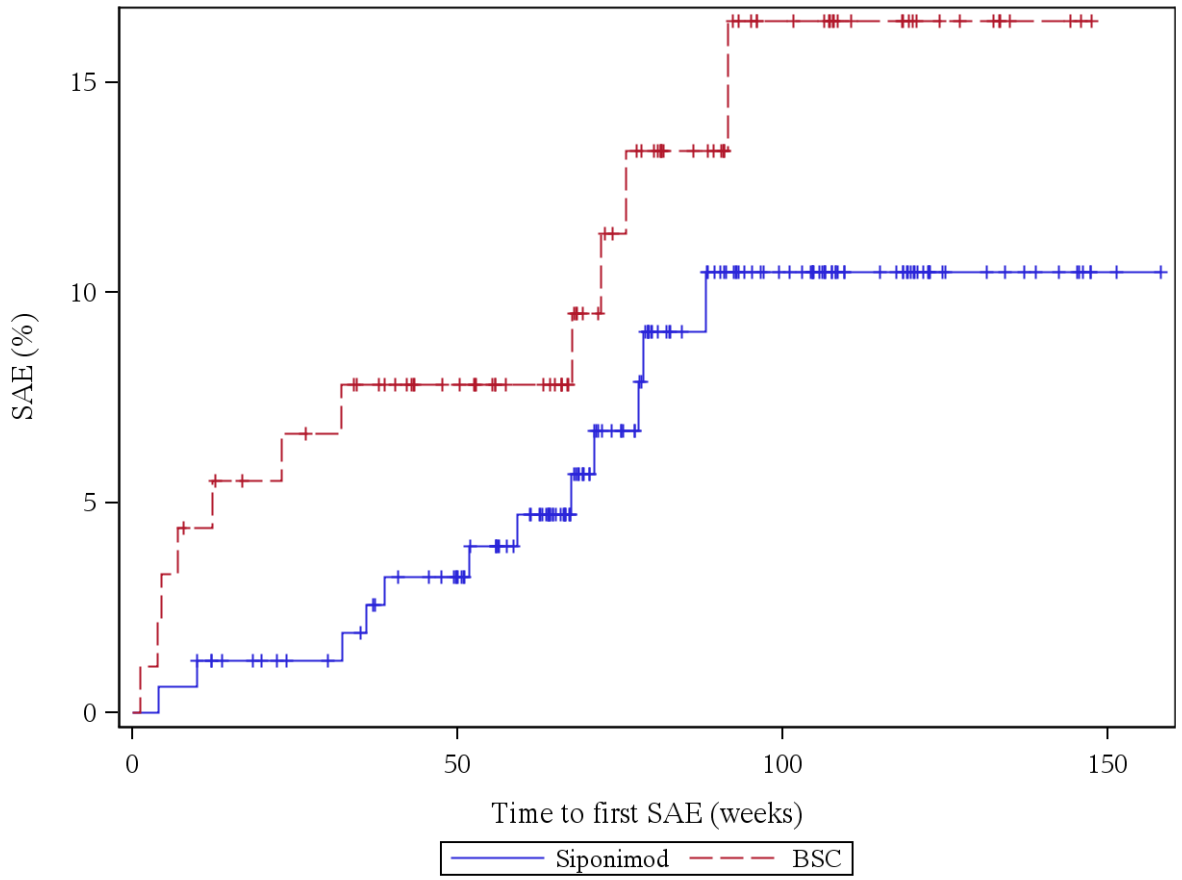


Patients at risk (Siponimod/BSC): Week 0: 26/12, Week 4: 26/12, Week 12: 25/12, Week 24: 23/11, Week 36: 20/11, Week 48: 19/9, Week 60: 17/6, Week 72: 12/5, Week 84: 10/4, Week 96: 7/2, Week 108: 4/1, Week 120: 3/0, Week 132: 2/0, Week 144: 0/0

Log rank test: p-value = 0,482
*: p < 0,05

Analysis population: A2304 SAF total population

Figure 12.2.1.3.2: SAE, Age = 31-40 years

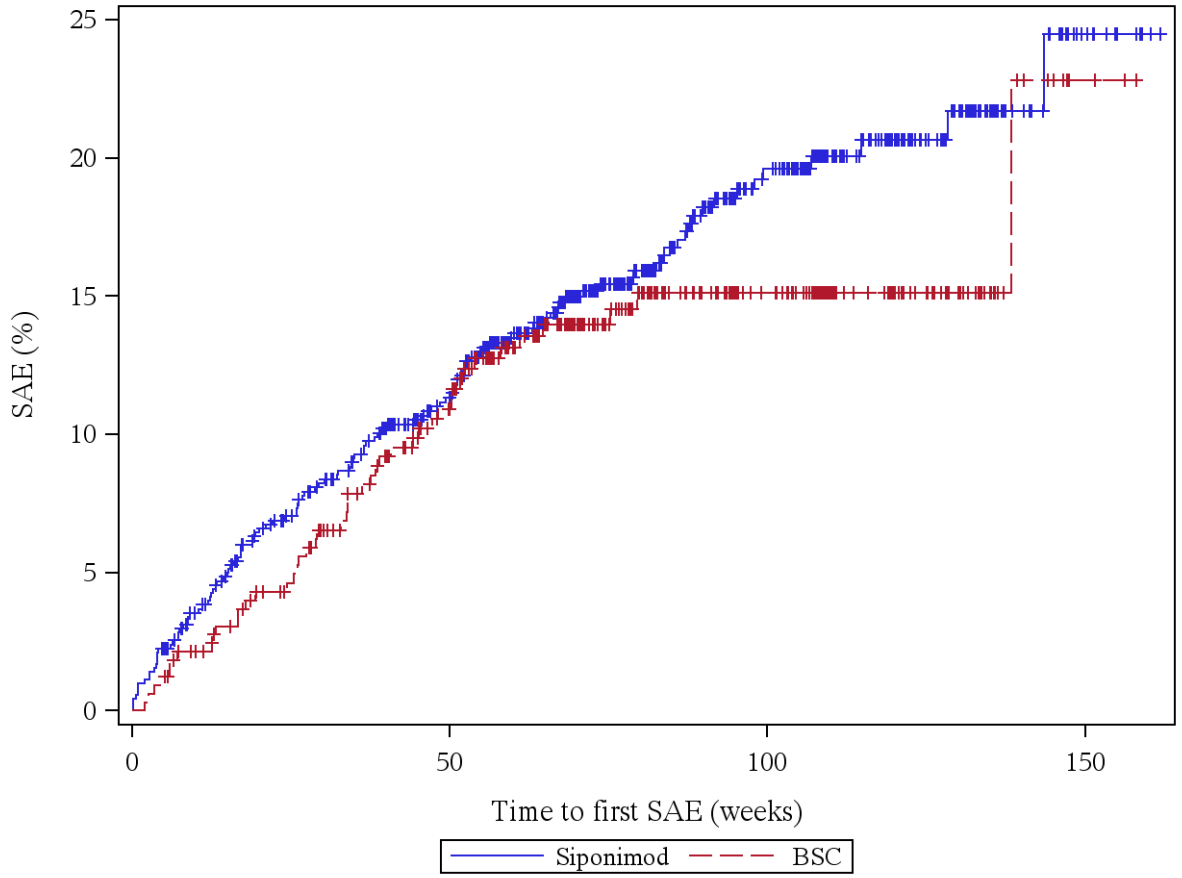


Patients at risk (Siponimod/BSC): Week 0: 161/91, Week 4: 160/89, Week 12: 158/86, Week 24: 151/82, Week 36: 147/78, Week 48: 141/70, Week 60: 124/62, Week 72: 87/47, Week 84: 65/35, Week 96: 51/22, Week 108: 34/16, Week 120: 22/10, Week 132: 11/7, Week 144: 7/3, Week 156: 1/0, Week 168: 0/0

Log rank test: p-value = 0,196
*: p < 0,05

Analysis population: A2304 SAF total population

Figure 12.2.1.3.3: SAE, Age = 41-55 years

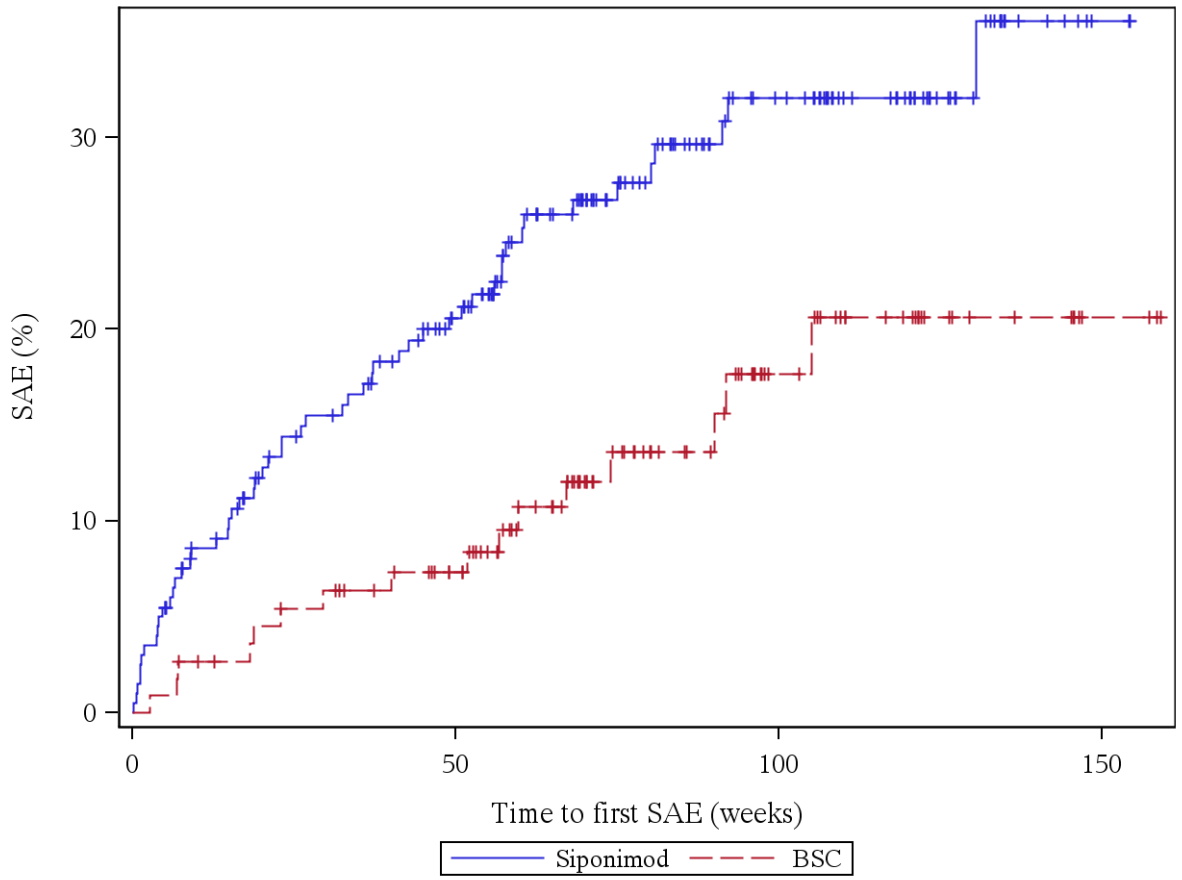


Patients at risk (Siponimod/BSC): Week 0: 712/331, Week 4: 697/328, Week 12: 665/317, Week 24: 628/301, Week 36: 595/278, Week 48: 549/252, Week 60: 483/213, Week 72: 381/169, Week 84: 297/126, Week 96: 228/98, Week 108: 164/71, Week 120: 108/44, Week 132: 60/22, Week 144: 27/8, Week 156: 6/2, Week 168: 0/0

Log rank test: p-value = 0,291
*: p < 0,05

Analysis population: A2304 SAF total population

Figure 12.2.1.3.4: SAE, Age = >55 years



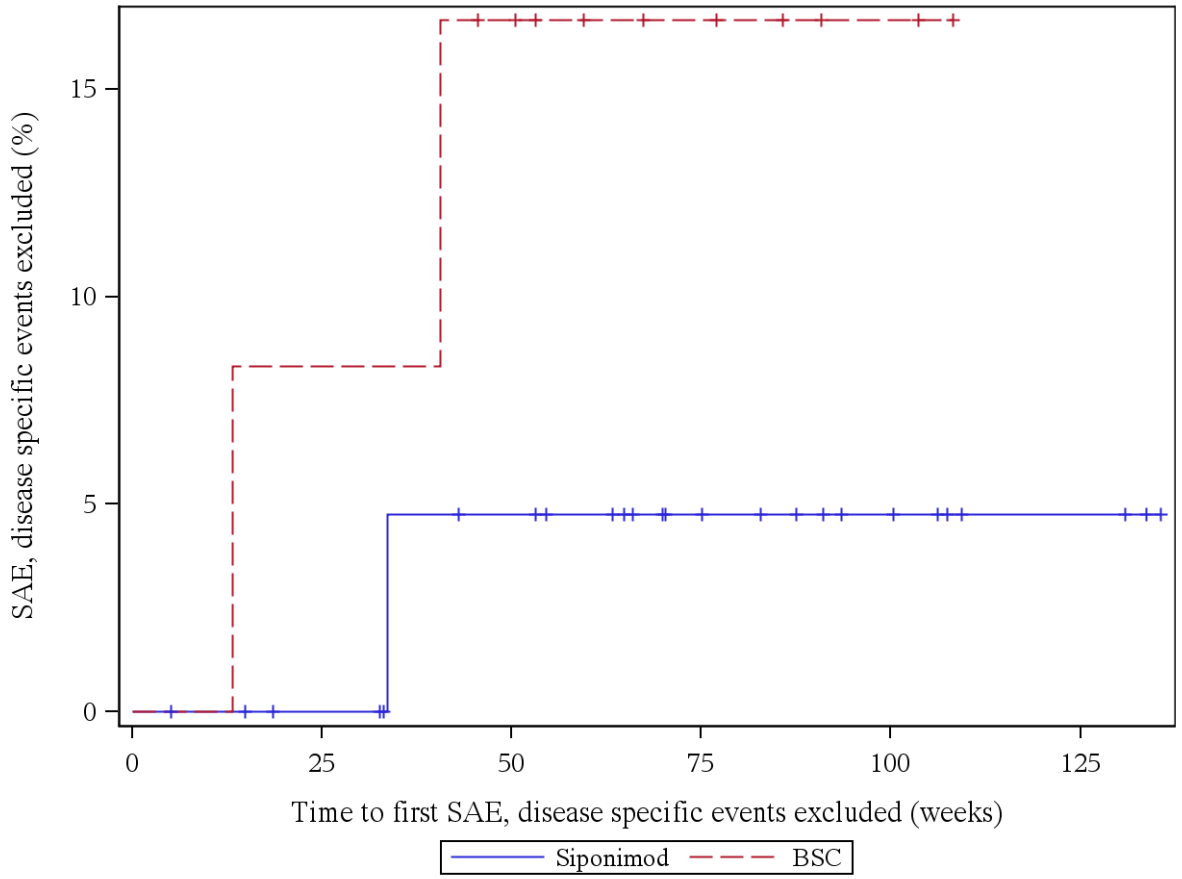
Patients at risk (Siponimod/BSC): Week 0: 200/112, Week 4: 190/111, Week 12: 176/107, Week 24: 157/102, Week 36: 150/98, Week 48: 136/92, Week 60: 106/73, Week 72: 84/56, Week 84: 65/46, Week 96: 51/35, Week 108: 40/24, Week 120: 31/18, Week 132: 15/9, Week 144: 6/8, Week 156: 0/3

Log rank test: p-value = 0,006 *
*: p < 0,05

Analysis population: A2304 SAF total population

12.2.1.4: Any SAE, disease specific events excluded

Figure 12.2.1.4.1: SAE, disease specific events excluded, Age = 18-30 years

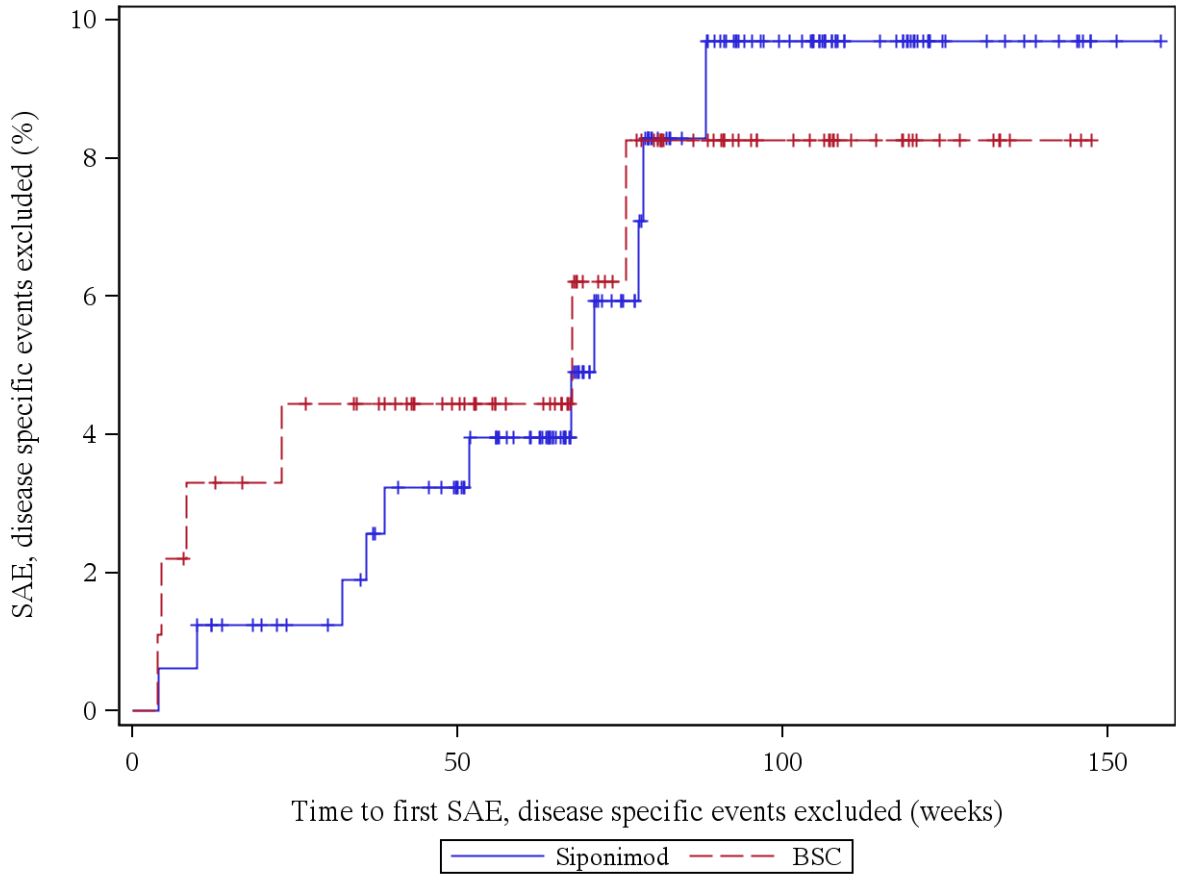


Patients at risk (Siponimod/BSC): Week 0: 26/12, Week 4: 26/12, Week 12: 25/12, Week 24: 23/11, Week 36: 20/11, Week 48: 19/9, Week 60: 17/6, Week 72: 12/5, Week 84: 10/4, Week 96: 7/2, Week 108: 4/1, Week 120: 3/0, Week 132: 2/0, Week 144: 0/0

Log rank test: p-value = 0,234
*: p < 0,05

Analysis population: A2304 SAF total population

Figure 12.2.1.4.2: SAE, disease specific events excluded, Age = 31-40 years

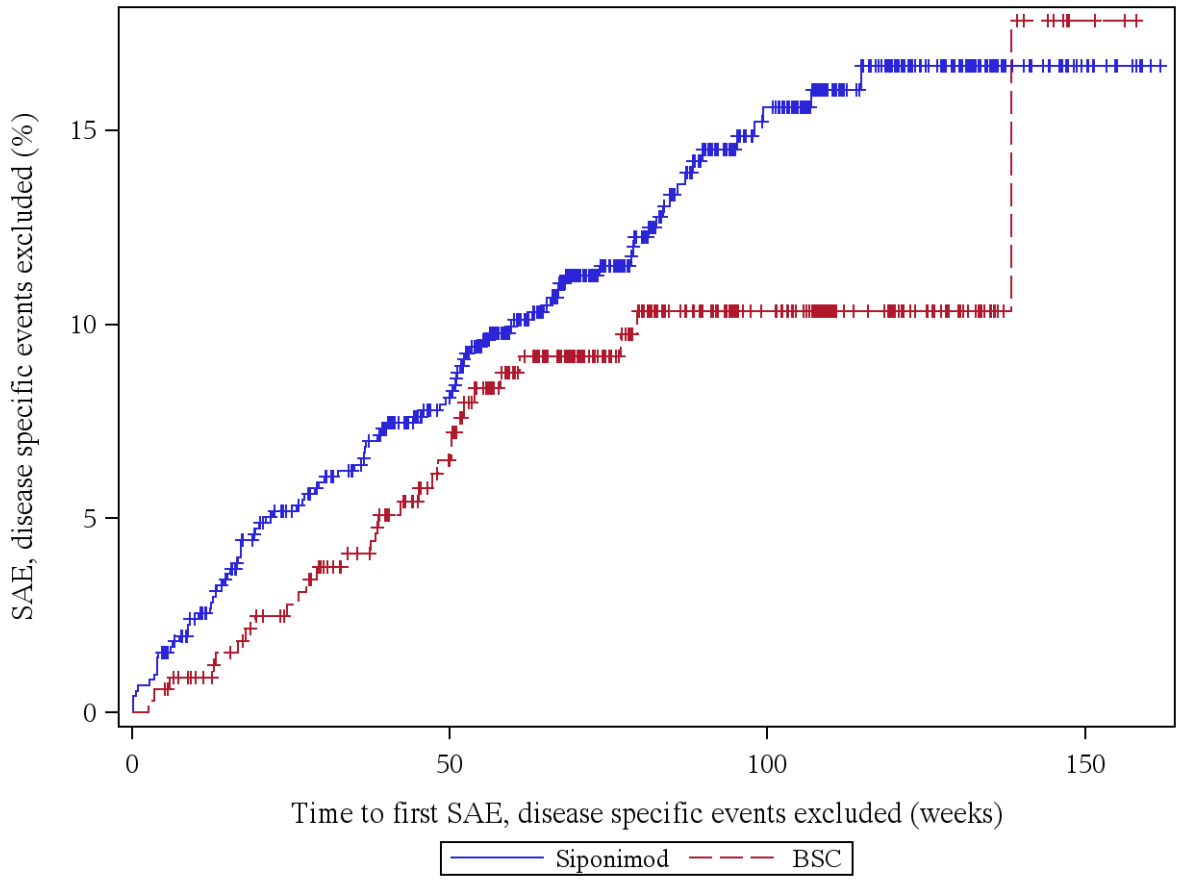


Patients at risk (Siponimod/BSC): Week 0: 161/91, Week 4: 160/90, Week 12: 158/87, Week 24: 151/84, Week 36: 147/81, Week 48: 141/73, Week 60: 125/63, Week 72: 88/48, Week 84: 66/36, Week 96: 52/24, Week 108: 34/17, Week 120: 22/10, Week 132: 11/7, Week 144: 7/3, Week 156: 1/0, Week 168: 0/0

Log rank test: p-value = 0,996
*: p < 0,05

Analysis population: A2304 SAF total population

Figure 12.2.1.4.3: SAE, disease specific events excluded, Age = 41-55 years

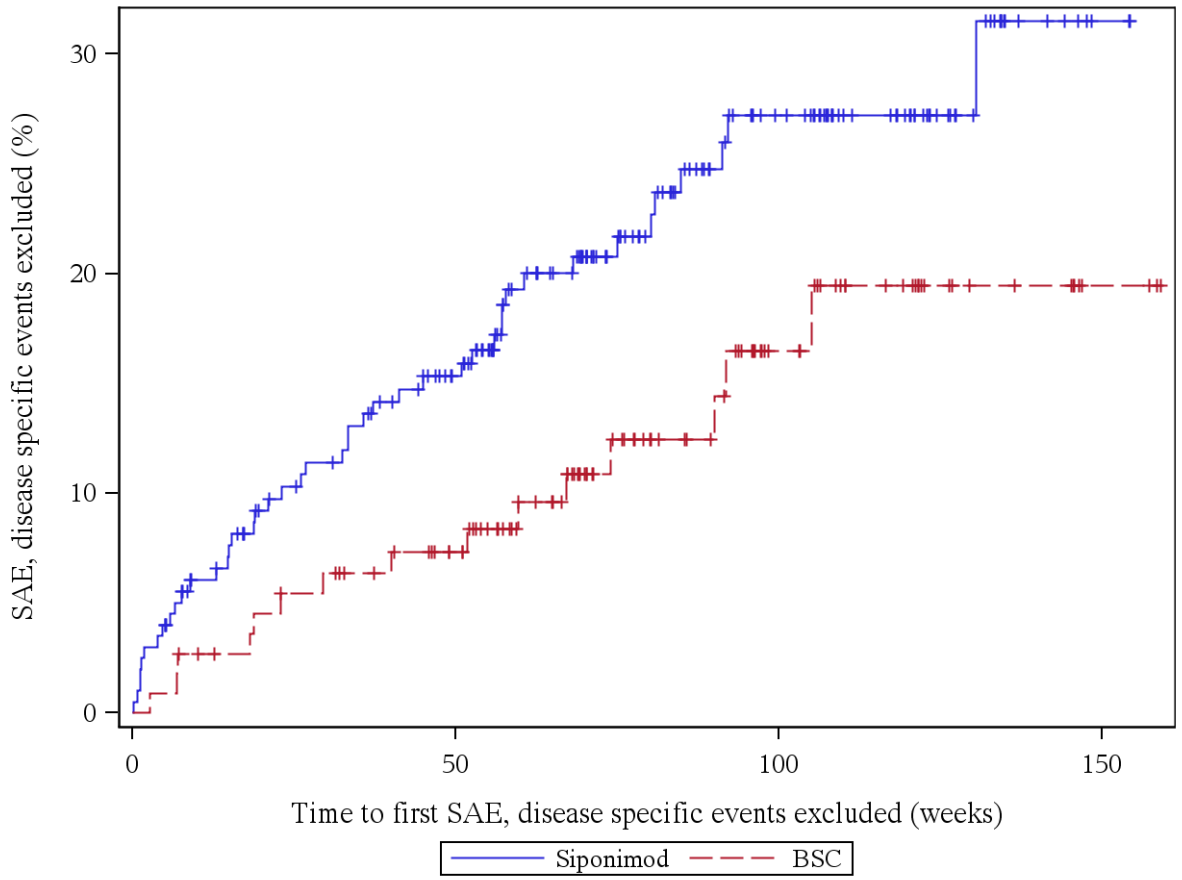


Patients at risk (Siponimod/BSC): Week 0: 712/331, Week 4: 702/329, Week 12: 673/320, Week 24: 637/306, Week 36: 612/287, Week 48: 566/261, Week 60: 500/220, Week 72: 398/173, Week 84: 309/130, Week 96: 239/100, Week 108: 173/72, Week 120: 115/45, Week 132: 67/23, Week 144: 31/9, Week 156: 7/2, Week 168: 0/0

Log rank test: p-value = 0,131
*: p < 0,05

Analysis population: A2304 SAF total population

Figure 12.2.1.4.4: SAE, disease specific events excluded, Age = >55 years



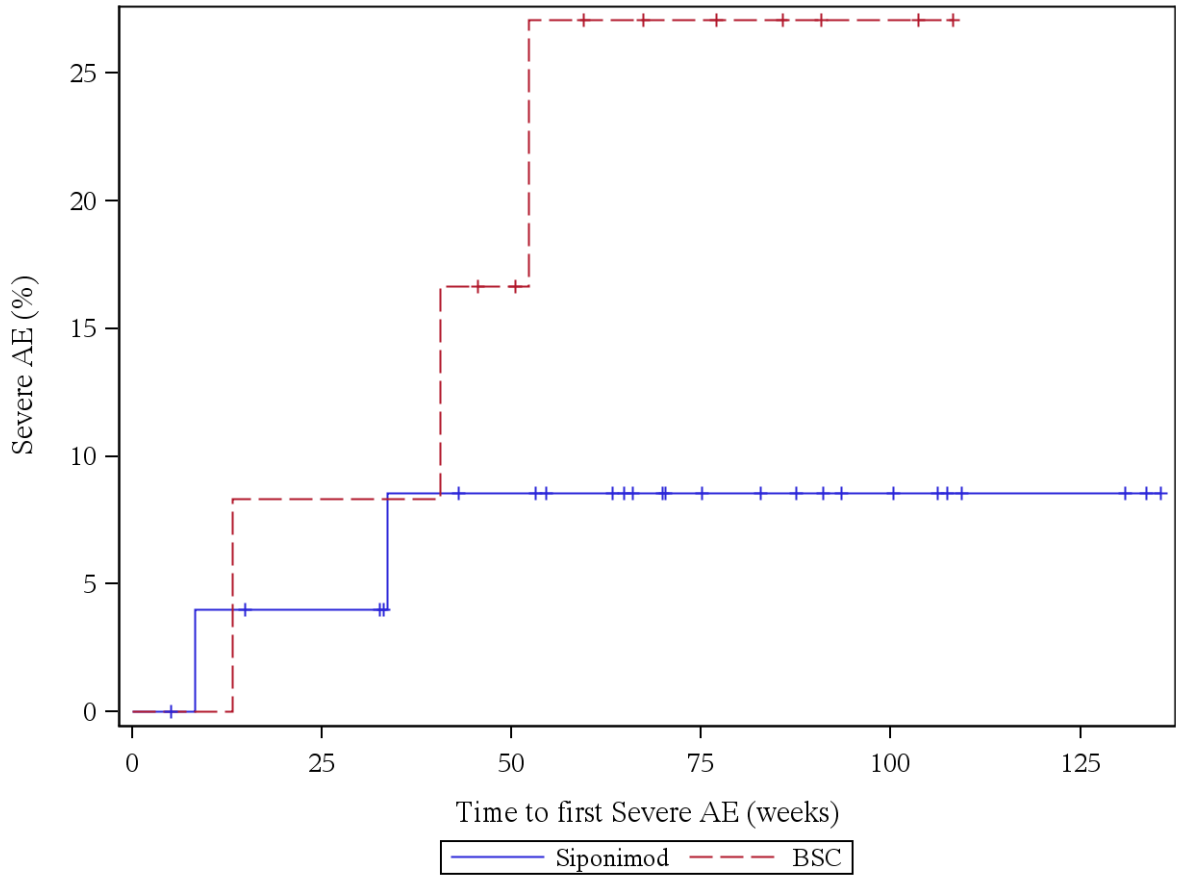
Patients at risk (Siponimod/BSC): Week 0: 200/112, Week 4: 193/111, Week 12: 180/107, Week 24: 164/102, Week 36: 156/98, Week 48: 144/92, Week 60: 113/74, Week 72: 90/57, Week 84: 70/47, Week 96: 54/36, Week 108: 41/24, Week 120: 31/18, Week 132: 15/9, Week 144: 6/8, Week 156: 0/3

Log rank test: p-value = 0,043 *
*: p < 0,05

Analysis population: A2304 SAF total population

12.2.1.5: Any severe AE

Figure 12.2.1.5.1: Severe AE, Age = 18-30 years

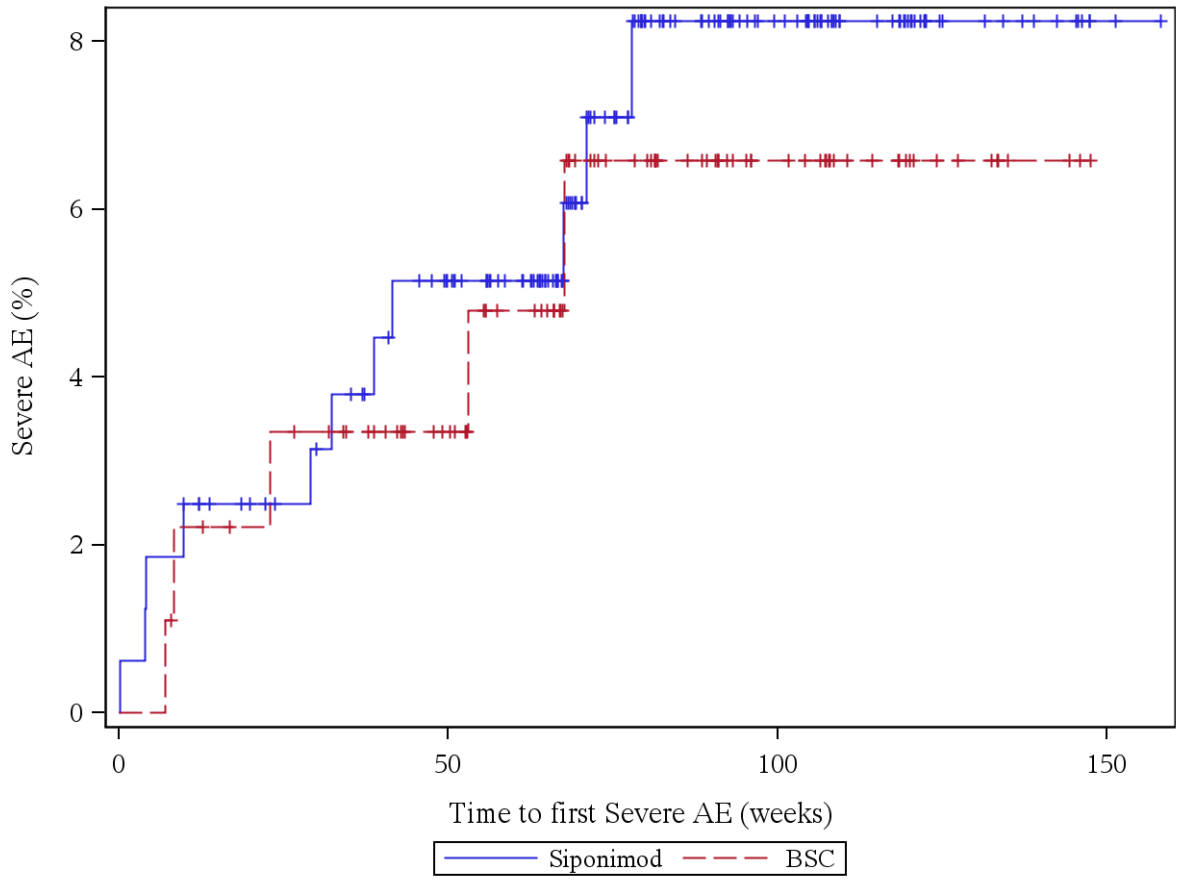


Patients at risk (Siponimod/BSC): Week 0: 26/12, Week 4: 26/12, Week 12: 24/12, Week 24: 23/11, Week 36: 20/11, Week 48: 19/9, Week 60: 17/6, Week 72: 12/5, Week 84: 10/4, Week 96: 7/2, Week 108: 4/1, Week 120: 3/0, Week 132: 2/0, Week 144: 0/0

Log rank test: p-value = 0,200
*: p < 0,05

Analysis population: A2304 SAF total population

Figure 12.2.1.5.2: Severe AE, Age = 31-40 years

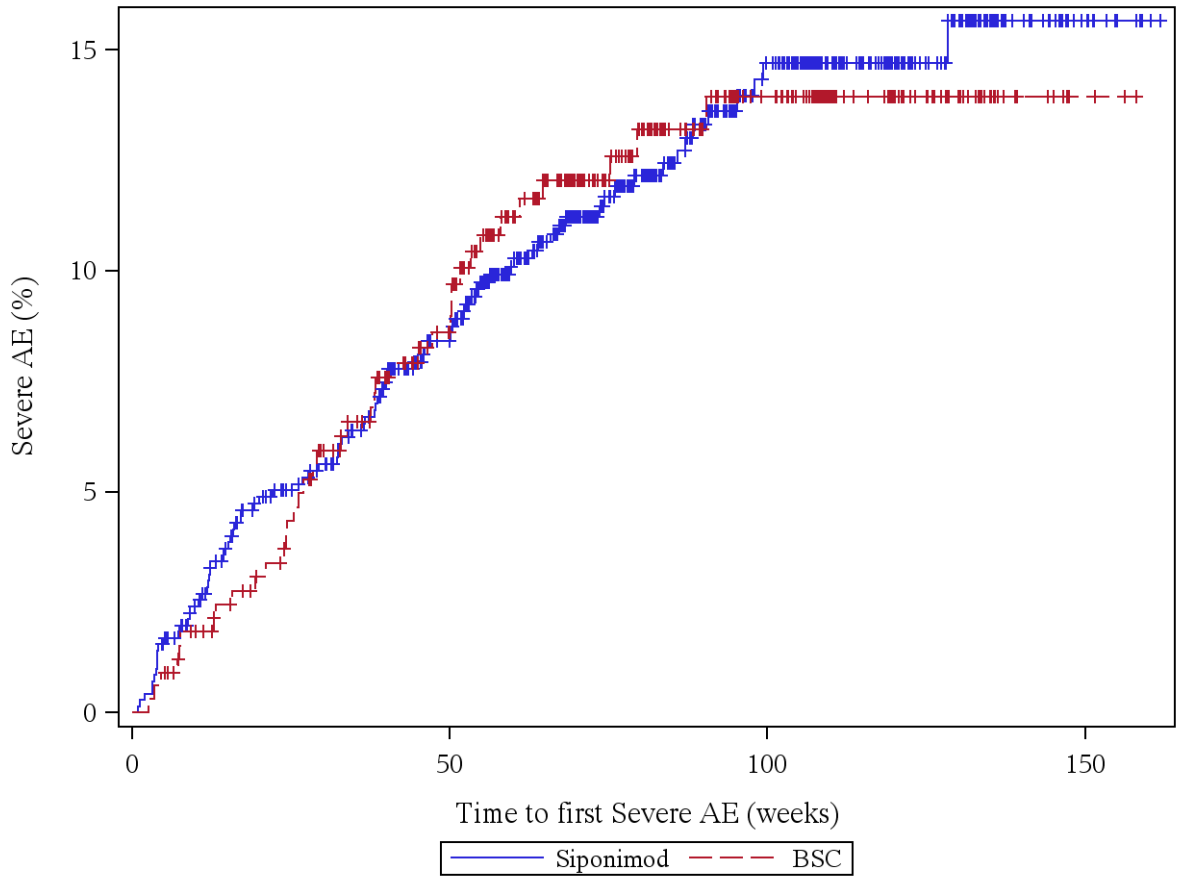


Patients at risk (Siponimod/BSC): Week 0: 161/91, Week 4: 159/91, Week 12: 156/88, Week 24: 149/85, Week 36: 145/81, Week 48: 138/73, Week 60: 124/62, Week 72: 88/47, Week 84: 66/36, Week 96: 52/24, Week 108: 35/17, Week 120: 22/10, Week 132: 11/7, Week 144: 7/3, Week 156: 1/0, Week 168: 0/0

Log rank test: p-value = 0,718
*: p < 0,05

Analysis population: A2304 SAF total population

Figure 12.2.1.5.3: Severe AE, Age = 41-55 years

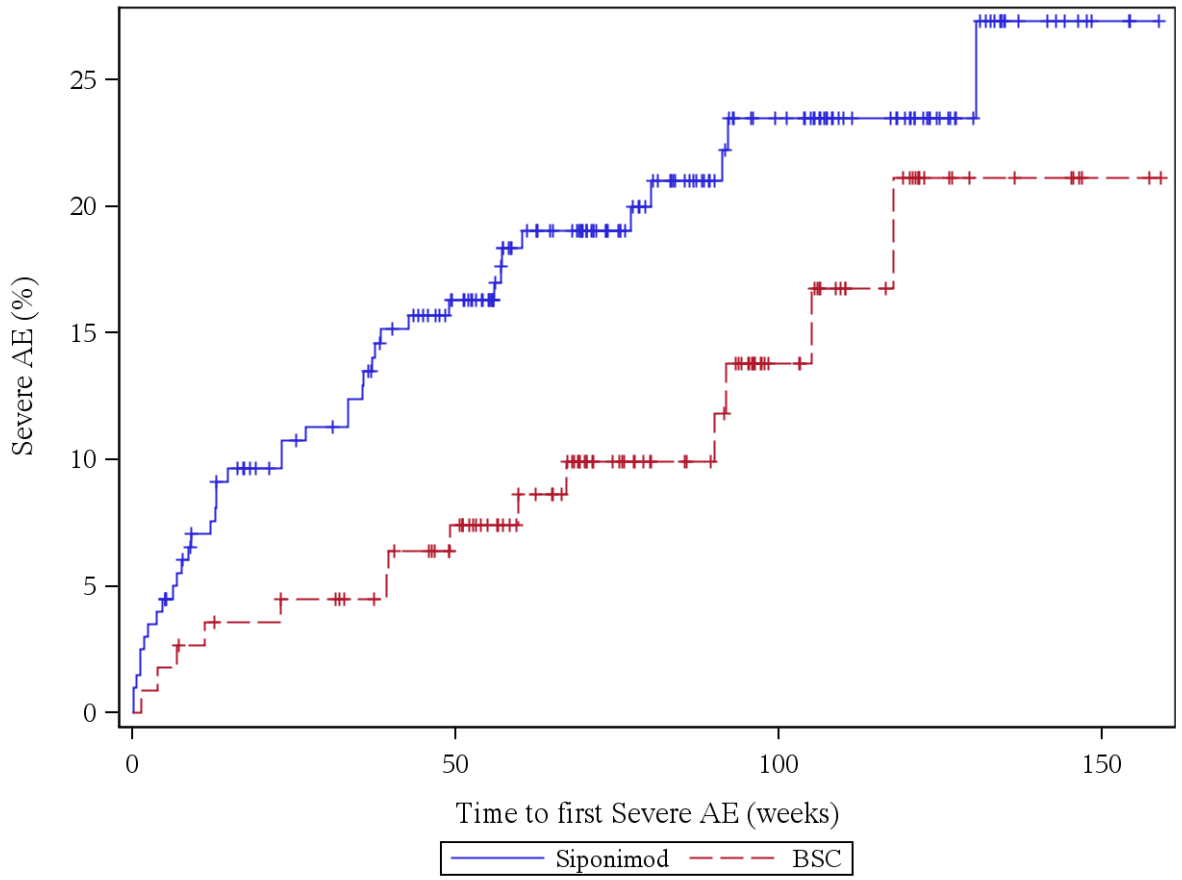


Patients at risk (Siponimod/BSC): Week 0: 712/331, Week 4: 702/329, Week 12: 670/318, Week 24: 637/304, Week 36: 611/283, Week 48: 562/257, Week 60: 498/218, Week 72: 401/170, Week 84: 313/126, Week 96: 241/98, Week 108: 175/70, Week 120: 119/43, Week 132: 69/21, Week 144: 31/8, Week 156: 6/2, Week 168: 0/0

Log rank test: p-value = 0,988
*: p < 0,05

Analysis population: A2304 SAF total population

Figure 12.2.1.5.4: Severe AE, Age = >55 years



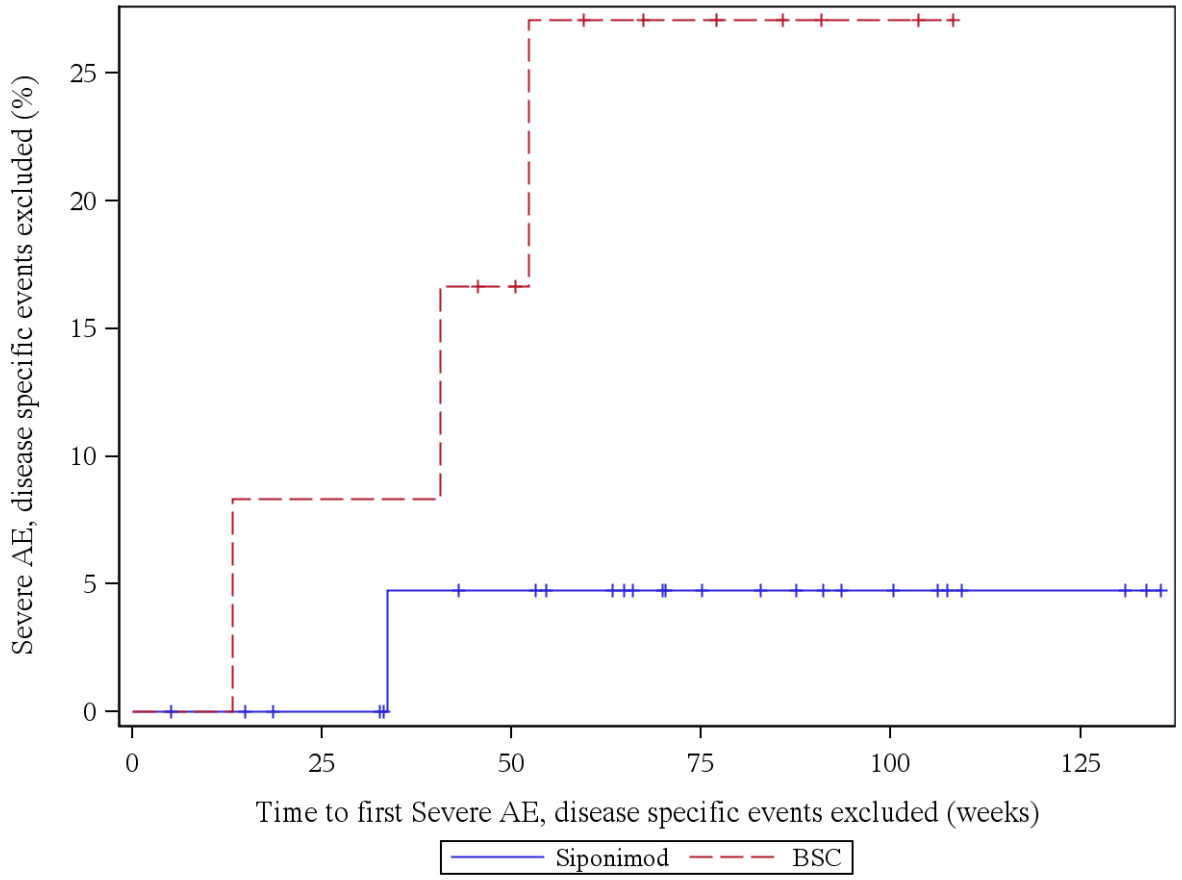
Patients at risk (Siponimod/BSC): Week 0: 200/112, Week 4: 192/110, Week 12: 178/107, Week 24: 165/104, Week 36: 158/101, Week 48: 144/94, Week 60: 114/75, Week 72: 93/59, Week 84: 73/50, Week 96: 56/37, Week 108: 44/24, Week 120: 35/17, Week 132: 17/7, Week 144: 7/6, Week 156: 1/2, Week 168: 0/0

Log rank test: p-value = 0,067
*: p < 0,05

Analysis population: A2304 SAF total population

12.2.1.6: Any severe AE, disease specific events excluded

Figure 12.2.1.6.1: Severe AE, disease specific events excluded, Age = 18-30 years

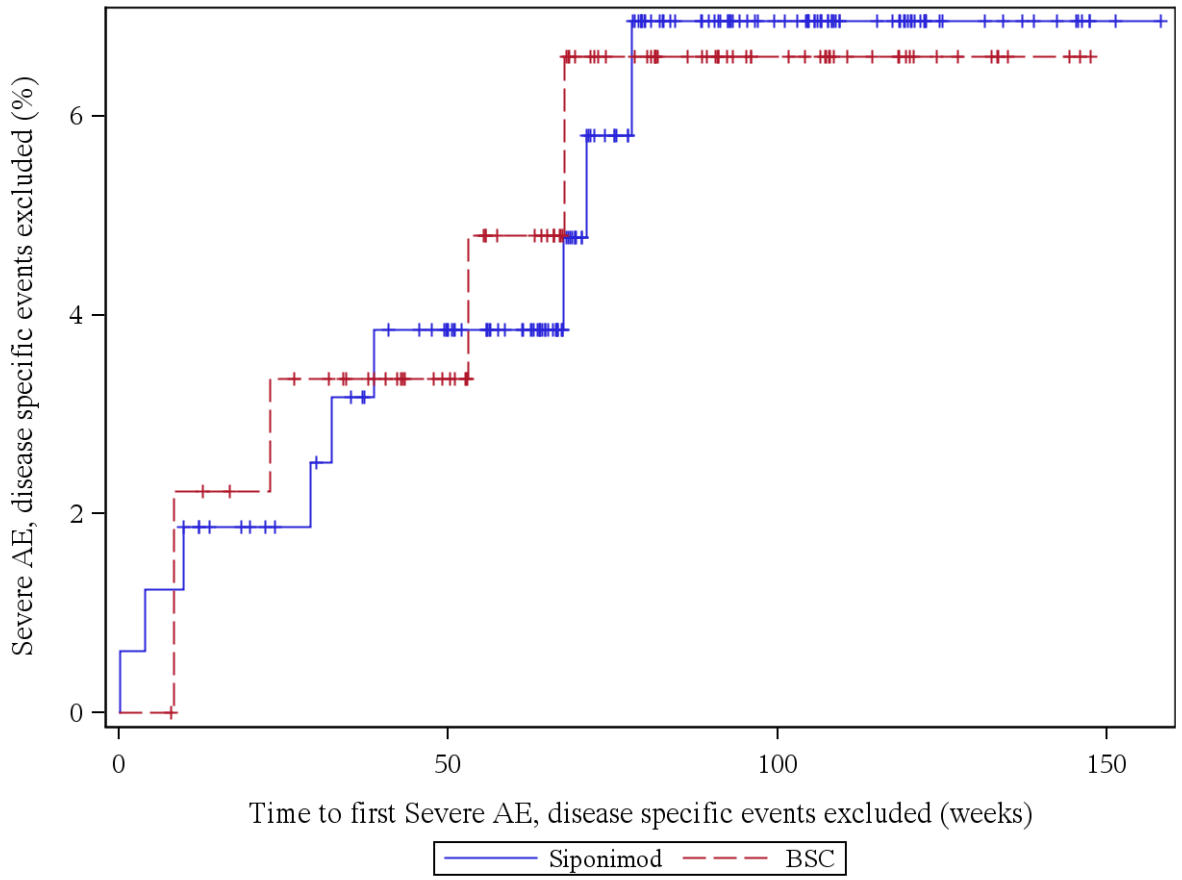


Patients at risk (Siponimod/BSC): Week 0: 26/12, Week 4: 26/12, Week 12: 25/12, Week 24: 23/11, Week 36: 20/11, Week 48: 19/9, Week 60: 17/6, Week 72: 12/5, Week 84: 10/4, Week 96: 7/2, Week 108: 4/1, Week 120: 3/0, Week 132: 2/0, Week 144: 0/0

Log rank test: p-value = 0,074
*: p < 0,05

Analysis population: A2304 SAF total population

Figure 12.2.1.6.2: Severe AE, disease specific events excluded, Age = 31-40 years

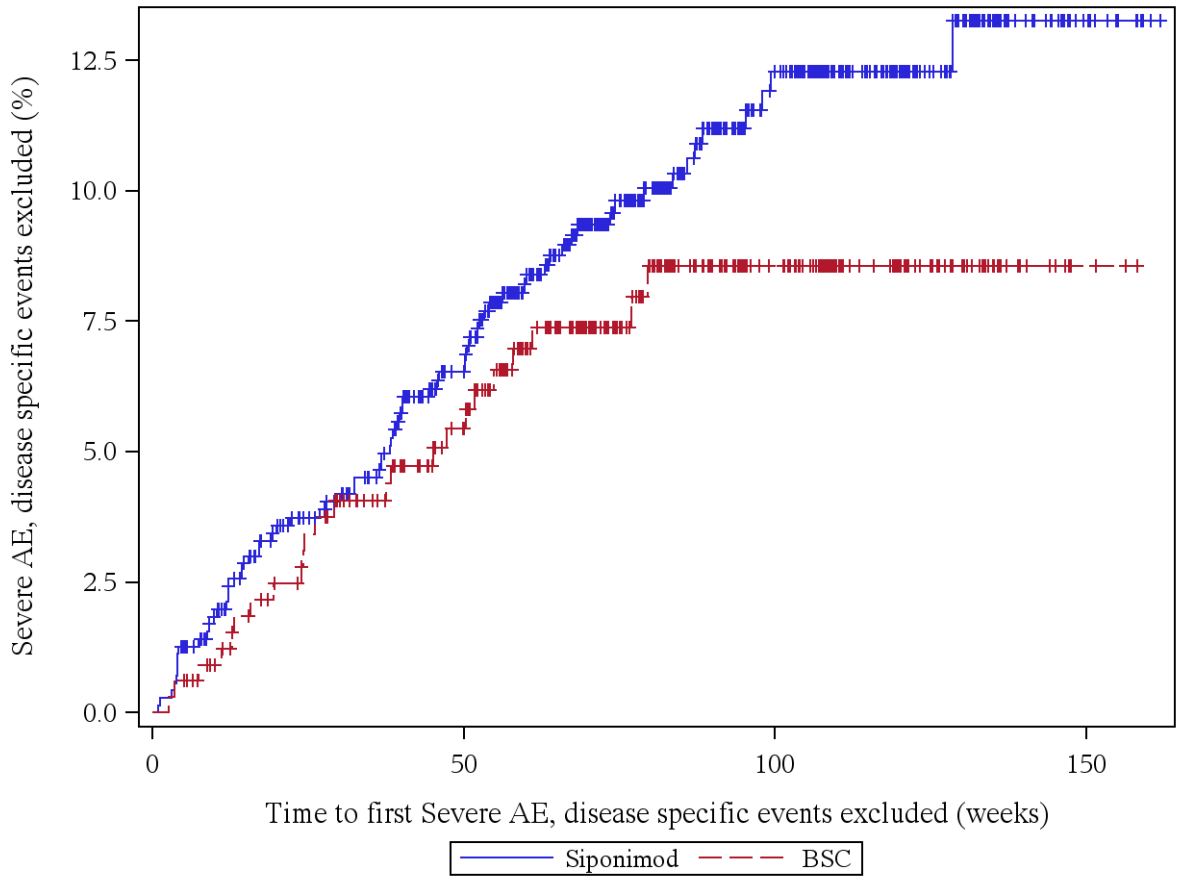


Patients at risk (Siponimod/BSC): Week 0: 161/91, Week 4: 159/91, Week 12: 157/88, Week 24: 150/85, Week 36: 146/81, Week 48: 140/73, Week 60: 125/62, Week 72: 89/47, Week 84: 67/36, Week 96: 53/24, Week 108: 35/17, Week 120: 22/10, Week 132: 11/7, Week 144: 7/3, Week 156: 1/0, Week 168: 0/0

Log rank test: p-value = 0,977
*: p < 0,05

Analysis population: A2304 SAF total population

Figure 12.2.1.6.3: Severe AE, disease specific events excluded, Age = 41-55 years

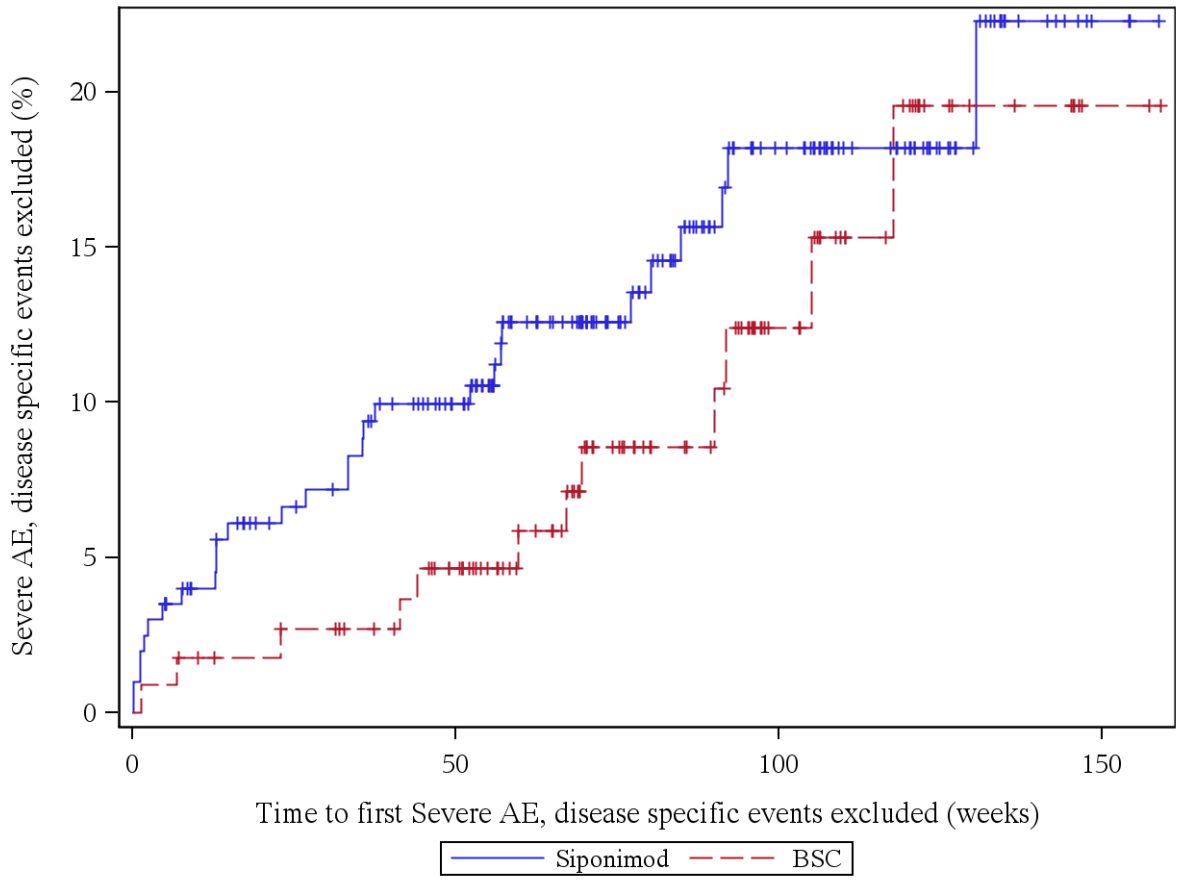


Patients at risk (Siponimod/BSC): Week 0: 712/331, Week 4: 704/329, Week 12: 675/319, Week 24: 644/306, Week 36: 621/288, Week 48: 570/263, Week 60: 506/225, Week 72: 408/175, Week 84: 320/131, Week 96: 247/100, Week 108: 181/72, Week 120: 123/45, Week 132: 71/23, Week 144: 31/9, Week 156: 6/2, Week 168: 0/0

Log rank test: p-value = 0,204
*: p < 0,05

Analysis population: A2304 SAF total population

Figure 12.2.1.6.4: Severe AE, disease specific events excluded, Age = >55 years



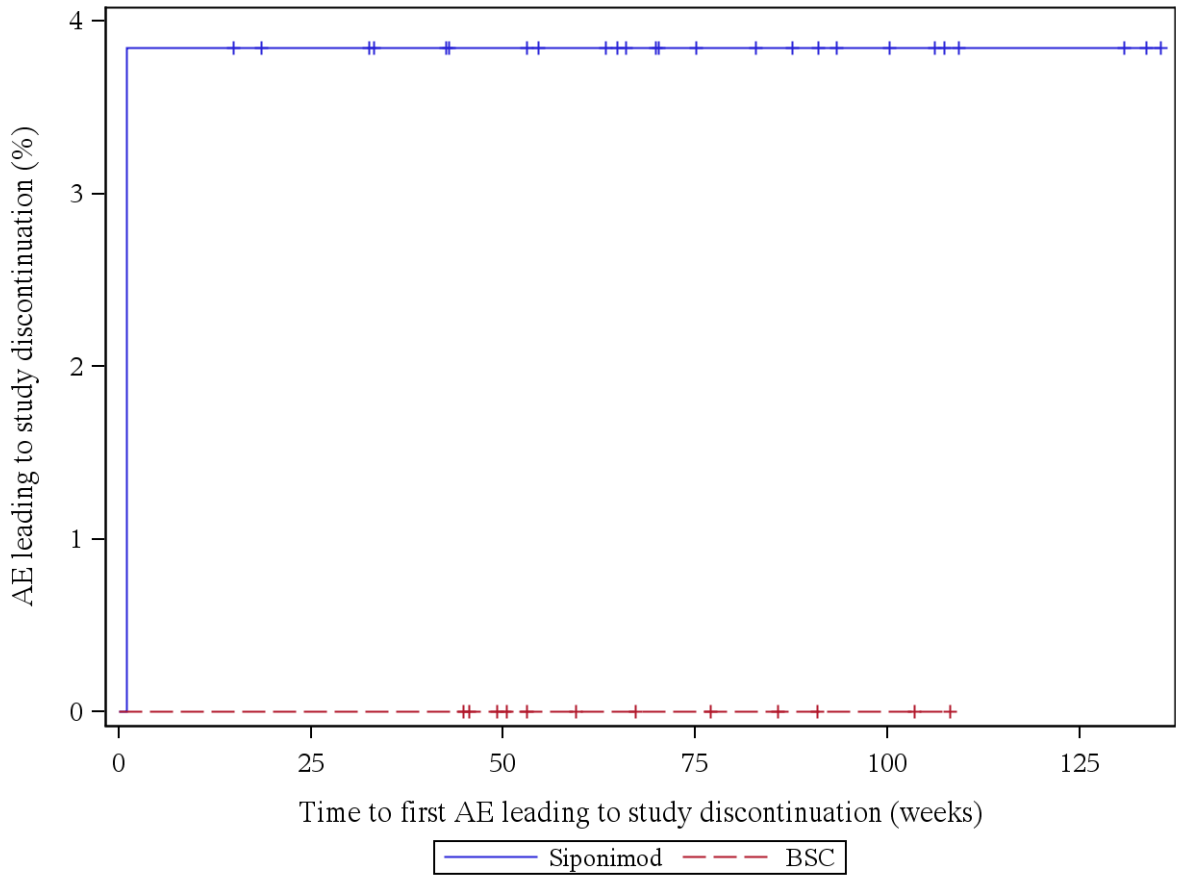
Patients at risk (Siponimod/BSC): Week 0: 200/112, Week 4: 194/111, Week 12: 184/108, Week 24: 172/105, Week 36: 165/102, Week 48: 154/95, Week 60: 122/77, Week 72: 99/60, Week 84: 78/51, Week 96: 58/38, Week 108: 45/25, Week 120: 35/18, Week 132: 17/8, Week 144: 7/7, Week 156: 1/2, Week 168: 0/0

Log rank test: p-value = 0,271
*: p < 0,05

Analysis population: A2304 SAF total population

12.2.1.7: Any AE leading to study discontinuation

Figure 12.2.1.7.1: AE leading to study discontinuation, Age = 18-30 years

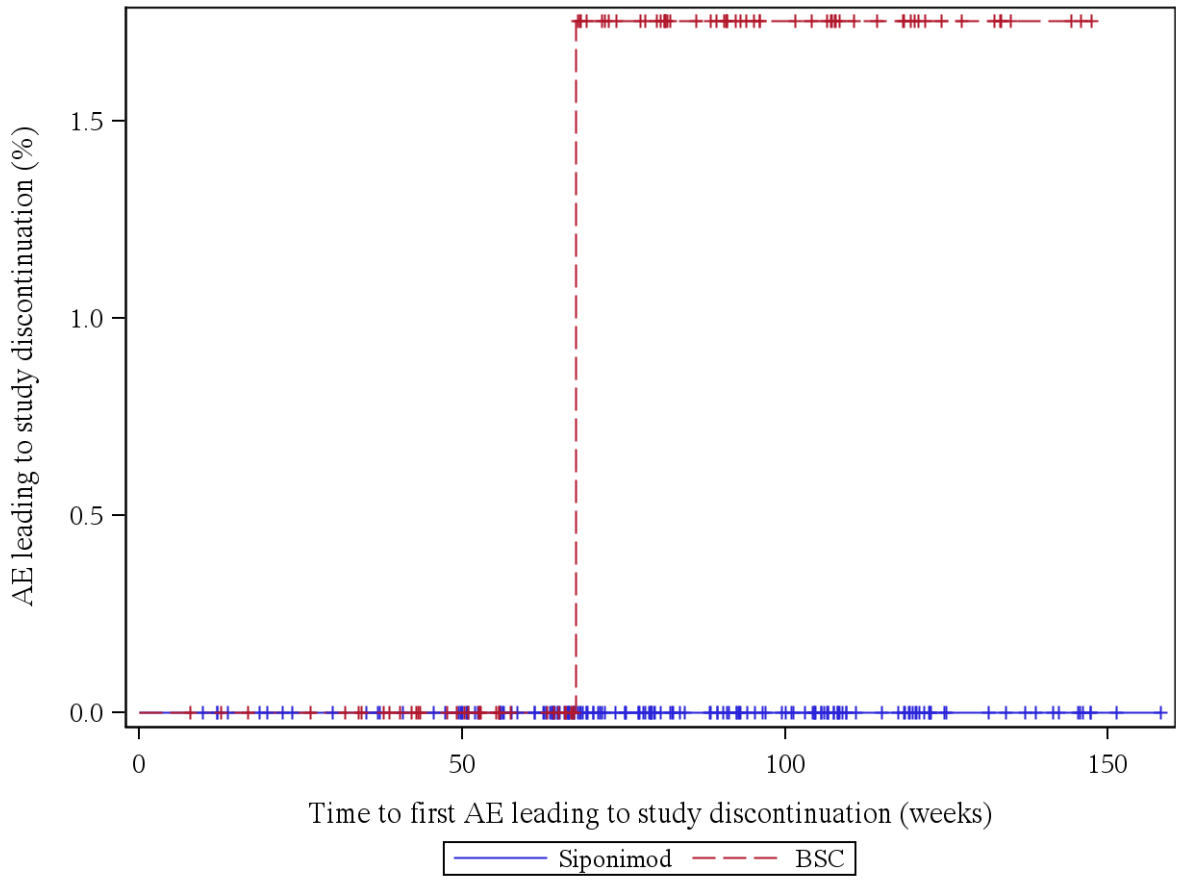


Patients at risk (Siponimod/BSC): Week 0: 26/12, Week 4: 25/12, Week 12: 25/12, Week 24: 23/12, Week 36: 21/12, Week 48: 19/10, Week 60: 17/6, Week 72: 12/5, Week 84: 10/4, Week 96: 7/2, Week 108: 4/1, Week 120: 3/0, Week 132: 2/0, Week 144: 0/0

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

Analysis population: A2304 SAF total population

Figure 12.2.1.7.2: AE leading to study discontinuation, Age = 31-40 years

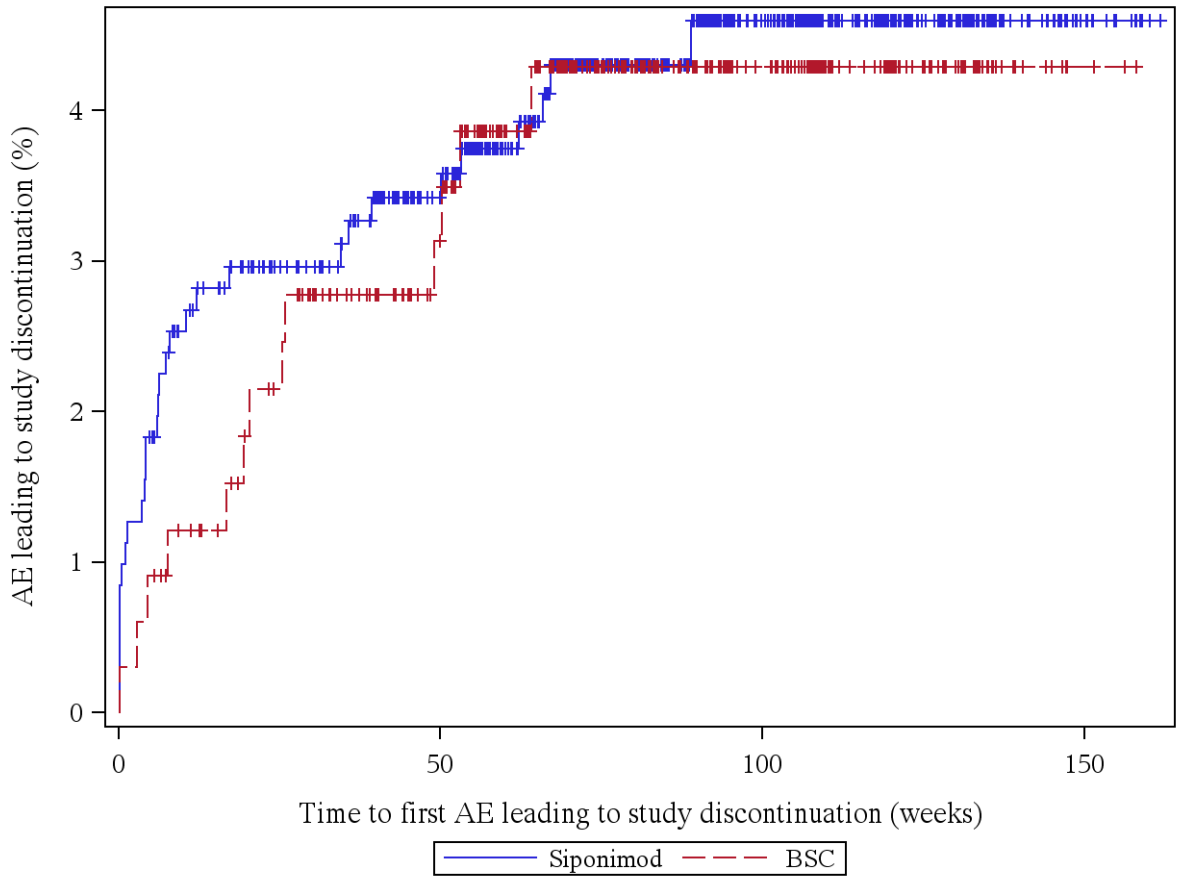


Patients at risk (Siponimod/BSC): Week 0: 161/91, Week 4: 161/91, Week 12: 160/90, Week 24: 153/88, Week 36: 151/84, Week 48: 146/76, Week 60: 130/66, Week 72: 95/51, Week 84: 73/38, Week 96: 58/25, Week 108: 38/18, Week 120: 23/11, Week 132: 12/7, Week 144: 7/3, Week 156: 1/0, Week 168: 0/0

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

Analysis population: A2304 SAF total population

Figure 12.2.1.7.3: AE leading to study discontinuation, Age = 41-55 years

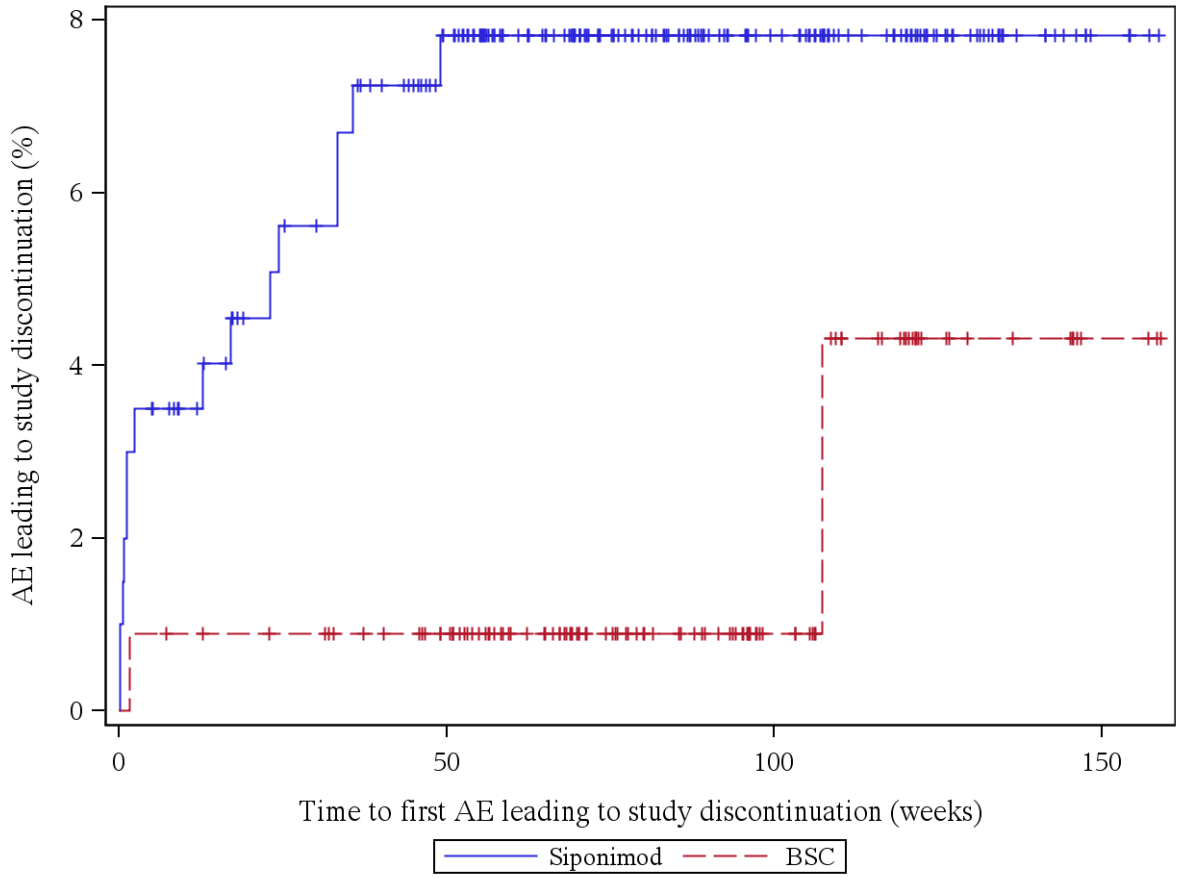


Patients at risk (Siponimod/BSC): Week 0: 712/331, Week 4: 701/329, Week 12: 680/322, Week 24: 659/311, Week 36: 639/296, Week 48: 597/275, Week 60: 538/234, Week 72: 436/183, Week 84: 345/140, Week 96: 268/107, Week 108: 197/78, Week 120: 133/49, Week 132: 78/24, Week 144: 35/9, Week 156: 7/2, Week 168: 0/0

Log rank test: p-value = 0,852
*: p < 0,05

Analysis population: A2304 SAF total population

Figure 12.2.1.7.4: AE leading to study discontinuation, Age = >55 years



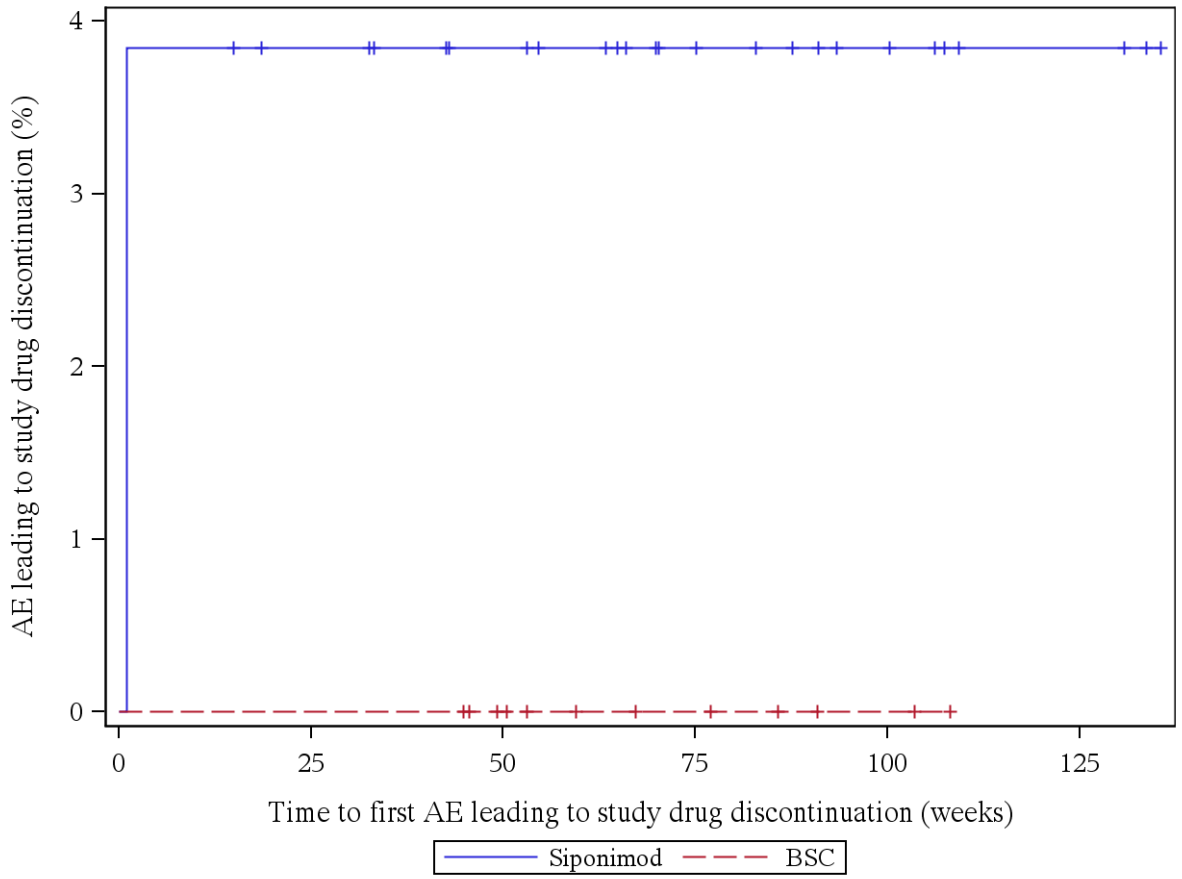
Patients at risk (Siponimod/BSC): Week 0: 200/112, Week 4: 193/111, Week 12: 186/110, Week 24: 177/108, Week 36: 171/105, Week 48: 160/100, Week 60: 131/81, Week 72: 107/65, Week 84: 87/55, Week 96: 67/42, Week 108: 52/28, Week 120: 41/20, Week 132: 21/9, Week 144: 9/8, Week 156: 2/3, Week 168: 0/0

Log rank test: p-value = 0,032 *
*: p < 0,05

Analysis population: A2304 SAF total population

12.2.1.8: Any AE leading to study drug discontinuation

Figure 12.2.1.8.1: AE leading to study drug discontinuation, Age = 18-30 years

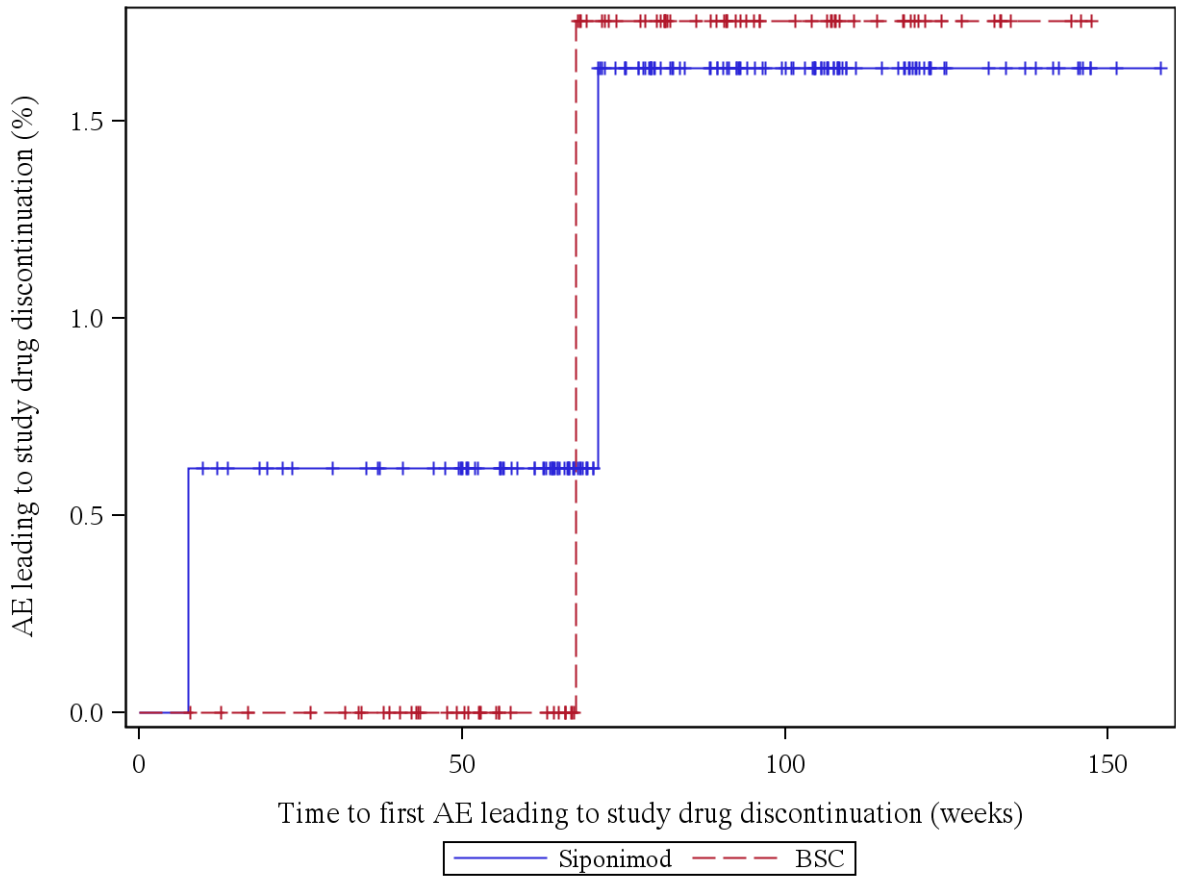


Patients at risk (Siponimod/BSC): Week 0: 26/12, Week 4: 25/12, Week 12: 25/12, Week 24: 23/12, Week 36: 21/12, Week 48: 19/10, Week 60: 17/6, Week 72: 12/5, Week 84: 10/4, Week 96: 7/2, Week 108: 4/1, Week 120: 3/0, Week 132: 2/0, Week 144: 0/0

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

Analysis population: A2304 SAF total population

Figure 12.2.1.8.2: AE leading to study drug discontinuation, Age = 31-40 years

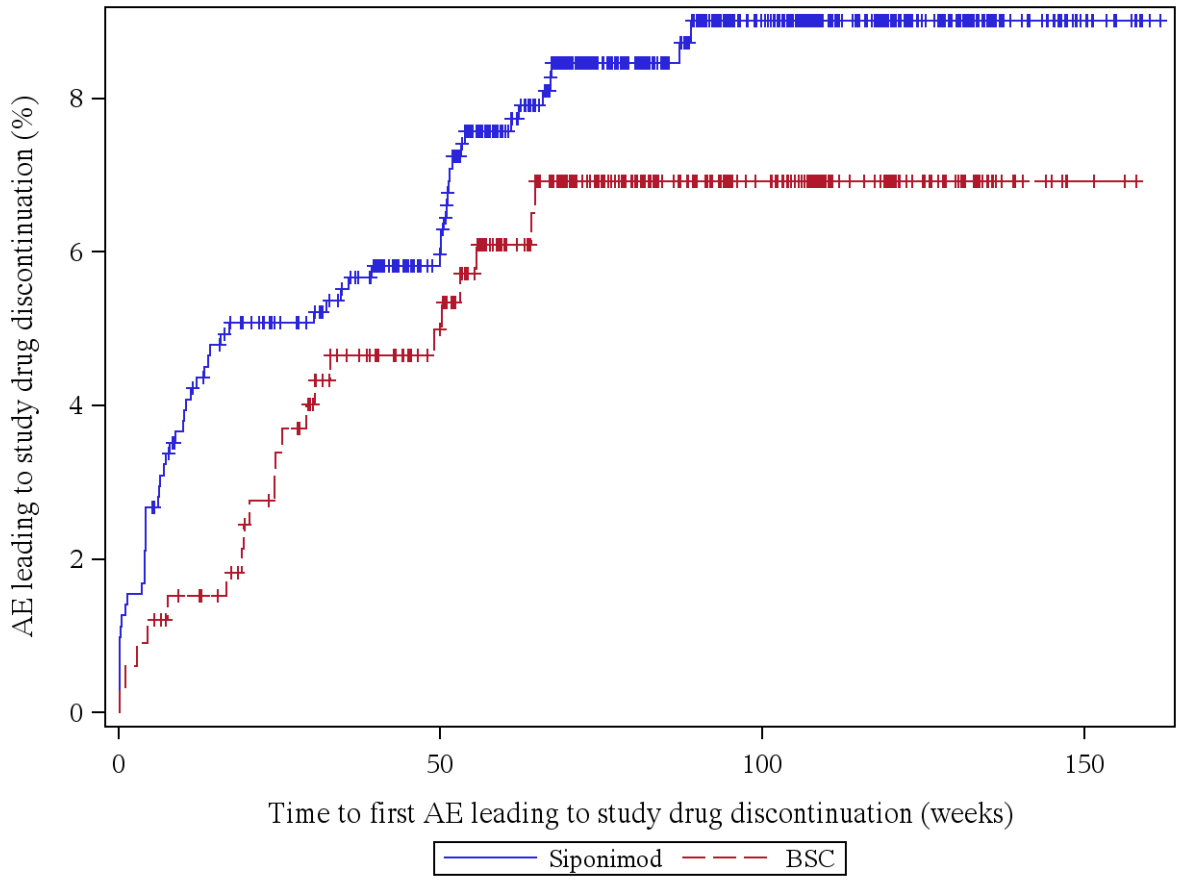


Patients at risk (Siponimod/BSC): Week 0: 161/91, Week 4: 161/91, Week 12: 159/90, Week 24: 153/88, Week 36: 151/84, Week 48: 146/76, Week 60: 130/66, Week 72: 94/51, Week 84: 73/38, Week 96: 58/25, Week 108: 38/18, Week 120: 23/11, Week 132: 12/7, Week 144: 7/3, Week 156: 1/0, Week 168: 0/0

Log rank test: p-value = 0,947
*: p < 0,05

Analysis population: A2304 SAF total population

Figure 12.2.1.8.3: AE leading to study drug discontinuation, Age = 41-55 years

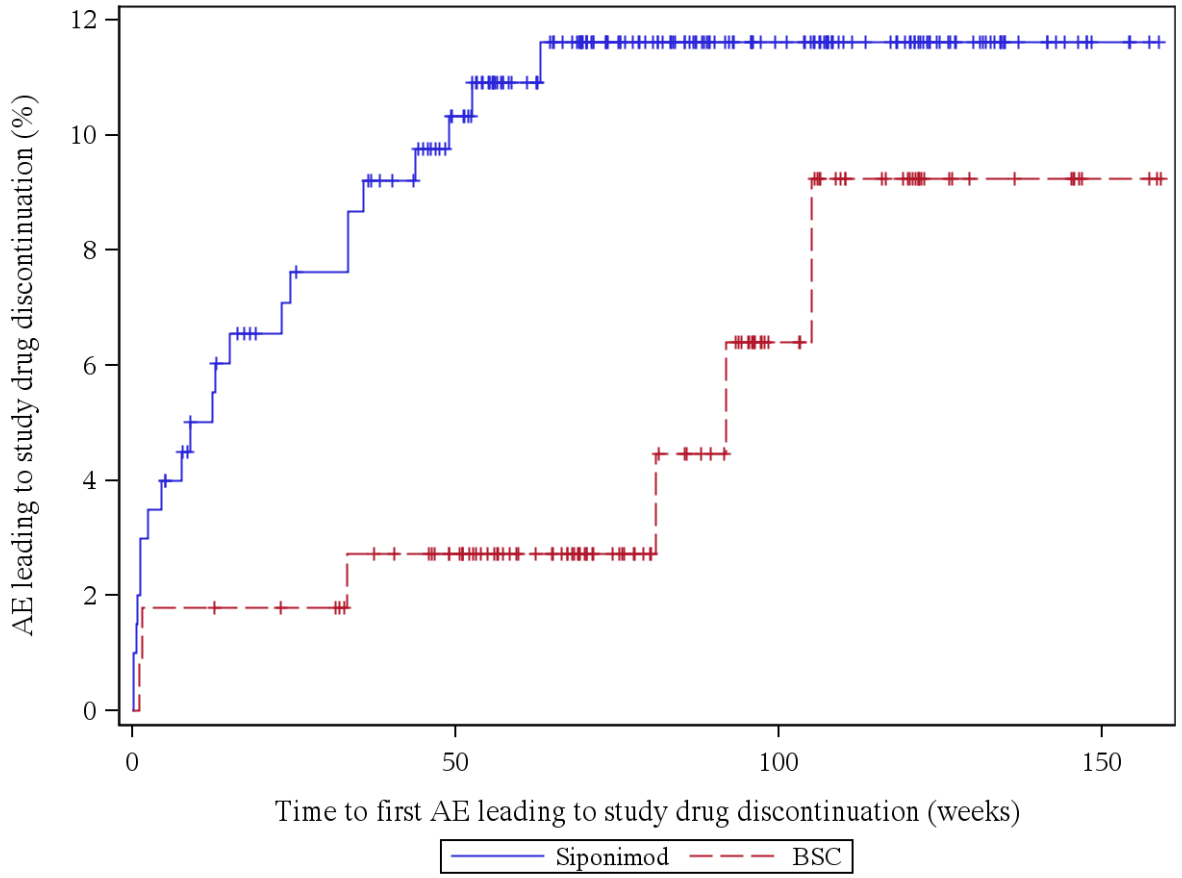


Patients at risk (Siponimod/BSC): Week 0: 712/331, Week 4: 697/328, Week 12: 675/322, Week 24: 656/311, Week 36: 637/293, Week 48: 597/274, Week 60: 535/233, Week 72: 433/183, Week 84: 344/140, Week 96: 268/107, Week 108: 197/78, Week 120: 133/49, Week 132: 78/24, Week 144: 35/9, Week 156: 7/2, Week 168: 0/0

Log rank test: p-value = 0,306
*: p < 0,05

Analysis population: A2304 SAF total population

Figure 12.2.1.8.4: AE leading to study drug discontinuation, Age = >55 years



Patients at risk (Siponimod/BSC): Week 0: 200/112, Week 4: 193/110, Week 12: 185/110, Week 24: 176/108, Week 36: 171/104, Week 48: 159/99, Week 60: 131/81, Week 72: 107/65, Week 84: 87/54, Week 96: 67/41, Week 108: 52/28, Week 120: 41/20, Week 132: 21/9, Week 144: 9/8, Week 156: 2/3, Week 168: 0/0

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

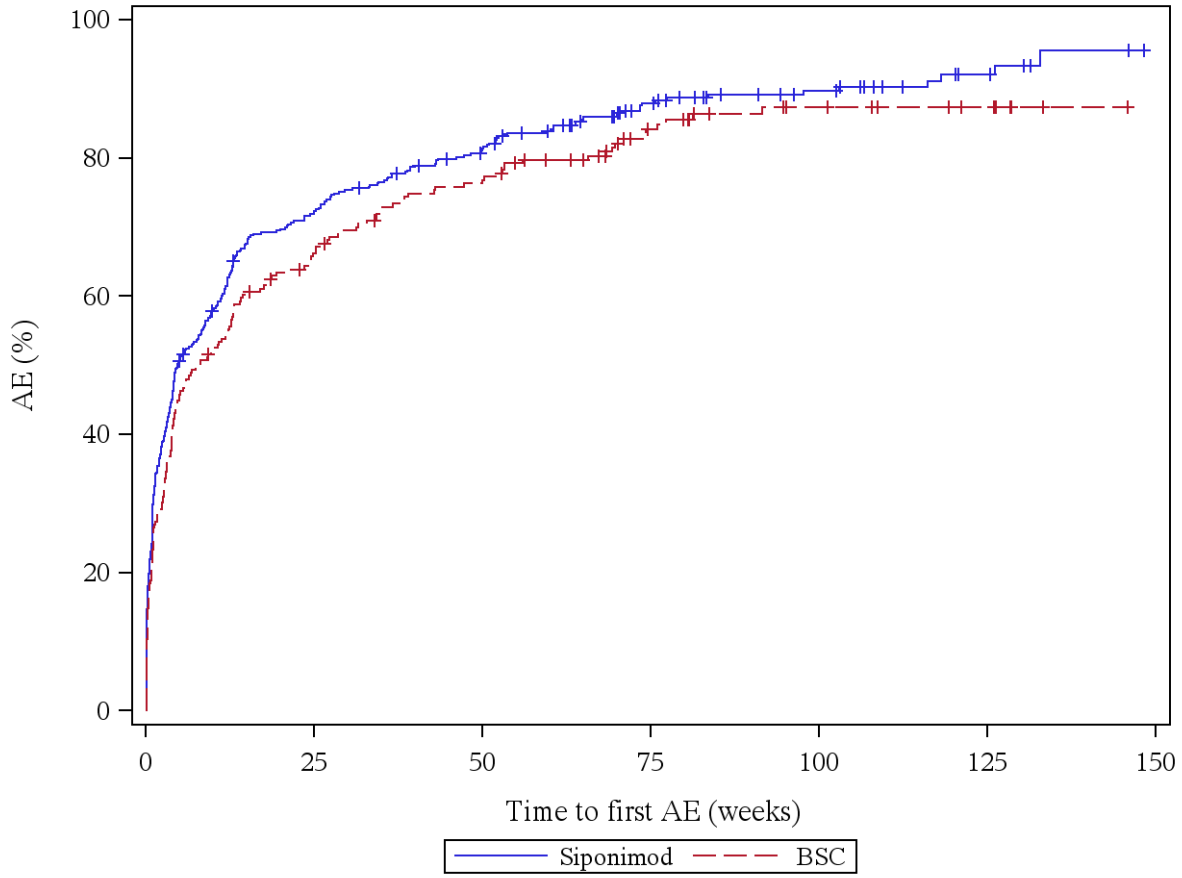
Analysis population: A2304 SAF total population

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

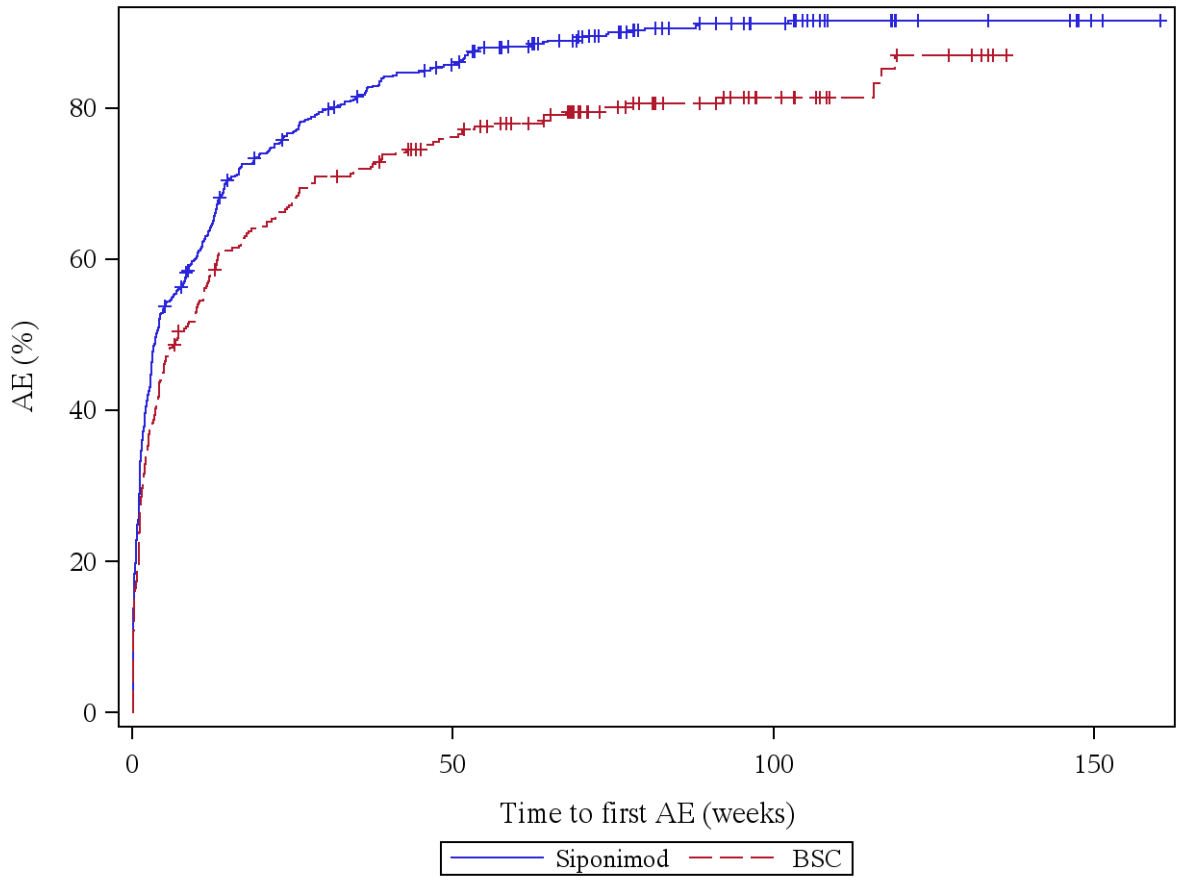


Patients at risk (Siponimod/BSC): Week 0: 435/223, Week 4: 234/131, Week 12: 165/101, Week 24: 121/76, Week 36: 96/56, Week 48: 80/49, Week 60: 60/38, Week 72: 38/25, Week 84: 24/14, Week 96: 21/11, Week 108: 14/9, Week 120: 9/7, Week 132: 3/2, Week 144: 2/1, Week 156: 0/0

Log rank test: p-value = 0,059
*: p < 0,05

Analysis population: A2304 SAF total population

Figure 12.3.1.1.2: AE, Gender = Female



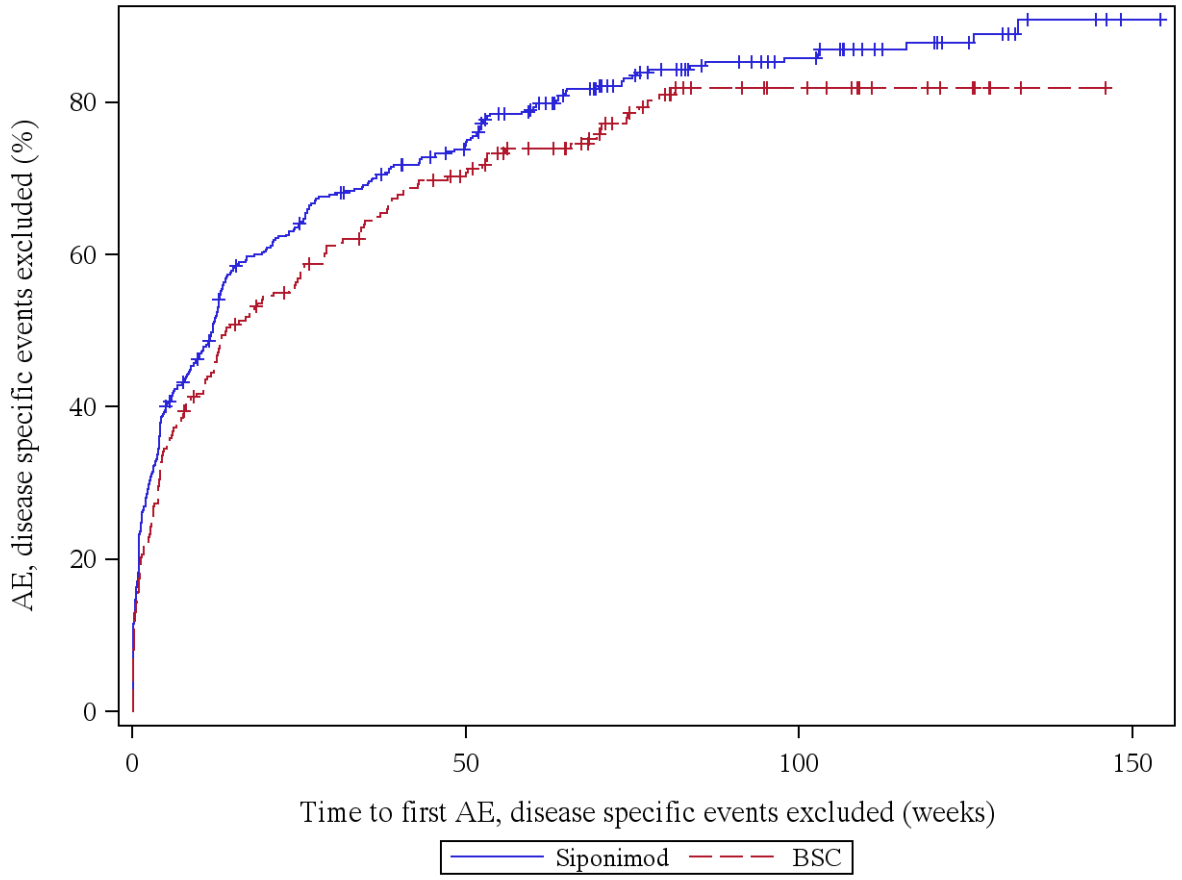
Patients at risk (Siponimod/BSC): Week 0: 664/323, Week 4: 326/188, Week 12: 237/135, Week 24: 152/106, Week 36: 114/88, Week 48: 89/71, Week 60: 65/58, Week 72: 47/40, Week 84: 32/26, Week 96: 25/20, Week 108: 14/12, Week 120: 8/6, Week 132: 7/4, Week 144: 6/0, Week 156: 1/0, Week 168: 0/0

Log rank test: p-value = <0,001 *
*: p < 0,05

Analysis population: A2304 SAF total population

12.3.1.2: Any AE, disease specific events excluded

Figure 12.3.1.2.1: AE, disease specific events excluded, Gender = Male

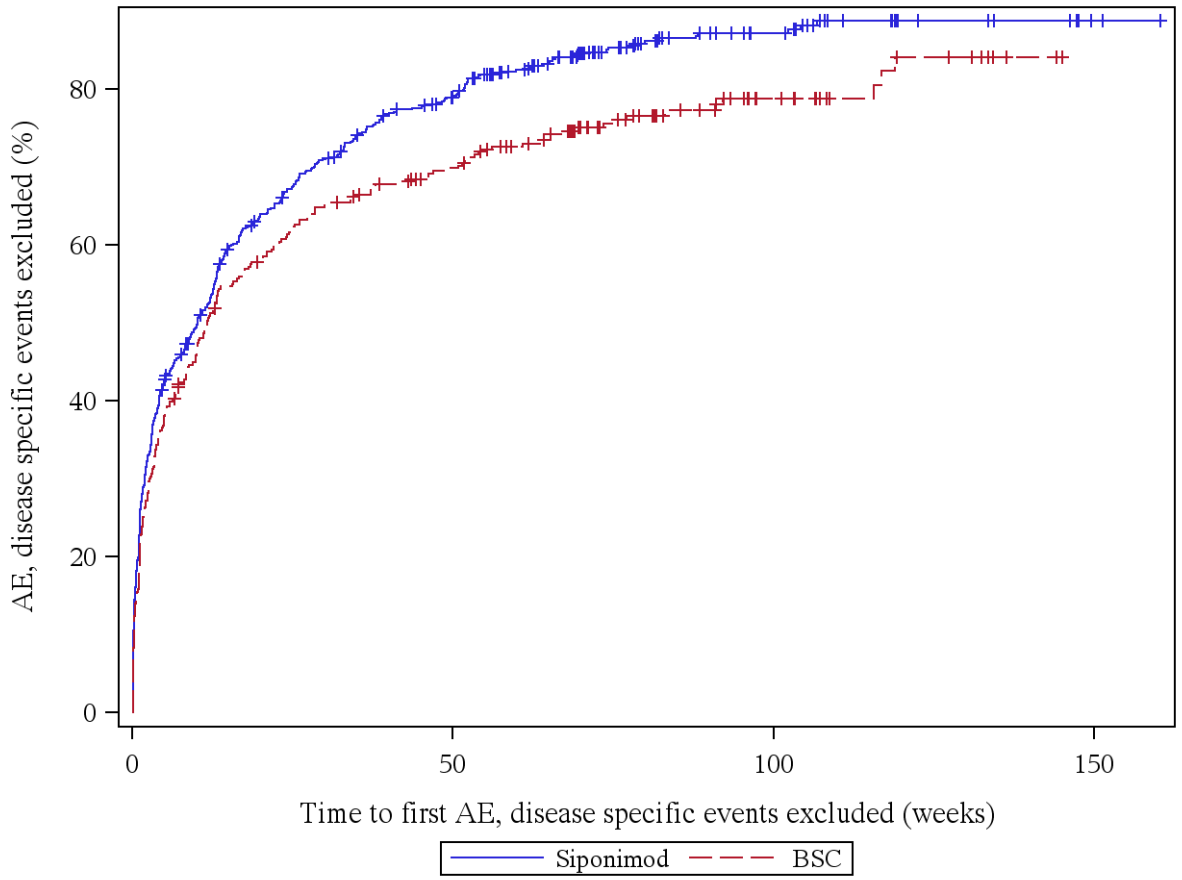


Patients at risk (Siponimod/BSC): Week 0: 435/223, Week 4: 278/155, Week 12: 213/122, Week 24: 155/95, Week 36: 123/74, Week 48: 104/60, Week 60: 74/46, Week 72: 50/31, Week 84: 34/17, Week 96: 28/14, Week 108: 19/11, Week 120: 14/7, Week 132: 7/2, Week 144: 4/1, Week 156: 0/0

Log rank test: p-value = 0,066
*: p < 0,05

Analysis population: A2304 SAF total population

Figure 12.3.1.2.2: AE, disease specific events excluded, Gender = Female



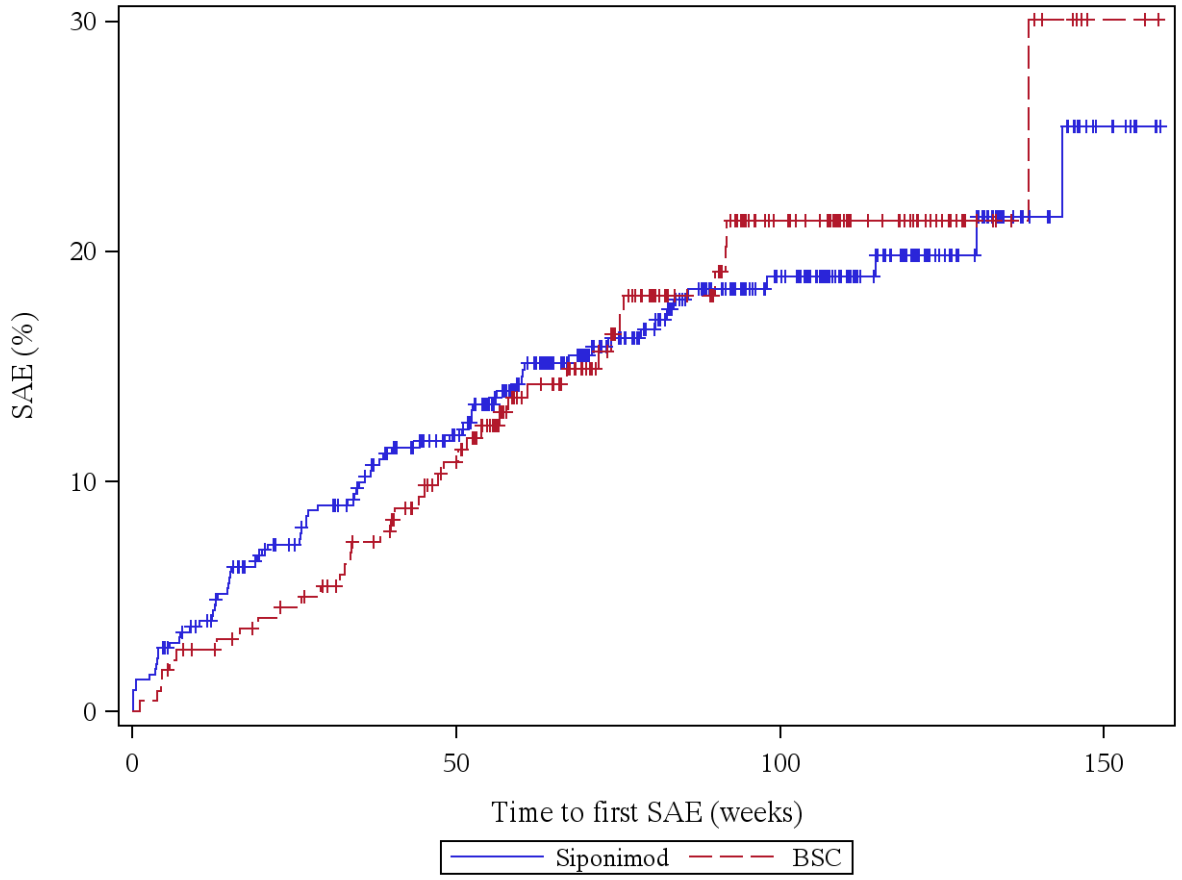
Patients at risk (Siponimod/BSC): Week 0: 664/323, Week 4: 402/209, Week 12: 308/156, Week 24: 211/122, Week 36: 158/102, Week 48: 128/88, Week 60: 91/72, Week 72: 61/51, Week 84: 38/33, Week 96: 30/23, Week 108: 17/14, Week 120: 9/8, Week 132: 8/6, Week 144: 6/2, Week 156: 1/0, Week 168: 0/0

Log rank test: p-value = 0,004 *
*: p < 0,05

Analysis population: A2304 SAF total population

12.3.1.3: Any SAE

Figure 12.3.1.3.1: SAE, Gender = Male

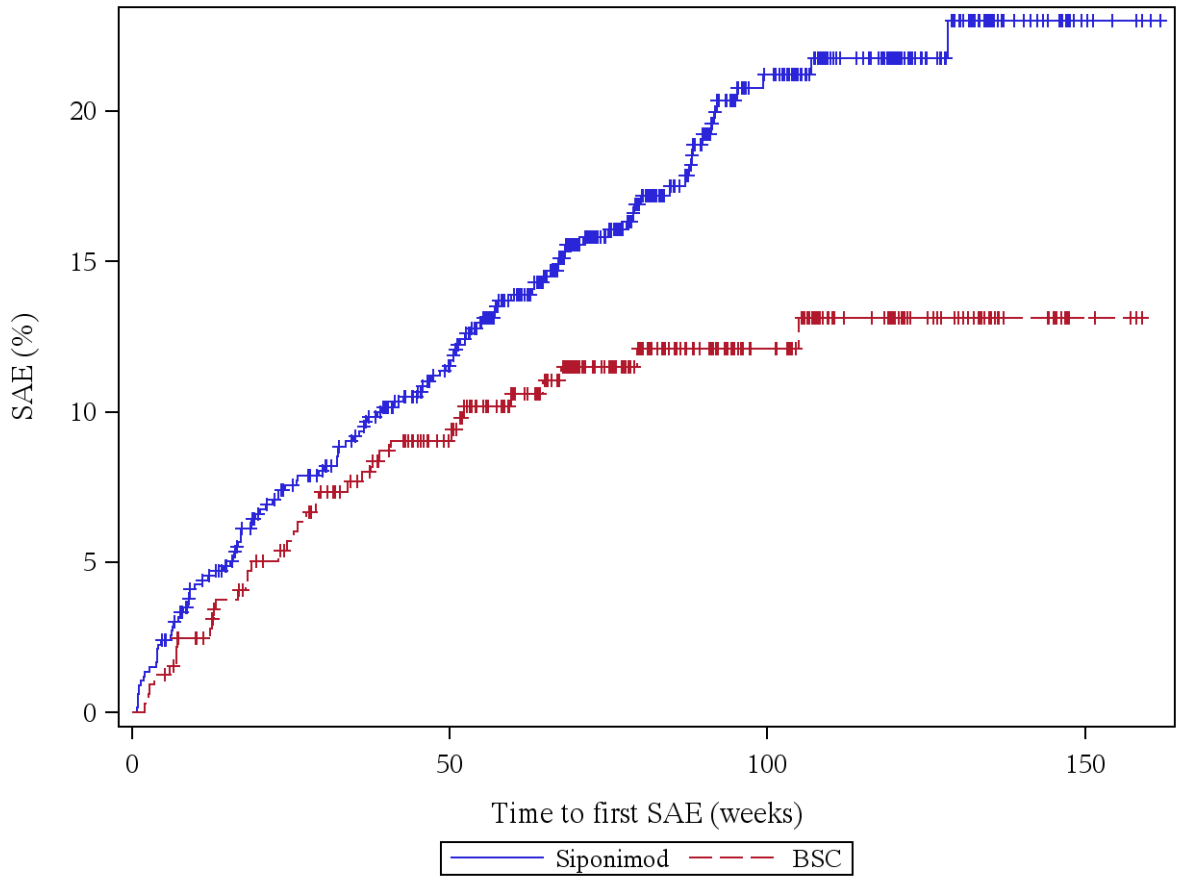


Patients at risk (Siponimod/BSC): Week 0: 435/223, Week 4: 423/221, Week 12: 408/214, Week 24: 380/206, Week 36: 358/193, Week 48: 335/174, Week 60: 283/141, Week 72: 226/111, Week 84: 185/82, Week 96: 152/58, Week 108: 108/46, Week 120: 74/30, Week 132: 39/12, Week 144: 19/6, Week 156: 3/2, Week 168: 0/0

Log rank test: p-value = 0,911
*: p < 0,05

Analysis population: A2304 SAF total population

Figure 12.3.1.3.2: SAE, Gender = Female



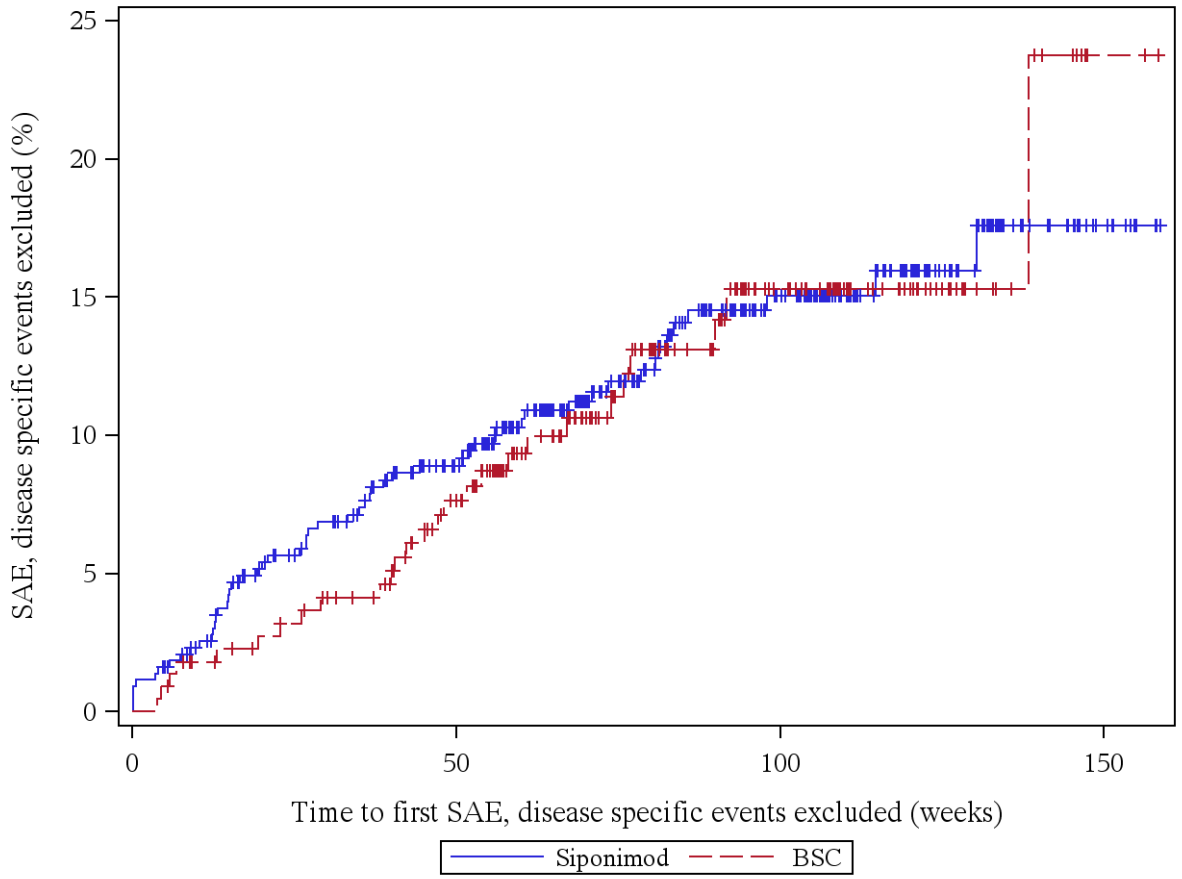
Patients at risk (Siponimod/BSC): Week 0: 664/323, Week 4: 650/319, Week 12: 616/308, Week 24: 579/290, Week 36: 554/272, Week 48: 510/249, Week 60: 447/213, Week 72: 338/166, Week 84: 252/129, Week 96: 185/99, Week 108: 134/66, Week 120: 90/42, Week 132: 49/26, Week 144: 21/13, Week 156: 4/3, Week 168: 0/0

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

Analysis population: A2304 SAF total population

12.3.1.4: Any SAE, disease specific events excluded

Figure 12.3.1.4.1: SAE, disease specific events excluded, Gender = Male

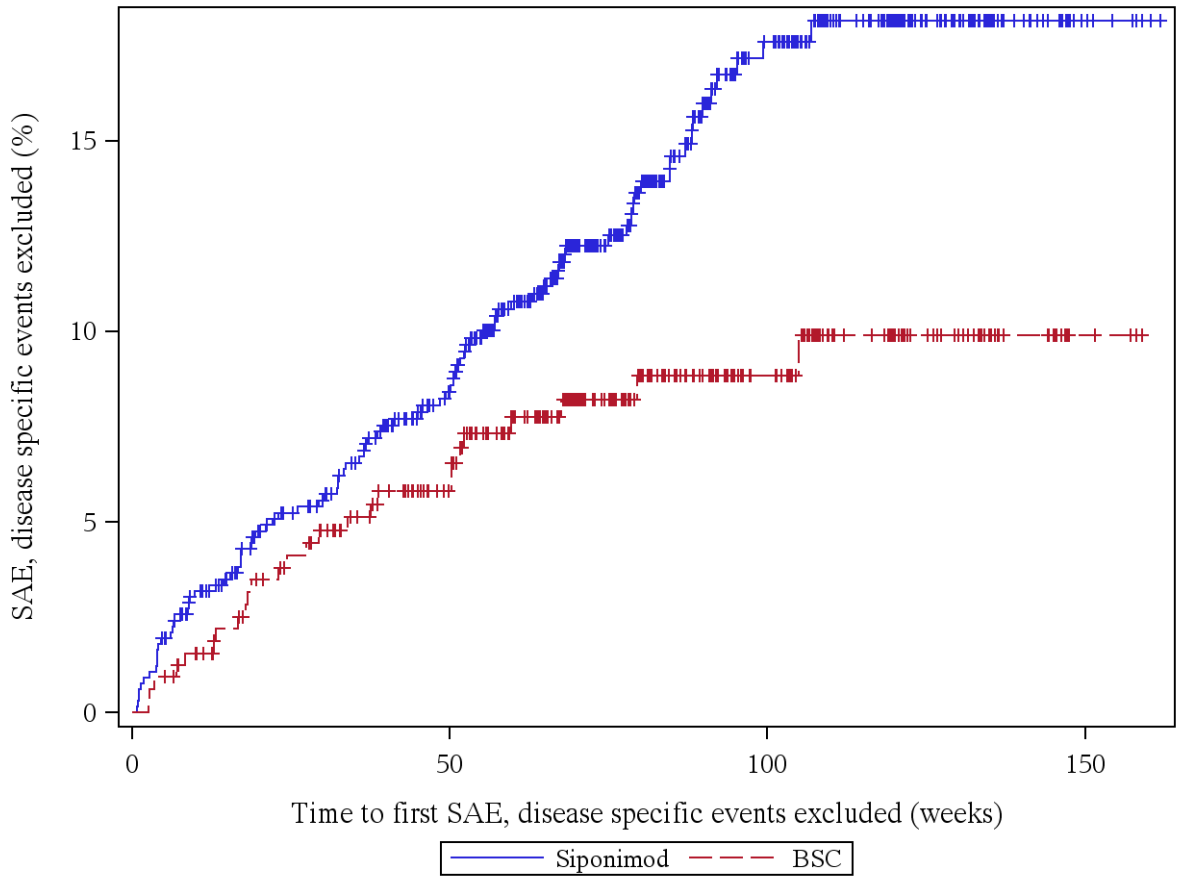


Patients at risk (Siponimod/BSC): Week 0: 435/223, Week 4: 428/222, Week 12: 413/215, Week 24: 386/208, Week 36: 368/199, Week 48: 346/178, Week 60: 296/146, Week 72: 237/115, Week 84: 195/86, Week 96: 161/62, Week 108: 113/48, Week 120: 78/31, Week 132: 43/13, Week 144: 22/7, Week 156: 3/2, Week 168: 0/0

Log rank test: p-value = 0,852
*: p < 0,05

Analysis population: A2304 SAF total population

Figure 12.3.1.4.2: SAE, disease specific events excluded, Gender = Female



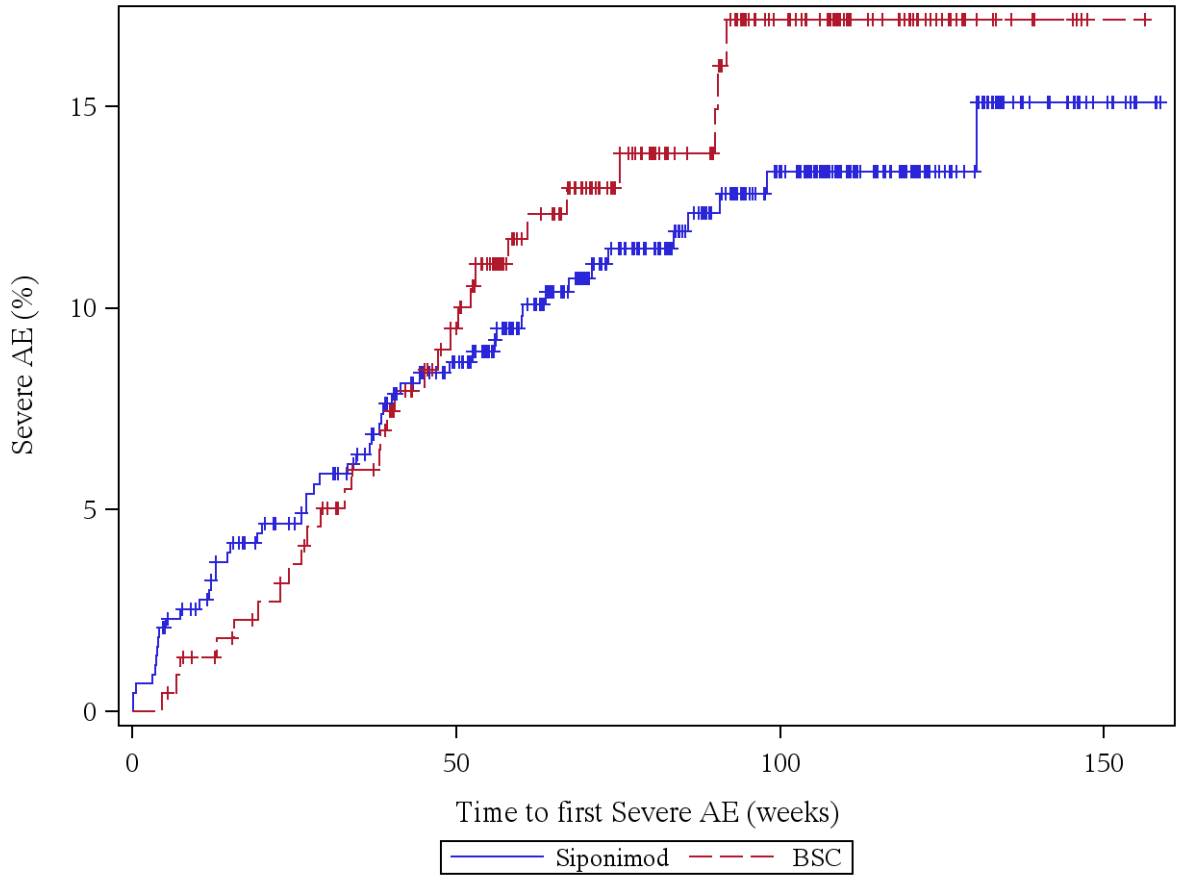
Patients at risk (Siponimod/BSC): Week 0: 664/323, Week 4: 653/320, Week 12: 623/311, Week 24: 589/295, Week 36: 567/278, Week 48: 524/257, Week 60: 459/217, Week 72: 351/168, Week 84: 260/131, Week 96: 191/100, Week 108: 139/66, Week 120: 93/42, Week 132: 52/26, Week 144: 22/13, Week 156: 5/3, Week 168: 0/0

Log rank test: p-value = 0,015 *
*: p < 0,05

Analysis population: A2304 SAF total population

12.3.1.5: Any severe AE

Figure 12.3.1.5.1: Severe AE, Gender = Male

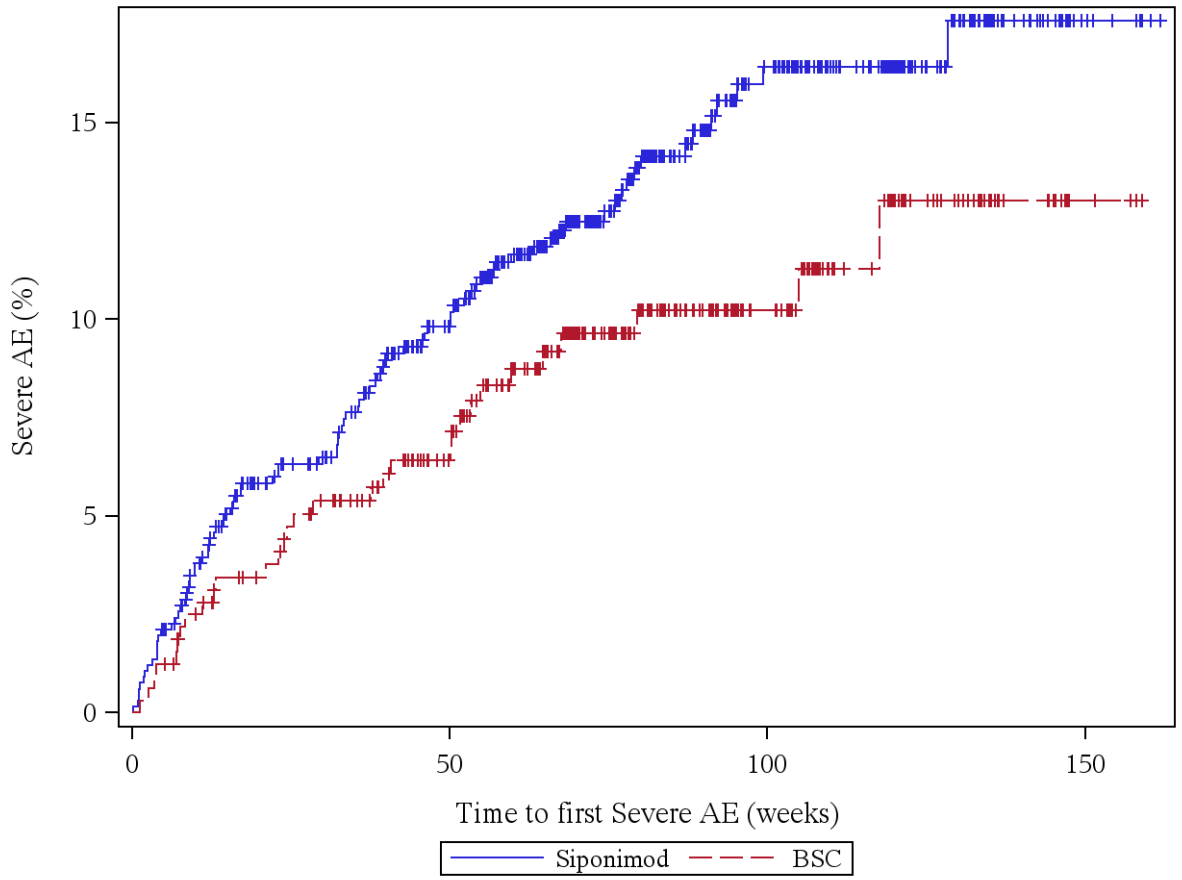


Patients at risk (Siponimod/BSC): Week 0: 435/223, Week 4: 427/223, Week 12: 412/217, Week 24: 394/209, Week 36: 376/195, Week 48: 351/175, Week 60: 301/143, Week 72: 242/112, Week 84: 200/84, Week 96: 161/61, Week 108: 112/46, Week 120: 78/28, Week 132: 42/10, Week 144: 21/5, Week 156: 3/1, Week 168: 0/0

Log rank test: p-value = 0,421
*: p < 0,05

Analysis population: A2304 SAF total population

Figure 12.3.1.5.2: Severe AE, Gender = Female



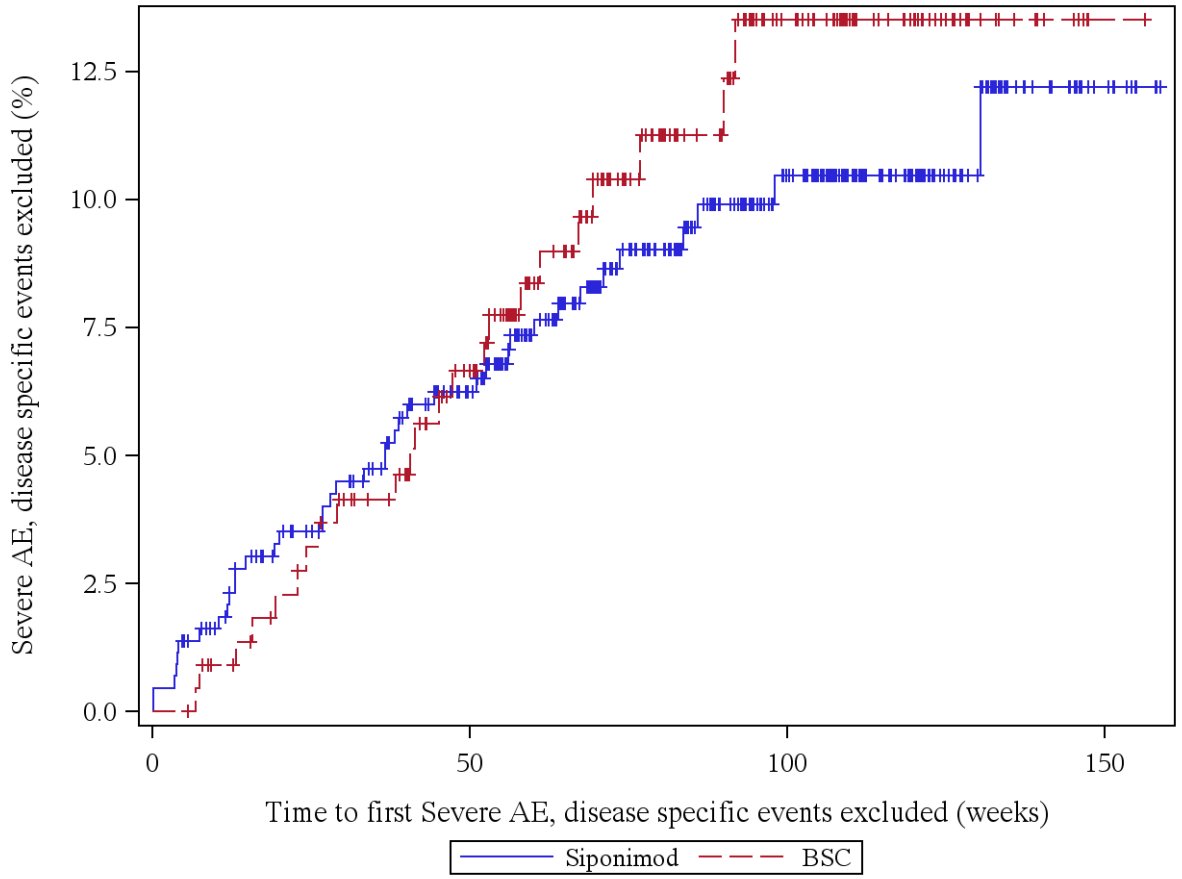
Patients at risk (Siponimod/BSC): Week 0: 664/323, Week 4: 652/319, Week 12: 616/308, Week 24: 580/295, Week 36: 558/281, Week 48: 512/258, Week 60: 452/218, Week 72: 352/169, Week 84: 262/132, Week 96: 195/100, Week 108: 146/66, Week 120: 101/42, Week 132: 57/25, Week 144: 24/12, Week 156: 5/3, Week 168: 0/0

Log rank test: p-value = 0,090
*: p < 0,05

Analysis population: A2304 SAF total population

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

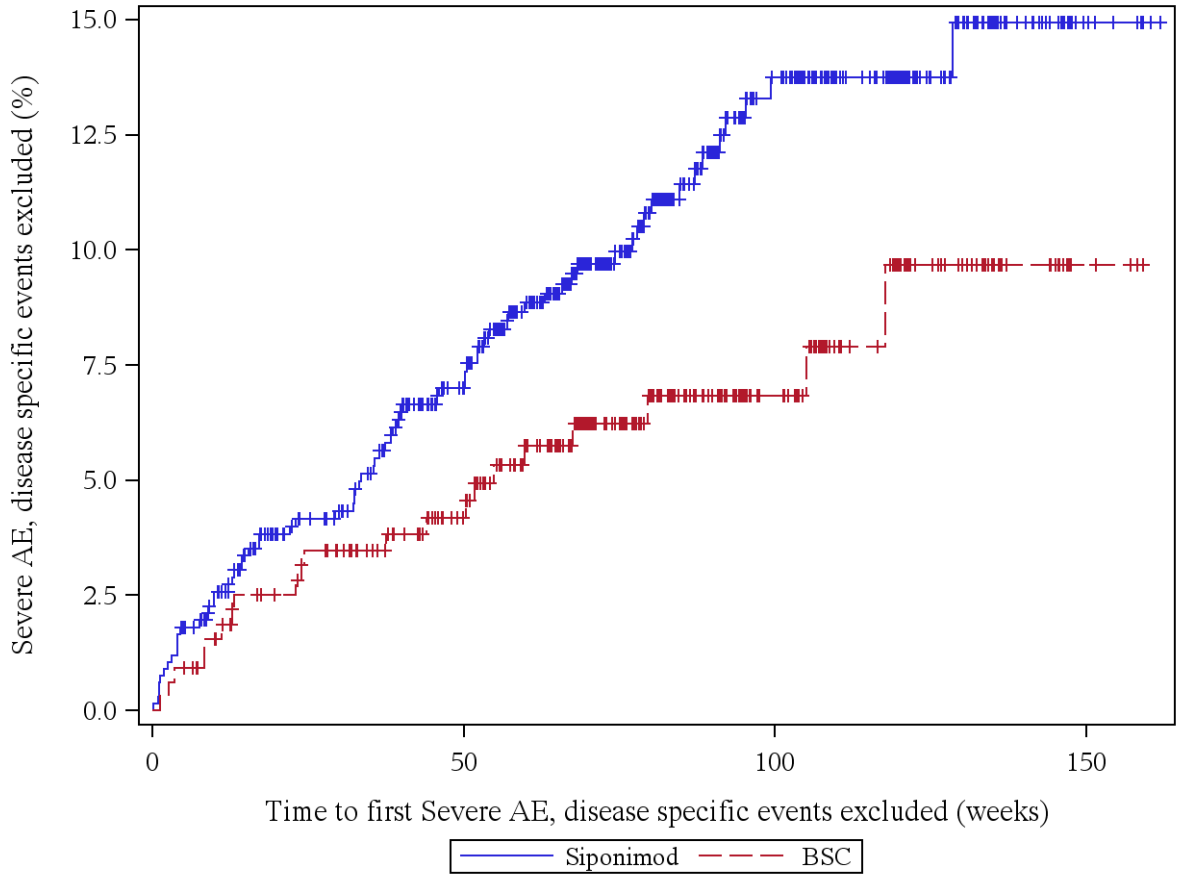


Patients at risk (Siponimod/BSC): Week 0: 435/223, Week 4: 430/223, Week 12: 415/217, Week 24: 398/209, Week 36: 382/198, Week 48: 359/178, Week 60: 309/147, Week 72: 248/114, Week 84: 206/86, Week 96: 167/63, Week 108: 116/48, Week 120: 81/30, Week 132: 43/12, Week 144: 21/6, Week 156: 3/1, Week 168: 0/0

Log rank test: p-value = 0,499
*: p < 0,05

Analysis population: A2304 SAF total population

Figure 12.3.1.6.2: Severe AE, disease specific events excluded, Gender = Female



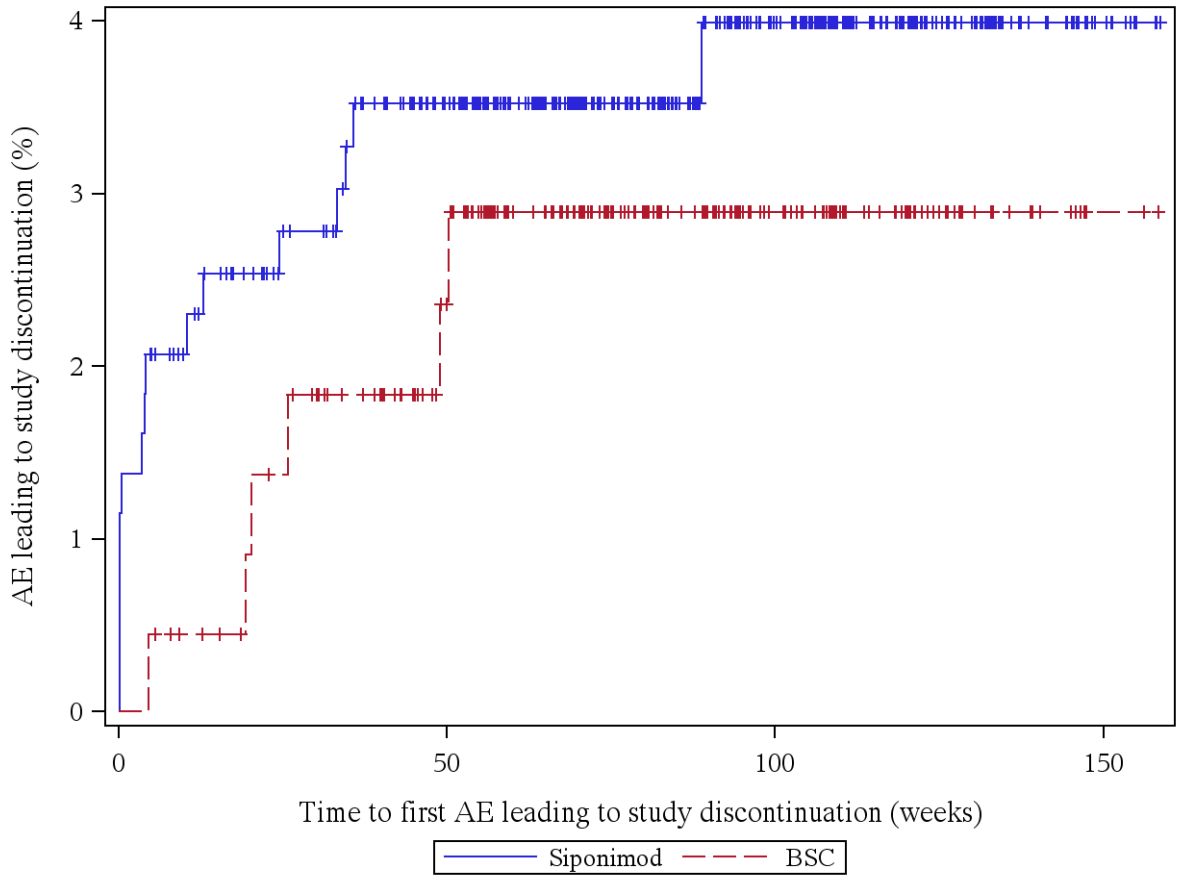
Patients at risk (Siponimod/BSC): Week 0: 664/323, Week 4: 653/320, Week 12: 626/310, Week 24: 591/298, Week 36: 570/284, Week 48: 524/262, Week 60: 461/223, Week 72: 360/173, Week 84: 269/136, Week 96: 198/101, Week 108: 149/67, Week 120: 102/43, Week 132: 58/26, Week 144: 24/13, Week 156: 5/3, Week 168: 0/0

Log rank test: p-value = 0,037 *
*: p < 0,05

Analysis population: A2304 SAF total population

12.3.1.7: Any AE leading to study discontinuation

Figure 12.3.1.7.1: AE leading to study discontinuation, Gender = Male

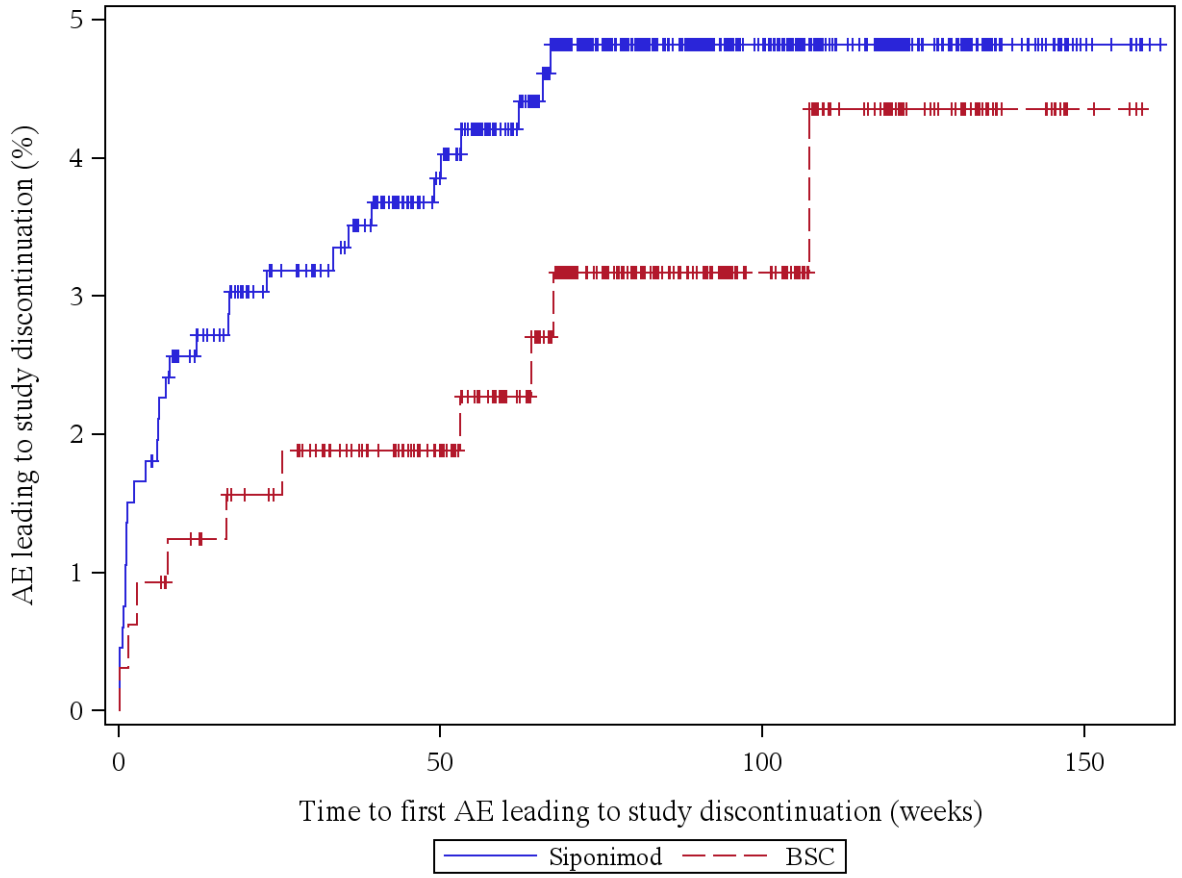


Patients at risk (Siponimod/BSC): Week 0: 435/223, Week 4: 427/223, Week 12: 417/219, Week 24: 403/213, Week 36: 389/204, Week 48: 371/188, Week 60: 324/154, Week 72: 262/124, Week 84: 220/93, Week 96: 177/68, Week 108: 125/52, Week 120: 85/33, Week 132: 47/13, Week 144: 23/7, Week 156: 3/2, Week 168: 0/0

Log rank test: p-value = 0,504
*: p < 0,05

Analysis population: A2304 SAF total population

Figure 12.3.1.7.2: AE leading to study discontinuation, Gender = Female



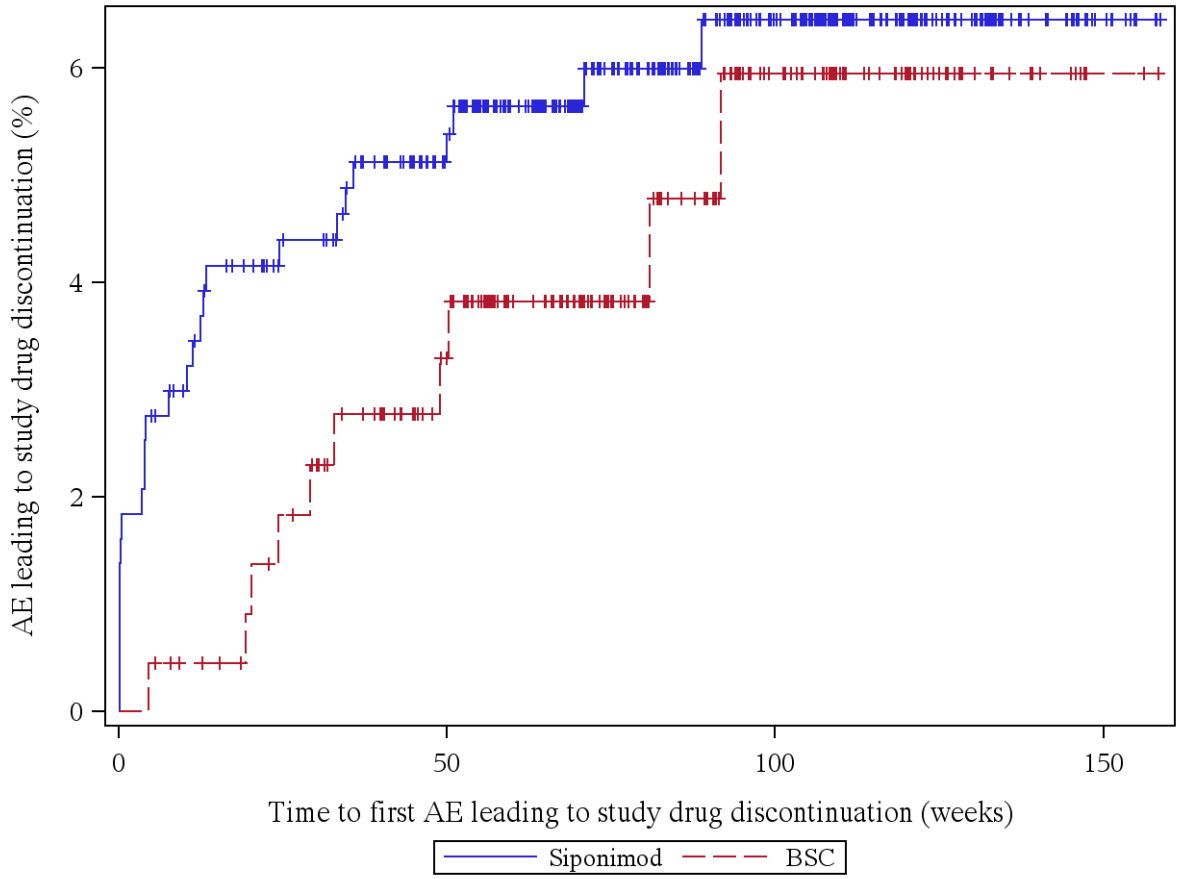
Patients at risk (Siponimod/BSC): Week 0: 664/323, Week 4: 653/320, Week 12: 634/315, Week 24: 609/306, Week 36: 593/293, Week 48: 551/273, Week 60: 492/233, Week 72: 388/180, Week 84: 295/144, Week 96: 223/108, Week 108: 166/73, Week 120: 115/47, Week 132: 66/27, Week 144: 28/13, Week 156: 7/3, Week 168: 0/0

Log rank test: p-value = 0,296
*: p < 0,05

Analysis population: A2304 SAF total population

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

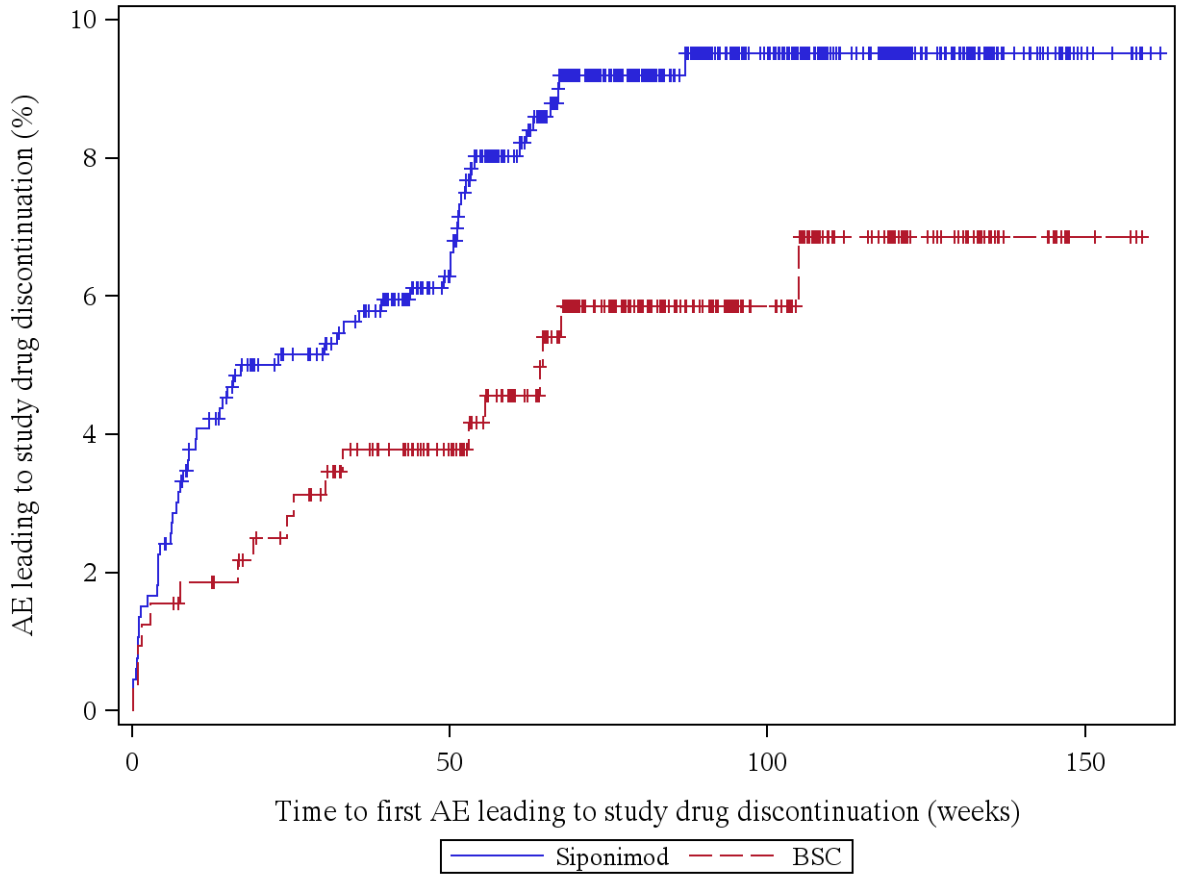


Patients at risk (Siponimod/BSC): Week 0: 435/223, Week 4: 424/223, Week 12: 414/219, Week 24: 402/213, Week 36: 389/202, Week 48: 371/187, Week 60: 323/154, Week 72: 261/124, Week 84: 220/92, Week 96: 177/67, Week 108: 125/52, Week 120: 85/33, Week 132: 47/13, Week 144: 23/7, Week 156: 3/2, Week 168: 0/0

Log rank test: p-value = 0,446
*: p < 0,05

Analysis population: A2304 SAF total population

Figure 12.3.1.8.2: AE leading to study drug discontinuation, Gender = Female



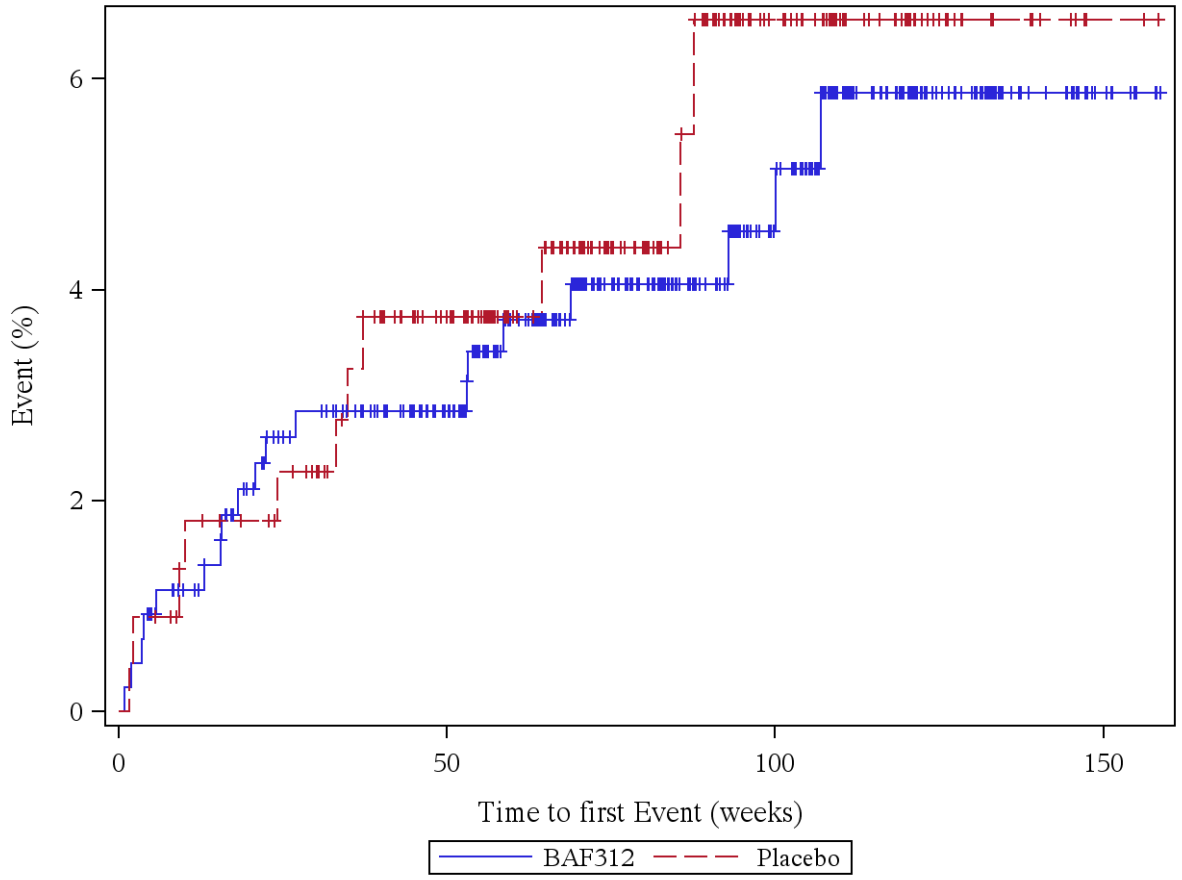
Patients at risk (Siponimod/BSC): Week 0: 664/323, Week 4: 652/318, Week 12: 630/315, Week 24: 606/306, Week 36: 591/291, Week 48: 550/272, Week 60: 490/232, Week 72: 385/180, Week 84: 294/144, Week 96: 223/108, Week 108: 166/73, Week 120: 115/47, Week 132: 66/27, Week 144: 28/13, Week 156: 7/3, Week 168: 0/0

Log rank test: p-value = 0,090
*: p < 0,05

Analysis population: A2304 SAF total population

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

Figure 12.3.5.1.1: Peripheral edema/swelling (AESI), Gender = Male

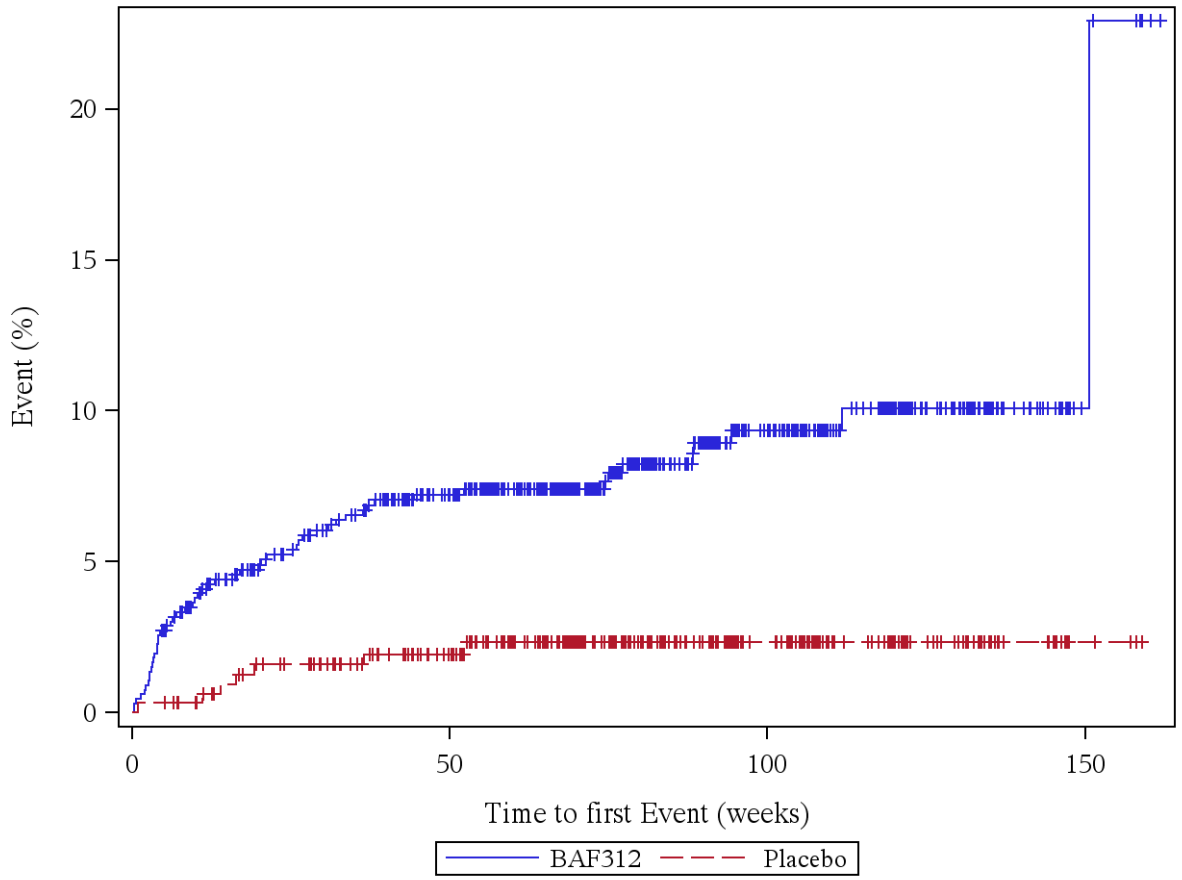


Patients at risk (BAF312/Placebo): Week 0: 435/223, Week 4: 431/221, Week 12: 418/215, Week 24: 395/210, Week 36: 383/197, Week 48: 362/181, Week 60: 312/151, Week 72: 252/119, Week 84: 211/89, Week 96: 170/62, Week 108: 120/46, Week 120: 82/27, Week 132: 45/11, Week 144: 22/6, Week 156: 3/2, Week 168: 0/0

Log rank test: p-value = 0,663
*: p < 0,05

Analysis population: A2304 SAF total population

Figure 12.3.5.1.2: Peripheral edema/swelling (AESI), Gender = Female

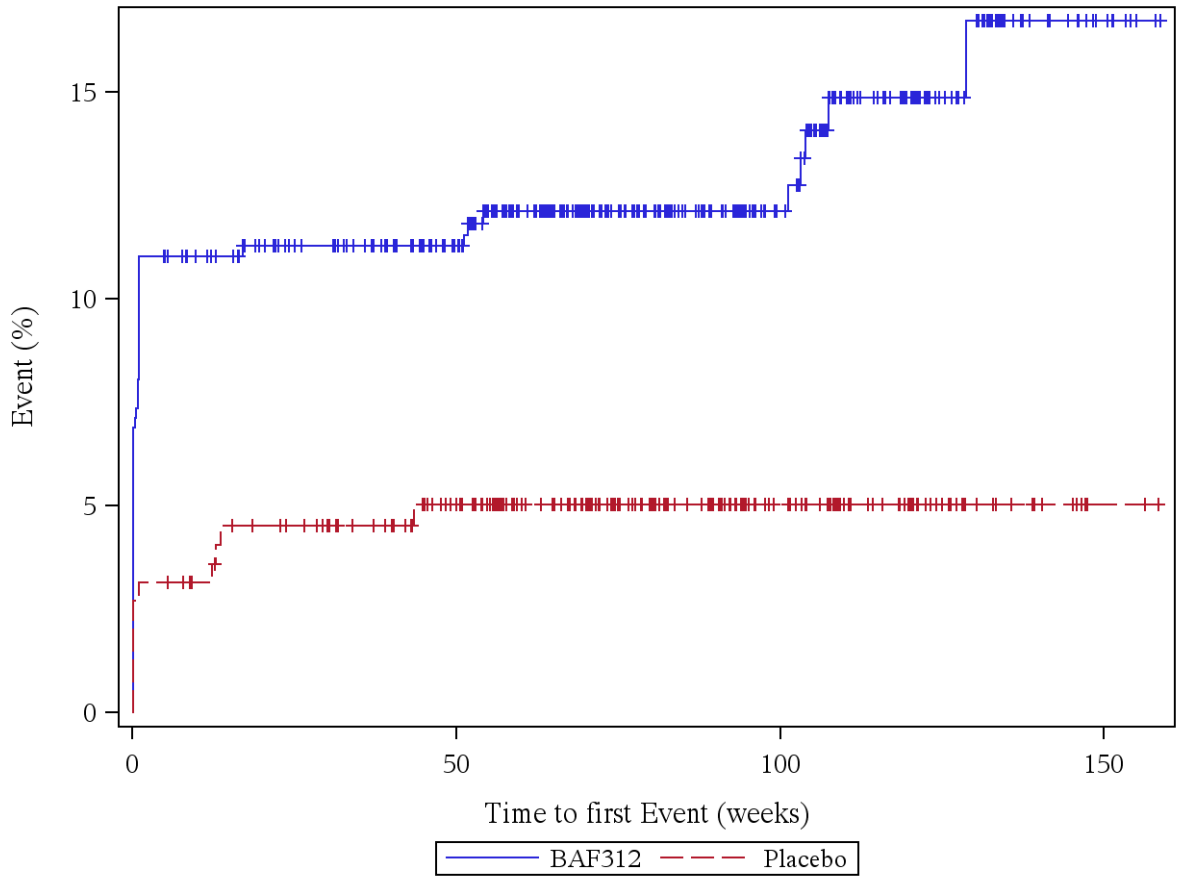


Patients at risk (BAF312/Placebo): Week 0: 664/323, Week 4: 649/322, Week 12: 609/314, Week 24: 580/302, Week 36: 560/288, Week 48: 514/268, Week 60: 458/227, Week 72: 364/176, Week 84: 272/140, Week 96: 202/106, Week 108: 149/73, Week 120: 99/46, Week 132: 57/26, Week 144: 23/13, Week 156: 5/3, Week 168: 0/0

Log rank test: p-value = <0,001 *
*: p < 0,05

Analysis population: A2304 SAF total population

Figure 12.3.5.1.3: Bradyarrhythmias and bradycardia (AESI), Gender = Male

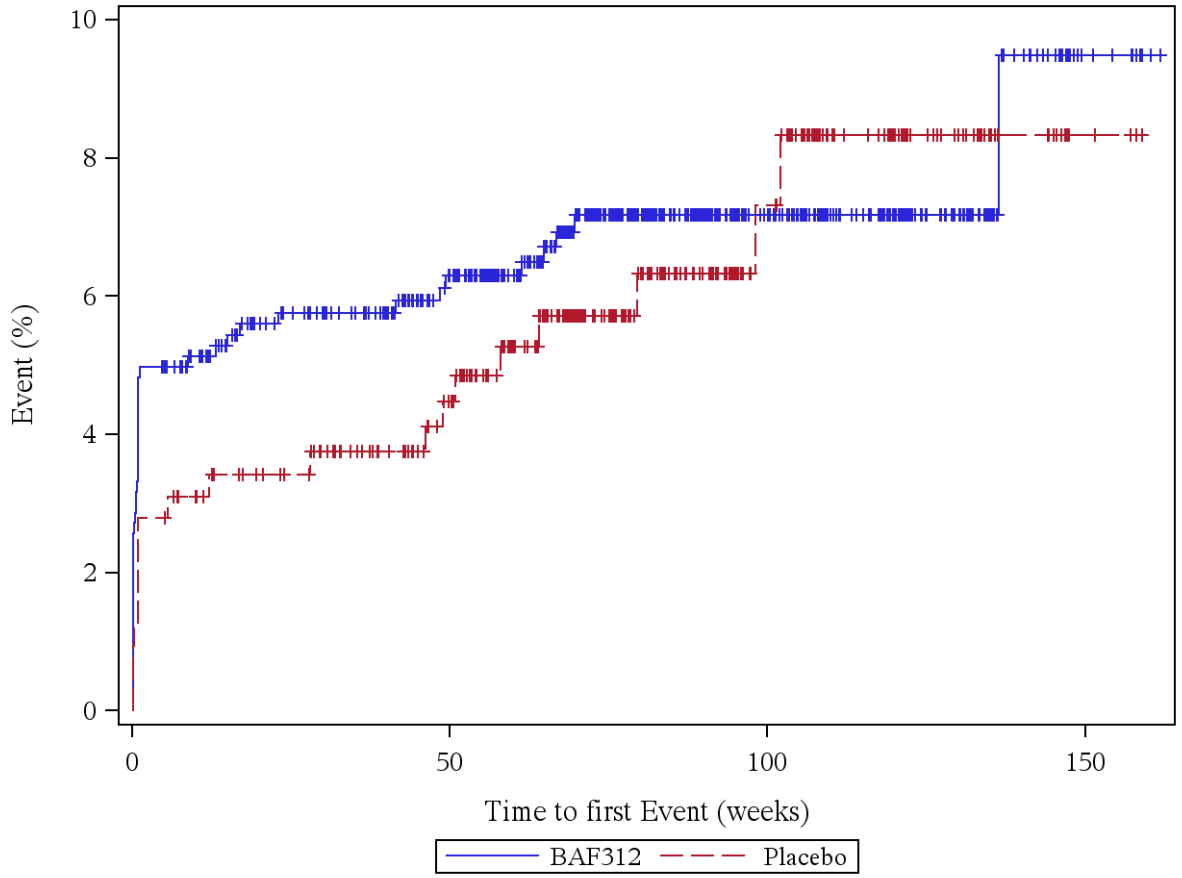


Patients at risk (BAF312/Placebo): Week 0: 435/223, Week 4: 387/216, Week 12: 378/212, Week 24: 361/204, Week 36: 351/194, Week 48: 330/178, Week 60: 284/147, Week 72: 226/120, Week 84: 185/90, Week 96: 147/67, Week 108: 101/51, Week 120: 72/33, Week 132: 37/13, Week 144: 16/7, Week 156: 2/2, Week 168: 0/0

Log rank test: p-value = 0,001 *
*: p < 0,05

Analysis population: A2304 SAF total population

Figure 12.3.5.1.4: Bradyarrhythmias and bradycardia (AESI), Gender = Female



Patients at risk (BAF312/Placebo): Week 0: 664/323, Week 4: 631/314, Week 12: 607/306, Week 24: 581/296, Week 36: 566/281, Week 48: 523/261, Week 60: 463/220, Week 72: 360/171, Week 84: 273/135, Week 96: 203/100, Week 108: 152/65, Week 120: 104/43, Week 132: 61/25, Week 144: 27/12, Week 156: 7/3, Week 168: 0/0

Log rank test: p-value = 0,657
*: p < 0,05

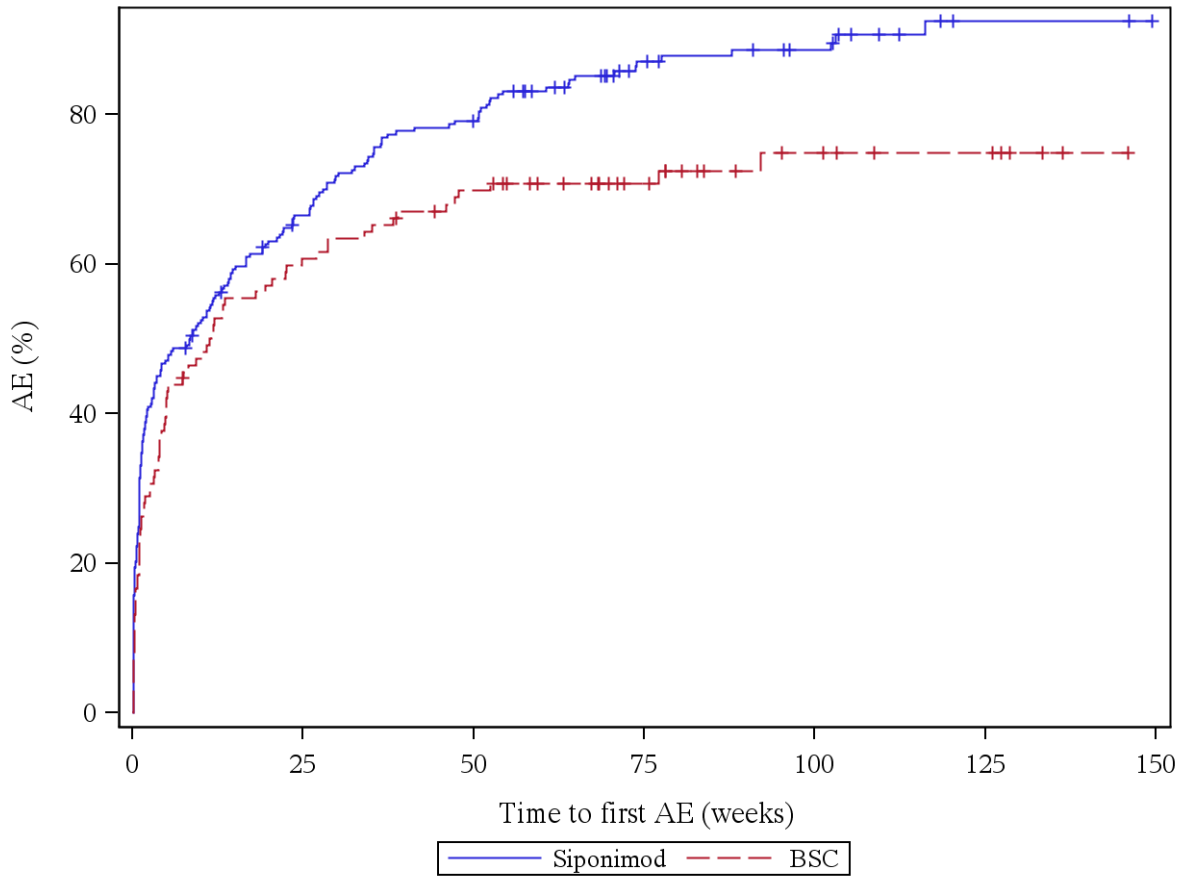
Analysis population: A2304 SAF total population

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

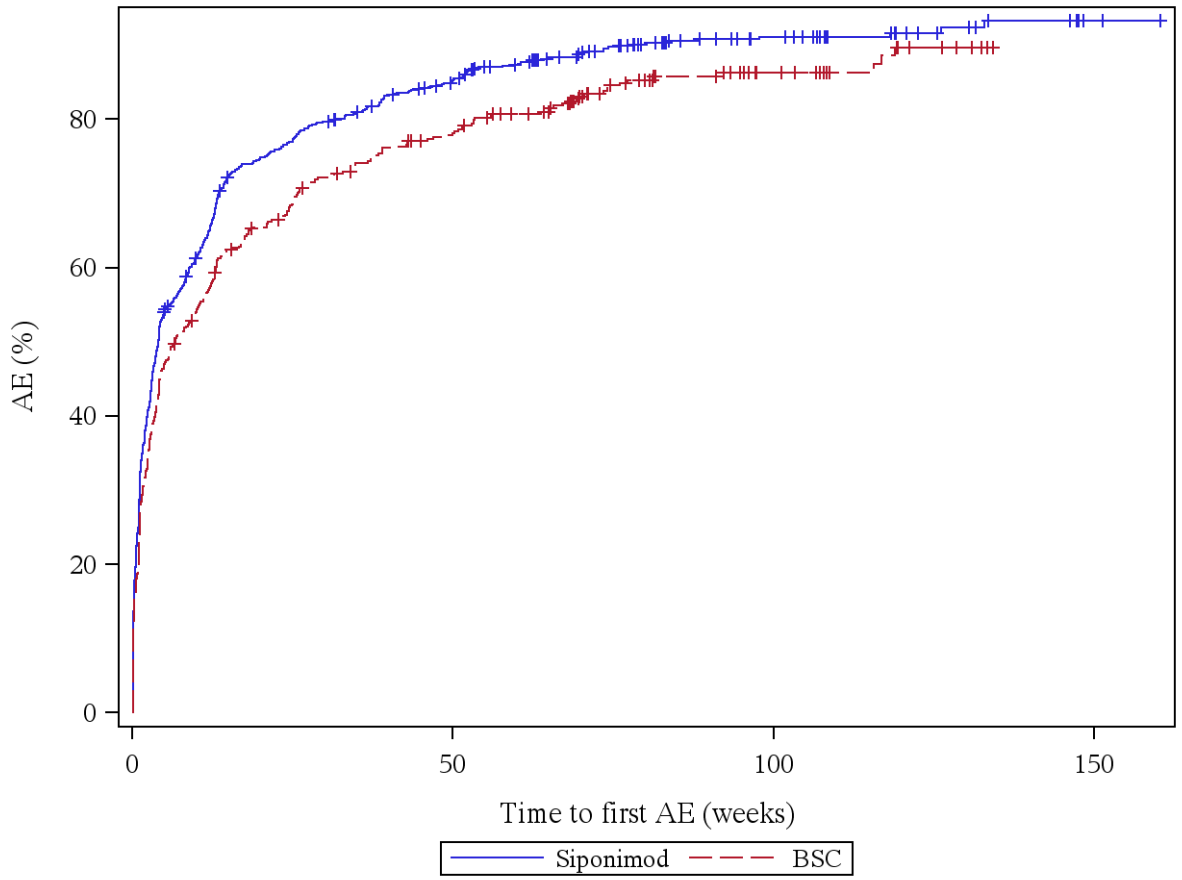


Patients at risk (Siponimod/BSC): Week 0: 242/114, Week 4: 133/72, Week 12: 106/53, Week 24: 77/45, Week 36: 56/39, Week 48: 48/32, Week 60: 34/26, Week 72: 22/19, Week 84: 16/12, Week 96: 13/9, Week 108: 7/7, Week 120: 3/6, Week 132: 2/3, Week 144: 2/1, Week 156: 0/0

Log rank test: p-value = 0,006 *
*: p < 0,05

Analysis population: A2304 SAF total population

Figure 12.4.1.1.2: AE, Previous MS DMT = Yes



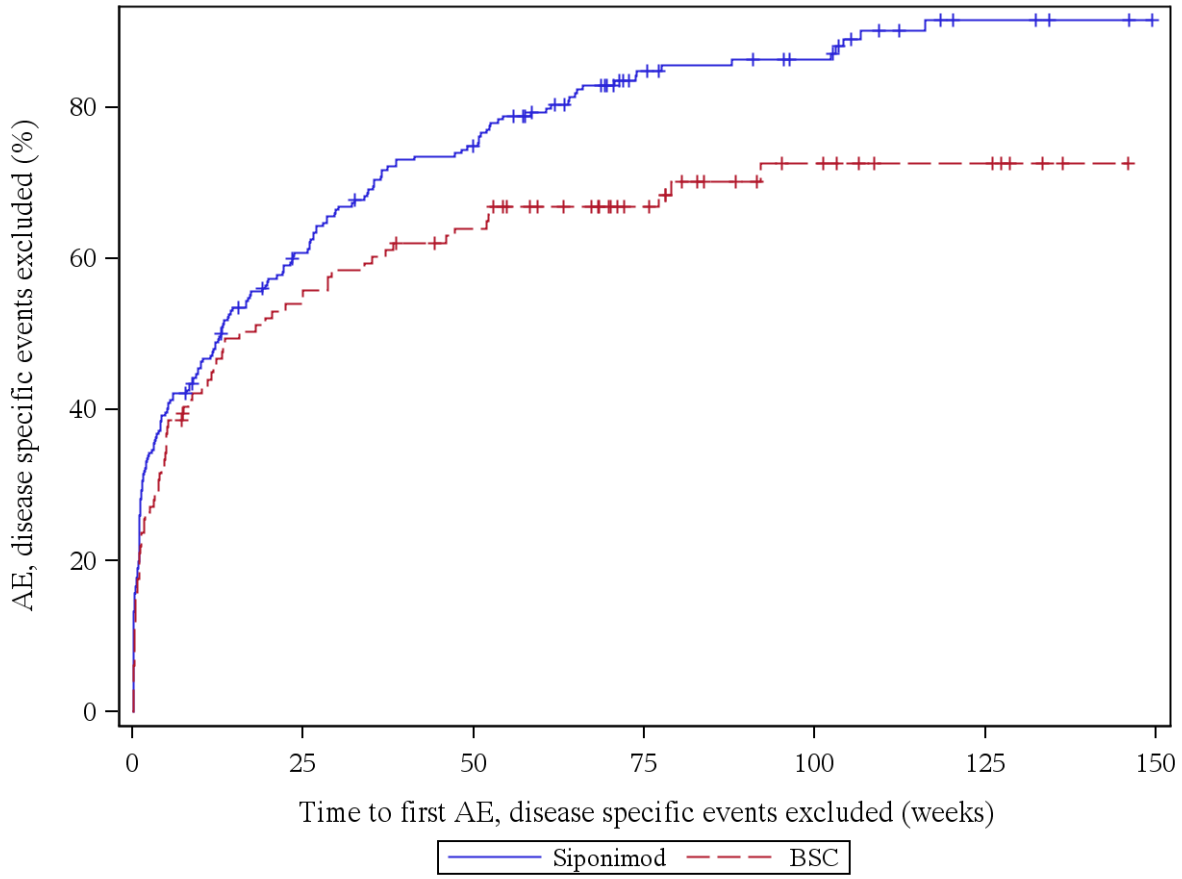
Patients at risk (Siponimod/BSC): Week 0: 857/432, Week 4: 427/247, Week 12: 296/183, Week 24: 196/137, Week 36: 154/105, Week 48: 121/88, Week 60: 91/70, Week 72: 63/46, Week 84: 40/28, Week 96: 33/22, Week 108: 21/14, Week 120: 14/7, Week 132: 8/3, Week 144: 6/0, Week 156: 1/0, Week 168: 0/0

Log rank test: p-value = 0,001 *
*: p < 0,05

Analysis population: A2304 SAF total population

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

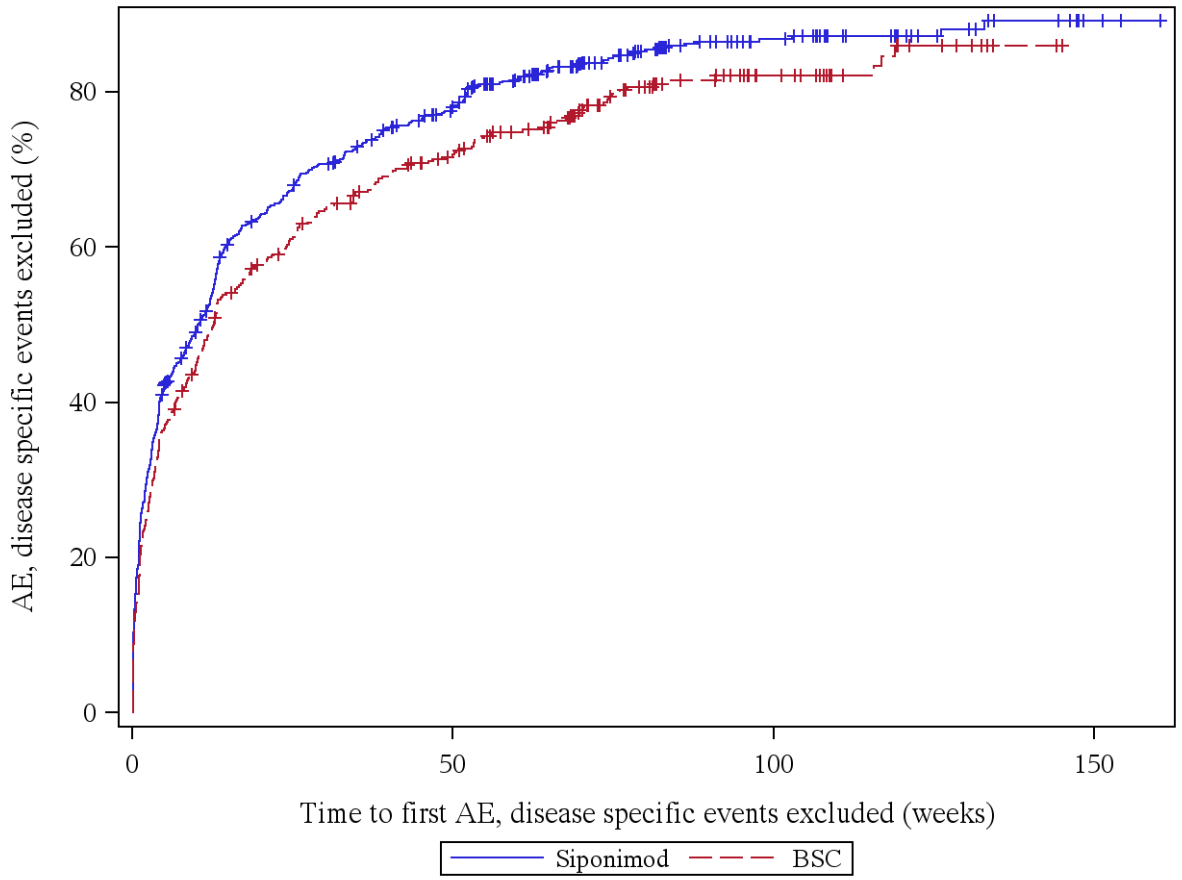


Patients at risk (Siponimod/BSC): Week 0: 242/114, Week 4: 152/78, Week 12: 124/60, Week 24: 90/51, Week 36: 67/44, Week 48: 59/38, Week 60: 42/30, Week 72: 26/22, Week 84: 20/14, Week 96: 17/10, Week 108: 9/7, Week 120: 5/6, Week 132: 4/3, Week 144: 2/1, Week 156: 0/0

Log rank test: p-value = 0,007 *
*: p < 0,05

Analysis population: A2304 SAF total population

Figure 12.4.1.2.2: AE, disease specific events excluded, Previous MS DMT = Yes



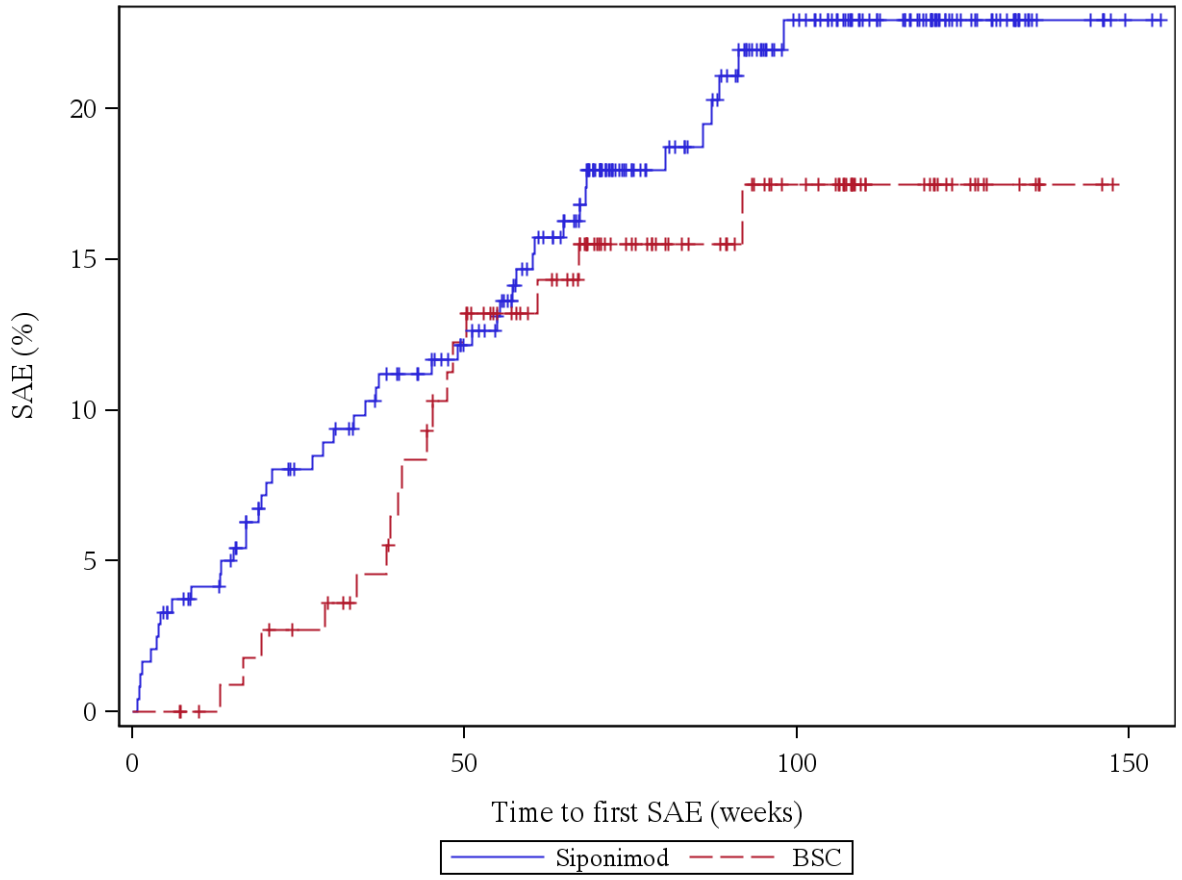
Patients at risk (Siponimod/BSC): Week 0: 857/432, Week 4: 528/286, Week 12: 397/218, Week 24: 276/166, Week 36: 214/132, Week 48: 173/110, Week 60: 123/88, Week 72: 85/60, Week 84: 52/36, Week 96: 41/27, Week 108: 27/18, Week 120: 18/9, Week 132: 11/5, Week 144: 8/2, Week 156: 1/0, Week 168: 0/0

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

Analysis population: A2304 SAF total population

12.4.1.3: Any SAE

Figure 12.4.1.3.1: SAE, Previous MS DMT = No

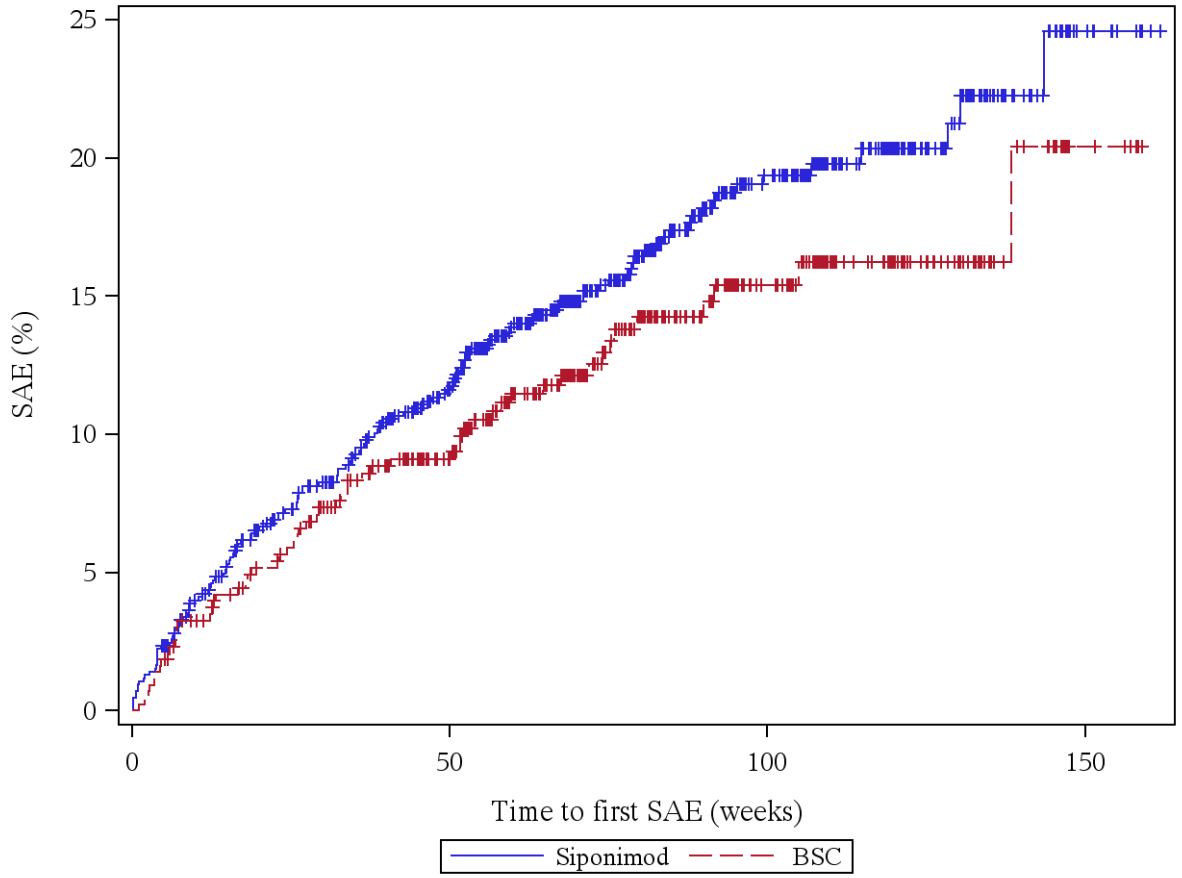


Patients at risk (Siponimod/BSC): Week 0: 242/114, Week 4: 235/114, Week 12: 226/111, Week 24: 207/106, Week 36: 198/101, Week 48: 185/91, Week 60: 162/78, Week 72: 123/58, Week 84: 103/47, Week 96: 81/38, Week 108: 62/27, Week 120: 44/16, Week 132: 20/6, Week 144: 8/2, Week 156: 0/0

Log rank test: p-value = 0,357
*: p < 0,05

Analysis population: A2304 SAF total population

Figure 12.4.1.3.2: SAE, Previous MS DMT = Yes



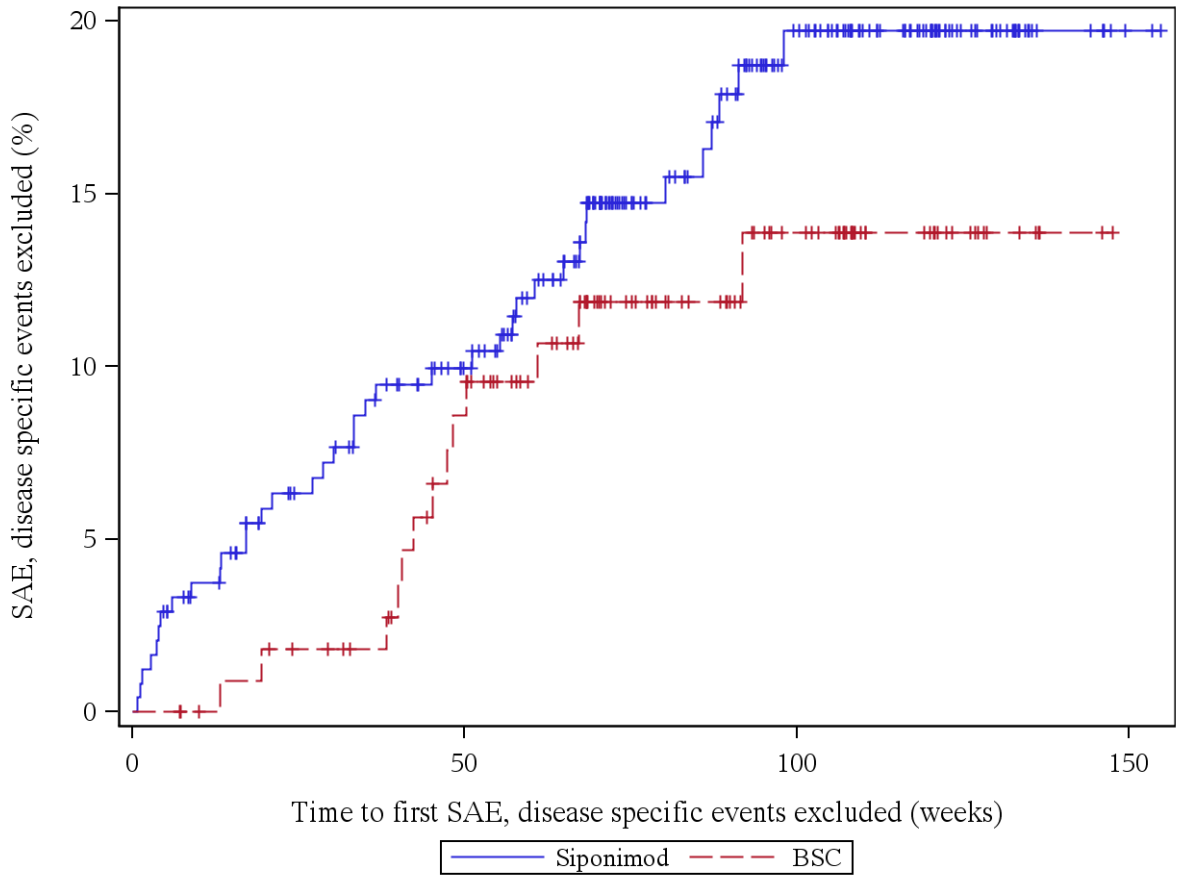
Patients at risk (Siponimod/BSC): Week 0: 857/432, Week 4: 838/426, Week 12: 798/411, Week 24: 752/390, Week 36: 714/364, Week 48: 660/332, Week 60: 568/276, Week 72: 441/219, Week 84: 334/164, Week 96: 256/119, Week 108: 180/85, Week 120: 120/56, Week 132: 68/32, Week 144: 32/17, Week 156: 7/5, Week 168: 0/0

Log rank test: p-value = 0,159
*: p < 0,05

Analysis population: A2304 SAF total population

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

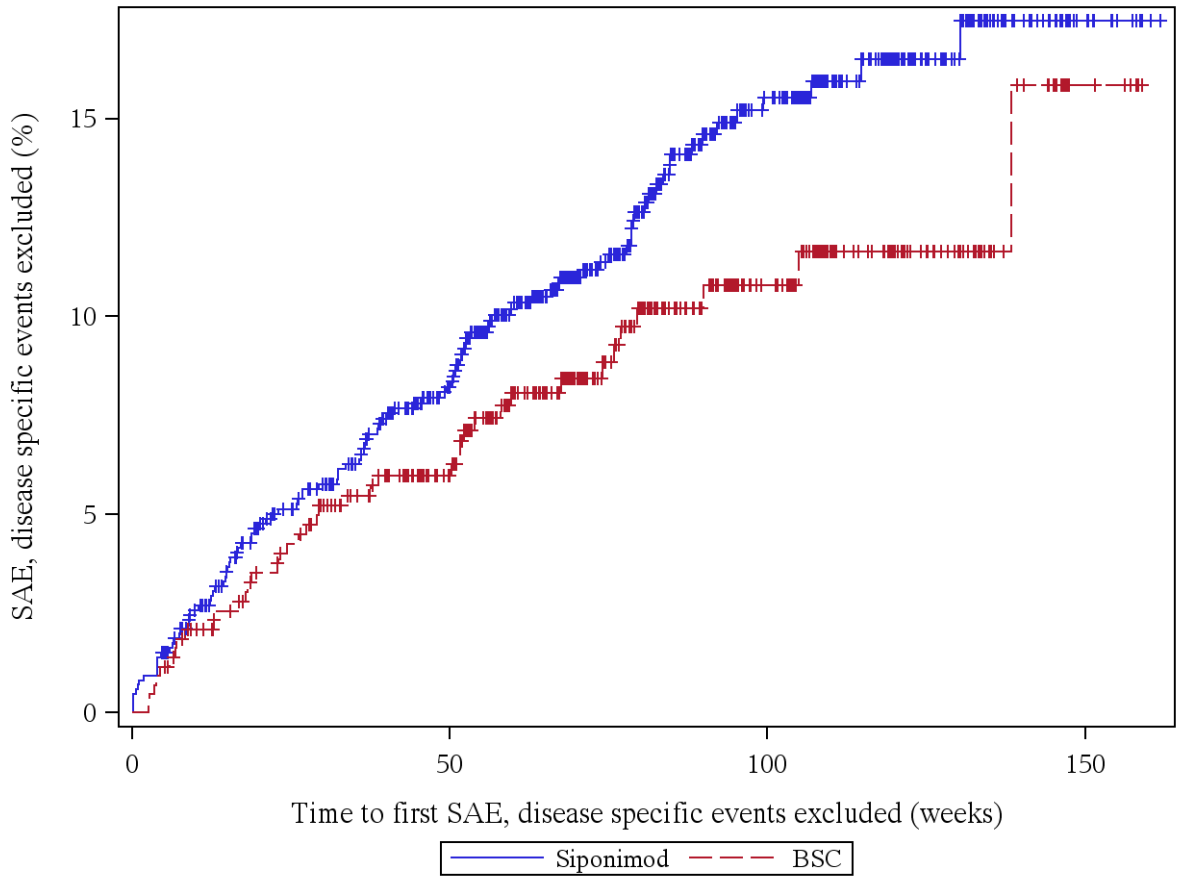


Patients at risk (Siponimod/BSC): Week 0: 242/114, Week 4: 236/114, Week 12: 227/111, Week 24: 211/107, Week 36: 201/104, Week 48: 189/94, Week 60: 167/81, Week 72: 128/61, Week 84: 107/50, Week 96: 85/39, Week 108: 64/27, Week 120: 45/16, Week 132: 21/6, Week 144: 8/2, Week 156: 0/0

Log rank test: p-value = 0,260
*: p < 0,05

Analysis population: A2304 SAF total population

Figure 12.4.1.4.2: SAE, disease specific events excluded, Previous MS DMT = Yes



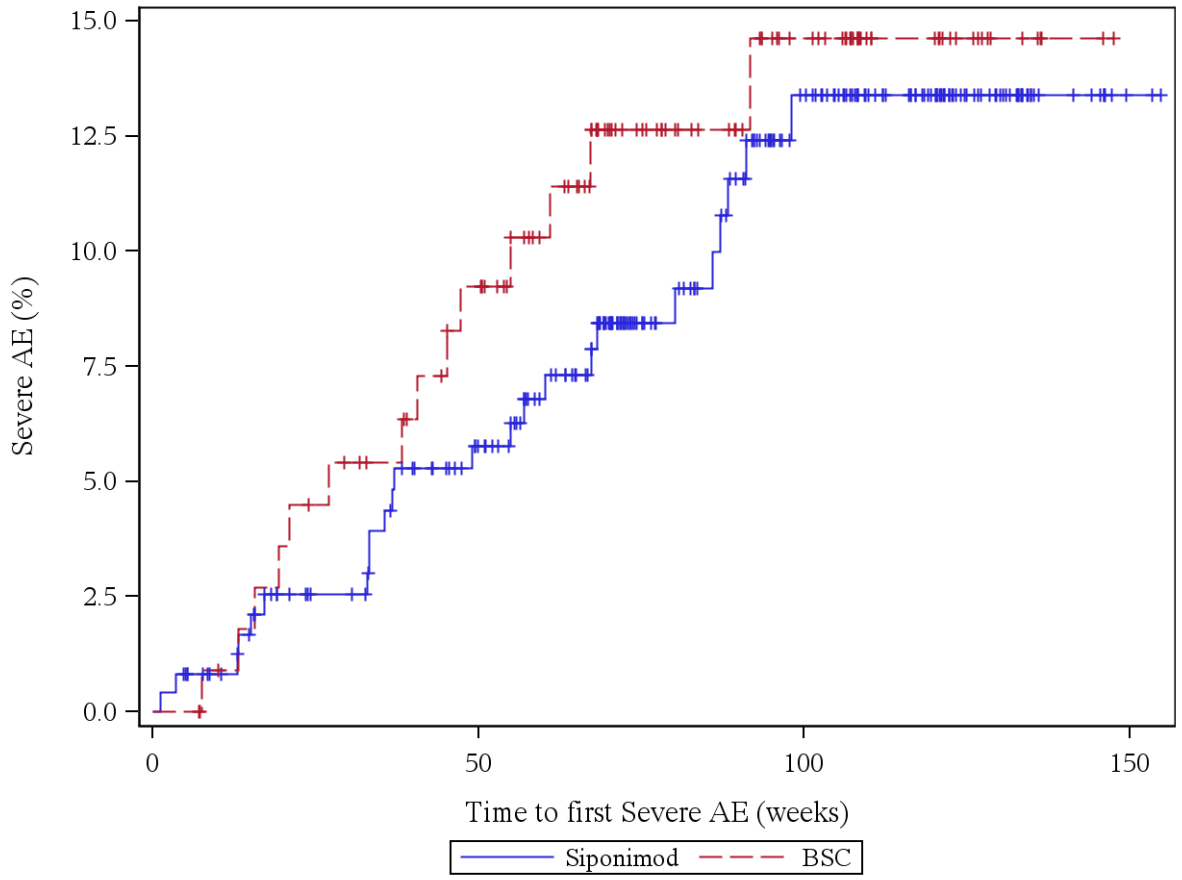
Patients at risk (Siponimod/BSC): Week 0: 857/432, Week 4: 845/428, Week 12: 809/415, Week 24: 764/396, Week 36: 734/373, Week 48: 681/341, Week 60: 588/282, Week 72: 460/222, Week 84: 348/167, Week 96: 267/123, Week 108: 188/87, Week 120: 126/57, Week 132: 74/33, Week 144: 36/18, Week 156: 8/5, Week 168: 0/0

Log rank test: p-value = 0,106
*: p < 0,05

Analysis population: A2304 SAF total population

12.4.1.5: Any severe AE

Figure 12.4.1.5.1: Severe AE, Previous MS DMT = No

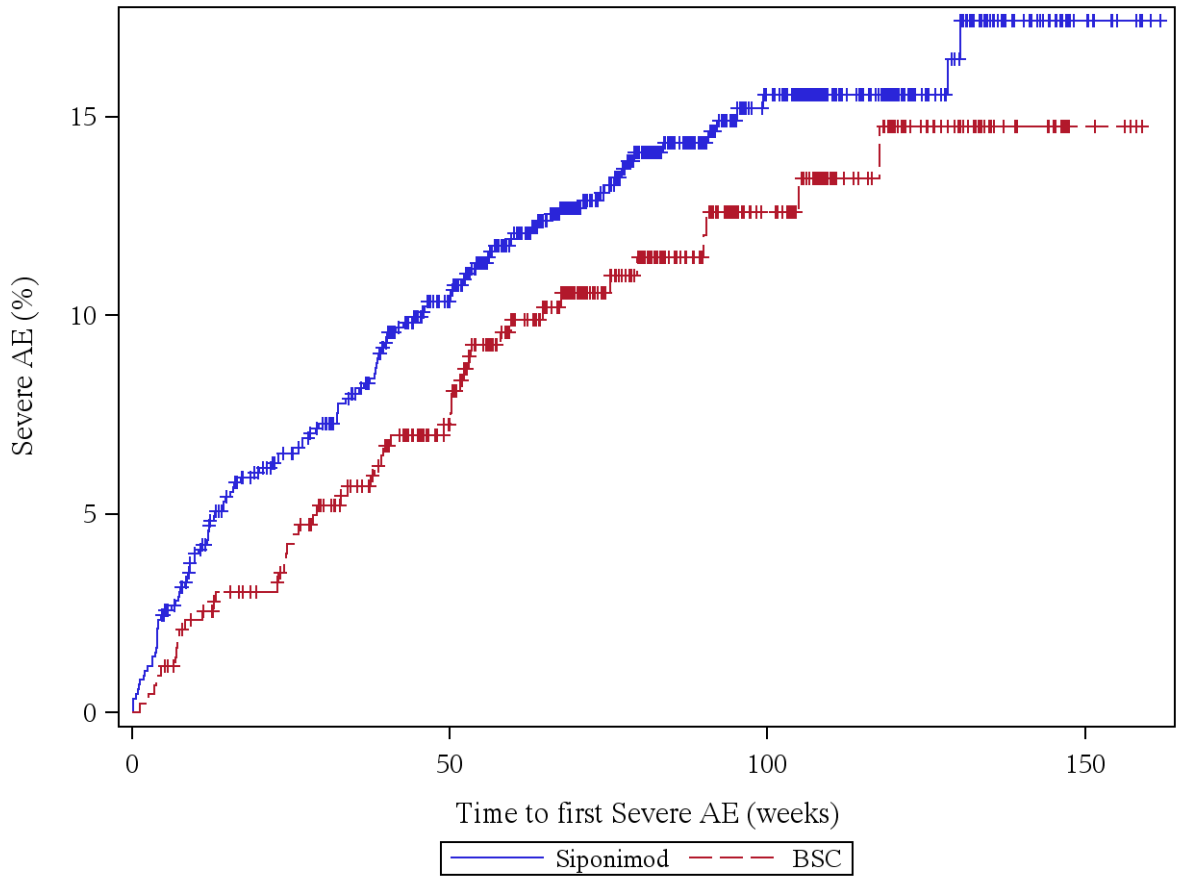


Patients at risk (Siponimod/BSC): Week 0: 242/114, Week 4: 240/114, Week 12: 232/110, Week 24: 217/105, Week 36: 209/101, Week 48: 197/93, Week 60: 176/80, Week 72: 138/59, Week 84: 115/48, Week 96: 92/38, Week 108: 71/26, Week 120: 53/16, Week 132: 24/6, Week 144: 9/2, Week 156: 0/0

Log rank test: p-value = 0,485
*: p < 0,05

Analysis population: A2304 SAF total population

Figure 12.4.1.5.2: Severe AE, Previous MS DMT = Yes



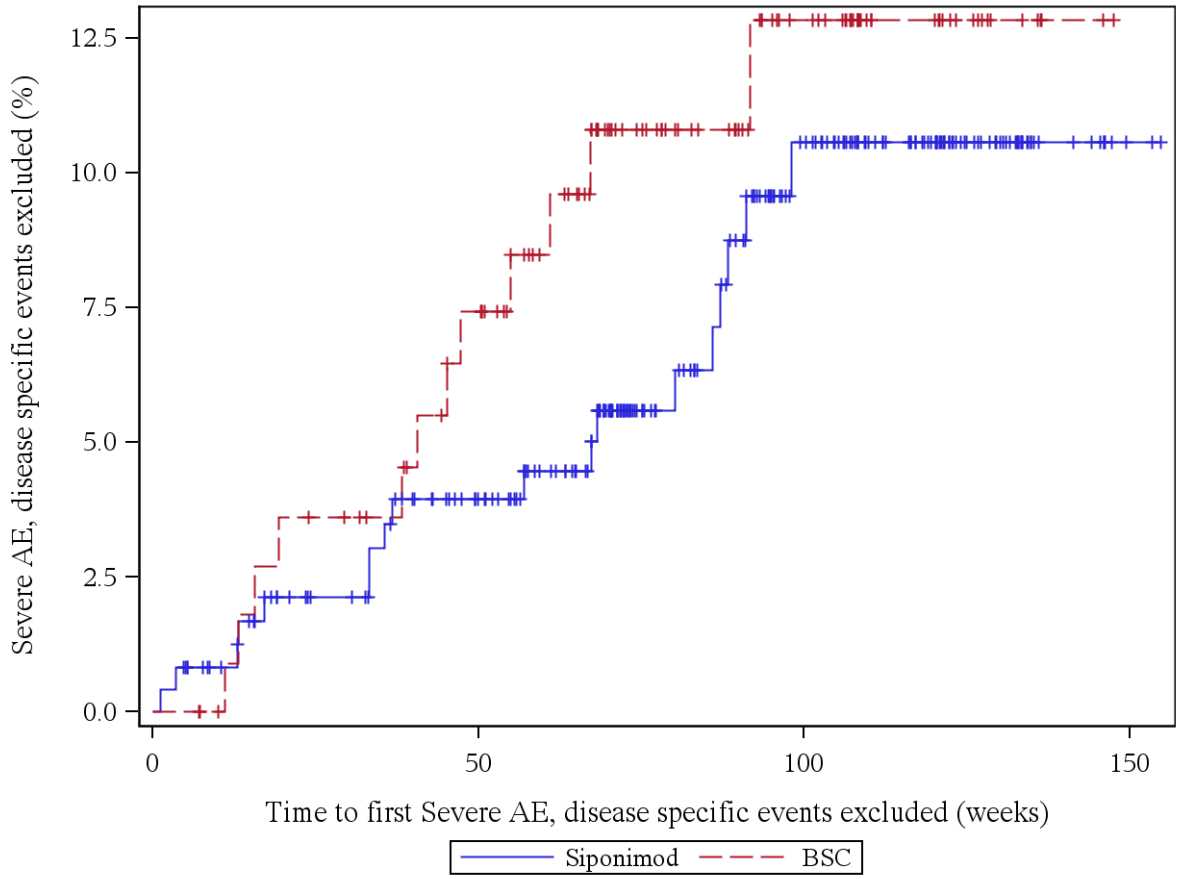
Patients at risk (Siponimod/BSC): Week 0: 857/432, Week 4: 839/428, Week 12: 796/415, Week 24: 757/399, Week 36: 725/375, Week 48: 666/340, Week 60: 577/281, Week 72: 456/222, Week 84: 347/168, Week 96: 264/123, Week 108: 187/86, Week 120: 126/54, Week 132: 75/29, Week 144: 36/15, Week 156: 8/4, Week 168: 0/0

Log rank test: p-value = 0,216
*: p < 0,05

Analysis population: A2304 SAF total population

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

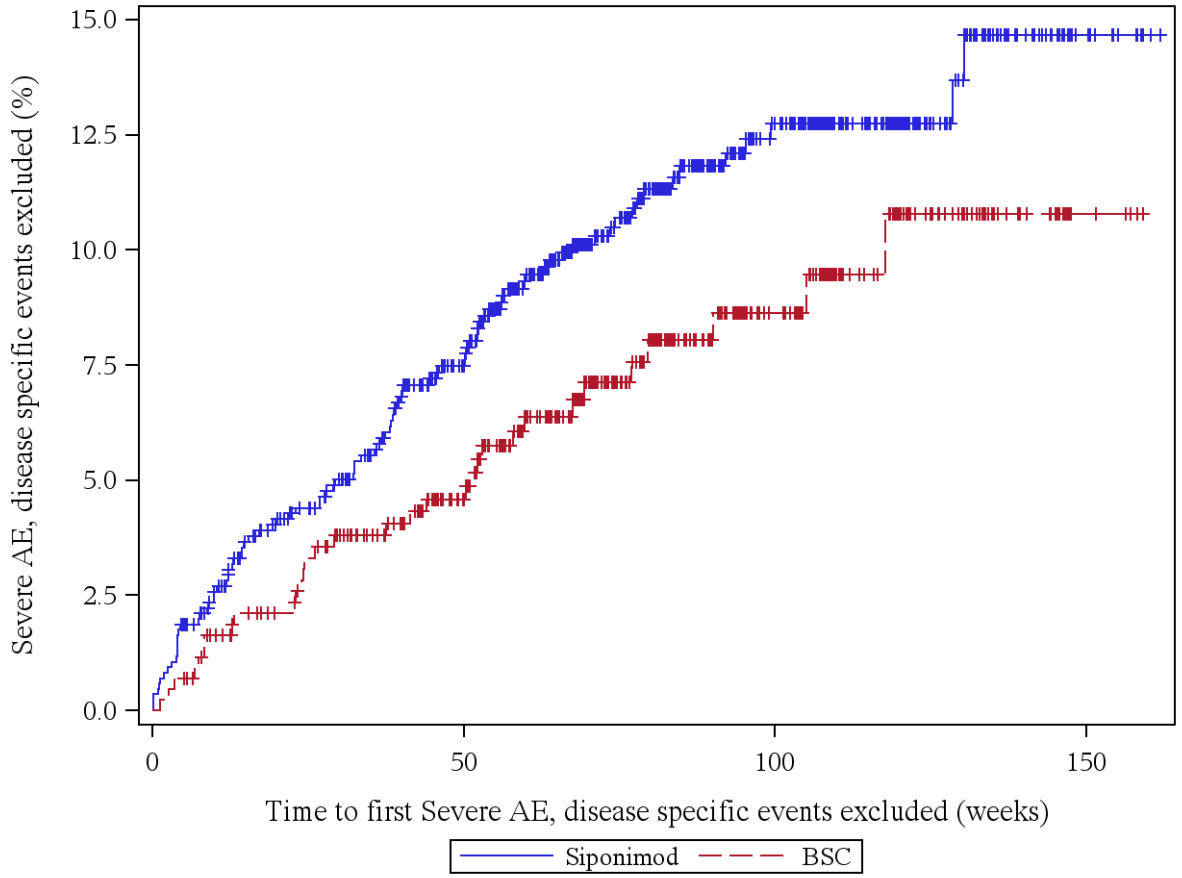


Patients at risk (Siponimod/BSC): Week 0: 242/114, Week 4: 240/114, Week 12: 232/110, Week 24: 218/106, Week 36: 211/103, Week 48: 199/95, Week 60: 180/82, Week 72: 142/61, Week 84: 118/50, Week 96: 95/38, Week 108: 73/26, Week 120: 54/16, Week 132: 25/6, Week 144: 9/2, Week 156: 0/0

Log rank test: p-value = 0,315
*: p < 0,05

Analysis population: A2304 SAF total population

Figure 12.4.1.6.2: Severe AE, disease specific events excluded, Previous MS DMT = Yes



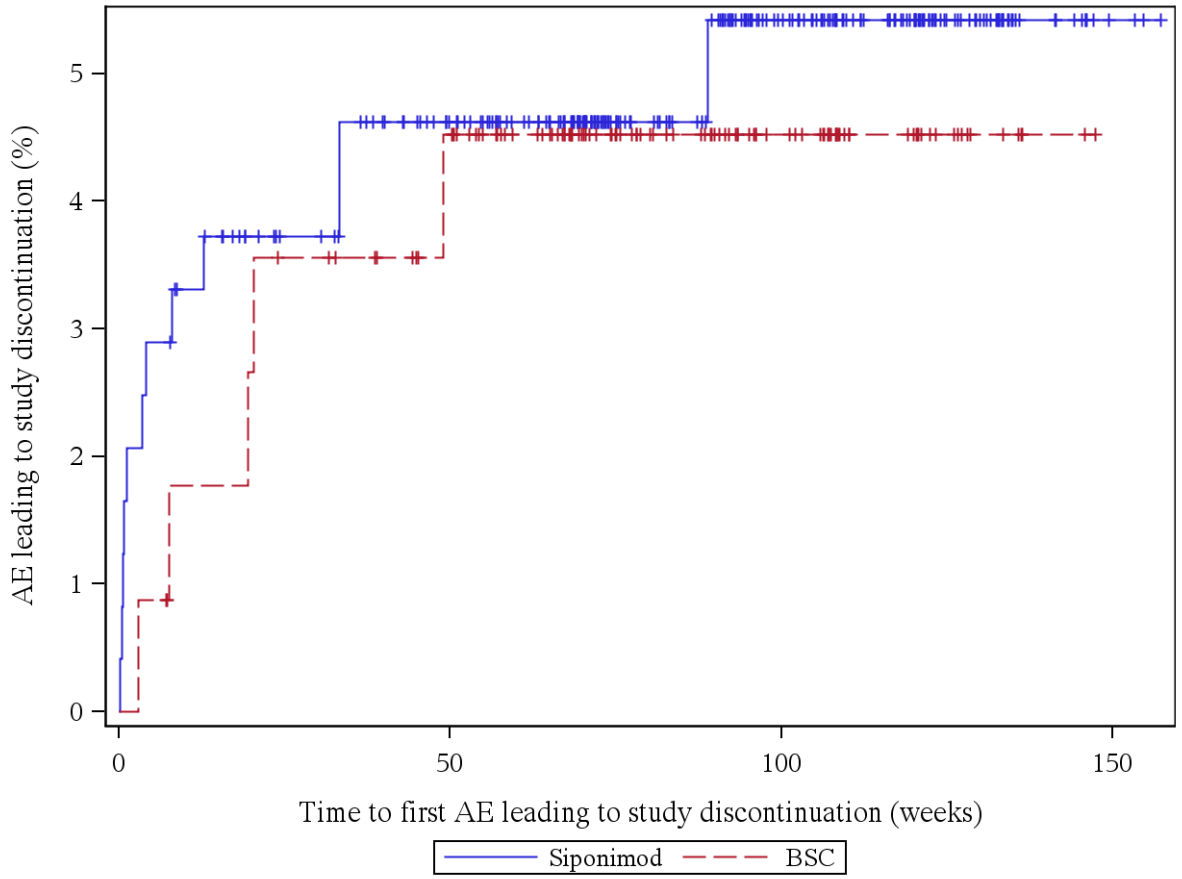
Patients at risk (Siponimod/BSC): Week 0: 857/432, Week 4: 843/429, Week 12: 809/417, Week 24: 771/401, Week 36: 741/379, Week 48: 684/345, Week 60: 590/288, Week 72: 466/226, Week 84: 357/172, Week 96: 270/126, Week 108: 192/89, Week 120: 129/57, Week 132: 76/32, Week 144: 36/17, Week 156: 8/4, Week 168: 0/0

Log rank test: p-value = 0,073
*: p < 0,05

Analysis population: A2304 SAF total population

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

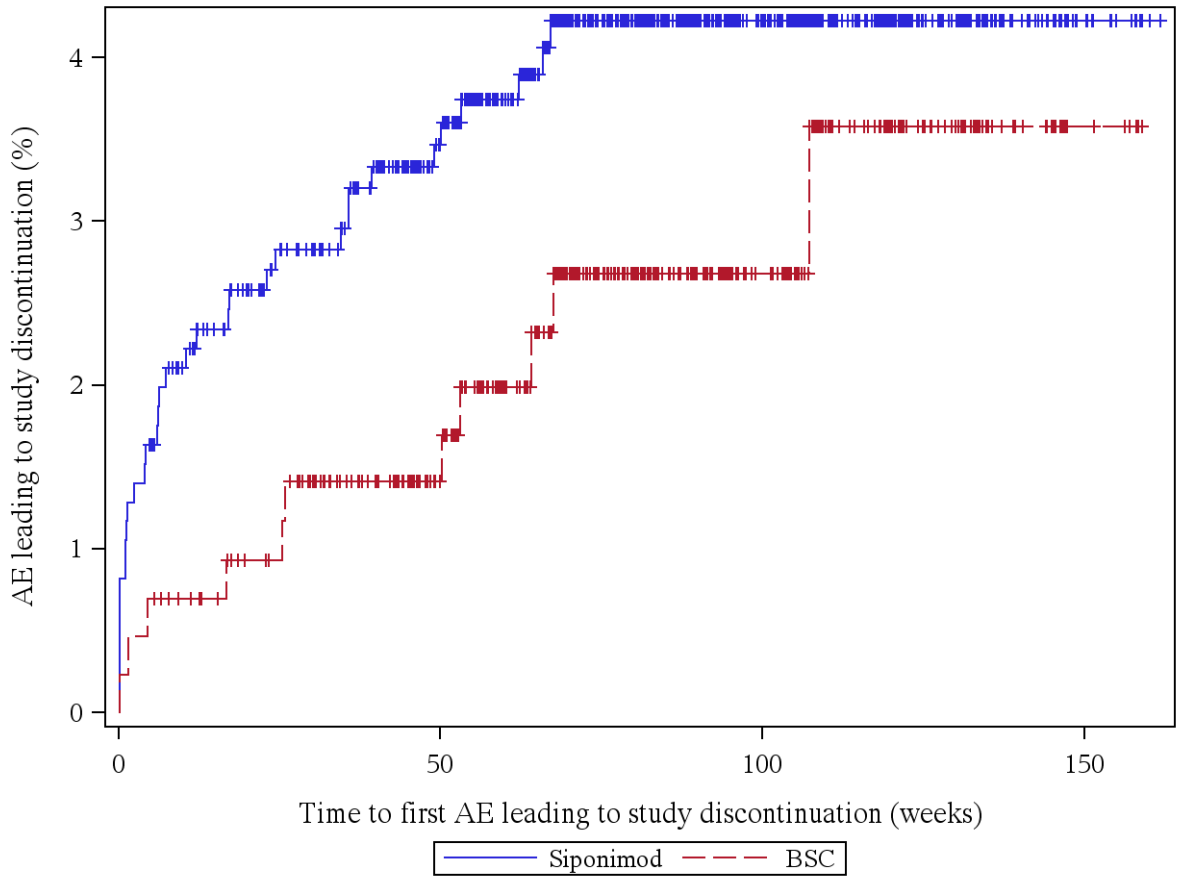


Patients at risk (Siponimod/BSC): Week 0: 242/114, Week 4: 236/113, Week 12: 231/110, Week 24: 220/107, Week 36: 214/105, Week 48: 203/100, Week 60: 185/86, Week 72: 147/67, Week 84: 122/54, Week 96: 98/41, Week 108: 76/28, Week 120: 57/17, Week 132: 27/6, Week 144: 10/2, Week 156: 1/0, Week 168: 0/0

Log rank test: p-value = 0,799
*: p < 0,05

Analysis population: A2304 SAF total population

Figure 12.4.1.7.2: AE leading to study discontinuation, Previous MS DMT = Yes



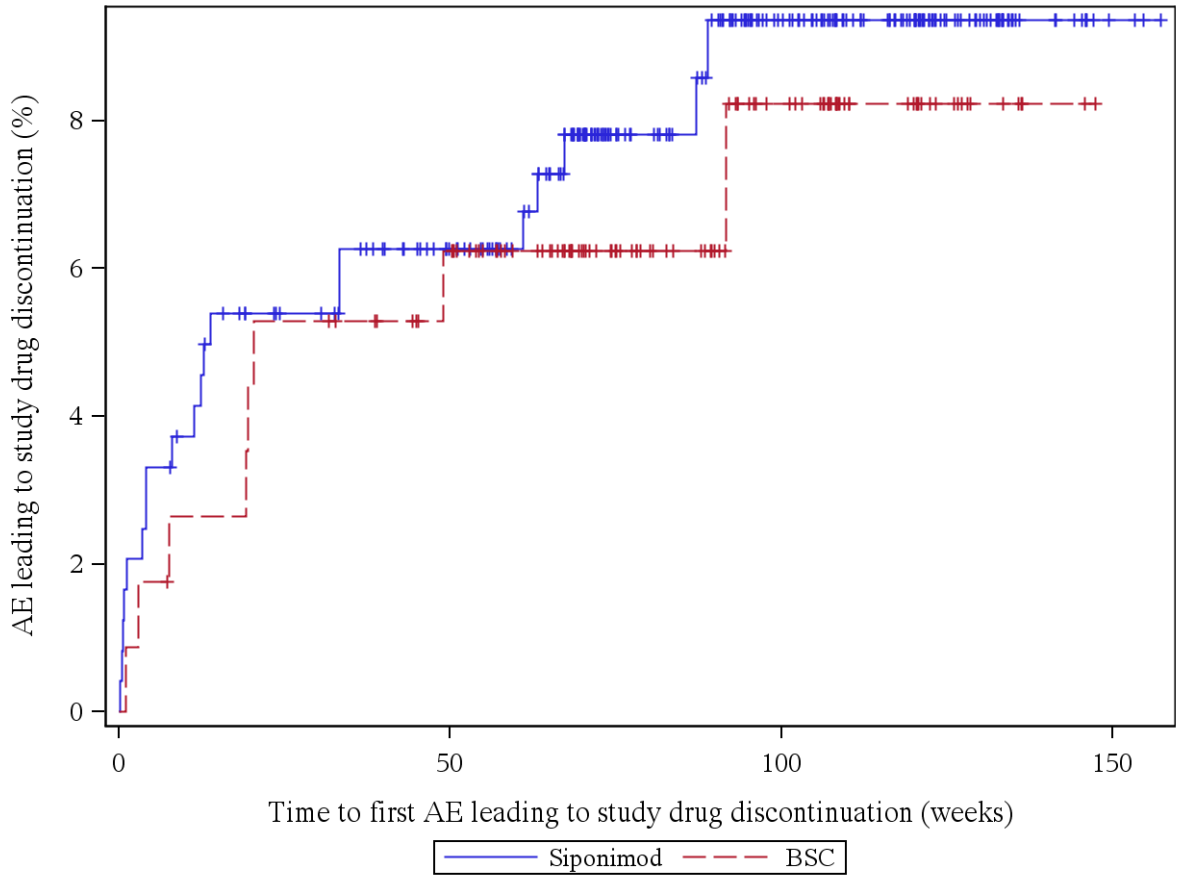
Patients at risk (Siponimod/BSC): Week 0: 857/432, Week 4: 844/430, Week 12: 820/424, Week 24: 792/412, Week 36: 768/392, Week 48: 719/361, Week 60: 631/301, Week 72: 503/237, Week 84: 393/183, Week 96: 302/135, Week 108: 215/97, Week 120: 143/63, Week 132: 86/34, Week 144: 41/18, Week 156: 9/5, Week 168: 0/0

Log rank test: p-value = 0,199
*: p < 0,05

Analysis population: A2304 SAF total population

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

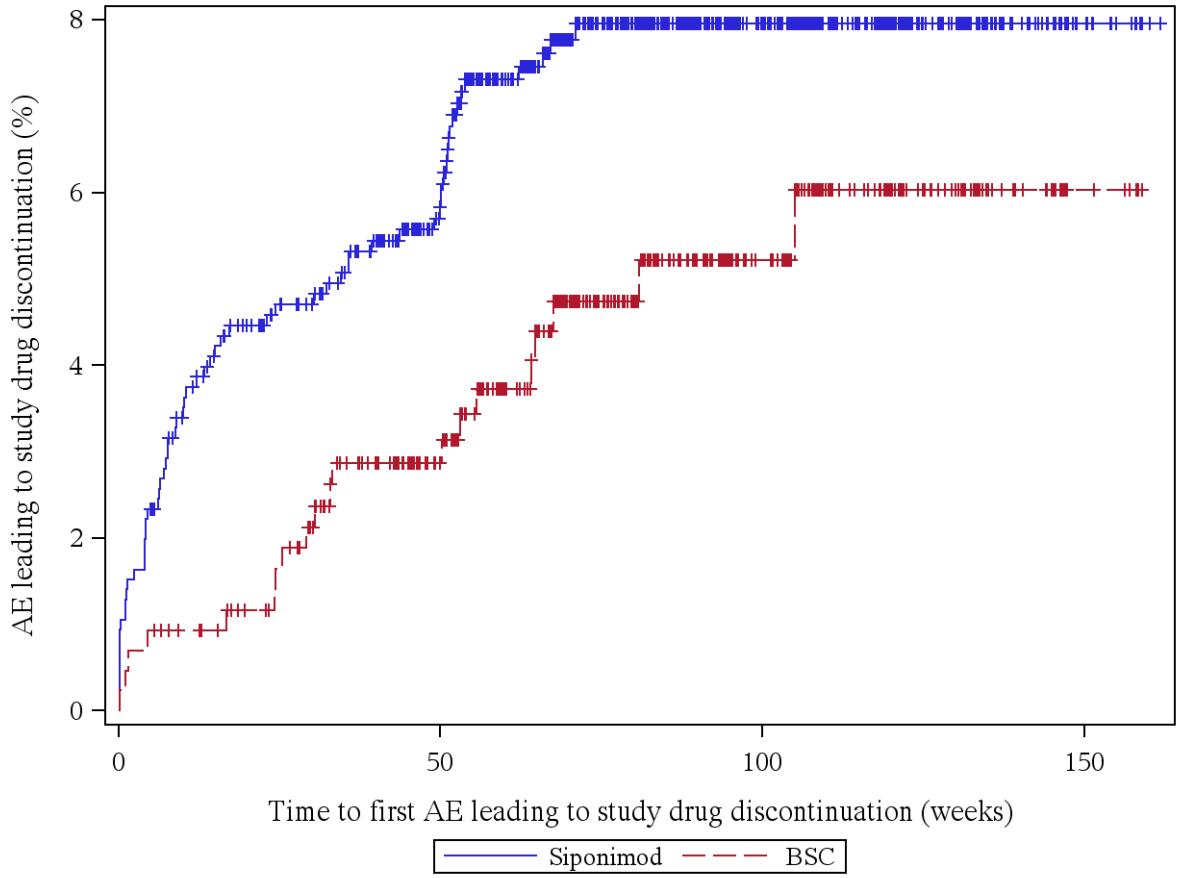


Patients at risk (Siponimod/BSC): Week 0: 242/114, Week 4: 236/112, Week 12: 230/110, Week 24: 220/107, Week 36: 214/105, Week 48: 203/100, Week 60: 185/86, Week 72: 145/67, Week 84: 121/54, Week 96: 98/40, Week 108: 76/28, Week 120: 57/17, Week 132: 27/6, Week 144: 10/2, Week 156: 1/0, Week 168: 0/0

Log rank test: p-value = 0,686
*: p < 0,05

Analysis population: A2304 SAF total population

Figure 12.4.1.8.2: AE leading to study drug discontinuation, Previous MS DMT = Yes



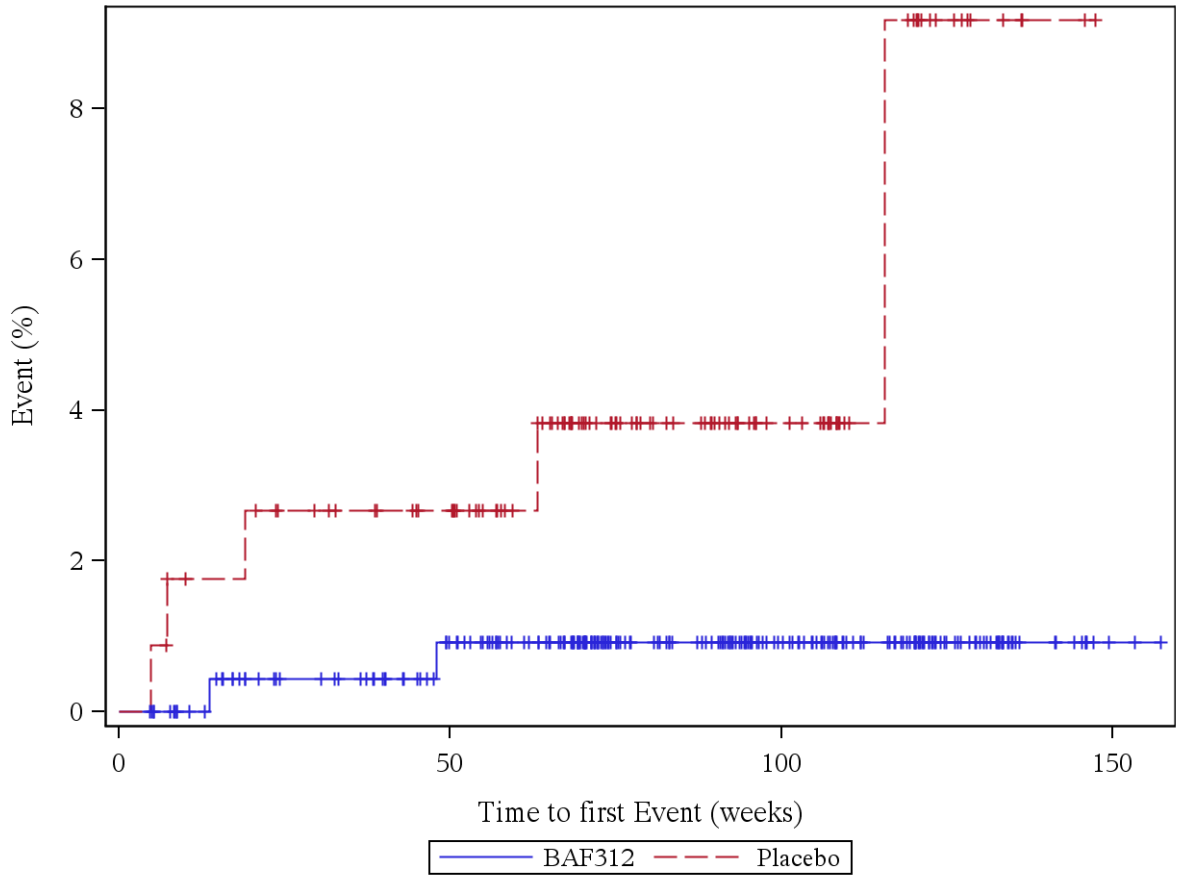
Patients at risk (Siponimod/BSC): Week 0: 857/432, Week 4: 840/429, Week 12: 814/424, Week 24: 788/412, Week 36: 766/388, Week 48: 718/359, Week 60: 628/300, Week 72: 501/237, Week 84: 393/182, Week 96: 302/135, Week 108: 215/97, Week 120: 143/63, Week 132: 86/34, Week 144: 41/18, Week 156: 9/5, Week 168: 0/0

Log rank test: p-value = 0,060
*: p < 0,05

Analysis population: A2304 SAF total population

v12.4.5: Time to First Adverse Event of Special Interest (SAF) by Previous MS DMT

Figure 12.4.5.1.1: Herpes simplex virus infections (AESI), Previous MS DMT = No

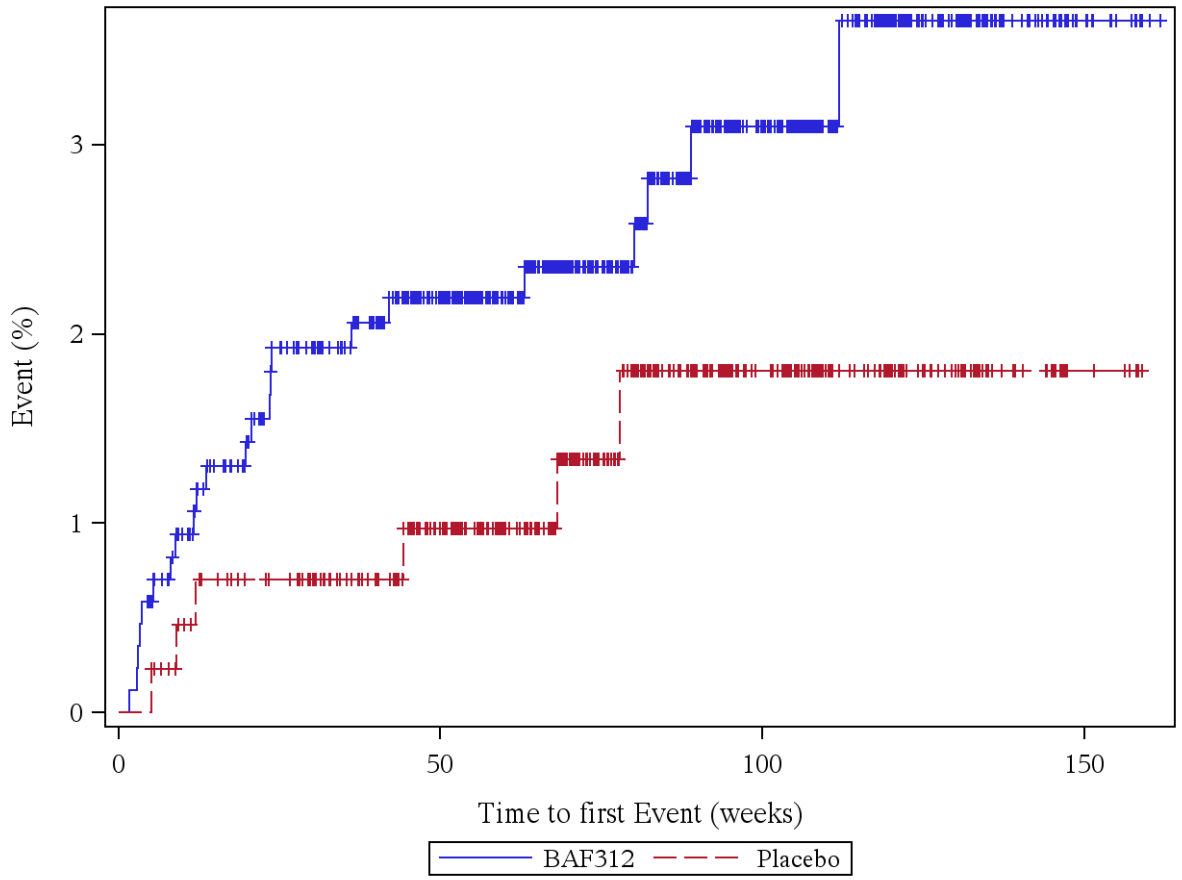


Patients at risk (BAF312/Placebo): Week 0: 242/114, Week 4: 242/114, Week 12: 232/109, Week 24: 219/105, Week 36: 215/102, Week 48: 201/97, Week 60: 183/83, Week 72: 145/63, Week 84: 120/50, Week 96: 96/37, Week 108: 74/25, Week 120: 56/15, Week 132: 26/5, Week 144: 9/2, Week 156: 1/0, Week 168: 0/0

Log rank test: p-value = 0,019 *
*: p < 0,05

Analysis population: A2304 SAF total population

Figure 12.4.5.1.2: Herpes simplex virus infections (AESI), Previous MS DMT = Yes

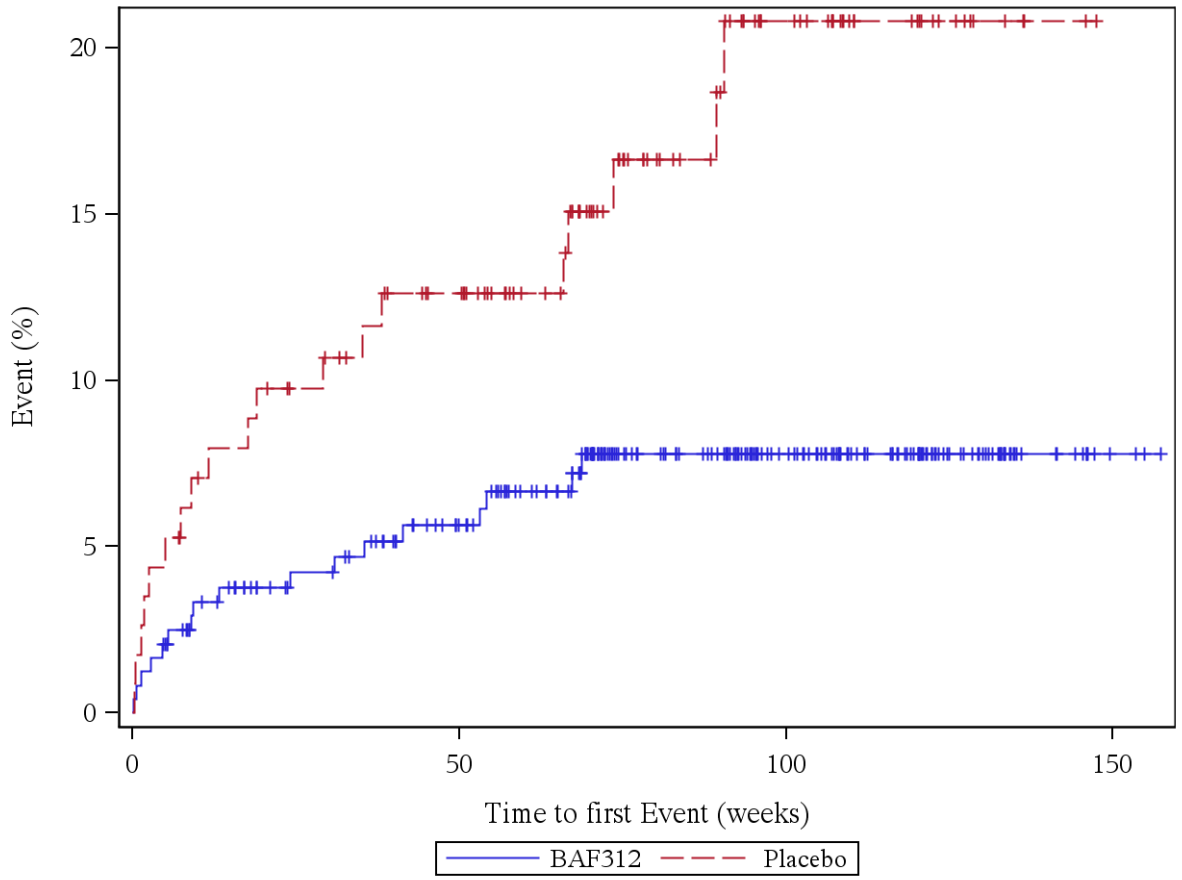


Patients at risk (BAF312/Placebo): Week 0: 857/432, Week 4: 852/432, Week 12: 818/421, Week 24: 781/410, Week 36: 759/389, Week 48: 705/357, Week 60: 616/298, Week 72: 491/236, Week 84: 384/181, Week 96: 296/133, Week 108: 212/96, Week 120: 139/63, Week 132: 84/34, Week 144: 41/18, Week 156: 9/5, Week 168: 0/0

Log rank test: p-value = 0,143
*: p < 0,05

Analysis population: A2304 SAF total population

Figure 12.4.5.2.1: Respiratory disorders (AESI), Previous MS DMT = No

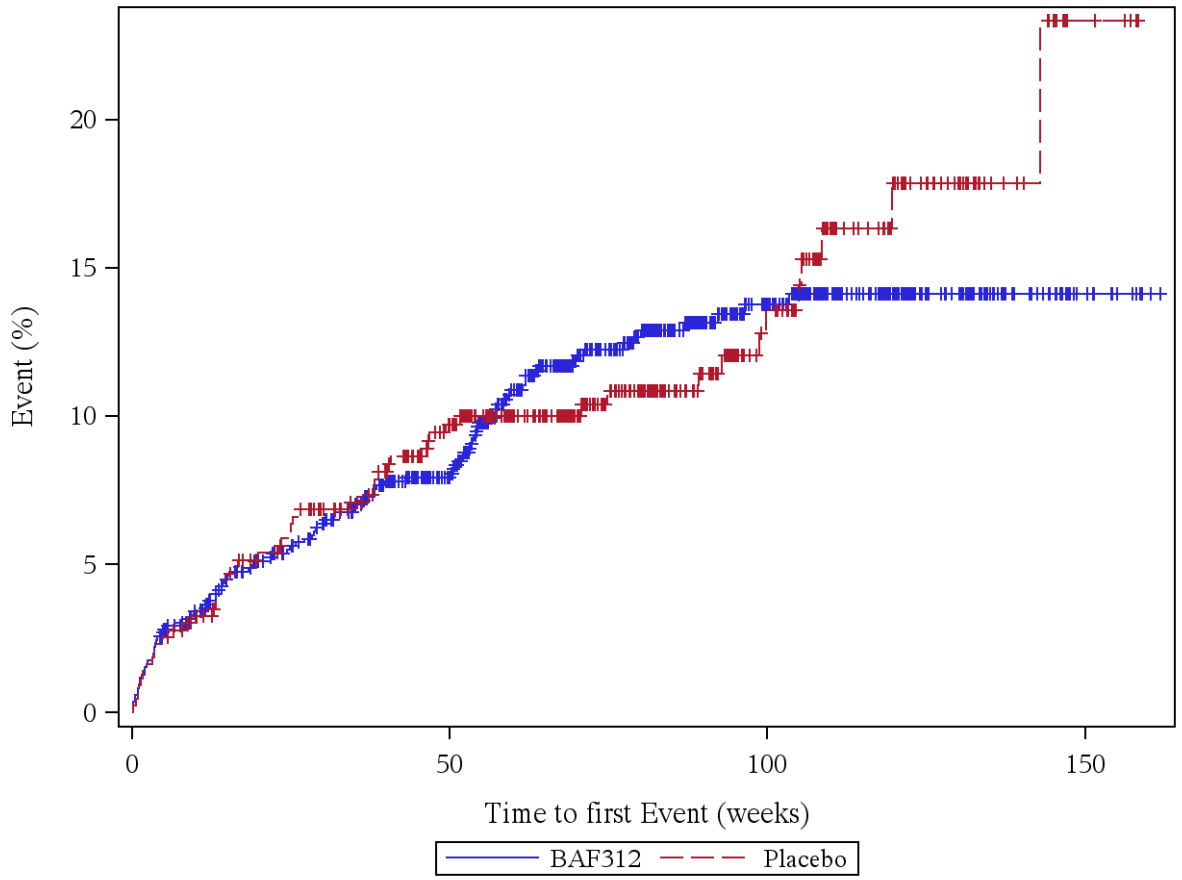


Patients at risk (BAF312/Placebo): Week 0: 242/114, Week 4: 238/109, Week 12: 224/102, Week 24: 211/97, Week 36: 205/92, Week 48: 192/86, Week 60: 174/73, Week 72: 137/55, Week 84: 116/42, Week 96: 92/30, Week 108: 73/21, Week 120: 54/13, Week 132: 27/5, Week 144: 10/2, Week 156: 1/0, Week 168: 0/0

Log rank test: p-value = 0,004 *
*: p < 0,05

Analysis population: A2304 SAF total population

Figure 12.4.5.2.2: Respiratory disorders (AESI), Previous MS DMT = Yes



Patients at risk (BAF312/Placebo): Week 0: 857/432, Week 4: 835/422, Week 12: 796/411, Week 24: 755/389, Week 36: 721/367, Week 48: 664/332, Week 60: 565/277, Week 72: 448/219, Week 84: 347/165, Week 96: 266/120, Week 108: 189/84, Week 120: 124/50, Week 132: 75/25, Week 144: 38/14, Week 156: 9/4, Week 168: 0/0

Log rank test: p-value = 0,811
*: p < 0,05

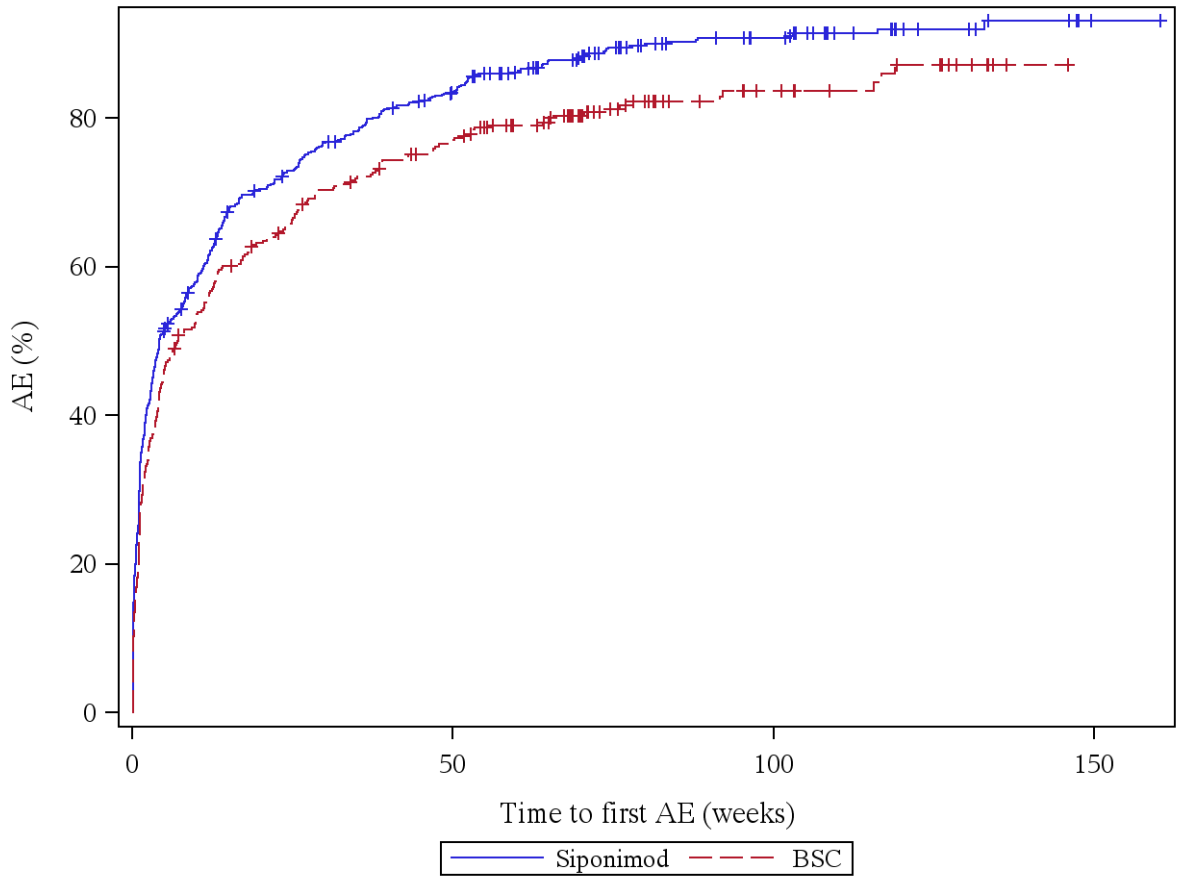
Analysis population: A2304 SAF total population

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

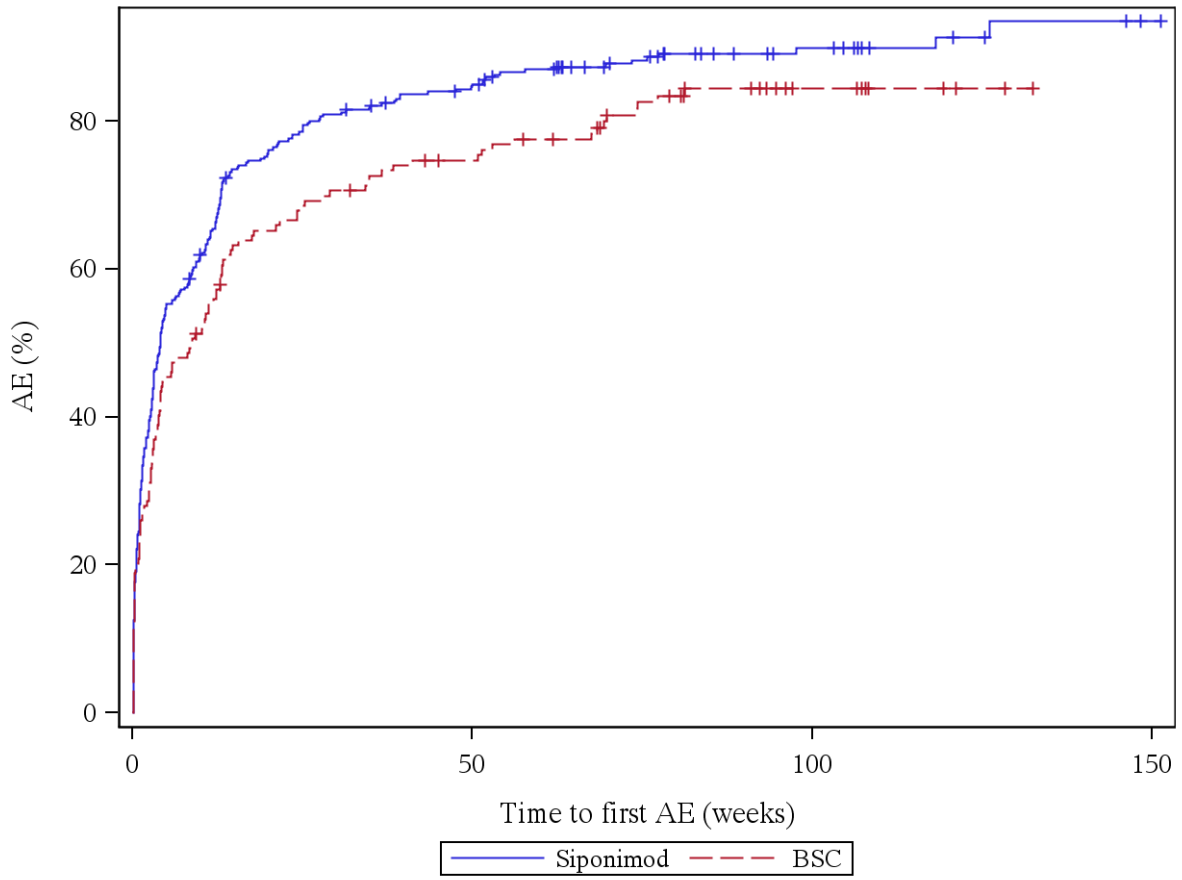


Patients at risk (Siponimod/BSC): Week 0: 755/392, Week 4: 386/228, Week 12: 285/169, Week 24: 200/132, Week 36: 152/104, Week 48: 120/85, Week 60: 87/66, Week 72: 58/43, Week 84: 38/26, Week 96: 32/21, Week 108: 20/16, Week 120: 11/10, Week 132: 7/5, Week 144: 5/1, Week 156: 1/0, Week 168: 0/0

Log rank test: p-value = 0,001 *
*: p < 0,05

Analysis population: A2304 SAF total population

Figure 12.5.1.1.2: AE, Previous IFN-beta-1b Treatment = Yes



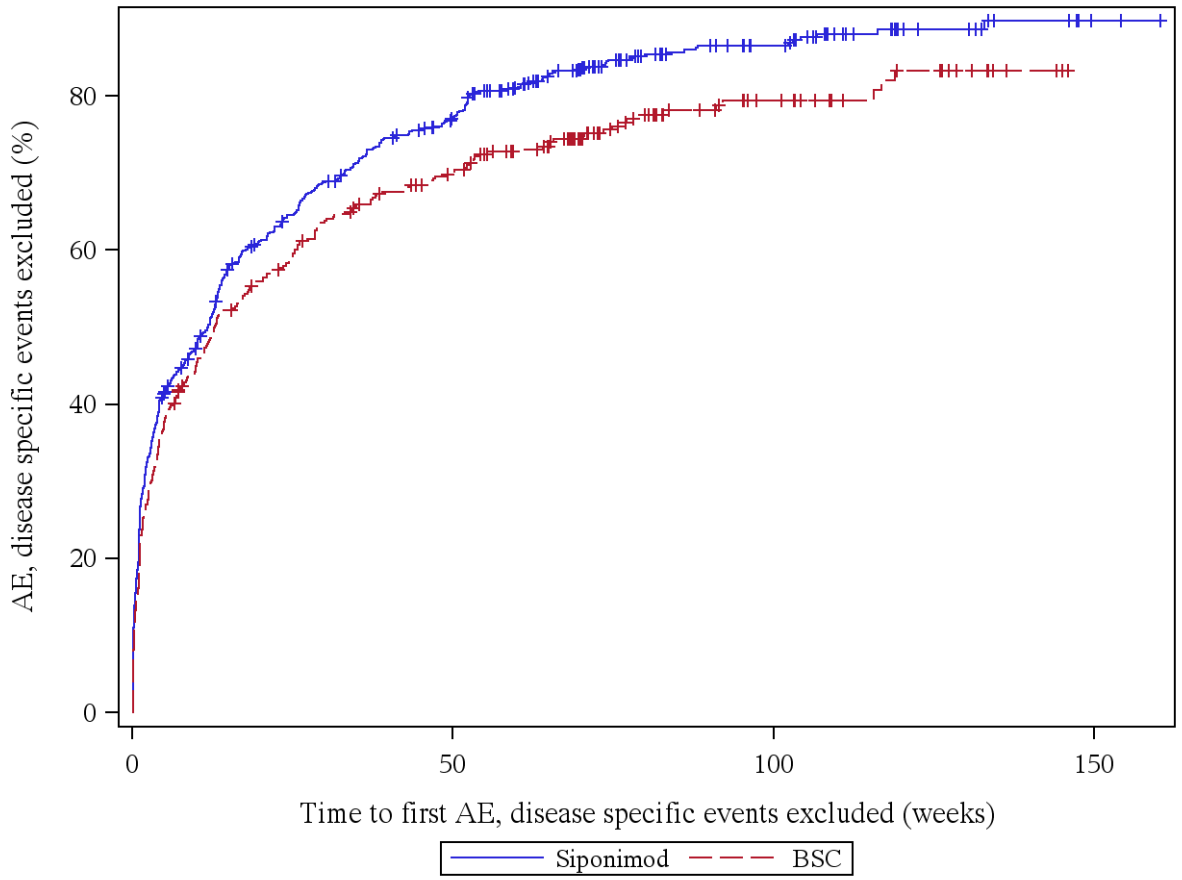
Patients at risk (Siponimod/BSC): Week 0: 344/154, Week 4: 174/91, Week 12: 117/67, Week 24: 73/50, Week 36: 58/40, Week 48: 49/35, Week 60: 38/30, Week 72: 27/22, Week 84: 18/14, Week 96: 14/10, Week 108: 8/5, Week 120: 6/3, Week 132: 3/1, Week 144: 3/0, Week 156: 0/0

Log rank test: p-value = 0,013 *
*: p < 0,05

Analysis population: A2304 SAF total population

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

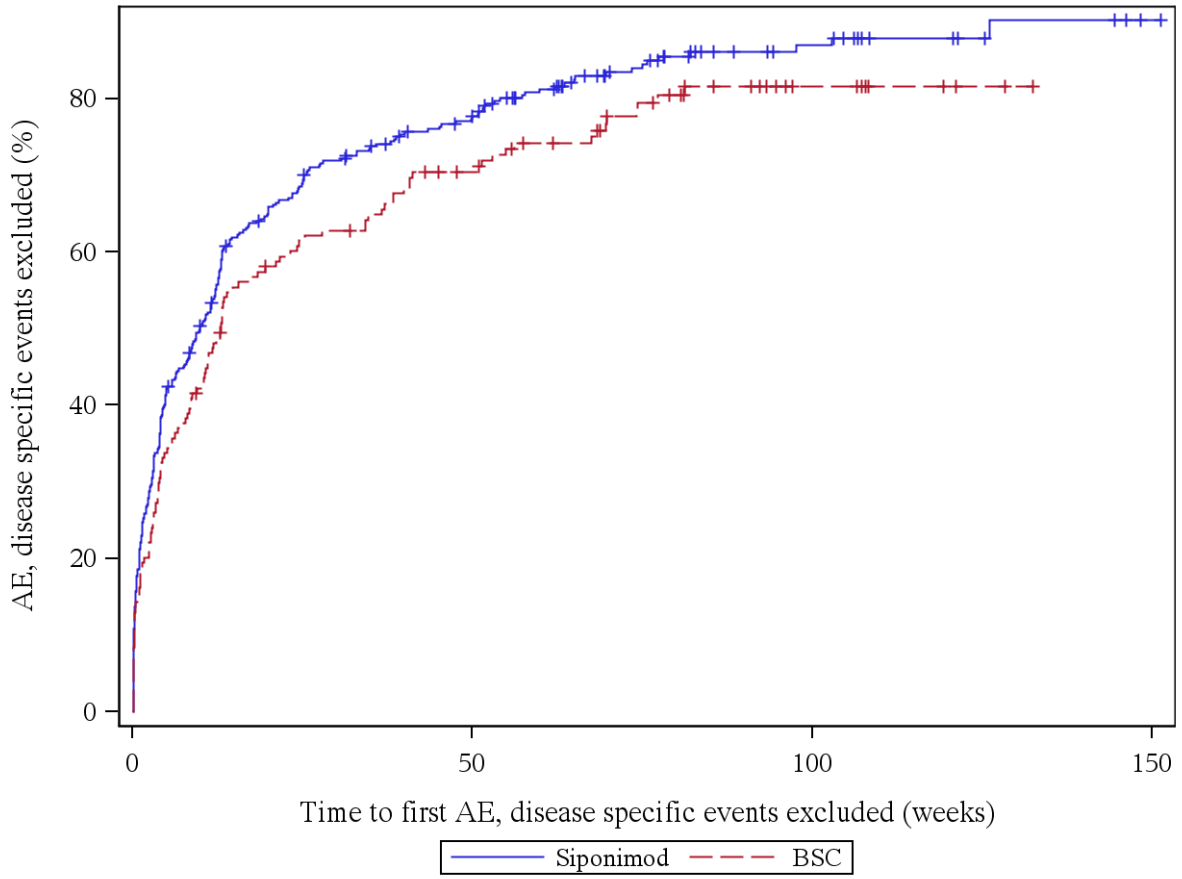


Patients at risk (Siponimod/BSC): Week 0: 755/392, Week 4: 461/257, Week 12: 367/199, Week 24: 259/158, Week 36: 199/125, Week 48: 163/108, Week 60: 116/86, Week 72: 78/58, Week 84: 52/35, Week 96: 42/27, Week 108: 27/20, Week 120: 15/12, Week 132: 11/7, Week 144: 6/3, Week 156: 1/0, Week 168: 0/0

Log rank test: p-value = 0,004 *
*: p < 0,05

Analysis population: A2304 SAF total population

Figure 12.5.1.2.2: AE, disease specific events excluded, Previous IFN-beta-1b Treatment = Yes



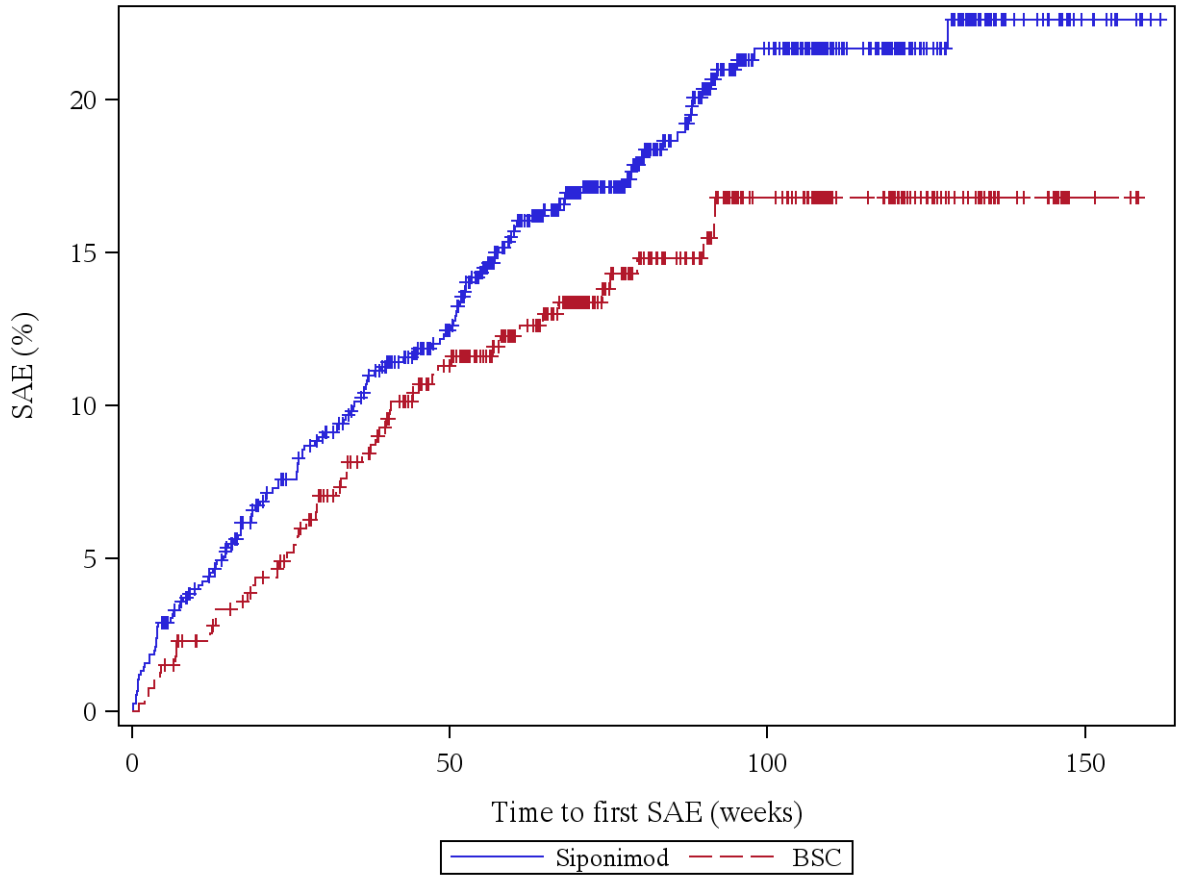
Patients at risk (Siponimod/BSC): Week 0: 344/154, Week 4: 219/107, Week 12: 154/79, Week 24: 107/59, Week 36: 82/51, Week 48: 69/40, Week 60: 49/32, Week 72: 33/24, Week 84: 20/15, Week 96: 16/10, Week 108: 9/5, Week 120: 8/3, Week 132: 4/1, Week 144: 4/0, Week 156: 0/0

Log rank test: p-value = 0,056
*: p < 0,05

Analysis population: A2304 SAF total population

12.5.1.3: Any SAE

Figure 12.5.1.3.1: SAE, Previous IFN-beta-1b Treatment = No

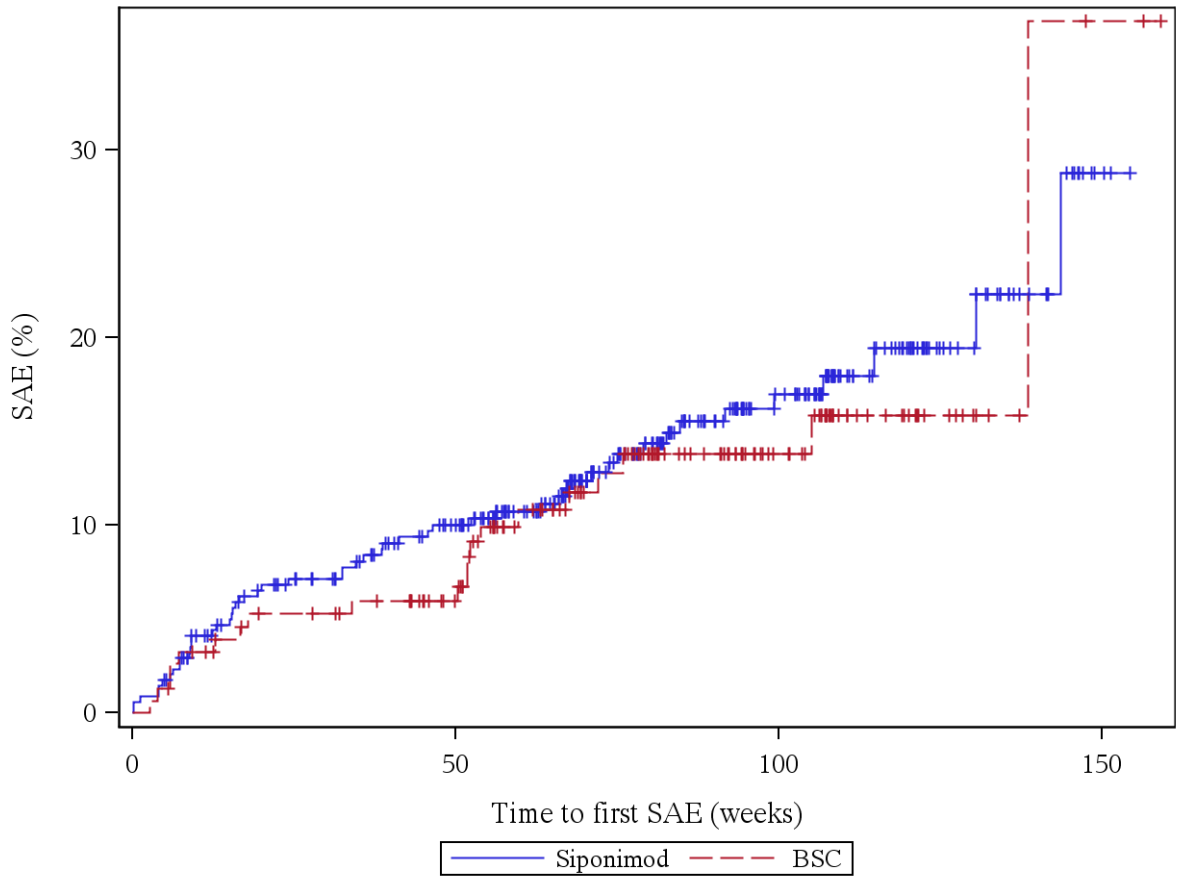


Patients at risk (Siponimod/BSC): Week 0: 755/392, Week 4: 734/388, Week 12: 704/376, Week 24: 658/357, Week 36: 625/330, Week 48: 574/299, Week 60: 494/253, Week 72: 384/191, Week 84: 295/144, Week 96: 230/105, Week 108: 169/84, Week 120: 119/56, Week 132: 64/32, Week 144: 29/16, Week 156: 7/3, Week 168: 0/0

Log rank test: p-value = 0,095
*: p < 0,05

Analysis population: A2304 SAF total population

Figure 12.5.1.3.2: SAE, Previous IFN-beta-1b Treatment = Yes



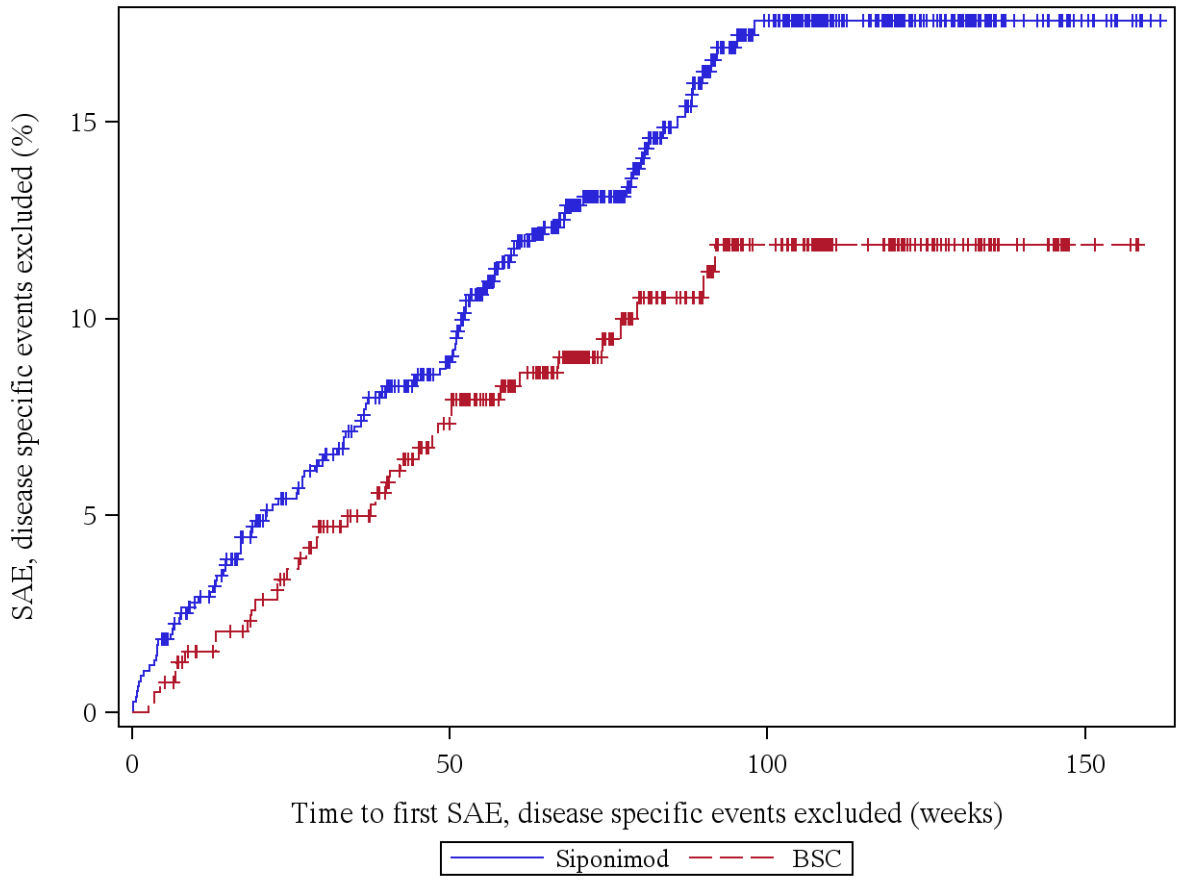
Patients at risk (Siponimod/BSC): Week 0: 344/154, Week 4: 339/152, Week 12: 320/146, Week 24: 301/139, Week 36: 287/135, Week 48: 271/124, Week 60: 236/101, Week 72: 180/86, Week 84: 142/67, Week 96: 107/52, Week 108: 73/28, Week 120: 45/16, Week 132: 24/6, Week 144: 11/3, Week 156: 0/2

Log rank test: p-value = 0,640
*: p < 0,05

Analysis population: A2304 SAF total population

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

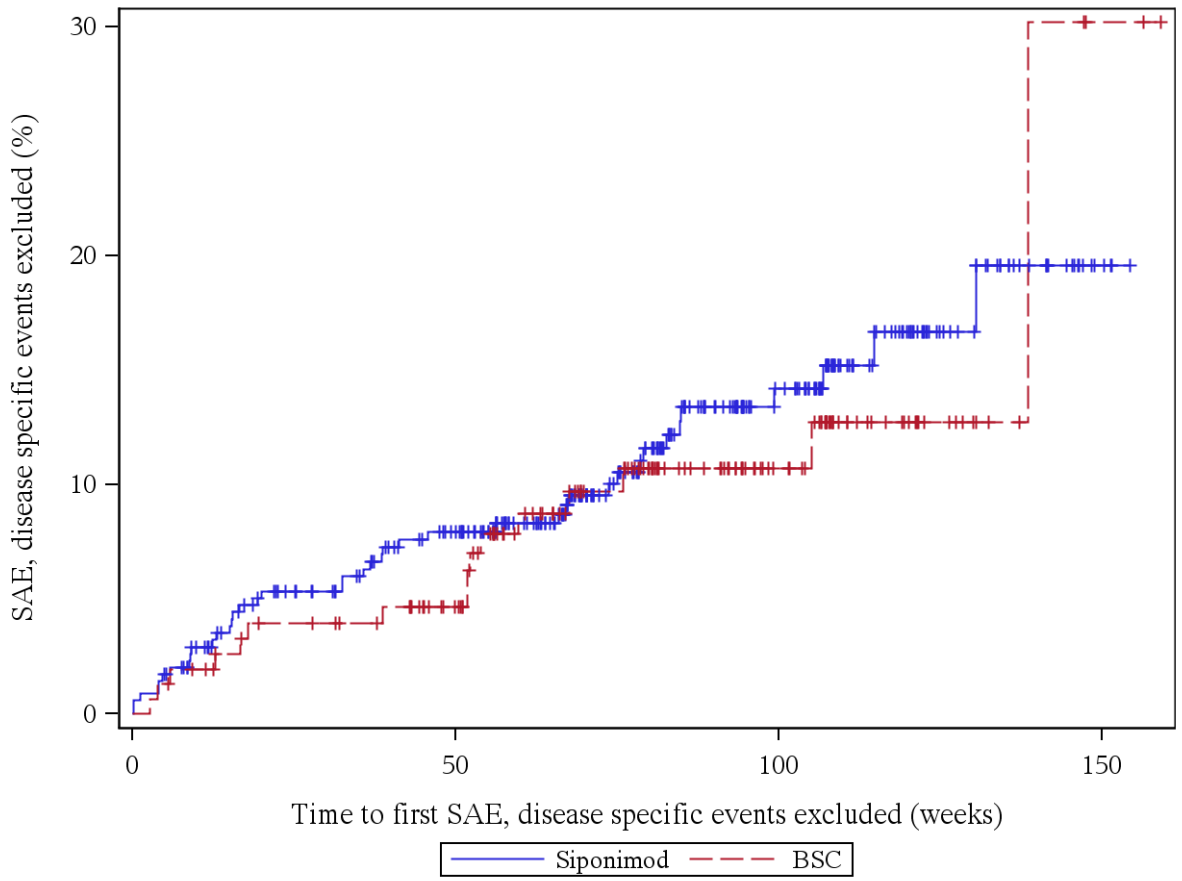


Patients at risk (Siponimod/BSC): Week 0: 755/392, Week 4: 742/390, Week 12: 713/378, Week 24: 671/362, Week 36: 643/339, Week 48: 594/309, Week 60: 514/259, Week 72: 402/195, Week 84: 310/148, Week 96: 243/108, Week 108: 177/84, Week 120: 125/56, Week 132: 70/32, Week 144: 32/16, Week 156: 8/3, Week 168: 0/0

Log rank test: p-value = 0,043 *
*: p < 0,05

Analysis population: A2304 SAF total population

Figure 12.5.1.4.2: SAE, disease specific events excluded, Previous IFN-beta-1b Treatment = Yes



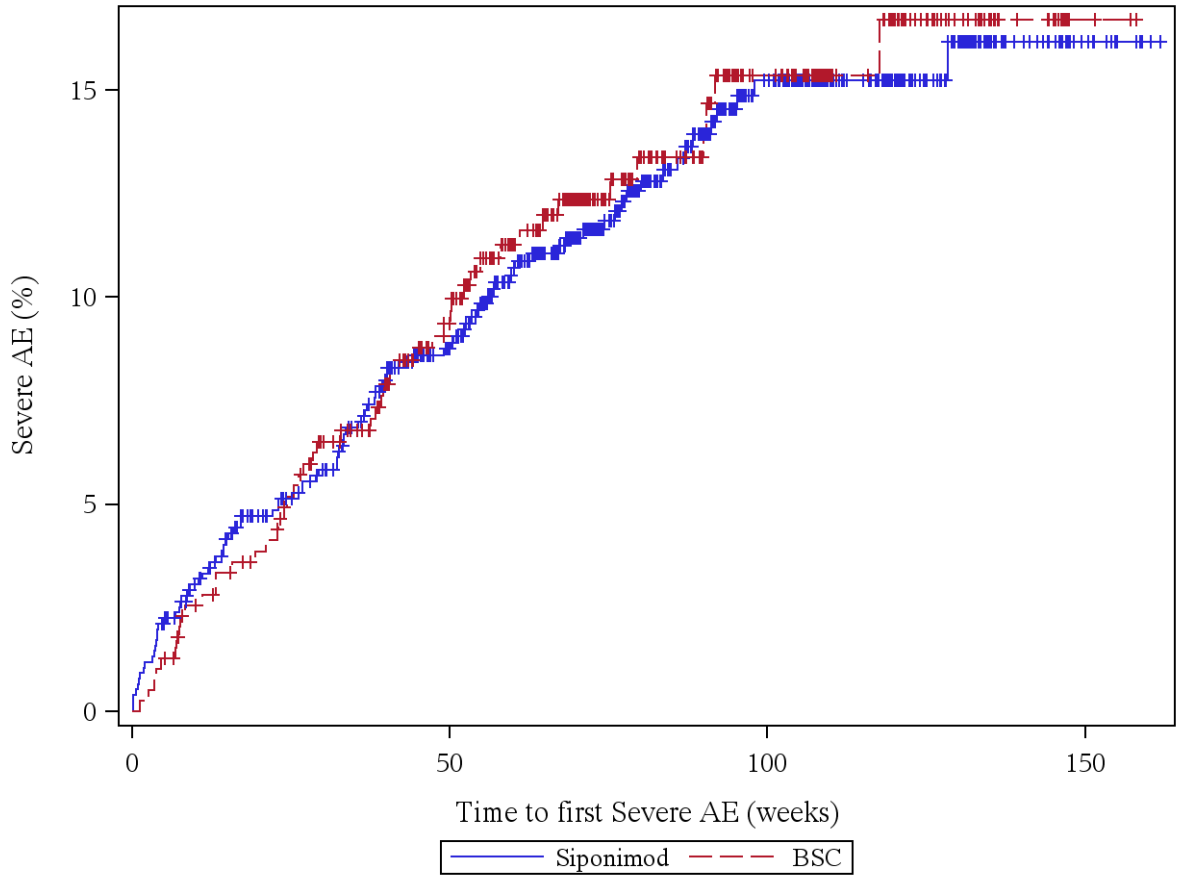
Patients at risk (Siponimod/BSC): Week 0: 344/154, Week 4: 339/152, Week 12: 323/148, Week 24: 304/141, Week 36: 292/138, Week 48: 276/126, Week 60: 241/104, Week 72: 186/88, Week 84: 145/69, Week 96: 109/54, Week 108: 75/30, Week 120: 46/17, Week 132: 25/7, Week 144: 12/4, Week 156: 0/2

Log rank test: p-value = 0,634
*: p < 0,05

Analysis population: A2304 SAF total population

12.5.1.5: Any severe AE

Figure 12.5.1.5.1: Severe AE, Previous IFN-beta-1b Treatment = No

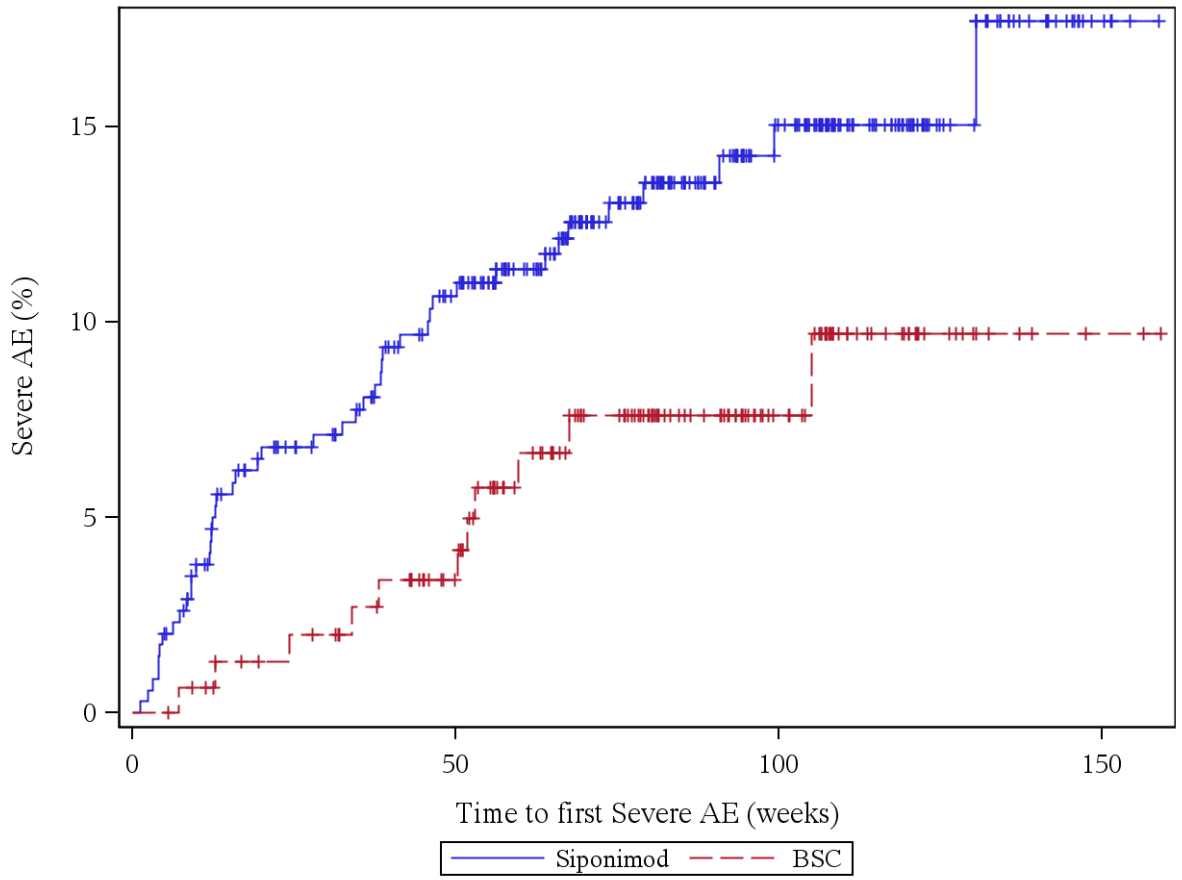


Patients at risk (Siponimod/BSC): Week 0: 755/392, Week 4: 740/388, Week 12: 708/375, Week 24: 673/359, Week 36: 645/337, Week 48: 593/306, Week 60: 518/255, Week 72: 411/191, Week 84: 316/146, Week 96: 248/107, Week 108: 181/82, Week 120: 131/54, Week 132: 72/29, Week 144: 33/14, Week 156: 7/2, Week 168: 0/0

Log rank test: p-value = 0,802
*: p < 0,05

Analysis population: A2304 SAF total population

Figure 12.5.1.5.2: Severe AE, Previous IFN-beta-1b Treatment = Yes



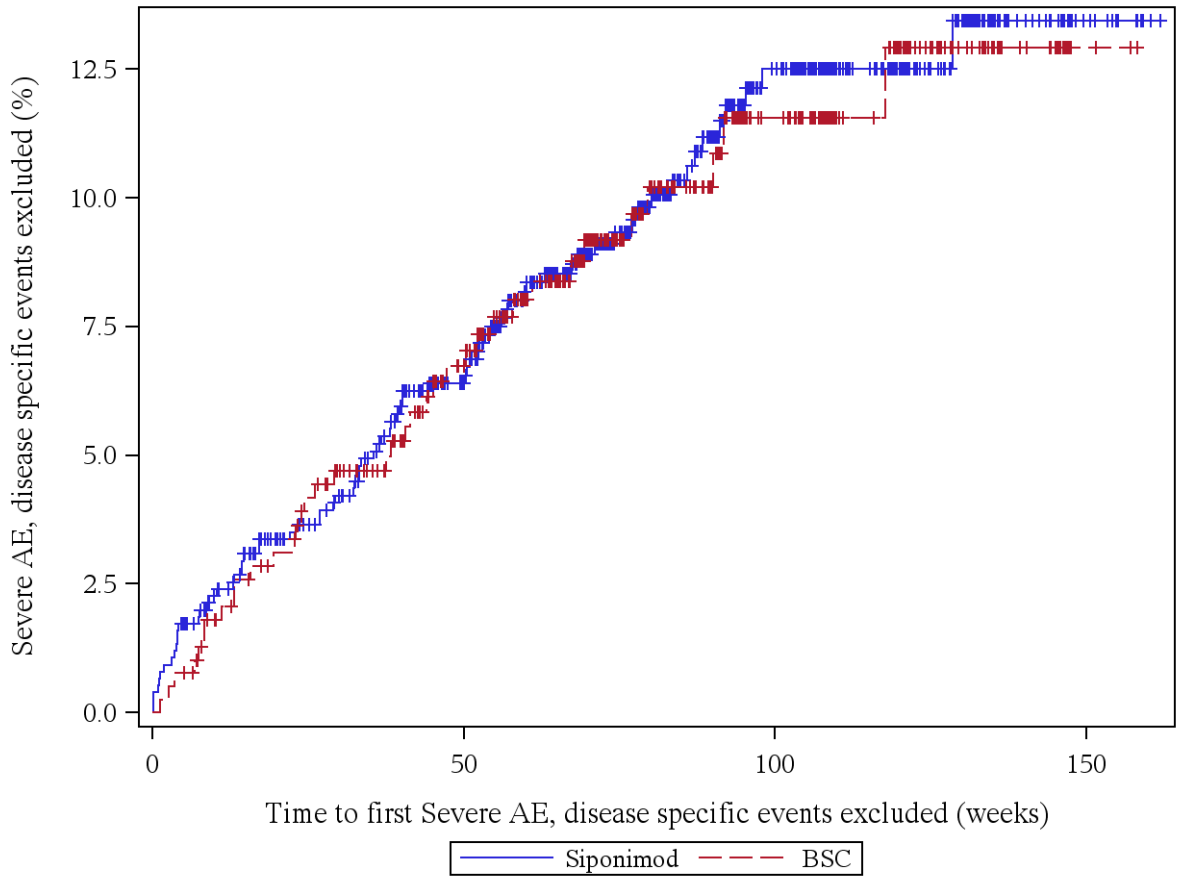
Patients at risk (Siponimod/BSC): Week 0: 344/154, Week 4: 339/154, Week 12: 320/150, Week 24: 301/145, Week 36: 289/139, Week 48: 270/127, Week 60: 235/106, Week 72: 183/90, Week 84: 146/70, Week 96: 108/54, Week 108: 77/30, Week 120: 48/16, Week 132: 27/6, Week 144: 12/3, Week 156: 1/2, Week 168: 0/0

Log rank test: p-value = 0,053
*: p < 0,05

Analysis population: A2304 SAF total population

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

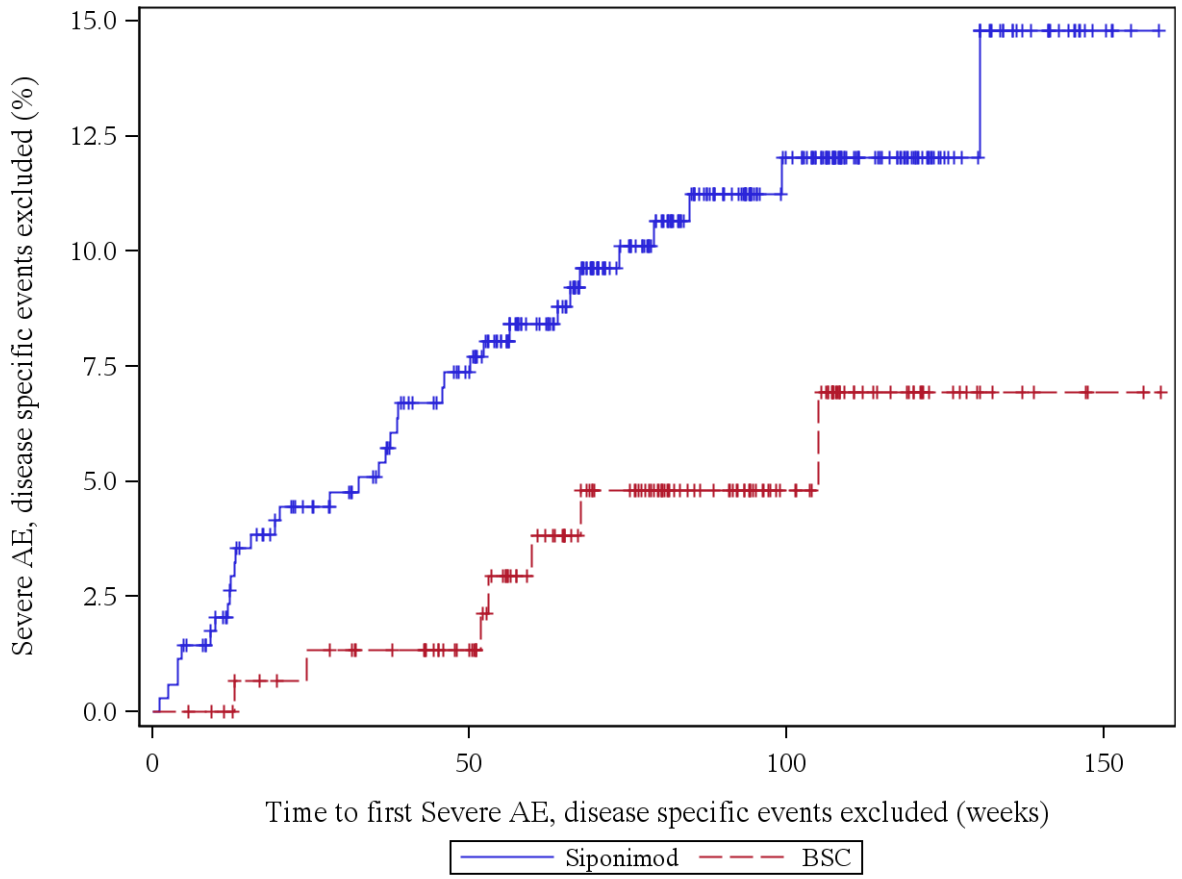


Patients at risk (Siponimod/BSC): Week 0: 755/392, Week 4: 743/389, Week 12: 715/376, Week 24: 682/361, Week 36: 657/341, Week 48: 605/310, Week 60: 529/261, Week 72: 421/196, Week 84: 325/151, Week 96: 253/109, Week 108: 185/84, Week 120: 133/56, Week 132: 74/31, Week 144: 33/15, Week 156: 7/2, Week 168: 0/0

Log rank test: p-value = 0,899
*: p < 0,05

Analysis population: A2304 SAF total population

Figure 12.5.1.6.2: Severe AE, disease specific events excluded, Previous IFN-beta-1b Treatment = Yes



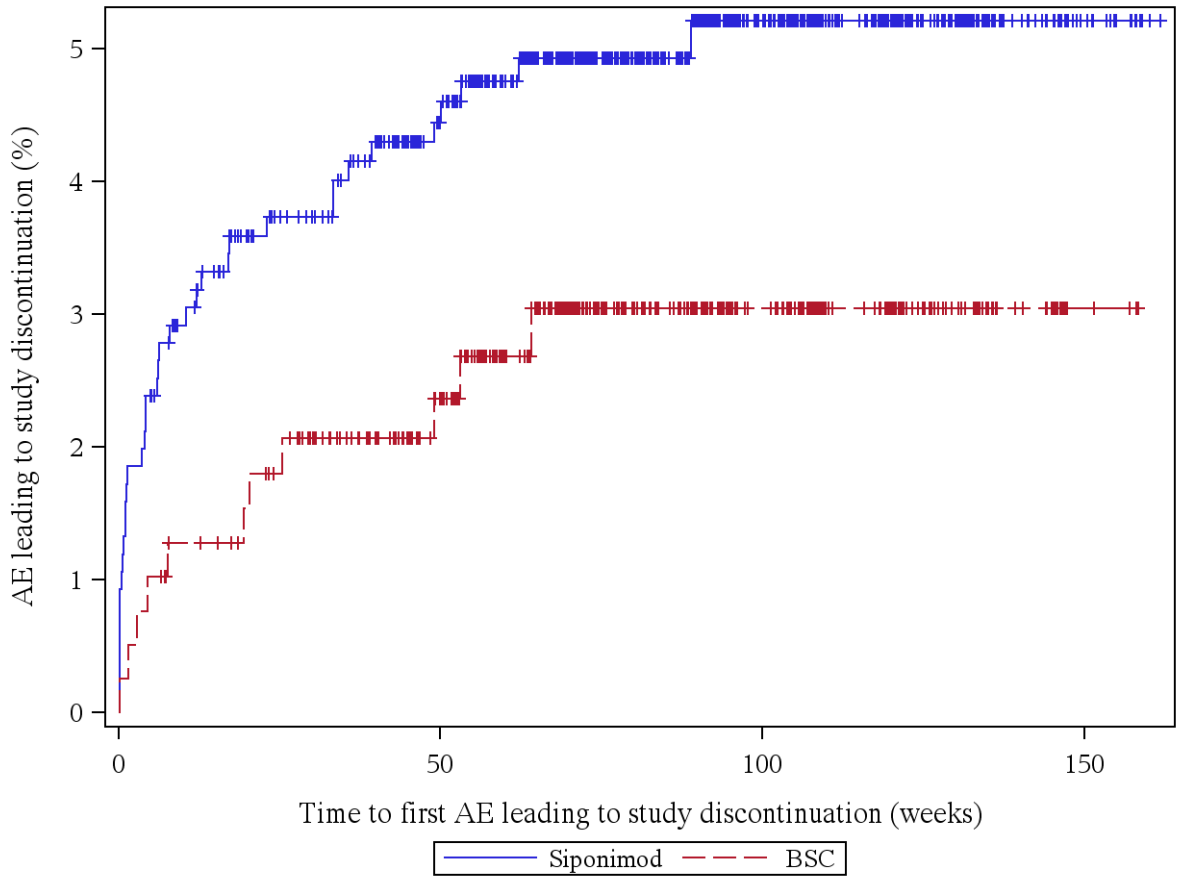
Patients at risk (Siponimod/BSC): Week 0: 344/154, Week 4: 340/154, Week 12: 326/151, Week 24: 307/146, Week 36: 295/141, Week 48: 278/130, Week 60: 241/109, Week 72: 187/91, Week 84: 150/71, Week 96: 112/55, Week 108: 80/31, Week 120: 50/17, Week 132: 27/7, Week 144: 12/4, Week 156: 1/2, Week 168: 0/0

Log rank test: p-value = 0,039 *
*: p < 0,05

Analysis population: A2304 SAF total population

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

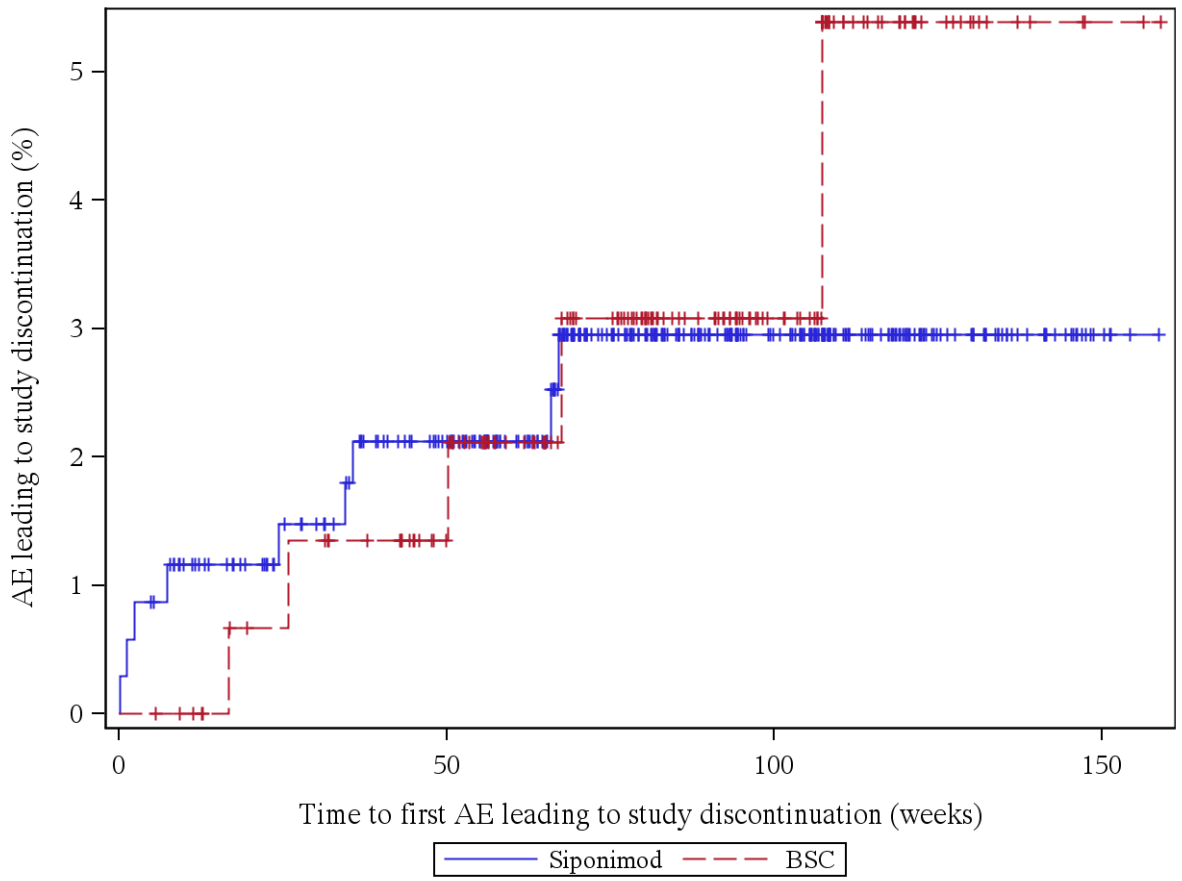


Patients at risk (Siponimod/BSC): Week 0: 755/392, Week 4: 739/389, Week 12: 721/383, Week 24: 696/373, Week 36: 678/355, Week 48: 632/330, Week 60: 563/276, Week 72: 453/210, Week 84: 354/164, Week 96: 278/119, Week 108: 204/92, Week 120: 147/62, Week 132: 82/33, Week 144: 37/16, Week 156: 9/3, Week 168: 0/0

Log rank test: p-value = 0,097
*: p < 0,05

Analysis population: A2304 SAF total population

Figure 12.5.1.7.2: AE leading to study discontinuation, Previous IFN-beta-1b Treatment = Yes



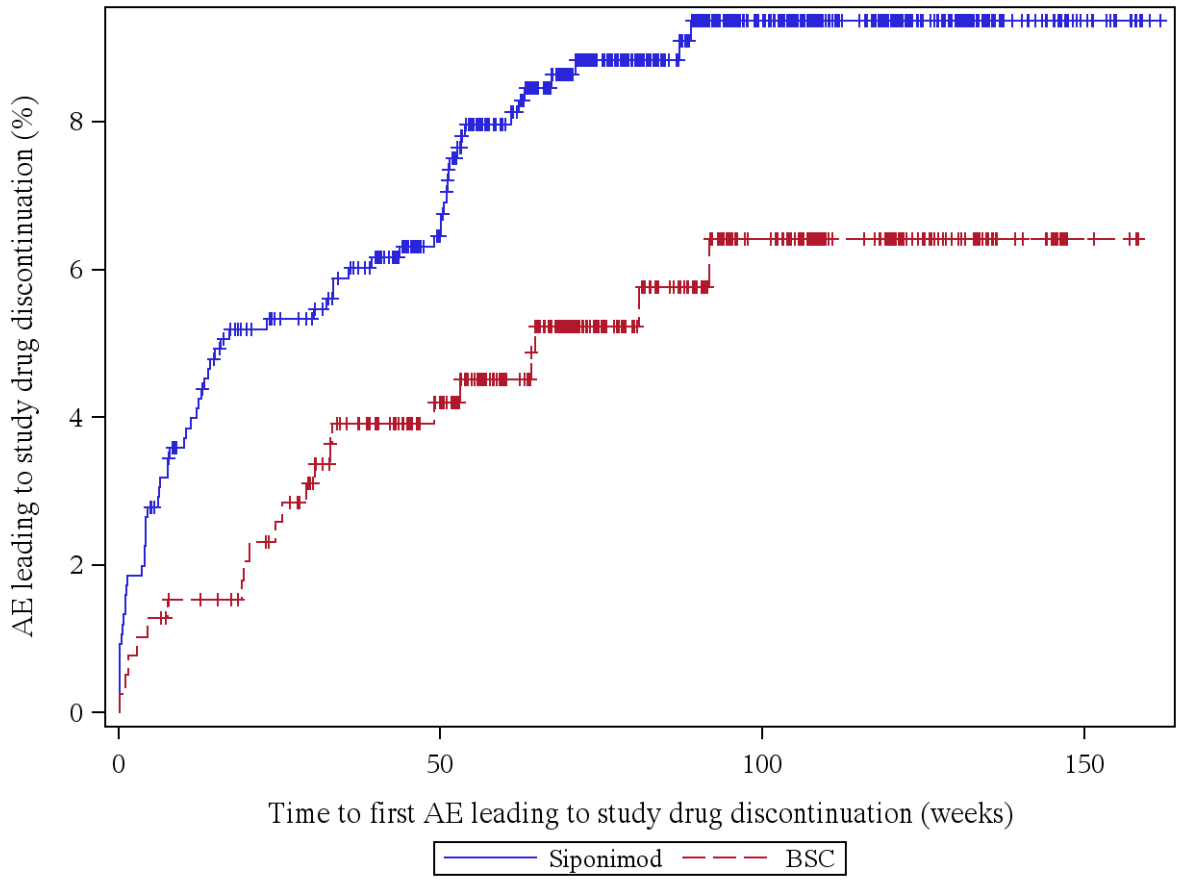
Patients at risk (Siponimod/BSC): Week 0: 344/154, Week 4: 341/154, Week 12: 330/151, Week 24: 316/146, Week 36: 304/142, Week 48: 290/131, Week 60: 253/111, Week 72: 197/94, Week 84: 161/73, Week 96: 122/57, Week 108: 87/33, Week 120: 53/18, Week 132: 31/7, Week 144: 14/4, Week 156: 1/2, Week 168: 0/0

Log rank test: p-value = 0,708
*: p < 0,05

Analysis population: A2304 SAF total population

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

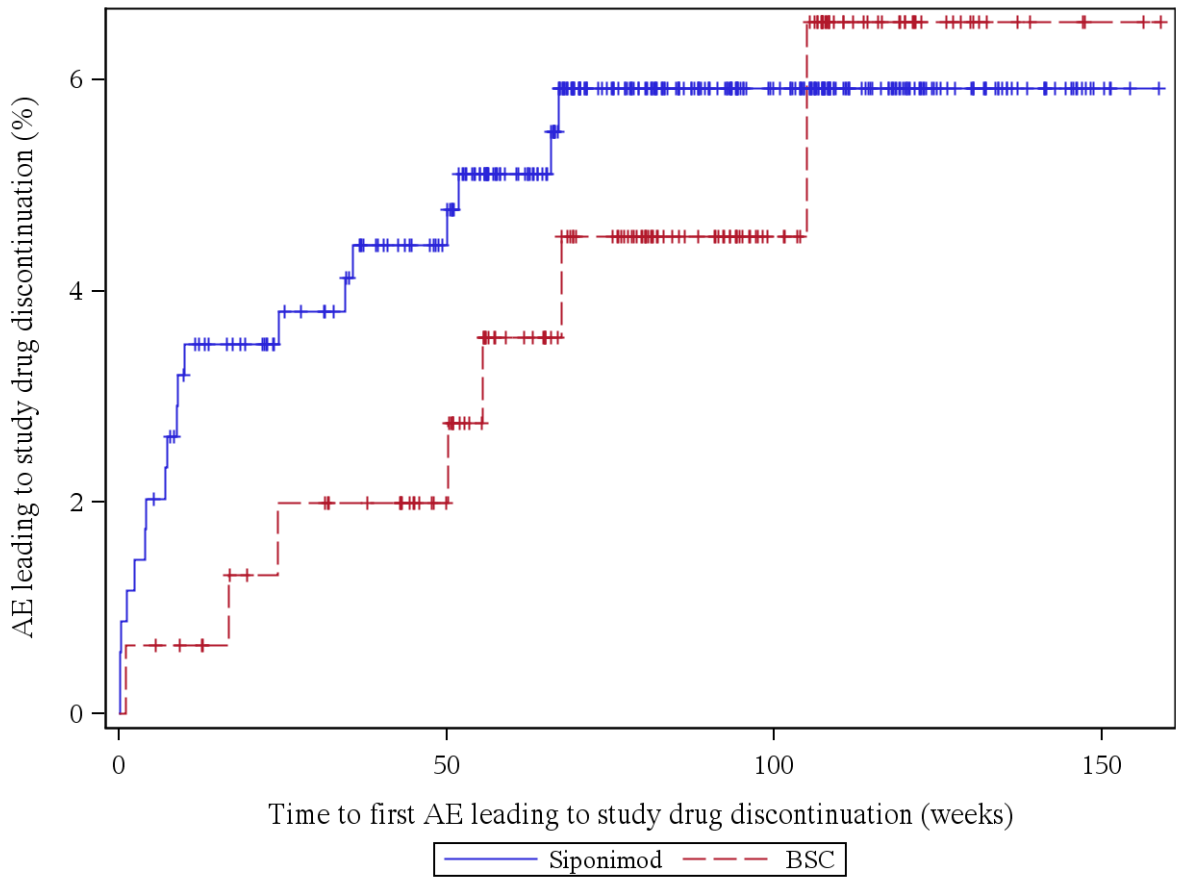


Patients at risk (Siponimod/BSC): Week 0: 755/392, Week 4: 738/388, Week 12: 717/383, Week 24: 694/373, Week 36: 676/351, Week 48: 631/328, Week 60: 561/276, Week 72: 450/210, Week 84: 353/163, Week 96: 278/118, Week 108: 204/92, Week 120: 147/62, Week 132: 82/33, Week 144: 37/16, Week 156: 9/3, Week 168: 0/0

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

Analysis population: A2304 SAF total population

Figure 12.5.1.8.2: AE leading to study drug discontinuation, Previous IFN-beta-1b Treatment = Yes



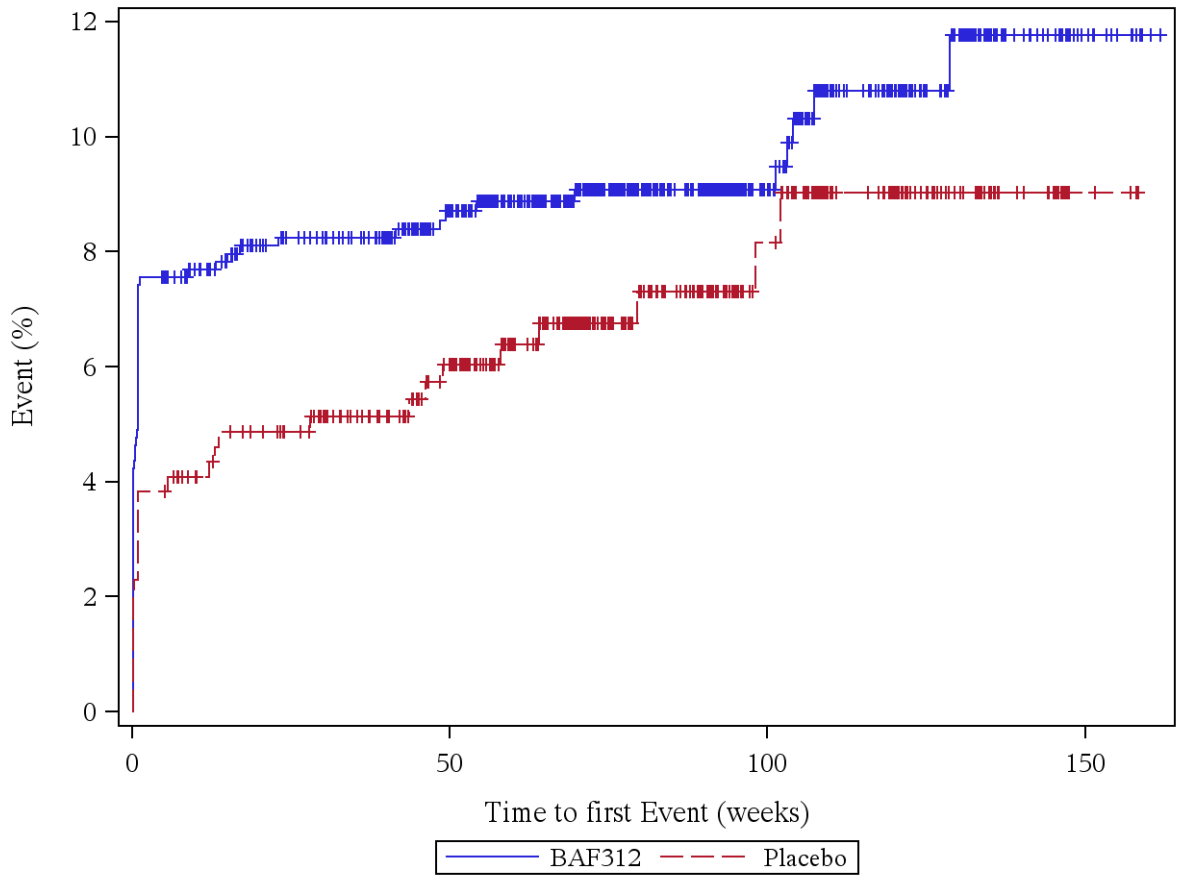
Patients at risk (Siponimod/BSC): Week 0: 344/154, Week 4: 338/153, Week 12: 327/151, Week 24: 314/146, Week 36: 304/142, Week 48: 290/131, Week 60: 252/110, Week 72: 196/94, Week 84: 161/73, Week 96: 122/57, Week 108: 87/33, Week 120: 53/18, Week 132: 31/7, Week 144: 14/4, Week 156: 1/2, Week 168: 0/0

Log rank test: p-value = 0,644
*: p < 0,05

Analysis population: A2304 SAF total population

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

Figure 12.5.5.1.1: Bradyarrhythmias and bradycardia (AESI), Previous IFN-beta-1b Treatment = No

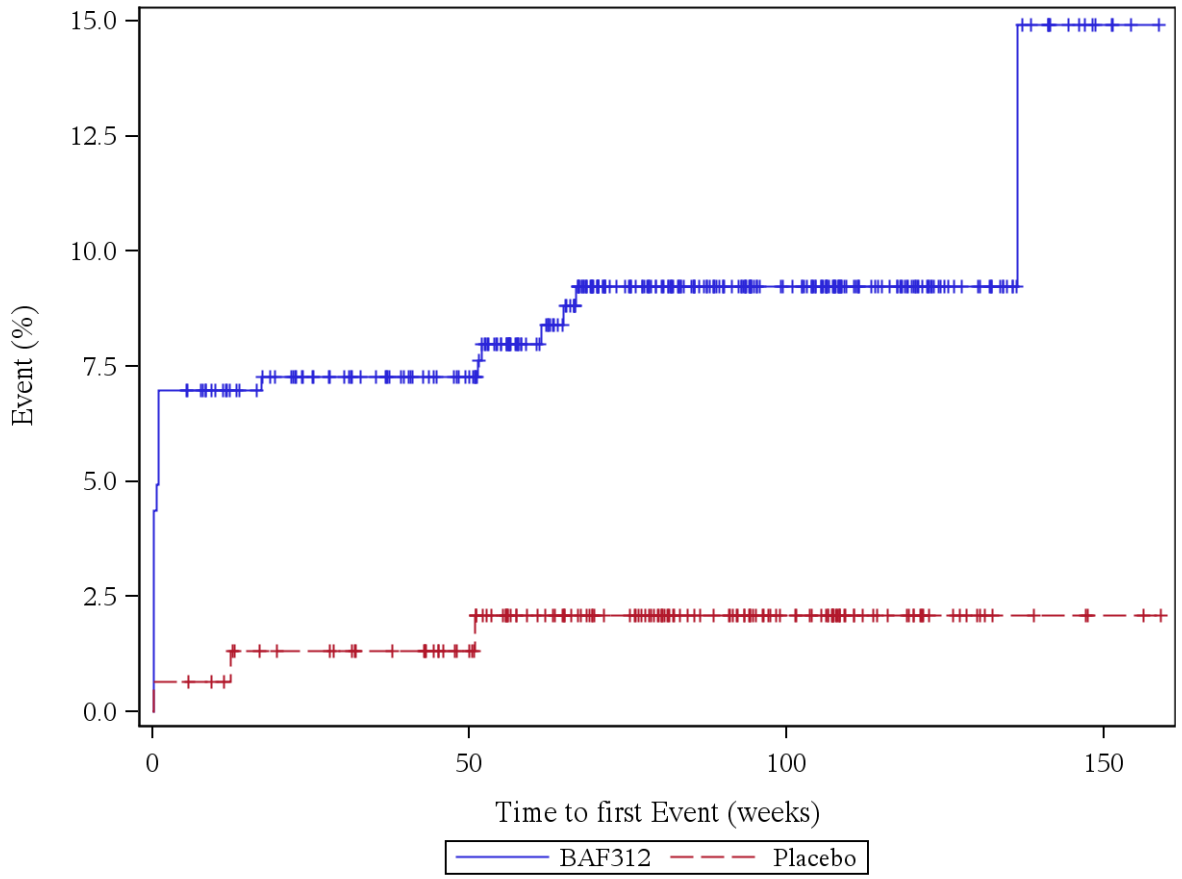


Patients at risk (BAF312/Placebo): Week 0: 755/392, Week 4: 698/377, Week 12: 676/368, Week 24: 647/355, Week 36: 632/335, Week 48: 583/310, Week 60: 516/258, Week 72: 409/199, Week 84: 315/154, Week 96: 245/112, Week 108: 177/84, Week 120: 130/59, Week 132: 72/32, Week 144: 34/15, Week 156: 8/3, Week 168: 0/0

Log rank test: p-value = 0,182
*: p < 0,05

Analysis population: A2304 SAF total population

Figure 12.5.5.1.2: Bradyarrhythmias and bradycardia (AESI), Previous IFN-beta-1b Treatment = Yes



Patients at risk (BAF312/Placebo): Week 0: 344/154, Week 4: 320/153, Week 12: 309/150, Week 24: 295/145, Week 36: 285/140, Week 48: 270/129, Week 60: 231/109, Week 72: 177/92, Week 84: 143/71, Week 96: 105/55, Week 108: 76/32, Week 120: 46/17, Week 132: 26/6, Week 144: 9/4, Week 156: 1/2, Week 168: 0/0

Log rank test: p-value = 0,004 *
*: p < 0,05

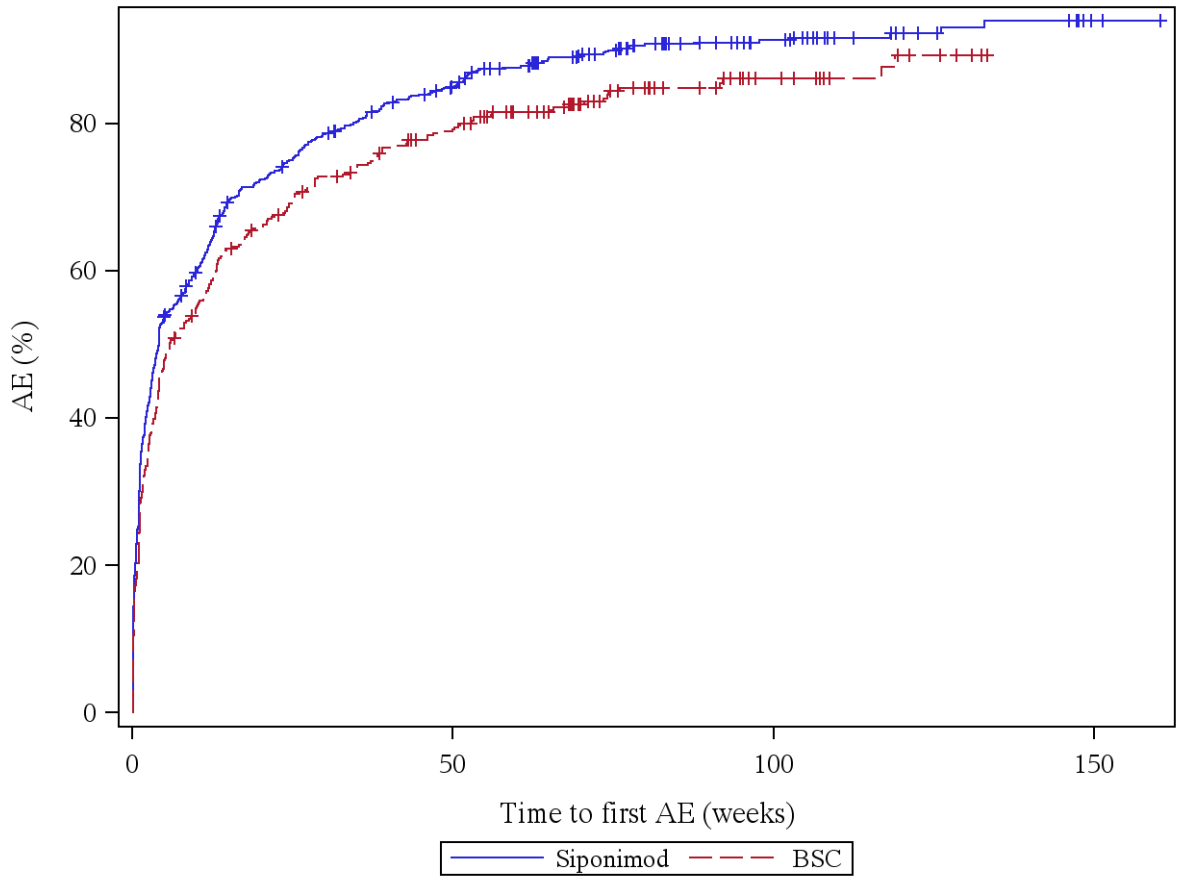
Analysis population: A2304 SAF total population

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

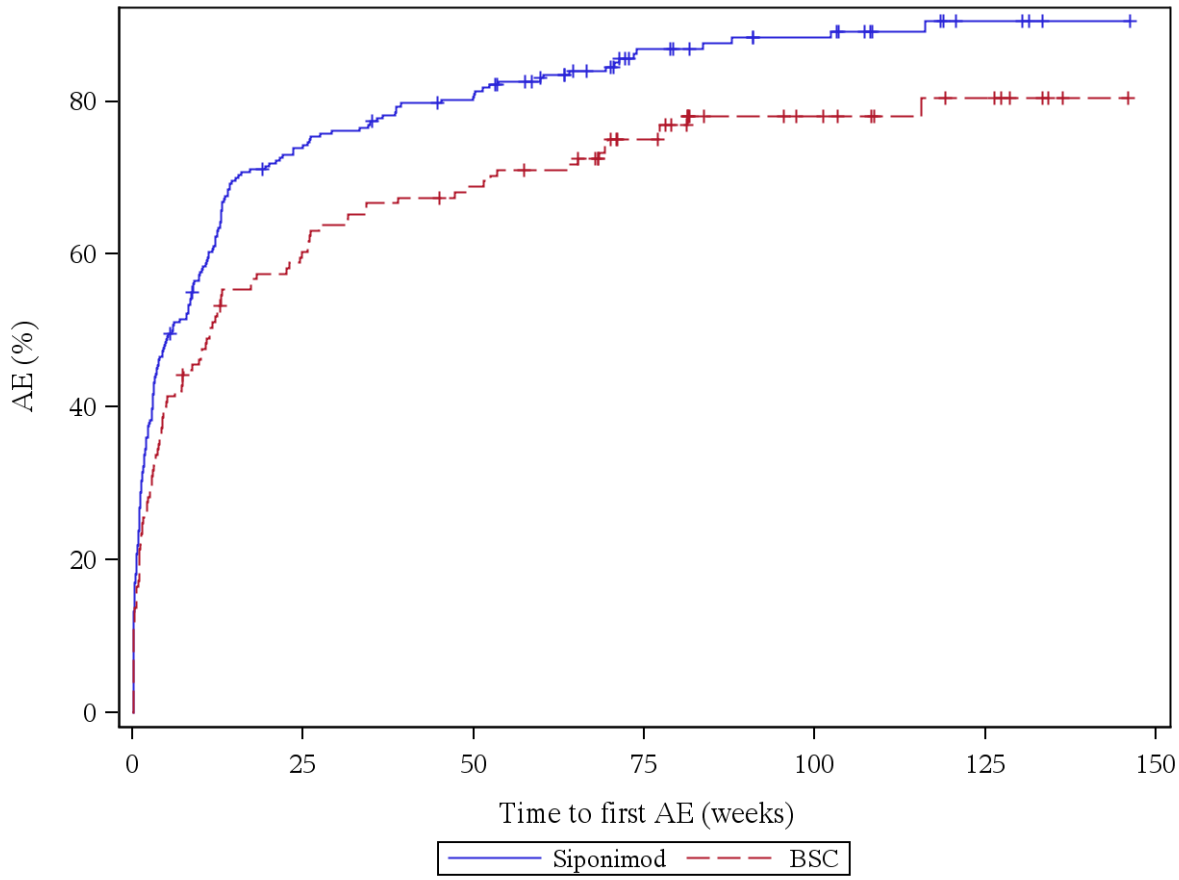


Patients at risk (Siponimod/BSC): Week 0: 835/401, Week 4: 419/226, Week 12: 301/166, Week 24: 206/124, Week 36: 154/97, Week 48: 120/76, Week 60: 88/57, Week 72: 60/38, Week 84: 39/25, Week 96: 32/17, Week 108: 18/10, Week 120: 12/6, Week 132: 8/2, Week 144: 7/0, Week 156: 1/0, Week 168: 0/0

Log rank test: p-value = 0,003 *
*: p < 0,05

Analysis population: A2304 SAF total population

Figure 12.6.1.1.2: AE, Rapid Evolvement = Yes



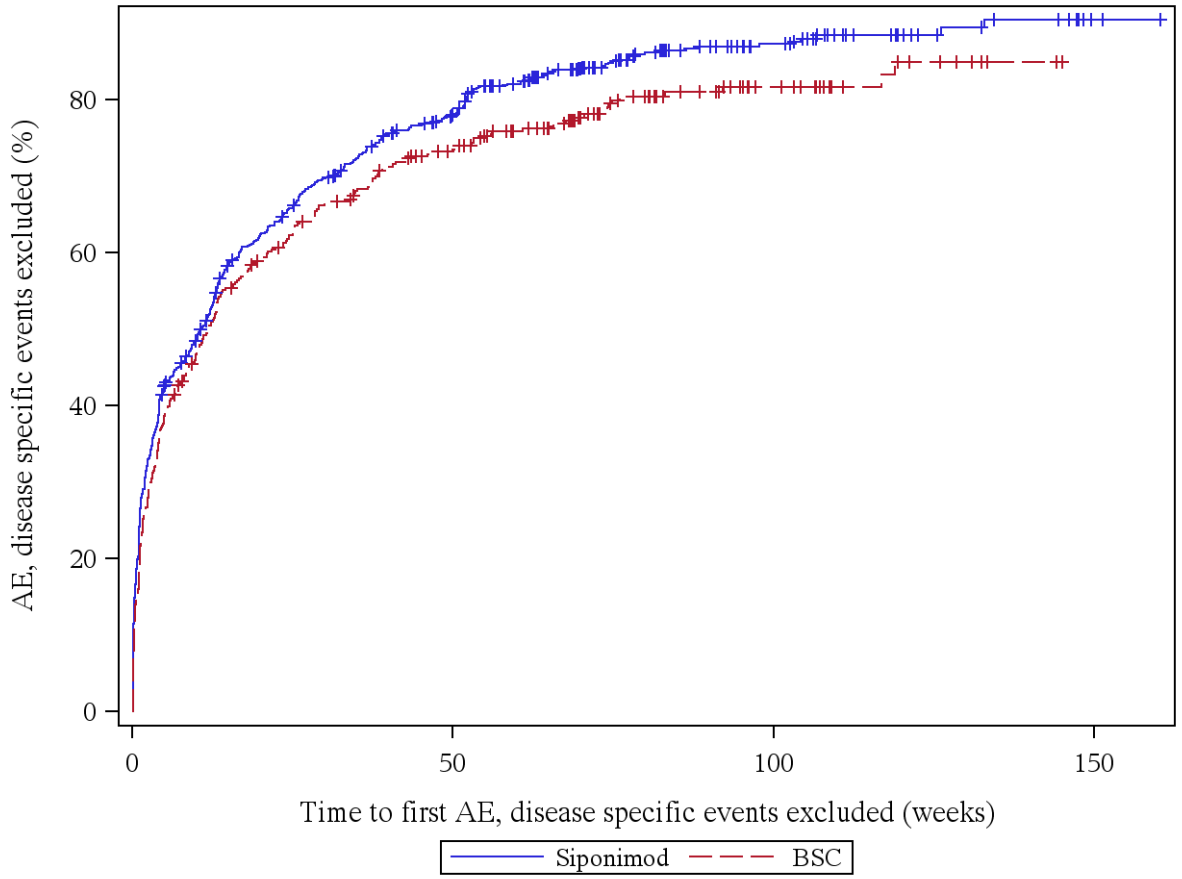
Patients at risk (Siponimod/BSC): Week 0: 264/145, Week 4: 141/93, Week 12: 101/70, Week 24: 67/58, Week 36: 56/47, Week 48: 49/44, Week 60: 37/39, Week 72: 25/27, Week 84: 17/15, Week 96: 14/14, Week 108: 10/11, Week 120: 5/7, Week 132: 2/4, Week 144: 1/1, Week 156: 0/0

Log rank test: p-value = 0,004 *
*: p < 0,05

Analysis population: A2304 SAF total population

12.6.1.2: Any AE, disease specific events excluded

Figure 12.6.1.2.1: AE, disease specific events excluded, Rapid Evolvement = No

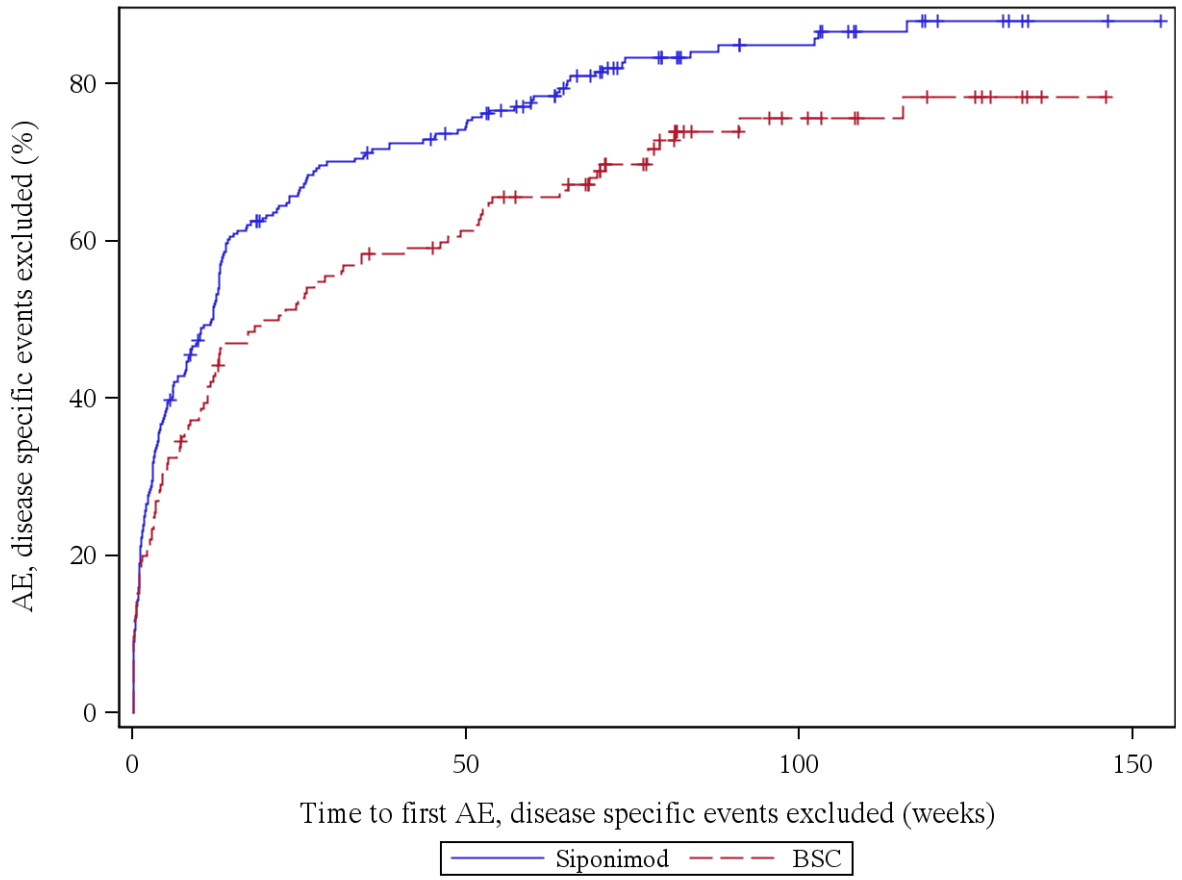


Patients at risk (Siponimod/BSC): Week 0: 835/401, Week 4: 511/260, Week 12: 392/195, Week 24: 280/148, Week 36: 211/118, Week 48: 169/94, Week 60: 118/73, Week 72: 80/50, Week 84: 52/33, Week 96: 41/23, Week 108: 24/14, Week 120: 16/8, Week 132: 11/4, Week 144: 8/2, Week 156: 1/0, Week 168: 0/0

Log rank test: p-value = 0,026 *
*: p < 0,05

Analysis population: A2304 SAF total population

Figure 12.6.1.2.2: AE, disease specific events excluded, Rapid Evolvement = Yes



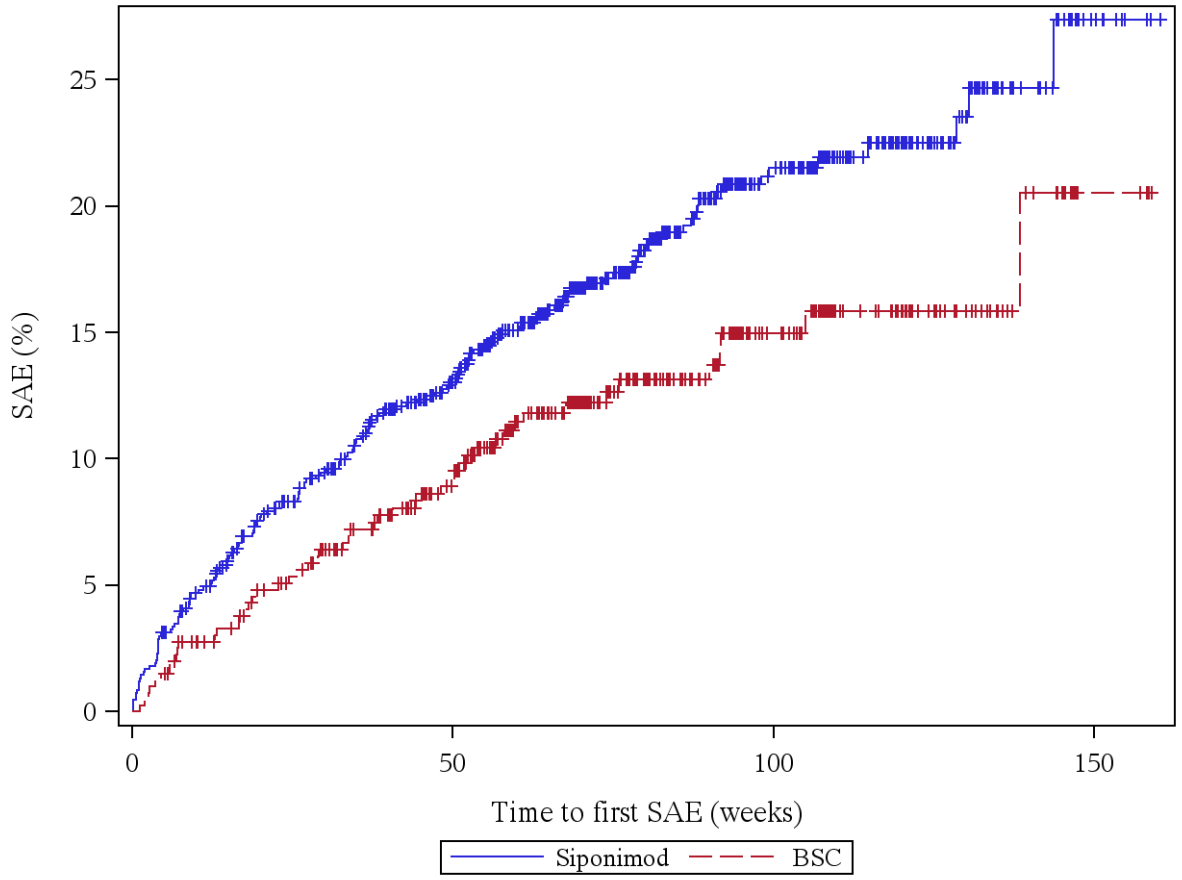
Patients at risk (Siponimod/BSC): Week 0: 264/145, Week 4: 169/104, Week 12: 129/83, Week 24: 86/69, Week 36: 70/58, Week 48: 63/54, Week 60: 47/45, Week 72: 31/32, Week 84: 20/17, Week 96: 17/14, Week 108: 12/11, Week 120: 7/7, Week 132: 4/4, Week 144: 2/1, Week 156: 0/0

Log rank test: p-value = 0,006 *
*: p < 0,05

Analysis population: A2304 SAF total population

12.6.1.3: Any SAE

Figure 12.6.1.3.1: SAE, Rapid Evolvement = No

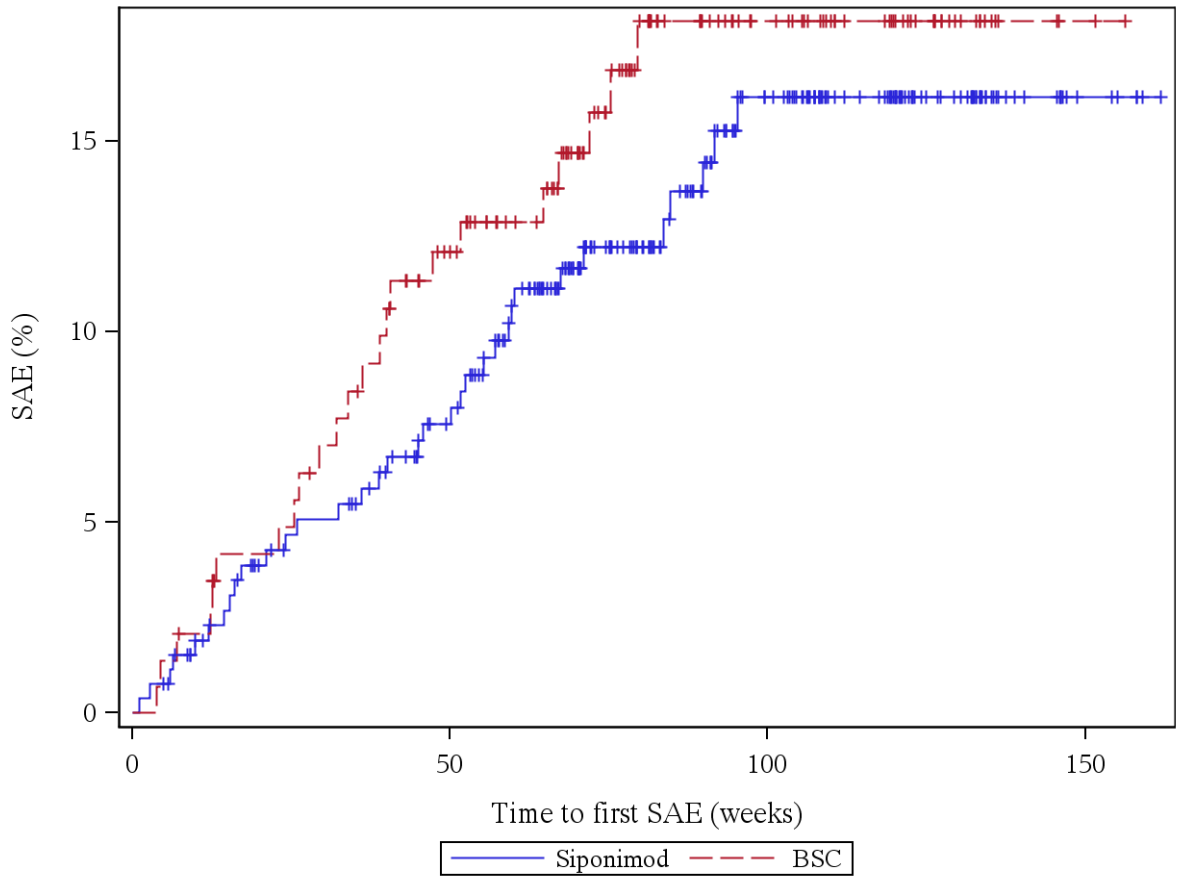


Patients at risk (Siponimod/BSC): Week 0: 835/401, Week 4: 811/396, Week 12: 774/381, Week 24: 722/362, Week 36: 682/338, Week 48: 630/308, Week 60: 537/252, Week 72: 416/198, Week 84: 316/157, Week 96: 246/113, Week 108: 170/76, Week 120: 111/48, Week 132: 56/27, Week 144: 27/15, Week 156: 3/4, Week 168: 0/0

Log rank test: p-value = 0,019 *
*: p < 0,05

Analysis population: A2304 SAF total population

Figure 12.6.1.3.2: SAE, Rapid Evolvement = Yes



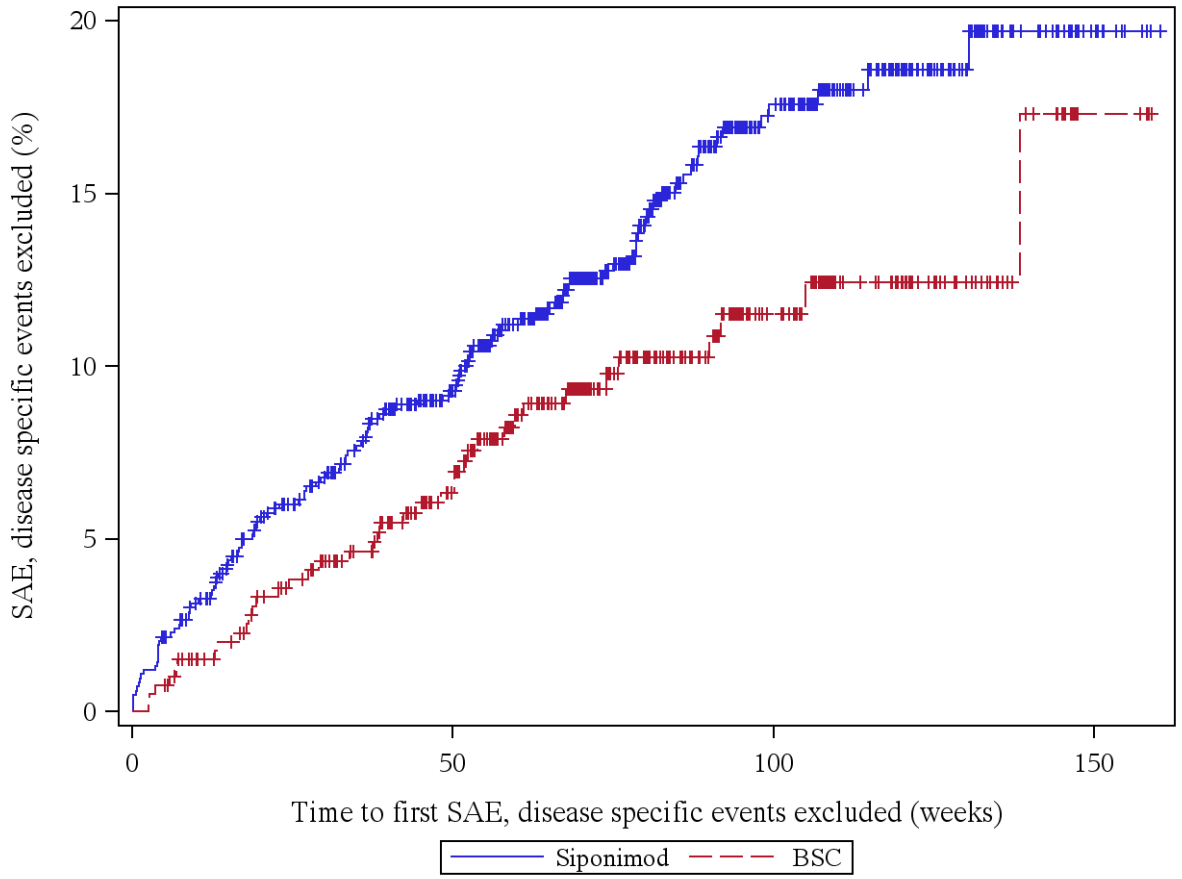
Patients at risk (Siponimod/BSC): Week 0: 264/145, Week 4: 262/144, Week 12: 250/141, Week 24: 237/134, Week 36: 230/127, Week 48: 215/115, Week 60: 193/102, Week 72: 148/79, Week 84: 121/54, Week 96: 91/44, Week 108: 72/36, Week 120: 53/24, Week 132: 32/11, Week 144: 13/4, Week 156: 4/1, Week 168: 0/0

Log rank test: p-value = 0,390
*: p < 0,05

Analysis population: A2304 SAF total population

12.6.1.4: Any SAE, disease specific events excluded

Figure 12.6.1.4.1: SAE, disease specific events excluded, Rapid Evolvement = No

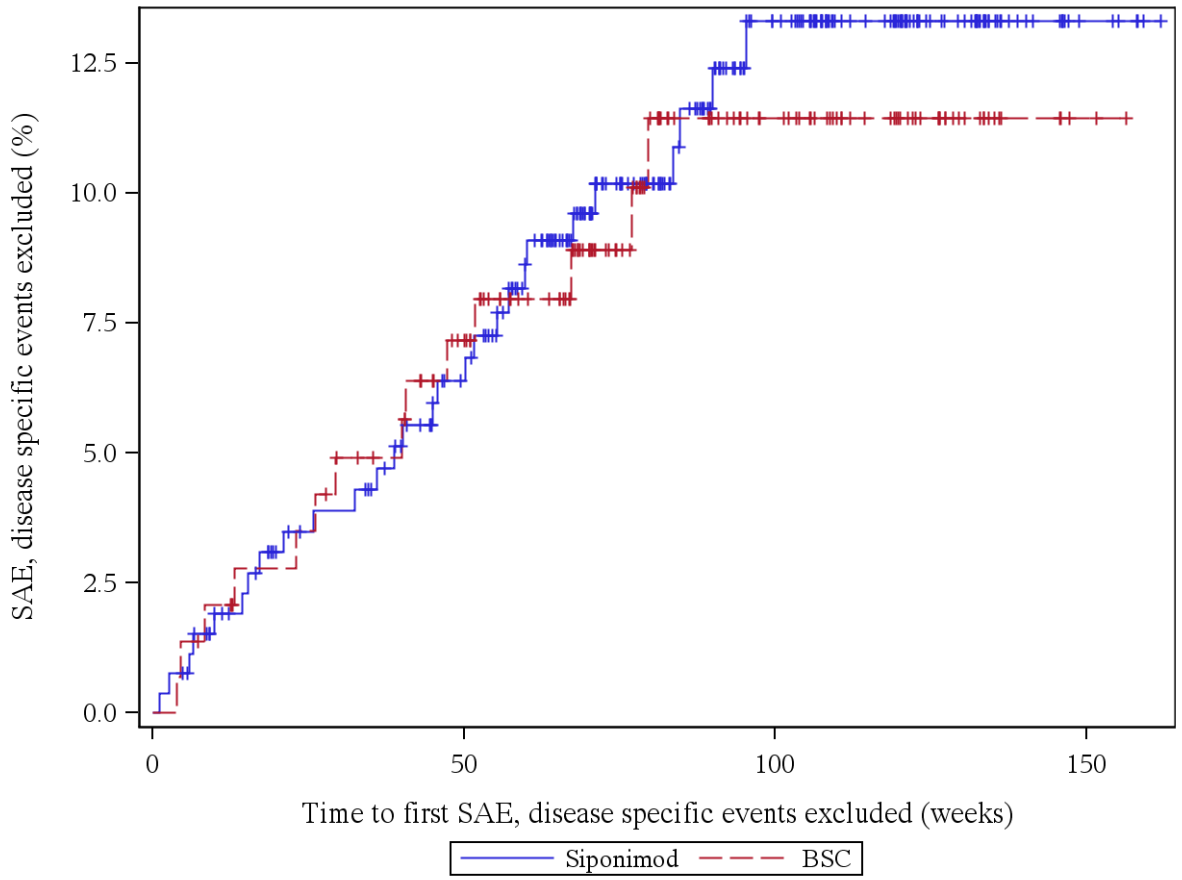


Patients at risk (Siponimod/BSC): Week 0: 835/401, Week 4: 819/398, Week 12: 785/385, Week 24: 737/367, Week 36: 703/347, Week 48: 653/315, Week 60: 559/258, Week 72: 437/201, Week 84: 331/160, Week 96: 259/115, Week 108: 179/76, Week 120: 117/48, Week 132: 62/27, Week 144: 31/15, Week 156: 4/4, Week 168: 0/0

Log rank test: p-value = 0,039 *
*: p < 0,05

Analysis population: A2304 SAF total population

Figure 12.6.1.4.2: SAE, disease specific events excluded, Rapid Evolvement = Yes



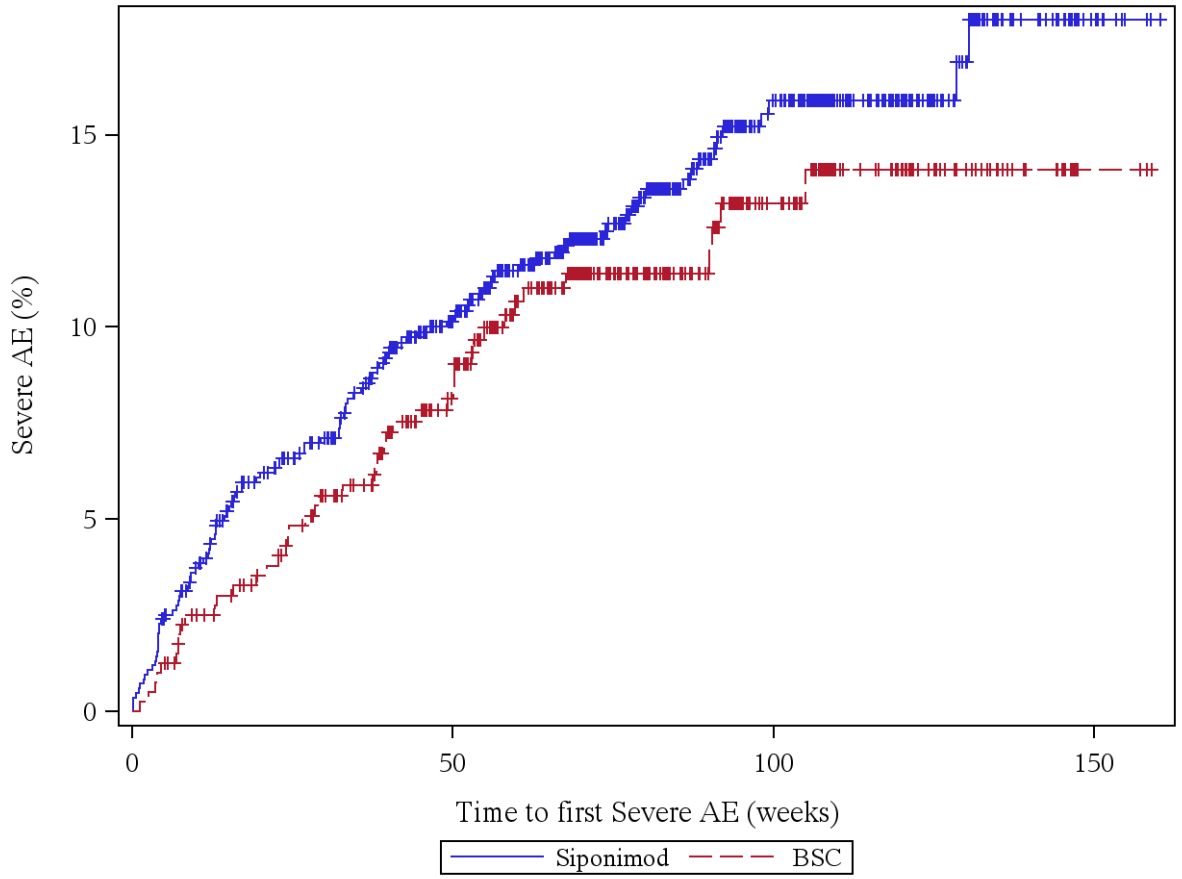
Patients at risk (Siponimod/BSC): Week 0: 264/145, Week 4: 262/144, Week 12: 251/141, Week 24: 238/136, Week 36: 232/130, Week 48: 217/120, Week 60: 196/105, Week 72: 151/82, Week 84: 124/57, Week 96: 93/47, Week 108: 73/38, Week 120: 54/25, Week 132: 33/12, Week 144: 13/5, Week 156: 4/1, Week 168: 0/0

Log rank test: p-value = 0,803
*: p < 0,05

Analysis population: A2304 SAF total population

12.6.1.5: Any severe AE

Figure 12.6.1.5.1: Severe AE, Rapid Evolvement = No

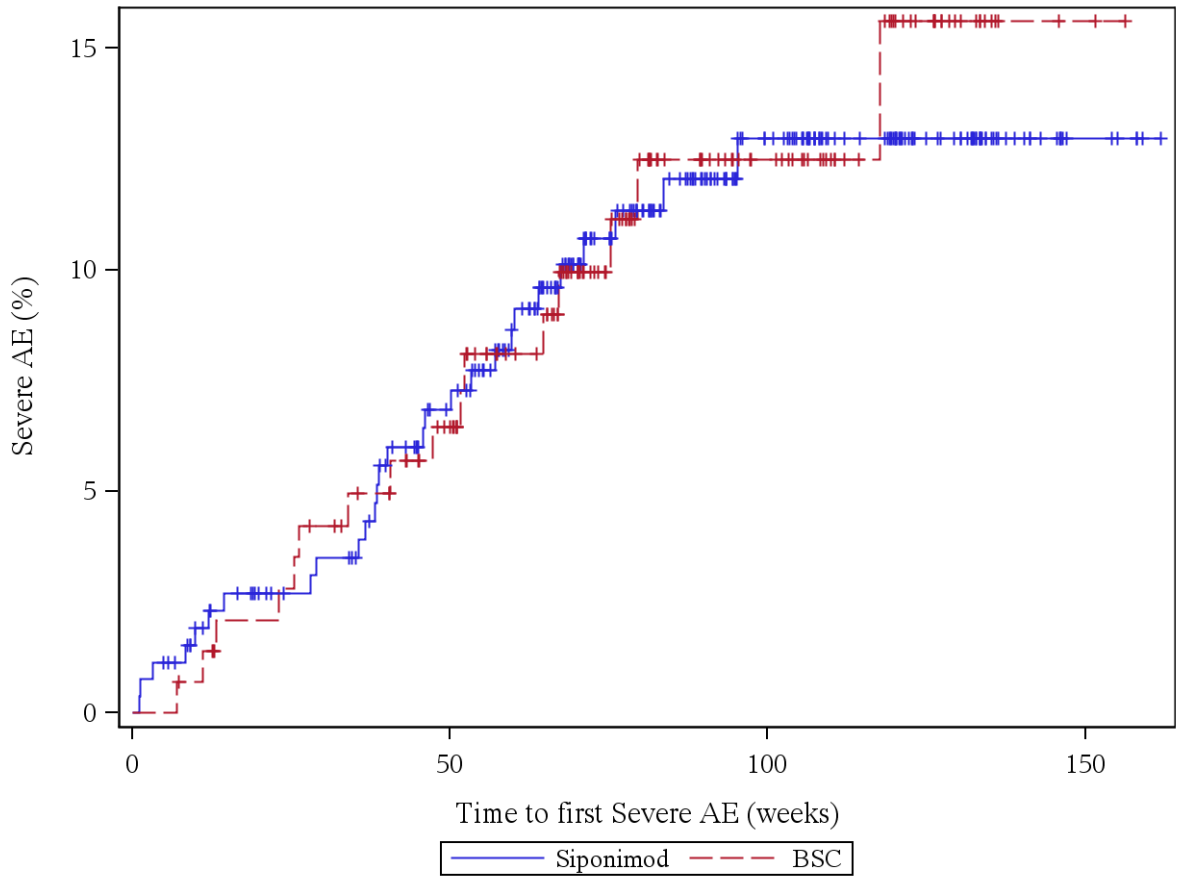


Patients at risk (Siponimod/BSC): Week 0: 835/401, Week 4: 818/397, Week 12: 778/383, Week 24: 735/367, Week 36: 701/346, Week 48: 648/312, Week 60: 559/257, Week 72: 445/200, Week 84: 340/161, Week 96: 263/116, Week 108: 186/76, Week 120: 123/48, Week 132: 64/25, Week 144: 33/14, Week 156: 4/3, Week 168: 0/0

Log rank test: p-value = 0,329
*: p < 0,05

Analysis population: A2304 SAF total population

Figure 12.6.1.5.2: Severe AE, Rapid Evolvement = Yes



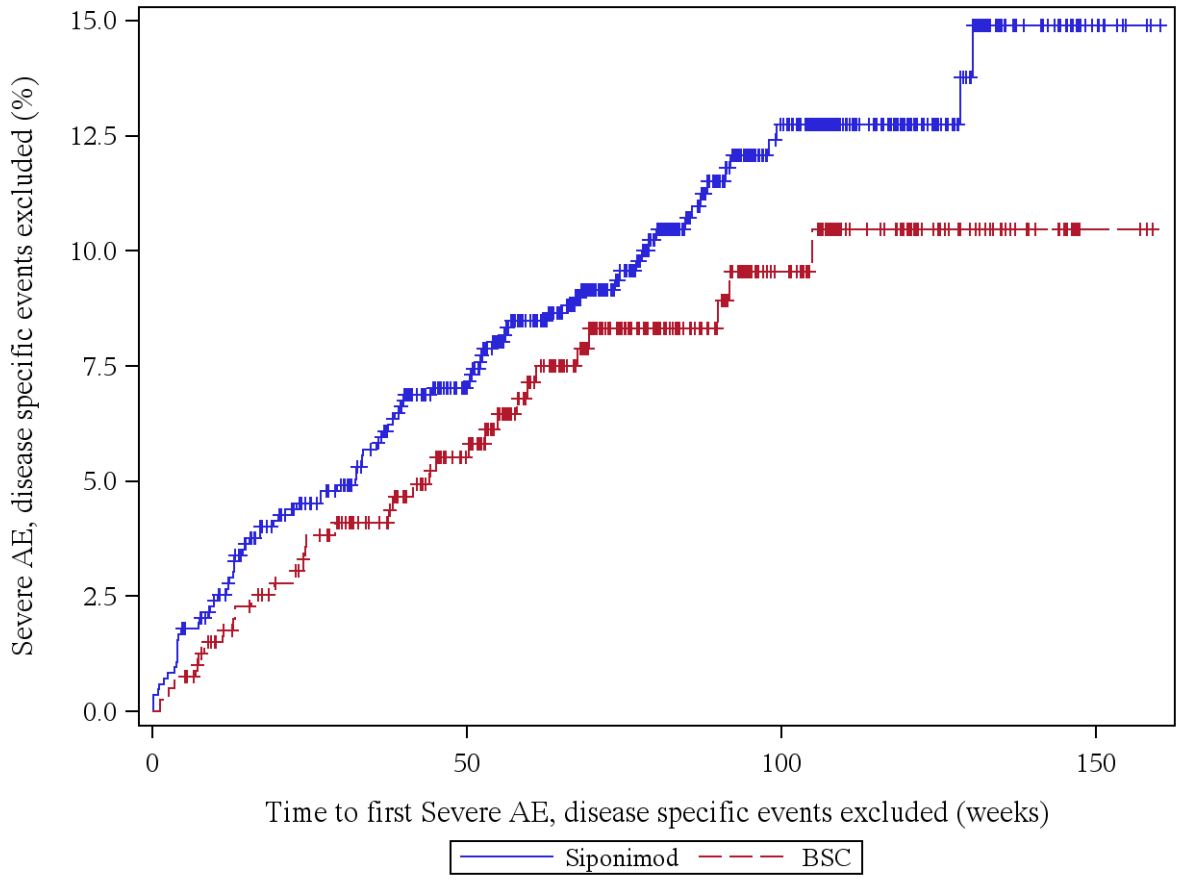
Patients at risk (Siponimod/BSC): Week 0: 264/145, Week 4: 261/145, Week 12: 250/142, Week 24: 239/137, Week 36: 233/130, Week 48: 215/121, Week 60: 194/104, Week 72: 149/81, Week 84: 122/55, Week 96: 93/45, Week 108: 72/36, Week 120: 56/22, Week 132: 35/10, Week 144: 12/3, Week 156: 4/1, Week 168: 0/0

Log rank test: p-value = 0,880
*: p < 0,05

Analysis population: A2304 SAF total population

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

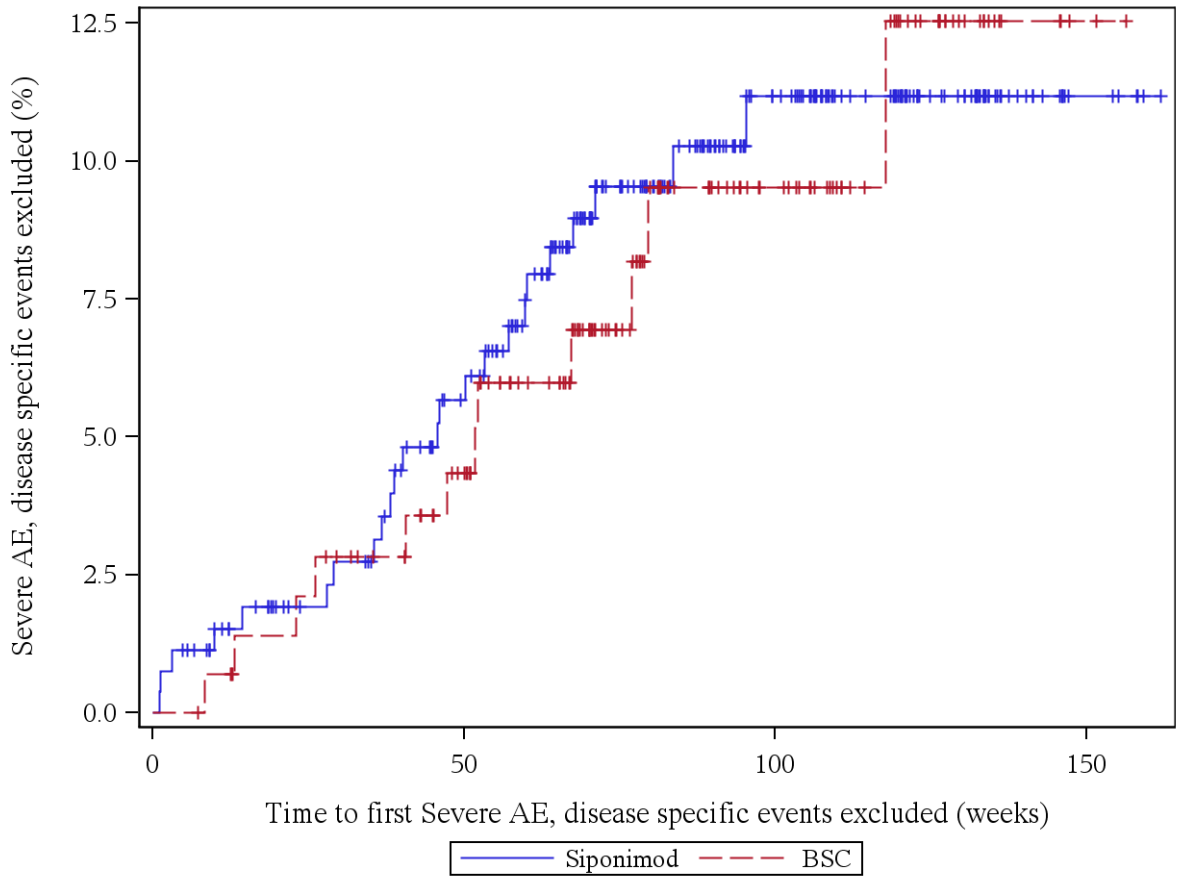


Patients at risk (Siponimod/BSC): Week 0: 835/401, Week 4: 822/398, Week 12: 789/384, Week 24: 749/369, Week 36: 718/350, Week 48: 666/317, Week 60: 574/264, Week 72: 458/204, Week 84: 351/165, Week 96: 271/117, Week 108: 192/77, Week 120: 127/49, Week 132: 66/26, Week 144: 33/14, Week 156: 4/3, Week 168: 0/0

Log rank test: p-value = 0,233
*: p < 0,05

Analysis population: A2304 SAF total population

Figure 12.6.1.6.2: Severe AE, disease specific events excluded, Rapid Evolvement = Yes



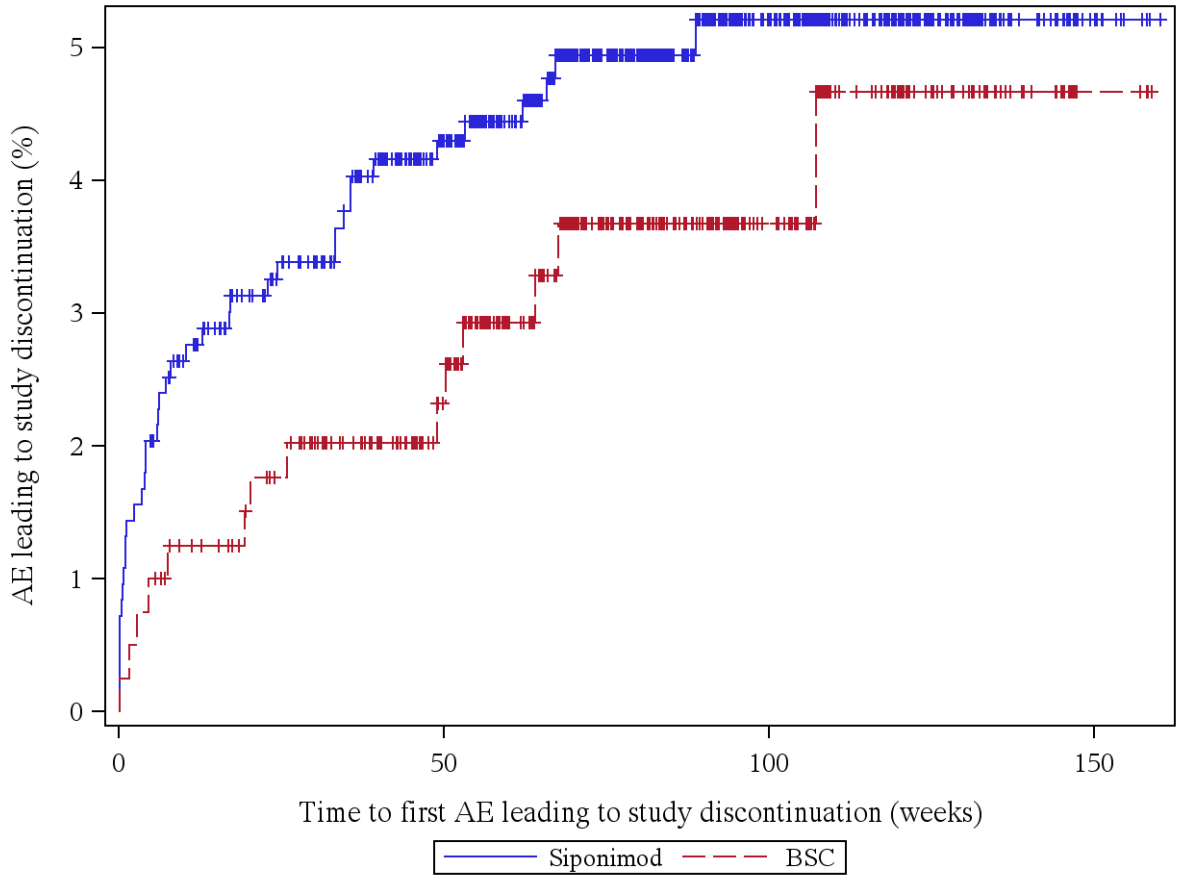
Patients at risk (Siponimod/BSC): Week 0: 264/145, Week 4: 261/145, Week 12: 252/143, Week 24: 240/138, Week 36: 234/132, Week 48: 217/123, Week 60: 196/106, Week 72: 150/83, Week 84: 124/57, Week 96: 94/47, Week 108: 73/38, Week 120: 56/24, Week 132: 35/12, Week 144: 12/5, Week 156: 4/1, Week 168: 0/0

Log rank test: p-value = 0,796
*: p < 0,05

Analysis population: A2304 SAF total population

12.6.1.7: Any AE leading to study discontinuation

Figure 12.6.1.7.1: AE leading to study discontinuation, Rapid Evolvement = No

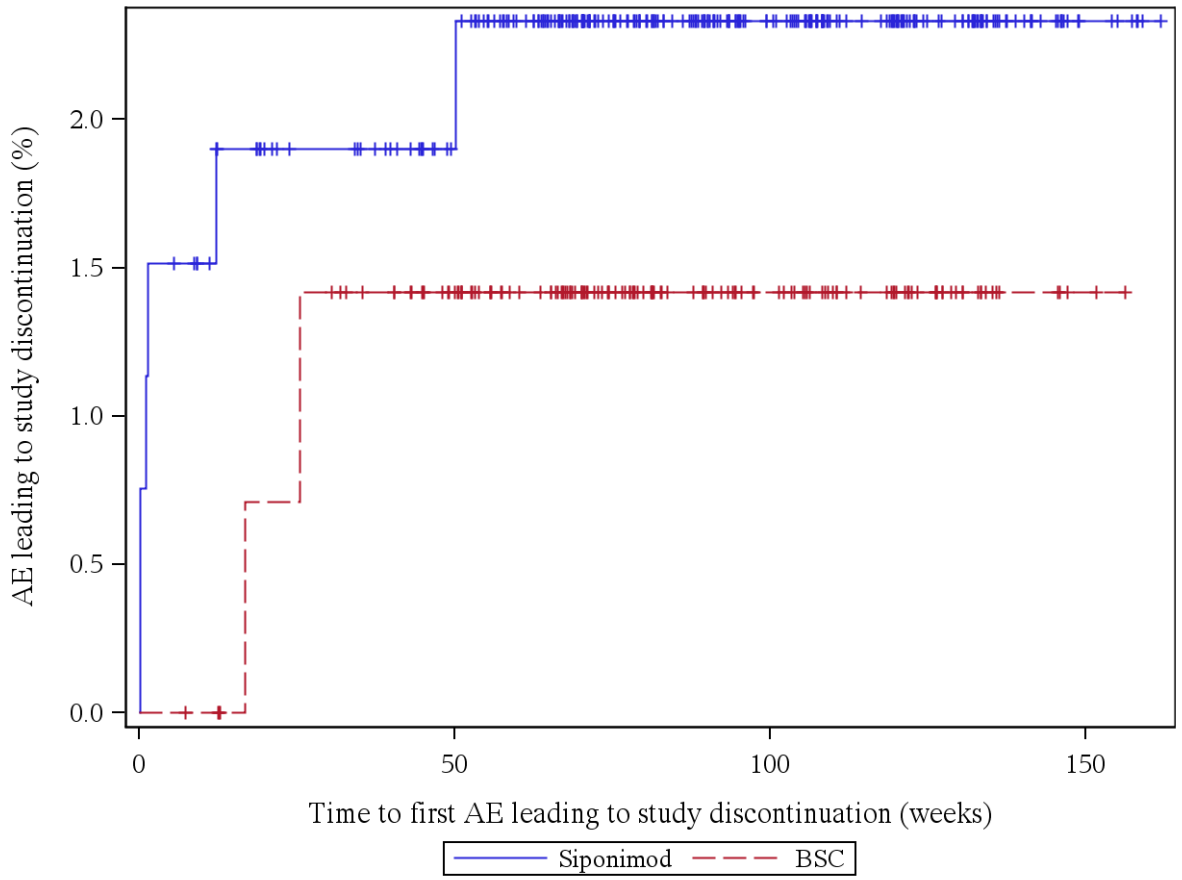


Patients at risk (Siponimod/BSC): Week 0: 835/401, Week 4: 820/398, Week 12: 796/390, Week 24: 768/379, Week 36: 741/362, Week 48: 692/334, Week 60: 605/278, Week 72: 482/217, Week 84: 375/175, Week 96: 292/126, Week 108: 205/85, Week 120: 136/53, Week 132: 72/28, Week 144: 35/15, Week 156: 5/4, Week 168: 0/0

Log rank test: p-value = 0,303
*: p < 0,05

Analysis population: A2304 SAF total population

Figure 12.6.1.7.2: AE leading to study discontinuation, Rapid Evolvement = Yes



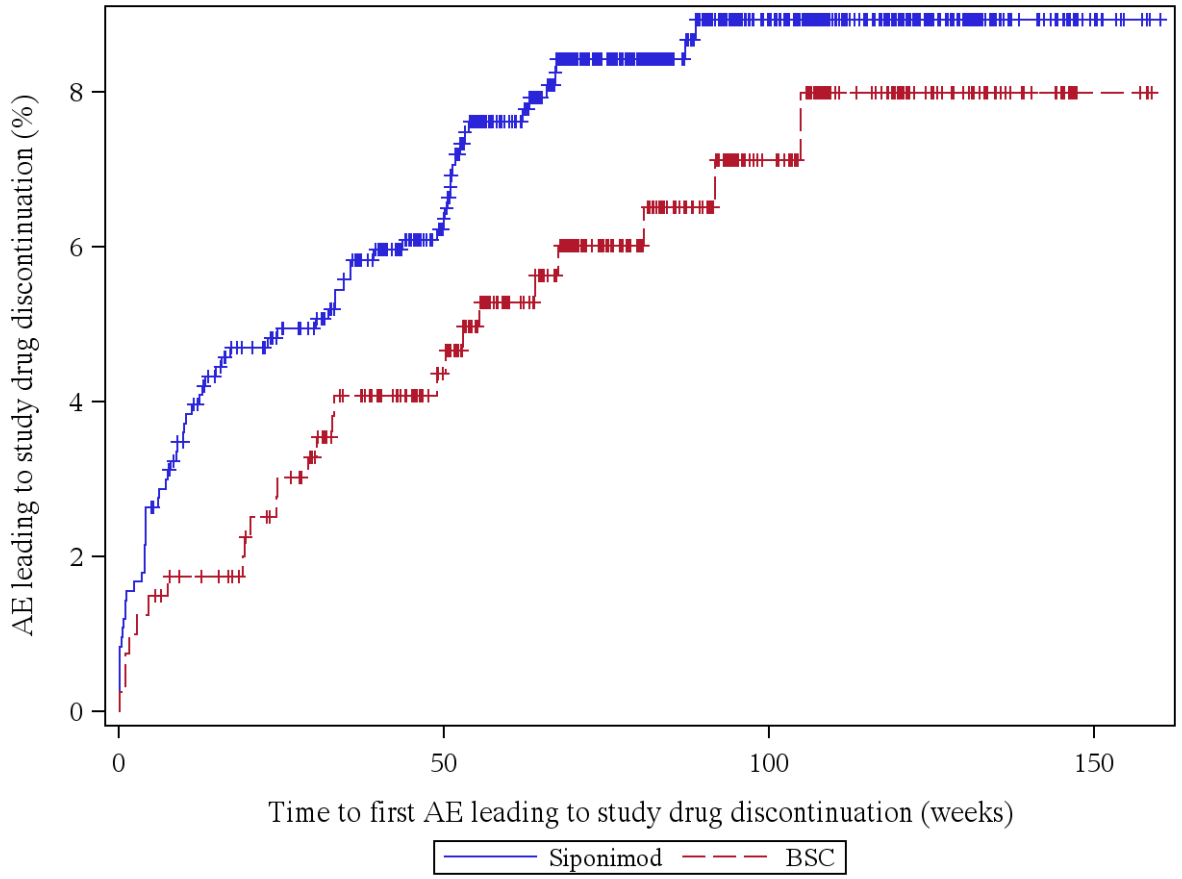
Patients at risk (Siponimod/BSC): Week 0: 264/145, Week 4: 260/145, Week 12: 255/144, Week 24: 244/140, Week 36: 241/135, Week 48: 230/127, Week 60: 211/109, Week 72: 168/87, Week 84: 140/62, Week 96: 108/50, Week 108: 86/40, Week 120: 64/27, Week 132: 41/12, Week 144: 16/5, Week 156: 5/1, Week 168: 0/0

Log rank test: p-value = 0,526
*: p < 0,05

Analysis population: A2304 SAF total population

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

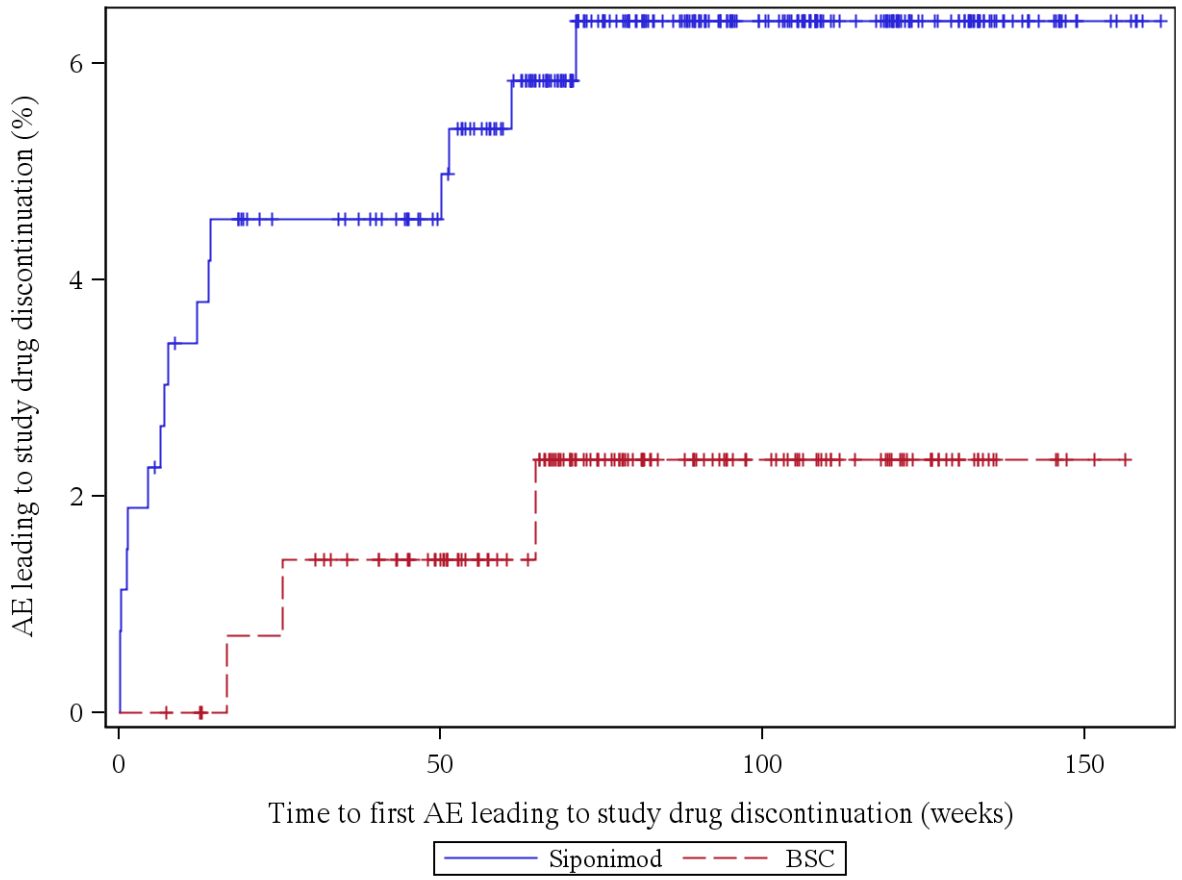


Patients at risk (Siponimod/BSC): Week 0: 835/401, Week 4: 817/396, Week 12: 791/390, Week 24: 765/379, Week 36: 739/358, Week 48: 691/332, Week 60: 602/277, Week 72: 480/217, Week 84: 375/174, Week 96: 292/125, Week 108: 205/85, Week 120: 136/53, Week 132: 72/28, Week 144: 35/15, Week 156: 5/4, Week 168: 0/0

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

Analysis population: A2304 SAF total population

Figure 12.6.1.8.2: AE leading to study drug discontinuation, Rapid Evolvement = Yes



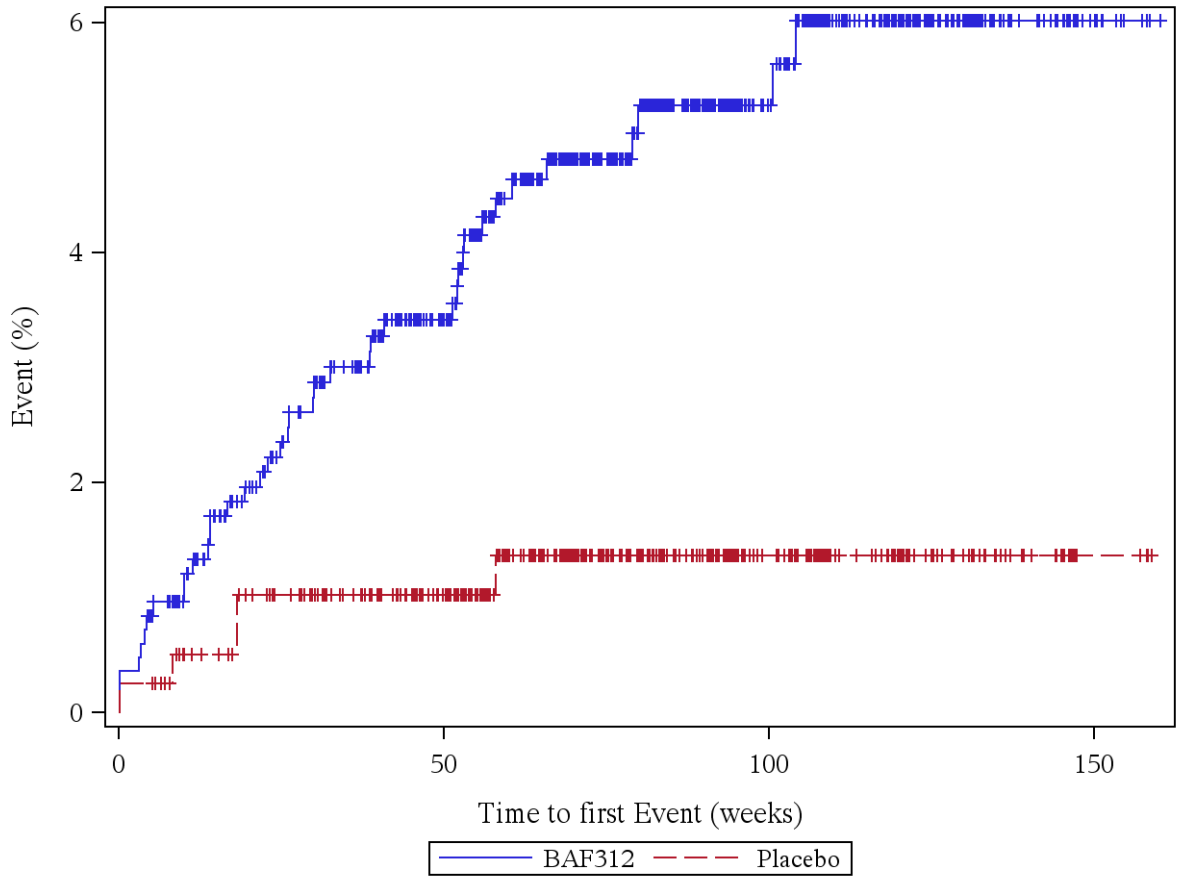
Patients at risk (Siponimod/BSC): Week 0: 264/145, Week 4: 259/145, Week 12: 253/144, Week 24: 243/140, Week 36: 241/135, Week 48: 230/127, Week 60: 211/109, Week 72: 166/87, Week 84: 139/62, Week 96: 108/50, Week 108: 86/40, Week 120: 64/27, Week 132: 41/12, Week 144: 16/5, Week 156: 5/1, Week 168: 0/0

Log rank test: p-value = 0,072
*: p < 0,05

Analysis population: A2304 SAF total population

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

Figure 12.6.2.1.1: BLOOD AND LYMPHATIC SYSTEM DISORDERS (SOC), Rapid Evolvement = No

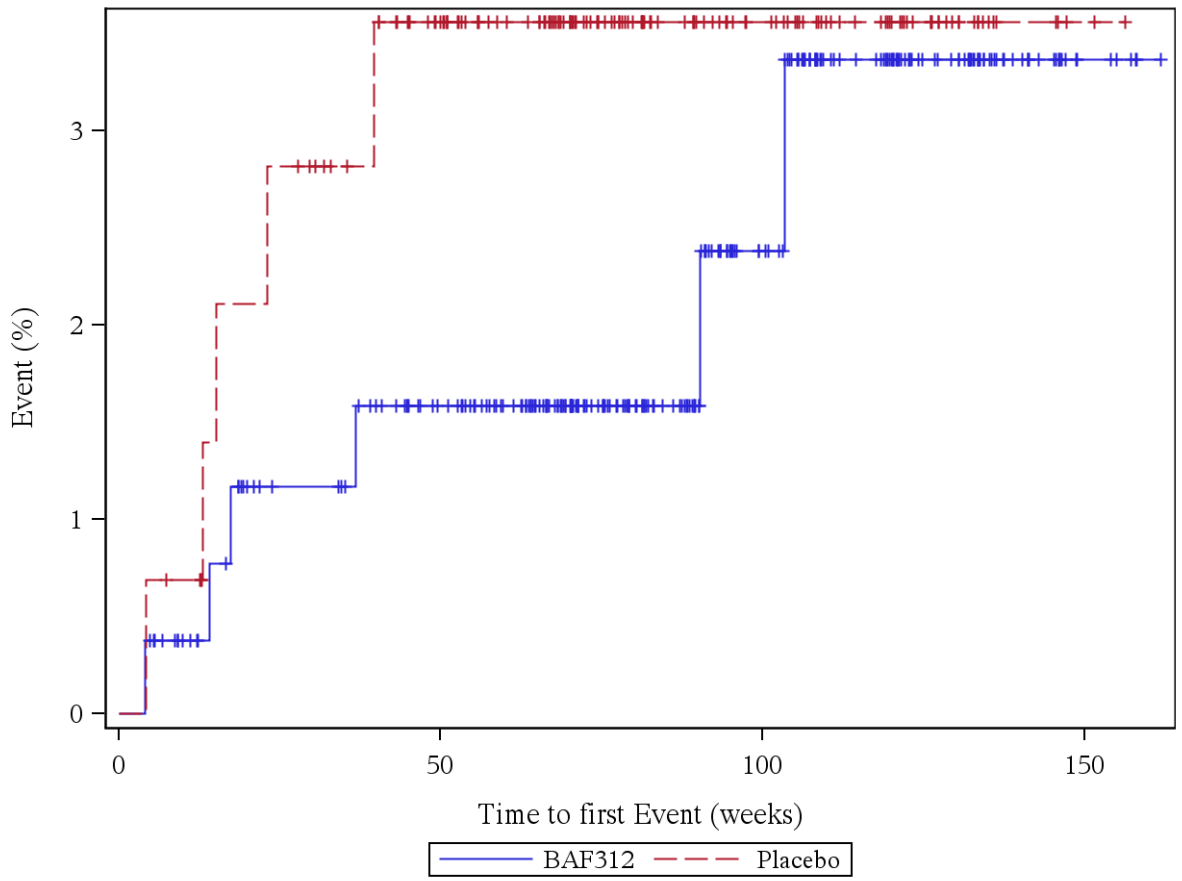


Patients at risk (BAF312/Placebo): Week 0: 835/401, Week 4: 829/400, Week 12: 793/389, Week 24: 755/376, Week 36: 727/358, Week 48: 672/330, Week 60: 580/274, Week 72: 465/214, Week 84: 361/172, Week 96: 280/124, Week 108: 196/84, Week 120: 130/51, Week 132: 69/27, Week 144: 35/15, Week 156: 5/4, Week 168: 0/0

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

Analysis population: A2304 SAF total population

Figure 12.6.2.1.2: BLOOD AND LYMPHATIC SYSTEM DISORDERS (SOC), Rapid Evolvement = Yes

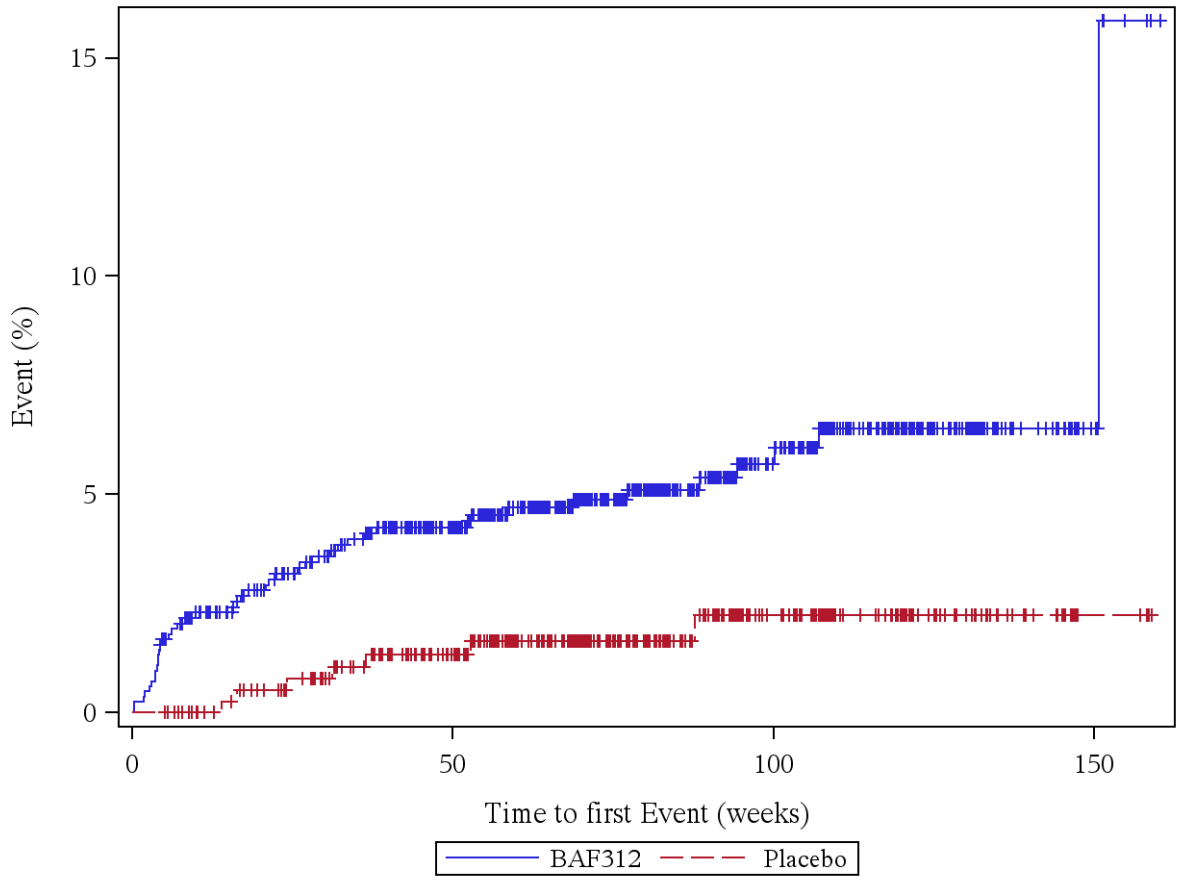


Patients at risk (BAF312/Placebo): Week 0: 264/145, Week 4: 263/145, Week 12: 254/143, Week 24: 241/137, Week 36: 238/131, Week 48: 226/122, Week 60: 209/105, Week 72: 167/83, Week 84: 138/59, Week 96: 105/48, Week 108: 83/38, Week 120: 61/26, Week 132: 39/12, Week 144: 15/5, Week 156: 4/1, Week 168: 0/0

Log rank test: p-value = 0,453
*: p < 0,05

Analysis population: A2304 SAF total population

Figure 12.6.2.2.1: OEDEMA PERIPHERAL (PT), Rapid Evolvement = No

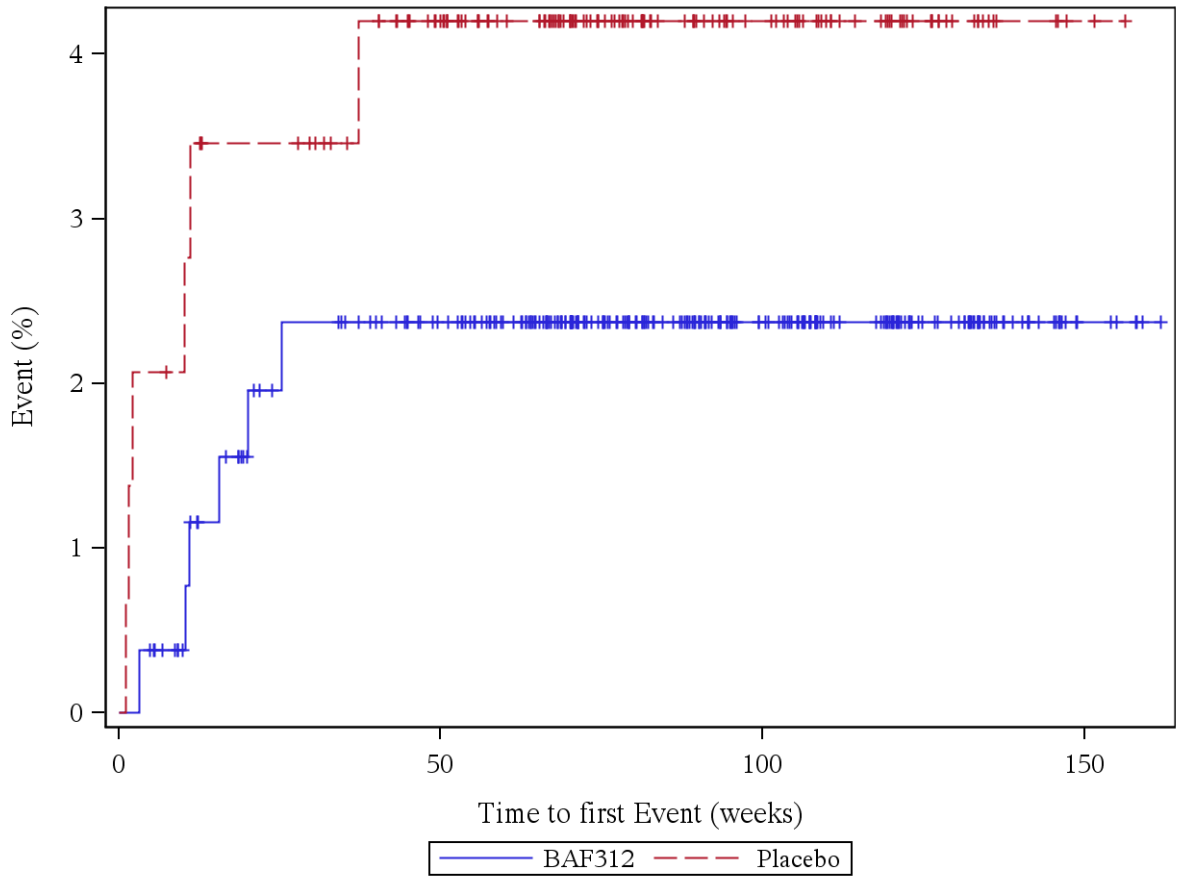


Patients at risk (BAF312/Placebo): Week 0: 835/401, Week 4: 824/401, Week 12: 785/391, Week 24: 749/378, Week 36: 722/358, Week 48: 666/330, Week 60: 578/276, Week 72: 462/215, Week 84: 358/173, Week 96: 277/125, Week 108: 193/85, Week 120: 125/52, Week 132: 65/27, Week 144: 32/15, Week 156: 4/4, Week 168: 0/0

Log rank test: p-value = 0,004 *
*: p < 0,05

Analysis population: A2304 SAF total population

Figure 12.6.2.2.2: OEDEMA PERIPHERAL (PT), Rapid Evolvement = Yes



Patients at risk (BAF312/Placebo): Week 0: 264/145, Week 4: 263/142, Week 12: 252/139, Week 24: 239/136, Week 36: 235/130, Week 48: 225/121, Week 60: 207/103, Week 72: 165/82, Week 84: 136/58, Week 96: 104/46, Week 108: 82/37, Week 120: 62/24, Week 132: 40/12, Week 144: 15/5, Week 156: 4/1, Week 168: 0/0

Log rank test: p-value = 0,294
*: p < 0,05

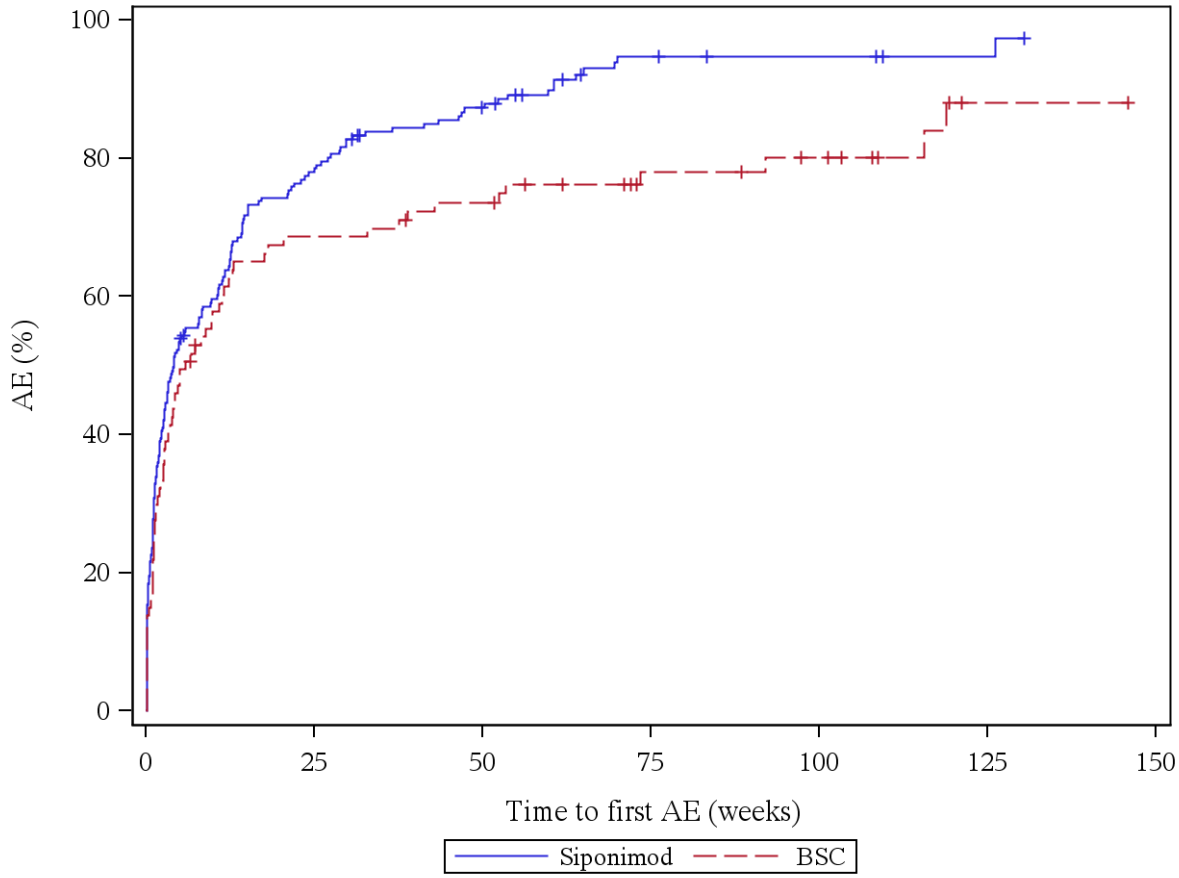
Analysis population: A2304 SAF total population

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

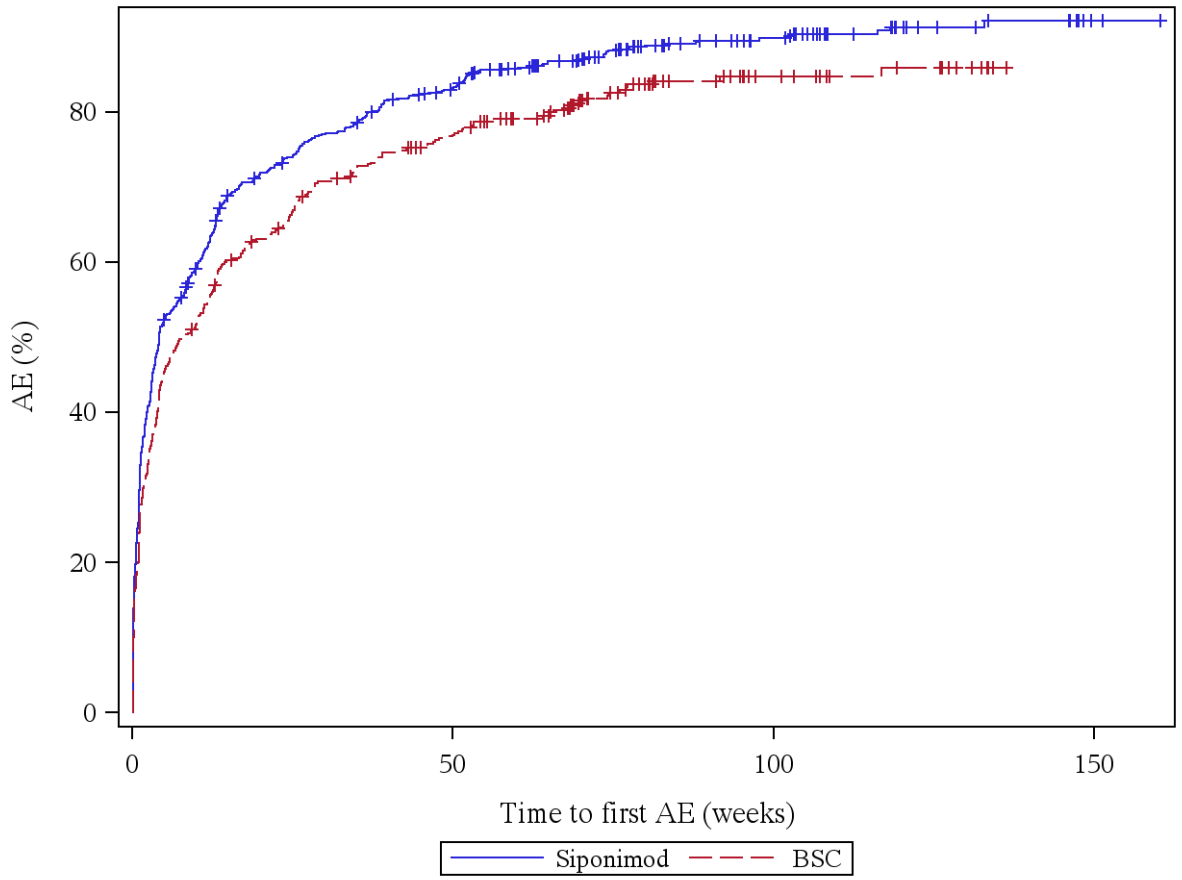


Patients at risk (Siponimod/BSC): Week 0: 195/87, Week 4: 98/49, Week 12: 69/32, Week 24: 43/26, Week 36: 28/25, Week 48: 22/21, Week 60: 14/17, Week 72: 6/14, Week 84: 4/12, Week 96: 4/10, Week 108: 4/6, Week 120: 2/2, Week 132: 0/1

Log rank test: p-value = 0,011 *
*: p < 0,05

Analysis population: A2304 SAF total population

Figure 12.7.1.1.2: AE, Moderate or Severe Disease Course = Yes



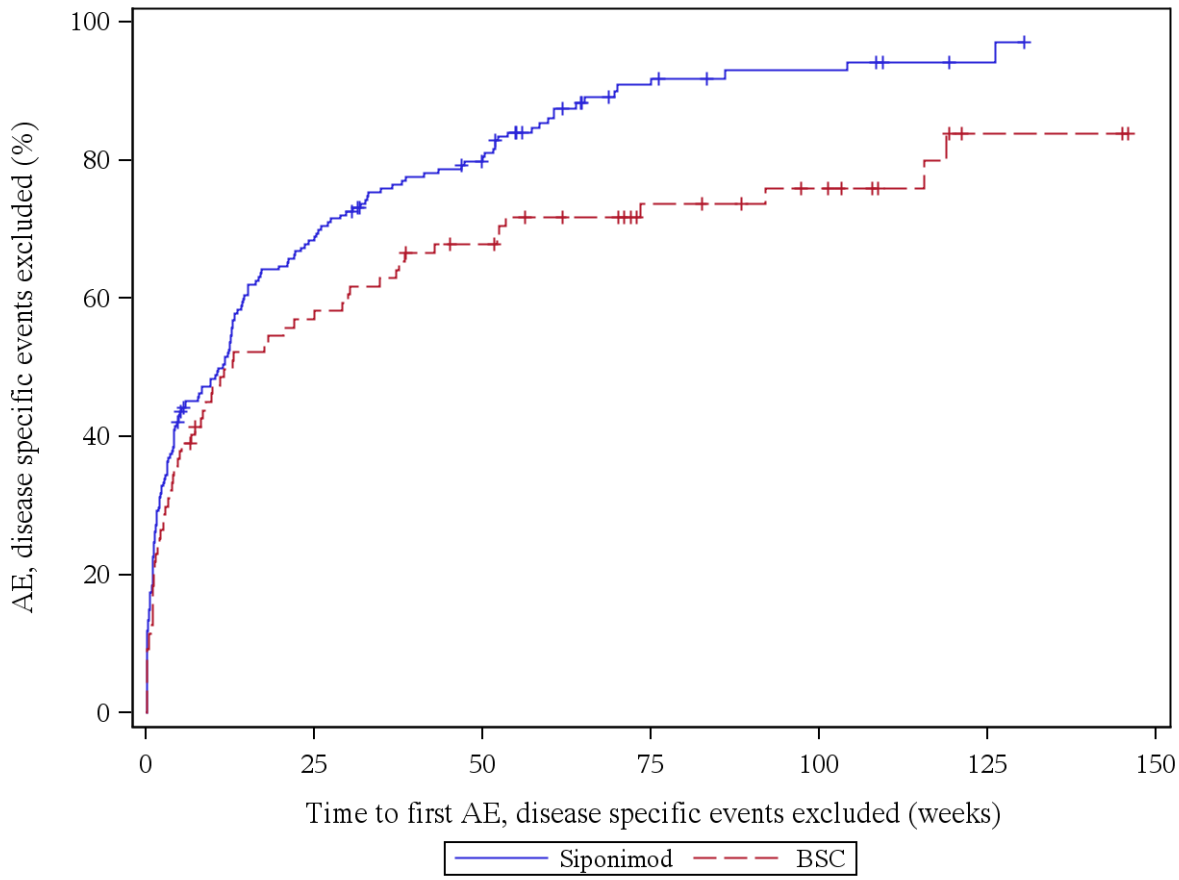
Patients at risk (Siponimod/BSC): Week 0: 904/459, Week 4: 462/270, Week 12: 333/204, Week 24: 230/156, Week 36: 182/119, Week 48: 147/99, Week 60: 111/79, Week 72: 79/51, Week 84: 52/28, Week 96: 42/21, Week 108: 24/15, Week 120: 15/11, Week 132: 10/5, Week 144: 8/0, Week 156: 1/0, Week 168: 0/0

Log rank test: p-value = 0,001 *
*: p < 0,05

Analysis population: A2304 SAF total population

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

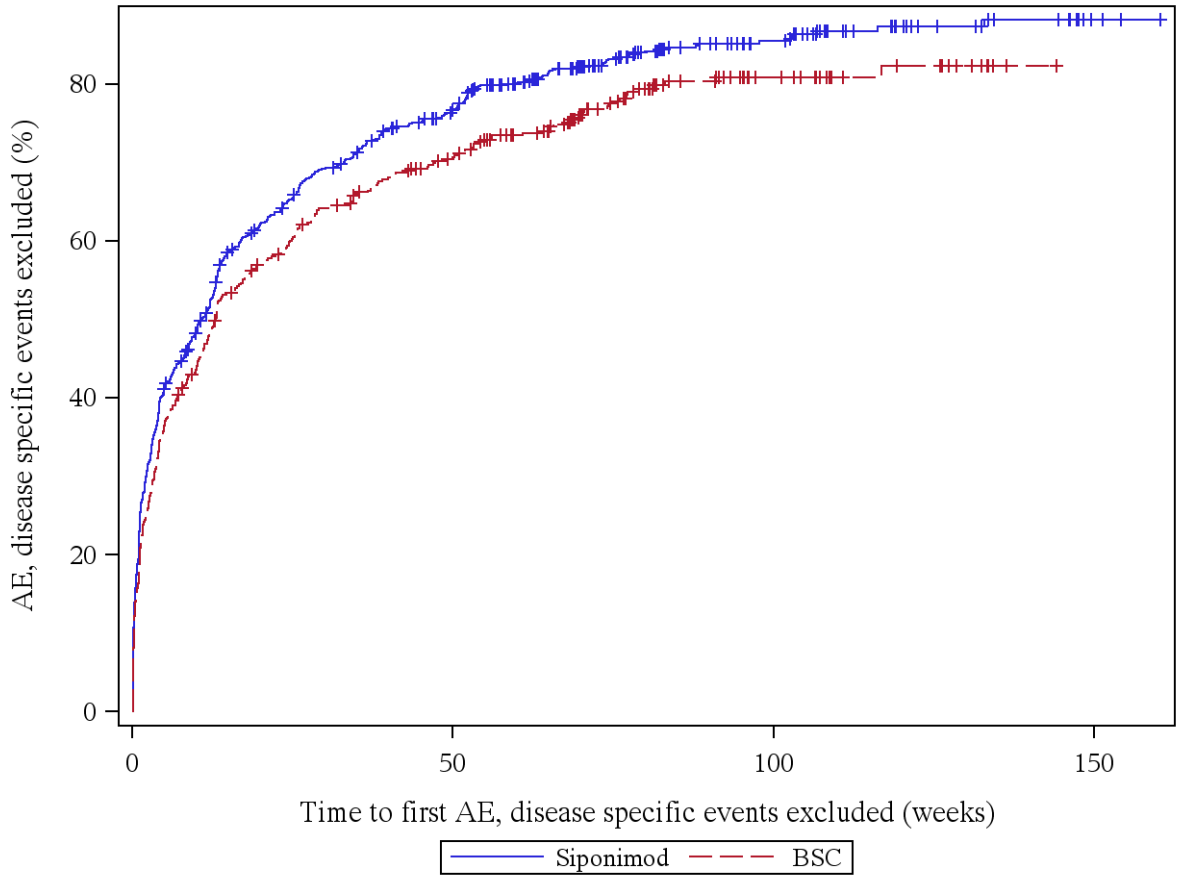


Patients at risk (Siponimod/BSC): Week 0: 195/87, Week 4: 120/57, Week 12: 92/42, Week 24: 61/36, Week 36: 43/31, Week 48: 35/25, Week 60: 20/20, Week 72: 10/16, Week 84: 7/13, Week 96: 6/11, Week 108: 5/7, Week 120: 2/3, Week 132: 0/2

Log rank test: p-value = 0,006 *
*: p < 0,05

Analysis population: A2304 SAF total population

Figure 12.7.1.2.2: AE, disease specific events excluded, Moderate or Severe Disease Course = Yes



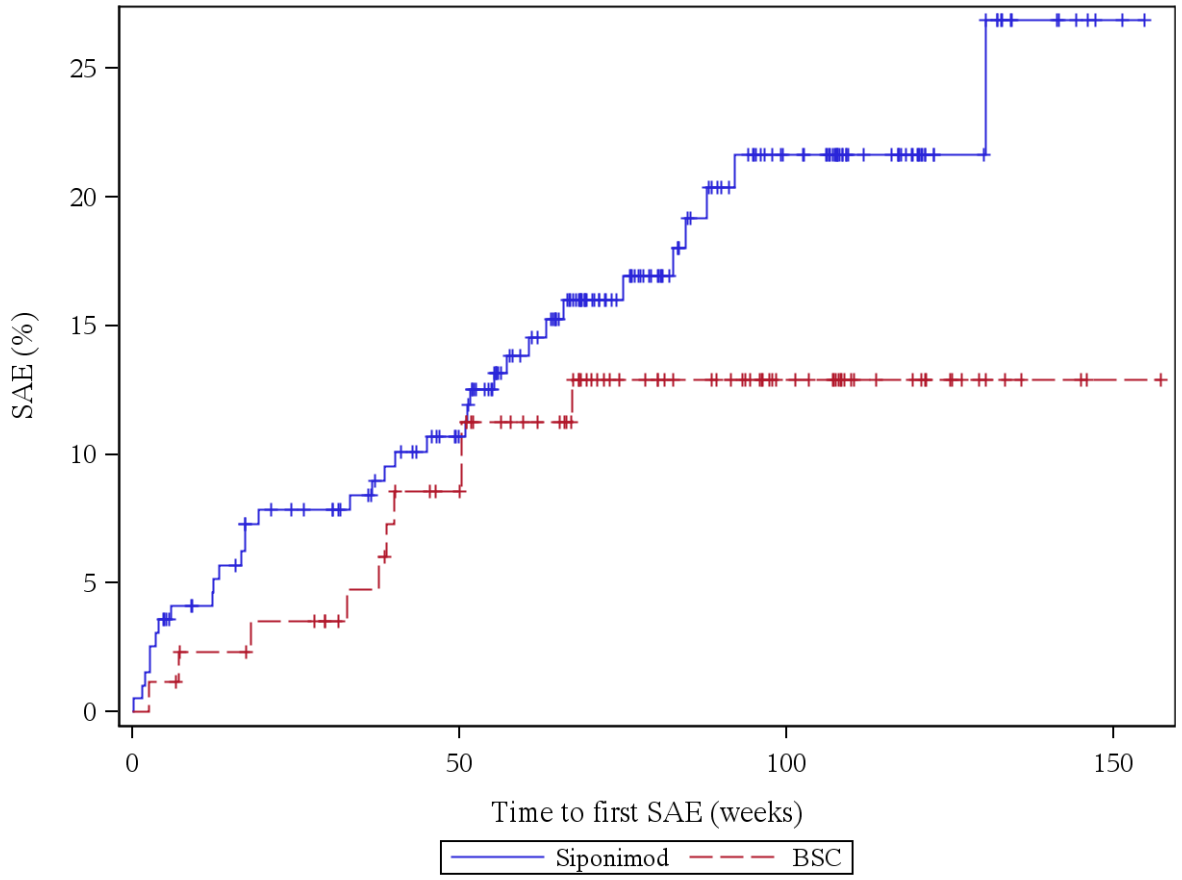
Patients at risk (Siponimod/BSC): Week 0: 904/459, Week 4: 560/307, Week 12: 429/236, Week 24: 305/181, Week 36: 238/145, Week 48: 197/123, Week 60: 145/98, Week 72: 101/66, Week 84: 65/37, Week 96: 52/26, Week 108: 31/18, Week 120: 21/12, Week 132: 15/6, Week 144: 10/1, Week 156: 1/0, Week 168: 0/0

Log rank test: p-value = 0,010 *
*: p < 0,05

Analysis population: A2304 SAF total population

12.7.1.3: Any SAE

Figure 12.7.1.3.1: SAE, Moderate or Severe Disease Course = No

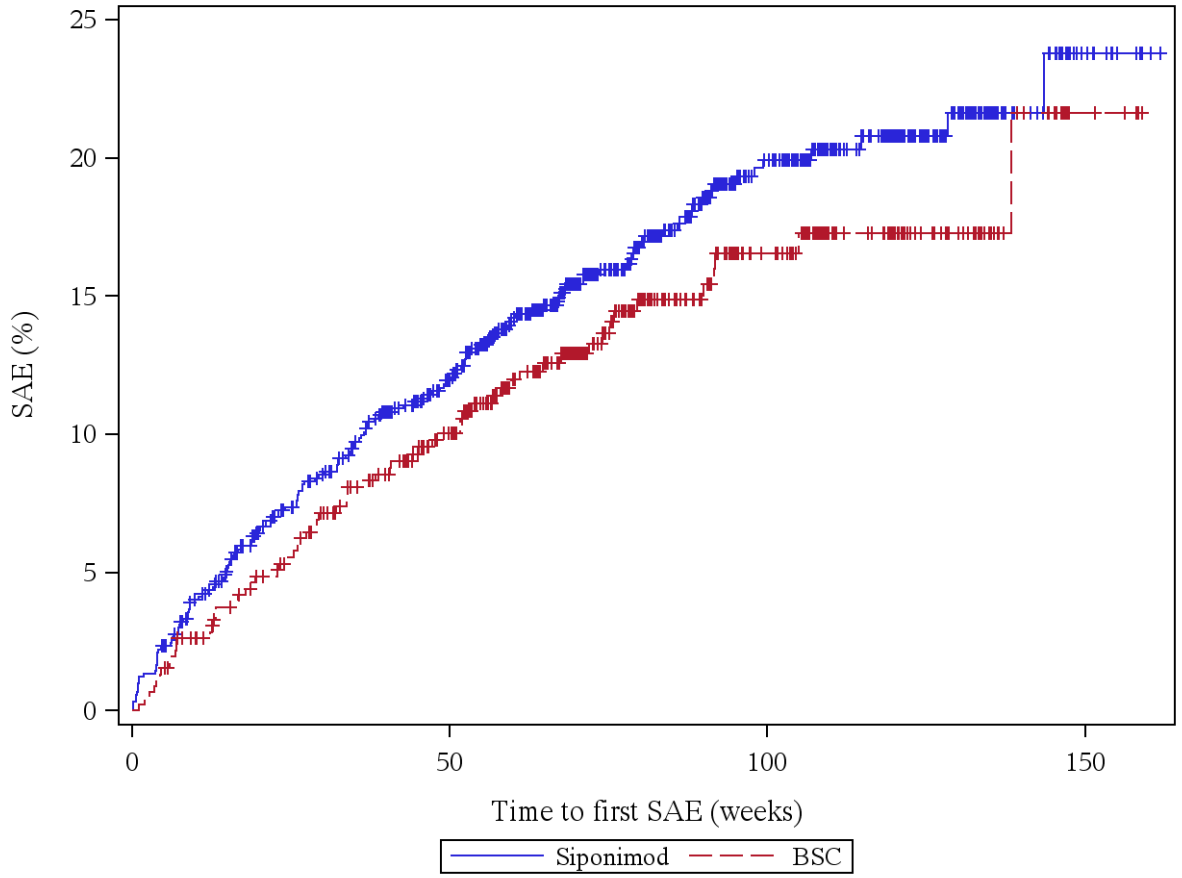


Patients at risk (Siponimod/BSC): Week 0: 195/87, Week 4: 188/86, Week 12: 181/83, Week 24: 170/81, Week 36: 162/76, Week 48: 150/69, Week 60: 124/59, Week 72: 95/45, Week 84: 71/38, Week 96: 56/31, Week 108: 39/20, Week 120: 24/13, Week 132: 13/5, Week 144: 5/3, Week 156: 0/1

Log rank test: p-value = 0,190
*: p < 0,05

Analysis population: A2304 SAF total population

Figure 12.7.1.3.2: SAE, Moderate or Severe Disease Course = Yes



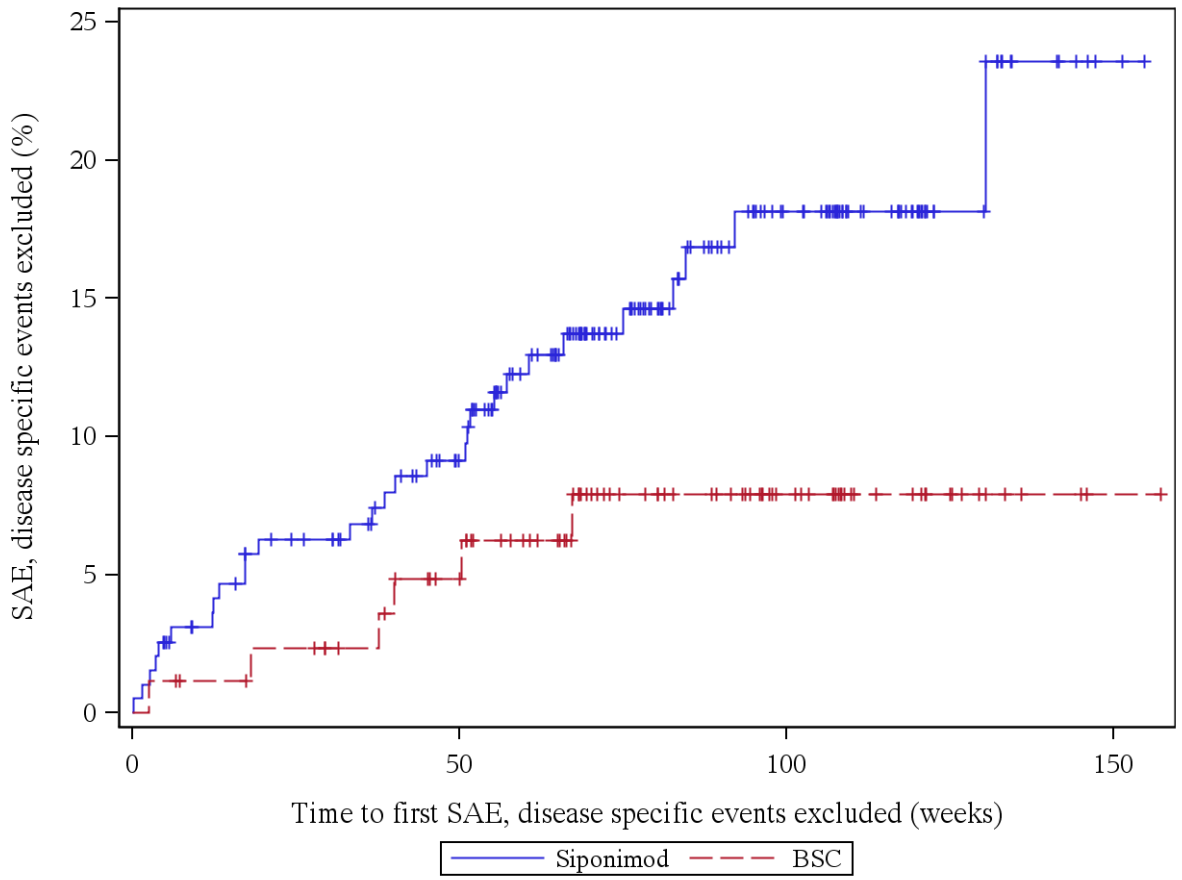
Patients at risk (Siponimod/BSC): Week 0: 904/459, Week 4: 885/454, Week 12: 843/439, Week 24: 789/415, Week 36: 750/389, Week 48: 695/354, Week 60: 606/295, Week 72: 469/232, Week 84: 366/173, Week 96: 281/126, Week 108: 203/92, Week 120: 140/59, Week 132: 75/33, Week 144: 35/16, Week 156: 7/4, Week 168: 0/0

Log rank test: p-value = 0,213
*: p < 0,05

Analysis population: A2304 SAF total population

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

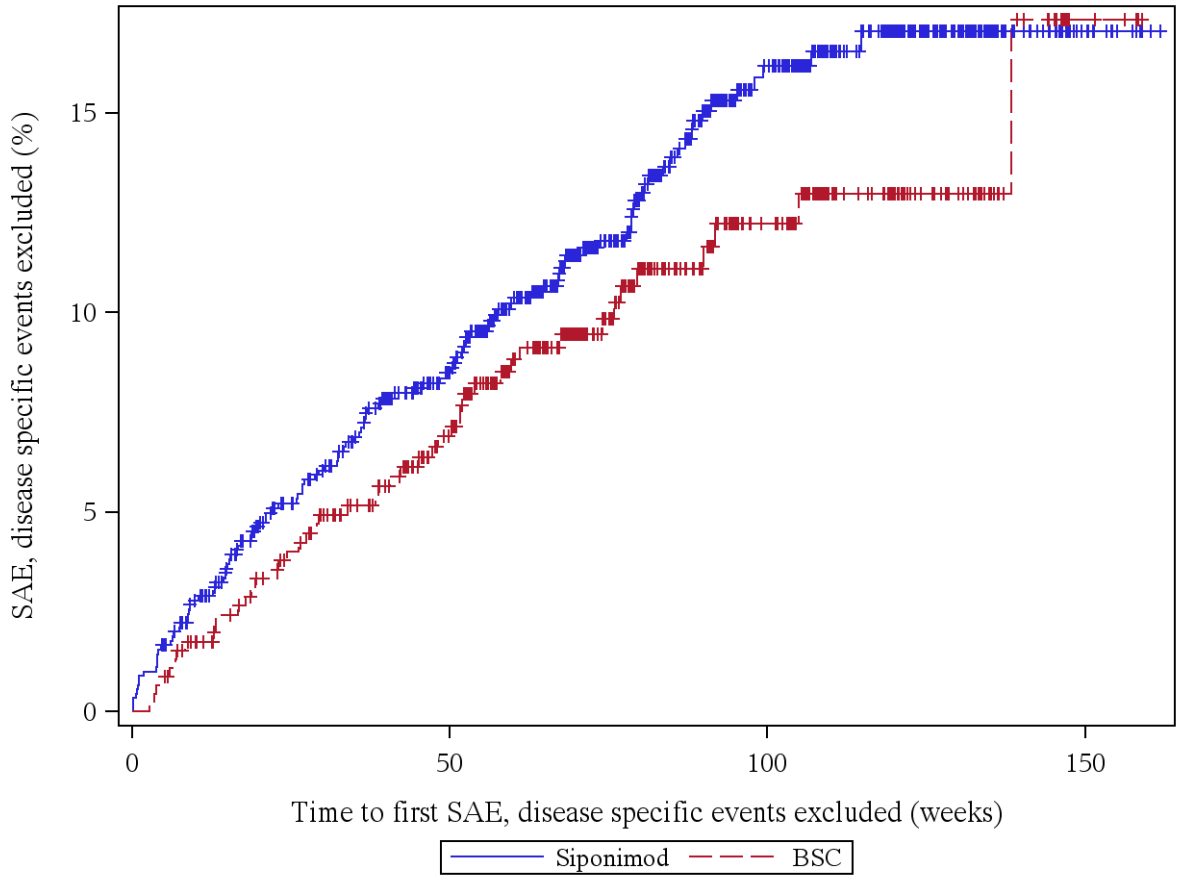


Patients at risk (Siponimod/BSC): Week 0: 195/87, Week 4: 190/86, Week 12: 183/84, Week 24: 173/82, Week 36: 165/78, Week 48: 153/71, Week 60: 127/62, Week 72: 99/46, Week 84: 74/39, Week 96: 59/32, Week 108: 41/20, Week 120: 25/13, Week 132: 13/5, Week 144: 5/3, Week 156: 0/1

Log rank test: p-value = 0,060
*: $p < 0,05$

Analysis population: A2304 SAF total population

Figure 12.7.1.4.2: SAE, disease specific events excluded, Moderate or Severe Disease Course = Yes



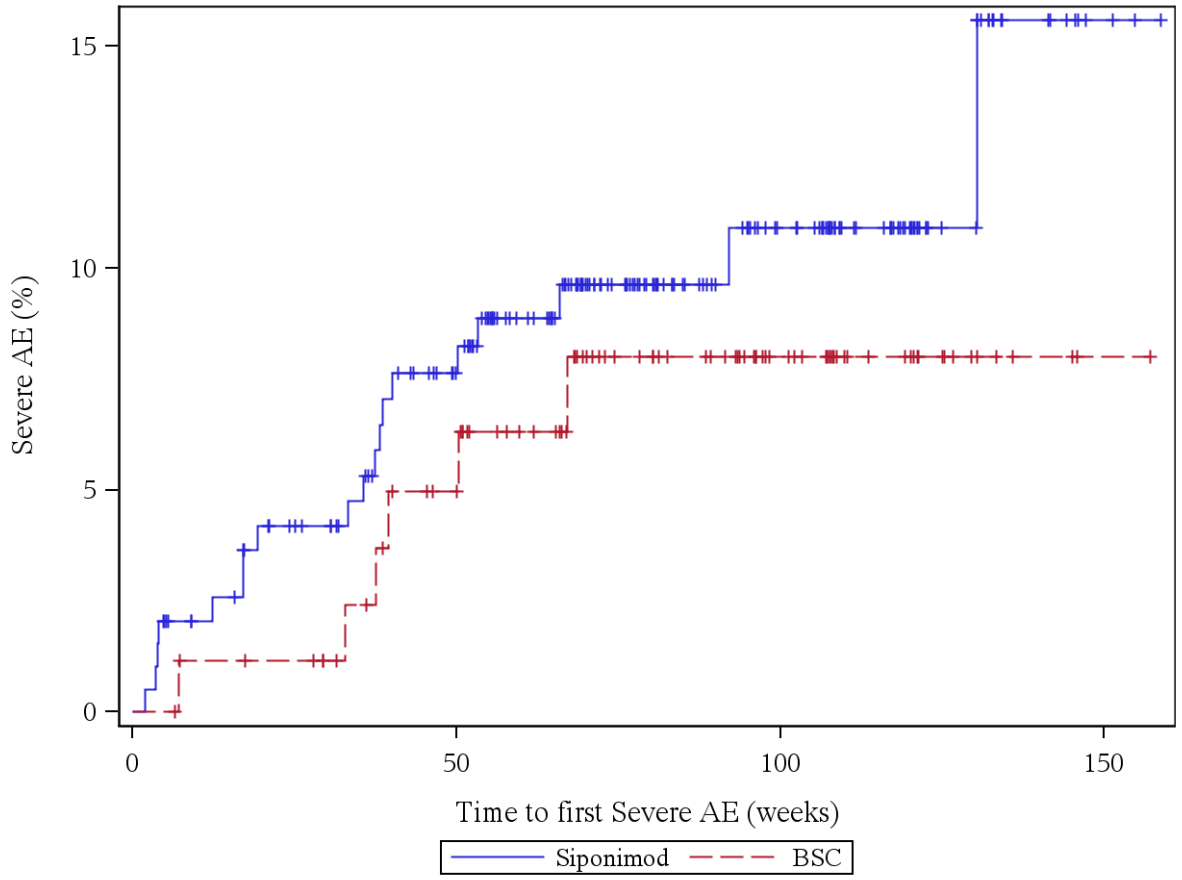
Patients at risk (Siponimod/BSC): Week 0: 904/459, Week 4: 891/456, Week 12: 853/442, Week 24: 802/421, Week 36: 770/399, Week 48: 717/364, Week 60: 628/301, Week 72: 489/237, Week 84: 381/178, Week 96: 293/130, Week 108: 211/94, Week 120: 146/60, Week 132: 82/34, Week 144: 39/17, Week 156: 8/4, Week 168: 0/0

Log rank test: p-value = 0,195
*: p < 0,05

Analysis population: A2304 SAF total population

12.7.1.5: Any severe AE

Figure 12.7.1.5.1: Severe AE, Moderate or Severe Disease Course = No

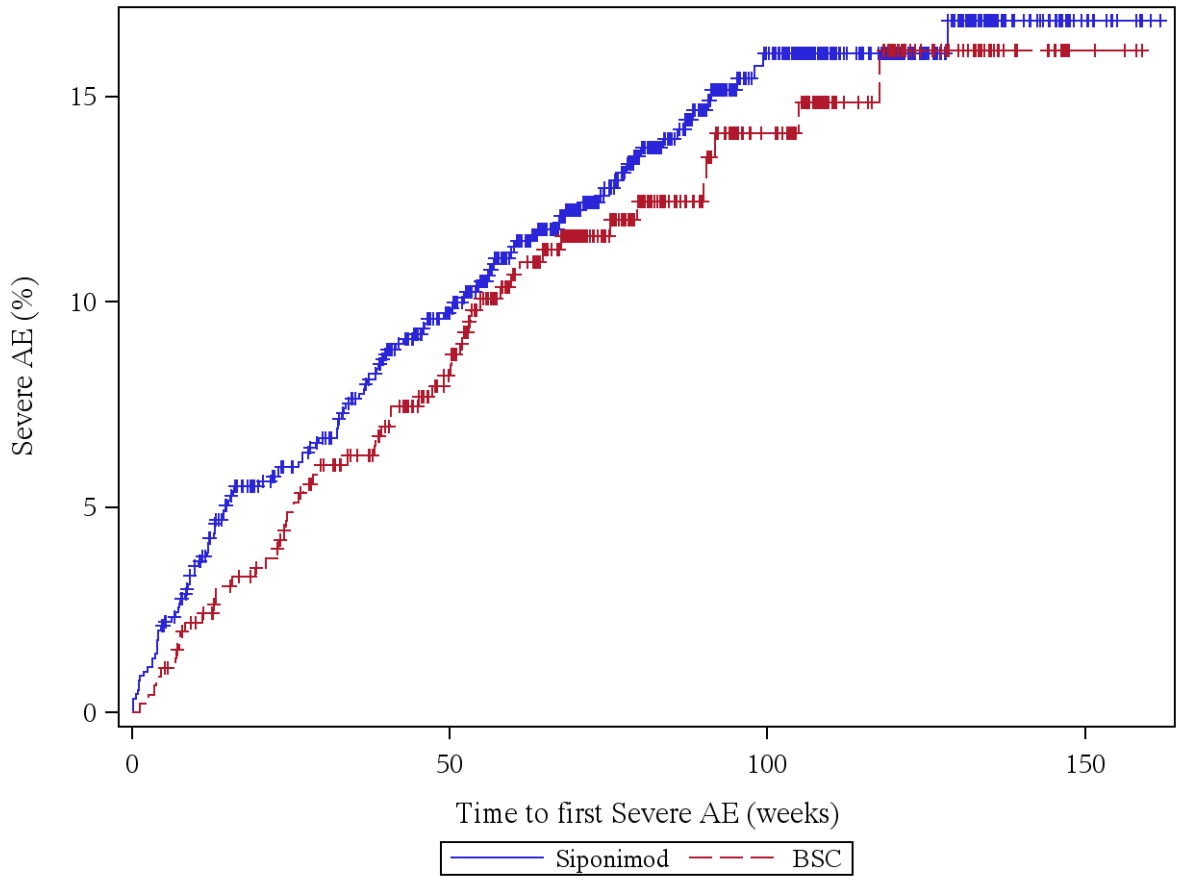


Patients at risk (Siponimod/BSC): Week 0: 195/87, Week 4: 191/87, Week 12: 185/84, Week 24: 176/83, Week 36: 166/78, Week 48: 154/71, Week 60: 129/61, Week 72: 101/48, Week 84: 78/41, Week 96: 65/33, Week 108: 48/21, Week 120: 31/14, Week 132: 15/5, Week 144: 7/3, Week 156: 1/1, Week 168: 0/0

Log rank test: p-value = 0,423
*: p < 0,05

Analysis population: A2304 SAF total population

Figure 12.7.1.5.2: Severe AE, Moderate or Severe Disease Course = Yes



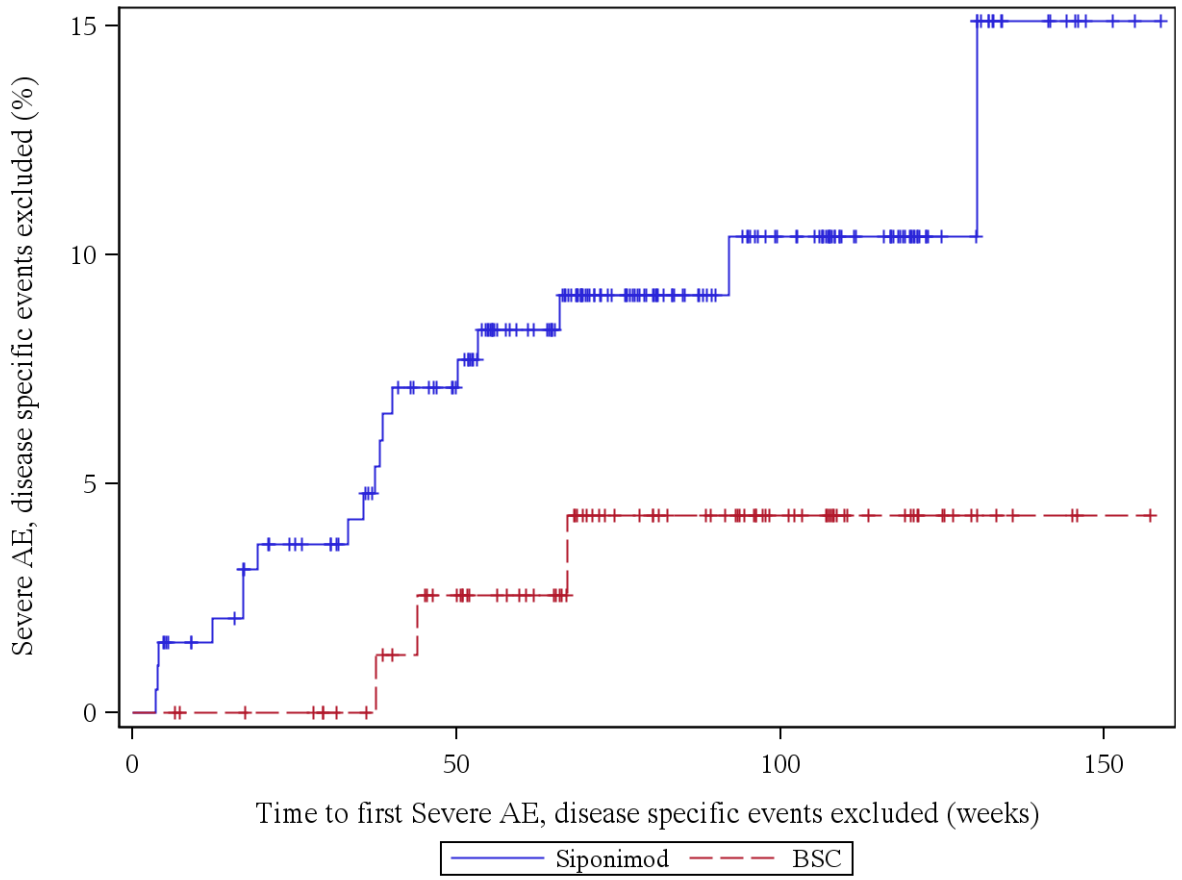
Patients at risk (Siponimod/BSC): Week 0: 904/459, Week 4: 888/455, Week 12: 843/441, Week 24: 798/421, Week 36: 768/398, Week 48: 709/362, Week 60: 624/300, Week 72: 493/233, Week 84: 384/175, Week 96: 291/128, Week 108: 210/91, Week 120: 148/56, Week 132: 84/30, Week 144: 38/14, Week 156: 7/3, Week 168: 0/0

Log rank test: p-value = 0,566
*: p < 0,05

Analysis population: A2304 SAF total population

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

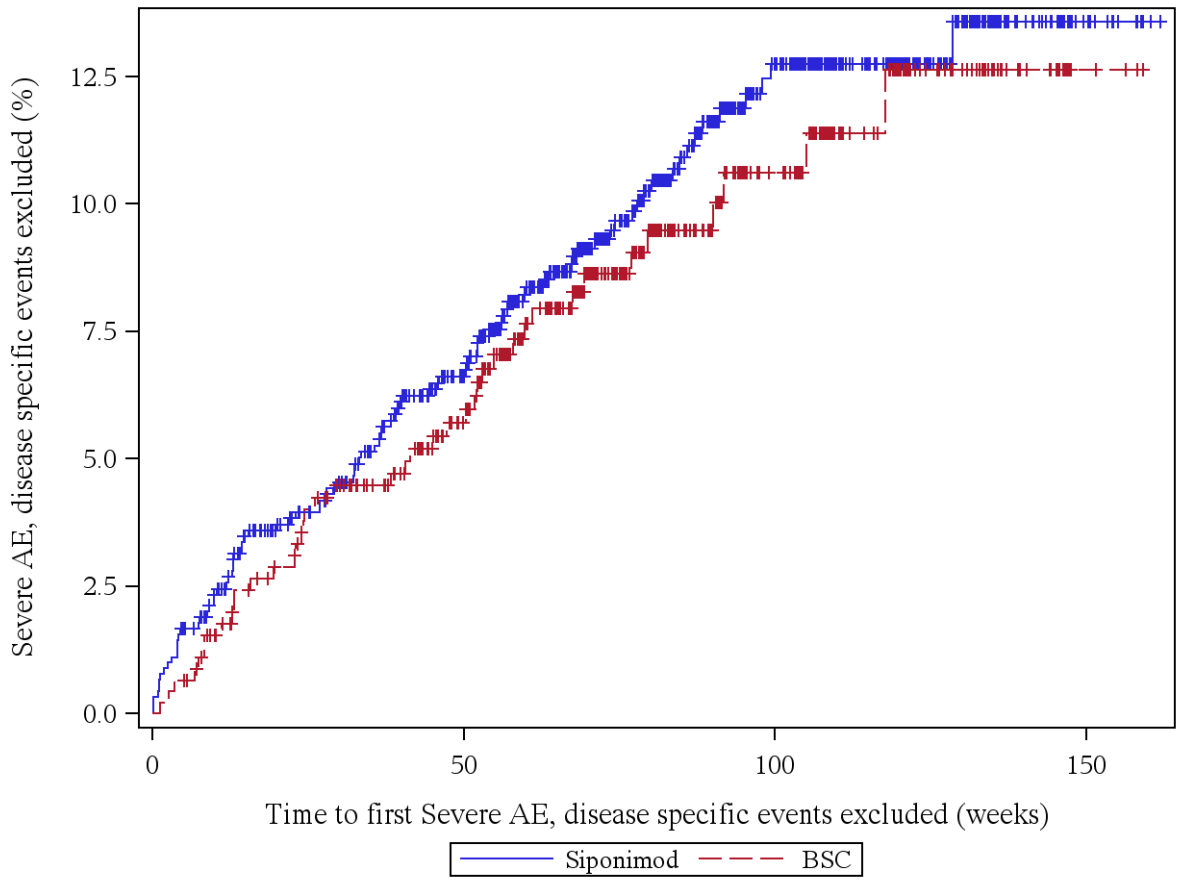


Patients at risk (Siponimod/BSC): Week 0: 195/87, Week 4: 192/87, Week 12: 186/85, Week 24: 177/84, Week 36: 167/80, Week 48: 155/72, Week 60: 130/63, Week 72: 102/48, Week 84: 79/41, Week 96: 65/33, Week 108: 48/21, Week 120: 31/14, Week 132: 15/5, Week 144: 7/3, Week 156: 1/1, Week 168: 0/0

Log rank test: p-value = 0,087
*: p < 0,05

Analysis population: A2304 SAF total population

Figure 12.7.1.6.2: Severe AE, disease specific events excluded, Moderate or Severe Disease Course = Yes



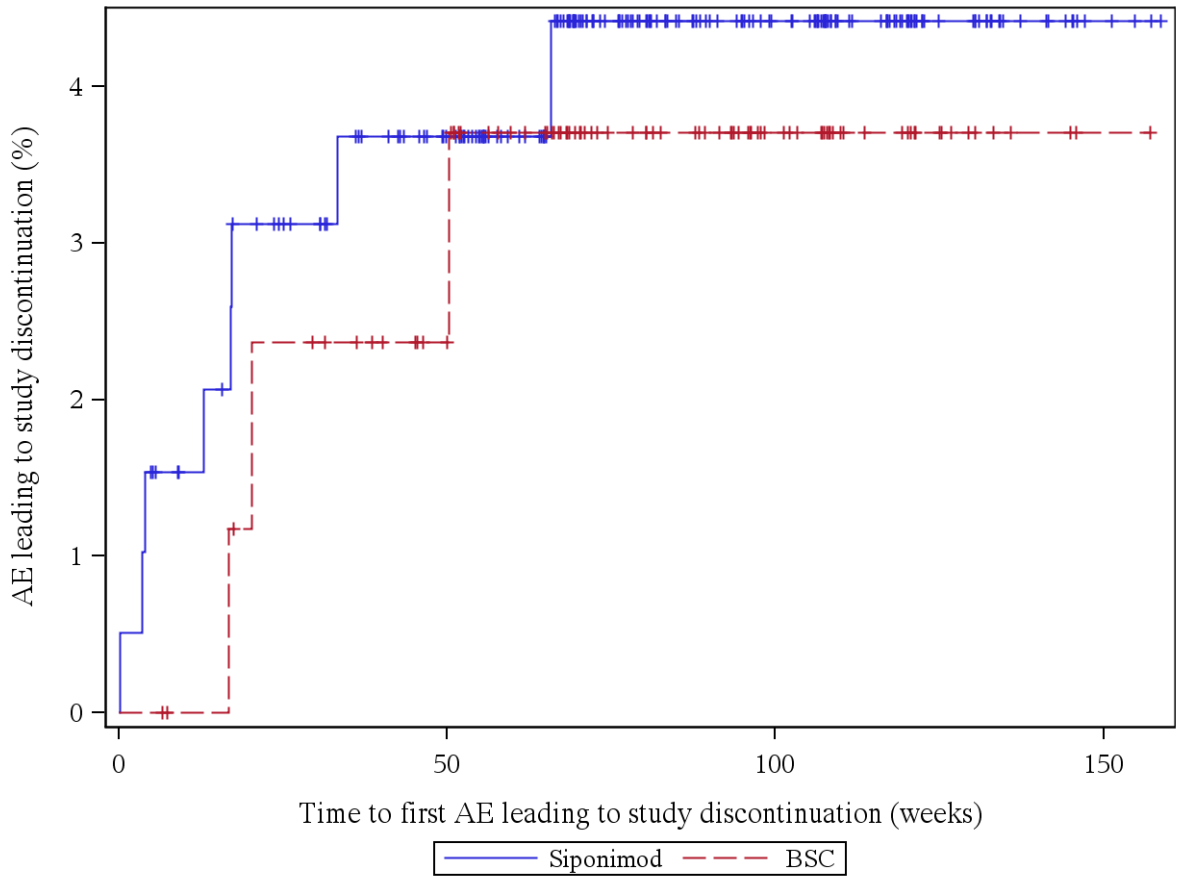
Patients at risk (Siponimod/BSC): Week 0: 904/459, Week 4: 891/456, Week 12: 855/442, Week 24: 812/423, Week 36: 785/402, Week 48: 728/368, Week 60: 640/307, Week 72: 506/239, Week 84: 396/181, Week 96: 300/131, Week 108: 217/94, Week 120: 152/59, Week 132: 86/33, Week 144: 38/16, Week 156: 7/3, Week 168: 0/0

Log rank test: p-value = 0,558
*: p < 0,05

Analysis population: A2304 SAF total population

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

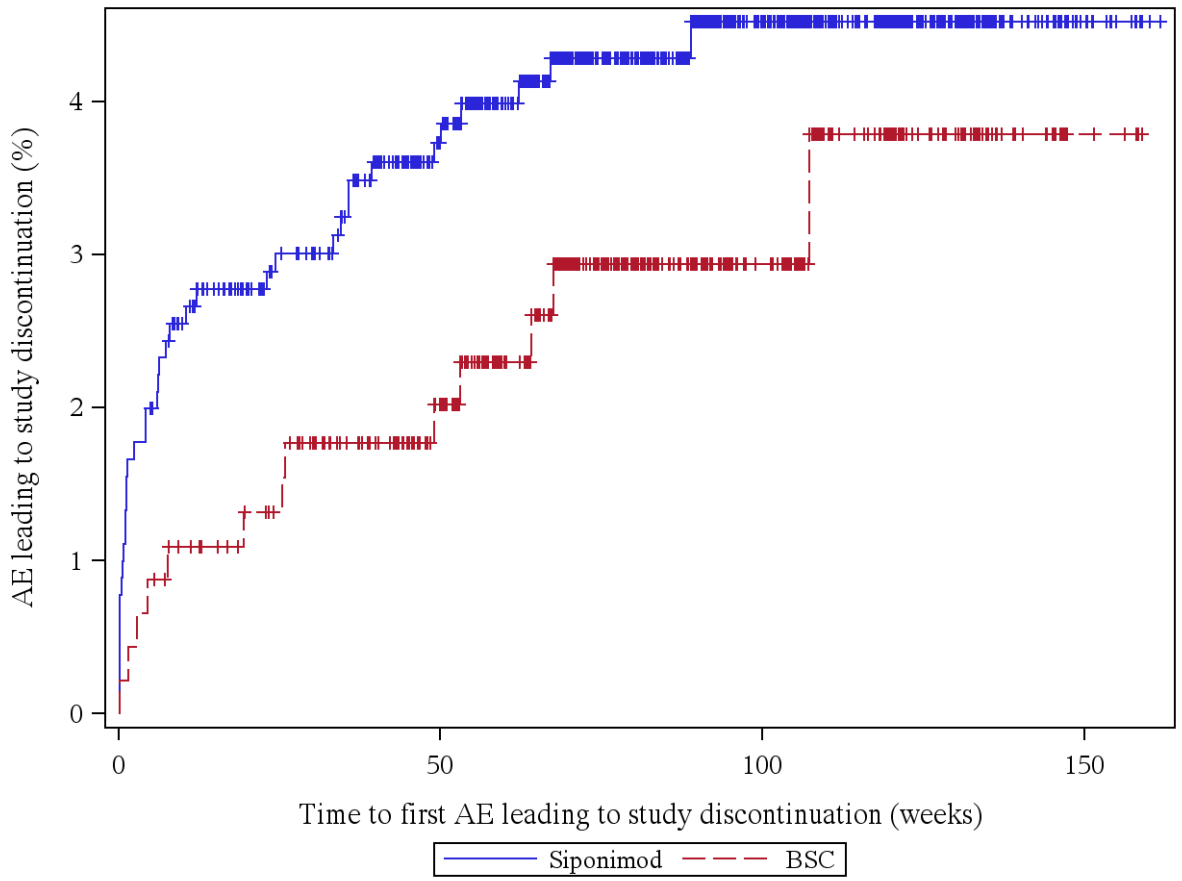


Patients at risk (Siponimod/BSC): Week 0: 195/87, Week 4: 192/87, Week 12: 187/85, Week 24: 180/82, Week 36: 171/80, Week 48: 162/74, Week 60: 139/64, Week 72: 109/49, Week 84: 85/42, Week 96: 71/33, Week 108: 51/21, Week 120: 34/14, Week 132: 19/5, Week 144: 9/3, Week 156: 2/1, Week 168: 0/0

Log rank test: p-value = 0,773
*: p < 0,05

Analysis population: A2304 SAF total population

Figure 12.7.1.7.2: AE leading to study discontinuation, Moderate or Severe Disease Course = Yes



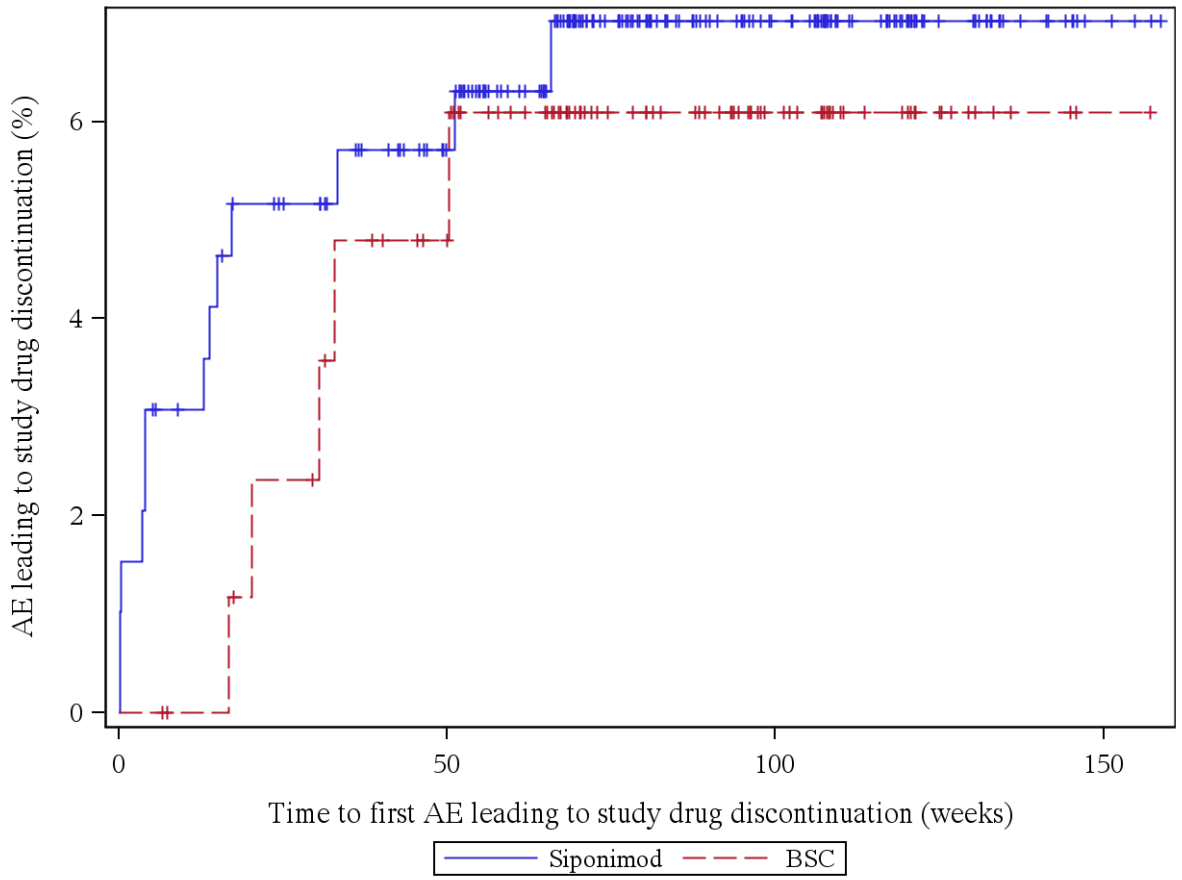
Patients at risk (Siponimod/BSC): Week 0: 904/459, Week 4: 888/456, Week 12: 864/449, Week 24: 832/437, Week 36: 811/417, Week 48: 760/387, Week 60: 677/323, Week 72: 541/255, Week 84: 430/195, Week 96: 329/143, Week 108: 240/104, Week 120: 166/66, Week 132: 94/35, Week 144: 42/17, Week 156: 8/4, Week 168: 0/0

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

Analysis population: A2304 SAF total population

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

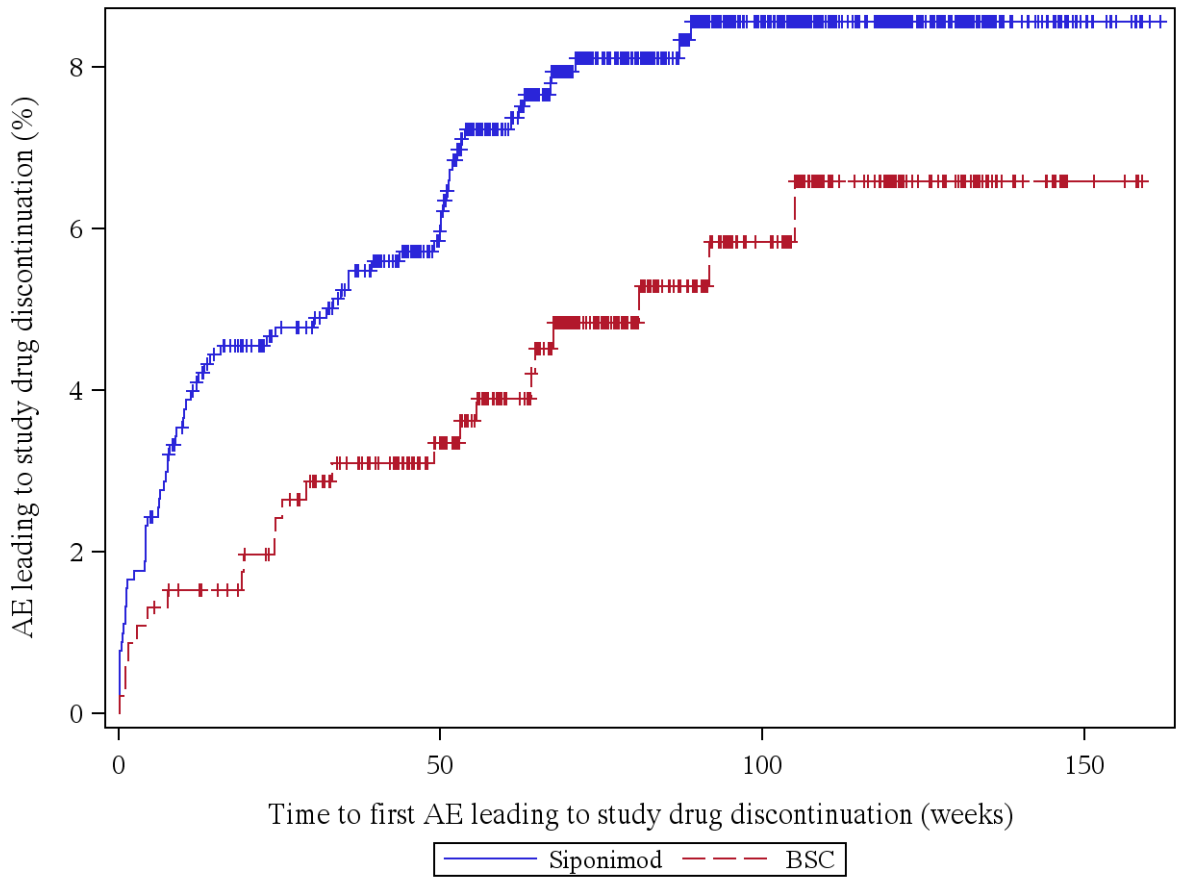


Patients at risk (Siponimod/BSC): Week 0: 195/87, Week 4: 189/87, Week 12: 186/85, Week 24: 179/82, Week 36: 171/78, Week 48: 162/74, Week 60: 139/64, Week 72: 109/49, Week 84: 85/42, Week 96: 71/33, Week 108: 51/21, Week 120: 34/14, Week 132: 19/5, Week 144: 9/3, Week 156: 2/1, Week 168: 0/0

Log rank test: p-value = 0,748
*: p < 0,05

Analysis population: A2304 SAF total population

Figure 12.7.1.8.2: AE leading to study drug discontinuation, Moderate or Severe Disease Course = Yes



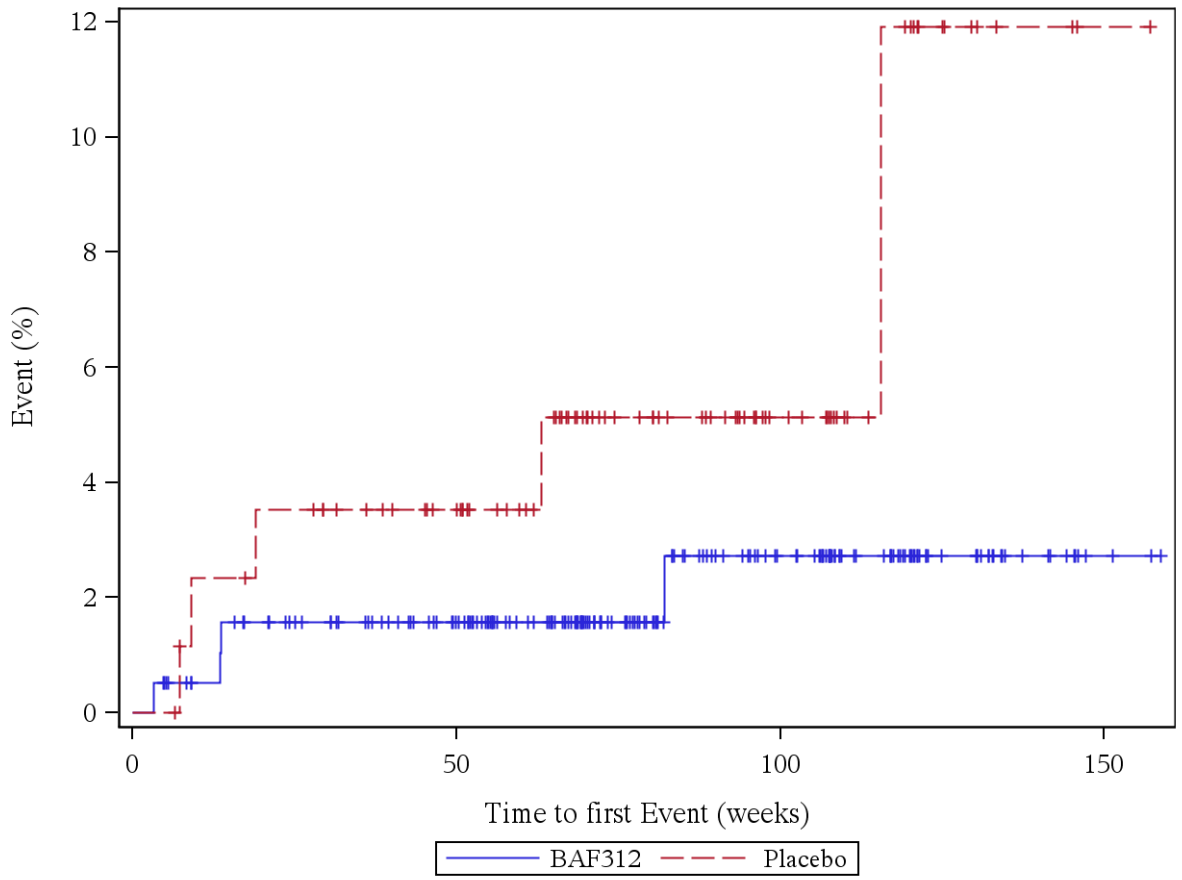
Patients at risk (Siponimod/BSC): Week 0: 904/459, Week 4: 887/454, Week 12: 858/449, Week 24: 829/437, Week 36: 809/415, Week 48: 759/385, Week 60: 674/322, Week 72: 537/255, Week 84: 429/194, Week 96: 329/142, Week 108: 240/104, Week 120: 166/66, Week 132: 94/35, Week 144: 42/17, Week 156: 8/4, Week 168: 0/0

Log rank test: p-value = 0,061
*: p < 0,05

Analysis population: A2304 SAF total population

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

Figure 12.7.5.1.1: Herpes simplex virus infections (AESI), Moderate or Severe Disease Course = No

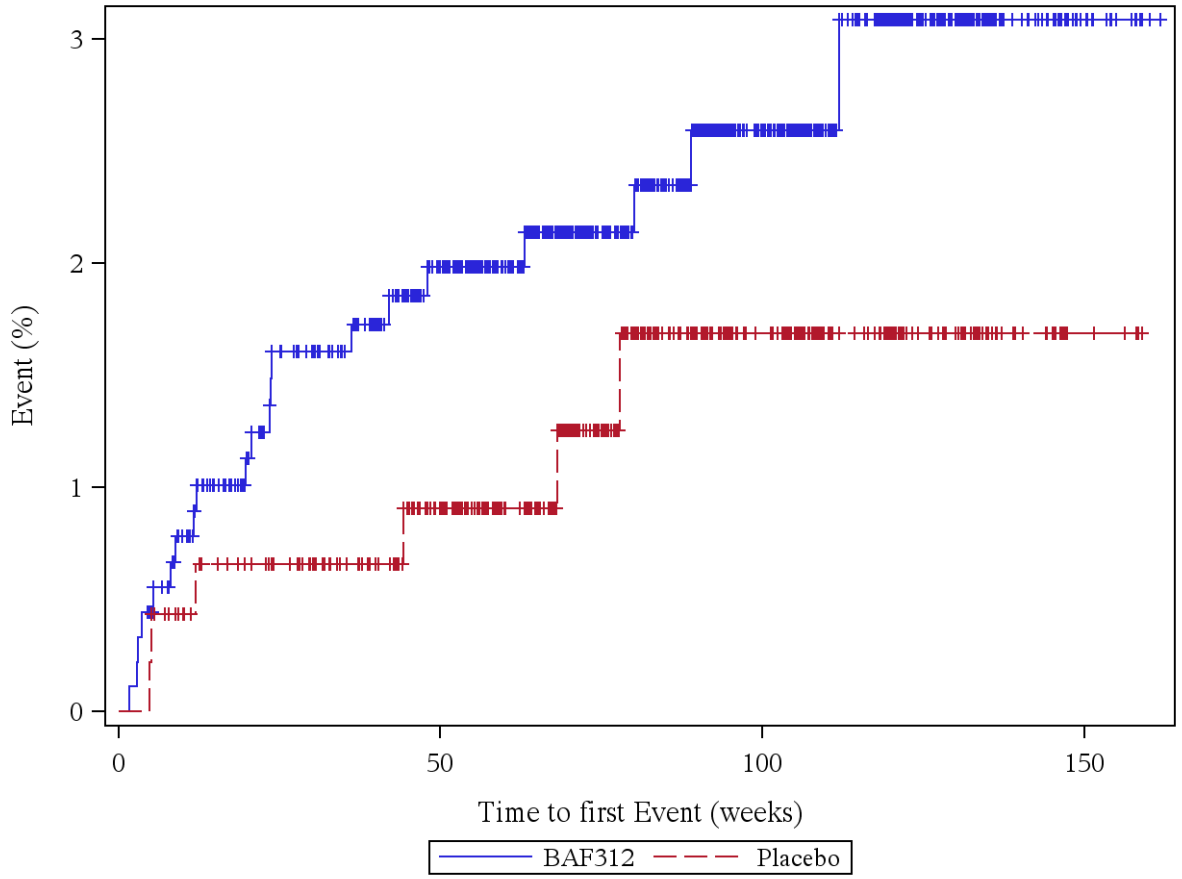


Patients at risk (BAF312/Placebo): Week 0: 195/87, Week 4: 194/87, Week 12: 187/83, Week 24: 179/81, Week 36: 171/77, Week 48: 160/71, Week 60: 136/62, Week 72: 106/46, Week 84: 81/39, Week 96: 69/30, Week 108: 50/19, Week 120: 33/12, Week 132: 18/4, Week 144: 8/3, Week 156: 2/1, Week 168: 0/0

Log rank test: p-value = 0,099
*: p < 0,05

Analysis population: A2304 SAF total population

Figure 12.7.5.1.2: Herpes simplex virus infections (AESI), Moderate or Severe Disease Course = Yes



Patients at risk (BAF312/Placebo): Week 0: 904/459, Week 4: 900/459, Week 12: 863/447, Week 24: 821/434, Week 36: 803/414, Week 48: 746/383, Week 60: 663/319, Week 72: 530/253, Week 84: 423/192, Week 96: 323/140, Week 108: 236/102, Week 120: 162/66, Week 132: 92/35, Week 144: 42/17, Week 156: 8/4, Week 168: 0/0

Log rank test: p-value = 0,212
*: p < 0,05

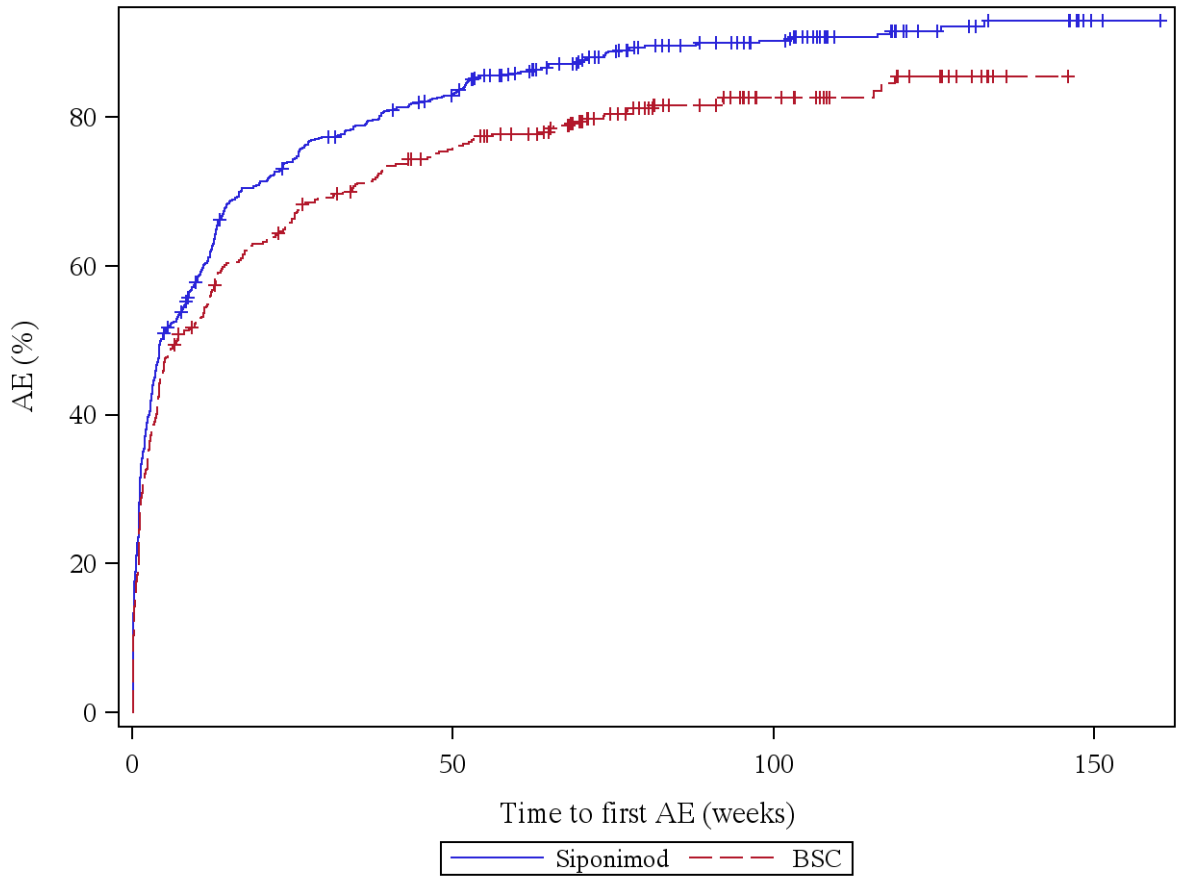
Analysis population: A2304 SAF total population

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

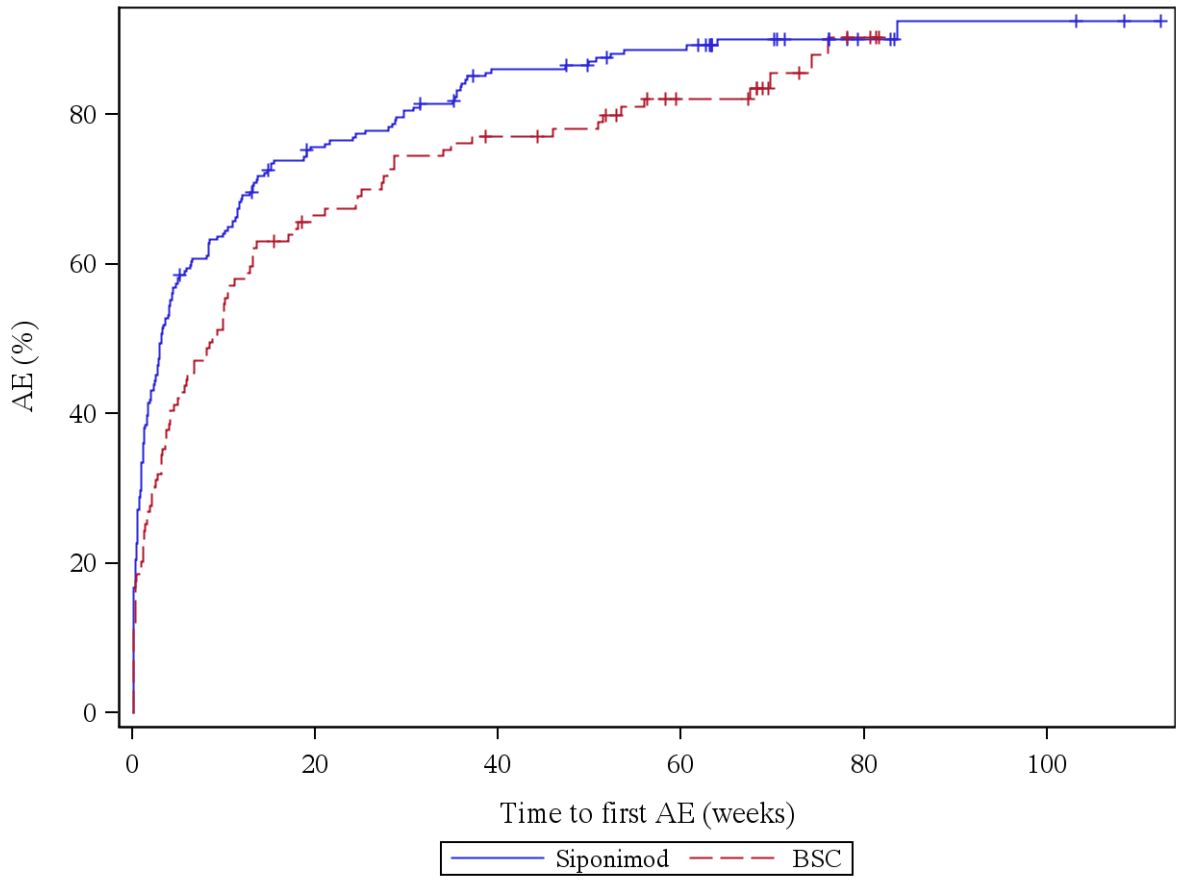


Patients at risk (Siponimod/BSC): Week 0: 860/427, Week 4: 451/246, Week 12: 329/186, Week 24: 220/145, Week 36: 176/117, Week 48: 142/97, Week 60: 104/82, Week 72: 75/58, Week 84: 53/40, Week 96: 43/31, Week 108: 26/21, Week 120: 17/13, Week 132: 10/6, Week 144: 8/1, Week 156: 1/0, Week 168: 0/0

Log rank test: p-value = <0,001 *
*: p < 0,05

Analysis population: A2304 SAF total population

Figure 12.8.1.1.2: AE, Region = Other



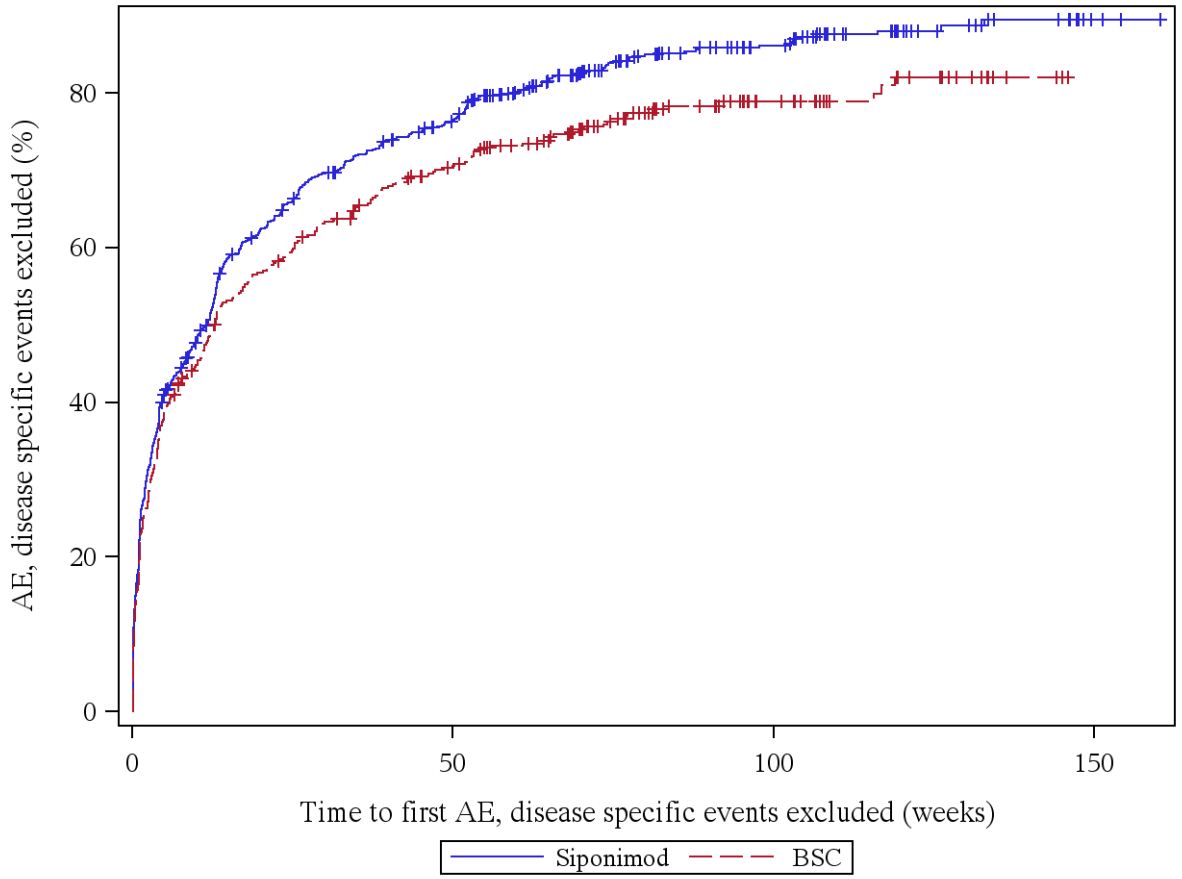
Patients at risk (Siponimod/BSC): Week 0: 239/119, Week 4: 109/73, Week 12: 73/50, Week 24: 53/37, Week 36: 34/27, Week 48: 27/23, Week 60: 21/14, Week 72: 10/7, Week 84: 3/0, Week 96: 3/0, Week 108: 2/0, Week 120: 0/0

Log rank test: p-value = 0,031 *
*: p < 0,05

Analysis population: A2304 SAF total population

12.8.1.2: Any AE, disease specific events excluded

Figure 12.8.1.2.1: AE, disease specific events excluded, Region = Europe

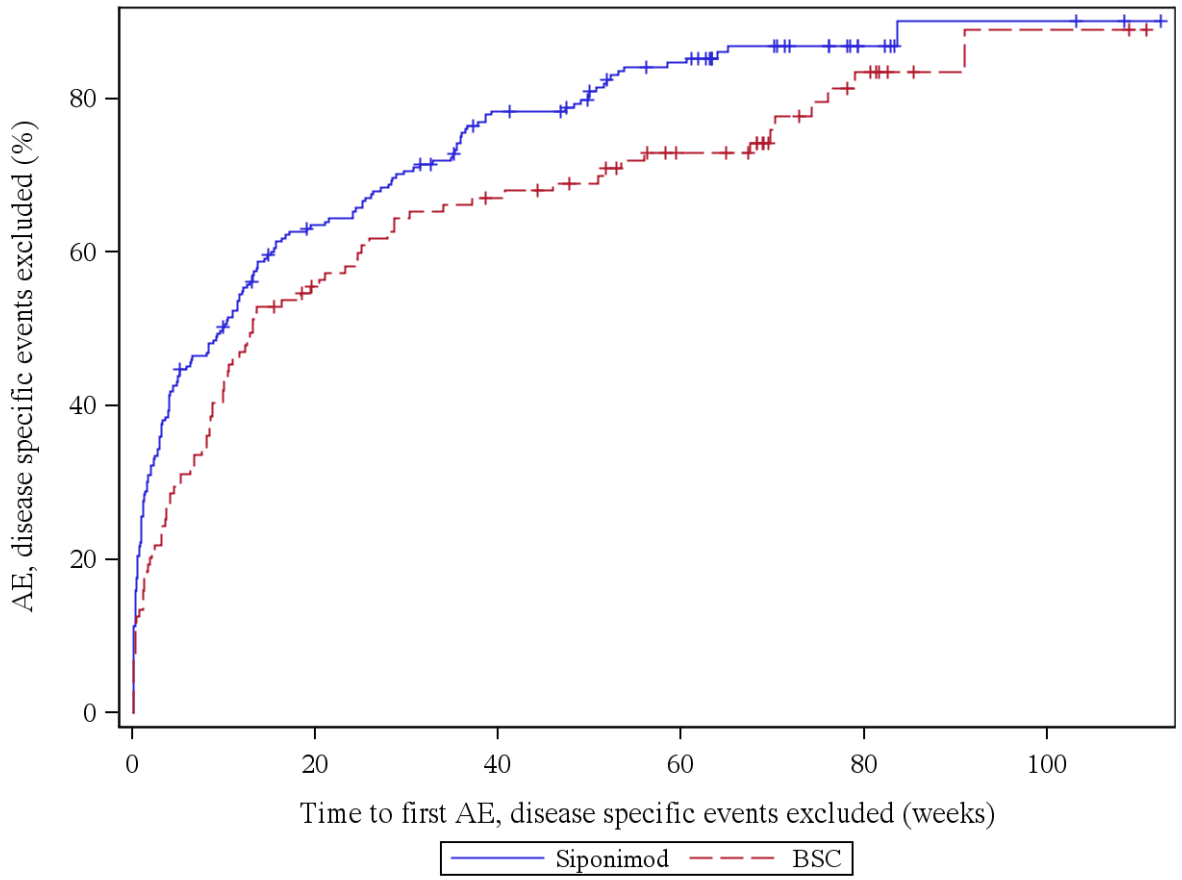


Patients at risk (Siponimod/BSC): Week 0: 860/427, Week 4: 540/277, Week 12: 415/215, Week 24: 285/170, Week 36: 228/138, Week 48: 190/116, Week 60: 138/95, Week 72: 98/69, Week 84: 69/46, Week 96: 55/35, Week 108: 34/23, Week 120: 23/15, Week 132: 15/8, Week 144: 10/3, Week 156: 1/0, Week 168: 0/0

Log rank test: p-value = 0,006 *
*: p < 0,05

Analysis population: A2304 SAF total population

Figure 12.8.1.2.2: AE, disease specific events excluded, Region = Other



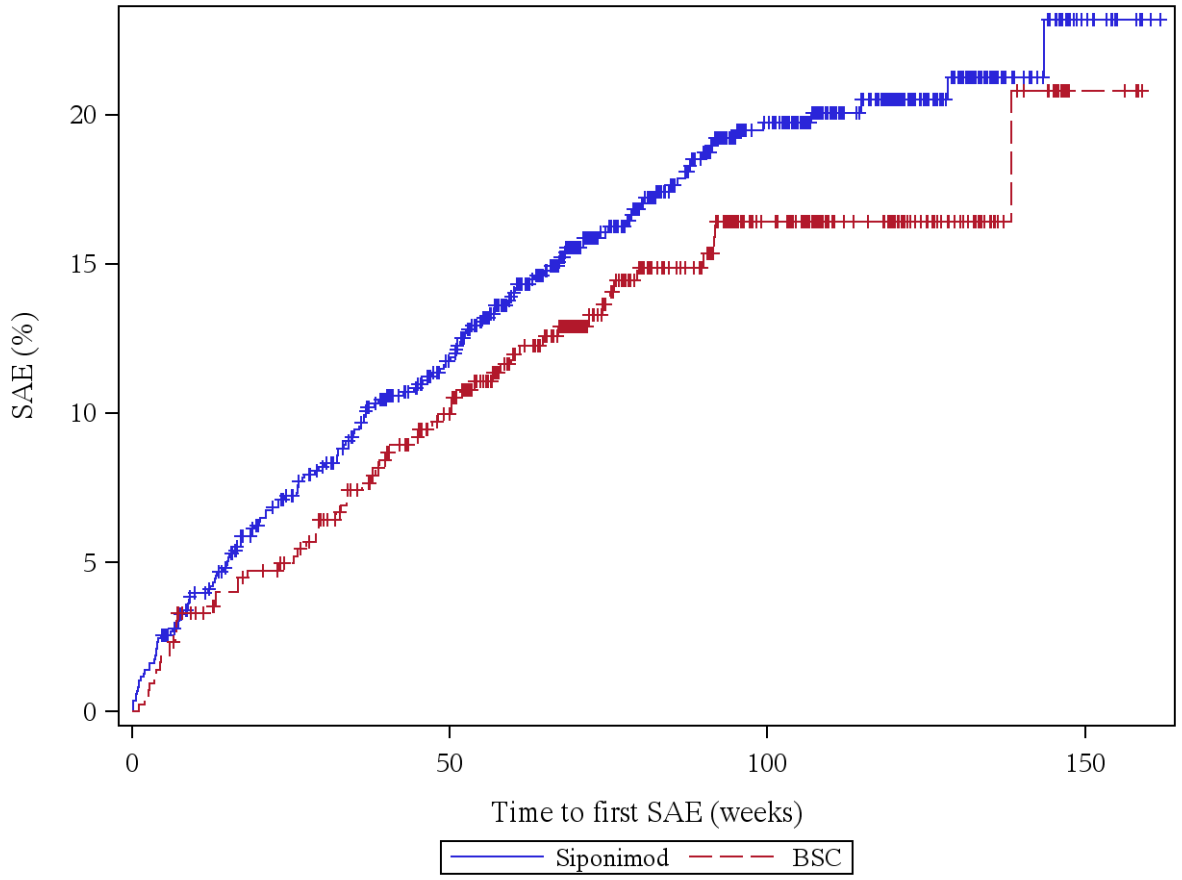
Patients at risk (Siponimod/BSC): Week 0: 239/119, Week 4: 140/87, Week 12: 106/63, Week 24: 81/47, Week 36: 53/38, Week 48: 42/32, Week 60: 27/23, Week 72: 13/13, Week 84: 3/4, Week 96: 3/2, Week 108: 2/2, Week 120: 0/0

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

Analysis population: A2304 SAF total population

12.8.1.3: Any SAE

Figure 12.8.1.3.1: SAE, Region = Europe

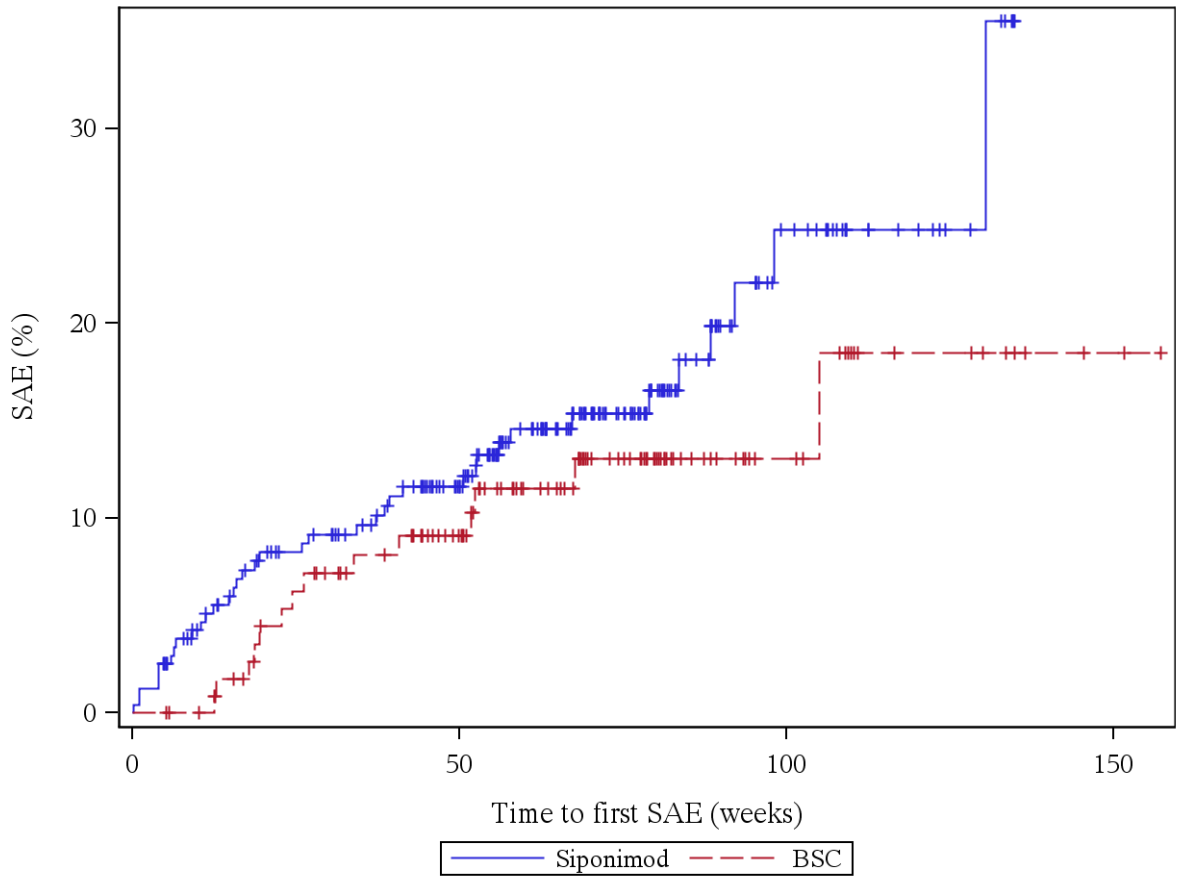


Patients at risk (Siponimod/BSC): Week 0: 860/427, Week 4: 840/421, Week 12: 809/406, Week 24: 761/392, Week 36: 724/370, Week 48: 677/340, Week 60: 602/291, Week 72: 476/230, Week 84: 386/184, Week 96: 306/139, Week 108: 223/98, Week 120: 152/64, Week 132: 82/32, Week 144: 40/16, Week 156: 7/4, Week 168: 0/0

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

Analysis population: A2304 SAF total population

Figure 12.8.1.3.2: SAE, Region = Other



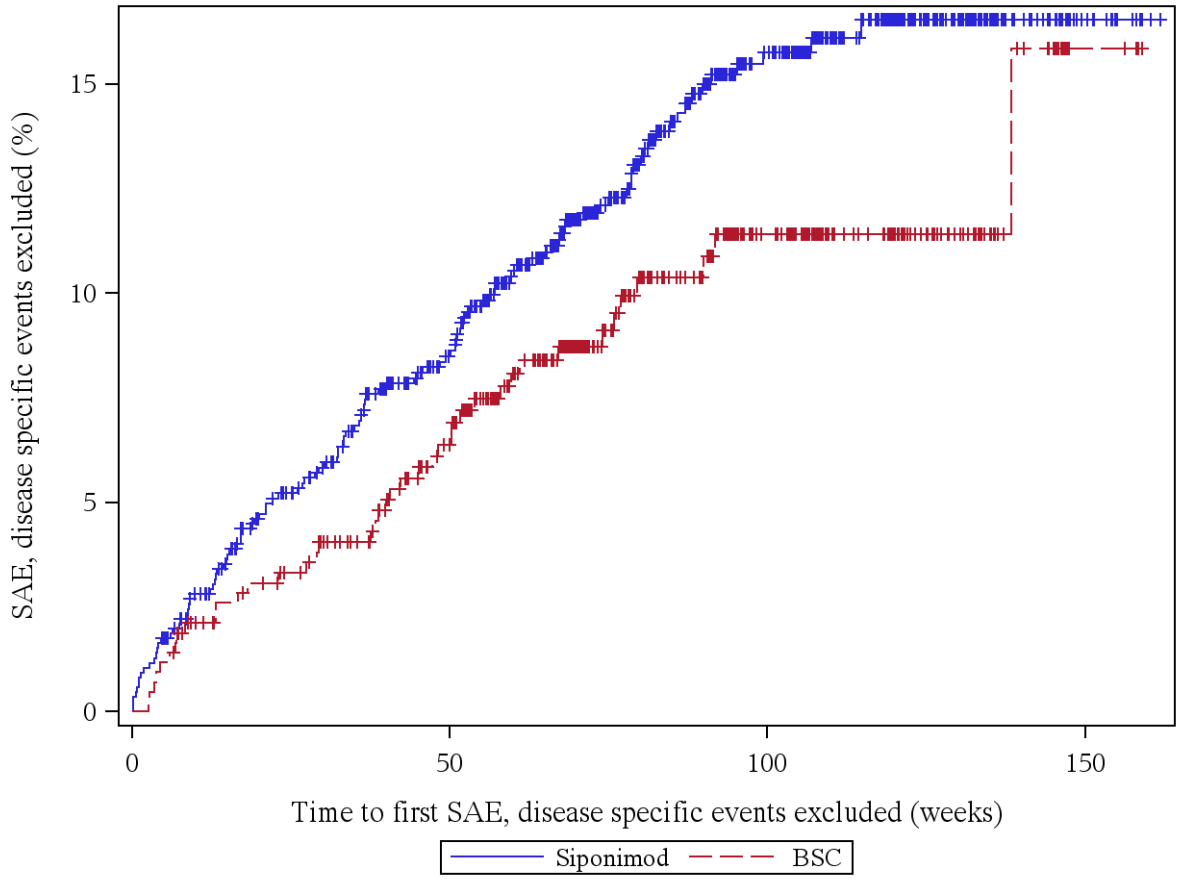
Patients at risk (Siponimod/BSC): Week 0: 239/119, Week 4: 233/119, Week 12: 215/116, Week 24: 198/104, Week 36: 188/95, Week 48: 168/83, Week 60: 128/63, Week 72: 88/47, Week 84: 51/27, Week 96: 31/18, Week 108: 19/14, Week 120: 12/8, Week 132: 6/6, Week 144: 0/3

Log rank test: p-value = 0,244
*: p < 0,05

Analysis population: A2304 SAF total population

12.8.1.4: Any SAE, disease specific events excluded

Figure 12.8.1.4.1: SAE, disease specific events excluded, Region = Europe

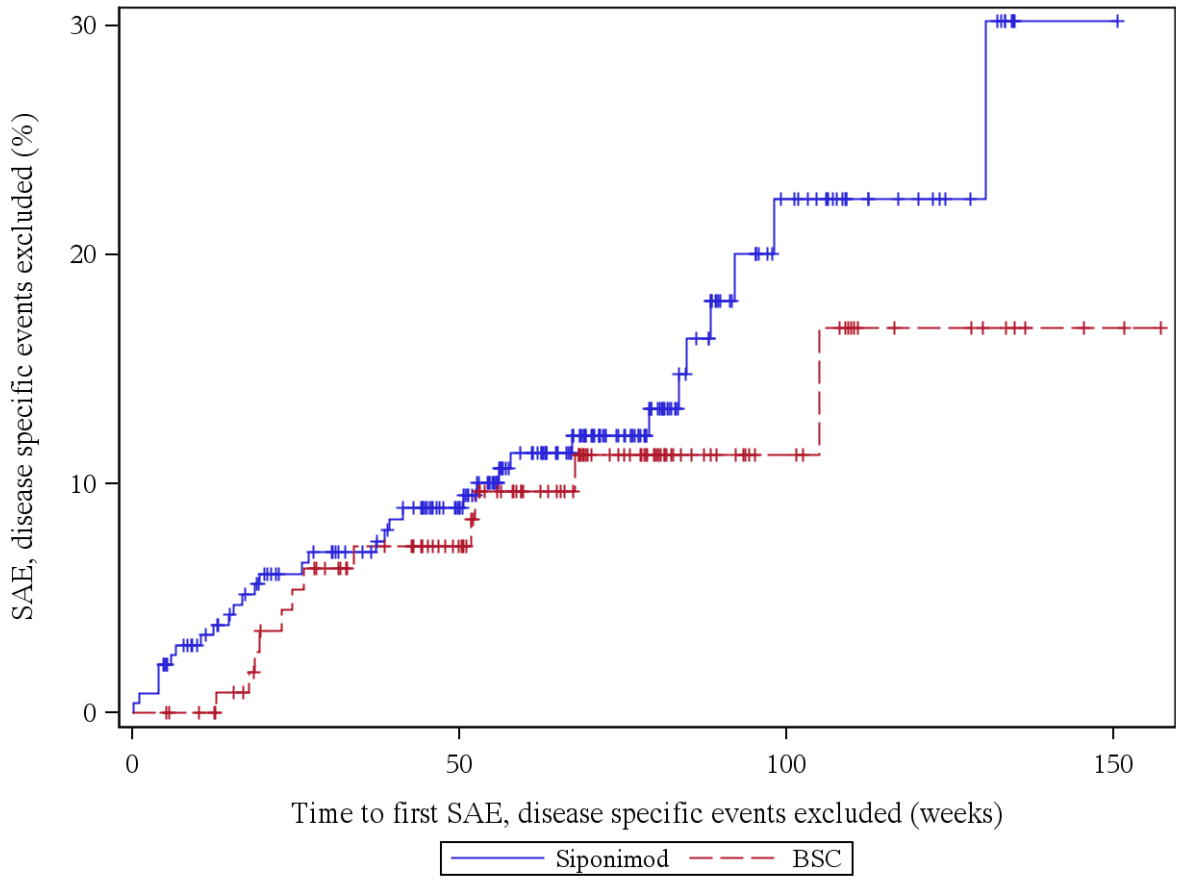


Patients at risk (Siponimod/BSC): Week 0: 860/427, Week 4: 847/423, Week 12: 817/410, Week 24: 773/398, Week 36: 742/382, Week 48: 697/351, Week 60: 621/300, Week 72: 495/236, Week 84: 399/190, Week 96: 317/144, Week 108: 230/100, Week 120: 156/65, Week 132: 86/33, Week 144: 43/17, Week 156: 8/4, Week 168: 0/0

Log rank test: p-value = 0,077
*: p < 0,05

Analysis population: A2304 SAF total population

Figure 12.8.1.4.2: SAE, disease specific events excluded, Region = Other



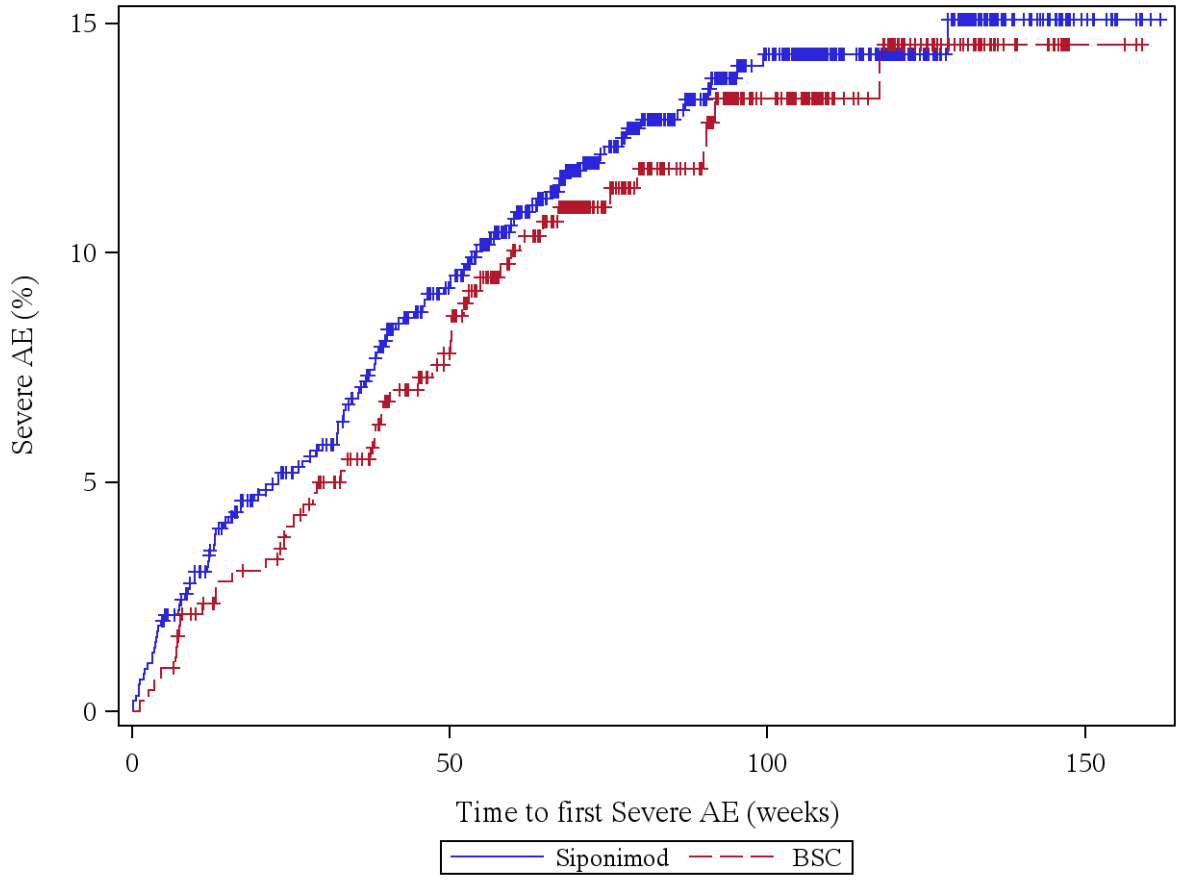
Patients at risk (Siponimod/BSC): Week 0: 239/119, Week 4: 234/119, Week 12: 219/116, Week 24: 202/105, Week 36: 193/95, Week 48: 173/84, Week 60: 134/63, Week 72: 93/47, Week 84: 56/27, Week 96: 35/18, Week 108: 22/14, Week 120: 15/8, Week 132: 9/6, Week 144: 1/3, Week 156: 0/1

Log rank test: p-value = 0,355
*: p < 0,05

Analysis population: A2304 SAF total population

12.8.1.5: Any severe AE

Figure 12.8.1.5.1: Severe AE, Region = Europe

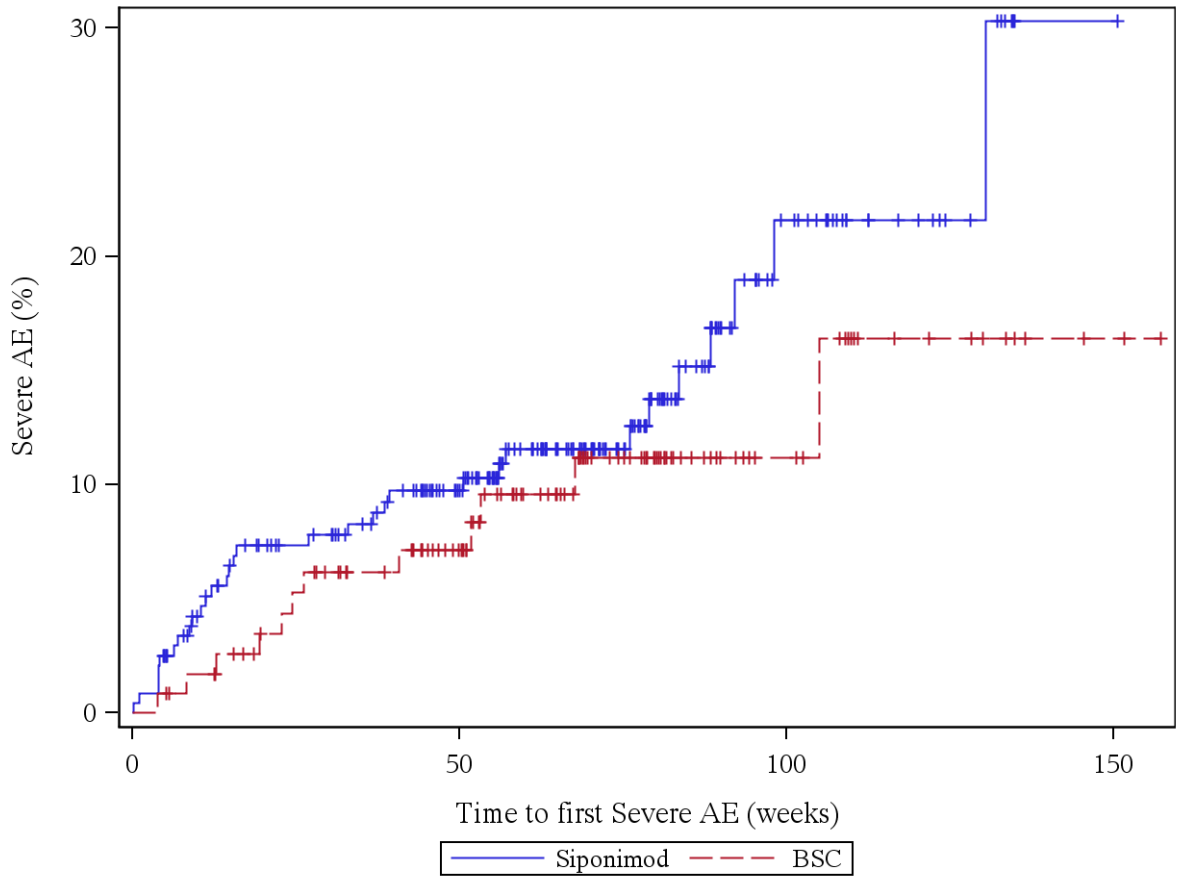


Patients at risk (Siponimod/BSC): Week 0: 860/427, Week 4: 845/424, Week 12: 814/410, Week 24: 774/398, Week 36: 743/379, Week 48: 692/348, Week 60: 621/297, Week 72: 499/234, Week 84: 405/188, Week 96: 323/142, Week 108: 238/97, Week 120: 165/61, Week 132: 91/29, Week 144: 44/14, Week 156: 8/3, Week 168: 0/0

Log rank test: p-value = 0,657
*: p < 0,05

Analysis population: A2304 SAF total population

Figure 12.8.1.5.2: Severe AE, Region = Other



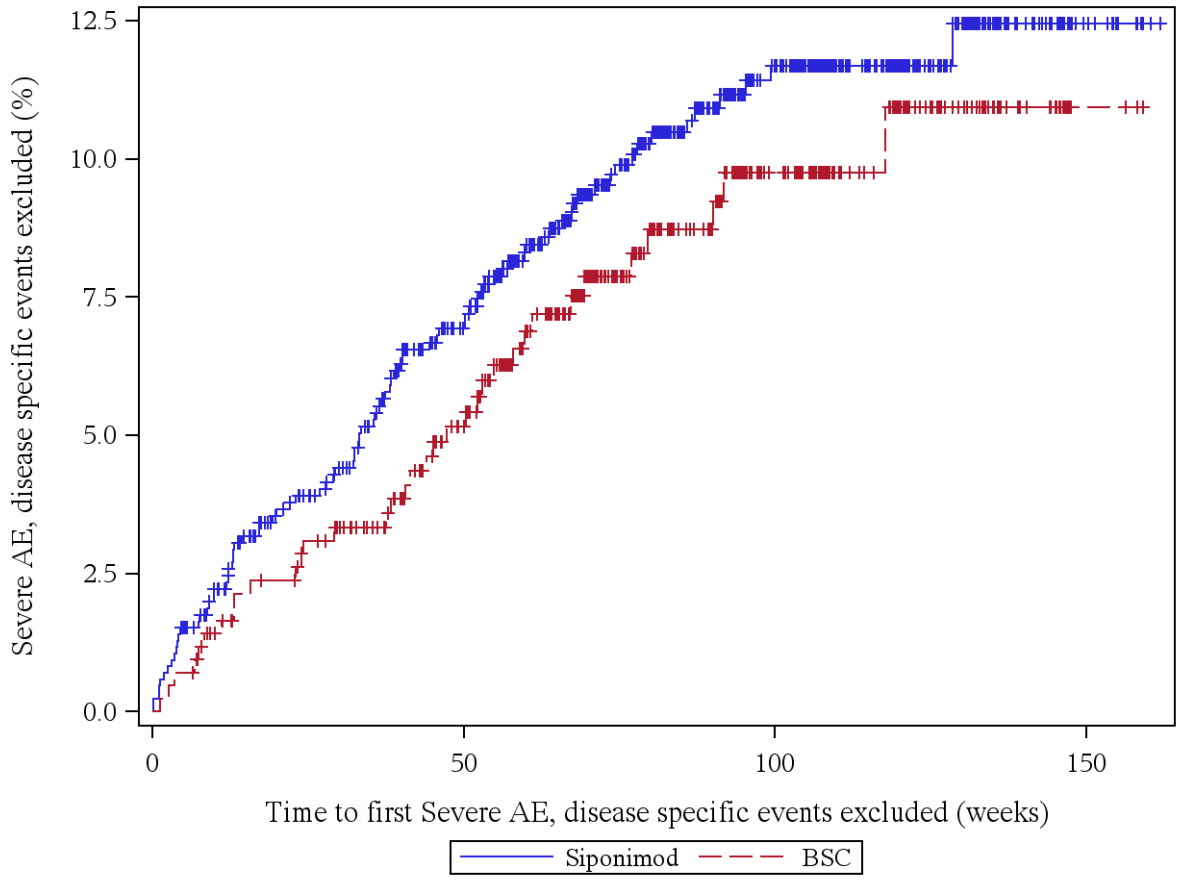
Patients at risk (Siponimod/BSC): Week 0: 239/119, Week 4: 234/118, Week 12: 214/115, Week 24: 200/106, Week 36: 191/97, Week 48: 171/85, Week 60: 132/64, Week 72: 95/47, Week 84: 57/28, Week 96: 33/19, Week 108: 20/15, Week 120: 14/9, Week 132: 8/6, Week 144: 1/3, Week 156: 0/1

Log rank test: p-value = 0,323
*: p < 0,05

Analysis population: A2304 SAF total population

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

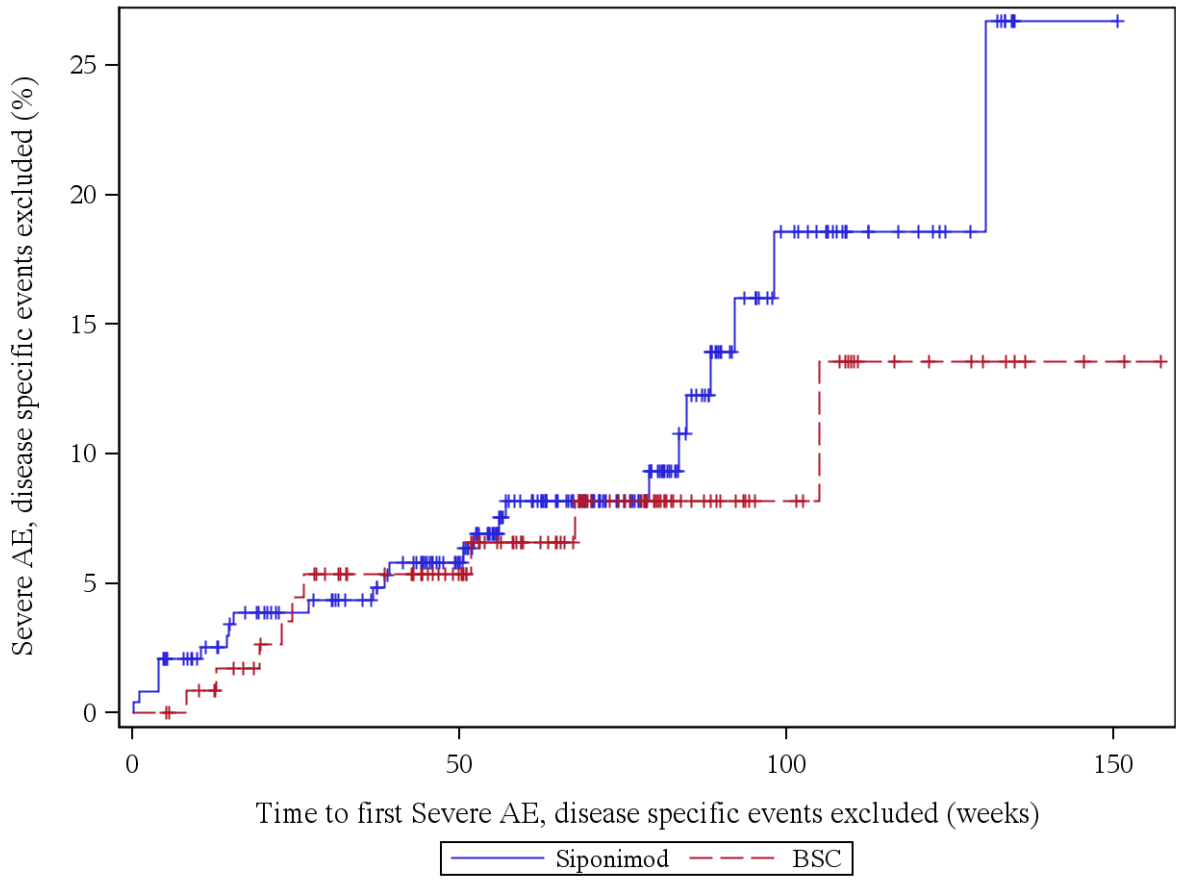


Patients at risk (Siponimod/BSC): Week 0: 860/427, Week 4: 849/424, Week 12: 820/412, Week 24: 782/401, Week 36: 753/385, Week 48: 705/354, Week 60: 633/305, Week 72: 509/239, Week 84: 414/193, Week 96: 330/145, Week 108: 243/100, Week 120: 168/64, Week 132: 92/32, Week 144: 44/16, Week 156: 8/3, Week 168: 0/0

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

Analysis population: A2304 SAF total population

Figure 12.8.1.6.2: Severe AE, disease specific events excluded, Region = Other



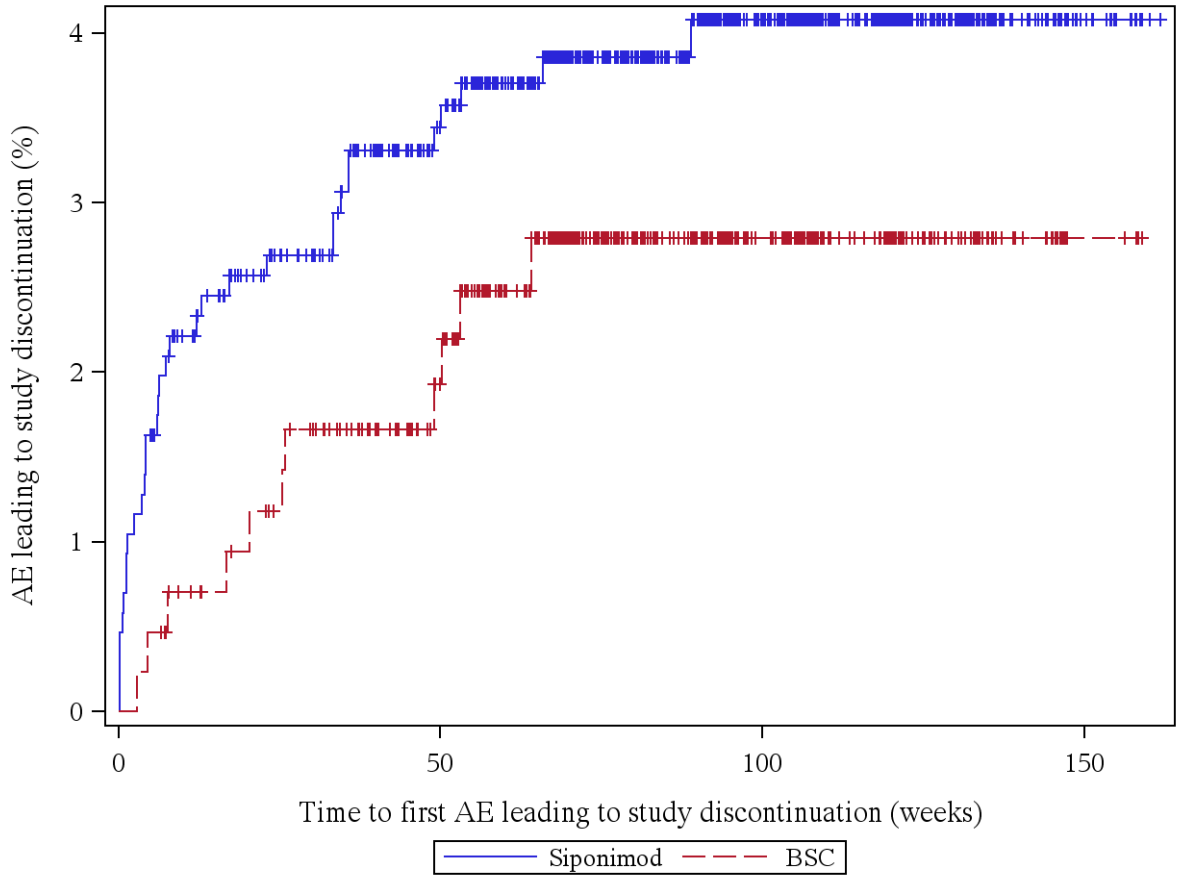
Patients at risk (Siponimod/BSC): Week 0: 239/119, Week 4: 234/119, Week 12: 221/115, Week 24: 207/106, Week 36: 199/97, Week 48: 178/86, Week 60: 137/65, Week 72: 99/48, Week 84: 61/29, Week 96: 35/19, Week 108: 22/15, Week 120: 15/9, Week 132: 9/6, Week 144: 1/3, Week 156: 0/1

Log rank test: p-value = 0,427
*: p < 0,05

Analysis population: A2304 SAF total population

12.8.1.7: Any AE leading to study discontinuation

Figure 12.8.1.7.1: AE leading to study discontinuation, Region = Europe

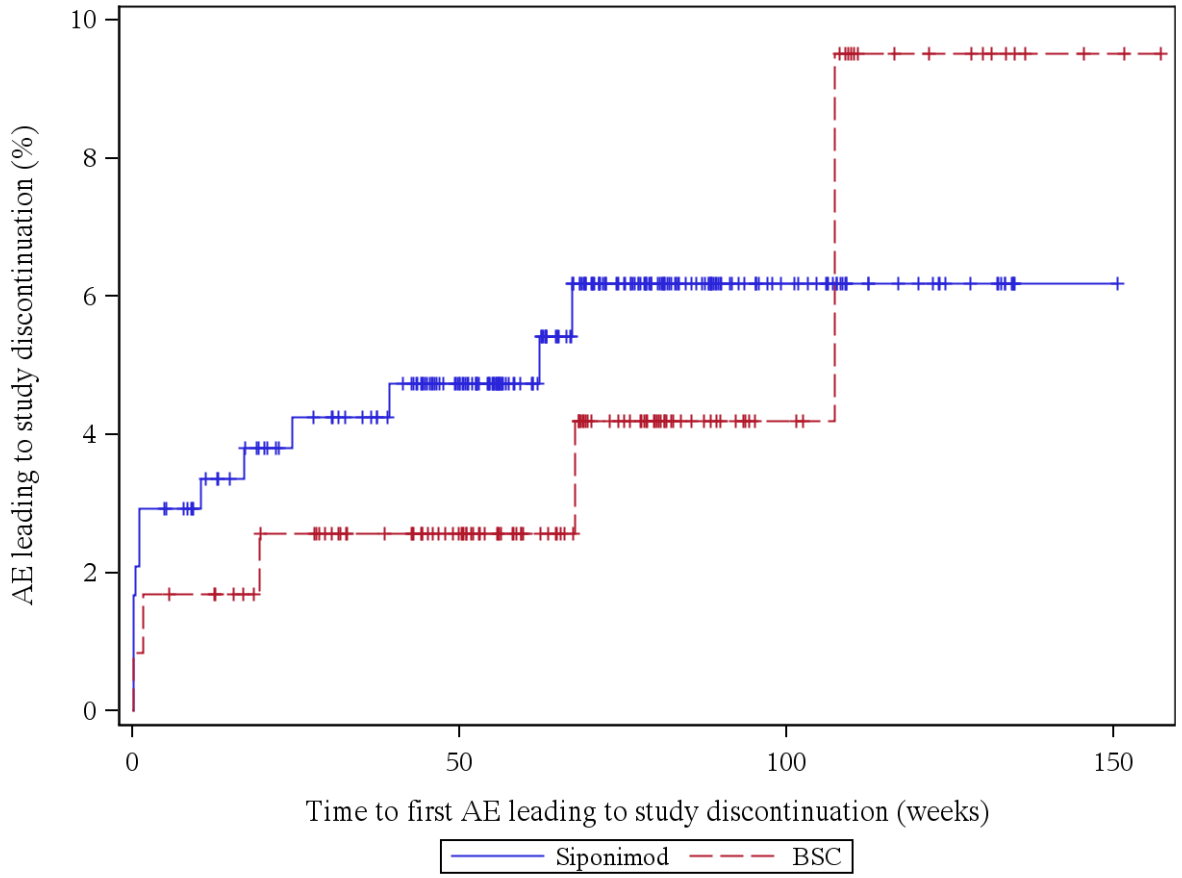


Patients at risk (Siponimod/BSC): Week 0: 860/427, Week 4: 848/426, Week 12: 828/418, Week 24: 800/410, Week 36: 777/397, Week 48: 739/372, Week 60: 673/320, Week 72: 549/254, Week 84: 452/207, Week 96: 362/156, Week 108: 266/109, Week 120: 183/70, Week 132: 102/34, Week 144: 50/17, Week 156: 10/4, Week 168: 0/0

Log rank test: p-value = 0,240
*: p < 0,05

Analysis population: A2304 SAF total population

Figure 12.8.1.7.2: AE leading to study discontinuation, Region = Other



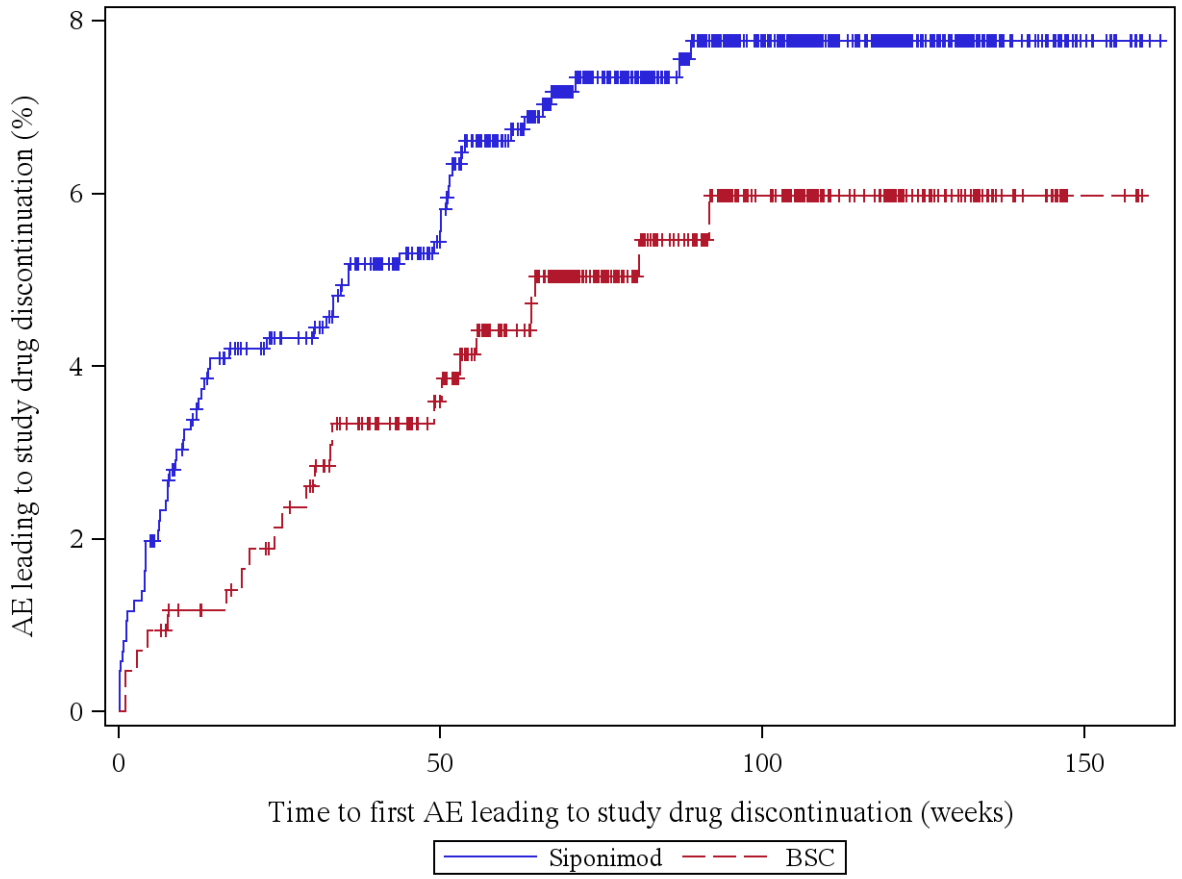
Patients at risk (Siponimod/BSC): Week 0: 239/119, Week 4: 232/117, Week 12: 223/116, Week 24: 212/109, Week 36: 205/100, Week 48: 183/89, Week 60: 143/67, Week 72: 101/50, Week 84: 63/30, Week 96: 38/20, Week 108: 25/16, Week 120: 17/10, Week 132: 11/6, Week 144: 1/3, Week 156: 0/1

Log rank test: p-value = 0,588
*: p < 0,05

Analysis population: A2304 SAF total population

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

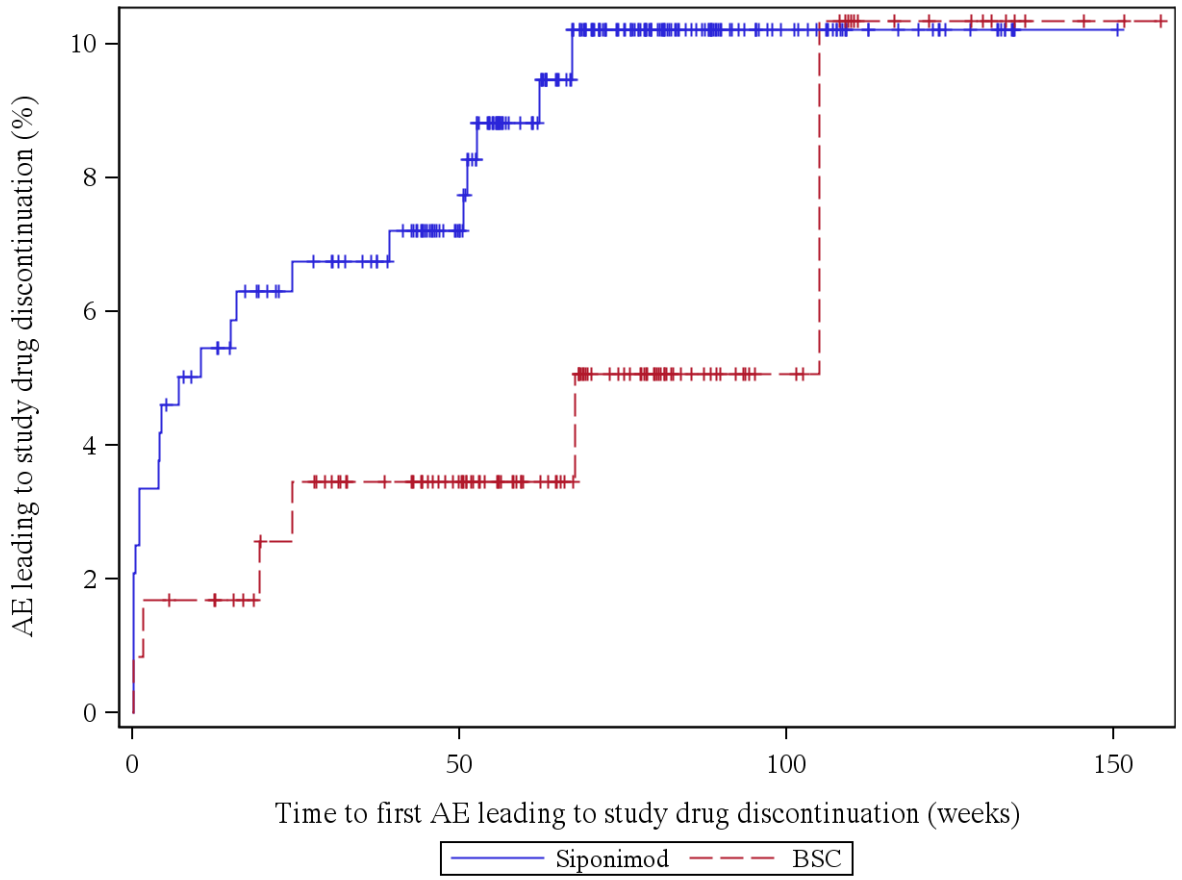


Patients at risk (Siponimod/BSC): Week 0: 860/427, Week 4: 846/424, Week 12: 821/418, Week 24: 796/410, Week 36: 775/393, Week 48: 738/370, Week 60: 670/319, Week 72: 545/254, Week 84: 451/206, Week 96: 362/155, Week 108: 266/109, Week 120: 183/70, Week 132: 102/34, Week 144: 50/17, Week 156: 10/4, Week 168: 0/0

Log rank test: p-value = 0,170
*: p < 0,05

Analysis population: A2304 SAF total population

Figure 12.8.1.8.2: AE leading to study drug discontinuation, Region = Other



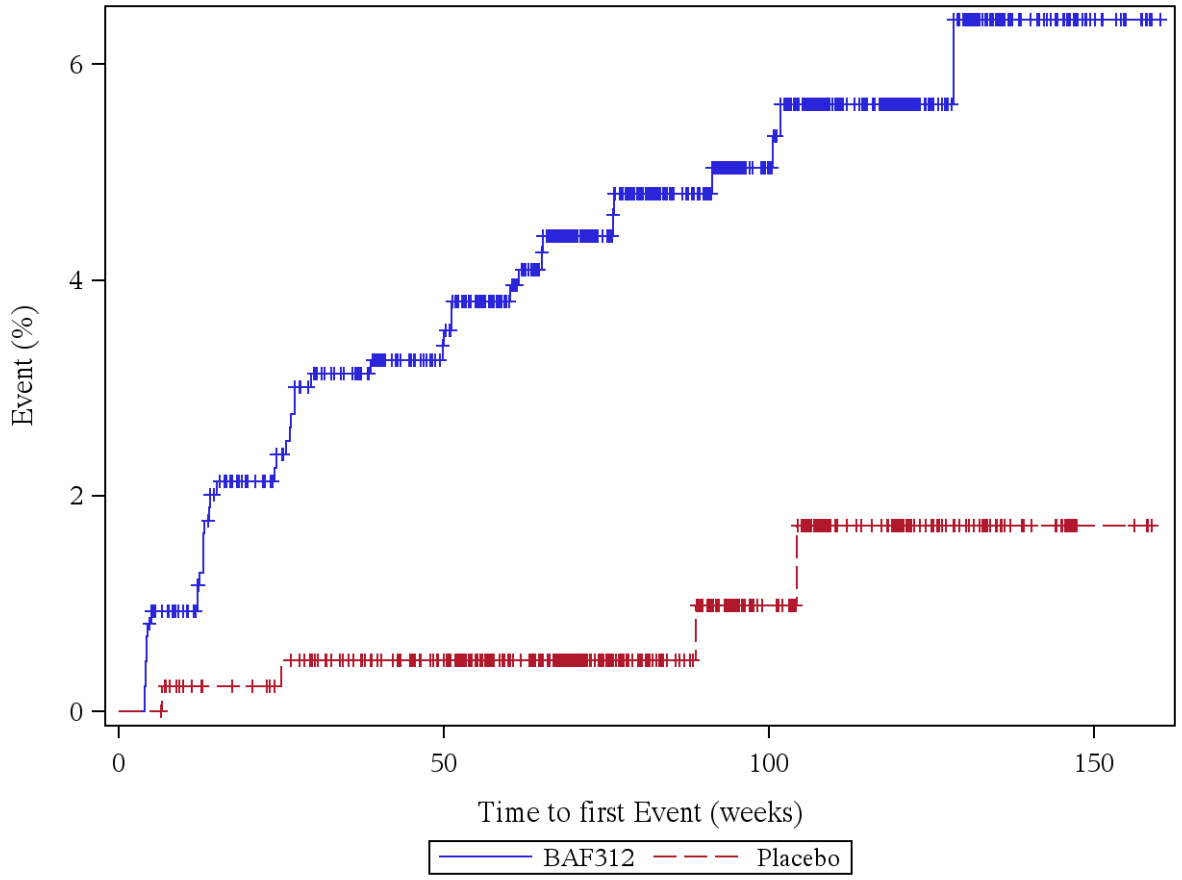
Patients at risk (Siponimod/BSC): Week 0: 239/119, Week 4: 230/117, Week 12: 223/116, Week 24: 212/109, Week 36: 205/100, Week 48: 183/89, Week 60: 143/67, Week 72: 101/50, Week 84: 63/30, Week 96: 38/20, Week 108: 25/16, Week 120: 17/10, Week 132: 11/6, Week 144: 1/3, Week 156: 0/1

Log rank test: p-value = 0,174
*: p < 0,05

Analysis population: A2304 SAF total population

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

Figure 12.8.2.1.1: GAMMA-GLUTAMYLTRANSFERASE INCREASED (PT), Region = Europe

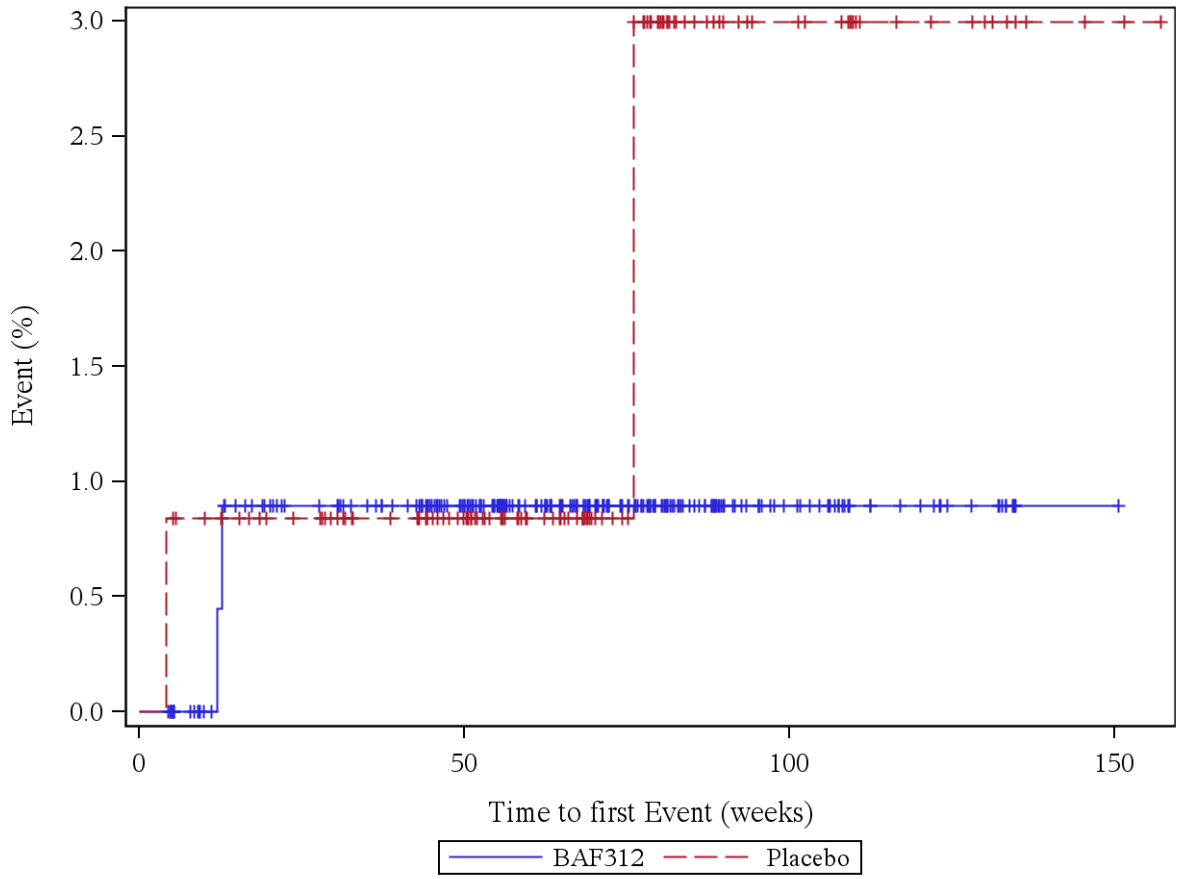


Patients at risk (BAF312/Placebo): Week 0: 860/427, Week 4: 858/427, Week 12: 827/418, Week 24: 787/411, Week 36: 762/395, Week 48: 719/371, Week 60: 650/320, Week 72: 524/254, Week 84: 425/206, Week 96: 341/155, Week 108: 249/108, Week 120: 170/69, Week 132: 95/34, Week 144: 45/17, Week 156: 9/4, Week 168: 0/0

Log rank test: p-value = 0,001 *
*: p < 0,05

Analysis population: A2304 SAF total population

Figure 12.8.2.1.2: GAMMA-GLUTAMYLTRANSFERASE INCREASED (PT), Region = Other



Patients at risk (BAF312/Placebo): Week 0: 239/119, Week 4: 239/119, Week 12: 223/115, Week 24: 210/108, Week 36: 203/99, Week 48: 181/88, Week 60: 141/66, Week 72: 101/49, Week 84: 63/28, Week 96: 38/20, Week 108: 25/17, Week 120: 17/10, Week 132: 11/6, Week 144: 1/3, Week 156: 0/1

Log rank test: p-value = 0,485
*: p < 0,05

Analysis population: A2304 SAF total population

Efficacy Tables

Novartis **Siponimod SPMS**
AMNOG Dossier Total Population **CBAF312A2304**

Table 2.1: All-cause Mortality (FAS), Binary Analysis

	Treatment groups		Comparison		
	BAF312 (N=1099)	**Placebo (N=546)**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
N'	1099	546			
All-cause mortality n (%)	4 (0.4)	4 (0.7)	0.49 [0.12;1.99] 0.321	0.50 [0.12;1.98] 0.321	0.00 [-0.01;0.00] 0.366

N': Number of patients in the analysis
OR: Odds Ratio
RR: Relative Risk
RD: Risk Difference

Table 3.1.1: Annualized Relapse Rate (FAS)

	Treatment groups		Comparison	
	BAF312 (N=1099)	**Placebo (N=546)**	**RR [95% CI]**	**p-value**
N'	1061	528		
Patients with at least one relapse	113	100		
Number of relapses	134	141		
Annualized Relapse Rate* [95% CI]	0.07 [0.06;0.09]	0.16 [0.12;0.21]	0.45 [0.34;0.59]	<.001

N': Number of patients in the analysis
* calculated from negative binomial model including the following variables: Treatment+Country+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=1099)	**Placebo (N=546)**	**RR [95% CI]**	**p-value**
Interaction Test				0.308
Age = 18-30				
N'	24	12		
Patients with at least one relapse	5	5		
Number of relapses	5	8		
Annualized Relapse Rate* [95% CI]	0.11 [0.04;0.32]	0.29 [0.11;0.78]	0.39 [0.10;1.57]	0.185
Age = 31-40				
N'	154	88		
Patients with at least one relapse	21	27		
Number of relapses	25	42		
Annualized Relapse Rate* [95% CI]	0.07 [0.05;0.12]	0.25 [0.16;0.38]	0.30 [0.16;0.54]	<.001
Age = 41-55				
N'	686	320		
Patients with at least one relapse	72	56		
Number of relapses	86	76		
Annualized Relapse Rate* [95% CI]	0.07 [0.05;0.09]	0.15 [0.11;0.20]	0.48 [0.33;0.68]	<.001
Age = >55				
N'	197	108		
Patients with at least one relapse	15	12		
Number of relapses	18	15		
Annualized Relapse Rate* [95% CI]	0.06 [0.04;0.10]	0.08 [0.05;0.15]	0.73 [0.34;1.55]	0.410

N': Number of patients in the analysis
* calculated from negative binomial model including the following variables: Treatment+Agegroup+Treatment*Agegroup+Country+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=1099)	**Placebo (N=546)**	**RR [95% CI]**	**p-value**
Interaction Test				0.037
Sex = F				
N'	643	315		
Patients with at least one relapse	83	63		
Number of relapses	99	85		
Annualized Relapse Rate* [95% CI]	0.09 [0.07;0.12]	0.16 [0.12;0.22]	0.55 [0.39;0.77]	<.001
Sex = M				
N'	418	213		
Patients with at least one relapse	30	37		
Number of relapses	35	56		
Annualized Relapse Rate* [95% CI]	0.05 [0.03;0.07]	0.16 [0.11;0.23]	0.29 [0.18;0.47]	<.001

N': Number of patients in the analysis
* calculated from negative binomial model including the following variables: Treatment+Sex+Treatment*Sex+Country+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=1099)	**Placebo (N=546)**	**RR [95% CI]**	**p-value**
Interaction Test				0.627
Previous MS-DMT = N				
N'	235	111		
Patients with at least one relapse	17	13		
Number of relapses	21	19		
Annualized Relapse Rate* [95% CI]	0.04 [0.03;0.07]	0.08 [0.05;0.14]	0.53 [0.26;1.05]	0.069
Previous MS-DMT = Y				
N'	826	417		
Patients with at least one relapse	96	87		
Number of relapses	113	122		
Annualized Relapse Rate* [95% CI]	0.08 [0.06;0.10]	0.18 [0.14;0.24]	0.43 [0.32;0.59]	<.001

N': Number of patients in the analysis
* calculated from negative binomial model including the following variables: Treatment+DMT+Treatment*DMT+Country+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=1099)	**Placebo (N=546)**	**RR [95% CI]**	**p-value**
Interaction Test				0.637
Previous IFN-beta 1b = N				
N'	726	380		
Patients with at least one relapse	76	68		
Number of relapses	85	100		
Annualized Relapse Rate* [95% CI]	0.06 [0.05;0.09]	0.15 [0.11;0.21]	0.42 [0.30;0.59]	<.001
Previous IFN-beta 1b = Y				
N'	335	148		
Patients with at least one relapse	37	32		
Number of relapses	49	41		
Annualized Relapse Rate* [95% CI]	0.08 [0.06;0.12]	0.17 [0.12;0.26]	0.49 [0.30;0.80]	0.005

N': Number of patients in the analysis
* calculated from negative binomial model including the following variables: Treatment+IFN+Treatment*IFN+Country+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=1099)	**Placebo (N=546)**	**RR [95% CI]**	**p-value**
Interaction Test				0.446
Rapid evolvement = N				
N'	810	389		
Patients with at least one relapse	80	63		
Number of relapses	95	92		
Annualized Relapse Rate* [95% CI]	0.07 [0.05;0.09]	0.15 [0.11;0.20]	0.48 [0.34;0.67]	<.001
Rapid evolvement = Y				
N'	251	139		
Patients with at least one relapse	33	37		
Number of relapses	39	49		
Annualized Relapse Rate* [95% CI]	0.07 [0.05;0.11]	0.19 [0.13;0.28]	0.38 [0.23;0.63]	<.001

N': Number of patients in the analysis
* calculated from negative binomial model including the following variables: Treatment+Rapid evolvement+Treatment*Rapid evolvement+Country+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=1099)	**Placebo (N=546)**	**RR [95% CI]**	**p-value**
Interaction Test				0.209
Moderate/severe disease course = N				
N'	192	84		
Patients with at least one relapse	11	17		
Number of relapses	13	20		
Annualized Relapse Rate* [95% CI]	0.04 [0.02;0.07]	0.13 [0.07;0.23]	0.28 [0.13;0.62]	0.002
Moderate/severe disease course = Y				
N'	869	444		
Patients with at least one relapse	102	83		
Number of relapses	121	121		
Annualized Relapse Rate* [95% CI]	0.08 [0.06;0.10]	0.17 [0.13;0.22]	0.48 [0.36;0.64]	<.001

N': Number of patients in the analysis
* calculated from negative binomial model including the following variables: Treatment+Course+Treatment*Course+Country+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=1099)	**Placebo (N=546)**	**RR [95% CI]**	**p-value**
Interaction Test				0.336
Region = Europe				
N'	832	417		
Patients with at least one relapse	97	82		
Number of relapses	117	118		
Annualized Relapse Rate* [95% CI]	0.09 [0.07;0.11]	0.18 [0.14;0.22]	0.48 [0.36;0.65]	<.001
Region = Others				
N'	229	111		
Patients with at least one relapse	16	18		
Number of relapses	17	23		
Annualized Relapse Rate* [95% CI]	0.07 [0.04;0.11]	0.20 [0.12;0.33]	0.33 [0.17;0.67]	0.002

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=1099)	**Placebo (N=546)**	**HR [95% CI]**	**p-value**
N'	1061	528		
Patients with at least one relapse	113	100		
Median in days* [95% KI]	[S > 50%]	[S > 50%]		
% of patients without relapse after 24 months* [95% KI]	89.00 [86.99;91.01]	79.59 [75.84;83.35]		
% of patients without relapse at EOS* [95% KI]	82.19 [74.71;89.66]	76.92 [72.20;81.65]		
			0.54 [0.41;0.70]	<.001

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=1099)	**Placebo (N=546)**	**HR [95% CI]**	**p-value**
Interaction Test				0.347
Age = 18-30				
N'	24	12		
Patients with at least one relapse	5	5		
Median in days* [95% KI]	[S > 50%]	[S > 50%]		
% of patients without relapse after 24 months* [95% KI]	73.43 [51.58;95.28]	58.33 [30.44;86.23]		
% of patients without relapse at EOS* [95% KI]	73.43 [51.58;95.28]	58.33 [30.44;86.23]		
			0.40 [0.11;1.45]	0.162
Age = 31-40				
N'	154	88		
Patients with at least one relapse	21	27		
Median in days* [95% KI]	[S > 50%]	[S > 50%]		
% of patients without relapse after 24 months* [95% KI]	85.30 [79.47;91.14]	66.57 [55.69;77.46]		
% of patients without relapse at EOS* [95% KI]	85.30 [79.47;91.14]	66.57 [55.69;77.46]		
			0.36 [0.20;0.63]	<.001

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=1099)	**Placebo (N=546)**	**HR [95% CI]**	**p-value**
Age = 41-55				
N'	686	320		
Patients with at least one relapse	72	56		
Median in days* [95% KI]	[S > 50%]	[S > 50%]		
% of patients without relapse after 24 months* [95% KI]	89.39 [86.92;91.86]	80.82 [76.15;85.50]		
% of patients without relapse at EOS* [95% KI]	78.96 [67.09;90.83]	79.70 [74.60;84.80]		
			0.57 [0.40;0.81]	0.002
Age = >55				
N'	197	108		
Patients with at least one relapse	15	12		
Median in days* [95% KI]	[S > 50%]	[S > 50%]		
% of patients without relapse after 24 months* [95% KI]	92.31 [88.43;96.19]	88.92 [82.08;95.76]		
% of patients without relapse at EOS* [95% KI]	90.26 [84.76;95.76]	78.81 [64.00;93.63]		
			0.80 [0.37;1.71]	0.562

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=1099)	**Placebo (N=546)**	**HR [95% CI]**	**p-value**
Interaction Test				0.093
Sex = F				
N'	643	315		
Patients with at least one relapse	83	63		
Median in days* [95% KI]	[S > 50%]	[S > 50%]		
% of patients without relapse after 24 months* [95% KI]	86.29 [83.41;89.17]	78.47 [73.44;83.50]		
% of patients without relapse at EOS* [95% KI]	77.89 [65.99;89.79]	73.99 [67.08;80.90]		
			0.63 [0.45;0.87]	0.006
Sex = M				
N'	418	213		
Patients with at least one relapse	30	37		
Median in days* [95% KI]	[S > 50%]	[S > 50%]		
% of patients without relapse after 24 months* [95% KI]	93.03 [90.47;95.59]	81.38 [75.88;86.88]		
% of patients without relapse at EOS* [95% KI]	87.98 [80.49;95.46]	81.38 [75.88;86.88]		
			0.38 [0.23;0.62]	<.001

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=1099)	**Placebo (N=546)**	**HR [95% CI]**	**p-value**
Interaction Test				0.857
Previous MS-DMT = N				
N'	235	111		
Patients with at least one relapse	17	13		
Median in days* [95% KI]	[S > 50%]	[S > 50%]		
% of patients without relapse after 24 months* [95% KI]	92.04 [88.37;95.70]	85.81 [77.73;93.89]		
% of patients without relapse at EOS* [95% KI]	92.04 [88.37;95.70]	81.52 [70.29;92.75]		
			0.58 [0.28;1.19]	0.138
Previous MS-DMT = Y				
N'	826	417		
Patients with at least one relapse	96	87		
Median in days* [95% KI]	[S > 50%]	[S > 50%]		
% of patients without relapse after 24 months* [95% KI]	88.14 [85.78;90.50]	78.01 [73.82;82.21]		
% of patients without relapse at EOS* [95% KI]	79.64 [70.56;88.73]	75.75 [70.57;80.93]		
			0.54 [0.40;0.72]	<.001

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=1099)	**Placebo (N=546)**	**HR [95% CI]**	**p-value**
Interaction Test				0.572
Previous IFN-beta 1b = N				
N'	726	380		
Patients with at least one relapse	76	68		
Median in days* [95% KI]	[S > 50%]	[S > 50%]		
% of patients without relapse after 24 months* [95% KI]	89.02 [86.57;91.46]	80.63 [76.19;85.06]		
% of patients without relapse at EOS* [95% KI]	81.51 [71.80;91.22]	77.08 [71.26;82.90]		
			0.56 [0.40;0.78]	<.001
Previous IFN-beta 1b = Y				
N'	335	148		
Patients with at least one relapse	37	32		
Median in days* [95% KI]	[S > 50%]	[S > 50%]		
% of patients without relapse after 24 months* [95% KI]	88.94 [85.40;92.48]	76.85 [69.74;83.97]		
% of patients without relapse at EOS* [95% KI]	84.37 [78.00;90.74]	76.85 [69.74;83.97]		
			0.47 [0.29;0.77]	0.002

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=1099)	**Placebo (N=546)**	**HR [95% CI]**	**p-value**
Interaction Test				0.289
Rapid evolvement = N				
N'	810	389		
Patients with at least one relapse	80	63		
Median in days* [95% KI]	[S > 50%]	[S > 50%]		
% of patients without relapse after 24 months* [95% KI]	89.87 [87.64;92.11]	82.54 [78.44;86.64]		
% of patients without relapse at EOS* [95% KI]	85.31 [80.62;90.00]	79.17 [73.12;85.22]		
			0.60 [0.43;0.83]	0.002
Rapid evolvement = Y				
N'	251	139		
Patients with at least one relapse	33	37		
Median in days* [95% KI]	[S > 50%]	[S > 50%]		
% of patients without relapse after 24 months* [95% KI]	86.24 [81.77;90.72]	72.08 [64.10;80.06]		
% of patients without relapse at EOS* [95% KI]	86.24 [81.77;90.72]	70.36 [61.90;78.83]		
			0.43 [0.27;0.70]	<.001

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=1099)	**Placebo (N=546)**	**HR [95% CI]**	**p-value**
Interaction Test				0.050
Moderate/severe disease course = N				
N'	192	84		
Patients with at least one relapse	11	17		
Median in days* [95% KI]	[S > 50%]	[S > 50%]		
% of patients without relapse after 24 months* [95% KI]	94.63 [91.39;97.87]	78.31 [69.06;87.55]		
% of patients without relapse at EOS* [95% KI]	92.84 [88.14;97.55]	78.31 [69.06;87.55]		
			0.27 [0.12;0.57]	<.001
Moderate/severe disease course = Y				
N'	869	444		
Patients with at least one relapse	102	83		
Median in days* [95% KI]	[S > 50%]	[S > 50%]		
% of patients without relapse after 24 months* [95% KI]	87.77 [85.43;90.11]	79.87 [75.77;83.97]		
% of patients without relapse at EOS* [95% KI]	79.88 [70.86;88.91]	76.62 [71.23;82.00]		
			0.60 [0.45;0.81]	<.001

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=1099)	**Placebo (N=546)**	**HR [95% CI]**	**p-value**
Interaction Test				0.403
Region = Europe				
N'	832	417		
Patients with at least one relapse	97	82		
Median in days* [95% KI]	[S > 50%]	[S > 50%]		
% of patients without relapse after 24 months* [95% KI]	88.08 [85.76;90.41]	79.00 [74.81;83.19]		
% of patients without relapse at EOS* [95% KI]	81.24 [73.46;89.02]	76.95 [71.96;81.95]		
			0.57 [0.43;0.77]	<.001
Region = Others				
N'	229	111		
Patients with at least one relapse	16	18		
Median in days* [95% KI]	[S > 50%]	[S > 50%]		
% of patients without relapse after 24 months* [95% KI]	92.88 [89.36;96.40]	81.80 [72.74;90.85]		
% of patients without relapse at EOS* [95% KI]	89.88 [83.18;96.59]	74.98 [59.73;90.23]		
			0.42 [0.21;0.82]	0.011

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=1099)	**Placebo (N=546)**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
N'	1099	546			
3-month CDP n (%)	289 (26.3)	173 (31.7)	0.77 [0.61;0.96] 0.022	0.83 [0.71;0.97] 0.021	-0.05 [-0.10;-0.01] 0.024

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=1099)	**Placebo (N=546)**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Interaction Test	p= 0.748				
Age = 18-30					
N'	26	12			
3-month CDP n (%)	7 (26.9)	6 (50.0)	0.37 [0.09;1.53] 0.170	0.54 [0.23;1.26] 0.153	-0.23 [-0.56;0.10] 0.171
Age = 31-40					
N'	161	91			
3-month CDP n (%)	50 (31.1)	35 (38.5)	0.72 [0.42;1.23] 0.233	0.81 [0.57;1.14] 0.227	-0.07 [-0.20;0.05] 0.238
Age = 41-55					
N'	712	331			
3-month CDP n (%)	189 (26.5)	102 (30.8)	0.81 [0.61;1.08] 0.153	0.86 [0.70;1.05] 0.149	-0.04 [-0.10;0.02] 0.159
Age = >55					
N'	200	112			
3-month CDP n (%)	43 (21.5)	30 (26.8)	0.75 [0.44;1.28] 0.291	0.80 [0.54;1.20] 0.287	-0.05 [-0.15;0.05] 0.299

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=1099)	**Placebo (N=546)**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Interaction Test	p= 0.569				
Sex = F					
N'	664	323			
3-month CDP n (%)	160 (24.1)	98 (30.3)	0.73 [0.54;0.98] 0.037	0.79 [0.64;0.98] 0.034	-0.06 [-0.12;0.00] 0.041
Sex = M					
N'	435	223			
3-month CDP n (%)	129 (29.7)	75 (33.6)	0.83 [0.59;1.18] 0.297	0.88 [0.70;1.11] 0.293	-0.04 [-0.12;0.04] 0.301

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=1099)	**Placebo (N=546)**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Interaction Test	p= 0.525				
Previous MS-DMT = N					
N'	242	114			
3-month CDP n (%)	57 (23.6)	36 (31.6)	0.67 [0.41;1.09] 0.109	0.75 [0.52;1.06] 0.103	-0.08 [-0.18;0.02] 0.118
Previous MS-DMT = Y					
N'	857	432			
3-month CDP n (%)	232 (27.1)	137 (31.7)	0.80 [0.62;1.03] 0.082	0.85 [0.72;1.02] 0.079	-0.05 [-0.10;0.01] 0.086

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=1099)	**Placebo (N=546)**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Interaction Test	p= 0.448				
Previous IFN-beta 1b = N					
N'	755	392			
3-month CDP n (%)	199 (26.4)	129 (32.9)	0.73 [0.56;0.95] 0.020	0.80 [0.67;0.96] 0.019	-0.07 [-0.12;-0.01] 0.022
Previous IFN-beta 1b = Y					
N'	344	154			
3-month CDP n (%)	90 (26.2)	44 (28.6)	0.89 [0.58;1.35] 0.575	0.92 [0.67;1.24] 0.573	-0.02 [-0.11;0.06] 0.579

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=1099)	**Placebo (N=546)**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Interaction Test	p= 0.280				
Rapid evolvement = N					
N'	835	401			
3-month CDP n (%)	207 (24.8)	113 (28.2)	0.84 [0.64;1.10] 0.203	0.88 [0.72;1.07] 0.200	-0.03 [-0.09;0.02] 0.209
Rapid evolvement = Y					
N'	264	145			
3-month CDP n (%)	82 (31.1)	60 (41.4)	0.64 [0.42;0.97] 0.036	0.75 [0.58;0.98] 0.033	-0.10 [-0.20;-0.01] 0.038

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=1099)	**Placebo (N=546)**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Interaction Test	p= 0.682				
Moderate/severe disease course = N					
N'	195	87			
3-month CDP n (%)	56 (28.7)	32 (36.8)	0.69 [0.41;1.18] 0.178	0.78 [0.55;1.11] 0.170	-0.08 [-0.20;0.04] 0.186
Moderate/severe disease course = Y					
N'	904	459			
3-month CDP n (%)	233 (25.8)	141 (30.7)	0.78 [0.61;1.00] 0.053	0.84 [0.70;1.00] 0.051	-0.05 [-0.10;0.00] 0.057

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=1099)	**Placebo (N=546)**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Interaction Test	p= 0.271				
Region = Europe					
N'	860	427			
3-month CDP n (%)	231 (26.9)	144 (33.7)	0.72 [0.56;0.93] 0.011	0.80 [0.67;0.95] 0.010	-0.07 [-0.12;-0.01] 0.012
Region = Others					
N'	239	119			
3-month CDP n (%)	58 (24.3)	29 (24.4)	0.99 [0.60;1.66] 0.983	1.00 [0.68;1.47] 0.983	0.00 [-0.10;0.09] 0.983

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=1099)	**Placebo (N=546)**	**HR [95% CI]**	**p-value**
N'	1096	545		
Patients with at least one CDP	288	173		
Median in days* [95% KI]	[S > 50%]	[S > 50%]		
% of patients without CDP after 24 months* [95% KI]	68.68 [65.45;71.91]	64.39 [59.78;68.99]		
% of patients without CDP at EOS* [95% KI]	64.21 [58.98;69.44]	56.36 [48.50;64.23]		
			0.79 [0.65;0.95]	0.013

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=1099)	**Placebo (N=546)**	**HR [95% CI]**	**p-value**
Interaction Test				0.879
Age = 18-30				
N'	25	12		
Patients with at least one CDP	7	6		
Median in days* [95% KI]	[S > 50%]	350 [279;NA]		
% of patients without CDP after 24 months* [95% KI]	59.78 [34.07;85.48]	81.80 [72.74;90.85]		
% of patients without CDP at EOS* [95% KI]	59.78 [34.07;85.48]	74.98 [59.73;90.23]		
			0.51 [0.17;1.52]	0.227
Age = 31-40				
N'	161	91		
Patients with at least one CDP	50	35		
Median in days* [95% KI]	[S > 50%]	[S > 50%]		
% of patients without CDP after 24 months* [95% KI]	65.62 [57.58;73.66]	55.05 [42.89;67.21]		
% of patients without CDP at EOS* [95% KI]	62.89 [53.56;72.21]	55.05 [42.89;67.21]		
			0.83 [0.53;1.28]	0.391

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

Table 4.2.2: 3-month CDP (FAS), Time-to-Event Analysis by Age

	Treatment groups		Comparison	
	BAF312 (N=1099)	**Placebo (N=546)**	**HR [95% CI]**	**p-value**
Age = 41-55				
N'	710	330		
Patients with at least one CDP	188	102		
Median in days* [95% KI]	[S > 50%]	[S > 50%]		
% of patients without CDP after 24 months* [95% KI]	68.40 [64.36;72.43]	65.31 [59.47;71.15]		
% of patients without CDP at EOS* [95% KI]	63.72 [56.97;70.47]	56.47 [46.47;66.48]		
			0.79 [0.62;1.01]	0.058
Age = >55				
N'	200	112		
Patients with at least one CDP	43	30		
Median in days* [95% KI]	[S > 50%]	[S > 50%]		
% of patients without CDP after 24 months* [95% KI]	73.60 [66.23;80.96]	72.09 [63.10;81.09]		
% of patients without CDP at EOS* [95% KI]	69.20 [60.10;78.30]	60.56 [42.33;78.78]		
			0.81 [0.51;1.29]	0.377

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=1099)	**Placebo (N=546)**	**HR [95% CI]**	**p-value**
Interaction Test				0.842
Sex = F				
N'	662	323		
Patients with at least one CDP	159	98		
Median in days* [95% KI]	[S > 50%]	[S > 50%]		
% of patients without CDP after 24 months* [95% KI]	70.70 [66.55;74.85]	66.26 [60.37;72.14]		
% of patients without CDP at EOS* [95% KI]	68.01 [62.95;73.06]	59.82 [50.29;69.35]		
			0.77 [0.60;1.00]	0.048
Sex = M				
N'	434	222		
Patients with at least one CDP	129	75		
Median in days* [95% KI]	[S > 50%]	[S > 50%]		
% of patients without CDP after 24 months* [95% KI]	65.82 [60.70;70.94]	61.64 [54.24;69.04]		
% of patients without CDP at EOS* [95% KI]	59.57 [50.39;68.74]	50.59 [36.87;64.30]		
			0.81 [0.60;1.07]	0.140

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=1099)	**Placebo (N=546)**	**HR [95% CI]**	**p-value**
Interaction Test				0.497
Previous MS-DMT = N				
N'	242	114		
Patients with at least one CDP	57	36		
Median in days* [95% KI]	[S > 50%]	[S > 50%]		
% of patients without CDP after 24 months* [95% KI]	68.76 [61.49;76.03]	64.45 [54.53;74.36]		
% of patients without CDP at EOS* [95% KI]	68.76 [61.49;76.03]	61.22 [49.97;72.48]		
			0.69 [0.45;1.06]	0.088
Previous MS-DMT = Y				
N'	854	431		
Patients with at least one CDP	231	137		
Median in days* [95% KI]	[S > 50%]	[S > 50%]		
% of patients without CDP after 24 months* [95% KI]	68.69 [65.09;72.28]	64.42 [59.24;69.60]		
% of patients without CDP at EOS* [95% KI]	65.42 [61.08;69.76]	55.84 [46.98;64.69]		
			0.82 [0.66;1.01]	0.062

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=1099)	**Placebo (N=546)**	**HR [95% CI]**	**p-value**
Interaction Test				0.404
Previous IFN-beta 1b = N				
N'	754	392		
Patients with at least one CDP	199	129		
Median in days* [95% KI]	[S > 50%]	[S > 50%]		
% of patients without CDP after 24 months* [95% KI]	68.31 [64.36;72.26]	62.83 [57.35;68.31]		
% of patients without CDP at EOS* [95% KI]	63.52 [56.80;70.24]	58.90 [51.96;65.83]		
			0.75 [0.60;0.94]	0.011
Previous IFN-beta 1b = Y				
N'	342	153		
Patients with at least one CDP	89	44		
Median in days* [95% KI]	[S > 50%]	923 [904;NA]		
% of patients without CDP after 24 months* [95% KI]	69.54 [63.94;75.13]	68.59 [60.27;76.92]		
% of patients without CDP at EOS* [95% KI]	66.05 [58.89;73.21]	40.92 [12.83;69.01]		
			0.90 [0.62;1.29]	0.567

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=1099)	**Placebo (N=546)**	**HR [95% CI]**	**p-value**
Interaction Test				0.180
Rapid evolvement = N				
N'	832	400		
Patients with at least one CDP	206	113		
Median in days* [95% KI]	[S > 50%]	[S > 50%]		
% of patients without CDP after 24 months* [95% KI]	70.27 [66.58;73.96]	67.64 [62.35;72.93]		
% of patients without CDP at EOS* [95% KI]	63.97 [56.49;71.46]	60.28 [51.47;69.09]		
			0.86 [0.69;1.09]	0.209
Rapid evolvement = Y				
N'	264	145		
Patients with at least one CDP	82	60		
Median in days* [95% KI]	[S > 50%]	904 [549;NA]		
% of patients without CDP after 24 months* [95% KI]	63.91 [57.28;70.55]	56.17 [47.35;65.00]		
% of patients without CDP at EOS* [95% KI]	62.64 [55.68;69.60]	47.40 [32.53;62.26]		
			0.65 [0.46;0.91]	0.013

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=1099)	**Placebo (N=546)**	**HR [95% CI]**	**p-value**
Interaction Test				0.703
Moderate/severe disease course = N				
N'	195	87		
Patients with at least one CDP	56	32		
Median in days* [95% KI]	992 [992;NA]	[S > 50%]		
% of patients without CDP after 24 months* [95% KI]	65.05 [56.96;73.14]	60.76 [49.74;71.78]		
% of patients without CDP at EOS* [95% KI]	65.05 [56.96;73.14]	55.69 [41.83;69.56]		
			0.73 [0.47;1.13]	0.153
Moderate/severe disease course = Y				
N'	901	458		
Patients with at least one CDP	232	141		
Median in days* [95% KI]	[S > 50%]	[S > 50%]		
% of patients without CDP after 24 months* [95% KI]	69.46 [65.94;72.98]	64.96 [59.87;70.06]		
% of patients without CDP at EOS* [95% KI]	66.39 [62.19;70.59]	56.37 [47.40;65.34]		
			0.80 [0.65;0.99]	0.036

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=1099)	**Placebo (N=546)**	**HR [95% CI]**	**p-value**
Interaction Test				0.269
Region = Europe				
N'	858	426		
Patients with at least one CDP	230	144		
Median in days* [95% KI]	[S > 50%]	[S > 50%]		
% of patients without CDP after 24 months* [95% KI]	69.04 [65.49;72.58]	63.50 [58.48;68.52]		
% of patients without CDP at EOS* [95% KI]	64.15 [58.51;69.80]	54.65 [46.07;63.23]		
			0.75 [0.61;0.92]	0.006
Region = Others				
N'	238	119		
Patients with at least one CDP	58	29		
Median in days* [95% KI]	[S > 50%]	[S > 50%]		
% of patients without CDP after 24 months* [95% KI]	67.80 [59.81;75.79]	67.16 [53.22;81.11]		
% of patients without CDP at EOS* [95% KI]	67.80 [59.81;75.79]	67.16 [53.22;81.11]		
			0.98 [0.63;1.54]	0.946

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=1099)	**Placebo (N=546)**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
N'	1099	546			
6-month CDP n (%)	219 (19.9)	139 (25.5)	0.73 [0.57;0.93] 0.011	0.78 [0.65;0.94] 0.010	-0.06 [-0.10;-0.01] 0.013

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=1099)	**Placebo (N=546)**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Interaction Test	p= 0.173				
Age = 18-30					
N'	26	12			
6-moth CDP n (%)	2 (7.7)	5 (41.7)	0.12 [0.02;0.74] 0.022	0.18 [0.04;0.82] 0.026	-0.34 [-0.64;-0.04] 0.025
Age = 31-40					
N'	161	91			
6-moth CDP n (%)	37 (23.0)	31 (34.1)	0.58 [0.33;1.02] 0.058	0.67 [0.45;1.01] 0.055	-0.11 [-0.23;0.01] 0.063
Age = 41-55					
N'	712	331			
6-moth CDP n (%)	145 (20.4)	79 (23.9)	0.82 [0.60;1.11] 0.200	0.85 [0.67;1.09] 0.197	-0.04 [-0.09;0.02] 0.209
Age = >55					
N'	200	112			
6-moth CDP n (%)	35 (17.5)	24 (21.4)	0.78 [0.44;1.39] 0.396	0.82 [0.51;1.30] 0.393	-0.04 [-0.13;0.05] 0.405

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=1099)	**Placebo (N=546)**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Interaction Test	p= 0.357				
Sex = F					
N'	664	323			
6-moth CDP n (%)	117 (17.6)	79 (24.5)	0.66 [0.48;0.91] 0.012	0.72 [0.56;0.93] 0.011	-0.07 [-0.12;-0.01] 0.015
Sex = M					
N'	435	223			
6-moth CDP n (%)	102 (23.4)	60 (26.9)	0.83 [0.57;1.20] 0.330	0.87 [0.66;1.15] 0.327	-0.03 [-0.11;0.04] 0.337

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=1099)	**Placebo (N=546)**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Interaction Test	p= 0.373				
Previous MS-DMT = N					
N'	242	114			
6-moth CDP n (%)	37 (15.3)	27 (23.7)	0.58 [0.33;1.01] 0.056	0.65 [0.41;1.01] 0.053	-0.08 [-0.17;0.01] 0.068
Previous MS-DMT = Y					
N'	857	432			
6-moth CDP n (%)	182 (21.2)	112 (25.9)	0.77 [0.59;1.01] 0.059	0.82 [0.67;1.01] 0.056	-0.05 [-0.10;0.00] 0.064

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=1099)	**Placebo (N=546)**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Interaction Test	p= 0.125				
Previous IFN-beta 1b = N					
N'	755	392			
6-moth CDP n (%)	144 (19.1)	105 (26.8)	0.64 [0.48;0.86] 0.003	0.71 [0.57;0.89] 0.002	-0.08 [-0.13;-0.03] 0.004
Previous IFN-beta 1b = Y					
N'	344	154			
6-moth CDP n (%)	75 (21.8)	34 (22.1)	0.98 [0.62;1.56] 0.945	0.99 [0.69;1.41] 0.945	0.00 [-0.08;0.08] 0.945

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=1099)	**Placebo (N=546)**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Interaction Test	p= 0.284				
Rapid evolvement = N					
N'	835	401			
6-moth CDP n (%)	154 (18.4)	88 (21.9)	0.80 [0.60;1.08] 0.147	0.84 [0.67;1.06] 0.144	-0.04 [-0.08;0.01] 0.155
Rapid evolvement = Y					
N'	264	145			
6-moth CDP n (%)	65 (24.6)	51 (35.2)	0.60 [0.39;0.94] 0.024	0.70 [0.52;0.95] 0.022	-0.11 [-0.20;-0.01] 0.027

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=1099)	**Placebo (N=546)**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Interaction Test	p= 0.465				
Moderate/severe disease course = N					
N'	195	87			
6-moth CDP n (%)	45 (23.1)	22 (25.3)	0.89 [0.49;1.59] 0.687	0.91 [0.59;1.42] 0.686	-0.02 [-0.13;0.09] 0.691
Moderate/severe disease course = Y					
N'	904	459			
6-moth CDP n (%)	174 (19.2)	117 (25.5)	0.70 [0.53;0.91] 0.008	0.76 [0.61;0.93] 0.007	-0.06 [-0.11;-0.01] 0.010

N': Number of patients in the analysis
OR: Odds Ratio
RR: Relative Risk
RD: Risk Difference

Table 5.1.8: 6-month CDP (FAS), Binary Analysis by Region

	Treatment groups		Comparison		
	BAF312 (N=1099)	**Placebo (N=546)**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Interaction Test	p= 0.586				
Region = Europe					
N'	860	427			
6-moth CDP n (%)	179 (20.8)	116 (27.2)	0.70 [0.54;0.92] 0.011	0.77 [0.63;0.94] 0.010	-0.06 [-0.11;-0.01] 0.013
Region = Others					
N'	239	119			
6-moth CDP n (%)	40 (16.7)	23 (19.3)	0.84 [0.48;1.48] 0.545	0.87 [0.54;1.38] 0.543	-0.03 [-0.11;0.06] 0.551

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=1099)	**Placebo (N=546)**	**HR [95% CI]**	**p-value**
N'	1096	545		
Patients with at least one CDP	218	139		
Median in days* [95% KI]	[S > 50%]	[S > 50%]		
% of patients without CDP after 24 months* [95% KI]	76.47 [73.58;79.35]	70.81 [66.47;75.14]		
% of patients without CDP at EOS* [95% KI]	75.33 [72.20;78.45]	70.02 [65.46;74.57]		
			0.74 [0.60;0.92]	0.006

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=1099)	**Placebo (N=546)**	**HR [95% CI]**	**p-value**
Interaction Test				0.302
Age = 18-30				
N'	25	12		
Patients with at least one CDP	2	5		
Median in days* [95% KI]	[S > 50%]	[S > 50%]		
% of patients without CDP after 24 months* [95% KI]	90.51 [77.87;100.0]	67.16 [53.22;81.11]		
% of patients without CDP at EOS* [95% KI]	90.51 [77.87;100.0]	67.16 [53.22;81.11]		
			0.17 [0.03;0.87]	0.034
Age = 31-40				
N'	161	91		
Patients with at least one CDP	37	31		
Median in days* [95% KI]	[S > 50%]	[S > 50%]		
% of patients without CDP after 24 months* [95% KI]	74.40 [67.08;81.72]	61.20 [49.57;72.82]		
% of patients without CDP at EOS* [95% KI]	74.40 [67.08;81.72]	61.20 [49.57;72.82]		
			0.67 [0.41;1.08]	0.100

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

Table 5.2.2: 6-month CDP (FAS), Time-to-Event Analysis by Age

	Treatment groups		Comparison	
	BAF312 (N=1099)	**Placebo (N=546)**	**HR [95% CI]**	**p-value**
Age = 41-55				
N'	710	330		
Patients with at least one CDP	144	79		
Median in days* [95% KI]	[S > 50%]	[S > 50%]		
% of patients without CDP after 24 months* [95% KI]	76.15 [72.57;79.73]	72.37 [66.89;77.84]		
% of patients without CDP at EOS* [95% KI]	75.13 [71.32;78.94]	70.92 [64.86;76.97]		
			0.78 [0.59;1.03]	0.082
Age = >55				
N'	200	112		
Patients with at least one CDP	35	24		
Median in days* [95% KI]	[S > 50%]	[S > 50%]		
% of patients without CDP after 24 months* [95% KI]	78.08 [71.21;84.96]	76.41 [68.00;84.82]		
% of patients without CDP at EOS* [95% KI]	75.79 [67.78;83.80]	76.41 [68.00;84.82]		
			0.83 [0.49;1.41]	0.495

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=1099)	**Placebo (N=546)**	**HR [95% CI]**	**p-value**
Interaction Test				0.435
Sex = F				
N'	662	323		
Patients with at least one CDP	116	79		
Median in days* [95% KI]	[S > 50%]	[S > 50%]		
% of patients without CDP after 24 months* [95% KI]	78.91 [75.27;82.54]	72.03 [66.44;77.62]		
% of patients without CDP at EOS* [95% KI]	77.33 [73.17;81.50]	72.03 [66.44;77.62]		
			0.69 [0.52;0.92]	0.011
Sex = M				
N'	434	222		
Patients with at least one CDP	102	60		
Median in days* [95% KI]	[S > 50%]	[S > 50%]		
% of patients without CDP after 24 months* [95% KI]	72.96 [68.28;77.63]	68.98 [62.05;75.91]		
% of patients without CDP at EOS* [95% KI]	72.34 [67.55;77.13]	67.16 [59.56;74.77]		
			0.82 [0.59;1.13]	0.218

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=1099)	**Placebo (N=546)**	**HR [95% CI]**	**p-value**
Interaction Test				0.288
Previous MS-DMT = N				
N'	242	114		
Patients with at least one CDP	37	27		
Median in days* [95% KI]	[S > 50%]	[S > 50%]		
% of patients without CDP after 24 months* [95% KI]	79.32 [73.08;85.57]	73.32 [64.44;82.20]		
% of patients without CDP at EOS* [95% KI]	79.32 [73.08;85.57]	73.32 [64.44;82.20]		
			0.58 [0.35;0.96]	0.035
Previous MS-DMT = Y				
N'	854	431		
Patients with at least one CDP	181	112		
Median in days* [95% KI]	[S > 50%]	[S > 50%]		
% of patients without CDP after 24 months* [95% KI]	75.72 [72.48;78.96]	70.24 [65.32;75.16]		
% of patients without CDP at EOS* [95% KI]	74.22 [70.61;77.82]	69.31 [64.14;74.49]		
			0.79 [0.62;1.00]	0.049

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=1099)	**Placebo (N=546)**	**HR [95% CI]**	**p-value**
Interaction Test				0.098
Previous IFN-beta 1b = N				
N'	754	392		
Patients with at least one CDP	144	105		
Median in days* [95% KI]	[S > 50%]	[S > 50%]		
% of patients without CDP after 24 months* [95% KI]	77.14 [73.66;80.62]	69.41 [64.24;74.59]		
% of patients without CDP at EOS* [95% KI]	76.11 [72.38;79.84]	69.41 [64.24;74.59]		
			0.66 [0.51;0.85]	0.001
Previous IFN-beta 1b = Y				
N'	342	153		
Patients with at least one CDP	74	34		
Median in days* [95% KI]	[S > 50%]	[S > 50%]		
% of patients without CDP after 24 months* [95% KI]	75.01 [69.87;80.15]	74.64 [66.86;82.42]		
% of patients without CDP at EOS* [95% KI]	73.48 [67.63;79.32]	71.40 [61.70;81.09]		
			0.99 [0.66;1.49]	0.957

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=1099)	**Placebo (N=546)**	**HR [95% CI]**	**p-value**
Interaction Test				0.210
Rapid evolvement = N				
N'	832	400		
Patients with at least one CDP	153	88		
Median in days* [95% KI]	[S > 50%]	[S > 50%]		
% of patients without CDP after 24 months* [95% KI]	78.21 [74.98;81.45]	74.27 [69.41;79.12]		
% of patients without CDP at EOS* [95% KI]	76.58 [72.91;80.26]	74.27 [69.41;79.12]		
			0.82 [0.63;1.07]	0.137
Rapid evolvement = Y				
N'	264	145		
Patients with at least one CDP	65	51		
Median in days* [95% KI]	[S > 50%]	[S > 50%]		
% of patients without CDP after 24 months* [95% KI]	71.19 [65.00;77.37]	62.02 [53.35;70.70]		
% of patients without CDP at EOS* [95% KI]	71.19 [65.00;77.37]	59.88 [50.55;69.22]		
			0.61 [0.42;0.89]	0.010

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=1099)	**Placebo (N=546)**	**HR [95% CI]**	**p-value**
Interaction Test				0.424
Moderate/severe disease course = N				
N'	195	87		
Patients with at least one CDP	45	22		
Median in days* [95% KI]	[S > 50%]	[S > 50%]		
% of patients without CDP after 24 months* [95% KI]	72.00 [64.67;79.33]	72.15 [62.09;82.20]		
% of patients without CDP at EOS* [95% KI]	72.00 [64.67;79.33]	72.15 [62.09;82.20]		
			0.89 [0.53;1.50]	0.670
Moderate/severe disease course = Y				
N'	901	458		
Patients with at least one CDP	173	117		
Median in days* [95% KI]	[S > 50%]	[S > 50%]		
% of patients without CDP after 24 months* [95% KI]	77.44 [74.32;80.56]	70.45 [65.62;75.29]		
% of patients without CDP at EOS* [95% KI]	76.04 [72.58;79.50]	69.51 [64.41;74.62]		
			0.71 [0.56;0.90]	0.004

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=1099)	**Placebo (N=546)**	**HR [95% CI]**	**p-value**
Interaction Test				0.584
Region = Europe				
N'	858	426		
Patients with at least one CDP	178	116		
Median in days* [95% KI]	[S > 50%]	[S > 50%]		
% of patients without CDP after 24 months* [95% KI]	76.08 [72.88;79.28]	69.79 [65.04;74.53]		
% of patients without CDP at EOS* [95% KI]	74.82 [71.35;78.28]	68.93 [63.96;73.91]		
			0.72 [0.57;0.91]	0.007
Region = Others				
N'	238	119		
Patients with at least one CDP	40	23		
Median in days* [95% KI]	[S > 50%]	[S > 50%]		
% of patients without CDP after 24 months* [95% KI]	78.73 [72.00;85.46]	72.99 [58.69;87.29]		
% of patients without CDP at EOS* [95% KI]	78.73 [72.00;85.46]	72.99 [58.69;87.29]		
			0.85 [0.51;1.41]	0.524

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=1099)	**Placebo (N=546)**	**Total (N=1645)**
Return Rate n (%)*			
Baseline	1067 (97.1)	536 (98.2)	1603 (97.4)
Month 06	959 (87.3)	482 (88.3)	1441 (87.6)
Month 12	862 (78.4)	411 (75.3)	1273 (77.4)
Month 18	605 (55.1)	285 (52.2)	890 (54.1)
Month 24	372 (33.8)	172 (31.5)	544 (33.1)

* 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=1099)	**Placebo (N=546)**	**Mean Difference [95% CI]**	**p-value**
N'	972	496		
Baseline Mean (SD)	0.04 (0.67)	0.05 (0.65)		
Month 12 Adjusted Mean Change (SE)	0.00 (0.01)	-0.02 (0.02)	0.02 [-0.03;0.07]	0.373
Month 24 Adjusted Mean Change (SE)	-0.07 (0.02)	-0.07 (0.03)	-0.01 [-0.08;0.07]	0.856

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=1099)	**Placebo (N=546)**	**Mean Difference [95% CI]**	**p-value**
Interaction Test				0.124
Age = 18-30				
N'	20	11		
Baseline Mean (SD)	-0.18 (0.79)	-0.03 (0.79)		
Month 12 Adjusted Mean Change (SE)	0.06 (0.10)	-0.15 (0.15)	0.22 [-0.14;0.57]	0.237
Month 24 Adjusted Mean Change (SE)	-0.08 (0.18)	-0.41 (0.23)	0.33 [-0.24;0.90]	0.254
Age = 31-40				
N'	142	86		
Baseline Mean (SD)	-0.04 (0.74)	0.09 (0.66)		
Month 12 Adjusted Mean Change (SE)	0.00 (0.04)	-0.02 (0.05)	0.02 [-0.10;0.14]	0.775
Month 24 Adjusted Mean Change (SE)	-0.08 (0.06)	-0.17 (0.07)	0.09 [-0.09;0.26]	0.351
Age = 41-55				
N'	631	294		
Baseline Mean (SD)	0.06 (0.65)	0.07 (0.62)		
Month 12 Adjusted Mean Change (SE)	-0.01 (0.02)	-0.02 (0.03)	0.01 [-0.05;0.07]	0.694
Month 24 Adjusted Mean Change (SE)	-0.10 (0.03)	-0.04 (0.04)	-0.06 [-0.15;0.03]	0.189
Age = >55				
N'	179	105		
Baseline Mean (SD)	0.03 (0.65)	-0.05 (0.68)		
Month 12 Adjusted Mean Change (SE)	0.02 (0.03)	-0.02 (0.04)	0.04 [-0.07;0.15]	0.476
Month 24 Adjusted Mean Change (SE)	0.01 (0.05)	-0.05 (0.07)	0.06 [-0.11;0.22]	0.489

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=1099)	**Placebo (N=546)**	**Mean Difference [95% CI]**	**p-value**
Interaction Test				0.004
Sex = F				
N'	578	295		
Baseline Mean (SD)	0.06 (0.71)	0.05 (0.66)		
Month 12 Adjusted Mean Change (SE)	0.03 (0.02)	-0.06 (0.03)	0.09 [0.03;0.15]	0.006
Month 24 Adjusted Mean Change (SE)	-0.05 (0.03)	-0.07 (0.04)	0.03 [-0.07;0.12]	0.574
Sex = M				
N'	394	201		
Baseline Mean (SD)	0.01 (0.61)	0.04 (0.62)		
Month 12 Adjusted Mean Change (SE)	-0.05 (0.02)	0.03 (0.03)	-0.07 [-0.15;0.00]	0.052
Month 24 Adjusted Mean Change (SE)	-0.12 (0.03)	-0.06 (0.05)	-0.05 [-0.17;0.06]	0.354

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=1099)	**Placebo (N=546)**	**Mean Difference [95% CI]**	**p-value**
Interaction Test				0.639
Previous MS-DMT = N				
N'	213	103		
Baseline Mean (SD)	0.15 (0.62)	0.06 (0.59)		
Month 12 Adjusted Mean Change (SE)	0.06 (0.03)	0.06 (0.04)	0.00 [-0.11;0.10]	0.962
Month 24 Adjusted Mean Change (SE)	0.00 (0.04)	0.03 (0.07)	-0.03 [-0.18;0.13]	0.720
Previous MS-DMT = Y				
N'	759	393		
Baseline Mean (SD)	0.01 (0.68)	0.04 (0.66)		
Month 12 Adjusted Mean Change (SE)	-0.02 (0.02)	-0.04 (0.02)	0.03 [-0.03;0.08]	0.330
Month 24 Adjusted Mean Change (SE)	-0.10 (0.02)	-0.09 (0.03)	0.00 [-0.08;0.08]	0.943

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=1099)	**Placebo (N=546)**	**Mean Difference [95% CI]**	**p-value**
Interaction Test				0.277
Previous IFN-beta 1b = N				
N'	669	351		
Baseline Mean (SD)	0.06 (0.69)	0.09 (0.61)		
Month 12 Adjusted Mean Change (SE)	-0.01 (0.02)	0.00 (0.02)	0.00 [-0.06;0.05]	0.883
Month 24 Adjusted Mean Change (SE)	-0.06 (0.03)	-0.05 (0.04)	-0.02 [-0.10;0.07]	0.699
Previous IFN-beta 1b = Y				
N'	303	145		
Baseline Mean (SD)	-0.01 (0.63)	-0.06 (0.73)		
Month 12 Adjusted Mean Change (SE)	0.02 (0.03)	-0.07 (0.04)	0.08 [0.00;0.17]	0.060
Month 24 Adjusted Mean Change (SE)	-0.10 (0.04)	-0.12 (0.06)	0.02 [-0.11;0.15]	0.762

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=1099)	**Placebo (N=546)**	**Mean Difference [95% CI]**	**p-value**
Interaction Test				0.240
Rapid evolvement = N				
N'	728	361		
Baseline Mean (SD)	0.00 (0.67)	0.02 (0.66)		
Month 12 Adjusted Mean Change (SE)	-0.01 (0.02)	-0.01 (0.02)	0.00 [-0.05;0.06]	0.948
Month 24 Adjusted Mean Change (SE)	-0.08 (0.02)	-0.05 (0.04)	-0.03 [-0.11;0.06]	0.548
Rapid evolvement = Y				
N'	244	135		
Baseline Mean (SD)	0.16 (0.66)	0.11 (0.61)		
Month 12 Adjusted Mean Change (SE)	0.03 (0.03)	-0.05 (0.04)	0.08 [-0.02;0.17]	0.102
Month 24 Adjusted Mean Change (SE)	-0.06 (0.04)	-0.10 (0.05)	0.04 [-0.09;0.17]	0.519

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=1099)	**Placebo (N=546)**	**Mean Difference [95% CI]**	**p-value**
Interaction Test				0.980
Moderate/severe disease course = N				
N'	181	82		
Baseline Mean (SD)	0.35 (0.49)	0.38 (0.47)		
Month 12 Adjusted Mean Change (SE)	0.07 (0.03)	0.05 (0.05)	0.02 [-0.09;0.13]	0.728
Month 24 Adjusted Mean Change (SE)	0.04 (0.05)	0.07 (0.07)	-0.03 [-0.19;0.14]	0.751
Moderate/severe disease course = Y				
N'	791	414		
Baseline Mean (SD)	-0.03 (0.68)	-0.02 (0.65)		
Month 12 Adjusted Mean Change (SE)	-0.02 (0.02)	-0.04 (0.02)	0.02 [-0.03;0.07]	0.446
Month 24 Adjusted Mean Change (SE)	-0.10 (0.02)	-0.10 (0.03)	0.00 [-0.08;0.08]	0.972

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=1099)	**Placebo (N=546)**	**Mean Difference [95% CI]**	**p-value**
Interaction Test				0.183
Region = Europe				
N'	770	394		
Baseline Mean (SD)	0.06 (0.67)	0.06 (0.63)		
Month 12 Adjusted Mean Change (SE)	0.00 (0.02)	-0.01 (0.02)	0.00 [-0.05;0.06]	0.907
Month 24 Adjusted Mean Change (SE)	-0.07 (0.02)	-0.05 (0.03)	-0.02 [-0.10;0.05]	0.542
Region = Others				
N'	202	102		
Baseline Mean (SD)	-0.03 (0.68)	-0.02 (0.70)		
Month 12 Adjusted Mean Change (SE)	0.01 (0.03)	-0.09 (0.05)	0.10 [-0.01;0.21]	0.074
Month 24 Adjusted Mean Change (SE)	-0.11 (0.06)	-0.21 (0.09)	0.10 [-0.12;0.32]	0.364

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=1099)	**Placebo (N=546)**	**Total (N=1645)**
Return Rate n (%)*			
Baseline	1082 (98.5)	538 (98.5)	1620 (98.5)
Month 06	995 (90.5)	501 (91.8)	1496 (90.9)
Month 12	906 (82.4)	440 (80.6)	1346 (81.8)
Month 18	634 (57.7)	309 (56.6)	943 (57.3)
Month 24	395 (35.9)	191 (35.0)	586 (35.6)

* 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=1099)	**Placebo (N=546)**	**Mean Difference [95% CI]**	**p-value**
N'	1011	509		
Baseline Mean (SD)	39.47 (14.39)	39.46 (13.86)		
Month 12 Adjusted Mean Change (SE)	2.25 (0.30)	1.80 (0.43)	0.45 [-0.57;1.47]	0.387
Month 24 Adjusted Mean Change (SE)	2.98 (0.40)	2.38 (0.58)	0.59 [-0.79;1.98]	0.401

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=1099)	**Placebo (N=546)**	**Mean Difference [95% CI]**	**p-value**
Interaction Test				0.932
Age = 18-30				
N'	23	12		
Baseline Mean (SD)	36.09 (16.47)	38.75 (15.59)		
Month 12 Adjusted Mean Change (SE)	3.85 (2.04)	2.90 (3.14)	0.95 [-6.40;8.30]	0.800
Month 24 Adjusted Mean Change (SE)	5.65 (3.32)	2.14 (4.01)	3.51 [-6.70;13.73]	0.500
Age = 31-40				
N'	150	88		
Baseline Mean (SD)	38.79 (14.38)	40.88 (13.85)		
Month 12 Adjusted Mean Change (SE)	3.06 (0.77)	3.19 (1.02)	-0.14 [-2.65;2.38]	0.915
Month 24 Adjusted Mean Change (SE)	1.85 (1.07)	1.71 (1.38)	0.14 [-3.29;3.57]	0.937
Age = 41-55				
N'	654	303		
Baseline Mean (SD)	40.07 (14.16)	39.54 (13.55)		
Month 12 Adjusted Mean Change (SE)	2.18 (0.37)	1.53 (0.55)	0.65 [-0.66;1.95]	0.332
Month 24 Adjusted Mean Change (SE)	3.21 (0.50)	2.61 (0.74)	0.61 [-1.15;2.36]	0.497
Age = >55				
N'	184	106		
Baseline Mean (SD)	38.34 (14.89)	38.14 (14.62)		
Month 12 Adjusted Mean Change (SE)	1.66 (0.72)	1.34 (0.93)	0.32 [-1.98;2.62]	0.786
Month 24 Adjusted Mean Change (SE)	2.65 (0.96)	2.45 (1.32)	0.19 [-3.01;3.40]	0.906

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=1099)	**Placebo (N=546)**	**Mean Difference [95% CI]**	**p-value**
Interaction Test				0.012
Sex = F				
N'	603	303		
Baseline Mean (SD)	38.80 (14.72)	38.98 (13.68)		
Month 12 Adjusted Mean Change (SE)	2.55 (0.39)	0.99 (0.55)	1.56 [0.23;2.88]	0.021
Month 24 Adjusted Mean Change (SE)	3.48 (0.54)	2.13 (0.74)	1.35 [-0.45;3.15]	0.141
Sex = M				
N'	408	206		
Baseline Mean (SD)	40.48 (13.84)	40.16 (14.14)		
Month 12 Adjusted Mean Change (SE)	1.82 (0.47)	2.99 (0.67)	-1.17 [-2.77;0.44]	0.153
Month 24 Adjusted Mean Change (SE)	2.30 (0.61)	2.62 (0.93)	-0.32 [-2.51;1.86]	0.771

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=1099)	**Placebo (N=546)**	**Mean Difference [95% CI]**	**p-value**
Interaction Test				0.928
Previous MS-DMT = N				
N'	220	105		
Baseline Mean (SD)	39.43 (13.68)	37.94 (14.25)		
Month 12 Adjusted Mean Change (SE)	2.54 (0.64)	2.65 (0.94)	-0.11 [-2.34;2.12]	0.923
Month 24 Adjusted Mean Change (SE)	3.35 (0.85)	1.93 (1.29)	1.42 [-1.61;4.45]	0.358
Previous MS-DMT = Y				
N'	791	404		
Baseline Mean (SD)	39.49 (14.58)	39.85 (13.75)		
Month 12 Adjusted Mean Change (SE)	2.17 (0.34)	1.58 (0.48)	0.59 [-0.56;1.74]	0.315
Month 24 Adjusted Mean Change (SE)	2.88 (0.46)	2.49 (0.65)	0.39 [-1.17;1.95]	0.624

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=1099)	**Placebo (N=546)**	**Mean Difference [95% CI]**	**p-value**
Interaction Test				0.495
Previous IFN-beta 1b = N				
N'	693	362		
Baseline Mean (SD)	39.94 (14.12)	39.84 (14.04)		
Month 12 Adjusted Mean Change (SE)	2.34 (0.36)	1.97 (0.51)	0.37 [-0.85;1.59]	0.553
Month 24 Adjusted Mean Change (SE)	3.59 (0.49)	2.47 (0.69)	1.12 [-0.53;2.78]	0.184
Previous IFN-beta 1b = Y				
N'	318	147		
Baseline Mean (SD)	38.47 (14.93)	38.52 (13.43)		
Month 12 Adjusted Mean Change (SE)	2.06 (0.54)	1.39 (0.79)	0.67 [-1.20;2.55]	0.482
Month 24 Adjusted Mean Change (SE)	1.63 (0.72)	2.20 (1.07)	-0.58 [-3.11;1.96]	0.655

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=1099)	**Placebo (N=546)**	**Mean Difference [95% CI]**	**p-value**
Interaction Test				0.079
Rapid evolvement = N				
N'	763	370		
Baseline Mean (SD)	38.96 (14.29)	39.73 (13.98)		
Month 12 Adjusted Mean Change (SE)	2.00 (0.35)	1.88 (0.50)	0.12 [-1.07;1.32]	0.843
Month 24 Adjusted Mean Change (SE)	2.55 (0.47)	2.99 (0.70)	-0.44 [-2.10;1.23]	0.607
Rapid evolvement = Y				
N'	248	139		
Baseline Mean (SD)	41.06 (14.58)	38.74 (13.59)		
Month 12 Adjusted Mean Change (SE)	3.00 (0.60)	1.58 (0.82)	1.41 [-0.57;3.40]	0.162
Month 24 Adjusted Mean Change (SE)	4.16 (0.77)	1.20 (1.02)	2.97 [0.45;5.49]	0.021

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=1099)	**Placebo (N=546)**	**Mean Difference [95% CI]**	**p-value**
Interaction Test				0.956
Moderate/severe disease course = N				
N'	182	82		
Baseline Mean (SD)	41.97 (13.12)	42.68 (12.71)		
Month 12 Adjusted Mean Change (SE)	3.04 (0.71)	2.75 (1.05)	0.29 [-2.19;2.78]	0.818
Month 24 Adjusted Mean Change (SE)	3.46 (0.93)	3.48 (1.35)	-0.02 [-3.23;3.19]	0.992
Moderate/severe disease course = Y				
N'	829	427		
Baseline Mean (SD)	38.93 (14.60)	38.84 (14.01)		
Month 12 Adjusted Mean Change (SE)	2.08 (0.33)	1.61 (0.47)	0.47 [-0.66;1.59]	0.416
Month 24 Adjusted Mean Change (SE)	2.88 (0.45)	2.15 (0.64)	0.73 [-0.81;2.27]	0.350

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=1099)	**Placebo (N=546)**	**Mean Difference [95% CI]**	**p-value**
Interaction Test				0.313
Region = Europe				
N'	799	404		
Baseline Mean (SD)	39.60 (14.12)	39.29 (13.92)		
Month 12 Adjusted Mean Change (SE)	2.46 (0.33)	2.29 (0.47)	0.18 [-0.96;1.31]	0.760
Month 24 Adjusted Mean Change (SE)	3.06 (0.43)	2.74 (0.62)	0.32 [-1.17;1.80]	0.676
Region = Others				
N'	212	105		
Baseline Mean (SD)	39.00 (15.37)	40.10 (13.70)		
Month 12 Adjusted Mean Change (SE)	1.30 (0.68)	-0.20 (0.98)	1.50 [-0.83;3.84]	0.208
Month 24 Adjusted Mean Change (SE)	3.00 (1.18)	0.92 (1.79)	2.08 [-2.13;6.29]	0.332

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=1099)	**Placebo (N=546)**	**Total (N=1645)**
Return Rate n (%)*			
Baseline	1089 (99.1)	545 (99.8)	1634 (99.3)
Month 03	1050 (95.5)	528 (96.7)	1578 (95.9)
Month 06	1021 (92.9)	518 (94.9)	1539 (93.6)
Month 09	985 (89.6)	492 (90.1)	1477 (89.8)
Month 12	928 (84.4)	453 (83.0)	1381 (84.0)
Month 15	818 (74.4)	408 (74.7)	1226 (74.5)
Month 18	654 (59.5)	316 (57.9)	970 (59.0)
Month 21	531 (48.3)	259 (47.4)	790 (48.0)
Month 24	404 (36.8)	195 (35.7)	599 (36.4)

* 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=1099)	**Placebo (N=546)**	**Mean Difference [95% CI]**	**p-value**
N'	1056	535		
Baseline Mean (SD)	34.07 (18.37)	34.48 (19.92)		
Month 12 Adjusted Mean Change (SE)	1.01 (0.44)	1.01 (0.63)	0.00 [-1.50;1.51]	0.996
Month 24 Adjusted Mean Change (SE)	2.31 (0.58)	3.52 (0.82)	-1.20 [-3.18;0.78]	0.233

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=1099)	**Placebo (N=546)**	**Mean Difference [95% CI]**	**p-value**
Interaction Test				0.671
Age = 18-30				
N'	23	12		
Baseline Mean (SD)	33.89 (11.17)	35.85 (16.04)		
Month 12 Adjusted Mean Change (SE)	8.69 (3.11)	2.26 (4.61)	6.43 [-4.47;17.33]	0.247
Month 24 Adjusted Mean Change (SE)	8.88 (4.86)	3.02 (5.77)	5.87 [-8.94;20.68]	0.437
Age = 31-40				
N'	157	91		
Baseline Mean (SD)	38.91 (23.00)	34.28 (19.46)		
Month 12 Adjusted Mean Change (SE)	0.90 (1.14)	0.90 (1.52)	0.00 [-3.73;3.73]	1.000
Month 24 Adjusted Mean Change (SE)	5.21 (1.52)	4.94 (1.99)	0.27 [-4.65;5.19]	0.914
Age = 41-55				
N'	688	321		
Baseline Mean (SD)	33.75 (18.68)	34.31 (20.37)		
Month 12 Adjusted Mean Change (SE)	0.75 (0.55)	0.56 (0.81)	0.19 [-1.73;2.11]	0.846
Month 24 Adjusted Mean Change (SE)	1.83 (0.71)	3.47 (1.06)	-1.64 [-4.15;0.87]	0.201
Age = >55				
N'	188	111		
Baseline Mean (SD)	31.25 (11.77)	34.97 (19.59)		
Month 12 Adjusted Mean Change (SE)	1.17 (1.06)	2.18 (1.37)	-1.01 [-4.39;2.38]	0.560
Month 24 Adjusted Mean Change (SE)	0.84 (1.40)	2.44 (1.83)	-1.60 [-6.12;2.93]	0.488

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=1099)	**Placebo (N=546)**	**Mean Difference [95% CI]**	**p-value**
Interaction Test				0.571
Sex = F				
N'	632	317		
Baseline Mean (SD)	31.92 (16.86)	33.39 (20.48)		
Month 12 Adjusted Mean Change (SE)	0.38 (0.57)	-0.30 (0.81)	0.68 [-1.26;2.63]	0.493
Month 24 Adjusted Mean Change (SE)	1.59 (0.77)	2.54 (1.06)	-0.96 [-3.52;1.61]	0.465
Sex = M				
N'	424	218		
Baseline Mean (SD)	37.28 (20.01)	36.06 (19.02)		
Month 12 Adjusted Mean Change (SE)	1.94 (0.70)	2.92 (0.98)	-0.97 [-3.33;1.38]	0.418
Month 24 Adjusted Mean Change (SE)	3.38 (0.89)	4.89 (1.31)	-1.52 [-4.63;1.60]	0.339

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=1099)	**Placebo (N=546)**	**Mean Difference [95% CI]**	**p-value**
Interaction Test				0.730
Previous MS-DMT = N				
N'	228	111		
Baseline Mean (SD)	32.54 (16.49)	34.67 (18.92)		
Month 12 Adjusted Mean Change (SE)	1.62 (0.95)	0.40 (1.38)	1.22 [-2.07;4.51]	0.467
Month 24 Adjusted Mean Change (SE)	2.05 (1.25)	2.24 (1.82)	-0.19 [-4.52;4.14]	0.931
Previous MS-DMT = Y				
N'	828	424		
Baseline Mean (SD)	34.50 (18.84)	34.42 (20.20)		
Month 12 Adjusted Mean Change (SE)	0.84 (0.50)	1.16 (0.70)	-0.32 [-2.01;1.37]	0.710
Month 24 Adjusted Mean Change (SE)	2.38 (0.65)	3.85 (0.92)	-1.47 [-3.69;0.76]	0.196

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=1099)	**Placebo (N=546)**	**Mean Difference [95% CI]**	**p-value**
Interaction Test				0.262
Previous IFN-beta 1b = N				
N'	725	385		
Baseline Mean (SD)	33.74 (18.57)	34.28 (19.50)		
Month 12 Adjusted Mean Change (SE)	1.39 (0.53)	1.13 (0.74)	0.27 [-1.53;2.06]	0.771
Month 24 Adjusted Mean Change (SE)	2.49 (0.70)	2.31 (0.97)	0.17 [-2.18;2.52]	0.885
Previous IFN-beta 1b = Y				
N'	331	150		
Baseline Mean (SD)	34.80 (17.94)	34.97 (21.03)		
Month 12 Adjusted Mean Change (SE)	0.16 (0.79)	0.68 (1.17)	-0.52 [-3.29;2.26]	0.714
Month 24 Adjusted Mean Change (SE)	1.92 (1.03)	6.25 (1.51)	-4.33 [-7.92;-0.74]	0.018

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=1099)	**Placebo (N=546)**	**Mean Difference [95% CI]**	**p-value**
Interaction Test				0.910
Rapid evolvement = N				
N'	799	392		
Baseline Mean (SD)	34.61 (18.94)	35.37 (20.80)		
Month 12 Adjusted Mean Change (SE)	1.21 (0.51)	0.90 (0.74)	0.31 [-1.44;2.07]	0.727
Month 24 Adjusted Mean Change (SE)	2.39 (0.68)	4.15 (0.99)	-1.76 [-4.11;0.59]	0.143
Rapid evolvement = Y				
N'	257	143		
Baseline Mean (SD)	32.40 (16.42)	32.02 (17.13)		
Month 12 Adjusted Mean Change (SE)	0.38 (0.88)	1.30 (1.20)	-0.93 [-3.85;1.99]	0.533
Month 24 Adjusted Mean Change (SE)	2.02 (1.13)	2.07 (1.50)	-0.05 [-3.75;3.64]	0.978

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=1099)	**Placebo (N=546)**	**Mean Difference [95% CI]**	**p-value**
Interaction Test				0.589
Moderate/severe disease course = N				
N'	189	85		
Baseline Mean (SD)	27.06 (8.43)	26.14 (5.52)		
Month 12 Adjusted Mean Change (SE)	-0.41 (1.05)	-1.03 (1.55)	0.62 [-3.05;4.28]	0.742
Month 24 Adjusted Mean Change (SE)	-0.36 (1.35)	-1.26 (1.98)	0.90 [-3.80;5.59]	0.708
Moderate/severe disease course = Y				
N'	867	450		
Baseline Mean (SD)	35.60 (19.56)	36.05 (21.23)		
Month 12 Adjusted Mean Change (SE)	1.32 (0.49)	1.40 (0.68)	-0.08 [-1.73;1.56]	0.921
Month 24 Adjusted Mean Change (SE)	2.89 (0.64)	4.53 (0.91)	-1.64 [-3.82;0.54]	0.139

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=1099)	**Placebo (N=546)**	**Mean Difference [95% CI]**	**p-value**
Interaction Test				0.740
Region = Europe				
N'	829	419		
Baseline Mean (SD)	33.84 (18.30)	33.51 (17.87)		
Month 12 Adjusted Mean Change (SE)	0.76 (0.49)	0.58 (0.70)	0.18 [-1.51;1.86]	0.837
Month 24 Adjusted Mean Change (SE)	2.37 (0.63)	3.07 (0.90)	-0.70 [-2.86;1.45]	0.521
Region = Others				
N'	227	116		
Baseline Mean (SD)	34.93 (18.64)	37.96 (25.82)		
Month 12 Adjusted Mean Change (SE)	1.96 (0.99)	2.86 (1.40)	-0.91 [-4.26;2.45]	0.596
Month 24 Adjusted Mean Change (SE)	0.86 (1.53)	6.89 (2.20)	-6.04 [-11.30;-0.77]	0.025

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=1099)	**Placebo (N=546)**	**Total (N=1645)**
Return Rate n (%)*			
Baseline	1090 (99.2)	544 (99.6)	1634 (99.3)
Month 03	1033 (94.0)	529 (96.9)	1562 (95.0)
Month 06	987 (89.8)	504 (92.3)	1491 (90.6)
Month 09	952 (86.6)	480 (87.9)	1432 (87.1)
Month 12	895 (81.4)	425 (77.8)	1320 (80.2)
Month 15	787 (71.6)	385 (70.5)	1172 (71.2)
Month 18	624 (56.8)	294 (53.8)	918 (55.8)
Month 21	498 (45.3)	239 (43.8)	737 (44.8)
Month 24	385 (35.0)	176 (32.2)	561 (34.1)

* 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=1099)	**Placebo (N=546)**	**Mean Difference [95% CI]**	**p-value**
N'	1045	532		
Baseline Mean (SD)	16.40 (18.95)	15.24 (17.81)		
Month 12 Adjusted Mean Change (SE)	4.28 (0.67)	4.24 (0.95)	0.03 [-2.24;2.31]	0.976
Month 24 Adjusted Mean Change (SE)	9.40 (1.05)	7.02 (1.52)	2.38 [-1.25;6.01]	0.199

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=1099)	**Placebo (N=546)**	**Mean Difference [95% CI]**	**p-value**
Interaction Test				0.727
Age = 18-30				
N'	23	12		
Baseline Mean (SD)	25.52 (33.05)	16.84 (16.30)		
Month 12 Adjusted Mean Change (SE)	1.20 (4.59)	14.40 (6.95)	-13.20 [-29.53;3.13]	0.113
Month 24 Adjusted Mean Change (SE)	13.52 (8.14)	10.39 (10.88)	3.13 [-23.56;29.82]	0.818
Age = 31-40				
N'	157	90		
Baseline Mean (SD)	17.57 (18.77)	15.73 (16.73)		
Month 12 Adjusted Mean Change (SE)	7.43 (1.73)	2.34 (2.28)	5.09 [-0.53;10.71]	0.076
Month 24 Adjusted Mean Change (SE)	10.10 (2.78)	9.88 (3.67)	0.22 [-8.83;9.27]	0.962
Age = 41-55				
N'	677	319		
Baseline Mean (SD)	16.06 (17.71)	14.39 (17.41)		
Month 12 Adjusted Mean Change (SE)	4.05 (0.82)	4.74 (1.22)	-0.69 [-3.58;2.20]	0.640
Month 24 Adjusted Mean Change (SE)	10.05 (1.29)	6.55 (1.95)	3.50 [-1.10;8.10]	0.135
Age = >55				
N'	188	111		
Baseline Mean (SD)	15.53 (20.90)	17.12 (19.88)		
Month 12 Adjusted Mean Change (SE)	2.80 (1.58)	3.68 (2.06)	-0.88 [-5.98;4.22]	0.735
Month 24 Adjusted Mean Change (SE)	5.77 (2.50)	5.87 (3.33)	-0.10 [-8.28;8.08]	0.981

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=1099)	**Placebo (N=546)**	**Mean Difference [95% CI]**	**p-value**
Interaction Test				0.011
Sex = F				
N'	622	315		
Baseline Mean (SD)	17.77 (19.93)	16.76 (18.96)		
Month 12 Adjusted Mean Change (SE)	3.11 (0.86)	5.77 (1.22)	-2.66 [-5.60;0.28]	0.076
Month 24 Adjusted Mean Change (SE)	8.15 (1.39)	7.90 (1.97)	0.25 [-4.48;4.98]	0.918
Sex = M				
N'	423	217		
Baseline Mean (SD)	14.37 (17.24)	13.04 (15.76)		
Month 12 Adjusted Mean Change (SE)	6.00 (1.05)	2.01 (1.48)	3.99 [0.43;7.55]	0.028
Month 24 Adjusted Mean Change (SE)	11.29 (1.62)	5.74 (2.39)	5.56 [-0.11;11.22]	0.055

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=1099)	**Placebo (N=546)**	**Mean Difference [95% CI]**	**p-value**
Interaction Test				0.886
Previous MS-DMT = N				
N'	227	110		
Baseline Mean (SD)	13.08 (14.38)	11.92 (11.27)		
Month 12 Adjusted Mean Change (SE)	0.88 (1.42)	1.04 (2.07)	-0.16 [-5.09;4.77]	0.950
Month 24 Adjusted Mean Change (SE)	5.93 (2.24)	3.44 (3.29)	2.49 [-5.33;10.32]	0.532
Previous MS-DMT = Y				
N'	818	422		
Baseline Mean (SD)	17.32 (19.95)	16.10 (19.06)		
Month 12 Adjusted Mean Change (SE)	5.23 (0.75)	5.08 (1.06)	0.15 [-2.40;2.70]	0.910
Month 24 Adjusted Mean Change (SE)	10.38 (1.19)	7.96 (1.71)	2.42 [-1.68;6.52]	0.246

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=1099)	**Placebo (N=546)**	**Mean Difference [95% CI]**	**p-value**
Interaction Test				0.223
Previous IFN-beta 1b = N				
N'	716	382		
Baseline Mean (SD)	16.25 (20.12)	14.01 (13.78)		
Month 12 Adjusted Mean Change (SE)	4.26 (0.80)	3.30 (1.12)	0.96 [-1.74;3.66]	0.485
Month 24 Adjusted Mean Change (SE)	9.50 (1.27)	6.24 (1.80)	3.26 [-1.08;7.59]	0.140
Previous IFN-beta 1b = Y				
N'	329	150		
Baseline Mean (SD)	16.71 (16.15)	18.37 (25.10)		
Month 12 Adjusted Mean Change (SE)	4.33 (1.20)	6.61 (1.77)	-2.28 [-6.47;1.91]	0.286
Month 24 Adjusted Mean Change (SE)	9.14 (1.88)	9.04 (2.83)	0.10 [-6.58;6.78]	0.976

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=1099)	**Placebo (N=546)**	**Mean Difference [95% CI]**	**p-value**
Interaction Test				0.156
Rapid evolvement = N				
N'	791	390		
Baseline Mean (SD)	17.56 (20.51)	16.01 (18.98)		
Month 12 Adjusted Mean Change (SE)	4.80 (0.77)	3.91 (1.11)	0.89 [-1.77;3.54]	0.512
Month 24 Adjusted Mean Change (SE)	9.60 (1.23)	6.47 (1.82)	3.13 [-1.18;7.44]	0.155
Rapid evolvement = Y				
N'	254	142		
Baseline Mean (SD)	12.79 (12.31)	13.11 (13.91)		
Month 12 Adjusted Mean Change (SE)	2.71 (1.33)	5.15 (1.81)	-2.45 [-6.86;1.96]	0.276
Month 24 Adjusted Mean Change (SE)	8.63 (2.05)	8.46 (2.79)	0.18 [-6.62;6.98]	0.960

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=1099)	**Placebo (N=546)**	**Mean Difference [95% CI]**	**p-value**
Interaction Test				0.581
Moderate/severe disease course = N				
N'	188	85		
Baseline Mean (SD)	7.97 (6.66)	7.39 (2.91)		
Month 12 Adjusted Mean Change (SE)	-0.26 (1.56)	0.46 (2.32)	-0.72 [-6.21;4.76]	0.796
Month 24 Adjusted Mean Change (SE)	0.46 (2.43)	0.31 (3.53)	0.15 [-8.26;8.57]	0.971
Moderate/severe disease course = Y				
N'	857	447		
Baseline Mean (SD)	18.24 (20.23)	16.73 (19.02)		
Month 12 Adjusted Mean Change (SE)	5.29 (0.74)	4.99 (1.03)	0.31 [-2.18;2.79]	0.809
Month 24 Adjusted Mean Change (SE)	11.37 (1.16)	8.43 (1.67)	2.94 [-1.06;6.93]	0.149

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=1099)	**Placebo (N=546)**	**Mean Difference [95% CI]**	**p-value**
Interaction Test				0.382
Region = Europe				
N'	822	416		
Baseline Mean (SD)	15.80 (18.57)	14.35 (16.91)		
Month 12 Adjusted Mean Change (SE)	4.57 (0.75)	3.81 (1.06)	0.76 [-1.79;3.31]	0.559
Month 24 Adjusted Mean Change (SE)	9.11 (1.14)	6.21 (1.65)	2.90 [-1.05;6.84]	0.149
Region = Others				
N'	223	116		
Baseline Mean (SD)	18.61 (20.19)	18.42 (20.46)		
Month 12 Adjusted Mean Change (SE)	2.99 (1.48)	5.90 (2.08)	-2.90 [-7.92;2.11]	0.256
Month 24 Adjusted Mean Change (SE)	11.88 (2.86)	11.61 (4.20)	0.27 [-9.71;10.25]	0.958

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=1099)	**Placebo (N=546)**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
N'	1099	546			
Worsening of T25W of ≥20% n(%)	436 (39.7)	226 (41.4)	0.93 [0.76;1.15] 0.502	0.96 [0.85;1.08] 0.501	-0.02 [-0.07;0.03] 0.504

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=1099)	**Placebo (N=546)**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Interaction Test	p= 0.756				
Age = 18-30					
N'	26	12			
Worsening of T25W of ≥20% n (%)	10 (38.5)	7 (58.3)	0.45 [0.11;1.80] 0.257	0.66 [0.33;1.30] 0.231	-0.20 [-0.53;0.14] 0.246
Age = 31-40					
N'	161	91			
Worsening of T25W of ≥20% n (%)	69 (42.9)	42 (46.2)	0.87 [0.52;1.47] 0.613	0.93 [0.70;1.23] 0.610	-0.03 [-0.16;0.09] 0.613
Age = 41-55					
N'	712	331			
Worsening of T25W of ≥20% n (%)	288 (40.4)	137 (41.4)	0.96 [0.74;1.25] 0.774	0.98 [0.84;1.14] 0.773	-0.01 [-0.07;0.05] 0.774
Age = >55					
N'	200	112			
Worsening of T25W of ≥20% n (%)	69 (34.5)	40 (35.7)	0.95 [0.58;1.54] 0.829	0.97 [0.71;1.32] 0.829	-0.01 [-0.12;0.10] 0.830

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=1099)	**Placebo (N=546)**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Interaction Test	p= 0.239				
Sex = F					
N'	664	323			
Worsening of T25W of ≥20% n (%)	242 (36.4)	131 (40.6)	0.84 [0.64;1.10] 0.212	0.90 [0.76;1.06] 0.207	-0.04 [-0.11;0.02] 0.214
Sex = M					
N'	435	223			
Worsening of T25W of ≥20% n (%)	194 (44.6)	95 (42.6)	1.08 [0.78;1.50] 0.625	1.05 [0.87;1.26] 0.627	0.02 [-0.06;0.10] 0.625

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=1099)	**Placebo (N=546)**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Interaction Test	p= 0.206				
Previous MS-DMT = N					
N'	242	114			
Worsening of T25W of ≥20% n (%)	73 (30.2)	43 (37.7)	0.71 [0.45;1.14] 0.157	0.80 [0.59;1.08] 0.150	-0.08 [-0.18;0.03] 0.163
Previous MS-DMT = Y					
N'	857	432			
Worsening of T25W of ≥20% n (%)	363 (42.4)	183 (42.4)	1.00 [0.79;1.26] 0.999	1.00 [0.87;1.14] 0.999	0.00 [-0.06;0.06] 0.999

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=1099)	**Placebo (N=546)**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Interaction Test	p= 0.287				
Previous IFN-beta 1b = N					
N'	755	392			
Worsening of T25W of ≥20% n (%)	290 (38.4)	151 (38.5)	1.00 [0.77;1.28] 0.971	1.00 [0.85;1.16] 0.971	0.00 [-0.06;0.06] 0.971
Previous IFN-beta 1b = Y					
N'	344	154			
Worsening of T25W of ≥20% n (%)	146 (42.4)	75 (48.7)	0.78 [0.53;1.14] 0.194	0.87 [0.71;1.07] 0.185	-0.06 [-0.16;0.03] 0.195

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=1099)	**Placebo (N=546)**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Interaction Test	p= 0.388				
Rapid evolvement = N					
N'	835	401			
Worsening of T25W of ≥20% n (%)	323 (38.7)	167 (41.6)	0.88 [0.69;1.13] 0.319	0.93 [0.80;1.07] 0.315	-0.03 [-0.09;0.03] 0.321
Rapid evolvement = Y					
N'	264	145			
Worsening of T25W of ≥20% n (%)	113 (42.8)	59 (40.7)	1.09 [0.72;1.65] 0.679	1.05 [0.83;1.34] 0.680	0.02 [-0.08;0.12] 0.678

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=1099)	**Placebo (N=546)**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Interaction Test	p= 0.578				
Moderate/severe disease course = N					
N'	195	87			
Worsening of T25W of ≥20% n (%)	55 (28.2)	23 (26.4)	1.09 [0.62;1.93] 0.759	1.07 [0.70;1.62] 0.760	0.02 [-0.09;0.13] 0.757
Moderate/severe disease course = Y					
N'	904	459			
Worsening of T25W of ≥20% n (%)	381 (42.1)	203 (44.2)	0.92 [0.73;1.15] 0.463	0.95 [0.84;1.08] 0.461	-0.02 [-0.08;0.03] 0.464

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=1099)	**Placebo (N=546)**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Interaction Test	p= 0.825				
Region = Europe					
N'	860	427			
Worsening of T25W of ≥20% n (%)	358 (41.6)	184 (43.1)	0.94 [0.74;1.19] 0.617	0.97 [0.84;1.11] 0.615	-0.01 [-0.07;0.04] 0.617
Region = Others					
N'	239	119			
Worsening of T25W of ≥20% n (%)	78 (32.6)	42 (35.3)	0.89 [0.56;1.41] 0.616	0.92 [0.68;1.25] 0.614	-0.03 [-0.13;0.08] 0.618

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=1099)	**Placebo (N=546)**	**HR [95% CI]**	**p-value**
N'	1087	543		
Patients with at least one worsening	432	225		
Median in days* [95% KI]	821 [722;NA]	804 [565;NA]		
% of patients without worsening after 24 months* [95% KI]	52.50 [48.87;56.14]	50.37 [45.25;55.48]		
% of patients without worsening at EOS* [95% KI]	47.99 [43.69;52.30]	44.16 [36.51;51.81]		
			0.94 [0.80;1.10]	0.440

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=1099)	**Placebo (N=546)**	**HR [95% CI]**	**p-value**
Interaction Test				0.300
Age = 18-30				
N'	25	12		
Patients with at least one worsening	10	7		
Median in days* [95% KI]	[S > 50%]	273 [103;455]		
% of patients without worsening after 24 months* [95% KI]	55.18 [34.44;75.91]	0.00 [0.00;100.0]		
% of patients without worsening at EOS* [95% KI]	55.18 [34.44;75.91]	0.00 [0.00;100.0]		
			0.41 [0.15;1.10]	0.077
Age = 31-40				
N'	160	90		
Patients with at least one worsening	69	41		
Median in days* [95% KI]	821 [449;NA]	556 [472;NA]		
% of patients without worsening after 24 months* [95% KI]	52.41 [43.73;61.09]	44.51 [32.35;56.67]		
% of patients without worsening at EOS* [95% KI]	49.33 [39.27;59.38]	44.51 [32.35;56.67]		
			1.03 [0.70;1.53]	0.866

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 6.6.2: Worsening of T25W of ≥20% (FAS), Time-to-Event Analysis by Age

	Treatment groups		Comparison	
	BAF312 (N=1099)	**Placebo (N=546)**	**HR [95% CI]**	**p-value**
Age = 41-55				
N'	703	329		
Patients with at least one worsening	284	137		
Median in days* [95% KI]	819 [717;NA]	722 [545;NA]		
% of patients without worsening after 24 months* [95% KI]	51.61 [47.05;56.17]	49.25 [42.49;56.01]		
% of patients without worsening at EOS* [95% KI]	46.57 [41.09;52.05]	45.80 [37.94;53.66]		
			0.89 [0.73;1.09]	0.269
Age = >55				
N'	199	112		
Patients with at least one worsening	69	40		
Median in days* [95% KI]	[S > 50%]	916 [906;NA]		
% of patients without worsening after 24 months* [95% KI]	55.34 [46.46;64.22]	61.34 [51.27;71.41]		
% of patients without worsening at EOS* [95% KI]	51.58 [41.90;61.26]	47.71 [29.30;66.12]		
			1.08 [0.73;1.60]	0.691

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=1099)	**Placebo (N=546)**	**HR [95% CI]**	**p-value**
Interaction Test				0.530
Sex = F				
N'	653	322		
Patients with at least one worsening	239	131		
Median in days* [95% KI]	[S > 50%]	916 [629;NA]		
% of patients without worsening after 24 months* [95% KI]	55.56 [50.86;60.27]	52.07 [45.55;58.59]		
% of patients without worsening at EOS* [95% KI]	52.55 [47.24;57.86]	48.60 [39.64;57.56]		
			0.90 [0.72;1.11]	0.318
Sex = M				
N'	434	221		
Patients with at least one worsening	193	94		
Median in days* [95% KI]	724 [617;855]	645 [542;NA]		
% of patients without worsening after 24 months* [95% KI]	48.45 [42.81;54.08]	47.88 [39.66;56.10]		
% of patients without worsening at EOS* [95% KI]	42.48 [35.76;49.20]	37.00 [23.01;50.98]		
			1.00 [0.78;1.28]	0.976

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=1099)	**Placebo (N=546)**	**HR [95% CI]**	**p-value**
Interaction Test				0.150
Previous MS-DMT = N				
N'	239	113		
Patients with at least one worsening	72	43		
Median in days* [95% KI]	[S > 50%]	[S > 50%]		
% of patients without worsening after 24 months* [95% KI]	59.93 [51.83;68.03]	56.48 [46.01;66.96]		
% of patients without worsening at EOS* [95% KI]	59.93 [51.83;68.03]	51.78 [38.73;64.82]		
			0.73 [0.50;1.07]	0.105
Previous MS-DMT = Y				
N'	848	430		
Patients with at least one worsening	360	182		
Median in days* [95% KI]	752 [633;855]	720 [547;NA]		
% of patients without worsening after 24 months* [95% KI]	50.45 [46.40;54.50]	48.93 [43.14;54.71]		
% of patients without worsening at EOS* [95% KI]	44.62 [39.63;49.62]	42.68 [34.17;51.18]		
			1.00 [0.83;1.19]	0.959

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=1099)	**Placebo (N=546)**	**HR [95% CI]**	**p-value**
Interaction Test				0.304
Previous IFN-beta 1b = N				
N'	747	390		
Patients with at least one worsening	288	150		
Median in days* [95% KI]	851 [724;NA]	906 [644;NA]		
% of patients without worsening after 24 months* [95% KI]	53.21 [48.78;57.63]	53.46 [47.37;59.54]		
% of patients without worsening at EOS* [95% KI]	49.91 [44.86;54.95]	48.03 [39.64;56.42]		
			0.99 [0.81;1.21]	0.950
Previous IFN-beta 1b = Y				
N'	340	153		
Patients with at least one worsening	144	75		
Median in days* [95% KI]	752 [555;NA]	539 [450;NA]		
% of patients without worsening after 24 months* [95% KI]	50.96 [44.58;57.33]	42.98 [33.68;52.28]		
% of patients without worsening at EOS* [95% KI]	43.81 [35.72;51.90]	34.38 [17.58;51.19]		
			0.83 [0.62;1.10]	0.191

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=1099)	**Placebo (N=546)**	**HR [95% CI]**	**p-value**
Interaction Test				0.682
Rapid evolvement = N				
N'	824	399		
Patients with at least one worsening	319	167		
Median in days* [95% KI]	821 [724;NA]	720 [546;916]		
% of patients without worsening after 24 months* [95% KI]	53.62 [49.41;57.82]	48.50 [42.31;54.68]		
% of patients without worsening at EOS* [95% KI]	47.65 [42.33;52.98]	39.25 [29.22;49.27]		
			0.92 [0.76;1.11]	0.389
Rapid evolvement = Y				
N'	263	144		
Patients with at least one worsening	113	58		
Median in days* [95% KI]	728 [582;NA]	[S > 50%]		
% of patients without worsening after 24 months* [95% KI]	49.33 [42.11;56.55]	54.70 [45.66;63.75]		
% of patients without worsening at EOS* [95% KI]	47.88 [40.34;55.42]	54.70 [45.66;63.75]		
			1.00 [0.72;1.37]	0.976

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=1099)	**Placebo (N=546)**	**HR [95% CI]**	**p-value**
Interaction Test				0.282
Moderate/severe disease course = N				
N'	194	87		
Patients with at least one worsening	55	23		
Median in days* [95% KI]	[S > 50%]	[S > 50%]		
% of patients without worsening after 24 months* [95% KI]	64.51 [55.72;73.29]	70.78 [60.25;81.31]		
% of patients without worsening at EOS* [95% KI]	55.38 [43.04;67.72]	66.06 [52.78;79.35]		
			1.21 [0.74;1.97]	0.451
Moderate/severe disease course = Y				
N'	893	456		
Patients with at least one worsening	377	202		
Median in days* [95% KI]	738 [635;NA]	635 [542;906]		
% of patients without worsening after 24 months* [95% KI]	50.01 [46.04;53.98]	46.30 [40.62;51.99]		
% of patients without worsening at EOS* [95% KI]	46.38 [41.85;50.91]	40.11 [31.73;48.49]		
			0.91 [0.76;1.08]	0.268

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 6.6.8: Worsening of T25W of ≥20% (FAS), Time-to-Event Analysis by Region

	Treatment groups		Comparison	
	BAF312 (N=1099)	**Placebo (N=546)**	**HR [95% CI]**	**p-value**
Interaction Test				0.695
Region = Europe				
N'	851	424		
Patients with at least one worsening	354	183		
Median in days* [95% KI]	820 [720;NA]	722 [547;NA]		
% of patients without worsening after 24 months* [95% KI]	52.11 [48.17;56.06]	49.72 [44.11;55.33]		
% of patients without worsening at EOS* [95% KI]	47.55 [42.93;52.18]	42.71 [34.24;51.17]		
			0.92 [0.77;1.10]	0.383
Region = Others				
N'	236	119		
Patients with at least one worsening	78	42		
Median in days* [95% KI]	738 [633;NA]	[S > 50%]		
% of patients without worsening after 24 months* [95% KI]	53.80 [43.70;63.89]	55.62 [44.42;66.83]		
% of patients without worsening at EOS* [95% KI]	49.95 [38.09;61.81]	55.62 [44.42;66.83]		
			1.00 [0.69;1.46]	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+Region+Treatment*Region+SPMS Group+BL EDSS+BL Value

Table 7.1.0: SDMT (FAS), Return Rates

	Treatment groups		
	BAF312 (N=1099)	**Placebo (N=546)**	**Total (N=1645)**
Return Rate n (%)*			
Baseline	1090 (99.2)	541 (99.1)	1631 (99.1)
Month 06	1004 (91.4)	512 (93.8)	1516 (92.2)
Month 12	924 (84.1)	448 (82.1)	1372 (83.4)
Month 18	644 (58.6)	313 (57.3)	957 (58.2)
Month 24	306 (27.8)	140 (25.6)	446 (27.1)
Month 30	87 (7.9)	35 (6.4)	122 (7.4)

* 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=1099)	**Placebo (N=546)**	**Mean Difference [95% CI]**	**p-value**
N'	1024	517		
Baseline Mean (SD)	38.92 (14.00)	39.80 (13.20)		
Month 12 Adjusted Mean Change (SE)	0.15 (0.29)	-0.94 (0.38)	1.09 [0.23;1.95]	0.013
Month 24 Adjusted Mean Change (SE)	1.42 (0.42)	-1.06 (0.59)	2.48 [1.11;3.85]	<.001

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=1099)	**Placebo (N=546)**	**Mean Difference [95% CI]**	**p-value**
Interaction Test				0.899
Age = 18-30				
N'	23	12		
Baseline Mean (SD)	36.04 (16.18)	40.00 (11.12)		
Month 12 Adjusted Mean Change (SE)	-0.74 (1.76)	0.16 (2.74)	-0.90 [-7.24;5.44]	0.781
Month 24 Adjusted Mean Change (SE)	3.82 (3.79)	-2.79 (3.96)	6.61 [-4.13;17.36]	0.227
Age = 31-40				
N'	151	87		
Baseline Mean (SD)	37.60 (15.08)	42.03 (14.52)		
Month 12 Adjusted Mean Change (SE)	0.02 (0.67)	-1.72 (0.89)	1.74 [-0.40;3.88]	0.111
Month 24 Adjusted Mean Change (SE)	0.67 (1.08)	-2.84 (1.38)	3.52 [0.10;6.93]	0.044
Age = 41-55				
N'	666	312		
Baseline Mean (SD)	39.70 (13.86)	39.58 (13.12)		
Month 12 Adjusted Mean Change (SE)	0.17 (0.35)	-0.75 (0.48)	0.93 [-0.17;2.02]	0.097
Month 24 Adjusted Mean Change (SE)	1.56 (0.51)	-0.67 (0.77)	2.22 [0.46;3.98]	0.013
Age = >55				
N'	184	106		
Baseline Mean (SD)	37.55 (13.14)	38.59 (12.44)		
Month 12 Adjusted Mean Change (SE)	0.32 (0.62)	-0.95 (0.81)	1.26 [-0.68;3.21]	0.203
Month 24 Adjusted Mean Change (SE)	1.40 (0.93)	-0.51 (1.27)	1.91 [-1.14;4.96]	0.218

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=1099)	**Placebo (N=546)**	**Mean Difference [95% CI]**	**p-value**
Interaction Test				0.238
Sex = F				
N'	615	308		
Baseline Mean (SD)	40.15 (14.26)	40.12 (13.95)		
Month 12 Adjusted Mean Change (SE)	0.55 (0.36)	-1.29 (0.48)	1.84 [0.73;2.95]	0.001
Month 24 Adjusted Mean Change (SE)	1.98 (0.54)	-0.98 (0.77)	2.97 [1.16;4.77]	0.001
Sex = M				
N'	409	209		
Baseline Mean (SD)	37.08 (13.40)	39.33 (12.03)		
Month 12 Adjusted Mean Change (SE)	-0.43 (0.42)	-0.39 (0.58)	-0.04 [-1.40;1.32]	0.954
Month 24 Adjusted Mean Change (SE)	0.66 (0.61)	-1.12 (0.91)	1.78 [-0.33;3.89]	0.099

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=1099)	**Placebo (N=546)**	**Mean Difference [95% CI]**	**p-value**
Interaction Test				0.708
Previous MS-DMT = N				
N'	221	107		
Baseline Mean (SD)	38.76 (14.57)	39.06 (11.94)		
Month 12 Adjusted Mean Change (SE)	-0.42 (0.57)	-0.73 (0.82)	0.30 [-1.59;2.20]	0.753
Month 24 Adjusted Mean Change (SE)	1.61 (0.83)	-1.53 (1.36)	3.14 [0.03;6.24]	0.047
Previous MS-DMT = Y				
N'	803	410		
Baseline Mean (SD)	38.97 (13.85)	40.00 (13.51)		
Month 12 Adjusted Mean Change (SE)	0.31 (0.32)	-1.00 (0.43)	1.31 [0.34;2.27]	0.008
Month 24 Adjusted Mean Change (SE)	1.37 (0.47)	-0.96 (0.65)	2.34 [0.80;3.87]	0.003

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=1099)	**Placebo (N=546)**	**Mean Difference [95% CI]**	**p-value**
Interaction Test				0.515
Previous IFN-beta 1b = N				
N'	701	370		
Baseline Mean (SD)	38.76 (14.03)	40.16 (13.14)		
Month 12 Adjusted Mean Change (SE)	0.72 (0.30)	-0.58 (0.42)	1.30 [0.28;2.32]	0.012
Month 24 Adjusted Mean Change (SE)	2.05 (0.47)	-0.49 (0.67)	2.54 [0.92;4.15]	0.002
Previous IFN-beta 1b = Y				
N'	323	147		
Baseline Mean (SD)	39.27 (13.95)	38.90 (13.35)		
Month 12 Adjusted Mean Change (SE)	-0.50 (0.45)	-1.11 (0.67)	0.61 [-0.97;2.19]	0.446
Month 24 Adjusted Mean Change (SE)	0.60 (0.71)	-1.86 (1.14)	2.45 [-0.19;5.09]	0.069

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 7.1.6 SDMT (FAS), Change from Baseline by Rapid Evolvement

	Treatment groups		Comparison	
	BAF312 (N=1099)	**Placebo (N=546)**	**Mean Difference [95% CI]**	**p-value**
Interaction Test				0.155
Rapid evolvement = N				
N'	773	375		
Baseline Mean (SD)	38.09 (13.94)	39.87 (12.80)		
Month 12 Adjusted Mean Change (SE)	0.48 (0.29)	-0.43 (0.42)	0.90 [-0.10;1.91]	0.078
Month 24 Adjusted Mean Change (SE)	1.79 (0.46)	-0.06 (0.73)	1.86 [0.16;3.55]	0.032
Rapid evolvement = Y				
N'	251	142		
Baseline Mean (SD)	41.48 (13.90)	39.61 (14.24)		
Month 12 Adjusted Mean Change (SE)	-0.06 (0.50)	-1.54 (0.68)	1.48 [-0.18;3.13]	0.080
Month 24 Adjusted Mean Change (SE)	1.07 (0.74)	-2.47 (0.97)	3.54 [1.15;5.93]	0.004

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 7.1.7 SDMT (FAS), Change from Baseline by Disease Course

	Treatment groups		Comparison	
	BAF312 (N=1099)	**Placebo (N=546)**	**Mean Difference [95% CI]**	**p-value**
Interaction Test				0.983
Moderate/severe disease course = N				
N'	183	83		
Baseline Mean (SD)	41.05 (12.74)	41.47 (11.97)		
Month 12 Adjusted Mean Change (SE)	1.20 (0.62)	0.11 (0.90)	1.09 [-1.00;3.19]	0.305
Month 24 Adjusted Mean Change (SE)	2.75 (0.92)	-0.18 (1.49)	2.93 [-0.47;6.34]	0.091
Moderate/severe disease course = Y				
N'	841	434		
Baseline Mean (SD)	38.46 (14.22)	39.48 (13.41)		
Month 12 Adjusted Mean Change (SE)	-0.06 (0.31)	-1.13 (0.41)	1.07 [0.13;2.02]	0.026
Month 24 Adjusted Mean Change (SE)	1.15 (0.46)	-1.21 (0.64)	2.36 [0.86;3.86]	0.002

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=1099)	**Placebo (N=546)**	**Mean Difference [95% CI]**	**p-value**
Interaction Test				N.E.
Region = Europe				
N'	806	408		
Baseline Mean (SD)	38.94 (13.84)	39.79 (12.53)		
Month 12 Adjusted Mean Change (SE)	0.45 (0.28)	-0.67 (0.40)	1.12 [0.17;2.08]	0.021
Month 24 Adjusted Mean Change (SE)	1.77 (0.42)	-0.96 (0.62)	2.73 [1.25;4.21]	<.001
Region = Others				
N'	218	109		
Baseline Mean (SD)	38.87 (14.61)	39.83 (15.51)		
Month 12 Adjusted Mean Change (SE)	-0.04 (0.58)	-1.00 (0.84)	0.95 [-1.05;2.96]	0.350
Month 24 Adjusted Mean Change (SE)	0.26 (1.05)	-0.31 (1.62)	0.57 [-3.30;4.45]	0.769

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=1099)	**Placebo (N=546)**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
N'	1099	546			
SDMT improvement by ≥4 points in 12 months	340 (30.9)	130 (23.8)	1.43 [1.13;1.81] 0.003	1.30 [1.09;1.55] 0.003	0.07 [0.03;0.12] 0.002

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=1099)	**Placebo (N=546)**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Interaction Test	p= 0.387				
Age = 18-30					
N'	26	12			
SDMT improvement by ≥4 points in 12 months	4 (15.4)	3 (25.0)	0.55 [0.10;2.94] 0.481	0.62 [0.16;2.33] 0.475	-0.10 [-0.38;0.19] 0.503
Age = 31-40					
N'	161	91			
SDMT improvement by ≥4 points in 12 months	41 (25.5)	20 (22.0)	1.21 [0.66;2.23] 0.535	1.16 [0.73;1.85] 0.538	0.03 [-0.07;0.14] 0.529
Age = 41-55					
N'	712	331			
SDMT improvement by ≥4 points in 12 months	227 (31.9)	84 (25.4)	1.38 [1.03;1.85] 0.033	1.26 [1.01;1.56] 0.036	0.07 [0.01;0.12] 0.028
Age = >55					
N'	200	112			
SDMT improvement by ≥4 points in 12 months	68 (34.0)	23 (20.5)	1.99 [1.16;3.43] 0.013	1.66 [1.10;2.50] 0.017	0.13 [0.04;0.23] 0.008

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=1099)	**Placebo (N=546)**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Interaction Test	p= 0.137				
Sex = F					
N'	664	323			
SDMT improvement by ≥4 points in 12 months	212 (31.9)	71 (22.0)	1.66 [1.22;2.27] 0.001	1.45 [1.15;1.83] 0.002	0.10 [0.04;0.16] <.001
Sex = M					
N'	435	223			
SDMT improvement by ≥4 points in 12 months	128 (29.4)	59 (26.5)	1.16 [0.81;1.66] 0.425	1.11 [0.86;1.45] 0.428	0.03 [-0.04;0.10] 0.419

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=1099)	**Placebo (N=546)**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Interaction Test	p= 0.551				
Previous MS-DMT = N					
N'	242	114			
SDMT improvement by ≥4 points in 12 months	70 (28.9)	28 (24.6)	1.25 [0.75;2.08] 0.390	1.18 [0.81;1.72] 0.396	0.04 [-0.05;0.14] 0.380
Previous MS-DMT = Y					
N'	857	432			
SDMT improvement by ≥4 points in 12 months	270 (31.5)	102 (23.6)	1.49 [1.14;1.94] 0.003	1.33 [1.10;1.62] 0.004	0.08 [0.03;0.13] 0.002

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=1099)	**Placebo (N=546)**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Interaction Test	p= 0.844				
Previous IFN-beta 1b = N					
N'	755	392			
SDMT improvement by ≥4 points in 12 months	248 (32.8)	98 (25.0)	1.47 [1.12;1.93] 0.006	1.31 [1.08;1.60] 0.007	0.08 [0.02;0.13] 0.005
Previous IFN-beta 1b = Y					
N'	344	154			
SDMT improvement by ≥4 points in 12 months	92 (26.7)	32 (20.8)	1.39 [0.88;2.20] 0.156	1.29 [0.90;1.83] 0.163	0.06 [-0.02;0.14] 0.141

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=1099)	**Placebo (N=546)**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Interaction Test	p= 0.470				
Rapid evolvement = N					
N'	835	401			
SDMT improvement by ≥4 points in 12 months	270 (32.3)	97 (24.2)	1.50 [1.14;1.96] 0.003	1.34 [1.10;1.63] 0.004	0.08 [0.03;0.13] 0.002
Rapid evolvement = Y					
N'	264	145			
SDMT improvement by ≥4 points in 12 months	70 (26.5)	33 (22.8)	1.22 [0.76;1.97] 0.403	1.17 [0.81;1.67] 0.407	0.04 [-0.05;0.12] 0.395

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=1099)	**Placebo (N=546)**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Interaction Test	p= 0.986				
Moderate/severe disease course = N					
N'	195	87			
SDMT improvement by ≥4 points in 12 months	71 (36.4)	25 (28.7)	1.42 [0.82;2.46] 0.210	1.27 [0.87;1.85] 0.221	0.08 [-0.04;0.19] 0.197
Moderate/severe disease course = Y					
N'	904	459			
SDMT improvement by ≥4 points in 12 months	269 (29.8)	105 (22.9)	1.43 [1.10;1.85] 0.007	1.30 [1.07;1.58] 0.008	0.07 [0.02;0.12] 0.006

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=1099)	**Placebo (N=546)**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Interaction Test	p= 0.187				
Region = Europe					
N'	860	427			
SDMT improvement by ≥4 points in 12 months	256 (29.8)	104 (24.4)	1.32 [1.01;1.72] 0.042	1.22 [1.00;1.49] 0.045	0.05 [0.00;0.11] 0.037
Region = Others					
N'	239	119			
SDMT improvement by ≥4 points in 12 months	84 (35.1)	26 (21.8)	1.94 [1.16;3.23] 0.011	1.61 [1.10;2.35] 0.014	0.13 [0.04;0.23] 0.007

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=1099)	**Placebo (N=546)**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
N'	1099	546			
SDMT worsening by ≥4 points in 12 months n	291 (26.5)	185 (33.9)	0.70 [0.56;0.88] 0.002	0.78 [0.67;0.91] 0.002	-0.07 [-0.12;-0.03] 0.002

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=1099)	**Placebo (N=546)**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Interaction Test	p= 0.557				
Age = 18-30					
N'	26	12			
SDMT worsening by ≥4 points in 12 months n	9 (34.6)	3 (25.0)	1.59 [0.34;7.38] 0.555	1.38 [0.45;4.22] 0.567	0.10 [-0.21;0.40] 0.538
Age = 31-40					
N'	161	91			
SDMT worsening by ≥4 points in 12 months n	42 (26.1)	36 (39.6)	0.54 [0.31;0.93] 0.027	0.66 [0.46;0.95] 0.025	-0.13 [-0.26;-0.01] 0.029
Age = 41-55					
N'	712	331			
SDMT worsening by ≥4 points in 12 months n	185 (26.0)	107 (32.3)	0.73 [0.55;0.98] 0.034	0.80 [0.66;0.98] 0.032	-0.06 [-0.12;0.00] 0.038
Age = >55					
N'	200	112			
SDMT worsening by ≥4 points in 12 months n	55 (27.5)	39 (34.8)	0.71 [0.43;1.17] 0.177	0.79 [0.56;1.11] 0.172	-0.07 [-0.18;0.03] 0.183

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=1099)	**Placebo (N=546)**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Interaction Test	p= 0.003				
Sex = F					
N'	664	323			
SDMT worsening by ≥4 points in 12 months n	166 (25.0)	124 (38.4)	0.53 [0.40;0.71] <.001	0.65 [0.54;0.79] <.001	-0.13 [-0.20;-0.07] <.001
Sex = M					
N'	435	223			
SDMT worsening by ≥4 points in 12 months n	125 (28.7)	61 (27.4)	1.07 [0.75;1.54] 0.710	1.05 [0.81;1.36] 0.710	0.01 [-0.06;0.09] 0.708

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=1099)	**Placebo (N=546)**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Interaction Test	p= 0.343				
Previous MS-DMT = N					
N'	242	114			
SDMT worsening by ≥4 points in 12 months n	69 (28.5)	36 (31.6)	0.86 [0.53;1.40] 0.554	0.90 [0.65;1.26] 0.551	-0.03 [-0.13;0.07] 0.558
Previous MS-DMT = Y					
N'	857	432			
SDMT worsening by ≥4 points in 12 months n	222 (25.9)	149 (34.5)	0.66 [0.52;0.85] 0.001	0.75 [0.63;0.89] 0.001	-0.09 [-0.14;-0.03] 0.002

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=1099)	**Placebo (N=546)**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Interaction Test	p= 0.436				
Previous IFN-beta 1b = N					
N'	755	392			
SDMT worsening by ≥4 points in 12 months n	195 (25.8)	135 (34.4)	0.66 [0.51;0.86] 0.002	0.75 [0.62;0.90] 0.002	-0.09 [-0.14;-0.03] 0.003
Previous IFN-beta 1b = Y					
N'	344	154			
SDMT worsening by ≥4 points in 12 months n	96 (27.9)	50 (32.5)	0.81 [0.53;1.21] 0.302	0.86 [0.65;1.14] 0.296	-0.05 [-0.13;0.04] 0.309

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=1099)	**Placebo (N=546)**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Interaction Test	p= 0.705				
Rapid evolvement = N					
N'	835	401			
SDMT worsening by ≥4 points in 12 months n	212 (25.4)	128 (31.9)	0.73 [0.56;0.94] 0.016	0.80 [0.66;0.96] 0.015	-0.07 [-0.12;-0.01] 0.019
Rapid evolvement = Y					
N'	264	145			
SDMT worsening by ≥4 points in 12 months n	79 (29.9)	57 (39.3)	0.66 [0.43;1.01] 0.054	0.76 [0.58;1.00] 0.051	-0.09 [-0.19;0.00] 0.057

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=1099)	**Placebo (N=546)**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Interaction Test	p= 0.108				
Moderate/severe disease course = N					
N'	195	87			
SDMT worsening by ≥4 points in 12 months n	38 (19.5)	30 (34.5)	0.46 [0.26;0.81] 0.007	0.57 [0.38;0.85] 0.006	-0.15 [-0.26;-0.04] 0.010
Moderate/severe disease course = Y					
N'	904	459			
SDMT worsening by ≥4 points in 12 months n	253 (28.0)	155 (33.8)	0.76 [0.60;0.97] 0.028	0.83 [0.70;0.98] 0.026	-0.06 [-0.11;-0.01] 0.030

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=1099)	**Placebo (N=546)**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Interaction Test	p= 0.401				
Region = Europe					
N'	860	427			
SDMT worsening by ≥4 points in 12 months n	228 (26.5)	140 (32.8)	0.74 [0.57;0.95] 0.019	0.81 [0.68;0.96] 0.018	-0.06 [-0.12;-0.01] 0.021
Region = Others					
N'	239	119			
SDMT worsening by ≥4 points in 12 months n	63 (26.4)	45 (37.8)	0.59 [0.37;0.94] 0.027	0.70 [0.51;0.95] 0.024	-0.11 [-0.22;-0.01] 0.030

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=1099)	**Placebo (N=546)**	**Total (N=1645)**
Return Rate n (%)*			
Baseline	1069 (97.3)	525 (96.2)	1594 (96.9)
Month 06	987 (89.8)	504 (92.3)	1491 (90.6)
Month 12	917 (83.4)	445 (81.5)	1362 (82.8)
Month 18	637 (58.0)	306 (56.0)	943 (57.3)
Month 24	301 (27.4)	138 (25.3)	439 (26.7)
Month 30	87 (7.9)	34 (6.2)	121 (7.4)

* 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=1099)	**Placebo (N=546)**	**Mean Difference [95% CI]**	**p-value**
N'	1003	498		
Baseline Mean (SD)	8.12 (3.40)	8.07 (3.36)		
Month 12 Adjusted Mean Change (SE)	-0.11 (0.09)	0.04 (0.12)	-0.15 [-0.42;0.12]	0.284
Month 24 Adjusted Mean Change (SE)	0.44 (0.13)	0.43 (0.19)	0.01 [-0.43;0.45]	0.964

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=1099)	**Placebo (N=546)**	**Mean Difference [95% CI]**	**p-value**
Interaction Test				0.455
Age = 18-30				
N'	23	12		
Baseline Mean (SD)	8.35 (3.14)	9.00 (2.45)		
Month 12 Adjusted Mean Change (SE)	-1.30 (0.53)	1.45 (0.85)	-2.75 [-4.72;-0.78]	0.006
Month 24 Adjusted Mean Change (SE)	-1.69 (1.19)	-0.21 (1.26)	-1.48 [-4.89;1.93]	0.395
Age = 31-40				
N'	150	83		
Baseline Mean (SD)	8.14 (3.75)	8.48 (3.16)		
Month 12 Adjusted Mean Change (SE)	-0.15 (0.20)	0.40 (0.27)	-0.55 [-1.21;0.12]	0.108
Month 24 Adjusted Mean Change (SE)	0.52 (0.35)	0.75 (0.46)	-0.22 [-1.35;0.91]	0.699
Age = 41-55				
N'	649	301		
Baseline Mean (SD)	8.15 (3.38)	8.07 (3.41)		
Month 12 Adjusted Mean Change (SE)	0.01 (0.10)	0.07 (0.14)	-0.06 [-0.40;0.28]	0.731
Month 24 Adjusted Mean Change (SE)	0.57 (0.16)	0.60 (0.24)	-0.04 [-0.60;0.53]	0.900
Age = >55				
N'	181	102		
Baseline Mean (SD)	7.99 (3.23)	7.62 (3.43)		
Month 12 Adjusted Mean Change (SE)	-0.14 (0.19)	-0.28 (0.25)	0.14 [-0.47;0.74]	0.653
Month 24 Adjusted Mean Change (SE)	0.27 (0.29)	-0.08 (0.39)	0.35 [-0.61;1.31]	0.476

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 8.1.3: BVMT-R Delayed Recall Score (FAS), Change from Baseline by Gender

	Treatment groups		Comparison	
	BAF312 (N=1099)	**Placebo (N=546)**	**Mean Difference [95% CI]**	**p-value**
Interaction Test				0.952
Sex = F				
N'	598	296		
Baseline Mean (SD)	8.15 (3.51)	7.79 (3.46)		
Month 12 Adjusted Mean Change (SE)	-0.06 (0.11)	-0.12 (0.15)	0.06 [-0.29;0.41]	0.731
Month 24 Adjusted Mean Change (SE)	0.45 (0.17)	0.17 (0.24)	0.28 [-0.30;0.85]	0.345
Sex = M				
N'	405	202		
Baseline Mean (SD)	8.08 (3.24)	8.48 (3.16)		
Month 12 Adjusted Mean Change (SE)	-0.18 (0.13)	0.28 (0.18)	-0.46 [-0.88;-0.03]	0.035
Month 24 Adjusted Mean Change (SE)	0.43 (0.19)	0.81 (0.29)	-0.38 [-1.06;0.30]	0.270

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=1099)	**Placebo (N=546)**	**Mean Difference [95% CI]**	**p-value**
Interaction Test				0.608
Previous MS-DMT = N				
N'	216	106		
Baseline Mean (SD)	8.31 (3.22)	8.27 (3.31)		
Month 12 Adjusted Mean Change (SE)	-0.03 (0.17)	-0.14 (0.25)	0.11 [-0.48;0.70]	0.714
Month 24 Adjusted Mean Change (SE)	0.53 (0.26)	0.42 (0.42)	0.11 [-0.87;1.09]	0.828
Previous MS-DMT = Y				
N'	787	392		
Baseline Mean (SD)	8.07 (3.45)	8.02 (3.37)		
Month 12 Adjusted Mean Change (SE)	-0.08 (0.09)	0.13 (0.13)	-0.22 [-0.52;0.09]	0.163
Month 24 Adjusted Mean Change (SE)	0.46 (0.15)	0.47 (0.21)	-0.01 [-0.51;0.48]	0.956

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+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=1099)	**Placebo (N=546)**	**Mean Difference [95% CI]**	**p-value**
Interaction Test				0.470
Previous IFN-beta 1b = N				
N'	688	354		
Baseline Mean (SD)	8.17 (3.39)	8.22 (3.35)		
Month 12 Adjusted Mean Change (SE)	-0.09 (0.10)	0.02 (0.14)	-0.11 [-0.44;0.21]	0.491
Month 24 Adjusted Mean Change (SE)	0.44 (0.16)	0.50 (0.22)	-0.06 [-0.57;0.46]	0.833
Previous IFN-beta 1b = Y				
N'	315	144		
Baseline Mean (SD)	8.02 (3.44)	7.69 (3.36)		
Month 12 Adjusted Mean Change (SE)	-0.15 (0.15)	0.07 (0.21)	-0.22 [-0.72;0.27]	0.382
Month 24 Adjusted Mean Change (SE)	0.42 (0.23)	0.24 (0.37)	0.19 [-0.67;1.04]	0.669

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=1099)	**Placebo (N=546)**	**Mean Difference [95% CI]**	**p-value**
Interaction Test				0.092
Rapid evolvement = N				
N'	759	365		
Baseline Mean (SD)	7.95 (3.39)	7.99 (3.36)		
Month 12 Adjusted Mean Change (SE)	-0.14 (0.10)	0.07 (0.14)	-0.21 [-0.53;0.10]	0.182
Month 24 Adjusted Mean Change (SE)	0.39 (0.15)	0.58 (0.24)	-0.19 [-0.73;0.35]	0.489
Rapid evolvement = Y				
N'	244	133		
Baseline Mean (SD)	8.65 (3.38)	8.28 (3.36)		
Month 12 Adjusted Mean Change (SE)	0.00 (0.17)	-0.04 (0.22)	0.04 [-0.49;0.56]	0.889
Month 24 Adjusted Mean Change (SE)	0.59 (0.25)	0.17 (0.32)	0.42 [-0.36;1.19]	0.290

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=1099)	**Placebo (N=546)**	**Mean Difference [95% CI]**	**p-value**
Interaction Test				0.319
Moderate/severe disease course = N				
N'	179	82		
Baseline Mean (SD)	8.52 (3.39)	8.61 (2.95)		
Month 12 Adjusted Mean Change (SE)	-0.20 (0.20)	0.23 (0.28)	-0.43 [-1.08;0.23]	0.201
Month 24 Adjusted Mean Change (SE)	0.58 (0.29)	0.76 (0.47)	-0.18 [-1.26;0.91]	0.748
Moderate/severe disease course = Y				
N'	824	416		
Baseline Mean (SD)	8.04 (3.40)	7.96 (3.43)		
Month 12 Adjusted Mean Change (SE)	-0.09 (0.10)	0.00 (0.13)	-0.09 [-0.38;0.21]	0.558
Month 24 Adjusted Mean Change (SE)	0.40 (0.15)	0.36 (0.21)	0.04 [-0.45;0.52]	0.885

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=1099)	**Placebo (N=546)**	**Mean Difference [95% CI]**	**p-value**
Interaction Test				0.229
Region = Europe				
N'	789	397		
Baseline Mean (SD)	8.26 (3.38)	8.22 (3.28)		
Month 12 Adjusted Mean Change (SE)	-0.07 (0.10)	0.03 (0.14)	-0.10 [-0.43;0.23]	0.549
Month 24 Adjusted Mean Change (SE)	0.50 (0.14)	0.56 (0.20)	-0.06 [-0.54;0.43]	0.816
Region = Others				
N'	214	101		
Baseline Mean (SD)	7.61 (3.44)	7.50 (3.60)		
Month 12 Adjusted Mean Change (SE)	0.00 (0.19)	0.44 (0.28)	-0.43 [-1.11;0.24]	0.206
Month 24 Adjusted Mean Change (SE)	0.24 (0.38)	-0.76 (0.58)	0.99 [-0.37;2.36]	0.154

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+

Table 8.2.0: BVMT-R Total Recall Score (FAS), Return Rates

	Treatment groups		
	BAF312 (N=1099)	**Placebo (N=546)**	**Total (N=1645)**
Return Rate n (%)*			
Baseline	1078 (98.1)	534 (97.8)	1612 (98.0)
Month 06	990 (90.1)	509 (93.2)	1499 (91.1)
Month 12	920 (83.7)	445 (81.5)	1365 (83.0)
Month 18	639 (58.1)	307 (56.2)	946 (57.5)
Month 24	302 (27.5)	138 (25.3)	440 (26.7)
Month 30	87 (7.9)	34 (6.2)	121 (7.4)

* 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=1099)	**Placebo (N=546)**	**Mean Difference [95% CI]**	**p-value**
N'	1011	508		
Baseline Mean (SD)	20.79 (8.77)	20.60 (8.73)		
Month 12 Adjusted Mean Change (SE)	0.21 (0.22)	0.56 (0.30)	-0.35 [-1.01;0.32]	0.307
Month 24 Adjusted Mean Change (SE)	1.78 (0.32)	1.33 (0.45)	0.45 [-0.59;1.49]	0.394

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=1099)	**Placebo (N=546)**	**Mean Difference [95% CI]**	**p-value**
Interaction Test				0.686
Age = 18-30				
N'	23	12		
Baseline Mean (SD)	21.09 (7.76)	22.08 (7.32)		
Month 12 Adjusted Mean Change (SE)	-0.96 (1.35)	3.42 (2.12)	-4.38 [-9.27;0.52]	0.080
Month 24 Adjusted Mean Change (SE)	2.39 (2.84)	2.27 (2.99)	0.12 [-7.97;8.21]	0.977
Age = 31-40				
N'	151	84		
Baseline Mean (SD)	21.05 (9.72)	22.04 (8.32)		
Month 12 Adjusted Mean Change (SE)	0.54 (0.51)	1.86 (0.69)	-1.32 [-2.97;0.34]	0.118
Month 24 Adjusted Mean Change (SE)	3.18 (0.82)	1.56 (1.08)	1.62 [-1.02;4.25]	0.228
Age = 41-55				
N'	655	309		
Baseline Mean (SD)	20.99 (8.62)	20.68 (8.72)		
Month 12 Adjusted Mean Change (SE)	0.32 (0.27)	0.40 (0.37)	-0.08 [-0.92;0.77]	0.857
Month 24 Adjusted Mean Change (SE)	1.73 (0.39)	1.89 (0.58)	-0.17 [-1.50;1.17]	0.807
Age = >55				
N'	182	103		
Baseline Mean (SD)	19.81 (8.60)	19.02 (9.10)		
Month 12 Adjusted Mean Change (SE)	-0.23 (0.48)	-0.27 (0.63)	0.04 [-1.47;1.55]	0.955
Month 24 Adjusted Mean Change (SE)	1.00 (0.70)	-0.38 (0.94)	1.38 [-0.90;3.67]	0.235

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=1099)	**Placebo (N=546)**	**Mean Difference [95% CI]**	**p-value**
Interaction Test				0.251
Sex = F				
N'	602	301		
Baseline Mean (SD)	20.95 (8.89)	20.02 (9.07)		
Month 12 Adjusted Mean Change (SE)	0.51 (0.28)	0.23 (0.37)	0.28 [-0.58;1.14]	0.519
Month 24 Adjusted Mean Change (SE)	2.21 (0.42)	0.50 (0.58)	1.71 [0.35;3.07]	0.014
Sex = M				
N'	409	207		
Baseline Mean (SD)	20.56 (8.60)	21.44 (8.16)		
Month 12 Adjusted Mean Change (SE)	-0.21 (0.32)	1.06 (0.45)	-1.27 [-2.32;-0.23]	0.017
Month 24 Adjusted Mean Change (SE)	1.23 (0.46)	2.52 (0.69)	-1.28 [-2.87;0.30]	0.113

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=1099)	**Placebo (N=546)**	**Mean Difference [95% CI]**	**p-value**
Interaction Test				0.416
Previous MS-DMT = N				
N'	218	108		
Baseline Mean (SD)	21.07 (8.12)	20.96 (8.41)		
Month 12 Adjusted Mean Change (SE)	0.54 (0.44)	-0.08 (0.63)	0.62 [-0.84;2.08]	0.403
Month 24 Adjusted Mean Change (SE)	2.07 (0.64)	0.68 (1.02)	1.40 [-0.92;3.72]	0.238
Previous MS-DMT = Y				
N'	793	400		
Baseline Mean (SD)	20.72 (8.94)	20.51 (8.82)		
Month 12 Adjusted Mean Change (SE)	0.12 (0.25)	0.72 (0.33)	-0.60 [-1.35;0.15]	0.115
Month 24 Adjusted Mean Change (SE)	1.69 (0.36)	1.47 (0.50)	0.22 [-0.95;1.39]	0.710

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=1099)	**Placebo (N=546)**	**Mean Difference [95% CI]**	**p-value**
Interaction Test				N.E.
Previous IFN-beta 1b = N				
N'	693	361		
Baseline Mean (SD)	20.97 (8.69)	20.83 (8.57)		
Month 12 Adjusted Mean Change (SE)	0.04 (0.27)	0.43 (0.36)	-0.39 [-1.18;0.40]	0.332
Month 24 Adjusted Mean Change (SE)	1.76 (0.38)	1.13 (0.52)	0.63 [-0.57;1.84]	0.301
Previous IFN-beta 1b = Y				
N'	318	147		
Baseline Mean (SD)	20.40 (8.94)	20.05 (9.13)		
Month 12 Adjusted Mean Change (SE)	0.40 (0.43)	0.54 (0.57)	-0.14 [-1.40;1.12]	0.826
Month 24 Adjusted Mean Change (SE)	1.59 (0.61)	1.77 (0.94)	-0.18 [-2.30;1.94]	0.865

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=1099)	**Placebo (N=546)**	**Mean Difference [95% CI]**	**p-value**
Interaction Test				0.937
Rapid evolvement = N				
N'	763	371		
Baseline Mean (SD)	20.35 (8.76)	20.49 (8.83)		
Month 12 Adjusted Mean Change (SE)	0.18 (0.25)	0.57 (0.35)	-0.39 [-1.17;0.39]	0.326
Month 24 Adjusted Mean Change (SE)	1.51 (0.37)	1.19 (0.56)	0.32 [-0.97;1.60]	0.628
Rapid evolvement = Y				
N'	248	137		
Baseline Mean (SD)	22.16 (8.67)	20.90 (8.47)		
Month 12 Adjusted Mean Change (SE)	0.30 (0.41)	0.53 (0.54)	-0.23 [-1.52;1.06]	0.728
Month 24 Adjusted Mean Change (SE)	2.49 (0.58)	1.53 (0.74)	0.97 [-0.85;2.79]	0.297

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=1099)	**Placebo (N=546)**	**Mean Difference [95% CI]**	**p-value**
Interaction Test				0.217
Moderate/severe disease course = N				
N'	180	83		
Baseline Mean (SD)	21.67 (8.33)	21.41 (8.11)		
Month 12 Adjusted Mean Change (SE)	0.18 (0.47)	0.27 (0.68)	-0.09 [-1.71;1.53]	0.917
Month 24 Adjusted Mean Change (SE)	1.66 (0.69)	1.76 (1.12)	-0.10 [-2.68;2.48]	0.940
Moderate/severe disease course = Y				
N'	831	425		
Baseline Mean (SD)	20.60 (8.86)	20.44 (8.85)		
Month 12 Adjusted Mean Change (SE)	0.16 (0.21)	0.53 (0.31)	-0.37 [-1.11;0.36]	0.317
Month 24 Adjusted Mean Change (SE)	1.72 (0.33)	1.10 (0.48)	0.62 [-0.53;1.77]	0.289

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+Age

Table 8.2.8 BVMT-R Total Recall Score (FAS), Change from Baseline by Region

	Treatment groups		Comparison	
	BAF312 (N=1099)	**Placebo (N=546)**	**Mean Difference [95% CI]**	**p-value**
Interaction Test				0.816
Region = Europe				
N'	796	402		
Baseline Mean (SD)	21.11 (8.78)	20.99 (8.73)		
Month 12 Adjusted Mean Change (SE)	0.20 (0.24)	0.40 (0.34)	-0.20 [-1.02;0.62]	0.630
Month 24 Adjusted Mean Change (SE)	1.81 (0.33)	1.37 (0.48)	0.44 [-0.71;1.58]	0.456
Region = Others				
N'	215	106		
Baseline Mean (SD)	19.63 (8.65)	19.14 (8.63)		
Month 12 Adjusted Mean Change (SE)	0.22 (0.48)	1.26 (0.69)	-1.04 [-2.69;0.62]	0.218
Month 24 Adjusted Mean Change (SE)	0.84 (0.91)	-1.44 (1.39)	2.28 [-0.97;5.54]	0.169

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+

Table 8.3.0: LCVA (FAS), Return Rates

	Treatment groups		
	BAF312 (N=1099)	**Placebo (N=546)**	**Total (N=1645)**
Return Rate n (%)*			
Baseline	1046 (95.2)	526 (96.3)	1572 (95.6)
Month 06	930 (84.6)	476 (87.2)	1406 (85.5)
Month 12	824 (75.0)	407 (74.5)	1231 (74.8)
Month 18	540 (49.1)	249 (45.6)	789 (48.0)
Month 24	327 (29.8)	141 (25.8)	468 (28.4)
Month 30	118 (10.7)	38 (7.0)	156 (9.5)

* 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=1099)	**Placebo (N=546)**	**Mean Difference [95% CI]**	**p-value**
N'	940	486		
Baseline Mean (SD)	0.37 (0.26)	0.36 (0.26)		
Month 12 Adjusted Mean Change (SE)	0.02 (0.01)	0.01 (0.01)	0.01 [-0.01;0.04]	0.366
Month 24 Adjusted Mean Change (SE)	0.01 (0.01)	0.00 (0.02)	0.00 [-0.03;0.04]	0.877

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=1099)	**Placebo (N=546)**	**Mean Difference [95% CI]**	**p-value**
Interaction Test				0.661
Age = 18-30				
N'	20	11		
Baseline Mean (SD)	0.61 (0.28)	0.25 (0.22)		
Month 12 Adjusted Mean Change (SE)	0.04 (0.05)	0.09 (0.08)	-0.05 [-0.23;0.14]	0.610
Month 24 Adjusted Mean Change (SE)	-0.03 (0.08)	0.09 (0.18)	-0.13 [-0.51;0.25]	0.515
Age = 31-40				
N'	140	81		
Baseline Mean (SD)	0.40 (0.29)	0.36 (0.28)		
Month 12 Adjusted Mean Change (SE)	0.04 (0.02)	0.03 (0.03)	0.01 [-0.05;0.07]	0.791
Month 24 Adjusted Mean Change (SE)	0.01 (0.03)	-0.07 (0.04)	0.08 [-0.02;0.18]	0.111
Age = 41-55				
N'	617	290		
Baseline Mean (SD)	0.35 (0.25)	0.35 (0.26)		
Month 12 Adjusted Mean Change (SE)	0.01 (0.01)	0.00 (0.01)	0.01 [-0.02;0.05]	0.432
Month 24 Adjusted Mean Change (SE)	0.01 (0.01)	0.01 (0.02)	0.00 [-0.05;0.04]	0.853
Age = >55				
N'	163	104		
Baseline Mean (SD)	0.40 (0.24)	0.40 (0.26)		
Month 12 Adjusted Mean Change (SE)	0.01 (0.02)	0.00 (0.02)	0.02 [-0.04;0.07]	0.587
Month 24 Adjusted Mean Change (SE)	0.00 (0.03)	0.02 (0.03)	-0.02 [-0.10;0.06]	0.621

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=1099)	**Placebo (N=546)**	**Mean Difference [95% CI]**	**p-value**
Interaction Test				0.016
Sex = F				
N'	569	287		
Baseline Mean (SD)	0.38 (0.26)	0.37 (0.27)		
Month 12 Adjusted Mean Change (SE)	0.02 (0.01)	0.02 (0.01)	0.01 [-0.02;0.04]	0.609
Month 24 Adjusted Mean Change (SE)	0.02 (0.01)	0.04 (0.02)	-0.02 [-0.07;0.03]	0.458
Sex = M				
N'	371	199		
Baseline Mean (SD)	0.35 (0.26)	0.34 (0.25)		
Month 12 Adjusted Mean Change (SE)	0.02 (0.01)	0.01 (0.02)	0.01 [-0.03;0.05]	0.484
Month 24 Adjusted Mean Change (SE)	0.02 (0.02)	-0.02 (0.03)	0.04 [-0.02;0.10]	0.162

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 8.3.4 LCVA (FAS), Change from Baseline by Previous MS DMT

	Treatment groups		Comparison	
	BAF312 (N=1099)	**Placebo (N=546)**	**Mean Difference [95% CI]**	**p-value**
Interaction Test				0.012
Previous MS-DMT = N				
N'	206	100		
Baseline Mean (SD)	0.36 (0.26)	0.38 (0.28)		
Month 12 Adjusted Mean Change (SE)	0.01 (0.02)	0.01 (0.02)	0.00 [-0.06;0.05]	0.880
Month 24 Adjusted Mean Change (SE)	0.00 (0.02)	0.00 (0.03)	0.00 [-0.07;0.08]	0.950
Previous MS-DMT = Y				
N'	734	386		
Baseline Mean (SD)	0.37 (0.26)	0.36 (0.26)		
Month 12 Adjusted Mean Change (SE)	0.02 (0.01)	0.00 (0.01)	0.02 [-0.01;0.04]	0.269
Month 24 Adjusted Mean Change (SE)	0.01 (0.01)	0.01 (0.02)	0.00 [-0.04;0.05]	0.861

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=1099)	**Placebo (N=546)**	**Mean Difference [95% CI]**	**p-value**
Interaction Test				0.968
Previous IFN-beta 1b = N				
N'	650	347		
Baseline Mean (SD)	0.37 (0.25)	0.36 (0.26)		
Month 12 Adjusted Mean Change (SE)	0.02 (0.01)	0.00 (0.01)	0.01 [-0.02;0.04]	0.485
Month 24 Adjusted Mean Change (SE)	0.01 (0.01)	0.02 (0.02)	0.00 [-0.05;0.04]	0.837
Previous IFN-beta 1b = Y				
N'	290	139		
Baseline Mean (SD)	0.38 (0.27)	0.37 (0.26)		
Month 12 Adjusted Mean Change (SE)	0.02 (0.01)	0.01 (0.02)	0.01 [-0.03;0.06]	0.575
Month 24 Adjusted Mean Change (SE)	0.00 (0.02)	-0.02 (0.03)	0.02 [-0.05;0.09]	0.576

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=1099)	**Placebo (N=546)**	**Mean Difference [95% CI]**	**p-value**
Interaction Test				0.091
Rapid evolvement = N				
N'	710	352		
Baseline Mean (SD)	0.37 (0.26)	0.36 (0.27)		
Month 12 Adjusted Mean Change (SE)	0.02 (0.01)	0.00 (0.01)	0.02 [-0.01;0.04]	0.312
Month 24 Adjusted Mean Change (SE)	0.02 (0.01)	-0.01 (0.02)	0.02 [-0.02;0.07]	0.304
Rapid evolvement = Y				
N'	230	134		
Baseline Mean (SD)	0.37 (0.26)	0.36 (0.24)		
Month 12 Adjusted Mean Change (SE)	0.02 (0.02)	0.01 (0.02)	0.00 [-0.05;0.05]	0.941
Month 24 Adjusted Mean Change (SE)	-0.01 (0.02)	0.03 (0.03)	-0.05 [-0.11;0.02]	0.197

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=1099)	**Placebo (N=546)**	**Mean Difference [95% CI]**	**p-value**
Interaction Test				0.066
Moderate/severe disease course = N				
N'	169	79		
Baseline Mean (SD)	0.33 (0.23)	0.35 (0.26)		
Month 12 Adjusted Mean Change (SE)	0.00 (0.02)	0.02 (0.03)	-0.02 [-0.08;0.04]	0.481
Month 24 Adjusted Mean Change (SE)	0.03 (0.02)	0.04 (0.04)	-0.01 [-0.10;0.08]	0.894
Moderate/severe disease course = Y				
N'	771	407		
Baseline Mean (SD)	0.38 (0.26)	0.36 (0.26)		
Month 12 Adjusted Mean Change (SE)	0.02 (0.01)	0.00 (0.01)	0.02 [-0.01;0.05]	0.191
Month 24 Adjusted Mean Change (SE)	0.00 (0.01)	0.00 (0.02)	0.00 [-0.04;0.04]	0.867

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=1099)	**Placebo (N=546)**	**Mean Difference [95% CI]**	**p-value**
Interaction Test				0.180
Region = Europe				
N'	752	390		
Baseline Mean (SD)	0.37 (0.26)	0.37 (0.27)		
Month 12 Adjusted Mean Change (SE)	0.03 (0.01)	0.02 (0.01)	0.01 [-0.02;0.04]	0.642
Month 24 Adjusted Mean Change (SE)	0.03 (0.01)	0.01 (0.02)	0.01 [-0.03;0.05]	0.507
Region = Others				
N'	188	96		
Baseline Mean (SD)	0.35 (0.25)	0.33 (0.24)		
Month 12 Adjusted Mean Change (SE)	-0.01 (0.02)	-0.04 (0.03)	0.03 [-0.03;0.09]	0.285
Month 24 Adjusted Mean Change (SE)	-0.03 (0.03)	0.05 (0.05)	-0.08 [-0.19;0.03]	0.165

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=1099)	**Placebo (N=546)**	**Total (N=1645)**
Return Rate n (%)*			
Baseline	1098 (99.9)	545 (99.8)	1643 (99.9)
Month 12	1024 (93.2)	509 (93.2)	1533 (93.2)
Month 24	626 (57.0)	305 (55.9)	931 (56.6)
Month 36	133 (12.1)	53 (9.7)	186 (11.3)

* 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=1099)	**Placebo (N=546)**	**Mean Difference [95% CI]**	**p-value**
N'	995	495		
Baseline Mean (SD)	15551.74 (16319.94)	14285.38 (15438.57)		
Month 12 Adjusted Mean Change (SE)	204.94 (67.47)	818.03 (87.29)	-613.09 [-800.20;-425.98]	<.001
Month 24 Adjusted Mean Change (SE)	162.90 (73.90)	940.41 (97.20)	-777.52 [-990.63;-564.40]	<.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=1099)	**Placebo (N=546)**	**Mean Difference [95% CI]**	**p-value**
Interaction Test				<.001
Age = 18-30				
N'	21	10		
Baseline Mean (SD)	20949.52 (18147.16)	20924.60 (17225.68)		
Month 12 Adjusted Mean Change (SE)	-89.36 (388.76)	2646.82 (553.66)	-2736.17 [-4043.82;-1428.53]	<.001
Month 24 Adjusted Mean Change (SE)	174.91 (447.26)	2930.22 (602.91)	-2755.31 [-4214.34;-1296.28]	<.001
Age = 31-40				
N'	149	83		
Baseline Mean (SD)	17911.99 (19081.43)	16064.82 (15955.19)		
Month 12 Adjusted Mean Change (SE)	301.72 (147.74)	1335.29 (194.10)	-1033.57 [-1501.05;-566.10]	<.001
Month 24 Adjusted Mean Change (SE)	233.40 (169.13)	993.73 (213.80)	-760.33 [-1284.56;-236.10]	0.005
Age = 41-55				
N'	642	297		
Baseline Mean (SD)	14683.47 (15248.04)	13383.41 (14396.17)		
Month 12 Adjusted Mean Change (SE)	233.89 (80.00)	814.31 (107.57)	-580.41 [-818.48;-342.35]	<.001
Month 24 Adjusted Mean Change (SE)	161.16 (87.67)	974.99 (121.11)	-813.82 [-1084.79;-542.85]	<.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+SPMS Group+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=1099)	**Placebo (N=546)**	**Mean Difference [95% CI]**	**p-value**
Age = >55				
N'	183	105		
Baseline Mean (SD)	16056.64 (17107.01)	14797.77 (17508.46)		
Month 12 Adjusted Mean Change (SE)	63.09 (135.96)	234.62 (176.40)	-171.53 [-587.58;244.52]	0.419
Month 24 Adjusted Mean Change (SE)	125.70 (153.76)	638.49 (202.93)	-512.79 [-995.80;-29.78]	0.037

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+SPMS Group+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=1099)	**Placebo (N=546)**	**Mean Difference [95% CI]**	**p-value**
Interaction Test				0.587
Sex = F				
N'	594	302		
Baseline Mean (SD)	15022.17 (16018.81)	15931.74 (17001.79)		
Month 12 Adjusted Mean Change (SE)	278.27 (81.42)	954.14 (106.54)	-675.86 [-916.33;-435.40]	<.001
Month 24 Adjusted Mean Change (SE)	237.83 (91.16)	932.02 (120.84)	-694.18 [-970.74;-417.62]	<.001
Sex = M				
N'	401	193		
Baseline Mean (SD)	16336.19 (16745.44)	11709.21 (12212.94)		
Month 12 Adjusted Mean Change (SE)	88.81 (95.26)	599.15 (132.59)	-510.34 [-809.56;-211.12]	<.001
Month 24 Adjusted Mean Change (SE)	47.33 (104.73)	935.45 (147.64)	-888.13 [-1224.46;-551.79]	<.001

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=1099)	**Placebo (N=546)**	**Mean Difference [95% CI]**	**p-value**
Interaction Test				0.009
Previous MS-DMT = N				
N'	215	103		
Baseline Mean (SD)	15412.61 (17623.09)	14770.50 (15546.45)		
Month 12 Adjusted Mean Change (SE)	395.17 (127.15)	672.61 (179.22)	-277.44 [-686.35;131.46]	0.183
Month 24 Adjusted Mean Change (SE)	269.66 (141.59)	894.32 (202.49)	-624.66 [-1088.97;-160.35]	0.008
Previous MS-DMT = Y				
N'	780	392		
Baseline Mean (SD)	15590.09 (15953.82)	14157.92 (15427.53)		
Month 12 Adjusted Mean Change (SE)	151.16 (74.28)	855.76 (96.41)	-704.60 [-915.41;-493.80]	<.001
Month 24 Adjusted Mean Change (SE)	133.24 (81.82)	951.96 (107.70)	-818.73 [-1059.32;-578.13]	<.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=1099)	**Placebo (N=546)**	**Mean Difference [95% CI]**	**p-value**
Interaction Test				0.054
Previous IFN-beta 1b = N				
N'	679	358		
Baseline Mean (SD)	15336.01 (16532.17)	14068.68 (15477.36)		
Month 12 Adjusted Mean Change (SE)	266.54 (77.35)	736.83 (100.56)	-470.29 [-692.71;-247.88]	<.001
Month 24 Adjusted Mean Change (SE)	178.23 (85.46)	888.54 (112.68)	-710.32 [-964.21;-456.42]	<.001
Previous IFN-beta 1b = Y				
N'	316	137		
Baseline Mean (SD)	16015.28 (15870.22)	14851.66 (15378.81)		
Month 12 Adjusted Mean Change (SE)	65.55 (106.42)	1023.06 (153.86)	-957.51 [-1307.37;-607.64]	<.001
Month 24 Adjusted Mean Change (SE)	124.71 (119.03)	1070.81 (172.96)	-946.10 [-1342.85;-549.34]	<.001

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=1099)	**Placebo (N=546)**	**Mean Difference [95% CI]**	**p-value**
Interaction Test				0.304
Rapid evolvement = N				
N'	753	362		
Baseline Mean (SD)	16054.59 (16646.21)	14168.51 (15767.86)		
Month 12 Adjusted Mean Change (SE)	231.58 (75.25)	705.34 (100.96)	-473.76 [-691.39;-256.13]	<.001
Month 24 Adjusted Mean Change (SE)	213.45 (83.39)	937.80 (114.80)	-724.35 [-977.01;-471.68]	<.001
Rapid evolvement = Y				
N'	242	133		
Baseline Mean (SD)	13987.09 (15186.70)	14603.50 (14557.23)		
Month 12 Adjusted Mean Change (SE)	108.07 (120.37)	1115.20 (156.05)	-1007.13 [-1377.03;-637.22]	<.001
Month 24 Adjusted Mean Change (SE)	3.21 (131.68)	983.79 (169.45)	-980.57 [-1385.82;-575.32]	<.001

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=1099)	**Placebo (N=546)**	**Mean Difference [95% CI]**	**p-value**
Interaction Test				0.035
Moderate/severe disease course = N				
N'	179	79		
Baseline Mean (SD)	15095.97 (15674.31)	14457.58 (13335.12)		
Month 12 Adjusted Mean Change (SE)	335.93 (138.78)	508.90 (201.34)	-172.97 [-634.31;288.36]	0.462
Month 24 Adjusted Mean Change (SE)	131.69 (154.81)	501.52 (221.76)	-369.82 [-884.17;144.52]	0.159
Moderate/severe disease course = Y				
N'	816	416		
Baseline Mean (SD)	15651.72 (16465.82)	14252.68 (15820.64)		
Month 12 Adjusted Mean Change (SE)	175.55 (71.74)	876.30 (93.33)	-700.76 [-905.85;-495.66]	<.001
Month 24 Adjusted Mean Change (SE)	169.47 (79.13)	1028.42 (104.84)	-858.95 [-1093.38;-624.53]	<.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=1099)	**Placebo (N=546)**	**Mean Difference [95% CI]**	**p-value**
Interaction Test				0.009
Region = Europe				
N'	790	393		
Baseline Mean (SD)	15716.80 (16777.73)	14134.29 (14611.25)		
Month 12 Adjusted Mean Change (SE)	187.13 (62.75)	887.36 (88.02)	-700.23 [-910.42;-490.04]	<.001
Month 24 Adjusted Mean Change (SE)	140.52 (69.11)	971.24 (97.66)	-830.71 [-1064.05;-597.38]	<.001
Region = Others				
N'	205	102		
Baseline Mean (SD)	14915.65 (14440.66)	14867.52 (18351.24)		
Month 12 Adjusted Mean Change (SE)	331.01 (122.97)	582.27 (172.41)	-251.26 [-663.64;161.13]	0.232
Month 24 Adjusted Mean Change (SE)	327.16 (159.34)	902.14 (224.78)	-574.98 [-1112.63;-37.33]	0.036

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+BL Number of T1 Lesions

Table 9.2.0: Number of New or Enlarging T2 Lesions (FAS), Return Rates

	Treatment groups		
	BAF312 (N=1099)	**Placebo (N=546)**	**Total (N=1645)**
Return Rate n (%)*			
Month 12	1023 (93.1)	509 (93.2)	1532 (93.1)
Month 24	626 (57.0)	304 (55.7)	930 (56.5)

* 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=1099)	**Placebo (N=546)**	**RR [95% CI]**	**p-value**
N'	997	496		
Month 12: Number of lesions relative to baseline [95% CI]*	1.00 [0.86;1.17]	3.78 [3.15;4.53]	0.27 [0.21;0.33]	<.001
Month 24: Number of lesions relative to Month 12 [95% CI]*	0.49 [0.37;0.64]	3.44 [2.80;4.22]	0.14 [0.10;0.20]	<.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+Country+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=1099)	**Placebo (N=546)**	**RR [95% CI]**	**p-value**
Interaction Test				0.869
Age = 18-30				
N'	21	10		
Month 12: Number of lesions relative to baseline [95% CI]*	2.36 [1.35;4.12]	10.13 [5.57;18.43]	0.23 [0.11;0.51]	<.001
Month 24: Number of lesions relative to Month 12 [95% CI]*	0.81 [0.47;1.41]	6.41 [3.19;12.86]	0.13 [0.05;0.30]	<.001
Age = 31-40				
N'	149	83		
Month 12: Number of lesions relative to baseline [95% CI]*	2.29 [1.67;3.15]	7.82 [5.41;11.30]	0.29 [0.18;0.48]	<.001
Month 24: Number of lesions relative to Month 12 [95% CI]*	1.23 [0.62;2.44]	6.89 [4.27;11.11]	0.18 [0.08;0.41]	<.001
Age = 41-55				
N'	644	298		
Month 12: Number of lesions relative to baseline [95% CI]*	1.01 [0.83;1.23]	4.23 [3.39;5.27]	0.24 [0.18;0.31]	<.001
Month 24: Number of lesions relative to Month 12 [95% CI]*	0.48 [0.35;0.66]	3.49 [2.73;4.46]	0.14 [0.09;0.20]	<.001
Age = >55				
N'	183	105		
Month 12: Number of lesions relative to baseline [95% CI]*	0.41 [0.28;0.61]	1.28 [0.85;1.94]	0.32 [0.19;0.56]	<.001
Month 24: Number of lesions relative to Month 12 [95% CI]*	0.21 [0.12;0.36]	1.59 [0.98;2.59]	0.13 [0.07;0.27]	<.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+Country+BL Number of T1 Lesions

Table 9.2.3: Number of New or Enlarging T2 Lesions (FAS) by Gender

	Treatment groups		Comparison	
	BAF312 (N=1099)	**Placebo (N=546)**	**RR [95% CI]**	**p-value**
Interaction Test				0.604
Sex = F				
N'	595	302		
Month 12: Number of lesions relative to baseline [95% CI]*	1.03 [0.85;1.24]	4.37 [3.50;5.45]	0.23 [0.18;0.30]	<.001
Month 24: Number of lesions relative to Month 12 [95% CI]*	0.58 [0.40;0.84]	3.27 [2.58;4.14]	0.18 [0.12;0.27]	<.001
Sex = M				
N'	402	194		
Month 12: Number of lesions relative to baseline [95% CI]*	0.96 [0.75;1.23]	2.86 [2.19;3.73]	0.34 [0.23;0.48]	<.001
Month 24: Number of lesions relative to Month 12 [95% CI]*	0.35 [0.25;0.49]	3.53 [2.53;4.93]	0.10 [0.06;0.16]	<.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+Country+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=1099)	**Placebo (N=546)**	**RR [95% CI]**	**p-value**
Interaction Test				0.030
Previous MS-DMT = N				
N'	215	103		
Month 12: Number of lesions relative to baseline [95% CI]*	0.81 [0.60;1.08]	4.89 [3.39;7.04]	0.16 [0.11;0.26]	<.001
Month 24: Number of lesions relative to Month 12 [95% CI]*	0.40 [0.24;0.65]	4.48 [3.08;6.54]	0.09 [0.05;0.16]	<.001
Previous MS-DMT = Y				
N'	782	393		
Month 12: Number of lesions relative to baseline [95% CI]*	1.05 [0.88;1.26]	3.50 [2.89;4.24]	0.30 [0.24;0.38]	<.001
Month 24: Number of lesions relative to Month 12 [95% CI]*	0.51 [0.37;0.69]	3.17 [2.51;3.99]	0.16 [0.11;0.23]	<.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+DMT+Visit+Treatment*DMT+Treatment*Visit+DMT*Visit+Treatment*Visit*DMT+Country+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=1099)	**Placebo (N=546)**	**RR [95% CI]**	**p-value**
Interaction Test				0.010
Previous IFN-beta 1b = N				
N'	679	358		
Month 12: Number of lesions relative to baseline [95% CI]*	0.90 [0.75;1.07]	3.77 [3.04;4.66]	0.24 [0.19;0.31]	<.001
Month 24: Number of lesions relative to Month 12 [95% CI]*	0.38 [0.27;0.53]	3.68 [2.90;4.67]	0.10 [0.07;0.15]	<.001
Previous IFN-beta 1b = Y				
N'	318	138		
Month 12: Number of lesions relative to baseline [95% CI]*	1.22 [0.95;1.58]	3.71 [2.78;4.95]	0.33 [0.23;0.48]	<.001
Month 24: Number of lesions relative to Month 12 [95% CI]*	0.72 [0.48;1.09]	2.80 [2.01;3.92]	0.26 [0.15;0.43]	<.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+IFN+Visit+Treatment*IFN+Treatment*Visit+IFN*Visit+Treatment*Visit*IFN+Country+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=1099)	**Placebo (N=546)**	**RR [95% CI]**	**p-value**
Interaction Test				0.377
Rapid evolvement = N				
N'	755	363		
Month 12: Number of lesions relative to baseline [95% CI]*	0.94 [0.79;1.12]	3.41 [2.79;4.18]	0.28 [0.22;0.35]	<.001
Month 24: Number of lesions relative to Month 12 [95% CI]*	0.55 [0.40;0.75]	3.57 [2.83;4.51]	0.15 [0.10;0.22]	<.001
Rapid evolvement = Y				
N'	242	133		
Month 12: Number of lesions relative to baseline [95% CI]*	1.17 [0.85;1.61]	4.74 [3.46;6.51]	0.25 [0.16;0.38]	<.001
Month 24: Number of lesions relative to Month 12 [95% CI]*	0.34 [0.21;0.55]	3.19 [2.26;4.51]	0.11 [0.06;0.19]	<.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+Country+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=1099)	**Placebo (N=546)**	**RR [95% CI]**	**p-value**
Interaction Test				0.549
Moderate/severe disease course = N				
N'	179	79		
Month 12: Number of lesions relative to baseline [95% CI]*	0.60 [0.43;0.84]	2.27 [1.53;3.37]	0.27 [0.16;0.44]	<.001
Month 24: Number of lesions relative to Month 12 [95% CI]*	0.33 [0.18;0.60]	1.64 [1.05;2.57]	0.20 [0.10;0.41]	<.001
Moderate/severe disease course = Y				
N'	818	417		
Month 12: Number of lesions relative to baseline [95% CI]*	1.09 [0.92;1.29]	4.04 [3.33;4.90]	0.27 [0.21;0.34]	<.001
Month 24: Number of lesions relative to Month 12 [95% CI]*	0.52 [0.39;0.70]	3.81 [3.07;4.74]	0.14 [0.10;0.19]	<.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+Country+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=1099)	**Placebo (N=546)**	**RR [95% CI]**	**p-value**
Interaction Test				0.045
Region = Europe				
N'	792	394		
Month 12: Number of lesions relative to baseline [95% CI]*	1.07 [0.92;1.24]	4.09 [3.43;4.89]	0.26 [0.21;0.33]	<.001
Month 24: Number of lesions relative to Month 12 [95% CI]*	0.44 [0.34;0.57]	3.85 [3.09;4.79]	0.11 [0.08;0.16]	<.001
Region = Others				
N'	205	102		
Month 12: Number of lesions relative to baseline [95% CI]*	0.96 [0.56;1.64]	3.40 [2.21;5.21]	0.28 [0.14;0.56]	<.001
Month 24: Number of lesions relative to Month 12 [95% CI]*	1.11 [0.59;2.10]	2.60 [1.68;4.04]	0.43 [0.20;0.93]	0.031

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=1099)	**Placebo (N=546)**	**Total (N=1645)**
Return Rate n (%)*			
Month 12	1019 (92.7)	507 (92.9)	1526 (92.8)
Month 24	622 (56.6)	304 (55.7)	926 (56.3)

* 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=1099)	**Placebo (N=546)**	**RR [95% CI]**	**p-value**
N'	996	496		
Month 12: Number of lesions [95% CI]*	0.08 [0.06;0.11]	0.64 [0.49;0.84]	0.13 [0.08;0.19]	<.001
Month 24: Number of lesions [95% CI]*	0.07 [0.04;0.14]	0.42 [0.29;0.61]	0.18 [0.09;0.36]	<.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 9.3.2: Number of T1 Gd-enhancing Lesions (FAS) by Age

	Treatment groups		Comparison	
	BAF312 (N=1099)	**Placebo (N=546)**	**RR [95% CI]**	**p-value**
Interaction Test				0.710
Age = 18-30				
N'	21	10		
Month 12: Number of lesions [95% CI]*	0.10 [0.03;0.33]	1.18 [0.57;2.44]	0.08 [0.02;0.34]	<.001
Month 24: Number of lesions [95% CI]*	0.01 [0.00;0.10]	0.40 [0.10;1.61]	0.04 [0.00;0.38]	0.006
Age = 31-40				
N'	149	83		
Month 12: Number of lesions [95% CI]*	0.18 [0.10;0.34]	1.10 [0.74;1.65]	0.17 [0.08;0.35]	<.001
Month 24: Number of lesions [95% CI]*	0.04 [0.01;0.17]	0.45 [0.22;0.93]	0.09 [0.02;0.44]	0.003
Age = 41-55				
N'	643	298		
Month 12: Number of lesions [95% CI]*	0.08 [0.05;0.12]	0.76 [0.53;1.09]	0.10 [0.06;0.18]	<.001
Month 24: Number of lesions [95% CI]*	0.09 [0.05;0.18]	0.47 [0.29;0.74]	0.20 [0.09;0.44]	<.001
Age = >55				
N'	183	105		
Month 12: Number of lesions [95% CI]*	0.03 [0.01;0.07]	0.19 [0.10;0.35]	0.15 [0.05;0.44]	<.001
Month 24: Number of lesions [95% CI]*	0.03 [0.01;0.09]	0.27 [0.13;0.55]	0.10 [0.02;0.40]	0.001

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 9.3.3: Number of T1 Gd-enhancing Lesions (FAS) by Gender

	Treatment groups		Comparison	
	BAF312 (N=1099)	**Placebo (N=546)**	**RR [95% CI]**	**p-value**
Interaction Test				0.095
Sex = F				
N'	594	302		
Month 12: Number of lesions [95% CI]*	0.09 [0.07;0.13]	0.76 [0.54;1.07]	0.12 [0.08;0.20]	<.001
Month 24: Number of lesions [95% CI]*	0.11 [0.06;0.23]	0.38 [0.27;0.55]	0.30 [0.14;0.66]	0.003
Sex = M				
N'	402	194		
Month 12: Number of lesions [95% CI]*	0.06 [0.03;0.13]	0.45 [0.30;0.68]	0.14 [0.06;0.32]	<.001
Month 24: Number of lesions [95% CI]*	0.03 [0.01;0.06]	0.46 [0.23;0.93]	0.06 [0.02;0.16]	<.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 9.3.4: Number of T1 Gd-enhancing Lesions (FAS) by Previous MS DMT

	Treatment groups		Comparison	
	BAF312 (N=1099)	**Placebo (N=546)**	**RR [95% CI]**	**p-value**
Interaction Test				0.355
Previous MS-DMT = N				
N'	215	103		
Month 12: Number of lesions [95% CI]*	0.06 [0.02;0.14]	0.63 [0.37;1.09]	0.09 [0.03;0.25]	<.001
Month 24: Number of lesions [95% CI]*	0.07 [0.03;0.17]	0.59 [0.35;1.00]	0.12 [0.04;0.34]	<.001
Previous MS-DMT = Y				
N'	781	393		
Month 12: Number of lesions [95% CI]*	0.09 [0.06;0.12]	0.64 [0.47;0.88]	0.14 [0.09;0.21]	<.001
Month 24: Number of lesions [95% CI]*	0.07 [0.04;0.16]	0.37 [0.23;0.60]	0.20 [0.08;0.48]	<.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+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=1099)	**Placebo (N=546)**	**RR [95% CI]**	**p-value**
Interaction Test				0.142
Previous IFN-beta 1b = N				
N'	678	358		
Month 12: Number of lesions [95% CI]*	0.08 [0.05;0.12]	0.67 [0.48;0.94]	0.12 [0.07;0.21]	<.001
Month 24: Number of lesions [95% CI]*	0.06 [0.03;0.10]	0.47 [0.31;0.73]	0.12 [0.06;0.24]	<.001
Previous IFN-beta 1b = Y				
N'	318	138		
Month 12: Number of lesions [95% CI]*	0.08 [0.05;0.13]	0.55 [0.38;0.81]	0.14 [0.08;0.26]	<.001
Month 24: Number of lesions [95% CI]*	0.11 [0.03;0.35]	0.29 [0.14;0.57]	0.38 [0.10;1.46]	0.160

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=1099)	**Placebo (N=546)**	**RR [95% CI]**	**p-value**
Interaction Test				0.189
Rapid evolvement = N				
N'	754	363		
Month 12: Number of lesions [95% CI]*	0.07 [0.05;0.10]	0.65 [0.46;0.91]	0.11 [0.07;0.18]	<.001
Month 24: Number of lesions [95% CI]*	0.08 [0.04;0.17]	0.52 [0.34;0.80]	0.15 [0.06;0.36]	<.001
Rapid evolvement = Y				
N'	242	133		
Month 12: Number of lesions [95% CI]*	0.10 [0.05;0.19]	0.61 [0.41;0.91]	0.17 [0.08;0.35]	<.001
Month 24: Number of lesions [95% CI]*	0.06 [0.03;0.13]	0.21 [0.11;0.38]	0.31 [0.12;0.79]	0.014

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=1099)	**Placebo (N=546)**	**RR [95% CI]**	**p-value**
Interaction Test				0.724
Moderate/severe disease course = N				
N'	179	79		
Month 12: Number of lesions [95% CI]*	0.05 [0.03;0.11]	0.46 [0.23;0.92]	0.11 [0.04;0.31]	<.001
Month 24: Number of lesions [95% CI]*	0.08 [0.03;0.17]	0.29 [0.12;0.66]	0.27 [0.08;0.86]	0.028
Moderate/severe disease course = Y				
N'	817	417		
Month 12: Number of lesions [95% CI]*	0.09 [0.06;0.12]	0.68 [0.50;0.90]	0.13 [0.08;0.20]	<.001
Month 24: Number of lesions [95% CI]*	0.07 [0.04;0.15]	0.45 [0.30;0.67]	0.17 [0.07;0.37]	<.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 9.3.8: Number of T1 Gd-enhancing Lesions (FAS) by Region

	Treatment groups		Comparison	
	BAF312 (N=1099)	**Placebo (N=546)**	**RR [95% CI]**	**p-value**
Interaction Test				0.001
Region = Europe				
N'	791	394		
Month 12: Number of lesions [95% CI]*	0.07 [0.05;0.10]	0.64 [0.48;0.85]	0.11 [0.07;0.17]	<.001
Month 24: Number of lesions [95% CI]*	0.04 [0.03;0.07]	0.45 [0.30;0.68]	0.10 [0.05;0.18]	<.001
Region = Others				
N'	205	102		
Month 12: Number of lesions [95% CI]*	0.11 [0.05;0.24]	0.62 [0.30;1.28]	0.18 [0.06;0.52]	0.002
Month 24: Number of lesions [95% CI]*	0.32 [0.11;0.93]	0.18 [0.08;0.40]	1.80 [0.47;6.89]	0.392

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=1099)	**Placebo (N=546)**	**Total (N=1645)**
Return Rate n (%)*			
Month 12	903 (82.2)	439 (80.4)	1342 (81.6)
Month 24	470 (42.8)	239 (43.8)	709 (43.1)
Month 36	80 (7.3)	31 (5.7)	111 (6.7)

* 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=1099)	**Placebo (N=546)**	**Mean Difference [95% CI]**	**p-value**
N'	894	436		
Normalized Brain Volume at Baseline (SD)	1425.03 (85.07)	1424.58 (87.59)		
Month 12 Adjusted Mean Change (SE)	-0.28 (0.03)	-0.46 (0.03)	0.17 [0.10;0.25]	<.001
Month 24 Adjusted Mean Change (SE)	-0.71 (0.04)	-0.84 (0.05)	0.13 [0.02;0.24]	0.020

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=1099)	**Placebo (N=546)**	**Mean Difference [95% CI]**	**p-value**
Interaction Test				0.138
Age = 18-30				
N'	19	8		
Baseline Mean (SD)	1469.35 (95.60)	1526.71 (117.87)		
Month 12 Adjusted Mean Change (SE)	-0.42 (0.15)	-0.54 (0.22)	0.12 [-0.41;0.64]	0.659
Month 24 Adjusted Mean Change (SE)	-1.02 (0.24)	-0.80 (0.32)	-0.22 [-0.99;0.56]	0.582
Age = 31-40				
N'	133	72		
Baseline Mean (SD)	1443.31 (92.77)	1443.69 (83.17)		
Month 12 Adjusted Mean Change (SE)	-0.25 (0.05)	-0.35 (0.07)	0.10 [-0.08;0.28]	0.270
Month 24 Adjusted Mean Change (SE)	-0.73 (0.08)	-0.67 (0.10)	-0.06 [-0.32;0.21]	0.676
Age = 41-55				
N'	582	263		
Baseline Mean (SD)	1424.03 (81.88)	1422.16 (87.66)		
Month 12 Adjusted Mean Change (SE)	-0.26 (0.03)	-0.46 (0.04)	0.20 [0.11;0.29]	<.001
Month 24 Adjusted Mean Change (SE)	-0.66 (0.04)	-0.87 (0.06)	0.21 [0.07;0.35]	0.003
Age = >55				
N'	160	93		
Baseline Mean (SD)	1408.20 (84.63)	1407.85 (80.67)		
Month 12 Adjusted Mean Change (SE)	-0.37 (0.05)	-0.54 (0.07)	0.17 [0.01;0.33]	0.038
Month 24 Adjusted Mean Change (SE)	-0.86 (0.08)	-0.91 (0.10)	0.05 [-0.20;0.30]	0.675

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+SPMS Group+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=1099)	**Placebo (N=546)**	**Mean Difference [95% CI]**	**p-value**
Interaction Test				0.461
Sex = F				
N'	529	269		
Baseline Mean (SD)	1429.44 (85.82)	1422.78 (86.28)		
Month 12 Adjusted Mean Change (SE)	-0.22 (0.03)	-0.43 (0.04)	0.21 [0.12;0.30]	<.001
Month 24 Adjusted Mean Change (SE)	-0.60 (0.04)	-0.79 (0.06)	0.19 [0.05;0.33]	0.007
Sex = M				
N'	365	167		
Baseline Mean (SD)	1418.62 (83.67)	1427.48 (89.85)		
Month 12 Adjusted Mean Change (SE)	-0.37 (0.04)	-0.50 (0.05)	0.13 [0.01;0.24]	0.032
Month 24 Adjusted Mean Change (SE)	-0.86 (0.05)	-0.92 (0.07)	0.06 [-0.11;0.23]	0.485

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=1099)	**Placebo (N=546)**	**Mean Difference [95% CI]**	**p-value**
Interaction Test				0.346
Previous MS-DMT = N				
N'	195	91		
Baseline Mean (SD)	1434.89 (85.96)	1427.32 (86.58)		
Month 12 Adjusted Mean Change (SE)	-0.40 (0.05)	-0.59 (0.07)	0.19 [0.03;0.35]	0.018
Month 24 Adjusted Mean Change (SE)	-0.84 (0.07)	-0.99 (0.10)	0.14 [-0.09;0.38]	0.225
Previous MS-DMT = Y				
N'	699	345		
Baseline Mean (SD)	1422.28 (84.68)	1423.86 (87.97)		
Month 12 Adjusted Mean Change (SE)	-0.25 (0.03)	-0.42 (0.04)	0.17 [0.09;0.26]	<.001
Month 24 Adjusted Mean Change (SE)	-0.67 (0.04)	-0.80 (0.05)	0.13 [0.01;0.25]	0.039

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=1099)	**Placebo (N=546)**	**Mean Difference [95% CI]**	**p-value**
Interaction Test				0.790
Previous IFN-beta 1b = N				
N'	603	319		
Baseline Mean (SD)	1428.27 (86.54)	1428.45 (85.53)		
Month 12 Adjusted Mean Change (SE)	-0.32 (0.03)	-0.48 (0.04)	0.15 [0.07;0.24]	<.001
Month 24 Adjusted Mean Change (SE)	-0.72 (0.04)	-0.85 (0.06)	0.13 [0.01;0.26]	0.041
Previous IFN-beta 1b = Y				
N'	291	117		
Baseline Mean (SD)	1418.30 (81.68)	1414.02 (92.53)		
Month 12 Adjusted Mean Change (SE)	-0.20 (0.04)	-0.41 (0.06)	0.21 [0.08;0.35]	0.002
Month 24 Adjusted Mean Change (SE)	-0.70 (0.06)	-0.81 (0.09)	0.11 [-0.09;0.31]	0.281

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=1099)	**Placebo (N=546)**	**Mean Difference [95% CI]**	**p-value**
Interaction Test				0.901
Rapid evolvement = N				
N'	676	315		
Baseline Mean (SD)	1421.93 (85.77)	1421.28 (86.63)		
Month 12 Adjusted Mean Change (SE)	-0.26 (0.03)	-0.47 (0.04)	0.21 [0.12;0.29]	<.001
Month 24 Adjusted Mean Change (SE)	-0.70 (0.04)	-0.82 (0.06)	0.12 [0.00;0.25]	0.059
Rapid evolvement = Y				
N'	218	121		
Baseline Mean (SD)	1434.63 (82.31)	1433.18 (89.84)		
Month 12 Adjusted Mean Change (SE)	-0.35 (0.05)	-0.42 (0.06)	0.08 [-0.07;0.22]	0.293
Month 24 Adjusted Mean Change (SE)	-0.75 (0.07)	-0.87 (0.08)	0.11 [-0.09;0.31]	0.270

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=1099)	**Placebo (N=546)**	**Mean Difference [95% CI]**	**p-value**
Interaction Test				0.637
Moderate/severe disease course = N				
N'	162	71		
Baseline Mean (SD)	1416.91 (77.90)	1402.06 (80.53)		
Month 12 Adjusted Mean Change (SE)	-0.29 (0.05)	-0.46 (0.08)	0.17 [0.00;0.35]	0.053
Month 24 Adjusted Mean Change (SE)	-0.69 (0.08)	-0.77 (0.11)	0.08 [-0.17;0.34]	0.525
Moderate/severe disease course = Y				
N'	732	365		
Baseline Mean (SD)	1426.82 (86.52)	1428.96 (88.34)		
Month 12 Adjusted Mean Change (SE)	-0.28 (0.03)	-0.46 (0.04)	0.18 [0.10;0.25]	<.001
Month 24 Adjusted Mean Change (SE)	-0.72 (0.04)	-0.85 (0.05)	0.14 [0.02;0.26]	0.022

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=1099)	**Placebo (N=546)**	**Mean Difference [95% CI]**	**p-value**
Interaction Test				0.483
Region = Europe				
N'	716	351		
Baseline Mean (SD)	1425.00 (84.18)	1420.01 (86.91)		
Month 12 Adjusted Mean Change (SE)	-0.27 (0.02)	-0.45 (0.03)	0.19 [0.11;0.27]	<.001
Month 24 Adjusted Mean Change (SE)	-0.70 (0.03)	-0.84 (0.05)	0.14 [0.02;0.25]	0.022
Region = Others				
N'	178	85		
Baseline Mean (SD)	1425.13 (88.82)	1443.46 (88.40)		
Month 12 Adjusted Mean Change (SE)	-0.34 (0.05)	-0.48 (0.07)	0.14 [-0.02;0.31]	0.084
Month 24 Adjusted Mean Change (SE)	-0.71 (0.09)	-0.83 (0.12)	0.11 [-0.18;0.41]	0.447

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 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=1099)	**Placebo (N=546)**	**Total (N=1645)**
Return Rate n (%)*			
Baseline	1066 (97.0)	530 (97.1)	1596 (97.0)
Month 06	992 (90.3)	509 (93.2)	1501 (91.2)
Month 12	909 (82.7)	441 (80.8)	1350 (82.1)
Month 18	634 (57.7)	306 (56.0)	940 (57.1)
Month 24	388 (35.3)	188 (34.4)	576 (35.0)
Month 30	146 (13.3)	61 (11.2)	207 (12.6)

* 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=1099)	**Placebo (N=546)**	**Mean Difference [95% CI]**	**p-value**
N'	1001	508		
Baseline Mean (SD)	51.20 (21.54)	50.53 (21.35)		
Month 06 Adjusted Mean Change (SE)	0.24 (0.61)	1.55 (0.80)		.
Month 12 Adjusted Mean Change (SE)	1.33 (0.65)	4.22 (0.87)	-2.89 [-4.83;-0.96]	0.003
Month 18 Adjusted Mean Change (SE)	2.79 (0.70)	5.09 (0.95)		.
Month 24 Adjusted Mean Change (SE)	3.31 (0.82)	4.67 (1.12)	-1.36 [-3.93;1.21]	0.300
Month 30 Adjusted Mean Change (SE)	3.79 (1.07)	6.37 (1.57)		.

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=1099)	Placebo (N=546)	Mean Difference [95% CI]	p-value
Interaction Test				0.023
Age = 18-30				
N'	22	10		
Baseline Mean (SD)	53.94 (27.03)	52.50 (17.24)		
Month 06 Adjusted Mean Change (SE)	-3.31 (3.59)	9.37 (5.28)	.	.
Month 12 Adjusted Mean Change (SE)	-2.60 (3.95)	11.08 (6.58)	-13.68 [-28.64;1.28]	0.073
Month 18 Adjusted Mean Change (SE)	-11.34 (4.63)	12.42 (6.92)	.	.
Month 24 Adjusted Mean Change (SE)	-11.43 (6.17)	16.06 (8.39)	-27.50 [-47.86;-7.13]	0.008
Month 30 Adjusted Mean Change (SE)	-10.86 (7.19)	23.48 (11.87)	.	.
Age = 31-40				
N'	147	86		
Baseline Mean (SD)	53.24 (22.88)	51.57 (21.13)		
Month 06 Adjusted Mean Change (SE)	2.51 (1.42)	2.24 (1.83)	.	.
Month 12 Adjusted Mean Change (SE)	2.01 (1.51)	4.73 (1.99)	-2.72 [-7.54;2.10]	0.268
Month 18 Adjusted Mean Change (SE)	4.07 (1.69)	6.34 (2.14)	.	.
Month 24 Adjusted Mean Change (SE)	3.77 (2.02)	5.57 (2.67)	-1.80 [-8.31;4.70]	0.587
Month 30 Adjusted Mean Change (SE)	1.66 (2.82)	10.71 (3.63)	.	.
Age = 41-55				
N'	653	307		
Baseline Mean (SD)	50.71 (21.31)	50.11 (21.72)		
Month 06 Adjusted Mean Change (SE)	0.13 (0.74)	1.47 (1.00)	.	.
Month 12 Adjusted Mean Change (SE)	1.46 (0.78)	4.43 (1.08)	-2.97 [-5.43;-0.51]	0.018
Month 18 Adjusted Mean Change (SE)	3.01 (0.84)	4.69 (1.20)	.	.
Month 24 Adjusted Mean Change (SE)	4.11 (0.98)	5.42 (1.40)	-1.31 [-4.52;1.91]	0.426
Month 30 Adjusted Mean Change (SE)	5.77 (1.29)	4.52 (2.05)	.	.

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=1099)	**Placebo (N=546)**	**Mean Difference [95% CI]**	**p-value**
Age = >55				
N'	179	105		
Baseline Mean (SD)	50.99 (20.54)	50.73 (21.03)		
Month 06 Adjusted Mean Change (SE)	-0.90 (1.30)	0.38 (1.68)	.	.
Month 12 Adjusted Mean Change (SE)	0.71 (1.41)	2.54 (1.83)	-1.83 [-6.23;2.57]	0.414
Month 18 Adjusted Mean Change (SE)	2.28 (1.55)	4.47 (2.01)	.	.
Month 24 Adjusted Mean Change (SE)	1.05 (1.85)	0.41 (2.45)	0.64 [-5.30;6.58]	0.833
Month 30 Adjusted Mean Change (SE)	-0.43 (2.30)	5.40 (3.18)	.	.

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=1099)	**Placebo (N=546)**	**Mean Difference [95% CI]**	**p-value**
Interaction Test				0.616
Sex = F				
N'	603	301		
Baseline Mean (SD)	52.04 (21.90)	52.08 (21.64)		
Month 06 Adjusted Mean Change (SE)	-0.37 (0.76)	1.18 (1.01)	.	.
Month 12 Adjusted Mean Change (SE)	0.96 (0.81)	4.10 (1.09)	-3.14 [-5.65;-0.63]	0.014
Month 18 Adjusted Mean Change (SE)	2.25 (0.89)	5.24 (1.21)	.	.
Month 24 Adjusted Mean Change (SE)	2.46 (1.05)	4.54 (1.42)	-2.08 [-5.43;1.27]	0.223
Month 30 Adjusted Mean Change (SE)	2.30 (1.38)	4.98 (2.02)	.	.
Sex = M				
N'	398	207		
Baseline Mean (SD)	49.92 (20.94)	48.29 (20.77)		
Month 06 Adjusted Mean Change (SE)	1.14 (0.89)	2.06 (1.21)	.	.
Month 12 Adjusted Mean Change (SE)	1.88 (0.95)	4.38 (1.32)	-2.50 [-5.56;0.55]	0.108
Month 18 Adjusted Mean Change (SE)	3.57 (1.02)	4.86 (1.44)	.	.
Month 24 Adjusted Mean Change (SE)	4.45 (1.19)	4.86 (1.75)	-0.41 [-4.46;3.64]	0.844
Month 30 Adjusted Mean Change (SE)	5.78 (1.58)	8.39 (2.44)	.	.

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=1099)	**Placebo (N=546)**	**Mean Difference [95% CI]**	**p-value**
Interaction Test				0.465
Previous MS-DMT = N				
N'	213	105		
Baseline Mean (SD)	47.85 (22.93)	46.63 (21.84)		
Month 06 Adjusted Mean Change (SE)	-1.05 (1.20)	0.81 (1.68)	.	.
Month 12 Adjusted Mean Change (SE)	-0.11 (1.29)	5.02 (1.84)	-5.12 [-9.39;-0.86]	0.019
Month 18 Adjusted Mean Change (SE)	1.66 (1.43)	4.06 (2.06)	.	.
Month 24 Adjusted Mean Change (SE)	2.45 (1.66)	5.48 (2.38)	-3.03 [-8.62;2.55]	0.287
Month 30 Adjusted Mean Change (SE)	5.06 (2.26)	9.89 (3.90)	.	.
Previous MS-DMT = Y				
N'	788	403		
Baseline Mean (SD)	52.10 (21.07)	51.55 (21.14)		
Month 06 Adjusted Mean Change (SE)	0.61 (0.68)	1.75 (0.89)	.	.
Month 12 Adjusted Mean Change (SE)	1.74 (0.72)	4.03 (0.96)	-2.29 [-4.47;-0.12]	0.039
Month 18 Adjusted Mean Change (SE)	3.11 (0.78)	5.35 (1.05)	.	.
Month 24 Adjusted Mean Change (SE)	3.55 (0.91)	4.45 (1.26)	-0.89 [-3.80;2.01]	0.546
Month 30 Adjusted Mean Change (SE)	3.50 (1.19)	5.73 (1.72)	.	.

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=1099)	**Placebo (N=546)**	**Mean Difference [95% CI]**	**p-value**
Interaction Test				0.490
Previous IFN-beta 1b = N				
N'	681	362		
Baseline Mean (SD)	50.70 (21.95)	49.80 (21.07)		
Month 06 Adjusted Mean Change (SE)	0.01 (0.71)	1.71 (0.94)	.	.
Month 12 Adjusted Mean Change (SE)	1.31 (0.76)	4.17 (1.02)	-2.86 [-5.17;-0.54]	0.016
Month 18 Adjusted Mean Change (SE)	2.24 (0.83)	4.94 (1.13)	.	.
Month 24 Adjusted Mean Change (SE)	2.57 (0.97)	4.42 (1.32)	-1.85 [-4.93;1.23]	0.238
Month 30 Adjusted Mean Change (SE)	3.40 (1.25)	6.78 (1.81)	.	.
Previous IFN-beta 1b = Y				
N'	320	146		
Baseline Mean (SD)	52.27 (20.63)	52.35 (22.01)		
Month 06 Adjusted Mean Change (SE)	0.72 (1.00)	1.16 (1.41)	.	.
Month 12 Adjusted Mean Change (SE)	1.37 (1.07)	4.35 (1.53)	-2.98 [-6.54;0.57]	0.100
Month 18 Adjusted Mean Change (SE)	3.97 (1.17)	5.44 (1.66)	.	.
Month 24 Adjusted Mean Change (SE)	4.90 (1.38)	5.29 (2.03)	-0.39 [-5.12;4.34]	0.872
Month 30 Adjusted Mean Change (SE)	4.57 (1.94)	4.74 (3.18)	.	.

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=1099)	**Placebo (N=546)**	**Mean Difference [95% CI]**	**p-value**
Interaction Test				0.543
Rapid evolvement = N				
N'	754	371		
Baseline Mean (SD)	51.58 (21.65)	50.70 (20.63)		
Month 06 Adjusted Mean Change (SE)	0.41 (0.69)	1.48 (0.93)	.	.
Month 12 Adjusted Mean Change (SE)	1.61 (0.73)	3.45 (1.01)	-1.85 [-4.11;0.42]	0.110
Month 18 Adjusted Mean Change (SE)	2.66 (0.80)	4.84 (1.13)	.	.
Month 24 Adjusted Mean Change (SE)	2.94 (0.94)	4.85 (1.35)	-1.91 [-4.99;1.17]	0.225
Month 30 Adjusted Mean Change (SE)	4.18 (1.27)	6.05 (1.93)	.	.
Rapid evolvement = Y				
N'	247	137		
Baseline Mean (SD)	50.05 (21.18)	50.09 (23.28)		
Month 06 Adjusted Mean Change (SE)	-0.34 (1.13)	1.70 (1.47)	.	.
Month 12 Adjusted Mean Change (SE)	0.47 (1.19)	6.22 (1.59)	-5.75 [-9.51;-1.98]	0.003
Month 18 Adjusted Mean Change (SE)	3.06 (1.28)	5.75 (1.69)	.	.
Month 24 Adjusted Mean Change (SE)	4.09 (1.48)	4.50 (1.97)	-0.41 [-5.14;4.32]	0.867
Month 30 Adjusted Mean Change (SE)	2.93 (1.89)	7.19 (2.71)	.	.

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=1099)	**Placebo (N=546)**	**Mean Difference [95% CI]**	**p-value**
Interaction Test				0.223
Moderate/severe disease course = N				
N'	181	80		
Baseline Mean (SD)	39.51 (20.35)	40.98 (20.68)		
Month 06 Adjusted Mean Change (SE)	-3.05 (1.31)	0.16 (1.90)	.	.
Month 12 Adjusted Mean Change (SE)	-3.50 (1.40)	2.70 (2.05)	-6.20 [-10.93;-1.46]	0.010
Month 18 Adjusted Mean Change (SE)	-1.47 (1.55)	2.85 (2.23)	.	.
Month 24 Adjusted Mean Change (SE)	-2.06 (1.76)	2.26 (2.58)	-4.32 [-10.35;1.70]	0.159
Month 30 Adjusted Mean Change (SE)	0.16 (2.35)	4.73 (4.42)	.	.
Moderate/severe disease course = Y				
N'	820	428		
Baseline Mean (SD)	53.78 (20.94)	52.32 (21.02)		
Month 06 Adjusted Mean Change (SE)	0.91 (0.66)	1.73 (0.86)	.	.
Month 12 Adjusted Mean Change (SE)	2.33 (0.70)	4.43 (0.93)	-2.09 [-4.21;0.02]	0.052
Month 18 Adjusted Mean Change (SE)	3.66 (0.76)	5.46 (1.03)	.	.
Month 24 Adjusted Mean Change (SE)	4.47 (0.89)	5.08 (1.23)	-0.61 [-3.45;2.23]	0.672
Month 30 Adjusted Mean Change (SE)	4.52 (1.18)	6.64 (1.69)	.	.

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=1099)	**Placebo (N=546)**	**Mean Difference [95% CI]**	**p-value**
Interaction Test				0.915
Region = Europe				
N'	784	397		
Baseline Mean (SD)	51.09 (21.44)	49.53 (21.06)		
Month 06 Adjusted Mean Change (SE)	0.48 (0.60)	2.20 (0.83)	.	.
Month 12 Adjusted Mean Change (SE)	1.77 (0.63)	4.94 (0.90)	-3.16 [-5.32;-1.00]	0.004
Month 18 Adjusted Mean Change (SE)	3.67 (0.69)	6.07 (0.98)	.	.
Month 24 Adjusted Mean Change (SE)	3.95 (0.81)	5.20 (1.16)	-1.25 [-4.03;1.52]	0.376
Month 30 Adjusted Mean Change (SE)	4.29 (1.10)	7.11 (1.70)	.	.
Region = Others				
N'	217	111		
Baseline Mean (SD)	51.60 (21.95)	54.12 (22.11)		
Month 06 Adjusted Mean Change (SE)	1.41 (1.13)	1.59 (1.59)	.	.
Month 12 Adjusted Mean Change (SE)	1.66 (1.25)	3.86 (1.78)	-2.20 [-6.47;2.07]	0.312
Month 18 Adjusted Mean Change (SE)	0.70 (1.51)	3.00 (2.21)	.	.
Month 24 Adjusted Mean Change (SE)	2.42 (2.11)	5.94 (3.08)	-3.52 [-10.84;3.80]	0.346
Month 30 Adjusted Mean Change (SE)	4.18 (2.89)	6.04 (3.86)	.	.

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=1099)	**Placebo (N=546)**	**Total (N=1645)**
Return Rate n (%)*			
Baseline	1064 (96.8)	529 (96.9)	1593 (96.8)
Month 06	986 (89.7)	507 (92.9)	1493 (90.8)
Month 12	909 (82.7)	441 (80.8)	1350 (82.1)
Month 18	632 (57.5)	306 (56.0)	938 (57.0)
Month 24	386 (35.1)	188 (34.4)	574 (34.9)
Month 30	146 (13.3)	61 (11.2)	207 (12.6)

* 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=1099)	**Placebo (N=546)**	**Mean Difference [95% CI]**	**p-value**
N'	998	506		
Baseline Mean (SD)	38.05 (23.32)	38.46 (23.87)		
Month 06 Adjusted Mean Change (SE)	-0.73 (0.66)	0.95 (0.86)		.
Month 12 Adjusted Mean Change (SE)	0.11 (0.71)	2.14 (0.95)	-2.03 [-4.15;0.09]	0.060
Month 18 Adjusted Mean Change (SE)	0.88 (0.79)	2.48 (1.08)		.
Month 24 Adjusted Mean Change (SE)	0.81 (0.96)	1.48 (1.33)	-0.66 [-3.73;2.40]	0.670
Month 30 Adjusted Mean Change (SE)	-1.05 (1.20)	2.82 (1.78)		.

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=1099)	Placebo (N=546)	Mean Difference [95% CI]	p-value
Interaction Test				0.044
Age = 18-30				
N'	22	10		
Baseline Mean (SD)	50.17 (29.91)	43.33 (20.59)		
Month 06 Adjusted Mean Change (SE)	-8.33 (3.83)	5.23 (5.63)	.	.
Month 12 Adjusted Mean Change (SE)	-4.81 (4.32)	5.39 (7.28)	-10.20 [-26.70;6.31]	0.226
Month 18 Adjusted Mean Change (SE)	-13.68 (5.31)	6.41 (7.92)	.	.
Month 24 Adjusted Mean Change (SE)	-4.95 (7.53)	11.64 (10.04)	-16.59 [-41.17;8.00]	0.186
Month 30 Adjusted Mean Change (SE)	-18.41 (8.10)	16.31 (13.60)	.	.
Age = 31-40				
N'	147	85		
Baseline Mean (SD)	40.19 (25.34)	39.69 (23.86)		
Month 06 Adjusted Mean Change (SE)	0.19 (1.52)	1.84 (1.96)	.	.
Month 12 Adjusted Mean Change (SE)	0.52 (1.64)	4.54 (2.18)	-4.02 [-9.29;1.25]	0.135
Month 18 Adjusted Mean Change (SE)	0.24 (1.93)	5.65 (2.43)	.	.
Month 24 Adjusted Mean Change (SE)	0.04 (2.40)	1.47 (3.19)	-1.43 [-9.20;6.34]	0.718
Month 30 Adjusted Mean Change (SE)	-2.83 (3.23)	8.57 (4.15)	.	.
Age = 41-55				
N'	650	306		
Baseline Mean (SD)	37.18 (22.96)	37.61 (23.48)		
Month 06 Adjusted Mean Change (SE)	-0.65 (0.79)	1.23 (1.07)	.	.
Month 12 Adjusted Mean Change (SE)	0.53 (0.85)	2.02 (1.18)	-1.48 [-4.18;1.21]	0.280
Month 18 Adjusted Mean Change (SE)	2.02 (0.95)	1.68 (1.37)	.	.
Month 24 Adjusted Mean Change (SE)	2.18 (1.15)	2.10 (1.65)	0.08 [-3.75;3.90]	0.968
Month 30 Adjusted Mean Change (SE)	0.51 (1.46)	0.14 (2.35)	.	.

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=1099)	**Placebo (N=546)**	**Mean Difference [95% CI]**	**p-value**
Age = >55				
N'	179	105		
Baseline Mean (SD)	37.97 (21.62)	39.47 (25.42)		
Month 06 Adjusted Mean Change (SE)	-0.80 (1.38)	-0.94 (1.79)	.	.
Month 12 Adjusted Mean Change (SE)	-1.14 (1.54)	0.32 (2.00)	-1.46 [-6.28;3.35]	0.550
Month 18 Adjusted Mean Change (SE)	-1.42 (1.77)	1.78 (2.29)	.	.
Month 24 Adjusted Mean Change (SE)	-3.19 (2.19)	-1.47 (2.93)	-1.72 [-8.81;5.38]	0.635
Month 30 Adjusted Mean Change (SE)	-3.49 (2.59)	3.44 (3.61)	.	.

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=1099)	**Placebo (N=546)**	**Mean Difference [95% CI]**	**p-value**
Interaction Test				0.104
Sex = F				
N'	602	301		
Baseline Mean (SD)	38.82 (23.11)	40.05 (24.68)		
Month 06 Adjusted Mean Change (SE)	-0.85 (0.73)	1.23 (1.03)	.	.
Month 12 Adjusted Mean Change (SE)	-0.17 (0.80)	3.06 (1.15)	-3.23 [-5.98;-0.49]	0.021
Month 18 Adjusted Mean Change (SE)	-0.05 (0.94)	3.48 (1.34)	.	.
Month 24 Adjusted Mean Change (SE)	0.32 (1.19)	2.99 (1.64)	-2.67 [-6.66;1.32]	0.189
Month 30 Adjusted Mean Change (SE)	-2.25 (1.52)	3.19 (2.27)	.	.
Sex = M				
N'	396	205		
Baseline Mean (SD)	36.89 (23.62)	36.12 (22.48)		
Month 06 Adjusted Mean Change (SE)	0.10 (0.91)	1.49 (1.25)	.	.
Month 12 Adjusted Mean Change (SE)	1.15 (0.98)	1.66 (1.39)	-0.51 [-3.85;2.83]	0.764
Month 18 Adjusted Mean Change (SE)	2.79 (1.11)	1.86 (1.60)	.	.
Month 24 Adjusted Mean Change (SE)	2.19 (1.36)	0.04 (2.05)	2.15 [-2.68;6.98]	0.382
Month 30 Adjusted Mean Change (SE)	1.20 (1.75)	3.05 (2.75)	.	.

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 10.2.4 MSIS-29 Psychological Impact Scale (FAS), Change from Baseline by Previous MS DMT

	Treatment groups		Comparison	
	BAF312 (N=1099)	**Placebo (N=546)**	**Mean Difference [95% CI]**	**p-value**
Interaction Test				0.720
Previous MS-DMT = N				
N'	213	105		
Baseline Mean (SD)	39.61 (23.96)	36.23 (23.37)		
Month 06 Adjusted Mean Change (SE)	-2.33 (1.28)	0.81 (1.79)	.	.
Month 12 Adjusted Mean Change (SE)	-0.81 (1.40)	3.11 (2.01)	-3.92 [-8.59;0.75]	0.100
Month 18 Adjusted Mean Change (SE)	-0.16 (1.63)	0.05 (2.34)	.	.
Month 24 Adjusted Mean Change (SE)	1.17 (1.97)	0.85 (2.80)	0.31 [-6.31;6.93]	0.926
Month 30 Adjusted Mean Change (SE)	-1.40 (2.55)	-2.41 (4.49)	.	.
Previous MS-DMT = Y				
N'	785	401		
Baseline Mean (SD)	37.63 (23.14)	39.04 (23.99)		
Month 06 Adjusted Mean Change (SE)	-0.28 (0.73)	1.00 (0.95)	.	.
Month 12 Adjusted Mean Change (SE)	0.38 (0.78)	1.91 (1.05)	-1.53 [-3.91;0.85]	0.208
Month 18 Adjusted Mean Change (SE)	1.17 (0.88)	3.08 (1.20)	.	.
Month 24 Adjusted Mean Change (SE)	0.72 (1.07)	1.63 (1.49)	-0.91 [-4.38;2.55]	0.605
Month 30 Adjusted Mean Change (SE)	-0.94 (1.34)	3.79 (1.94)	.	.

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=1099)	**Placebo (N=546)**	**Mean Difference [95% CI]**	**p-value**
Interaction Test				0.773
Previous IFN-beta 1b = N				
N'	679	361		
Baseline Mean (SD)	38.25 (23.49)	38.24 (23.90)		
Month 06 Adjusted Mean Change (SE)	-1.12 (0.76)	1.00 (1.00)	.	.
Month 12 Adjusted Mean Change (SE)	0.88 (0.82)	2.55 (1.11)	-1.66 [-4.19;0.87]	0.198
Month 18 Adjusted Mean Change (SE)	0.16 (0.94)	2.77 (1.28)	.	.
Month 24 Adjusted Mean Change (SE)	0.27 (1.14)	2.06 (1.56)	-1.78 [-5.45;1.88]	0.339
Month 30 Adjusted Mean Change (SE)	-0.23 (1.40)	2.65 (2.04)	.	.
Previous IFN-beta 1b = Y				
N'	319	145		
Baseline Mean (SD)	37.63 (22.99)	39.00 (23.86)		
Month 06 Adjusted Mean Change (SE)	0.11 (1.07)	0.80 (1.51)	.	.
Month 12 Adjusted Mean Change (SE)	-1.63 (1.17)	1.17 (1.67)	-2.80 [-6.68;1.08]	0.157
Month 18 Adjusted Mean Change (SE)	2.36 (1.32)	1.74 (1.89)	.	.
Month 24 Adjusted Mean Change (SE)	1.91 (1.62)	0.02 (2.42)	1.89 [-3.74;7.52]	0.510
Month 30 Adjusted Mean Change (SE)	-3.31 (2.19)	3.63 (3.62)	.	.

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=1099)	**Placebo (N=546)**	**Mean Difference [95% CI]**	**p-value**
Interaction Test				0.614
Rapid evolvement = N				
N'	751	369		
Baseline Mean (SD)	37.80 (23.06)	37.48 (23.41)		
Month 06 Adjusted Mean Change (SE)	-0.40 (0.66)	1.20 (0.93)	.	.
Month 12 Adjusted Mean Change (SE)	0.55 (0.72)	2.30 (1.04)	-1.75 [-4.23;0.73]	0.167
Month 18 Adjusted Mean Change (SE)	1.46 (0.84)	2.26 (1.23)	.	.
Month 24 Adjusted Mean Change (SE)	0.87 (1.06)	1.54 (1.56)	-0.67 [-4.37;3.03]	0.723
Month 30 Adjusted Mean Change (SE)	-0.96 (1.39)	3.08 (2.16)	.	.
Rapid evolvement = Y				
N'	247	137		
Baseline Mean (SD)	38.81 (24.11)	41.09 (24.97)		
Month 06 Adjusted Mean Change (SE)	-0.72 (1.15)	1.69 (1.53)	.	.
Month 12 Adjusted Mean Change (SE)	-0.21 (1.23)	2.99 (1.69)	-3.20 [-7.30;0.90]	0.126
Month 18 Adjusted Mean Change (SE)	0.24 (1.40)	4.10 (1.88)	.	.
Month 24 Adjusted Mean Change (SE)	1.55 (1.69)	2.51 (2.27)	-0.97 [-6.53;4.59]	0.733
Month 30 Adjusted Mean Change (SE)	-0.53 (2.07)	3.40 (3.04)	.	.

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 10.2.7 MSIS-29 Psychological Impact Scale (FAS), Change from Baseline by Disease Course

	Treatment groups		Comparison	
	BAF312 (N=1099)	**Placebo (N=546)**	**Mean Difference [95% CI]**	**p-value**
Interaction Test				0.400
Moderate/severe disease course = N				
N'	180	80		
Baseline Mean (SD)	33.42 (21.56)	38.89 (23.04)		
Month 06 Adjusted Mean Change (SE)	-2.69 (1.40)	0.36 (2.02)	.	.
Month 12 Adjusted Mean Change (SE)	-2.60 (1.52)	2.92 (2.24)	-5.51 [-10.71;-0.31]	0.038
Month 18 Adjusted Mean Change (SE)	-2.91 (1.75)	0.39 (2.53)	.	.
Month 24 Adjusted Mean Change (SE)	-3.37 (2.06)	-0.18 (3.03)	-3.19 [-10.31;3.92]	0.379
Month 30 Adjusted Mean Change (SE)	-3.32 (2.63)	0.52 (5.09)	.	.
Moderate/severe disease course = Y				
N'	818	426		
Baseline Mean (SD)	39.07 (23.58)	38.38 (24.04)		
Month 06 Adjusted Mean Change (SE)	-0.34 (0.71)	1.03 (0.92)	.	.
Month 12 Adjusted Mean Change (SE)	0.67 (0.76)	1.95 (1.02)	-1.28 [-3.60;1.04]	0.279
Month 18 Adjusted Mean Change (SE)	1.66 (0.86)	2.88 (1.17)	.	.
Month 24 Adjusted Mean Change (SE)	1.74 (1.05)	1.80 (1.46)	-0.06 [-3.45;3.34]	0.973
Month 30 Adjusted Mean Change (SE)	-0.60 (1.32)	3.15 (1.90)	.	.

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=1099)	**Placebo (N=546)**	**Mean Difference [95% CI]**	**p-value**
Interaction Test				0.703
Region = Europe				
N'	782	396		
Baseline Mean (SD)	37.50 (23.04)	37.81 (23.35)		
Month 06 Adjusted Mean Change (SE)	-0.77 (0.64)	1.16 (0.90)	.	.
Month 12 Adjusted Mean Change (SE)	0.60 (0.69)	2.48 (0.99)	-1.88 [-4.26;0.49]	0.120
Month 18 Adjusted Mean Change (SE)	1.17 (0.79)	3.11 (1.12)	.	.
Month 24 Adjusted Mean Change (SE)	1.43 (0.96)	1.85 (1.37)	-0.42 [-3.70;2.87]	0.804
Month 30 Adjusted Mean Change (SE)	-0.01 (1.22)	3.71 (1.91)	.	.
Region = Others				
N'	216	110		
Baseline Mean (SD)	40.04 (24.25)	40.81 (25.62)		
Month 06 Adjusted Mean Change (SE)	0.59 (1.22)	1.98 (1.71)	.	.
Month 12 Adjusted Mean Change (SE)	-0.69 (1.38)	2.49 (1.96)	-3.17 [-7.88;1.53]	0.186
Month 18 Adjusted Mean Change (SE)	0.89 (1.75)	0.99 (2.57)	.	.
Month 24 Adjusted Mean Change (SE)	-1.59 (2.60)	1.79 (3.80)	-3.38 [-12.42;5.65]	0.462
Month 30 Adjusted Mean Change (SE)	-6.80 (3.24)	0.08 (4.29)	.	.

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=1099)	**Placebo (N=546)**	**Total (N=1645)**
Return Rate n (%)*			
Baseline	1084 (98.6)	536 (98.2)	1620 (98.5)
Month 06	1012 (92.1)	517 (94.7)	1529 (92.9)
Month 12	910 (82.8)	438 (80.2)	1348 (81.9)
Month 18	646 (58.8)	308 (56.4)	954 (58.0)
Month 24	305 (27.8)	143 (26.2)	448 (27.2)
Month 30	87 (7.9)	35 (6.4)	122 (7.4)

* 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=1099)	**Placebo (N=546)**	**Mean Difference [95% CI]**	**p-value**
N'	1017	514		
Baseline Mean (SD)	0.61 (0.23)	0.59 (0.23)		
Month 06 Adjusted Mean Change (SE)	-0.02 (0.01)	-0.02 (0.01)		.
Month 12 Adjusted Mean Change (SE)	-0.02 (0.01)	-0.05 (0.01)	0.03 [0.00;0.05]	0.037
Month 18 Adjusted Mean Change (SE)	-0.04 (0.01)	-0.04 (0.01)		.
Month 24 Adjusted Mean Change (SE)	-0.04 (0.01)	-0.07 (0.02)	0.03 [0.00;0.07]	0.088
Month 30 Adjusted Mean Change (SE)	-0.01 (0.02)	-0.11 (0.03)		.

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=1099)	**Placebo (N=546)**	**Mean Difference [95% CI]**	**p-value**
Interaction Test				0.075
Age = 18-30				
N'	23	11		
Baseline Mean (SD)	0.51 (0.31)	0.57 (0.30)		
Month 06 Adjusted Mean Change (SE)	0.09 (0.05)	-0.05 (0.07)	.	.
Month 12 Adjusted Mean Change (SE)	0.04 (0.05)	-0.04 (0.08)	0.08 [-0.11;0.27]	0.426
Month 18 Adjusted Mean Change (SE)	0.06 (0.07)	-0.28 (0.09)	.	.
Month 24 Adjusted Mean Change (SE)	-0.16 (0.10)	-0.42 (0.11)	0.26 [-0.04;0.55]	0.094
Age = 31-40				
N'	151	85		
Baseline Mean (SD)	0.59 (0.25)	0.60 (0.22)		
Month 06 Adjusted Mean Change (SE)	-0.01 (0.02)	-0.06 (0.02)	.	.
Month 12 Adjusted Mean Change (SE)	-0.02 (0.02)	-0.07 (0.03)	0.05 [-0.01;0.12]	0.105
Month 18 Adjusted Mean Change (SE)	-0.05 (0.02)	-0.08 (0.03)	.	.
Month 24 Adjusted Mean Change (SE)	-0.04 (0.03)	-0.09 (0.04)	0.04 [-0.05;0.14]	0.373
Month 30 Adjusted Mean Change (SE)	0.07 (0.05)	-0.04 (0.09)	.	.
Age = 41-55				
N'	658	310		
Baseline Mean (SD)	0.61 (0.22)	0.58 (0.24)		
Month 06 Adjusted Mean Change (SE)	-0.03 (0.01)	-0.01 (0.01)	.	.
Month 12 Adjusted Mean Change (SE)	-0.03 (0.01)	-0.04 (0.01)	0.01 [-0.02;0.04]	0.610
Month 18 Adjusted Mean Change (SE)	-0.05 (0.01)	-0.02 (0.02)	.	.
Month 24 Adjusted Mean Change (SE)	-0.04 (0.01)	-0.05 (0.02)	0.00 [-0.04;0.05]	0.858
Month 30 Adjusted Mean Change (SE)	-0.04 (0.02)	-0.15 (0.04)	.	.

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+

Table 10.3.2: EQ-5D Utility Score (FAS), Change from Baseline by Age

	Treatment groups		Comparison	
	BAF312 (N=1099)	**Placebo (N=546)**	**Mean Difference [95% CI]**	**p-value**
Age = >55				
N'	185	108		
Baseline Mean (SD)	0.62 (0.21)	0.61 (0.22)		
Month 06 Adjusted Mean Change (SE)	-0.02 (0.02)	0.00 (0.02)	.	.
Month 12 Adjusted Mean Change (SE)	-0.01 (0.02)	-0.04 (0.02)	0.02 [-0.03;0.08]	0.423
Month 18 Adjusted Mean Change (SE)	-0.05 (0.02)	-0.03 (0.03)	.	.
Month 24 Adjusted Mean Change (SE)	-0.05 (0.03)	-0.08 (0.03)	0.04 [-0.05;0.12]	0.392
Month 30 Adjusted Mean Change (SE)	0.01 (0.04)	-0.02 (0.05)	.	.

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+

Table 10.3.3: EQ-5D Utility Score (FAS), Change from Baseline by Gender

	Treatment groups		Comparison	
	BAF312 (N=1099)	**Placebo (N=546)**	**Mean Difference [95% CI]**	**p-value**
Interaction Test				0.144
Sex = F				
N'	611	305		
Baseline Mean (SD)	0.61 (0.23)	0.58 (0.25)		
Month 06 Adjusted Mean Change (SE)	-0.02 (0.01)	-0.02 (0.01)	.	.
Month 12 Adjusted Mean Change (SE)	-0.03 (0.01)	-0.06 (0.01)	0.03 [0.00;0.06]	0.059
Month 18 Adjusted Mean Change (SE)	-0.03 (0.01)	-0.06 (0.02)	.	.
Month 24 Adjusted Mean Change (SE)	-0.03 (0.01)	-0.10 (0.02)	0.07 [0.02;0.12]	0.008
Month 30 Adjusted Mean Change (SE)	0.00 (0.03)	-0.10 (0.04)	.	.
Sex = M				
N'	406	209		
Baseline Mean (SD)	0.61 (0.22)	0.61 (0.21)		
Month 06 Adjusted Mean Change (SE)	-0.02 (0.01)	-0.02 (0.01)	.	.
Month 12 Adjusted Mean Change (SE)	-0.01 (0.01)	-0.03 (0.02)	0.02 [-0.02;0.06]	0.324
Month 18 Adjusted Mean Change (SE)	-0.05 (0.01)	-0.01 (0.02)	.	.
Month 24 Adjusted Mean Change (SE)	-0.05 (0.02)	-0.04 (0.02)	-0.01 [-0.07;0.04]	0.637
Month 30 Adjusted Mean Change (SE)	-0.03 (0.03)	-0.12 (0.05)	.	.

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=1099)	**Placebo (N=546)**	**Mean Difference [95% CI]**	**p-value**
Interaction Test				0.564
Previous MS-DMT = N				
N'	219	108		
Baseline Mean (SD)	0.62 (0.22)	0.62 (0.23)		
Month 06 Adjusted Mean Change (SE)	-0.03 (0.01)	-0.03 (0.02)	.	.
Month 12 Adjusted Mean Change (SE)	-0.02 (0.01)	-0.03 (0.02)	0.01 [-0.05;0.06]	0.794
Month 18 Adjusted Mean Change (SE)	-0.04 (0.02)	0.00 (0.03)	.	.
Month 24 Adjusted Mean Change (SE)	-0.02 (0.02)	-0.11 (0.04)	0.08 [0.00;0.17]	0.049
Month 30 Adjusted Mean Change (SE)	-0.03 (0.05)	-0.23 (0.09)	.	.
Previous MS-DMT = Y				
N'	798	406		
Baseline Mean (SD)	0.61 (0.23)	0.59 (0.24)		
Month 06 Adjusted Mean Change (SE)	-0.02 (0.01)	-0.02 (0.01)	.	.
Month 12 Adjusted Mean Change (SE)	-0.02 (0.01)	-0.05 (0.01)	0.03 [0.00;0.06]	0.028
Month 18 Adjusted Mean Change (SE)	-0.04 (0.01)	-0.05 (0.01)	.	.
Month 24 Adjusted Mean Change (SE)	-0.04 (0.01)	-0.07 (0.02)	0.02 [-0.02;0.06]	0.336
Month 30 Adjusted Mean Change (SE)	-0.01 (0.02)	-0.09 (0.03)	.	.

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=1099)	**Placebo (N=546)**	**Mean Difference [95% CI]**	**p-value**
Interaction Test				0.459
Previous IFN-beta 1b = N				
N'	693	367		
Baseline Mean (SD)	0.61 (0.23)	0.60 (0.24)		
Month 06 Adjusted Mean Change (SE)	-0.02 (0.01)	-0.02 (0.01)	.	.
Month 12 Adjusted Mean Change (SE)	-0.03 (0.01)	-0.04 (0.01)	0.02 [-0.01;0.04]	0.270
Month 18 Adjusted Mean Change (SE)	-0.05 (0.01)	-0.05 (0.01)	.	.
Month 24 Adjusted Mean Change (SE)	-0.04 (0.01)	-0.08 (0.02)	0.04 [0.00;0.08]	0.075
Month 30 Adjusted Mean Change (SE)	-0.01 (0.02)	-0.13 (0.04)	.	.
Previous IFN-beta 1b = Y				
N'	324	147		
Baseline Mean (SD)	0.60 (0.22)	0.59 (0.23)		
Month 06 Adjusted Mean Change (SE)	-0.02 (0.01)	-0.02 (0.02)	.	.
Month 12 Adjusted Mean Change (SE)	-0.01 (0.01)	-0.06 (0.02)	0.05 [0.00;0.09]	0.033
Month 18 Adjusted Mean Change (SE)	-0.03 (0.01)	-0.02 (0.02)	.	.
Month 24 Adjusted Mean Change (SE)	-0.03 (0.02)	-0.04 (0.03)	0.01 [-0.06;0.08]	0.822
Month 30 Adjusted Mean Change (SE)	-0.01 (0.04)	-0.02 (0.07)	.	.

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=1099)	**Placebo (N=546)**	**Mean Difference [95% CI]**	**p-value**
Interaction Test				0.264
Rapid evolvement = N				
N'	768	375		
Baseline Mean (SD)	0.61 (0.23)	0.60 (0.22)		
Month 06 Adjusted Mean Change (SE)	-0.02 (0.01)	-0.03 (0.01)	.	.
Month 12 Adjusted Mean Change (SE)	-0.03 (0.01)	-0.05 (0.01)	0.02 [-0.01;0.05]	0.124
Month 18 Adjusted Mean Change (SE)	-0.04 (0.01)	-0.04 (0.02)	.	.
Month 24 Adjusted Mean Change (SE)	-0.04 (0.01)	-0.07 (0.02)	0.03 [-0.02;0.08]	0.217
Month 30 Adjusted Mean Change (SE)	-0.01 (0.02)	-0.11 (0.04)	.	.
Rapid evolvement = Y				
N'	249	139		
Baseline Mean (SD)	0.61 (0.23)	0.57 (0.26)		
Month 06 Adjusted Mean Change (SE)	-0.03 (0.01)	0.00 (0.02)	.	.
Month 12 Adjusted Mean Change (SE)	-0.02 (0.02)	-0.03 (0.02)	0.01 [-0.04;0.06]	0.704
Month 18 Adjusted Mean Change (SE)	-0.04 (0.02)	-0.02 (0.02)	.	.
Month 24 Adjusted Mean Change (SE)	-0.06 (0.02)	-0.07 (0.03)	0.01 [-0.06;0.08]	0.716
Month 30 Adjusted Mean Change (SE)	-0.03 (0.04)	-0.06 (0.06)	.	.

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+

Table 10.3.7 EQ-5D Utility Score (FAS), Change from Baseline by Disease Course

	Treatment groups		Comparison	
	BAF312 (N=1099)	**Placebo (N=546)**	**Mean Difference [95% CI]**	**p-value**
Interaction Test				0.763
Moderate/severe disease course = N				
N'	182	84		
Baseline Mean (SD)	0.70 (0.17)	0.65 (0.19)		
Month 06 Adjusted Mean Change (SE)	0.01 (0.02)	0.01 (0.02)	.	.
Month 12 Adjusted Mean Change (SE)	0.01 (0.02)	-0.04 (0.02)	0.05 [-0.01;0.11]	0.102
Month 18 Adjusted Mean Change (SE)	-0.02 (0.02)	0.01 (0.03)	.	.
Month 24 Adjusted Mean Change (SE)	0.01 (0.03)	-0.03 (0.04)	0.04 [-0.05;0.13]	0.390
Month 30 Adjusted Mean Change (SE)	0.04 (0.05)	-0.08 (0.09)	.	.
Moderate/severe disease course = Y				
N'	835	430		
Baseline Mean (SD)	0.59 (0.23)	0.58 (0.24)		
Month 06 Adjusted Mean Change (SE)	-0.03 (0.01)	-0.03 (0.01)	.	.
Month 12 Adjusted Mean Change (SE)	-0.03 (0.01)	-0.05 (0.01)	0.02 [-0.01;0.05]	0.125
Month 18 Adjusted Mean Change (SE)	-0.05 (0.01)	-0.05 (0.01)	.	.
Month 24 Adjusted Mean Change (SE)	-0.05 (0.01)	-0.08 (0.02)	0.03 [-0.01;0.07]	0.148
Month 30 Adjusted Mean Change (SE)	-0.02 (0.02)	-0.11 (0.03)	.	.

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=1099)	**Placebo (N=546)**	**Mean Difference [95% CI]**	**p-value**
Interaction Test				N.E.
Region = Europe				
N'	803	403		
Baseline Mean (SD)	0.61 (0.22)	0.61 (0.22)		
Month 06 Adjusted Mean Change (SE)	-0.02 (0.01)	-0.02 (0.01)	.	.
Month 12 Adjusted Mean Change (SE)	-0.03 (0.01)	-0.05 (0.01)	0.02 [0.00;0.05]	0.065
Month 18 Adjusted Mean Change (SE)	-0.04 (0.01)	-0.05 (0.01)	.	.
Month 24 Adjusted Mean Change (SE)	-0.04 (0.01)	-0.07 (0.02)	0.03 [-0.01;0.07]	0.145
Month 30 Adjusted Mean Change (SE)	-0.02 (0.02)	-0.11 (0.03)	.	.
Region = Others				
N'	214	111		
Baseline Mean (SD)	0.60 (0.25)	0.55 (0.27)		
Month 06 Adjusted Mean Change (SE)	-0.02 (0.01)	-0.02 (0.02)	.	.
Month 12 Adjusted Mean Change (SE)	0.00 (0.02)	-0.03 (0.02)	0.03 [-0.03;0.09]	0.315
Month 18 Adjusted Mean Change (SE)	-0.02 (0.02)	0.02 (0.03)	.	.
Month 24 Adjusted Mean Change (SE)	-0.03 (0.03)	-0.13 (0.05)	0.10 [-0.01;0.21]	0.068
Month 30 Adjusted Mean Change (SE)	0.06 (0.12)	-0.14 (0.15)	.	.

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=1099)	**Placebo (N=546)**	**Total (N=1645)**
Return Rate n (%)*			
Baseline	1082 (98.5)	537 (98.4)	1619 (98.4)
Month 06	1004 (91.4)	512 (93.8)	1516 (92.2)
Month 12	907 (82.5)	439 (80.4)	1346 (81.8)
Month 18	643 (58.5)	308 (56.4)	951 (57.8)
Month 24	306 (27.8)	143 (26.2)	449 (27.3)
Month 30	87 (7.9)	36 (6.6)	123 (7.5)

* 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=1099)	**Placebo (N=546)**	**Mean Difference [95% CI]**	**p-value**
N'	1016	514		
Baseline Mean (SD)	57.97 (18.93)	56.28 (19.25)		
Month 06 Adjusted Mean Change (SE)	-1.03 (0.53)	-0.91 (0.74)		.
Month 12 Adjusted Mean Change (SE)	-2.08 (0.57)	-3.88 (0.82)	1.79 [-0.16;3.75]	0.072
Month 18 Adjusted Mean Change (SE)	-2.17 (0.67)	-3.27 (0.96)		.
Month 24 Adjusted Mean Change (SE)	-2.06 (0.90)	-3.00 (1.31)	0.94 [-2.18;4.07]	0.555
Month 30 Adjusted Mean Change (SE)	-3.70 (1.74)	-5.90 (2.67)		.

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=1099)	**Placebo (N=546)**	**Mean Difference [95% CI]**	**p-value**
Interaction Test				N.E.
Age = 18-30				
N'	23	11		
Baseline Mean (SD)	57.30 (14.37)	47.82 (21.33)		
Age = 31-40				
N'	150	86		
Baseline Mean (SD)	57.03 (21.54)	56.55 (17.58)		
Month 06 Adjusted Mean Change (SE)	-2.22 (1.42)	-3.92 (1.87)	.	.
Month 12 Adjusted Mean Change (SE)	-3.29 (1.62)	-5.55 (2.19)	2.26 [-3.10;7.62]	0.407
Month 18 Adjusted Mean Change (SE)	-2.01 (1.85)	-7.38 (2.37)	.	.
Month 24 Adjusted Mean Change (SE)	-2.93 (2.25)	-6.26 (2.87)	3.32 [-3.92;10.57]	0.364
Month 30 Adjusted Mean Change (SE)	-5.45 (4.04)	-0.65 (7.22)	.	.
Age = 41-55				
N'	660	311		
Baseline Mean (SD)	57.58 (18.55)	56.01 (19.72)		
Month 06 Adjusted Mean Change (SE)	-0.69 (0.65)	-1.39 (0.94)	.	.
Month 12 Adjusted Mean Change (SE)	-1.99 (0.70)	-3.68 (1.04)	1.69 [-0.78;4.15]	0.180
Month 18 Adjusted Mean Change (SE)	-2.16 (0.82)	-2.72 (1.25)	.	.
Month 24 Adjusted Mean Change (SE)	-2.18 (1.14)	-4.15 (1.78)	1.97 [-2.19;6.13]	0.353
Month 30 Adjusted Mean Change (SE)	-3.78 (2.39)	-7.46 (3.92)	.	.

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=1099)	**Placebo (N=546)**	**Mean Difference [95% CI]**	**p-value**
Age = >55				
N'	183	106		
Baseline Mean (SD)	60.26 (18.48)	57.74 (18.93)		
Month 06 Adjusted Mean Change (SE)	-1.51 (1.26)	3.06 (1.64)	.	.
Month 12 Adjusted Mean Change (SE)	-1.21 (1.27)	-3.16 (1.65)	1.96 [-2.15;6.06]	0.349
Month 18 Adjusted Mean Change (SE)	-2.78 (1.59)	-1.47 (2.05)	.	.
Month 24 Adjusted Mean Change (SE)	-1.29 (2.05)	2.43 (2.73)	-3.72 [-10.50;3.06]	0.279
Month 30 Adjusted Mean Change (SE)	-5.50 (3.49)	-1.69 (4.11)	.	.

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=1099)	**Placebo (N=546)**	**Mean Difference [95% CI]**	**p-value**
Interaction Test				0.843
Sex = F				
N'	609	306		
Baseline Mean (SD)	58.79 (19.02)	57.24 (19.42)		
Month 06 Adjusted Mean Change (SE)	-0.61 (0.68)	0.74 (0.96)	.	.
Month 12 Adjusted Mean Change (SE)	-2.08 (0.74)	-3.20 (1.06)	1.13 [-1.41;3.66]	0.383
Month 18 Adjusted Mean Change (SE)	-1.24 (0.89)	-2.73 (1.25)	.	.
Month 24 Adjusted Mean Change (SE)	-1.92 (1.21)	-3.10 (1.72)	1.18 [-2.95;5.31]	0.575
Month 30 Adjusted Mean Change (SE)	-1.40 (2.27)	-3.95 (3.65)	.	.
Sex = M				
N'	407	208		
Baseline Mean (SD)	56.75 (18.77)	54.87 (18.95)		
Month 06 Adjusted Mean Change (SE)	-1.67 (0.84)	-3.32 (1.16)	.	.
Month 12 Adjusted Mean Change (SE)	-2.11 (0.90)	-4.88 (1.29)	2.78 [-0.29;5.85]	0.076
Month 18 Adjusted Mean Change (SE)	-3.42 (1.03)	-4.06 (1.51)	.	.
Month 24 Adjusted Mean Change (SE)	-2.28 (1.35)	-2.90 (2.04)	0.62 [-4.19;5.42]	0.801
Month 30 Adjusted Mean Change (SE)	-6.93 (2.71)	-8.28 (3.89)	.	.

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=1099)	**Placebo (N=546)**	**Mean Difference [95% CI]**	**p-value**
Interaction Test				0.952
Previous MS-DMT = N				
N'	218	108		
Baseline Mean (SD)	60.55 (17.74)	58.54 (20.81)		
Month 06 Adjusted Mean Change (SE)	-2.64 (1.28)	-1.28 (1.82)	.	.
Month 12 Adjusted Mean Change (SE)	-2.66 (1.36)	-5.56 (1.98)	2.90 [-1.81;7.61]	0.227
Month 18 Adjusted Mean Change (SE)	-4.23 (1.63)	-0.24 (2.35)	.	.
Month 24 Adjusted Mean Change (SE)	-4.38 (2.05)	-1.02 (3.21)	-3.36 [-10.84;4.12]	0.378
Month 30 Adjusted Mean Change (SE)	-3.66 (4.49)	-12.79 (7.99)	.	.
Previous MS-DMT = Y				
N'	798	406		
Baseline Mean (SD)	57.27 (19.20)	55.68 (18.79)		
Month 06 Adjusted Mean Change (SE)	-1.07 (0.67)	-0.24 (0.94)	.	.
Month 12 Adjusted Mean Change (SE)	-2.47 (0.72)	-3.04 (1.02)	0.58 [-1.86;3.02]	0.643
Month 18 Adjusted Mean Change (SE)	-2.13 (0.83)	-3.26 (1.19)	.	.
Month 24 Adjusted Mean Change (SE)	-1.90 (1.09)	-2.93 (1.55)	1.03 [-2.69;4.75]	0.586
Month 30 Adjusted Mean Change (SE)	-4.03 (1.93)	-4.54 (2.88)	.	.

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+

Table 10.4.5 EQ-5D VAS Thermometer (FAS), Change from Baseline by Previous IFN-beta-1b treatment

	Treatment groups		Comparison	
	BAF312 (N=1099)	**Placebo (N=546)**	**Mean Difference [95% CI]**	**p-value**
Interaction Test				N.E.
Previous IFN-beta 1b = N				
N'	693	369		
Baseline Mean (SD)	58.27 (18.71)	56.61 (19.31)		
Month 06 Adjusted Mean Change (SE)	-1.24 (0.63)	-1.34 (0.86)	.	.
Month 12 Adjusted Mean Change (SE)	-2.57 (0.67)	-4.44 (0.94)	1.87 [-0.39;4.14]	0.105
Month 18 Adjusted Mean Change (SE)	-2.21 (0.81)	-2.92 (1.15)	.	.
Month 24 Adjusted Mean Change (SE)	-2.34 (1.09)	-3.60 (1.51)	1.26 [-2.40;4.92]	0.499
Month 30 Adjusted Mean Change (SE)	-2.28 (2.01)	-6.02 (2.86)	.	.
Previous IFN-beta 1b = Y				
N'	323	145		
Baseline Mean (SD)	57.33 (19.41)	55.45 (19.14)		
Month 06 Adjusted Mean Change (SE)	-0.59 (0.99)	0.14 (1.46)	.	.
Month 12 Adjusted Mean Change (SE)	-1.05 (1.08)	-2.45 (1.61)	1.40 [-2.41;5.21]	0.470
Month 18 Adjusted Mean Change (SE)	-2.14 (1.20)	-3.96 (1.77)	.	.
Month 24 Adjusted Mean Change (SE)	-1.46 (1.62)	-0.91 (2.67)	-0.55 [-6.71;5.62]	0.861
Month 30 Adjusted Mean Change (SE)	-6.50 (3.61)	-8.99 (6.73)	.	.

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=1099)	**Placebo (N=546)**	**Mean Difference [95% CI]**	**p-value**
Interaction Test				0.918
Rapid evolvement = N				
N'	768	374		
Baseline Mean (SD)	58.54 (18.96)	58.24 (18.91)		
Month 06 Adjusted Mean Change (SE)	-1.46 (0.68)	-0.67 (0.98)	.	.
Month 12 Adjusted Mean Change (SE)	-2.88 (0.73)	-4.24 (1.06)	1.36 [-1.17;3.89]	0.291
Month 18 Adjusted Mean Change (SE)	-3.00 (0.86)	-3.71 (1.27)	.	.
Month 24 Adjusted Mean Change (SE)	-1.49 (1.13)	-2.67 (1.73)	1.19 [-2.87;5.24]	0.566
Month 30 Adjusted Mean Change (SE)	-4.96 (2.10)	-4.57 (3.19)	.	.
Rapid evolvement = Y				
N'	248	140		
Baseline Mean (SD)	56.21 (18.78)	51.04 (19.24)		
Month 06 Adjusted Mean Change (SE)	-1.24 (1.21)	0.09 (1.60)	.	.
Month 12 Adjusted Mean Change (SE)	-1.39 (1.27)	-1.84 (1.72)	0.44 [-3.74;4.63]	0.836
Month 18 Adjusted Mean Change (SE)	-1.33 (1.45)	-0.22 (1.93)	.	.
Month 24 Adjusted Mean Change (SE)	-4.58 (1.80)	-1.90 (2.36)	-2.67 [-8.50;3.16]	0.368
Month 30 Adjusted Mean Change (SE)	-1.86 (3.28)	-7.32 (5.11)	.	.

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+

Table 10.4.7 EQ-5D VAS Thermometer (FAS), Change from Baseline by Disease Course

	Treatment groups		Comparison	
	BAF312 (N=1099)	**Placebo (N=546)**	**Mean Difference [95% CI]**	**p-value**
Interaction Test				0.036
Moderate/severe disease course = N				
N'	181	83		
Baseline Mean (SD)	64.10 (18.02)	61.61 (19.00)		
Month 06 Adjusted Mean Change (SE)	3.15 (1.26)	0.42 (1.85)	.	.
Month 12 Adjusted Mean Change (SE)	0.36 (1.37)	-2.21 (1.99)	2.57 [-2.15;7.30]	0.286
Month 18 Adjusted Mean Change (SE)	1.13 (1.63)	-3.02 (2.30)	.	.
Month 24 Adjusted Mean Change (SE)	3.23 (2.10)	-2.71 (3.29)	5.94 [-1.72;13.60]	0.128
Month 30 Adjusted Mean Change (SE)	4.59 (4.28)	-10.90 (7.93)	.	.
Moderate/severe disease course = Y				
N'	835	431		
Baseline Mean (SD)	56.65 (18.88)	55.25 (19.15)		
Month 06 Adjusted Mean Change (SE)	-1.92 (0.58)	-1.17 (0.81)	.	.
Month 12 Adjusted Mean Change (SE)	-2.60 (0.63)	-4.22 (0.89)	1.62 [-0.53;3.76]	0.139
Month 18 Adjusted Mean Change (SE)	-2.86 (0.74)	-3.32 (1.06)	.	.
Month 24 Adjusted Mean Change (SE)	-3.22 (0.99)	-3.06 (1.42)	-0.16 [-3.57;3.25]	0.927
Month 30 Adjusted Mean Change (SE)	-5.37 (1.90)	-5.23 (2.83)	.	.

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=1099)	**Placebo (N=546)**	**Mean Difference [95% CI]**	**p-value**
Interaction Test				0.095
Region = Europe				
N'	802	404		
Baseline Mean (SD)	56.87 (18.68)	54.90 (19.02)		
Month 06 Adjusted Mean Change (SE)	-1.97 (0.67)	-0.69 (0.94)	.	.
Month 12 Adjusted Mean Change (SE)	-2.94 (0.71)	-3.87 (1.01)	0.93 [-1.50;3.35]	0.454
Month 18 Adjusted Mean Change (SE)	-2.63 (0.81)	-2.67 (1.16)	.	.
Month 24 Adjusted Mean Change (SE)	-2.62 (1.02)	-2.16 (1.49)	-0.47 [-4.02;3.09]	0.797
Month 30 Adjusted Mean Change (SE)	-4.59 (1.80)	-4.09 (2.81)	.	.
Region = Others				
N'	214	110		
Baseline Mean (SD)	62.12 (19.35)	61.35 (19.32)		
Month 06 Adjusted Mean Change (SE)	0.73 (1.30)	0.37 (1.81)	.	.
Month 12 Adjusted Mean Change (SE)	-0.84 (1.41)	-2.46 (2.00)	1.62 [-3.18;6.42]	0.508
Month 18 Adjusted Mean Change (SE)	-2.88 (1.82)	-3.05 (2.64)	.	.
Month 24 Adjusted Mean Change (SE)	-2.18 (2.91)	-6.56 (4.05)	4.38 [-5.41;14.18]	0.380
Month 30 Adjusted Mean Change (SE)	1.20 (7.87)	-20.41 (9.13)	.	.

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+

Table 10.5.0: MSWS-12 Converted Score (FAS), Return Rates

	Treatment groups		
	BAF312 (N=1099)	**Placebo (N=546)**	**Total (N=1645)**
Return Rate n (%)*			
Baseline	1089 (99.1)	539 (98.7)	1628 (99.0)
Month 06	1012 (92.1)	518 (94.9)	1530 (93.0)
Month 12	925 (84.2)	452 (82.8)	1377 (83.7)
Month 18	516 (47.0)	246 (45.1)	762 (46.3)
Month 24	403 (36.7)	195 (35.7)	598 (36.4)
Month 30	144 (13.1)	59 (10.8)	203 (12.3)

* 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=1099)	**Placebo (N=546)**	**Mean Difference [95% CI]**	**p-value**
N'	1022	516		
Baseline Mean (SD)	68.34 (23.39)	67.39 (22.28)		
Month 06 Adjusted Mean Change (SE)	0.11 (0.64)	1.09 (0.84)		.
Month 12 Adjusted Mean Change (SE)	1.53 (0.68)	3.36 (0.91)	-1.83 [-3.85;0.19]	0.076
Month 18 Adjusted Mean Change (SE)	3.28 (0.74)	5.01 (1.01)		.
Month 24 Adjusted Mean Change (SE)	4.16 (0.85)	5.38 (1.17)	-1.23 [-3.89;1.44]	0.367
Month 30 Adjusted Mean Change (SE)	4.39 (1.10)	7.47 (1.63)		.

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=1099)	Placebo (N=546)	Mean Difference [95% CI]	p-value
Interaction Test				0.699
Age = 18-30				
N'	23	11		
Baseline Mean (SD)	64.40 (24.03)	71.40 (19.37)		
Month 06 Adjusted Mean Change (SE)	-1.82 (3.92)	4.08 (5.61)	.	.
Month 12 Adjusted Mean Change (SE)	-0.71 (4.30)	11.02 (6.80)	-11.73 [-27.41;3.94]	0.142
Month 18 Adjusted Mean Change (SE)	1.56 (4.80)	10.03 (7.57)	.	.
Month 24 Adjusted Mean Change (SE)	-9.60 (6.72)	4.20 (8.28)	-13.80 [-34.65;7.05]	0.194
Month 30 Adjusted Mean Change (SE)	-5.32 (7.58)	6.30 (12.35)	.	.
Age = 31-40				
N'	150	88		
Baseline Mean (SD)	67.67 (23.85)	68.18 (22.68)		
Month 06 Adjusted Mean Change (SE)	0.59 (1.57)	1.37 (2.01)	.	.
Month 12 Adjusted Mean Change (SE)	2.75 (1.67)	1.51 (2.19)	1.24 [-4.08;6.56]	0.648
Month 18 Adjusted Mean Change (SE)	4.85 (1.88)	7.66 (2.34)	.	.
Month 24 Adjusted Mean Change (SE)	5.67 (2.20)	8.04 (2.84)	-2.37 [-9.34;4.60]	0.504
Month 30 Adjusted Mean Change (SE)	2.19 (2.98)	8.97 (3.96)	.	.
Age = 41-55				
N'	664	309		
Baseline Mean (SD)	68.97 (23.02)	67.67 (22.28)		
Month 06 Adjusted Mean Change (SE)	-0.79 (0.82)	0.53 (1.11)	.	.
Month 12 Adjusted Mean Change (SE)	0.50 (0.87)	3.38 (1.21)	-2.88 [-5.61;-0.15]	0.039
Month 18 Adjusted Mean Change (SE)	2.47 (0.93)	4.02 (1.36)	.	.
Month 24 Adjusted Mean Change (SE)	3.78 (1.07)	4.56 (1.53)	-0.78 [-4.30;2.74]	0.665
Month 30 Adjusted Mean Change (SE)	5.46 (1.38)	8.02 (2.16)	.	.

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

Table 10.5.2: MSWS-12 Converted Score (FAS), Change from Baseline by Age

	Treatment groups		Comparison	
	BAF312 (N=1099)	**Placebo (N=546)**	**Mean Difference [95% CI]**	**p-value**
Age = >55				
N'	185	108		
Baseline Mean (SD)	67.10 (24.33)	65.52 (22.38)		
Month 06 Adjusted Mean Change (SE)	1.79 (1.43)	2.17 (1.85)	.	.
Month 12 Adjusted Mean Change (SE)	3.10 (1.55)	4.58 (2.00)	-1.48 [-6.30;3.33]	0.546
Month 18 Adjusted Mean Change (SE)	4.06 (1.70)	4.80 (2.14)	.	.
Month 24 Adjusted Mean Change (SE)	4.43 (1.98)	5.72 (2.66)	-1.29 [-7.69;5.11]	0.692
Month 30 Adjusted Mean Change (SE)	2.19 (2.43)	5.45 (3.44)	.	.

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

Table 10.5.3: MSWS-12 Converted Score (FAS), Change from Baseline by Gender

	Treatment groups		Comparison	
	BAF312 (N=1099)	**Placebo (N=546)**	**Mean Difference [95% CI]**	**p-value**
Interaction Test				0.381
Sex = F				
N'	615	307		
Baseline Mean (SD)	68.77 (23.78)	67.81 (23.13)		
Month 06 Adjusted Mean Change (SE)	-0.68 (0.79)	0.70 (1.05)	.	.
Month 12 Adjusted Mean Change (SE)	0.27 (0.84)	3.29 (1.14)	-3.02 [-5.63;-0.40]	0.024
Month 18 Adjusted Mean Change (SE)	2.69 (0.93)	5.10 (1.30)	.	.
Month 24 Adjusted Mean Change (SE)	2.93 (1.09)	4.97 (1.46)	-2.04 [-5.49;1.41]	0.247
Month 30 Adjusted Mean Change (SE)	2.85 (1.42)	6.32 (2.09)	.	.
Sex = M				
N'	407	209		
Baseline Mean (SD)	67.68 (22.81)	66.77 (20.99)		
Month 06 Adjusted Mean Change (SE)	1.24 (0.93)	1.58 (1.26)	.	.
Month 12 Adjusted Mean Change (SE)	3.34 (0.99)	3.38 (1.38)	-0.04 [-3.23;3.14]	0.979
Month 18 Adjusted Mean Change (SE)	4.11 (1.08)	4.87 (1.51)	.	.
Month 24 Adjusted Mean Change (SE)	5.79 (1.23)	5.99 (1.84)	-0.20 [-4.44;4.03]	0.925
Month 30 Adjusted Mean Change (SE)	6.47 (1.63)	9.12 (2.54)	.	.

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=1099)	**Placebo (N=546)**	**Mean Difference [95% CI]**	**p-value**
Interaction Test				0.668
Previous MS-DMT = N				
N'	221	107		
Baseline Mean (SD)	61.37 (25.03)	61.97 (22.07)		
Month 06 Adjusted Mean Change (SE)	-0.60 (1.25)	-0.07 (1.75)	.	.
Month 12 Adjusted Mean Change (SE)	0.92 (1.33)	5.09 (1.92)	-4.17 [-8.61;0.27]	0.065
Month 18 Adjusted Mean Change (SE)	2.16 (1.47)	3.25 (2.16)	.	.
Month 24 Adjusted Mean Change (SE)	4.51 (1.72)	4.91 (2.47)	-0.40 [-6.18;5.38]	0.892
Month 30 Adjusted Mean Change (SE)	0.89 (2.35)	7.51 (3.97)	.	.
Previous MS-DMT = Y				
N'	801	409		
Baseline Mean (SD)	70.26 (22.56)	68.80 (22.14)		
Month 06 Adjusted Mean Change (SE)	0.31 (0.71)	1.39 (0.93)	.	.
Month 12 Adjusted Mean Change (SE)	1.71 (0.75)	2.92 (1.01)	-1.22 [-3.49;1.06]	0.295
Month 18 Adjusted Mean Change (SE)	3.60 (0.83)	5.47 (1.12)	.	.
Month 24 Adjusted Mean Change (SE)	4.05 (0.95)	5.50 (1.31)	-1.45 [-4.47;1.57]	0.346
Month 30 Adjusted Mean Change (SE)	5.25 (1.21)	7.49 (1.77)	.	.

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=1099)	**Placebo (N=546)**	**Mean Difference [95% CI]**	**p-value**
Interaction Test				0.898
Previous IFN-beta 1b = N				
N'	699	369		
Baseline Mean (SD)	67.00 (23.79)	66.44 (21.90)		
Month 06 Adjusted Mean Change (SE)	0.20 (0.74)	0.64 (0.98)	.	.
Month 12 Adjusted Mean Change (SE)	1.51 (0.79)	3.66 (1.06)	-2.15 [-4.57;0.27]	0.081
Month 18 Adjusted Mean Change (SE)	2.91 (0.87)	5.14 (1.19)	.	.
Month 24 Adjusted Mean Change (SE)	3.57 (1.00)	5.51 (1.37)	-1.94 [-5.12;1.24]	0.232
Month 30 Adjusted Mean Change (SE)	4.25 (1.28)	6.99 (1.88)	.	.
Previous IFN-beta 1b = Y				
N'	323	147		
Baseline Mean (SD)	71.23 (22.28)	69.76 (23.09)		
Month 06 Adjusted Mean Change (SE)	-0.10 (1.05)	2.16 (1.48)	.	.
Month 12 Adjusted Mean Change (SE)	1.55 (1.12)	2.61 (1.61)	-1.06 [-4.79;2.66]	0.576
Month 18 Adjusted Mean Change (SE)	4.06 (1.23)	4.71 (1.79)	.	.
Month 24 Adjusted Mean Change (SE)	5.42 (1.43)	5.05 (2.13)	0.37 [-4.57;5.31]	0.883
Month 30 Adjusted Mean Change (SE)	4.58 (2.01)	9.15 (3.26)	.	.

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=1099)	**Placebo (N=546)**	**Mean Difference [95% CI]**	**p-value**
Interaction Test				0.523
Rapid evolvement = N				
N'	775	377		
Baseline Mean (SD)	68.78 (23.46)	67.15 (22.34)		
Month 06 Adjusted Mean Change (SE)	0.40 (0.72)	1.56 (0.97)	.	.
Month 12 Adjusted Mean Change (SE)	1.96 (0.76)	2.79 (1.05)	-0.83 [-3.19;1.53]	0.492
Month 18 Adjusted Mean Change (SE)	3.49 (0.84)	4.81 (1.20)	.	.
Month 24 Adjusted Mean Change (SE)	3.82 (0.98)	4.98 (1.41)	-1.16 [-4.37;2.05]	0.477
Month 30 Adjusted Mean Change (SE)	5.05 (1.30)	7.68 (2.01)	.	.
Rapid evolvement = Y				
N'	247	139		
Baseline Mean (SD)	66.96 (23.20)	68.02 (22.16)		
Month 06 Adjusted Mean Change (SE)	-0.80 (1.18)	-0.17 (1.53)	.	.
Month 12 Adjusted Mean Change (SE)	0.23 (1.25)	4.84 (1.66)	-4.61 [-8.55;-0.67]	0.022
Month 18 Adjusted Mean Change (SE)	2.66 (1.35)	5.46 (1.77)	.	.
Month 24 Adjusted Mean Change (SE)	4.86 (1.55)	6.19 (2.02)	-1.33 [-6.21;3.55]	0.593
Month 30 Adjusted Mean Change (SE)	2.80 (1.96)	7.19 (2.76)	.	.

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=1099)	**Placebo (N=546)**	**Mean Difference [95% CI]**	**p-value**
Interaction Test				0.123
Moderate/severe disease course = N				
N'	182	84		
Baseline Mean (SD)	52.84 (22.52)	53.99 (22.24)		
Month 06 Adjusted Mean Change (SE)	-3.67 (1.39)	-0.85 (1.95)	.	.
Month 12 Adjusted Mean Change (SE)	-4.30 (1.48)	1.90 (2.11)	-6.20 [-11.09;-1.31]	0.013
Month 18 Adjusted Mean Change (SE)	-2.13 (1.64)	0.81 (2.29)	.	.
Month 24 Adjusted Mean Change (SE)	1.43 (1.86)	4.78 (2.64)	-3.36 [-9.56;2.85]	0.289
Month 30 Adjusted Mean Change (SE)	0.85 (2.44)	10.35 (4.50)	.	.
Moderate/severe disease course = Y				
N'	840	432		
Baseline Mean (SD)	71.69 (22.21)	69.99 (21.35)		
Month 06 Adjusted Mean Change (SE)	0.87 (0.69)	1.37 (0.90)	.	.
Month 12 Adjusted Mean Change (SE)	2.73 (0.73)	3.53 (0.98)	-0.81 [-3.01;1.40]	0.474
Month 18 Adjusted Mean Change (SE)	4.39 (0.80)	5.83 (1.10)	.	.
Month 24 Adjusted Mean Change (SE)	4.63 (0.93)	5.37 (1.28)	-0.75 [-3.71;2.21]	0.621
Month 30 Adjusted Mean Change (SE)	5.07 (1.21)	7.08 (1.75)	.	.

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=1099)	**Placebo (N=546)**	**Mean Difference [95% CI]**	**p-value**
Interaction Test				0.729
Region = Europe				
N'	805	405		
Baseline Mean (SD)	67.86 (23.46)	66.11 (21.70)		
Month 06 Adjusted Mean Change (SE)	-0.22 (0.65)	1.63 (0.92)	.	.
Month 12 Adjusted Mean Change (SE)	1.72 (0.70)	3.99 (1.00)	-2.27 [-4.66;0.12]	0.063
Month 18 Adjusted Mean Change (SE)	3.70 (0.75)	5.57 (1.08)	.	.
Month 24 Adjusted Mean Change (SE)	4.33 (0.87)	5.45 (1.24)	-1.12 [-4.10;1.86]	0.461
Month 30 Adjusted Mean Change (SE)	4.66 (1.15)	7.97 (1.78)	.	.
Region = Others				
N'	217	111		
Baseline Mean (SD)	70.11 (23.12)	72.03 (23.79)		
Month 06 Adjusted Mean Change (SE)	1.58 (1.26)	0.90 (1.76)	.	.
Month 12 Adjusted Mean Change (SE)	0.88 (1.40)	3.03 (1.98)	-2.15 [-6.90;2.61]	0.377
Month 18 Adjusted Mean Change (SE)	1.42 (1.67)	4.15 (2.48)	.	.
Month 24 Adjusted Mean Change (SE)	3.80 (2.34)	9.31 (3.41)	-5.51 [-13.62;2.60]	0.183
Month 30 Adjusted Mean Change (SE)	2.94 (3.03)	8.27 (4.21)	.	.

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+

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Table 13.1: C-SSRS (FAS), Binary Analysis

	Treatment groups		Comparison		
	BAF312 (N=1099)	**Placebo (N=546)**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
N'	1079	542			
Any suicidal ideation (Cat.1-5)	121 (11.2)	58 (10.7)	1.05 [0.76;1.47] 0.756	1.05 [0.78;1.41] 0.756	0.01 [-0.03;0.04] 0.754
Cat.1 - Wish to be dead	115 (10.7)	56 (10.3)	1.04 [0.74;1.45] 0.840	1.03 [0.76;1.40] 0.840	0.00 [-0.03;0.03] 0.840
Cat.2 - Non-specific active suicidal thoughts	36 (3.3)	14 (2.6)	1.30 [0.70;2.43] 0.408	1.29 [0.70;2.37] 0.410	0.01 [-0.01;0.02] 0.388
Cat.3 - Active suicidal ideation with any methods (not plan) without intent to act	24 (2.2)	7 (1.3)	1.74 [0.74;4.06] 0.196	1.72 [0.75;3.97] 0.202	0.01 [0.00;0.02] 0.158
Cat.4 - Active suicidal ideation with some intent to act, without specific plan	15 (1.4)	2 (0.4)	3.81 [0.87;16.71] 0.057	3.77 [0.86;16.42] 0.077	0.01 [0.00;0.02] 0.021
Cat.5 - Active suicidal ideation with specific plan and intent	5 (0.5)	0 (0.0)	5.55 [0.31;100.6] 0.112	5.53 [0.31;99.84] 0.247	0.00 [0.00;0.01] 0.025
Any suicidal behavior (Cat.6-10)	25 (2.3)	7 (1.3)	1.81 [0.78;4.22] 0.161	1.79 [0.78;4.12] 0.168	0.01 [0.00;0.02] 0.124
Cat.6 - Preparatory acts or behavior	9 (0.8)	0 (0.0)	9.63 [0.56;165.7] 0.033	9.55 [0.56;163.8] 0.120	0.01 [0.00;0.01] 0.003
Cat.7 - Aborted attempt	12 (1.1)	4 (0.7)	1.51 [0.49;4.71] 0.472	1.51 [0.49;4.65] 0.476	0.00 [-0.01;0.01] 0.442
Cat.8 - Interrupted attempt	11 (1.0)	2 (0.4)	2.78 [0.61;12.59] 0.166	2.76 [0.61;12.42] 0.185	0.01 [0.00;0.01] 0.105
Cat.9 - Actual attempt	4 (0.4)	2 (0.4)	1.00 [0.18;5.50] 0.996	1.00 [0.18;5.47] 0.996	0.00 [-0.01;0.01] 0.996

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Table 13.1: C-SSRS (FAS), Binary Analysis

	Treatment groups		Comparison		
	BAF312 (N=1099)	**Placebo (N=546)**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Cat.10 - Completed suicide	1 (0.1)	0 (0.0)	1.51 [0.06;37.10] 0.478	1.51 [0.06;36.97] 0.801	0.00 [0.00;0.00] 0.317
Any suicidal ideation or behavior (Cat.1-10)	128 (11.9)	61 (11.3)	1.06 [0.77;1.47] 0.719	1.05 [0.79;1.40] 0.719	0.01 [-0.03;0.04] 0.717
Self-injurious behavior, without suicidal intent	3 (0.3)	1 (0.2)	1.51 [0.16;14.53] 0.720	1.51 [0.16;14.45] 0.722	0.00 [0.00;0.01] 0.702

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=1099)	**Placebo (N=546)**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
N' Age=18-30	24	12			
N' Age=31-40	160	91			
N' Age=41-55	700	327			
N' Age=>55	195	112			
Any suicidal ideation (Cat.1-5)					
Interaction Test	p= 0.884				
Age = 18-30	2 (8.3)	2 (16.7)	0.45 [0.06;3.70] 0.461	0.50 [0.08;3.13] 0.459	-0.08 [-0.32;0.15] 0.493
Age = 31-40	16 (10.0)	9 (9.9)	1.01 [0.43;2.39] 0.978	1.01 [0.47;2.19] 0.978	0.00 [-0.08;0.08] 0.978
Age = 41-55	81 (11.6)	35 (10.7)	1.09 [0.72;1.66] 0.682	1.08 [0.74;1.57] 0.683	0.01 [-0.03;0.05] 0.678
Age = >55	22 (11.3)	12 (10.7)	1.06 [0.50;2.23] 0.879	1.05 [0.54;2.05] 0.879	0.01 [-0.07;0.08] 0.878
Any suicidal behavior (Cat.6-10)					
Interaction Test	p= 0.824				
Age = 18-30	1 (4.2)	0 (0.0)	-	1.56 [0.07;35.67] 0.781	0.04 [-0.04;0.12] 0.307
Age = 31-40	4 (2.5)	0 (0.0)	-	5.14 [0.28;94.46] 0.270	0.03 [0.00;0.05] 0.043
Age = 41-55	16 (2.3)	4 (1.2)	1.89 [0.63;5.70] 0.259	1.87 [0.63;5.55] 0.260	0.01 [-0.01;0.03] 0.200

Table 13.2: C-SSRS (FAS), Binary Analysis by Age

	Treatment groups		Comparison		
	BAF312 (N=1099)	**Placebo (N=546)**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Age = >55	4 (2.1)	3 (2.7)	0.76 [0.17;3.46] 0.724	0.77 [0.17;3.36] 0.724	-0.01 [-0.04;0.03] 0.732
Any suicidal ideation or behavior (Cat.1-10)					
Interaction Test	p= 0.975				
Age = 18-30	3 (12.5)	2 (16.7)	0.71 [0.10;4.97] 0.733	0.75 [0.14;3.90] 0.732	-0.04 [-0.29;0.21] 0.743
Age = 31-40	18 (11.3)	9 (9.9)	1.15 [0.50;2.69] 0.738	1.14 [0.53;2.43] 0.739	0.01 [-0.06;0.09] 0.734
Age = 41-55	84 (12.0)	37 (11.3)	1.07 [0.71;1.61] 0.751	1.06 [0.74;1.53] 0.751	0.01 [-0.04;0.05] 0.749
Age = >55	23 (11.8)	13 (11.6)	1.02 [0.49;2.10] 0.961	1.02 [0.54;1.93] 0.961	0.00 [-0.07;0.08] 0.961

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=1099)	**Placebo (N=546)**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
N' Sex=F	650	320			
N' Sex=M	429	222			
Any suicidal ideation (Cat.1-5)					
Interaction Test	p= 0.958				
Sex = F	79 (12.2)	37 (11.6)	1.06 [0.70;1.60] 0.790	1.05 [0.73;1.52] 0.790	0.01 [-0.04;0.05] 0.788
Sex = M	42 (9.8)	21 (9.5)	1.04 [0.60;1.80] 0.892	1.03 [0.63;1.70] 0.892	0.00 [-0.04;0.05] 0.892
Any suicidal behavior (Cat.6-10)					
Interaction Test	p= 0.335				
Sex = F	13 (2.0)	5 (1.6)	1.29 [0.45;3.64] 0.636	1.28 [0.46;3.56] 0.636	0.00 [-0.01;0.02] 0.621
Sex = M	12 (2.8)	2 (0.9)	3.16 [0.70;14.26] 0.134	3.10 [0.70;13.75] 0.136	0.02 [0.00;0.04] 0.062
Any suicidal ideation or behavior (Cat.1-10)					
Interaction Test	p= 0.794				
Sex = F	83 (12.8)	40 (12.5)	1.02 [0.68;1.53] 0.906	1.02 [0.72;1.45] 0.906	0.00 [-0.04;0.05] 0.905
Sex = M	45 (10.5)	21 (9.5)	1.12 [0.65;1.93] 0.680	1.11 [0.68;1.81] 0.681	0.01 [-0.04;0.06] 0.675

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=1099)	**Placebo (N=546)**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
N' Previous MS-DMT=N	236	112			
N' Previous MS-DMT=Y	843	430			
Any suicidal ideation (Cat.1-5)					
Interaction Test	p= 0.608				
Previous MS-DMT = N	26 (11.0)	10 (8.9)	1.26 [0.59;2.72] 0.551	1.23 [0.62;2.47] 0.553	0.02 [-0.05;0.09] 0.536
Previous MS-DMT = Y	95 (11.3)	48 (11.2)	1.01 [0.70;1.46] 0.955	1.01 [0.73;1.40] 0.955	0.00 [-0.04;0.04] 0.955
Any suicidal behavior (Cat.6-10)					
Interaction Test	p= 0.962				
Previous MS-DMT = N	4 (1.7)	1 (0.9)	1.91 [0.21;17.31] 0.564	1.90 [0.21;16.79] 0.564	0.01 [-0.02;0.03] 0.512
Previous MS-DMT = Y	21 (2.5)	6 (1.4)	1.81 [0.72;4.51] 0.206	1.79 [0.73;4.39] 0.207	0.01 [0.00;0.03] 0.160
Any suicidal ideation or behavior (Cat.1-10)					
Interaction Test	p= 0.461				
Previous MS-DMT = N	28 (11.9)	10 (8.9)	1.37 [0.64;2.93] 0.414	1.33 [0.67;2.64] 0.417	0.03 [-0.04;0.10] 0.391
Previous MS-DMT = Y	100 (11.9)	51 (11.9)	1.00 [0.70;1.43] 0.999	1.00 [0.73;1.37] 0.999	0.00 [-0.04;0.04] 0.999

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=1099)	**Placebo (N=546)**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
N' Previous IFN-beta 1b=N	740	390			
N' Previous IFN-beta 1b=Y	339	152			
Any suicidal ideation (Cat.1-5)					
Interaction Test	p= 0.887				
Previous IFN-beta 1b = N	87 (11.8)	43 (11.0)	1.08 [0.73;1.58] 0.714	1.07 [0.76;1.50] 0.715	0.01 [-0.03;0.05] 0.712
Previous IFN-beta 1b = Y	34 (10.0)	15 (9.9)	1.02 [0.54;1.93] 0.956	1.02 [0.57;1.81] 0.956	0.00 [-0.06;0.06] 0.956
Any suicidal behavior (Cat.6-10)					
Interaction Test	p= 0.674				
Previous IFN-beta 1b = N	19 (2.6)	5 (1.3)	2.03 [0.75;5.48] 0.162	2.00 [0.75;5.32] 0.164	0.01 [0.00;0.03] 0.114
Previous IFN-beta 1b = Y	6 (1.8)	2 (1.3)	1.35 [0.27;6.77] 0.714	1.35 [0.27;6.59] 0.715	0.00 [-0.02;0.03] 0.698
Any suicidal ideation or behavior (Cat.1-10)					
Interaction Test	p= 0.840				
Previous IFN-beta 1b = N	92 (12.4)	45 (11.5)	1.09 [0.74;1.59] 0.662	1.08 [0.77;1.51] 0.662	0.01 [-0.03;0.05] 0.658
Previous IFN-beta 1b = Y	36 (10.6)	16 (10.5)	1.01 [0.54;1.88] 0.975	1.01 [0.58;1.76] 0.975	0.00 [-0.06;0.06] 0.975

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=1099)	**Placebo (N=546)**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
N' Rapid evolvement=N	820	398			
N' Rapid evolvement=Y	259	144			
Any suicidal ideation (Cat.1-5)					
Interaction Test	p= 0.933				
Rapid evolvement = N	96 (11.7)	45 (11.3)	1.04 [0.71;1.52] 0.838	1.04 [0.74;1.44] 0.838	0.00 [-0.03;0.04] 0.837
Rapid evolvement = Y	25 (9.7)	13 (9.0)	1.08 [0.53;2.18] 0.837	1.07 [0.56;2.02] 0.837	0.01 [-0.05;0.07] 0.836
Any suicidal behavior (Cat.6-10)					
Interaction Test	p= 0.413				
Rapid evolvement = N	19 (2.3)	4 (1.0)	2.34 [0.79;6.91] 0.125	2.31 [0.79;6.73] 0.127	0.01 [0.00;0.03] 0.070
Rapid evolvement = Y	6 (2.3)	3 (2.1)	1.11 [0.27;4.53] 0.879	1.11 [0.28;4.38] 0.879	0.00 [-0.03;0.03] 0.878
Any suicidal ideation or behavior (Cat.1-10)					
Interaction Test	p= 0.750				
Rapid evolvement = N	102 (12.4)	46 (11.6)	1.09 [0.75;1.57] 0.659	1.08 [0.78;1.49] 0.659	0.01 [-0.03;0.05] 0.655
Rapid evolvement = Y	26 (10.0)	15 (10.4)	0.96 [0.49;1.88] 0.904	0.96 [0.53;1.76] 0.904	0.00 [-0.07;0.06] 0.905

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=1099)	**Placebo (N=546)**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
N' Moderate/severe disease course=N	191	86			
N' Moderate/severe disease course=Y	888	456			
Any suicidal ideation (Cat.1-5)					
Interaction Test	p= 0.569				
Moderate/severe disease course = N	15 (7.9)	8 (9.3)	0.83 [0.34;2.04] 0.686	0.84 [0.37;1.92] 0.685	-0.01 [-0.09;0.06] 0.694
Moderate/severe disease course = Y	106 (11.9)	50 (11.0)	1.10 [0.77;1.57] 0.598	1.09 [0.79;1.49] 0.599	0.01 [-0.03;0.05] 0.594
Any suicidal behavior (Cat.6-10)					
Interaction Test	p= 0.379				
Moderate/severe disease course = N	4 (2.1)	2 (2.3)	0.90 [0.16;5.00] 0.903	0.90 [0.17;4.82] 0.903	0.00 [-0.04;0.04] 0.904
Moderate/severe disease course = Y	21 (2.4)	5 (1.1)	2.18 [0.82;5.83] 0.119	2.16 [0.82;5.68] 0.120	0.01 [0.00;0.03] 0.072
Any suicidal ideation or behavior (Cat.1-10)					
Interaction Test	p= 0.670				
Moderate/severe disease course = N	16 (8.4)	8 (9.3)	0.89 [0.37;2.17] 0.800	0.90 [0.40;2.02] 0.800	-0.01 [-0.08;0.06] 0.803

Table 13.7: C-SSRS (FAS), Binary Analysis by Disease Course

	Treatment groups		Comparison		
	BAF312 (N=1099)	**Placebo (N=546)**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Moderate/severe disease course = Y	112 (12.6)	53 (11.6)	1.10 [0.77;1.55] 0.601	1.09 [0.80;1.47] 0.601	0.01 [-0.03;0.05] 0.596

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=1099)	**Placebo (N=546)**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
N' Region=Europe	845	423			
N' Region=Others	234	119			
Any suicidal ideation (Cat.1-5)					
Interaction Test	p= 0.119				
Region = Europe	96 (11.4)	40 (9.5)	1.23 [0.83;1.81] 0.302	1.20 [0.85;1.70] 0.304	0.02 [-0.02;0.05] 0.288
Region = Others	25 (10.7)	18 (15.1)	0.67 [0.35;1.29] 0.230	0.71 [0.40;1.24] 0.227	-0.04 [-0.12;0.03] 0.249
Any suicidal behavior (Cat.6-10)					
Interaction Test	p= 0.818				
Region = Europe	19 (2.2)	5 (1.2)	1.92 [0.71;5.19] 0.196	1.90 [0.72;5.06] 0.198	0.01 [0.00;0.03] 0.145
Region = Others	6 (2.6)	2 (1.7)	1.54 [0.31;7.75] 0.601	1.53 [0.31;7.44] 0.601	0.01 [-0.02;0.04] 0.573
Any suicidal ideation or behavior (Cat.1-10)					
Interaction Test	p= 0.199				
Region = Europe	99 (11.7)	42 (9.9)	1.20 [0.82;1.76] 0.340	1.18 [0.84;1.66] 0.342	0.02 [-0.02;0.05] 0.328
Region = Others	29 (12.4)	19 (16.0)	0.74 [0.40;1.39] 0.356	0.78 [0.45;1.32] 0.353	-0.04 [-0.11;0.04] 0.370

N': Number of patients in the analysis
OR: Odds Ratio
RR: Relative Risk
RD: Risk Difference

Efficacy Figures

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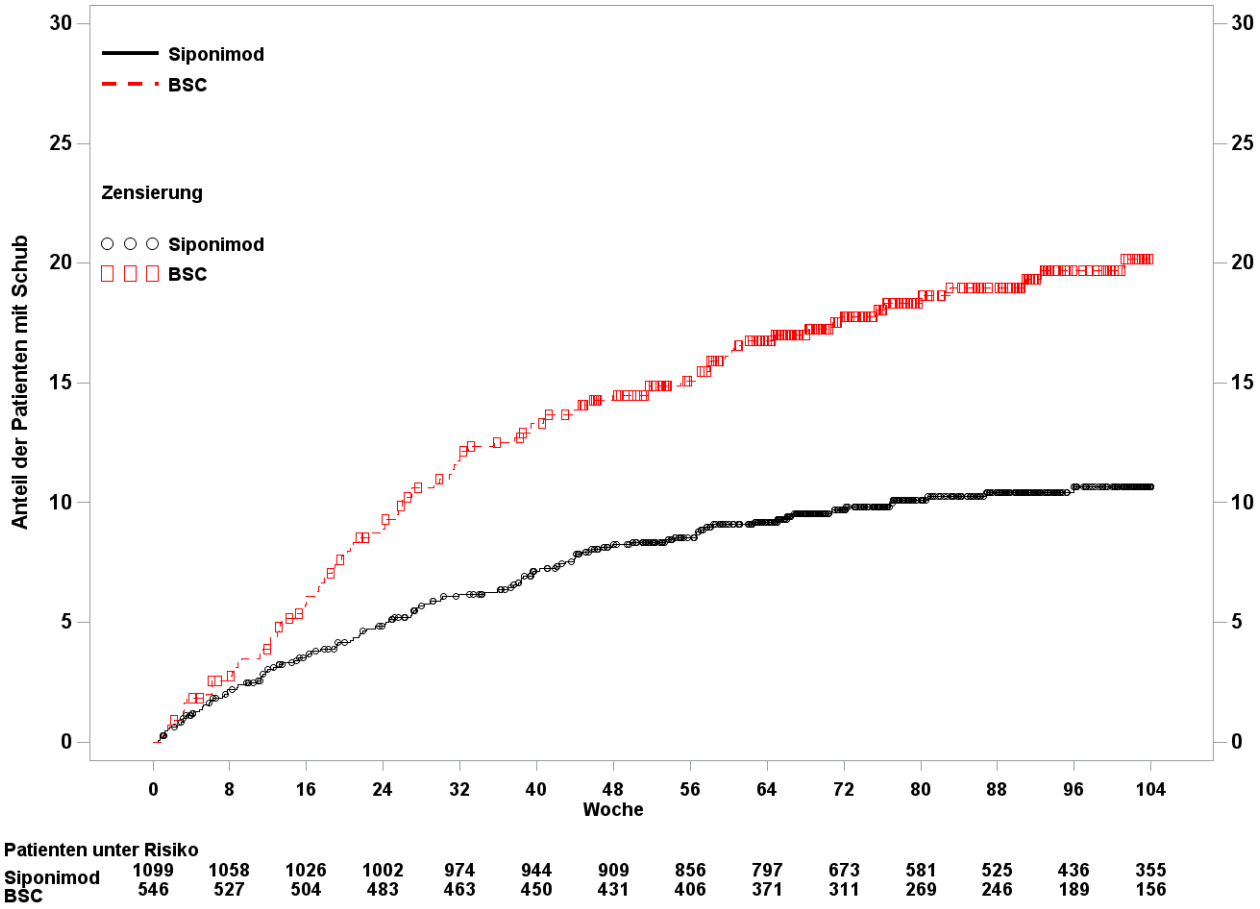
Figure 3.2.1: Time to First Relapse (FAS)



Patienten unter Risiko

Siponimod	1099	1058	1026	1002	974	944	909	856	797	673	581	525	436	355
BSC	546	527	504	483	463	450	431	406	371	311	269	246	189	156

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Figure 4.2.1: Time to First 3-month CDP (FAS)

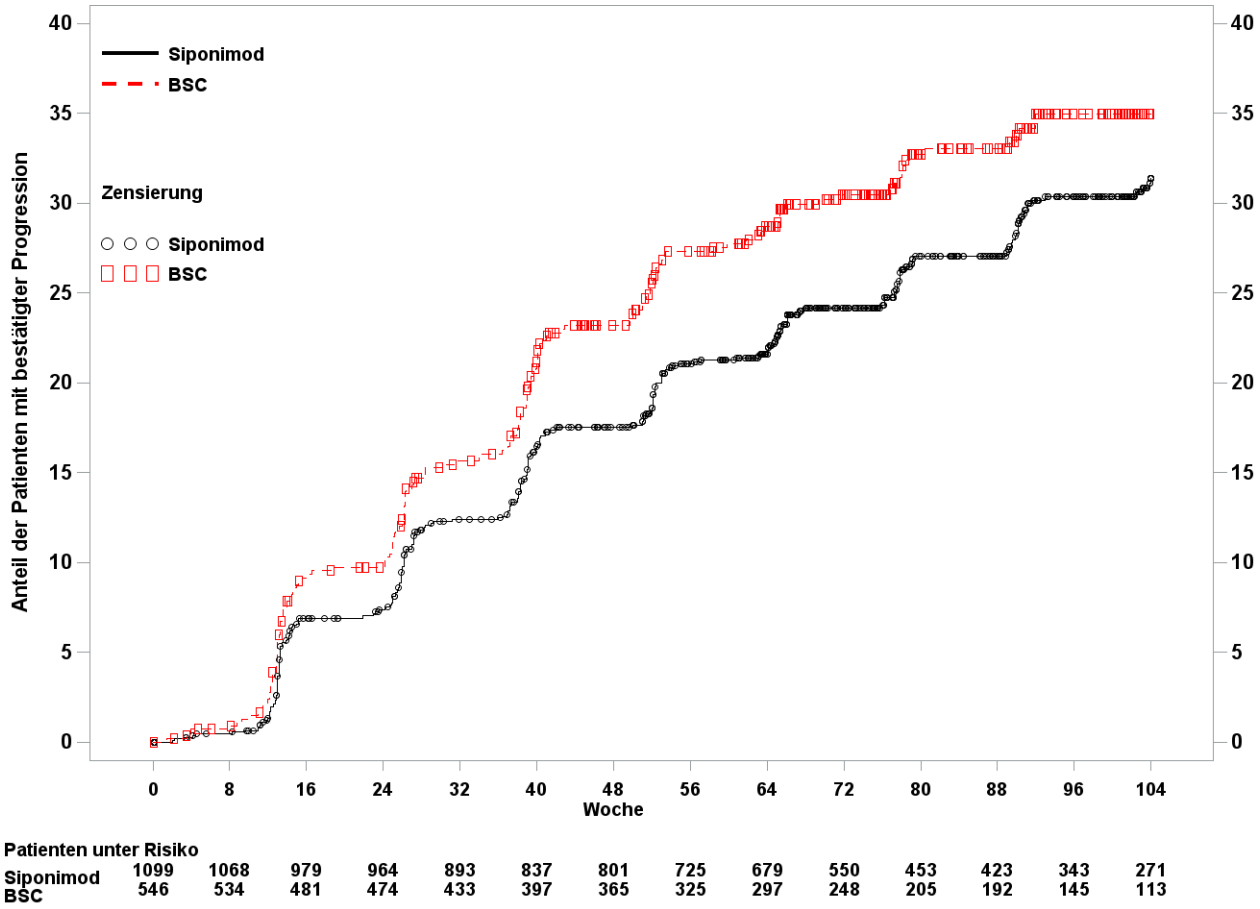

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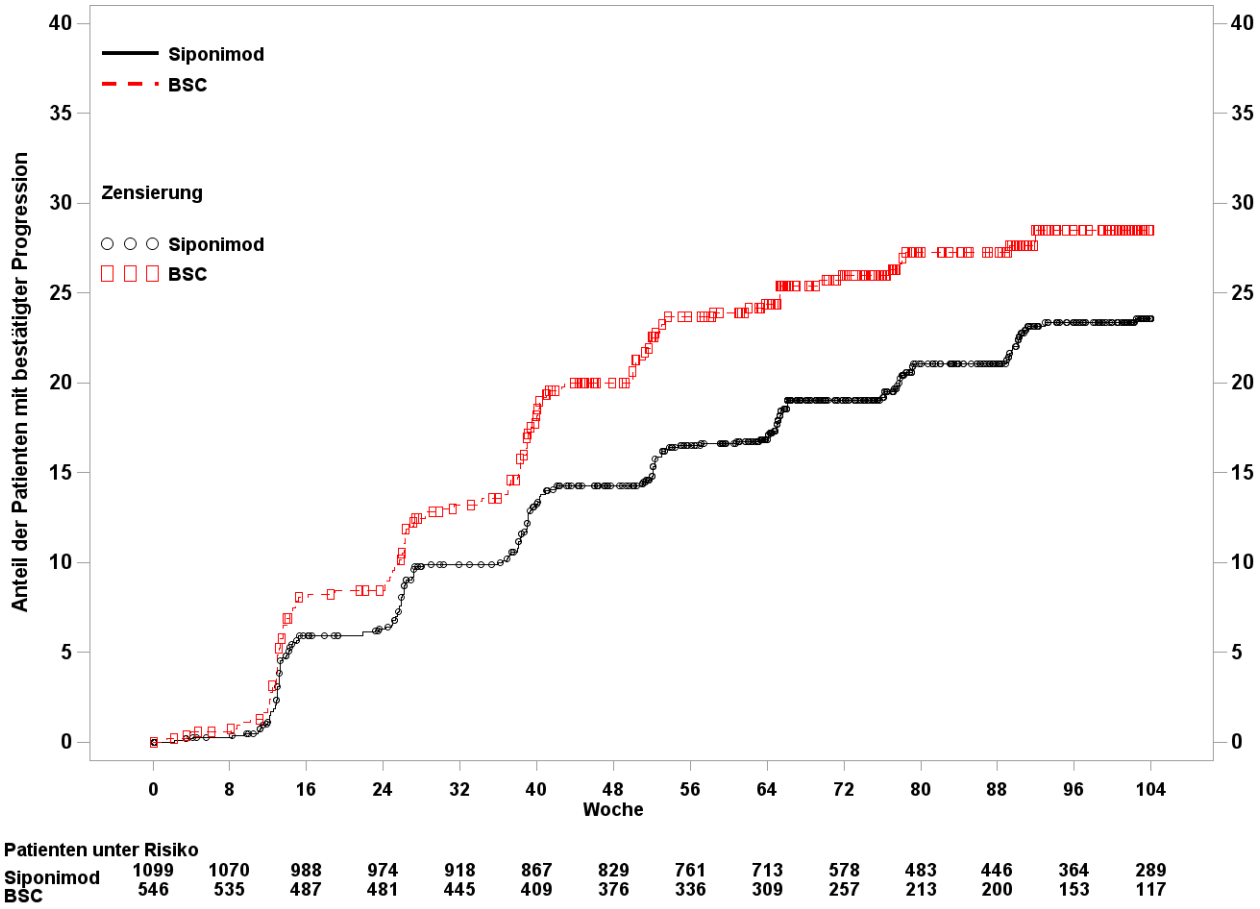
Figure 5.2.1: Time to First 6-month CDP (FAS)



Patienten unter Risiko

Siponimod	1099	1070	988	974	918	867	829	761	713	578	483	446	364	289
BSC	546	535	487	481	445	409	376	336	309	257	213	200	153	117

Figure 6.6.1: Time to First Worsening of T25W of ≥20% (FAS)

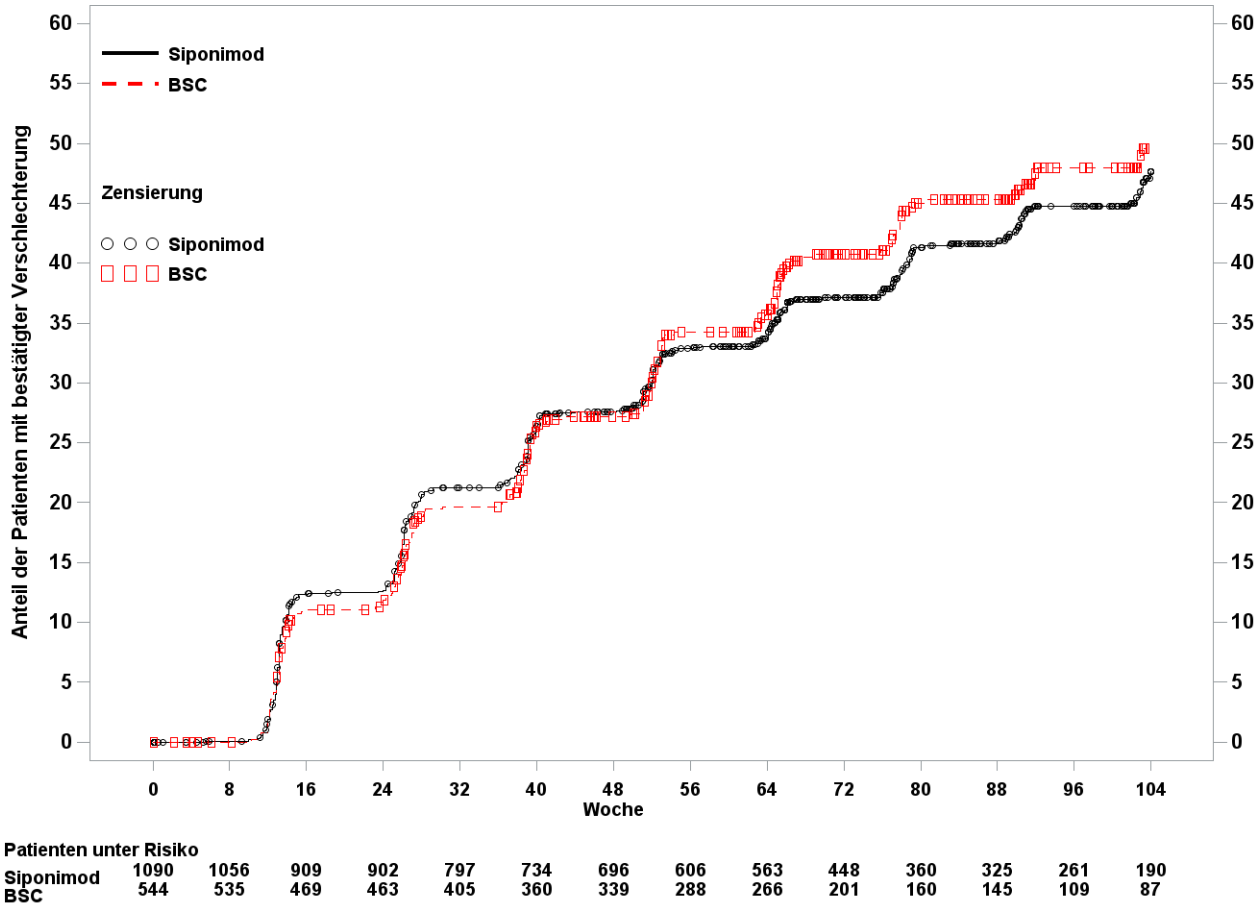


Figure 10.1.1: MSIS-29 Physical Impact Scale, Time course (FAS)

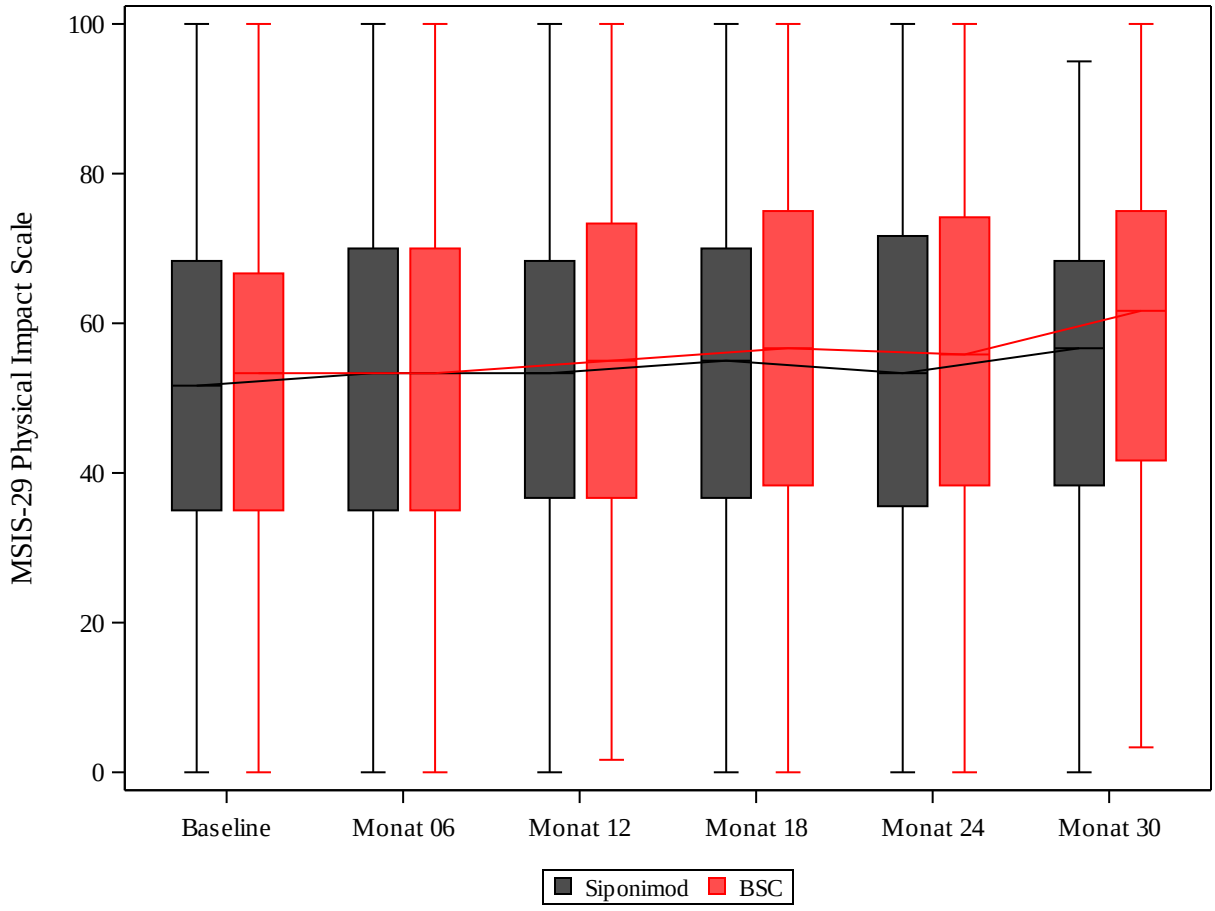


Figure 10.1.2: MSIS-29 Physical Impact Scale, Time course (FAS) by Age

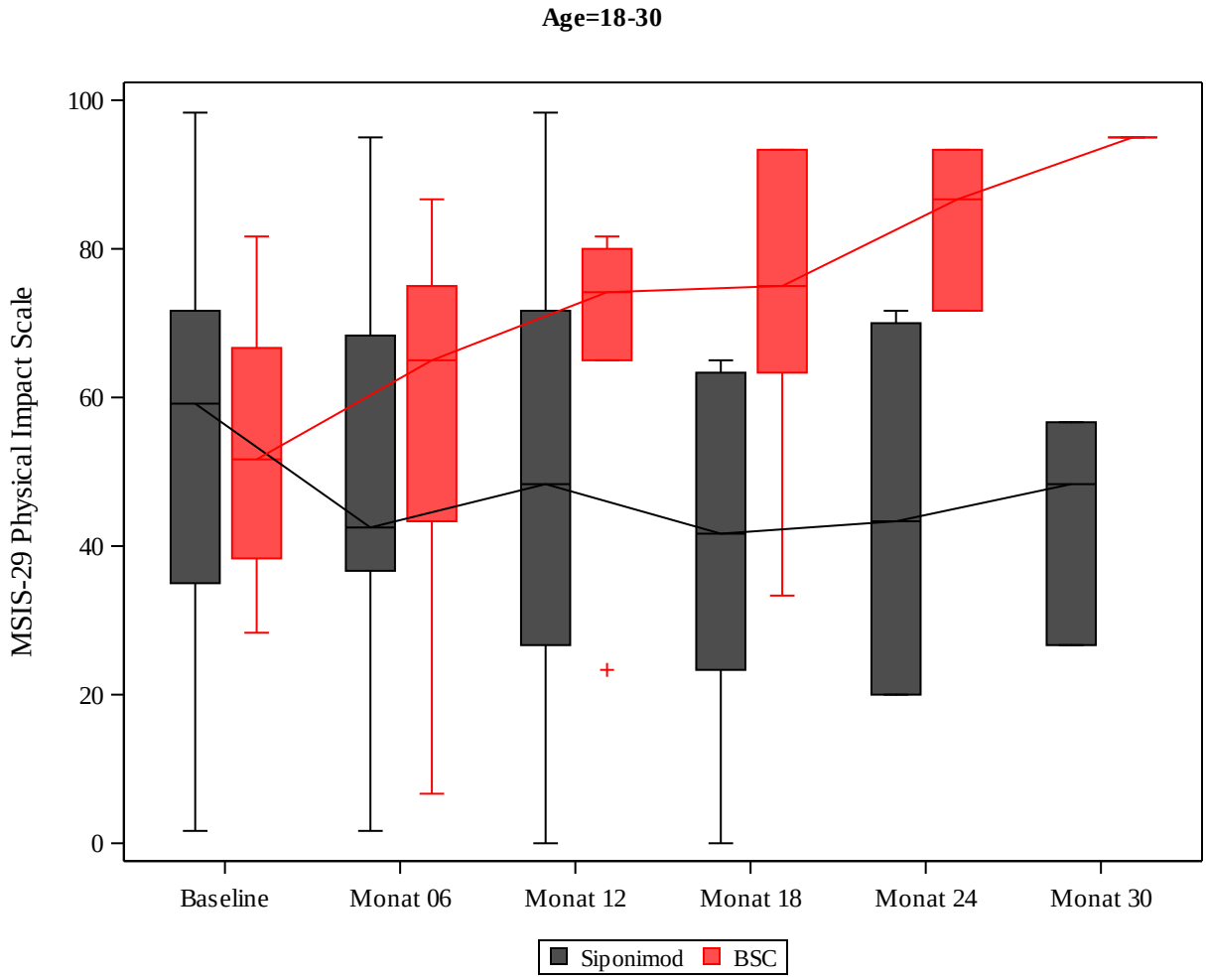


Figure 10.1.2: MSIS-29 Physical Impact Scale, Time course (FAS) by Age

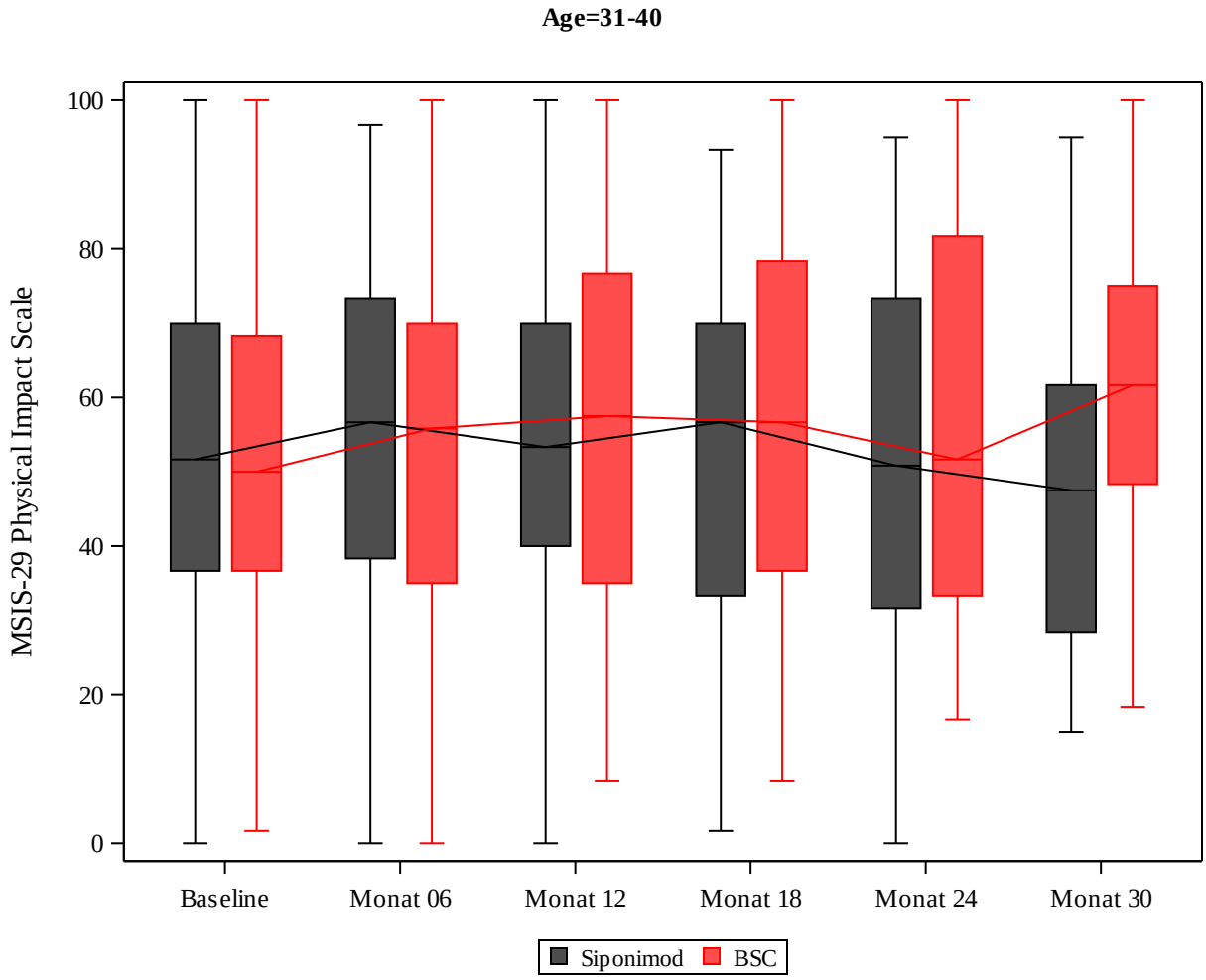


Figure 10.1.2: MSIS-29 Physical Impact Scale, Time course (FAS) by Age

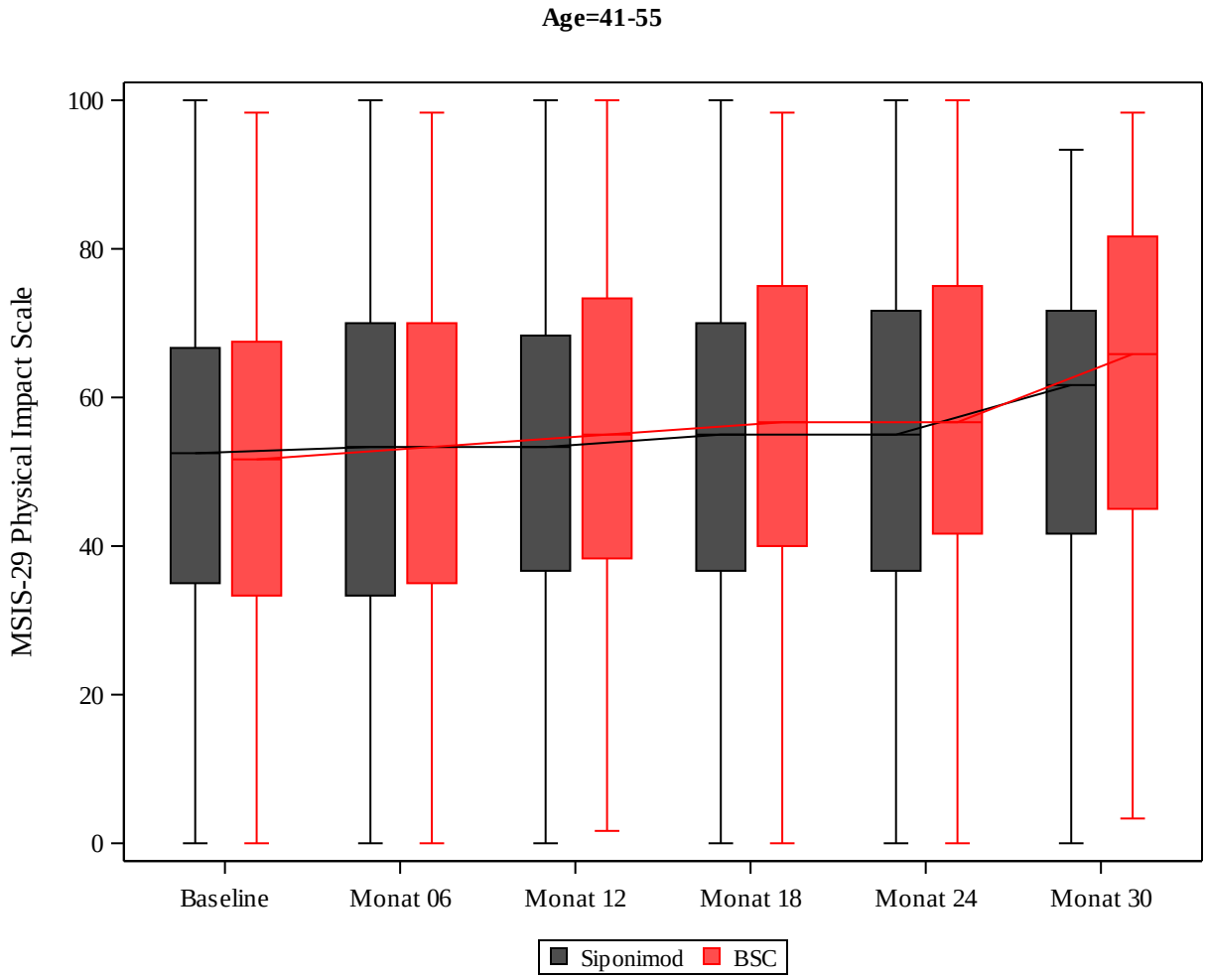


Figure 10.1.2: MSIS-29 Physical Impact Scale, Time course (FAS) by Age

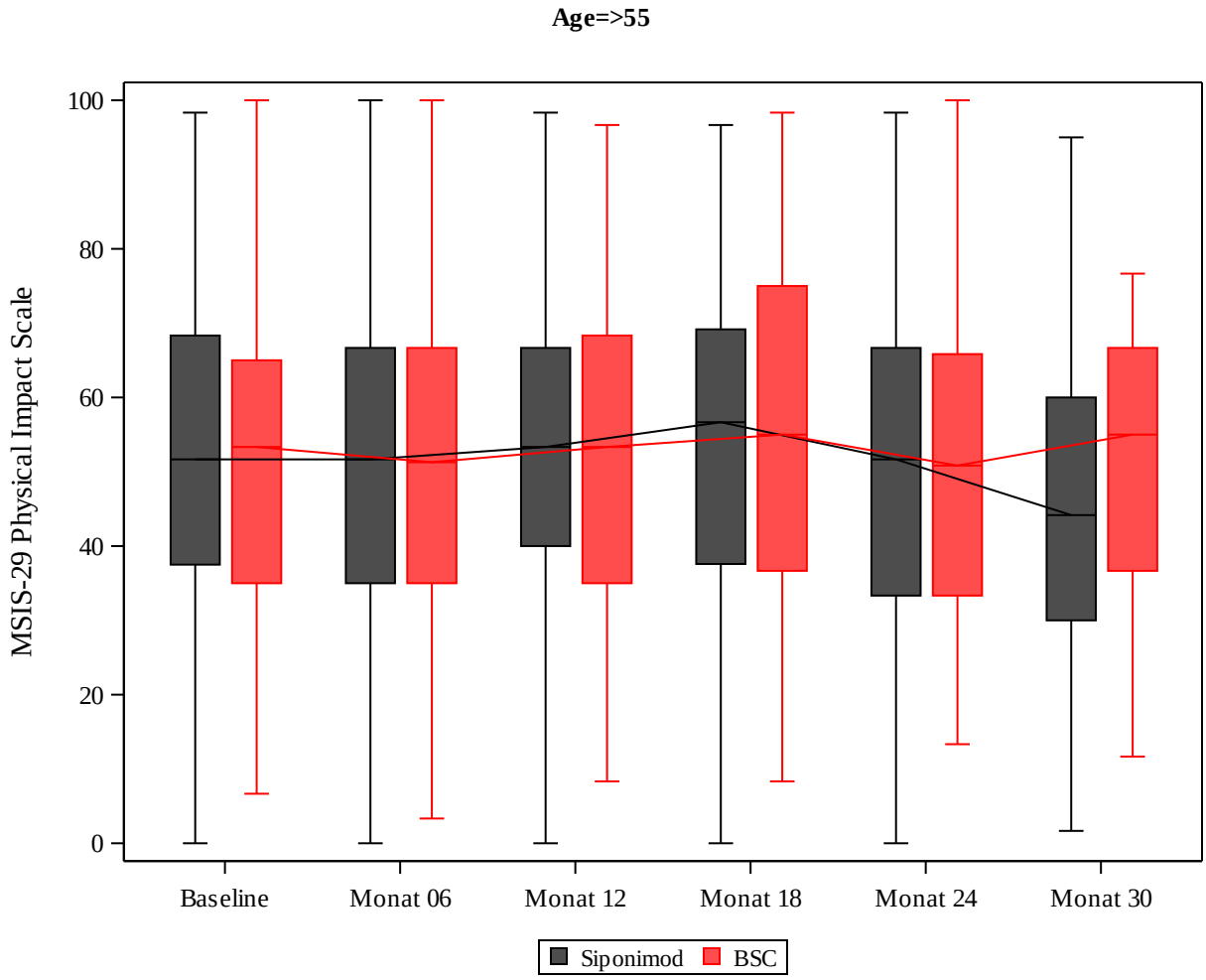
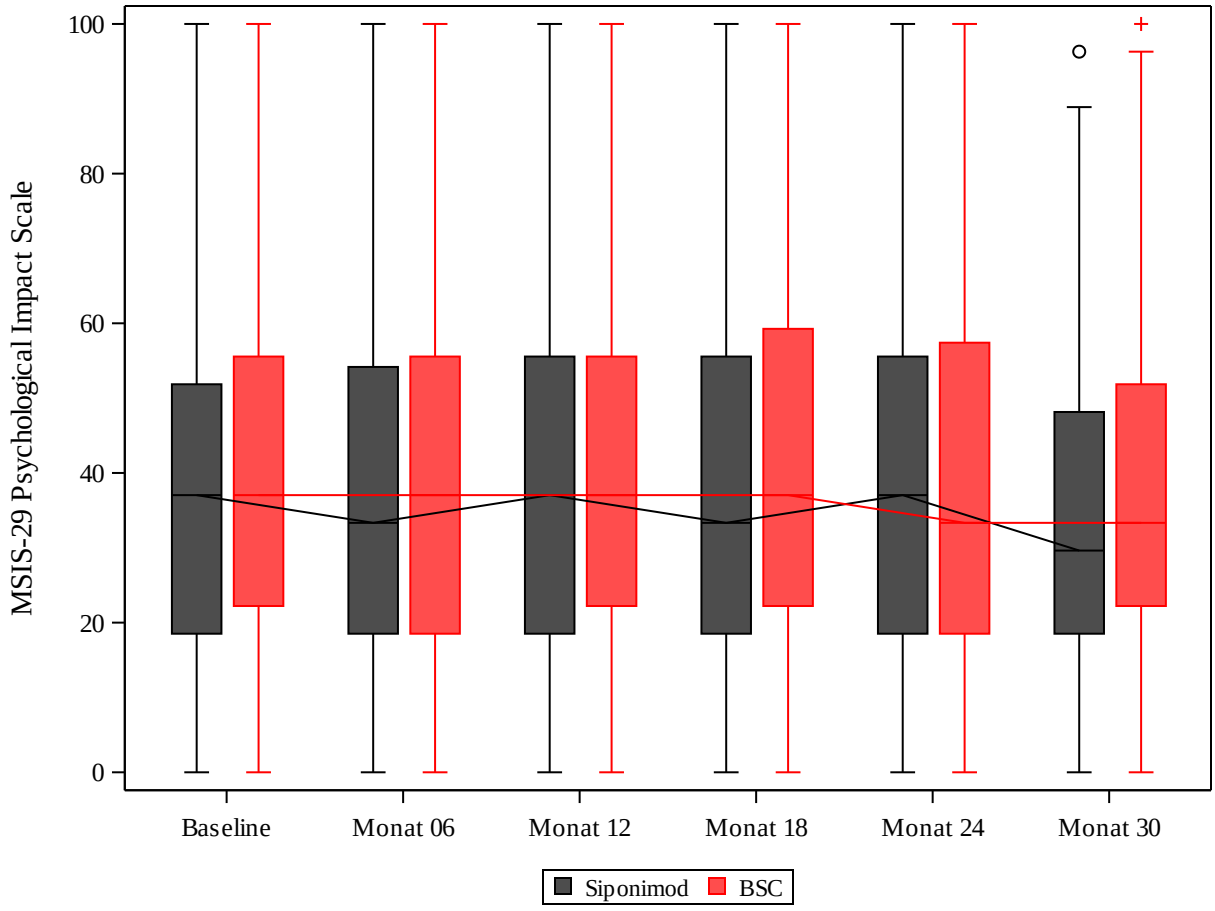


Figure 10.2.1: MSIS-29 Psychological Impact Scale, Time course (FAS)



Novartis **Siponimod SPMS**
AMNOG Dossier Total Population **CBAF312A2304**

Figure 10.2.2: MSIS-29 Psychological Impact Scale, Time course (FAS) by Age

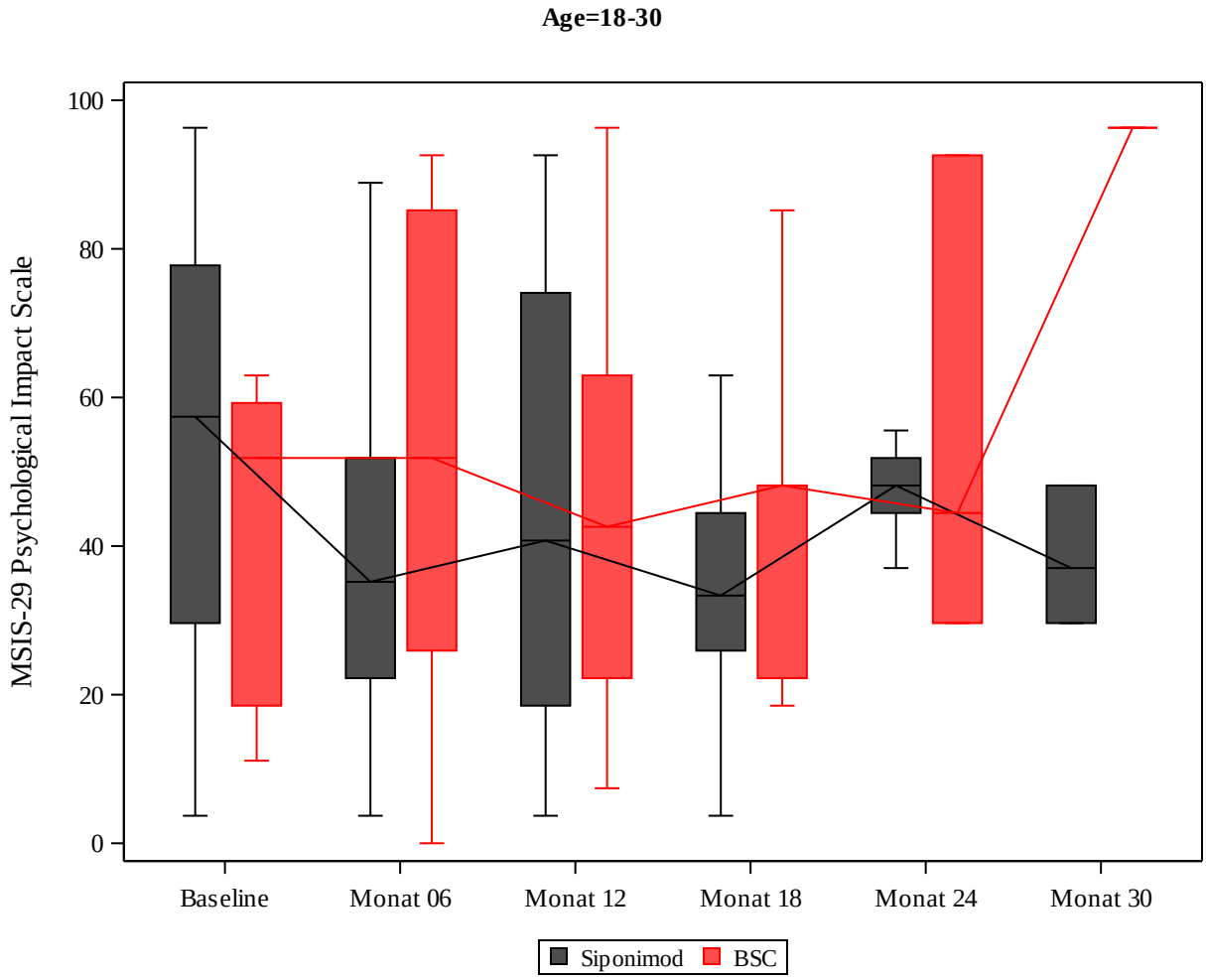
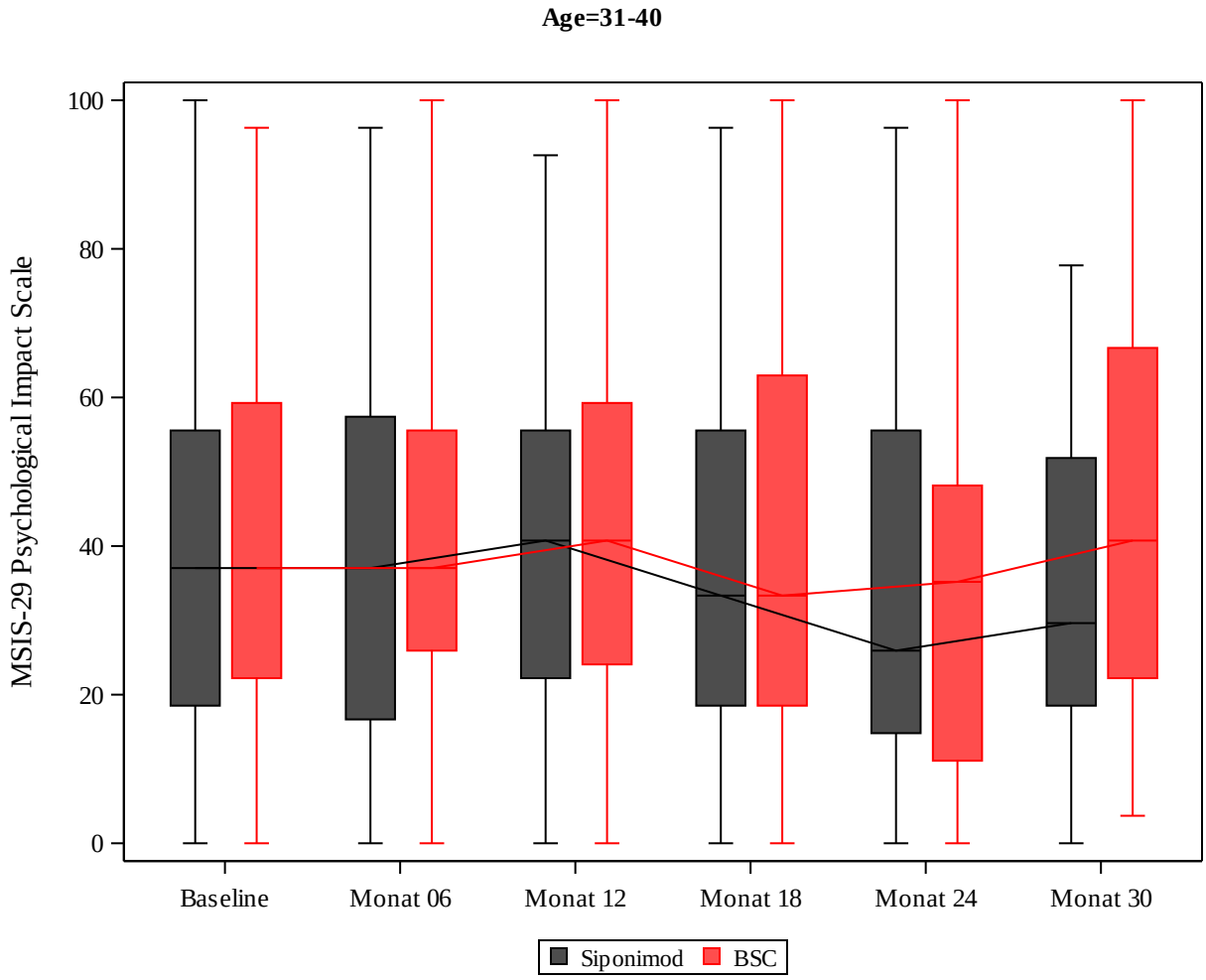
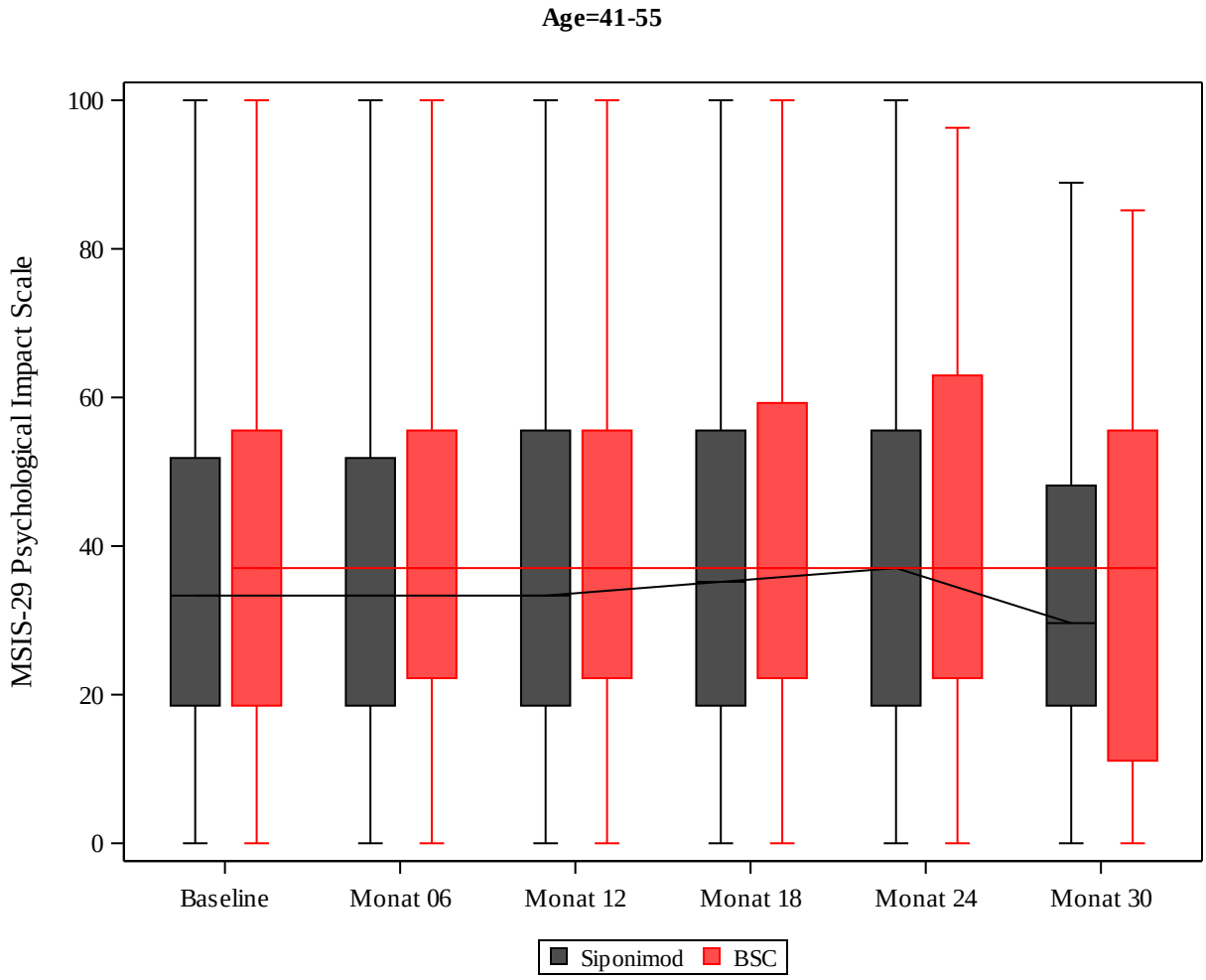


Figure 10.2.2: MSIS-29 Psychological Impact Scale, Time course (FAS) by Age



Novartis **Siponimod SPMS**
AMNOG Dossier Total Population **CBAF312A2304**

Figure 10.2.2: MSIS-29 Psychological Impact Scale, Time course (FAS) by Age



Novartis **Siponimod SPMS**
AMNOG Dossier Total Population **CBAF312A2304**

Figure 10.2.2: MSIS-29 Psychological Impact Scale, Time course (FAS) by Age

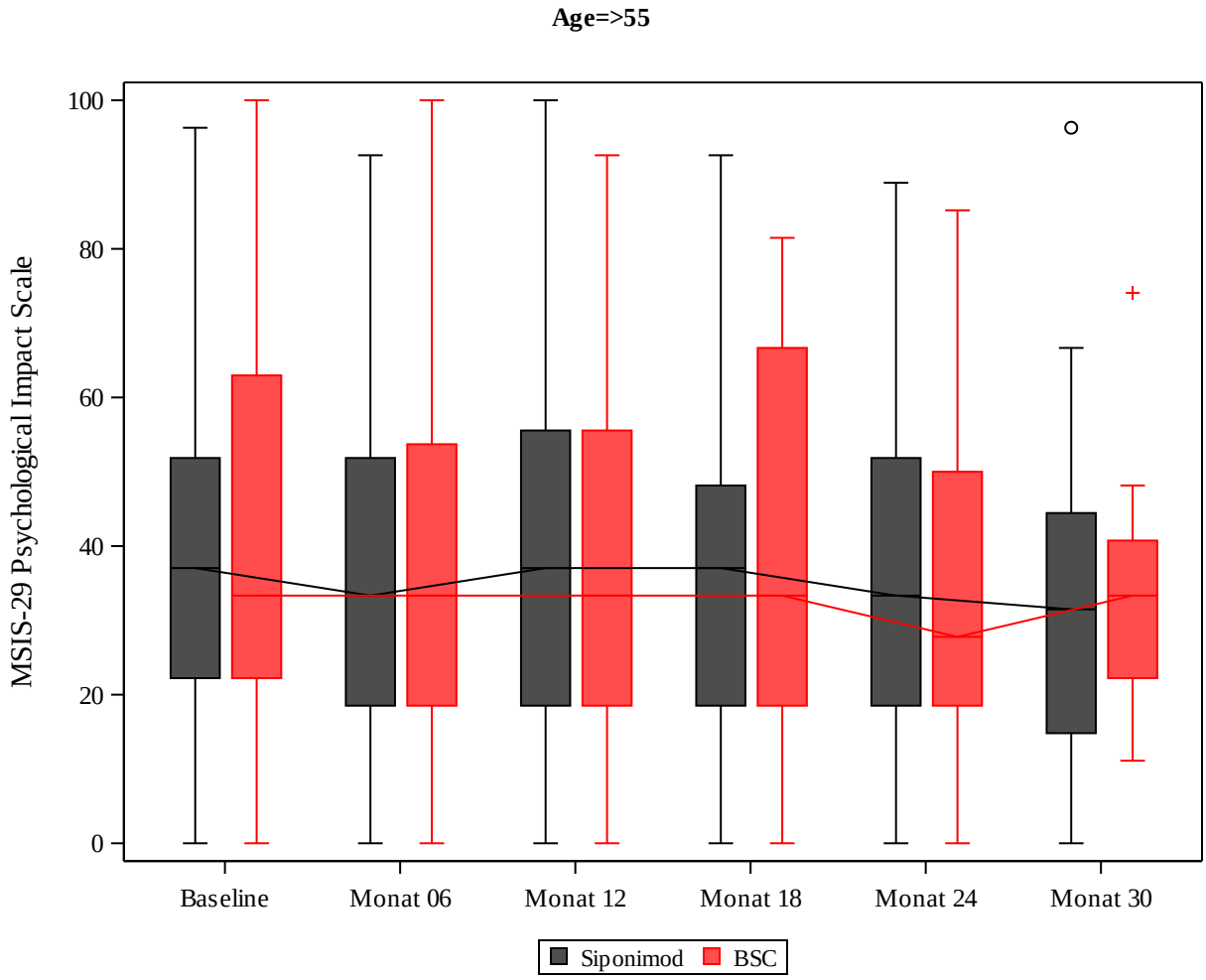


Figure 10.3.1: EQ-5D Utility Score, Time course (FAS)

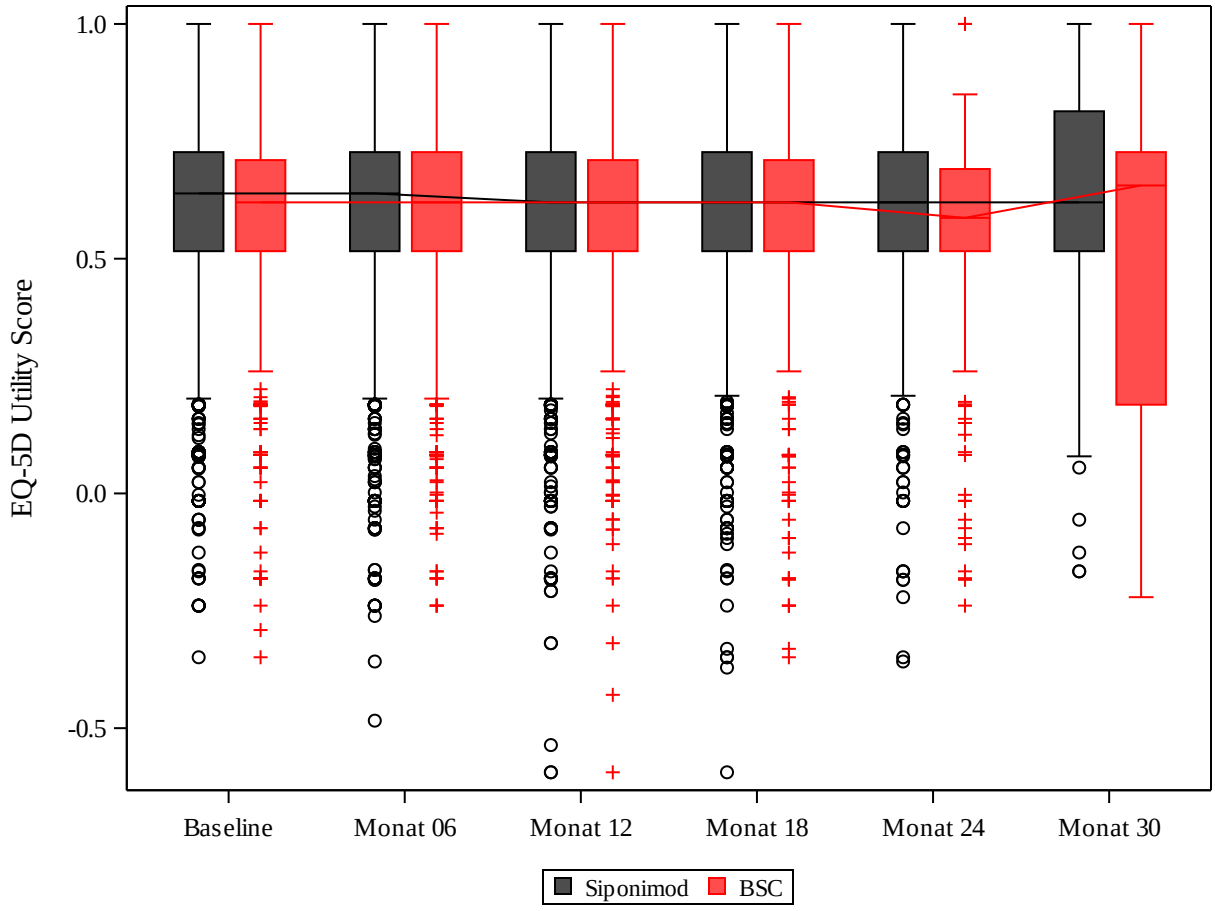


Figure 10.4.1: EQ-5D VAS Thermometer, Time course (FAS)

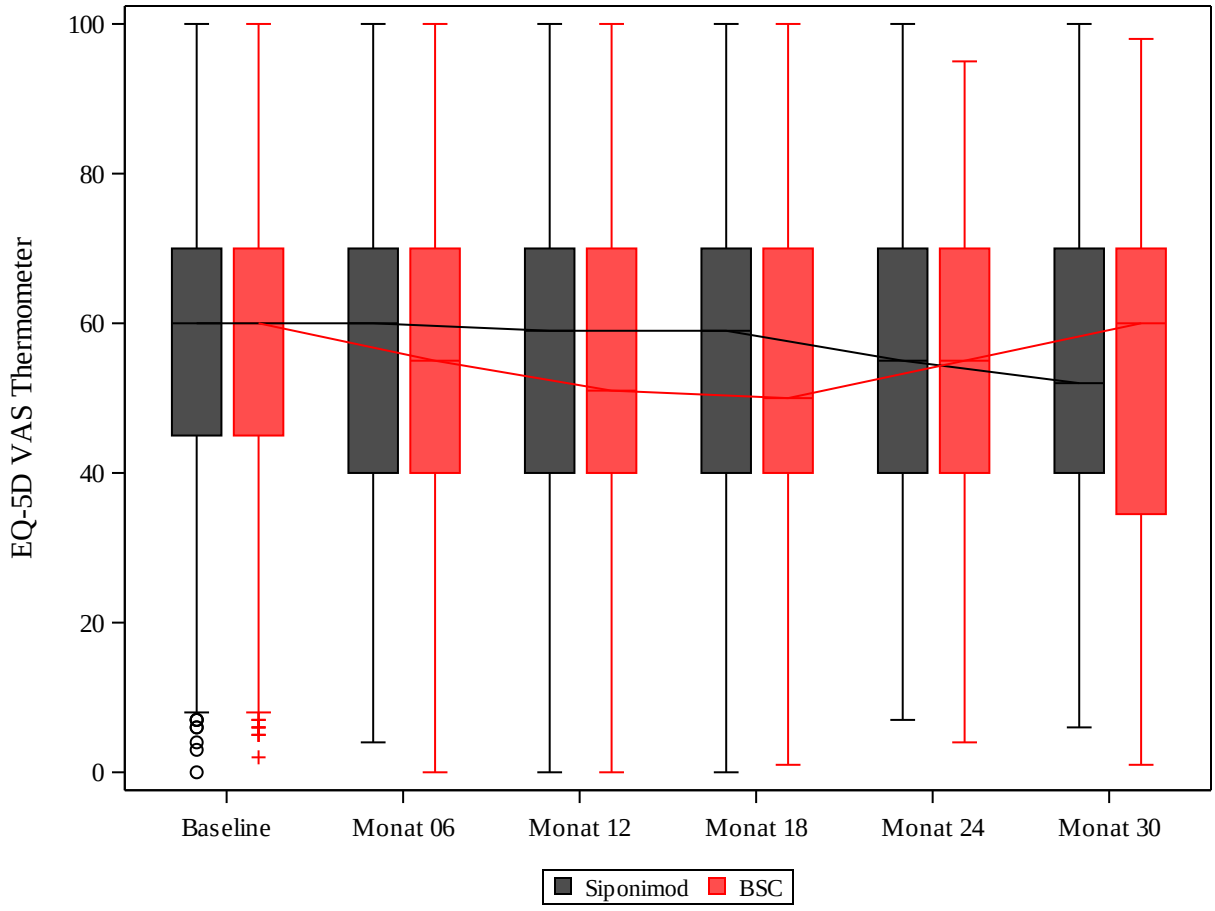


Figure 10.4.7: EQ-5D VAS Thermometer, Time course (FAS) by Disease Course

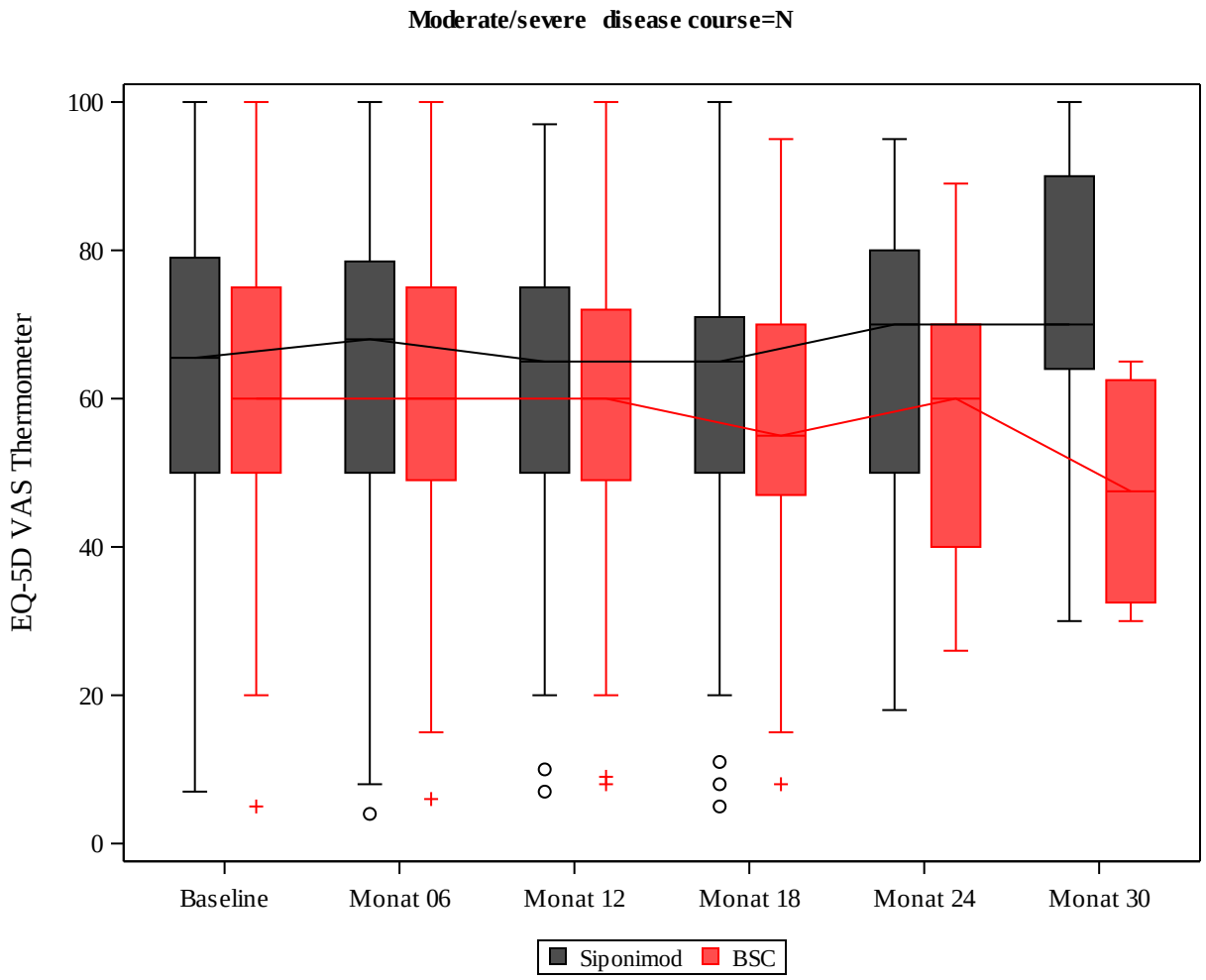
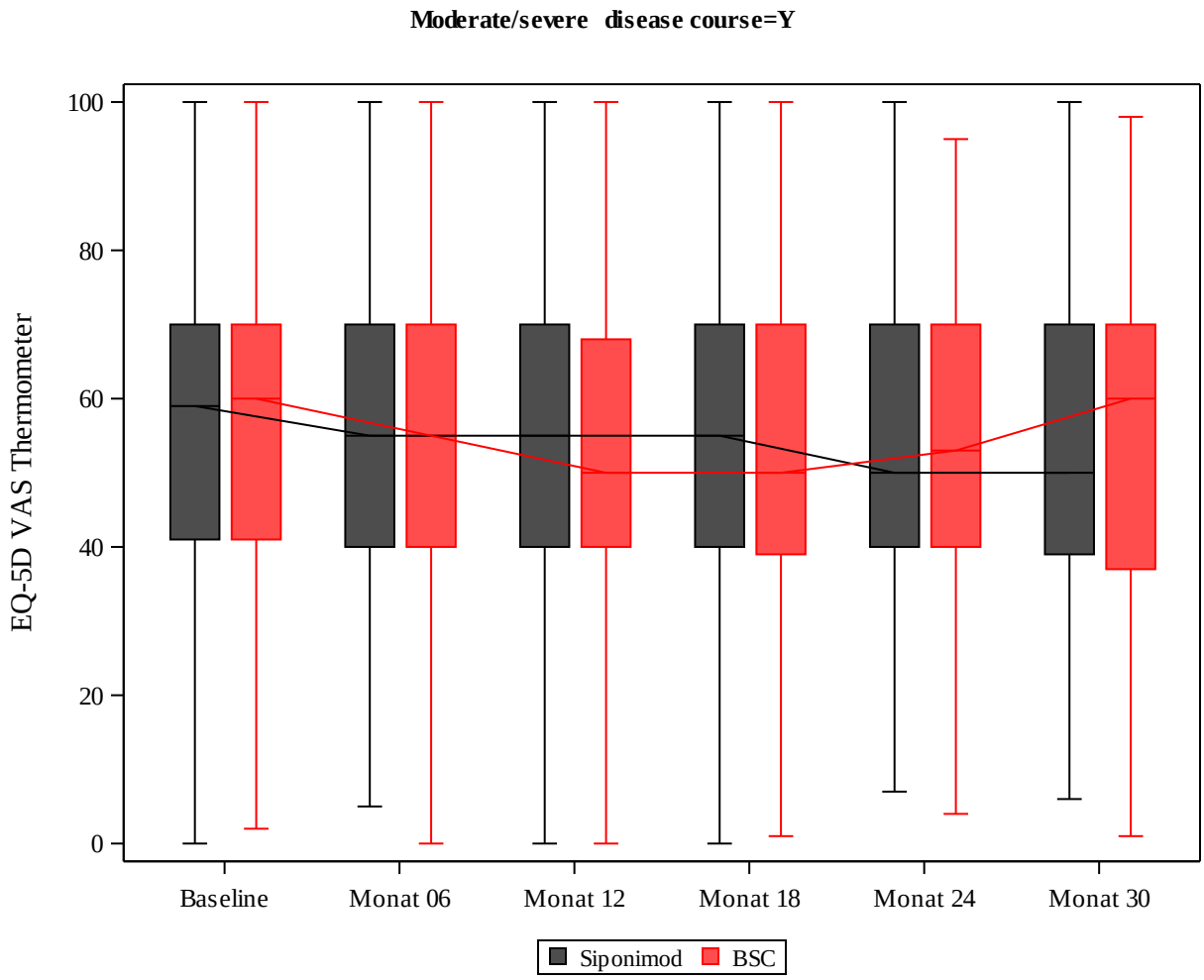


Figure 10.4.7: EQ-5D VAS Thermometer, Time course (FAS) by Disease Course



Novartis **Siponimod SPMS**
AMNOG Dossier Total Population **CBAF312A2304**

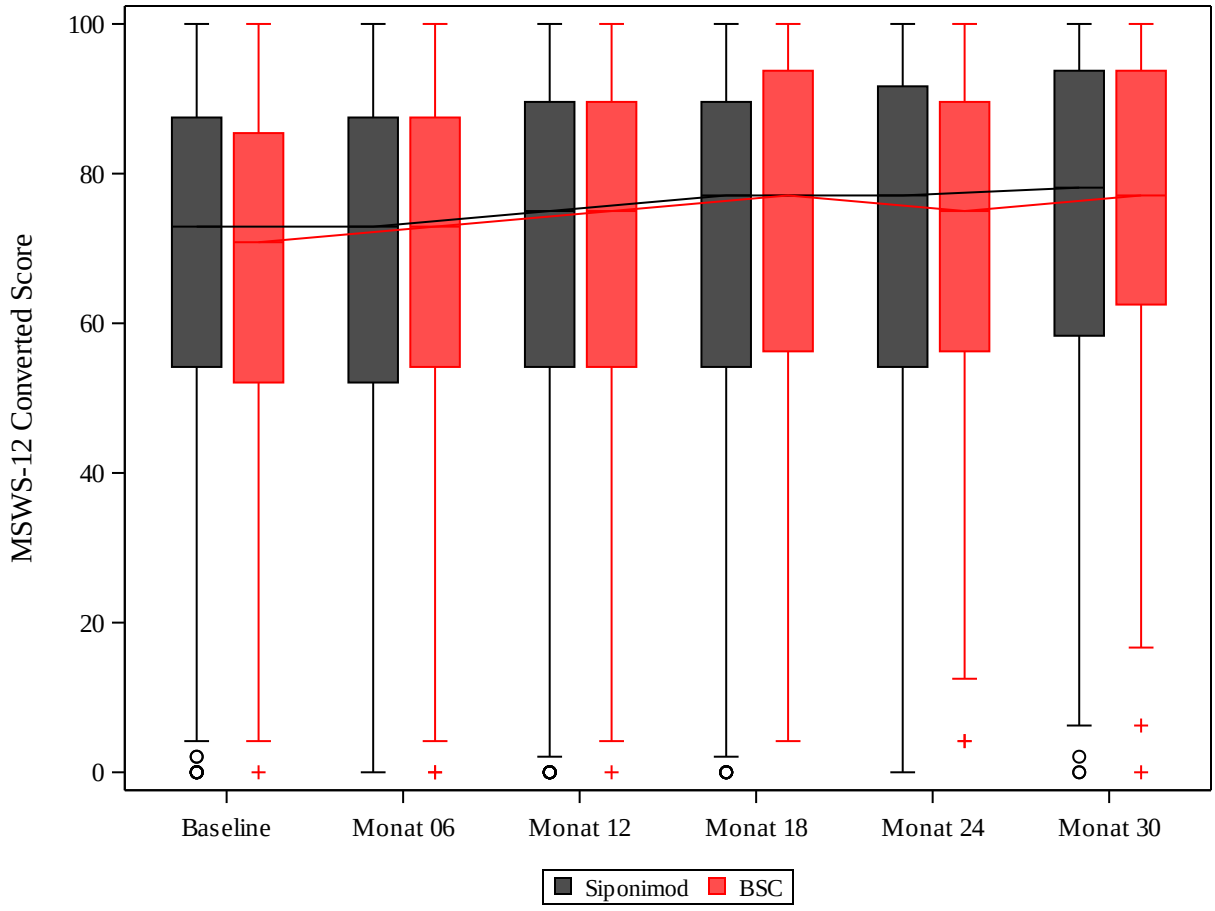



Figure 10.5.1: MSWS-12 Converted Score, Time course (FAS)