2.7.4 Summary of Clinical Safety

9.7. Listings of Subjects Who Died by Individual Study – All Studies With Data

＊新薬承認情報提供時に置換えた

Table 297: Listing of Deaths: Study 109MS301

Listing of deaths:
Study 109MS301
Page 1 of 2
BG00012 240 mg BID

Study ID	Subject(a) Sex/Age/Race	Study day(b)	Date of death	Cause of death	AE related	AE description	Relationship to study drug
109MS301	136* F/5[redacted]/WHITE	99	16DEC2008	CRANIOCEREBRAL TRAUMA	Y	CRANIOCEREBRAL TRAUMA	NOT RELATED

(a) *=Death occurred after subject withdrew from study.
(b) #=On or after the subject switched to alternate MS medication.
Abbreviations: M=Male; F=Female; N=No; Y=Yes.

SOURCE: BG12MS/JAPAN/ISS/L-DEATH-LST-301.SAS DATE: 02DEC2015

＊新薬承認情報提供時に置換えた

Listing of deaths:
Study 109MS301
Page 2 of 2
BG00012 240 mg TID

Study ID	Subject(a) Sex/Age/Race	Study day(b)	Date of death	Cause of death	AE related	AE description	Relationship to study drug
109MS301	210* F/3[redacted]/BLACK OR AFRICAN AMERICAN	62	29NOV2008	MOTOR VEHICLE ACCIDENT	Y	MOTOR VEHICLE ACCIDENT	NOT RELATED

(a) *=Death occurred after subject withdrew from study.
(b) #=On or after the subject switched to alternate MS medication.
Abbreviations: M=Male; F=Female; N=No; Y=Yes.

SOURCE: BG12MS/JAPAN/ISS/L-DEATH-LST-301.SAS DATE: 02DEC2015

＊新薬承認情報提供時に置換えた

Table 298: Listing of Deaths: Study 109MS302

Listing of deaths:
Study 109MS302
Page 1 of 3
Placebo

Study ID	Subject(a) Sex/Age/Race	Study day(b)	Date of death	Cause of death	AE related	AE description	Relationship to study drug
109MS302	384* F/5[redacted]/WHITE	344#	17DEC2009	ISCHEMIC STROKE	Y	CEREBRAL OEDEMA, COMA, ISCHEMIC STROKE	UNLIKELY

(a) *=Death occurred after subject withdrew from study.
(b) #=On or after the subject switched to alternate MS medication.
Abbreviations: M=Male; F=Female; N=No; Y=Yes.

SOURCE: BG12MS/JAPAN/ISS/L-DEATH-LST-302.SAS DATE: 02DEC2015

＊新薬承認情報提供時に置換えた

Listing of deaths:
Study 109MS302
Page 2 of 3
BG00012 240 mg TID

Study ID	Subject(a) Sex/Age/Race	Study day(b)	Date of death	Cause of death	AE related	AE description	Relationship to study drug
109MS302	345* F/5[redacted]/WHITE	218	17MAR2010	MULTIPLE SCLEROSIS, TUMEFACTIVE FORM	Y	MS RELAPSE	POSSIBLY

(a) *=Death occurred after subject withdrew from study.
(b) #=On or after the subject switched to alternate MS medication.
Abbreviations: M=Male; F=Female; N=No; Y=Yes.

SOURCE: BG12MS/JAPAN/ISS/L-DEATH-LST-302.SAS DATE: 02DEC2015

＊新薬承認情報提供時に置換えた

Listing of deaths:
Study 109MS302
Page 3 of 3
GA

Study ID	Subject(a) Sex/Age/Race	Study day(b)	Date of death	Cause of death	AE related	AE description	Relationship to study drug
109MS302	350* M/2[redacted]/WHITE	529	16APR2010	SUICIDE	Y	SUICIDE	UNLIKELY

(a) *=Death occurred after subject withdrew from study.
(b) #=On or after the subject switched to alternate MS medication.
Abbreviations: M=Male; F=Female; N=No; Y=Yes.

SOURCE: BG12MS/JAPAN/ISS/L-DEATH-LST-302.SAS DATE: 02DEC2015

＊新薬承認情報提供時に置換えた

Table 299: Listing of Deaths: Study 109MS303

Listing of deaths:
Study 109MS303
Page 1 of 2
BG00012 240 mg BID

Study ID	Subject(a) Sex/Age/Race	Study day(b)	Date of death	Cause of death	AE related	AE description	Relationship to study drug
109MS303	348* F/3[redacted]/ASIAN	150#	01DEC2011	TERMINAL CARDIO RESPIRATORY ARREST DUE TO TYPE I RESPIRATORY FAILURE DUE TO ASPIRATION PNEUMONIA	Y	BEDSORE ON LEFT BUTTOCK, RECURRENCE OF BEDSORE (INFECTED) OF LEFT FOOT.	NOT RELATED
	353* F/4[redacted]/ASIAN	473	06APR2012	MESPTHELIEMA.	Y	MALIGNANT MESOTHELIOMA-RIGHT	NOT RELATED
	349* F/3[redacted]/ASIAN	177	29JUN2011	MULTIPLE SCLEROSIS-RELAPSE CARDIO RESPIRATORY ARREST	Y	MS RELAPSE	NOT RELATED

(a) *=Death occurred after subject withdrew from study.
(b) #=On or after the subject switched to alternate MS medication.
Abbreviations: M=Male; F=Female; N=No; Y=Yes.

SOURCE: BG12MS/JAPAN/ISS/L-DEATH-LST-303.SAS DATE: 02DEC2015

＊新薬承認情報提供時に置換えた

Listing of deaths:
Study 109MS303
Page 2 of 2
BG00012 240 mg TID

Study ID	Subject(a) Sex/Age/Race	Study day(b)	Date of death	Cause of death	AE related	AE description	Relationship to study drug
109MS303	354* F/4[redacted]/WHITE	1705	13OCT2014	ASPIRATIONS PNEUMONIA	Y	ASPITATIONS PNEUMONIA/ DUE TO PML, PML	RELATED
	388* M/4[redacted]/WHITE	1632	25MAR2014	SUICIDE	Y	SUICIDE	UNLIKELY
	351* F/4[redacted]/WHITE	92	14DEC2010	PATIENT TOOK AN OVERDOSE OF PARACETAMOL ON 10 DEC 2010 PATIENT WENT INTO A COMA AND DEMISED ON 14 DEC 2010	Y	DEPRESSION (WORSENING), LIVER FAILURE, PARACETAMOL INTOXICATION, SUICIDE	NOT RELATED
	352* F/4[redacted]/WHITE	999	06AUG2013	THE PATIENT EXPERIENCED SERIOUS SAE "CARDIAC ARREST" ON 06 AUG 2013 WHICH WAS FATAL.		CARDIAC ARREST	

(a) *=Death occurred after subject withdrew from study.
(b) #=On or after the subject switched to alternate MS medication.
Abbreviations: M=Male; F=Female; N=No; Y=Yes.

SOURCE: BG12MS/JAPAN/ISS/L-DEATH-LST-303.SAS DATE: 02DEC2015

＊新薬承認情報提供時に置換えた

9.8. Listings of Subjects With SAEs by Individual Study – All Studies With Data

＊新薬承認情報提供時に置換えた

Table 303: Listing of Serious Adverse Events: Study 109MS301

Listing of serious adverse events:
Study 109MS301
Page 1 of 72
Treatment group: Placebo

Subject Sex/Age Race	MedDRA Preferred Term	Study Day Onset (a)(b)	Study Day Res	Dur (days)	Relationship to Study Drug	Severity	Serious	Action Taken With Study Drug	Outcome
[redacted] M/2[redacted] WHITE	意識消失	620	620	1	UNLIKELY	SEVERE	Yes	NONE	RESOLVED
502* F/4[redacted] BLACK OR AFRICAN AMERICAN	骨盤内炎症性疾患	396	472	77	UNLIKELY	SEVERE	Yes	DI	RESOLVED
	骨盤腔内腫瘤	396	472	77	UNLIKELY	SEVERE	Yes	DI	RESOLVED
	骨盤痛	396	472	77	UNLIKELY	SEVERE	Yes	DI	RESOLVED
503* F/3[redacted] WHITE	胃腸出血	247	252	6	POSSIBLY	MODERATE	Yes	DI	RESOLVED
	胃腸出血	320	321	2	UNLIKELY	MODERATE	Yes	DI	RESOLVED

(a) #=On or after the subject switched to alternate MS medication
(b) ^=Adverse Event with onset prior to dosing
Abbreviations: Res=Resolution, NR=Not Recovered/Not Resolved, Dur=Duration, NONE=Dose Not Changed, DW=Drug Withdrawn, DI=Drug Interrupted, DR=Dose Reduced, M=Male, F=Female

SOURCE: BG12MS/JAPAN/ISS/L-AE-SER-301.SAS DATE: 02DEC2015

＊新薬承認情報提供時に置換えた

Listing of serious adverse events:
Study 109MS301
Page 2 of 72
Treatment group: Placebo

Subject Sex/Age Race	MedDRA Preferred Term	Study Day Onset (a)(b)	Study Day Res	Dur (days)	Relationship to Study Drug	Severity	Serious	Action Taken With Study Drug	Outcome
[redacted] F/3[redacted] WHITE	肺炎	531	543	13	POSSIBLY	MODERATE	Yes	DI	RESOLVED
	敗血症	531	543	13	POSSIBLY	MODERATE	Yes	DI	RESOLVED
[redacted] F/3[redacted] WHITE	片頭痛	407	409	3	UNRELATED	MODERATE	Yes	NONE	RESOLVED
002* F/4[redacted] BLACK OR AFRICAN AMERICAN	多発性硬化症	415#	420	6	UNRELATED	MODERATE	Yes	NONE	RESOLVED

(a) #=On or after the subject switched to alternate MS medication
(b) ^=Adverse Event with onset prior to dosing
Abbreviations: Res=Resolution, NR=Not Recovered/Not Resolved, Dur=Duration, NONE=Dose Not Changed, DW=Drug Withdrawn, DI=Drug Interrupted, DR=Dose Reduced, M=Male, F=Female

SOURCE: BG12MS/JAPAN/ISS/L-AE-SER-301.SAS DATE: 02DEC2015

＊新薬承認情報提供時に置換えた

Listing of serious adverse events:
Study 109MS301
Page 3 of 72
Treatment group: Placebo

Subject Sex/Age Race	MedDRA Preferred Term	Study Day Onset (a)(b)	Study Day Res	Dur (days)	Relationship to Study Drug	Severity	Serious	Action Taken With Study Drug	Outcome
511* F/4[redacted] WHITE	インフルエンザ様疾患	653	658	6	POSSIBLY	MODERATE	Yes	DI	RESOLVED
512* F/4[redacted] WHITE	自殺念慮	132	132	1	UNRELATED	MILD	Yes	NONE	RESOLVED
513* F/5[redacted] ASIAN	貧血	157	165	9	UNRELATED	SEVERE	Yes	NONE	RESOLVED
	腹膜出血	157	157	1	UNRELATED	SEVERE	Yes	DI	RESOLVED
	月経障害	264	264	1	UNRELATED	SEVERE	Yes	DI	RESOLVED
	子宮平滑筋腫	264	264	1	UNRELATED	SEVERE	Yes	DI	RESOLVED

(a) #=On or after the subject switched to alternate MS medication
(b) ^=Adverse Event with onset prior to dosing
Abbreviations: Res=Resolution, NR=Not Recovered/Not Resolved, Dur=Duration, NONE=Dose Not Changed, DW=Drug Withdrawn, DI=Drug Interrupted, DR=Dose Reduced, M=Male, F=Female

SOURCE: BG12MS/JAPAN/ISS/L-AE-SER-301.SAS DATE: 02DEC2015

＊新薬承認情報提供時に置換えた

Listing of serious adverse events:
Study 109MS301
Page 4 of 72
Treatment group: Placebo

Subject Sex/Age Race	MedDRA Preferred Term	Study Day Onset (a)(b)	Study Day Res	Dur (days)	Relationship to Study Drug	Severity	Serious	Action Taken With Study Drug	Outcome
[redacted] F/3[redacted] WHITE	多発性硬化症再発	281	290	10	UNRELATED	MODERATE	Yes	NONE	RESOLVED
	多発性硬化症再発	425	430	6	UNRELATED	MODERATE	Yes	NONE	RESOLVED
006* F/2[redacted] WHITE	多発性硬化症再発	152	224	73	UNRELATED	MODERATE	Yes	DW	RESOLVED
[redacted] F/3[redacted] WHITE	多発性硬化症再発	211	221	11	UNRELATED	MODERATE	Yes	NONE	RESOLVED
	多発性硬化症再発	650	662	13	UNRELATED	MODERATE	Yes	NONE	RESOLVED

(a) #=On or after the subject switched to alternate MS medication
(b) ^=Adverse Event with onset prior to dosing
Abbreviations: Res=Resolution, NR=Not Recovered/Not Resolved, Dur=Duration, NONE=Dose Not Changed, DW=Drug Withdrawn, DI=Drug Interrupted, DR=Dose Reduced, M=Male, F=Female

SOURCE: BG12MS/JAPAN/ISS/L-AE-SER-301.SAS DATE: 02DEC2015

＊新薬承認情報提供時に置換えた

Listing of serious adverse events:
Study 109MS301
Page 5 of 72
Treatment group: Placebo

Subject Sex/Age Race	MedDRA Preferred Term	Study Day Onset (a)(b)	Study Day Res	Dur (days)	Relationship to Study Drug	Severity	Serious	Action Taken With Study Drug	Outcome
516* M/3[redacted] WHITE	肝酵素上昇	283	293	11	UNLIKELY	MODERATE	Yes	DI	RESOLVED
	多発性硬化症再発	659	669	11	UNRELATED	MODERATE	Yes	NONE	RESOLVED
[redacted] F/3[redacted] WHITE	多発性硬化症再発	189	197	9	UNRELATED	MODERATE	Yes	NONE	RESOLVED
	多発性硬化症再発	670	681	12	UNRELATED	MODERATE	Yes	NONE	RESOLVED
[redacted] F/2[redacted] WHITE	多発性硬化症再発	225	281	57	UNRELATED	MODERATE	Yes	NONE	RESOLVED

(a) #=On or after the subject switched to alternate MS medication
(b) ^=Adverse Event with onset prior to dosing
Abbreviations: Res=Resolution, NR=Not Recovered/Not Resolved, Dur=Duration, NONE=Dose Not Changed, DW=Drug Withdrawn, DI=Drug Interrupted, DR=Dose Reduced, M=Male, F=Female

SOURCE: BG12MS/JAPAN/ISS/L-AE-SER-301.SAS DATE: 02DEC2015

＊新薬承認情報提供時に置換えた

Listing of serious adverse events:
Study 109MS301
Page 6 of 72
Treatment group: Placebo

Subject Sex/Age Race	MedDRA Preferred Term	Study Day Onset (a)(b)	Study Day Res	Dur (days)	Relationship to Study Drug	Severity	Serious	Action Taken With Study Drug	Outcome
007* F/2[redacted] ASIAN	多発性硬化症再発	175	178	4	UNRELATED	SEVERE	Yes	DW	RESOLVED
[redacted] F/4[redacted] ASIAN	多発性硬化症再発	173	282	110	UNRELATED	MILD	Yes	NONE	RESOLVED
[redacted] F/3[redacted] ASIAN	多発性硬化症再発	83	87	5	UNRELATED	SEVERE	Yes	NONE	RESOLVED
008* F/4[redacted] ASIAN	多発性硬化症再発	271	521	251	POSSIBLY	SEVERE	Yes	DW	RESOLVED
	多発性硬化症再発	575#	579	5	UNRELATED	SEVERE	Yes	NONE	RESOLVED

(a) #=On or after the subject switched to alternate MS medication
(b) ^=Adverse Event with onset prior to dosing
Abbreviations: Res=Resolution, NR=Not Recovered/Not Resolved, Dur=Duration, NONE=Dose Not Changed, DW=Drug Withdrawn, DI=Drug Interrupted, DR=Dose Reduced, M=Male, F=Female

SOURCE: BG12MS/JAPAN/ISS/L-AE-SER-301.SAS DATE: 02DEC2015

＊新薬承認情報提供時に置換えた

Listing of serious adverse events:
Study 109MS301
Page 7 of 72
Treatment group: Placebo

Subject Sex/Age Race	MedDRA Preferred Term	Study Day Onset (a)(b)	Study Day Res	Dur (days)	Relationship to Study Drug	Severity	Serious	Action Taken With Study Drug	Outcome
008* F/4[redacted] ASIAN	多発性硬化症再発	627#	631	5	UNRELATED	SEVERE	Yes	NONE	RESOLVED
[redacted] M/2[redacted] ASIAN	多発性硬化症再発	88	136	49	UNRELATED	MODERATE	Yes	NONE	RESOLVED
[redacted] M/3[redacted] ASIAN	多発性硬化症再発	2	45	44	UNLIKELY	SEVERE	Yes	NONE	RESOLVED
[redacted] M/3[redacted] ASIAN	多発性硬化症再発	9	17	9	UNRELATED	SEVERE	Yes	NONE	RESOLVED

(a) #=On or after the subject switched to alternate MS medication
(b) ^=Adverse Event with onset prior to dosing
Abbreviations: Res=Resolution, NR=Not Recovered/Not Resolved, Dur=Duration, NONE=Dose Not Changed, DW=Drug Withdrawn, DI=Drug Interrupted, DR=Dose Reduced, M=Male, F=Female

SOURCE: BG12MS/JAPAN/ISS/L-AE-SER-301.SAS DATE: 02DEC2015

＊新薬承認情報提供時に置換えた

Listing of serious adverse events:
Study 109MS301
Page 8 of 72
Treatment group: Placebo

Subject Sex/Age Race	MedDRA Preferred Term	Study Day Onset (a)(b)	Study Day Res	Dur (days)	Relationship to Study Drug	Severity	Serious	Action Taken With Study Drug	Outcome
524* F/2[redacted] ASIAN	痙攣	83	85	3	UNRELATED	SEVERE	Yes	NONE	RESOLVED
	多発性硬化症再発	324	368	45	UNRELATED	SEVERE	Yes	NONE	RESOLVED
525* F/2[redacted] ASIAN	多発性硬化症再発	70	76	7	UNRELATED	SEVERE	Yes	NONE	RESOLVED
	多発性硬化症再発	274	284	11	UNLIKELY	MODERATE	Yes	NONE	RESOLVED
	Ｈ１Ｎ１インフルエンザ	308	313	6	UNRELATED	SEVERE	Yes	NONE	RESOLVED
	多発性硬化症再発	589	595	7	UNRELATED	SEVERE	Yes	NONE	RESOLVED

(a) #=On or after the subject switched to alternate MS medication
(b) ^=Adverse Event with onset prior to dosing
Abbreviations: Res=Resolution, NR=Not Recovered/Not Resolved, Dur=Duration, NONE=Dose Not Changed, DW=Drug Withdrawn, DI=Drug Interrupted, DR=Dose Reduced, M=Male, F=Female

SOURCE: BG12MS/JAPAN/ISS/L-AE-SER-301.SAS DATE: 02DEC2015

＊新薬承認情報提供時に置換えた

Listing of serious adverse events:
Study 109MS301
Page 9 of 72
Treatment group: Placebo

Subject Sex/Age Race	MedDRA Preferred Term	Study Day Onset (a)(b)	Study Day Res	Dur (days)	Relationship to Study Drug	Severity	Serious	Action Taken With Study Drug	Outcome
528* F/2[redacted] ASIAN	多発性関節炎	280	308	29	POSSIBLY	MODERATE	Yes	NONE	RESOLVED
010* M/2[redacted] ASIAN	消化器結核	235	542	308	POSSIBLY	MODERATE	Yes	DW	RESOLVED
	大発作痙攣	425	426	2	UNRELATED	MILD	Yes	NONE	RESOLVED
	多発性硬化症再発	431	433	3	UNRELATED	MODERATE	Yes	NONE	RESOLVED
530* M/2[redacted] ASIAN	脳症	197	201	5	UNRELATED	MODERATE	Yes	NONE	RESOLVED
	多発性硬化症再発	365	421	57	UNRELATED	MILD	Yes	NONE	RESOLVED

(a) #=On or after the subject switched to alternate MS medication
(b) ^=Adverse Event with onset prior to dosing
Abbreviations: Res=Resolution, NR=Not Recovered/Not Resolved, Dur=Duration, NONE=Dose Not Changed, DW=Drug Withdrawn, DI=Drug Interrupted, DR=Dose Reduced, M=Male, F=Female

SOURCE: BG12MS/JAPAN/ISS/L-AE-SER-301.SAS DATE: 02DEC2015

＊新薬承認情報提供時に置換えた

Listing of serious adverse events:
Study 109MS301
Page 10 of 72
Treatment group: Placebo

Subject Sex/Age Race	MedDRA Preferred Term	Study Day Onset (a)(b)	Study Day Res	Dur (days)	Relationship to Study Drug	Severity	Serious	Action Taken With Study Drug	Outcome
530* M/2[redacted] ASIAN	多発性硬化症再発	543	546	4	UNRELATED	MODERATE	Yes	NONE	RESOLVED
	多発性硬化症再発	617	619	3	UNRELATED	MODERATE	Yes	NONE	RESOLVED
532* M/5[redacted] ASIAN	腱断裂	141	172	32	UNRELATED	MODERATE	Yes	NONE	RESOLVED
[redacted] F/4[redacted] ASIAN	多発性硬化症再発	100	106	7	UNRELATED	MODERATE	Yes	NONE	RESOLVED
	多発性硬化症再発	431			UNRELATED	MODERATE	Yes	NONE	RESOLVED
	多発性硬化症再発	62 0	625	6	UNRELATED	MODERATE	Yes	NONE	RESOLVED

(a) #=On or after the subject switched to alternate MS medication
(b) ^=Adverse Event with onset prior to dosing
Abbreviations: Res=Resolution, NR=Not Recovered/Not Resolved, Dur=Duration, NONE=Dose Not Changed, DW=Drug Withdrawn, DI=Drug Interrupted, DR=Dose Reduced, M=Male, F=Female

SOURCE: BG12MS/JAPAN/ISS/L-AE-SER-301.SAS DATE: 02DEC2015

＊新薬承認情報提供時に置換えた

Listing of serious adverse events:
Study 109MS301
Page 11 of 72
Treatment group: Placebo

Subject Sex/Age Race	MedDRA Preferred Term	Study Day Onset (a)(b)	Study Day Res	Dur (days)	Relationship to Study Drug	Severity	Serious	Action Taken With Study Drug	Outcome
353* F/4[redacted] ASIAN	多発性硬化症再発	181	254	74	UNRELATED	MODERATE	Yes	NONE	RESOLVED
	感染性下痢	187	188	2	UNRELATED	MODERATE	Yes	NONE	RESOLVED
	ライター症候群	200	204	5	UNRELATED	MODERATE	Yes	NONE	RESOLVED
[redacted] F/5[redacted] WHITE	多発性硬化症再発	337	340	4	UNRELATED	SEVERE	Yes	NONE	RESOLVED
[redacted] F/4[redacted] WHITE	多発性硬化症再発	470	472	3	UNRELATED	MODERATE	Yes	NONE	RESOLVED
355* F/3[redacted] WHITE	多発性硬化症再発	260	261	2	UNLIKELY	SEVERE	Yes	NONE	RESOLVED

(a) #=On or after the subject switched to alternate MS medication
(b) ^=Adverse Event with onset prior to dosing
Abbreviations: Res=Resolution, NR=Not Recovered/Not Resolved, Dur=Duration, NONE=Dose Not Changed, DW=Drug Withdrawn, DI=Drug Interrupted, DR=Dose Reduced, M=Male, F=Female

SOURCE: BG12MS/JAPAN/ISS/L-AE-SER-301.SAS DATE: 02DEC2015

＊新薬承認情報提供時に置換えた

Listing of serious adverse events:
Study 109MS301
Page 12 of 72
Treatment group: Placebo

Subject Sex/Age Race	MedDRA Preferred Term	Study Day Onset (a)(b)	Study Day Res	Dur (days)	Relationship to Study Drug	Severity	Serious	Action Taken With Study Drug	Outcome
537* F/4[redacted] WHITE	子宮平滑筋腫	308	313	6	UNRELATED	MODERATE	Yes	NONE	RESOLVED
	基底細胞癌	402	451	50	UNLIKELY	MODERATE	Yes	NONE	RESOLVED
[redacted] F/3[redacted] WHITE	多発性硬化症再発	65	77	13	UNLIKELY	MODERATE	Yes	NONE	RESOLVED
016* M/2[redacted] WHITE	鼓膜炎	597#	604	8	UNRELATED	MODERATE	Yes	NONE	RESOLVED
	外耳炎	597#	604	8	UNRELATED	MODERATE	Yes	NONE	RESOLVED
543* F/3[redacted] WHITE	鼻咽頭炎	149	155	7	UNLIKELY	MILD	Yes	NONE	RESOLVED

(a) #=On or after the subject switched to alternate MS medication
(b) ^=Adverse Event with onset prior to dosing
Abbreviations: Res=Resolution, NR=Not Recovered/Not Resolved, Dur=Duration, NONE=Dose Not Changed, DW=Drug Withdrawn, DI=Drug Interrupted, DR=Dose Reduced, M=Male, F=Female

SOURCE: BG12MS/JAPAN/ISS/L-AE-SER-301.SAS DATE: 02DEC2015

＊新薬承認情報提供時に置換えた

Listing of serious adverse events:
Study 109MS301
Page 13 of 72
Treatment group: Placebo

Subject Sex/Age Race	MedDRA Preferred Term	Study Day Onset (a)(b)	Study Day Res	Dur (days)	Relationship to Study Drug	Severity	Serious	Action Taken With Study Drug	Outcome
[redacted] F/2[redacted] WHITE	多発性硬化症再発	278	282	5	UNRELATED	MILD	Yes	NONE	RESOLVED
020* F/2[redacted] WHITE	多発性硬化症再発	184	187	4	UNRELATED	MILD	Yes	NONE	RESOLVED
	多発性硬化症再発	320	344	25	UNRELATED	MILD	Yes	DW	RESOLVED
021* F/4[redacted] WHITE	多発性硬化症再発	124	131	8	UNRELATED	MILD	Yes	DW	RESOLVED
552* M/3[redacted] WHITE	血管腫	106	107	2	UNRELATED	MILD	Yes	NONE	RESOLVED

(a) #=On or after the subject switched to alternate MS medication
(b) ^=Adverse Event with onset prior to dosing
Abbreviations: Res=Resolution, NR=Not Recovered/Not Resolved, Dur=Duration, NONE=Dose Not Changed, DW=Drug Withdrawn, DI=Drug Interrupted, DR=Dose Reduced, M=Male, F=Female

SOURCE: BG12MS/JAPAN/ISS/L-AE-SER-301.SAS DATE: 02DEC2015

＊新薬承認情報提供時に置換えた

Listing of serious adverse events:
Study 109MS301
Page 14 of 72
Treatment group: Placebo

Subject Sex/Age Race	MedDRA Preferred Term	Study Day Onset (a)(b)	Study Day Res	Dur (days)	Relationship to Study Drug	Severity	Serious	Action Taken With Study Drug	Outcome
554* F/4[redacted] WHITE	小球性貧血	330	335	6	UNRELATED	MODERATE	Yes	NONE	RESOLVED
	大腿骨頚部骨折	507	560	54	UNRELATED	SEVERE	Yes	NONE	RESOLVED
024* F/3[redacted] WHITE	多発性硬化症再発	64	86	23	UNRELATED	SEVERE	Yes	NONE	RESOLVED
[redacted] F/4[redacted] WHITE	多発性硬化症再発	143	151	9	UNLIKELY	SEVERE	Yes	NONE	RESOLVED
025* F/3[redacted] WHITE	多発性硬化症再発	497#	527	31	UNRELATED	MODERATE	Yes	NONE	RESOLVED

(a) #=On or after the subject switched to alternate MS medication
(b) ^=Adverse Event with onset prior to dosing
Abbreviations: Res=Resolution, NR=Not Recovered/Not Resolved, Dur=Duration, NONE=Dose Not Changed, DW=Drug Withdrawn, DI=Drug Interrupted, DR=Dose Reduced, M=Male, F=Female

SOURCE: BG12MS/JAPAN/ISS/L-AE-SER-301.SAS DATE: 02DEC2015

＊新薬承認情報提供時に置換えた

Listing of serious adverse events:
Study 109MS301
Page 15 of 72
Treatment group: Placebo

Subject Sex/Age Race	MedDRA Preferred Term	Study Day Onset (a)(b)	Study Day Res	Dur (days)	Relationship to Study Drug	Severity	Serious	Action Taken With Study Drug	Outcome
558* F/4[redacted] WHITE	変形性関節症	352	374	23	UNRELATED	SEVERE	Yes	DI	RESOLVED
028* F/4[redacted] WHITE	大腸炎	138	142	5	POSSIBLY	MODERATE	Yes	NONE	RESOLVED
	潰瘍性大腸炎	250	263	14	UNRELATED	MODERATE	Yes	NONE	RESOLVED
[redacted] F/3[redacted] WHITE	多発性硬化症再発	641	NR		UNRELATED	MODERATE	Yes	NONE	NOT RESOLVED
035* F/4[redacted] WHITE	多発性硬化症再発	472	483	12	UNRELATED	MODERATE	Yes	DW	RESOLVED

(a) #=On or after the subject switched to alternate MS medication
(b) ^=Adverse Event with onset prior to dosing
Abbreviations: Res=Resolution, NR=Not Recovered/Not Resolved, Dur=Duration, NONE=Dose Not Changed, DW=Drug Withdrawn, DI=Drug Interrupted, DR=Dose Reduced, M=Male, F=Female

SOURCE: BG12MS/JAPAN/ISS/L-AE-SER-301.SAS DATE: 02DEC2015

＊新薬承認情報提供時に置換えた

Listing of serious adverse events:
Study 109MS301
Page 16 of 72
Treatment group: Placebo

Subject Sex/Age Race	MedDRA Preferred Term	Study Day Onset (a)(b)	Study Day Res	Dur (days)	Relationship to Study Drug	Severity	Serious	Action Taken With Study Drug	Outcome
[redacted] F/4[redacted] WHITE	多発性硬化症再発	495	499	5	UNRELATED	MODERATE	Yes	NONE	RESOLVED
[redacted] F/3[redacted] WHITE	多発性硬化症再発	281	286	6	UNLIKELY	MODERATE	Yes	NONE	RESOLVED
	多発性硬化症再発	653	658	6	UNLIKELY	MODERATE	Yes	NONE	RESOLVED
[redacted] F/2[redacted] WHITE	多発性硬化症再発	52	56	5	UNLIKELY	MILD	Yes	NONE	RESOLVED
	多発性硬化症再発	99	103	5	UNLIKELY	MILD	Yes	NONE	RESOLVED
	多発性硬化症再発	229	232	4	UNLIKELY	MODERATE	Yes	NONE	RESOLVED

(a) #=On or after the subject switched to alternate MS medication
(b) ^=Adverse Event with onset prior to dosing
Abbreviations: Res=Resolution, NR=Not Recovered/Not Resolved, Dur=Duration, NONE=Dose Not Changed, DW=Drug Withdrawn, DI=Drug Interrupted, DR=Dose Reduced, M=Male, F=Female

SOURCE: BG12MS/JAPAN/ISS/L-AE-SER-301.SAS DATE: 02DEC2015

＊新薬承認情報提供時に置換えた

Listing of serious adverse events:
Study 109MS301
Page 17 of 72
Treatment group: Placebo

Subject Sex/Age Race	MedDRA Preferred Term	Study Day Onset (a)(b)	Study Day Res	Dur (days)	Relationship to Study Drug	Severity	Serious	Action Taken With Study Drug	Outcome
[redacted] F/2[redacted] WHITE	多発性硬化症再発	477#	480	4	UNRELATED	MODERATE	Yes	NONE	RESOLVED
[redacted] M/4[redacted] WHITE	多発性硬化症再発	565	569	5	UNLIKELY	MODERATE	Yes	NONE	RESOLVED
[redacted] F/4[redacted] WHITE	多発性硬化症再発	151	157	7	UNLIKELY	SEVERE	Yes	NONE	RESOLVED
	多発性硬化症再発	306	312	7	UNLIKELY	SEVERE	Yes	NONE	RESOLVED
	多発性硬化症再発	422	428	7	UNLIKELY	SEVERE	Yes	NONE	RESOLVED
	多発性硬化症再発	564	574	11	UNLIKELY	SEVERE	Yes	NONE	RESOLVED

(a) #=On or after the subject switched to alternate MS medication
(b) ^=Adverse Event with onset prior to dosing
Abbreviations: Res=Resolution, NR=Not Recovered/Not Resolved, Dur=Duration, NONE=Dose Not Changed, DW=Drug Withdrawn, DI=Drug Interrupted, DR=Dose Reduced, M=Male, F=Female

SOURCE: BG12MS/JAPAN/ISS/L-AE-SER-301.SAS DATE: 02DEC2015

＊新薬承認情報提供時に置換えた

Listing of serious adverse events:
Study 109MS301
Page 18 of 72
Treatment group: Placebo

Subject Sex/Age Race	MedDRA Preferred Term	Study Day Onset (a)(b)	Study Day Res	Dur (days)	Relationship to Study Drug	Severity	Serious	Action Taken With Study Drug	Outcome
[redacted] F/4[redacted] WHITE	多発性硬化症再発	62 0	627	8	UNLIKELY	SEVERE	Yes	NONE	RESOLVED
[redacted] F/4[redacted] WHITE	多発性硬化症再発	453	460	8	UNLIKELY	MODERATE	Yes	NONE	RESOLVED
[redacted] F/4[redacted] WHITE	多発性硬化症再発	425	429	5	UNLIKELY	MODERATE	Yes	NONE	RESOLVED
570* F/3[redacted] WHITE	子宮出血	232	233	2	UNLIKELY	MODERATE	Yes	NONE	RESOLVED

(a) #=On or after the subject switched to alternate MS medication
(b) ^=Adverse Event with onset prior to dosing
Abbreviations: Res=Resolution, NR=Not Recovered/Not Resolved, Dur=Duration, NONE=Dose Not Changed, DW=Drug Withdrawn, DI=Drug Interrupted, DR=Dose Reduced, M=Male, F=Female

SOURCE: BG12MS/JAPAN/ISS/L-AE-SER-301.SAS DATE: 02DEC2015

＊新薬承認情報提供時に置換えた

Listing of serious adverse events:
Study 109MS301
Page 19 of 72
Treatment group: Placebo

Subject Sex/Age Race	MedDRA Preferred Term	Study Day Onset (a)(b)	Study Day Res	Dur (days)	Relationship to Study Drug	Severity	Serious	Action Taken With Study Drug	Outcome
571* F/3[redacted] WHITE	多発性硬化症再発	170	175	6	UNLIKELY	MODERATE	Yes	NONE	RESOLVED
	多発性硬化症再発	212	218	7	UNLIKELY	MODERATE	Yes	NONE	RESOLVED
	卵巣嚢胞	456	464	9	UNLIKELY	SEVERE	Yes	DI	RESOLVED
[redacted] F/2[redacted] WHITE	多発性硬化症再発	309	313	5	UNLIKELY	MILD	Yes	NONE	RESOLVED
[redacted] F/5[redacted] WHITE	多発性硬化症再発	196	200	5	UNLIKELY	MILD	Yes	NONE	RESOLVED

(a) #=On or after the subject switched to alternate MS medication
(b) ^=Adverse Event with onset prior to dosing
Abbreviations: Res=Resolution, NR=Not Recovered/Not Resolved, Dur=Duration, NONE=Dose Not Changed, DW=Drug Withdrawn, DI=Drug Interrupted, DR=Dose Reduced, M=Male, F=Female

SOURCE: BG12MS/JAPAN/ISS/L-AE-SER-301.SAS DATE: 02DEC2015

＊新薬承認情報提供時に置換えた

Listing of serious adverse events:
Study 109MS301
Page 20 of 72
Treatment group: Placebo

Subject Sex/Age Race	MedDRA Preferred Term	Study Day Onset (a)(b)	Study Day Res	Dur (days)	Relationship to Study Drug	Severity	Serious	Action Taken With Study Drug	Outcome
[redacted] F/4[redacted] WHITE	多発性硬化症再発	57	66	10	UNRELATED	MODERATE	Yes	NONE	RESOLVED
	多発性硬化症再発	311	319	9	UNRELATED	MODERATE	Yes	NONE	RESOLVED
	多発性硬化症再発	480#	498	19	UNRELATED	MODERATE	Yes	NONE	RESOLVED
[redacted] F/3[redacted] WHITE	多発性硬化症再発	74	78	5	UNRELATED	MILD	Yes	NONE	RESOLVED
	多発性硬化症再発	413#	419	7	UNRELATED	MILD	Yes	NONE	RESOLVED
[redacted] F/4[redacted] WHITE	多発性硬化症再発	394	398	5	UNRELATED	MILD	Yes	NONE	RESOLVED

(a) #=On or after the subject switched to alternate MS medication
(b) ^=Adverse Event with onset prior to dosing
Abbreviations: Res=Resolution, NR=Not Recovered/Not Resolved, Dur=Duration, NONE=Dose Not Changed, DW=Drug Withdrawn, DI=Drug Interrupted, DR=Dose Reduced, M=Male, F=Female

SOURCE: BG12MS/JAPAN/ISS/L-AE-SER-301.SAS DATE: 02DEC2015

＊新薬承認情報提供時に置換えた

Listing of serious adverse events:
Study 109MS301
Page 21 of 72
Treatment group: Placebo

Subject Sex/Age Race	MedDRA Preferred Term	Study Day Onset (a)(b)	Study Day Res	Dur (days)	Relationship to Study Drug	Severity	Serious	Action Taken With Study Drug	Outcome
[redacted] F/4[redacted] WHITE	多発性硬化症再発	197	203	7	UNRELATED	MODERATE	Yes	NONE	RESOLVED
[redacted] F/2[redacted] WHITE	多発性硬化症再発	13	19	7	UNRELATED	MODERATE	Yes	NONE	RESOLVED
[redacted] M/4[redacted] WHITE	多発性硬化症再発	597	601	5	UNRELATED	MODERATE	Yes	NONE	RESOLVED
[redacted] F/3[redacted] WHITE	多発性硬化症再発	313	349	37	UNLIKELY	MODERATE	Yes	NONE	RESOLVED

(a) #=On or after the subject switched to alternate MS medication
(b) ^=Adverse Event with onset prior to dosing
Abbreviations: Res=Resolution, NR=Not Recovered/Not Resolved, Dur=Duration, NONE=Dose Not Changed, DW=Drug Withdrawn, DI=Drug Interrupted, DR=Dose Reduced, M=Male, F=Female

SOURCE: BG12MS/JAPAN/ISS/L-AE-SER-301.SAS DATE: 02DEC2015

＊新薬承認情報提供時に置換えた

Listing of serious adverse events:
Study 109MS301
Page 22 of 72
Treatment group: Placebo

Subject Sex/Age Race	MedDRA Preferred Term	Study Day Onset (a)(b)	Study Day Res	Dur (days)	Relationship to Study Drug	Severity	Serious	Action Taken With Study Drug	Outcome
[redacted] F/3[redacted] WHITE	多発性硬化症再発	132	167	36	UNLIKELY	MODERATE	Yes	NONE	RESOLVED
[redacted] F/4[redacted] WHITE	多発性硬化症再発	170	198	29	UNLIKELY	MODERATE	Yes	NONE	RESOLVED
	多発性硬化症再発	477	493	17	UNLIKELY	MODERATE	Yes	NONE	RESOLVED
[redacted] F/3[redacted] WHITE	多発性硬化症再発	156	213	58	UNLIKELY	MODERATE	Yes	NONE	RESOLVED
[redacted] F/3[redacted] WHITE	多発性硬化症再発	245	349	105	UNLIKELY	MILD	Yes	NONE	RESOLVED

(a) #=On or after the subject switched to alternate MS medication
(b) ^=Adverse Event with onset prior to dosing
Abbreviations: Res=Resolution, NR=Not Recovered/Not Resolved, Dur=Duration, NONE=Dose Not Changed, DW=Drug Withdrawn, DI=Drug Interrupted, DR=Dose Reduced, M=Male, F=Female

SOURCE: BG12MS/JAPAN/ISS/L-AE-SER-301.SAS DATE: 02DEC2015

＊新薬承認情報提供時に置換えた

Listing of serious adverse events:
Study 109MS301
Page 23 of 72
Treatment group: Placebo

Subject Sex/Age Race	MedDRA Preferred Term	Study Day Onset (a)(b)	Study Day Res	Dur (days)	Relationship to Study Drug	Severity	Serious	Action Taken With Study Drug	Outcome
[redacted] F/3[redacted] WHITE	多発性硬化症再発	666	771	106	UNLIKELY	MODERATE	Yes	NONE	RESOLVED
[redacted] M/3[redacted] WHITE	多発性硬化症再発	5	7	3	UNRELATED	MODERATE	Yes	NONE	RESOLVED
[redacted] M/4[redacted] WHITE	多発性硬化症再発	621	628	8	UNRELATED	MODERATE	Yes	NONE	RESOLVED
[redacted] F/4[redacted] HISPANIC	多発性硬化症再発	477	482	6	UNRELATED	MODERATE	Yes	NONE	RESOLVED

(a) #=On or after the subject switched to alternate MS medication
(b) ^=Adverse Event with onset prior to dosing
Abbreviations: Res=Resolution, NR=Not Recovered/Not Resolved, Dur=Duration, NONE=Dose Not Changed, DW=Drug Withdrawn, DI=Drug Interrupted, DR=Dose Reduced, M=Male, F=Female

SOURCE: BG12MS/JAPAN/ISS/L-AE-SER-301.SAS DATE: 02DEC2015

＊新薬承認情報提供時に置換えた

Listing of serious adverse events:
Study 109MS301
Page 24 of 72
Treatment group: Placebo

Subject Sex/Age Race	MedDRA Preferred Term	Study Day Onset (a)(b)	Study Day Res	Dur (days)	Relationship to Study Drug	Severity	Serious	Action Taken With Study Drug	Outcome
346* F/3[redacted] HISPANIC	アレルギー性皮膚炎	647	649	3	UNRELATED	SEVERE	Yes	NONE	RESOLVED
038* F/4[redacted] WHITE	うつ病	172	174	3	UNRELATED	MODERATE	Yes	NONE	RESOLVED
[redacted] F/4[redacted]	多発性硬化症再発	452	481	30	UNRELATED	SEVERE	Yes	NONE	RESOLVED
579* F/3[redacted]	下肢静止不能症候群	614	NR		UNLIKELY	MODERATE	Yes	NONE	NOT RESOLVED
580* M/4[redacted]	肛門膿瘍	420	422	3	POSSIBLY	SEVERE	Yes	NONE	RESOLVED

(a) #=On or after the subject switched to alternate MS medication
(b) ^=Adverse Event with onset prior to dosing
Abbreviations: Res=Resolution, NR=Not Recovered/Not Resolved, Dur=Duration, NONE=Dose Not Changed, DW=Drug Withdrawn, DI=Drug Interrupted, DR=Dose Reduced, M=Male, F=Female

SOURCE: BG12MS/JAPAN/ISS/L-AE-SER-301.SAS DATE: 02DEC2015

＊新薬承認情報提供時に置換えた

Listing of serious adverse events:
Study 109MS301
Page 25 of 72
Treatment group: Placebo

Subject Sex/Age Race	MedDRA Preferred Term	Study Day Onset (a)(b)	Study Day Res	Dur (days)	Relationship to Study Drug	Severity	Serious	Action Taken With Study Drug	Outcome
043* F/4[redacted]	末梢性虚血	403	410	8	POSSIBLY	SEVERE	Yes	DW	RESOLVED
046* F/3[redacted] WHITE	多発性硬化症再発	301	304	4	UNRELATED	SEVERE	Yes	NONE	RESOLVED
047* F/4[redacted] WHITE	多発性硬化症再発	134	146	13	UNRELATED	SEVERE	Yes	NONE	RESOLVED
048* F/4[redacted] WHITE	多発性硬化症再発	227			UNRELATED	SEVERE	Yes	DW	RESOLVED

(a) #=On or after the subject switched to alternate MS medication
(b) ^=Adverse Event with onset prior to dosing
Abbreviations: Res=Resolution, NR=Not Recovered/Not Resolved, Dur=Duration, NONE=Dose Not Changed, DW=Drug Withdrawn, DI=Drug Interrupted, DR=Dose Reduced, M=Male, F=Female

SOURCE: BG12MS/JAPAN/ISS/L-AE-SER-301.SAS DATE: 02DEC2015

＊新薬承認情報提供時に置換えた

Listing of serious adverse events:
Study 109MS301
Page 26 of 72
Treatment group: Placebo

Subject Sex/Age Race	MedDRA Preferred Term	Study Day Onset (a)(b)	Study Day Res	Dur (days)	Relationship to Study Drug	Severity	Serious	Action Taken With Study Drug	Outcome
582* F/4[redacted] WHITE	滑液嚢腫	357	357	1	UNRELATED	SEVERE	Yes	NONE	RESOLVED
589* F/4[redacted] WHITE	腱断裂	612	635	24	UNRELATED	MODERATE	Yes	NONE	RESOLVED
590* M/4[redacted] WHITE	脛骨骨折	250	377	128	UNRELATED	MODERATE	Yes	NONE	RESOLVED
051* F/3[redacted] WHITE	乳癌	561	NR		UNRELATED	SEVERE	Yes	DW	NOT RESOLVED

(a) #=On or after the subject switched to alternate MS medication
(b) ^=Adverse Event with onset prior to dosing
Abbreviations: Res=Resolution, NR=Not Recovered/Not Resolved, Dur=Duration, NONE=Dose Not Changed, DW=Drug Withdrawn, DI=Drug Interrupted, DR=Dose Reduced, M=Male, F=Female

SOURCE: BG12MS/JAPAN/ISS/L-AE-SER-301.SAS DATE: 02DEC2015

＊新薬承認情報提供時に置換えた

Listing of serious adverse events:
Study 109MS301
Page 27 of 72
Treatment group: Placebo

Subject Sex/Age Race	MedDRA Preferred Term	Study Day Onset (a)(b)	Study Day Res	Dur (days)	Relationship to Study Drug	Severity	Serious	Action Taken With Study Drug	Outcome
[redacted] M/5[redacted] WHITE	多発性硬化症再発	576	583	8	UNRELATED	MODERATE	Yes	NONE	RESOLVED
368* F/3[redacted] WHITE	うつ病	25	30	6	UNLIKELY	MODERATE	Yes	NONE	RESOLVED

(a) #=On or after the subject switched to alternate MS medication
(b) ^=Adverse Event with onset prior to dosing
Abbreviations: Res=Resolution, NR=Not Recovered/Not Resolved, Dur=Duration, NONE=Dose Not Changed, DW=Drug Withdrawn, DI=Drug Interrupted, DR=Dose Reduced, M=Male, F=Female

SOURCE: BG12MS/JAPAN/ISS/L-AE-SER-301.SAS DATE: 02DEC2015

＊新薬承認情報提供時に置換えた

Listing of serious adverse events:
Study 109MS301
Page 28 of 72
Treatment group: BG00012 240 mg BID

Subject Sex/Age Race	MedDRA Preferred Term	Study Day Onset (a)(b)	Study Day Res	Dur (days)	Relationship to Study Drug	Severity	Serious	Action Taken With Study Drug	Outcome
[redacted] M/5[redacted] WHITE	抑うつ気分を伴う適応障害	510			UNRELATED	SEVERE	Yes	NONE	RESOLVED
	自殺念慮	510			UNRELATED	SEVERE	Yes	NONE	RESOLVED
[redacted] F/4[redacted] WHITE	多発性硬化症再発	386	389	4	UNRELATED	SEVERE	Yes	NONE	RESOLVED
[redacted] F/4[redacted] WHITE	多発性硬化症再発	590	596	7	UNRELATED	MODERATE	Yes	NONE	RESOLVED
120* F/3[redacted] WHITE	多発性硬化症再発	439	453	15	UNRELATED	MODERATE	Yes	NONE	RESOLVED

(a) #=On or after the subject switched to alternate MS medication
(b) ^=Adverse Event with onset prior to dosing
Abbreviations: Res=Resolution, NR=Not Recovered/Not Resolved, Dur=Duration, NONE=Dose Not Changed, DW=Drug Withdrawn, DI=Drug Interrupted, DR=Dose Reduced, M=Male, F=Female

SOURCE: BG12MS/JAPAN/ISS/L-AE-SER-301.SAS DATE: 02DEC2015

＊新薬承認情報提供時に置換えた

Listing of serious adverse events:
Study 109MS301
Page 29 of 72
Treatment group: BG00012 240 mg BID

Subject Sex/Age Race	MedDRA Preferred Term	Study Day Onset (a)(b)	Study Day Res	Dur (days)	Relationship to Study Drug	Severity	Serious	Action Taken With Study Drug	Outcome
[redacted] F/3[redacted] WHITE	多発性硬化症再発	90	98	9	UNRELATED	MODERATE	Yes	NONE	RESOLVED
[redacted] F/3[redacted] WHITE	多発性硬化症再発	85	96	12	UNLIKELY	MODERATE	Yes	NONE	RESOLVED
517* F/3[redacted] ASIAN	半月板障害	291	391	101	UNRELATED	MODERATE	Yes	NONE	RESOLVED
[redacted] F/3[redacted] ASIAN	血尿	-8^	-1	8	UNRELATED	MILD	Yes	NONE	RESOLVED
	蛋白尿	-8^	-1	8	UNRELATED	MILD	Yes	NONE	RESOLVED

(a) #=On or after the subject switched to alternate MS medication
(b) ^=Adverse Event with onset prior to dosing
Abbreviations: Res=Resolution, NR=Not Recovered/Not Resolved, Dur=Duration, NONE=Dose Not Changed, DW=Drug Withdrawn, DI=Drug Interrupted, DR=Dose Reduced, M=Male, F=Female

SOURCE: BG12MS/JAPAN/ISS/L-AE-SER-301.SAS DATE: 02DEC2015

＊新薬承認情報提供時に置換えた

Listing of serious adverse events:
Study 109MS301
Page 30 of 72
Treatment group: BG00012 240 mg BID

Subject Sex/Age Race	MedDRA Preferred Term	Study Day Onset (a)(b)	Study Day Res	Dur (days)	Relationship to Study Drug	Severity	Serious	Action Taken With Study Drug	Outcome
[redacted] F/3[redacted] ASIAN	多発性硬化症再発	685	692	8	UNRELATED	SEVERE	Yes	NONE	RESOLVED
[redacted] M/4[redacted] ASIAN	多発性硬化症再発	610	651	42	UNLIKELY	SEVERE	Yes	DI	RESOLVED
521* F/5[redacted] ASIAN	発熱	329	341	13	UNRELATED	MODERATE	Yes	NONE	RESOLVED
	嘔吐	329	341	13	UNRELATED	MODERATE	Yes	NONE	RESOLVED
	発熱	388	396	9	UNRELATED	MODERATE	Yes	NONE	RESOLVED
523* M/2[redacted] ASIAN	胸水	555	904	350	POSSIBLY	SEVERE	Yes	NONE	RESOLVED

(a) #=On or after the subject switched to alternate MS medication
(b) ^=Adverse Event with onset prior to dosing
Abbreviations: Res=Resolution, NR=Not Recovered/Not Resolved, Dur=Duration, NONE=Dose Not Changed, DW=Drug Withdrawn, DI=Drug Interrupted, DR=Dose Reduced, M=Male, F=Female

SOURCE: BG12MS/JAPAN/ISS/L-AE-SER-301.SAS DATE: 02DEC2015

＊新薬承認情報提供時に置換えた

Listing of serious adverse events:
Study 109MS301
Page 31 of 72
Treatment group: BG00012 240 mg BID

Subject Sex/Age Race	MedDRA Preferred Term	Study Day Onset (a)(b)	Study Day Res	Dur (days)	Relationship to Study Drug	Severity	Serious	Action Taken With Study Drug	Outcome
[redacted] F/2[redacted] ASIAN	多発性硬化症再発	297	315	19	UNRELATED	MODERATE	Yes	NONE	RESOLVED
	胃腸炎	317	322	6	UNRELATED	MODERATE	Yes	NONE	RESOLVED
	多発性硬化症再発	479	535	57	UNRELATED	MODERATE	Yes	NONE	RESOLVED
	多発性硬化症再発	628	630	3	UNRELATED	MODERATE	Yes	NONE	RESOLVED
[redacted] M/2[redacted] ASIAN	ウイルス感染	552	554	3	UNRELATED	MODERATE	Yes	NONE	RESOLVED
[redacted] M/2[redacted] ASIAN	多発性硬化症再発	41	46	6	UNRELATED	MODERATE	Yes	NONE	RESOLVED

(a) #=On or after the subject switched to alternate MS medication
(b) ^=Adverse Event with onset prior to dosing
Abbreviations: Res=Resolution, NR=Not Recovered/Not Resolved, Dur=Duration, NONE=Dose Not Changed, DW=Drug Withdrawn, DI=Drug Interrupted, DR=Dose Reduced, M=Male, F=Female

SOURCE: BG12MS/JAPAN/ISS/L-AE-SER-301.SAS DATE: 02DEC2015

＊新薬承認情報提供時に置換えた

Listing of serious adverse events:
Study 109MS301
Page 32 of 72
Treatment group: BG00012 240 mg BID

Subject Sex/Age Race	MedDRA Preferred Term	Study Day Onset (a)(b)	Study Day Res	Dur (days)	Relationship to Study Drug	Severity	Serious	Action Taken With Study Drug	Outcome
[redacted] M/2[redacted] ASIAN	多発性硬化症再発	179	182	4	UNRELATED	SEVERE	Yes	NONE	RESOLVED
	多発性硬化症再発	246	281	36	UNRELATED	SEVERE	Yes	NONE	RESOLVED
	多発性硬化症再発	448	508	61	UNRELATED	MODERATE	Yes	NONE	RESOLVED
534* F/2[redacted] ASIAN	多発性硬化症再発	149	154	6	UNRELATED	SEVERE	Yes	NONE	RESOLVED
	ウイルス感染後疲労症候群	548	550	3	UNRELATED	MODERATE	Yes	NONE	RESOLVED
349* F/2[redacted] ASIAN	多発性硬化症再発	75	80	6	UNRELATED	SEVERE	Yes	NONE	RESOLVED

(a) #=On or after the subject switched to alternate MS medication
(b) ^=Adverse Event with onset prior to dosing
Abbreviations: Res=Resolution, NR=Not Recovered/Not Resolved, Dur=Duration, NONE=Dose Not Changed, DW=Drug Withdrawn, DI=Drug Interrupted, DR=Dose Reduced, M=Male, F=Female

SOURCE: BG12MS/JAPAN/ISS/L-AE-SER-301.SAS DATE: 02DEC2015

＊新薬承認情報提供時に置換えた

Listing of serious adverse events:
Study 109MS301
Page 33 of 72
Treatment group: BG00012 240 mg BID

Subject Sex/Age Race	MedDRA Preferred Term	Study Day Onset (a)(b)	Study Day Res	Dur (days)	Relationship to Study Drug	Severity	Serious	Action Taken With Study Drug	Outcome
349* F/2[redacted] ASIAN	多発性硬化症再発	130			UNLIKELY	SEVERE	Yes	NONE	RESOLVED
	副鼻腔炎	220	223	4	UNRELATED	MODERATE	Yes	NONE	RESOLVED
	多発性硬化症再発	224	277	54	UNRELATED	SEVERE	Yes	NONE	RESOLVED
	多発性硬化症再発	256	277	22	UNRELATED	SEVERE	Yes	NONE	RESOLVED
	多発性硬化症再発	299	321	23	UNRELATED	SEVERE	Yes	NONE	RESOLVED
	多発性硬化症再発	341#	352	12	UNRELATED	SEVERE	Yes	NONE	RESOLVED
	多発性硬化症再発	378#	384	7	UNRELATED	SEVERE	Yes	NONE	RESOLVED
	失神	390#	401	12	UNRELATED	MODERATE	Yes	NONE	RESOLVED
	尿路感染	394#	400	7	UNRELATED	MODERATE	Yes	NONE	RESOLVED

(a) #=On or after the subject switched to alternate MS medication
(b) ^=Adverse Event with onset prior to dosing
Abbreviations: Res=Resolution, NR=Not Recovered/Not Resolved, Dur=Duration, NONE=Dose Not Changed, DW=Drug Withdrawn, DI=Drug Interrupted, DR=Dose Reduced, M=Male, F=Female

SOURCE: BG12MS/JAPAN/ISS/L-AE-SER-301.SAS DATE: 02DEC2015

＊新薬承認情報提供時に置換えた

Listing of serious adverse events:
Study 109MS301
Page 34 of 72
Treatment group: BG00012 240 mg BID

Subject Sex/Age Race	MedDRA Preferred Term	Study Day Onset (a)(b)	Study Day Res	Dur (days)	Relationship to Study Drug	Severity	Serious	Action Taken With Study Drug	Outcome
349* F/2[redacted] ASIAN	多発性硬化症再発	408#	431	24	UNRELATED	SEVERE	Yes	NONE	RESOLVED
	多発性硬化症再発	453#	NR		UNRELATED	SEVERE	Yes	NONE	NOT RESOLVED
	多発性硬化症再発	568#	NR		UNRELATED	MODERATE	Yes	NONE	NOT RESOLVED
	尿路感染	648#	657	10	UNRELATED	MODERATE	Yes	NONE	RESOLVED
536* F/3[redacted] IRISH/TURKISH	卵巣嚢胞破裂	78	92	15	UNLIKELY	SEVERE	Yes	DI	RESOLVED
	術後発熱	185	187	3	UNRELATED	MODERATE	Yes	DI	RESOLVED
	処置による低血圧	185	187	3	UNRELATED	MODERATE	Yes	DI	RESOLVED

(a) #=On or after the subject switched to alternate MS medication
(b) ^=Adverse Event with onset prior to dosing
Abbreviations: Res=Resolution, NR=Not Recovered/Not Resolved, Dur=Duration, NONE=Dose Not Changed, DW=Drug Withdrawn, DI=Drug Interrupted, DR=Dose Reduced, M=Male, F=Female

SOURCE: BG12MS/JAPAN/ISS/L-AE-SER-301.SAS DATE: 02DEC2015

＊新薬承認情報提供時に置換えた

Listing of serious adverse events:
Study 109MS301
Page 35 of 72
Treatment group: BG00012 240 mg BID

Subject Sex/Age Race	MedDRA Preferred Term	Study Day Onset (a)(b)	Study Day Res	Dur (days)	Relationship to Study Drug	Severity	Serious	Action Taken With Study Drug	Outcome
123* F/4[redacted] WHITE	過敏症	1	1	1	RELATED	MODERATE	Yes	DW	RESOLVED
[redacted] F/3[redacted] WHITE	多発性硬化症再発	226	228	3	UNRELATED	SEVERE	Yes	NONE	RESOLVED
	多発性硬化症再発	286	287	2	UNRELATED	SEVERE	Yes	NONE	RESOLVED
308* F/4[redacted] WHITE	卵巣嚢胞	323	324	2	UNRELATED	MODERATE	Yes	NONE	RESOLVED
539* F/4[redacted] WHITE	子宮内膜症	77	NR		UNRELATED	MILD	Yes	NONE	NOT RESOLVED

(a) #=On or after the subject switched to alternate MS medication
(b) ^=Adverse Event with onset prior to dosing
Abbreviations: Res=Resolution, NR=Not Recovered/Not Resolved, Dur=Duration, NONE=Dose Not Changed, DW=Drug Withdrawn, DI=Drug Interrupted, DR=Dose Reduced, M=Male, F=Female

SOURCE: BG12MS/JAPAN/ISS/L-AE-SER-301.SAS DATE: 02DEC2015

＊新薬承認情報提供時に置換えた

Listing of serious adverse events:
Study 109MS301
Page 36 of 72
Treatment group: BG00012 240 mg BID

Subject Sex/Age Race	MedDRA Preferred Term	Study Day Onset (a)(b)	Study Day Res	Dur (days)	Relationship to Study Drug	Severity	Serious	Action Taken With Study Drug	Outcome
540* F/3[redacted] WHITE	脳振盪	443	444	2	UNRELATED	MILD	Yes	NONE	RESOLVED
	全般性不安障害	497	587	91	UNRELATED	MODERATE	Yes	NONE	RESOLVED
	自己愛性人格障害	497	587	91	UNRELATED	SEVERE	Yes	NONE	RESOLVED
125* F/4[redacted] WHITE	胃腸障害	13	54	42	POSSIBLY	SEVERE	Yes	DW	RESOLVED
545* F/4[redacted] WHITE	子宮摘出	413	416	4	UNRELATED	MODERATE	Yes	DI	RESOLVED

(a) #=On or after the subject switched to alternate MS medication
(b) ^=Adverse Event with onset prior to dosing
Abbreviations: Res=Resolution, NR=Not Recovered/Not Resolved, Dur=Duration, NONE=Dose Not Changed, DW=Drug Withdrawn, DI=Drug Interrupted, DR=Dose Reduced, M=Male, F=Female

SOURCE: BG12MS/JAPAN/ISS/L-AE-SER-301.SAS DATE: 02DEC2015

＊新薬承認情報提供時に置換えた

Listing of serious adverse events:
Study 109MS301
Page 37 of 72
Treatment group: BG00012 240 mg BID

Subject Sex/Age Race	MedDRA Preferred Term	Study Day Onset (a)(b)	Study Day Res	Dur (days)	Relationship to Study Drug	Severity	Serious	Action Taken With Study Drug	Outcome
126* F/2[redacted] WHITE	虫垂炎	30	30	1	UNLIKELY	MODERATE	Yes	NONE	RESOLVED
127* M/4[redacted] WHITE	躁病	127	150	24	UNRELATED	MILD	Yes	DI	RESOLVED
	多発性硬化症再発	173	177	5	UNRELATED	SEVERE	Yes	NONE	RESOLVED
	神経学的症状	295	299	5	UNRELATED	MILD	Yes	NONE	RESOLVED
548* F/2[redacted] WHITE	シェーグレン症候群	527	535	9	UNLIKELY	MODERATE	Yes	NONE	RESOLVED

(a) #=On or after the subject switched to alternate MS medication
(b) ^=Adverse Event with onset prior to dosing
Abbreviations: Res=Resolution, NR=Not Recovered/Not Resolved, Dur=Duration, NONE=Dose Not Changed, DW=Drug Withdrawn, DI=Drug Interrupted, DR=Dose Reduced, M=Male, F=Female

SOURCE: BG12MS/JAPAN/ISS/L-AE-SER-301.SAS DATE: 02DEC2015

＊新薬承認情報提供時に置換えた

Listing of serious adverse events:
Study 109MS301
Page 38 of 72
Treatment group: BG00012 240 mg BID

Subject Sex/Age Race	MedDRA Preferred Term	Study Day Onset (a)(b)	Study Day Res	Dur (days)	Relationship to Study Drug	Severity	Serious	Action Taken With Study Drug	Outcome
550* F/2[redacted] WHITE	女性不妊手術	670	671	2	UNRELATED	SEVERE	Yes	DI	RESOLVED
[redacted] F/5[redacted] WHITE	多発性硬化症再発	17	19	3	UNRELATED	MILD	Yes	NONE	RESOLVED
	多発性硬化症再発	91	104	14	UNRELATED	MILD	Yes	NONE	RESOLVED
[redacted] F/2[redacted] WHITE	多発性硬化症再発	95	99	5	UNRELATED	MILD	Yes	NONE	RESOLVED
132* F/5[redacted] WHITE	移行上皮癌	644	660	17	POSSIBLY	SEVERE	Yes	DW	RESOLVED

(a) #=On or after the subject switched to alternate MS medication
(b) ^=Adverse Event with onset prior to dosing
Abbreviations: Res=Resolution, NR=Not Recovered/Not Resolved, Dur=Duration, NONE=Dose Not Changed, DW=Drug Withdrawn, DI=Drug Interrupted, DR=Dose Reduced, M=Male, F=Female

SOURCE: BG12MS/JAPAN/ISS/L-AE-SER-301.SAS DATE: 02DEC2015

＊新薬承認情報提供時に置換えた

Listing of serious adverse events:
Study 109MS301
Page 39 of 72
Treatment group: BG00012 240 mg BID

Subject Sex/Age Race	MedDRA Preferred Term	Study Day Onset (a)(b)	Study Day Res	Dur (days)	Relationship to Study Drug	Severity	Serious	Action Taken With Study Drug	Outcome
559* F/3[redacted] WHITE	胆石症	606	610	5	UNLIKELY	SEVERE	Yes	DI	RESOLVED
562* F/3[redacted] WHITE	胃腸炎	18	21	4	UNRELATED	SEVERE	Yes	DI	RESOLVED
[redacted] F/2[redacted] WHITE	多発性硬化症再発	624	643	20	UNRELATED	MILD	Yes	NONE	RESOLVED
136* F/5[redacted] WHITE	交通事故	5	5	1	UNRELATED	SEVERE	Yes	DW	RESOLVED
	外傷性脳損傷	5	99	95	UNRELATED	SEVERE	Yes	DW	RESOLVED

(a) #=On or after the subject switched to alternate MS medication
(b) ^=Adverse Event with onset prior to dosing
Abbreviations: Res=Resolution, NR=Not Recovered/Not Resolved, Dur=Duration, NONE=Dose Not Changed, DW=Drug Withdrawn, DI=Drug Interrupted, DR=Dose Reduced, M=Male, F=Female

SOURCE: BG12MS/JAPAN/ISS/L-AE-SER-301.SAS DATE: 02DEC2015

＊新薬承認情報提供時に置換えた

Listing of serious adverse events:
Study 109MS301
Page 40 of 72
Treatment group: BG00012 240 mg BID

Subject Sex/Age Race	MedDRA Preferred Term	Study Day Onset (a)(b)	Study Day Res	Dur (days)	Relationship to Study Drug	Severity	Serious	Action Taken With Study Drug	Outcome
564* F/4[redacted] WHITE	卵巣嚢胞	653#	656	4	UNRELATED	MILD	Yes	NONE	RESOLVED
[redacted] F/4[redacted] WHITE	多発性硬化症再発	511	516	6	UNRELATED	MILD	Yes	NONE	RESOLVED
566* F/4[redacted] WHITE	結腸内視鏡検査	520	521	2	UNRELATED	MILD	Yes	NONE	RESOLVED
	多発性硬化症再発	590	594	5	UNLIKELY	MODERATE	Yes	NONE	RESOLVED
567* F/4[redacted] WHITE	尿管瘤	292	302	11	UNRELATED	MODERATE	Yes	DI	RESOLVED

(a) #=On or after the subject switched to alternate MS medication
(b) ^=Adverse Event with onset prior to dosing
Abbreviations: Res=Resolution, NR=Not Recovered/Not Resolved, Dur=Duration, NONE=Dose Not Changed, DW=Drug Withdrawn, DI=Drug Interrupted, DR=Dose Reduced, M=Male, F=Female

SOURCE: BG12MS/JAPAN/ISS/L-AE-SER-301.SAS DATE: 02DEC2015

＊新薬承認情報提供時に置換えた

Listing of serious adverse events:
Study 109MS301
Page 41 of 72
Treatment group: BG00012 240 mg BID

Subject Sex/Age Race	MedDRA Preferred Term	Study Day Onset (a)(b)	Study Day Res	Dur (days)	Relationship to Study Drug	Severity	Serious	Action Taken With Study Drug	Outcome
[redacted] F/4[redacted] WHITE	多発性硬化症再発	341	347	7	UNLIKELY	SEVERE	Yes	NONE	RESOLVED
	多発性硬化症再発	550	554	5	UNLIKELY	SEVERE	Yes	NONE	RESOLVED
141* F/4[redacted] WHITE	多発性硬化症再発	397	401	5	UNLIKELY	MODERATE	Yes	NONE	RESOLVED
	胆汁うっ滞性肝炎	446	457	12	POSSIBLY	SEVERE	Yes	DW	RESOLVED
568* F/3[redacted] WHITE	甲状腺腫	371	374	4	UNLIKELY	MODERATE	Yes	NONE	RESOLVED

(a) #=On or after the subject switched to alternate MS medication
(b) ^=Adverse Event with onset prior to dosing
Abbreviations: Res=Resolution, NR=Not Recovered/Not Resolved, Dur=Duration, NONE=Dose Not Changed, DW=Drug Withdrawn, DI=Drug Interrupted, DR=Dose Reduced, M=Male, F=Female

SOURCE: BG12MS/JAPAN/ISS/L-AE-SER-301.SAS DATE: 02DEC2015

＊新薬承認情報提供時に置換えた

Listing of serious adverse events:
Study 109MS301
Page 42 of 72
Treatment group: BG00012 240 mg BID

Subject Sex/Age Race	MedDRA Preferred Term	Study Day Onset (a)(b)	Study Day Res	Dur (days)	Relationship to Study Drug	Severity	Serious	Action Taken With Study Drug	Outcome
[redacted] F/3[redacted] WHITE	多発性硬化症再発	167	171	5	UNLIKELY	MODERATE	Yes	NONE	RESOLVED
569* M/5[redacted] WHITE	多発性硬化症再発	371	377	7	UNLIKELY	MODERATE	Yes	NONE	RESOLVED
	神経鞘腫	531	541	11	UNLIKELY	SEVERE	Yes	NONE	RESOLVED
[redacted] F/4[redacted] WHITE	多発性硬化症再発	597	603	7	UNLIKELY	MODERATE	Yes	NONE	RESOLVED
572* F/5[redacted] WHITE	多発性硬化症再発	65	70	6	UNLIKELY	MILD	Yes	NONE	RESOLVED

(a) #=On or after the subject switched to alternate MS medication
(b) ^=Adverse Event with onset prior to dosing
Abbreviations: Res=Resolution, NR=Not Recovered/Not Resolved, Dur=Duration, NONE=Dose Not Changed, DW=Drug Withdrawn, DI=Drug Interrupted, DR=Dose Reduced, M=Male, F=Female

SOURCE: BG12MS/JAPAN/ISS/L-AE-SER-301.SAS DATE: 02DEC2015

＊新薬承認情報提供時に置換えた

Listing of serious adverse events:
Study 109MS301
Page 43 of 72
Treatment group: BG00012 240 mg BID

Subject Sex/Age Race	MedDRA Preferred Term	Study Day Onset (a)(b)	Study Day Res	Dur (days)	Relationship to Study Drug	Severity	Serious	Action Taken With Study Drug	Outcome
[redacted] F/5[redacted] WHITE	一過性脳虚血発作	584	590	7	UNLIKELY	MILD	Yes	NONE	RESOLVED
[redacted] M/4[redacted] WHITE	多発性硬化症再発	39	43	5	UNLIKELY	MILD	Yes	NONE	RESOLVED
574* F/4[redacted] WHITE	胃腸炎	15	19	5	POSSIBLY	MODERATE	Yes	DI	RESOLVED
[redacted] F/3[redacted] WHITE	多発性硬化症再発	114	118	5	UNRELATED	MODERATE	Yes	NONE	RESOLVED

(a) #=On or after the subject switched to alternate MS medication
(b) ^=Adverse Event with onset prior to dosing
Abbreviations: Res=Resolution, NR=Not Recovered/Not Resolved, Dur=Duration, NONE=Dose Not Changed, DW=Drug Withdrawn, DI=Drug Interrupted, DR=Dose Reduced, M=Male, F=Female

SOURCE: BG12MS/JAPAN/ISS/L-AE-SER-301.SAS DATE: 02DEC2015

＊新薬承認情報提供時に置換えた

Listing of serious adverse events:
Study 109MS301
Page 44 of 72
Treatment group: BG00012 240 mg BID

Subject Sex/Age Race	MedDRA Preferred Term	Study Day Onset (a)(b)	Study Day Res	Dur (days)	Relationship to Study Drug	Severity	Serious	Action Taken With Study Drug	Outcome
[redacted] F/3[redacted] WHITE	多発性硬化症再発	57	62	6	UNRELATED	MODERATE	Yes	NONE	RESOLVED
	多発性硬化症再発	111	115	5	UNLIKELY	MODERATE	Yes	NONE	RESOLVED
[redacted] F/4[redacted] WHITE	多発性硬化症再発	135	139	5	UNRELATED	MODERATE	Yes	NONE	RESOLVED
363* F/4[redacted] WHITE	肺の良性新生物	105	113	9	UNRELATED	SEVERE	Yes	DI	RESOLVED
[redacted] M/2[redacted] WHITE	多発性硬化症再発	68	73	6	UNLIKELY	MODERATE	Yes	NONE	RESOLVED

(a) #=On or after the subject switched to alternate MS medication
(b) ^=Adverse Event with onset prior to dosing
Abbreviations: Res=Resolution, NR=Not Recovered/Not Resolved, Dur=Duration, NONE=Dose Not Changed, DW=Drug Withdrawn, DI=Drug Interrupted, DR=Dose Reduced, M=Male, F=Female

SOURCE: BG12MS/JAPAN/ISS/L-AE-SER-301.SAS DATE: 02DEC2015

＊新薬承認情報提供時に置換えた

Listing of serious adverse events:
Study 109MS301
Page 45 of 72
Treatment group: BG00012 240 mg BID

Subject Sex/Age Race	MedDRA Preferred Term	Study Day Onset (a)(b)	Study Day Res	Dur (days)	Relationship to Study Drug	Severity	Serious	Action Taken With Study Drug	Outcome
[redacted] M/2[redacted] WHITE	多発性硬化症再発	308	337	30	UNLIKELY	MODERATE	Yes	NONE	RESOLVED
	多発性硬化症再発	352#	392	41	UNLIKELY	MODERATE	Yes	NONE	RESOLVED
	多発性硬化症再発	425#	442	18	UNLIKELY	MODERATE	Yes	NONE	RESOLVED
	多発性硬化症再発	530#	560	31	UNLIKELY	MODERATE	Yes	NONE	RESOLVED
	多発性硬化症再発	588#	596	9	UNLIKELY	MODERATE	Yes	NONE	RESOLVED
[redacted] F/5[redacted] WHITE	多発性硬化症再発	117	125	9	UNLIKELY	MODERATE	Yes	NONE	RESOLVED

(a) #=On or after the subject switched to alternate MS medication
(b) ^=Adverse Event with onset prior to dosing
Abbreviations: Res=Resolution, NR=Not Recovered/Not Resolved, Dur=Duration, NONE=Dose Not Changed, DW=Drug Withdrawn, DI=Drug Interrupted, DR=Dose Reduced, M=Male, F=Female

SOURCE: BG12MS/JAPAN/ISS/L-AE-SER-301.SAS DATE: 02DEC2015

＊新薬承認情報提供時に置換えた

Listing of serious adverse events:
Study 109MS301
Page 46 of 72
Treatment group: BG00012 240 mg BID

Subject Sex/Age Race	MedDRA Preferred Term	Study Day Onset (a)(b)	Study Day Res	Dur (days)	Relationship to Study Drug	Severity	Serious	Action Taken With Study Drug	Outcome
359* F/5[redacted] WHITE	舌咽神経痛	427	490	64	UNLIKELY	SEVERE	Yes	NONE	RESOLVED
[redacted] M/3[redacted] WHITE	多発性硬化症再発	183	225	43	UNLIKELY	MODERATE	Yes	NONE	RESOLVED
[redacted] F/2[redacted] WHITE	多発性硬化症再発	590	602	13	UNLIKELY	MODERATE	Yes	NONE	RESOLVED
144* F/4[redacted] WHITE	多発性硬化症再発	27	121	95	UNLIKELY	MODERATE	Yes	NONE	RESOLVED
	多発性硬化症再発	316#	331	16	UNRELATED	MODERATE	Yes	NONE	RESOLVED

(a) #=On or after the subject switched to alternate MS medication
(b) ^=Adverse Event with onset prior to dosing
Abbreviations: Res=Resolution, NR=Not Recovered/Not Resolved, Dur=Duration, NONE=Dose Not Changed, DW=Drug Withdrawn, DI=Drug Interrupted, DR=Dose Reduced, M=Male, F=Female

SOURCE: BG12MS/JAPAN/ISS/L-AE-SER-301.SAS DATE: 02DEC2015

＊新薬承認情報提供時に置換えた

Listing of serious adverse events:
Study 109MS301
Page 47 of 72
Treatment group: BG00012 240 mg BID

Subject Sex/Age Race	MedDRA Preferred Term	Study Day Onset (a)(b)	Study Day Res	Dur (days)	Relationship to Study Drug	Severity	Serious	Action Taken With Study Drug	Outcome
576* F/4[redacted] HISPANIC	胃腸炎	293	296	4	UNRELATED	SEVERE	Yes	NONE	RESOLVED
[redacted] F/5[redacted] HISPANIC	多発性硬化症再発	338	353	16	UNRELATED	MODERATE	Yes	NONE	RESOLVED
577* F/4[redacted] WHITE	静脈瘤	400	405	6	UNRELATED	MODERATE	Yes	NONE	RESOLVED
148* M/3[redacted]	うつ病	254	256	3	UNLIKELY	SEVERE	Yes	DI	RESOLVED
[redacted] F/3[redacted]	多発性硬化症再発	431	433	3	UNRELATED	MILD	Yes	NONE	RESOLVED

(a) #=On or after the subject switched to alternate MS medication
(b) ^=Adverse Event with onset prior to dosing
Abbreviations: Res=Resolution, NR=Not Recovered/Not Resolved, Dur=Duration, NONE=Dose Not Changed, DW=Drug Withdrawn, DI=Drug Interrupted, DR=Dose Reduced, M=Male, F=Female

SOURCE: BG12MS/JAPAN/ISS/L-AE-SER-301.SAS DATE: 02DEC2015

＊新薬承認情報提供時に置換えた

Listing of serious adverse events:
Study 109MS301
Page 48 of 72
Treatment group: BG00012 240 mg BID

Subject Sex/Age Race	MedDRA Preferred Term	Study Day Onset (a)(b)	Study Day Res	Dur (days)	Relationship to Study Drug	Severity	Serious	Action Taken With Study Drug	Outcome
149* F/2[redacted]	自殺企図	590#	591	2	UNRELATED	MILD	Yes	NONE	RESOLVED
150* F/2[redacted]	第７脳神経麻痺	235	840	606	UNLIKELY	MODERATE	Yes	NONE	RESOLVED
153* M/3[redacted] WHITE	肺炎	329	344	16	UNRELATED	SEVERE	Yes	DI	RESOLVED
	てんかん	534	554	21	UNRELATED	SEVERE	Yes	DW	RESOLVED
	誤嚥性肺炎	535	554	20	UNRELATED	SEVERE	Yes	DW	RESOLVED
154* F/2[redacted] WHITE	潮紅	1	1	1	RELATED	MODERATE	Yes	DW	RESOLVED

(a) #=On or after the subject switched to alternate MS medication
(b) ^=Adverse Event with onset prior to dosing
Abbreviations: Res=Resolution, NR=Not Recovered/Not Resolved, Dur=Duration, NONE=Dose Not Changed, DW=Drug Withdrawn, DI=Drug Interrupted, DR=Dose Reduced, M=Male, F=Female

SOURCE: BG12MS/JAPAN/ISS/L-AE-SER-301.SAS DATE: 02DEC2015

＊新薬承認情報提供時に置換えた

Listing of serious adverse events:
Study 109MS301
Page 49 of 72
Treatment group: BG00012 240 mg BID

Subject Sex/Age Race	MedDRA Preferred Term	Study Day Onset (a)(b)	Study Day Res	Dur (days)	Relationship to Study Drug	Severity	Serious	Action Taken With Study Drug	Outcome
347* F/2[redacted] WHITE	スティーブンス・ジョンソン症候群	504	645	142	UNLIKELY	MODERATE	Yes	NONE	RESOLVED
[redacted] F/4[redacted] WHITE	多発性硬化症再発	110	112	3	UNLIKELY	MODERATE	Yes	NONE	RESOLVED
583* F/3[redacted] WHITE	裂孔ヘルニア	356	358	3	UNRELATED	MODERATE	Yes	DI	RESOLVED
584* F/3[redacted] WHITE	腹部ヘルニア	260	263	4	UNRELATED	SEVERE	Yes	NONE	RESOLVED

(a) #=On or after the subject switched to alternate MS medication
(b) ^=Adverse Event with onset prior to dosing
Abbreviations: Res=Resolution, NR=Not Recovered/Not Resolved, Dur=Duration, NONE=Dose Not Changed, DW=Drug Withdrawn, DI=Drug Interrupted, DR=Dose Reduced, M=Male, F=Female

SOURCE: BG12MS/JAPAN/ISS/L-AE-SER-301.SAS DATE: 02DEC2015

＊新薬承認情報提供時に置換えた

Listing of serious adverse events:
Study 109MS301
Page 50 of 72
Treatment group: BG00012 240 mg BID

Subject Sex/Age Race	MedDRA Preferred Term	Study Day Onset (a)(b)	Study Day Res	Dur (days)	Relationship to Study Drug	Severity	Serious	Action Taken With Study Drug	Outcome
160* F/3[redacted] WHITE	便秘	14	48	35	RELATED	SEVERE	Yes	DW	RESOLVED
586* F/5[redacted] WHITE	肺炎	635	642	8	POSSIBLY	MODERATE	Yes	NONE	RESOLVED
[redacted] M/2[redacted] WHITE	多発性硬化症再発	519	525	7	UNRELATED	MODERATE	Yes	NONE	RESOLVED
[redacted] M/3[redacted] WHITE	多発性硬化症再発	226	232	7	UNRELATED	MODERATE	Yes	NONE	RESOLVED

(a) #=On or after the subject switched to alternate MS medication
(b) ^=Adverse Event with onset prior to dosing
Abbreviations: Res=Resolution, NR=Not Recovered/Not Resolved, Dur=Duration, NONE=Dose Not Changed, DW=Drug Withdrawn, DI=Drug Interrupted, DR=Dose Reduced, M=Male, F=Female

SOURCE: BG12MS/JAPAN/ISS/L-AE-SER-301.SAS DATE: 02DEC2015

＊新薬承認情報提供時に置換えた

Listing of serious adverse events:
Study 109MS301
Page 51 of 72
Treatment group: BG00012 240 mg BID

Subject Sex/Age Race	MedDRA Preferred Term	Study Day Onset (a)(b)	Study Day Res	Dur (days)	Relationship to Study Drug	Severity	Serious	Action Taken With Study Drug	Outcome
[redacted] F/4[redacted] WHITE	多発性硬化症再発	448#	453	6	UNRELATED	MODERATE	Yes	NONE	RESOLVED
[redacted] F/5[redacted] WHITE	多発性硬化症再発	12	16	5	UNRELATED	MILD	Yes	NONE	RESOLVED
	多発性硬化症再発	329	333	5	UNRELATED	MILD	Yes	NONE	RESOLVED

(a) #=On or after the subject switched to alternate MS medication
(b) ^=Adverse Event with onset prior to dosing
Abbreviations: Res=Resolution, NR=Not Recovered/Not Resolved, Dur=Duration, NONE=Dose Not Changed, DW=Drug Withdrawn, DI=Drug Interrupted, DR=Dose Reduced, M=Male, F=Female

SOURCE: BG12MS/JAPAN/ISS/L-AE-SER-301.SAS DATE: 02DEC2015

＊新薬承認情報提供時に置換えた

Listing of serious adverse events:
Study 109MS301
Page 52 of 72
Treatment group: BG00012 240 mg TID

Subject Sex/Age Race	MedDRA Preferred Term	Study Day Onset (a)(b)	Study Day Res	Dur (days)	Relationship to Study Drug	Severity	Serious	Action Taken With Study Drug	Outcome
500* F/4[redacted] WHITE	腺筋症	504	561	58	UNRELATED	MODERATE	Yes	DI	RESOLVED
	卵巣嚢胞	504	561	58	UNRELATED	MODERATE	Yes	DI	RESOLVED
208* F/5[redacted] WHITE	下腹部痛	394	396	3	POSSIBLY	MODERATE	Yes	DW	RESOLVED
210* F/3[redacted] BLACK OR AFRICAN AMERICAN	交通事故	62	62	1	UNRELATED	SEVERE	Yes	DW	RESOLVED

(a) #=On or after the subject switched to alternate MS medication
(b) ^=Adverse Event with onset prior to dosing
Abbreviations: Res=Resolution, NR=Not Recovered/Not Resolved, Dur=Duration, NONE=Dose Not Changed, DW=Drug Withdrawn, DI=Drug Interrupted, DR=Dose Reduced, M=Male, F=Female

SOURCE: BG12MS/JAPAN/ISS/L-AE-SER-301.SAS DATE: 02DEC2015

＊新薬承認情報提供時に置換えた

Listing of serious adverse events:
Study 109MS301
Page 53 of 72
Treatment group: BG00012 240 mg TID

Subject Sex/Age Race	MedDRA Preferred Term	Study Day Onset (a)(b)	Study Day Res	Dur (days)	Relationship to Study Drug	Severity	Serious	Action Taken With Study Drug	Outcome
504* F/4[redacted] WHITE	背部痛	49	50	2	UNLIKELY	MODERATE	Yes	DI	RESOLVED
216* F/4[redacted] WHITE	子宮頚部癌	556	595	40	UNLIKELY	MODERATE	Yes	DW	RESOLVED
221* F/3[redacted] WHITE	うっ血性心不全	477	668	192	UNLIKELY	SEVERE	Yes	DW	RESOLVED
224* F/3[redacted] WHITE	便秘	210#	301	92	UNRELATED	SEVERE	Yes	NONE	RESOLVED

(a) #=On or after the subject switched to alternate MS medication
(b) ^=Adverse Event with onset prior to dosing
Abbreviations: Res=Resolution, NR=Not Recovered/Not Resolved, Dur=Duration, NONE=Dose Not Changed, DW=Drug Withdrawn, DI=Drug Interrupted, DR=Dose Reduced, M=Male, F=Female

SOURCE: BG12MS/JAPAN/ISS/L-AE-SER-301.SAS DATE: 02DEC2015

＊新薬承認情報提供時に置換えた

Listing of serious adverse events:
Study 109MS301
Page 54 of 72
Treatment group: BG00012 240 mg TID

Subject Sex/Age Race	MedDRA Preferred Term	Study Day Onset (a)(b)	Study Day Res	Dur (days)	Relationship to Study Drug	Severity	Serious	Action Taken With Study Drug	Outcome
509* M/3[redacted] BLACK OR AFRICAN AMERICAN	深部静脈血栓症	106	NR		UNRELATED	SEVERE	Yes	NONE	NOT RESOLVED
[redacted] F/3[redacted] WHITE	血中ブドウ糖増加	95	171	77	UNRELATED	MILD	Yes	NONE	RESOLVED
	多発性硬化症再発	95	100	6	UNRELATED	MILD	Yes	NONE	RESOLVED
514* M/4[redacted] WHITE	非心臓性胸痛	72	73	2	UNRELATED	MODERATE	Yes	NONE	RESOLVED

(a) #=On or after the subject switched to alternate MS medication
(b) ^=Adverse Event with onset prior to dosing
Abbreviations: Res=Resolution, NR=Not Recovered/Not Resolved, Dur=Duration, NONE=Dose Not Changed, DW=Drug Withdrawn, DI=Drug Interrupted, DR=Dose Reduced, M=Male, F=Female

SOURCE: BG12MS/JAPAN/ISS/L-AE-SER-301.SAS DATE: 02DEC2015

＊新薬承認情報提供時に置換えた

Listing of serious adverse events:
Study 109MS301
Page 55 of 72
Treatment group: BG00012 240 mg TID

Subject Sex/Age Race	MedDRA Preferred Term	Study Day Onset (a)(b)	Study Day Res	Dur (days)	Relationship to Study Drug	Severity	Serious	Action Taken With Study Drug	Outcome
232* F/4[redacted] HISPANIC	潮紅	152	152	1	POSSIBLY	SEVERE	Yes	DW	RESOLVED
	そう痒症	152	152	1	POSSIBLY	SEVERE	Yes	DW	RESOLVED
233* F/3[redacted] WHITE	アナフィラキシー様反応	13	16	4	RELATED	SEVERE	Yes	DW	RESOLVED
235* M/4[redacted] WHITE	虚血性脳卒中	139	140	2	UNLIKELY	SEVERE	Yes	DW	RESOLVED
[redacted] F/4[redacted] WHITE	多発性硬化症再発	593	606	14	UNRELATED	MODERATE	Yes	NONE	RESOLVED

(a) #=On or after the subject switched to alternate MS medication
(b) ^=Adverse Event with onset prior to dosing
Abbreviations: Res=Resolution, NR=Not Recovered/Not Resolved, Dur=Duration, NONE=Dose Not Changed, DW=Drug Withdrawn, DI=Drug Interrupted, DR=Dose Reduced, M=Male, F=Female

SOURCE: BG12MS/JAPAN/ISS/L-AE-SER-301.SAS DATE: 02DEC2015

＊新薬承認情報提供時に置換えた

Listing of serious adverse events:
Study 109MS301
Page 56 of 72
Treatment group: BG00012 240 mg TID

Subject Sex/Age Race	MedDRA Preferred Term	Study Day Onset (a)(b)	Study Day Res	Dur (days)	Relationship to Study Drug	Severity	Serious	Action Taken With Study Drug	Outcome
235* M/3[redacted] WHITE	多発性硬化症再発	46	57	12	UNRELATED	MODERATE	Yes	NONE	RESOLVED
	多発性硬化症再発	375	389	15	UNRELATED	MODERATE	Yes	NONE	RESOLVED
236* F/3[redacted] WHITE	多発性硬化症再発	673	701	29	UNLIKELY	MODERATE	Yes	NONE	RESOLVED
237* F/2[redacted] ASIAN	間脳性内分泌障害	53	142	90	UNLIKELY	SEVERE	Yes	DI	RESOLVED
	多発性硬化症再発	665	673	9	UNRELATED	SEVERE	Yes	NONE	RESOLVED

(a) #=On or after the subject switched to alternate MS medication
(b) ^=Adverse Event with onset prior to dosing
Abbreviations: Res=Resolution, NR=Not Recovered/Not Resolved, Dur=Duration, NONE=Dose Not Changed, DW=Drug Withdrawn, DI=Drug Interrupted, DR=Dose Reduced, M=Male, F=Female

SOURCE: BG12MS/JAPAN/ISS/L-AE-SER-301.SAS DATE: 02DEC2015

＊新薬承認情報提供時に置換えた

Listing of serious adverse events:
Study 109MS301
Page 57 of 72
Treatment group: BG00012 240 mg TID

Subject Sex/Age Race	MedDRA Preferred Term	Study Day Onset (a)(b)	Study Day Res	Dur (days)	Relationship to Study Drug	Severity	Serious	Action Taken With Study Drug	Outcome
520* F/2[redacted] ASIAN	多発性硬化症再発	43	78	36	UNRELATED	MODERATE	Yes	NONE	RESOLVED
	胃炎	450	455	6	UNLIKELY	SEVERE	Yes	NONE	RESOLVED
	神経学的症状	450	455	6	UNLIKELY	MODERATE	Yes	NONE	RESOLVED
235* F/4[redacted] ASIAN	急性冠動脈症候群	174	192	19	UNLIKELY	SEVERE	Yes	DW	RESOLVED
356* F/3[redacted] ASIAN	橈骨骨折	123	196	74	UNRELATED	MODERATE	Yes	NONE	RESOLVED
236* M/5[redacted] ASIAN	多発性硬化症再発	504	507	4	UNRELATED	MODERATE	Yes	DW	RESOLVED

(a) #=On or after the subject switched to alternate MS medication
(b) ^=Adverse Event with onset prior to dosing
Abbreviations: Res=Resolution, NR=Not Recovered/Not Resolved, Dur=Duration, NONE=Dose Not Changed, DW=Drug Withdrawn, DI=Drug Interrupted, DR=Dose Reduced, M=Male, F=Female

SOURCE: BG12MS/JAPAN/ISS/L-AE-SER-301.SAS DATE: 02DEC2015

＊新薬承認情報提供時に置換えた

Listing of serious adverse events:
Study 109MS301
Page 58 of 72
Treatment group: BG00012 240 mg TID

Subject Sex/Age Race	MedDRA Preferred Term	Study Day Onset (a)(b)	Study Day Res	Dur (days)	Relationship to Study Drug	Severity	Serious	Action Taken With Study Drug	Outcome
237* M/5[redacted] ASIAN	医学的観察	655	666	12	UNRELATED	MILD	Yes	NONE	RESOLVED
	発熱	669#	673	5	UNRELATED	MODERATE	Yes	NONE	RESOLVED
[redacted] F/4[redacted] ASIAN	多発性硬化症再発	414	657	244	UNRELATED	MODERATE	Yes	NONE	RESOLVED
	多発性硬化症再発	538	657	120	UNRELATED	MODERATE	Yes	NONE	RESOLVED
518* F/2[redacted] ASIAN	多発性硬化症再発	12	19	8	UNRELATED	SEVERE	Yes	NONE	RESOLVED
	蜂巣炎	20	295	276	UNRELATED	SEVERE	Yes	NONE	RESOLVED

(a) #=On or after the subject switched to alternate MS medication
(b) ^=Adverse Event with onset prior to dosing
Abbreviations: Res=Resolution, NR=Not Recovered/Not Resolved, Dur=Duration, NONE=Dose Not Changed, DW=Drug Withdrawn, DI=Drug Interrupted, DR=Dose Reduced, M=Male, F=Female

SOURCE: BG12MS/JAPAN/ISS/L-AE-SER-301.SAS DATE: 02DEC2015

＊新薬承認情報提供時に置換えた

Listing of serious adverse events:
Study 109MS301
Page 59 of 72
Treatment group: BG00012 240 mg TID

Subject Sex/Age Race	MedDRA Preferred Term	Study Day Onset (a)(b)	Study Day Res	Dur (days)	Relationship to Study Drug	Severity	Serious	Action Taken With Study Drug	Outcome
238* F/3[redacted] ASIAN	副鼻腔炎	25	33	9	UNRELATED	MILD	Yes	NONE	RESOLVED
	胃炎	49	54	6	POSSIBLY	MODERATE	Yes	DR	RESOLVED
	多発性硬化症再発	88	95	8	UNRELATED	SEVERE	Yes	NONE	RESOLVED
	多発性硬化症再発	144	147	4	UNRELATED	MODERATE	Yes	NONE	RESOLVED
	ウイルス感染	154	157	4	UNRELATED	MODERATE	Yes	NONE	RESOLVED
	多発性硬化症再発	216	223	8	UNRELATED	SEVERE	Yes	NONE	RESOLVED
	多発性硬化症再発	305	368	64	UNRELATED	SEVERE	Yes	NONE	RESOLVED
[redacted] F/3[redacted] ASIAN	胃腸炎	6	9	4	UNRELATED	MODERATE	Yes	NONE	RESOLVED

(a) #=On or after the subject switched to alternate MS medication
(b) ^=Adverse Event with onset prior to dosing
Abbreviations: Res=Resolution, NR=Not Recovered/Not Resolved, Dur=Duration, NONE=Dose Not Changed, DW=Drug Withdrawn, DI=Drug Interrupted, DR=Dose Reduced, M=Male, F=Female

SOURCE: BG12MS/JAPAN/ISS/L-AE-SER-301.SAS DATE: 02DEC2015

＊新薬承認情報提供時に置換えた

Listing of serious adverse events:
Study 109MS301
Page 60 of 72
Treatment group: BG00012 240 mg TID

Subject Sex/Age Race	MedDRA Preferred Term	Study Day Onset (a)(b)	Study Day Res	Dur (days)	Relationship to Study Drug	Severity	Serious	Action Taken With Study Drug	Outcome
[redacted] F/3[redacted] ASIAN	多発性硬化症再発	6			UNRELATED	MODERATE	Yes	NONE	RESOLVED
	多発性硬化症再発	44	50	7	UNRELATED	MODERATE	Yes	NONE	RESOLVED
[redacted] F/3[redacted] ASIAN	多発性硬化症再発	22	224	203	UNRELATED	SEVERE	Yes	NONE	RESOLVED
[redacted] F/5[redacted] WHITE	多発性硬化症再発	205	209	5	UNRELATED	MODERATE	Yes	NONE	RESOLVED
	多発性硬化症再発	343	376	34	UNRELATED	MODERATE	Yes	DW	RESOLVED

(a) #=On or after the subject switched to alternate MS medication
(b) ^=Adverse Event with onset prior to dosing
Abbreviations: Res=Resolution, NR=Not Recovered/Not Resolved, Dur=Duration, NONE=Dose Not Changed, DW=Drug Withdrawn, DI=Drug Interrupted, DR=Dose Reduced, M=Male, F=Female

SOURCE: BG12MS/JAPAN/ISS/L-AE-SER-301.SAS DATE: 02DEC2015

＊新薬承認情報提供時に置換えた

Listing of serious adverse events:
Study 109MS301
Page 61 of 72
Treatment group: BG00012 240 mg TID

Subject Sex/Age Race	MedDRA Preferred Term	Study Day Onset (a)(b)	Study Day Res	Dur (days)	Relationship to Study Drug	Severity	Serious	Action Taken With Study Drug	Outcome
[redacted] F/4[redacted] WHITE	検査	611	612	2	UNRELATED	MODERATE	Yes	NONE	RESOLVED
546* F/4[redacted] WHITE	インフルエンザ	613	629	17	UNLIKELY	MODERATE	Yes	NONE	RESOLVED
547* F/2[redacted] WHITE	頭痛	125			UNLIKELY	MILD	Yes	NONE	RESOLVED
	多発性硬化症再発	126	129	4	UNLIKELY	MODERATE	Yes	NONE	RESOLVED
	多発性硬化症再発	168	170	3	UNLIKELY	MODERATE	Yes	NONE	RESOLVED

(a) #=On or after the subject switched to alternate MS medication
(b) ^=Adverse Event with onset prior to dosing
Abbreviations: Res=Resolution, NR=Not Recovered/Not Resolved, Dur=Duration, NONE=Dose Not Changed, DW=Drug Withdrawn, DI=Drug Interrupted, DR=Dose Reduced, M=Male, F=Female

SOURCE: BG12MS/JAPAN/ISS/L-AE-SER-301.SAS DATE: 02DEC2015

＊新薬承認情報提供時に置換えた

Listing of serious adverse events:
Study 109MS301
Page 62 of 72
Treatment group: BG00012 240 mg TID

Subject Sex/Age Race	MedDRA Preferred Term	Study Day Onset (a)(b)	Study Day Res	Dur (days)	Relationship to Study Drug	Severity	Serious	Action Taken With Study Drug	Outcome
246* F/5[redacted] WHITE	心不全	118	NR		UNLIKELY	MODERATE	Yes	NONE	NOT RESOLVED
549* F/3[redacted] WHITE	扁桃周囲膿瘍	496	498	3	UNLIKELY	SEVERE	Yes	NONE	RESOLVED
247* F/4[redacted] WHITE	乳癌	468	476	9	UNLIKELY	MODERATE	Yes	DW	RESOLVED
551* M/2[redacted] WHITE	低血糖症	208	209	2	UNLIKELY	SEVERE	Yes	NONE	RESOLVED
	Ｈ１Ｎ１インフルエンザ	470	476	7	UNRELATED	MODERATE	Yes	NONE	RESOLVED

(a) #=On or after the subject switched to alternate MS medication
(b) ^=Adverse Event with onset prior to dosing
Abbreviations: Res=Resolution, NR=Not Recovered/Not Resolved, Dur=Duration, NONE=Dose Not Changed, DW=Drug Withdrawn, DI=Drug Interrupted, DR=Dose Reduced, M=Male, F=Female

SOURCE: BG12MS/JAPAN/ISS/L-AE-SER-301.SAS DATE: 02DEC2015

＊新薬承認情報提供時に置換えた

Listing of serious adverse events:
Study 109MS301
Page 63 of 72
Treatment group: BG00012 240 mg TID

Subject Sex/Age Race	MedDRA Preferred Term	Study Day Onset (a)(b)	Study Day Res	Dur (days)	Relationship to Study Drug	Severity	Serious	Action Taken With Study Drug	Outcome
553* F/4[redacted] WHITE	頭位性回転性めまい	97	101	5	UNRELATED	SEVERE	Yes	NONE	RESOLVED
555* F/3[redacted] WHITE	横静脈洞血栓症	745	NR		POSSIBLY	SEVERE	Yes	NONE	NOT RESOLVED
249* M/5[redacted] WHITE	手首関節骨折	71	240	170	UNRELATED	SEVERE	Yes	NONE	RESOLVED
[redacted] F/3[redacted] WHITE	多発性硬化症再発	89	94	6	UNRELATED	MODERATE	Yes	NONE	RESOLVED
	多発性硬化症再発	170	174	5	UNRELATED	MODERATE	Yes	NONE	RESOLVED

(a) #=On or after the subject switched to alternate MS medication
(b) ^=Adverse Event with onset prior to dosing
Abbreviations: Res=Resolution, NR=Not Recovered/Not Resolved, Dur=Duration, NONE=Dose Not Changed, DW=Drug Withdrawn, DI=Drug Interrupted, DR=Dose Reduced, M=Male, F=Female

SOURCE: BG12MS/JAPAN/ISS/L-AE-SER-301.SAS DATE: 02DEC2015

＊新薬承認情報提供時に置換えた

Listing of serious adverse events:
Study 109MS301
Page 64 of 72
Treatment group: BG00012 240 mg TID

Subject Sex/Age Race	MedDRA Preferred Term	Study Day Onset (a)(b)	Study Day Res	Dur (days)	Relationship to Study Drug	Severity	Serious	Action Taken With Study Drug	Outcome
557* F/3[redacted] WHITE	アレルギー検査	193	195	3	UNRELATED	MILD	Yes	NONE	RESOLVED
	多発性硬化症	266	287	22	UNRELATED	MILD	Yes	NONE	RESOLVED
	多発性硬化症再発	476	481	6	UNLIKELY	MODERATE	Yes	NONE	RESOLVED
[redacted] M/1[redacted] WHITE	手骨折	-20^	10	31	UNRELATED	MODERATE	Yes	NONE	RESOLVED
399* F/3[redacted] WHITE	甲状腺腫	135	141	7	UNRELATED	MILD	Yes	DI	RESOLVED

(a) #=On or after the subject switched to alternate MS medication
(b) ^=Adverse Event with onset prior to dosing
Abbreviations: Res=Resolution, NR=Not Recovered/Not Resolved, Dur=Duration, NONE=Dose Not Changed, DW=Drug Withdrawn, DI=Drug Interrupted, DR=Dose Reduced, M=Male, F=Female

SOURCE: BG12MS/JAPAN/ISS/L-AE-SER-301.SAS DATE: 02DEC2015

＊新薬承認情報提供時に置換えた

Listing of serious adverse events:
Study 109MS301
Page 65 of 72
Treatment group: BG00012 240 mg TID

Subject Sex/Age Race	MedDRA Preferred Term	Study Day Onset (a)(b)	Study Day Res	Dur (days)	Relationship to Study Drug	Severity	Serious	Action Taken With Study Drug	Outcome
560* F/5[redacted] WHITE	卵巣嚢胞	538	541	4	UNLIKELY	MODERATE	Yes	NONE	RESOLVED
561* F/3[redacted] WHITE	外陰部膿瘍	125	131	7	POSSIBLY	MODERATE	Yes	NONE	RESOLVED
	腎仙痛	628	629	2	UNLIKELY	MODERATE	Yes	NONE	RESOLVED
256* F/2[redacted] WHITE	自然流産	621#	621	1	UNRELATED	SEVERE	Yes	NONE	RESOLVED
563* F/3[redacted] WHITE	多発性硬化症再発	149	152	4	UNRELATED	MILD	Yes	NONE	RESOLVED
	静脈瘤	425	431	7	UNRELATED	MILD	Yes	NONE	RESOLVED

(a) #=On or after the subject switched to alternate MS medication
(b) ^=Adverse Event with onset prior to dosing
Abbreviations: Res=Resolution, NR=Not Recovered/Not Resolved, Dur=Duration, NONE=Dose Not Changed, DW=Drug Withdrawn, DI=Drug Interrupted, DR=Dose Reduced, M=Male, F=Female

SOURCE: BG12MS/JAPAN/ISS/L-AE-SER-301.SAS DATE: 02DEC2015

＊新薬承認情報提供時に置換えた

Listing of serious adverse events:
Study 109MS301
Page 66 of 72
Treatment group: BG00012 240 mg TID

Subject Sex/Age Race	MedDRA Preferred Term	Study Day Onset (a)(b)	Study Day Res	Dur (days)	Relationship to Study Drug	Severity	Serious	Action Taken With Study Drug	Outcome
565* F/5[redacted] WHITE	子宮平滑筋腫	392	393	2	UNRELATED	MILD	Yes	NONE	RESOLVED
[redacted] M/2[redacted] WHITE	多発性硬化症再発	47	51	5	UNLIKELY	SEVERE	Yes	NONE	RESOLVED
	多発性硬化症再発	511	517	7	UNLIKELY	MODERATE	Yes	NONE	RESOLVED
[redacted] M/4[redacted] WHITE	多発性硬化症再発	211	215	5	UNLIKELY	MODERATE	Yes	NONE	RESOLVED
[redacted] F/4[redacted] WHITE	多発性硬化症再発	454	462	9	UNLIKELY	MODERATE	Yes	NONE	RESOLVED

(a) #=On or after the subject switched to alternate MS medication
(b) ^=Adverse Event with onset prior to dosing
Abbreviations: Res=Resolution, NR=Not Recovered/Not Resolved, Dur=Duration, NONE=Dose Not Changed, DW=Drug Withdrawn, DI=Drug Interrupted, DR=Dose Reduced, M=Male, F=Female

SOURCE: BG12MS/JAPAN/ISS/L-AE-SER-301.SAS DATE: 02DEC2015

＊新薬承認情報提供時に置換えた

Listing of serious adverse events:
Study 109MS301
Page 67 of 72
Treatment group: BG00012 240 mg TID

Subject Sex/Age Race	MedDRA Preferred Term	Study Day Onset (a)(b)	Study Day Res	Dur (days)	Relationship to Study Drug	Severity	Serious	Action Taken With Study Drug	Outcome
[redacted] M/4[redacted] WHITE	多発性硬化症再発	436	440	5	UNLIKELY	MODERATE	Yes	NONE	RESOLVED
[redacted] F/5[redacted] WHITE	多発性硬化症再発	433	437	5	UNLIKELY	MODERATE	Yes	NONE	RESOLVED
	多発性硬化症再発	594	597	4	UNRELATED	MODERATE	Yes	NONE	RESOLVED
	多発性硬化症再発	665	670	6	UNRELATED	MODERATE	Yes	NONE	RESOLVED
573* F/5[redacted] WHITE	静脈ステント挿入	673	674	2	UNRELATED	MODERATE	Yes	NONE	RESOLVED

(a) #=On or after the subject switched to alternate MS medication
(b) ^=Adverse Event with onset prior to dosing
Abbreviations: Res=Resolution, NR=Not Recovered/Not Resolved, Dur=Duration, NONE=Dose Not Changed, DW=Drug Withdrawn, DI=Drug Interrupted, DR=Dose Reduced, M=Male, F=Female

SOURCE: BG12MS/JAPAN/ISS/L-AE-SER-301.SAS DATE: 02DEC2015

＊新薬承認情報提供時に置換えた

Listing of serious adverse events:
Study 109MS301
Page 68 of 72
Treatment group: BG00012 240 mg TID

Subject Sex/Age Race	MedDRA Preferred Term	Study Day Onset (a)(b)	Study Day Res	Dur (days)	Relationship to Study Drug	Severity	Serious	Action Taken With Study Drug	Outcome
[redacted] F/4[redacted] WHITE	多発性硬化症再発	437	442	6	UNRELATED	MODERATE	Yes	NONE	RESOLVED
[redacted] F/5[redacted] WHITE	多発性硬化症再発	235	240	6	UNRELATED	MODERATE	Yes	NONE	RESOLVED
[redacted] F/2[redacted] WHITE	多発性硬化症再発	569	571	3	UNRELATED	MODERATE	Yes	NONE	RESOLVED
[redacted] F/3[redacted] WHITE	多発性硬化症再発	222	226	5	UNRELATED	MODERATE	Yes	NONE	RESOLVED

(a) #=On or after the subject switched to alternate MS medication
(b) ^=Adverse Event with onset prior to dosing
Abbreviations: Res=Resolution, NR=Not Recovered/Not Resolved, Dur=Duration, NONE=Dose Not Changed, DW=Drug Withdrawn, DI=Drug Interrupted, DR=Dose Reduced, M=Male, F=Female

SOURCE: BG12MS/JAPAN/ISS/L-AE-SER-301.SAS DATE: 02DEC2015

＊新薬承認情報提供時に置換えた

Listing of serious adverse events:
Study 109MS301
Page 69 of 72
Treatment group: BG00012 240 mg TID

Subject Sex/Age Race	MedDRA Preferred Term	Study Day Onset (a)(b)	Study Day Res	Dur (days)	Relationship to Study Drug	Severity	Serious	Action Taken With Study Drug	Outcome
[redacted] F/4[redacted] WHITE	多発性硬化症再発	329	337	9	UNLIKELY	MILD	Yes	NONE	RESOLVED
575* M/ 3[redacted] WHITE	陰嚢水瘤	519	528	10	UNLIKELY	MODERATE	Yes	NONE	RESOLVED
578* F/3[redacted] WHITE	足関節部骨折	570	647	78	UNRELATED	SEVERE	Yes	NONE	RESOLVED
263* F/3[redacted]	胃炎	18	NR		POSSIBLY	MODERATE	Yes	DW	NOT RESOLVED

(a) #=On or after the subject switched to alternate MS medication
(b) ^=Adverse Event with onset prior to dosing
Abbreviations: Res=Resolution, NR=Not Recovered/Not Resolved, Dur=Duration, NONE=Dose Not Changed, DW=Drug Withdrawn, DI=Drug Interrupted, DR=Dose Reduced, M=Male, F=Female

SOURCE: BG12MS/JAPAN/ISS/L-AE-SER-301.SAS DATE: 02DEC2015

＊新薬承認情報提供時に置換えた

Listing of serious adverse events:
Study 109MS301
Page 70 of 72
Treatment group: BG00012 240 mg TID

Subject Sex/Age Race	MedDRA Preferred Term	Study Day Onset (a)(b)	Study Day Res	Dur (days)	Relationship to Study Drug	Severity	Serious	Action Taken With Study Drug	Outcome
581* M/2[redacted] WHITE	意識変容状態	72	75	4	UNRELATED	MODERATE	Yes	NONE	RESOLVED
	頭痛	72	75	4	UNRELATED	SEVERE	Yes	NONE	RESOLVED
	発熱	72	75	4	UNRELATED	SEVERE	Yes	NONE	RESOLVED
268* F/3[redacted] WHITE	多発性硬化症再発	169	307	139	UNLIKELY	MODERATE	Yes	NONE	RESOLVED
	一過性全健忘	366	368	3	POSSIBLY	MODERATE	Yes	NONE	RESOLVED
585* F/3[redacted] WHITE	尿路感染	46	56	11	POSSIBLY	SEVERE	Yes	NONE	RESOLVED

(a) #=On or after the subject switched to alternate MS medication
(b) ^=Adverse Event with onset prior to dosing
Abbreviations: Res=Resolution, NR=Not Recovered/Not Resolved, Dur=Duration, NONE=Dose Not Changed, DW=Drug Withdrawn, DI=Drug Interrupted, DR=Dose Reduced, M=Male, F=Female

SOURCE: BG12MS/JAPAN/ISS/L-AE-SER-301.SAS DATE: 02DEC2015

＊新薬承認情報提供時に置換えた

Listing of serious adverse events:
Study 109MS301
Page 71 of 72
Treatment group: BG00012 240 mg TID

Subject Sex/Age Race	MedDRA Preferred Term	Study Day Onset (a)(b)	Study Day Res	Dur (days)	Relationship to Study Drug	Severity	Serious	Action Taken With Study Drug	Outcome
587* F/5[redacted] WHITE	ウイルス性迷路炎	580#	582	3	UNRELATED	SEVERE	Yes	NONE	RESOLVED
272* M/5[redacted] WHITE	過敏症	29	85	57	RELATED	MODERATE	Yes	DW	RESOLVED
273* F/3[redacted] MIXED SOUTH AFRICAN	多発性硬化症再発	424	588	165	UNRELATED	SEVERE	Yes	DW	RESOLVED
	嘔吐	424	588	165	UNRELATED	SEVERE	Yes	DW	RESOLVED

(a) #=On or after the subject switched to alternate MS medication
(b) ^=Adverse Event with onset prior to dosing
Abbreviations: Res=Resolution, NR=Not Recovered/Not Resolved, Dur=Duration, NONE=Dose Not Changed, DW=Drug Withdrawn, DI=Drug Interrupted, DR=Dose Reduced, M=Male, F=Female

SOURCE: BG12MS/JAPAN/ISS/L-AE-SER-301.SAS DATE: 02DEC2015

＊新薬承認情報提供時に置換えた

Listing of serious adverse events:
Study 109MS301
Page 72 of 72
Treatment group: BG00012 240 mg TID

Subject Sex/Age Race	MedDRA Preferred Term	Study Day Onset (a)(b)	Study Day Res	Dur (days)	Relationship to Study Drug	Severity	Serious	Action Taken With Study Drug	Outcome
[redacted] F/4[redacted] WHITE	多発性硬化症再発	450	455	6	UNRELATED	MODERATE	Yes	DW	RESOLVED
[redacted] F/4[redacted] WHITE	多発性硬化症再発	641	645	5	UNRELATED	MODERATE	Yes	NONE	RESOLVED
[redacted] M/4[redacted] WHITE	多発性硬化症再発	95	99	5	UNLIKELY	MODERATE	Yes	NONE	RESOLVED
	多発性硬化症再発	165	170	6	UNLIKELY	MODERATE	Yes	NONE	RESOLVED
	多発性硬化症再発	387	390	4	UNLIKELY	MODERATE	Yes	NONE	RESOLVED

(a) #=On or after the subject switched to alternate MS medication
(b) ^=Adverse Event with onset prior to dosing
Abbreviations: Res=Resolution, NR=Not Recovered/Not Resolved, Dur=Duration, NONE=Dose Not Changed, DW=Drug Withdrawn, DI=Drug Interrupted, DR=Dose Reduced, M=Male, F=Female

SOURCE: BG12MS/JAPAN/ISS/L-AE-SER-301.SAS DATE: 02DEC2015

＊新薬承認情報提供時に置換えた

Table 304: Listing of Serious Adverse Events: Study 109MS302

Listing of serious adverse events:
Study 109MS302
Page 1 of 75
Treatment group: Placebo

Subject Sex/Age Race	MedDRA Preferred Term	Study Day Onset (a) (b)	Study Day Res	Dur (days)	Relationship to Study Drug	Severity	Serious	Action Taken with Study Drug	Outcome
[redacted] F/3[redacted] ASIAN	多発性硬化症再発	88	116	29	UNRELATED	MODERATE	Yes	NONE	RESOLVED
[redacted] F/3[redacted] ASIAN	多発性硬化症再発	482	534	53	UNRELATED	MODERATE	Yes	NONE	RESOLVED
591* F/3[redacted] ASIAN	多発性硬化症再発	209	213	5	UNRELATED	MODERATE	Yes	NONE	RESOLVED
056* F/4[redacted] ASIAN	痙攣	11	13	3	UNLIKELY	MODERATE	Yes	NONE	RESOLVED
	大発作痙攣	297	301	5	POSSIBLY	MODERATE	Yes	DW	RESOLVED

(a) #=On or after the subject switched to alternate MS medication
(b) ^=Adverse Event with onset prior to dosing
Abbreviations: Res=Resolution, NR=Not Recovered/Not Resolved, Dur=Duration, NONE=Dose Not Changed, DW=Drug Withdrawn, DI=Drug Interrupted, DR=Dose Reduced, M=Male, F=Female

SOURCE: BG12MS/JAPAN/ISS/L-AE-SER-302.SAS DATE: 02DEC2015

＊新薬承認情報提供時に置換えた

Listing of serious adverse events:
Study 109MS302
Page 2 of 75
Treatment group: Placebo

Subject Sex/Age Race	MedDRA Preferred Term	Study Day Onset (a) (b)	Study Day Res	Dur (days)	Relationship to Study Drug	Severity	Serious	Action Taken with Study Drug	Outcome
600* M/3[redacted] ASIAN	靭帯損傷	219	287	69	UNRELATED	MODERATE	Yes	DI	RESOLVED
	半月板障害	219	287	69	UNRELATED	MODERATE	Yes	DI	RESOLVED
601* M/3[redacted] ASIAN	治療薬毒性	566	568	3	UNRELATED	MODERATE	Yes	NONE	RESOLVED
058* M/2[redacted] ASIAN	二次性進行型多発性硬化症	424#	433	10	UNLIKELY	MODERATE	Yes	NONE	RESOLVED
[redacted] M/3[redacted] ASIAN	多発性硬化症再発	163	167	5	UNLIKELY	MODERATE	Yes	NONE	RESOLVED

(a) #=On or after the subject switched to alternate MS medication
(b) ^=Adverse Event with onset prior to dosing
Abbreviations: Res=Resolution, NR=Not Recovered/Not Resolved, Dur=Duration, NONE=Dose Not Changed, DW=Drug Withdrawn, DI=Drug Interrupted, DR=Dose Reduced, M=Male, F=Female

SOURCE: BG12MS/JAPAN/ISS/L-AE-SER-302.SAS DATE: 02DEC2015

＊新薬承認情報提供時に置換えた

Listing of serious adverse events:
Study 109MS302
Page 3 of 75
Treatment group: Placebo

Subject Sex/Age Race	MedDRA Preferred Term	Study Day Onset (a) (b)	Study Day Res	Dur (days)	Relationship to Study Drug	Severity	Serious	Action Taken with Study Drug	Outcome
[redacted] M/2[redacted] ASIAN	多発性硬化症再発	179	190	12	UNLIKELY	MODERATE	Yes	DI	RESOLVED
602* M/3[redacted] ASIAN	痙攣	532	532	1	POSSIBLY	MILD	Yes	NONE	RESOLVED
059* F/3[redacted] ASIAN	多発性硬化症再発	132	135	4	UNRELATED	MODERATE	Yes	NONE	RESOLVED
	多発性硬化症再発	244	249	6	UNRELATED	MILD	Yes	NONE	RESOLVED
	多発性硬化症再発	285	322	38	UNRELATED	MODERATE	Yes	NONE	RESOLVED
	多発性硬化症再発	442#	NR		UNRELATED	SEVERE	Yes	NONE	NOT RESOLVED

(a) #=On or after the subject switched to alternate MS medication
(b) ^=Adverse Event with onset prior to dosing
Abbreviations: Res=Resolution, NR=Not Recovered/Not Resolved, Dur=Duration, NONE=Dose Not Changed, DW=Drug Withdrawn, DI=Drug Interrupted, DR=Dose Reduced, M=Male, F=Female

SOURCE: BG12MS/JAPAN/ISS/L-AE-SER-302.SAS DATE: 02DEC2015

＊新薬承認情報提供時に置換えた

Listing of serious adverse events:
Study 109MS302
Page 4 of 75
Treatment group: Placebo

Subject Sex/Age Race	MedDRA Preferred Term	Study Day Onset (a) (b)	Study Day Res	Dur (days)	Relationship to Study Drug	Severity	Serious	Action Taken with Study Drug	Outcome
607* F/3[redacted] BLACK OR AFRICAN AMERICAN	線維腫	155	168	14	UNLIKELY	SEVERE	Yes	DI	RESOLVED
609* M/2[redacted] WHITE	ホームズ・アディー瞳孔	75	77	3	UNRELATED	SEVERE	Yes	NONE	RESOLVED
061* M/4[redacted] WHITE	多発性硬化症再発	613#	618	6	UNRELATED	SEVERE	Yes	NONE	RESOLVED
611* F/2[redacted] WHITE	自然流産	33	33	1	UNLIKELY	SEVERE	Yes	DI	RESOLVED

(a) #=On or after the subject switched to alternate MS medication
(b) ^=Adverse Event with onset prior to dosing
Abbreviations: Res=Resolution, NR=Not Recovered/Not Resolved, Dur=Duration, NONE=Dose Not Changed, DW=Drug Withdrawn, DI=Drug Interrupted, DR=Dose Reduced, M=Male, F=Female

SOURCE: BG12MS/JAPAN/ISS/L-AE-SER-302.SAS DATE: 02DEC2015

＊新薬承認情報提供時に置換えた

Listing of serious adverse events:
Study 109MS302
Page 5 of 75
Treatment group: Placebo

Subject Sex/Age Race	MedDRA Preferred Term	Study Day Onset (a) (b)	Study Day Res	Dur (days)	Relationship to Study Drug	Severity	Serious	Action Taken with Study Drug	Outcome
611* F/2[redacted] WHITE	多発性硬化症	527#	530	4	UNRELATED	SEVERE	Yes	NONE	RESOLVED
612* F/5[redacted] WHITE	肺炎	120	204	85	UNLIKELY	MODERATE	Yes	NONE	RESOLVED
062* F/2[redacted] WHITE	急性胆嚢炎	383#	387	5	UNLIKELY	SEVERE	Yes	NONE	RESOLVED
	胆石症	383#	387	5	UNLIKELY	SEVERE	Yes	NONE	RESOLVED
063* F/4[redacted] WHITE	急性膵炎	167	171	5	UNLIKELY	SEVERE	Yes	NONE	RESOLVED

(a) #=On or after the subject switched to alternate MS medication
(b) ^=Adverse Event with onset prior to dosing
Abbreviations: Res=Resolution, NR=Not Recovered/Not Resolved, Dur=Duration, NONE=Dose Not Changed, DW=Drug Withdrawn, DI=Drug Interrupted, DR=Dose Reduced, M=Male, F=Female

SOURCE: BG12MS/JAPAN/ISS/L-AE-SER-302.SAS DATE: 02DEC2015

＊新薬承認情報提供時に置換えた

Listing of serious adverse events:
Study 109MS302
Page 6 of 75
Treatment group: Placebo

Subject Sex/Age Race	MedDRA Preferred Term	Study Day Onset (a) (b)	Study Day Res	Dur (days)	Relationship to Study Drug	Severity	Serious	Action Taken with Study Drug	Outcome
064* F/3[redacted] BLACK OR AFRICAN AMERICAN	糖尿病性ケトアシドーシス	59	59	1	UNRELATED	SEVERE	Yes	NONE	RESOLVED
	肝酵素上昇	226	261	36	POSSIBLY	SEVERE	Yes	DW	RESOLVED
370* F/4[redacted] WHITE	悪心	3	6	4	POSSIBLY	SEVERE	Yes	DI	RESOLVED
	嘔吐	3	5	3	POSSIBLY	SEVERE	Yes	DI	RESOLVED
	不安	6	6	1	UNRELATED	MODERATE	Yes	DI	RESOLVED
627* M/3[redacted] WHITE	視力低下	568	631	64	UNRELATED	SEVERE	Yes	DI	RESOLVED

(a) #=On or after the subject switched to alternate MS medication
(b) ^=Adverse Event with onset prior to dosing
Abbreviations: Res=Resolution, NR=Not Recovered/Not Resolved, Dur=Duration, NONE=Dose Not Changed, DW=Drug Withdrawn, DI=Drug Interrupted, DR=Dose Reduced, M=Male, F=Female

SOURCE: BG12MS/JAPAN/ISS/L-AE-SER-302.SAS DATE: 02DEC2015

＊新薬承認情報提供時に置換えた

Listing of serious adverse events:
Study 109MS302
Page 7 of 75
Treatment group: Placebo

Subject Sex/Age Race	MedDRA Preferred Term	Study Day Onset (a) (b)	Study Day Res	Dur (days)	Relationship to Study Drug	Severity	Serious	Action Taken with Study Drug	Outcome
630* M/3[redacted] WHITE	てんかん	587	589	3	POSSIBLY	SEVERE	Yes	NONE	RESOLVED
	多発性硬化症	682	686	5	RELATED	MILD	Yes	NONE	RESOLVED
[redacted] M/4[redacted] WHITE	多発性硬化症再発	588	597	10	UNLIKELY	SEVERE	Yes	NONE	RESOLVED
[redacted] F/2[redacted] WHITE	多発性硬化症再発	283	344	62	UNRELATED	SEVERE	Yes	NONE	RESOLVED
	眼痛	491	494	4	UNRELATED	MILD	Yes	NONE	RESOLVED
632* F/5[redacted] WHITE	敗血症	177	185	9	POSSIBLY	SEVERE	Yes	NONE	RESOLVED

(a) #=On or after the subject switched to alternate MS medication
(b) ^=Adverse Event with onset prior to dosing
Abbreviations: Res=Resolution, NR=Not Recovered/Not Resolved, Dur=Duration, NONE=Dose Not Changed, DW=Drug Withdrawn, DI=Drug Interrupted, DR=Dose Reduced, M=Male, F=Female

SOURCE: BG12MS/JAPAN/ISS/L-AE-SER-302.SAS DATE: 02DEC2015

＊新薬承認情報提供時に置換えた

Listing of serious adverse events:
Study 109MS302
Page 8 of 75
Treatment group: Placebo

Subject Sex/Age Race	MedDRA Preferred Term	Study Day Onset (a) (b)	Study Day Res	Dur (days)	Relationship to Study Drug	Severity	Serious	Action Taken with Study Drug	Outcome
[redacted] F/3[redacted] WHITE	多発性硬化症再発	86	92	7	UNRELATED	SEVERE	Yes	DI	RESOLVED
	多発性硬化症再発	212	215	4	UNLIKELY	SEVERE	Yes	NONE	RESOLVED
067* F/2[redacted] WHITE	多発性硬化症再発	139	141	3	UNLIKELY	SEVERE	Yes	NONE	RESOLVED
[redacted] M/3[redacted] WHITE	多発性硬化症再発	30	39	10	UNRELATED	MODERATE	Yes	NONE	RESOLVED
633* F/3[redacted] WHITE	多発性硬化症再発	396	422	27	UNLIKELY	MODERATE	Yes	NONE	RESOLVED

(a) #=On or after the subject switched to alternate MS medication
(b) ^=Adverse Event with onset prior to dosing
Abbreviations: Res=Resolution, NR=Not Recovered/Not Resolved, Dur=Duration, NONE=Dose Not Changed, DW=Drug Withdrawn, DI=Drug Interrupted, DR=Dose Reduced, M=Male, F=Female

SOURCE: BG12MS/JAPAN/ISS/L-AE-SER-302.SAS DATE: 02DEC2015

＊新薬承認情報提供時に置換えた

Listing of serious adverse events:
Study 109MS302
Page 9 of 75
Treatment group: Placebo

Subject Sex/Age Race	MedDRA Preferred Term	Study Day Onset (a) (b)	Study Day Res	Dur (days)	Relationship to Study Drug	Severity	Serious	Action Taken with Study Drug	Outcome
633* F/3[redacted] WHITE	社会問題	508	522	15	UNRELATED	MILD	Yes	NONE	RESOLVED
070* F/3[redacted] WHITE	多発性硬化症再発	110	114	5	UNRELATED	MILD	Yes	NONE	RESOLVED
[redacted] F/3[redacted] WHITE	多発性硬化症再発	45	51	7	UNLIKELY	MILD	Yes	NONE	RESOLVED
	多発性硬化症再発	177	184	8	UNLIKELY	MODERATE	Yes	NONE	RESOLVED
	多発性硬化症再発	410	421	12	UNLIKELY	MODERATE	Yes	NONE	RESOLVED

(a) #=On or after the subject switched to alternate MS medication
(b) ^=Adverse Event with onset prior to dosing
Abbreviations: Res=Resolution, NR=Not Recovered/Not Resolved, Dur=Duration, NONE=Dose Not Changed, DW=Drug Withdrawn, DI=Drug Interrupted, DR=Dose Reduced, M=Male, F=Female

SOURCE: BG12MS/JAPAN/ISS/L-AE-SER-302.SAS DATE: 02DEC2015

＊新薬承認情報提供時に置換えた

Listing of serious adverse events:
Study 109MS302
Page 10 of 75
Treatment group: Placebo

Subject Sex/Age Race	MedDRA Preferred Term	Study Day Onset (a) (b)	Study Day Res	Dur (days)	Relationship to Study Drug	Severity	Serious	Action Taken with Study Drug	Outcome
634* F/2[redacted] WHITE	妊娠浮腫	491	501	11	UNRELATED	MODERATE	Yes	NONE	RESOLVED
636* F/3[redacted] WHITE	気管炎	58	63	6	UNRELATED	MILD	Yes	NONE	RESOLVED
[redacted] F/5[redacted] WHITE	多発性硬化症再発	178	194	17	UNRELATED	SEVERE	Yes	NONE	RESOLVED
[redacted] F/4[redacted] WHITE	多発性硬化症再発	259	290	32	UNRELATED	MODERATE	Yes	NONE	RESOLVED

(a) #=On or after the subject switched to alternate MS medication
(b) ^=Adverse Event with onset prior to dosing
Abbreviations: Res=Resolution, NR=Not Recovered/Not Resolved, Dur=Duration, NONE=Dose Not Changed, DW=Drug Withdrawn, DI=Drug Interrupted, DR=Dose Reduced, M=Male, F=Female

SOURCE: BG12MS/JAPAN/ISS/L-AE-SER-302.SAS DATE: 02DEC2015

＊新薬承認情報提供時に置換えた

Listing of serious adverse events:
Study 109MS302
Page 11 of 75
Treatment group: Placebo

Subject Sex/Age Race	MedDRA Preferred Term	Study Day Onset (a) (b)	Study Day Res	Dur (days)	Relationship to Study Drug	Severity	Serious	Action Taken with Study Drug	Outcome
[redacted] F/2[redacted] WHITE	多発性硬化症再発	217	NR		UNRELATED	MODERATE	Yes	NONE	NOT RESOLVED
639* F/4[redacted] WHITE	腱断裂	343	362	20	UNRELATED	MILD	Yes	NONE	RESOLVED
	腱断裂	343	362	20	UNRELATED	MILD	Yes	NONE	RESOLVED
[redacted] M/3[redacted] WHITE	多発性硬化症再発	545	549	5	UNLIKELY	SEVERE	Yes	NONE	RESOLVED
649* F/2[redacted] WHITE	手骨折	455	479	25	UNRELATED	MODERATE	Yes	NONE	RESOLVED

(a) #=On or after the subject switched to alternate MS medication
(b) ^=Adverse Event with onset prior to dosing
Abbreviations: Res=Resolution, NR=Not Recovered/Not Resolved, Dur=Duration, NONE=Dose Not Changed, DW=Drug Withdrawn, DI=Drug Interrupted, DR=Dose Reduced, M=Male, F=Female

SOURCE: BG12MS/JAPAN/ISS/L-AE-SER-302.SAS DATE: 02DEC2015

＊新薬承認情報提供時に置換えた

Listing of serious adverse events:
Study 109MS302
Page 12 of 75
Treatment group: Placebo

Subject Sex/Age Race	MedDRA Preferred Term	Study Day Onset (a) (b)	Study Day Res	Dur (days)	Relationship to Study Drug	Severity	Serious	Action Taken with Study Drug	Outcome
651* F/2[redacted] WHITE	子宮頚部円錐切除	58	60	3	UNRELATED	MODERATE	Yes	NONE	RESOLVED
077* F/4[redacted] WHITE	バルトリン嚢腫	18	21	4	UNLIKELY	MODERATE	Yes	NONE	RESOLVED
	細菌性心内膜炎	57	117	61	POSSIBLY	SEVERE	Yes	DW	RESOLVED
654* F/4[redacted] WHITE	無力症	51	63	13	UNLIKELY	MODERATE	Yes	NONE	RESOLVED
[redacted] F/2[redacted] WHITE	多発性硬化症再発	455	463	9	UNLIKELY	SEVERE	Yes	NONE	RESOLVED

(a) #=On or after the subject switched to alternate MS medication
(b) ^=Adverse Event with onset prior to dosing
Abbreviations: Res=Resolution, NR=Not Recovered/Not Resolved, Dur=Duration, NONE=Dose Not Changed, DW=Drug Withdrawn, DI=Drug Interrupted, DR=Dose Reduced, M=Male, F=Female

SOURCE: BG12MS/JAPAN/ISS/L-AE-SER-302.SAS DATE: 02DEC2015

＊新薬承認情報提供時に置換えた

Listing of serious adverse events:
Study 109MS302
Page 13 of 75
Treatment group: Placebo

Subject Sex/Age Race	MedDRA Preferred Term	Study Day Onset (a) (b)	Study Day Res	Dur (days)	Relationship to Study Drug	Severity	Serious	Action Taken with Study Drug	Outcome
[redacted] F/3[redacted] WHITE	多発性硬化症再発	236	244	9	UNLIKELY	MODERATE	Yes	NONE	RESOLVED
	多発性硬化症再発	364	370	7	UNLIKELY	MODERATE	Yes	NONE	RESOLVED
[redacted] F/5[redacted] WHITE	多発性硬化症再発	65	70	6	UNLIKELY	MILD	Yes	NONE	RESOLVED
	多発性硬化症再発	179	183	5	UNLIKELY	MILD	Yes	NONE	RESOLVED
	多発性硬化症再発	429#	434	6	UNLIKELY	MILD	Yes	NONE	RESOLVED
[redacted] F/3[redacted] WHITE	多発性硬化症再発	163	170	8	UNLIKELY	MILD	Yes	NONE	RESOLVED

(a) #=On or after the subject switched to alternate MS medication
(b) ^=Adverse Event with onset prior to dosing
Abbreviations: Res=Resolution, NR=Not Recovered/Not Resolved, Dur=Duration, NONE=Dose Not Changed, DW=Drug Withdrawn, DI=Drug Interrupted, DR=Dose Reduced, M=Male, F=Female

SOURCE: BG12MS/JAPAN/ISS/L-AE-SER-302.SAS DATE: 02DEC2015

＊新薬承認情報提供時に置換えた

Listing of serious adverse events:
Study 109MS302
Page 14 of 75
Treatment group: Placebo

Subject Sex/Age Race	MedDRA Preferred Term	Study Day Onset (a) (b)	Study Day Res	Dur (days)	Relationship to Study Drug	Severity	Serious	Action Taken with Study Drug	Outcome
080* F/3[redacted] WHITE	乳房新生物	352			UNLIKELY	MODERATE	Yes	DW	RESOLVED
081* F/2[redacted] WHITE	多発性硬化症再発	90	96	7	UNRELATED	MODERATE	Yes	NONE	RESOLVED
	多発性硬化症再発	268	272	5	UNRELATED	MODERATE	Yes	NONE	RESOLVED
	多発性硬化症再発	341	346	6	UNRELATED	MODERATE	Yes	NONE	RESOLVED
	多発性硬化症再発	483#	490	8	UNRELATED	MODERATE	Yes	NONE	RESOLVED
	多発性硬化症再発	635#	638	4	UNRELATED	MILD	Yes	NONE	RESOLVED

(a) #=On or after the subject switched to alternate MS medication
(b) ^=Adverse Event with onset prior to dosing
Abbreviations: Res=Resolution, NR=Not Recovered/Not Resolved, Dur=Duration, NONE=Dose Not Changed, DW=Drug Withdrawn, DI=Drug Interrupted, DR=Dose Reduced, M=Male, F=Female

SOURCE: BG12MS/JAPAN/ISS/L-AE-SER-302.SAS DATE: 02DEC2015

＊新薬承認情報提供時に置換えた

Listing of serious adverse events:
Study 109MS302
Page 15 of 75
Treatment group: Placebo

Subject Sex/Age Race	MedDRA Preferred Term	Study Day Onset (a) (b)	Study Day Res	Dur (days)	Relationship to Study Drug	Severity	Serious	Action Taken with Study Drug	Outcome
[redacted] F/4[redacted] WHITE	多発性硬化症再発	417	423	7	UNRELATED	MODERATE	Yes	NONE	RESOLVED
	多発性硬化症再発	596	602	7	UNRELATED	MODERATE	Yes	NONE	RESOLVED
[redacted] M/4[redacted] WHITE	多発性硬化症再発	38	42	5	UNRELATED	SEVERE	Yes	NONE	RESOLVED
[redacted] F/2[redacted] WHITE	多発性硬化症再発	50	55	6	UNLIKELY	MODERATE	Yes	NONE	RESOLVED
	多発性硬化症再発	225	230	6	UNLIKELY	MODERATE	Yes	NONE	RESOLVED

(a) #=On or after the subject switched to alternate MS medication
(b) ^=Adverse Event with onset prior to dosing
Abbreviations: Res=Resolution, NR=Not Recovered/Not Resolved, Dur=Duration, NONE=Dose Not Changed, DW=Drug Withdrawn, DI=Drug Interrupted, DR=Dose Reduced, M=Male, F=Female

SOURCE: BG12MS/JAPAN/ISS/L-AE-SER-302.SAS DATE: 02DEC2015

＊新薬承認情報提供時に置換えた

Listing of serious adverse events:
Study 109MS302
Page 16 of 75
Treatment group: Placebo

Subject Sex/Age Race	MedDRA Preferred Term	Study Day Onset (a) (b)	Study Day Res	Dur (days)	Relationship to Study Drug	Severity	Serious	Action Taken with Study Drug	Outcome
[redacted] F/3[redacted] WHITE	多発性硬化症再発	141	148	8	UNRELATED	MILD	Yes	NONE	RESOLVED
	多発性硬化症再発	180	188	9	UNRELATED	MILD	Yes	NONE	RESOLVED
	多発性硬化症再発	380#	389	10	UNRELATED	MILD	Yes	NONE	RESOLVED
663* F/4[redacted] WHITE	子宮出血	133	134	2	UNRELATED	MILD	Yes	NONE	RESOLVED
	眼外傷	541	549	9	UNRELATED	MODERATE	Yes	NONE	RESOLVED
664* F/4[redacted] WHITE	多発性硬化症再発	37	43	7	UNRELATED	MILD	Yes	NONE	RESOLVED
	ボレリア感染	95	112	18	UNRELATED	MILD	Yes	NONE	RESOLVED

(a) #=On or after the subject switched to alternate MS medication
(b) ^=Adverse Event with onset prior to dosing
Abbreviations: Res=Resolution, NR=Not Recovered/Not Resolved, Dur=Duration, NONE=Dose Not Changed, DW=Drug Withdrawn, DI=Drug Interrupted, DR=Dose Reduced, M=Male, F=Female

SOURCE: BG12MS/JAPAN/ISS/L-AE-SER-302.SAS DATE: 02DEC2015

＊新薬承認情報提供時に置換えた

Listing of serious adverse events:
Study 109MS302
Page 17 of 75
Treatment group: Placebo

Subject Sex/Age Race	MedDRA Preferred Term	Study Day Onset (a) (b)	Study Day Res	Dur (days)	Relationship to Study Drug	Severity	Serious	Action Taken with Study Drug	Outcome
664* F/4[redacted] WHITE	インフルエンザ	171	176	6	UNRELATED	MILD	Yes	NONE	RESOLVED
	多発性硬化症再発	452	457	6	UNRELATED	MILD	Yes	NONE	RESOLVED
[redacted] F/2[redacted] WHITE	多発性硬化症再発	76	80	5	UNRELATED	MILD	Yes	NONE	RESOLVED
	多発性硬化症再発	136	140	5	UNRELATED	MILD	Yes	NONE	RESOLVED
[redacted] F/2[redacted] WHITE	多発性硬化症再発	680	682	3	UNRELATED	MODERATE	Yes	NONE	RESOLVED

(a) #=On or after the subject switched to alternate MS medication
(b) ^=Adverse Event with onset prior to dosing
Abbreviations: Res=Resolution, NR=Not Recovered/Not Resolved, Dur=Duration, NONE=Dose Not Changed, DW=Drug Withdrawn, DI=Drug Interrupted, DR=Dose Reduced, M=Male, F=Female

SOURCE: BG12MS/JAPAN/ISS/L-AE-SER-302.SAS DATE: 02DEC2015

＊新薬承認情報提供時に置換えた

Listing of serious adverse events:
Study 109MS302
Page 18 of 75
Treatment group: Placebo

Subject Sex/Age Race	MedDRA Preferred Term	Study Day Onset (a) (b)	Study Day Res	Dur (days)	Relationship to Study Drug	Severity	Serious	Action Taken with Study Drug	Outcome
[redacted] M/4[redacted] WHITE	多発性硬化症再発	145	163	19	UNRELATED	MODERATE	Yes	NONE	RESOLVED
	多発性硬化症再発	477	481	5	UNRELATED	MODERATE	Yes	NONE	RESOLVED
	多発性硬化症再発	642	646	5	UNRELATED	MODERATE	Yes	NONE	RESOLVED
082* M/3[redacted] WHITE	多発性硬化症再発	252	256	5	UNLIKELY	MODERATE	Yes	NONE	RESOLVED
	多発性硬化症再発	368	371	4	UNLIKELY	MODERATE	Yes	NONE	RESOLVED
083* F/4[redacted] WHITE	多発性硬化症再発	32	35	4	UNLIKELY	MODERATE	Yes	NONE	RESOLVED

(a) #=On or after the subject switched to alternate MS medication
(b) ^=Adverse Event with onset prior to dosing
Abbreviations: Res=Resolution, NR=Not Recovered/Not Resolved, Dur=Duration, NONE=Dose Not Changed, DW=Drug Withdrawn, DI=Drug Interrupted, DR=Dose Reduced, M=Male, F=Female

SOURCE: BG12MS/JAPAN/ISS/L-AE-SER-302.SAS DATE: 02DEC2015

＊新薬承認情報提供時に置換えた

Listing of serious adverse events:
Study 109MS302
Page 19 of 75
Treatment group: Placebo

Subject Sex/Age Race	MedDRA Preferred Term	Study Day Onset (a) (b)	Study Day Res	Dur (days)	Relationship to Study Drug	Severity	Serious	Action Taken with Study Drug	Outcome
083* F/4[redacted] WHITE	多発性硬化症再発	280	283	4	UNLIKELY	MODERATE	Yes	NONE	RESOLVED
[redacted] M/2[redacted] WHITE	多発性硬化症再発	40	43	4	UNRELATED	MODERATE	Yes	NONE	RESOLVED
[redacted] F/2[redacted] WHITE	多発性硬化症再発	87	91	5	UNRELATED	SEVERE	Yes	NONE	RESOLVED
[redacted] F/4[redacted] WHITE	多発性硬化症再発	391	395	5	UNRELATED	MILD	Yes	NONE	RESOLVED

(a) #=On or after the subject switched to alternate MS medication
(b) ^=Adverse Event with onset prior to dosing
Abbreviations: Res=Resolution, NR=Not Recovered/Not Resolved, Dur=Duration, NONE=Dose Not Changed, DW=Drug Withdrawn, DI=Drug Interrupted, DR=Dose Reduced, M=Male, F=Female

SOURCE: BG12MS/JAPAN/ISS/L-AE-SER-302.SAS DATE: 02DEC2015

＊新薬承認情報提供時に置換えた

Listing of serious adverse events:
Study 109MS302
Page 20 of 75
Treatment group: Placebo

Subject Sex/Age Race	MedDRA Preferred Term	Study Day Onset (a) (b)	Study Day Res	Dur (days)	Relationship to Study Drug	Severity	Serious	Action Taken with Study Drug	Outcome
672* F/5[redacted] WHITE	膀胱憩室	173	177	5	UNRELATED	SEVERE	Yes	NONE	RESOLVED
[redacted] M/4[redacted]	多発性硬化症再発	225	238	14	UNRELATED	MODERATE	Yes	NONE	RESOLVED
	多発性硬化症再発	534	540	7	UNRELATED	MODERATE	Yes	NONE	RESOLVED
[redacted] F/4[redacted]	多発性硬化症再発	643	658	16	UNRELATED	MODERATE	Yes	NONE	RESOLVED
675* M/3[redacted]	鼻茸	557	557	1	UNRELATED	MODERATE	Yes	NONE	RESOLVED
	鼻甲介切除	557	557	1	UNRELATED	MODERATE	Yes	NONE	RESOLVED

(a) #=On or after the subject switched to alternate MS medication
(b) ^=Adverse Event with onset prior to dosing
Abbreviations: Res=Resolution, NR=Not Recovered/Not Resolved, Dur=Duration, NONE=Dose Not Changed, DW=Drug Withdrawn, DI=Drug Interrupted, DR=Dose Reduced, M=Male, F=Female

SOURCE: BG12MS/JAPAN/ISS/L-AE-SER-302.SAS DATE: 02DEC2015

＊新薬承認情報提供時に置換えた

Listing of serious adverse events:
Study 109MS302
Page 21 of 75
Treatment group: Placebo

Subject Sex/Age Race	MedDRA Preferred Term	Study Day Onset (a) (b)	Study Day Res	Dur (days)	Relationship to Study Drug	Severity	Serious	Action Taken with Study Drug	Outcome
676* F/2[redacted]	自然流産	425	425	1	POSSIBLY	MODERATE	Yes	DI	RESOLVED
678* F/1[redacted] WHITE	腎下垂症	210	219	10	UNLIKELY	MILD	Yes	NONE	RESOLVED
[redacted] F/5[redacted] WHITE	多発性硬化症再発	132	149	18	UNLIKELY	MILD	Yes	NONE	RESOLVED
	多発性硬化症再発	617	631	15	UNLIKELY	SEVERE	Yes	NONE	RESOLVED
[redacted] F/2[redacted] WHITE	多発性硬化症再発	29	37	9	UNLIKELY	MILD	Yes	NONE	RESOLVED

(a) #=On or after the subject switched to alternate MS medication
(b) ^=Adverse Event with onset prior to dosing
Abbreviations: Res=Resolution, NR=Not Recovered/Not Resolved, Dur=Duration, NONE=Dose Not Changed, DW=Drug Withdrawn, DI=Drug Interrupted, DR=Dose Reduced, M=Male, F=Female

SOURCE: BG12MS/JAPAN/ISS/L-AE-SER-302.SAS DATE: 02DEC2015

＊新薬承認情報提供時に置換えた

Listing of serious adverse events:
Study 109MS302
Page 22 of 75
Treatment group: Placebo

Subject Sex/Age Race	MedDRA Preferred Term	Study Day Onset (a) (b)	Study Day Res	Dur (days)	Relationship to Study Drug	Severity	Serious	Action Taken with Study Drug	Outcome
[redacted] F/2[redacted] WHITE	多発性硬化症再発	633	645	13	UNRELATED	SEVERE	Yes	NONE	RESOLVED
[redacted] M/2[redacted] WHITE	多発性硬化症再発	208	222	15	UNRELATED	MODERATE	Yes	NONE	RESOLVED
[redacted] M/2[redacted] WHITE	多発性硬化症再発	5	16	12	UNRELATED	MODERATE	Yes	NONE	RESOLVED
[redacted] F/2[redacted] WHITE	多発性硬化症再発	363	373	11	UNRELATED	MILD	Yes	NONE	RESOLVED

(a) #=On or after the subject switched to alternate MS medication
(b) ^=Adverse Event with onset prior to dosing
Abbreviations: Res=Resolution, NR=Not Recovered/Not Resolved, Dur=Duration, NONE=Dose Not Changed, DW=Drug Withdrawn, DI=Drug Interrupted, DR=Dose Reduced, M=Male, F=Female

SOURCE: BG12MS/JAPAN/ISS/L-AE-SER-302.SAS DATE: 02DEC2015

＊新薬承認情報提供時に置換えた

Listing of serious adverse events:
Study 109MS302
Page 23 of 75
Treatment group: Placebo

Subject Sex/Age Race	MedDRA Preferred Term	Study Day Onset (a) (b)	Study Day Res	Dur (days)	Relationship to Study Drug	Severity	Serious	Action Taken with Study Drug	Outcome
089* F/4[redacted] WHITE	脳血管発作	117	NR		UNLIKELY	SEVERE	Yes	DW	NOT RESOLVED
684* F/3[redacted] HISPANIC	片頭痛	145	146	2	UNRELATED	MODERATE	Yes	NONE	RESOLVED
	多発性硬化症再発	161	169	9	UNRELATED	MODERATE	Yes	NONE	RESOLVED
[redacted] F/3[redacted] HISPANIC	多発性硬化症再発	376	394	19	UNRELATED	MODERATE	Yes	DI	RESOLVED
[redacted] F/3[redacted] HISPANIC	多発性硬化症再発	266	270	5	UNRELATED	MILD	Yes	NONE	RESOLVED

(a) #=On or after the subject switched to alternate MS medication
(b) ^=Adverse Event with onset prior to dosing
Abbreviations: Res=Resolution, NR=Not Recovered/Not Resolved, Dur=Duration, NONE=Dose Not Changed, DW=Drug Withdrawn, DI=Drug Interrupted, DR=Dose Reduced, M=Male, F=Female

SOURCE: BG12MS/JAPAN/ISS/L-AE-SER-302.SAS DATE: 02DEC2015

＊新薬承認情報提供時に置換えた

Listing of serious adverse events:
Study 109MS302
Page 24 of 75
Treatment group: Placebo

Subject Sex/Age Race	MedDRA Preferred Term	Study Day Onset (a) (b)	Study Day Res	Dur (days)	Relationship to Study Drug	Severity	Serious	Action Taken with Study Drug	Outcome
[redacted] F/4[redacted] WHITE	多発性硬化症再発	281	296	16	UNLIKELY	SEVERE	Yes	NONE	RESOLVED
[redacted] F/3[redacted] WHITE	多発性硬化症再発	479	483	5	POSSIBLY	MODERATE	Yes	NONE	RESOLVED
[redacted] F/4[redacted] WHITE	多発性硬化症再発	27	36	10	UNLIKELY	MODERATE	Yes	NONE	RESOLVED
344* F/5[redacted] WHITE	脳浮腫	342#	344	3	UNLIKELY	SEVERE	Yes	NONE	RESOLVED
	昏睡	342#	344	3	UNLIKELY	SEVERE	Yes	NONE	RESOLVED
	虚血性脳卒中	342#	344	3	UNLIKELY	SEVERE	Yes	NONE	RESOLVED

(a) #=On or after the subject switched to alternate MS medication
(b) ^=Adverse Event with onset prior to dosing
Abbreviations: Res=Resolution, NR=Not Recovered/Not Resolved, Dur=Duration, NONE=Dose Not Changed, DW=Drug Withdrawn, DI=Drug Interrupted, DR=Dose Reduced, M=Male, F=Female

SOURCE: BG12MS/JAPAN/ISS/L-AE-SER-302.SAS DATE: 02DEC2015

＊新薬承認情報提供時に置換えた

Listing of serious adverse events:
Study 109MS302
Page 25 of 75
Treatment group: Placebo

Subject Sex/Age Race	MedDRA Preferred Term	Study Day Onset (a) (b)	Study Day Res	Dur (days)	Relationship to Study Drug	Severity	Serious	Action Taken with Study Drug	Outcome
094* F/3[redacted] WHITE	多発性硬化症再発	241	248	8	UNRELATED	MODERATE	Yes	NONE	RESOLVED
	多発性硬化症再発	589	595	7	UNRELATED	SEVERE	Yes	DW	RESOLVED
[redacted] F/3[redacted] WHITE	多発性硬化症再発	309	317	9	UNRELATED	MODERATE	Yes	NONE	RESOLVED

(a) #=On or after the subject switched to alternate MS medication
(b) ^=Adverse Event with onset prior to dosing
Abbreviations: Res=Resolution, NR=Not Recovered/Not Resolved, Dur=Duration, NONE=Dose Not Changed, DW=Drug Withdrawn, DI=Drug Interrupted, DR=Dose Reduced, M=Male, F=Female

SOURCE: BG12MS/JAPAN/ISS/L-AE-SER-302.SAS DATE: 02DEC2015

＊新薬承認情報提供時に置換えた

Listing of serious adverse events:
Study 109MS302
Page 26 of 75
Treatment group: BG00012 240 mg BID

Subject Sex/Age Race	MedDRA Preferred Term	Study Day Onset (a) (b)	Study Day Res	Dur (days)	Relationship to Study Drug	Severity	Serious	Action Taken with Study Drug	Outcome
592* F/5[redacted] ASIAN	転倒	113	113	1	UNRELATED	MILD	Yes	NONE	RESOLVED
	足骨折	113	146	34	UNRELATED	MILD	Yes	NONE	RESOLVED
	月経過多	441	443	3	UNRELATED	SEVERE	Yes	NONE	RESOLVED
593* F/2[redacted] ASIAN	蜂巣炎	285	336	52	UNRELATED	MODERATE	Yes	NONE	RESOLVED
[redacted] F/2[redacted] ASIAN	多発性硬化症再発	121	142	22	UNRELATED	SEVERE	Yes	NONE	RESOLVED
	多発性硬化症再発	240	249	10	UNRELATED	MODERATE	Yes	NONE	RESOLVED

(a) #=On or after the subject switched to alternate MS medication
(b) ^=Adverse Event with onset prior to dosing
Abbreviations: Res=Resolution, NR=Not Recovered/Not Resolved, Dur=Duration, NONE=Dose Not Changed, DW=Drug Withdrawn, DI=Drug Interrupted, DR=Dose Reduced, M=Male, F=Female

SOURCE: BG12MS/JAPAN/ISS/L-AE-SER-302.SAS DATE: 02DEC2015

＊新薬承認情報提供時に置換えた

Listing of serious adverse events:
Study 109MS302
Page 27 of 75
Treatment group: BG00012 240 mg BID

Subject Sex/Age Race	MedDRA Preferred Term	Study Day Onset (a) (b)	Study Day Res	Dur (days)	Relationship to Study Drug	Severity	Serious	Action Taken with Study Drug	Outcome
[redacted] M/1[redacted] ASIAN	多発性硬化症再発	131	133	3	UNRELATED	MODERATE	Yes	NONE	RESOLVED
163* F/1[redacted] ASIAN	多発性硬化症再発	71	167	97	UNRELATED	MILD	Yes	NONE	RESOLVED
	多発性硬化症再発	372	393	22	UNLIKELY	MODERATE	Yes	NONE	RESOLVED
	多発性硬化症再発	581	588	8	UNLIKELY	SEVERE	Yes	DW	RESOLVED
	部分発作	581	588	8	UNLIKELY	SEVERE	Yes	DW	RESOLVED
598* F/5[redacted] ASIAN	ウイルス感染	486	488	3	UNRELATED	MODERATE	Yes	NONE	RESOLVED

(a) #=On or after the subject switched to alternate MS medication
(b) ^=Adverse Event with onset prior to dosing
Abbreviations: Res=Resolution, NR=Not Recovered/Not Resolved, Dur=Duration, NONE=Dose Not Changed, DW=Drug Withdrawn, DI=Drug Interrupted, DR=Dose Reduced, M=Male, F=Female

SOURCE: BG12MS/JAPAN/ISS/L-AE-SER-302.SAS DATE: 02DEC2015

＊新薬承認情報提供時に置換えた

Listing of serious adverse events:
Study 109MS302
Page 28 of 75
Treatment group: BG00012 240 mg BID

Subject Sex/Age Race	MedDRA Preferred Term	Study Day Onset (a) (b)	Study Day Res	Dur (days)	Relationship to Study Drug	Severity	Serious	Action Taken with Study Drug	Outcome
[redacted] F/2[redacted] ASIAN	多発性硬化症再発	62	67	6	UNLIKELY	MODERATE	Yes	NONE	RESOLVED
59* F/5[redacted] ASIAN	大腿骨骨折	378	431	54	UNRELATED	SEVERE	Yes	NONE	RESOLVED
604* F/4[redacted] ASIAN	蜂巣炎	192	222	31	POSSIBLY	MODERATE	Yes	DI	RESOLVED
[redacted] F/3[redacted] ASIAN	多発性硬化症再発	348	354	7	UNRELATED	SEVERE	Yes	NONE	RESOLVED

(a) #=On or after the subject switched to alternate MS medication
(b) ^=Adverse Event with onset prior to dosing
Abbreviations: Res=Resolution, NR=Not Recovered/Not Resolved, Dur=Duration, NONE=Dose Not Changed, DW=Drug Withdrawn, DI=Drug Interrupted, DR=Dose Reduced, M=Male, F=Female

SOURCE: BG12MS/JAPAN/ISS/L-AE-SER-302.SAS DATE: 02DEC2015

＊新薬承認情報提供時に置換えた

Listing of serious adverse events:
Study 109MS302
Page 29 of 75
Treatment group: BG00012 240 mg BID

Subject Sex/Age Race	MedDRA Preferred Term	Study Day Onset (a) (b)	Study Day Res	Dur (days)	Relationship to Study Drug	Severity	Serious	Action Taken with Study Drug	Outcome
164* F/2[redacted] ASIAN	多発性硬化症再発	57	66	10	POSSIBLY	MODERATE	Yes	DI	RESOLVED
	動悸	592#	592	1	UNRELATED	SEVERE	Yes	NONE	RESOLVED
606* F/4[redacted] WHITE	多発性硬化症再発	266	284	19	UNRELATED	SEVERE	Yes	DI	RESOLVED
	背部痛	330	332	3	UNRELATED	SEVERE	Yes	NONE	RESOLVED
610* M/3[redacted] WHITE	腹痛	152	153	2	UNRELATED	MODERATE	Yes	NONE	RESOLVED
614* M/5[redacted] WHITE	憩室穿孔	187	195	9	UNLIKELY	SEVERE	Yes	DI	RESOLVED

(a) #=On or after the subject switched to alternate MS medication
(b) ^=Adverse Event with onset prior to dosing
Abbreviations: Res=Resolution, NR=Not Recovered/Not Resolved, Dur=Duration, NONE=Dose Not Changed, DW=Drug Withdrawn, DI=Drug Interrupted, DR=Dose Reduced, M=Male, F=Female

SOURCE: BG12MS/JAPAN/ISS/L-AE-SER-302.SAS DATE: 02DEC2015

＊新薬承認情報提供時に置換えた

Listing of serious adverse events:
Study 109MS302
Page 30 of 75
Treatment group: BG00012 240 mg BID

Subject Sex/Age Race	MedDRA Preferred Term	Study Day Onset (a) (b)	Study Day Res	Dur (days)	Relationship to Study Drug	Severity	Serious	Action Taken with Study Drug	Outcome
617* F/3[redacted] WHITE	腹痛	576	577	2	UNRELATED	SEVERE	Yes	NONE	RESOLVED
	悪心	576	577	2	UNRELATED	SEVERE	Yes	NONE	RESOLVED
	嘔吐	576	577	2	UNRELATED	SEVERE	Yes	NONE	RESOLVED
[redacted] F/5[redacted] WHITE	多発性硬化症再発	176	261	86	UNRELATED	SEVERE	Yes	NONE	RESOLVED
624* F/3[redacted] WHITE	過量投与	280	284	5	UNRELATED	SEVERE	Yes	NONE	RESOLVED
628* F/3[redacted] WHITE	胃腸炎	6	7	2	UNRELATED	MODERATE	Yes	DI	RESOLVED

(a) #=On or after the subject switched to alternate MS medication
(b) ^=Adverse Event with onset prior to dosing
Abbreviations: Res=Resolution, NR=Not Recovered/Not Resolved, Dur=Duration, NONE=Dose Not Changed, DW=Drug Withdrawn, DI=Drug Interrupted, DR=Dose Reduced, M=Male, F=Female

SOURCE: BG12MS/JAPAN/ISS/L-AE-SER-302.SAS DATE: 02DEC2015

＊新薬承認情報提供時に置換えた

Listing of serious adverse events:
Study 109MS302
Page 31 of 75
Treatment group: BG00012 240 mg BID

Subject Sex/Age Race	MedDRA Preferred Term	Study Day Onset (a) (b)	Study Day Res	Dur (days)	Relationship to Study Drug	Severity	Serious	Action Taken with Study Drug	Outcome
178* M/4[redacted] WHITE	多発性硬化症再発	224	226	3	UNRELATED	MODERATE	Yes	NONE	RESOLVED
[redacted] M/4[redacted] WHITE	多発性硬化症再発	275	NR		UNLIKELY	SEVERE	Yes	DI	NOT RESOLVED
[redacted] M/3[redacted] WHITE	多発性硬化症再発	13	19	7	POSSIBLY	SEVERE	Yes	NONE	RESOLVED
[redacted] F/2[redacted] WHITE	多発性硬化症再発	334	339	6	UNRELATED	MILD	Yes	NONE	RESOLVED

(a) #=On or after the subject switched to alternate MS medication
(b) ^=Adverse Event with onset prior to dosing
Abbreviations: Res=Resolution, NR=Not Recovered/Not Resolved, Dur=Duration, NONE=Dose Not Changed, DW=Drug Withdrawn, DI=Drug Interrupted, DR=Dose Reduced, M=Male, F=Female

SOURCE: BG12MS/JAPAN/ISS/L-AE-SER-302.SAS DATE: 02DEC2015

＊新薬承認情報提供時に置換えた

Listing of serious adverse events:
Study 109MS302
Page 32 of 75
Treatment group: BG00012 240 mg BID

Subject Sex/Age Race	MedDRA Preferred Term	Study Day Onset (a) (b)	Study Day Res	Dur (days)	Relationship to Study Drug	Severity	Serious	Action Taken with Study Drug	Outcome
637* M/5[redacted] WHITE	滑液包炎	437	504	68	UNRELATED	SEVERE	Yes	NONE	RESOLVED
640* F/4[redacted] WHITE	膀胱機能障害	186	189	4	UNRELATED	MODERATE	Yes	NONE	RESOLVED
[redacted] F/2[redacted] WHITE	多発性硬化症再発	565	566	2	UNLIKELY	MILD	Yes	DI	RESOLVED
642* M/2[redacted] WHITE	靭帯断裂	164	343	180	UNRELATED	MODERATE	Yes	NONE	RESOLVED

(a) #=On or after the subject switched to alternate MS medication
(b) ^=Adverse Event with onset prior to dosing
Abbreviations: Res=Resolution, NR=Not Recovered/Not Resolved, Dur=Duration, NONE=Dose Not Changed, DW=Drug Withdrawn, DI=Drug Interrupted, DR=Dose Reduced, M=Male, F=Female

SOURCE: BG12MS/JAPAN/ISS/L-AE-SER-302.SAS DATE: 02DEC2015

＊新薬承認情報提供時に置換えた

Listing of serious adverse events:
Study 109MS302
Page 33 of 75
Treatment group: BG00012 240 mg BID

Subject Sex/Age Race	MedDRA Preferred Term	Study Day Onset (a) (b)	Study Day Res	Dur (days)	Relationship to Study Drug	Severity	Serious	Action Taken with Study Drug	Outcome
644* M/5[redacted] WHITE	Ｈ１Ｎ１インフルエンザ	301	319	19	UNRELATED	MODERATE	Yes	NONE	RESOLVED
645* M/4[redacted] WHITE	顔面骨骨折	197	205	9	UNRELATED	MODERATE	Yes	NONE	RESOLVED
648* F/4[redacted] WHITE	喘息	521	526	6	UNRELATED	MODERATE	Yes	NONE	RESOLVED
[redacted] M/4[redacted] WHITE	多発性硬化症再発	57	61	5	UNRELATED	MILD	Yes	NONE	RESOLVED

(a) #=On or after the subject switched to alternate MS medication
(b) ^=Adverse Event with onset prior to dosing
Abbreviations: Res=Resolution, NR=Not Recovered/Not Resolved, Dur=Duration, NONE=Dose Not Changed, DW=Drug Withdrawn, DI=Drug Interrupted, DR=Dose Reduced, M=Male, F=Female

SOURCE: BG12MS/JAPAN/ISS/L-AE-SER-302.SAS DATE: 02DEC2015

＊新薬承認情報提供時に置換えた

Listing of serious adverse events:
Study 109MS302
Page 34 of 75
Treatment group: BG00012 240 mg BID

Subject Sex/Age Race	MedDRA Preferred Term	Study Day Onset (a) (b)	Study Day Res	Dur (days)	Relationship to Study Drug	Severity	Serious	Action Taken with Study Drug	Outcome
653* F/4[redacted] WHITE	背部痛	524	533	10	UNRELATED	MODERATE	Yes	NONE	RESOLVED
[redacted] M/4[redacted] WHITE	多発性硬化症再発	338	342	5	UNLIKELY	MODERATE	Yes	NONE	RESOLVED
[redacted] F/2[redacted] WHITE	多発性硬化症再発	133	138	6	UNLIKELY	SEVERE	Yes	NONE	RESOLVED
	多発性硬化症再発	504	508	5	UNLIKELY	SEVERE	Yes	NONE	RESOLVED
[redacted] F/3[redacted] WHITE	多発性硬化症再発	540	544	5	UNLIKELY	MODERATE	Yes	NONE	RESOLVED

(a) #=On or after the subject switched to alternate MS medication
(b) ^=Adverse Event with onset prior to dosing
Abbreviations: Res=Resolution, NR=Not Recovered/Not Resolved, Dur=Duration, NONE=Dose Not Changed, DW=Drug Withdrawn, DI=Drug Interrupted, DR=Dose Reduced, M=Male, F=Female

SOURCE: BG12MS/JAPAN/ISS/L-AE-SER-302.SAS DATE: 02DEC2015

＊新薬承認情報提供時に置換えた

Listing of serious adverse events:
Study 109MS302
Page 35 of 75
Treatment group: BG00012 240 mg BID

Subject Sex/Age Race	MedDRA Preferred Term	Study Day Onset (a) (b)	Study Day Res	Dur (days)	Relationship to Study Drug	Severity	Serious	Action Taken with Study Drug	Outcome
191* M/3[redacted] WHITE	多発性硬化症再発	111	117	7	UNRELATED	MODERATE	Yes	NONE	RESOLVED
[redacted] M/5[redacted] WHITE	多発性硬化症再発	53	60	8	UNLIKELY	MILD	Yes	NONE	RESOLVED
	多発性硬化症再発	601#	607	7	UNLIKELY	MILD	Yes	NONE	RESOLVED
[redacted] F/2[redacted] WHITE	多発性硬化症再発	5	10	6	UNLIKELY	MILD	Yes	NONE	RESOLVED
	多発性硬化症再発	131	135	5	UNLIKELY	MILD	Yes	NONE	RESOLVED
	多発性硬化症再発	621#	625	5	UNLIKELY	MILD	Yes	NONE	RESOLVED

(a) #=On or after the subject switched to alternate MS medication
(b) ^=Adverse Event with onset prior to dosing
Abbreviations: Res=Resolution, NR=Not Recovered/Not Resolved, Dur=Duration, NONE=Dose Not Changed, DW=Drug Withdrawn, DI=Drug Interrupted, DR=Dose Reduced, M=Male, F=Female

SOURCE: BG12MS/JAPAN/ISS/L-AE-SER-302.SAS DATE: 02DEC2015

＊新薬承認情報提供時に置換えた

Listing of serious adverse events:
Study 109MS302
Page 36 of 75
Treatment group: BG00012 240 mg BID

Subject Sex/Age Race	MedDRA Preferred Term	Study Day Onset (a) (b)	Study Day Res	Dur (days)	Relationship to Study Drug	Severity	Serious	Action Taken with Study Drug	Outcome
[redacted] F/2[redacted] WHITE	多発性硬化症再発	14	20	7	UNRELATED	MODERATE	Yes	NONE	RESOLVED
[redacted] F/4[redacted] WHITE	多発性硬化症再発	188	194	7	UNRELATED	MODERATE	Yes	NONE	RESOLVED
660* F/4[redacted] WHITE	多発性硬化症再発	37	42	6	UNRELATED	MODERATE	Yes	NONE	RESOLVED
	関節痛	602	611	10	UNRELATED	MODERATE	Yes	NONE	RESOLVED
[redacted] F/3[redacted] WHITE	多発性硬化症再発	370	375	6	UNRELATED	MILD	Yes	NONE	RESOLVED

(a) #=On or after the subject switched to alternate MS medication
(b) ^=Adverse Event with onset prior to dosing
Abbreviations: Res=Resolution, NR=Not Recovered/Not Resolved, Dur=Duration, NONE=Dose Not Changed, DW=Drug Withdrawn, DI=Drug Interrupted, DR=Dose Reduced, M=Male, F=Female

SOURCE: BG12MS/JAPAN/ISS/L-AE-SER-302.SAS DATE: 02DEC2015

＊新薬承認情報提供時に置換えた

Listing of serious adverse events:
Study 109MS302
Page 37 of 75
Treatment group: BG00012 240 mg BID

Subject Sex/Age Race	MedDRA Preferred Term	Study Day Onset (a) (b)	Study Day Res	Dur (days)	Relationship to Study Drug	Severity	Serious	Action Taken with Study Drug	Outcome
[redacted] F/3[redacted] WHITE	多発性硬化症再発	29	33	5	UNRELATED	MILD	Yes	NONE	RESOLVED
665* F/4[redacted] WHITE	多発性硬化症再発	213	218	6	UNRELATED	MODERATE	Yes	NONE	RESOLVED
	子宮平滑筋腫	554	559	6	UNRELATED	MODERATE	Yes	NONE	RESOLVED
[redacted] F/2[redacted] WHITE	多発性硬化症再発	46	50	5	UNRELATED	MODERATE	Yes	NONE	RESOLVED
[redacted] M/4[redacted] WHITE	多発性硬化症再発	34	43	10	UNRELATED	MODERATE	Yes	NONE	RESOLVED

(a) #=On or after the subject switched to alternate MS medication
(b) ^=Adverse Event with onset prior to dosing
Abbreviations: Res=Resolution, NR=Not Recovered/Not Resolved, Dur=Duration, NONE=Dose Not Changed, DW=Drug Withdrawn, DI=Drug Interrupted, DR=Dose Reduced, M=Male, F=Female

SOURCE: BG12MS/JAPAN/ISS/L-AE-SER-302.SAS DATE: 02DEC2015

＊新薬承認情報提供時に置換えた

Listing of serious adverse events:
Study 109MS302
Page 38 of 75
Treatment group: BG00012 240 mg BID

Subject Sex/Age Race	MedDRA Preferred Term	Study Day Onset (a) (b)	Study Day Res	Dur (days)	Relationship to Study Drug	Severity	Serious	Action Taken with Study Drug	Outcome
[redacted] M/2[redacted] WHITE	多発性硬化症再発	27	44	18	UNLIKELY	MODERATE	Yes	NONE	RESOLVED
	多発性硬化症再発	129	167	39	UNLIKELY	MODERATE	Yes	NONE	RESOLVED
[redacted] F/3[redacted] WHITE	多発性硬化症再発	11	22	12	UNLIKELY	MODERATE	Yes	NONE	RESOLVED
	多発性硬化症再発	320	325	6	UNLIKELY	MILD	Yes	NONE	RESOLVED
	多発性硬化症再発	541	545	5	UNLIKELY	MODERATE	Yes	NONE	RESOLVED
669* F/3[redacted] WHITE	乳房腫瘤摘除	339	340	2	UNRELATED	MODERATE	Yes	NONE	RESOLVED

(a) #=On or after the subject switched to alternate MS medication
(b) ^=Adverse Event with onset prior to dosing
Abbreviations: Res=Resolution, NR=Not Recovered/Not Resolved, Dur=Duration, NONE=Dose Not Changed, DW=Drug Withdrawn, DI=Drug Interrupted, DR=Dose Reduced, M=Male, F=Female

SOURCE: BG12MS/JAPAN/ISS/L-AE-SER-302.SAS DATE: 02DEC2015

＊新薬承認情報提供時に置換えた

Listing of serious adverse events:
Study 109MS302
Page 39 of 75
Treatment group: BG00012 240 mg BID

Subject Sex/Age Race	MedDRA Preferred Term	Study Day Onset (a) (b)	Res	Dur (days)	Relationship to Study Drug	Severity	Serious	Action Taken with Study Drug	Outcome
193* F/2[redacted] WHITE	双極１型障害	610	628	19	UNRELATED	MODERATE	Yes	NONE	RESOLVED
	双極１型障害	637	NR		UNRELATED	SEVERE	Yes	DW	NOT RESOLVED
[redacted] F/4[redacted] WHITE	多発性硬化症再発	337	341	5	UNRELATED	MILD	Yes	NONE	RESOLVED
670* F/5[redacted] WHITE	多発性硬化症再発	563	570	8	UNRELATED	MODERATE	Yes	NONE	RESOLVED
	尿路感染	563	570	8	UNRELATED	MODERATE	Yes	NONE	RESOLVED
[redacted] F/4[redacted] WHITE	多発性硬化症再発	253	258	6	UNRELATED	MODERATE	Yes	DI	RESOLVED

(a) #=On or after the subject switched to alternate MS medication
(b) ^=Adverse Event with onset prior to dosing
Abbreviations: Res=Resolution, NR=Not Recovered/Not Resolved, Dur=Duration, NONE=Dose Not Changed, DW=Drug Withdrawn, DI=Drug Interrupted, DR=Dose Reduced, M=Male, F=Female

SOURCE: BG12MS/JAPAN/ISS/L-AE-SER-302.SAS DATE: 02DEC2015

＊新薬承認情報提供時に置換えた

Listing of serious adverse events:
Study 109MS302
Page 40 of 75
Treatment group: BG00012 240 mg BID

Subject Sex/Age Race	MedDRA Preferred Term	Study Day Onset (a) (b)	Study Day Res	Dur (days)	Relationship to Study Drug	Severity	Serious	Action Taken with Study Drug	Outcome
[redacted] F/4[redacted] WHITE	多発性硬化症再発	341	346	6	UNRELATED	MODERATE	Yes	DI	RESOLVED
[redacted] F/4[redacted] WHITE	多発性硬化症再発	183	187	5	UNRELATED	SEVERE	Yes	NONE	RESOLVED
[redacted] F/3[redacted]	治療食	30	64	35	UNRELATED	MILD	Yes	NONE	RESOLVED
194* M/3[redacted]	心房頻脈	576#	578	3	UNRELATED	MODERATE	Yes	NONE	RESOLVED
195* M/3[redacted]	多発性硬化症再発	70	72	3	UNRELATED	MODERATE	Yes	NONE	RESOLVED

(a) #=On or after the subject switched to alternate MS medication
(b) ^=Adverse Event with onset prior to dosing
Abbreviations: Res=Resolution, NR=Not Recovered/Not Resolved, Dur=Duration, NONE=Dose Not Changed, DW=Drug Withdrawn, DI=Drug Interrupted, DR=Dose Reduced, M=Male, F=Female

SOURCE: BG12MS/JAPAN/ISS/L-AE-SER-302.SAS DATE: 02DEC2015

＊新薬承認情報提供時に置換えた

Listing of serious adverse events:
Study 109MS302
Page 41 of 75
Treatment group: BG00012 240 mg BID

Subject Sex/Age Race	MedDRA Preferred Term	Study Day Onset (a) (b)	Study Day Res	Dur (days)	Relationship to Study Drug	Severity	Serious	Action Taken with Study Drug	Outcome
[redacted] M/2[redacted] WHITE	多発性硬化症再発	176	198	23	UNLIKELY	MILD	Yes	NONE	RESOLVED
	多発性硬化症再発	219	232	14	UNLIKELY	MILD	Yes	NONE	RESOLVED
	多発性硬化症再発	552	561	10	UNRELATED	MILD	Yes	NONE	RESOLVED
685* M/2[redacted] HISPANIC	胃腸炎	13	25	13	RELATED	MODERATE	Yes	DR	RESOLVED
[redacted] F/3[redacted] WHITE	多発性硬化症再発	317	325	9	UNLIKELY	MODERATE	Yes	NONE	RESOLVED

(a) #=On or after the subject switched to alternate MS medication
(b) ^=Adverse Event with onset prior to dosing
Abbreviations: Res=Resolution, NR=Not Recovered/Not Resolved, Dur=Duration, NONE=Dose Not Changed, DW=Drug Withdrawn, DI=Drug Interrupted, DR=Dose Reduced, M=Male, F=Female

SOURCE: BG12MS/JAPAN/ISS/L-AE-SER-302.SAS DATE: 02DEC2015

＊新薬承認情報提供時に置換えた

Listing of serious adverse events:
Study 109MS302
Page 42 of 75
Treatment group: BG00012 240 mg BID

Subject Sex/Age Race	MedDRA Preferred Term	Study Day Onset (a) (b)	Study Day Res	Dur (days)	Relationship to Study Drug	Severity	Serious	Action Taken with Study Drug	Outcome
[redacted] F/5[redacted] WHITE	多発性硬化症再発	253	260	8	UNRELATED	MODERATE	Yes	NONE	RESOLVED
[redacted] F/5[redacted] WHITE	多発性硬化症再発	361	365	5	UNLIKELY	MODERATE	Yes	NONE	RESOLVED
689* M/3[redacted] WHITE	外傷性血腫	250	253	4	UNRELATED	MILD	Yes	NONE	RESOLVED

(a) #=On or after the subject switched to alternate MS medication
(b) ^=Adverse Event with onset prior to dosing
Abbreviations: Res=Resolution, NR=Not Recovered/Not Resolved, Dur=Duration, NONE=Dose Not Changed, DW=Drug Withdrawn, DI=Drug Interrupted, DR=Dose Reduced, M=Male, F=Female

SOURCE: BG12MS/JAPAN/ISS/L-AE-SER-302.SAS DATE: 02DEC2015

＊新薬承認情報提供時に置換えた

Listing of serious adverse events:
Study 109MS302
Page 43 of 75
Treatment group: BG00012 240 mg TID

Subject Sex/Age Race	MedDRA Preferred Term	Study Day Onset (a) (b)	Study Day Res	Dur (days)	Relationship to Study Drug	Severity	Serious	Action Taken with Study Drug	Outcome
594* F/4[redacted] ASIAN	発熱	38	42	5	UNRELATED	SEVERE	Yes	NONE	RESOLVED
	尿中β２ミクログロブリン増加	274	276	3	POSSIBLY	MILD	Yes	NONE	RESOLVED
596* F/2[redacted] ASIAN	十二指腸炎	18	19	2	POSSIBLY	SEVERE	Yes	DI	RESOLVED
597* F/2[redacted] ASIAN	胃腸炎	14	16	3	UNRELATED	MODERATE	Yes	NONE	RESOLVED
[redacted] M/3[redacted] ASIAN	多発性硬化症再発	589	591	3	UNRELATED	MODERATE	Yes	NONE	RESOLVED

(a) #=On or after the subject switched to alternate MS medication
(b) ^=Adverse Event with onset prior to dosing
Abbreviations: Res=Resolution, NR=Not Recovered/Not Resolved, Dur=Duration, NONE=Dose Not Changed, DW=Drug Withdrawn, DI=Drug Interrupted, DR=Dose Reduced, M=Male, F=Female

SOURCE: BG12MS/JAPAN/ISS/L-AE-SER-302.SAS DATE: 02DEC2015

＊新薬承認情報提供時に置換えた

Listing of serious adverse events:
Study 109MS302
Page 44 of 75
Treatment group: BG00012 240 mg TID

Subject Sex/Age Race	MedDRA Preferred Term	Study Day Onset (a) (b)	Study Day Res	Dur (days)	Relationship to Study Drug	Severity	Serious	Action Taken with Study Drug	Outcome
603* F/2[redacted] ASIAN	片頭痛	104	120	17	POSSIBLY	SEVERE	Yes	NONE	RESOLVED
	多発性硬化症再発	110	154	45	POSSIBLY	SEVERE	Yes	NONE	RESOLVED
613* F/3[redacted] WHITE	椎間板手術	645	645	1	UNRELATED	MODERATE	Yes	NONE	RESOLVED
615* F/4[redacted] WHITE	腸閉塞	360	365	6	UNRELATED	SEVERE	Yes	DI	RESOLVED
656* M/4[redacted] WHITE	アルコール中毒	573			UNRELATED	MODERATE	Yes	NONE	RESOLVED

(a) #=On or after the subject switched to alternate MS medication
(b) ^=Adverse Event with onset prior to dosing
Abbreviations: Res=Resolution, NR=Not Recovered/Not Resolved, Dur=Duration, NONE=Dose Not Changed, DW=Drug Withdrawn, DI=Drug Interrupted, DR=Dose Reduced, M=Male, F=Female

SOURCE: BG12MS/JAPAN/ISS/L-AE-SER-302.SAS DATE: 02DEC2015

＊新薬承認情報提供時に置換えた

Listing of serious adverse events:
Study 109MS302
Page 45 of 75
Treatment group: BG00012 240 mg TID

Subject Sex/Age Race	MedDRA Preferred Term	Study Day Onset (a) (b)	Study Day Res	Dur (days)	Relationship to Study Drug	Severity	Serious	Action Taken with Study Drug	Outcome
619* F/3[redacted] WHITE	大発作痙攣	172	172	1	UNLIKELY	SEVERE	Yes	NONE	RESOLVED
621* M/4[redacted] WHITE	無力症	244	245	2	UNRELATED	SEVERE	Yes	DI	RESOLVED
	構語障害	244	245	2	UNRELATED	SEVERE	Yes	DI	RESOLVED
623* F/2[redacted] WHITE	頭痛	526	528	3	UNRELATED	SEVERE	Yes	NONE	RESOLVED
	肉離れ	526	528	3	UNRELATED	SEVERE	Yes	NONE	RESOLVED
	後頭神経痛	526	528	3	UNRELATED	SEVERE	Yes	NONE	RESOLVED
	良性頭蓋内圧亢進	550	NR		UNRELATED	MODERATE	Yes	NONE	NOT RESOLVED
	嘔吐	646	648	3	UNRELATED	MODERATE	Yes	NONE	RESOLVED

(a) #=On or after the subject switched to alternate MS medication
(b) ^=Adverse Event with onset prior to dosing
Abbreviations: Res=Resolution, NR=Not Recovered/Not Resolved, Dur=Duration, NONE=Dose Not Changed, DW=Drug Withdrawn, DI=Drug Interrupted, DR=Dose Reduced, M=Male, F=Female

SOURCE: BG12MS/JAPAN/ISS/L-AE-SER-302.SAS DATE: 02DEC2015

＊新薬承認情報提供時に置換えた

Listing of serious adverse events:
Study 109MS302
Page 46 of 75
Treatment group: BG00012 240 mg TID

Subject Sex/Age Race	MedDRA Preferred Term	Study Day Onset (a) (b)	Study Day Res	Dur (days)	Relationship to Study Drug	Severity	Serious	Action Taken with Study Drug	Outcome
287* F/4[redacted] WHITE	自殺企図	187	193	7	UNRELATED	SEVERE	Yes	NONE	RESOLVED
625* F/4[redacted] WHITE	肉離れ	224	225	2	UNRELATED	MODERATE	Yes	DI	RESOLVED
	蜂巣炎	639	649	11	POSSIBLY	MODERATE	Yes	NONE	RESOLVED
626* F/5[redacted] WHITE	手首関節骨折	483	484	2	UNRELATED	SEVERE	Yes	NONE	RESOLVED
629* F/4[redacted] WHITE	下肢静止不能症候群	616	620	5	UNRELATED	MILD	Yes	NONE	RESOLVED

(a) #=On or after the subject switched to alternate MS medication
(b) ^=Adverse Event with onset prior to dosing
Abbreviations: Res=Resolution, NR=Not Recovered/Not Resolved, Dur=Duration, NONE=Dose Not Changed, DW=Drug Withdrawn, DI=Drug Interrupted, DR=Dose Reduced, M=Male, F=Female

SOURCE: BG12MS/JAPAN/ISS/L-AE-SER-302.SAS DATE: 02DEC2015

＊新薬承認情報提供時に置換えた

Listing of serious adverse events:
Study 109MS302
Page 47 of 75
Treatment group: BG00012 240 mg TID

Subject Sex/Age Race	MedDRA Preferred Term	Study Day Onset (a) (b)	Study Day Res	Dur (days)	Relationship to Study Drug	Severity	Serious	Action Taken with Study Drug	Outcome
289* F/4[redacted] WHITE	脱水	21	24	4	POSSIBLY	SEVERE	Yes	DI	RESOLVED
	ウイルス性胃腸炎	21	24	4	POSSIBLY	SEVERE	Yes	DI	RESOLVED
[redacted] F/2[redacted] WHITE	多発性硬化症再発	244	248	5	UNLIKELY	MODERATE	Yes	NONE	RESOLVED
631* F/2[redacted] WHITE	急性腎盂腎炎	187	199	13	UNRELATED	MODERATE	Yes	NONE	RESOLVED
	膀胱穿孔	210	233	24	UNRELATED	SEVERE	Yes	NONE	RESOLVED
	ダグラス窩膿瘍	210	233	24	UNRELATED	SEVERE	Yes	NONE	RESOLVED

(a) #=On or after the subject switched to alternate MS medication
(b) ^=Adverse Event with onset prior to dosing
Abbreviations: Res=Resolution, NR=Not Recovered/Not Resolved, Dur=Duration, NONE=Dose Not Changed, DW=Drug Withdrawn, DI=Drug Interrupted, DR=Dose Reduced, M=Male, F=Female

SOURCE: BG12MS/JAPAN/ISS/L-AE-SER-302.SAS DATE: 02DEC2015

＊新薬承認情報提供時に置換えた

Listing of serious adverse events:
Study 109MS302
Page 48 of 75
Treatment group: BG00012 240 mg TID

Subject Sex/Age Race	MedDRA Preferred Term	Study Day Onset (a) (b)	Study Day Res	Dur (days)	Relationship to Study Drug	Severity	Serious	Action Taken with Study Drug	Outcome
[redacted] M/3[redacted] WHITE	多発性硬化症再発	127	148	22	UNRELATED	MODERATE	Yes	NONE	RESOLVED
[redacted] M/2[redacted] WHITE	多発性硬化症再発	31	51	21	UNRELATED	MODERATE	Yes	NONE	RESOLVED
[redacted] M/4[redacted] WHITE	多発性硬化症再発	27	36	10	UNRELATED	MILD	Yes	NONE	RESOLVED
294* F/4[redacted] WHITE	冠動脈疾患	458#	460	3	UNRELATED	MODERATE	Yes	NONE	RESOLVED
	狭心症	520#			UNRELATED	SEVERE	Yes	NONE	RESOLVED

(a) #=On or after the subject switched to alternate MS medication
(b) ^=Adverse Event with onset prior to dosing
Abbreviations: Res=Resolution, NR=Not Recovered/Not Resolved, Dur=Duration, NONE=Dose Not Changed, DW=Drug Withdrawn, DI=Drug Interrupted, DR=Dose Reduced, M=Male, F=Female

SOURCE: BG12MS/JAPAN/ISS/L-AE-SER-302.SAS DATE: 02DEC2015

＊新薬承認情報提供時に置換えた

Listing of serious adverse events:
Study 109MS302
Page 49 of 75
Treatment group: BG00012 240 mg TID

Subject Sex/Age Race	MedDRA Preferred Term	Study Day Onset (a) (b)	Study Day Res	Dur (days)	Relationship to Study Drug	Severity	Serious	Action Taken with Study Drug	Outcome
296* F/2[redacted] WHITE	多発性硬化症再発	331	332	2	UNLIKELY	MILD	Yes	DI	RESOLVED
[redacted] F/3[redacted] WHITE	多発性硬化症再発	396	407	12	UNRELATED	MILD	Yes	NONE	RESOLVED
647* F/4[redacted] WHITE	胆管結石	53	65	13	UNLIKELY	MILD	Yes	DI	RESOLVED
	胆石症	53	65	13	UNLIKELY	MILD	Yes	DI	RESOLVED
652* F/4[redacted] WHITE	変形性脊椎症	435	447	13	UNRELATED	MILD	Yes	NONE	RESOLVED

(a) #=On or after the subject switched to alternate MS medication
(b) ^=Adverse Event with onset prior to dosing
Abbreviations: Res=Resolution, NR=Not Recovered/Not Resolved, Dur=Duration, NONE=Dose Not Changed, DW=Drug Withdrawn, DI=Drug Interrupted, DR=Dose Reduced, M=Male, F=Female

SOURCE: BG12MS/JAPAN/ISS/L-AE-SER-302.SAS DATE: 02DEC2015

＊新薬承認情報提供時に置換えた

Listing of serious adverse events:
Study 109MS302
Page 50 of 75
Treatment group: BG00012 240 mg TID

Subject Sex/Age Race	MedDRA Preferred Term	Study Day Onset (a) (b)	Study Day Res	Dur (days)	Relationship to Study Drug	Severity	Serious	Action Taken with Study Drug	Outcome
[redacted] F/3[redacted] WHITE	多発性硬化症再発	177	181	5	UNLIKELY	MODERATE	Yes	NONE	RESOLVED
	多発性硬化症再発	388	393	6	UNLIKELY	MODERATE	Yes	NONE	RESOLVED
[redacted] M/5[redacted] WHITE	多発性硬化症再発	280	285	6	UNLIKELY	SEVERE	Yes	NONE	RESOLVED
[redacted] M/1[redacted] WHITE	多発性硬化症再発	168	173	6	UNRELATED	MODERATE	Yes	NONE	RESOLVED
[redacted] F/2[redacted] WHITE	多発性硬化症再発	556	560	5	UNLIKELY	MODERATE	Yes	NONE	RESOLVED

(a) #=On or after the subject switched to alternate MS medication
(b) ^=Adverse Event with onset prior to dosing
Abbreviations: Res=Resolution, NR=Not Recovered/Not Resolved, Dur=Duration, NONE=Dose Not Changed, DW=Drug Withdrawn, DI=Drug Interrupted, DR=Dose Reduced, M=Male, F=Female

SOURCE: BG12MS/JAPAN/ISS/L-AE-SER-302.SAS DATE: 02DEC2015

＊新薬承認情報提供時に置換えた

Listing of serious adverse events:
Study 109MS302
Page 51 of 75
Treatment group: BG00012 240 mg TID

Subject Sex/Age Race	MedDRA Preferred Term	Study Day Onset (a) (b)	Study Day Res	Dur (days)	Relationship to Study Drug	Severity	Serious	Action Taken with Study Drug	Outcome
[redacted] F/5[redacted] WHITE	多発性硬化症再発	228	235	8	UNLIKELY	MODERATE	Yes	NONE	RESOLVED
[redacted] F/5[redacted] WHITE	多発性硬化症再発	400	404	5	UNLIKELY	MILD	Yes	NONE	RESOLVED
[redacted] F/5[redacted] WHITE	多発性硬化症再発	393	397	5	UNRELATED	MODERATE	Yes	NONE	RESOLVED
[redacted] F/3[redacted] WHITE	多発性硬化症再発	77	168	92	UNRELATED	MODERATE	Yes	NONE	RESOLVED
	多発性硬化症再発	296	300	5	UNRELATED	MODERATE	Yes	NONE	RESOLVED

(a) #=On or after the subject switched to alternate MS medication
(b) ^=Adverse Event with onset prior to dosing
Abbreviations: Res=Resolution, NR=Not Recovered/Not Resolved, Dur=Duration, NONE=Dose Not Changed, DW=Drug Withdrawn, DI=Drug Interrupted, DR=Dose Reduced, M=Male, F=Female

SOURCE: BG12MS/JAPAN/ISS/L-AE-SER-302.SAS DATE: 02DEC2015

＊新薬承認情報提供時に置換えた

Listing of serious adverse events:
Study 109MS302
Page 52 of 75
Treatment group: BG00012 240 mg TID

Subject Sex/Age Race	MedDRA Preferred Term	Study Day Onset (a) (b)	Study Day Res	Dur (days)	Relationship to Study Drug	Severity	Serious	Action Taken with Study Drug	Outcome
661* F/4[redacted] WHITE	多発性硬化症再発	91	96	6	UNRELATED	MODERATE	Yes	NONE	RESOLVED
	不正子宮出血	295	296	2	UNRELATED	MILD	Yes	NONE	RESOLVED
[redacted] M/2[redacted] WHITE	多発性硬化症再発	253	257	5	UNRELATED	MODERATE	Yes	NONE	RESOLVED
667* M/3[redacted] WHITE	多発性硬化症再発	25	29	5	UNRELATED	MODERATE	Yes	NONE	RESOLVED
	腹痛	500#	506	7	UNLIKELY	SEVERE	Yes	NONE	RESOLVED
668* F/5[redacted] WHITE	変形性関節症	649	653	5	UNRELATED	MODERATE	Yes	NONE	RESOLVED

(a) #=On or after the subject switched to alternate MS medication
(b) ^=Adverse Event with onset prior to dosing
Abbreviations: Res=Resolution, NR=Not Recovered/Not Resolved, Dur=Duration, NONE=Dose Not Changed, DW=Drug Withdrawn, DI=Drug Interrupted, DR=Dose Reduced, M=Male, F=Female

SOURCE: BG12MS/JAPAN/ISS/L-AE-SER-302.SAS DATE: 02DEC2015

＊新薬承認情報提供時に置換えた

Listing of serious adverse events:
Study 109MS302
Page 53 of 75
Treatment group: BG00012 240 mg TID

Subject Sex/Age Race	MedDRA Preferred Term	Study Day Onset (a) (b)	Study Day Res	Dur (days)	Relationship to Study Drug	Severity	Serious	Action Taken with Study Drug	Outcome
311* M/4[redacted] WHITE	尿路感染	59	66	8	UNRELATED	SEVERE	Yes	DW	RESOLVED
673* F/5[redacted]	多発性硬化症再発	148	169	22	UNRELATED	MODERATE	Yes	NONE	RESOLVED
	多発性硬化症再発	463	469	7	UNRELATED	MODERATE	Yes	NONE	RESOLVED
	うつ病	533	536	4	UNRELATED	SEVERE	Yes	NONE	RESOLVED
	尿失禁	590	592	3	UNRELATED	MODERATE	Yes	NONE	RESOLVED
	多発性硬化症再発	647	651	5	UNRELATED	MILD	Yes	NONE	RESOLVED
674* F/3[redacted]	大腿骨骨折	448	558	111	UNRELATED	SEVERE	Yes	DI	RESOLVED
	交通事故	448	448	1	UNRELATED	SEVERE	Yes	DI	RESOLVED

(a) #=On or after the subject switched to alternate MS medication
(b) ^=Adverse Event with onset prior to dosing
Abbreviations: Res=Resolution, NR=Not Recovered/Not Resolved, Dur=Duration, NONE=Dose Not Changed, DW=Drug Withdrawn, DI=Drug Interrupted, DR=Dose Reduced, M=Male, F=Female

SOURCE: BG12MS/JAPAN/ISS/L-AE-SER-302.SAS DATE: 02DEC2015

＊新薬承認情報提供時に置換えた

Listing of serious adverse events:
Study 109MS302
Page 54 of 75
Treatment group: BG00012 240 mg TID

Subject Sex/Age Race	MedDRA Preferred Term	Study Day Onset (a) (b)	Study Day Res	Dur (days)	Relationship to Study Drug	Severity	Serious	Action Taken with Study Drug	Outcome
677* F/3[redacted]	臍ヘルニア	314	319	6	UNRELATED	MODERATE	Yes	NONE	RESOLVED
[redacted] F/3[redacted]	多発性硬化症再発	50			UNRELATED	MILD	Yes	NONE	RESOLVED
[redacted] M/2[redacted] WHITE	多発性硬化症再発	12	21	10	UNRELATED	MODERATE	Yes	NONE	RESOLVED
	多発性硬化症再発	442	450	9	UNRELATED	MODERATE	Yes	NONE	RESOLVED
[redacted] F/3[redacted] WHITE	多発性硬化症再発	552	561	10	UNLIKELY	MILD	Yes	NONE	RESOLVED

(a) #=On or after the subject switched to alternate MS medication
(b) ^=Adverse Event with onset prior to dosing
Abbreviations: Res=Resolution, NR=Not Recovered/Not Resolved, Dur=Duration, NONE=Dose Not Changed, DW=Drug Withdrawn, DI=Drug Interrupted, DR=Dose Reduced, M=Male, F=Female

SOURCE: BG12MS/JAPAN/ISS/L-AE-SER-302.SAS DATE: 02DEC2015

＊新薬承認情報提供時に置換えた

Listing of serious adverse events:
Study 109MS302
Page 55 of 75
Treatment group: BG00012 240 mg TID

Subject Sex/Age Race	MedDRA Preferred Term	Study Day Onset (a) (b)	Study Day Res	Dur (days)	Relationship to Study Drug	Severity	Serious	Action Taken with Study Drug	Outcome
681* F/4[redacted] WHITE	胃腸出血	111	134	24	POSSIBLY	MODERATE	Yes	DI	RESOLVED
	多発性硬化症再発	474	485	12	UNRELATED	MILD	Yes	NONE	RESOLVED
	多発性硬化症再発	548	558	11	UNRELATED	MILD	Yes	NONE	RESOLVED
682* F/3[redacted] WHITE	多発性硬化症再発	585	620	36	UNRELATED	MILD	Yes	NONE	RESOLVED
	徐脈	591	620	30	POSSIBLY	MILD	Yes	NONE	RESOLVED
	末梢性浮腫	591	620	30	UNRELATED	MILD	Yes	NONE	RESOLVED
316* F/4[redacted] HISPANIC	多発性硬化症再発	43	47	5	UNRELATED	MODERATE	Yes	DW	RESOLVED

(a) #=On or after the subject switched to alternate MS medication
(b) ^=Adverse Event with onset prior to dosing
Abbreviations: Res=Resolution, NR=Not Recovered/Not Resolved, Dur=Duration, NONE=Dose Not Changed, DW=Drug Withdrawn, DI=Drug Interrupted, DR=Dose Reduced, M=Male, F=Female

SOURCE: BG12MS/JAPAN/ISS/L-AE-SER-302.SAS DATE: 02DEC2015

＊新薬承認情報提供時に置換えた

Listing of serious adverse events:
Study 109MS302
Page 56 of 75
Treatment group: BG00012 240 mg TID

Subject Sex/Age Race	MedDRA Preferred Term	Study Day Onset (a) (b)	Study Day Res	Dur (days)	Relationship to Study Drug	Severity	Serious	Action Taken with Study Drug	Outcome
683* M/4[redacted] HISPANIC	胃腸炎	293	295	3	UNRELATED	MODERATE	Yes	NONE	RESOLVED
686* F/2[redacted] LATINA	骨盤内炎症性疾患	510	512	3	UNRELATED	MILD	Yes	DI	RESOLVED
[redacted] M/4[redacted] WHITE	多発性硬化症再発	93	95	3	UNLIKELY	MODERATE	Yes	NONE	RESOLVED
345* F/5[redacted] WHITE	多発性硬化症再発	203	218	16	UNRELATED	SEVERE	Yes	NONE	RESOLVED

(a) #=On or after the subject switched to alternate MS medication
(b) ^=Adverse Event with onset prior to dosing
Abbreviations: Res=Resolution, NR=Not Recovered/Not Resolved, Dur=Duration, NONE=Dose Not Changed, DW=Drug Withdrawn, DI=Drug Interrupted, DR=Dose Reduced, M=Male, F=Female

SOURCE: BG12MS/JAPAN/ISS/L-AE-SER-302.SAS DATE: 02DEC2015

＊新薬承認情報提供時に置換えた

Listing of serious adverse events:
Study 109MS302
Page 57 of 75
Treatment group: BG00012 240 mg TID

Subject Sex/Age Race	MedDRA Preferred Term	Study Day Onset (a) (b)	Study Day Res	Dur (days)	Relationship to Study Drug	Severity	Serious	Action Taken with Study Drug	Outcome
[redacted] F/5[redacted] WHITE	多発性硬化症再発	93	99	7	UNRELATED	MODERATE	Yes	NONE	RESOLVED
	多発性硬化症再発	416	421	6	UNRELATED	MODERATE	Yes	NONE	RESOLVED
[redacted] M/2[redacted] WHITE	多発性硬化症再発	297	300	4	UNRELATED	MODERATE	Yes	NONE	RESOLVED
690* F/4[redacted] WHITE	閉塞性ヘルニア	569	576	8	UNRELATED	MODERATE	Yes	DI	RESOLVED

(a) #=On or after the subject switched to alternate MS medication
(b) ^=Adverse Event with onset prior to dosing
Abbreviations: Res=Resolution, NR=Not Recovered/Not Resolved, Dur=Duration, NONE=Dose Not Changed, DW=Drug Withdrawn, DI=Drug Interrupted, DR=Dose Reduced, M=Male, F=Female

SOURCE: BG12MS/JAPAN/ISS/L-AE-SER-302.SAS DATE: 02DEC2015

＊新薬承認情報提供時に置換えた

Listing of serious adverse events:
Study 109MS302
Page 58 of 75
Treatment group: GA

Subject Sex/Age Race	MedDRA Preferred Term	Study Day Onset (a) (b)	Study Day Res	Dur (days)	Relationship to Study Drug	Severity	Serious	Action Taken with Study Drug	Outcome
595* F/4[redacted] ASIAN	多発性硬化症再発	252	293	42	UNRELATED	MODERATE	Yes	NONE	RESOLVED
	多発性硬化症再発	517	532	16	UNRELATED	SEVERE	Yes	NONE	RESOLVED
	そう痒性皮疹	594#	616	23	UNRELATED	SEVERE	Yes	NONE	RESOLVED
320* F/4[redacted] ASIAN	アナフィラキシー反応	127	128	2	POSSIBLY	MODERATE	Yes	DW	RESOLVED
321* F/3[redacted] ASIAN	股関節手術	314#	332	19	UNRELATED	SEVERE	Yes	NONE	RESOLVED
	股関節手術	510#	523	14	UNRELATED	SEVERE	Yes	NONE	RESOLVED

(a) #=On or after the subject switched to alternate MS medication
(b) ^=Adverse Event with onset prior to dosing
Abbreviations: Res=Resolution, NR=Not Recovered/Not Resolved, Dur=Duration, NONE=Dose Not Changed, DW=Drug Withdrawn, DI=Drug Interrupted, DR=Dose Reduced, M=Male, F=Female

SOURCE: BG12MS/JAPAN/ISS/L-AE-SER-302.SAS DATE: 02DEC2015

＊新薬承認情報提供時に置換えた

Listing of serious adverse events:
Study 109MS302
Page 59 of 75
Treatment group: GA

Subject Sex/Age Race	MedDRA Preferred Term	Study Day Onset (a) (b)	Study Day Res	Dur (days)	Relationship to Study Drug	Severity	Serious	Action Taken with Study Drug	Outcome
[redacted] M/3[redacted] ASIAN	多発性硬化症再発	543	548	6	UNRELATED	SEVERE	Yes	DI	RESOLVED
605* F/3[redacted] ASIAN	多発性硬化症再発	226	231	6	UNLIKELY	MODERATE	Yes	NONE	RESOLVED
	褥瘡性潰瘍	406#	513	108	UNLIKELY	MODERATE	Yes	NONE	RESOLVED
608* M/4[redacted] WHITE	基底細胞癌	652	652	1	UNRELATED	SEVERE	Yes	NONE	RESOLVED

(a) #=On or after the subject switched to alternate MS medication
(b) ^=Adverse Event with onset prior to dosing
Abbreviations: Res=Resolution, NR=Not Recovered/Not Resolved, Dur=Duration, NONE=Dose Not Changed, DW=Drug Withdrawn, DI=Drug Interrupted, DR=Dose Reduced, M=Male, F=Female

SOURCE: BG12MS/JAPAN/ISS/L-AE-SER-302.SAS DATE: 02DEC2015

＊新薬承認情報提供時に置換えた

Listing of serious adverse events:
Study 109MS302
Page 60 of 75
Treatment group: GA

Subject Sex/Age Race	MedDRA Preferred Term	Study Day Onset (a) (b)	Study Day Res	Dur (days)	Relationship to Study Drug	Severity	Serious	Action Taken with Study Drug	Outcome
[redacted] F/5[redacted] BLACK OR AFRICAN AMERICAN	多発性硬化症再発	6	8	3	UNRELATED	SEVERE	Yes	NONE	RESOLVED
618* F/5[redacted] WHITE	自殺企図	644	645	2	UNRELATED	SEVERE	Yes	NONE	RESOLVED
620* F/2[redacted] WHITE	うつ病	8	34	27	UNLIKELY	SEVERE	Yes	NONE	RESOLVED
	多発性硬化症再発	92	95	4	UNLIKELY	MODERATE	Yes	NONE	RESOLVED

(a) #=On or after the subject switched to alternate MS medication
(b) ^=Adverse Event with onset prior to dosing
Abbreviations: Res=Resolution, NR=Not Recovered/Not Resolved, Dur=Duration, NONE=Dose Not Changed, DW=Drug Withdrawn, DI=Drug Interrupted, DR=Dose Reduced, M=Male, F=Female

SOURCE: BG12MS/JAPAN/ISS/L-AE-SER-302.SAS DATE: 02DEC2015

＊新薬承認情報提供時に置換えた

Listing of serious adverse events:
Study 109MS302
Page 61 of 75
Treatment group: GA

Subject Sex/Age Race	MedDRA Preferred Term	Study Day Onset (a) (b)	Study Day Res	Dur (days)	Relationship to Study Drug	Severity	Serious	Action Taken with Study Drug	Outcome
622* M/2[redacted] WHITE	大発作痙攣	617	617	1	UNRELATED	SEVERE	Yes	NONE	RESOLVED
[redacted] F/5[redacted] WHITE	外傷性血腫	-8^	78	87	UNRELATED	MODERATE	Yes	NONE	RESOLVED
331* F/2[redacted] WHITE	多発性硬化症再発	69	71	3	UNRELATED	SEVERE	Yes	DI	RESOLVED
[redacted] M/3[redacted] WHITE	多発性硬化症再発	595	597	3	UNRELATED	MILD	Yes	NONE	RESOLVED

(a) #=On or after the subject switched to alternate MS medication
(b) ^=Adverse Event with onset prior to dosing
Abbreviations: Res=Resolution, NR=Not Recovered/Not Resolved, Dur=Duration, NONE=Dose Not Changed, DW=Drug Withdrawn, DI=Drug Interrupted, DR=Dose Reduced, M=Male, F=Female

SOURCE: BG12MS/JAPAN/ISS/L-AE-SER-302.SAS DATE: 02DEC2015

＊新薬承認情報提供時に置換えた

Listing of serious adverse events:
Study 109MS302
Page 62 of 75
Treatment group: GA

Subject Sex/Age Race	MedDRA Preferred Term	Study Day Onset (a) (b)	Study Day Res	Dur (days)	Relationship to Study Drug	Severity	Serious	Action Taken with Study Drug	Outcome
[redacted] F/4[redacted] WHITE	多発性硬化症再発	98	117	20	UNRELATED	MILD	Yes	NONE	RESOLVED
[redacted] F/5[redacted] WHITE	多発性硬化症再発	38	43	6	UNLIKELY	SEVERE	Yes	NONE	RESOLVED
	多発性硬化症再発	172	177	6	UNLIKELY	MODERATE	Yes	NONE	RESOLVED
[redacted] F/4[redacted] WHITE	多発性硬化症再発	668	674	7	UNRELATED	SEVERE	Yes	NONE	RESOLVED
310* F/3[redacted] WHITE	過敏症	91	93	3	RELATED	SEVERE	Yes	DW	RESOLVED

(a) #=On or after the subject switched to alternate MS medication
(b) ^=Adverse Event with onset prior to dosing
Abbreviations: Res=Resolution, NR=Not Recovered/Not Resolved, Dur=Duration, NONE=Dose Not Changed, DW=Drug Withdrawn, DI=Drug Interrupted, DR=Dose Reduced, M=Male, F=Female

SOURCE: BG12MS/JAPAN/ISS/L-AE-SER-302.SAS DATE: 02DEC2015

＊新薬承認情報提供時に置換えた

Listing of serious adverse events:
Study 109MS302
Page 63 of 75
Treatment group: GA

Subject Sex/Age Race	MedDRA Preferred Term	Study Day Onset (a) (b)	Study Day Res	Dur (days)	Relationship to Study Drug	Severity	Serious	Action Taken with Study Drug	Outcome
324* F/3[redacted] WHITE	末梢性浮腫	194	342	149	POSSIBLY	MODERATE	Yes	DW	RESOLVED
[redacted] M/2[redacted] WHITE	多発性硬化症再発	204	221	18	UNRELATED	MODERATE	Yes	NONE	RESOLVED
635* F/4[redacted] WHITE	子宮出血	320	321	2	UNRELATED	MILD	Yes	NONE	RESOLVED
638* F/5[redacted] WHITE	橈骨骨折	387	387	1	UNRELATED	SEVERE	Yes	NONE	RESOLVED

(a) #=On or after the subject switched to alternate MS medication
(b) ^=Adverse Event with onset prior to dosing
Abbreviations: Res=Resolution, NR=Not Recovered/Not Resolved, Dur=Duration, NONE=Dose Not Changed, DW=Drug Withdrawn, DI=Drug Interrupted, DR=Dose Reduced, M=Male, F=Female

SOURCE: BG12MS/JAPAN/ISS/L-AE-SER-302.SAS DATE: 02DEC2015

＊新薬承認情報提供時に置換えた

Listing of serious adverse events:
Study 109MS302
Page 64 of 75
Treatment group: GA

Subject Sex/Age Race	MedDRA Preferred Term	Study Day Onset (a) (b)	Study Day Res	Dur (days)	Relationship to Study Drug	Severity	Serious	Action Taken with Study Drug	Outcome
339* F/2[redacted] WHITE	多発性硬化症再発	154	254	101	UNRELATED	MODERATE	Yes	NONE	RESOLVED
641* M/3[redacted] WHITE	自殺念慮	53	92	40	UNRELATED	SEVERE	Yes	NONE	RESOLVED
	交通事故	162	162	1	UNRELATED	SEVERE	Yes	NONE	RESOLVED
	むち打ち損傷	178	226	49	UNRELATED	MODERATE	Yes	NONE	RESOLVED
	うつ病	399	505	107	UNRELATED	SEVERE	Yes	NONE	RESOLVED
643* F/3[redacted] WHITE	失語症	16	19	4	UNLIKELY	MILD	Yes	DI	RESOLVED
	意識消失	16	19	4	UNLIKELY	MILD	Yes	DI	RESOLVED

(a) #=On or after the subject switched to alternate MS medication
(b) ^=Adverse Event with onset prior to dosing
Abbreviations: Res=Resolution, NR=Not Recovered/Not Resolved, Dur=Duration, NONE=Dose Not Changed, DW=Drug Withdrawn, DI=Drug Interrupted, DR=Dose Reduced, M=Male, F=Female

SOURCE: BG12MS/JAPAN/ISS/L-AE-SER-302.SAS DATE: 02DEC2015

＊新薬承認情報提供時に置換えた

Listing of serious adverse events:
Study 109MS302
Page 65 of 75
Treatment group: GA

Subject Sex/Age Race	MedDRA Preferred Term	Study Day Onset (a) (b)	Study Day Res	Dur (days)	Relationship to Study Drug	Severity	Serious	Action Taken with Study Drug	Outcome
646* F/4[redacted] WHITE	子宮頚部癌	336	NR		UNLIKELY	MODERATE	Yes	NONE	NOT RESOLVED
[redacted] F/3[redacted] WHITE	不妊手術	121	124	4	UNRELATED	MODERATE	Yes	DI	RESOLVED
650* F/3[redacted] WHITE	多発性硬化症再発	595	599	5	UNRELATED	MODERATE	Yes	NONE	RESOLVED
[redacted] M/3[redacted] WHITE	多発性硬化症再発	143	150	8	UNLIKELY	SEVERE	Yes	NONE	RESOLVED

(a) #=On or after the subject switched to alternate MS medication
(b) ^=Adverse Event with onset prior to dosing
Abbreviations: Res=Resolution, NR=Not Recovered/Not Resolved, Dur=Duration, NONE=Dose Not Changed, DW=Drug Withdrawn, DI=Drug Interrupted, DR=Dose Reduced, M=Male, F=Female

SOURCE: BG12MS/JAPAN/ISS/L-AE-SER-302.SAS DATE: 02DEC2015

＊新薬承認情報提供時に置換えた

Listing of serious adverse events:
Study 109MS302
Page 66 of 75
Treatment group: GA

Subject Sex/Age Race	MedDRA Preferred Term	Study Day Onset (a) (b)	Study Day Res	Dur (days)	Relationship to Study Drug	Severity	Serious	Action Taken with Study Drug	Outcome
[redacted] F/3[redacted] WHITE	多発性硬化症再発	200	204	5	UNLIKELY	SEVERE	Yes	NONE	RESOLVED
655* M/4[redacted] WHITE	肺炎	518	539	22	UNLIKELY	MODERATE	Yes	DI	RESOLVED
	膿胸	518	539	22	UNLIKELY	MODERATE	Yes	DI	RESOLVED
[redacted] F/2[redacted] WHITE	多発性硬化症再発	3	9	7	UNRELATED	MODERATE	Yes	NONE	RESOLVED
383* F/4[redacted] WHITE	多発性硬化症再発	240	244	5	UNRELATED	MODERATE	Yes	NONE	RESOLVED

(a) #=On or after the subject switched to alternate MS medication
(b) ^=Adverse Event with onset prior to dosing
Abbreviations: Res=Resolution, NR=Not Recovered/Not Resolved, Dur=Duration, NONE=Dose Not Changed, DW=Drug Withdrawn, DI=Drug Interrupted, DR=Dose Reduced, M=Male, F=Female

SOURCE: BG12MS/JAPAN/ISS/L-AE-SER-302.SAS DATE: 02DEC2015

＊新薬承認情報提供時に置換えた

Listing of serious adverse events:
Study 109MS302
Page 67 of 75
Treatment group: GA

Subject Sex/Age Race	MedDRA Preferred Term	Study Day Onset (a) (b)	Study Day Res	Dur (days)	Relationship to Study Drug	Severity	Serious	Action Taken with Study Drug	Outcome
[redacted] F/3[redacted] WHITE	多発性硬化症再発	448	452	5	UNRELATED	MODERATE	Yes	NONE	RESOLVED
	多発性硬化症再発	539	546	8	UNRELATED	MODERATE	Yes	NONE	RESOLVED
616* F/4[redacted] WHITE	多発性硬化症再発	280	287	8	UNRELATED	MODERATE	Yes	NONE	RESOLVED
	深部静脈血栓症	290	293	4	UNRELATED	MODERATE	Yes	NONE	RESOLVED
657* F/5[redacted] WHITE	子宮平滑筋腫	320	323	4	UNRELATED	MODERATE	Yes	NONE	RESOLVED

(a) #=On or after the subject switched to alternate MS medication
(b) ^=Adverse Event with onset prior to dosing
Abbreviations: Res=Resolution, NR=Not Recovered/Not Resolved, Dur=Duration, NONE=Dose Not Changed, DW=Drug Withdrawn, DI=Drug Interrupted, DR=Dose Reduced, M=Male, F=Female

SOURCE: BG12MS/JAPAN/ISS/L-AE-SER-302.SAS DATE: 02DEC2015

＊新薬承認情報提供時に置換えた

Listing of serious adverse events:
Study 109MS302
Page 68 of 75
Treatment group: GA

Subject Sex/Age Race	MedDRA Preferred Term	Study Day Onset (a) (b)	Study Day Res	Dur (days)	Relationship to Study Drug	Severity	Serious	Action Taken with Study Drug	Outcome
658* M/1[redacted] WHITE	脳血管障害	417	418	2	UNRELATED	MILD	Yes	NONE	RESOLVED
659* F/5[redacted] WHITE	大腿骨骨折	39	43	5	UNRELATED	MODERATE	Yes	NONE	RESOLVED
	多発性硬化症再発	454	460	7	UNRELATED	MODERATE	Yes	NONE	RESOLVED
[redacted] F/3[redacted] WHITE	多発性硬化症再発	74	87	14	UNRELATED	MODERATE	Yes	NONE	RESOLVED
335* F/4[redacted] WHITE	子宮内膜癌	182	244	63	UNLIKELY	MODERATE	Yes	DW	RESOLVED

(a) #=On or after the subject switched to alternate MS medication
(b) ^=Adverse Event with onset prior to dosing
Abbreviations: Res=Resolution, NR=Not Recovered/Not Resolved, Dur=Duration, NONE=Dose Not Changed, DW=Drug Withdrawn, DI=Drug Interrupted, DR=Dose Reduced, M=Male, F=Female

SOURCE: BG12MS/JAPAN/ISS/L-AE-SER-302.SAS DATE: 02DEC2015

＊新薬承認情報提供時に置換えた

Listing of serious adverse events:
Study 109MS302
Page 69 of 75
Treatment group: GA

Subject Sex/Age Race	MedDRA Preferred Term	Study Day Onset (a) (b)	Study Day Res	Dur (days)	Relationship to Study Drug	Severity	Serious	Action Taken with Study Drug	Outcome
335* F/4[redacted] WHITE	アナフィラキシー反応	216	219	4	RELATED	SEVERE	Yes	DW	RESOLVED
[redacted] M/4[redacted] WHITE	多発性硬化症再発	337	341	5	UNRELATED	MODERATE	Yes	NONE	RESOLVED
662* M/3[redacted] WHITE	多発性硬化症再発	281	285	5	UNRELATED	MILD	Yes	NONE	RESOLVED
	多発性硬化症再発	562	566	5	UNRELATED	MILD	Yes	NONE	RESOLVED
	肺炎	641	655	15	UNLIKELY	MILD	Yes	DI	RESOLVED

(a) #=On or after the subject switched to alternate MS medication
(b) ^=Adverse Event with onset prior to dosing
Abbreviations: Res=Resolution, NR=Not Recovered/Not Resolved, Dur=Duration, NONE=Dose Not Changed, DW=Drug Withdrawn, DI=Drug Interrupted, DR=Dose Reduced, M=Male, F=Female

SOURCE: BG12MS/JAPAN/ISS/L-AE-SER-302.SAS DATE: 02DEC2015

＊新薬承認情報提供時に置換えた

Listing of serious adverse events:
Study 109MS302
Page 70 of 75
Treatment group: GA

Subject Sex/Age Race	MedDRA Preferred Term	Study Day Onset (a) (b)	Study Day Res	Dur (days)	Relationship to Study Drug	Severity	Serious	Action Taken with Study Drug	Outcome
666* F/2[redacted] WHITE	虫垂炎	121	123	3	UNLIKELY	MODERATE	Yes	NONE	RESOLVED
[redacted] M/2[redacted] WHITE	多発性硬化症再発	14	19	6	UNLIKELY	MILD	Yes	NONE	RESOLVED
	多発性硬化症再発	117	123	7	UNRELATED	MODERATE	Yes	NONE	RESOLVED
	多発性硬化症再発	412#	418	7	UNRELATED	MODERATE	Yes	NONE	RESOLVED
	多発性硬化症再発	461#	465	5	UNRELATED	MODERATE	Yes	NONE	RESOLVED
	多発性硬化症再発	609#	614	6	UNRELATED	MODERATE	Yes	NONE	RESOLVED

(a) #=On or after the subject switched to alternate MS medication
(b) ^=Adverse Event with onset prior to dosing
Abbreviations: Res=Resolution, NR=Not Recovered/Not Resolved, Dur=Duration, NONE=Dose Not Changed, DW=Drug Withdrawn, DI=Drug Interrupted, DR=Dose Reduced, M=Male, F=Female

SOURCE: BG12MS/JAPAN/ISS/L-AE-SER-302.SAS DATE: 02DEC2015

＊新薬承認情報提供時に置換えた

Listing of serious adverse events:
Study 109MS302
Page 71 of 75
Treatment group: GA

Subject Sex/Age Race	MedDRA Preferred Term	Study Day Onset (a) (b)	Study Day Res	Dur (days)	Relationship to Study Drug	Severity	Serious	Action Taken with Study Drug	Outcome
[redacted] F/4[redacted] WHITE	多発性硬化症再発	620	645	26	UNRELATED	MODERATE	Yes	NONE	RESOLVED
[redacted] F/3[redacted] WHITE	多発性硬化症再発	277	281	5	UNLIKELY	MODERATE	Yes	NONE	RESOLVED
[redacted] F/2[redacted] WHITE	多発性硬化症再発	4	9	6	UNRELATED	MODERATE	Yes	NONE	RESOLVED
[redacted] F/3[redacted] WHITE	多発性硬化症再発	417	424	8	UNRELATED	MODERATE	Yes	NONE	RESOLVED

(a) #=On or after the subject switched to alternate MS medication
(b) ^=Adverse Event with onset prior to dosing
Abbreviations: Res=Resolution, NR=Not Recovered/Not Resolved, Dur=Duration, NONE=Dose Not Changed, DW=Drug Withdrawn, DI=Drug Interrupted, DR=Dose Reduced, M=Male, F=Female

SOURCE: BG12MS/JAPAN/ISS/L-AE-SER-302.SAS DATE: 02DEC2015

＊新薬承認情報提供時に置換えた

Listing of serious adverse events:
Study 109MS302
Page 72 of 75
Treatment group: GA

Subject Sex/Age Race	MedDRA Preferred Term	Study Day Onset (a) (b)	Study Day Res	Dur (days)	Relationship to Study Drug	Severity	Serious	Action Taken with Study Drug	Outcome
[redacted] F/4[redacted] WHITE	多発性硬化症再発	176	190	15	UNRELATED	MODERATE	Yes	DI	RESOLVED
[redacted] M/4[redacted] WHITE	多発性硬化症再発	220	224	5	UNRELATED	MODERATE	Yes	NONE	RESOLVED
[redacted] F/4[redacted]	多発性硬化症再発	270	278	9	UNRELATED	MODERATE	Yes	NONE	RESOLVED
	多発性硬化症再発	599	602	4	UNRELATED	MILD	Yes	NONE	RESOLVED
[redacted] M/2[redacted]	多発性硬化症再発	160	183	24	UNRELATED	MODERATE	Yes	NONE	RESOLVED

(a) #=On or after the subject switched to alternate MS medication
(b) ^=Adverse Event with onset prior to dosing
Abbreviations: Res=Resolution, NR=Not Recovered/Not Resolved, Dur=Duration, NONE=Dose Not Changed, DW=Drug Withdrawn, DI=Drug Interrupted, DR=Dose Reduced, M=Male, F=Female

SOURCE: BG12MS/JAPAN/ISS/L-AE-SER-302.SAS DATE: 02DEC2015

＊新薬承認情報提供時に置換えた

Listing of serious adverse events:
Study 109MS302
Page 73 of 75
Treatment group: GA

Subject Sex/Age Race	MedDRA Preferred Term	Study Day Onset (a) (b)	Study Day Res	Dur (days)	Relationship to Study Drug	Severity	Serious	Action Taken with Study Drug	Outcome
679* M/3[redacted] WHITE	前庭性運動失調	302	321	20	UNLIKELY	MILD	Yes	NONE	RESOLVED
[redacted] M/2[redacted] WHITE	多発性硬化症再発	126	140	15	UNRELATED	MODERATE	Yes	NONE	RESOLVED
680* F/4[redacted] WHITE	転移性甲状腺癌	91	100	10	UNLIKELY	MODERATE	Yes	DI	RESOLVED
[redacted] M/4[redacted] WHITE	多発性硬化症再発	176	198	23	UNLIKELY	MILD	Yes	NONE	RESOLVED

(a) #=On or after the subject switched to alternate MS medication
(b) ^=Adverse Event with onset prior to dosing
Abbreviations: Res=Resolution, NR=Not Recovered/Not Resolved, Dur=Duration, NONE=Dose Not Changed, DW=Drug Withdrawn, DI=Drug Interrupted, DR=Dose Reduced, M=Male, F=Female

SOURCE: BG12MS/JAPAN/ISS/L-AE-SER-302.SAS DATE: 02DEC2015

＊新薬承認情報提供時に置換えた

Listing of serious adverse events:
Study 109MS302
Page 74 of 75
Treatment group: GA

Subject Sex/Age Race	MedDRA Preferred Term	Study Day Onset (a) (b)	Study Day Res	Dur (days)	Relationship to Study Drug	Severity	Serious	Action Taken with Study Drug	Outcome
350* M/2[redacted] WHITE	胆石症	393	399	7	UNRELATED	MILD	Yes	NONE	RESOLVED
	自殺既遂	529	529	1	UNLIKELY	SEVERE	Yes	DW	RESOLVED
342* F/3[redacted] WHITE	心筋炎	25	70	46	POSSIBLY	SEVERE	Yes	DW	RESOLVED
[redacted] F/4[redacted] WHITE	多発性硬化症再発	37	45	9	UNRELATED	MODERATE	Yes	NONE	RESOLVED
[redacted] F/3[redacted] WHITE	痙攣	-28^	-24	5	UNRELATED	MILD	Yes	NONE	RESOLVED
	部分発作	31	31	1	UNRELATED	MILD	Yes	NONE	RESOLVED

(a) #=On or after the subject switched to alternate MS medication
(b) ^=Adverse Event with onset prior to dosing
Abbreviations: Res=Resolution, NR=Not Recovered/Not Resolved, Dur=Duration, NONE=Dose Not Changed, DW=Drug Withdrawn, DI=Drug Interrupted, DR=Dose Reduced, M=Male, F=Female

SOURCE: BG12MS/JAPAN/ISS/L-AE-SER-302.SAS DATE: 02DEC2015

＊新薬承認情報提供時に置換えた

Listing of serious adverse events:
Study 109MS302
Page 75 of 75
Treatment group: GA

Subject Sex/Age Race	MedDRA Preferred Term	Study Day Onset (a) (b)	Study Day Res	Dur (days)	Relationship to Study Drug	Severity	Serious	Action Taken with Study Drug	Outcome
687* F/4[redacted] WHITE	不正子宮出血	614	615	2	UNLIKELY	MODERATE	Yes	NONE	RESOLVED
[redacted] M/3[redacted] WHITE	多発性硬化症再発	563	568	6	UNRELATED	MODERATE	Yes	NONE	RESOLVED
688* M/4[redacted] WHITE	ウイルス感染	136	141	6	UNLIKELY	MODERATE	Yes	DI	RESOLVED

(a) #=On or after the subject switched to alternate MS medication
(b) ^=Adverse Event with onset prior to dosing
Abbreviations: Res=Resolution, NR=Not Recovered/Not Resolved, Dur=Duration, NONE=Dose Not Changed, DW=Drug Withdrawn, DI=Drug Interrupted, DR=Dose Reduced, M=Male, F=Female

SOURCE: BG12MS/JAPAN/ISS/L-AE-SER-302.SAS DATE: 02DEC2015

＊新薬承認情報提供時に置換えた

Table 305: Listing of Serious Adverse Events: Study 109MS303

Listing of serious adverse events:
Study 109MS303
Page 1 of 138
Treatment group: BG00012 240 mg BID

Subject Sex/Age Race	MedDRA Preferred Term	Study Day Onset (a)(b)	Res	Dur (days)	Relationship to Study Drug	Severity	Serious	Action Taken With Study Drug	Outcome
[redacted] F/5[redacted] WHITE	深部静脈血栓症	280	468	189	POSSIBLY	MODERATE	Yes	NONE	RESOLVED
592* F/5[redacted] ASIAN	急性冠動脈症候群	1347#	NR		UNRELATED	MODERATE	Yes	DI	NOT RESOLVED
	うっ血性心不全	1347#	NR		UNRELATED	MODERATE	Yes	DI	NOT RESOLVED
	左室機能不全	1347#	NR		UNRELATED	MODERATE	Yes	DI	NOT RESOLVED
	尿路感染	1347#	NR		UNRELATED	MODERATE	Yes	DI	NOT RESOLVED
[redacted] M/3[redacted] ASIAN	転倒	113	116	4	UNRELATED	MODERATE	Yes	NONE	RESOLVED
	靭帯損傷	113	116	4	UNRELATED	MODERATE	Yes	NONE	RESOLVED

(a) #=On or after the subject switched to alternate MS medication
(b) ^=Adverse Event with onset prior to dosing
Abbreviations: Res=Resolution, NR=Not Recovered/Not Resolved, Dur=Duration, NONE=Dose Not Changed, DW=Drug Withdrawn, DI=Drug Interrupted, DR=Dose Reduced, M=Male, F=Female

SOURCE: BG12MS/JAPAN/ISS/L-AE-SER-303.SAS DATE: 02DEC2015

＊新薬承認情報提供時に置換えた

Listing of serious adverse events:
Study 109MS303
Page 2 of 138
Treatment group: BG00012 240 mg BID

Subject Sex/Age Race	MedDRA Preferred Term	Study Day Onset (a)(b)	Res	Dur (days)	Relationship to Study Drug	Severity	Serious	Action Taken With Study Drug	Outcome
[redacted] M/3[redacted] ASIAN	靭帯断裂	158	161	4	UNRELATED	SEVERE	Yes	NONE	RESOLVED
	発熱	458	465	8	UNRELATED	MODERATE	Yes	NONE	RESOLVED
	尿路感染	458	465	8	UNRELATED	MODERATE	Yes	NONE	RESOLVED
[redacted] M/2[redacted] ASIAN	ツツガ虫病	232	246	15	UNRELATED	SEVERE	Yes	NONE	RESOLVED
591* F/3[redacted] ASIAN	蜂巣炎	330	392	63	UNLIKELY	MODERATE	Yes	NONE	RESOLVED
163* F/2[redacted] ASIAN	多発性硬化症再発	376	425	50	POSSIBLY	SEVERE	Yes	NONE	RESOLVED

(a) #=On or after the subject switched to alternate MS medication
(b) ^=Adverse Event with onset prior to dosing
Abbreviations: Res=Resolution, NR=Not Recovered/Not Resolved, Dur=Duration, NONE=Dose Not Changed, DW=Drug Withdrawn, DI=Drug Interrupted, DR=Dose Reduced, M=Male, F=Female

SOURCE: BG12MS/JAPAN/ISS/L-AE-SER-303.SAS DATE: 02DEC2015

＊新薬承認情報提供時に置換えた

Listing of serious adverse events:
Study 109MS303
Page 3 of 138
Treatment group: BG00012 240 mg BID

Subject Sex/Age Race	MedDRA Preferred Term	Study Day Onset (a)(b)	Res	Dur (days)	Relationship to Study Drug	Severity	Serious	Action Taken With Study Drug	Outcome
163* F/2[redacted] ASIAN	尿路感染	466	474	9	UNLIKELY	SEVERE	Yes	NONE	RESOLVED
[redacted] M/2[redacted] ASIAN	デング熱	1274	1284	11	UNRELATED	SEVERE	Yes	NONE	RESOLVED
604* F/4[redacted] ASIAN	発熱	1190	1194	5	UNRELATED	MODERATE	Yes	NONE	RESOLVED
	血小板減少症	1190	1194	5	UNRELATED	MODERATE	Yes	NONE	RESOLVED
[redacted] F/4[redacted] ASIAN	多発性硬化症再発	1077	1179	103	UNRELATED	MODERATE	Yes	NONE	RESOLVED

(a) #=On or after the subject switched to alternate MS medication
(b) ^=Adverse Event with onset prior to dosing
Abbreviations: Res=Resolution, NR=Not Recovered/Not Resolved, Dur=Duration, NONE=Dose Not Changed, DW=Drug Withdrawn, DI=Drug Interrupted, DR=Dose Reduced, M=Male, F=Female

SOURCE: BG12MS/JAPAN/ISS/L-AE-SER-303.SAS DATE: 02DEC2015

＊新薬承認情報提供時に置換えた

Listing of serious adverse events:
Study 109MS303
Page 4 of 138
Treatment group: BG00012 240 mg BID

Subject Sex/Age Race	MedDRA Preferred Term	Study Day Onset (a)(b)	Res	Dur (days)	Relationship to Study Drug	Severity	Serious	Action Taken With Study Drug	Outcome
[redacted] F/3[redacted] ASIAN	多発性硬化症再発	930	947	18	UNRELATED	SEVERE	Yes	NONE	RESOLVED
	多発性硬化症再発	1464	NR		UNRELATED	SEVERE	Yes	NONE	NOT RESOLVED
348* F/3[redacted] ASIAN	治癒不良	93	103	11	UNRELATED	MODERATE	Yes	NONE	RESOLVED
	褥瘡性潰瘍	141	150	10	UNRELATED	SEVERE	Yes	NONE	RESOLVED
	感染性皮膚潰瘍	141	150	10	UNRELATED	SEVERE	Yes	NONE	RESOLVED
[redacted] F/4[redacted] WHITE	乳房の上皮内癌	66	778	713	UNLIKELY	SEVERE	Yes	DW	RESOLVED

(a) #=On or after the subject switched to alternate MS medication
(b) ^=Adverse Event with onset prior to dosing
Abbreviations: Res=Resolution, NR=Not Recovered/Not Resolved, Dur=Duration, NONE=Dose Not Changed, DW=Drug Withdrawn, DI=Drug Interrupted, DR=Dose Reduced, M=Male, F=Female

SOURCE: BG12MS/JAPAN/ISS/L-AE-SER-303.SAS DATE: 02DEC2015

＊新薬承認情報提供時に置換えた

Listing of serious adverse events:
Study 109MS303
Page 5 of 138
Treatment group: BG00012 240 mg BID

Subject Sex/Age Race	MedDRA Preferred Term	Study Day Onset (a)(b)	Res	Dur (days)	Relationship to Study Drug	Severity	Serious	Action Taken With Study Drug	Outcome
[redacted] F/3[redacted] BLACK OR AFRICAN AMERICAN	乳癌	794	NR		UNLIKELY	SEVERE	Yes	DW	NOT RESOLVED
[redacted] F/4[redacted] WHITE	アルコール症	1123	1126	4	UNRELATED	SEVERE	Yes	DI	RESOLVED
[redacted] F/3[redacted] WHITE	消化管壊死	22	77	56	POSSIBLY	SEVERE	Yes	DW	RESOLVED
	術後ヘルニア	22	77	56	POSSIBLY	SEVERE	Yes	DW	RESOLVED
	小腸閉塞	22	77	56	POSSIBLY	SEVERE	Yes	DW	RESOLVED

(a) #=On or after the subject switched to alternate MS medication
(b) ^=Adverse Event with onset prior to dosing
Abbreviations: Res=Resolution, NR=Not Recovered/Not Resolved, Dur=Duration, NONE=Dose Not Changed, DW=Drug Withdrawn, DI=Drug Interrupted, DR=Dose Reduced, M=Male, F=Female

SOURCE: BG12MS/JAPAN/ISS/L-AE-SER-303.SAS DATE: 02DEC2015

＊新薬承認情報提供時に置換えた

Listing of serious adverse events:
Study 109MS303
Page 6 of 138
Treatment group: BG00012 240 mg BID

Subject Sex/Age Race	MedDRA Preferred Term	Study Day Onset (a)(b)	Res	Dur (days)	Relationship to Study Drug	Severity	Serious	Action Taken With Study Drug	Outcome
[redacted] M/4[redacted] WHITE	ウォルフ・パーキンソン・ホワイト症候群	1698	1700	3	UNRELATED	MODERATE	Yes	NONE	RESOLVED
[redacted] M/3[redacted] WHITE	憩室炎	647	659	13	UNLIKELY	SEVERE	Yes	NONE	RESOLVED
[redacted] M/4[redacted] WHITE	椎間板突出	778	1067	290	UNRELATED	SEVERE	Yes	NONE	RESOLVED
[redacted] M/4[redacted] WHITE	関節炎	31	NR		UNLIKELY	MODERATE	Yes	NONE	NOT RESOLVED

(a) #=On or after the subject switched to alternate MS medication
(b) ^=Adverse Event with onset prior to dosing
Abbreviations: Res=Resolution, NR=Not Recovered/Not Resolved, Dur=Duration, NONE=Dose Not Changed, DW=Drug Withdrawn, DI=Drug Interrupted, DR=Dose Reduced, M=Male, F=Female

SOURCE: BG12MS/JAPAN/ISS/L-AE-SER-303.SAS DATE: 02DEC2015

＊新薬承認情報提供時に置換えた

Listing of serious adverse events:
Study 109MS303
Page 7 of 138
Treatment group: BG00012 240 mg BID

Subject Sex/Age Race	MedDRA Preferred Term	Study Day Onset (a)(b)	Res	Dur (days)	Relationship to Study Drug	Severity	Serious	Action Taken With Study Drug	Outcome
[redacted] F/5[redacted] WHITE	脱水	834	839	6	UNRELATED	SEVERE	Yes	NONE	RESOLVED
	多発性硬化症再発	834	839	6	UNRELATED	SEVERE	Yes	DW	RESOLVED
	尿路感染	834	844	11	UNRELATED	SEVERE	Yes	NONE	RESOLVED
[redacted] M/3[redacted] WHITE	一過性全健忘	815	817	3	UNLIKELY	MODERATE	Yes	NONE	RESOLVED
[redacted] F/4[redacted] WHITE	胆嚢炎	428	431	4	UNRELATED	SEVERE	Yes	DI	RESOLVED
	膵炎	428	431	4	UNRELATED	SEVERE	Yes	DI	RESOLVED

(a) #=On or after the subject switched to alternate MS medication
(b) ^=Adverse Event with onset prior to dosing
Abbreviations: Res=Resolution, NR=Not Recovered/Not Resolved, Dur=Duration, NONE=Dose Not Changed, DW=Drug Withdrawn, DI=Drug Interrupted, DR=Dose Reduced, M=Male, F=Female

SOURCE: BG12MS/JAPAN/ISS/L-AE-SER-303.SAS DATE: 02DEC2015

＊新薬承認情報提供時に置換えた

Listing of serious adverse events:
Study 109MS303
Page 8 of 138
Treatment group: BG00012 240 mg BID

Subject Sex/Age Race	MedDRA Preferred Term	Study Day Onset (a)(b)	Res	Dur (days)	Relationship to Study Drug	Severity	Serious	Action Taken With Study Drug	Outcome
365* F/4[redacted] WHITE	腎細胞癌	398	400	3	RELATED	SEVERE	Yes	DW	RESOLVED
[redacted] F/5[redacted] WHITE	転移性新生物	1311	NR		POSSIBLY	SEVERE	Yes	DW	NOT RESOLVED
	痙攣	1353	1355	3	UNRELATED	MODERATE	Yes	NONE	RESOLVED
[redacted] F/2[redacted] WHITE	椎間板突出	476	476	1	UNRELATED	SEVERE	Yes	NONE	RESOLVED
[redacted] M/4[redacted] WHITE	急性心筋梗塞	28	28	1	UNLIKELY	SEVERE	Yes	NONE	RESOLVED

(a) #=On or after the subject switched to alternate MS medication
(b) ^=Adverse Event with onset prior to dosing
Abbreviations: Res=Resolution, NR=Not Recovered/Not Resolved, Dur=Duration, NONE=Dose Not Changed, DW=Drug Withdrawn, DI=Drug Interrupted, DR=Dose Reduced, M=Male, F=Female

SOURCE: BG12MS/JAPAN/ISS/L-AE-SER-303.SAS DATE: 02DEC2015

＊新薬承認情報提供時に置換えた

Listing of serious adverse events:
Study 109MS303
Page 9 of 138
Treatment group: BG00012 240 mg BID

Subject Sex/Age Race	MedDRA Preferred Term	Study Day Onset (a)(b)	Res	Dur (days)	Relationship to Study Drug	Severity	Serious	Action Taken With Study Drug	Outcome
[redacted] M/4[redacted] WHITE	ストレス	440	441	2	UNRELATED	SEVERE	Yes	NONE	RESOLVED
[redacted] F/4[redacted] WHITE	子宮平滑筋腫	1183	1183	1	UNLIKELY	SEVERE	Yes	NONE	RESOLVED
361* F/4[redacted] WHITE	腎結石症	469	473	5	UNRELATED	MODERATE	Yes	NONE	RESOLVED
182* F/5[redacted] WHITE	転倒	140	140	1	UNRELATED	SEVERE	Yes	DI	RESOLVED
	股関節部骨折	142	172	31	UNRELATED	SEVERE	Yes	DI	RESOLVED

(a) #=On or after the subject switched to alternate MS medication
(b) ^=Adverse Event with onset prior to dosing
Abbreviations: Res=Resolution, NR=Not Recovered/Not Resolved, Dur=Duration, NONE=Dose Not Changed, DW=Drug Withdrawn, DI=Drug Interrupted, DR=Dose Reduced, M=Male, F=Female

SOURCE: BG12MS/JAPAN/ISS/L-AE-SER-303.SAS DATE: 02DEC2015

＊新薬承認情報提供時に置換えた

Listing of serious adverse events:
Study 109MS303
Page 10 of 138
Treatment group: BG00012 240 mg BID

Subject Sex/Age Race	MedDRA Preferred Term	Study Day Onset (a)(b)	Res	Dur (days)	Relationship to Study Drug	Severity	Serious	Action Taken With Study Drug	Outcome
[redacted] M/3[redacted] HISPANIC	椎間板突出	599	601	3	UNRELATED	MODERATE	Yes	NONE	RESOLVED
[redacted] M/2[redacted] HISPANIC.	喘息	1277	1309	33	UNRELATED	SEVERE	Yes	NONE	RESOLVED
	肺炎	1277	1309	33	UNRELATED	MODERATE	Yes	NONE	RESOLVED
[redacted] F/4[redacted] WHITE	多発性硬化症再発	29	37	9	UNRELATED	MILD	Yes	NONE	RESOLVED

(a) #=On or after the subject switched to alternate MS medication
(b) ^=Adverse Event with onset prior to dosing
Abbreviations: Res=Resolution, NR=Not Recovered/Not Resolved, Dur=Duration, NONE=Dose Not Changed, DW=Drug Withdrawn, DI=Drug Interrupted, DR=Dose Reduced, M=Male, F=Female

SOURCE: BG12MS/JAPAN/ISS/L-AE-SER-303.SAS DATE: 02DEC2015

＊新薬承認情報提供時に置換えた

Listing of serious adverse events:
Study 109MS303
Page 11 of 138
Treatment group: BG00012 240 mg BID

Subject Sex/Age Race	MedDRA Preferred Term	Study Day Onset (a)(b)	Study Day Res	Dur (days)	Relationship to Study Drug	Severity	Serious	Action Taken With Study Drug	Outcome
[redacted] F/3[redacted] WHITE	多発性硬化症再発	786	789	4	UNRELATED	MODERATE	Yes	NONE	RESOLVED
[redacted] F/5[redacted] WHITE	多発性硬化症再発	1382	1386	5	UNRELATED	MODERATE	Yes	NONE	RESOLVED
[redacted] M/3[redacted] WHITE	多発性硬化症再発	1359	1373	15	UNRELATED	SEVERE	Yes	NONE	RESOLVED
[redacted] F/5[redacted] WHITE	胃炎	85	91	7	POSSIBLY	MILD	Yes	DR	RESOLVED
	子宮ポリープ	1169	1170	2	UNRELATED	MILD	Yes	NONE	RESOLVED

(a) #=On or after the subject switched to alternate MS medication
(b) ^=Adverse Event with onset prior to dosing
Abbreviations: Res=Resolution, NR=Not Recovered/Not Resolved, Dur=Duration, NONE=Dose Not Changed, DW=Drug Withdrawn, DI=Drug Interrupted, DR=Dose Reduced, M=Male, F=Female

SOURCE: BG12MS/JAPAN/ISS/L-AE-SER-303.SAS DATE: 02DEC2015

＊新薬承認情報提供時に置換えた

Listing of serious adverse events:
Study 109MS303
Page 12 of 138
Treatment group: BG00012 240 mg BID

Subject Sex/Age Race	MedDRA Preferred Term	Study Day Onset (a)(b)	Res	Dur (days)	Relationship to Study Drug	Severity	Serious	Action Taken With Study Drug	Outcome
[redacted] M/3[redacted] WHITE	神経根炎	693	716	24	UNRELATED	SEVERE	Yes	NONE	RESOLVED
[redacted] M/3[redacted] WHITE	多発性硬化症再発	324	332	9	UNRELATED	SEVERE	Yes	NONE	RESOLVED
[redacted] M/3[redacted] ASIAN	多発性硬化症再発	714#	875	162	UNRELATED	SEVERE	Yes	NONE	RESOLVED
[redacted] F/4[redacted] ASIAN	多発性硬化症再発	332	422	91	UNRELATED	SEVERE	Yes	NONE	RESOLVED
	不全対麻痺	385	422	38	UNRELATED	SEVERE	Yes	NONE	RESOLVED

(a) #=On or after the subject switched to alternate MS medication
(b) ^=Adverse Event with onset prior to dosing
Abbreviations: Res=Resolution, NR=Not Recovered/Not Resolved, Dur=Duration, NONE=Dose Not Changed, DW=Drug Withdrawn, DI=Drug Interrupted, DR=Dose Reduced, M=Male, F=Female

SOURCE: BG12MS/JAPAN/ISS/L-AE-SER-303.SAS DATE: 02DEC2015

＊新薬承認情報提供時に置換えた

Listing of serious adverse events:
Study 109MS303
Page 13 of 138
Treatment group: BG00012 240 mg BID

Subject Sex/Age Race	MedDRA Preferred Term	Study Day Onset (a)(b)	Res	Dur (days)	Relationship to Study Drug	Severity	Serious	Action Taken With Study Drug	Outcome
[redacted] F/3[redacted] ASIAN	多発性硬化症再発	736	765	30	UNRELATED	SEVERE	Yes	NONE	RESOLVED
[redacted] F/2[redacted] ASIAN	股関節形成	184	196	13	UNRELATED	SEVERE	Yes	NONE	RESOLVED
	ウイルス性髄膜炎	263	267	5	POSSIBLY	MODERATE	Yes	NONE	RESOLVED
	尿路感染	263	267	5	POSSIBLY	MODERATE	Yes	NONE	RESOLVED
[redacted] F/3[redacted] ASIAN	胃炎	25	31	7	POSSIBLY	SEVERE	Yes	NONE	RESOLVED
	食道カンジダ症	25	31	7	POSSIBLY	SEVERE	Yes	NONE	RESOLVED

(a) #=On or after the subject switched to alternate MS medication
(b) ^=Adverse Event with onset prior to dosing
Abbreviations: Res=Resolution, NR=Not Recovered/Not Resolved, Dur=Duration, NONE=Dose Not Changed, DW=Drug Withdrawn, DI=Drug Interrupted, DR=Dose Reduced, M=Male, F=Female

SOURCE: BG12MS/JAPAN/ISS/L-AE-SER-303.SAS DATE: 02DEC2015

＊新薬承認情報提供時に置換えた

Listing of serious adverse events:
Study 109MS303
Page 14 of 138
Treatment group: BG00012 240 mg BID

Subject Sex/Age Race	MedDRA Preferred Term	Study Day Onset (a)(b)	Res	Dur (days)	Relationship to Study Drug	Severity	Serious	Action Taken With Study Drug	Outcome
[redacted] F/3[redacted] ASIAN	不全対麻痺	336	341	6	UNRELATED	MODERATE	Yes	NONE	RESOLVED
	四肢不全麻痺	382	388	7	UNRELATED	MODERATE	Yes	NONE	RESOLVED
	多発性硬化症再発	673	691	19	UNRELATED	MODERATE	Yes	NONE	RESOLVED
526* F/2[redacted] ASIAN	多発性硬化症再発	72	82	11	UNRELATED	SEVERE	Yes	NONE	RESOLVED
	多発性硬化症再発	122	124	3	UNRELATED	MILD	Yes	NONE	RESOLVED
	再発寛解型多発性硬化症	225	227	3	UNRELATED	MODERATE	Yes	NONE	RESOLVED
	多発性硬化症再発	553	556	4	UNRELATED	MODERATE	Yes	NONE	RESOLVED

(a) #=On or after the subject switched to alternate MS medication
(b) ^=Adverse Event with onset prior to dosing
Abbreviations: Res=Resolution, NR=Not Recovered/Not Resolved, Dur=Duration, NONE=Dose Not Changed, DW=Drug Withdrawn, DI=Drug Interrupted, DR=Dose Reduced, M=Male, F=Female

SOURCE: BG12MS/JAPAN/ISS/L-AE-SER-303.SAS DATE: 02DEC2015

＊新薬承認情報提供時に置換えた

Listing of serious adverse events:
Study 109MS303
Page 15 of 138
Treatment group: BG00012 240 mg BID

Subject Sex/Age Race	MedDRA Preferred Term	Study Day Onset (a)(b)	Res	Dur (days)	Relationship to Study Drug	Severity	Serious	Action Taken With Study Drug	Outcome
527* M/2[redacted] ASIAN	多発性硬化症再発	140	142	3	UNRELATED	MODERATE	Yes	NONE	RESOLVED
	デング熱	166	171	6	UNRELATED	MODERATE	Yes	NONE	RESOLVED
	多発性硬化症再発	336	359	24	UNRELATED	MODERATE	Yes	NONE	RESOLVED
	多発性硬化症再発	386	388	3	UNRELATED	MODERATE	Yes	NONE	RESOLVED
	ウイルス感染	576	578	3	UNRELATED	MODERATE	Yes	NONE	RESOLVED
[redacted] F/2[redacted] ASIAN	多発性硬化症再発	504	506	3	UNRELATED	MODERATE	Yes	NONE	RESOLVED
	多発性硬化症再発	680	682	3	UNRELATED	MODERATE	Yes	NONE	RESOLVED

(a) #=On or after the subject switched to alternate MS medication
(b) ^=Adverse Event with onset prior to dosing
Abbreviations: Res=Resolution, NR=Not Recovered/Not Resolved, Dur=Duration, NONE=Dose Not Changed, DW=Drug Withdrawn, DI=Drug Interrupted, DR=Dose Reduced, M=Male, F=Female

SOURCE: BG12MS/JAPAN/ISS/L-AE-SER-303.SAS DATE: 02DEC2015

＊新薬承認情報提供時に置換えた

Listing of serious adverse events:
Study 109MS303
Page 16 of 138
Treatment group: BG00012 240 mg BID

Subject Sex/Age Race	MedDRA Preferred Term	Study Day Onset (a)(b)	Study Day Res	Dur (days)	Relationship to Study Drug	Severity	Serious	Action Taken With Study Drug	Outcome
[redacted] M/2[redacted] ASIAN	多発性硬化症再発	85	87	3	UNRELATED	MODERATE	Yes	NONE	RESOLVED
[redacted] F/3[redacted] ASIAN	多発性硬化症再発	669	671	3	UNRELATED	MODERATE	Yes	NONE	RESOLVED
[redacted] M/2[redacted] ASIAN	多発性硬化症再発	59	64	6	UNRELATED	MODERATE	Yes	NONE	RESOLVED
	多発性硬化症再発	600	605	6	UNRELATED	SEVERE	Yes	NONE	RESOLVED
534* F/2[redacted] ASIAN	多発性硬化症再発	378	395	18	UNRELATED	MODERATE	Yes	NONE	RESOLVED

(a) #=On or after the subject switched to alternate MS medication
(b) ^=Adverse Event with onset prior to dosing
Abbreviations: Res=Resolution, NR=Not Recovered/Not Resolved, Dur=Duration, NONE=Dose Not Changed, DW=Drug Withdrawn, DI=Drug Interrupted, DR=Dose Reduced, M=Male, F=Female

SOURCE: BG12MS/JAPAN/ISS/L-AE-SER-303.SAS DATE: 02DEC2015

＊新薬承認情報提供時に置換えた

Listing of serious adverse events:
Study 109MS303
Page 17 of 138
Treatment group: BG00012 240 mg BID

Subject Sex/Age Race	MedDRA Preferred Term	Study Day Onset (a)(b)	Res	Dur (days)	Relationship to Study Drug	Severity	Serious	Action Taken With Study Drug	Outcome
353* F/4[redacted] ASIAN	悪性中皮腫	361	473	113	UNRELATED	SEVERE	Yes	DW	RESOLVED
349* F/3[redacted] ASIAN	多発性硬化症再発	31	59	29	UNRELATED	SEVERE	Yes	NONE	RESOLVED
	多発性硬化症再発	68	102	35	UNRELATED	SEVERE	Yes	NONE	RESOLVED
	尿路感染	133	165	33	UNRELATED	MODERATE	Yes	NONE	RESOLVED
	尿路感染	176	NR		UNRELATED	MODERATE	Yes	NONE	NOT RESOLVED
	多発性硬化症再発	177	177	1	UNRELATED	SEVERE	Yes	NONE	RESOLVED
[redacted] M/4[redacted] WHITE	肛門癌	1247	1341	95	POSSIBLY	MODERATE	Yes	DW	RESOLVED

(a) #=On or after the subject switched to alternate MS medication
(b) ^=Adverse Event with onset prior to dosing
Abbreviations: Res=Resolution, NR=Not Recovered/Not Resolved, Dur=Duration, NONE=Dose Not Changed, DW=Drug Withdrawn, DI=Drug Interrupted, DR=Dose Reduced, M=Male, F=Female

SOURCE: BG12MS/JAPAN/ISS/L-AE-SER-303.SAS DATE: 02DEC2015

＊新薬承認情報提供時に置換えた

Listing of serious adverse events:
Study 109MS303
Page 18 of 138
Treatment group: BG00012 240 mg BID

Subject Sex/Age Race	MedDRA Preferred Term	Study Day Onset (a)(b)	Res	Dur (days)	Relationship to Study Drug	Severity	Serious	Action Taken With Study Drug	Outcome
[redacted] F/4[redacted] WHITE	多発性硬化症再発	673	752	80	UNRELATED	MODERATE	Yes	NONE	RESOLVED
[redacted] F/4[redacted] WHITE	乳房線維化	844	849	6	UNRELATED	MODERATE	Yes	NONE	RESOLVED
072* M/4[redacted] WHITE	転倒	1391	1391	1	UNRELATED	MODERATE	Yes	NONE	RESOLVED
	大腿骨骨折	1391	NR		UNRELATED	MODERATE	Yes	NONE	NOT RESOLVED
[redacted] F/3[redacted] WHITE	子宮頚部扁平上皮癌	391	401	11	POSSIBLY	SEVERE	Yes	NONE	RESOLVED

(a) #=On or after the subject switched to alternate MS medication
(b) ^=Adverse Event with onset prior to dosing
Abbreviations: Res=Resolution, NR=Not Recovered/Not Resolved, Dur=Duration, NONE=Dose Not Changed, DW=Drug Withdrawn, DI=Drug Interrupted, DR=Dose Reduced, M=Male, F=Female

SOURCE: BG12MS/JAPAN/ISS/L-AE-SER-303.SAS DATE: 02DEC2015

＊新薬承認情報提供時に置換えた

Listing of serious adverse events:
Study 109MS303
Page 19 of 138
Treatment group: BG00012 240 mg BID

Subject Sex/Age Race	MedDRA Preferred Term	Study Day Onset (a)(b)	Res	Dur (days)	Relationship to Study Drug	Severity	Serious	Action Taken With Study Drug	Outcome
637* M/5[redacted] WHITE	滑液包炎	214			UNRELATED	MODERATE	Yes	NONE	RESOLVED
	半月板障害	532	533	2	UNRELATED	MODERATE	Yes	NONE	RESOLVED
	薬物過敏症	794	806	13	UNRELATED	SEVERE	Yes	NONE	RESOLVED
[redacted] F/4[redacted] WHITE	胃出血	1413	1415	3	UNRELATED	SEVERE	Yes	DR	RESOLVED
[redacted] F/4[redacted] WHITE	卵巣嚢胞	858	863	6	UNLIKELY	MILD	Yes	NONE	RESOLVED
540* F/3[redacted] WHITE	多発性硬化症再発	708	716	9	UNRELATED	MODERATE	Yes	NONE	RESOLVED

(a) #=On or after the subject switched to alternate MS medication
(b) ^=Adverse Event with onset prior to dosing
Abbreviations: Res=Resolution, NR=Not Recovered/Not Resolved, Dur=Duration, NONE=Dose Not Changed, DW=Drug Withdrawn, DI=Drug Interrupted, DR=Dose Reduced, M=Male, F=Female

SOURCE: BG12MS/JAPAN/ISS/L-AE-SER-303.SAS DATE: 02DEC2015

＊新薬承認情報提供時に置換えた

Listing of serious adverse events:
Study 109MS303
Page 20 of 138
Treatment group: BG00012 240 mg BID

Subject Sex/Age Race	MedDRA Preferred Term	Study Day Onset (a)(b)	Res	Dur (days)	Relationship to Study Drug	Severity	Serious	Action Taken With Study Drug	Outcome
540* F/3[redacted] WHITE	薬物乱用	1339	1400	62	UNRELATED	MODERATE	Yes	NONE	RESOLVED
	月経過多	1735	1736	2	UNRELATED	MODERATE	Yes	NONE	RESOLVED
[redacted] F/4[redacted] WHITE	関節周囲炎	1262	1265	4	UNRELATED	MODERATE	Yes	NONE	RESOLVED
[redacted] F/2[redacted] WHITE	多発性硬化症再発	1627	NR		UNRELATED	MODERATE	Yes	NONE	NOT RESOLVED
[redacted] F/4[redacted] WHITE	過量投与	832	832	1	UNRELATED	MILD	Yes	NONE	RESOLVED
	悪性黒色腫	1012	1052	41	UNLIKELY	SEVERE	Yes	NONE	RESOLVED

(a) #=On or after the subject switched to alternate MS medication
(b) ^=Adverse Event with onset prior to dosing
Abbreviations: Res=Resolution, NR=Not Recovered/Not Resolved, Dur=Duration, NONE=Dose Not Changed, DW=Drug Withdrawn, DI=Drug Interrupted, DR=Dose Reduced, M=Male, F=Female

SOURCE: BG12MS/JAPAN/ISS/L-AE-SER-303.SAS DATE: 02DEC2015

＊新薬承認情報提供時に置換えた

Listing of serious adverse events:
Study 109MS303
Page 21 of 138
Treatment group: BG00012 240 mg BID

Subject Sex/Age Race	MedDRA Preferred Term	Study Day Onset (a)(b)	Res	Dur (days)	Relationship to Study Drug	Severity	Serious	Action Taken With Study Drug	Outcome
[redacted] F/4[redacted] WHITE	転移性悪性黒色腫	1440	NR		UNLIKELY	SEVERE	Yes	DW	NOT RESOLVED
[redacted] M/3[redacted] WHITE	髄膜腫	696	780	85	UNLIKELY	MODERATE	Yes	DI	RESOLVED
	脳出血	1526	1533	8	UNRELATED	SEVERE	Yes	NONE	RESOLVED
[redacted] F/2[redacted] WHITE	軟骨疾患	840	846	7	UNRELATED	SEVERE	Yes	NONE	RESOLVED
548* F/2[redacted] WHITE	横紋筋融解	148	157	10	UNRELATED	MILD	Yes	DI	RESOLVED

(a) #=On or after the subject switched to alternate MS medication
(b) ^=Adverse Event with onset prior to dosing
Abbreviations: Res=Resolution, NR=Not Recovered/Not Resolved, Dur=Duration, NONE=Dose Not Changed, DW=Drug Withdrawn, DI=Drug Interrupted, DR=Dose Reduced, M=Male, F=Female

SOURCE: BG12MS/JAPAN/ISS/L-AE-SER-303.SAS DATE: 02DEC2015

＊新薬承認情報提供時に置換えた

Listing of serious adverse events:
Study 109MS303
Page 22 of 138
Treatment group: BG00012 240 mg BID

Subject Sex/Age Race	MedDRA Preferred Term	Study Day Onset (a)(b)	Res	Dur (days)	Relationship to Study Drug	Severity	Serious	Action Taken With Study Drug	Outcome
[redacted] F/5[redacted] WHITE	多発性硬化症再発	51	89	39	POSSIBLY	MILD	Yes	NONE	RESOLVED
	背部痛	251	256	6	UNRELATED	MODERATE	Yes	NONE	RESOLVED
	肩回旋筋腱板症候群	1436	NR		UNRELATED	MODERATE	Yes	NONE	NOT RESOLVED
[redacted] F/3[redacted] WHITE	慢性扁桃炎	1393	1413	21	RELATED	MODERATE	Yes	NONE	RESOLVED
[redacted] F/4[redacted] WHITE	乳房の良性新生物	114	116	3	UNRELATED	MODERATE	Yes	NONE	RESOLVED
[redacted] M/3[redacted] WHITE	鼻咽頭炎	817	822	6	UNRELATED	SEVERE	Yes	NONE	RESOLVED

(a) #=On or after the subject switched to alternate MS medication
(b) ^=Adverse Event with onset prior to dosing
Abbreviations: Res=Resolution, NR=Not Recovered/Not Resolved, Dur=Duration, NONE=Dose Not Changed, DW=Drug Withdrawn, DI=Drug Interrupted, DR=Dose Reduced, M=Male, F=Female

SOURCE: BG12MS/JAPAN/ISS/L-AE-SER-303.SAS DATE: 02DEC2015

＊新薬承認情報提供時に置換えた

Listing of serious adverse events:
Study 109MS303
Page 23 of 138
Treatment group: BG00012 240 mg BID

Subject Sex/Age Race	MedDRA Preferred Term	Study Day Onset (a)(b)	Res	Dur (days)	Relationship to Study Drug	Severity	Serious	Action Taken With Study Drug	Outcome
[redacted] M/3[redacted] WHITE	多発性硬化症再発	1109	1113	5	POSSIBLY	MODERATE	Yes	DW	RESOLVED
[redacted] F/3[redacted] WHITE	燃え尽き症候群	729	763	35	UNRELATED	MILD	Yes	NONE	RESOLVED
[redacted] F/3[redacted] WHITE	再発寛解型多発性硬化症	939#	967	29	UNRELATED	MILD	Yes	NONE	RESOLVED
[redacted] F/5[redacted] WHITE	慢性閉塞性肺疾患	707	734	28	UNRELATED	MILD	Yes	NONE	RESOLVED

(a) #=On or after the subject switched to alternate MS medication
(b) ^=Adverse Event with onset prior to dosing
Abbreviations: Res=Resolution, NR=Not Recovered/Not Resolved, Dur=Duration, NONE=Dose Not Changed, DW=Drug Withdrawn, DI=Drug Interrupted, DR=Dose Reduced, M=Male, F=Female

SOURCE: BG12MS/JAPAN/ISS/L-AE-SER-303.SAS DATE: 02DEC2015

＊新薬承認情報提供時に置換えた

Listing of serious adverse events:
Study 109MS303
Page 24 of 138
Treatment group: BG00012 240 mg BID

Subject Sex/Age Race	MedDRA Preferred Term	Study Day Onset (a)(b)	Res	Dur (days)	Relationship to Study Drug	Severity	Serious	Action Taken With Study Drug	Outcome
[redacted] F/3[redacted] WHITE	失神	940	941	2	UNLIKELY	MODERATE	Yes	NONE	RESOLVED
	歯膿瘍	942	946	5	UNLIKELY	SEVERE	Yes	NONE	RESOLVED
[redacted] F/4[redacted] WHITE	検査	1219	1227	9	POSSIBLY	MILD	Yes	NONE	RESOLVED
[redacted] M/4[redacted] WHITE	多発性硬化症再発	458	512	55	UNRELATED	MILD	Yes	NONE	RESOLVED
[redacted] F/3[redacted] WHITE	心房細動	1058	NR		POSSIBLY	MODERATE	Yes	DW	NOT RESOLVED

(a) #=On or after the subject switched to alternate MS medication
(b) ^=Adverse Event with onset prior to dosing
Abbreviations: Res=Resolution, NR=Not Recovered/Not Resolved, Dur=Duration, NONE=Dose Not Changed, DW=Drug Withdrawn, DI=Drug Interrupted, DR=Dose Reduced, M=Male, F=Female

SOURCE: BG12MS/JAPAN/ISS/L-AE-SER-303.SAS DATE: 02DEC2015

＊新薬承認情報提供時に置換えた

Listing of serious adverse events:
Study 109MS303
Page 25 of 138
Treatment group: BG00012 240 mg BID

Subject Sex/Age Race	MedDRA Preferred Term	Study Day Onset (a)(b)	Res	Dur (days)	Relationship to Study Drug	Severity	Serious	Action Taken With Study Drug	Outcome
[redacted] M/4[redacted] WHITE	神経痛	263	277	15	UNRELATED	MODERATE	Yes	NONE	RESOLVED
[redacted] M/4[redacted] WHITE	多発性硬化症再発	3	8	6	UNRELATED	MODERATE	Yes	NONE	RESOLVED
[redacted] F/3[redacted] WHITE	誤嚥性肺炎	1015	1018	4	UNRELATED	SEVERE	Yes	NONE	RESOLVED
[redacted] M/4[redacted] WHITE	痙攣	1395	1439	45	UNRELATED	SEVERE	Yes	DI	RESOLVED

(a) #=On or after the subject switched to alternate MS medication
(b) ^=Adverse Event with onset prior to dosing
Abbreviations: Res=Resolution, NR=Not Recovered/Not Resolved, Dur=Duration, NONE=Dose Not Changed, DW=Drug Withdrawn, DI=Drug Interrupted, DR=Dose Reduced, M=Male, F=Female

SOURCE: BG12MS/JAPAN/ISS/L-AE-SER-303.SAS DATE: 02DEC2015

＊新薬承認情報提供時に置換えた

Listing of serious adverse events:
Study 109MS303
Page 26 of 138
Treatment group: BG00012 240 mg BID

Subject Sex/Age Race	MedDRA Preferred Term	Study Day Onset (a)(b)	Res	Dur (days)	Relationship to Study Drug	Severity	Serious	Action Taken With Study Drug	Outcome
[redacted] M/4[redacted] WHITE	甲状腺癌	575	585	11	UNRELATED	MODERATE	Yes	NONE	RESOLVED
[redacted] F/4[redacted] WHITE	線維嚢胞性乳腺疾患	1450	1452	3	UNRELATED	MODERATE	Yes	NONE	RESOLVED
644* M/5[redacted] WHITE	冠動脈疾患	216	267	52	UNRELATED	MILD	Yes	NONE	RESOLVED
	経皮的冠インターベンション	261	270	10	UNLIKELY	MODERATE	Yes	NONE	RESOLVED
[redacted] M/4[redacted] WHITE	多発性外傷	386	491	106	UNRELATED	MODERATE	Yes	NONE	RESOLVED

(a) #=On or after the subject switched to alternate MS medication
(b) ^=Adverse Event with onset prior to dosing
Abbreviations: Res=Resolution, NR=Not Recovered/Not Resolved, Dur=Duration, NONE=Dose Not Changed, DW=Drug Withdrawn, DI=Drug Interrupted, DR=Dose Reduced, M=Male, F=Female

SOURCE: BG12MS/JAPAN/ISS/L-AE-SER-303.SAS DATE: 02DEC2015

＊新薬承認情報提供時に置換えた

Listing of serious adverse events:
Study 109MS303
Page 27 of 138
Treatment group: BG00012 240 mg BID

Subject Sex/Age Race	MedDRA Preferred Term	Study Day Onset (a)(b)	Res	Dur (days)	Relationship to Study Drug	Severity	Serious	Action Taken With Study Drug	Outcome
[redacted] M/4[redacted] WHITE	交通事故	386	491	106	UNRELATED	MODERATE	Yes	NONE	RESOLVED
[redacted] F/5[redacted] WHITE	発熱	155	163	9	POSSIBLY	MODERATE	Yes	NONE	RESOLVED
	上気道感染	155	163	9	POSSIBLY	MODERATE	Yes	NONE	RESOLVED
	転倒	697	701	5	UNRELATED	SEVERE	Yes	NONE	RESOLVED
	足骨折	697	701	5	UNRELATED	SEVERE	Yes	NONE	RESOLVED
	背部痛	931	942	12	UNRELATED	SEVERE	Yes	NONE	RESOLVED
	脊椎すべり症	1631	1662	32	UNRELATED	MODERATE	Yes	NONE	RESOLVED
	挫傷	1665	1667	3	UNRELATED	MODERATE	Yes	NONE	RESOLVED
	転倒	1665	1667	3	UNRELATED	MODERATE	Yes	NONE	RESOLVED

(a) #=On or after the subject switched to alternate MS medication
(b) ^=Adverse Event with onset prior to dosing
Abbreviations: Res=Resolution, NR=Not Recovered/Not Resolved, Dur=Duration, NONE=Dose Not Changed, DW=Drug Withdrawn, DI=Drug Interrupted, DR=Dose Reduced, M=Male, F=Female

SOURCE: BG12MS/JAPAN/ISS/L-AE-SER-303.SAS DATE: 02DEC2015

＊新薬承認情報提供時に置換えた

Listing of serious adverse events:
Study 109MS303
Page 28 of 138
Treatment group: BG00012 240 mg BID

Subject Sex/Age Race	MedDRA Preferred Term	Study Day Onset (a)(b)	Res	Dur (days)	Relationship to Study Drug	Severity	Serious	Action Taken With Study Drug	Outcome
[redacted] M/3[redacted] WHITE	臍帯ヘルニア修復	337	338	2	UNRELATED	MODERATE	Yes	NONE	RESOLVED
	脳挫傷	1494	1506	13	UNRELATED	MODERATE	Yes	NONE	RESOLVED
	挫傷	1494	1506	13	UNRELATED	MODERATE	Yes	NONE	RESOLVED
	骨格損傷	1494	1506	13	UNRELATED	MODERATE	Yes	NONE	RESOLVED
[redacted] F/3[redacted] WHITE	転倒	1677	1677	1	UNRELATED	MODERATE	Yes	NONE	RESOLVED
	橈骨骨折	1677	1807	131	UNRELATED	MODERATE	Yes	NONE	RESOLVED
030* F/2[redacted] WHITE	四肢奇形	1739	1745	7	UNRELATED	SEVERE	Yes	NONE	RESOLVED

(a) #=On or after the subject switched to alternate MS medication
(b) ^=Adverse Event with onset prior to dosing
Abbreviations: Res=Resolution, NR=Not Recovered/Not Resolved, Dur=Duration, NONE=Dose Not Changed, DW=Drug Withdrawn, DI=Drug Interrupted, DR=Dose Reduced, M=Male, F=Female

SOURCE: BG12MS/JAPAN/ISS/L-AE-SER-303.SAS DATE: 02DEC2015

＊新薬承認情報提供時に置換えた

Listing of serious adverse events:
Study 109MS303
Page 29 of 138
Treatment group: BG00012 240 mg BID

Subject Sex/Age Race	MedDRA Preferred Term	Study Day Onset (a)(b)	Res	Dur (days)	Relationship to Study Drug	Severity	Serious	Action Taken With Study Drug	Outcome
[redacted] M/ 3[redacted] WHITE	交通事故	716	716	1	UNRELATED	MODERATE	Yes	NONE	RESOLVED
	剥離骨折	717	754	38	UNRELATED	MODERATE	Yes	NONE	RESOLVED
	恥骨骨折	717	754	38	UNRELATED	MODERATE	Yes	NONE	RESOLVED
	白血球減少症	1025	1032	8	UNLIKELY	MODERATE	Yes	NONE	RESOLVED
	気道感染	1025	1040	16	UNLIKELY	MODERATE	Yes	NONE	RESOLVED
[redacted] M/3[redacted] WHITE	多発性硬化症再発	940	952	13	UNRELATED	MODERATE	Yes	NONE	RESOLVED
[redacted] M/3[redacted] WHITE	静脈瘤手術	268	270	3	UNRELATED	MODERATE	Yes	NONE	RESOLVED

(a) #=On or after the subject switched to alternate MS medication
(b) ^=Adverse Event with onset prior to dosing
Abbreviations: Res=Resolution, NR=Not Recovered/Not Resolved, Dur=Duration, NONE=Dose Not Changed, DW=Drug Withdrawn, DI=Drug Interrupted, DR=Dose Reduced, M=Male, F=Female

SOURCE: BG12MS/JAPAN/ISS/L-AE-SER-303.SAS DATE: 02DEC2015

＊新薬承認情報提供時に置換えた

Listing of serious adverse events:
Study 109MS303
Page 30 of 138
Treatment group: BG00012 240 mg BID

Subject Sex/Age Race	MedDRA Preferred Term	Study Day Onset (a)(b)	Res	Dur (days)	Relationship to Study Drug	Severity	Serious	Action Taken With Study Drug	Outcome
[redacted] M/3[redacted] WHITE	多発性硬化症再発	2013	2046	34	UNRELATED	SEVERE	Yes	DW	RESOLVED
032* F/4[redacted] WHITE	急性精神病	703	808	106	UNRELATED	SEVERE	Yes	NONE	RESOLVED
	不正子宮出血	703	710	8	UNRELATED	SEVERE	Yes	NONE	RESOLVED
	子宮平滑筋腫	978	992	15	UNRELATED	SEVERE	Yes	NONE	RESOLVED
[redacted] F/5[redacted] WHITE	膀胱瘤	1518	1524	7	UNRELATED	MILD	Yes	NONE	RESOLVED
653* F/4[redacted] WHITE	背部痛	1007	1013	7	UNRELATED	MODERATE	Yes	NONE	RESOLVED

(a) #=On or after the subject switched to alternate MS medication
(b) ^=Adverse Event with onset prior to dosing
Abbreviations: Res=Resolution, NR=Not Recovered/Not Resolved, Dur=Duration, NONE=Dose Not Changed, DW=Drug Withdrawn, DI=Drug Interrupted, DR=Dose Reduced, M=Male, F=Female

SOURCE: BG12MS/JAPAN/ISS/L-AE-SER-303.SAS DATE: 02DEC2015

＊新薬承認情報提供時に置換えた

Listing of serious adverse events:
Study 109MS303
Page 31 of 138
Treatment group: BG00012 240 mg BID

Subject Sex/Age Race	MedDRA Preferred Term	Study Day Onset (a)(b)	Res	Dur (days)	Relationship to Study Drug	Severity	Serious	Action Taken With Study Drug	Outcome
653* F/4[redacted] WHITE	多発性硬化症再発	1589	NR		UNRELATED	SEVERE	Yes	NONE	NOT RESOLVED
	多発性硬化症再発	1595	1601	7	UNRELATED	SEVERE	Yes	NONE	RESOLVED
[redacted] M/3[redacted] WHITE	大動脈弁置換	976	984	9	UNRELATED	MODERATE	Yes	NONE	RESOLVED
[redacted] M/3[redacted] WHITE	穿孔性十二指腸潰瘍	737	762	26	UNRELATED	SEVERE	Yes	DI	RESOLVED
[redacted] M/4[redacted] WHITE	多発性硬化症再発	236	242	7	UNRELATED	MODERATE	Yes	NONE	RESOLVED

(a) #=On or after the subject switched to alternate MS medication
(b) ^=Adverse Event with onset prior to dosing
Abbreviations: Res=Resolution, NR=Not Recovered/Not Resolved, Dur=Duration, NONE=Dose Not Changed, DW=Drug Withdrawn, DI=Drug Interrupted, DR=Dose Reduced, M=Male, F=Female

SOURCE: BG12MS/JAPAN/ISS/L-AE-SER-303.SAS DATE: 02DEC2015

＊新薬承認情報提供時に置換えた

Listing of serious adverse events:
Study 109MS303
Page 32 of 138
Treatment group: BG00012 240 mg BID

Subject Sex/Age Race	MedDRA Preferred Term	Study Day Onset (a)(b)	Res	Dur (days)	Relationship to Study Drug	Severity	Serious	Action Taken With Study Drug	Outcome
[redacted] F/2[redacted] WHITE	肺炎	147	166	20	UNRELATED	MODERATE	Yes	NONE	RESOLVED
366* F/4[redacted] WHITE	子宮内膜癌	431	438	8	UNRELATED	MODERATE	Yes	NONE	RESOLVED
	腎細胞癌	562	570	9	UNRELATED	MODERATE	Yes	NONE	RESOLVED
[redacted] F/4[redacted] WHITE	糖尿病	643	645	3	UNRELATED	MILD	Yes	NONE	RESOLVED
[redacted] F/4[redacted] WHITE	多発性硬化症再発	95	99	5	UNRELATED	MODERATE	Yes	NONE	RESOLVED

(a) #=On or after the subject switched to alternate MS medication
(b) ^=Adverse Event with onset prior to dosing
Abbreviations: Res=Resolution, NR=Not Recovered/Not Resolved, Dur=Duration, NONE=Dose Not Changed, DW=Drug Withdrawn, DI=Drug Interrupted, DR=Dose Reduced, M=Male, F=Female

SOURCE: BG12MS/JAPAN/ISS/L-AE-SER-303.SAS DATE: 02DEC2015

＊新薬承認情報提供時に置換えた

Listing of serious adverse events:
Study 109MS303
Page 33 of 138
Treatment group: BG00012 240 mg BID

Subject Sex/Age Race	MedDRA Preferred Term	Study Day Onset (a)(b)	Res	Dur (days)	Relationship to Study Drug	Severity	Serious	Action Taken With Study Drug	Outcome
566* F/4[redacted] WHITE	多発性硬化症再発	280	284	5	UNLIKELY	MILD	Yes	NONE	RESOLVED
	多発性硬化症再発	830	834	5	UNRELATED	MILD	Yes	NONE	RESOLVED
	多発性硬化症再発	1148	1152	5	UNRELATED	MILD	Yes	NONE	RESOLVED
[redacted] M/4[redacted] WHITE	多発性硬化症再発	72	76	5	UNLIKELY	MILD	Yes	NONE	RESOLVED
	多発性硬化症再発	395	399	5	UNLIKELY	MILD	Yes	NONE	RESOLVED
	多発性硬化症再発	1199	1203	5	UNRELATED	MILD	Yes	NONE	RESOLVED

(a) #=On or after the subject switched to alternate MS medication
(b) ^=Adverse Event with onset prior to dosing
Abbreviations: Res=Resolution, NR=Not Recovered/Not Resolved, Dur=Duration, NONE=Dose Not Changed, DW=Drug Withdrawn, DI=Drug Interrupted, DR=Dose Reduced, M=Male, F=Female

SOURCE: BG12MS/JAPAN/ISS/L-AE-SER-303.SAS DATE: 02DEC2015

＊新薬承認情報提供時に置換えた

Listing of serious adverse events:
Study 109MS303
Page 34 of 138
Treatment group: BG00012 240 mg BID

Subject Sex/Age Race	MedDRA Preferred Term	Study Day Onset (a)(b)	Res	Dur (days)	Relationship to Study Drug	Severity	Serious	Action Taken With Study Drug	Outcome
[redacted] F/3[redacted] WHITE	下肢骨折	285	288	4	UNRELATED	MODERATE	Yes	NONE	RESOLVED
	直腸膿瘍	510	510	1	UNLIKELY	MODERATE	Yes	NONE	RESOLVED
	直腸膿瘍	578			UNLIKELY	MODERATE	Yes	NONE	RESOLVED
	多発性硬化症再発	623	627	5	UNRELATED	MILD	Yes	NONE	RESOLVED
[redacted] F/4[redacted] WHITE	多発性硬化症再発	1767	1771	5	UNRELATED	SEVERE	Yes	NONE	RESOLVED
	多発性硬化症再発	1767	1772	6	UNRELATED	MODERATE	Yes	NONE	RESOLVED
567* F/4[redacted] WHITE	多発性硬化症再発	1015	1019	5	UNRELATED	MODERATE	Yes	NONE	RESOLVED

(a) #=On or after the subject switched to alternate MS medication
(b) ^=Adverse Event with onset prior to dosing
Abbreviations: Res=Resolution, NR=Not Recovered/Not Resolved, Dur=Duration, NONE=Dose Not Changed, DW=Drug Withdrawn, DI=Drug Interrupted, DR=Dose Reduced, M=Male, F=Female

SOURCE: BG12MS/JAPAN/ISS/L-AE-SER-303.SAS DATE: 02DEC2015

Listing of serious adverse events:
Study 109MS303
Page 35 of 138
Treatment group: BG00012 240 mg BID

Subject Sex/Age Race	MedDRA Preferred Term	Study Day Onset (a)(b)	Res	Dur (days)	Relationship to Study Drug	Severity	Serious	Action Taken With Study Drug	Outcome
[redacted] F/2[redacted] WHITE	多発性硬化症再発	99	103	5	UNLIKELY	MODERATE	Yes	NONE	RESOLVED
	多発性硬化症再発	232	236	5	UNLIKELY	MODERATE	Yes	NONE	RESOLVED
	多発性硬化症再発	389	393	5	UNLIKELY	MODERATE	Yes	DW	RESOLVED
	多発性硬化症再発	445#	447	3	UNRELATED	MODERATE	Yes	NONE	RESOLVED
[redacted] M/5[redacted] WHITE	亜イレウス	1325	1331	7	UNLIKELY	MODERATE	Yes	NONE	RESOLVED
[redacted] F/2[redacted] WHITE	切開部位血腫	134	138	5	UNRELATED	MODERATE	Yes	NONE	RESOLVED

(a) #=On or after the subject switched to alternate MS medication
(b) ^=Adverse Event with onset prior to dosing
Abbreviations: Res=Resolution, NR=Not Recovered/Not Resolved, Dur=Duration, NONE=Dose Not Changed, DW=Drug Withdrawn, DI=Drug Interrupted, DR=Dose Reduced, M=Male, F=Female

SOURCE: BG12MS/JAPAN/ISS/L-AE-SER-303.SAS DATE: 02DEC2015

＊新薬承認情報提供時に置換えた

Listing of serious adverse events:
Study 109MS303
Page 36 of 138
Treatment group: BG00012 240 mg BID

Subject Sex/Age Race	MedDRA Preferred Term	Study Day Onset (a)(b)	Study Day Res	Dur (days)	Relationship to Study Drug	Severity	Serious	Action Taken With Study Drug	Outcome
[redacted] M/ 3[redacted] WHITE	多発性硬化症再発	757	761	5	UNRELATED	SEVERE	Yes	NONE	RESOLVED
	多発性硬化症再発	1100	1104	5	UNRELATED	MODERATE	Yes	NONE	RESOLVED
[redacted] F/4[redacted] WHITE	気管支炎	1699	1744	46	UNRELATED	SEVERE	Yes	DI	RESOLVED
[redacted] F/2[redacted] WHITE	多発性硬化症再発	761	766	6	UNLIKELY	MODERATE	Yes	NONE	RESOLVED
	多発性硬化症再発	1129	1134	6	UNLIKELY	MODERATE	Yes	NONE	RESOLVED
	多発性硬化症再発	1765	1769	5	UNRELATED	MODERATE	Yes	NONE	RESOLVED

(a) #=On or after the subject switched to alternate MS medication
(b) ^=Adverse Event with onset prior to dosing
Abbreviations: Res=Resolution, NR=Not Recovered/Not Resolved, Dur=Duration, NONE=Dose Not Changed, DW=Drug Withdrawn, DI=Drug Interrupted, DR=Dose Reduced, M=Male, F=Female

SOURCE: BG12MS/JAPAN/ISS/L-AE-SER-303.SAS DATE: 02DEC2015

＊新薬承認情報提供時に置換えた

Listing of serious adverse events:
Study 109MS303
Page 37 of 138
Treatment group: BG00012 240 mg BID

Subject Sex/Age Race	MedDRA Preferred Term	Study Day Onset (a)(b)	Study Day Res	Dur (days)	Relationship to Study Drug	Severity	Serious	Action Taken With Study Drug	Outcome
[redacted] F/4[redacted] WHITE	多発性硬化症再発	1264	1268	5	UNRELATED	MODERATE	Yes	NONE	RESOLVED
655* M/4[redacted] WHITE	多発性硬化症再発	700	704	5	UNRELATED	MILD	Yes	DW	RESOLVED
568* F/3[redacted] WHITE	多発性硬化症再発	1892	1896	5	UNRELATED	MODERATE	Yes	NONE	RESOLVED
[redacted] F/4[redacted] WHITE	多発性硬化症再発	261	266	6	UNLIKELY	MODERATE	Yes	NONE	RESOLVED
	多発性硬化症再発	601	605	5	UNLIKELY	MODERATE	Yes	NONE	RESOLVED

(a) #=On or after the subject switched to alternate MS medication
(b) ^=Adverse Event with onset prior to dosing
Abbreviations: Res=Resolution, NR=Not Recovered/Not Resolved, Dur=Duration, NONE=Dose Not Changed, DW=Drug Withdrawn, DI=Drug Interrupted, DR=Dose Reduced, M=Male, F=Female

SOURCE: BG12MS/JAPAN/ISS/L-AE-SER-303.SAS DATE: 02DEC2015

＊新薬承認情報提供時に置換えた

Listing of serious adverse events:
Study 109MS303
Page 38 of 138
Treatment group: BG00012 240 mg BID

Subject Sex/Age Race	MedDRA Preferred Term	Study Day Onset (a)(b)	Study Day Res	Dur (days)	Relationship to Study Drug	Severity	Serious	Action Taken With Study Drug	Outcome
[redacted] F/4[redacted] WHITE	多発性硬化症再発	1172	1176	5	UNLIKELY	MODERATE	Yes	NONE	RESOLVED
570* F/4[redacted] WHITE	子宮内膜増殖症	1032	1034	3	UNRELATED	SEVERE	Yes	NONE	RESOLVED
	胆石症	1155	1163	9	UNRELATED	MODERATE	Yes	NONE	RESOLVED
572* F/5[redacted] WHITE	気管支炎	833	841	9	UNRELATED	MILD	Yes	NONE	RESOLVED
	肺動脈血栓症	925	925	1	UNRELATED	MILD	Yes	NONE	RESOLVED

(a) #=On or after the subject switched to alternate MS medication
(b) ^=Adverse Event with onset prior to dosing
Abbreviations: Res=Resolution, NR=Not Recovered/Not Resolved, Dur=Duration, NONE=Dose Not Changed, DW=Drug Withdrawn, DI=Drug Interrupted, DR=Dose Reduced, M=Male, F=Female

SOURCE: BG12MS/JAPAN/ISS/L-AE-SER-303.SAS DATE: 02DEC2015

＊新薬承認情報提供時に置換えた

Listing of serious adverse events:
Study 109MS303
Page 39 of 138
Treatment group: BG00012 240 mg BID

Subject Sex/Age Race	MedDRA Preferred Term	Study Day Onset (a)(b)	Res	Dur (days)	Relationship to Study Drug	Severity	Serious	Action Taken With Study Drug	Outcome
[redacted] M/3[redacted] WHITE	多発性硬化症再発	770	776	7	UNLIKELY	MILD	Yes	NONE	RESOLVED
[redacted] F/3[redacted] WHITE	多発性硬化症再発	251	257	7	UNLIKELY	MODERATE	Yes	NONE	RESOLVED
[redacted] F/4[redacted] WHITE	多発性硬化症再発	512	517	6	UNLIKELY	MODERATE	Yes	NONE	RESOLVED
	多発性硬化症再発	1267	1280	14	UNLIKELY	MODERATE	Yes	NONE	RESOLVED
[redacted] M/5[redacted] WHITE	虫垂炎	186	195	10	UNLIKELY	MODERATE	Yes	NONE	RESOLVED

(a) #=On or after the subject switched to alternate MS medication
(b) ^=Adverse Event with onset prior to dosing
Abbreviations: Res=Resolution, NR=Not Recovered/Not Resolved, Dur=Duration, NONE=Dose Not Changed, DW=Drug Withdrawn, DI=Drug Interrupted, DR=Dose Reduced, M=Male, F=Female

SOURCE: BG12MS/JAPAN/ISS/L-AE-SER-303.SAS DATE: 02DEC2015

＊新薬承認情報提供時に置換えた

Listing of serious adverse events:
Study 109MS303
Page 40 of 138
Treatment group: BG00012 240 mg BID

Subject Sex/Age Race	MedDRA Preferred Term	Study Day Onset (a)(b)	Res	Dur (days)	Relationship to Study Drug	Severity	Serious	Action Taken With Study Drug	Outcome
[redacted] M/5[redacted] WHITE	虫垂切除	433	438	6	UNLIKELY	MODERATE	Yes	DI	RESOLVED
[redacted] F/4[redacted] WHITE	多発性硬化症再発	1032	1037	6	UNLIKELY	MODERATE	Yes	NONE	RESOLVED
[redacted] F/2[redacted] WHITE	多発性硬化症再発	1284	1289	6	UNRELATED	MODERATE	Yes	NONE	RESOLVED
[redacted] M/5[redacted] WHITE	多発性硬化症再発	217	222	6	UNRELATED	MODERATE	Yes	NONE	RESOLVED

(a) #=On or after the subject switched to alternate MS medication
(b) ^=Adverse Event with onset prior to dosing
Abbreviations: Res=Resolution, NR=Not Recovered/Not Resolved, Dur=Duration, NONE=Dose Not Changed, DW=Drug Withdrawn, DI=Drug Interrupted, DR=Dose Reduced, M=Male, F=Female

SOURCE: BG12MS/JAPAN/ISS/L-AE-SER-303.SAS DATE: 02DEC2015

＊新薬承認情報提供時に置換えた

Listing of serious adverse events:
Study 109MS303
Page 41 of 138
Treatment group: BG00012 240 mg BID

Subject Sex/Age Race	MedDRA Preferred Term	Study Day Onset (a)(b)	Res	Dur (days)	Relationship to Study Drug	Severity	Serious	Action Taken With Study Drug	Outcome
[redacted] F/3[redacted] WHITE	多発性硬化症再発	1045	1051	7	UNLIKELY	MILD	Yes	NONE	RESOLVED
	多発性硬化症再発	1478	1482	5	UNRELATED	MILD	Yes	NONE	RESOLVED
[redacted] F/5[redacted] WHITE	頭痛	99	104	6	UNLIKELY	MODERATE	Yes	NONE	RESOLVED
	脛骨骨折	329	415	87	UNLIKELY	MILD	Yes	NONE	RESOLVED
	多発性硬化症再発	564	569	6	UNLIKELY	MILD	Yes	NONE	RESOLVED
	多発性硬化症再発	768	772	5	UNLIKELY	MILD	Yes	NONE	RESOLVED
	多発性硬化症再発	1250	1254	5	UNLIKELY	MILD	Yes	NONE	RESOLVED

(a) #=On or after the subject switched to alternate MS medication
(b) ^=Adverse Event with onset prior to dosing
Abbreviations: Res=Resolution, NR=Not Recovered/Not Resolved, Dur=Duration, NONE=Dose Not Changed, DW=Drug Withdrawn, DI=Drug Interrupted, DR=Dose Reduced, M=Male, F=Female

SOURCE: BG12MS/JAPAN/ISS/L-AE-SER-303.SAS DATE: 02DEC2015

＊新薬承認情報提供時に置換えた

Listing of serious adverse events:
Study 109MS303
Page 42 of 138
Treatment group: BG00012 240 mg BID

Subject Sex/Age Race	MedDRA Preferred Term	Study Day Onset (a)(b)	Study Day Res	Dur (days)	Relationship to Study Drug	Severity	Serious	Action Taken With Study Drug	Outcome
[redacted] F/2[redacted] WHITE	多発性硬化症再発	745	749	5	UNLIKELY	MILD	Yes	NONE	RESOLVED
	多発性硬化症再発	1072	1077	6	UNLIKELY	MILD	Yes	NONE	RESOLVED
[redacted] F/4[redacted] WHITE	多発性硬化症再発	293	324	32	UNRELATED	MODERATE	Yes	NONE	RESOLVED
[redacted] F/5[redacted] WHITE	脳血管不全	137	138	2	UNRELATED	MILD	Yes	NONE	RESOLVED
	多発性硬化症再発	566	570	5	UNRELATED	MODERATE	Yes	NONE	RESOLVED
	多発性硬化症再発	933	937	5	UNRELATED	MODERATE	Yes	NONE	RESOLVED

(a) #=On or after the subject switched to alternate MS medication
(b) ^=Adverse Event with onset prior to dosing
Abbreviations: Res=Resolution, NR=Not Recovered/Not Resolved, Dur=Duration, NONE=Dose Not Changed, DW=Drug Withdrawn, DI=Drug Interrupted, DR=Dose Reduced, M=Male, F=Female

SOURCE: BG12MS/JAPAN/ISS/L-AE-SER-303.SAS DATE: 02DEC2015

＊新薬承認情報提供時に置換えた

Listing of serious adverse events:
Study 109MS303
Page 43 of 138
Treatment group: BG00012 240 mg BID

Subject Sex/Age Race	MedDRA Preferred Term	Study Day Onset (a)(b)	Study Day Res	Dur (days)	Relationship to Study Drug	Severity	Serious	Action Taken With Study Drug	Outcome
[redacted] F/5[redacted] WHITE	創傷	1537	1538	2	UNRELATED	MODERATE	Yes	NONE	RESOLVED
	多発性硬化症再発	1727	1731	5	UNRELATED	MODERATE	Yes	NONE	RESOLVED
[redacted] M/3[redacted] WHITE	多発性硬化症再発	512	521	10	UNRELATED	MILD	Yes	NONE	RESOLVED
	多発性硬化症再発	760	768	9	UNRELATED	MODERATE	Yes	NONE	RESOLVED
[redacted] M/3[redacted] WHITE	多発性硬化症再発	582	585	4	UNLIKELY	MODERATE	Yes	NONE	RESOLVED
	多発性硬化症再発	921	925	5	UNLIKELY	MODERATE	Yes	NONE	RESOLVED

(a) #=On or after the subject switched to alternate MS medication
(b) ^=Adverse Event with onset prior to dosing
Abbreviations: Res=Resolution, NR=Not Recovered/Not Resolved, Dur=Duration, NONE=Dose Not Changed, DW=Drug Withdrawn, DI=Drug Interrupted, DR=Dose Reduced, M=Male, F=Female

SOURCE: BG12MS/JAPAN/ISS/L-AE-SER-303.SAS DATE: 02DEC2015

＊新薬承認情報提供時に置換えた

Listing of serious adverse events:
Study 109MS303
Page 44 of 138
Treatment group: BG00012 240 mg BID

Subject Sex/Age Race	MedDRA Preferred Term	Study Day Onset (a)(b)	Res	Dur (days)	Relationship to Study Drug	Severity	Serious	Action Taken With Study Drug	Outcome
[redacted] M/3[redacted] WHITE	多発性硬化症再発	1261	1267	7	UNLIKELY	MODERATE	Yes	NONE	RESOLVED
[redacted] F/5[redacted] WHITE	多発性硬化症再発	12	27	16	UNLIKELY	SEVERE	Yes	DW	RESOLVED
[redacted] F/3[redacted] WHITE	子宮平滑筋腫	1722	1730	9	UNRELATED	MODERATE	Yes	DI	RESOLVED
[redacted] F/4[redacted] WHITE	尿路感染	124	133	10	UNRELATED	MILD	Yes	NONE	RESOLVED

(a) #=On or after the subject switched to alternate MS medication
(b) ^=Adverse Event with onset prior to dosing
Abbreviations: Res=Resolution, NR=Not Recovered/Not Resolved, Dur=Duration, NONE=Dose Not Changed, DW=Drug Withdrawn, DI=Drug Interrupted, DR=Dose Reduced, M=Male, F=Female

SOURCE: BG12MS/JAPAN/ISS/L-AE-SER-303.SAS DATE: 02DEC2015

＊新薬承認情報提供時に置換えた

Listing of serious adverse events:
Study 109MS303
Page 45 of 138
Treatment group: BG00012 240 mg BID

Subject Sex/Age Race	MedDRA Preferred Term	Study Day Onset (a)(b)	Res	Dur (days)	Relationship to Study Drug	Severity	Serious	Action Taken With Study Drug	Outcome
[redacted] F/4[redacted] WHITE	多発性硬化症再発	38	52	15	UNRELATED	MILD	Yes	NONE	RESOLVED
[redacted] F/4[redacted] WHITE	多発性硬化症再発	709	714	6	UNRELATED	MODERATE	Yes	NONE	RESOLVED
	大腿骨頚部骨折	714	722	9	UNRELATED	MODERATE	Yes	NONE	RESOLVED
662* M/3[redacted] WHITE	多発性硬化症再発	70	75	6	UNRELATED	MILD	Yes	NONE	RESOLVED
	多発性硬化症再発	306	311	6	UNRELATED	MODERATE	Yes	NONE	RESOLVED
	多発性硬化症再発	740	745	6	UNRELATED	MODERATE	Yes	NONE	RESOLVED

(a) #=On or after the subject switched to alternate MS medication
(b) ^=Adverse Event with onset prior to dosing
Abbreviations: Res=Resolution, NR=Not Recovered/Not Resolved, Dur=Duration, NONE=Dose Not Changed, DW=Drug Withdrawn, DI=Drug Interrupted, DR=Dose Reduced, M=Male, F=Female

SOURCE: BG12MS/JAPAN/ISS/L-AE-SER-303.SAS DATE: 02DEC2015

＊新薬承認情報提供時に置換えた

Listing of serious adverse events:
Study 109MS303
Page 46 of 138
Treatment group: BG00012 240 mg BID

Subject Sex/Age Race	MedDRA Preferred Term	Study Day Onset (a)(b)	Res	Dur (days)	Relationship to Study Drug	Severity	Serious	Action Taken With Study Drug	Outcome
662* M/3[redacted] WHITE	多発性硬化症再発	1231	1237	7	UNRELATED	MODERATE	Yes	NONE	RESOLVED
	多発性硬化症再発	1650	1657	8	UNRELATED	MODERATE	Yes	NONE	RESOLVED
	多発性硬化症再発	1933	1938	6	UNRELATED	MODERATE	Yes	NONE	RESOLVED
[redacted] F/3[redacted] WHITE	多発性硬化症再発	794	798	5	UNRELATED	MODERATE	Yes	NONE	RESOLVED
	多発性硬化症再発	1155	1159	5	UNRELATED	MODERATE	Yes	NONE	RESOLVED
	多発性硬化症再発	1261	1265	5	UNRELATED	MODERATE	Yes	NONE	RESOLVED

(a) #=On or after the subject switched to alternate MS medication
(b) ^=Adverse Event with onset prior to dosing
Abbreviations: Res=Resolution, NR=Not Recovered/Not Resolved, Dur=Duration, NONE=Dose Not Changed, DW=Drug Withdrawn, DI=Drug Interrupted, DR=Dose Reduced, M=Male, F=Female

SOURCE: BG12MS/JAPAN/ISS/L-AE-SER-303.SAS DATE: 02DEC2015

＊新薬承認情報提供時に置換えた

Listing of serious adverse events:
Study 109MS303
Page 47 of 138
Treatment group: BG00012 240 mg BID

Subject Sex/Age Race	MedDRA Preferred Term	Study Day Onset (a)(b)	Res	Dur (days)	Relationship to Study Drug	Severity	Serious	Action Taken With Study Drug	Outcome
663* F/4[redacted] WHITE	白内障	211	213	3	UNRELATED	MODERATE	Yes	NONE	RESOLVED
	多発性硬化症再発	841	845	5	UNRELATED	MODERATE	Yes	NONE	RESOLVED
	多発性硬化症再発	1513	1518	6	UNRELATED	MODERATE	Yes	NONE	RESOLVED
[redacted] M/4[redacted] WHITE	肺扁平上皮癌、病期不明	183	218	36	POSSIBLY	SEVERE	Yes	DW	RESOLVED
	処置後感染	309	334	26	UNRELATED	MODERATE	Yes	NONE	RESOLVED
[redacted] F/3[redacted] WHITE	多発性硬化症再発	761	765	5	UNRELATED	MODERATE	Yes	NONE	RESOLVED

(a) #=On or after the subject switched to alternate MS medication
(b) ^=Adverse Event with onset prior to dosing
Abbreviations: Res=Resolution, NR=Not Recovered/Not Resolved, Dur=Duration, NONE=Dose Not Changed, DW=Drug Withdrawn, DI=Drug Interrupted, DR=Dose Reduced, M=Male, F=Female

SOURCE: BG12MS/JAPAN/ISS/L-AE-SER-303.SAS DATE: 02DEC2015

＊新薬承認情報提供時に置換えた

Listing of serious adverse events:
Study 109MS303
Page 48 of 138
Treatment group: BG00012 240 mg BID

Subject Sex/Age Race	MedDRA Preferred Term	Study Day Onset (a)(b)	Study Day Res	Dur (days)	Relationship to Study Drug	Severity	Serious	Action Taken With Study Drug	Outcome
[redacted] F/3[redacted] WHITE	多発性硬化症再発	1009	1014	6	UNRELATED	MODERATE	Yes	NONE	RESOLVED
665* F/4[redacted] WHITE	多発性硬化症再発	1016	1021	6	UNRELATED	MODERATE	Yes	NONE	RESOLVED
363* F/5[redacted] WHITE	多発性硬化症再発	303	308	6	UNRELATED	MODERATE	Yes	NONE	RESOLVED
	ネフローゼ症候群	378	426	49	POSSIBLY	MODERATE	Yes	DW	RESOLVED
[redacted] F/3[redacted] WHITE	多発性硬化症再発	284	288	5	UNRELATED	MODERATE	Yes	NONE	RESOLVED
	多発性硬化症	1131	1135	5	UNRELATED	MODERATE	Yes	NONE	RESOLVED

(a) #=On or after the subject switched to alternate MS medication
(b) ^=Adverse Event with onset prior to dosing
Abbreviations: Res=Resolution, NR=Not Recovered/Not Resolved, Dur=Duration, NONE=Dose Not Changed, DW=Drug Withdrawn, DI=Drug Interrupted, DR=Dose Reduced, M=Male, F=Female

SOURCE: BG12MS/JAPAN/ISS/L-AE-SER-303.SAS DATE: 02DEC2015

＊新薬承認情報提供時に置換えた

Listing of serious adverse events:
Study 109MS303
Page 49 of 138
Treatment group: BG00012 240 mg BID

Subject Sex/Age Race	MedDRA Preferred Term	Study Day Onset (a)(b)	Res	Dur (days)	Relationship to Study Drug	Severity	Serious	Action Taken With Study Drug	Outcome
[redacted] F/3[redacted] WHITE	多発性硬化症再発	1471	1475	5	UNRELATED	MODERATE	Yes	NONE	RESOLVED
[redacted] F/4[redacted] WHITE	多発性硬化症再発	751	757	7	UNRELATED	MODERATE	Yes	NONE	RESOLVED
	多発性硬化症再発	1017	1024	8	UNRELATED	MODERATE	Yes	NONE	RESOLVED
	多発性硬化症再発	1516	1520	5	UNRELATED	MODERATE	Yes	NONE	RESOLVED
[redacted] F/3[redacted] WHITE	多発性硬化症再発	98	102	5	UNLIKELY	MODERATE	Yes	NONE	RESOLVED
	多発性硬化症再発	184	188	5	UNLIKELY	MODERATE	Yes	NONE	RESOLVED

(a) #=On or after the subject switched to alternate MS medication
(b) ^=Adverse Event with onset prior to dosing
Abbreviations: Res=Resolution, NR=Not Recovered/Not Resolved, Dur=Duration, NONE=Dose Not Changed, DW=Drug Withdrawn, DI=Drug Interrupted, DR=Dose Reduced, M=Male, F=Female

SOURCE: BG12MS/JAPAN/ISS/L-AE-SER-303.SAS DATE: 02DEC2015

＊新薬承認情報提供時に置換えた

Listing of serious adverse events:
Study 109MS303
Page 50 of 138
Treatment group: BG00012 240 mg BID

Subject Sex/Age Race	MedDRA Preferred Term	Study Day Onset (a)(b)	Res	Dur (days)	Relationship to Study Drug	Severity	Serious	Action Taken With Study Drug	Outcome
[redacted] F/3[redacted] WHITE	多発性硬化症再発	1163	1168	6	UNLIKELY	MODERATE	Yes	NONE	RESOLVED
	多発性硬化症再発	1647	1652	6	UNRELATED	MODERATE	Yes	NONE	RESOLVED
[redacted] M/5[redacted] WHITE	多発性硬化症再発	1087	1092	6	UNRELATED	MODERATE	Yes	NONE	RESOLVED
	妄想	1278	1325	48	UNLIKELY	MODERATE	Yes	NONE	RESOLVED
	身体疾患による気分障害	1352	1359	8	UNLIKELY	MODERATE	Yes	NONE	RESOLVED
359* F/5[redacted] WHITE	多発性硬化症再発	831	843	13	UNRELATED	MODERATE	Yes	NONE	RESOLVED

(a) #=On or after the subject switched to alternate MS medication
(b) ^=Adverse Event with onset prior to dosing
Abbreviations: Res=Resolution, NR=Not Recovered/Not Resolved, Dur=Duration, NONE=Dose Not Changed, DW=Drug Withdrawn, DI=Drug Interrupted, DR=Dose Reduced, M=Male, F=Female

SOURCE: BG12MS/JAPAN/ISS/L-AE-SER-303.SAS DATE: 02DEC2015

＊新薬承認情報提供時に置換えた

Listing of serious adverse events:
Study 109MS303
Page 51 of 138
Treatment group: BG00012 240 mg BID

Subject Sex/Age Race	MedDRA Preferred Term	Study Day Onset (a)(b)	Res	Dur (days)	Relationship to Study Drug	Severity	Serious	Action Taken With Study Drug	Outcome
359* F/5[redacted] WHITE	腟感染	915	932	18	UNRELATED	MODERATE	Yes	NONE	RESOLVED
	尿路感染	1415	1419	5	UNRELATED	MODERATE	Yes	NONE	RESOLVED
	腟感染	1415	1419	5	UNRELATED	MODERATE	Yes	NONE	RESOLVED
	神経因性膀胱	1457	1460	4	UNRELATED	MODERATE	Yes	NONE	RESOLVED
	細菌尿	1698	NR		UNRELATED	SEVERE	Yes	NONE	NOT RESOLVED
[redacted] F/3[redacted] WHITE	多発性硬化症再発	586	591	6	UNRELATED	MODERATE	Yes	NONE	RESOLVED
[redacted] F/4[redacted] WHITE	妊娠合併症	1388	1390	3	UNRELATED	SEVERE	Yes	NONE	RESOLVED

(a) #=On or after the subject switched to alternate MS medication
(b) ^=Adverse Event with onset prior to dosing
Abbreviations: Res=Resolution, NR=Not Recovered/Not Resolved, Dur=Duration, NONE=Dose Not Changed, DW=Drug Withdrawn, DI=Drug Interrupted, DR=Dose Reduced, M=Male, F=Female

SOURCE: BG12MS/JAPAN/ISS/L-AE-SER-303.SAS DATE: 02DEC2015

＊新薬承認情報提供時に置換えた

Listing of serious adverse events:
Study 109MS303
Page 52 of 138
Treatment group: BG00012 240 mg BID

Subject Sex/Age Race	MedDRA Preferred Term	Study Day Onset (a)(b)	Res	Dur (days)	Relationship to Study Drug	Severity	Serious	Action Taken With Study Drug	Outcome
[redacted] M/3[redacted] WHITE	多発性硬化症再発	53	85	33	UNRELATED	MODERATE	Yes	NONE	RESOLVED
[redacted] F/2[redacted] WHITE	多発性硬化症再発	191	195	5	UNRELATED	MODERATE	Yes	NONE	RESOLVED
	多発性硬化症再発	494	499	6	UNRELATED	MODERATE	Yes	NONE	RESOLVED
[redacted] F/4[redacted] WHITE	神経症	1454	1458	5	UNRELATED	MODERATE	Yes	NONE	RESOLVED
[redacted] M/2[redacted] WHITE	多発性硬化症再発	352	356	5	UNRELATED	MODERATE	Yes	NONE	RESOLVED

(a) #=On or after the subject switched to alternate MS medication
(b) ^=Adverse Event with onset prior to dosing
Abbreviations: Res=Resolution, NR=Not Recovered/Not Resolved, Dur=Duration, NONE=Dose Not Changed, DW=Drug Withdrawn, DI=Drug Interrupted, DR=Dose Reduced, M=Male, F=Female

SOURCE: BG12MS/JAPAN/ISS/L-AE-SER-303.SAS DATE: 02DEC2015

＊新薬承認情報提供時に置換えた

Listing of serious adverse events:
Study 109MS303
Page 53 of 138
Treatment group: BG00012 240 mg BID

Subject Sex/Age Race	MedDRA Preferred Term	Study Day Onset (a)(b)	Res	Dur (days)	Relationship to Study Drug	Severity	Serious	Action Taken With Study Drug	Outcome
[redacted] F/3[redacted] WHITE	幻覚	272	276	5	UNLIKELY	MODERATE	Yes	NONE	RESOLVED
[redacted] F/3[redacted] WHITE	多発性硬化症再発	441	445	5	UNLIKELY	MODERATE	Yes	NONE	RESOLVED
	多発性硬化症再発	703	707	5	UNRELATED	MILD	Yes	NONE	RESOLVED
	多発性硬化症再発	1347	1351	5	UNRELATED	MODERATE	Yes	NONE	RESOLVED
[redacted] F/4[redacted] WHITE	子宮平滑筋腫	1327	1333	7	UNRELATED	MILD	Yes	NONE	RESOLVED

(a) #=On or after the subject switched to alternate MS medication
(b) ^=Adverse Event with onset prior to dosing
Abbreviations: Res=Resolution, NR=Not Recovered/Not Resolved, Dur=Duration, NONE=Dose Not Changed, DW=Drug Withdrawn, DI=Drug Interrupted, DR=Dose Reduced, M=Male, F=Female

SOURCE: BG12MS/JAPAN/ISS/L-AE-SER-303.SAS DATE: 02DEC2015

＊新薬承認情報提供時に置換えた

Listing of serious adverse events:
Study 109MS303
Page 54 of 138
Treatment group: BG00012 240 mg BID

Subject Sex/Age Race	MedDRA Preferred Term	Study Day Onset (a)(b)	Res	Dur (days)	Relationship to Study Drug	Severity	Serious	Action Taken With Study Drug	Outcome
[redacted] F/4[redacted] WHITE	足変形	241	244	4	UNRELATED	MILD	Yes	NONE	RESOLVED
[redacted] M/2[redacted] WHITE	胃食道逆流性疾患	46	50	5	POSSIBLY	MODERATE	Yes	NONE	RESOLVED
[redacted] F/4[redacted] WHITE	椎間板障害	591	593	3	UNRELATED	SEVERE	Yes	NONE	RESOLVED
669* F/4[redacted] WHITE	多発性硬化症再発	368	371	4	UNRELATED	MILD	Yes	NONE	RESOLVED

(a) #=On or after the subject switched to alternate MS medication
(b) ^=Adverse Event with onset prior to dosing
Abbreviations: Res=Resolution, NR=Not Recovered/Not Resolved, Dur=Duration, NONE=Dose Not Changed, DW=Drug Withdrawn, DI=Drug Interrupted, DR=Dose Reduced, M=Male, F=Female

SOURCE: BG12MS/JAPAN/ISS/L-AE-SER-303.SAS DATE: 02DEC2015

＊新薬承認情報提供時に置換えた

Listing of serious adverse events:
Study 109MS303
Page 55 of 138
Treatment group: BG00012 240 mg BID

Subject Sex/Age Race	MedDRA Preferred Term	Study Day Onset (a)(b)	Res	Dur (days)	Relationship to Study Drug	Severity	Serious	Action Taken With Study Drug	Outcome
362* F/2[redacted] WHITE	血尿	603	607	5	UNLIKELY	MILD	Yes	NONE	RESOLVED
367* F/5[redacted] WHITE	腎細胞癌	951	961	11	UNRELATED	SEVERE	Yes	DW	RESOLVED
[redacted] F/2[redacted] WHITE	多発性硬化症再発	517	521	5	UNRELATED	MILD	Yes	NONE	RESOLVED
[redacted] F/5[redacted] WHITE	多発性硬化症再発	100	107	8	UNRELATED	MILD	Yes	NONE	RESOLVED
	多発性硬化症再発	220	225	6	UNRELATED	MODERATE	Yes	NONE	RESOLVED

(a) #=On or after the subject switched to alternate MS medication
(b) ^=Adverse Event with onset prior to dosing
Abbreviations: Res=Resolution, NR=Not Recovered/Not Resolved, Dur=Duration, NONE=Dose Not Changed, DW=Drug Withdrawn, DI=Drug Interrupted, DR=Dose Reduced, M=Male, F=Female

SOURCE: BG12MS/JAPAN/ISS/L-AE-SER-303.SAS DATE: 02DEC2015

＊新薬承認情報提供時に置換えた

Listing of serious adverse events:
Study 109MS303
Page 56 of 138
Treatment group: BG00012 240 mg BID

Subject Sex/Age Race	MedDRA Preferred Term	Study Day Onset (a)(b)	Res	Dur (days)	Relationship to Study Drug	Severity	Serious	Action Taken With Study Drug	Outcome
[redacted] F/5[redacted] WHITE	多発性硬化症再発	330	334	5	UNRELATED	MODERATE	Yes	NONE	RESOLVED
[redacted] M/4[redacted] WHITE	多発性硬化症再発	1215	1350	136	UNRELATED	MODERATE	Yes	NONE	NOT RESOLVED
	精巣上体炎	1225	1233	9	POSSIBLY	SEVERE	Yes	NONE	RESOLVED
	精巣上体炎	1225	1233	9	UNRELATED	MODERATE	Yes	NONE	RESOLVED
[redacted] F/4[redacted] WHITE	多発性硬化症再発	1177	1181	5	UNRELATED	MODERATE	Yes	DR	RESOLVED
[redacted] F/4[redacted] WHITE	単純ヘルペス	1012	1016	5	POSSIBLY	MODERATE	Yes	NONE	RESOLVED

(a) #=On or after the subject switched to alternate MS medication
(b) ^=Adverse Event with onset prior to dosing
Abbreviations: Res=Resolution, NR=Not Recovered/Not Resolved, Dur=Duration, NONE=Dose Not Changed, DW=Drug Withdrawn, DI=Drug Interrupted, DR=Dose Reduced, M=Male, F=Female

SOURCE: BG12MS/JAPAN/ISS/L-AE-SER-303.SAS DATE: 02DEC2015

＊新薬承認情報提供時に置換えた

Listing of serious adverse events:
Study 109MS303
Page 57 of 138
Treatment group: BG00012 240 mg BID

Subject Sex/Age Race	MedDRA Preferred Term	Study Day Onset (a)(b)	Study Day Res	Dur (days)	Relationship to Study Drug	Severity	Serious	Action Taken With Study Drug	Outcome
[redacted] F/4[redacted] WHITE	単純ヘルペス	1020	1026	7	POSSIBLY	MODERATE	Yes	DI	RESOLVED
[redacted] F/4[redacted] WHITE	バセドウ病	919	924	6	UNRELATED	SEVERE	Yes	NONE	RESOLVED
	副鼻腔炎	919	924	6	POSSIBLY	SEVERE	Yes	NONE	RESOLVED
[redacted] F/4[redacted] WHITE	皮膚潰瘍	281	309	29	UNLIKELY	SEVERE	Yes	NONE	RESOLVED
[redacted] F/4[redacted] WHITE	挫傷	469	475	7	UNRELATED	SEVERE	Yes	DI	RESOLVED
	靱帯断裂	469	475	7	UNRELATED	MODERATE	Yes	DI	RESOLVED

(a) #=On or after the subject switched to alternate MS medication
(b) ^=Adverse Event with onset prior to dosing
Abbreviations: Res=Resolution, NR=Not Recovered/Not Resolved, Dur=Duration, NONE=Dose Not Changed, DW=Drug Withdrawn, DI=Drug Interrupted, DR=Dose Reduced, M=Male, F=Female

SOURCE: BG12MS/JAPAN/ISS/L-AE-SER-303.SAS DATE: 02DEC2015

＊新薬承認情報提供時に置換えた

Listing of serious adverse events:
Study 109MS303
Page 58 of 138
Treatment group: BG00012 240 mg BID

Subject Sex/Age Race	MedDRA Preferred Term	Study Day Onset (a)(b)	Res	Dur (days)	Relationship to Study Drug	Severity	Serious	Action Taken With Study Drug	Outcome
[redacted] F/4[redacted] WHITE	半月板障害	469	475	7	UNRELATED	MODERATE	Yes	DI	RESOLVED
[redacted] F/4[redacted]	多発性硬化症再発	172	176	5	UNRELATED	MILD	Yes	NONE	RESOLVED
	子宮頚部新生物	882	921	40	POSSIBLY	MODERATE	Yes	DI	RESOLVED
[redacted] F/3[redacted]	腹壁形成	609	610	2	UNRELATED	MILD	Yes	NONE	RESOLVED
	乳房形成	609	610	2	UNRELATED	MILD	Yes	NONE	RESOLVED
[redacted] M/3[redacted]	虫垂炎	424	425	2	UNRELATED	SEVERE	Yes	NONE	RESOLVED
[redacted] F/3[redacted]	多発性硬化症再発	134	136	3	UNRELATED	MODERATE	Yes	NONE	RESOLVED

(a) #=On or after the subject switched to alternate MS medication
(b) ^=Adverse Event with onset prior to dosing
Abbreviations: Res=Resolution, NR=Not Recovered/Not Resolved, Dur=Duration, NONE=Dose Not Changed, DW=Drug Withdrawn, DI=Drug Interrupted, DR=Dose Reduced, M=Male, F=Female

SOURCE: BG12MS/JAPAN/ISS/L-AE-SER-303.SAS DATE: 02DEC2015

＊新薬承認情報提供時に置換えた

Listing of serious adverse events:
Study 109MS303
Page 59 of 138
Treatment group: BG00012 240 mg BID

Subject Sex/Age Race	MedDRA Preferred Term	Study Day Onset (a)(b)	Res	Dur (days)	Relationship to Study Drug	Severity	Serious	Action Taken With Study Drug	Outcome
[redacted] F/3[redacted]	転倒	492	492	1	UNRELATED	SEVERE	Yes	NONE	RESOLVED
	橈骨骨折	492	494	3	UNRELATED	SEVERE	Yes	NONE	RESOLVED
[redacted] F/4[redacted] Other	膀胱腫瘍修復	84	142	59	UNRELATED	SEVERE	Yes	DI	RESOLVED
[redacted] F/3[redacted]	多発性硬化症再発	79	99	21	UNRELATED	MILD	Yes	NONE	RESOLVED
[redacted] F/4[redacted]	変形性関節症	1357	NR		UNRELATED	SEVERE	Yes	NONE	NOT RESOLVED
[redacted] F/3[redacted]	乳癌	808	NR		POSSIBLY	SEVERE	Yes	DW	NOT RESOLVED

(a) #=On or after the subject switched to alternate MS medication
(b) ^=Adverse Event with onset prior to dosing
Abbreviations: Res=Resolution, NR=Not Recovered/Not Resolved, Dur=Duration, NONE=Dose Not Changed, DW=Drug Withdrawn, DI=Drug Interrupted, DR=Dose Reduced, M=Male, F=Female

SOURCE: BG12MS/JAPAN/ISS/L-AE-SER-303.SAS DATE: 02DEC2015

＊新薬承認情報提供時に置換えた

Listing of serious adverse events:
Study 109MS303
Page 60 of 138
Treatment group: BG00012 240 mg BID

Subject Sex/Age Race	MedDRA Preferred Term	Study Day Onset (a)(b)	Res	Dur (days)	Relationship to Study Drug	Severity	Serious	Action Taken With Study Drug	Outcome
[redacted] M/5[redacted] WHITE	構語障害	630	633	4	UNRELATED	MODERATE	Yes	NONE	RESOLVED
[redacted] M/4[redacted] WHITE	転倒	139	139	1	UNRELATED	MODERATE	Yes	NONE	RESOLVED
	足骨折	144	160	17	UNRELATED	MODERATE	Yes	NONE	RESOLVED
	転倒	1134	1134	1	UNRELATED	SEVERE	Yes	NONE	RESOLVED
	大腿骨骨折	1134	1145	12	UNRELATED	SEVERE	Yes	NONE	RESOLVED
	便秘	1817	1853	37	UNRELATED	MODERATE	Yes	NONE	RESOLVED
[redacted] F/4[redacted] WHITE	女性不妊手術	274	277	4	UNRELATED	SEVERE	Yes	NONE	RESOLVED
	卵巣嚢腫摘出術	274	277	4	UNRELATED	SEVERE	Yes	NONE	RESOLVED

(a) #=On or after the subject switched to alternate MS medication
(b) ^=Adverse Event with onset prior to dosing
Abbreviations: Res=Resolution, NR=Not Recovered/Not Resolved, Dur=Duration, NONE=Dose Not Changed, DW=Drug Withdrawn, DI=Drug Interrupted, DR=Dose Reduced, M=Male, F=Female

SOURCE: BG12MS/JAPAN/ISS/L-AE-SER-303.SAS DATE: 02DEC2015

＊新薬承認情報提供時に置換えた

Listing of serious adverse events:
Study 109MS303
Page 61 of 138
Treatment group: BG00012 240 mg BID

Subject Sex/Age Race	MedDRA Preferred Term	Study Day Onset (a)(b)	Res	Dur (days)	Relationship to Study Drug	Severity	Serious	Action Taken With Study Drug	Outcome
[redacted] F/4[redacted] WHITE	肥満	922	927	6	UNRELATED	MODERATE	Yes	NONE	RESOLVED
[redacted] F/4[redacted] WHITE	乳癌	960	NR		UNLIKELY	SEVERE	Yes	DW	NOT RESOLVED
582* F/4[redacted] WHITE	自殺企図	37	38	2	UNLIKELY	MILD	Yes	NONE	RESOLVED
	乳房壊死	888	986	99	UNRELATED	MODERATE	Yes	NONE	RESOLVED
[redacted] M/4[redacted] WHITE	背部痛	517	529	13	UNRELATED	SEVERE	Yes	NONE	RESOLVED
	精神病的行動	1022	1057	36	UNLIKELY	SEVERE	Yes	DI	RESOLVED

(a) #=On or after the subject switched to alternate MS medication
(b) ^=Adverse Event with onset prior to dosing
Abbreviations: Res=Resolution, NR=Not Recovered/Not Resolved, Dur=Duration, NONE=Dose Not Changed, DW=Drug Withdrawn, DI=Drug Interrupted, DR=Dose Reduced, M=Male, F=Female

SOURCE: BG12MS/JAPAN/ISS/L-AE-SER-303.SAS DATE: 02DEC2015

＊新薬承認情報提供時に置換えた

Listing of serious adverse events:
Study 109MS303
Page 62 of 138
Treatment group: BG00012 240 mg BID

Subject Sex/Age Race	MedDRA Preferred Term	Study Day Onset (a)(b)	Res	Dur (days)	Relationship to Study Drug	Severity	Serious	Action Taken With Study Drug	Outcome
[redacted] F/5[redacted] WHITE	胃腸炎	15	21	7	UNLIKELY	SEVERE	Yes	DI	RESOLVED
584* F/3[redacted] WHITE	臍ヘルニア	1257	1257	1	UNRELATED	SEVERE	Yes	NONE	RESOLVED
[redacted] F/5[redacted] WHITE	片頭痛	1047	1048	2	POSSIBLY	SEVERE	Yes	NONE	RESOLVED
[redacted] F/2[redacted] SCOTTISH+PORTUGUESE/SOUTH AFRICAN	子宮平滑筋腫	924	927	4	UNRELATED	MODERATE	Yes	NONE	RESOLVED

(a) #=On or after the subject switched to alternate MS medication
(b) ^=Adverse Event with onset prior to dosing
Abbreviations: Res=Resolution, NR=Not Recovered/Not Resolved, Dur=Duration, NONE=Dose Not Changed, DW=Drug Withdrawn, DI=Drug Interrupted, DR=Dose Reduced, M=Male, F=Female

SOURCE: BG12MS/JAPAN/ISS/L-AE-SER-303.SAS DATE: 02DEC2015

＊新薬承認情報提供時に置換えた

Listing of serious adverse events:
Study 109MS303
Page 63 of 138
Treatment group: BG00012 240 mg BID

Subject Sex/Age Race	MedDRA Preferred Term	Study Day Onset (a)(b)	Res	Dur (days)	Relationship to Study Drug	Severity	Serious	Action Taken With Study Drug	Outcome
[redacted] F/2[redacted] WHITE	急性精神病	547	610	64	UNLIKELY	SEVERE	Yes	DI	RESOLVED
[redacted] F/4[redacted] WHITE	鉄欠乏性貧血	128	142	15	UNRELATED	MODERATE	Yes	NONE	RESOLVED
[redacted] M/2[redacted] WHITE	多発性硬化症再発	893	904	12	UNRELATED	MILD	Yes	NONE	RESOLVED
	多発性硬化症再発	1147	1152	6	UNRELATED	MODERATE	Yes	NONE	RESOLVED
	多発性硬化症再発	1152	1159	8	UNRELATED	MODERATE	Yes	NONE	RESOLVED

(a) #=On or after the subject switched to alternate MS medication
(b) ^=Adverse Event with onset prior to dosing
Abbreviations: Res=Resolution, NR=Not Recovered/Not Resolved, Dur=Duration, NONE=Dose Not Changed, DW=Drug Withdrawn, DI=Drug Interrupted, DR=Dose Reduced, M=Male, F=Female

SOURCE: BG12MS/JAPAN/ISS/L-AE-SER-303.SAS DATE: 02DEC2015

＊新薬承認情報提供時に置換えた

Listing of serious adverse events:
Study 109MS303
Page 64 of 138
Treatment group: BG00012 240 mg BID

Subject Sex/Age Race	MedDRA Preferred Term	Study Day Onset (a)(b)	Res	Dur (days)	Relationship to Study Drug	Severity	Serious	Action Taken With Study Drug	Outcome
[redacted] M/5[redacted] WHITE	多発性硬化症再発	476	503	28	UNLIKELY	MILD	Yes	NONE	RESOLVED
[redacted] F/2[redacted] WHITE	胃腸の炎症	119	123	5	POSSIBLY	MODERATE	Yes	NONE	RESOLVED
	多発性硬化症再発	476	490	15	UNLIKELY	MILD	Yes	NONE	RESOLVED
[redacted] F/4[redacted] WHITE	子宮平滑筋腫	271	313	43	UNRELATED	MODERATE	Yes	DI	RESOLVED
	足関節部骨折	1173	1286	114	UNRELATED	SEVERE	Yes	NONE	RESOLVED
	交通事故	1173	1286	114	UNLIKELY	SEVERE	Yes	NONE	RESOLVED

(a) #=On or after the subject switched to alternate MS medication
(b) ^=Adverse Event with onset prior to dosing
Abbreviations: Res=Resolution, NR=Not Recovered/Not Resolved, Dur=Duration, NONE=Dose Not Changed, DW=Drug Withdrawn, DI=Drug Interrupted, DR=Dose Reduced, M=Male, F=Female

SOURCE: BG12MS/JAPAN/ISS/L-AE-SER-303.SAS DATE: 02DEC2015

＊新薬承認情報提供時に置換えた

Listing of serious adverse events:
Study 109MS303
Page 65 of 138
Treatment group: BG00012 240 mg BID

Subject Sex/Age Race	MedDRA Preferred Term	Study Day Onset (a)(b)	Res	Dur (days)	Relationship to Study Drug	Severity	Serious	Action Taken With Study Drug	Outcome
[redacted] F/4[redacted] WHITE	変形性関節症	1094	1402	309	UNRELATED	MODERATE	Yes	NONE	RESOLVED
[redacted] F/5[redacted] WHITE	痙攣	672	686	15	UNLIKELY	SEVERE	Yes	DI	RESOLVED
	神経膠腫	749	871	123	UNRELATED	SEVERE	Yes	DW	RESOLVED
[redacted] M/3[redacted] WHITE	多発性硬化症再発	1203	1261	59	UNRELATED	SEVERE	Yes	NONE	RESOLVED
[redacted] F/3[redacted] WHITE	多発性硬化症再発	29	61	33	UNRELATED	MODERATE	Yes	NONE	RESOLVED

(a) #=On or after the subject switched to alternate MS medication
(b) ^=Adverse Event with onset prior to dosing
Abbreviations: Res=Resolution, NR=Not Recovered/Not Resolved, Dur=Duration, NONE=Dose Not Changed, DW=Drug Withdrawn, DI=Drug Interrupted, DR=Dose Reduced, M=Male, F=Female

SOURCE: BG12MS/JAPAN/ISS/L-AE-SER-303.SAS DATE: 02DEC2015

＊新薬承認情報提供時に置換えた

Listing of serious adverse events:
Study 109MS303
Page 66 of 138
Treatment group: BG00012 240 mg BID

Subject Sex/Age Race	MedDRA Preferred Term	Study Day Onset (a)(b)	Res	Dur (days)	Relationship to Study Drug	Severity	Serious	Action Taken With Study Drug	Outcome
[redacted] F/3[redacted] WHITE	多発性硬化症再発	925	930	6	UNRELATED	SEVERE	Yes	NONE	RESOLVED
	多発性硬化症再発	1687	1702	16	UNRELATED	SEVERE	Yes	NONE	RESOLVED
[redacted] F/4[redacted] WHITE	多発性硬化症再発	57	58	2	UNRELATED	MODERATE	Yes	NONE	RESOLVED
[redacted] F/4[redacted] HISPANIC	不安障害	1306	1309	4	UNRELATED	MODERATE	Yes	NONE	RESOLVED
[redacted] F/5[redacted] HISPANIC	リンパ球減少症	169	NR		POSSIBLY	MODERATE	Yes	DI	NOT RESOLVED

(a) #=On or after the subject switched to alternate MS medication
(b) ^=Adverse Event with onset prior to dosing
Abbreviations: Res=Resolution, NR=Not Recovered/Not Resolved, Dur=Duration, NONE=Dose Not Changed, DW=Drug Withdrawn, DI=Drug Interrupted, DR=Dose Reduced, M=Male, F=Female

SOURCE: BG12MS/JAPAN/ISS/L-AE-SER-303.SAS DATE: 02DEC2015

＊新薬承認情報提供時に置換えた

Listing of serious adverse events:
Study 109MS303
Page 67 of 138
Treatment group: BG00012 240 mg BID

Subject Sex/Age Race	MedDRA Preferred Term	Study Day Onset (a)(b)	Res	Dur (days)	Relationship to Study Drug	Severity	Serious	Action Taken With Study Drug	Outcome
685* M/2[redacted] HISPANIC	多発性硬化症再発	22	29	8	UNRELATED	MODERATE	Yes	NONE	RESOLVED
	多発性硬化症再発	859	862	4	UNRELATED	MODERATE	Yes	NONE	RESOLVED
	多発性硬化症再発	1021	1029	9	UNRELATED	MODERATE	Yes	NONE	RESOLVED
	多発性硬化症再発	1227	1232	6	UNRELATED	MODERATE	Yes	NONE	RESOLVED
[redacted] F/3[redacted] HISPANIC	多発性硬化症再発	1214	1226	13	UNRELATED	MODERATE	Yes	NONE	RESOLVED
[redacted] F/4[redacted] WHITE	筋痙直	1176	1187	12	UNRELATED	MODERATE	Yes	NONE	RESOLVED

(a) #=On or after the subject switched to alternate MS medication
(b) ^=Adverse Event with onset prior to dosing
Abbreviations: Res=Resolution, NR=Not Recovered/Not Resolved, Dur=Duration, NONE=Dose Not Changed, DW=Drug Withdrawn, DI=Drug Interrupted, DR=Dose Reduced, M=Male, F=Female

SOURCE: BG12MS/JAPAN/ISS/L-AE-SER-303.SAS DATE: 02DEC2015

＊新薬承認情報提供時に置換えた

Listing of serious adverse events:
Study 109MS303
Page 68 of 138
Treatment group: BG00012 240 mg BID

Subject Sex/Age Race	MedDRA Preferred Term	Study Day Onset (a)(b)	Study Day Res	Dur (days)	Relationship to Study Drug	Severity	Serious	Action Taken With Study Drug	Outcome
[redacted] F/2[redacted] WHITE	胃腸粘膜障害	85	92	8	RELATED	MODERATE	Yes	DR	RESOLVED
[redacted] F/4[redacted] WHITE	多発性硬化症再発	22	26	5	UNRELATED	MODERATE	Yes	NONE	RESOLVED
[redacted] F/5[redacted] WHITE	緑内障	882	886	5	UNLIKELY	MODERATE	Yes	NONE	RESOLVED
[redacted] F/3[redacted] WHITE	腹膜炎	16	23	8	UNRELATED	SEVERE	Yes	DI	RESOLVED

(a) #=On or after the subject switched to alternate MS medication
(b) ^=Adverse Event with onset prior to dosing
Abbreviations: Res=Resolution, NR=Not Recovered/Not Resolved, Dur=Duration, NONE=Dose Not Changed, DW=Drug Withdrawn, DI=Drug Interrupted, DR=Dose Reduced, M=Male, F=Female

SOURCE: BG12MS/JAPAN/ISS/L-AE-SER-303.SAS DATE: 02DEC2015

Listing of serious adverse events:
Study 109MS303
Page 69 of 138
Treatment group: BG00012 240 mg BID

Subject Sex/Age Race	MedDRA Preferred Term	Study Day Onset (a)(b)	Res	Dur (days)	Relationship to Study Drug	Severity	Serious	Action Taken With Study Drug	Outcome
[redacted] F/3[redacted] WHITE	卵巣良性腫瘍	130	136	7	UNRELATED	SEVERE	Yes	DW	RESOLVED
[redacted] M/4[redacted] WHITE	骨壊死	32	43	12	UNRELATED	MODERATE	Yes	DI	RESOLVED
	慢性腎盂腎炎	1029	1034	6	UNLIKELY	MODERATE	Yes	NONE	RESOLVED
	多発性硬化症再発	1386	1391	6	UNLIKELY	MODERATE	Yes	NONE	RESOLVED
[redacted] F/4[redacted] WHITE	多発性硬化症再発	326	342	17	UNLIKELY	SEVERE	Yes	DI	RESOLVED
	多発性硬化症再発	846	854	9	UNRELATED	MODERATE	Yes	NONE	RESOLVED

(a) #=On or after the subject switched to alternate MS medication
(b) ^=Adverse Event with onset prior to dosing
Abbreviations: Res=Resolution, NR=Not Recovered/Not Resolved, Dur=Duration, NONE=Dose Not Changed, DW=Drug Withdrawn, DI=Drug Interrupted, DR=Dose Reduced, M=Male, F=Female

SOURCE: BG12MS/JAPAN/ISS/L-AE-SER-303.SAS DATE: 02DEC2015

＊新薬承認情報提供時に置換えた

Listing of serious adverse events:
Study 109MS303
Page 70 of 138
Treatment group: BG00012 240 mg TID

Subject Sex/Age Race	MedDRA Preferred Term	Study Day Onset (a)(b)	Res	Dur (days)	Relationship to Study Drug	Severity	Serious	Action Taken With Study Drug	Outcome
500* F/5[redacted] WHITE	非心臓性胸痛	1656	NR		UNRELATED	MODERATE	Yes	NONE	NOT RESOLVED
[redacted] F/4[redacted] WHITE	尿路性敗血症	1231	1242	12	UNLIKELY	SEVERE	Yes	DI	RESOLVED
[redacted] F/3[redacted] ASIAN	急性腎盂腎炎	19	35	17	UNRELATED	MODERATE	Yes	NONE	RESOLVED
	尿路感染	19	35	17	UNRELATED	MODERATE	Yes	NONE	RESOLVED
595* F/5[redacted] ASIAN	乳癌	117	1026	910	UNRELATED	SEVERE	Yes	DW	RESOLVED
	貧血	127#	166	40	UNRELATED	MODERATE	Yes	NONE	RESOLVED

(a) #=On or after the subject switched to alternate MS medication
(b) ^=Adverse Event with onset prior to dosing
Abbreviations: Res=Resolution, NR=Not Recovered/Not Resolved, Dur=Duration, NONE=Dose Not Changed, DW=Drug Withdrawn, DI=Drug Interrupted, DR=Dose Reduced, M=Male, F=Female

SOURCE: BG12MS/JAPAN/ISS/L-AE-SER-303.SAS DATE: 02DEC2015

＊新薬承認情報提供時に置換えた

Listing of serious adverse events:
Study 109MS303
Page 71 of 138
Treatment group: BG00012 240 mg TID

Subject Sex/Age Race	MedDRA Preferred Term	Study Day Onset (a)(b)	Res	Dur (days)	Relationship to Study Drug	Severity	Serious	Action Taken With Study Drug	Outcome
595* F/5[redacted] ASIAN	好中球減少症	127#	129	3	UNRELATED	MODERATE	Yes	NONE	RESOLVED
	口腔カンジダ症	127#	132	6	UNRELATED	MODERATE	Yes	NONE	RESOLVED
	発熱	127#	129	3	UNRELATED	MODERATE	Yes	NONE	RESOLVED
597* F/2[redacted] ASIAN	多発性硬化症再発	365	368	4	POSSIBLY	SEVERE	Yes	NONE	RESOLVED
[redacted] M/3[redacted] ASIAN	多発性硬化症再発	512	514	3	RELATED	MODERATE	Yes	NONE	RESOLVED
[redacted] M/3[redacted] ASIAN	多発性硬化症再発	942	957	16	UNRELATED	MODERATE	Yes	NONE	RESOLVED

(a) #=On or after the subject switched to alternate MS medication
(b) ^=Adverse Event with onset prior to dosing
Abbreviations: Res=Resolution, NR=Not Recovered/Not Resolved, Dur=Duration, NONE=Dose Not Changed, DW=Drug Withdrawn, DI=Drug Interrupted, DR=Dose Reduced, M=Male, F=Female

SOURCE: BG12MS/JAPAN/ISS/L-AE-SER-303.SAS DATE: 02DEC2015

＊新薬承認情報提供時に置換えた

Listing of serious adverse events:
Study 109MS303
Page 72 of 138
Treatment group: BG00012 240 mg TID

Subject Sex/Age Race	MedDRA Preferred Term	Study Day Onset (a)(b)	Study Day Res	Dur (days)	Relationship to Study Drug	Severity	Serious	Action Taken With Study Drug	Outcome
[redacted] M/3[redacted] ASIAN	多発性硬化症再発	1294	1297	4	UNRELATED	MODERATE	Yes	NONE	RESOLVED
[redacted] M/3[redacted] ASIAN	多発性硬化症再発	17	21	5	UNRELATED	MODERATE	Yes	NONE	RESOLVED
602* M/3[redacted] ASIAN	痙攣	321	322	2	UNRELATED	MODERATE	Yes	NONE	RESOLVED
[redacted] F/3[redacted] ASIAN	多発性硬化症再発	877	1202	326	UNRELATED	MODERATE	Yes	NONE	RESOLVED

(a) #=On or after the subject switched to alternate MS medication
(b) ^=Adverse Event with onset prior to dosing
Abbreviations: Res=Resolution, NR=Not Recovered/Not Resolved, Dur=Duration, NONE=Dose Not Changed, DW=Drug Withdrawn, DI=Drug Interrupted, DR=Dose Reduced, M=Male, F=Female

SOURCE: BG12MS/JAPAN/ISS/L-AE-SER-303.SAS DATE: 02DEC2015

＊新薬承認情報提供時に置換えた

Listing of serious adverse events:
Study 109MS303
Page 73 of 138
Treatment group: BG00012 240 mg TID

Subject Sex/Age Race	MedDRA Preferred Term	Study Day Onset (a)(b)	Res	Dur (days)	Relationship to Study Drug	Severity	Serious	Action Taken With Study Drug	Outcome
[redacted] M/2[redacted] ASIAN	多発性硬化症再発	577	586	10	UNRELATED	SEVERE	Yes	NONE	RESOLVED
609* M/2[redacted] WHITE	多発性硬化症再発	1503	1546	44	RELATED	SEVERE	Yes	NONE	RESOLVED
[redacted] F/5[redacted] BLACK OR AFRICAN AMERICAN	多発性硬化症再発	126	168	43	UNRELATED	SEVERE	Yes	DW	RESOLVED
[redacted] F/4[redacted] WHITE	多発性硬化症再発	960	991	32	UNRELATED	SEVERE	Yes	NONE	RESOLVED

(a) #=On or after the subject switched to alternate MS medication
(b) ^=Adverse Event with onset prior to dosing
Abbreviations: Res=Resolution, NR=Not Recovered/Not Resolved, Dur=Duration, NONE=Dose Not Changed, DW=Drug Withdrawn, DI=Drug Interrupted, DR=Dose Reduced, M=Male, F=Female

SOURCE: BG12MS/JAPAN/ISS/L-AE-SER-303.SAS DATE: 02DEC2015

＊新薬承認情報提供時に置換えた

Listing of serious adverse events:
Study 109MS303
Page 74 of 138
Treatment group: BG00012 240 mg TID

Subject Sex/Age Race	MedDRA Preferred Term	Study Day Onset (a)(b)	Study Day Res	Dur (days)	Relationship to Study Drug	Severity	Serious	Action Taken With Study Drug	Outcome
[redacted] F/4[redacted] WHITE	フューム吸引性呼吸障害	1467	1468	2	UNRELATED	MODERATE	Yes	NONE	RESOLVED
506* F/3[redacted] WHITE	片頭痛	862	865	4	UNRELATED	MODERATE	Yes	NONE	RESOLVED
[redacted] F/5[redacted] WHITE	子宮平滑筋腫	1129	1138	10	UNLIKELY	SEVERE	Yes	NONE	RESOLVED
[redacted] M/5[redacted] WHITE	心房細動	1143	1143	1	UNRELATED	SEVERE	Yes	NONE	RESOLVED
	心停止	1143	1143	1	UNRELATED	SEVERE	Yes	NONE	RESOLVED
	息詰まり	1143	1143	1	UNRELATED	SEVERE	Yes	NONE	RESOLVED

(a) #=On or after the subject switched to alternate MS medication
(b) ^=Adverse Event with onset prior to dosing
Abbreviations: Res=Resolution, NR=Not Recovered/Not Resolved, Dur=Duration, NONE=Dose Not Changed, DW=Drug Withdrawn, DI=Drug Interrupted, DR=Dose Reduced, M=Male, F=Female

SOURCE: BG12MS/JAPAN/ISS/L-AE-SER-303.SAS DATE: 02DEC2015

＊新薬承認情報提供時に置換えた

Listing of serious adverse events:
Study 109MS303
Page 75 of 138
Treatment group: BG00012 240 mg TID

Subject Sex/Age Race	MedDRA Preferred Term	Study Day Onset (a)(b)	Study Day Res	Dur (days)	Relationship to Study Drug	Severity	Serious	Action Taken With Study Drug	Outcome
[redacted] M/5[redacted] WHITE	多発性硬化症再発	1497	1500	4	UNRELATED	MODERATE	Yes	NONE	RESOLVED
[redacted] F/5[redacted] WHITE	感覚鈍麻	280	284	5	UNRELATED	MODERATE	Yes	NONE	RESOLVED
	交通事故	280	280	1	UNRELATED	MODERATE	Yes	NONE	RESOLVED
	胃食道逆流性疾患	549	549	1	UNRELATED	MODERATE	Yes	NONE	RESOLVED
	非心臓性胸痛	1350	1380	31	UNRELATED	MODERATE	Yes	NONE	RESOLVED
[redacted] F/4[redacted] WHITE	大腸炎	1241	1245	5	UNRELATED	MODERATE	Yes	NONE	RESOLVED

(a) #=On or after the subject switched to alternate MS medication
(b) ^=Adverse Event with onset prior to dosing
Abbreviations: Res=Resolution, NR=Not Recovered/Not Resolved, Dur=Duration, NONE=Dose Not Changed, DW=Drug Withdrawn, DI=Drug Interrupted, DR=Dose Reduced, M=Male, F=Female

SOURCE: BG12MS/JAPAN/ISS/L-AE-SER-303.SAS DATE: 02DEC2015

＊新薬承認情報提供時に置換えた

Listing of serious adverse events:
Study 109MS303
Page 76 of 138
Treatment group: BG00012 240 mg TID

Subject Sex/Age Race	MedDRA Preferred Term	Study Day Onset (a)(b)	Res	Dur (days)	Relationship to Study Drug	Severity	Serious	Action Taken With Study Drug	Outcome
[redacted] F/4[redacted] WHITE	慢性骨髄性白血病	910	NR		POSSIBLY	SEVERE	Yes	DW	NOT RESOLVED
[redacted] M/5[redacted] WHITE	蜂巣炎	477	479	3	UNLIKELY	MODERATE	Yes	NONE	RESOLVED
	帯状疱疹	477	479	3	UNLIKELY	MODERATE	Yes	NONE	RESOLVED
[redacted] M/4[redacted] WHITE	変形性関節症	1246	1250	5	UNRELATED	SEVERE	Yes	NONE	RESOLVED
[redacted] M/5[redacted] WHITE	注意力障害	251	251	1	UNRELATED	SEVERE	Yes	NONE	RESOLVED
	交通事故	251	251	1	UNLIKELY	SEVERE	Yes	NONE	RESOLVED

(a) #=On or after the subject switched to alternate MS medication
(b) ^=Adverse Event with onset prior to dosing
Abbreviations: Res=Resolution, NR=Not Recovered/Not Resolved, Dur=Duration, NONE=Dose Not Changed, DW=Drug Withdrawn, DI=Drug Interrupted, DR=Dose Reduced, M=Male, F=Female

SOURCE: BG12MS/JAPAN/ISS/L-AE-SER-303.SAS DATE: 02DEC2015

＊新薬承認情報提供時に置換えた

Listing of serious adverse events:
Study 109MS303
Page 77 of 138
Treatment group: BG00012 240 mg TID

Subject Sex/Age Race	MedDRA Preferred Term	Study Day Onset (a)(b)	Res	Dur (days)	Relationship to Study Drug	Severity	Serious	Action Taken With Study Drug	Outcome
[redacted] F/4[redacted] WHITE	三叉神経痛	945	960	16	UNRELATED	SEVERE	Yes	NONE	RESOLVED
[redacted] M/3[redacted] WHITE	多発性硬化症再発	64	68	5	UNLIKELY	MODERATE	Yes	NONE	RESOLVED
	多発性硬化症再発	687	691	5	UNLIKELY	MODERATE	Yes	NONE	RESOLVED
	多発性硬化症再発	858	862	5	UNLIKELY	MODERATE	Yes	NONE	RESOLVED
	多発性硬化症再発	1267	1271	5	UNLIKELY	MODERATE	Yes	NONE	RESOLVED
	多発性硬化症再発	1457	1461	5	UNRELATED	MODERATE	Yes	NONE	RESOLVED

(a) #=On or after the subject switched to alternate MS medication
(b) ^=Adverse Event with onset prior to dosing
Abbreviations: Res=Resolution, NR=Not Recovered/Not Resolved, Dur=Duration, NONE=Dose Not Changed, DW=Drug Withdrawn, DI=Drug Interrupted, DR=Dose Reduced, M=Male, F=Female

SOURCE: BG12MS/JAPAN/ISS/L-AE-SER-303.SAS DATE: 02DEC2015

＊新薬承認情報提供時に置換えた

Listing of serious adverse events:
Study 109MS303
Page 78 of 138
Treatment group: BG00012 240 mg TID

Subject Sex/Age Race	MedDRA Preferred Term	Study Day Onset (a)(b)	Res	Dur (days)	Relationship to Study Drug	Severity	Serious	Action Taken With Study Drug	Outcome
[redacted] F/5[redacted] WHITE	乳癌	487	499	13	UNRELATED	MODERATE	Yes	DW	RESOLVED
[redacted] F/5[redacted] WHITE	扁平上皮癌	1218	1227	10	UNRELATED	SEVERE	Yes	NONE	RESOLVED
510* F/4[redacted] WHITE	唾液腺癌	388	895	508	POSSIBLY	MODERATE	Yes	NONE	RESOLVED
[redacted] F/5[redacted] WHITE	変形性関節症	69	72	4	UNRELATED	MODERATE	Yes	NONE	RESOLVED

(a) #=On or after the subject switched to alternate MS medication
(b) ^=Adverse Event with onset prior to dosing
Abbreviations: Res=Resolution, NR=Not Recovered/Not Resolved, Dur=Duration, NONE=Dose Not Changed, DW=Drug Withdrawn, DI=Drug Interrupted, DR=Dose Reduced, M=Male, F=Female

SOURCE: BG12MS/JAPAN/ISS/L-AE-SER-303.SAS DATE: 02DEC2015

＊新薬承認情報提供時に置換えた

Listing of serious adverse events:
Study 109MS303
Page 79 of 138
Treatment group: BG00012 240 mg TID

Subject Sex/Age Race	MedDRA Preferred Term	Study Day Onset (a)(b)	Res	Dur (days)	Relationship to Study Drug	Severity	Serious	Action Taken With Study Drug	Outcome
626* F/5[redacted] WHITE	腓骨骨折	1199	1334	136	UNRELATED	SEVERE	Yes	NONE	RESOLVED
	脛骨骨折	1199	1334	136	UNRELATED	SEVERE	Yes	NONE	RESOLVED
[redacted] M/4[redacted] WHITE	非心臓性胸痛	772	775	4	UNLIKELY	MODERATE	Yes	NONE	RESOLVED
[redacted] F/4[redacted] WHITE	慢性閉塞性肺疾患	1199	1202	4	UNRELATED	SEVERE	Yes	DI	RESOLVED
	細菌性肺炎	1485	1488	4	UNRELATED	SEVERE	Yes	DI	RESOLVED
[redacted] F/4[redacted] WHITE	骨髄炎	1573	NR		UNRELATED	SEVERE	Yes	DI	NOT RESOLVED

(a) #=On or after the subject switched to alternate MS medication
(b) ^=Adverse Event with onset prior to dosing
Abbreviations: Res=Resolution, NR=Not Recovered/Not Resolved, Dur=Duration, NONE=Dose Not Changed, DW=Drug Withdrawn, DI=Drug Interrupted, DR=Dose Reduced, M=Male, F=Female

SOURCE: BG12MS/JAPAN/ISS/L-AE-SER-303.SAS DATE: 02DEC2015

＊新薬承認情報提供時に置換えた

Listing of serious adverse events:
Study 109MS303
Page 80 of 138
Treatment group: BG00012 240 mg TID

Subject Sex/Age Race	MedDRA Preferred Term	Study Day Onset (a)(b)	Res	Dur (days)	Relationship to Study Drug	Severity	Serious	Action Taken With Study Drug	Outcome
[redacted] F/5[redacted] BLACK OR AFRICAN AMERICAN	急性胆嚢炎	195	199	5	UNRELATED	SEVERE	Yes	NONE	RESOLVED
[redacted] F/4[redacted] WHITE	リンパ球数減少	1514	NR		RELATED	MILD	Yes	DI	NOT RESOLVED
[redacted] F/3[redacted] BLACK OR AFRICAN AMERICAN	脱水	203	205	3	UNLIKELY	SEVERE	Yes	NONE	RESOLVED
	尿路感染	203	205	3	UNLIKELY	MILD	Yes	NONE	RESOLVED
	肺サルコイドーシス	284	322	39	UNRELATED	SEVERE	Yes	NONE	RESOLVED

(a) #=On or after the subject switched to alternate MS medication
(b) ^=Adverse Event with onset prior to dosing
Abbreviations: Res=Resolution, NR=Not Recovered/Not Resolved, Dur=Duration, NONE=Dose Not Changed, DW=Drug Withdrawn, DI=Drug Interrupted, DR=Dose Reduced, M=Male, F=Female

SOURCE: BG12MS/JAPAN/ISS/L-AE-SER-303.SAS DATE: 02DEC2015

＊新薬承認情報提供時に置換えた

Listing of serious adverse events:
Study 109MS303
Page 81 of 138
Treatment group: BG00012 240 mg TID

Subject Sex/Age Race	MedDRA Preferred Term	Study Day Onset (a)(b)	Res	Dur (days)	Relationship to Study Drug	Severity	Serious	Action Taken With Study Drug	Outcome
629* F/4[redacted] WHITE	神経痛	1345	1348	4	UNRELATED	MODERATE	Yes	NONE	RESOLVED
[redacted] F/4[redacted] WHITE	医療機器変更	1316	1327	12	UNRELATED	MODERATE	Yes	NONE	RESOLVED
[redacted] M/3[redacted] WHITE	扁桃周囲膿瘍	1205	1206	2	UNRELATED	MODERATE	Yes	NONE	RESOLVED
[redacted] F/3[redacted] HISPANIC	多発性硬化症再発	1308	1318	11	UNRELATED	MILD	Yes	NONE	RESOLVED

(a) #=On or after the subject switched to alternate MS medication
(b) ^=Adverse Event with onset prior to dosing
Abbreviations: Res=Resolution, NR=Not Recovered/Not Resolved, Dur=Duration, NONE=Dose Not Changed, DW=Drug Withdrawn, DI=Drug Interrupted, DR=Dose Reduced, M=Male, F=Female

SOURCE: BG12MS/JAPAN/ISS/L-AE-SER-303.SAS DATE: 02DEC2015

＊新薬承認情報提供時に置換えた

Listing of serious adverse events:
Study 109MS303
Page 82 of 138
Treatment group: BG00012 240 mg TID

Subject Sex/Age Race	MedDRA Preferred Term	Study Day Onset (a)(b)	Res	Dur (days)	Relationship to Study Drug	Severity	Serious	Action Taken With Study Drug	Outcome
[redacted] M/3[redacted] WHITE	多発性硬化症再発	589	593	5	UNRELATED	MILD	Yes	NONE	RESOLVED
	多発性硬化症再発	1653	1676	24	UNRELATED	MODERATE	Yes	NONE	RESOLVED
[redacted] M/2[redacted] WHITE	関節痛	412	497	86	UNRELATED	MILD	Yes	NONE	RESOLVED
[redacted] F/2[redacted] WHITE	多発性硬化症再発	784	805	22	UNRELATED	MODERATE	Yes	NONE	RESOLVED
	多発性硬化症再発	835	874	40	UNRELATED	MODERATE	Yes	DW	RESOLVED

(a) #=On or after the subject switched to alternate MS medication
(b) ^=Adverse Event with onset prior to dosing
Abbreviations: Res=Resolution, NR=Not Recovered/Not Resolved, Dur=Duration, NONE=Dose Not Changed, DW=Drug Withdrawn, DI=Drug Interrupted, DR=Dose Reduced, M=Male, F=Female

SOURCE: BG12MS/JAPAN/ISS/L-AE-SER-303.SAS DATE: 02DEC2015

＊新薬承認情報提供時に置換えた

Listing of serious adverse events:
Study 109MS303
Page 83 of 138
Treatment group: BG00012 240 mg TID

Subject Sex/Age Race	MedDRA Preferred Term	Study Day Onset (a)(b)	Study Day Res	Dur (days)	Relationship to Study Drug	Severity	Serious	Action Taken With Study Drug	Outcome
[redacted] F/4[redacted] WHITE	多発性硬化症再発	361	364	4	UNRELATED	MODERATE	Yes	NONE	RESOLVED
	感覚鈍麻	1154	1157	4	UNRELATED	MILD	Yes	NONE	RESOLVED
[redacted] M/4[redacted] WHITE	多発性硬化症再発	360	365	6	UNRELATED	MODERATE	Yes	NONE	RESOLVED
[redacted] M/5[redacted] WHITE	多発性硬化症再発	12	23	12	UNRELATED	MODERATE	Yes	NONE	RESOLVED
	多発性硬化症再発	715	729	15	UNRELATED	MODERATE	Yes	NONE	RESOLVED

(a) #=On or after the subject switched to alternate MS medication
(b) ^=Adverse Event with onset prior to dosing
Abbreviations: Res=Resolution, NR=Not Recovered/Not Resolved, Dur=Duration, NONE=Dose Not Changed, DW=Drug Withdrawn, DI=Drug Interrupted, DR=Dose Reduced, M=Male, F=Female

SOURCE: BG12MS/JAPAN/ISS/L-AE-SER-303.SAS DATE: 02DEC2015

＊新薬承認情報提供時に置換えた

Listing of serious adverse events:
Study 109MS303
Page 84 of 138
Treatment group: BG00012 240 mg TID

Subject Sex/Age Race	MedDRA Preferred Term	Study Day Onset (a)(b)	Res	Dur (days)	Relationship to Study Drug	Severity	Serious	Action Taken With Study Drug	Outcome
[redacted] M/5[redacted] WHITE	腸閉塞	1149	1159	11	UNLIKELY	SEVERE	Yes	NONE	RESOLVED
	腸の軸捻転	1149	1159	11	UNLIKELY	SEVERE	Yes	NONE	RESOLVED
[redacted] F/2[redacted] WHITE	痙攣	1336	1343	8	UNRELATED	MODERATE	Yes	DI	RESOLVED
[redacted] M/3[redacted] WHITE	多発性硬化症再発	656	665	10	UNRELATED	MODERATE	Yes	NONE	RESOLVED
	多発性硬化症再発	1345	1357	13	UNRELATED	MODERATE	Yes	NONE	RESOLVED
	多発性硬化症再発	1446	1454	9	UNRELATED	MODERATE	Yes	NONE	RESOLVED

(a) #=On or after the subject switched to alternate MS medication
(b) ^=Adverse Event with onset prior to dosing
Abbreviations: Res=Resolution, NR=Not Recovered/Not Resolved, Dur=Duration, NONE=Dose Not Changed, DW=Drug Withdrawn, DI=Drug Interrupted, DR=Dose Reduced, M=Male, F=Female

SOURCE: BG12MS/JAPAN/ISS/L-AE-SER-303.SAS DATE: 02DEC2015

＊新薬承認情報提供時に置換えた

Listing of serious adverse events:
Study 109MS303
Page 85 of 138
Treatment group: BG00012 240 mg TID

Subject Sex/Age Race	MedDRA Preferred Term	Study Day Onset (a)(b)	Res	Dur (days)	Relationship to Study Drug	Severity	Serious	Action Taken With Study Drug	Outcome
[redacted] M/4[redacted] WHITE	肺結核腫	293	316	24	UNRELATED	SEVERE	Yes	DI	RESOLVED
	心筋梗塞	556	583	28	UNRELATED	MODERATE	Yes	NONE	RESOLVED
[redacted] F/5[redacted] WHITE	慢性胆嚢炎	41	45	5	UNRELATED	MODERATE	Yes	DI	RESOLVED
	胆石症	41	45	5	UNRELATED	MODERATE	Yes	DI	RESOLVED
[redacted] F/5[redacted] WHITE	脳振盪	79	121	43	UNRELATED	MODERATE	Yes	NONE	RESOLVED
	脳振盪	79	121	43	UNRELATED	MODERATE	Yes	NONE	RESOLVED
	尺骨骨折	79	223	145	UNRELATED	MODERATE	Yes	NONE	RESOLVED

(a) #=On or after the subject switched to alternate MS medication
(b) ^=Adverse Event with onset prior to dosing
Abbreviations: Res=Resolution, NR=Not Recovered/Not Resolved, Dur=Duration, NONE=Dose Not Changed, DW=Drug Withdrawn, DI=Drug Interrupted, DR=Dose Reduced, M=Male, F=Female

SOURCE: BG12MS/JAPAN/ISS/L-AE-SER-303.SAS DATE: 02DEC2015

＊新薬承認情報提供時に置換えた

Listing of serious adverse events:
Study 109MS303
Page 86 of 138
Treatment group: BG00012 240 mg TID

Subject Sex/Age Race	MedDRA Preferred Term	Study Day Onset (a)(b)	Res	Dur (days)	Relationship to Study Drug	Severity	Serious	Action Taken With Study Drug	Outcome
[redacted] F/2[redacted] WHITE	多発性硬化症再発	137	141	5	UNRELATED	MODERATE	Yes	NONE	RESOLVED
	多発性硬化症再発	266	273	8	UNRELATED	MILD	Yes	NONE	RESOLVED
	多発性硬化症再発	556	560	5	UNRELATED	MODERATE	Yes	NONE	RESOLVED
	多発性硬化症再発	792	796	5	UNRELATED	MODERATE	Yes	NONE	RESOLVED
	多発性硬化症再発	912	917	6	UNRELATED	MODERATE	Yes	NONE	RESOLVED
	多発性硬化症再発	1144	1163	20	UNRELATED	MODERATE	Yes	NONE	RESOLVED
[redacted] M/2[redacted] WHITE	多発性硬化症再発	395	405	11	UNRELATED	MODERATE	Yes	NONE	RESOLVED

(a) #=On or after the subject switched to alternate MS medication
(b) ^=Adverse Event with onset prior to dosing
Abbreviations: Res=Resolution, NR=Not Recovered/Not Resolved, Dur=Duration, NONE=Dose Not Changed, DW=Drug Withdrawn, DI=Drug Interrupted, DR=Dose Reduced, M=Male, F=Female

SOURCE: BG12MS/JAPAN/ISS/L-AE-SER-303.SAS DATE: 02DEC2015

＊新薬承認情報提供時に置換えた

Listing of serious adverse events:
Study 109MS303
Page 87 of 138
Treatment group: BG00012 240 mg TID

Subject Sex/Age Race	MedDRA Preferred Term	Study Day Onset (a)(b)	Res	Dur (days)	Relationship to Study Drug	Severity	Serious	Action Taken With Study Drug	Outcome
[redacted] M/3[redacted] ASIAN	多発性硬化症再発	602	644	43	UNRELATED	SEVERE	Yes	NONE	RESOLVED
519* F/2[redacted] ASIAN	多発性硬化症再発	147	153	7	UNRELATED	SEVERE	Yes	NONE	RESOLVED
[redacted] F/4[redacted] ASIAN	多発性硬化症再発	437	469	33	UNRELATED	MODERATE	Yes	NONE	RESOLVED
[redacted] F/3[redacted] ASIAN	多発性硬化症再発	165	167	3	UNRELATED	MODERATE	Yes	NONE	RESOLVED

(a) #=On or after the subject switched to alternate MS medication
(b) ^=Adverse Event with onset prior to dosing
Abbreviations: Res=Resolution, NR=Not Recovered/Not Resolved, Dur=Duration, NONE=Dose Not Changed, DW=Drug Withdrawn, DI=Drug Interrupted, DR=Dose Reduced, M=Male, F=Female

SOURCE: BG12MS/JAPAN/ISS/L-AE-SER-303.SAS DATE: 02DEC2015

＊新薬承認情報提供時に置換えた

Listing of serious adverse events:
Study 109MS303
Page 88 of 138
Treatment group: BG00012 240 mg TID

Subject Sex/Age Race	MedDRA Preferred Term	Study Day Onset (a)(b)	Study Day Res	Dur (days)	Relationship to Study Drug	Severity	Serious	Action Taken With Study Drug	Outcome
[redacted] F/2[redacted] ASIAN	多発性硬化症再発	313	319	7	UNRELATED	MODERATE	Yes	NONE	RESOLVED
[redacted] F/3[redacted] ASIAN	多発性硬化症再発	267	269	3	UNRELATED	MODERATE	Yes	NONE	RESOLVED
360* M/4[redacted] ASIAN	腎結石症	75	76	2	UNRELATED	MILD	Yes	NONE	RESOLVED
[redacted] F/4[redacted] ASIAN	頚腕症候群	534	537	4	UNRELATED	MODERATE	Yes	NONE	RESOLVED
	神経痛	588	591	4	UNRELATED	MODERATE	Yes	NONE	RESOLVED
	関節周囲炎	660	661	2	UNRELATED	SEVERE	Yes	NONE	RESOLVED

(a) #=On or after the subject switched to alternate MS medication
(b) ^=Adverse Event with onset prior to dosing
Abbreviations: Res=Resolution, NR=Not Recovered/Not Resolved, Dur=Duration, NONE=Dose Not Changed, DW=Drug Withdrawn, DI=Drug Interrupted, DR=Dose Reduced, M=Male, F=Female

SOURCE: BG12MS/JAPAN/ISS/L-AE-SER-303.SAS DATE: 02DEC2015

＊新薬承認情報提供時に置換えた

Listing of serious adverse events:
Study 109MS303
Page 89 of 138
Treatment group: BG00012 240 mg TID

Subject Sex/Age Race	MedDRA Preferred Term	Study Day Onset (a)(b)	Res	Dur (days)	Relationship to Study Drug	Severity	Serious	Action Taken With Study Drug	Outcome
238* F/4[redacted] ASIAN	多発性硬化症再発	122	143	22	UNRELATED	MODERATE	Yes	NONE	RESOLVED
	多発性硬化症再発	694	703	10	UNRELATED	SEVERE	Yes	NONE	RESOLVED
535* F/4[redacted] ASIAN	多発性硬化症再発	398	403	6	UNRELATED	MODERATE	Yes	NONE	RESOLVED
[redacted] F/5[redacted] WHITE	尿路感染	1199	1204	6	UNRELATED	MODERATE	Yes	NONE	RESOLVED
	粉砕骨折	1295	1385	91	UNRELATED	SEVERE	Yes	DI	RESOLVED

(a) #=On or after the subject switched to alternate MS medication
(b) ^=Adverse Event with onset prior to dosing
Abbreviations: Res=Resolution, NR=Not Recovered/Not Resolved, Dur=Duration, NONE=Dose Not Changed, DW=Drug Withdrawn, DI=Drug Interrupted, DR=Dose Reduced, M=Male, F=Female

SOURCE: BG12MS/JAPAN/ISS/L-AE-SER-303.SAS DATE: 02DEC2015

＊新薬承認情報提供時に置換えた

Listing of serious adverse events:
Study 109MS303
Page 90 of 138
Treatment group: BG00012 240 mg TID

Subject Sex/Age Race	MedDRA Preferred Term	Study Day Onset (a)(b)	Res	Dur (days)	Relationship to Study Drug	Severity	Serious	Action Taken With Study Drug	Outcome
[redacted] M/4[redacted] WHITE	多発骨折	548	840	293	UNLIKELY	SEVERE	Yes	NONE	RESOLVED
	鎖骨骨折	1285	1520	236	UNRELATED	MODERATE	Yes	NONE	RESOLVED
	交通事故	1285	1285	1	UNRELATED	MODERATE	Yes	NONE	RESOLVED
[redacted] F/4[redacted] WHITE	三叉神経痛	1878	1884	7	UNRELATED	MODERATE	Yes	DI	RESOLVED
	胆道仙痛	1977	1984	8	UNRELATED	SEVERE	Yes	NONE	RESOLVED
[redacted] F/2[redacted] WHITE	うつ病	565	686	122	UNRELATED	MODERATE	Yes	NONE	RESOLVED

(a) #=On or after the subject switched to alternate MS medication
(b) ^=Adverse Event with onset prior to dosing
Abbreviations: Res=Resolution, NR=Not Recovered/Not Resolved, Dur=Duration, NONE=Dose Not Changed, DW=Drug Withdrawn, DI=Drug Interrupted, DR=Dose Reduced, M=Male, F=Female

SOURCE: BG12MS/JAPAN/ISS/L-AE-SER-303.SAS DATE: 02DEC2015

＊新薬承認情報提供時に置換えた

Listing of serious adverse events:
Study 109MS303
Page 91 of 138
Treatment group: BG00012 240 mg TID

Subject Sex/Age Race	MedDRA Preferred Term	Study Day Onset (a)(b)	Res	Dur (days)	Relationship to Study Drug	Severity	Serious	Action Taken With Study Drug	Outcome
542* F/4[redacted] WHITE	人工内耳植込み	19	25	7	UNRELATED	MODERATE	Yes	NONE	RESOLVED
	前庭神経炎	32	37	6	UNRELATED	MODERATE	Yes	NONE	RESOLVED
	膀胱頚部吊り上げ術	463	466	4	UNRELATED	MODERATE	Yes	NONE	RESOLVED
	聴力低下	1099	1104	6	UNRELATED	SEVERE	Yes	NONE	RESOLVED
	潰瘍性大腸炎	1454	1463	10	UNRELATED	SEVERE	Yes	DI	RESOLVED
[redacted] F/5[redacted] WHITE	関節周囲炎	1024	1029	6	UNRELATED	MODERATE	Yes	NONE	RESOLVED
[redacted] M/5[redacted] WHITE	肋骨骨折	983	994	12	UNRELATED	MILD	Yes	NONE	RESOLVED

(a) #=On or after the subject switched to alternate MS medication
(b) ^=Adverse Event with onset prior to dosing
Abbreviations: Res=Resolution, NR=Not Recovered/Not Resolved, Dur=Duration, NONE=Dose Not Changed, DW=Drug Withdrawn, DI=Drug Interrupted, DR=Dose Reduced, M=Male, F=Female

SOURCE: BG12MS/JAPAN/ISS/L-AE-SER-303.SAS DATE: 02DEC2015

＊新薬承認情報提供時に置換えた

Listing of serious adverse events:
Study 109MS303
Page 92 of 138
Treatment group: BG00012 240 mg TID

Subject Sex/Age Race	MedDRA Preferred Term	Study Day Onset (a)(b)	Res	Dur (days)	Relationship to Study Drug	Severity	Serious	Action Taken With Study Drug	Outcome
[redacted] F/5[redacted] WHITE	自己免疫性甲状腺炎	460	NR		UNLIKELY	MILD	Yes	NONE	NOT RESOLVED
	筋骨格痛	1176	1187	12	UNRELATED	MILD	Yes	NONE	RESOLVED
	乳癌	1225	1295		UNRELATED	SEVERE	Yes	DW	RESOLVED
	卵巣嚢胞	1286	1292	7	UNRELATED	SEVERE	Yes	NONE	RESOLVED
546* F/4[redacted] WHITE	転倒	327	327	1	UNRELATED	MODERATE	Yes	NONE	RESOLVED
	上肢骨折	327	667	341	UNRELATED	SEVERE	Yes	NONE	RESOLVED
	医療機器除去	665	667	3	UNRELATED	MODERATE	Yes	NONE	RESOLVED
547* F/3[redacted] WHITE	高血糖	65	66	2	UNLIKELY	MILD	Yes	NONE	RESOLVED

(a) #=On or after the subject switched to alternate MS medication
(b) ^=Adverse Event with onset prior to dosing
Abbreviations: Res=Resolution, NR=Not Recovered/Not Resolved, Dur=Duration, NONE=Dose Not Changed, DW=Drug Withdrawn, DI=Drug Interrupted, DR=Dose Reduced, M=Male, F=Female

SOURCE: BG12MS/JAPAN/ISS/L-AE-SER-303.SAS DATE: 02DEC2015

＊新薬承認情報提供時に置換えた

Listing of serious adverse events:
Study 109MS303
Page 93 of 138
Treatment group: BG00012 240 mg TID

Subject Sex/Age Race	MedDRA Preferred Term	Study Day Onset (a)(b)	Res	Dur (days)	Relationship to Study Drug	Severity	Serious	Action Taken With Study Drug	Outcome
[redacted] F/3[redacted] WHITE	多発性硬化症再発	397	429	33	UNRELATED	SEVERE	Yes	DW	RESOLVED
	多発性硬化症再発	445#	450	6	UNRELATED	SEVERE	Yes	NONE	RESOLVED
	多発性硬化症再発	461#	484	24	UNRELATED	SEVERE	Yes	DW	RESOLVED
[redacted] F/4[redacted] WHITE	複雑部分発作	32	37	6	UNRELATED	SEVERE	Yes	NONE	RESOLVED
	てんかん	1342	1347	6	UNRELATED	SEVERE	Yes	NONE	RESOLVED
[redacted] F/3[redacted] WHITE	多発性硬化症再発	777	782	6	UNRELATED	MODERATE	Yes	NONE	RESOLVED
	腹痛	976	978	3	POSSIBLY	SEVERE	Yes	NONE	RESOLVED

(a) #=On or after the subject switched to alternate MS medication
(b) ^=Adverse Event with onset prior to dosing
Abbreviations: Res=Resolution, NR=Not Recovered/Not Resolved, Dur=Duration, NONE=Dose Not Changed, DW=Drug Withdrawn, DI=Drug Interrupted, DR=Dose Reduced, M=Male, F=Female

SOURCE: BG12MS/JAPAN/ISS/L-AE-SER-303.SAS DATE: 02DEC2015

＊新薬承認情報提供時に置換えた

Listing of serious adverse events:
Study 109MS303
Page 94 of 138
Treatment group: BG00012 240 mg TID

Subject Sex/Age Race	MedDRA Preferred Term	Study Day Onset (a)(b)	Study Day Res	Dur (days)	Relationship to Study Drug	Severity	Serious	Action Taken With Study Drug	Outcome
[redacted] M/3[redacted] WHITE	虫垂炎	1503	1506	4	POSSIBLY	MILD	Yes	NONE	RESOLVED
[redacted] F/4[redacted] WHITE	多発性硬化症再発	13	18	6	UNRELATED	MILD	Yes	NONE	RESOLVED
	多発性硬化症再発	404	409	6	UNRELATED	MODERATE	Yes	NONE	RESOLVED
	多発性硬化症再発	593	598	6	UNRELATED	MODERATE	Yes	NONE	RESOLVED
	多発性硬化症再発	1001	1010	10	UNRELATED	MILD	Yes	NONE	RESOLVED
	多発性硬化症再発	1671	1676	6	UNRELATED	MILD	Yes	NONE	RESOLVED
	多発性硬化症再発	1671	1676	6	UNRELATED	MODERATE	Yes	NONE	RESOLVED

(a) #=On or after the subject switched to alternate MS medication
(b) ^=Adverse Event with onset prior to dosing
Abbreviations: Res=Resolution, NR=Not Recovered/Not Resolved, Dur=Duration, NONE=Dose Not Changed, DW=Drug Withdrawn, DI=Drug Interrupted, DR=Dose Reduced, M=Male, F=Female

SOURCE: BG12MS/JAPAN/ISS/L-AE-SER-303.SAS DATE: 02DEC2015

＊新薬承認情報提供時に置換えた

Listing of serious adverse events:
Study 109MS303
Page 95 of 138
Treatment group: BG00012 240 mg TID

Subject Sex/Age Race	MedDRA Preferred Term	Study Day Onset (a)(b)	Study Day Res	Dur (days)	Relationship to Study Drug	Severity	Serious	Action Taken With Study Drug	Outcome
[redacted] F/4[redacted] WHITE	多発性硬化症再発	1818	1823	6	UNRELATED	MODERATE	Yes	NONE	RESOLVED
[redacted] F/3[redacted] WHITE	多発性硬化症再発	839	847	9	RELATED	MILD	Yes	NONE	RESOLVED
	多発性硬化症再発	1159	1203	45	POSSIBLY	MODERATE	Yes	NONE	RESOLVED
[redacted] F/4[redacted] WHITE	子宮内膜症	1481	1486	6	UNRELATED	SEVERE	Yes	NONE	RESOLVED
[redacted] M/2[redacted] WHITE	アナフィラキシー反応	236	237	2	UNRELATED	SEVERE	Yes	NONE	RESOLVED

(a) #=On or after the subject switched to alternate MS medication
(b) ^=Adverse Event with onset prior to dosing
Abbreviations: Res=Resolution, NR=Not Recovered/Not Resolved, Dur=Duration, NONE=Dose Not Changed, DW=Drug Withdrawn, DI=Drug Interrupted, DR=Dose Reduced, M=Male, F=Female

SOURCE: BG12MS/JAPAN/ISS/L-AE-SER-303.SAS DATE: 02DEC2015

＊新薬承認情報提供時に置換えた

Listing of serious adverse events:
Study 109MS303
Page 96 of 138
Treatment group: BG00012 240 mg TID

Subject Sex/Age Race	MedDRA Preferred Term	Study Day Onset (a)(b)	Res	Dur (days)	Relationship to Study Drug	Severity	Serious	Action Taken With Study Drug	Outcome
[redacted] F/3[redacted] WHITE	慢性副鼻腔炎	1086	1094	9	UNRELATED	MODERATE	Yes	DI	RESOLVED
	子宮平滑筋腫	1282	1329	48	UNRELATED	MODERATE	Yes	NONE	RESOLVED
[redacted] F/4[redacted] WHITE	多発性硬化症	766	794	29	UNRELATED	MODERATE	Yes	NONE	RESOLVED
	月経過多	1504	1506	3	UNRELATED	MODERATE	Yes	DI	RESOLVED
[redacted] F/5[redacted] WHITE	突発難聴	339	NR		UNRELATED	MODERATE	Yes	NONE	NOT RESOLVED
354* F/4[redacted] WHITE	多発性硬化症再発	1635	1702	68		SEVERE	Yes	DW	RESOLVED

(a) #=On or after the subject switched to alternate MS medication
(b) ^=Adverse Event with onset prior to dosing
Abbreviations: Res=Resolution, NR=Not Recovered/Not Resolved, Dur=Duration, NONE=Dose Not Changed, DW=Drug Withdrawn, DI=Drug Interrupted, DR=Dose Reduced, M=Male, F=Female

SOURCE: BG12MS/JAPAN/ISS/L-AE-SER-303.SAS DATE: 02DEC2015

＊新薬承認情報提供時に置換えた

Listing of serious adverse events:
Study 109MS303
Page 97 of 138
Treatment group: BG00012 240 mg TID

Subject Sex/Age Race	MedDRA Preferred Term	Study Day Onset (a)(b)	Res	Dur (days)	Relationship to Study Drug	Severity	Serious	Action Taken With Study Drug	Outcome
354* F/4[redacted] WHITE	進行性多巣性白質脳症	1703	1705	3	RELATED	SEVERE	Yes	NONE	RESOLVED
	進行性多巣性白質脳症	1703	1705	3	RELATED	SEVERE	Yes	NONE	RESOLVED
551* M/2[redacted] WHITE	糖尿病	369	379	11	UNRELATED	MODERATE	Yes	NONE	RESOLVED
	うつ病	470	672	203	UNRELATED	MODERATE	Yes	NONE	RESOLVED
	ノロウイルス性胃腸炎	689	690	2	UNRELATED	MILD	Yes	NONE	RESOLVED
[redacted] F/4[redacted] WHITE	胃炎	29	37	9	POSSIBLY	SEVERE	Yes	DW	RESOLVED

(a) #=On or after the subject switched to alternate MS medication
(b) ^=Adverse Event with onset prior to dosing
Abbreviations: Res=Resolution, NR=Not Recovered/Not Resolved, Dur=Duration, NONE=Dose Not Changed, DW=Drug Withdrawn, DI=Drug Interrupted, DR=Dose Reduced, M=Male, F=Female

SOURCE: BG12MS/JAPAN/ISS/L-AE-SER-303.SAS DATE: 02DEC2015

＊新薬承認情報提供時に置換えた

Listing of serious adverse events:
Study 109MS303
Page 98 of 138
Treatment group: BG00012 240 mg TID

Subject Sex/Age Race	MedDRA Preferred Term	Study Day Onset (a)(b)	Res	Dur (days)	Relationship to Study Drug	Severity	Serious	Action Taken With Study Drug	Outcome
555* F/3[redacted] WHITE	多発性硬化症再発	402	465	64	UNRELATED	MODERATE	Yes	NONE	RESOLVED
	多発性硬化症再発	1378	1399	22	UNRELATED	MILD	Yes	NONE	RESOLVED
[redacted] F/2[redacted] WHITE	子宮内膜炎	977	986	10	UNRELATED	MILD	Yes	NONE	RESOLVED
	クローン病	1040	1050	11	UNRELATED	MODERATE	Yes	NONE	RESOLVED
[redacted] F/2[redacted] WHITE	譫妄	29	36	8	UNLIKELY	SEVERE	Yes	NONE	RESOLVED

(a) #=On or after the subject switched to alternate MS medication
(b) ^=Adverse Event with onset prior to dosing
Abbreviations: Res=Resolution, NR=Not Recovered/Not Resolved, Dur=Duration, NONE=Dose Not Changed, DW=Drug Withdrawn, DI=Drug Interrupted, DR=Dose Reduced, M=Male, F=Female

SOURCE: BG12MS/JAPAN/ISS/L-AE-SER-303.SAS DATE: 02DEC2015

＊新薬承認情報提供時に置換えた

Listing of serious adverse events:
Study 109MS303
Page 99 of 138
Treatment group: BG00012 240 mg TID

Subject Sex/Age Race	MedDRA Preferred Term	Study Day Onset (a)(b)	Res	Dur (days)	Relationship to Study Drug	Severity	Serious	Action Taken With Study Drug	Outcome
[redacted] M/4[redacted] WHITE	深部静脈血栓症	272	504	233	UNLIKELY	SEVERE	Yes	NONE	RESOLVED
	多発性硬化症再発	1257	1268	12	UNRELATED	SEVERE	Yes	NONE	RESOLVED
	多発性硬化症再発	1384	1415	32	UNLIKELY	SEVERE	Yes	DW	RESOLVED
[redacted] M/4[redacted] WHITE	骨痛	291	292	2	UNRELATED	MODERATE	Yes	NONE	RESOLVED
[redacted] F/4[redacted] WHITE	挫傷	941			UNRELATED	MODERATE	Yes	NONE	RESOLVED
	交通事故	941	941	1	UNRELATED	MODERATE	Yes	NONE	RESOLVED
	骨格損傷	941			UNRELATED	MODERATE	Yes	NONE	RESOLVED

(a) #=On or after the subject switched to alternate MS medication
(b) ^=Adverse Event with onset prior to dosing
Abbreviations: Res=Resolution, NR=Not Recovered/Not Resolved, Dur=Duration, NONE=Dose Not Changed, DW=Drug Withdrawn, DI=Drug Interrupted, DR=Dose Reduced, M=Male, F=Female

SOURCE: BG12MS/JAPAN/ISS/L-AE-SER-303.SAS DATE: 02DEC2015

Listing of serious adverse events:
Study 109MS303
Page 100 of 138
Treatment group: BG00012 240 mg TID

Subject Sex/Age Race	MedDRA Preferred Term	Study Day Onset (a)(b)	Res	Dur (days)	Relationship to Study Drug	Severity	Serious	Action Taken With Study Drug	Outcome
[redacted] F/4[redacted] WHITE	脊柱変形	941			UNRELATED	MODERATE	Yes	NONE	RESOLVED
	胸椎骨折	941			UNRELATED	MODERATE	Yes	NONE	RESOLVED
[redacted] F/4[redacted] WHITE	月経過多	647	649	3	UNRELATED	MILD	Yes	NONE	RESOLVED
	月経過多	655	660	6	UNRELATED	MILD	Yes	NONE	RESOLVED
	甲状腺摘除	922	925	4	UNRELATED	MILD	Yes	NONE	RESOLVED
	膝関節形成	1124	1134	11	UNRELATED	MODERATE	Yes	NONE	RESOLVED
	術後ケア	1138	1168	31	UNRELATED	MILD	Yes	NONE	RESOLVED
[redacted] F/3[redacted] WHITE	多発性硬化症再発	576	757	182	UNRELATED	SEVERE	Yes	NONE	RESOLVED

(a) #=On or after the subject switched to alternate MS medication
(b) ^=Adverse Event with onset prior to dosing
Abbreviations: Res=Resolution, NR=Not Recovered/Not Resolved, Dur=Duration, NONE=Dose Not Changed, DW=Drug Withdrawn, DI=Drug Interrupted, DR=Dose Reduced, M=Male, F=Female

SOURCE: BG12MS/JAPAN/ISS/L-AE-SER-303.SAS DATE: 02DEC2015

Listing of serious adverse events:
Study 109MS303
Page 101 of 138
Treatment group: BG00012 240 mg TID

Subject Sex/Age Race	MedDRA Preferred Term	Study Day Onset (a)(b)	Res	Dur (days)	Relationship to Study Drug	Severity	Serious	Action Taken With Study Drug	Outcome
557* F/3[redacted] WHITE	脳虚血	1325	1429	105	UNLIKELY	MODERATE	Yes	NONE	RESOLVED
[redacted] M/5[redacted] WHITE	腺リンパ腫	190	NR		UNLIKELY	SEVERE	Yes	NONE	NOT RESOLVED
	扁桃周囲炎	1167	1178	12	POSSIBLY	MILD	Yes	NONE	RESOLVED
[redacted] F/3[redacted] WHITE	視神経炎	791	854	64	UNRELATED	SEVERE	Yes	NONE	RESOLVED
	多発性硬化症再発	1008	NR		UNRELATED	MILD	Yes	NONE	NOT RESOLVED
	多発性硬化症再発	1031	1041	11	UNRELATED	MODERATE	Yes	NONE	RESOLVED

(a) #=On or after the subject switched to alternate MS medication
(b) ^=Adverse Event with onset prior to dosing
Abbreviations: Res=Resolution, NR=Not Recovered/Not Resolved, Dur=Duration, NONE=Dose Not Changed, DW=Drug Withdrawn, DI=Drug Interrupted, DR=Dose Reduced, M=Male, F=Female

SOURCE: BG12MS/JAPAN/ISS/L-AE-SER-303.SAS DATE: 02DEC2015

＊新薬承認情報提供時に置換えた

Listing of serious adverse events:
Study 109MS303
Page 102 of 138
Treatment group: BG00012 240 mg TID

Subject Sex/Age Race	MedDRA Preferred Term	Study Day Onset (a)(b)	Res	Dur (days)	Relationship to Study Drug	Severity	Serious	Action Taken With Study Drug	Outcome
[redacted] F/3[redacted] WHITE	多発性硬化症再発	1074	1084	11	UNRELATED	MODERATE	Yes	NONE	RESOLVED
[redacted] F/4[redacted] WHITE	筋骨格痛	1371	1376	6	UNRELATED	MODERATE	Yes	NONE	RESOLVED
	多発性硬化症再発	1473	NR		RELATED	SEVERE	Yes	DW	NOT RESOLVED
	ＩＮＲ減少	1589	1590	2	UNRELATED	MILD	Yes	NONE	RESOLVED
[redacted] F/4[redacted] WHITE	卵巣嚢胞破裂	1268	1269	2	UNRELATED	SEVERE	Yes	NONE	RESOLVED

(a) #=On or after the subject switched to alternate MS medication
(b) ^=Adverse Event with onset prior to dosing
Abbreviations: Res=Resolution, NR=Not Recovered/Not Resolved, Dur=Duration, NONE=Dose Not Changed, DW=Drug Withdrawn, DI=Drug Interrupted, DR=Dose Reduced, M=Male, F=Female

SOURCE: BG12MS/JAPAN/ISS/L-AE-SER-303.SAS DATE: 02DEC2015

Listing of serious adverse events:
Study 109MS303
Page 103 of 138
Treatment group: BG00012 240 mg TID

Subject Sex/Age Race	MedDRA Preferred Term	Study Day Onset (a)(b)	Res	Dur (days)	Relationship to Study Drug	Severity	Serious	Action Taken With Study Drug	Outcome
[redacted] F/2[redacted] WHITE	動物咬傷	797	799	3	UNRELATED	MODERATE	Yes	NONE	RESOLVED
	蜂巣炎	797	799	3	UNRELATED	MODERATE	Yes	NONE	RESOLVED
558* F/4[redacted] WHITE	肺塞栓症	340	350	11	UNRELATED	MODERATE	Yes	DI	RESOLVED
[redacted] F/4[redacted] WHITE	転倒	890	890	1	UNRELATED	MODERATE	Yes	DI	RESOLVED
	股関節部骨折	891	1014	124	UNRELATED	MODERATE	Yes	DI	RESOLVED
[redacted] M/3[redacted] WHITE	気管支肺炎	1325	1338	14	UNRELATED	MILD	Yes	DI	RESOLVED

(a) #=On or after the subject switched to alternate MS medication
(b) ^=Adverse Event with onset prior to dosing
Abbreviations: Res=Resolution, NR=Not Recovered/Not Resolved, Dur=Duration, NONE=Dose Not Changed, DW=Drug Withdrawn, DI=Drug Interrupted, DR=Dose Reduced, M=Male, F=Female

SOURCE: BG12MS/JAPAN/ISS/L-AE-SER-303.SAS DATE: 02DEC2015

＊新薬承認情報提供時に置換えた

Listing of serious adverse events:
Study 109MS303
Page 104 of 138
Treatment group: BG00012 240 mg TID

Subject Sex/Age Race	MedDRA Preferred Term	Study Day Onset (a)(b)	Study Day Res	Dur (days)	Relationship to Study Drug	Severity	Serious	Action Taken With Study Drug	Outcome
[redacted] M/3[redacted] WHITE	胃腸出血	1049	1079	31	UNLIKELY	MILD	Yes	DR	RESOLVED
[redacted] M/3[redacted] WHITE	多発性硬化症再発	218	220	3	UNRELATED	SEVERE	Yes	NONE	RESOLVED
[redacted] M/3[redacted] WHITE	多発性硬化症再発	804	811	8	UNRELATED	SEVERE	Yes	NONE	RESOLVED
	大うつ病	921	945	25	UNRELATED	SEVERE	Yes	NONE	RESOLVED
	多発性硬化症再発	921	945	25	UNRELATED	SEVERE	Yes	NONE	RESOLVED

(a) #=On or after the subject switched to alternate MS medication
(b) ^=Adverse Event with onset prior to dosing
Abbreviations: Res=Resolution, NR=Not Recovered/Not Resolved, Dur=Duration, NONE=Dose Not Changed, DW=Drug Withdrawn, DI=Drug Interrupted, DR=Dose Reduced, M=Male, F=Female

SOURCE: BG12MS/JAPAN/ISS/L-AE-SER-303.SAS DATE: 02DEC2015

Listing of serious adverse events:
Study 109MS303
Page 105 of 138
Treatment group: BG00012 240 mg TID

Subject Sex/Age Race	MedDRA Preferred Term	Study Day Onset (a)(b)	Res	Dur (days)	Relationship to Study Drug	Severity	Serious	Action Taken With Study Drug	Outcome
561* F/4[redacted] WHITE	肋骨骨折	259	260	2	UNLIKELY	MODERATE	Yes	NONE	RESOLVED
[redacted] F/3[redacted] WHITE	胆石症	951	954	4	UNRELATED	MODERATE	Yes	DI	RESOLVED
[redacted] F/4[redacted] WHITE	子宮内膜症	1310	1319	10	UNRELATED	SEVERE	Yes	NONE	RESOLVED
[redacted] M/4[redacted] WHITE	ロタウイルス胃腸炎	1463	1465	3	UNRELATED	SEVERE	Yes	NONE	RESOLVED

(a) #=On or after the subject switched to alternate MS medication
(b) ^=Adverse Event with onset prior to dosing
Abbreviations: Res=Resolution, NR=Not Recovered/Not Resolved, Dur=Duration, NONE=Dose Not Changed, DW=Drug Withdrawn, DI=Drug Interrupted, DR=Dose Reduced, M=Male, F=Female

SOURCE: BG12MS/JAPAN/ISS/L-AE-SER-303.SAS DATE: 02DEC2015

＊新薬承認情報提供時に置換えた

Listing of serious adverse events:
Study 109MS303
Page 106 of 138
Treatment group: BG00012 240 mg TID

Subject Sex/Age Race	MedDRA Preferred Term	Study Day Onset (a)(b)	Res	Dur (days)	Relationship to Study Drug	Severity	Serious	Action Taken With Study Drug	Outcome
[redacted] F/4[redacted] WHITE	バニオン手術	462	465	4	UNRELATED	MILD	Yes	DI	RESOLVED
[redacted] M/3[redacted] WHITE	虫垂炎	885	893	9	UNLIKELY	SEVERE	Yes	DI	RESOLVED
[redacted] F/4[redacted] WHITE	不正子宮出血	1541	1541	1	UNRELATED	MILD	Yes	NONE	RESOLVED
[redacted] F/4[redacted] WHITE	胆道仙痛	950	954	5	UNLIKELY	MODERATE	Yes	NONE	RESOLVED

(a) #=On or after the subject switched to alternate MS medication
(b) ^=Adverse Event with onset prior to dosing
Abbreviations: Res=Resolution, NR=Not Recovered/Not Resolved, Dur=Duration, NONE=Dose Not Changed, DW=Drug Withdrawn, DI=Drug Interrupted, DR=Dose Reduced, M=Male, F=Female

SOURCE: BG12MS/JAPAN/ISS/L-AE-SER-303.SAS DATE: 02DEC2015

Listing of serious adverse events:
Study 109MS303
Page 107 of 138
Treatment group: BG00012 240 mg TID

Subject Sex/Age Race	MedDRA Preferred Term	Study Day Onset (a)(b)	Res	Dur (days)	Relationship to Study Drug	Severity	Serious	Action Taken With Study Drug	Outcome
[redacted] F/3[redacted] WHITE	胆管結石	1397	1405	9	UNLIKELY	MILD	Yes	NONE	RESOLVED
	障害者	1513	1681	169	UNRELATED	MODERATE	Yes	NONE	RESOLVED
[redacted] M/3[redacted] WHITE	多発性硬化症再発	205	209	5	UNLIKELY	MILD	Yes	NONE	RESOLVED
	多発性硬化症再発	517	521	5	UNLIKELY	MILD	Yes	NONE	RESOLVED
	多発性硬化症再発	1093	1097	5	UNRELATED	MILD	Yes	NONE	RESOLVED
	多発性硬化症再発	1461	1465	5	UNRELATED	MILD	Yes	NONE	RESOLVED

(a) #=On or after the subject switched to alternate MS medication
(b) ^=Adverse Event with onset prior to dosing
Abbreviations: Res=Resolution, NR=Not Recovered/Not Resolved, Dur=Duration, NONE=Dose Not Changed, DW=Drug Withdrawn, DI=Drug Interrupted, DR=Dose Reduced, M=Male, F=Female

SOURCE: BG12MS/JAPAN/ISS/L-AE-SER-303.SAS DATE: 02DEC2015

Listing of serious adverse events:
Study 109MS303
Page 108 of 138
Treatment group: BG00012 240 mg TID

Subject Sex/Age Race	MedDRA Preferred Term	Study Day Onset (a)(b)	Res	Dur (days)	Relationship to Study Drug	Severity	Serious	Action Taken With Study Drug	Outcome
[redacted] F/3[redacted] WHITE	多発性硬化症再発	1010	1014	5	UNLIKELY	MODERATE	Yes	NONE	RESOLVED
[redacted] F/3[redacted] WHITE	多発性硬化症再発	252	256	5	UNLIKELY	MODERATE	Yes	NONE	RESOLVED
[redacted] M/4[redacted] WHITE	多発性硬化症再発	292	297	6	UNRELATED	MODERATE	Yes	NONE	RESOLVED
[redacted] M/3[redacted] WHITE	多発性硬化症再発	823	827	5	UNLIKELY	MODERATE	Yes	NONE	RESOLVED

(a) #=On or after the subject switched to alternate MS medication
(b) ^=Adverse Event with onset prior to dosing
Abbreviations: Res=Resolution, NR=Not Recovered/Not Resolved, Dur=Duration, NONE=Dose Not Changed, DW=Drug Withdrawn, DI=Drug Interrupted, DR=Dose Reduced, M=Male, F=Female

SOURCE: BG12MS/JAPAN/ISS/L-AE-SER-303.SAS DATE: 02DEC2015

Listing of serious adverse events:
Study 109MS303
Page 109 of 138
Treatment group: BG00012 240 mg TID

Subject Sex/Age Race	MedDRA Preferred Term	Study Day Onset (a)(b)	Study Day Res	Dur (days)	Relationship to Study Drug	Severity	Serious	Action Taken With Study Drug	Outcome
[redacted] M/5[redacted] WHITE	多発性硬化症再発	1121	1126	6	UNLIKELY	MODERATE	Yes	NONE	RESOLVED
[redacted] F/5[redacted] WHITE	多発性硬化症再発	64	69	6	UNLIKELY	MODERATE	Yes	NONE	RESOLVED
[redacted] F/5[redacted] WHITE	アレルギー性皮膚炎	468	476	9	UNLIKELY	MODERATE	Yes	NONE	RESOLVED
	多発性硬化症再発	933	937	5	UNLIKELY	MODERATE	Yes	NONE	RESOLVED
	虫垂炎	1154	1157	4	UNLIKELY	SEVERE	Yes	NONE	RESOLVED

(a) #=On or after the subject switched to alternate MS medication
(b) ^=Adverse Event with onset prior to dosing
Abbreviations: Res=Resolution, NR=Not Recovered/Not Resolved, Dur=Duration, NONE=Dose Not Changed, DW=Drug Withdrawn, DI=Drug Interrupted, DR=Dose Reduced, M=Male, F=Female

SOURCE: BG12MS/JAPAN/ISS/L-AE-SER-303.SAS DATE: 02DEC2015

Listing of serious adverse events:
Study 109MS303
Page 110 of 138
Treatment group: BG00012 240 mg TID

Subject Sex/Age Race	MedDRA Preferred Term	Study Day Onset (a)(b)	Res	Dur (days)	Relationship to Study Drug	Severity	Serious	Action Taken With Study Drug	Outcome
[redacted] F/5[redacted] WHITE	多発性硬化症再発	1144	1148	5	UNLIKELY	MODERATE	Yes	NONE	RESOLVED
	失神	1405	1413	9	UNRELATED	SEVERE	Yes	NONE	RESOLVED
[redacted] F/4[redacted] WHITE	多発性硬化症再発	1032	1036	5	UNLIKELY	MODERATE	Yes	NONE	RESOLVED
	多発性硬化症再発	1704	1710	7	UNRELATED	MODERATE	Yes	NONE	RESOLVED
[redacted] M/3[redacted] WHITE	多発性硬化症再発	229	233	5	UNLIKELY	MILD	Yes	NONE	RESOLVED

(a) #=On or after the subject switched to alternate MS medication
(b) ^=Adverse Event with onset prior to dosing
Abbreviations: Res=Resolution, NR=Not Recovered/Not Resolved, Dur=Duration, NONE=Dose Not Changed, DW=Drug Withdrawn, DI=Drug Interrupted, DR=Dose Reduced, M=Male, F=Female

SOURCE: BG12MS/JAPAN/ISS/L-AE-SER-303.SAS DATE: 02DEC2015

Listing of serious adverse events:
Study 109MS303
Page 111 of 138
Treatment group: BG00012 240 mg TID

Subject Sex/Age Race	MedDRA Preferred Term	Study Day Onset (a)(b)	Res	Dur (days)	Relationship to Study Drug	Severity	Serious	Action Taken With Study Drug	Outcome
[redacted] F/4[redacted] WHITE	多発性硬化症再発	941	945	5	UNLIKELY	MILD	Yes	NONE	RESOLVED
[redacted] F/4[redacted] WHITE	多発性硬化症再発	507	511	5	UNLIKELY	MILD	Yes	NONE	RESOLVED
[redacted] F/5[redacted] WHITE	直腸癌	419	NR		UNLIKELY	SEVERE	Yes	DW	NOT RESOLVED
	骨盤膿瘍	457	467	11	UNLIKELY	SEVERE	Yes	NONE	RESOLVED
[redacted] M/4[redacted] WHITE	心筋梗塞	1014	1020	7	UNRELATED	SEVERE	Yes	NONE	RESOLVED

(a) #=On or after the subject switched to alternate MS medication
(b) ^=Adverse Event with onset prior to dosing
Abbreviations: Res=Resolution, NR=Not Recovered/Not Resolved, Dur=Duration, NONE=Dose Not Changed, DW=Drug Withdrawn, DI=Drug Interrupted, DR=Dose Reduced, M=Male, F=Female

SOURCE: BG12MS/JAPAN/ISS/L-AE-SER-303.SAS DATE: 02DEC2015

Listing of serious adverse events:
Study 109MS303
Page 112 of 138
Treatment group: BG00012 240 mg TID

Subject Sex/Age Race	MedDRA Preferred Term	Study Day Onset (a)(b)	Res	Dur (days)	Relationship to Study Drug	Severity	Serious	Action Taken With Study Drug	Outcome
[redacted] M/2[redacted] WHITE	多発性硬化症再発	574	579	6	UNLIKELY	MODERATE	Yes	NONE	RESOLVED
	多発性硬化症再発	762	766	5	UNLIKELY	MODERATE	Yes	NONE	RESOLVED
	多発性硬化症再発	1358	1362	5	UNLIKELY	MODERATE	Yes	NONE	RESOLVED
	多発性硬化症再発	1856	1860	5	UNRELATED	MODERATE	Yes	NONE	RESOLVED
[redacted] M/2[redacted] WHITE	多発性硬化症再発	71	75	5	UNLIKELY	MODERATE	Yes	NONE	RESOLVED
[redacted] F/4[redacted] WHITE	多発性硬化症再発	1485	1489	5	UNRELATED	MODERATE	Yes	NONE	RESOLVED

(a) #=On or after the subject switched to alternate MS medication
(b) ^=Adverse Event with onset prior to dosing
Abbreviations: Res=Resolution, NR=Not Recovered/Not Resolved, Dur=Duration, NONE=Dose Not Changed, DW=Drug Withdrawn, DI=Drug Interrupted, DR=Dose Reduced, M=Male, F=Female

SOURCE: BG12MS/JAPAN/ISS/L-AE-SER-303.SAS DATE: 02DEC2015

Listing of serious adverse events:
Study 109MS303
Page 113 of 138
Treatment group: BG00012 240 mg TID

Subject Sex/Age Race	MedDRA Preferred Term	Study Day Onset (a)(b)	Study Day Res	Dur (days)	Relationship to Study Drug	Severity	Serious	Action Taken With Study Drug	Outcome
[redacted] F/4[redacted] WHITE	多発性硬化症再発	1842	1846	5	UNRELATED	MODERATE	Yes	NONE	RESOLVED
[redacted] M/2[redacted] WHITE	多発性硬化症再発	1618	1623	6	UNRELATED	MODERATE	Yes	NONE	RESOLVED
383* F/5[redacted] WHITE	慢性胆嚢炎	56	63	8	UNLIKELY	MODERATE	Yes	DI	RESOLVED
	胆石症	56	63	8	UNLIKELY	MODERATE	Yes	DI	RESOLVED
[redacted] F/5[redacted] WHITE	多発性硬化症再発	120	126	7	UNLIKELY	MODERATE	Yes	NONE	RESOLVED

(a) #=On or after the subject switched to alternate MS medication
(b) ^=Adverse Event with onset prior to dosing
Abbreviations: Res=Resolution, NR=Not Recovered/Not Resolved, Dur=Duration, NONE=Dose Not Changed, DW=Drug Withdrawn, DI=Drug Interrupted, DR=Dose Reduced, M=Male, F=Female

SOURCE: BG12MS/JAPAN/ISS/L-AE-SER-303.SAS DATE: 02DEC2015

＊新薬承認情報提供時に置換えた

Listing of serious adverse events:
Study 109MS303
Page 114 of 138
Treatment group: BG00012 240 mg TID

Subject Sex/Age Race	MedDRA Preferred Term	Study Day Onset (a)(b)	Res	Dur (days)	Relationship to Study Drug	Severity	Serious	Action Taken With Study Drug	Outcome
[redacted] F/5[redacted] WHITE	多発性硬化症再発	352	361	10	UNLIKELY	MODERATE	Yes	NONE	RESOLVED
	多発性硬化症再発	603	608	6	UNLIKELY	MODERATE	Yes	NONE	RESOLVED
[redacted] F/5[redacted] WHITE	多発性硬化症再発	43	47	5	UNLIKELY	MODERATE	Yes	NONE	RESOLVED
[redacted] F/3[redacted] WHITE	変形性関節症	1075	1088	14	UNRELATED	MILD	Yes	NONE	RESOLVED
[redacted] F/2[redacted] WHITE	胆石症	710	712	3	UNRELATED	MILD	Yes	NONE	RESOLVED

(a) #=On or after the subject switched to alternate MS medication
(b) ^=Adverse Event with onset prior to dosing
Abbreviations: Res=Resolution, NR=Not Recovered/Not Resolved, Dur=Duration, NONE=Dose Not Changed, DW=Drug Withdrawn, DI=Drug Interrupted, DR=Dose Reduced, M=Male, F=Female

SOURCE: BG12MS/JAPAN/ISS/L-AE-SER-303.SAS DATE: 02DEC2015

Listing of serious adverse events:
Study 109MS303
Page 115 of 138
Treatment group: BG00012 240 mg TID

Subject Sex/Age Race	MedDRA Preferred Term	Study Day Onset (a)(b)	Study Day Res	Dur (days)	Relationship to Study Drug	Severity	Serious	Action Taken With Study Drug	Outcome
[redacted] F/2[redacted] WHITE	多発性硬化症再発	1312	1317	6	UNRELATED	MILD	Yes	NONE	RESOLVED
[redacted] F/2[redacted] WHITE	多発性硬化症再発	504	512	9	UNRELATED	MODERATE	Yes	NONE	RESOLVED
573* F/5[redacted] WHITE	子宮ポリープ	554	554	1	UNRELATED	MILD	Yes	NONE	RESOLVED
	多発性硬化症再発	836	841	6	UNRELATED	MODERATE	Yes	NONE	RESOLVED
	交通事故	1003	1003	1	UNRELATED	MODERATE	Yes	NONE	RESOLVED
	交通事故	1003	1003	1	UNRELATED	MODERATE	Yes	NONE	RESOLVED
	脾破裂	1003	1003	1	UNRELATED	SEVERE	Yes	NONE	RESOLVED

(a) #=On or after the subject switched to alternate MS medication
(b) ^=Adverse Event with onset prior to dosing
Abbreviations: Res=Resolution, NR=Not Recovered/Not Resolved, Dur=Duration, NONE=Dose Not Changed, DW=Drug Withdrawn, DI=Drug Interrupted, DR=Dose Reduced, M=Male, F=Female

SOURCE: BG12MS/JAPAN/ISS/L-AE-SER-303.SAS DATE: 02DEC2015

＊新薬承認情報提供時に置換えた

Listing of serious adverse events:
Study 109MS303
Page 116 of 138
Treatment group: BG00012 240 mg TID

Subject Sex/Age Race	MedDRA Preferred Term	Study Day Onset (a)(b)	Res	Dur (days)	Relationship to Study Drug	Severity	Serious	Action Taken With Study Drug	Outcome
657* F/5[redacted] WHITE	多発性硬化症再発	254	256	3	UNRELATED	MODERATE	Yes	NONE	RESOLVED
	多発性硬化症再発	1487	1489	3	UNRELATED	MODERATE	Yes	NONE	RESOLVED
658* M/2[redacted] WHITE	多発性硬化症再発	483	487	5	UNRELATED	MODERATE	Yes	NONE	RESOLVED
659* F/5[redacted] WHITE	多発性硬化症再発	32	37	6	UNRELATED	MODERATE	Yes	NONE	RESOLVED
	多発性硬化症再発	1305	1310	6	UNRELATED	MODERATE	Yes	NONE	RESOLVED

(a) #=On or after the subject switched to alternate MS medication
(b) ^=Adverse Event with onset prior to dosing
Abbreviations: Res=Resolution, NR=Not Recovered/Not Resolved, Dur=Duration, NONE=Dose Not Changed, DW=Drug Withdrawn, DI=Drug Interrupted, DR=Dose Reduced, M=Male, F=Female

SOURCE: BG12MS/JAPAN/ISS/L-AE-SER-303.SAS DATE: 02DEC2015

＊新薬承認情報提供時に置換えた

Listing of serious adverse events:
Study 109MS303
Page 117 of 138
Treatment group: BG00012 240 mg TID

Subject Sex/Age Race	MedDRA Preferred Term	Study Day Onset (a)(b)	Res	Dur (days)	Relationship to Study Drug	Severity	Serious	Action Taken With Study Drug	Outcome
[redacted] M/2[redacted] WHITE	視神経炎	108	113	6	UNRELATED	MODERATE	Yes	NONE	RESOLVED
[redacted] F/3[redacted] WHITE	多発性硬化症再発	669	840	172	UNRELATED	SEVERE	Yes	NONE	RESOLVED
	多発性硬化症再発	888	894	7	UNRELATED	MODERATE	Yes	NONE	RESOLVED
	多発性硬化症再発	980	984	5	UNRELATED	MODERATE	Yes	NONE	RESOLVED
	多発性硬化症再発	1114	1119	6	UNRELATED	MODERATE	Yes	NONE	RESOLVED
	多発性硬化症再発	1338	1342	5	UNRELATED	MODERATE	Yes	NONE	RESOLVED

(a) #=On or after the subject switched to alternate MS medication
(b) ^=Adverse Event with onset prior to dosing
Abbreviations: Res=Resolution, NR=Not Recovered/Not Resolved, Dur=Duration, NONE=Dose Not Changed, DW=Drug Withdrawn, DI=Drug Interrupted, DR=Dose Reduced, M=Male, F=Female

SOURCE: BG12MS/JAPAN/ISS/L-AE-SER-303.SAS DATE: 02DEC2015

Listing of serious adverse events:
Study 109MS303
Page 118 of 138
Treatment group: BG00012 240 mg TID

Subject Sex/Age Race	MedDRA Preferred Term	Study Day Onset (a)(b)	Study Day Res	Dur (days)	Relationship to Study Drug	Severity	Serious	Action Taken With Study Drug	Outcome
[redacted] F/2[redacted] WHITE	多発性硬化症再発	1489	1493	5	UNRELATED	MODERATE	Yes	NONE	RESOLVED
661* F/4[redacted] WHITE	多発性硬化症再発	85	93	9	UNRELATED	MODERATE	Yes	NONE	RESOLVED
[redacted] F/4[redacted] WHITE	多発性硬化症再発	1834	1836	3	UNRELATED	MODERATE	Yes	NONE	RESOLVED
[redacted] F/2[redacted] WHITE	多発性硬化症再発	642	646	5	UNRELATED	MODERATE	Yes	NONE	RESOLVED
	単径ヘルニア	735	736	2	UNRELATED	MILD	Yes	NONE	RESOLVED
	外科手術	735	736	2	UNRELATED	MILD	Yes	NONE	RESOLVED

(a) #=On or after the subject switched to alternate MS medication
(b) ^=Adverse Event with onset prior to dosing
Abbreviations: Res=Resolution, NR=Not Recovered/Not Resolved, Dur=Duration, NONE=Dose Not Changed, DW=Drug Withdrawn, DI=Drug Interrupted, DR=Dose Reduced, M=Male, F=Female

SOURCE: BG12MS/JAPAN/ISS/L-AE-SER-303.SAS DATE: 02DEC2015

＊新薬承認情報提供時に置換えた

Listing of serious adverse events:
Study 109MS303
Page 119 of 138
Treatment group: BG00012 240 mg TID

Subject Sex/Age Race	MedDRA Preferred Term	Study Day Onset (a)(b)	Res	Dur (days)	Relationship to Study Drug	Severity	Serious	Action Taken With Study Drug	Outcome
[redacted] F/2[redacted] WHITE	潰瘍性角膜炎	1246	1252	7	UNLIKELY	MODERATE	Yes	NONE	RESOLVED
[redacted] F/5[redacted] WHITE	多発性硬化症再発	888	892	5	UNRELATED	MODERATE	Yes	NONE	RESOLVED
	甲状腺癌	1010	1014	5	POSSIBLY	SEVERE	Yes	DI	RESOLVED
664* F/4[redacted] WHITE	不正子宮出血	564	565	2	UNRELATED	MODERATE	Yes	NONE	RESOLVED
	多発性硬化症再発	725	729	5	UNRELATED	MODERATE	Yes	NONE	RESOLVED
	多発性硬化症再発	817	823	7	UNRELATED	MODERATE	Yes	NONE	RESOLVED

(a) #=On or after the subject switched to alternate MS medication
(b) ^=Adverse Event with onset prior to dosing
Abbreviations: Res=Resolution, NR=Not Recovered/Not Resolved, Dur=Duration, NONE=Dose Not Changed, DW=Drug Withdrawn, DI=Drug Interrupted, DR=Dose Reduced, M=Male, F=Female

SOURCE: BG12MS/JAPAN/ISS/L-AE-SER-303.SAS DATE: 02DEC2015

＊新薬承認情報提供時に置換えた

Listing of serious adverse events:
Study 109MS303
Page 120 of 138
Treatment group: BG00012 240 mg TID

Subject Sex/Age Race	MedDRA Preferred Term	Study Day Onset (a)(b)	Res	Dur (days)	Relationship to Study Drug	Severity	Serious	Action Taken With Study Drug	Outcome
[redacted] F/4[redacted] WHITE	多発性硬化症再発	1128	1134	7	UNRELATED	MODERATE	Yes	NONE	RESOLVED
	関節捻挫	1216	1216	1	UNRELATED	MODERATE	Yes	NONE	RESOLVED
	子宮頚部上皮異形成	1254			UNRELATED	MODERATE	Yes	NONE	RESOLVED
[redacted] F/2[redacted] WHITE	多発性硬化症再発	668	673	6	UNRELATED	MODERATE	Yes	NONE	RESOLVED
[redacted] M/3[redacted] WHITE	多発性硬化症再発	99	105	7	UNLIKELY	MODERATE	Yes	NONE	RESOLVED
[redacted] F/3[redacted] WHITE	慢性副鼻腔炎	1297	1303	7	UNRELATED	MODERATE	Yes	NONE	RESOLVED

(a) #=On or after the subject switched to alternate MS medication
(b) ^=Adverse Event with onset prior to dosing
Abbreviations: Res=Resolution, NR=Not Recovered/Not Resolved, Dur=Duration, NONE=Dose Not Changed, DW=Drug Withdrawn, DI=Drug Interrupted, DR=Dose Reduced, M=Male, F=Female

SOURCE: BG12MS/JAPAN/ISS/L-AE-SER-303.SAS DATE: 02DEC2015

Listing of serious adverse events:
Study 109MS303
Page 121 of 138
Treatment group: BG00012 240 mg TID

Subject Sex/Age Race	MedDRA Preferred Term	Study Day Onset (a)(b)	Res	Dur (days)	Relationship to Study Drug	Severity	Serious	Action Taken With Study Drug	Outcome
[redacted] F/3[redacted] WHITE	咽頭の良性新生物	1297	1303	7	UNRELATED	MODERATE	Yes	NONE	RESOLVED
[redacted] M/2[redacted] WHITE	十二指腸炎	16	62	47	POSSIBLY	MODERATE	Yes	DI	RESOLVED
	胃炎	16	62	47	POSSIBLY	MODERATE	Yes	DI	RESOLVED
	虫垂炎	131	136	6	UNRELATED	MODERATE	Yes	DR	RESOLVED
	多発性硬化症再発	580	584	5	UNRELATED	MODERATE	Yes	NONE	RESOLVED
[redacted] F/4[redacted] WHITE	多発性硬化症再発	877	881	5	UNRELATED	MODERATE	Yes	NONE	RESOLVED

(a) #=On or after the subject switched to alternate MS medication
(b) ^=Adverse Event with onset prior to dosing
Abbreviations: Res=Resolution, NR=Not Recovered/Not Resolved, Dur=Duration, NONE=Dose Not Changed, DW=Drug Withdrawn, DI=Drug Interrupted, DR=Dose Reduced, M=Male, F=Female

SOURCE: BG12MS/JAPAN/ISS/L-AE-SER-303.SAS DATE: 02DEC2015

Listing of serious adverse events:
Study 109MS303
Page 122 of 138
Treatment group: BG00012 240 mg TID

Subject Sex/Age Race	MedDRA Preferred Term	Study Day Onset (a)(b)	Study Day Res	Dur (days)	Relationship to Study Drug	Severity	Serious	Action Taken With Study Drug	Outcome
[redacted] F/3[redacted] WHITE	帝王切開	1143	1143	1	UNRELATED	MILD	Yes	NONE	RESOLVED
[redacted] F/2[redacted] WHITE	子宮頚部上皮異形成	475	476	2	UNRELATED	MODERATE	Yes	NONE	RESOLVED
	子宮頚部上皮異形成	524	531	8	UNRELATED	MODERATE	Yes	NONE	RESOLVED
668* F/5[redacted] WHITE	変形性関節症	877	886	10	UNRELATED	SEVERE	Yes	NONE	RESOLVED
[redacted] F/4[redacted] WHITE	脊椎圧迫骨折	567	570	4	UNRELATED	MODERATE	Yes	NONE	RESOLVED

(a) #=On or after the subject switched to alternate MS medication
(b) ^=Adverse Event with onset prior to dosing
Abbreviations: Res=Resolution, NR=Not Recovered/Not Resolved, Dur=Duration, NONE=Dose Not Changed, DW=Drug Withdrawn, DI=Drug Interrupted, DR=Dose Reduced, M=Male, F=Female

SOURCE: BG12MS/JAPAN/ISS/L-AE-SER-303.SAS DATE: 02DEC2015

Listing of serious adverse events:
Study 109MS303
Page 123 of 138
Treatment group: BG00012 240 mg TID

Subject Sex/Age Race	MedDRA Preferred Term	Study Day Onset (a)(b)	Res	Dur (days)	Relationship to Study Drug	Severity	Serious	Action Taken With Study Drug	Outcome
[redacted] F/3[redacted] WHITE	自然流産	300	300	1	POSSIBLY	MODERATE	Yes	DW	RESOLVED
[redacted] F/3[redacted] WHITE	多発性硬化症再発	752	773	22	UNLIKELY	MILD	Yes	NONE	RESOLVED
[redacted] F/3[redacted] WHITE	乳癌	901	NR		POSSIBLY	SEVERE	Yes	DW	NOT RESOLVED
[redacted] F/3[redacted] WHITE	膵癌	1208	NR		UNLIKELY	MILD	Yes	DW	NOT RESOLVED

(a) #=On or after the subject switched to alternate MS medication
(b) ^=Adverse Event with onset prior to dosing
Abbreviations: Res=Resolution, NR=Not Recovered/Not Resolved, Dur=Duration, NONE=Dose Not Changed, DW=Drug Withdrawn, DI=Drug Interrupted, DR=Dose Reduced, M=Male, F=Female

SOURCE: BG12MS/JAPAN/ISS/L-AE-SER-303.SAS DATE: 02DEC2015

Listing of serious adverse events:
Study 109MS303
Page 124 of 138
Treatment group: BG00012 240 mg TID

Subject Sex/Age Race	MedDRA Preferred Term	Study Day Onset (a)(b)	Res	Dur (days)	Relationship to Study Drug	Severity	Serious	Action Taken With Study Drug	Outcome
[redacted] F/3[redacted] WHITE	多発性硬化症再発	362	366	5	UNRELATED	MODERATE	Yes	NONE	RESOLVED
[redacted] F/4[redacted] WHITE	多発性硬化症再発	297	301	5	UNRELATED	MILD	Yes	NONE	RESOLVED
[redacted] M/3[redacted] WHITE	多発性硬化症再発	342	346	5	UNRELATED	MILD	Yes	NONE	RESOLVED
[redacted] F/5[redacted] WHITE	気管支肺炎	545	555	11	UNLIKELY	SEVERE	Yes	DI	RESOLVED

(a) #=On or after the subject switched to alternate MS medication
(b) ^=Adverse Event with onset prior to dosing
Abbreviations: Res=Resolution, NR=Not Recovered/Not Resolved, Dur=Duration, NONE=Dose Not Changed, DW=Drug Withdrawn, DI=Drug Interrupted, DR=Dose Reduced, M=Male, F=Female

SOURCE: BG12MS/JAPAN/ISS/L-AE-SER-303.SAS DATE: 02DEC2015

Listing of serious adverse events:
Study 109MS303
Page 125 of 138
Treatment group: BG00012 240 mg TID

Subject Sex/Age Race	MedDRA Preferred Term	Study Day Onset (a)(b)	Study Day Res	Dur (days)	Relationship to Study Drug	Severity	Serious	Action Taken With Study Drug	Outcome
[redacted] M/4[redacted] WHITE	外科手術	270	282	13	UNRELATED	MILD	Yes	NONE	RESOLVED
	多発性硬化症再発	346	351	6	UNRELATED	MILD	Yes	NONE	RESOLVED
[redacted] F/4[redacted] WHITE	多発性硬化症再発	24	29	6	UNRELATED	MILD	Yes	NONE	RESOLVED
[redacted] F/5[redacted] WHITE	転倒	1269	1269	1	UNRELATED	SEVERE	Yes	NONE	RESOLVED
	大腿骨頚部骨折	1269	1277	9	UNRELATED	SEVERE	Yes	NONE	RESOLVED

(a) #=On or after the subject switched to alternate MS medication
(b) ^=Adverse Event with onset prior to dosing
Abbreviations: Res=Resolution, NR=Not Recovered/Not Resolved, Dur=Duration, NONE=Dose Not Changed, DW=Drug Withdrawn, DI=Drug Interrupted, DR=Dose Reduced, M=Male, F=Female

SOURCE: BG12MS/JAPAN/ISS/L-AE-SER-303.SAS DATE: 02DEC2015

Listing of serious adverse events:
Study 109MS303
Page 126 of 138
Treatment group: BG00012 240 mg TID

Subject Sex/Age Race	MedDRA Preferred Term	Study Day Onset (a)(b)	Res	Dur (days)	Relationship to Study Drug	Severity	Serious	Action Taken With Study Drug	Outcome
[redacted] F/3[redacted] WHITE	多発性硬化症再発	215	220	6	POSSIBLY	MILD	Yes	NONE	RESOLVED
	瘢痕ヘルニア	367	368	2	UNRELATED	MILD	Yes	NONE	RESOLVED
[redacted] M/3[redacted] WHITE	多発性硬化症再発	194	198	5	POSSIBLY	MILD	Yes	NONE	RESOLVED
	多発性硬化症再発	929	935	7	UNRELATED	MILD	Yes	NONE	RESOLVED
	多発性硬化症再発	1311	1316	6	UNRELATED	MILD	Yes	NONE	RESOLVED
[redacted] M/4[redacted] WHITE	悪性黒色腫	9	121	113	POSSIBLY	SEVERE	Yes	DW	RESOLVED

(a) #=On or after the subject switched to alternate MS medication
(b) ^=Adverse Event with onset prior to dosing
Abbreviations: Res=Resolution, NR=Not Recovered/Not Resolved, Dur=Duration, NONE=Dose Not Changed, DW=Drug Withdrawn, DI=Drug Interrupted, DR=Dose Reduced, M=Male, F=Female

SOURCE: BG12MS/JAPAN/ISS/L-AE-SER-303.SAS DATE: 02DEC2015

Listing of serious adverse events:
Study 109MS303
Page 127 of 138
Treatment group: BG00012 240 mg TID

Subject Sex/Age Race	MedDRA Preferred Term	Study Day Onset (a)(b)	Res	Dur (days)	Relationship to Study Drug	Severity	Serious	Action Taken With Study Drug	Outcome
673* F/2[redacted] WHITE	肥満	443	448	6	UNRELATED	SEVERE	Yes	NONE	RESOLVED
[redacted] F/4[redacted] WHITE	乳癌	455	760	306	POSSIBLY	SEVERE	Yes	DW	RESOLVED
[redacted] F/4[redacted] WHITE	精神病性障害	575	585	11	UNRELATED	SEVERE	Yes	NONE	RESOLVED
[redacted] F/5[redacted]	うつ病	226	268	43	UNRELATED	MODERATE	Yes	NONE	RESOLVED
	多発性硬化症再発	347	351	5	UNRELATED	MODERATE	Yes	NONE	RESOLVED

(a) #=On or after the subject switched to alternate MS medication
(b) ^=Adverse Event with onset prior to dosing
Abbreviations: Res=Resolution, NR=Not Recovered/Not Resolved, Dur=Duration, NONE=Dose Not Changed, DW=Drug Withdrawn, DI=Drug Interrupted, DR=Dose Reduced, M=Male, F=Female

SOURCE: BG12MS/JAPAN/ISS/L-AE-SER-303.SAS DATE: 02DEC2015

＊新薬承認情報提供時に置換えた

Listing of serious adverse events:
Study 109MS303
Page 128 of 138
Treatment group: BG00012 240 mg TID

Subject Sex/Age Race	MedDRA Preferred Term	Study Day Onset (a)(b)	Study Day Res	Dur (days)	Relationship to Study Drug	Severity	Serious	Action Taken With Study Drug	Outcome
[redacted] F/5[redacted]	多発性硬化症再発	394	397	4	UNRELATED	MODERATE	Yes	NONE	RESOLVED
	多発性硬化症再発	589	595	7	UNRELATED	MODERATE	Yes	NONE	RESOLVED
	多発性硬化症再発	1173	1176	4	UNRELATED	MILD	Yes	NONE	RESOLVED
	上腕骨骨折	1225			UNRELATED	MODERATE	Yes	NONE	RESOLVED
	うつ病	1264	NR		UNRELATED	MODERATE	Yes	NONE	NOT RESOLVED
	免疫グロブリン	1340	1346	7	UNRELATED	MILD	Yes	NONE	RESOLVED
[redacted] F/4[redacted]	多発性硬化症再発	69	71	3	UNRELATED	MILD	Yes	NONE	RESOLVED
	多発性硬化症再発	424	428	5	UNRELATED	MODERATE	Yes	NONE	RESOLVED
[redacted] F/37	多発性硬化症再発	1338	1340	3	UNRELATED	MODERATE	Yes	NONE	RESOLVED

(a) #=On or after the subject switched to alternate MS medication
(b) ^=Adverse Event with onset prior to dosing
Abbreviations: Res=Resolution, NR=Not Recovered/Not Resolved, Dur=Duration, NONE=Dose Not Changed, DW=Drug Withdrawn, DI=Drug Interrupted, DR=Dose Reduced, M=Male, F=Female

SOURCE: BG12MS/JAPAN/ISS/L-AE-SER-303.SAS DATE: 02DEC2015

Listing of serious adverse events:
Study 109MS303
Page 129 of 138
Treatment group: BG00012 240 mg TID

Subject Sex/Age Race	MedDRA Preferred Term	Study Day Onset (a)(b)	Res	Dur (days)	Relationship to Study Drug	Severity	Serious	Action Taken With Study Drug	Outcome
[redacted] F/5[redacted]	多発性硬化症再発	610			UNRELATED	MILD	Yes	NONE	RESOLVED
	発疹	988	989	2	UNRELATED	MILD	Yes	DR	RESOLVED
[redacted] F/4[redacted]	多発性硬化症再発	476	478	3	UNRELATED	MODERATE	Yes	NONE	RESOLVED
[redacted] F/4[redacted]	網膜虚血	933	933	1	UNLIKELY	MODERATE	Yes	NONE	RESOLVED
[redacted] F/4[redacted]	痔核	1329	NR		UNRELATED	MODERATE	Yes	NONE	NOT RESOLVED
579* F/3[redacted]	胃炎	14	21	8	RELATED	SEVERE	Yes	DW	RESOLVED

(a) #=On or after the subject switched to alternate MS medication
(b) ^=Adverse Event with onset prior to dosing
Abbreviations: Res=Resolution, NR=Not Recovered/Not Resolved, Dur=Duration, NONE=Dose Not Changed, DW=Drug Withdrawn, DI=Drug Interrupted, DR=Dose Reduced, M=Male, F=Female

SOURCE: BG12MS/JAPAN/ISS/L-AE-SER-303.SAS DATE: 02DEC2015

＊新薬承認情報提供時に置換えた

Listing of serious adverse events:
Study 109MS303
Page 130 of 138
Treatment group: BG00012 240 mg TID

Subject Sex/Age Race	MedDRA Preferred Term	Study Day Onset (a)(b)	Res	Dur (days)	Relationship to Study Drug	Severity	Serious	Action Taken With Study Drug	Outcome
[redacted] F/2[redacted]	多発性硬化症再発	192			UNRELATED	MODERATE	Yes	DW	RESOLVED
[redacted] F/3[redacted]	感染性下痢	715	723	9	UNRELATED	MODERATE	Yes	NONE	RESOLVED
[redacted] F/4[redacted]	足変形	1663	1663	1	UNRELATED	MODERATE	Yes	NONE	RESOLVED
[redacted] F/4[redacted]	神経性無食欲症	648	704	57	UNRELATED	MODERATE	Yes	NONE	RESOLVED
[redacted] F/4[redacted] WHITE	卵巣嚢胞	430	430	1	UNRELATED	MODERATE	Yes	NONE	RESOLVED

(a) #=On or after the subject switched to alternate MS medication
(b) ^=Adverse Event with onset prior to dosing
Abbreviations: Res=Resolution, NR=Not Recovered/Not Resolved, Dur=Duration, NONE=Dose Not Changed, DW=Drug Withdrawn, DI=Drug Interrupted, DR=Dose Reduced, M=Male, F=Female

SOURCE: BG12MS/JAPAN/ISS/L-AE-SER-303.SAS DATE: 02DEC2015

＊新薬承認情報提供時に置換えた

Listing of serious adverse events:
Study 109MS303
Page 131 of 138
Treatment group: BG00012 240 mg TID

Subject Sex/Age Race	MedDRA Preferred Term	Study Day Onset (a)(b)	Study Day Res	Dur (days)	Relationship to Study Drug	Severity	Serious	Action Taken With Study Drug	Outcome
[redacted] F/4[redacted] WHITE	関節損傷	631	633	3	UNRELATED	SEVERE	Yes	DI	RESOLVED
388* M/4[redacted] WHITE	自殺既遂	1632	1632	1	UNLIKELY	SEVERE	Yes	DW	RESOLVED
[redacted] F/4[redacted] WHITE	精神的機能代償不全	1290	1438	149	UNRELATED	SEVERE	Yes	NONE	RESOLVED
	多発性硬化症再発	1689	1691	3	UNRELATED	MODERATE	Yes	NONE	RESOLVED
[redacted] F/3[redacted] WHITE	細胞遺伝学的異常	540	540	1	UNLIKELY	SEVERE	Yes	NONE	RESOLVED

(a) #=On or after the subject switched to alternate MS medication
(b) ^=Adverse Event with onset prior to dosing
Abbreviations: Res=Resolution, NR=Not Recovered/Not Resolved, Dur=Duration, NONE=Dose Not Changed, DW=Drug Withdrawn, DI=Drug Interrupted, DR=Dose Reduced, M=Male, F=Female

SOURCE: BG12MS/JAPAN/ISS/L-AE-SER-303.SAS DATE: 02DEC2015

＊新薬承認情報提供時に置換えた

Listing of serious adverse events:
Study 109MS303
Page 132 of 138
Treatment group: BG00012 240 mg TID

Subject Sex/Age Race	MedDRA Preferred Term	Study Day Onset (a)(b)	Res	Dur (days)	Relationship to Study Drug	Severity	Serious	Action Taken With Study Drug	Outcome
[redacted] M/4[redacted] WHITE	胸膜炎	844	939	96	UNRELATED	MILD	Yes	NONE	RESOLVED
	漿膜炎	1030	1122	93	UNRELATED	MODERATE	Yes	NONE	RESOLVED
	帯状疱疹	1783	1796	14	RELATED	MODERATE	Yes	NONE	RESOLVED
[redacted] F/3[redacted] WHITE	胃潰瘍	1444	1454	11	UNRELATED	MODERATE	Yes	DI	RESOLVED
679* M/3[redacted] WHITE	霧視	134	144	11	UNRELATED	MILD	Yes	NONE	RESOLVED
[redacted] F/3[redacted] WHITE	稽留流産	206	213	8	UNRELATED	MODERATE	Yes	DI	RESOLVED

(a) #=On or after the subject switched to alternate MS medication
(b) ^=Adverse Event with onset prior to dosing
Abbreviations: Res=Resolution, NR=Not Recovered/Not Resolved, Dur=Duration, NONE=Dose Not Changed, DW=Drug Withdrawn, DI=Drug Interrupted, DR=Dose Reduced, M=Male, F=Female

SOURCE: BG12MS/JAPAN/ISS/L-AE-SER-303.SAS DATE: 02DEC2015

＊新薬承認情報提供時に置換えた

Listing of serious adverse events:
Study 109MS303
Page 133 of 138
Treatment group: BG00012 240 mg TID

Subject Sex/Age Race	MedDRA Preferred Term	Study Day Onset (a)(b)	Res	Dur (days)	Relationship to Study Drug	Severity	Serious	Action Taken With Study Drug	Outcome
[redacted] M/2[redacted] WHITE	多発性硬化症再発	297	306	10	UNRELATED	MILD	Yes	NONE	RESOLVED
[redacted] F/3[redacted] WHITE	多発性硬化症再発	868	876	9	UNLIKELY	MILD	Yes	NONE	RESOLVED
	多発性硬化症再発	977	991	15	UNLIKELY	MILD	Yes	NONE	RESOLVED
[redacted] F/4[redacted] WHITE	ウイルス感染	1529	1533	5	UNLIKELY	SEVERE	Yes	NONE	RESOLVED
589* F/4[redacted] WHITE	手根管除圧	1454	1454	1	UNRELATED	MODERATE	Yes	NONE	RESOLVED

(a) #=On or after the subject switched to alternate MS medication
(b) ^=Adverse Event with onset prior to dosing
Abbreviations: Res=Resolution, NR=Not Recovered/Not Resolved, Dur=Duration, NONE=Dose Not Changed, DW=Drug Withdrawn, DI=Drug Interrupted, DR=Dose Reduced, M=Male, F=Female

SOURCE: BG12MS/JAPAN/ISS/L-AE-SER-303.SAS DATE: 02DEC2015

＊新薬承認情報提供時に置換えた

Listing of serious adverse events:
Study 109MS303
Page 134 of 138
Treatment group: BG00012 240 mg TID

Subject Sex/Age Race	MedDRA Preferred Term	Study Day Onset (a)(b)	Res	Dur (days)	Relationship to Study Drug	Severity	Serious	Action Taken With Study Drug	Outcome
589* F/4[redacted] WHITE	線維腫	1454	1454	1	UNRELATED	MODERATE	Yes	NONE	RESOLVED
[redacted] F/4[redacted] WHITE	好酸球増加症	43	57	15	RELATED	MILD	Yes	DW	RESOLVED
[redacted] F/4[redacted] WHITE	血小板減少症	844	NR		POSSIBLY	SEVERE	Yes	DW	NOT RESOLVED
[redacted] F/4[redacted] WHITE	多発性硬化症再発	1390	1400	11	UNRELATED	MODERATE	Yes	NONE	RESOLVED

(a) #=On or after the subject switched to alternate MS medication
(b) ^=Adverse Event with onset prior to dosing
Abbreviations: Res=Resolution, NR=Not Recovered/Not Resolved, Dur=Duration, NONE=Dose Not Changed, DW=Drug Withdrawn, DI=Drug Interrupted, DR=Dose Reduced, M=Male, F=Female

SOURCE: BG12MS/JAPAN/ISS/L-AE-SER-303.SAS DATE: 02DEC2015

＊新薬承認情報提供時に置換えた

Listing of serious adverse events:
Study 109MS303
Page 135 of 138
Treatment group: BG00012 240 mg TID

Subject Sex/Age Race	MedDRA Preferred Term	Study Day Onset (a)(b)	Res	Dur (days)	Relationship to Study Drug	Severity	Serious	Action Taken With Study Drug	Outcome
682* F/3[redacted] WHITE	末梢性浮腫	135	148	14	POSSIBLY	MODERATE	Yes	DW	RESOLVED
351* F/4[redacted] WHITE	自殺既遂	88	92	5	UNRELATED	SEVERE	Yes	DW	RESOLVED
	薬物毒性	88	92	5	UNRELATED	SEVERE	Yes	DW	RESOLVED
	肝不全	88	92	5	UNRELATED	SEVERE	Yes	DW	RESOLVED
[redacted] M/4[redacted] WHITE	多発性硬化症再発	306	310	5	UNLIKELY	MILD	Yes	NONE	RESOLVED
052* F/4[redacted] WHITE	不正子宮出血	316	318	3	UNLIKELY	MODERATE	Yes	NONE	RESOLVED

(a) #=On or after the subject switched to alternate MS medication
(b) ^=Adverse Event with onset prior to dosing
Abbreviations: Res=Resolution, NR=Not Recovered/Not Resolved, Dur=Duration, NONE=Dose Not Changed, DW=Drug Withdrawn, DI=Drug Interrupted, DR=Dose Reduced, M=Male, F=Female

SOURCE: BG12MS/JAPAN/ISS/L-AE-SER-303.SAS DATE: 02DEC2015

＊新薬承認情報提供時に置換えた

Listing of serious adverse events:
Study 109MS303
Page 136 of 138
Treatment group: BG00012 240 mg TID

Subject Sex/Age Race	MedDRA Preferred Term	Study Day Onset (a)(b)	Res	Dur (days)	Relationship to Study Drug	Severity	Serious	Action Taken With Study Drug	Outcome
052* F/4[redacted] WHITE	多発性硬化症再発	696	710	15	UNLIKELY	MODERATE	Yes	NONE	RESOLVED
[redacted] M/4[redacted] WHITE	事故	1103	1107	5	UNRELATED	MODERATE	Yes	NONE	RESOLVED
	転倒	1103	1107	5	UNRELATED	MODERATE	Yes	NONE	RESOLVED
	下肢骨折	1103	1107	5	UNRELATED	MODERATE	Yes	NONE	RESOLVED
	急性胆嚢炎	1473	1481	9	UNRELATED	MODERATE	Yes	NONE	RESOLVED
	胆石症	1473	1481	9	UNRELATED	MODERATE	Yes	NONE	RESOLVED
[redacted] F/4[redacted] WHITE	多発性硬化症再発	27	33	7	UNRELATED	MILD	Yes	NONE	RESOLVED
	多発性硬化症再発	765	770	6	UNRELATED	MODERATE	Yes	NONE	RESOLVED

(a) #=On or after the subject switched to alternate MS medication
(b) ^=Adverse Event with onset prior to dosing
Abbreviations: Res=Resolution, NR=Not Recovered/Not Resolved, Dur=Duration, NONE=Dose Not Changed, DW=Drug Withdrawn, DI=Drug Interrupted, DR=Dose Reduced, M=Male, F=Female

SOURCE: BG12MS/JAPAN/ISS/L-AE-SER-303.SAS DATE: 02DEC2015

＊新薬承認情報提供時に置換えた

Listing of serious adverse events:
Study 109MS303
Page 137 of 138
Treatment group: BG00012 240 mg TID

Subject Sex/Age Race	MedDRA Preferred Term	Study Day Onset (a)(b)	Res	Dur (days)	Relationship to Study Drug	Severity	Serious	Action Taken With Study Drug	Outcome
[redacted] F/4[redacted] WHITE	多発性硬化症再発	1443	1449	7	UNRELATED	MODERATE	Yes	NONE	RESOLVED
352* F/4[redacted] WHITE	身体疾患による精神病性障害	981	985	5	UNLIKELY	MODERATE	Yes	DW	RESOLVED
	心停止	999	999	1	UNLIKELY	SEVERE	Yes	NONE	RESOLVED
[redacted] F/4[redacted] WHITE	甲状腺腫	834	NR		UNLIKELY	MILD	Yes	NONE	NOT RESOLVED
	多発性硬化症再発	1430	1437	8	UNLIKELY	MODERATE	Yes	NONE	RESOLVED

(a) #=On or after the subject switched to alternate MS medication
(b) ^=Adverse Event with onset prior to dosing
Abbreviations: Res=Resolution, NR=Not Recovered/Not Resolved, Dur=Duration, NONE=Dose Not Changed, DW=Drug Withdrawn, DI=Drug Interrupted, DR=Dose Reduced, M=Male, F=Female

SOURCE: BG12MS/JAPAN/ISS/L-AE-SER-303.SAS DATE: 02DEC2015

＊新薬承認情報提供時に置換えた

Listing of serious adverse events:
Study 109MS303
Page 138 of 138
Treatment group: BG00012 240 mg TID

Subject Sex/Age Race	MedDRA Preferred Term	Study Day Onset (a)(b)	Res	Dur (days)	Relationship to Study Drug	Severity	Serious	Action Taken With Study Drug	Outcome
[redacted] F/3[redacted] WHITE	細菌性消化管感染	84	87	4	UNLIKELY	MODERATE	Yes	NONE	RESOLVED
	平滑筋腫	243	250	8	POSSIBLY	MODERATE	Yes	NONE	RESOLVED
	多発性硬化症再発	841	848	8	UNLIKELY	MODERATE	Yes	NONE	RESOLVED
[redacted] M/3[redacted] WHITE	多発性硬化症再発	1176	1190	15	UNRELATED	SEVERE	Yes	NONE	RESOLVED
[redacted] F/5[redacted] WHITE	多発性硬化症再発	141	147	7	UNLIKELY	MODERATE	Yes	NONE	RESOLVED

(a) #=On or after the subject switched to alternate MS medication
(b) ^=Adverse Event with onset prior to dosing
Abbreviations: Res=Resolution, NR=Not Recovered/Not Resolved, Dur=Duration, NONE=Dose Not Changed, DW=Drug Withdrawn, DI=Drug Interrupted, DR=Dose Reduced, M=Male, F=Female

SOURCE: BG12MS/JAPAN/ISS/L-AE-SER-303.SAS DATE: 02DEC2015

Table 306: Listing of Serious Adverse Events - Overall

Listing of serious adverse events
- Overall
Page 1 of 10
Treatment group: Placebo

Subject Number	MedDRA Preferred Term (c)	Study Day		Dur (days)	Severity (d)	Concomitant Treat Given	Action Taken with Study Drug	Relationship to Study Drug	Resulted in Withdrawal from Study	Serious
		Onset (a)(b)	Res							
[redacted]	多発性硬化症再発	148	150	3	MILD	Yes	NONE	NOT RELATED	No	Yes
[redacted]	多発性硬化症再発	92	104	13	MODERATE	Yes	NONE	NOT RELATED	No	Yes
[redacted]	多発性硬化症再発	5	12	8	MODERATE	Yes	NONE	NOT RELATED	No	Yes
	多発性硬化症再発	67	98	32	MODERATE	Yes	NONE	NOT RELATED	No	Yes
	多発性硬化症再発	109	146	38	MODERATE	Yes	NONE	NOT RELATED	No	Yes

(a) #=On or after the subject switched to alternate MS medication.
(b) ^=Adverse Event with onset prior to dosing.
(c) *=Adverse Event caused subject to discontinue study drug, **=Adverse Event caused subject to discontinue the study, ***=Adverse Event caused subject to discontinue both study drug and study.
(d) Investigator assessment.
Abbreviations: Res=Resolution, NR=Not Recovered/Not Resolved, Dur=Duration, NONE=Dose Not Changed, DW=Drug Withdrawn, DI=Drug Interrupted, DR=Dose Reduced

SOURCE: BG12MS/109MS305/PART1/L-AE-SER.SAS DATE: 25SEP2015

Listing of serious adverse events
- Overall
Page 2 of 10
Treatment group: Placebo

Subject Number	MedDRA Preferred Term (c)	Study Day		Dur (days)	Severity (d)	Concomitant Treat Given	Action Taken with Study Drug	Relationship to Study Drug	Resulted in Withdrawal from Study	Serious
		Onset (a)(b)	Res							
[redacted]	多発性硬化症再発	159	194	36	MODERATE	Yes	NONE	NOT RELATED	No	Yes
371*	多発性硬化症再発	58	71	14	MODERATE	Yes	NONE	NOT RELATED	No	Yes
[redacted]	多発性硬化症再発***	60	93	34	MODERATE	Yes	DW	NOT RELATED	Yes	Yes
[redacted]	多発性硬化症再発	5	20	16	MILD	Yes	NONE	NOT RELATED	No	Yes

(a) #=On or after the subject switched to alternate MS medication.
(b) ^=Adverse Event with onset prior to dosing.
(c) *=Adverse Event caused subject to discontinue study drug, **=Adverse Event caused subject to discontinue the study, ***=Adverse Event caused subject to discontinue both study drug and study.
(d) Investigator assessment.
Abbreviations: Res=Resolution, NR=Not Recovered/Not Resolved, Dur=Duration, NONE=Dose Not Changed, DW=Drug Withdrawn, DI=Drug Interrupted, DR=Dose Reduced

SOURCE: BG12MS/109MS305/PART1/L-AE-SER.SAS DATE: 25SEP2015

＊新薬承認情報提供時に置換えた

Listing of serious adverse events
- Overall
Page 3 of 10
Treatment group: Placebo

Subject Number	MedDRA Preferred Term (c)	Study Day Onset (a)(b)	Study Day Res	Dur (days)	Severity (d)	Concomitant Treat Given	Action Taken with Study Drug	Relationship to Study Drug	Resulted in Withdrawal from Study	Serious
[redacted]	多発性硬化症再発	36	73	38	MILD	Yes	NONE	NOT RELATED	No	Yes
692*	多発性硬化症再発	138	143	6	MODERATE	Yes	NONE	RELATED	No	Yes
	卵管癌	173	190	18	SEVERE	Yes	NONE	NOT RELATED	No	Yes
696*	多発性硬化症再発	140	280	141	MODERATE	Yes	NONE	RELATED	No	Yes
[redacted]	多発性硬化症再発	72	73	2	MILD	Yes	NONE	NOT RELATED	No	Yes

(a) #=On or after the subject switched to alternate MS medication.
(b) ^=Adverse Event with onset prior to dosing.
(c) *=Adverse Event caused subject to discontinue study drug, **=Adverse Event caused subject to discontinue the study, ***=Adverse Event caused subject to discontinue both study drug and study.
(d) Investigator assessment.
Abbreviations: Res=Resolution, NR=Not Recovered/Not Resolved, Dur=Duration, NONE=Dose Not Changed, DW=Drug Withdrawn, DI=Drug Interrupted, DR=Dose Reduced

SOURCE: BG12MS/109MS305/PART1/L-AE-SER.SAS DATE: 25SEP2015

＊新薬承認情報提供時に置換えた

Listing of serious adverse events
- Overall
Page 4 of 10
Treatment group: Placebo

Subject Number	MedDRA Preferred Term (c)	Study Day		Dur (days)	Severity (d)	Concomitant Treat Given	Action Taken with Study Drug	Relationship to Study Drug	Resulted in Withdrawal from Study	Serious
		Onset (a)(b)	Res							
[redacted]	多発性硬化症再発	72	79	8	MODERATE	Yes	NONE	NOT RELATED	No	Yes
[redacted]	多発性硬化症再発	4	25	22	MILD	Yes	NONE	NOT RELATED	No	Yes
	多発性硬化症再発	100#	123	24	MODERATE	Yes	NONE	NOT RELATED	No	Yes
[redacted]	多発性硬化症再発	129	143	15	MILD	Yes	NONE	NOT RELATED	No	Yes
700*	多発性硬化症再発	98	112	15	MILD	Yes	NONE	NOT RELATED	No	Yes

(a) #=On or after the subject switched to alternate MS medication.
(b) ^=Adverse Event with onset prior to dosing.
(c) *=Adverse Event caused subject to discontinue study drug, **=Adverse Event caused subject to discontinue the study, ***=Adverse Event caused subject to discontinue both study drug and study.
(d) Investigator assessment.
Abbreviations: Res=Resolution, NR=Not Recovered/Not Resolved, Dur=Duration, NONE=Dose Not Changed, DW=Drug Withdrawn, DI=Drug Interrupted, DR=Dose Reduced

SOURCE: BG12MS/109MS305/PART1/L-AE-SER.SAS DATE: 25SEP2015

＊新薬承認情報提供時に置換えた

Listing of serious adverse events
- Overall
Page 5 of 10
Treatment group: Placebo

Subject Number	MedDRA Preferred Term (c)	Study Day		Dur (days)	Severity (d)	Concomitant Treat Given	Action Taken with Study Drug	Relationship to Study Drug	Resulted in Withdrawal from Study	Serious
		Onset (a)(b)	Res							
[redacted]	多発性硬化症再発	61	63	3	SEVERE	Yes	NONE	NOT RELATED	No	Yes
704*	多発性硬化症再発	6	10	5	MILD	Yes	NONE	NOT RELATED	No	Yes
	多発性硬化症再発	51	55	5	MILD	Yes	NONE	NOT RELATED	No	Yes
	多発性硬化症再発	122	133	12	MILD	Yes	NONE	NOT RELATED	No	Yes
[redacted]	多発性硬化症再発	99	105	7	MILD	Yes	NONE	NOT RELATED	No	Yes

(a) #=On or after the subject switched to alternate MS medication.
(b) ^=Adverse Event with onset prior to dosing.
(c) *=Adverse Event caused subject to discontinue study drug, **=Adverse Event caused subject to discontinue the study, ***=Adverse Event caused subject to discontinue both study drug and study.
(d) Investigator assessment.
Abbreviations: Res=Resolution, NR=Not Recovered/Not Resolved, Dur=Duration, NONE=Dose Not Changed, DW=Drug Withdrawn, DI=Drug Interrupted, DR=Dose Reduced

SOURCE: BG12MS/109MS305/PART1/L-AE-SER.SAS DATE: 25SEP2015

＊新薬承認情報提供時に置換えた

Listing of serious adverse events
- Overall
Page 6 of 10
Treatment group: BG00012 240 mg BID

Subject Number	MedDRA Preferred Term (c)	Study Day		Dur (days)	Severity (d)	Concomitant Treat Given	Action Taken with Study Drug	Relationship to Study Drug	Resulted in Withdrawal from Study	Serious
		Onset (a)(b)	Res							
691*	上腕骨骨折	33	98	66	SEVERE	Yes	NONE	NOT RELATED	No	Yes
	交通事故	33	33	1	SEVERE	No	NONE	NOT RELATED	No	Yes
	脛骨骨折	33	98	66	SEVERE	Yes	NONE	NOT RELATED	No	Yes
[redacted]	多発性硬化症再発	169	173	5	MILD	Yes	NONE	NOT RELATED	No	Yes
[redacted]	多発性硬化症再発	6	20	15	MILD	Yes	NONE	NOT RELATED	No	Yes
[redacted]	多発性硬化症再発	56	59	4	MODERATE	Yes	NONE	RELATED	No	Yes

(a) #=On or after the subject switched to alternate MS medication.
(b) ^=Adverse Event with onset prior to dosing.
(c) *=Adverse Event caused subject to discontinue study drug, **=Adverse Event caused subject to discontinue the study, ***=Adverse Event caused subject to discontinue both study drug and study.
(d) Investigator assessment.
Abbreviations: Res=Resolution, NR=Not Recovered/Not Resolved, Dur=Duration, NONE=Dose Not Changed, DW=Drug Withdrawn, DI=Drug Interrupted, DR=Dose Reduced

SOURCE: BG12MS/109MS305/PART1/L-AE-SER.SAS DATE: 25SEP2015

＊新薬承認情報提供時に置換えた

Listing of serious adverse events
- Overall
Page 7 of 10
Treatment group: BG00012 240 mg BID

Subject Number	MedDRA Preferred Term (c)	Study Day		Dur (days)	Severity (d)	Concomitant Treat Given	Action Taken with Study Drug	Relationship to Study Drug	Resulted in Withdrawal from Study	Serious
		Onset (a)(b)	Res							
[redacted]	多発性硬化症再発	43	46	4	MILD	Yes	NONE	NOT RELATED	No	Yes
	多発性硬化症再発	162	164	3	MILD	Yes	NONE	NOT RELATED	No	Yes
693*	不安	6	7	2	MODERATE	No	NONE	NOT RELATED	No	Yes
[redacted]	多発性硬化症再発	92	140	49	SEVERE	Yes	NONE	NOT RELATED	No	Yes
[redacted]	多発性硬化症再発	39	52	14	MODERATE	Yes	NONE	NOT RELATED	No	Yes

(a) #=On or after the subject switched to alternate MS medication.
(b) ^=Adverse Event with onset prior to dosing.
(c) *=Adverse Event caused subject to discontinue study drug, **=Adverse Event caused subject to discontinue the study, ***=Adverse Event caused subject to discontinue both study drug and study.
(d) Investigator assessment.
Abbreviations: Res=Resolution, NR=Not Recovered/Not Resolved, Dur=Duration, NONE=Dose Not Changed, DW=Drug Withdrawn, DI=Drug Interrupted, DR=Dose Reduced

SOURCE: BG12MS/109MS305/PART1/L-AE-SER.SAS DATE: 25SEP2015

＊新薬承認情報提供時に置換えた

Listing of serious adverse events
- Overall
Page 8 of 10
Treatment group: BG00012 240 mg BID

Subject Number	MedDRA Preferred Term (c)	Study Day Onset (a)(b)	Study Day Res	Dur (days)	Severity (d)	Concomitant Treat Given	Action Taken with Study Drug	Relationship to Study Drug	Resulted in Withdrawal from Study	Serious
[redacted]	多発性硬化症再発	78	88	11	MODERATE	Yes	NONE	NOT RELATED	No	Yes
	多発性硬化症再発	112	123	12	MODERATE	Yes	NONE	NOT RELATED	No	Yes
[redacted]	多発性硬化症再発	169	218	50	MODERATE	Yes	NONE	NOT RELATED	No	Yes
694*	腎盂腎炎	15	24	10	MODERATE	Yes	NONE	NOT RELATED	No	Yes
	腎盂腎炎	33	109	77	MODERATE	Yes	NONE	NOT RELATED	No	Yes
[redacted]	多発性硬化症再発	98	168	71	MILD	Yes	NONE	NOT RELATED	No	Yes

(a) #=On or after the subject switched to alternate MS medication.
(b) ^=Adverse Event with onset prior to dosing.
(c) *=Adverse Event caused subject to discontinue study drug, **=Adverse Event caused subject to discontinue the study, ***=Adverse Event caused subject to discontinue both study drug and study.
(d) Investigator assessment.
Abbreviations: Res=Resolution, NR=Not Recovered/Not Resolved, Dur=Duration, NONE=Dose Not Changed, DW=Drug Withdrawn, DI=Drug Interrupted, DR=Dose Reduced

SOURCE: BG12MS/109MS305/PART1/L-AE-SER.SAS DATE: 25SEP2015

＊新薬承認情報提供時に置換えた

Listing of serious adverse events
- Overall
Page 9 of 10
Treatment group: BG00012 240 mg BID

Subject Number	MedDRA Preferred Term (c)	Study Day		Dur (days)	Severity (d)	Concomitant Treat Given	Action Taken with Study Drug	Relationship to Study Drug	Resulted in Withdrawal from Study	Serious
		Onset (a)(b)	Res							
[redacted]	多発性硬化症再発	2	84	83	MILD	Yes	NONE	NOT RELATED	No	Yes
[redacted]	多発性硬化症再発	29	43	15	SEVERE	Yes	NONE	NOT RELATED	No	Yes
	多発性硬化症再発	122	182	61	SEVERE	Yes	NONE	NOT RELATED	No	Yes
[redacted]	多発性硬化症再発	7	11	5	MODERATE	Yes	NONE	NOT RELATED	No	Yes
	多発性硬化症再発	144	147	4	MODERATE	Yes	NONE	NOT RELATED	No	Yes

(a) #=On or after the subject switched to alternate MS medication.
(b) ^=Adverse Event with onset prior to dosing.
(c) *=Adverse Event caused subject to discontinue study drug, **=Adverse Event caused subject to discontinue the study, ***=Adverse Event caused subject to discontinue both study drug and study.
(d) Investigator assessment.
Abbreviations: Res=Resolution, NR=Not Recovered/Not Resolved, Dur=Duration, NONE=Dose Not Changed, DW=Drug Withdrawn, DI=Drug Interrupted, DR=Dose Reduced

SOURCE: BG12MS/109MS305/PART1/L-AE-SER.SAS DATE: 25SEP2015

Listing of serious adverse events
- Overall
Page 10 of 10
Treatment group: BG00012 240 mg BID

Subject Number	MedDRA Preferred Term (c)	Study Day			Severity (d)	Concomitant Treat Given	Action Taken with Study Drug	Relationship to Study Drug	Resulted in Withdrawal from Study	Serious
		Onset (a)(b)	Res	Dur (days)						
[redacted]	多発性硬化症再発	55	90	36	SEVERE	Yes	NONE	NOT RELATED	No	Yes

(a) #=On or after the subject switched to alternate MS medication.
(b) ^=Adverse Event with onset prior to dosing.
(c) *=Adverse Event caused subject to discontinue study drug, **=Adverse Event caused subject to discontinue the study, ***=Adverse Event caused subject to discontinue both study drug and study.
(d) Investigator assessment.
Abbreviations: Res=Resolution, NR=Not Recovered/Not Resolved, Dur=Duration, NONE=Dose Not Changed, DW=Drug Withdrawn, DI=Drug Interrupted, DR=Dose Reduced

SOURCE: BG12MS/109MS305/PART1/L-AE-SER.SAS DATE: 25SEP2015

9.9. Listings of Subjects Who Discontinued Treatment Due to AEs by Individual Study – All Evaluation Studies With Data

Table 307: Listing of Adverse Events That Led to Discontinuation of Study Drug: Study 109MS301

Listing of adverse events that led to discontinuation of study drug:
Study 109MS301
Page 1 of 53
Treatment group: Placebo

Subject Sex/Age Race	MedDRA Preferred Term	Study Day Onset (a) (b)	Res	Dur (days)	Relationship to Study Drug	Severity	Serious	Action Taken with Study Drug	Outcome
001* M/2[redacted] WHITE	血中クレアチニン増加	541	552	12	UNLIKELY	MILD	No	DW	RESOLVED
002* F/4[redacted] BLACK OR AFRICAN AMERICAN	多発性硬化症	254	337	84	UNRELATED	MODERATE	No	DW	RESOLVED
003* F/5[redacted] WHITE	血尿	51	56	6	POSSIBLY	MODERATE	No	DW	RESOLVED
004* F/3[redacted] WHITE	アラニン・アミノトランスフェラーゼ増加	279	349	71	RELATED	SEVERE	No	DW	RESOLVED

(a) #=On or after the subject switched to alternate MS medication
(b) ^=Adverse Event with onset prior to dosing
Abbreviations: Res=Resolution, NR=Not Recovered/Not Resolved, Dur=Duration, NONE=Dose Not Changed, DW=Drug Withdrawn, DI=Drug Interrupted, DR=Dose Reduced, M=Male, F=Female

SOURCE: BG12MS/JAPAN/ISS/L-AE-DISCON-301.SAS

DATE: 02DEC2015

＊新薬承認情報提供時に置換えた

Listing of adverse events that led to discontinuation of study drug:
Study 109MS301
Page 2 of 53
Treatment group: Placebo

Subject Sex/Age Race	MedDRA Preferred Term	Study Day Onset (a) (b)	Res	Dur (days)	Relationship to Study Drug	Severity	Serious	Action Taken with Study Drug	Outcome
004* F/3[redacted] WHITE	アスパラギン酸アミノトランスフェラーゼ増加	279	349	71	RELATED	SEVERE	No	DW	RESOLVED
	γ－グルタミルトランスフェラーゼ増加	279	349	71	RELATED	SEVERE	No	DW	RESOLVED
005* F/5[redacted] WHITE	多発性硬化症	363	468	106	UNLIKELY	MODERATE	No	DW	RESOLVED
006* F/2[redacted] WHITE	多発性硬化症再発	152	224	73	UNRELATED	MODERATE	Yes	DW	RESOLVED
007* F/2[redacted] ASIAN	多発性硬化症再発	175	178	4	UNRELATED	SEVERE	Yes	DW	RESOLVED

(a) #=On or after the subject switched to alternate MS medication
(b) ^=Adverse Event with onset prior to dosing
Abbreviations: Res=Resolution, NR=Not Recovered/Not Resolved, Dur=Duration, NONE=Dose Not Changed, DW=Drug Withdrawn, DI=Drug Interrupted, DR=Dose Reduced, M=Male, F=Female

SOURCE: BG12MS/JAPAN/ISS/L-AE-DISCON-301.SAS

DATE: 02DEC2015

＊新薬承認情報提供時に置換えた

Listing of adverse events that led to discontinuation of study drug:
Study 109MS301
Page 3 of 53
Treatment group: Placebo

Subject Sex/Age Race	MedDRA Preferred Term	Study Day Onset (a) (b)	Res	Dur (days)	Relationship to Study Drug	Severity	Serious	Action Taken with Study Drug	Outcome
008* F/4[redacted] ASIAN	多発性硬化症再発	271	521	251	POSSIBLY	SEVERE	Yes	DW	RESOLVED
009* F/3[redacted] ASIAN	肝酵素上昇	29	175	147	POSSIBLY	MODERATE	No	DW	RESOLVED
010* M/2[redacted] ASIAN	消化器結核	235	542	308	POSSIBLY	MODERATE	Yes	DW	RESOLVED
011* M/2[redacted] WHITE	多発性硬化症再発	362			UNRELATED	MILD	No	DW	RESOLVED

(a) #=On or after the subject switched to alternate MS medication
(b) ^=Adverse Event with onset prior to dosing
Abbreviations: Res=Resolution, NR=Not Recovered/Not Resolved, Dur=Duration, NONE=Dose Not Changed, DW=Drug Withdrawn, DI=Drug Interrupted, DR=Dose Reduced, M=Male, F=Female

SOURCE: BG12MS/JAPAN/ISS/L-AE-DISCON-301.SAS

DATE: 02DEC2015

＊新薬承認情報提供時に置換えた

Listing of adverse events that led to discontinuation of study drug:
Study 109MS301
Page 4 of 53
Treatment group: Placebo

Subject Sex/Age Race	MedDRA Preferred Term	Study Day Onset (a) (b)	Res	Dur (days)	Relationship to Study Drug	Severity	Serious	Action Taken with Study Drug	Outcome
012* M/2[redacted] WHITE	多発性硬化症再発	345	407	63	UNRELATED	MODERATE	No	DW	RESOLVED
013* F/5[redacted] WHITE	筋痙直	2	9	8	POSSIBLY	SEVERE	No	DW	RESOLVED
	そう痒症	3	12	10	POSSIBLY	MODERATE	No	DW	RESOLVED
	帯状疱疹	5	8	4	POSSIBLY	MODERATE	No	DW	RESOLVED
014* F/3[redacted] WHITE	多発性硬化症再発	2	29	28	UNRELATED	MODERATE	No	DW	RESOLVED
015* F/4[redacted] WHITE	胃腸障害	607	NR		POSSIBLY	MILD	No	DW	NOT RESOLVED

(a) #=On or after the subject switched to alternate MS medication
(b) ^=Adverse Event with onset prior to dosing
Abbreviations: Res=Resolution, NR=Not Recovered/Not Resolved, Dur=Duration, NONE=Dose Not Changed, DW=Drug Withdrawn, DI=Drug Interrupted, DR=Dose Reduced, M=Male, F=Female

SOURCE: BG12MS/JAPAN/ISS/L-AE-DISCON-301.SAS

DATE: 02DEC2015

＊新薬承認情報提供時に置換えた

Listing of adverse events that led to discontinuation of study drug:
Study 109MS301
Page 5 of 53
Treatment group: Placebo

Subject Sex/Age Race	MedDRA Preferred Term	Study Day Onset (a) (b)	Res	Dur (days)	Relationship to Study Drug	Severity	Serious	Action Taken with Study Drug	Outcome
016* M/2[redacted] WHITE	多発性硬化症再発	117	209	93	UNRELATED	MILD	No	DW	RESOLVED
017* M/2[redacted] WHITE	多発性硬化症再発	451	466	16	UNLIKELY	MILD	No	DW	RESOLVED
018* M/4[redacted] WHITE	肝酵素上昇	57	149	93	POSSIBLY	SEVERE	No	DW	RESOLVED
019* F/2[redacted] WHITE	多発性硬化症再発	396	402	7	UNRELATED	MODERATE	No	DW	RESOLVED

(a) #=On or after the subject switched to alternate MS medication
(b) ^=Adverse Event with onset prior to dosing
Abbreviations: Res=Resolution, NR=Not Recovered/Not Resolved, Dur=Duration, NONE=Dose Not Changed, DW=Drug Withdrawn, DI=Drug Interrupted, DR=Dose Reduced, M=Male, F=Female

SOURCE: BG12MS/JAPAN/ISS/L-AE-DISCON-301.SAS

DATE: 02DEC2015

＊新薬承認情報提供時に置換えた

Listing of adverse events that led to discontinuation of study drug:
Study 109MS301
Page 6 of 53
Treatment group: Placebo

Subject Sex/Age Race	MedDRA Preferred Term	Study Day Onset (a) (b)	Res	Dur (days)	Relationship to Study Drug	Severity	Serious	Action Taken with Study Drug	Outcome
020* F/2[redacted] WHITE	多発性硬化症再発	315	320	6	UNRELATED	MILD	No	DW	RESOLVED
	多発性硬化症再発	320	344	25	UNRELATED	MILD	Yes	DW	RESOLVED
021* F/4[redacted] WHITE	多発性硬化症再発	124	131	8	UNRELATED	MILD	Yes	DW	RESOLVED
022* F/4[redacted] WHITE	肝酵素上昇	1	29	29	UNRELATED	MILD	No	DW	RESOLVED
023* F/3[redacted] WHITE	多発性硬化症再発	70	130	61	UNLIKELY	MILD	No	DW	RESOLVED

(a) #=On or after the subject switched to alternate MS medication
(b) ^=Adverse Event with onset prior to dosing
Abbreviations: Res=Resolution, NR=Not Recovered/Not Resolved, Dur=Duration, NONE=Dose Not Changed, DW=Drug Withdrawn, DI=Drug Interrupted, DR=Dose Reduced, M=Male, F=Female

SOURCE: BG12MS/JAPAN/ISS/L-AE-DISCON-301.SAS

DATE: 02DEC2015

＊新薬承認情報提供時に置換えた

Listing of adverse events that led to discontinuation of study drug:
Study 109MS301
Page 7 of 53
Treatment group: Placebo

Subject Sex/Age Race	MedDRA Preferred Term	Study Day Onset (a) (b)	Res	Dur (days)	Relationship to Study Drug	Severity	Serious	Action Taken with Study Drug	Outcome
024* F/3[redacted] WHITE	感覚鈍麻	87	NR		UNLIKELY	MODERATE	No	DW	NOT RESOLVED
025* F/3[redacted] WHITE	多発性硬化症再発	406	429	24	UNLIKELY	MODERATE	No	DW	RESOLVED
026* F/4[redacted] WHITE	動悸	72	NR		POSSIBLY	MILD	No	DW	NOT RESOLVED
	腹部膨満	88	NR		POSSIBLY	MODERATE	No	DW	NOT RESOLVED
027* F/2[redacted] WHITE	多発性硬化症再発	459	NR		UNLIKELY	MODERATE	No	DW	NOT RESOLVED

(a) #=On or after the subject switched to alternate MS medication
(b) ^=Adverse Event with onset prior to dosing
Abbreviations: Res=Resolution, NR=Not Recovered/Not Resolved, Dur=Duration, NONE=Dose Not Changed, DW=Drug Withdrawn, DI=Drug Interrupted, DR=Dose Reduced, M=Male, F=Female

SOURCE: BG12MS/JAPAN/ISS/L-AE-DISCON-301.SAS

DATE: 02DEC2015

＊新薬承認情報提供時に置換えた

Listing of adverse events that led to discontinuation of study drug:
Study 109MS301
Page 8 of 53
Treatment group: Placebo

Subject Sex/Age Race	MedDRA Preferred Term	Study Day Onset (a) (b)	Res	Dur (days)	Relationship to Study Drug	Severity	Serious	Action Taken with Study Drug	Outcome
028* F/4[redacted] WHITE	下痢	123	171	49	POSSIBLY	MODERATE	No	DW	RESOLVED
029* F/1[redacted] WHITE	多発性硬化症再発	79	NR		UNRELATED	MODERATE	No	DW	NOT RESOLVED
030* F/2[redacted] WHITE	多発性硬化症再発	286	309	24	UNRELATED	MILD	No	DW	RESOLVED
031* F/2[redacted] WHITE	胃腸障害	310	NR		RELATED	MODERATE	No	DW	NOT RESOLVED

(a) #=On or after the subject switched to alternate MS medication
(b) ^=Adverse Event with onset prior to dosing
Abbreviations: Res=Resolution, NR=Not Recovered/Not Resolved, Dur=Duration, NONE=Dose Not Changed, DW=Drug Withdrawn, DI=Drug Interrupted, DR=Dose Reduced, M=Male, F=Female

SOURCE: BG12MS/JAPAN/ISS/L-AE-DISCON-301.SAS

DATE: 02DEC2015

＊新薬承認情報提供時に置換えた

Listing of adverse events that led to discontinuation of study drug:
Study 109MS301
Page 9 of 53
Treatment group: Placebo

Subject Sex/Age Race	MedDRA Preferred Term	Study Day Onset (a) (b)	Res	Dur (days)	Relationship to Study Drug	Severity	Serious	Action Taken with Study Drug	Outcome
032* F/4[redacted] WHITE	多発性硬化症再発	266	309	44	UNRELATED	MILD	No	DW	RESOLVED
033* M/3[redacted] WHITE	多発性硬化症再発	368	464	97	UNRELATED	MODERATE	No	DW	RESOLVED
034* M/3[redacted] WHITE	多発性硬化症再発	363	393	31	UNLIKELY	MILD	No	DW	RESOLVED
035* F/4[redacted] WHITE	多発性硬化症再発	472	483	12	UNRELATED	MODERATE	Yes	DW	RESOLVED

(a) #=On or after the subject switched to alternate MS medication
(b) ^=Adverse Event with onset prior to dosing
Abbreviations: Res=Resolution, NR=Not Recovered/Not Resolved, Dur=Duration, NONE=Dose Not Changed, DW=Drug Withdrawn, DI=Drug Interrupted, DR=Dose Reduced, M=Male, F=Female

SOURCE: BG12MS/JAPAN/ISS/L-AE-DISCON-301.SAS

DATE: 02DEC2015

＊新薬承認情報提供時に置換えた

Listing of adverse events that led to discontinuation of study drug:
Study 109MS301
Page 10 of 53
Treatment group: Placebo

Subject Sex/Age Race	MedDRA Preferred Term	Study Day Onset (a) (b)	Res	Dur (days)	Relationship to Study Drug	Severity	Serious	Action Taken with Study Drug	Outcome
036* F/2[redacted] WHITE	そう痒症	663	669	7	POSSIBLY	MODERATE	No	DW	RESOLVED
	乾皮症	663	669	7	POSSIBLY	MODERATE	No	DW	RESOLVED
037* F/3[redacted] WHITE	背部痛	113			POSSIBLY	MODERATE	No	DW	RESOLVED
038* F/4[redacted] WHITE	多発性硬化症再発	352	422	71	UNRELATED	MODERATE	No	DW	RESOLVED
039* F/3[redacted] WHITE	潮紅	249	314	66	RELATED	MODERATE	No	DW	RESOLVED

(a) #=On or after the subject switched to alternate MS medication
(b) ^=Adverse Event with onset prior to dosing
Abbreviations: Res=Resolution, NR=Not Recovered/Not Resolved, Dur=Duration, NONE=Dose Not Changed, DW=Drug Withdrawn, DI=Drug Interrupted, DR=Dose Reduced, M=Male, F=Female

SOURCE: BG12MS/JAPAN/ISS/L-AE-DISCON-301.SAS

DATE: 02DEC2015

＊新薬承認情報提供時に置換えた

Listing of adverse events that led to discontinuation of study drug:
Study 109MS301
Page 11 of 53
Treatment group: Placebo

Subject Sex/Age Race	MedDRA Preferred Term	Study Day Onset (a) (b)	Res	Dur (days)	Relationship to Study Drug	Severity	Serious	Action Taken with Study Drug	Outcome
040* F/3[redacted]	上腹部痛	1	NR		POSSIBLY	SEVERE	No	DW	NOT RESOLVED
041* F/4[redacted]	歯肉炎	46	NR		POSSIBLY	MILD	No	DW	NOT RESOLVED
042* M/3[redacted]	多発性硬化症再発	273	327	55	UNRELATED	MODERATE	No	DW	RESOLVED
043* F/4[redacted]	末梢性虚血	403	410	8	POSSIBLY	SEVERE	Yes	DW	RESOLVED
044* F/3[redacted]	多発性硬化症再発	159	171	13	UNRELATED	MODERATE	No	DW	RESOLVED

(a) #=On or after the subject switched to alternate MS medication
(b) ^=Adverse Event with onset prior to dosing
Abbreviations: Res=Resolution, NR=Not Recovered/Not Resolved, Dur=Duration, NONE=Dose Not Changed, DW=Drug Withdrawn, DI=Drug Interrupted, DR=Dose Reduced, M=Male, F=Female

SOURCE: BG12MS/JAPAN/ISS/L-AE-DISCON-301.SAS

DATE: 02DEC2015

＊新薬承認情報提供時に置換えた

Listing of adverse events that led to discontinuation of study drug:
Study 109MS301
Page 12 of 53
Treatment group: Placebo

Subject Sex/Age Race	MedDRA Preferred Term	Study Day Onset (a) (b)	Res	Dur (days)	Relationship to Study Drug	Severity	Serious	Action Taken with Study Drug	Outcome
045* F/4[redacted] WHITE	多発性硬化症再発	323	505	183	UNRELATED	MODERATE	No	DW	RESOLVED
046* F/3[redacted] WHITE	多発性硬化症再発	416			UNRELATED	MODERATE	No	DW	RESOLVED
047* F/4[redacted] WHITE	多発性硬化症再発	133	365	233	UNLIKELY	MODERATE	No	DW	RESOLVED
048* F/4[redacted] WHITE	多発性硬化症再発	227			UNRELATED	SEVERE	Yes	DW	RESOLVED

(a) #=On or after the subject switched to alternate MS medication
(b) ^=Adverse Event with onset prior to dosing
Abbreviations: Res=Resolution, NR=Not Recovered/Not Resolved, Dur=Duration, NONE=Dose Not Changed, DW=Drug Withdrawn, DI=Drug Interrupted, DR=Dose Reduced, M=Male, F=Female

SOURCE: BG12MS/JAPAN/ISS/L-AE-DISCON-301.SAS

DATE: 02DEC2015

＊新薬承認情報提供時に置換えた

Listing of adverse events that led to discontinuation of study drug:
Study 109MS301
Page 13 of 53
Treatment group: Placebo

Subject Sex/Age Race	MedDRA Preferred Term	Study Day Onset (a) (b)	Res	Dur (days)	Relationship to Study Drug	Severity	Serious	Action Taken with Study Drug	Outcome
049* F/5[redacted] WHITE	インフルエンザ様疾患	9	101	93	POSSIBLY	SEVERE	No	DW	RESOLVED
	細菌性咽頭炎	89	101	13	POSSIBLY	MODERATE	No	DW	RESOLVED
050* M/5[redacted] WHITE	多発性硬化症再発	413	NR		UNRELATED	SEVERE	No	DW	NOT RESOLVED
051* F/3[redacted] WHITE	乳癌	561	NR		UNRELATED	SEVERE	Yes	DW	NOT RESOLVED
052* F/4[redacted] WHITE	多発性硬化症再発	514	537	24	UNRELATED	MODERATE	No	DW	RESOLVED

(a) #=On or after the subject switched to alternate MS medication
(b) ^=Adverse Event with onset prior to dosing
Abbreviations: Res=Resolution, NR=Not Recovered/Not Resolved, Dur=Duration, NONE=Dose Not Changed, DW=Drug Withdrawn, DI=Drug Interrupted, DR=Dose Reduced, M=Male, F=Female

SOURCE: BG12MS/JAPAN/ISS/L-AE-DISCON-301.SAS

DATE: 02DEC2015

＊新薬承認情報提供時に置換えた

Listing of adverse events that led to discontinuation of study drug:
Study 109MS301
Page 14 of 53
Treatment group: Placebo

Subject Sex/Age Race	MedDRA Preferred Term	Study Day Onset (a) (b)	Res	Dur (days)	Relationship to Study Drug	Severity	Serious	Action Taken with Study Drug	Outcome
053* F/3[redacted] WHITE	多発性硬化症再発	154	158	5	UNLIKELY	MODERATE	No	DW	RESOLVED
054* M/2[redacted] WHITE	多発性硬化症再発	119	147	29	UNRELATED	MODERATE	No	DW	RESOLVED
055* F/3[redacted] WHITE	頭痛	6	12	7	RELATED	SEVERE	No	DW	RESOLVED

(a) #=On or after the subject switched to alternate MS medication
(b) ^=Adverse Event with onset prior to dosing
Abbreviations: Res=Resolution, NR=Not Recovered/Not Resolved, Dur=Duration, NONE=Dose Not Changed, DW=Drug Withdrawn, DI=Drug Interrupted, DR=Dose Reduced, M=Male, F=Female

SOURCE: BG12MS/JAPAN/ISS/L-AE-DISCON-301.SAS

DATE: 02DEC2015

＊新薬承認情報提供時に置換えた

Listing of adverse events that led to discontinuation of study drug:
Study 109MS301
Page 15 of 53
Treatment group: BG00012 240 mg BID

Subject Sex/Age Race	MedDRA Preferred Term	Study Day Onset (a) (b)	Res	Dur (days)	Relationship to Study Drug	Severity	Serious	Action Taken with Study Drug	Outcome
095* F/4[redacted] FATHER E.INDIAN, MOTHER M-EASTBLACK	そう痒症	2	24	23	POSSIBLY	MODERATE	No	DW	RESOLVED
096* M/4[redacted] WHITE	過敏症	1	1	1	RELATED	SEVERE	No	DW	RESOLVED
097* F/3[redacted] WHITE	腹部不快感	10	22	13	RELATED	SEVERE	No	DW	RESOLVED
	消化不良	10	22	13	RELATED	SEVERE	No	DW	RESOLVED

(a) #=On or after the subject switched to alternate MS medication
(b) ^=Adverse Event with onset prior to dosing
Abbreviations: Res=Resolution, NR=Not Recovered/Not Resolved, Dur=Duration, NONE=Dose Not Changed, DW=Drug Withdrawn, DI=Drug Interrupted, DR=Dose Reduced, M=Male, F=Female

SOURCE: BG12MS/JAPAN/ISS/L-AE-DISCON-301.SAS

DATE: 02DEC2015

＊新薬承認情報提供時に置換えた

Listing of adverse events that led to discontinuation of study drug:
Study 109MS301
Page 16 of 53
Treatment group: BG00012 240 mg BID

Subject Sex/Age Race	MedDRA Preferred Term	Study Day Onset (a) (b)	Res	Dur (days)	Relationship to Study Drug	Severity	Serious	Action Taken with Study Drug	Outcome
098* F/3[redacted] WHITE	嘔吐	84	94	11	RELATED	MODERATE	No	DW	RESOLVED
099* F/4[redacted] WHITE	腹部不快感	31	41	11	POSSIBLY	MILD	No	DW	RESOLVED
	疲労	31	41	11	POSSIBLY	MODERATE	No	DW	RESOLVED
	悪心	31	41	11	POSSIBLY	MILD	No	DW	RESOLVED
	傾眠	31	41	11	POSSIBLY	MODERATE	No	DW	RESOLVED
	嘔吐	32	34	3	POSSIBLY	MILD	No	DW	RESOLVED
	下痢	33	41	9	POSSIBLY	MODERATE	No	DW	RESOLVED
	便失禁	37	37	1	UNLIKELY	MODERATE	No	DW	RESOLVED
100* M/4[redacted] WHITE	蛋白尿	203	308	106	POSSIBLY	MILD	No	DW	RESOLVED

(a) #=On or after the subject switched to alternate MS medication
(b) ^=Adverse Event with onset prior to dosing
Abbreviations: Res=Resolution, NR=Not Recovered/Not Resolved, Dur=Duration, NONE=Dose Not Changed, DW=Drug Withdrawn, DI=Drug Interrupted, DR=Dose Reduced, M=Male, F=Female

SOURCE: BG12MS/JAPAN/ISS/L-AE-DISCON-301.SAS

DATE: 02DEC2015

＊新薬承認情報提供時に置換えた

Listing of adverse events that led to discontinuation of study drug:
Study 109MS301
Page 17 of 53
Treatment group: BG00012 240 mg BID

Subject Sex/Age Race	MedDRA Preferred Term	Study Day Onset (a) (b)	Res	Dur (days)	Relationship to Study Drug	Severity	Serious	Action Taken with Study Drug	Outcome
101* F/3[redacted] WHITE	上腹部痛	3	48	46	RELATED	MODERATE	No	DW	RESOLVED
	悪心	3	48	46	RELATED	MODERATE	No	DW	RESOLVED
	嘔吐	3	48	46	RELATED	MODERATE	No	DW	RESOLVED
103* F/2[redacted] WHITE	潮紅	1	9	9	RELATED	MILD	No	DW	RESOLVED
104* F/4[redacted] WHITE	発疹	2	19	18	RELATED	MODERATE	No	DW	RESOLVED
105* F/3[redacted] WHITE	過敏症	82	82	1	RELATED	MILD	No	DW	RESOLVED

(a) #=On or after the subject switched to alternate MS medication
(b) ^=Adverse Event with onset prior to dosing
Abbreviations: Res=Resolution, NR=Not Recovered/Not Resolved, Dur=Duration, NONE=Dose Not Changed, DW=Drug Withdrawn, DI=Drug Interrupted, DR=Dose Reduced, M=Male, F=Female

SOURCE: BG12MS/JAPAN/ISS/L-AE-DISCON-301.SAS

DATE: 02DEC2015

＊新薬承認情報提供時に置換えた

Listing of adverse events that led to discontinuation of study drug:
Study 109MS301
Page 18 of 53
Treatment group: BG00012 240 mg BID

Subject Sex/Age Race	MedDRA Preferred Term	Study Day Onset (a) (b)	Res	Dur (days)	Relationship to Study Drug	Severity	Serious	Action Taken with Study Drug	Outcome
106* F/4[redacted] WHITE	下痢	119			RELATED	SEVERE	No	DW	RESOLVED
107* F/5[redacted] WHITE	多汗症	229	231	3	POSSIBLY	SEVERE	No	DW	RESOLVED
108* F/3[redacted] WHITE	悪心	8	40	33	POSSIBLY	MODERATE	No	DW	RESOLVED
	下痢	13	41	29	POSSIBLY	MILD	No	DW	RESOLVED

(a) #=On or after the subject switched to alternate MS medication
(b) ^=Adverse Event with onset prior to dosing
Abbreviations: Res=Resolution, NR=Not Recovered/Not Resolved, Dur=Duration, NONE=Dose Not Changed, DW=Drug Withdrawn, DI=Drug Interrupted, DR=Dose Reduced, M=Male, F=Female

SOURCE: BG12MS/JAPAN/ISS/L-AE-DISCON-301.SAS

DATE: 02DEC2015

＊新薬承認情報提供時に置換えた

Listing of adverse events that led to discontinuation of study drug:
Study 109MS301
Page 19 of 53
Treatment group: BG00012 240 mg BID

Subject Sex/Age Race	MedDRA Preferred Term	Study Day Onset (a) (b)	Res	Dur (days)	Relationship to Study Drug	Severity	Serious	Action Taken with Study Drug	Outcome
109* F/3[redacted] BLACK OR AFRICAN AMERICAN	甲状腺腫	175	NR		POSSIBLY	MILD	No	DW	NOT RESOLVED
110* F/5[redacted] WHITE	発疹	1	122	122	RELATED	MILD	No	DW	RESOLVED
111* M/3[redacted] WHITE	多発性硬化症再発	268	339	72	RELATED	MODERATE	No	DW	RESOLVED

(a) #=On or after the subject switched to alternate MS medication
(b) ^=Adverse Event with onset prior to dosing
Abbreviations: Res=Resolution, NR=Not Recovered/Not Resolved, Dur=Duration, NONE=Dose Not Changed, DW=Drug Withdrawn, DI=Drug Interrupted, DR=Dose Reduced, M=Male, F=Female

SOURCE: BG12MS/JAPAN/ISS/L-AE-DISCON-301.SAS

DATE: 02DEC2015

＊新薬承認情報提供時に置換えた

Listing of adverse events that led to discontinuation of study drug:
Study 109MS301
Page 20 of 53
Treatment group: BG00012 240 mg BID

Subject Sex/Age Race	MedDRA Preferred Term	Study Day Onset (a) (b)	Res	Dur (days)	Relationship to Study Drug	Severity	Serious	Action Taken with Study Drug	Outcome
112* M/5[redacted] BLACK OR AFRICAN AMERICAN	尿中アルブミン陽性	1	85	85	UNRELATED	MILD	No	DW	RESOLVED
113* F/5[redacted] WHITE	血尿	28	168	141	POSSIBLY	MILD	No	DW	RESOLVED
114* F/4[redacted] WHITE	下痢	16	21	6	POSSIBLY	MODERATE	No	DW	RESOLVED
115* F/3[redacted] WHITE	潮紅	35	154	120	POSSIBLY	MODERATE	No	DW	RESOLVED

(a) #=On or after the subject switched to alternate MS medication
(b) ^=Adverse Event with onset prior to dosing
Abbreviations: Res=Resolution, NR=Not Recovered/Not Resolved, Dur=Duration, NONE=Dose Not Changed, DW=Drug Withdrawn, DI=Drug Interrupted, DR=Dose Reduced, M=Male, F=Female

SOURCE: BG12MS/JAPAN/ISS/L-AE-DISCON-301.SAS

DATE: 02DEC2015

＊新薬承認情報提供時に置換えた

Listing of adverse events that led to discontinuation of study drug:
Study 109MS301
Page 21 of 53
Treatment group: BG00012 240 mg BID

Subject Sex/Age Race	MedDRA Preferred Term	Study Day Onset (a) (b)	Res	Dur (days)	Relationship to Study Drug	Severity	Serious	Action Taken with Study Drug	Outcome
115* F/3[redacted] WHITE	全身性皮疹	35	154	120	POSSIBLY	MODERATE	No	DW	RESOLVED
116* M/3[redacted] WHITE	上腹部痛	21	22	2	RELATED	SEVERE	No	DW	RESOLVED
117* M/4[redacted] WHITE	胃炎	18			POSSIBLY	MODERATE	No	DW	RESOLVED
118* F/3[redacted] HISPANIC OR LATINO	多発性硬化症再発	365	374	10	UNRELATED	MODERATE	No	DW	RESOLVED

(a) #=On or after the subject switched to alternate MS medication
(b) ^=Adverse Event with onset prior to dosing
Abbreviations: Res=Resolution, NR=Not Recovered/Not Resolved, Dur=Duration, NONE=Dose Not Changed, DW=Drug Withdrawn, DI=Drug Interrupted, DR=Dose Reduced, M=Male, F=Female

SOURCE: BG12MS/JAPAN/ISS/L-AE-DISCON-301.SAS

DATE: 02DEC2015

＊新薬承認情報提供時に置換えた

Listing of adverse events that led to discontinuation of study drug:
Study 109MS301
Page 22 of 53
Treatment group: BG00012 240 mg BID

Subject Sex/Age Race	MedDRA Preferred Term	Study Day Onset (a) (b)	Res	Dur (days)	Relationship to Study Drug	Severity	Serious	Action Taken with Study Drug	Outcome
119* F/4[redacted] WHITE	過敏症	30	40	11	POSSIBLY	MODERATE	No	DW	RESOLVED
120* F/3[redacted] WHITE	潮紅	28	43	16	RELATED	MILD	No	DW	RESOLVED
	胃腸障害	28	43	16	RELATED	MILD	No	DW	RESOLVED
121* F/3[redacted] ASIAN	腫脹	8	13	6	RELATED	MODERATE	No	DW	RESOLVED
122* F/5[redacted] WHITE	潮紅	8	8	1	RELATED	MODERATE	No	DW	RESOLVED

(a) #=On or after the subject switched to alternate MS medication
(b) ^=Adverse Event with onset prior to dosing
Abbreviations: Res=Resolution, NR=Not Recovered/Not Resolved, Dur=Duration, NONE=Dose Not Changed, DW=Drug Withdrawn, DI=Drug Interrupted, DR=Dose Reduced, M=Male, F=Female

SOURCE: BG12MS/JAPAN/ISS/L-AE-DISCON-301.SAS

DATE: 02DEC2015

＊新薬承認情報提供時に置換えた

Listing of adverse events that led to discontinuation of study drug:
Study 109MS301
Page 23 of 53
Treatment group: BG00012 240 mg BID

Subject Sex/Age Race	MedDRA Preferred Term	Study Day Onset (a) (b)	Res	Dur (days)	Relationship to Study Drug	Severity	Serious	Action Taken with Study Drug	Outcome
123* F/4[redacted] WHITE	過敏症	1	1	1	RELATED	MODERATE	Yes	DW	RESOLVED
125* F/4[redacted] WHITE	胃腸障害	11	13	3	POSSIBLY	SEVERE	No	DW	RESOLVED
	胃腸障害	13	54	42	POSSIBLY	SEVERE	Yes	DW	RESOLVED
126* F/2[redacted] WHITE	腹痛	398	420	23	POSSIBLY	MODERATE	No	DW	RESOLVED
127* M/4[redacted] WHITE	蛋白尿	225	NR		POSSIBLY	MILD	No	DW	NOT RESOLVED

(a) #=On or after the subject switched to alternate MS medication
(b) ^=Adverse Event with onset prior to dosing
Abbreviations: Res=Resolution, NR=Not Recovered/Not Resolved, Dur=Duration, NONE=Dose Not Changed, DW=Drug Withdrawn, DI=Drug Interrupted, DR=Dose Reduced, M=Male, F=Female

SOURCE: BG12MS/JAPAN/ISS/L-AE-DISCON-301.SAS

DATE: 02DEC2015

＊新薬承認情報提供時に置換えた

Listing of adverse events that led to discontinuation of study drug:
Study 109MS301
Page 24 of 53
Treatment group: BG00012 240 mg BID

Subject Sex/Age Race	MedDRA Preferred Term	Study Day Onset (a) (b)	Res	Dur (days)	Relationship to Study Drug	Severity	Serious	Action Taken with Study Drug	Outcome
128* F/3[redacted] WHITE	アレルギー性皮膚炎	1	4	4	RELATED	MODERATE	No	DW	RESOLVED
129* F/4[redacted] WHITE	上腹部痛	32	86	55	RELATED	SEVERE	No	DW	RESOLVED
130* F/3[redacted] WHITE	全身紅斑	2	11	10	RELATED	MODERATE	No	DW	RESOLVED
	全身性そう痒症	2	11	10	RELATED	MODERATE	No	DW	RESOLVED
131* M/5[redacted] WHITE	全身紅斑	2	2	1	RELATED	MODERATE	No	DW	RESOLVED
	高血圧	2	2	1	RELATED	MODERATE	No	DW	RESOLVED

(a) #=On or after the subject switched to alternate MS medication
(b) ^=Adverse Event with onset prior to dosing
Abbreviations: Res=Resolution, NR=Not Recovered/Not Resolved, Dur=Duration, NONE=Dose Not Changed, DW=Drug Withdrawn, DI=Drug Interrupted, DR=Dose Reduced, M=Male, F=Female

SOURCE: BG12MS/JAPAN/ISS/L-AE-DISCON-301.SAS

DATE: 02DEC2015

＊新薬承認情報提供時に置換えた

Listing of adverse events that led to discontinuation of study drug:
Study 109MS301
Page 25 of 53
Treatment group: BG00012 240 mg BID

Subject Sex/Age Race	MedDRA Preferred Term	Study Day Onset (a) (b)	Res	Dur (days)	Relationship to Study Drug	Severity	Serious	Action Taken with Study Drug	Outcome
131* M/5[redacted] WHITE	粘膜乾燥	2	2	1	RELATED	MODERATE	No	DW	RESOLVED
	発熱	2	2	1	RELATED	MODERATE	No	DW	RESOLVED
132* F/5[redacted] WHITE	腎新生物	633	644	12	POSSIBLY	MODERATE	No	DW	RESOLVED
	移行上皮癌	644	660	17	POSSIBLY	SEVERE	Yes	DW	RESOLVED
133* F/5[redacted] WHITE	体重減少	1	NR		POSSIBLY	MODERATE	No	DW	NOT RESOLVED
	悪心	14	22	9	RELATED	SEVERE	No	DW	RESOLVED
	嘔吐	14	22	9	RELATED	SEVERE	No	DW	RESOLVED

(a) #=On or after the subject switched to alternate MS medication
(b) ^=Adverse Event with onset prior to dosing
Abbreviations: Res=Resolution, NR=Not Recovered/Not Resolved, Dur=Duration, NONE=Dose Not Changed, DW=Drug Withdrawn, DI=Drug Interrupted, DR=Dose Reduced, M=Male, F=Female

SOURCE: BG12MS/JAPAN/ISS/L-AE-DISCON-301.SAS

DATE: 02DEC2015

＊新薬承認情報提供時に置換えた

Listing of adverse events that led to discontinuation of study drug:
Study 109MS301
Page 26 of 53
Treatment group: BG00012 240 mg BID

Subject Sex/Age Race	MedDRA Preferred Term	Study Day Onset (a) (b)	Res	Dur (days)	Relationship to Study Drug	Severity	Serious	Action Taken with Study Drug	Outcome
134* F/3[redacted] WHITE	消化不良	61	75	15	RELATED	MILD	No	DW	RESOLVED
135* F/5[redacted] WHITE	多発性硬化症再発	190	280	91	UNRELATED	MODERATE	No	DW	RESOLVED
136* F/5[redacted] WHITE	交通事故	5	5	1	UNRELATED	SEVERE	Yes	DW	RESOLVED
	外傷性脳損傷	5	99	95	UNRELATED	SEVERE	Yes	DW	RESOLVED
137* F/4[redacted] WHITE	多発性硬化症再発	82	194	113	UNRELATED	MILD	No	DW	RESOLVED

(a) #=On or after the subject switched to alternate MS medication
(b) ^=Adverse Event with onset prior to dosing
Abbreviations: Res=Resolution, NR=Not Recovered/Not Resolved, Dur=Duration, NONE=Dose Not Changed, DW=Drug Withdrawn, DI=Drug Interrupted, DR=Dose Reduced, M=Male, F=Female

SOURCE: BG12MS/JAPAN/ISS/L-AE-DISCON-301.SAS

DATE: 02DEC2015

＊新薬承認情報提供時に置換えた

Listing of adverse events that led to discontinuation of study drug:
Study 109MS301
Page 27 of 53
Treatment group: BG00012 240 mg BID

Subject Sex/Age Race	MedDRA Preferred Term	Study Day Onset (a) (b)	Res	Dur (days)	Relationship to Study Drug	Severity	Serious	Action Taken with Study Drug	Outcome
138* F/3[redacted] WHITE	消化不良	477	513	37	RELATED	SEVERE	No	DW	RESOLVED
	紅斑	477	513	37	RELATED	SEVERE	No	DW	RESOLVED
139* M/3[redacted] WHITE	潮紅	7	21	15	RELATED	SEVERE	No	DW	RESOLVED
140* F/2[redacted] WHITE	妊娠	664	NR		UNRELATED	MODERATE	No	DW	NOT RESOLVED
141* F/4[redacted] WHITE	胆汁うっ滞性肝炎	446	457	12	POSSIBLY	SEVERE	Yes	DW	RESOLVED

(a) #=On or after the subject switched to alternate MS medication
(b) ^=Adverse Event with onset prior to dosing
Abbreviations: Res=Resolution, NR=Not Recovered/Not Resolved, Dur=Duration, NONE=Dose Not Changed, DW=Drug Withdrawn, DI=Drug Interrupted, DR=Dose Reduced, M=Male, F=Female

SOURCE: BG12MS/JAPAN/ISS/L-AE-DISCON-301.SAS

DATE: 02DEC2015

＊新薬承認情報提供時に置換えた

Listing of adverse events that led to discontinuation of study drug:
Study 109MS301
Page 28 of 53
Treatment group: BG00012 240 mg BID

Subject Sex/Age Race	MedDRA Preferred Term	Study Day Onset (a) (b)	Res	Dur (days)	Relationship to Study Drug	Severity	Serious	Action Taken with Study Drug	Outcome
142* M/4[redacted] WHITE	全身性皮疹	351	368	18	RELATED	SEVERE	No	DW	RESOLVED
143* F/3[redacted] WHITE	上腹部痛	55	74	20	RELATED	SEVERE	No	DW	RESOLVED
144* F/4[redacted] WHITE	下痢	1	14	14	RELATED	MODERATE	No	DW	RESOLVED
	嘔吐	26	26	1	RELATED	MODERATE	No	DW	RESOLVED
145* F/3[redacted] WHITE	胃腸炎	12	34	23	RELATED	SEVERE	No	DW	RESOLVED

(a) #=On or after the subject switched to alternate MS medication
(b) ^=Adverse Event with onset prior to dosing
Abbreviations: Res=Resolution, NR=Not Recovered/Not Resolved, Dur=Duration, NONE=Dose Not Changed, DW=Drug Withdrawn, DI=Drug Interrupted, DR=Dose Reduced, M=Male, F=Female

SOURCE: BG12MS/JAPAN/ISS/L-AE-DISCON-301.SAS

DATE: 02DEC2015

＊新薬承認情報提供時に置換えた

Listing of adverse events that led to discontinuation of study drug:
Study 109MS301
Page 29 of 53
Treatment group: BG00012 240 mg BID

Subject Sex/Age Race	MedDRA Preferred Term	Study Day Onset (a) (b)	Res	Dur (days)	Relationship to Study Drug	Severity	Serious	Action Taken with Study Drug	Outcome
146* F/3[redacted] WHITE	潮紅	424	NR		RELATED	SEVERE	No	DW	NOT RESOLVED
147* F/4[redacted] WHITE	潮紅	168	287	120	RELATED	MILD	No	DW	RESOLVED
148* M/3[redacted]	うつ病	256	NR		UNLIKELY	MODERATE	No	DW	NOT RESOLVED
149* F/2[redacted]	発疹	1			RELATED	MODERATE	No	DW	RESOLVED
150* F/2[redacted]	異常行動	1	138	138	POSSIBLY	MILD	No	DW	RESOLVED

(a) #=On or after the subject switched to alternate MS medication
(b) ^=Adverse Event with onset prior to dosing
Abbreviations: Res=Resolution, NR=Not Recovered/Not Resolved, Dur=Duration, NONE=Dose Not Changed, DW=Drug Withdrawn, DI=Drug Interrupted, DR=Dose Reduced, M=Male, F=Female

SOURCE: BG12MS/JAPAN/ISS/L-AE-DISCON-301.SAS

DATE: 02DEC2015

＊新薬承認情報提供時に置換えた

Listing of adverse events that led to discontinuation of study drug:
Study 109MS301
Page 30 of 53
Treatment group: BG00012 240 mg BID

Subject Sex/Age Race	MedDRA Preferred Term	Study Day Onset (a) (b)	Res	Dur (days)	Relationship to Study Drug	Severity	Serious	Action Taken with Study Drug	Outcome
151* M/2[redacted]	腹痛	44	56	13	POSSIBLY	MODERATE	No	DW	RESOLVED
152* F/4[redacted]	潮紅	156	188	33	RELATED	MODERATE	No	DW	RESOLVED
	頭痛	156	188	33	POSSIBLY	MODERATE	No	DW	RESOLVED
153* M/3[redacted] WHITE	てんかん	534	554	21	UNRELATED	SEVERE	Yes	DW	RESOLVED
	誤嚥性肺炎	535	554	20	UNRELATED	SEVERE	Yes	DW	RESOLVED
154* F/2[redacted] WHITE	潮紅	1	1	1	RELATED	MODERATE	Yes	DW	RESOLVED

(a) #=On or after the subject switched to alternate MS medication
(b) ^=Adverse Event with onset prior to dosing
Abbreviations: Res=Resolution, NR=Not Recovered/Not Resolved, Dur=Duration, NONE=Dose Not Changed, DW=Drug Withdrawn, DI=Drug Interrupted, DR=Dose Reduced, M=Male, F=Female

SOURCE: BG12MS/JAPAN/ISS/L-AE-DISCON-301.SAS

DATE: 02DEC2015

＊新薬承認情報提供時に置換えた

Listing of adverse events that led to discontinuation of study drug:
Study 109MS301
Page 31 of 53
Treatment group: BG00012 240 mg BID

Subject Sex/Age Race	MedDRA Preferred Term	Study Day Onset (a) (b)	Res	Dur (days)	Relationship to Study Drug	Severity	Serious	Action Taken with Study Drug	Outcome
155* F/4[redacted] WHITE	腹痛	1	38	38	POSSIBLY	MODERATE	No	DW	RESOLVED
	悪心	1	NR		POSSIBLY	MODERATE	No	DW	NOT RESOLVED
	上腹部痛	15	NR		POSSIBLY	MODERATE	No	DW	NOT RESOLVED
156* F/3[redacted] WHITE	アレルギー性皮膚炎	1	1	1	POSSIBLY	MODERATE	No	DW	RESOLVED
	アレルギー性そう痒症	1	1	1	POSSIBLY	MODERATE	No	DW	RESOLVED
157* M/3[redacted] WHITE	好中球増加症	23	NR		POSSIBLY	MILD	No	DW	NOT RESOLVED

(a) #=On or after the subject switched to alternate MS medication
(b) ^=Adverse Event with onset prior to dosing
Abbreviations: Res=Resolution, NR=Not Recovered/Not Resolved, Dur=Duration, NONE=Dose Not Changed, DW=Drug Withdrawn, DI=Drug Interrupted, DR=Dose Reduced, M=Male, F=Female

SOURCE: BG12MS/JAPAN/ISS/L-AE-DISCON-301.SAS

DATE: 02DEC2015

＊新薬承認情報提供時に置換えた

Listing of adverse events that led to discontinuation of study drug:
Study 109MS301
Page 32 of 53
Treatment group: BG00012 240 mg BID

Subject Sex/Age Race	MedDRA Preferred Term	Study Day Onset (a) (b)	Res	Dur (days)	Relationship to Study Drug	Severity	Serious	Action Taken with Study Drug	Outcome
158* F/5[redacted] WHITE	多発性硬化症再発	172	NR		UNRELATED	MODERATE	No	DW	NOT RESOLVED
159* F/4[redacted] PERSIAN	肝機能検査異常	65	140	76	RELATED	SEVERE	No	DW	RESOLVED
160* F/3[redacted] WHITE	便秘	14	48	35	RELATED	SEVERE	Yes	DW	RESOLVED
161* F/4[redacted] WHITE	潮紅	1	NR		POSSIBLY	MILD	No	DW	NOT RESOLVED

(a) #=On or after the subject switched to alternate MS medication
(b) ^=Adverse Event with onset prior to dosing
Abbreviations: Res=Resolution, NR=Not Recovered/Not Resolved, Dur=Duration, NONE=Dose Not Changed, DW=Drug Withdrawn, DI=Drug Interrupted, DR=Dose Reduced, M=Male, F=Female

SOURCE: BG12MS/JAPAN/ISS/L-AE-DISCON-301.SAS

DATE: 02DEC2015

＊新薬承認情報提供時に置換えた

Listing of adverse events that led to discontinuation of study drug:
Study 109MS301
Page 33 of 53
Treatment group: BG00012 240 mg TID

Subject Sex/Age Race	MedDRA Preferred Term	Study Day Onset (a) (b)	Res	Dur (days)	Relationship to Study Drug	Severity	Serious	Action Taken with Study Drug	Outcome
207* F/3[redacted] WHITE	胃腸障害	35	52	18	RELATED	MODERATE	No	DW	RESOLVED
208* F/5[redacted] WHITE	多発性硬化症再発	327	421	95	UNRELATED	MODERATE	No	DW	RESOLVED
209* F/5[redacted] WHITE	下腹部痛	394	396	3	POSSIBLY	MODERATE	Yes	DW	RESOLVED
210* F/3[redacted] BLACK OR AFRICAN AMERICAN	交通事故	62	62	1	UNRELATED	SEVERE	Yes	DW	RESOLVED

(a) #=On or after the subject switched to alternate MS medication
(b) ^=Adverse Event with onset prior to dosing
Abbreviations: Res=Resolution, NR=Not Recovered/Not Resolved, Dur=Duration, NONE=Dose Not Changed, DW=Drug Withdrawn, DI=Drug Interrupted, DR=Dose Reduced, M=Male, F=Female

SOURCE: BG12MS/JAPAN/ISS/L-AE-DISCON-301.SAS DATE: 02DEC2015

＊新薬承認情報提供時に置換えた

Listing of adverse events that led to discontinuation of study drug:
Study 109MS301
Page 34 of 53
Treatment group: BG00012 240 mg TID

Subject Sex/Age Race	MedDRA Preferred Term	Study Day Onset (a) (b)	Res	Dur (days)	Relationship to Study Drug	Severity	Serious	Action Taken with Study Drug	Outcome
211* M/5[redacted] WHITE	腹痛	3	NR		POSSIBLY	MILD	No	DW	NOT RESOLVED
	平衡障害	3	NR		UNLIKELY	MILD	No	DW	NOT RESOLVED
	胸痛	3	NR		POSSIBLY	MILD	No	DW	NOT RESOLVED
	不快感	3	NR		POSSIBLY	MILD	No	DW	NOT RESOLVED
	疲労	3	NR		POSSIBLY	MODERATE	No	DW	NOT RESOLVED
	頭痛	3	NR		UNLIKELY	MILD	No	DW	NOT RESOLVED
	四肢痛	3	NR		UNLIKELY	MILD	No	DW	NOT RESOLVED
	霧視	3	NR		POSSIBLY	MILD	No	DW	NOT RESOLVED
212* F/4[redacted] WHITE	腹痛	28	38	11	POSSIBLY	MODERATE	No	DW	RESOLVED
	背部痛	28	38	11	POSSIBLY	SEVERE	No	DW	RESOLVED
	下痢	28	38	11	POSSIBLY	MILD	No	DW	RESOLVED
	腹部膨満	29	38	10	POSSIBLY	SEVERE	No	DW	RESOLVED

(a) #=On or after the subject switched to alternate MS medication
(b) ^=Adverse Event with onset prior to dosing
Abbreviations: Res=Resolution, NR=Not Recovered/Not Resolved, Dur=Duration, NONE=Dose Not Changed, DW=Drug Withdrawn, DI=Drug Interrupted, DR=Dose Reduced, M=Male, F=Female

SOURCE: BG12MS/JAPAN/ISS/L-AE-DISCON-301.SAS

DATE: 02DEC2015

＊新薬承認情報提供時に置換えた

Listing of adverse events that led to discontinuation of study drug:
Study 109MS301
Page 35 of 53
Treatment group: BG00012 240 mg TID

Subject Sex/Age Race	MedDRA Preferred Term	Study Day Onset (a) (b)	Res	Dur (days)	Relationship to Study Drug	Severity	Serious	Action Taken with Study Drug	Outcome
212* F/4[redacted] WHITE	側腹部痛	30	38	9	POSSIBLY	MODERATE	No	DW	RESOLVED
213* F/5[redacted] WHITE	悪心	379	NR		UNLIKELY	MILD	No	DW	NOT RESOLVED
	嘔吐	379	NR		UNLIKELY	MILD	No	DW	NOT RESOLVED
214* F/3[redacted] WHITE	そう痒性皮疹	29	32	4	POSSIBLY	MILD	No	DW	RESOLVED
	そう痒性皮疹	29	32	4	POSSIBLY	MILD	No	DW	RESOLVED
	そう痒性皮疹	31	32	2	POSSIBLY	MILD	No	DW	RESOLVED
	そう痒性皮疹	31	32	2	POSSIBLY	MILD	No	DW	RESOLVED

(a) #=On or after the subject switched to alternate MS medication
(b) ^=Adverse Event with onset prior to dosing
Abbreviations: Res=Resolution, NR=Not Recovered/Not Resolved, Dur=Duration, NONE=Dose Not Changed, DW=Drug Withdrawn, DI=Drug Interrupted, DR=Dose Reduced, M=Male, F=Female

SOURCE: BG12MS/JAPAN/ISS/L-AE-DISCON-301.SAS

DATE: 02DEC2015

＊新薬承認情報提供時に置換えた

Listing of adverse events that led to discontinuation of study drug:
Study 109MS301
Page 36 of 53
Treatment group: BG00012 240 mg TID

Subject Sex/Age Race	MedDRA Preferred Term	Study Day Onset (a) (b)	Res	Dur (days)	Relationship to Study Drug	Severity	Serious	Action Taken with Study Drug	Outcome
215* F/4[redacted] WHITE	眼帯状疱疹	88	NR		UNLIKELY	SEVERE	No	DW	NOT RESOLVED
216* F/3[redacted] WHITE	全身性皮疹	11	14	4	POSSIBLY	MODERATE	No	DW	RESOLVED
217* F/4[redacted] WHITE	子宮頚部癌	556	595	40	UNLIKELY	MODERATE	Yes	DW	RESOLVED
218* F/4[redacted] WHITE	蕁麻疹	15	35	21	POSSIBLY	MODERATE	No	DW	RESOLVED
	上腹部痛	20	35	16	POSSIBLY	SEVERE	No	DW	RESOLVED
	憩室炎	22	NR		POSSIBLY	MODERATE	No	DW	NOT RESOLVED

(a) #=On or after the subject switched to alternate MS medication
(b) ^=Adverse Event with onset prior to dosing
Abbreviations: Res=Resolution, NR=Not Recovered/Not Resolved, Dur=Duration, NONE=Dose Not Changed, DW=Drug Withdrawn, DI=Drug Interrupted, DR=Dose Reduced, M=Male, F=Female

SOURCE: BG12MS/JAPAN/ISS/L-AE-DISCON-301.SAS

DATE: 02DEC2015

＊新薬承認情報提供時に置換えた

Listing of adverse events that led to discontinuation of study drug:
Study 109MS301
Page 37 of 53
Treatment group: BG00012 240 mg TID

Subject Sex/Age Race	MedDRA Preferred Term	Study Day Onset (a) (b)	Res	Dur (days)	Relationship to Study Drug	Severity	Serious	Action Taken with Study Drug	Outcome
219* F/3[redacted] WHITE	腹部膨満	20	34	15	RELATED	MODERATE	No	DW	RESOLVED
	下痢	20	32	13	RELATED	MODERATE	No	DW	RESOLVED
	悪心	20	53	34	RELATED	MODERATE	No	DW	RESOLVED
	耳不快感	21	24	4	RELATED	MILD	No	DW	RESOLVED
	腹痛	23	34	12	RELATED	MODERATE	No	DW	RESOLVED
220* F/4[redacted] WHITE	潮紅	1	82	82	POSSIBLY	MILD	No	DW	RESOLVED
	腹部膨満	12	83	72	POSSIBLY	MILD	No	DW	RESOLVED

(a) #=On or after the subject switched to alternate MS medication
(b) ^=Adverse Event with onset prior to dosing
Abbreviations: Res=Resolution, NR=Not Recovered/Not Resolved, Dur=Duration, NONE=Dose Not Changed, DW=Drug Withdrawn, DI=Drug Interrupted, DR=Dose Reduced, M=Male, F=Female

SOURCE: BG12MS/JAPAN/ISS/L-AE-DISCON-301.SAS

DATE: 02DEC2015

Listing of adverse events that led to discontinuation of study drug:
Study 109MS301
Page 38 of 53
Treatment group: BG00012 240 mg TID

Subject Sex/Age Race	MedDRA Preferred Term	Study Day Onset (a) (b)	Res	Dur (days)	Relationship to Study Drug	Severity	Serious	Action Taken with Study Drug	Outcome
221* F/4[redacted] BLACK OR AFRICAN AMERICAN	嘔吐	10	29	20	RELATED	MILD	No	DW	RESOLVED
222* F/3[redacted] WHITE	うっ血性心不全	477	668	192	UNLIKELY	SEVERE	Yes	DW	RESOLVED
	心筋症	478	NR		UNLIKELY	MODERATE	No	DW	NOT RESOLVED
223* F/4[redacted] WHITE	肝機能検査異常	362	408	47	RELATED	MODERATE	No	DW	RESOLVED

(a) #=On or after the subject switched to alternate MS medication
(b) ^=Adverse Event with onset prior to dosing
Abbreviations: Res=Resolution, NR=Not Recovered/Not Resolved, Dur=Duration, NONE=Dose Not Changed, DW=Drug Withdrawn, DI=Drug Interrupted, DR=Dose Reduced, M=Male, F=Female

SOURCE: BG12MS/JAPAN/ISS/L-AE-DISCON-301.SAS

DATE: 02DEC2015

＊新薬承認情報提供時に置換えた

Listing of adverse events that led to discontinuation of study drug:
Study 109MS301
Page 39 of 53
Treatment group: BG00012 240 mg TID

Subject Sex/Age Race	MedDRA Preferred Term	Study Day Onset (a) (b)	Res	Dur (days)	Relationship to Study Drug	Severity	Serious	Action Taken with Study Drug	Outcome
224* F/3[redacted] WHITE	多発性硬化症再発	43			UNRELATED	MODERATE	No	DW	RESOLVED
225* F/4[redacted] WHITE	肝障害	29	65	37	POSSIBLY	MODERATE	No	DW	RESOLVED
226* M/4[redacted] WHITE	腹痛	12	53	42	RELATED	MODERATE	No	DW	RESOLVED
	下痢	12	53	42	RELATED	MODERATE	No	DW	RESOLVED
227* F/5[redacted] WHITE	腹痛	11	NR		POSSIBLY	MILD	No	DW	NOT RESOLVED

(a) #=On or after the subject switched to alternate MS medication
(b) ^=Adverse Event with onset prior to dosing
Abbreviations: Res=Resolution, NR=Not Recovered/Not Resolved, Dur=Duration, NONE=Dose Not Changed, DW=Drug Withdrawn, DI=Drug Interrupted, DR=Dose Reduced, M=Male, F=Female

SOURCE: BG12MS/JAPAN/ISS/L-AE-DISCON-301.SAS

DATE: 02DEC2015

＊新薬承認情報提供時に置換えた

Listing of adverse events that led to discontinuation of study drug:
Study 109MS301
Page 40 of 53
Treatment group: BG00012 240 mg TID

Subject Sex/Age Race	MedDRA Preferred Term	Study Day Onset (a) (b)	Res	Dur (days)	Relationship to Study Drug	Severity	Serious	Action Taken with Study Drug	Outcome
228* F/4[redacted] WHITE	耳鳴	3	5	3	POSSIBLY	MILD	No	DW	RESOLVED
	下痢	5	5	1	RELATED	MILD	No	DW	RESOLVED
	悪心	5	5	1	RELATED	MODERATE	No	DW	RESOLVED
	膣出血	5	5	1	UNLIKELY	MILD	No	DW	RESOLVED
	回転性めまい	5	5	1	POSSIBLY	MODERATE	No	DW	RESOLVED
	嘔吐	5	5	1	RELATED	MODERATE	No	DW	RESOLVED
229* F/4[redacted] WHITE	鼓腸	1	20	20	RELATED	MODERATE	No	DW	RESOLVED
	腹痛	11	20	10	RELATED	SEVERE	No	DW	RESOLVED
	悪心	11	15	5	RELATED	MODERATE	No	DW	RESOLVED

(a) #=On or after the subject switched to alternate MS medication
(b) ^=Adverse Event with onset prior to dosing
Abbreviations: Res=Resolution, NR=Not Recovered/Not Resolved, Dur=Duration, NONE=Dose Not Changed, DW=Drug Withdrawn, DI=Drug Interrupted, DR=Dose Reduced, M=Male, F=Female

SOURCE: BG12MS/JAPAN/ISS/L-AE-DISCON-301.SAS

DATE: 02DEC2015

＊新薬承認情報提供時に置換えた

Listing of adverse events that led to discontinuation of study drug:
Study 109MS301
Page 41 of 53
Treatment group: BG00012 240 mg TID

Subject Sex/Age Race	MedDRA Preferred Term	Study Day Onset (a) (b)	Res	Dur (days)	Relationship to Study Drug	Severity	Serious	Action Taken with Study Drug	Outcome
230* F/4[redacted] WHITE	上腹部痛	22	26	5	RELATED	SEVERE	No	DW	RESOLVED
	上腹部痛	22	26	5	RELATED	SEVERE	No	DW	RESOLVED
	悪心	22	26	5	RELATED	SEVERE	No	DW	RESOLVED
231* F/2[redacted] PATIENT IS MIXED, BLACK AND WHITE.	上腹部痛	67	68	2	RELATED	SEVERE	No	DW	RESOLVED
232* F/4[redacted] HISPANIC	潮紅	152	152	1	POSSIBLY	SEVERE	Yes	DW	RESOLVED
	そう痒症	152	152	1	POSSIBLY	SEVERE	Yes	DW	RESOLVED

(a) #=On or after the subject switched to alternate MS medication
(b) ^=Adverse Event with onset prior to dosing
Abbreviations: Res=Resolution, NR=Not Recovered/Not Resolved, Dur=Duration, NONE=Dose Not Changed, DW=Drug Withdrawn, DI=Drug Interrupted, DR=Dose Reduced, M=Male, F=Female

SOURCE: BG12MS/JAPAN/ISS/L-AE-DISCON-301.SAS

DATE: 02DEC2015

＊新薬承認情報提供時に置換えた

Listing of adverse events that led to discontinuation of study drug:
Study 109MS301
Page 42 of 53
Treatment group: BG00012 240 mg TID

Subject Sex/Age Race	MedDRA Preferred Term	Study Day Onset (a) (b)	Res	Dur (days)	Relationship to Study Drug	Severity	Serious	Action Taken with Study Drug	Outcome
233* F/3[redacted] WHITE	アナフィラキシー様反応	13	16	4	RELATED	SEVERE	Yes	DW	RESOLVED
234* F/4[redacted] WHITE	潮紅	113	116	4	POSSIBLY	MODERATE	No	DW	RESOLVED
235* M/4[redacted] WHITE	虚血性脳卒中	139	140	2	UNLIKELY	SEVERE	Yes	DW	RESOLVED
236* F/4[redacted] ASIAN	急性冠動脈症候群	174	192	19	UNLIKELY	SEVERE	Yes	DW	RESOLVED

(a) #=On or after the subject switched to alternate MS medication
(b) ^=Adverse Event with onset prior to dosing
Abbreviations: Res=Resolution, NR=Not Recovered/Not Resolved, Dur=Duration, NONE=Dose Not Changed, DW=Drug Withdrawn, DI=Drug Interrupted, DR=Dose Reduced, M=Male, F=Female

SOURCE: BG12MS/JAPAN/ISS/L-AE-DISCON-301.SAS

DATE: 02DEC2015

＊新薬承認情報提供時に置換えた

Listing of adverse events that led to discontinuation of study drug:
Study 109MS301
Page 43 of 53
Treatment group: BG00012 240 mg TID

Subject Sex/Age Race	MedDRA Preferred Term	Study Day Onset (a) (b)	Res	Dur (days)	Relationship to Study Drug	Severity	Serious	Action Taken with Study Drug	Outcome
237* M/5[redacted] ASIAN	多発性硬化症再発	504	507	4	UNRELATED	MODERATE	Yes	DW	RESOLVED
	二次性進行型多発性硬化症	588	NR		UNRELATED	MODERATE	No	DW	NOT RESOLVED
238* F/3[redacted] ASIAN	多発性硬化症再発	334	335	2	UNRELATED	SEVERE	No	DW	RESOLVED
239* F/4[redacted] ASIAN	腎機能障害	222	NR		POSSIBLY	MODERATE	No	DW	NOT RESOLVED
240* F/2[redacted] WHITE	尿中蛋白陽性	21	80	60	RELATED	SEVERE	No	DW	RESOLVED

(a) #=On or after the subject switched to alternate MS medication
(b) ^=Adverse Event with onset prior to dosing
Abbreviations: Res=Resolution, NR=Not Recovered/Not Resolved, Dur=Duration, NONE=Dose Not Changed, DW=Drug Withdrawn, DI=Drug Interrupted, DR=Dose Reduced, M=Male, F=Female

SOURCE: BG12MS/JAPAN/ISS/L-AE-DISCON-301.SAS

DATE: 02DEC2015

＊新薬承認情報提供時に置換えた

Listing of adverse events that led to discontinuation of study drug:
Study 109MS301
Page 44 of 53
Treatment group: BG00012 240 mg TID

Subject Sex/Age Race	MedDRA Preferred Term	Study Day Onset (a) (b)	Res	Dur (days)	Relationship to Study Drug	Severity	Serious	Action Taken with Study Drug	Outcome
240* F/2[redacted] WHITE	腹部不快感	56			RELATED	MODERATE	No	DW	RESOLVED
	下痢	56			RELATED	MODERATE	No	DW	RESOLVED
	潮紅	56			RELATED	MODERATE	No	DW	RESOLVED
241* F/4[redacted] WHITE	下痢	15	18	4	RELATED	SEVERE	No	DW	RESOLVED
	嘔吐	15	18	4	RELATED	SEVERE	No	DW	RESOLVED
	灼熱感	21	21	1	RELATED	SEVERE	No	DW	RESOLVED
	発熱	21	21	1	RELATED	MODERATE	No	DW	RESOLVED
242* F/5[redacted] WHITE	多発性硬化症再発	343	376	34	UNRELATED	MODERATE	Yes	DW	RESOLVED

(a) #=On or after the subject switched to alternate MS medication
(b) ^=Adverse Event with onset prior to dosing
Abbreviations: Res=Resolution, NR=Not Recovered/Not Resolved, Dur=Duration, NONE=Dose Not Changed, DW=Drug Withdrawn, DI=Drug Interrupted, DR=Dose Reduced, M=Male, F=Female

SOURCE: BG12MS/JAPAN/ISS/L-AE-DISCON-301.SAS

DATE: 02DEC2015

＊新薬承認情報提供時に置換えた

Listing of adverse events that led to discontinuation of study drug:
Study 109MS301
Page 45 of 53
Treatment group: BG00012 240 mg TID

Subject Sex/Age Race	MedDRA Preferred Term	Study Day Onset (a) (b)	Res	Dur (days)	Relationship to Study Drug	Severity	Serious	Action Taken with Study Drug	Outcome
243* F/2[redacted] WHITE	上腹部痛	13	21	9	RELATED	SEVERE	No	DW	RESOLVED
244* F/4[redacted] WHITE	アラニン・アミノトランスフェラーゼ増加	335	372	38	POSSIBLY	MODERATE	No	DW	RESOLVED
	アスパラギン酸アミノトランスフェラーゼ増加	372	448	77	POSSIBLY	SEVERE	No	DW	RESOLVED
245* F/4[redacted] WHITE	過敏症	1	1	1	POSSIBLY	SEVERE	No	DW	RESOLVED

(a) #=On or after the subject switched to alternate MS medication
(b) ^=Adverse Event with onset prior to dosing
Abbreviations: Res=Resolution, NR=Not Recovered/Not Resolved, Dur=Duration, NONE=Dose Not Changed, DW=Drug Withdrawn, DI=Drug Interrupted, DR=Dose Reduced, M=Male, F=Female

SOURCE: BG12MS/JAPAN/ISS/L-AE-DISCON-301.SAS

DATE: 02DEC2015

＊新薬承認情報提供時に置換えた

Listing of adverse events that led to discontinuation of study drug:
Study 109MS301
Page 46 of 53
Treatment group: BG00012 240 mg TID

Subject Sex/Age Race	MedDRA Preferred Term	Study Day Onset (a) (b)	Res	Dur (days)	Relationship to Study Drug	Severity	Serious	Action Taken with Study Drug	Outcome
246* F/5[redacted] WHITE	咳嗽	1	114	114	RELATED	MODERATE	No	DW	RESOLVED
247* F/4[redacted] WHITE	乳癌	462	468	7	UNLIKELY	MODERATE	No	DW	RESOLVED
	乳癌	468	476	9	UNLIKELY	MODERATE	Yes	DW	RESOLVED
248* M/4[redacted] WHITE	腹痛	2	NR		POSSIBLY	MODERATE	No	DW	NOT RESOLVED
	蟻走感	2	4	3	POSSIBLY	MODERATE	No	DW	RESOLVED
	多汗症	2	4	3	POSSIBLY	MODERATE	No	DW	RESOLVED

(a) #=On or after the subject switched to alternate MS medication
(b) ^=Adverse Event with onset prior to dosing
Abbreviations: Res=Resolution, NR=Not Recovered/Not Resolved, Dur=Duration, NONE=Dose Not Changed, DW=Drug Withdrawn, DI=Drug Interrupted, DR=Dose Reduced, M=Male, F=Female

SOURCE: BG12MS/JAPAN/ISS/L-AE-DISCON-301.SAS

DATE: 02DEC2015

＊新薬承認情報提供時に置換えた

Listing of adverse events that led to discontinuation of study drug:
Study 109MS301
Page 47 of 53
Treatment group: BG00012 240 mg TID

Subject Sex/Age Race	MedDRA Preferred Term	Study Day Onset (a) (b)	Res	Dur (days)	Relationship to Study Drug	Severity	Serious	Action Taken with Study Drug	Outcome
249* M/5[redacted] WHITE	全身紅斑	155	155	1	RELATED	SEVERE	No	DW	RESOLVED
250* M/4[redacted] WHITE	腎臓痛	2	6	5	POSSIBLY	MODERATE	No	DW	RESOLVED
251* M/3[redacted] WHITE	アレルギー性皮膚炎	257	273	17	POSSIBLY	MODERATE	No	DW	RESOLVED
252* F/5[redacted] WHITE	アラニン・アミノトランスフェラーゼ増加	29	47	19	RELATED	MODERATE	No	DW	RESOLVED

(a) #=On or after the subject switched to alternate MS medication
(b) ^=Adverse Event with onset prior to dosing
Abbreviations: Res=Resolution, NR=Not Recovered/Not Resolved, Dur=Duration, NONE=Dose Not Changed, DW=Drug Withdrawn, DI=Drug Interrupted, DR=Dose Reduced, M=Male, F=Female

SOURCE: BG12MS/JAPAN/ISS/L-AE-DISCON-301.SAS

DATE: 02DEC2015

＊新薬承認情報提供時に置換えた

Listing of adverse events that led to discontinuation of study drug:
Study 109MS301
Page 48 of 53
Treatment group: BG00012 240 mg TID

Subject Sex/Age Race	MedDRA Preferred Term	Study Day Onset (a) (b)	Res	Dur (days)	Relationship to Study Drug	Severity	Serious	Action Taken with Study Drug	Outcome
253* F/5[redacted] WHITE	潮紅	1	4	4	RELATED	MODERATE	No	DW	RESOLVED
254* F/4[redacted] WHITE	多発性硬化症再発	209	225	17	UNRELATED	MILD	No	DW	RESOLVED
255* M/2[redacted] WHITE	肝機能検査異常	309	NR		POSSIBLY	MODERATE	No	DW	NOT RESOLVED
256* F/2[redacted] WHITE	多発性硬化症再発	476	483	8	UNRELATED	MILD	No	DW	RESOLVED

(a) #=On or after the subject switched to alternate MS medication
(b) ^=Adverse Event with onset prior to dosing
Abbreviations: Res=Resolution, NR=Not Recovered/Not Resolved, Dur=Duration, NONE=Dose Not Changed, DW=Drug Withdrawn, DI=Drug Interrupted, DR=Dose Reduced, M=Male, F=Female

SOURCE: BG12MS/JAPAN/ISS/L-AE-DISCON-301.SAS

DATE: 02DEC2015

＊新薬承認情報提供時に置換えた

Listing of adverse events that led to discontinuation of study drug:
Study 109MS301
Page 49 of 53
Treatment group: BG00012 240 mg TID

Subject Sex/Age Race	MedDRA Preferred Term	Study Day Onset (a) (b)	Res	Dur (days)	Relationship to Study Drug	Severity	Serious	Action Taken with Study Drug	Outcome
256* F/3[redacted] WHITE	過敏症	2	34	33	RELATED	MODERATE	No	DW	RESOLVED
257* F/2[redacted] WHITE	アレルギー性皮膚炎	2	4	3	RELATED	MODERATE	No	DW	RESOLVED
258* M/3[redacted] WHITE	多発性硬化症再発	155	168	14	UNLIKELY	MODERATE	No	DW	RESOLVED
259* F/4[redacted] WHITE	関節痛	259	349	91	POSSIBLY	MODERATE	No	DW	RESOLVED

(a) #=On or after the subject switched to alternate MS medication
(b) ^=Adverse Event with onset prior to dosing
Abbreviations: Res=Resolution, NR=Not Recovered/Not Resolved, Dur=Duration, NONE=Dose Not Changed, DW=Drug Withdrawn, DI=Drug Interrupted, DR=Dose Reduced, M=Male, F=Female

SOURCE: BG12MS/JAPAN/ISS/L-AE-DISCON-301.SAS

DATE: 02DEC2015

＊新薬承認情報提供時に置換えた

Listing of adverse events that led to discontinuation of study drug:
Study 109MS301
Page 50 of 53
Treatment group: BG00012 240 mg TID

Subject Sex/Age Race	MedDRA Preferred Term	Study Day Onset (a) (b)	Res	Dur (days)	Relationship to Study Drug	Severity	Serious	Action Taken with Study Drug	Outcome
800* F/4[redacted] HISPANIC	高血糖	3	NR		UNLIKELY	MODERATE	No	DW	NOT RESOLVED
261* F/3[redacted]	アレルギー性皮膚炎	1	1	1	RELATED	MILD	No	DW	RESOLVED
262* F/4[redacted]	紅斑	71	139		RELATED	MODERATE	No	DW	RESOLVED
	皮膚灼熱感	71	139		RELATED	MODERATE	No	DW	RESOLVED
263* F/3[redacted]	胃炎	8	18	11	POSSIBLY	MODERATE	No	DW	RESOLVED
	胃炎	18	NR		POSSIBLY	MODERATE	Yes	DW	NOT RESOLVED
264* F/3[redacted]	潮紅	1	3	3	RELATED	MODERATE	No	DW	RESOLVED

(a) #=On or after the subject switched to alternate MS medication
(b) ^=Adverse Event with onset prior to dosing
Abbreviations: Res=Resolution, NR=Not Recovered/Not Resolved, Dur=Duration, NONE=Dose Not Changed, DW=Drug Withdrawn, DI=Drug Interrupted, DR=Dose Reduced, M=Male, F=Female

SOURCE: BG12MS/JAPAN/ISS/L-AE-DISCON-301.SAS

DATE: 02DEC2015

＊新薬承認情報提供時に置換えた

Listing of adverse events that led to discontinuation of study drug:
Study 109MS301
Page 51 of 53
Treatment group: BG00012 240 mg TID

Subject Sex/Age Race	MedDRA Preferred Term	Study Day Onset (a) (b)	Res	Dur (days)	Relationship to Study Drug	Severity	Serious	Action Taken with Study Drug	Outcome
265* F/4[redacted] WHITE	下痢	9	29	21	RELATED	MODERATE	No	DW	RESOLVED
	悪心	9	29	21	RELATED	MODERATE	No	DW	RESOLVED
	上腹部痛	10	29	20	RELATED	MODERATE	No	DW	RESOLVED
266* F/4[redacted] ARABIC	上腹部痛	2	23	22	POSSIBLY	MODERATE	No	DW	RESOLVED
	嘔吐	10	23	14	POSSIBLY	MODERATE	No	DW	RESOLVED
269* F/4[redacted] WHITE	下痢	15	48	34	POSSIBLY	MILD	No	DW	RESOLVED

(a) #=On or after the subject switched to alternate MS medication
(b) ^=Adverse Event with onset prior to dosing
Abbreviations: Res=Resolution, NR=Not Recovered/Not Resolved, Dur=Duration, NONE=Dose Not Changed, DW=Drug Withdrawn, DI=Drug Interrupted, DR=Dose Reduced, M=Male, F=Female

SOURCE: BG12MS/JAPAN/ISS/L-AE-DISCON-301.SAS

DATE: 02DEC2015

＊新薬承認情報提供時に置換えた

Listing of adverse events that led to discontinuation of study drug:
Study 109MS301
Page 52 of 53
Treatment group: BG00012 240 mg TID

Subject Sex/Age Race	MedDRA Preferred Term	Study Day Onset (a) (b)	Res	Dur (days)	Relationship to Study Drug	Severity	Serious	Action Taken with Study Drug	Outcome
270* F/4[redacted] WHITE	頭痛	13	14	2	POSSIBLY	SEVERE	No	DW	RESOLVED
271* F/3[redacted] WHITE	灼熱感	392	392	1	POSSIBLY	MODERATE	No	DW	RESOLVED
	過敏症	392	392	1	POSSIBLY	MODERATE	No	DW	RESOLVED
272* M/5[redacted] WHITE	過敏症	29	85	57	RELATED	MODERATE	Yes	DW	RESOLVED

(a) #=On or after the subject switched to alternate MS medication
(b) ^=Adverse Event with onset prior to dosing
Abbreviations: Res=Resolution, NR=Not Recovered/Not Resolved, Dur=Duration, NONE=Dose Not Changed, DW=Drug Withdrawn, DI=Drug Interrupted, DR=Dose Reduced, M=Male, F=Female

SOURCE: BG12MS/JAPAN/ISS/L-AE-DISCON-301.SAS

DATE: 02DEC2015

＊新薬承認情報提供時に置換えた

Listing of adverse events that led to discontinuation of study drug:
Study 109MS301
Page 53 of 53
Treatment group: BG00012 240 mg TID

Subject Sex/Age Race	MedDRA Preferred Term	Study Day Onset (a) (b)	Res	Dur (days)	Relationship to Study Drug	Severity	Serious	Action Taken with Study Drug	Outcome
273* F/3[redacted] MIXED SOUTH AFRICAN	多発性硬化症再発	420	424	5	UNRELATED	SEVERE	No	DW	RESOLVED
	多発性硬化症再発	424	588	165	UNRELATED	SEVERE	Yes	DW	RESOLVED
	嘔吐	424	588	165	UNRELATED	SEVERE	Yes	DW	RESOLVED
274* M/3[redacted] WHITE	多発性硬化症	419	700	282	UNLIKELY	MILD	No	DW	RESOLVED
275* F/4[redacted] WHITE	多発性硬化症再発	450	455	6	UNRELATED	MODERATE	Yes	DW	RESOLVED

(a) #=On or after the subject switched to alternate MS medication
(b) ^=Adverse Event with onset prior to dosing
Abbreviations: Res=Resolution, NR=Not Recovered/Not Resolved, Dur=Duration, NONE=Dose Not Changed, DW=Drug Withdrawn, DI=Drug Interrupted, DR=Dose Reduced, M=Male, F=Female

SOURCE: BG12MS/JAPAN/ISS/L-AE-DISCON-301.SAS

DATE: 02DEC2015

＊新薬承認情報提供時に置換えた

Table 308: Listing of Adverse Events That Led to Discontinuation of Study Drug: Study 109MS302

Listing of adverse events that led to discontinuation of study drug:
Study 109MS302
Page 1 of 48
Treatment group: Placebo

Subject Sex/Age Race	MedDRA Preferred Term	Study Day Onset (a) (b)	Study Day Res	Dur (days)	Relationship to Study Drug	Severity	Serious	Action Taken With Study Drug	Outcome
056* F/4[redacted] ASIAN	大発作痙攣	297	301	5	POSSIBLY	MODERATE	Yes	DW	RESOLVED
057* M/5[redacted] ASIAN	発疹	5	66	62	RELATED	SEVERE	No	DW	RESOLVED
058* M/2[redacted] ASIAN	多発性硬化症再発	368#	370	3	UNRELATED	MODERATE	No	DW	RESOLVED
059* F/3[redacted] ASIAN	多発性硬化症再発	322	441	120	UNRELATED	MODERATE	No	DW	RESOLVED

(a) #=On or after the subject switched to alternate MS medication
(b) ^=Adverse Event with onset prior to dosing
Abbreviations: Res=Resolution, NR=Not Recovered/Not Resolved, Dur=Duration, NONE=Dose Not Changed, DW=Drug Withdrawn, DI=Drug Interrupted, DR=Dose Reduced, M=Male, F=Female

SOURCE: BG12MS/JAPAN/ISS/L-AE-DISCON-302.SAS DATE: 02DEC2015

＊新薬承認情報提供時に置換えた

Listing of adverse events that led to discontinuation of study drug:
Study 109MS302
Page 2 of 48
Treatment group: Placebo

Subject Sex/Age Race	MedDRA Preferred Term	Study Day Onset (a) (b)	Study Day Res	Dur (days)	Relationship to Study Drug	Severity	Serious	Action Taken With Study Drug	Outcome
060* M/3[redacted] ASIAN	多発性硬化症再発	633	673	41	UNRELATED	MILD	No	DW	RESOLVED
061* M/4[redacted] WHITE	多発性硬化症再発	162	187	26	UNRELATED	MODERATE	No	DW	RESOLVED
062* F/2[redacted] WHITE	心電図ＰＲ延長	162	214	53	POSSIBLY	MODERATE	No	DW	RESOLVED
063* F/4[redacted] WHITE	多発性硬化症再発	256	262	7	UNRELATED	MODERATE	No	DW	RESOLVED

(a) #=On or after the subject switched to alternate MS medication
(b) ^=Adverse Event with onset prior to dosing
Abbreviations: Res=Resolution, NR=Not Recovered/Not Resolved, Dur=Duration, NONE=Dose Not Changed, DW=Drug Withdrawn, DI=Drug Interrupted, DR=Dose Reduced, M=Male, F=Female

SOURCE: BG12MS/JAPAN/ISS/L-AE-DISCON-302.SAS DATE: 02DEC2015

＊新薬承認情報提供時に置換えた

Listing of adverse events that led to discontinuation of study drug:
Study 109MS302
Page 3 of 48
Treatment group: Placebo

Subject Sex/Age Race	MedDRA Preferred Term	Study Day Onset (a) (b)	Study Day Res	Dur (days)	Relationship to Study Drug	Severity	Serious	Action Taken With Study Drug	Outcome
064* F/3[redacted] BLACK OR AFRICAN AMERICAN	肝酵素上昇	226	261	36	POSSIBLY	SEVERE	Yes	DW	RESOLVED
065* F/4[redacted] WHITE	多発性硬化症再発	292	300	9	UNRELATED	MODERATE	No	DW	RESOLVED
066* F/3[redacted] WHITE	性的興奮障害	1	NR		POSSIBLY	MILD	No	DW	NOT RESOLVED
067* F/2[redacted] WHITE	肝酵素上昇	209	NR		POSSIBLY	MODERATE	No	DW	NOT RESOLVED

(a) #=On or after the subject switched to alternate MS medication
(b) ^=Adverse Event with onset prior to dosing
Abbreviations: Res=Resolution, NR=Not Recovered/Not Resolved, Dur=Duration, NONE=Dose Not Changed, DW=Drug Withdrawn, DI=Drug Interrupted, DR=Dose Reduced, M=Male, F=Female

SOURCE: BG12MS/JAPAN/ISS/L-AE-DISCON-302.SAS DATE: 02DEC2015

＊新薬承認情報提供時に置換えた

Listing of adverse events that led to discontinuation of study drug:
Study 109MS302
Page 4 of 48
Treatment group: Placebo

Subject Sex/Age Race	MedDRA Preferred Term	Study Day Onset (a) (b)	Study Day Res	Dur (days)	Relationship to Study Drug	Severity	Serious	Action Taken With Study Drug	Outcome
068* F/2[redacted] WHITE	トランスアミナーゼ上昇	1	81	81	UNLIKELY	SEVERE	No	DW	RESOLVED
069* F/5[redacted] WHITE	消化不良	188	206	19	RELATED	MODERATE	No	DW	RESOLVED
070* F/3[redacted] WHITE	アラニン・アミノトランスフェラーゼ増加	183	253	71	POSSIBLY	MODERATE	No	DW	RESOLVED
071* M/3[redacted] WHITE	アラニン・アミノトランスフェラーゼ増加	427	486	60	POSSIBLY	MODERATE	No	DW	RESOLVED

(a) #=On or after the subject switched to alternate MS medication
(b) ^=Adverse Event with onset prior to dosing
Abbreviations: Res=Resolution, NR=Not Recovered/Not Resolved, Dur=Duration, NONE=Dose Not Changed, DW=Drug Withdrawn, DI=Drug Interrupted, DR=Dose Reduced, M=Male, F=Female

SOURCE: BG12MS/JAPAN/ISS/L-AE-DISCON-302.SAS DATE: 02DEC2015

＊新薬承認情報提供時に置換えた

Listing of adverse events that led to discontinuation of study drug:
Study 109MS302
Page 5 of 48
Treatment group: Placebo

Subject Sex/Age Race	MedDRA Preferred Term	Study Day Onset (a) (b)	Study Day Res	Dur (days)	Relationship to Study Drug	Severity	Serious	Action Taken With Study Drug	Outcome
071* M/3[redacted] WHITE	アスパラギン酸アミノトランスフェラーゼ増加	427	486	60	POSSIBLY	MODERATE	No	DW	RESOLVED
072* M/4[redacted] WHITE	多発性硬化症再発	139	237	99	UNRELATED	MODERATE	No	DW	RESOLVED
073* F/4[redacted] WHITE	多発性硬化症再発	110	151	42	UNLIKELY	MODERATE	No	DW	RESOLVED
074* F/5[redacted] WHITE	蛋白尿	59	250	192	POSSIBLY	MODERATE	No	DW	RESOLVED

(a) #=On or after the subject switched to alternate MS medication
(b) ^=Adverse Event with onset prior to dosing
Abbreviations: Res=Resolution, NR=Not Recovered/Not Resolved, Dur=Duration, NONE=Dose Not Changed, DW=Drug Withdrawn, DI=Drug Interrupted, DR=Dose Reduced, M=Male, F=Female

SOURCE: BG12MS/JAPAN/ISS/L-AE-DISCON-302.SAS DATE: 02DEC2015

＊新薬承認情報提供時に置換えた

Listing of adverse events that led to discontinuation of study drug:
Study 109MS302
Page 6 of 48
Treatment group: Placebo

Subject Sex/Age Race	MedDRA Preferred Term	Study Day Onset (a) (b)	Study Day Res	Dur (days)	Relationship to Study Drug	Severity	Serious	Action Taken With Study Drug	Outcome
075* F/4[redacted] WHITE	多発性硬化症再発	256	289	34	POSSIBLY	MILD	No	DW	RESOLVED
076* F/5[redacted] WHITE	肝酵素上昇	564	NR		UNLIKELY	MILD	No	DW	NOT RESOLVED
077* F/4[redacted] WHITE	細菌性心内膜炎	57	117	61	POSSIBLY	SEVERE	Yes	DW	RESOLVED
078* M/3[redacted] WHITE	アラニン・アミノトランスフェラーゼ増加	589	NR		POSSIBLY	MODERATE	No	DW	NOT RESOLVED

(a) #=On or after the subject switched to alternate MS medication
(b) ^=Adverse Event with onset prior to dosing
Abbreviations: Res=Resolution, NR=Not Recovered/Not Resolved, Dur=Duration, NONE=Dose Not Changed, DW=Drug Withdrawn, DI=Drug Interrupted, DR=Dose Reduced, M=Male, F=Female

SOURCE: BG12MS/JAPAN/ISS/L-AE-DISCON-302.SAS DATE: 02DEC2015

＊新薬承認情報提供時に置換えた

Listing of adverse events that led to discontinuation of study drug:
Study 109MS302
Page 7 of 48
Treatment group: Placebo

Subject Sex/Age Race	MedDRA Preferred Term	Study Day Onset (a) (b)	Study Day Res	Dur (days)	Relationship to Study Drug	Severity	Serious	Action Taken With Study Drug	Outcome
079* M/2[redacted] WHITE	視力低下	341	NR		POSSIBLY	MODERATE	No	DW	NOT RESOLVED
080* F/3[redacted] WHITE	乳房新生物	352			UNLIKELY	MODERATE	Yes	DW	RESOLVED
081* F/2[redacted] WHITE	多発性硬化症再発	339	341	3	UNRELATED	MODERATE	No	DW	RESOLVED
082* M/3[redacted] WHITE	多発性硬化症再発	367	368	2	UNLIKELY	MODERATE	No	DW	RESOLVED

(a) #=On or after the subject switched to alternate MS medication
(b) ^=Adverse Event with onset prior to dosing
Abbreviations: Res=Resolution, NR=Not Recovered/Not Resolved, Dur=Duration, NONE=Dose Not Changed, DW=Drug Withdrawn, DI=Drug Interrupted, DR=Dose Reduced, M=Male, F=Female

SOURCE: BG12MS/JAPAN/ISS/L-AE-DISCON-302.SAS DATE: 02DEC2015

＊新薬承認情報提供時に置換えた

Listing of adverse events that led to discontinuation of study drug:
Study 109MS302
Page 8 of 48
Treatment group: Placebo

Subject Sex/Age Race	MedDRA Preferred Term	Study Day Onset (a) (b)	Study Day Res	Dur (days)	Relationship to Study Drug	Severity	Serious	Action Taken With Study Drug	Outcome
083* F/4[redacted] WHITE	多発性硬化症再発	277	280	4	UNLIKELY	MODERATE	No	DW	RESOLVED
084* F/4[redacted] WHITE	食欲亢進	35	NR		UNLIKELY	MILD	No	DW	NOT RESOLVED
085* M/3[redacted]	多発性硬化症再発	215	NR		UNRELATED	MODERATE	No	DW	NOT RESOLVED
086* M/4[redacted] WHITE	多発性硬化症再発	80	105	26	UNRELATED	MODERATE	No	DW	RESOLVED

(a) #=On or after the subject switched to alternate MS medication
(b) ^=Adverse Event with onset prior to dosing
Abbreviations: Res=Resolution, NR=Not Recovered/Not Resolved, Dur=Duration, NONE=Dose Not Changed, DW=Drug Withdrawn, DI=Drug Interrupted, DR=Dose Reduced, M=Male, F=Female

SOURCE: BG12MS/JAPAN/ISS/L-AE-DISCON-302.SAS DATE: 02DEC2015

＊新薬承認情報提供時に置換えた

Listing of adverse events that led to discontinuation of study drug:
Study 109MS302
Page 9 of 48
Treatment group: Placebo

Subject Sex/Age Race	MedDRA Preferred Term	Study Day Onset (a) (b)	Study Day Res	Dur (days)	Relationship to Study Drug	Severity	Serious	Action Taken With Study Drug	Outcome
087* F/3[redacted] WHITE	多発性硬化症再発	62	NR		UNRELATED	MODERATE	No	DW	NOT RESOLVED
088* F/3[redacted] WHITE	アラニン・アミノトランスフェラーゼ増加	57	121	65	RELATED	MODERATE	No	DW	RESOLVED
	アスパラギン酸アミノトランスフェラーゼ増加	57	121	65	RELATED	MODERATE	No	DW	RESOLVED
089* F/4[redacted] WHITE	脳血管発作	117	NR		UNLIKELY	SEVERE	Yes	DW	NOT RESOLVED

(a) #=On or after the subject switched to alternate MS medication
(b) ^=Adverse Event with onset prior to dosing
Abbreviations: Res=Resolution, NR=Not Recovered/Not Resolved, Dur=Duration, NONE=Dose Not Changed, DW=Drug Withdrawn, DI=Drug Interrupted, DR=Dose Reduced, M=Male, F=Female

SOURCE: BG12MS/JAPAN/ISS/L-AE-DISCON-302.SAS DATE: 02DEC2015

＊新薬承認情報提供時に置換えた

Listing of adverse events that led to discontinuation of study drug:
Study 109MS302
Page 10 of 48
Treatment group: Placebo

Subject Sex/Age Race	MedDRA Preferred Term	Study Day Onset (a) (b)	Study Day Res	Dur (days)	Relationship to Study Drug	Severity	Serious	Action Taken With Study Drug	Outcome
090* F/4[redacted] WHITE	中毒性肝炎	476	533	58	RELATED	MODERATE	No	DW	RESOLVED
091* F/3[redacted] HISPANIC	多発性硬化症再発	492	533	42	UNRELATED	MODERATE	No	DW	RESOLVED
092* M/3[redacted] WHITE	多発性硬化症再発	181			UNRELATED	MODERATE	No	DW	RESOLVED
093* F/3[redacted] WHITE	肝障害	338	683	346	UNRELATED	MODERATE	No	DW	RESOLVED

(a) #=On or after the subject switched to alternate MS medication
(b) ^=Adverse Event with onset prior to dosing
Abbreviations: Res=Resolution, NR=Not Recovered/Not Resolved, Dur=Duration, NONE=Dose Not Changed, DW=Drug Withdrawn, DI=Drug Interrupted, DR=Dose Reduced, M=Male, F=Female

SOURCE: BG12MS/JAPAN/ISS/L-AE-DISCON-302.SAS DATE: 02DEC2015

＊新薬承認情報提供時に置換えた

Listing of adverse events that led to discontinuation of study drug:
Study 109MS302
Page 11 of 48
Treatment group: Placebo

Subject Sex/Age Race	MedDRA Preferred Term	Study Day Onset (a) (b)	Study Day Res	Dur (days)	Relationship to Study Drug	Severity	Serious	Action Taken With Study Drug	Outcome
094* F/3[redacted] WHITE	多発性硬化症再発	589	595	7	UNRELATED	SEVERE	Yes	DW	RESOLVED

(a) #=On or after the subject switched to alternate MS medication
(b) ^=Adverse Event with onset prior to dosing
Abbreviations: Res=Resolution, NR=Not Recovered/Not Resolved, Dur=Duration, NONE=Dose Not Changed, DW=Drug Withdrawn, DI=Drug Interrupted, DR=Dose Reduced, M=Male, F=Female

SOURCE: BG12MS/JAPAN/ISS/L-AE-DISCON-302.SAS DATE: 02DEC2015

＊新薬承認情報提供時に置換えた

Listing of adverse events that led to discontinuation of study drug:
Study 109MS302
Page 12 of 48
Treatment group: BG00012 240 mg BID

Subject Sex/Age Race	MedDRA Preferred Term	Study Day Onset (a) (b)	Study Day Res	Dur (days)	Relationship to Study Drug	Severity	Serious	Action Taken With Study Drug	Outcome
162* F/4[redacted] WHITE	潮紅	290	509	220	POSSIBLY	SEVERE	No	DW	RESOLVED
163* F/1[redacted] ASIAN	多発性硬化症再発	581	588	8	UNLIKELY	SEVERE	Yes	DW	RESOLVED
	部分発作	581	588	8	UNLIKELY	SEVERE	Yes	DW	RESOLVED
164* F/2[redacted] ASIAN	多発性硬化症	514	NR		UNLIKELY	MILD	No	DW	NOT RESOLVED
165* F/5[redacted] WHITE	下痢	2	NR		POSSIBLY	MODERATE	No	DW	NOT RESOLVED

(a) #=On or after the subject switched to alternate MS medication
(b) ^=Adverse Event with onset prior to dosing
Abbreviations: Res=Resolution, NR=Not Recovered/Not Resolved, Dur=Duration, NONE=Dose Not Changed, DW=Drug Withdrawn, DI=Drug Interrupted, DR=Dose Reduced, M=Male, F=Female

SOURCE: BG12MS/JAPAN/ISS/L-AE-DISCON-302.SAS DATE: 02DEC2015

＊新薬承認情報提供時に置換えた

Listing of adverse events that led to discontinuation of study drug:
Study 109MS302
Page 13 of 48
Treatment group: BG00012 240 mg BID

Subject Sex/Age Race	MedDRA Preferred Term	Study Day Onset (a) (b)	Study Day Res	Dur (days)	Relationship to Study Drug	Severity	Serious	Action Taken With Study Drug	Outcome
166* F/4[redacted] WHITE	腹部圧痛	337	393	57	POSSIBLY	MILD	No	DW	RESOLVED
167* F/4[redacted] WHITE	灼熱感	1	17	17	RELATED	MODERATE	No	DW	RESOLVED
	潮紅	1	17	17	RELATED	MODERATE	No	DW	RESOLVED
	全身性そう痒症	1	17	17	RELATED	MODERATE	No	DW	RESOLVED
	咳嗽	4	20	17	UNRELATED	MILD	No	DW	RESOLVED
168* F/3[redacted] WHITE	振戦	135	139	5	POSSIBLY	MODERATE	No	DW	RESOLVED
	蕁麻疹	135	139	5	POSSIBLY	MODERATE	No	DW	RESOLVED

(a) #=On or after the subject switched to alternate MS medication
(b) ^=Adverse Event with onset prior to dosing
Abbreviations: Res=Resolution, NR=Not Recovered/Not Resolved, Dur=Duration, NONE=Dose Not Changed, DW=Drug Withdrawn, DI=Drug Interrupted, DR=Dose Reduced, M=Male, F=Female

SOURCE: BG12MS/JAPAN/ISS/L-AE-DISCON-302.SAS DATE: 02DEC2015

＊新薬承認情報提供時に置換えた

Listing of adverse events that led to discontinuation of study drug:
Study 109MS302
Page 14 of 48
Treatment group: BG00012 240 mg BID

Subject Sex/Age Race	MedDRA Preferred Term	Study Day Onset (a) (b)	Study Day Res	Dur (days)	Relationship to Study Drug	Severity	Serious	Action Taken With Study Drug	Outcome
169* F/4[redacted] WHITE	腹痛	41	105	65	RELATED	SEVERE	No	DW	RESOLVED
170* F/4[redacted] WHITE	潮紅	8	24	17	RELATED	MODERATE	No	DW	RESOLVED
	そう痒症	8	24	17	RELATED	MODERATE	No	DW	RESOLVED
171* F/5[redacted] WHITE	高熱	1	182		RELATED	MILD	No	DW	RESOLVED
	蕁麻疹	1	182		RELATED	MODERATE	No	DW	RESOLVED
	ざ瘡様皮膚炎	1	182	182	RELATED	MODERATE	No	DW	RESOLVED
	潮紅	1	213	213	RELATED	MODERATE	No	DW	RESOLVED
	発疹	45	194	150	RELATED	MODERATE	No	DW	RESOLVED
	そう痒症	74	75	2	RELATED	MODERATE	No	DW	RESOLVED

(a) #=On or after the subject switched to alternate MS medication
(b) ^=Adverse Event with onset prior to dosing
Abbreviations: Res=Resolution, NR=Not Recovered/Not Resolved, Dur=Duration, NONE=Dose Not Changed, DW=Drug Withdrawn, DI=Drug Interrupted, DR=Dose Reduced, M=Male, F=Female

SOURCE: BG12MS/JAPAN/ISS/L-AE-DISCON-302.SAS DATE: 02DEC2015

＊新薬承認情報提供時に置換えた

Listing of adverse events that led to discontinuation of study drug:
Study 109MS302
Page 15 of 48
Treatment group: BG00012 240 mg BID

Subject Sex/Age Race	MedDRA Preferred Term	Study Day Onset (a) (b)	Study Day Res	Dur (days)	Relationship to Study Drug	Severity	Serious	Action Taken With Study Drug	Outcome
172* F/3[redacted] WHITE	潮紅	8	28	21	POSSIBLY	MODERATE	No	DW	RESOLVED
	頭痛	8	28	21	POSSIBLY	MODERATE	No	DW	RESOLVED
	四肢痛	8	28	21	POSSIBLY	MODERATE	No	DW	RESOLVED
	背部痛	18	29	12	POSSIBLY	MODERATE	No	DW	RESOLVED
	胸部不快感	18	29	12	POSSIBLY	MODERATE	No	DW	RESOLVED
173* F/3[redacted] HISPANIC	潮紅	1	12	12	RELATED	MODERATE	No	DW	RESOLVED
174* M/5[redacted] WHITE	浮動性めまい	70	83	14	UNLIKELY	MILD	No	DW	RESOLVED

(a) #=On or after the subject switched to alternate MS medication
(b) ^=Adverse Event with onset prior to dosing
Abbreviations: Res=Resolution, NR=Not Recovered/Not Resolved, Dur=Duration, NONE=Dose Not Changed, DW=Drug Withdrawn, DI=Drug Interrupted, DR=Dose Reduced, M=Male, F=Female

SOURCE: BG12MS/JAPAN/ISS/L-AE-DISCON-302.SAS DATE: 02DEC2015

＊新薬承認情報提供時に置換えた

Listing of adverse events that led to discontinuation of study drug:
Study 109MS302
Page 16 of 48
Treatment group: BG00012 240 mg BID

Subject Sex/Age Race	MedDRA Preferred Term	Study Day Onset (a) (b)	Study Day Res	Dur (days)	Relationship to Study Drug	Severity	Serious	Action Taken With Study Drug	Outcome
175* F/4[redacted] WHITE	多発性硬化症再発	161	281	121	UNLIKELY	MODERATE	No	DW	RESOLVED
176* M/2[redacted] WHITE	多発性硬化症再発	53			UNRELATED	MILD	No	DW	RESOLVED
177* F/4[redacted] WHITE	紅斑	1	4	4	RELATED	MODERATE	No	DW	RESOLVED
178* M/4[redacted] WHITE	多発性硬化症再発	516	525	10	UNLIKELY	MILD	No	DW	RESOLVED

(a) #=On or after the subject switched to alternate MS medication
(b) ^=Adverse Event with onset prior to dosing
Abbreviations: Res=Resolution, NR=Not Recovered/Not Resolved, Dur=Duration, NONE=Dose Not Changed, DW=Drug Withdrawn, DI=Drug Interrupted, DR=Dose Reduced, M=Male, F=Female

SOURCE: BG12MS/JAPAN/ISS/L-AE-DISCON-302.SAS DATE: 02DEC2015

＊新薬承認情報提供時に置換えた

Listing of adverse events that led to discontinuation of study drug:
Study 109MS302
Page 17 of 48
Treatment group: BG00012 240 mg BID

Subject Sex/Age Race	MedDRA Preferred Term	Study Day Onset (a) (b)	Study Day Res	Dur (days)	Relationship to Study Drug	Severity	Serious	Action Taken With Study Drug	Outcome
179* F/3[redacted] WHITE	アラニン・アミノトランスフェラーゼ増加	1	NR		UNRELATED	MODERATE	No	DW	NOT
	アスパラギン酸アミノトランスフェラーゼ増加	1	NR		UNRELATED	MODERATE	No	DW	NOT
180* F/3[redacted] WHITE	発疹	36	53	18	POSSIBLY	MODERATE	No	DW	RESOLVED
181* F/5[redacted] WHITE	肝酵素上昇	142	NR		POSSIBLY	MODERATE No	No	DW	NOT

(a) #=On or after the subject switched to alternate MS medication
(b) ^=Adverse Event with onset prior to dosing
Abbreviations: Res=Resolution, NR=Not Recovered/Not Resolved, Dur=Duration, NONE=Dose Not Changed, DW=Drug Withdrawn, DI=Drug Interrupted, DR=Dose Reduced, M=Male, F=Female

SOURCE: BG12MS/JAPAN/ISS/L-AE-DISCON-302.SAS DATE: 02DEC2015

＊新薬承認情報提供時に置換えた

Listing of adverse events that led to discontinuation of study drug:
Study 109MS302
Page 18 of 48
Treatment group: BG00012 240 mg BID

Subject Sex/Age Race	MedDRA Preferred Term	Study Day Onset (a) (b)	Study Day Res	Dur (days)	Relationship to Study Drug	Severity	Serious	Action Taken With Study Drug	Outcome
182* F/5[redacted] WHITE	多発性硬化症	97	207	111	UNLIKELY	MODERATE	No	DW	RESOLVED
183* F/4[redacted] WHITE	アラニン・アミノトランスフェラーゼ増加	277	NR		POSSIBLY	MODERATE	No	DW	NOT RESOLVED
	アスパラギン酸アミノトランスフェラーゼ増加	277	337	61	POSSIBLY	MODERATE	No	DW	RESOLVED
184* F/5[redacted] WHITE	潮紅	352	533		POSSIBLY	MILD	No	DW	RESOLVED

(a) #=On or after the subject switched to alternate MS medication
(b) ^=Adverse Event with onset prior to dosing
Abbreviations: Res=Resolution, NR=Not Recovered/Not Resolved, Dur=Duration, NONE=Dose Not Changed, DW=Drug Withdrawn, DI=Drug Interrupted, DR=Dose Reduced, M=Male, F=Female

SOURCE: BG12MS/JAPAN/ISS/L-AE-DISCON-302.SAS DATE: 02DEC2015

＊新薬承認情報提供時に置換えた

Listing of adverse events that led to discontinuation of study drug:
Study 109MS302
Page 19 of 48
Treatment group: BG00012 240 mg BID

Subject Sex/Age Race	MedDRA Preferred Term	Study Day Onset (a) (b)	Study Day Res	Dur (days)	Relationship to Study Drug	Severity	Serious	Action Taken With Study Drug	Outcome
185* F/3[redacted] WHITE	潮紅	394	476	83	POSSIBLY	MODERATE	No	DW	RESOLVED
186* F/3[redacted] WHITE	潮紅	29	70	42	RELATED	MILD	No	DW	RESOLVED
187* M/3[redacted] WHITE	潮紅	9			POSSIBLY	MODERATE	No	DW	RESOLVED
188* F/4[redacted] WHITE	上腹部痛	595	660	66	RELATED	MODERATE	No	DW	RESOLVED
	下痢	611	660	50	RELATED	MODERATE	No	DW	RESOLVED

(a) #=On or after the subject switched to alternate MS medication
(b) ^=Adverse Event with onset prior to dosing
Abbreviations: Res=Resolution, NR=Not Recovered/Not Resolved, Dur=Duration, NONE=Dose Not Changed, DW=Drug Withdrawn, DI=Drug Interrupted, DR=Dose Reduced, M=Male, F=Female

SOURCE: BG12MS/JAPAN/ISS/L-AE-DISCON-302.SAS DATE: 02DEC2015

＊新薬承認情報提供時に置換えた

Listing of adverse events that led to discontinuation of study drug:
Study 109MS302
Page 20 of 48
Treatment group: BG00012 240 mg BID

Subject Sex/Age Race	MedDRA Preferred Term	Study Day Onset (a) (b)	Study Day Res	Dur (days)	Relationship to Study Drug	Severity	Serious	Action Taken With Study Drug	Outcome
189* F/4[redacted] WHITE	潮紅	230	309	80	RELATED	SEVERE	No	DW	RESOLVED
190* M/2[redacted] WHITE	肝機能検査異常	57	NR		RELATED	MODERATE	No	DW	NOT RESOLVED
191* M/3[redacted] WHITE	アラニン･アミノトランスフェラーゼ増加	29	NR		UNLIKELY	MODERATE	No	DW	NOT RESOLVED
	アスパラギン酸アミノトランスフェラーゼ増加	29	NR		UNLIKELY	MODERATE	No	DW	NOT RESOLVED
	γ－グルタミルトランスフェラーゼ増加	56	NR		UNLIKELY	MODERATE	No	DW	NOT RESOLVED

(a) #=On or after the subject switched to alternate MS medication
(b) ^=Adverse Event with onset prior to dosing
Abbreviations: Res=Resolution, NR=Not Recovered/Not Resolved, Dur=Duration, NONE=Dose Not Changed, DW=Drug Withdrawn, DI=Drug Interrupted, DR=Dose Reduced, M=Male, F=Female

SOURCE: BG12MS/JAPAN/ISS/L-AE-DISCON-302.SAS DATE: 02DEC2015

＊新薬承認情報提供時に置換えた

Listing of adverse events that led to discontinuation of study drug:
Study 109MS302
Page 21 of 48
Treatment group: BG00012 240 mg BID

Subject Sex/Age Race	MedDRA Preferred Term	Study Day Onset (a) (b)	Study Day Res	Dur (days)	Relationship to Study Drug	Severity	Serious	Action Taken With Study Drug	Outcome
192* F/3[redacted] WHITE	血中乳酸脱水素酵素増加	593	671	79	POSSIBLY	SEVERE	No	DW	RESOLVED
193* F/2[redacted] WHITE	双極１型障害	637	NR		UNRELATED	SEVERE	Yes	DW	NOT RESOLVED
194* M/3[redacted]	多発性硬化症再発	375			UNRELATED	MODERATE	No	DW	RESOLVED
195* M/3[redacted]	多発性硬化症再発	480	NR		UNRELATED	MODERATE	No	DW	NOT RESOLVED
196* F/2[redacted] WHITE	頭痛	2	10	9	POSSIBLY	MODERATE	No	DW	RESOLVED

(a) #=On or after the subject switched to alternate MS medication
(b) ^=Adverse Event with onset prior to dosing
Abbreviations: Res=Resolution, NR=Not Recovered/Not Resolved, Dur=Duration, NONE=Dose Not Changed, DW=Drug Withdrawn, DI=Drug Interrupted, DR=Dose Reduced, M=Male, F=Female

SOURCE: BG12MS/JAPAN/ISS/L-AE-DISCON-302.SAS DATE: 02DEC2015

＊新薬承認情報提供時に置換えた

Listing of adverse events that led to discontinuation of study drug:
Study 109MS302
Page 22 of 48
Treatment group: BG00012 240 mg BID

Subject Sex/Age Race	MedDRA Preferred Term	Study Day Onset (a) (b)	Study Day Res	Dur (days)	Relationship to Study Drug	Severity	Serious	Action Taken With Study Drug	Outcome
196* F/2[redacted] WHITE	悪心	10	10	1	POSSIBLY	MODERATE	No	DW	RESOLVED
	嘔吐	10	10	1	POSSIBLY	MODERATE	No	DW	RESOLVED
197* F/4[redacted] WHITE	腹痛	21	25	5	RELATED	MODERATE	No	DW	RESOLVED
198* F/3[redacted] WHITE	頭痛	69	72	4	POSSIBLY	MODERATE	No	DW	RESOLVED
	嘔吐	69	72	4	RELATED	MODERATE	No	DW	RESOLVED
199* M/2[redacted] WHITE	頭痛	1	7	7	RELATED	SEVERE	No	DW	RESOLVED

(a) #=On or after the subject switched to alternate MS medication
(b) ^=Adverse Event with onset prior to dosing
Abbreviations: Res=Resolution, NR=Not Recovered/Not Resolved, Dur=Duration, NONE=Dose Not Changed, DW=Drug Withdrawn, DI=Drug Interrupted, DR=Dose Reduced, M=Male, F=Female

SOURCE: BG12MS/JAPAN/ISS/L-AE-DISCON-302.SAS DATE: 02DEC2015

＊新薬承認情報提供時に置換えた

Listing of adverse events that led to discontinuation of study drug:
Study 109MS302
Page 23 of 48
Treatment group: BG00012 240 mg BID

Subject Sex/Age Race	MedDRA Preferred Term	Study Day Onset (a) (b)	Study Day Res	Dur (days)	Relationship to Study Drug	Severity	Serious	Action Taken With Study Drug	Outcome
200* M/3[redacted] WHITE	潮紅	336	365	30	RELATED	MODERATE	No	DW	RESOLVED
201* M/3[redacted] WHITE	下腹部痛	31	54	24	POSSIBLY	MILD	No	DW	RESOLVED
	ほてり	31	54	24	POSSIBLY	MODERATE	No	DW	RESOLVED
	そう痒症	31	54	24	POSSIBLY	MILD	No	DW	RESOLVED
	好酸球数増加	33	43	11	POSSIBLY	MILD	No	DW	RESOLVED
	好酸球百分率増加	33	43	11	POSSIBLY	MILD	No	DW	RESOLVED
203* M/3[redacted] WHITE	嘔吐	31	34	4	RELATED	SEVERE	No	DW	RESOLVED

(a) #=On or after the subject switched to alternate MS medication
(b) ^=Adverse Event with onset prior to dosing
Abbreviations: Res=Resolution, NR=Not Recovered/Not Resolved, Dur=Duration, NONE=Dose Not Changed, DW=Drug Withdrawn, DI=Drug Interrupted, DR=Dose Reduced, M=Male, F=Female

SOURCE: BG12MS/JAPAN/ISS/L-AE-DISCON-302.SAS DATE: 02DEC2015

＊新薬承認情報提供時に置換えた

Listing of adverse events that led to discontinuation of study drug:
Study 109MS302
Page 24 of 48
Treatment group: BG00012 240 mg BID

Subject Sex/Age Race	MedDRA Preferred Term	Study Day Onset (a) (b)	Study Day Res	Dur (days)	Relationship to Study Drug	Severity	Serious	Action Taken With Study Drug	Outcome
204* F/3[redacted] WHITE	潮紅	561	NR		POSSIBLY	MODERATE	No	DW	NOT RESOLVED
205* F/3[redacted] WHITE	回転性めまい	97	118	22	POSSIBLY	MODERATE	No	DW	RESOLVED
206* F/5[redacted] WHITE	潮紅	331	NR		POSSIBLY	MODERATE	No	DW	NOT RESOLVED

(a) #=On or after the subject switched to alternate MS medication
(b) ^=Adverse Event with onset prior to dosing
Abbreviations: Res=Resolution, NR=Not Recovered/Not Resolved, Dur=Duration, NONE=Dose Not Changed, DW=Drug Withdrawn, DI=Drug Interrupted, DR=Dose Reduced, M=Male, F=Female

SOURCE: BG12MS/JAPAN/ISS/L-AE-DISCON-302.SAS DATE: 02DEC2015

＊新薬承認情報提供時に置換えた

Listing of adverse events that led to discontinuation of study drug:
Study 109MS302
Page 25 of 48
Treatment group: BG00012 240 mg TID

Subject Sex/Age Race	MedDRA Preferred Term	Study Day Onset (a) (b)	Study Day Res	Dur (days)	Relationship to Study Drug	Severity	Serious	Action Taken With Study Drug	Outcome
276* M/5[redacted] WHITE	腹痛	23	25	3	RELATED	MODERATE	No	DW	RESOLVED
277* F/4[redacted] WHITE	多発性硬化症再発	107	119	13	POSSIBLY	MODERATE	No	DW	RESOLVED
278* F/3[redacted] WHITE	下痢	11	22	12	RELATED	MILD	No	DW	RESOLVED
	悪心	11	22	12	RELATED	MILD	No	DW	RESOLVED
	嘔吐	11	22	12	RELATED	MILD	No	DW	RESOLVED
279* F/2[redacted] WHITE	潮紅	585	587	3	POSSIBLY	MODERATE	No	DW	RESOLVED

(a) #=On or after the subject switched to alternate MS medication
(b) ^=Adverse Event with onset prior to dosing
Abbreviations: Res=Resolution, NR=Not Recovered/Not Resolved, Dur=Duration, NONE=Dose Not Changed, DW=Drug Withdrawn, DI=Drug Interrupted, DR=Dose Reduced, M=Male, F=Female

SOURCE: BG12MS/JAPAN/ISS/L-AE-DISCON-302.SAS DATE: 02DEC2015

＊新薬承認情報提供時に置換えた

Listing of adverse events that led to discontinuation of study drug:
Study 109MS302
Page 26 of 48
Treatment group: BG00012 240 mg TID

Subject Sex/Age Race	MedDRA Preferred Term	Study Day Onset (a) (b)	Study Day Res	Dur (days)	Relationship to Study Drug	Severity	Serious	Action Taken With Study Drug	Outcome
280* F/3[redacted] WHITE	多発性硬化症	171	NR		UNLIKELY	MODERATE	No	DW	NOT RESOLVED
281* F/3[redacted] WHITE	蕁麻疹	54	64	11	POSSIBLY	MODERATE	No	DW	RESOLVED
282* F/3[redacted] WHITE	蛋白尿	29	716	688	POSSIBLY	MILD	No	DW	RESOLVED
	慢性腎不全	29	716	688	POSSIBLY	MILD	No	DW	RESOLVED
284* M/3[redacted] WHITE	潮紅	40	55	16	POSSIBLY	MILD	No	DW	RESOLVED
	気分変化	40	55	16	POSSIBLY	MODERATE	No	DW	RESOLVED

(a) #=On or after the subject switched to alternate MS medication
(b) ^=Adverse Event with onset prior to dosing
Abbreviations: Res=Resolution, NR=Not Recovered/Not Resolved, Dur=Duration, NONE=Dose Not Changed, DW=Drug Withdrawn, DI=Drug Interrupted, DR=Dose Reduced, M=Male, F=Female

SOURCE: BG12MS/JAPAN/ISS/L-AE-DISCON-302.SAS DATE: 02DEC2015

＊新薬承認情報提供時に置換えた

Listing of adverse events that led to discontinuation of study drug:
Study 109MS302
Page 27 of 48
Treatment group: BG00012 240 mg TID

Subject Sex/Age Race	MedDRA Preferred Term	Study Day Onset (a) (b)	Study Day Res	Dur (days)	Relationship to Study Drug	Severity	Serious	Action Taken With Study Drug	Outcome
285* F/2[redacted] WHITE	ほてり	579	599	21	RELATED	MODERATE	No	DW	RESOLVED
286* F/3[redacted] WHITE	悪心	11	32	22	RELATED	MODERATE	No	DW	RESOLVED
	嘔吐	11	32	22	RELATED	MODERATE	No	DW	RESOLVED
287* F/4[redacted] WHITE	多発性硬化症再発	359	504	146	UNLIKELY	MODERATE	No	DW	RESOLVED
288* F/5[redacted] HISPANIC	帯状疱疹	300	308	9	POSSIBLY	MODERATE	No	DW	RESOLVED

(a) #=On or after the subject switched to alternate MS medication
(b) ^=Adverse Event with onset prior to dosing
Abbreviations: Res=Resolution, NR=Not Recovered/Not Resolved, Dur=Duration, NONE=Dose Not Changed, DW=Drug Withdrawn, DI=Drug Interrupted, DR=Dose Reduced, M=Male, F=Female

SOURCE: BG12MS/JAPAN/ISS/L-AE-DISCON-302.SAS DATE: 02DEC2015

＊新薬承認情報提供時に置換えた

Listing of adverse events that led to discontinuation of study drug:
Study 109MS302
Page 28 of 48
Treatment group: BG00012 240 mg TID

Subject Sex/Age Race	MedDRA Preferred Term	Study Day Onset (a) (b)	Study Day Res	Dur (days)	Relationship to Study Drug	Severity	Serious	Action Taken With Study Drug	Outcome
289* F/4[redacted] WHITE	悪心	58	59	2	RELATED	MILD	No	DW	RESOLVED
290* F/4[redacted] WHITE	胸痛	7	7	1	POSSIBLY	MILD	No	DW	RESOLVED
291* F/3[redacted] WHITE	脱毛症	26	39	14	POSSIBLY	SEVERE	No	DW	RESOLVED
	狭心症	26	NR		POSSIBLY	SEVERE	No	DW	NOT RESOLVED
292* F/3[redacted] WHITE	上腹部痛	349	430	82	POSSIBLY	MODERATE	No	DW	RESOLVED

(a) #=On or after the subject switched to alternate MS medication
(b) ^=Adverse Event with onset prior to dosing
Abbreviations: Res=Resolution, NR=Not Recovered/Not Resolved, Dur=Duration, NONE=Dose Not Changed, DW=Drug Withdrawn, DI=Drug Interrupted, DR=Dose Reduced, M=Male, F=Female

SOURCE: BG12MS/JAPAN/ISS/L-AE-DISCON-302.SAS DATE: 02DEC2015

＊新薬承認情報提供時に置換えた

Listing of adverse events that led to discontinuation of study drug:
Study 109MS302
Page 29 of 48
Treatment group: BG00012 240 mg TID

Subject Sex/Age Race	MedDRA Preferred Term	Study Day Onset (a) (b)	Study Day Res	Dur (days)	Relationship to Study Drug	Severity	Serious	Action Taken With Study Drug	Outcome
293* F/4[redacted] WHITE	上腹部痛	2	16	15	POSSIBLY	MODERATE	No	DW	RESOLVED
	下痢	2	16	15	POSSIBLY	MODERATE	No	DW	RESOLVED
	上腹部痛	18	61	44	POSSIBLY	MODERATE	No	DW	RESOLVED
	下痢	18	61	44	POSSIBLY	MODERATE	No	DW	RESOLVED
	上腹部痛	72	109	38	POSSIBLY	MODERATE	No	DW	RESOLVED
	下痢	72	109	38	POSSIBLY	MODERATE	No	DW	RESOLVED
294* F/4[redacted] WHITE	浮動性めまい	1	22	22	POSSIBLY	MILD	No	DW	RESOLVED
295* F/4[redacted] WHITE	消化管感染	5	NR		POSSIBLY	SEVERE	No	DW	NOT RESOLVED
	体重減少	5	NR		POSSIBLY	MODERATE	No	DW	NOT RESOLVED

(a) #=On or after the subject switched to alternate MS medication
(b) ^=Adverse Event with onset prior to dosing
Abbreviations: Res=Resolution, NR=Not Recovered/Not Resolved, Dur=Duration, NONE=Dose Not Changed, DW=Drug Withdrawn, DI=Drug Interrupted, DR=Dose Reduced, M=Male, F=Female

SOURCE: BG12MS/JAPAN/ISS/L-AE-DISCON-302.SAS DATE: 02DEC2015

＊新薬承認情報提供時に置換えた

Listing of adverse events that led to discontinuation of study drug:
Study 109MS302
Page 30 of 48
Treatment group: BG00012 240 mg TID

Subject Sex/Age Race	MedDRA Preferred Term	Study Day Onset (a) (b)	Study Day Res	Dur (days)	Relationship to Study Drug	Severity	Serious	Action Taken With Study Drug	Outcome
296* F/2[redacted] WHITE	下痢	142	363		RELATED	MODERATE	No	DW	RESOLVED
297* F/3[redacted] WHITE	悪心	8	27	20	RELATED	SEVERE	No	DW	RESOLVED
298* F/3[redacted] WHITE	潮紅	99	116	18	RELATED	SEVERE	No	DW	RESOLVED
299* F/3[redacted] WHITE	腹部不快感	21	49	29	RELATED	MODERATE	No	DW	RESOLVED
	下痢	21	49	29	RELATED	MODERATE	No	DW	RESOLVED
	悪心	21	49	29	RELATED	MODERATE	No	DW	RESOLVED

(a) #=On or after the subject switched to alternate MS medication
(b) ^=Adverse Event with onset prior to dosing
Abbreviations: Res=Resolution, NR=Not Recovered/Not Resolved, Dur=Duration, NONE=Dose Not Changed, DW=Drug Withdrawn, DI=Drug Interrupted, DR=Dose Reduced, M=Male, F=Female

SOURCE: BG12MS/JAPAN/ISS/L-AE-DISCON-302.SAS DATE: 02DEC2015

＊新薬承認情報提供時に置換えた

Listing of adverse events that led to discontinuation of study drug:
Study 109MS302
Page 31 of 48
Treatment group: BG00012 240 mg TID

Subject Sex/Age Race	MedDRA Preferred Term	Study Day Onset (a) (b)	Study Day Res	Dur (days)	Relationship to Study Drug	Severity	Serious	Action Taken With Study Drug	Outcome
299* F/3[redacted] WHITE	発疹	40	49	10	RELATED	MODERATE	No	DW	RESOLVED
	気道感染	49			POSSIBLY	MODERATE	No	DW	RESOLVED
300* F/2[redacted] WHITE	嘔吐	15	30	16	RELATED	MODERATE	No	DW	RESOLVED
301* F/3[redacted] WHITE	上腹部痛	8	25	18	POSSIBLY	MODERATE	No	DW	RESOLVED
	下痢	8	25	18	POSSIBLY	MODERATE	No	DW	RESOLVED
	悪心	8	25	18	POSSIBLY	MODERATE	No	DW	RESOLVED

(a) #=On or after the subject switched to alternate MS medication
(b) ^=Adverse Event with onset prior to dosing
Abbreviations: Res=Resolution, NR=Not Recovered/Not Resolved, Dur=Duration, NONE=Dose Not Changed, DW=Drug Withdrawn, DI=Drug Interrupted, DR=Dose Reduced, M=Male, F=Female

SOURCE: BG12MS/JAPAN/ISS/L-AE-DISCON-302.SAS DATE: 02DEC2015

＊新薬承認情報提供時に置換えた

Listing of adverse events that led to discontinuation of study drug:
Study 109MS302
Page 32 of 48
Treatment group: BG00012 240 mg TID

Subject Sex/Age Race	MedDRA Preferred Term	Study Day Onset (a) (b)	Study Day Res	Dur (days)	Relationship to Study Drug	Severity	Serious	Action Taken With Study Drug	Outcome
302* F/3[redacted] WHITE	腹痛	21	22	2	RELATED	MODERATE	No	DW	RESOLVED
	腹部硬直	21	22	2	RELATED	MODERATE	No	DW	RESOLVED
303* F/3[redacted] WHITE	胃腸障害	2	22	21	RELATED	MODERATE	No	DW	RESOLVED
304* F/5[redacted] WHITE	そう痒症	363	477	115	POSSIBLY	MILD	No	DW	RESOLVED
	潮紅	428	477	50	POSSIBLY	MODERATE	No	DW	RESOLVED
305* F/2[redacted] WHITE	胃腸障害	28	34	7	RELATED	SEVERE	No	DW	RESOLVED

(a) #=On or after the subject switched to alternate MS medication
(b) ^=Adverse Event with onset prior to dosing
Abbreviations: Res=Resolution, NR=Not Recovered/Not Resolved, Dur=Duration, NONE=Dose Not Changed, DW=Drug Withdrawn, DI=Drug Interrupted, DR=Dose Reduced, M=Male, F=Female

SOURCE: BG12MS/JAPAN/ISS/L-AE-DISCON-302.SAS DATE: 02DEC2015

＊新薬承認情報提供時に置換えた

Listing of adverse events that led to discontinuation of study drug:
Study 109MS302
Page 33 of 48
Treatment group: BG00012 240 mg TID

Subject Sex/Age Race	MedDRA Preferred Term	Study Day Onset (a) (b)	Study Day Res	Dur (days)	Relationship to Study Drug	Severity	Serious	Action Taken With Study Drug	Outcome
306* M/5[redacted] WHITE	嘔吐	24	25	2	RELATED	MODERATE	No	DW	RESOLVED
307* F/4[redacted] WHITE	白血球数減少	56	NR		POSSIBLY	MILD	No	DW	NOT RESOLVED
308* M/4[redacted] WHITE	下痢	29	31	3	RELATED	SEVERE	No	DW	RESOLVED
309* M/2[redacted] WHITE	腎結石症	340	NR		RELATED	MILD	No	DW	NOT RESOLVED

(a) #=On or after the subject switched to alternate MS medication
(b) ^=Adverse Event with onset prior to dosing
Abbreviations: Res=Resolution, NR=Not Recovered/Not Resolved, Dur=Duration, NONE=Dose Not Changed, DW=Drug Withdrawn, DI=Drug Interrupted, DR=Dose Reduced, M=Male, F=Female

SOURCE: BG12MS/JAPAN/ISS/L-AE-DISCON-302.SAS DATE: 02DEC2015

＊新薬承認情報提供時に置換えた

Listing of adverse events that led to discontinuation of study drug:
Study 109MS302
Page 34 of 48
Treatment group: BG00012 240 mg TID

Subject Sex/Age Race	MedDRA Preferred Term	Study Day Onset (a) (b)	Study Day Res	Dur (days)	Relationship to Study Drug	Severity	Serious	Action Taken With Study Drug	Outcome
310* F/3[redacted] WHITE	胃腸障害	18	57	40	POSSIBLY	SEVERE	No	DW	RESOLVED
311* M/4[redacted] WHITE	尿路感染	59	66	8	UNRELATED	SEVERE	Yes	DW	RESOLVED
313* F/3[redacted]	悪寒	167	167	1	RELATED	MODERATE	No	DW	RESOLVED
	潮紅	167	167	1	RELATED	SEVERE	No	DW	RESOLVED
	ほてり	167	167	1	RELATED	MODERATE	No	DW	RESOLVED
314* M/4[redacted] WHITE	背部痛	1	1	1	RELATED	MODERATE	No	DW	RESOLVED
	潮紅	1	1	1	RELATED	MILD	No	DW	RESOLVED

(a) #=On or after the subject switched to alternate MS medication
(b) ^=Adverse Event with onset prior to dosing
Abbreviations: Res=Resolution, NR=Not Recovered/Not Resolved, Dur=Duration, NONE=Dose Not Changed, DW=Drug Withdrawn, DI=Drug Interrupted, DR=Dose Reduced, M=Male, F=Female

SOURCE: BG12MS/JAPAN/ISS/L-AE-DISCON-302.SAS DATE: 02DEC2015

＊新薬承認情報提供時に置換えた

Listing of adverse events that led to discontinuation of study drug:
Study 109MS302
Page 35 of 48
Treatment group: BG00012 240 mg TID

Subject Sex/Age Race	MedDRA Preferred Term	Study Day Onset (a) (b)	Study Day Res	Dur (days)	Relationship to Study Drug	Severity	Serious	Action Taken With Study Drug	Outcome
315* M/2[redacted] WHITE	過敏症	121	127	7	POSSIBLY	MODERATE	No	DW	RESOLVED
316* F/4[redacted] HISPANIC	多発性硬化症再発	40	43	4	UNRELATED	MODERATE	No	DW	RESOLVED
	多発性硬化症再発	43	47	5	UNRELATED	MODERATE	Yes	DW	RESOLVED
317* F/4[redacted] WHITE	全身性皮疹	32	34	3	POSSIBLY	MODERATE	No	DW	RESOLVED
318* F/3[redacted] WHITE	上腹部痛	13	23	11	RELATED	MODERATE	No	DW	RESOLVED

(a) #=On or after the subject switched to alternate MS medication
(b) ^=Adverse Event with onset prior to dosing
Abbreviations: Res=Resolution, NR=Not Recovered/Not Resolved, Dur=Duration, NONE=Dose Not Changed, DW=Drug Withdrawn, DI=Drug Interrupted, DR=Dose Reduced, M=Male, F=Female

SOURCE: BG12MS/JAPAN/ISS/L-AE-DISCON-302.SAS DATE: 02DEC2015

＊新薬承認情報提供時に置換えた

Listing of adverse events that led to discontinuation of study drug:
Study 109MS302
Page 36 of 48
Treatment group: BG00012 240 mg TID

Subject Sex/Age Race	MedDRA Preferred Term	Study Day Onset (a) (b)	Study Day Res	Dur (days)	Relationship to Study Drug	Severity	Serious	Action Taken With Study Drug	Outcome
318* F/3[redacted] WHITE	下痢	13	23	11	RELATED	MODERATE	No	DW	RESOLVED

(a) #=On or after the subject switched to alternate MS medication
(b) ^=Adverse Event with onset prior to dosing
Abbreviations: Res=Resolution, NR=Not Recovered/Not Resolved, Dur=Duration, NONE=Dose Not Changed, DW=Drug Withdrawn, DI=Drug Interrupted, DR=Dose Reduced, M=Male, F=Female

SOURCE: BG12MS/JAPAN/ISS/L-AE-DISCON-302.SAS DATE: 02DEC2015

＊新薬承認情報提供時に置換えた

Listing of adverse events that led to discontinuation of study drug:
Study 109MS302
Page 37 of 48
Treatment group: GA

Subject Sex/Age Race	MedDRA Preferred Term	Study Day Onset (a) (b)	Study Day Res	Dur (days)	Relationship to Study Drug	Severity	Serious	Action Taken With Study Drug	Outcome
319* F/4[redacted] WHITE	うつ病	2	27	26	UNLIKELY	MODERATE	No	DW	RESOLVED
320* F/4[redacted] ASIAN	アナフィラキシー反応	127	128	2	POSSIBLY	MODERATE	Yes	DW	RESOLVED
321* F/3[redacted] ASIAN	多発性硬化症	251	590	340	UNRELATED	SEVERE	No	DW	RESOLVED
322* F/2[redacted] ASIAN	アラニン・アミノトランスフェラーゼ増加	337	421	85	POSSIBLY	MILD	No	DW	RESOLVED

(a) #=On or after the subject switched to alternate MS medication
(b) ^=Adverse Event with onset prior to dosing
Abbreviations: Res=Resolution, NR=Not Recovered/Not Resolved, Dur=Duration, NONE=Dose Not Changed, DW=Drug Withdrawn, DI=Drug Interrupted, DR=Dose Reduced, M=Male, F=Female

SOURCE: BG12MS/JAPAN/ISS/L-AE-DISCON-302.SAS DATE: 02DEC2015

＊新薬承認情報提供時に置換えた

Listing of adverse events that led to discontinuation of study drug:
Study 109MS302
Page 38 of 48
Treatment group: GA

Subject Sex/Age Race	MedDRA Preferred Term	Study Day Onset (a) (b)	Study Day Res	Dur (days)	Relationship to Study Drug	Severity	Serious	Action Taken With Study Drug	Outcome
322* F/2[redacted] ASIAN	アスパラギン酸アミノトランスフェラーゼ増加	337	437	101	POSSIBLY	MILD	No	DW	RESOLVED
323* F/4[redacted] WHITE	注射部位結節	55	260	206	RELATED	MILD	No	DW	RESOLVED
202* F/3[redacted] WHITE	多発性硬化症再発	193	NR		UNRELATED	MODERATE	No	DW	NOT RESOLVED
325* F/2[redacted] WHITE	注射部位紅斑	12	29	18	RELATED	MODERATE	No	DW	RESOLVED
	注射部位そう痒感	12	29	18	RELATED	MODERATE	No	DW	RESOLVED
	注射部位腫脹	12	12	1	RELATED	MODERATE	No	DW	RESOLVED

(a) #=On or after the subject switched to alternate MS medication
(b) ^=Adverse Event with onset prior to dosing
Abbreviations: Res=Resolution, NR=Not Recovered/Not Resolved, Dur=Duration, NONE=Dose Not Changed, DW=Drug Withdrawn, DI=Drug Interrupted, DR=Dose Reduced, M=Male, F=Female

SOURCE: BG12MS/JAPAN/ISS/L-AE-DISCON-302.SAS DATE: 02DEC2015

＊新薬承認情報提供時に置換えた

Listing of adverse events that led to discontinuation of study drug:
Study 109MS302
Page 39 of 48
Treatment group: GA

Subject Sex/Age Race	MedDRA Preferred Term	Study Day Onset (a) (b)	Study Day Res	Dur (days)	Relationship to Study Drug	Severity	Serious	Action Taken With Study Drug	Outcome
325* F/2[redacted] WHITE	注射部位熱感	12	29	18	RELATED	MODERATE	No	DW	RESOLVED
326* F/4[redacted] WHITE	注射部位紅斑	1	75	75	RELATED	SEVERE	No	DW	RESOLVED
	注射部位腫瘤	1	75	75	RELATED	MODERATE	No	DW	RESOLVED
327* F/3[redacted] WHITE	注射部位紅斑	1	29	29	RELATED	MODERATE	No	DW	RESOLVED
	注射部位疼痛	1	29	29	RELATED	MODERATE	No	DW	RESOLVED
	注射部位そう痒感	1	29	29	RELATED	MODERATE	No	DW	RESOLVED
	注射部位腫脹	1	29	29	RELATED	MODERATE	No	DW	RESOLVED
	頻脈	1	29	29	RELATED	MODERATE	No	DW	RESOLVED

(a) #=On or after the subject switched to alternate MS medication
(b) ^=Adverse Event with onset prior to dosing
Abbreviations: Res=Resolution, NR=Not Recovered/Not Resolved, Dur=Duration, NONE=Dose Not Changed, DW=Drug Withdrawn, DI=Drug Interrupted, DR=Dose Reduced, M=Male, F=Female

SOURCE: BG12MS/JAPAN/ISS/L-AE-DISCON-302.SAS DATE: 02DEC2015

＊新薬承認情報提供時に置換えた

Listing of adverse events that led to discontinuation of study drug:
Study 109MS302
Page 40 of 48
Treatment group: GA

Subject Sex/Age Race	MedDRA Preferred Term	Study Day Onset (a) (b)	Res	Dur (days)	Relationship to Study Drug	Severity	Serious	Action Taken With Study Drug	Outcome
328* F/3[redacted] HISPANIC	呼吸困難	514	525	12	RELATED	MODERATE	No	DW	RESOLVED
329* M/3[redacted] WHITE	多発性硬化症再発	555	631	77	UNRELATED	MODERATE	No	DW	RESOLVED
330* F/3[redacted] WHITE	悪心	2	NR		POSSIBLY	MILD	No	DW	NOT RESOLVED
	注射部位疼痛	9	NR		RELATED	MILD	No	DW	NOT RESOLVED
	齲歯	21	79	59	UNRELATED	MILD	No	DW	RESOLVED
331* F/2[redacted] WHITE	肝酵素上昇	85	NR		UNRELATED	MILD	No	DW	NOT RESOLVED

(a) #=On or after the subject switched to alternate MS medication
(b) ^=Adverse Event with onset prior to dosing
Abbreviations: Res=Resolution, NR=Not Recovered/Not Resolved, Dur=Duration, NONE=Dose Not Changed, DW=Drug Withdrawn, DI=Drug Interrupted, DR=Dose Reduced, M=Male, F=Female

SOURCE: BG12MS/JAPAN/ISS/L-AE-DISCON-302.SAS DATE: 02DEC2015

＊新薬承認情報提供時に置換えた

Listing of adverse events that led to discontinuation of study drug:
Study 109MS302
Page 41 of 48
Treatment group: GA

Subject Sex/Age Race	MedDRA Preferred Term	Study Day Onset (a) (b)	Study Day Res	Dur (days)	Relationship to Study Drug	Severity	Serious	Action Taken With Study Drug	Outcome
331* F/2[redacted] WHITE	アラニン・アミノトランスフェラーゼ異常	113	NR		POSSIBLY	MODERATE	No	DW	NOT RESOLVED
	アスパラギン酸アミノトランスフェラーゼ増加	113	NR		POSSIBLY	MODERATE	No	DW	NOT RESOLVED
	血中アルカリホスファターゼ異常	113	NR		POSSIBLY	MODERATE	No	DW	NOT RESOLVED
	γ－グルタミルトランスフェラーゼ増加	113	NR		POSSIBLY	MODERATE	No	DW	NOT RESOLVED
333* M/5[redacted] WHITE	多発性硬化症再発	353	369	17	UNRELATED	MILD	No	DW	RESOLVED

(a) #=On or after the subject switched to alternate MS medication
(b) ^=Adverse Event with onset prior to dosing
Abbreviations: Res=Resolution, NR=Not Recovered/Not Resolved, Dur=Duration, NONE=Dose Not Changed, DW=Drug Withdrawn, DI=Drug Interrupted, DR=Dose Reduced, M=Male, F=Female

SOURCE: BG12MS/JAPAN/ISS/L-AE-DISCON-302.SAS DATE: 02DEC2015

＊新薬承認情報提供時に置換えた

Listing of adverse events that led to discontinuation of study drug:
Study 109MS302
Page 42 of 48
Treatment group: GA

Subject Sex/Age Race	MedDRA Preferred Term	Study Day Onset (a) (b)	Study Day Res	Dur (days)	Relationship to Study Drug	Severity	Serious	Action Taken With Study Drug	Outcome
310* F/3[redacted] WHITE	過敏症	91	93	3	RELATED	SEVERE	Yes	DW	RESOLVED
324* F/3[redacted] WHITE	末梢性浮腫	194	342	149	POSSIBLY	MODERATE	Yes	DW	RESOLVED
336* F/4[redacted] WHITE	多発性硬化症再発	428	490	63	POSSIBLY	MODERATE	No	DW	RESOLVED
337* F/2[redacted] WHITE	注射部位疼痛	1	57	57	RELATED	MODERATE	No	DW	RESOLVED
	注射部位硬結	19	57	39	RELATED	MILD	No	DW	RESOLVED

(a) #=On or after the subject switched to alternate MS medication
(b) ^=Adverse Event with onset prior to dosing
Abbreviations: Res=Resolution, NR=Not Recovered/Not Resolved, Dur=Duration, NONE=Dose Not Changed, DW=Drug Withdrawn, DI=Drug Interrupted, DR=Dose Reduced, M=Male, F=Female

SOURCE: BG12MS/JAPAN/ISS/L-AE-DISCON-302.SAS DATE: 02DEC2015

＊新薬承認情報提供時に置換えた

Listing of adverse events that led to discontinuation of study drug:
Study 109MS302
Page 43 of 48
Treatment group: GA

Subject Sex/Age Race	MedDRA Preferred Term	Study Day Onset (a) (b)	Study Day Res	Dur (days)	Relationship to Study Drug	Severity	Serious	Action Taken With Study Drug	Outcome
337* F/2[redacted] WHITE	注射部位そう痒感	19	57	39	RELATED	MODERATE	No	DW	RESOLVED
338* F/4[redacted] WHITE	注射部位反応	15	113	99	RELATED	MODERATE	No	DW	RESOLVED
339* F/2[redacted] WHITE	多発性硬化症再発	420	NR		RELATED	MODERATE	No	DW	NOT RESOLVED
340* F/2[redacted] WHITE	無力症	44	44	1	POSSIBLY	MODERATE	No	DW	RESOLVED
	浮動性めまい	44	44	1	POSSIBLY	MODERATE	No	DW	RESOLVED
	紅斑	44	44	1	POSSIBLY	MILD	No	DW	RESOLVED

(a) #=On or after the subject switched to alternate MS medication
(b) ^=Adverse Event with onset prior to dosing
Abbreviations: Res=Resolution, NR=Not Recovered/Not Resolved, Dur=Duration, NONE=Dose Not Changed, DW=Drug Withdrawn, DI=Drug Interrupted, DR=Dose Reduced, M=Male, F=Female

SOURCE: BG12MS/JAPAN/ISS/L-AE-DISCON-302.SAS DATE: 02DEC2015

＊新薬承認情報提供時に置換えた

Listing of adverse events that led to discontinuation of study drug:
Study 109MS302
Page 44 of 48
Treatment group: GA

Subject Sex/Age Race	MedDRA Preferred Term	Study Day Onset (a) (b)	Study Day Res	Dur (days)	Relationship to Study Drug	Severity	Serious	Action Taken With Study Drug	Outcome
340* F/2[redacted] WHITE	顔面腫脹	44	44	1	POSSIBLY	MILD	No	DW	RESOLVED
341* F/3[redacted] WHITE	無力症	41	42	2	POSSIBLY	MILD	No	DW	RESOLVED
	胸痛	41	41	1	POSSIBLY	MODERATE	No	DW	RESOLVED
	呼吸困難	41	41	1	POSSIBLY	MODERATE	No	DW	RESOLVED
	紅斑	41	41	1	POSSIBLY	MODERATE	No	DW	RESOLVED
	筋力低下	41	NR		POSSIBLY	MILD	No	DW	NOT RESOLVED
	頻尿	41	NR		UNLIKELY	MILD	No	DW	NOT RESOLVED
	顔面腫脹	41	41	1	POSSIBLY	MODERATE	No	DW	RESOLVED
	振戦	41	41	1	POSSIBLY	MILD	No	DW	RESOLVED

(a) #=On or after the subject switched to alternate MS medication
(b) ^=Adverse Event with onset prior to dosing
Abbreviations: Res=Resolution, NR=Not Recovered/Not Resolved, Dur=Duration, NONE=Dose Not Changed, DW=Drug Withdrawn, DI=Drug Interrupted, DR=Dose Reduced, M=Male, F=Female

SOURCE: BG12MS/JAPAN/ISS/L-AE-DISCON-302.SAS DATE: 02DEC2015

＊新薬承認情報提供時に置換えた

Listing of adverse events that led to discontinuation of study drug:
Study 109MS302
Page 45 of 48
Treatment group: GA

Subject Sex/Age Race	MedDRA Preferred Term	Study Day Onset (a) (b)	Study Day Res	Dur (days)	Relationship to Study Drug	Severity	Serious	Action Taken With Study Drug	Outcome
334* F/3[redacted] WHITE	上腹部痛	61	61	1	RELATED	MILD	No	DW	RESOLVED
	無力症	61	61	1	RELATED	MODERATE	No	DW	RESOLVED
	浮動性めまい	61	61	1	RELATED	MODERATE	No	DW	RESOLVED
	頭痛	61	61	1	RELATED	MODERATE	No	DW	RESOLVED
343* F/4[redacted] WHITE	壊死	283	505	223	RELATED	MILD	No	DW	RESOLVED
383* F/4[redacted] WHITE	非心臓性胸痛	460	460	1	RELATED	MODERATE	No	DW	RESOLVED

(a) #=On or after the subject switched to alternate MS medication
(b) ^=Adverse Event with onset prior to dosing
Abbreviations: Res=Resolution, NR=Not Recovered/Not Resolved, Dur=Duration, NONE=Dose Not Changed, DW=Drug Withdrawn, DI=Drug Interrupted, DR=Dose Reduced, M=Male, F=Female

SOURCE: BG12MS/JAPAN/ISS/L-AE-DISCON-302.SAS DATE: 02DEC2015

＊新薬承認情報提供時に置換えた

Listing of adverse events that led to discontinuation of study drug:
Study 109MS302
Page 46 of 48
Treatment group: GA

Subject Sex/Age Race	MedDRA Preferred Term	Study Day Onset (a) (b)	Study Day Res	Dur (days)	Relationship to Study Drug	Severity	Serious	Action Taken With Study Drug	Outcome
384* F/3[redacted] WHITE	アラニン・アミノトランスフェラーゼ増加	250	NR		POSSIBLY	SEVERE	No	DW	NOT RESOLVED
	アスパラギン酸アミノトランスフェラーゼ増加	250	NR		POSSIBLY	SEVERE	No	DW	NOT RESOLVED
335* F/4[redacted] WHITE	子宮内膜癌	182	244	63	UNLIKELY	MODERATE	Yes	DW	RESOLVED
	アナフィラキシー反応	216	219	4	RELATED	SEVERE	Yes	DW	RESOLVED
385* F/3[redacted] WHITE	多発性硬化症再発	6	10	5	UNRELATED	MODERATE	No	DW	RESOLVED

(a) #=On or after the subject switched to alternate MS medication
(b) ^=Adverse Event with onset prior to dosing
Abbreviations: Res=Resolution, NR=Not Recovered/Not Resolved, Dur=Duration, NONE=Dose Not Changed, DW=Drug Withdrawn, DI=Drug Interrupted, DR=Dose Reduced, M=Male, F=Female

SOURCE: BG12MS/JAPAN/ISS/L-AE-DISCON-302.SAS DATE: 02DEC2015

＊新薬承認情報提供時に置換えた

Listing of adverse events that led to discontinuation of study drug:
Study 109MS302
Page 47 of 48
Treatment group: GA

Subject Sex/Age Race	MedDRA Preferred Term	Study Day Onset (a) (b)	Study Day Res	Dur (days)	Relationship to Study Drug	Severity	Serious	Action Taken With Study Drug	Outcome
386* F/2[redacted]	トランスアミナーゼ上昇	222			POSSIBLY	MODERATE	No	DW	RESOLVED
387* F/4[redacted] WHITE	注射部位疼痛	1	34	34	RELATED	MODERATE	No	DW	RESOLVED
350* M/2[redacted] WHITE	自殺既遂	529	529	1	UNLIKELY	SEVERE	Yes	DW	RESOLVED
389* F/3[redacted] WHITE	ネフローゼ症候群	330	423	94	POSSIBLY	SEVERE	No	DW	RESOLVED

(a) #=On or after the subject switched to alternate MS medication
(b) ^=Adverse Event with onset prior to dosing
Abbreviations: Res=Resolution, NR=Not Recovered/Not Resolved, Dur=Duration, NONE=Dose Not Changed, DW=Drug Withdrawn, DI=Drug Interrupted, DR=Dose Reduced, M=Male, F=Female

SOURCE: BG12MS/JAPAN/ISS/L-AE-DISCON-302.SAS DATE: 02DEC2015

＊新薬承認情報提供時に置換えた

Listing of adverse events that led to discontinuation of study drug:
Study 109MS302
Page 48 of 48
Treatment group: GA

Subject Sex/Age Race	MedDRA Preferred Term	Study Day Onset (a) (b)	Study Day Res	Dur (days)	Relationship to Study Drug	Severity	Serious	Action Taken With Study Drug	Outcome
390* F/5[redacted] HISPANIC	頭痛	15	NR		RELATED	MODERATE	No	DW	NOT RESOLVED
	悪心	15	NR		RELATED	MODERATE	No	DW	NOT RESOLVED
	皮膚硬結	15	NR		RELATED	MODERATE	No	DW	NOT RESOLVED
	頻脈	15	NR		RELATED	MODERATE	No	DW	NOT RESOLVED
	嘔吐	15	NR		RELATED	MODERATE	No	DW	NOT RESOLVED
342* F/3[redacted] WHITE	心房細動	25	70	46	POSSIBLY	SEVERE	No	DW	RESOLVED
	心筋炎	25	70	46	POSSIBLY	SEVERE	Yes	DW	RESOLVED
391* M/3[redacted] WHITE	ミクロアルブミン尿	1	NR		POSSIBLY	MODERATE	No	DW	NOT RESOLVED

(a) #=On or after the subject switched to alternate MS medication
(b) ^=Adverse Event with onset prior to dosing
Abbreviations: Res=Resolution, NR=Not Recovered/Not Resolved, Dur=Duration, NONE=Dose Not Changed, DW=Drug Withdrawn, DI=Drug Interrupted, DR=Dose Reduced, M=Male, F=Female

SOURCE: BG12MS/JAPAN/ISS/L-AE-DISCON-302.SAS DATE: 02DEC2015

＊新薬承認情報提供時に置換えた

Table 310: Listing of Adverse Events That Led to the Discontinuation of Study Drug - Overall

Listing of adverse events that led to the discontinuation of study drug - Overall

Treatment Group	Subject Number	Onset Day of Event (a)	Day of Last Dose	Adverse Event		Severity (c)	Relationship to Study Drug(c)
				Investigator Term	Preferred Term (MedDRA) (b)		
BG00012 240 mg BID	372*	1	6	CONCURRENT DRUG INDUCED HEPATIC DISORDER	肝障害	MILD	NOT RELATED
Placebo	[redacted]	140	161	LFTS RAISED	肝機能検査異常	MILD	NOT RELATED
	[redacted]	60	70	RELAPSE OF MULTIPLE SCLEROSIS	多発性硬化症再発*	MODERATE	NOT RELATED

(a) #=On or after the subject switched to alternate MS medication.
(b) *=Adverse Event was serious.
(c) Investigator assessment.

SOURCE: BG12MS/109MS305/PART1/L-AE-DISCON.SAS DATE: 25SEP2015

＊新薬承認情報提供時に置換えた

9.10. Incidence of AEs With At Least 2% Higher in Any Treatment Group by Individual Study – All Evaluation Studies

Table 314: Incidence of Adverse Events At Least 2% Higher in Any Treatment Group by System Organ Class and Preferred Term and Causal Association to Study Drug: Study 109MS301

Incidence of adverse events at least 2% higher in any treatment group by system organ class and preferred term and causal association to study drug: Study 109MS301
Page 1 of 9

	Irrespective of causal association			Causal association cannot be ruled out		
	Placebo (N=408)	BG00012 240 mg BID (N=410)	BG00012 240 mg TID (N=416)	Placebo (N=408)	BG00012 240 mg BID (N=410)	BG00012 240 mg TID (N=416)
Number of subjects with an event	387 (95)	395 (96)	396 (95)	202 (50)	299 (73)	304 (73)
感染症および寄生虫症	232 (57)	242 (59)	259 (62)	34 (8)	39 (10)	48 (12)
鼻咽頭炎	101 (25)	108 (26)	109 (26)	16 (4)	15 (4)	19 (5)
尿路感染	53 (13)	55 (13)	54 (13)	6 (1)	7 (2)	12 (3)
胃腸炎	21 (5)	28 (7)	21 (5)	2 (<1)	4 (<1)	7 (2)
インフルエンザ	39 (10)	34 (8)	48 (12)	2 (<1)	1 (<1)	7 (2)
上気道感染	53 (13)	63 (15)	51 (12)	8 (2)	13 (3)	6 (1)
気管支炎	18 (4)	21 (5)	26 (6)	2 (<1)	3 (<1)	5 (1)
鼻炎	19 (5)	12 (3)	16 (4)	4 (<1)	2 (<1)	5 (1)
副鼻腔炎	20 (5)	17 (4)	34 (8)	2 (<1)	2 (<1)	4 (<1)
膀胱炎	13 (3)	6 (1)	16 (4)	1 (<1)	1 (<1)	3 (<1)
耳感染	8 (2)	2 (<1)	9 (2)	1 (<1)	0	2 (<1)
口腔ヘルペス	14 (3)	14 (3)	8 (2)	8 (2)	4 (<1)	2 (<1)
咽頭炎	18 (4)	18 (4)	16 (4)	2 (<1)	2 (<1)	1 (<1)
ウイルス感染	14 (3)	14 (3)	13 (3)	0	1 (<1)	1 (<1)

NOTE 1: Numbers in parentheses are percentages.
2: Data after subjects switched to alternative MS treatment are excluded.
3: A subject was counted only once within each system organ class or preferred term.

SOURCE: BG12MS/JAPAN/ISS/T-AE-SOCPT-CAUS2-301.SAS DATE: 02DEC2015

Incidence of adverse events at least 2% higher in any treatment group by
system organ class and preferred term and causal association to study drug:
Study 109MS301
Page 2 of 9

	Irrespective of causal association			Causal association cannot be ruled out		
	Placebo (N=408)	BG00012 240 mg BID (N=410)	BG00012 240 mg TID (N=416)	Placebo (N=408)	BG00012 240 mg BID (N=410)	BG00012 240 mg TID (N=416)
気道感染	5 (1)	11 (3)	10 (2)	0	1 (<1)	0
腟感染	2 (<1)	9 (2)	4 (<1)	1 (<1)	0	0
血液およびリンパ系障害	1 (<1)	14 (3)	13 (3)	1 (<1)	12 (3)	12 (3)
リンパ球減少症	1 (<1)	14 (3)	13 (3)	1 (<1)	12 (3)	12 (3)
免疫系障害	0	11 (3)	6 (1)	0	7 (2)	5 (1)
過敏症	0	11 (3)	6 (1)	0	7 (2)	5 (1)
代謝および栄養障害	9 (2)	10 (2)	10 (2)	2 (<1)	5 (1)	5 (1)
食欲減退	9 (2)	10 (2)	10 (2)	2 (<1)	5 (1)	5 (1)
精神障害	66 (16)	63 (15)	67 (16)	5 (1)	4 (<1)	7 (2)
不眠症	19 (5)	20 (5)	20 (5)	2 (<1)	1 (<1)	6 (1)
うつ病	33 (8)	29 (7)	33 (8)	3 (<1)	1 (<1)	1 (<1)

NOTE 1: Numbers in parentheses are percentages.
2: Data after subjects switched to alternative MS treatment are excluded.
3: A subject was counted only once within each system organ class or preferred term.

SOURCE: BG12MS/JAPAN/ISS/T-AE-SOCPT-CAUS2-301.SAS DATE: 02DEC2015

Incidence of adverse events at least 2% higher in any treatment group by system organ class and preferred term and causal association to study drug:
Study 109MS301
Page 3 of 9

	Irrespective of causal association			Causal association cannot be ruled out		
	Placebo (N=408)	BG00012 240 mg BID (N=410)	BG00012 240 mg TID (N=416)	Placebo (N=408)	BG00012 240 mg BID (N=410)	BG00012 240 mg TID (N=416)
不安	13 (3)	15 (4)	16 (4)	0	3 (<1)	0
抑うつ気分	10 (2)	9 (2)	7 (2)	0	0	0
神経系障害	268 (66)	216 (53)	206 (50)	49 (12)	55 (13)	61 (15)
頭痛	80 (20)	81 (20)	80 (19)	26 (6)	28 (7)	28 (7)
錯感覚	38 (9)	35 (9)	38 (9)	4 (<1)	9 (2)	12 (3)
片頭痛	15 (4)	14 (3)	16 (4)	3 (<1)	3 (<1)	7 (2)
灼熱感	5 (1)	14 (3)	16 (4)	1 (<1)	7 (2)	6 (1)
多発性硬化症再発	189 (46)	111 (27)	114 (27)	12 (3)	7 (2)	6 (1)
浮動性めまい	23 (6)	19 (5)	22 (5)	6 (1)	8 (2)	3 (<1)
異常感覚	5 (1)	11 (3)	3 (<1)	1 (<1)	6 (1)	2 (<1)
平衡障害	6 (1)	8 (2)	9 (2)	0	0	1 (<1)
感覚鈍麻	27 (7)	20 (5)	24 (6)	1 (<1)	0	1 (<1)
振戦	9 (2)	9 (2)	4 (<1)	0	2 (<1)	1 (<1)
多発性硬化症	11 (3)	3 (<1)	7 (2)	1 (<1)	0	0
筋痙直	16 (4)	10 (2)	9 (2)	2 (<1)	1 (<1)	0

NOTE 1: Numbers in parentheses are percentages.
2: Data after subjects switched to alternative MS treatment are excluded.
3: A subject was counted only once within each system organ class or preferred term.

SOURCE: BG12MS/JAPAN/ISS/T-AE-SOCPT-CAUS2-301.SAS DATE: 02DEC2015

Incidence of adverse events at least 2% higher in any treatment group by system organ class and preferred term and causal association to study drug:
Study 109MS301
Page 4 of 9

	Irrespective of causal association			Causal association cannot be ruled out		
	Placebo (N=408)	BG00012 240 mg BID (N=410)	BG00012 240 mg TID (N=416)	Placebo (N=408)	BG00012 240 mg BID (N=410)	BG00012 240 mg TID (N=416)
眼障害	23 (6)	15 (4)	17 (4)	2 (<1)	1 (<1)	1 (<1)
霧視	14 (3)	10 (2)	10 (2)	2 (<1)	1 (<1)	1 (<1)
眼痛	10 (2)	5 (1)	9 (2)	1 (<1)	0	0
耳および迷路障害	15 (4)	13 (3)	29 (7)	2 (<1)	4 (<1)	7 (2)
回転性めまい	15 (4)	13 (3)	29 (7)	2 (<1)	4 (<1)	7 (2)
血管障害	35 (9)	187 (46)	159 (38)	24 (6)	170 (41)	148 (36)
潮紅	20 (5)	154 (38)	132 (32)	18 (4)	145 (35)	129 (31)
ほてり	8 (2)	31 (8)	29 (7)	6 (1)	26 (6)	25 (6)
高血圧	12 (3)	7 (2)	9 (2)	2 (<1)	3 (<1)	0
呼吸器、胸郭および縦隔障害	38 (9)	52 (13)	43 (10)	2 (<1)	10 (2)	8 (2)
鼻漏	5 (1)	10 (2)	7 (2)	0	7 (2)	4 (<1)
咳嗽	18 (4)	22 (5)	19 (5)	1 (<1)	1 (<1)	3 (<1)
口腔咽頭痛	19 (5)	25 (6)	21 (5)	1 (<1)	2 (<1)	1 (<1)

NOTE 1: Numbers in parentheses are percentages.
2: Data after subjects switched to alternative MS treatment are excluded.
3: A subject was counted only once within each system organ class or preferred term.

SOURCE: BG12MS/JAPAN/ISS/T-AE-SOCPT-CAUS2-301.SAS DATE: 02DEC2015

Incidence of adverse events at least 2% higher in any treatment group by system organ class and preferred term and causal association to study drug:
Study 109MS301
Page 5 of 9

	Irrespective of causal association			Causal association cannot be ruled out		
	Placebo (N=408)	BG00012 240 mg BID (N=410)	BG00012 240 mg TID (N=416)	Placebo (N=408)	BG00012 240 mg BID (N=410)	BG00012 240 mg TID (N=416)
胃腸障害	147 (36)	201 (49)	206 (50)	82 (20)	138 (34)	149 (36)
下痢	55 (13)	62 (15)	78 (19)	28 (7)	38 (9)	49 (12)
悪心	38 (9)	53 (13)	54 (13)	23 (6)	40 (10)	43 (10)
上腹部痛	28 (7)	40 (10)	52 (13)	21 (5)	33 (8)	42 (10)
腹痛	22 (5)	46 (11)	37 (9)	15 (4)	29 (7)	25 (6)
嘔吐	24 (6)	40 (10)	30 (7)	7 (2)	18 (4)	22 (5)
胃腸障害	6 (1)	9 (2)	20 (5)	4 (<1)	9 (2)	17 (4)
消化不良	12 (3)	23 (6)	24 (6)	7 (2)	15 (4)	15 (4)
胃食道逆流性疾患	7 (2)	8 (2)	16 (4)	4 (<1)	4 (<1)	11 (3)
便秘	19 (5)	14 (3)	18 (4)	7 (2)	4 (<1)	9 (2)
腹部膨満	8 (2)	4 (<1)	9 (2)	5 (1)	3 (<1)	7 (2)
胃炎	6 (1)	12 (3)	11 (3)	1 (<1)	5 (1)	7 (2)
腹部不快感	9 (2)	12 (3)	8 (2)	7 (2)	9 (2)	6 (1)
口内乾燥	6 (1)	14 (3)	5 (1)	0	8 (2)	3 (<1)
歯痛	14 (3)	12 (3)	15 (4)	1 (<1)	1 (<1)	0

NOTE 1: Numbers in parentheses are percentages.
2: Data after subjects switched to alternative MS treatment are excluded.
3: A subject was counted only once within each system organ class or preferred term.

SOURCE: BG12MS/JAPAN/ISS/T-AE-SOCPT-CAUS2-301.SAS DATE: 02DEC2015

Incidence of adverse events at least 2% higher in any treatment group by
system organ class and preferred term and causal association to study drug:
Study 109MS301
Page 6 of 9

	Irrespective of causal association			Causal association cannot be ruled out		
	Placebo (N=408)	BG00012 240 mg BID (N=410)	BG00012 240 mg TID (N=416)	Placebo (N=408)	BG00012 240 mg BID (N=410)	BG00012 240 mg TID (N=416)
皮膚および皮下組織障害	60 (15)	111 (27)	109 (26)	31 (8)	86 (21)	84 (20)
紅斑	5 (1)	20 (5)	33 (8)	2 (<1)	17 (4)	28 (7)
そう痒症	19 (5)	42 (10)	34 (8)	12 (3)	34 (8)	27 (6)
発疹	13 (3)	34 (8)	27 (6)	5 (1)	22 (5)	15 (4)
多汗症	7 (2)	11 (3)	16 (4)	5 (1)	9 (2)	10 (2)
寝汗	5 (1)	11 (3)	13 (3)	2 (<1)	7 (2)	7 (2)
蕁麻疹	4 (<1)	6 (1)	9 (2)	0	5 (1)	7 (2)
脱毛症	13 (3)	7 (2)	5 (1)	8 (2)	1 (<1)	4 (<1)
アレルギー性皮膚炎	3 (<1)	9 (2)	6 (1)	1 (<1)	3 (<1)	3 (<1)
筋骨格系および結合組織障害	142 (35)	134 (33)	127 (31)	12 (3)	11 (3)	16 (4)
関節痛	39 (10)	46 (11)	37 (9)	4 (<1)	6 (1)	5 (1)
筋痙縮	20 (5)	13 (3)	27 (6)	1 (<1)	2 (<1)	4 (<1)
背部痛	57 (14)	59 (14)	46 (11)	2 (<1)	1 (<1)	3 (<1)
頚部痛	13 (3)	11 (3)	8 (2)	0	0	3 (<1)

NOTE 1: Numbers in parentheses are percentages.
2: Data after subjects switched to alternative MS treatment are excluded.
3: A subject was counted only once within each system organ class or preferred term.

SOURCE: BG12MS/JAPAN/ISS/T-AE-SOCPT-CAUS2-301.SAS DATE: 02DEC2015

Incidence of adverse events at least 2% higher in any treatment group by system organ class and preferred term and causal association to study drug:
Study 109MS301
Page 7 of 9

	Irrespective of causal association			Causal association cannot be ruled out		
	Placebo (N=408)	BG00012 240 mg BID (N=410)	BG00012 240 mg TID (N=416)	Placebo (N=408)	BG00012 240 mg BID (N=410)	BG00012 240 mg TID (N=416)
四肢痛	29 (7)	37 (9)	29 (7)	1 (<1)	2 (<1)	2 (<1)
筋力低下	26 (6)	12 (3)	14 (3)	3 (<1)	0	1 (<1)
筋肉痛	15 (4)	6 (1)	6 (1)	5 (1)	1 (<1)	1 (<1)
筋骨格痛	21 (5)	11 (3)	10 (2)	0	0	0
腎および尿路障害	68 (17)	69 (17)	80 (19)	26 (6)	37 (9)	28 (7)
蛋白尿	34 (8)	38 (9)	50 (12)	17 (4)	18 (4)	17 (4)
血尿	19 (5)	26 (6)	26 (6)	7 (2)	9 (2)	7 (2)
ケトン尿	5 (1)	5 (1)	12 (3)	2 (<1)	5 (1)	6 (1)
ミクロアルブミン尿	11 (3)	21 (5)	17 (4)	4 (<1)	11 (3)	4 (<1)
排尿困難	8 (2)	4 (<1)	9 (2)	0	1 (<1)	2 (<1)
頻尿	9 (2)	5 (1)	4 (<1)	1 (<1)	1 (<1)	1 (<1)
一般・全身障害および投与部位の状態	99 (24)	86 (21)	102 (25)	17 (4)	20 (5)	20 (5)
疲労	54 (13)	57 (14)	63 (15)	9 (2)	13 (3)	15 (4)
発熱	21 (5)	16 (4)	19 (5)	3 (<1)	1 (<1)	5 (1)

NOTE 1: Numbers in parentheses are percentages.
2: Data after subjects switched to alternative MS treatment are excluded.
3: A subject was counted only once within each system organ class or preferred term.

SOURCE: BG12MS/JAPAN/ISS/T-AE-SOCPT-CAUS2-301.SAS DATE: 02DEC2015

Incidence of adverse events at least 2% higher in any treatment group by
system organ class and preferred term and causal association to study drug:
Study 109MS301
Page 8 of 9

	Irrespective of causal association			Causal association cannot be ruled out		
	Placebo (N=408)	BG00012 240 mg BID (N=410)	BG00012 240 mg TID (N=416)	Placebo (N=408)	BG00012 240 mg BID (N=410)	BG00012 240 mg TID (N=416)
胸痛	10 (2)	8 (2)	11 (3)	0	1 (<1)	2 (<1)
無力症	8 (2)	11 (3)	10 (2)	0	3 (<1)	1 (<1)
インフルエンザ様疾患	11 (3)	8 (2)	8 (2)	4 (<1)	1 (<1)	0
末梢性浮腫	12 (3)	2 (<1)	7 (2)	4 (<1)	1 (<1)	0
臨床検査	55 (13)	76 (19)	84 (20)	27 (7)	32 (8)	47 (11)
アラニン・アミノトランスフェラーゼ増加	13 (3)	29 (7)	27 (6)	8 (2)	19 (5)	20 (5)
尿中アルブミン陽性	12 (3)	24 (6)	22 (5)	8 (2)	6 (1)	13 (3)
アスパラギン酸アミノトランスフェラーゼ増加	7 (2)	17 (4)	17 (4)	4 (<1)	10 (2)	11 (3)
尿中蛋白陽性	12 (3)	10 (2)	13 (3)	8 (2)	2 (<1)	8 (2)
γ－グルタミルトランスフェラーゼ増加	12 (3)	14 (3)	7 (2)	2 (<1)	9 (2)	7 (2)
血中副甲状腺ホルモン増加	4 (<1)	7 (2)	10 (2)	2 (<1)	2 (<1)	5 (1)
尿中血陽性	3 (<1)	6 (1)	10 (2)	1 (<1)	1 (<1)	5 (1)

NOTE 1: Numbers in parentheses are percentages.
2: Data after subjects switched to alternative MS treatment are excluded.
3: A subject was counted only once within each system organ class or preferred term.

SOURCE: BG12MS/JAPAN/ISS/T-AE-SOCPT-CAUS2-301.SAS DATE: 02DEC2015

Incidence of adverse events at least 2% higher in any treatment group by system organ class and preferred term and causal association to study drug:
Study 109MS301
Page 9 of 9

	Irrespective of causal association			Causal association cannot be ruled out		
	Placebo (N=408)	BG00012 240 mg BID (N=410)	BG00012 240 mg TID (N=416)	Placebo (N=408)	BG00012 240 mg BID (N=410)	BG00012 240 mg TID (N=416)
血中ブドウ糖増加	4 (<1)	6 (1)	10 (2)	1 (<1)	0	2 (<1)
尿中白血球陽性	7 (2)	11 (3)	11 (3)	0	2 (<1)	1 (<1)
白血球数増加	9 (2)	2 (<1)	2 (<1)	1 (<1)	1 (<1)	0
傷害、中毒および処置合併症	35 (9)	22 (5)	31 (7)	2 (<1)	0	0
挫傷	11 (3)	11 (3)	18 (4)	1 (<1)	0	0
転倒	11 (3)	13 (3)	9 (2)	1 (<1)	0	0
関節捻挫	13 (3)	5 (1)	7 (2)	0	0	0

NOTE 1: Numbers in parentheses are percentages.
2: Data after subjects switched to alternative MS treatment are excluded.
3: A subject was counted only once within each system organ class or preferred term.

SOURCE: BG12MS/JAPAN/ISS/T-AE-SOCPT-CAUS2-301.SAS DATE: 02DEC2015

Table 315: Incidence of Adverse Events At Least 2% Higher in Any Treatment Group by System Organ Class and Preferred Term and Causal Association to Study Drug: Study 109MS302

Incidence of adverse events at least 2% higher in any treatment group by
system organ class and preferred term and causal association to study drug:
Study 109MS302
Page 1 of 16

	Irrespective of causal association			
	Placebo (N=363)	BG00012 240 mg BID (N=359)	BG00012 240 mg TID (N=344)	GA (N=351)
Number of subjects with an event	333 (92)	338 (94)	316 (92)	304 (87)
感染症および寄生虫症	165 (45)	175 (49)	178 (52)	149 (42)
鼻咽頭炎	58 (16)	62 (17)	63 (18)	51 (15)
尿路感染	42 (12)	52 (14)	41 (12)	46 (13)
インフルエンザ	22 (6)	20 (6)	25 (7)	15 (4)
上気道感染	34 (9)	36 (10)	47 (14)	27 (8)
ウイルス性胃腸炎	8 (2)	9 (3)	13 (4)	6 (2)
口腔ヘルペス	12 (3)	9 (3)	5 (1)	6 (2)
気道感染	9 (2)	6 (2)	10 (3)	9 (3)
外陰腟真菌感染	5 (1)	2 (<1)	9 (3)	5 (1)
胃腸炎	7 (2)	14 (4)	13 (4)	5 (1)
副鼻腔炎	11 (3)	18 (5)	18 (5)	11 (3)
気管支炎	14 (4)	14 (4)	22 (6)	16 (5)
膀胱炎	8 (2)	5 (1)	3 (<1)	5 (1)

NOTE 1: Numbers in parentheses are percentages.
2: Data after subjects switched to alternative MS treatment are excluded.
3: A subject was counted only once within each system organ class or preferred term.

SOURCE: BG12MS/JAPAN/ISS/T-AE-SOCPT-CAUS2-302.SAS

DATE: 02DEC2015

Incidence of adverse events at least 2% higher in any treatment group by
system organ class and preferred term and causal association to study drug:
Study 109MS302
Page 2 of 16

	Causal association cannot be ruled out			
	Placebo (N=363)	BG00012 240 mg BID (N=359)	BG00012 240 mg TID (N=344)	GA (N=351)
Number of subjects with an event	146 (40)	236 (66)	234 (68)	152 (43)
感染症および寄生虫症	24 (7)	27 (8)	24 (7)	16 (5)
鼻咽頭炎	7 (2)	7 (2)	8 (2)	5 (1)
尿路感染	8 (2)	8 (2)	5 (1)	4 (1)
インフルエンザ	2 (<1)	1 (<1)	3 (<1)	1 (<1)
上気道感染	1 (<1)	4 (1)	3 (<1)	2 (<1)
ウイルス性胃腸炎	1 (<1)	1 (<1)	2 (<1)	0
口腔ヘルペス	2 (<1)	5 (1)	2 (<1)	0
気道感染	0	0	2 (<1)	0
外陰腟真菌感染	1 (<1)	1 (<1)	2 (<1)	0
胃腸炎	3 (<1)	1 (<1)	1 (<1)	1 (<1)
副鼻腔炎	3 (<1)	0	1 (<1)	0
気管支炎	2 (<1)	2 (<1)	0	0
膀胱炎	0	0	0	0

NOTE 1: Numbers in parentheses are percentages.
2: Data after subjects switched to alternative MS treatment are excluded.
3: A subject was counted only once within each system organ class or preferred term.

SOURCE: BG12MS/JAPAN/ISS/T-AE-SOCPT-CAUS2-302.SAS

DATE: 02DEC2015

Incidence of adverse events at least 2% higher in any treatment group by
system organ class and preferred term and causal association to study drug:
Study 109MS302
Page 3 of 16

	Irrespective of causal association			
	Placebo (N=363)	BG00012 240 mg BID (N=359)	BG00012 240 mg TID (N=344)	GA (N=351)
耳感染	4 (1)	3 (<1)	9 (3)	2 (<1)
咽頭炎	13 (4)	13 (4)	11 (3)	14 (4)
鼻炎	7 (2)	14 (4)	7 (2)	8 (2)
血液およびリンパ系障害	9 (2)	7 (2)	13 (4)	4 (1)
貧血	9 (2)	7 (2)	13 (4)	4 (1)
精神障害	55 (15)	45 (13)	32 (9)	48 (14)
うつ病	35 (10)	24 (7)	15 (4)	30 (9)
不安	14 (4)	16 (4)	10 (3)	7 (2)
不眠症	18 (5)	15 (4)	10 (3)	13 (4)
神経系障害	210 (58)	158 (44)	144 (42)	156 (44)
頭痛	49 (13)	52 (14)	46 (13)	46 (13)
多発性硬化症再発	155 (43)	110 (31)	85 (25)	119 (34)
灼熱感	8 (2)	7 (2)	9 (3)	0
浮動性めまい	15 (4)	14 (4)	8 (2)	9 (3)
錯感覚	31 (9)	21 (6)	21 (6)	15 (4)

NOTE 1: Numbers in parentheses are percentages.
2: Data after subjects switched to alternative MS treatment are excluded.
3: A subject was counted only once within each system organ class or preferred term.

SOURCE: BG12MS/JAPAN/ISS/T-AE-SOCPT-CAUS2-302.SAS DATE: 02DEC2015

Incidence of adverse events at least 2% higher in any treatment group by
system organ class and preferred term and causal association to study drug:
Study 109MS302
Page 4 of 16

	Causal association cannot be ruled out			
	Placebo (N=363)	BG00012 240 mg BID (N=359)	BG00012 240 mg TID (N=344)	GA (N=351)
耳感染	0	0	0	0
咽頭炎	0	1 (<1)	0	2 (<1)
鼻炎	0	2 (<1)	0	2 (<1)
血液およびリンパ系障害	0	1 (<1)	2 (<1)	1 (<1)
貧血	0	1 (<1)	2 (<1)	1 (<1)
精神障害	5 (1)	7 (2)	7 (2)	4 (1)
うつ病	2 (<1)	4 (1)	3 (<1)	2 (<1)
不安	1 (<1)	3 (<1)	2 (<1)	1 (<1)
不眠症	2 (<1)	2 (<1)	2 (<1)	1 (<1)
神経系障害	29 (8)	33 (9)	26 (8)	15 (4)
頭痛	15 (4)	19 (5)	13 (4)	7 (2)
多発性硬化症再発	11 (3)	8 (2)	5 (1)	4 (1)
灼熱感	2 (<1)	4 (1)	4 (1)	0
浮動性めまい	4 (1)	4 (1)	4 (1)	4 (1)
錯感覚	1 (<1)	1 (<1)	4 (1)	1 (<1)

NOTE 1: Numbers in parentheses are percentages.
2: Data after subjects switched to alternative MS treatment are excluded.
3: A subject was counted only once within each system organ class or preferred term.

SOURCE: BG12MS/JAPAN/ISS/T-AE-SOCPT-CAUS2-302.SAS DATE: 02DEC2015

Incidence of adverse events at least 2% higher in any treatment group by
system organ class and preferred term and causal association to study drug:
Study 109MS302
Page 5 of 16

	Irrespective of causal association			
	Placebo (N=363)	BG00012 240 mg BID (N=359)	BG00012 240 mg TID (N=344)	GA (N=351)
感覚鈍麻	21 (6)	11 (3)	19 (6)	16 (5)
筋痙直	11 (3)	7 (2)	7 (2)	7 (2)
眼障害	23 (6)	18 (5)	19 (6)	17 (5)
眼痛	4 (1)	8 (2)	7 (2)	6 (2)
霧視	7 (2)	3 (<1)	8 (2)	6 (2)
視力低下	10 (3)	1 (<1)	1 (<1)	4 (1)
結膜炎	3 (<1)	8 (2)	5 (1)	3 (<1)
耳および迷路障害	22 (6)	9 (3)	13 (4)	15 (4)
回転性めまい	22 (6)	9 (3)	13 (4)	15 (4)
血管障害	31 (9)	125 (35)	104 (30)	21 (6)
潮紅	13 (4)	110 (31)	83 (24)	6 (2)
ほてり	8 (2)	18 (5)	19 (6)	4 (1)
高血圧	12 (3)	5 (1)	11 (3)	13 (4)

NOTE 1: Numbers in parentheses are percentages.
2: Data after subjects switched to alternative MS treatment are excluded.
3: A subject was counted only once within each system organ class or preferred term.

SOURCE: BG12MS/JAPAN/ISS/T-AE-SOCPT-CAUS2-302.SAS DATE: 02DEC2015

Incidence of adverse events at least 2% higher in any treatment group by
system organ class and preferred term and causal association to study drug:
Study 109MS302
Page 6 of 16

	Causal association cannot be ruled out			
	Placebo (N=363)	BG00012 240 mg BID (N=359)	BG00012 240 mg TID (N=344)	GA (N=351)
感覚鈍麻	1 (<1)	1 (<1)	1 (<1)	2 (<1)
筋痙直	0	0	0	0
眼障害	3 (<1)	1 (<1)	2 (<1)	2 (<1)
眼痛	0	0	1 (<1)	1 (<1)
霧視	2 (<1)	0	1 (<1)	0
視力低下	1 (<1)	0	1 (<1)	1 (<1)
結膜炎	0	1 (<1)	0	1 (<1)
耳および迷路障害	3 (<1)	4 (1)	1 (<1)	1 (<1)
回転性めまい	3 (<1)	4 (1)	1 (<1)	1 (<1)
血管障害	18 (5)	120 (33)	89 (26)	7 (2)
潮紅	11 (3)	107 (30)	79 (23)	6 (2)
ほてり	5 (1)	16 (4)	16 (5)	2 (<1)
高血圧	2 (<1)	1 (<1)	1 (<1)	0

NOTE 1: Numbers in parentheses are percentages.
2: Data after subjects switched to alternative MS treatment are excluded.
3: A subject was counted only once within each system organ class or preferred term.

SOURCE: BG12MS/JAPAN/ISS/T-AE-SOCPT-CAUS2-302.SAS DATE: 02DEC2015

Incidence of adverse events at least 2% higher in any treatment group by
system organ class and preferred term and causal association to study drug:
Study 109MS302
Page 7 of 16

	Irrespective of causal association			
	Placebo (N=363)	BG00012 240 mg BID (N=359)	BG00012 240 mg TID (N=344)	GA (N=351)
呼吸器、胸郭および縦隔障害	26 (7)	24 (7)	35 (10)	23 (7)
咳嗽	17 (5)	16 (4)	18 (5)	9 (3)
口腔咽頭痛	14 (4)	12 (3)	21 (6)	15 (4)
胃腸障害	95 (26)	136 (38)	147 (43)	52 (15)
悪心	29 (8)	40 (11)	51 (15)	15 (4)
下痢	28 (8)	45 (13)	50 (15)	14 (4)
上腹部痛	17 (5)	36 (10)	33 (10)	4 (1)
腹痛	15 (4)	27 (8)	26 (8)	4 (1)
嘔吐	13 (4)	25 (7)	23 (7)	8 (2)
胃腸障害	2 (<1)	9 (3)	14 (4)	2 (<1)
消化不良	8 (2)	12 (3)	16 (5)	6 (2)
胃炎	5 (1)	10 (3)	9 (3)	4 (1)
便秘	14 (4)	9 (3)	11 (3)	9 (3)
歯痛	5 (1)	6 (2)	11 (3)	4 (1)
皮膚および皮下組織障害	33 (9)	64 (18)	70 (20)	27 (8)

NOTE 1: Numbers in parentheses are percentages.
2: Data after subjects switched to alternative MS treatment are excluded.
3: A subject was counted only once within each system organ class or preferred term.

SOURCE: BG12MS/JAPAN/ISS/T-AE-SOCPT-CAUS2-302.SAS DATE: 02DEC2015

Incidence of adverse events at least 2% higher in any treatment group by
system organ class and preferred term and causal association to study drug:
Study 109MS302
Page 8 of 16

	Causal association cannot be ruled out			
	Placebo (N=363)	BG00012 240 mg BID (N=359)	BG00012 240 mg TID (N=344)	GA (N=351)
呼吸器、胸郭および縦隔障害	1 (<1)	3 (<1)	3 (<1)	2 (<1)
咳嗽	1 (<1)	3 (<1)	2 (<1)	0
口腔咽頭痛	0	0	1 (<1)	2 (<1)
胃腸障害	41 (11)	92 (26)	101 (29)	12 (3)
悪心	19 (5)	33 (9)	40 (12)	7 (2)
下痢	10 (3)	26 (7)	33 (10)	1 (<1)
上腹部痛	9 (2)	29 (8)	27 (8)	2 (<1)
腹痛	7 (2)	19 (5)	17 (5)	1 (<1)
嘔吐	3 (<1)	14 (4)	15 (4)	2 (<1)
胃腸障害	2 (<1)	8 (2)	13 (4)	0
消化不良	3 (<1)	7 (2)	7 (2)	0
胃炎	2 (<1)	6 (2)	4 (1)	1 (<1)
便秘	1 (<1)	5 (1)	2 (<1)	0
歯痛	0	0	0	0
皮膚および皮下組織障害	14 (4)	53 (15)	50 (15)	13 (4)

NOTE 1: Numbers in parentheses are percentages.
2: Data after subjects switched to alternative MS treatment are excluded.
3: A subject was counted only once within each system organ class or preferred term.

SOURCE: BG12MS/JAPAN/ISS/T-AE-SOCPT-CAUS2-302.SAS DATE: 02DEC2015

Incidence of adverse events at least 2% higher in any treatment group by
system organ class and preferred term and causal association to study drug:
Study 109MS302
Page 9 of 16

	Irrespective of causal association			
	Placebo (N=363)	BG00012 240 mg BID (N=359)	BG00012 240 mg TID (N=344)	GA (N=351)
そう痒症	11 (3)	20 (6)	24 (7)	7 (2)
紅斑	5 (1)	16 (4)	21 (6)	6 (2)
発疹	13 (4)	24 (7)	28 (8)	8 (2)
多汗症	3 (<1)	6 (2)	10 (3)	5 (1)
脱毛症	6 (2)	10 (3)	6 (2)	7 (2)
筋骨格系および結合組織障害	93 (26)	85 (24)	95 (28)	72 (21)
筋肉痛	11 (3)	7 (2)	7 (2)	4 (1)
四肢痛	29 (8)	21 (6)	26 (8)	21 (6)
関節痛	26 (7)	20 (6)	27 (8)	17 (5)
背部痛	33 (9)	35 (10)	36 (10)	32 (9)
筋痙縮	14 (4)	13 (4)	21 (6)	8 (2)
筋力低下	10 (3)	6 (2)	10 (3)	6 (2)
筋骨格痛	5 (1)	3 (<1)	11 (3)	8 (2)
筋骨格硬直	5 (1)	1 (<1)	0	9 (3)
頚部痛	9 (2)	16 (4)	12 (3)	5 (1)

NOTE 1: Numbers in parentheses are percentages.
2: Data after subjects switched to alternative MS treatment are excluded.
3: A subject was counted only once within each system organ class or preferred term.

SOURCE: BG12MS/JAPAN/ISS/T-AE-SOCPT-CAUS2-302.SAS DATE: 02DEC2015

Incidence of adverse events at least 2% higher in any treatment group by
system organ class and preferred term and causal association to study drug:
Study 109MS302
Page 10 of 16

	Causal association cannot be ruled out			
	Placebo (N=363)	BG00012 240 mg BID (N=359)	BG00012 240 mg TID (N=344)	GA (N=351)
そう痒症	6 (2)	18 (5)	19 (6)	3 (<1)
紅斑	2 (<1)	14 (4)	18 (5)	5 (1)
発疹	5 (1)	19 (5)	18 (5)	3 (<1)
多汗症	1 (<1)	5 (1)	7 (2)	3 (<1)
脱毛症	1 (<1)	7 (2)	1 (<1)	1 (<1)
筋骨格系および結合組織障害	8 (2)	8 (2)	12 (3)	5 (1)
筋肉痛	3 (<1)	1 (<1)	4 (1)	1 (<1)
四肢痛	2 (<1)	2 (<1)	3 (<1)	0
関節痛	1 (<1)	1 (<1)	2 (<1)	0
背部痛	1 (<1)	1 (<1)	2 (<1)	2 (<1)
筋痙縮	2 (<1)	3 (<1)	2 (<1)	1 (<1)
筋力低下	0	0	1 (<1)	1 (<1)
筋骨格痛	1 (<1)	0	0	0
筋骨格硬直	1 (<1)	0	0	1 (<1)
頚部痛	0	2 (<1)	0	1 (<1)

NOTE 1: Numbers in parentheses are percentages.
2: Data after subjects switched to alternative MS treatment are excluded.
3: A subject was counted only once within each system organ class or preferred term.

SOURCE: BG12MS/JAPAN/ISS/T-AE-SOCPT-CAUS2-302.SAS DATE: 02DEC2015

Incidence of adverse events at least 2% higher in any treatment group by
system organ class and preferred term and causal association to study drug:
Study 109MS302
Page 11 of 16

	Irrespective of causal association			
	Placebo (N=363)	BG00012 240 mg BID (N=359)	BG00012 240 mg TID (N=344)	GA (N=351)
腎および尿路障害	44 (12)	40 (11)	52 (15)	44 (13)
蛋白尿	25 (7)	29 (8)	35 (10)	30 (9)
ミクロアルブミン尿	13 (4)	14 (4)	19 (6)	15 (4)
血尿	15 (4)	7 (2)	15 (4)	10 (3)
一般・全身障害および投与部位の状態	67 (18)	64 (18)	71 (21)	104 (30)
疲労	33 (9)	37 (10)	33 (10)	30 (9)
インフルエンザ様疾患	0	2 (<1)	7 (2)	3 (<1)
無力症	12 (3)	13 (4)	7 (2)	15 (4)
疼痛	4 (1)	8 (2)	7 (2)	5 (1)
発熱	19 (5)	11 (3)	25 (7)	17 (5)
注射部位紅斑	0	0	0	31 (9)
注射部位疼痛	0	0	0	29 (8)
注射部位そう痒感	0	0	0	13 (4)
注射部位腫脹	0	0	0	10 (3)
末梢性浮腫	7 (2)	5 (1)	9 (3)	4 (1)

NOTE 1: Numbers in parentheses are percentages.
2: Data after subjects switched to alternative MS treatment are excluded.
3: A subject was counted only once within each system organ class or preferred term.

SOURCE: BG12MS/JAPAN/ISS/T-AE-SOCPT-CAUS2-302.SAS DATE: 02DEC2015

Incidence of adverse events at least 2% higher in any treatment group by
system organ class and preferred term and causal association to study drug:
Study 109MS302
Page 12 of 16

	Causal association cannot be ruled out			
	Placebo (N=363)	BG00012 240 mg BID (N=359)	BG00012 240 mg TID (N=344)	GA (N=351)
腎および尿路障害	18 (5)	18 (5)	27 (8)	9 (3)
蛋白尿	10 (3)	12 (3)	18 (5)	5 (1)
ミクロアルブミン尿	5 (1)	8 (2)	10 (3)	3 (<1)
血尿	5 (1)	2 (<1)	5 (1)	2 (<1)
一般・全身障害および投与部位の状態	11 (3)	21 (6)	16 (5)	71 (20)
疲労	8 (2)	13 (4)	8 (2)	6 (2)
インフルエンザ様疾患	0	0	4 (1)	2 (<1)
無力症	3 (<1)	6 (2)	3 (<1)	5 (1)
疼痛	0	1 (<1)	1 (<1)	3 (<1)
発熱	0	1 (<1)	1 (<1)	6 (2)
注射部位紅斑	0	0	0	30 (9)
注射部位疼痛	0	0	0	27 (8)
注射部位そう痒感	0	0	0	13 (4)
注射部位腫脹	0	0	0	10 (3)
末梢性浮腫	1 (<1)	2 (<1)	0	1 (<1)

NOTE 1: Numbers in parentheses are percentages.
2: Data after subjects switched to alternative MS treatment are excluded.
3: A subject was counted only once within each system organ class or preferred term.

SOURCE: BG12MS/JAPAN/ISS/T-AE-SOCPT-CAUS2-302.SAS DATE: 02DEC2015

Incidence of adverse events at least 2% higher in any treatment group by
system organ class and preferred term and causal association to study drug:
Study 109MS302
Page 13 of 16

	Irrespective of causal association			
	Placebo (N=363)	BG00012 240 mg BID (N=359)	BG00012 240 mg TID (N=344)	GA (N=351)
臨床検査	60 (17)	67 (19)	64 (19)	66 (19)
アラニン・アミノトランスフェラーゼ増加	25 (7)	16 (4)	22 (6)	20 (6)
アスパラギン酸アミノトランスフェラーゼ増加	11 (3)	16 (4)	12 (3)	14 (4)
尿中アルブミン陽性	15 (4)	22 (6)	14 (4)	18 (5)
尿中β２ミクログロブリン増加	11 (3)	7 (2)	9 (3)	5 (1)
白血球数減少	0	9 (3)	7 (2)	1 (<1)
尿中蛋白陽性	10 (3)	18 (5)	7 (2)	15 (4)
血中副甲状腺ホルモン増加	2 (<1)	8 (2)	7 (2)	2 (<1)
尿中血陽性	4 (1)	10 (3)	8 (2)	4 (1)
γ－グルタミルトランスフェラーゼ増加	7 (2)	6 (2)	5 (1)	8 (2)
血中ブドウ糖増加	3 (<1)	4 (1)	8 (2)	7 (2)

NOTE 1: Numbers in parentheses are percentages.
2: Data after subjects switched to alternative MS treatment are excluded.
3: A subject was counted only once within each system organ class or preferred term.

SOURCE: BG12MS/JAPAN/ISS/T-AE-SOCPT-CAUS2-302.SAS DATE: 02DEC2015

Incidence of adverse events at least 2% higher in any treatment group by
system organ class and preferred term and causal association to study drug:
Study 109MS302
Page 14 of 16

	Causal association cannot be ruled out			
	Placebo (N=363)	BG00012 240 mg BID (N=359)	BG00012 240 mg TID (N=344)	GA (N=351)
臨床検査	29 (8)	33 (9)	33 (10)	20 (6)
アラニン・アミノトランスフェラーゼ増加	17 (5)	9 (3)	14 (4)	10 (3)
アスパラギン酸アミノトランスフェラーゼ増加	5 (1)	8 (2)	7 (2)	9 (3)
尿中アルブミン陽性	4 (1)	11 (3)	6 (2)	5 (1)
尿中β２ミクログロブリン増加	4 (1)	3 (<1)	6 (2)	1 (<1)
白血球数減少	0	5 (1)	6 (2)	1 (<1)
尿中蛋白陽性	4 (1)	7 (2)	4 (1)	2 (<1)
血中副甲状腺ホルモン増加	1 (<1)	2 (<1)	2 (<1)	0
尿中血陽性	1 (<1)	4 (1)	2 (<1)	0
γ－グルタミルトランスフェラーゼ増加	5 (1)	3 (<1)	2 (<1)	3 (<1)
血中ブドウ糖増加	1 (<1)	1 (<1)	0	0

NOTE 1: Numbers in parentheses are percentages.
2: Data after subjects switched to alternative MS treatment are excluded.
3: A subject was counted only once within each system organ class or preferred term.

SOURCE: BG12MS/JAPAN/ISS/T-AE-SOCPT-CAUS2-302.SAS DATE: 02DEC2015

Incidence of adverse events at least 2% higher in any treatment group by
system organ class and preferred term and causal association to study drug:
Study 109MS302
Page 15 of 16

	Irrespective of causal association			
	Placebo (N=363)	BG00012 240 mg BID (N=359)	BG00012 240 mg TID (N=344)	GA (N=351)
尿中白血球陽性	6 (2)	3 (<1)	4 (1)	9 (3)
傷害、中毒および処置合併症	19 (5)	22 (6)	22 (6)	17 (5)
挫傷	8 (2)	10 (3)	7 (2)	5 (1)
転倒	11 (3)	9 (3)	13 (4)	14 (4)
関節捻挫	3 (<1)	8 (2)	6 (2)	3 (<1)

NOTE 1: Numbers in parentheses are percentages.
2: Data after subjects switched to alternative MS treatment are excluded.
3: A subject was counted only once within each system organ class or preferred term.

SOURCE: BG12MS/JAPAN/ISS/T-AE-SOCPT-CAUS2-302.SAS DATE: 02DEC2015

Incidence of adverse events at least 2% higher in any treatment group by
system organ class and preferred term and causal association to study drug:
Study 109MS302
Page 16 of 16

	Causal association cannot be ruled out			
	Placebo (N=363)	BG00012 240 mg BID (N=359)	BG00012 240 mg TID (N=344)	GA (N=351)
尿中白血球陽性	0	0	0	0
傷害、中毒および処置合併症	1 (<1)	0	0	0
挫傷	1 (<1)	0	0	0
転倒	0	0	0	0
関節捻挫	0	0	0	0

NOTE 1: Numbers in parentheses are percentages.
2: Data after subjects switched to alternative MS treatment are excluded.
3: A subject was counted only once within each system organ class or preferred term.

SOURCE: BG12MS/JAPAN/ISS/T-AE-SOCPT-CAUS2-302.SAS DATE: 02DEC2015

Table 317: Incidence of Adverse Events At Least 2% Higher in Any Treatment Group by System Organ Class and Preferred Term and Causal Association to Study Drug - Part I (Placebo-controlled period) (PMDA specific requirements)

Incidence of adverse events with an incidence of >=2% in any treatment group by system organ class
and preferred term and causal association to study drug
-Part I (Placebo-controlled period) (PMDA specific requirements)
Page 1 of 4

	Irrespective of causal association		Causal association cannot be ruled out	
	Placebo (N=113)	BG00012 240 mg BID (N=111)	Placebo (N=113)	BG00012 240 mg BID (N=111)
Number of subjects with an event	87 (77)	96 (86)	30 (27)	62 (56)
感染症および寄生虫症	39 (35)	38 (34)	2 (2)	2 (2)
鼻咽頭炎	28 (25)	26 (23)	2 (2)	0
上気道感染	11 (10)	5 (5)	0	0
胃腸炎	0	4 (4)	0	1 (<1)
咽頭炎	1 (<1)	3 (3)	0	0
尿路感染	1 (<1)	3 (3)	0	1 (<1)
精神障害	4 (4)	3 (3)	1 (<1)	0
不眠症	4 (4)	3 (3)	1 (<1)	0
神経系障害	38 (34)	29 (26)	3 (3)	4 (4)
多発性硬化症再発	35 (31)	25 (23)	2 (2)	1 (<1)
頭痛	2 (2)	4 (4)	0	1 (<1)
浮動性めまい	1 (<1)	3 (3)	0	2 (2)
感覚鈍麻	0	3 (3)	0	0

NOTE 1: Numbers in parentheses are percentages.
2: Data after subjects switched to alternative MS medications are excluded.
3: A subject was counted only once within each system organ class or preferred term.

SOURCE: BG12MS/109MS305/PART1/T-AE-SOCPT-CAUS2.SAS DATE: 06OCT2015

Incidence of adverse events with an incidence of >=2% in any treatment group by system organ class
and preferred term and causal association to study drug
-Part I (Placebo-controlled period) (PMDA specific requirements)
Page 2 of 4

	Irrespective of causal association		Causal association cannot be ruled out	
	Placebo (N=113)	BG00012 240 mg BID (N=111)	Placebo (N=113)	BG00012 240 mg BID (N=111)
傾眠	5 (4)	0	1 (<1)	0
血管障害	10 (9)	30 (27)	9 (8)	28 (25)
潮紅	9 (8)	24 (22)	8 (7)	23 (21)
ほてり	1 (<1)	7 (6)	1 (<1)	6 (5)
胃腸障害	21 (19)	36 (32)	11 (10)	25 (23)
悪心	6 (5)	11 (10)	3 (3)	7 (6)
下痢	6 (5)	11 (10)	1 (<1)	10 (9)
腹痛	0	8 (7)	0	7 (6)
上腹部痛	6 (5)	5 (5)	4 (4)	4 (4)
嘔吐	0	5 (5)	0	4 (4)
便秘	0	3 (3)	0	0
消化不良	3 (3)	2 (2)	2 (2)	1 (<1)
齲歯	3 (3)	1 (<1)	0	0
口内炎	3 (3)	0	3 (3)	0
皮膚および皮下組織障害	5 (4)	13 (12)	1 (<1)	10 (9)

NOTE 1: Numbers in parentheses are percentages.
2: Data after subjects switched to alternative MS medications are excluded.
3: A subject was counted only once within each system organ class or preferred term.

SOURCE: BG12MS/109MS305/PART1/T-AE-SOCPT-CAUS2.SAS DATE: 06OCT2015

Incidence of adverse events with an incidence of >=2% in any treatment group by system organ class
and preferred term and causal association to study drug
-Part I (Placebo-controlled period) (PMDA specific requirements)
Page 3 of 4

	Irrespective of causal association		Causal association cannot be ruled out	
	Placebo (N=113)	BG00012 240 mg BID (N=111)	Placebo (N=113)	BG00012 240 mg BID (N=111)
そう痒症	2 (2)	8 (7)	0	6 (5)
紅斑	0	4 (4)	0	3 (3)
発疹	0	3 (3)	0	3 (3)
蕁麻疹	3 (3)	2 (2)	1 (<1)	1 (<1)
筋骨格系および結合組織障害	8 (7)	4 (4)	0	0
背部痛	3 (3)	3 (3)	0	0
関節痛	5 (4)	1 (<1)	0	0
腎および尿路障害	3 (3)	4 (4)	0	2 (2)
蛋白尿	0	3 (3)	0	1 (<1)
ミクロアルブミン尿	0	3 (3)	0	2 (2)
排尿困難	3 (3)	0	0	0
一般・全身障害および投与部位の状態	5 (4)	2 (2)	0	1 (<1)
発熱	5 (4)	2 (2)	0	1 (<1)

NOTE 1: Numbers in parentheses are percentages.
2: Data after subjects switched to alternative MS medications are excluded.
3: A subject was counted only once within each system organ class or preferred term.

SOURCE: BG12MS/109MS305/PART1/T-AE-SOCPT-CAUS2.SAS DATE: 06OCT2015

Incidence of adverse events with an incidence of >=2% in any treatment group by system organ class
and preferred term and causal association to study drug
-Part I (Placebo-controlled period) (PMDA specific requirements)
Page 4 of 4

	Irrespective of causal association		Causal association cannot be ruled out	
	Placebo (N=113)	BG00012 240 mg BID (N=111)	Placebo (N=113)	BG00012 240 mg BID (N=111)
臨床検査	2 (2)	7 (6)	1 (<1)	6 (5)
アラニン・アミノトランスフェラーゼ増加	2 (2)	7 (6)	1 (<1)	6 (5)
アスパラギン酸アミノトランスフェラーゼ増加	1 (<1)	4 (4)	0	4 (4)

NOTE 1: Numbers in parentheses are percentages.
2: Data after subjects switched to alternative MS medications are excluded.
3: A subject was counted only once within each system organ class or preferred term.

SOURCE: BG12MS/109MS305/PART1/T-AE-SOCPT-CAUS2.SAS DATE: 06OCT2015

9.11. Incidence of Adverse Events At Least 2% Higher for Any Treatment Group and the Entire Study Period by Preferred Term and Interval: Studies C-1900, 109MS301, 109MS302, 109MS303, 109MS305

Table 320: Incidence of Adverse Events At Least 2% Higher for Any Treatment Group and the Entire Study Period by Preferred Term and 3-Months Interval: Study 109MS301

Incidence of adverse events at least 2% higher for any treatment group and the entire study period by preferred term and 3-months interval: Study 109MS301

Page 1 of 48

	Placebo				
	0-3 months	>3-6 months	>6-9 months	>9-12 months	>12-15 months
Number of subjects followed in the interval	408 (100)	394 (100)	373 (100)	351 (100)	324 (100)
Number of subjects with an event	287 (70)	238 (60)	221 (59)	199 (57)	172 (53)
Number of subjects with deaths	0	0	0	0	0
Number of subjects with SAEs other than deaths	13 (3)	16 (4)	21 (6)	19 (5)	10 (3)
Number of subjects who discontinued	8 (2)	5 (1)	1 (<1)	2 (<1)	3 (<1)
潮紅	16 (4)	1 (<1)	2 (<1)	2 (<1)	0
多発性硬化症再発	47 (12)	40 (10)	43 (12)	40 (11)	33 (10)
鼻咽頭炎	31 (8)	19 (5)	19 (5)	19 (5)	26 (8)
頭痛	47 (12)	11 (3)	15 (4)	10 (3)	12 (4)
下痢	25 (6)	7 (2)	11 (3)	6 (2)	6 (2)
疲労	18 (4)	12 (3)	9 (2)	5 (1)	4 (1)
上気道感染	18 (4)	10 (3)	10 (3)	5 (1)	9 (3)
尿路感染	13 (3)	15 (4)	6 (2)	7 (2)	9 (3)
悪心	27 (7)	3 (<1)	5 (1)	3 (<1)	2 (<1)

NOTE 1: Numbers in parentheses are percentages.
2: Data after subjects switched to alternative MS treatment are excluded.
3: A subject was counted only once within each interval for each preferred term.
4: Preferred terms are presented by decreasing order of incidence in overall Total BG00012.

SOURCE: BG12MS/JAPAN/ISS/T-AE-PT-2PCT-3MON-301.SAS DATE: 02DEC2015

Incidence of adverse events at least 2% higher for any treatment group and the entire study period by preferred term and 3-months interval: Study 109MS301
Page 2 of 48

	Placebo			
	>15-18 months	>18-21 months	>21-24 months	>24 months
Number of subjects followed in the interval	303 (100)	286 (100)	281 (100)	203 (100)
Number of subjects with an event	171 (56)	165 (58)	145 (52)	26 (13)
Number of subjects with deaths	0	0	0	0
Number of subjects with SAEs other than deaths	13 (4)	7 (2)	17 (6)	0
Number of subjects who discontinued	2 (<1)	1 (<1)	1 (<1)	0
潮紅	1 (<1)	1 (<1)	1 (<1)	0
多発性硬化症再発	30 (10)	27 (9)	22 (8)	2 (<1)
鼻咽頭炎	23 (8)	16 (6)	13 (5)	2 (<1)
頭痛	9 (3)	6 (2)	6 (2)	2 (<1)
下痢	6 (2)	4 (1)	5 (2)	2 (<1)
疲労	6 (2)	7 (2)	5 (2)	0
上気道感染	8 (3)	3 (1)	8 (3)	1 (<1)
尿路感染	6 (2)	13 (5)	11 (4)	0
悪心	3 (<1)	1 (<1)	6 (2)	0

NOTE 1: Numbers in parentheses are percentages.
2: Data after subjects switched to alternative MS treatment are excluded.
3: A subject was counted only once within each interval for each preferred term.
4: Preferred terms are presented by decreasing order of incidence in overall Total BG00012.

SOURCE: BG12MS/JAPAN/ISS/T-AE-PT-2PCT-3MON-301.SAS DATE: 02DEC2015

Incidence of adverse events at least 2% higher for any treatment group and the entire study period by preferred term and 3-months interval: Study 109MS301
Page 3 of 48

	Placebo				
	0-3 months	>3-6 months	>6-9 months	>9-12 months	>12-15 months
背部痛	12 (3)	12 (3)	10 (3)	7 (2)	6 (2)
上腹部痛	16 (4)	2 (<1)	2 (<1)	3 (<1)	0
蛋白尿	11 (3)	13 (3)	6 (2)	4 (1)	5 (2)
腹痛	14 (3)	4 (1)	5 (1)	3 (<1)	1 (<1)
関節痛	10 (2)	10 (3)	10 (3)	2 (<1)	4 (1)
インフルエンザ	11 (3)	8 (2)	7 (2)	10 (3)	5 (2)
そう痒症	10 (2)	1 (<1)	4 (1)	0	2 (<1)
錯感覚	7 (2)	7 (2)	3 (<1)	8 (2)	4 (1)
嘔吐	10 (2)	2 (<1)	4 (1)	2 (<1)	1 (<1)
四肢痛	12 (3)	7 (2)	5 (1)	4 (1)	1 (<1)
うつ病	7 (2)	9 (2)	4 (1)	2 (<1)	1 (<1)
発疹	8 (2)	1 (<1)	0	4 (1)	0
ほてり	5 (1)	0	0	0	1 (<1)
アラニン・アミノトランスフェラーゼ増加	0	1 (<1)	2 (<1)	4 (1)	1 (<1)
紅斑	2 (<1)	0	0	1 (<1)	0
血尿	3 (<1)	4 (1)	6 (2)	2 (<1)	2 (<1)
副鼻腔炎	1 (<1)	4 (1)	2 (<1)	6 (2)	5 (2)
胃腸炎	4 (<1)	4 (1)	4 (1)	2 (<1)	5 (2)
気管支炎	2 (<1)	3 (<1)	4 (1)	1 (<1)	5 (2)
消化不良	7 (2)	3 (<1)	2 (<1)	0	0
尿中アルブミン陽性	1 (<1)	5 (1)	2 (<1)	1 (<1)	2 (<1)

NOTE 1: Numbers in parentheses are percentages.
2: Data after subjects switched to alternative MS treatment are excluded.
3: A subject was counted only once within each interval for each preferred term.
4: Preferred terms are presented by decreasing order of incidence in overall Total BG00012.

SOURCE: BG12MS/JAPAN/ISS/T-AE-PT-2PCT-3MON-301.SAS DATE: 02DEC2015

Incidence of adverse events at least 2% higher for any treatment group and the entire study period by preferred term and 3-months interval: Study 109MS301
Page 4 of 48

	Placebo			
	>15-18 months	>18-21 months	>21-24 months	>24 months
背部痛	5 (2)	6 (2)	10 (4)	1 (<1)
上腹部痛	1 (<1)	1 (<1)	3 (1)	0
蛋白尿	1 (<1)	2 (<1)	1 (<1)	0
腹痛	1 (<1)	1 (<1)	1 (<1)	0
関節痛	4 (1)	2 (<1)	3 (1)	0
インフルエンザ	1 (<1)	3 (1)	2 (<1)	0
そう痒症	3 (<1)	1 (<1)	2 (<1)	0
錯感覚	4 (1)	6 (2)	3 (1)	0
嘔吐	4 (1)	0	4 (1)	1 (<1)
四肢痛	2 (<1)	4 (1)	1 (<1)	0
うつ病	7 (2)	4 (1)	4 (1)	0
発疹	1 (<1)	0	1 (<1)	0
ほてり	1 (<1)	0	1 (<1)	0
アラニン・アミノトランスフェラーゼ増加	4 (1)	2 (<1)	0	1 (<1)
紅斑	0	1 (<1)	1 (<1)	0
血尿	4 (1)	2 (<1)	2 (<1)	1 (<1)
副鼻腔炎	4 (1)	3 (1)	0	0
胃腸炎	2 (<1)	1 (<1)	1 (<1)	0
気管支炎	5 (2)	2 (<1)	0	0
消化不良	1 (<1)	0	0	0
尿中アルブミン陽性	1 (<1)	1 (<1)	2 (<1)	0

NOTE 1: Numbers in parentheses are percentages.
2: Data after subjects switched to alternative MS treatment are excluded.
3: A subject was counted only once within each interval for each preferred term.
4: Preferred terms are presented by decreasing order of incidence in overall Total BG00012.

SOURCE: BG12MS/JAPAN/ISS/T-AE-PT-2PCT-3MON-301.SAS DATE: 02DEC2015

Incidence of adverse events at least 2% higher for any treatment group and the entire study period by preferred term and 3-months interval: Study 109MS301
Page 5 of 48

	Placebo				
	0-3 months	>3-6 months	>6-9 months	>9-12 months	>12-15 months
口腔咽頭痛	3 (<1)	2 (<1)	3 (<1)	3 (<1)	2 (<1)
感覚鈍麻	8 (2)	9 (2)	4 (1)	4 (1)	1 (<1)
回転性めまい	6 (1)	5 (1)	1 (<1)	0	2 (<1)
咳嗽	2 (<1)	6 (2)	2 (<1)	2 (<1)	1 (<1)
浮動性めまい	8 (2)	4 (1)	3 (<1)	0	2 (<1)
不眠症	5 (1)	1 (<1)	3 (<1)	2 (<1)	3 (<1)
筋痙縮	6 (1)	2 (<1)	2 (<1)	3 (<1)	3 (<1)
ミクロアルブミン尿	1 (<1)	1 (<1)	1 (<1)	3 (<1)	2 (<1)
発熱	5 (1)	1 (<1)	8 (2)	3 (<1)	5 (2)
アスパラギン酸アミノトランスフェラーゼ増加	1 (<1)	1 (<1)	0	4 (1)	0
咽頭炎	5 (1)	5 (1)	2 (<1)	0	4 (1)
便秘	9 (2)	3 (<1)	0	5 (1)	2 (<1)
不安	5 (1)	3 (<1)	2 (<1)	0	0
灼熱感	2 (<1)	0	2 (<1)	1 (<1)	0
片頭痛	3 (<1)	5 (1)	2 (<1)	1 (<1)	3 (<1)
挫傷	1 (<1)	2 (<1)	1 (<1)	4 (1)	0
胃腸障害	4 (<1)	0	0	2 (<1)	0
鼻炎	5 (1)	4 (1)	4 (1)	2 (<1)	1 (<1)
多汗症	4 (<1)	0	1 (<1)	0	1 (<1)
リンパ球減少症	0	0	1 (<1)	0	0
歯痛	5 (1)	1 (<1)	3 (<1)	1 (<1)	2 (<1)

NOTE 1: Numbers in parentheses are percentages.
2: Data after subjects switched to alternative MS treatment are excluded.
3: A subject was counted only once within each interval for each preferred term.
4: Preferred terms are presented by decreasing order of incidence in overall Total BG00012.

SOURCE: BG12MS/JAPAN/ISS/T-AE-PT-2PCT-3MON-301.SAS DATE: 02DEC2015

Incidence of adverse events at least 2% higher for any treatment group and the entire study period by preferred term and 3-months interval: Study 109MS301
Page 6 of 48

	Placebo			
	>15-18 months	>18-21 months	>21-24 months	>24 months
口腔咽頭痛	3 (<1)	1 (<1)	3 (1)	0
感覚鈍麻	3 (<1)	4 (1)	2 (<1)	0
回転性めまい	3 (<1)	0	1 (<1)	0
咳嗽	1 (<1)	1 (<1)	4 (1)	0
浮動性めまい	0	4 (1)	3 (1)	0
不眠症	4 (1)	1 (<1)	2 (<1)	0
筋痙縮	2 (<1)	5 (2)	0	0
ミクロアルブミン尿	2 (<1)	1 (<1)	2 (<1)	1 (<1)
発熱	1 (<1)	3 (1)	0	0
アスパラギン酸アミノトランスフェラーゼ増加	2 (<1)	1 (<1)	0	0
咽頭炎	1 (<1)	0	4 (1)	1 (<1)
便秘	1 (<1)	2 (<1)	2 (<1)	0
不安	2 (<1)	1 (<1)	0	0
灼熱感	1 (<1)	0	0	0
片頭痛	4 (1)	1 (<1)	2 (<1)	0
挫傷	3 (<1)	0	0	0
胃腸障害	0	2 (<1)	1 (<1)	0
鼻炎	3 (<1)	2 (<1)	1 (<1)	0
多汗症	0	0	1 (<1)	0
リンパ球減少症	0	0	0	0
歯痛	0	2 (<1)	0	0

NOTE 1: Numbers in parentheses are percentages.
2: Data after subjects switched to alternative MS treatment are excluded.
3: A subject was counted only once within each interval for each preferred term.
4: Preferred terms are presented by decreasing order of incidence in overall Total BG00012.

SOURCE: BG12MS/JAPAN/ISS/T-AE-PT-2PCT-3MON-301.SAS DATE: 02DEC2015

Incidence of adverse events at least 2% higher for any treatment group and the entire study period by preferred term and 3-months interval: Study 109MS301
Page 7 of 48

	Placebo				
	0-3 months	>3-6 months	>6-9 months	>9-12 months	>12-15 months
ウイルス感染	4 (<1)	2 (<1)	3 (<1)	4 (1)	3 (<1)
筋力低下	6 (1)	9 (2)	3 (<1)	1 (<1)	1 (<1)
胃食道逆流性疾患	4 (<1)	0	0	1 (<1)	2 (<1)
寝汗	2 (<1)	3 (<1)	0	1 (<1)	0
胃炎	0	2 (<1)	0	1 (<1)	0
尿中蛋白陽性	2 (<1)	1 (<1)	2 (<1)	1 (<1)	4 (1)
膀胱炎	4 (<1)	1 (<1)	3 (<1)	1 (<1)	2 (<1)
転倒	1 (<1)	3 (<1)	2 (<1)	1 (<1)	2 (<1)
口腔ヘルペス	3 (<1)	1 (<1)	5 (1)	3 (<1)	5 (2)
尿中白血球陽性	0	1 (<1)	1 (<1)	3 (<1)	0
無力症	1 (<1)	2 (<1)	0	0	1 (<1)
γ－グルタミルトランスフェラーゼ増加	2 (<1)	1 (<1)	1 (<1)	7 (2)	2 (<1)
筋骨格痛	4 (<1)	7 (2)	2 (<1)	3 (<1)	3 (<1)
気道感染	1 (<1)	1 (<1)	0	2 (<1)	0
腹部不快感	4 (<1)	1 (<1)	2 (<1)	1 (<1)	0
食欲減退	3 (<1)	2 (<1)	2 (<1)	1 (<1)	0
霧視	3 (<1)	0	3 (<1)	3 (<1)	1 (<1)
胸痛	6 (1)	1 (<1)	1 (<1)	0	1 (<1)
口内乾燥	2 (<1)	1 (<1)	2 (<1)	0	0
筋痙直	4 (<1)	3 (<1)	4 (1)	5 (1)	1 (<1)
頚部痛	3 (<1)	3 (<1)	3 (<1)	2 (<1)	1 (<1)

NOTE 1: Numbers in parentheses are percentages.
2: Data after subjects switched to alternative MS treatment are excluded.
3: A subject was counted only once within each interval for each preferred term.
4: Preferred terms are presented by decreasing order of incidence in overall Total BG00012.

SOURCE: BG12MS/JAPAN/ISS/T-AE-PT-2PCT-3MON-301.SAS DATE: 02DEC2015

Incidence of adverse events at least 2% higher for any treatment group and the entire study period by preferred term and 3-months interval: Study 109MS301
Page 8 of 48

	Placebo			
	>15-18 months	>18-21 months	>21-24 months	>24 months
ウイルス感染	1 (<1)	0	0	0
筋力低下	4 (1)	2 (<1)	1 (<1)	0
胃食道逆流性疾患	1 (<1)	0	0	0
寝汗	0	0	0	0
胃炎	1 (<1)	1 (<1)	1 (<1)	0
尿中蛋白陽性	0	1 (<1)	2 (<1)	0
膀胱炎	2 (<1)	0	3 (1)	1 (<1)
転倒	1 (<1)	4 (1)	1 (<1)	0
口腔ヘルペス	4 (1)	3 (1)	2 (<1)	0
尿中白血球陽性	1 (<1)	1 (<1)	0	1 (<1)
無力症	2 (<1)	1 (<1)	1 (<1)	0
γ－グルタミルトランスフェラーゼ増加	1 (<1)	1 (<1)	0	0
筋骨格痛	3 (<1)	2 (<1)	1 (<1)	0
気道感染	1 (<1)	0	0	0
腹部不快感	1 (<1)	1 (<1)	0	0
食欲減退	0	0	1 (<1)	0
霧視	0	4 (1)	1 (<1)	0
胸痛	0	0	1 (<1)	0
口内乾燥	0	1 (<1)	0	0
筋痙直	1 (<1)	2 (<1)	1 (<1)	0
頚部痛	3 (<1)	2 (<1)	0	0

NOTE 1: Numbers in parentheses are percentages.
2: Data after subjects switched to alternative MS treatment are excluded.
3: A subject was counted only once within each interval for each preferred term.
4: Preferred terms are presented by decreasing order of incidence in overall Total BG00012.

SOURCE: BG12MS/JAPAN/ISS/T-AE-PT-2PCT-3MON-301.SAS DATE: 02DEC2015

Incidence of adverse events at least 2% higher for any treatment group and the entire study period by preferred term and 3-months interval: Study 109MS301
Page 9 of 48

	Placebo				
	0-3 months	>3-6 months	>6-9 months	>9-12 months	>12-15 months
平衡障害	0	1 (<1)	1 (<1)	0	2 (<1)
血中副甲状腺ホルモン増加	0	0	0	2 (<1)	0
ケトン尿	2 (<1)	2 (<1)	0	0	0
鼻漏	2 (<1)	1 (<1)	1 (<1)	0	0
血中ブドウ糖増加	2 (<1)	0	1 (<1)	2 (<1)	1 (<1)
尿中血陽性	1 (<1)	0	0	0	1 (<1)
抑うつ気分	2 (<1)	4 (1)	1 (<1)	0	0
高血圧	2 (<1)	3 (<1)	2 (<1)	0	1 (<1)
インフルエンザ様疾患	6 (1)	1 (<1)	0	0	3 (<1)
アレルギー性皮膚炎	0	0	1 (<1)	0	0
蕁麻疹	0	3 (<1)	0	0	0
異常感覚	2 (<1)	0	0	0	0
眼痛	1 (<1)	3 (<1)	0	1 (<1)	1 (<1)
腹部膨満	5 (1)	1 (<1)	2 (<1)	0	0
排尿困難	0	3 (<1)	1 (<1)	1 (<1)	1 (<1)
振戦	4 (<1)	0	0	3 (<1)	0
腟感染	0	0	0	0	0
脱毛症	5 (1)	3 (<1)	2 (<1)	1 (<1)	1 (<1)
関節捻挫	1 (<1)	1 (<1)	1 (<1)	3 (<1)	1 (<1)
筋肉痛	7 (2)	4 (1)	1 (<1)	1 (<1)	2 (<1)
耳感染	0	1 (<1)	1 (<1)	2 (<1)	2 (<1)

NOTE 1: Numbers in parentheses are percentages.
2: Data after subjects switched to alternative MS treatment are excluded.
3: A subject was counted only once within each interval for each preferred term.
4: Preferred terms are presented by decreasing order of incidence in overall Total BG00012.

SOURCE: BG12MS/JAPAN/ISS/T-AE-PT-2PCT-3MON-301.SAS DATE: 02DEC2015

Incidence of adverse events at least 2% higher for any treatment group and the entire study period by preferred term and 3-months interval: Study 109MS301
Page 10 of 48

	Placebo			
	>15-18 months	>18-21 months	>21-24 months	>24 months
平衡障害	3 (<1)	0	0	0
血中副甲状腺ホルモン増加	0	0	1 (<1)	1 (<1)
ケトン尿	1 (<1)	0	0	0
鼻漏	0	0	1 (<1)	0
血中ブドウ糖増加	0	1 (<1)	1 (<1)	0
尿中血陽性	1 (<1)	0	1 (<1)	0
抑うつ気分	2 (<1)	2 (<1)	1 (<1)	0
高血圧	2 (<1)	2 (<1)	1 (<1)	0
インフルエンザ様疾患	1 (<1)	2 (<1)	4 (1)	0
アレルギー性皮膚炎	0	1 (<1)	1 (<1)	1 (<1)
蕁麻疹	0	0	1 (<1)	0
異常感覚	1 (<1)	1 (<1)	2 (<1)	0
眼痛	1 (<1)	3 (1)	0	0
腹部膨満	1 (<1)	0	0	0
排尿困難	2 (<1)	0	1 (<1)	0
振戦	0	2 (<1)	1 (<1)	0
腟感染	2 (<1)	0	0	0
脱毛症	1 (<1)	0	0	0
関節捻挫	1 (<1)	0	5 (2)	0
筋肉痛	1 (<1)	0	0	0
耳感染	3 (<1)	0	0	0

NOTE 1: Numbers in parentheses are percentages.
2: Data after subjects switched to alternative MS treatment are excluded.
3: A subject was counted only once within each interval for each preferred term.
4: Preferred terms are presented by decreasing order of incidence in overall Total BG00012.

SOURCE: BG12MS/JAPAN/ISS/T-AE-PT-2PCT-3MON-301.SAS DATE: 02DEC2015

Incidence of adverse events at least 2% higher for any treatment group and the entire study period by preferred term and 3-months interval: Study 109MS301
Page 11 of 48

	Placebo				
	0-3 months	>3-6 months	>6-9 months	>9-12 months	>12-15 months
多発性硬化症	3 (<1)	1 (<1)	1 (<1)	3 (<1)	3 (<1)
末梢性浮腫	7 (2)	0	1 (<1)	2 (<1)	1 (<1)
頻尿	2 (<1)	2 (<1)	1 (<1)	2 (<1)	0
白血球数増加	2 (<1)	1 (<1)	1 (<1)	1 (<1)	1 (<1)

NOTE 1: Numbers in parentheses are percentages.
2: Data after subjects switched to alternative MS treatment are excluded.
3: A subject was counted only once within each interval for each preferred term.
4: Preferred terms are presented by decreasing order of incidence in overall Total BG00012.

SOURCE: BG12MS/JAPAN/ISS/T-AE-PT-2PCT-3MON-301.SAS DATE: 02DEC2015

Incidence of adverse events at least 2% higher for any treatment group and the entire study period by preferred term and 3-months interval: Study 109MS301
Page 12 of 48

	Placebo			
	>15-18 months	>18-21 months	>21-24 months	>24 months
多発性硬化症	2 (<1)	2 (<1)	0	1 (<1)
末梢性浮腫	0	1 (<1)	1 (<1)	0
頻尿	1 (<1)	0	1 (<1)	0
白血球数増加	1 (<1)	3 (1)	0	0

NOTE 1: Numbers in parentheses are percentages.
2: Data after subjects switched to alternative MS treatment are excluded.
3: A subject was counted only once within each interval for each preferred term.
4: Preferred terms are presented by decreasing order of incidence in overall Total BG00012.

SOURCE: BG12MS/JAPAN/ISS/T-AE-PT-2PCT-3MON-301.SAS DATE: 02DEC2015

Incidence of adverse events at least 2% higher for any treatment group and the entire study period by preferred term and 3-months interval: Study 109MS301
Page 13 of 48

	BG00012 240 mg BID				
	0-3 months	>3-6 months	>6-9 months	>9-12 months	>12-15 months
Number of subjects followed in the interval	410 (100)	381 (100)	364 (100)	349 (100)	334 (100)
Number of subjects with an event	339 (83)	229 (60)	215 (59)	187 (54)	192 (57)
Number of subjects with deaths	0	1 (<1)	0	0	0
Number of subjects with SAEs other than deaths	19 (5)	14 (4)	8 (2)	14 (4)	10 (3)
Number of subjects who discontinued	30 (7)	1 (<1)	4 (1)	0	1 (<1)
潮紅	122 (30)	30 (8)	14 (4)	19 (5)	14 (4)
多発性硬化症再発	24 (6)	29 (8)	21 (6)	17 (5)	20 (6)
鼻咽頭炎	27 (7)	23 (6)	28 (8)	26 (7)	19 (6)
頭痛	41 (10)	14 (4)	10 (3)	14 (4)	12 (4)
下痢	41 (10)	9 (2)	5 (1)	8 (2)	3 (<1)
疲労	27 (7)	8 (2)	8 (2)	6 (2)	6 (2)
上気道感染	22 (5)	10 (3)	15 (4)	13 (4)	17 (5)
尿路感染	17 (4)	18 (5)	9 (2)	10 (3)	7 (2)
悪心	40 (10)	4 (1)	6 (2)	6 (2)	2 (<1)

NOTE 1: Numbers in parentheses are percentages.
2: Data after subjects switched to alternative MS treatment are excluded.
3: A subject was counted only once within each interval for each preferred term.
4: Preferred terms are presented by decreasing order of incidence in overall Total BG00012.

SOURCE: BG12MS/JAPAN/ISS/T-AE-PT-2PCT-3MON-301.SAS DATE: 02DEC2015

Incidence of adverse events at least 2% higher for any treatment group and the entire study period by preferred term and 3-months interval: Study 109MS301
Page 14 of 48

	BG00012 240 mg BID			
	>15-18 months	>18-21 months	>21-24 months	>24 months
Number of subjects followed in the interval	323 (100)	317 (100)	310 (100)	220 (100)
Number of subjects with an event	180 (56)	146 (46)	149 (48)	33 (15)
Number of subjects with deaths	0	0	0	0
Number of subjects with SAEs other than deaths	8 (2)	12 (4)	11 (4)	1 (<1)
Number of subjects who discontinued	2 (<1)	1 (<1)	1 (<1)	0
潮紅	10 (3)	4 (1)	2 (<1)	0
多発性硬化症再発	14 (4)	15 (5)	17 (5)	3 (1)
鼻咽頭炎	20 (6)	15 (5)	22 (7)	0
頭痛	14 (4)	10 (3)	8 (3)	3 (1)
下痢	2 (<1)	4 (1)	3 (<1)	0
疲労	7 (2)	5 (2)	2 (<1)	0
上気道感染	7 (2)	10 (3)	8 (3)	0
尿路感染	8 (2)	7 (2)	5 (2)	2 (<1)
悪心	2 (<1)	3 (<1)	3 (<1)	1 (<1)

NOTE 1: Numbers in parentheses are percentages.
2: Data after subjects switched to alternative MS treatment are excluded.
3: A subject was counted only once within each interval for each preferred term.
4: Preferred terms are presented by decreasing order of incidence in overall Total BG00012.

SOURCE: BG12MS/JAPAN/ISS/T-AE-PT-2PCT-3MON-301.SAS DATE: 02DEC2015

Incidence of adverse events at least 2% higher for any treatment group and the entire study period by preferred term and 3-months interval: Study 109MS301
Page 15 of 48

	BG00012 240 mg BID				
	0-3 months	>3-6 months	>6-9 months	>9-12 months	>12-15 months
背部痛	15 (4)	12 (3)	10 (3)	9 (3)	12 (4)
上腹部痛	29 (7)	6 (2)	6 (2)	5 (1)	4 (1)
蛋白尿	8 (2)	10 (3)	11 (3)	5 (1)	8 (2)
腹痛	29 (7)	5 (1)	6 (2)	8 (2)	2 (<1)
関節痛	14 (3)	6 (2)	6 (2)	4 (1)	6 (2)
インフルエンザ	7 (2)	8 (2)	5 (1)	5 (1)	4 (1)
そう痒症	24 (6)	7 (2)	8 (2)	6 (2)	3 (<1)
錯感覚	13 (3)	5 (1)	5 (1)	5 (1)	3 (<1)
嘔吐	23 (6)	3 (<1)	4 (1)	6 (2)	2 (<1)
四肢痛	7 (2)	9 (2)	7 (2)	6 (2)	2 (<1)
うつ病	5 (1)	3 (<1)	7 (2)	5 (1)	5 (1)
発疹	18 (4)	8 (2)	6 (2)	4 (1)	4 (1)
ほてり	24 (6)	4 (1)	1 (<1)	3 (<1)	0
アラニン・アミノトランスフェラーゼ増加	13 (3)	8 (2)	1 (<1)	2 (<1)	1 (<1)
紅斑	11 (3)	2 (<1)	0	0	0
血尿	4 (<1)	7 (2)	2 (<1)	5 (1)	5 (1)
副鼻腔炎	4 (<1)	1 (<1)	5 (1)	0	1 (<1)
胃腸炎	10 (2)	4 (1)	1 (<1)	4 (1)	8 (2)
気管支炎	6 (1)	6 (2)	3 (<1)	2 (<1)	2 (<1)
消化不良	12 (3)	3 (<1)	2 (<1)	5 (1)	2 (<1)
尿中アルブミン陽性	3 (<1)	7 (2)	8 (2)	1 (<1)	2 (<1)

NOTE 1: Numbers in parentheses are percentages.
2: Data after subjects switched to alternative MS treatment are excluded.
3: A subject was counted only once within each interval for each preferred term.
4: Preferred terms are presented by decreasing order of incidence in overall Total BG00012.

SOURCE: BG12MS/JAPAN/ISS/T-AE-PT-2PCT-3MON-301.SAS DATE: 02DEC2015

Incidence of adverse events at least 2% higher for any treatment group and the entire study period by preferred term and 3-months interval: Study 109MS301
Page 16 of 48

	BG00012 240 mg BID			
	>15-18 months	>18-21 months	>21-24 months	>24 months
背部痛	9 (3)	5 (2)	7 (2)	0
上腹部痛	0	1 (<1)	0	0
蛋白尿	6 (2)	4 (1)	3 (<1)	1 (<1)
腹痛	1 (<1)	1 (<1)	2 (<1)	0
関節痛	7 (2)	6 (2)	4 (1)	0
インフルエンザ	6 (2)	3 (<1)	6 (2)	0
そう痒症	3 (<1)	1 (<1)	3 (<1)	0
錯感覚	4 (1)	3 (<1)	2 (<1)	0
嘔吐	2 (<1)	0	3 (<1)	2 (<1)
四肢痛	6 (2)	4 (1)	4 (1)	0
うつ病	2 (<1)	2 (<1)	3 (<1)	2 (<1)
発疹	3 (<1)	0	2 (<1)	0
ほてり	1 (<1)	0	0	0
アラニン・アミノトランスフェラーゼ増加	4 (1)	1 (<1)	4 (1)	1 (<1)
紅斑	4 (1)	3 (<1)	1 (<1)	0
血尿	3 (<1)	6 (2)	8 (3)	1 (<1)
副鼻腔炎	1 (<1)	3 (<1)	2 (<1)	0
胃腸炎	2 (<1)	2 (<1)	0	0
気管支炎	2 (<1)	3 (<1)	2 (<1)	0
消化不良	1 (<1)	1 (<1)	1 (<1)	0
尿中アルブミン陽性	1 (<1)	2 (<1)	2 (<1)	1 (<1)

NOTE 1: Numbers in parentheses are percentages.
2: Data after subjects switched to alternative MS treatment are excluded.
3: A subject was counted only once within each interval for each preferred term.
4: Preferred terms are presented by decreasing order of incidence in overall Total BG00012.

SOURCE: BG12MS/JAPAN/ISS/T-AE-PT-2PCT-3MON-301.SAS DATE: 02DEC2015

Incidence of adverse events at least 2% higher for any treatment group and the entire study period by preferred term and 3-months interval: Study 109MS301
Page 17 of 48

	BG00012 240 mg BID				
	0-3 months	>3-6 months	>6-9 months	>9-12 months	>12-15 months
口腔咽頭痛	5 (1)	4 (1)	2 (<1)	5 (1)	2 (<1)
感覚鈍麻	5 (1)	4 (1)	4 (1)	5 (1)	3 (<1)
回転性めまい	3 (<1)	4 (1)	2 (<1)	0	2 (<1)
咳嗽	5 (1)	4 (1)	1 (<1)	2 (<1)	3 (<1)
浮動性めまい	5 (1)	2 (<1)	4 (1)	3 (<1)	3 (<1)
不眠症	4 (<1)	2 (<1)	6 (2)	5 (1)	2 (<1)
筋痙縮	3 (<1)	1 (<1)	1 (<1)	3 (<1)	3 (<1)
ミクロアルブミン尿	3 (<1)	6 (2)	2 (<1)	1 (<1)	9 (3)
発熱	3 (<1)	3 (<1)	0	2 (<1)	3 (<1)
アスパラギン酸アミノトランスフェラーゼ増加	7 (2)	4 (1)	1 (<1)	1 (<1)	1 (<1)
咽頭炎	4 (<1)	3 (<1)	1 (<1)	3 (<1)	4 (1)
便秘	5 (1)	2 (<1)	1 (<1)	0	6 (2)
不安	5 (1)	5 (1)	4 (1)	2 (<1)	2 (<1)
灼熱感	10 (2)	0	1 (<1)	3 (<1)	0
片頭痛	4 (<1)	4 (1)	4 (1)	2 (<1)	2 (<1)
挫傷	1 (<1)	2 (<1)	2 (<1)	3 (<1)	2 (<1)
胃腸障害	9 (2)	1 (<1)	0	1 (<1)	0
鼻炎	3 (<1)	3 (<1)	0	1 (<1)	2 (<1)
多汗症	3 (<1)	2 (<1)	2 (<1)	3 (<1)	0
リンパ球減少症	2 (<1)	3 (<1)	2 (<1)	1 (<1)	1 (<1)
歯痛	1 (<1)	2 (<1)	1 (<1)	2 (<1)	2 (<1)

NOTE 1: Numbers in parentheses are percentages.
2: Data after subjects switched to alternative MS treatment are excluded.
3: A subject was counted only once within each interval for each preferred term.
4: Preferred terms are presented by decreasing order of incidence in overall Total BG00012.

SOURCE: BG12MS/JAPAN/ISS/T-AE-PT-2PCT-3MON-301.SAS DATE: 02DEC2015

Incidence of adverse events at least 2% higher for any treatment group and the entire study period by preferred term and 3-months interval: Study 109MS301
Page 18 of 48

	BG00012 240 mg BID			
	>15-18 months	>18-21 months	>21-24 months	>24 months
口腔咽頭痛	4 (1)	4 (1)	2 (<1)	0
感覚鈍麻	1 (<1)	1 (<1)	0	0
回転性めまい	1 (<1)	0	2 (<1)	0
咳嗽	5 (2)	2 (<1)	3 (<1)	0
浮動性めまい	1 (<1)	1 (<1)	2 (<1)	1 (<1)
不眠症	2 (<1)	2 (<1)	1 (<1)	0
筋痙縮	3 (<1)	1 (<1)	3 (<1)	1 (<1)
ミクロアルブミン尿	1 (<1)	3 (<1)	1 (<1)	3 (1)
発熱	2 (<1)	4 (1)	1 (<1)	1 (<1)
アスパラギン酸アミノトランスフェラーゼ増加	3 (<1)	0	1 (<1)	0
咽頭炎	4 (1)	2 (<1)	3 (<1)	0
便秘	0	0	1 (<1)	0
不安	0	0	0	0
灼熱感	1 (<1)	0	1 (<1)	0
片頭痛	1 (<1)	1 (<1)	1 (<1)	0
挫傷	0	2 (<1)	1 (<1)	0
胃腸障害	0	0	0	0
鼻炎	2 (<1)	2 (<1)	0	0
多汗症	0	0	2 (<1)	0
リンパ球減少症	3 (<1)	2 (<1)	3 (<1)	0
歯痛	2 (<1)	1 (<1)	2 (<1)	0

NOTE 1: Numbers in parentheses are percentages.
2: Data after subjects switched to alternative MS treatment are excluded.
3: A subject was counted only once within each interval for each preferred term.
4: Preferred terms are presented by decreasing order of incidence in overall Total BG00012.

SOURCE: BG12MS/JAPAN/ISS/T-AE-PT-2PCT-3MON-301.SAS DATE: 02DEC2015

Incidence of adverse events at least 2% higher for any treatment group and the entire study period by preferred term and 3-months interval: Study 109MS301
Page 19 of 48

	BG00012 240 mg BID				
	0-3 months	>3-6 months	>6-9 months	>9-12 months	>12-15 months
ウイルス感染	3 (<1)	2 (<1)	0	1 (<1)	1 (<1)
筋力低下	2 (<1)	2 (<1)	3 (<1)	0	3 (<1)
胃食道逆流性疾患	5 (1)	1 (<1)	1 (<1)	1 (<1)	1 (<1)
寝汗	6 (1)	1 (<1)	3 (<1)	1 (<1)	0
胃炎	4 (<1)	3 (<1)	0	2 (<1)	1 (<1)
尿中蛋白陽性	5 (1)	1 (<1)	1 (<1)	1 (<1)	2 (<1)
膀胱炎	1 (<1)	3 (<1)	0	0	0
転倒	0	3 (<1)	4 (1)	1 (<1)	3 (<1)
口腔ヘルペス	4 (<1)	4 (1)	2 (<1)	2 (<1)	1 (<1)
尿中白血球陽性	0	3 (<1)	2 (<1)	2 (<1)	2 (<1)
無力症	8 (2)	0	1 (<1)	1 (<1)	0
γ－グルタミルトランスフェラーゼ増加	2 (<1)	3 (<1)	2 (<1)	0	2 (<1)
筋骨格痛	2 (<1)	1 (<1)	1 (<1)	3 (<1)	2 (<1)
気道感染	3 (<1)	2 (<1)	2 (<1)	1 (<1)	1 (<1)
腹部不快感	7 (2)	0	1 (<1)	2 (<1)	2 (<1)
食欲減退	4 (<1)	2 (<1)	0	1 (<1)	1 (<1)
霧視	3 (<1)	1 (<1)	1 (<1)	1 (<1)	0
胸痛	2 (<1)	2 (<1)	0	2 (<1)	0
口内乾燥	13 (3)	1 (<1)	0	1 (<1)	0
筋痙直	1 (<1)	5 (1)	0	0	1 (<1)
頚部痛	0	4 (1)	2 (<1)	1 (<1)	1 (<1)

NOTE 1: Numbers in parentheses are percentages.
2: Data after subjects switched to alternative MS treatment are excluded.
3: A subject was counted only once within each interval for each preferred term.
4: Preferred terms are presented by decreasing order of incidence in overall Total BG00012.

SOURCE: BG12MS/JAPAN/ISS/T-AE-PT-2PCT-3MON-301.SAS DATE: 02DEC2015

Incidence of adverse events at least 2% higher for any treatment group and the entire study period by preferred term and 3-months interval: Study 109MS301
Page 20 of 48

	BG00012 240 mg BID			
	>15-18 months	>18-21 months	>21-24 months	>24 months
ウイルス感染	1 (<1)	6 (2)	2 (<1)	0
筋力低下	2 (<1)	0	2 (<1)	0
胃食道逆流性疾患	0	0	1 (<1)	0
寝汗	0	0	0	0
胃炎	2 (<1)	0	0	0
尿中蛋白陽性	0	1 (<1)	1 (<1)	1 (<1)
膀胱炎	1 (<1)	0	2 (<1)	0
転倒	1 (<1)	1 (<1)	1 (<1)	0
口腔ヘルペス	2 (<1)	1 (<1)	2 (<1)	0
尿中白血球陽性	1 (<1)	2 (<1)	1 (<1)	0
無力症	0	1 (<1)	0	0
γ－グルタミルトランスフェラーゼ増加	1 (<1)	2 (<1)	4 (1)	0
筋骨格痛	2 (<1)	1 (<1)	2 (<1)	0
気道感染	1 (<1)	0	1 (<1)	0
腹部不快感	1 (<1)	0	1 (<1)	0
食欲減退	1 (<1)	0	2 (<1)	0
霧視	3 (<1)	1 (<1)	0	0
胸痛	0	2 (<1)	0	0
口内乾燥	0	0	0	0
筋痙直	2 (<1)	1 (<1)	1 (<1)	0
頚部痛	3 (<1)	0	1 (<1)	0

NOTE 1: Numbers in parentheses are percentages.
2: Data after subjects switched to alternative MS treatment are excluded.
3: A subject was counted only once within each interval for each preferred term.
4: Preferred terms are presented by decreasing order of incidence in overall Total BG00012.

SOURCE: BG12MS/JAPAN/ISS/T-AE-PT-2PCT-3MON-301.SAS DATE: 02DEC2015

Incidence of adverse events at least 2% higher for any treatment group and the entire study period by preferred term and 3-months interval: Study 109MS301
Page 21 of 48

	BG00012 240 mg BID				
	0-3 months	>3-6 months	>6-9 months	>9-12 months	>12-15 months
平衡障害	0	1 (<1)	1 (<1)	3 (<1)	1 (<1)
血中副甲状腺ホルモン増加	1 (<1)	1 (<1)	0	1 (<1)	1 (<1)
過敏症	7 (2)	0	0	0	3 (<1)
ケトン尿	1 (<1)	2 (<1)	1 (<1)	1 (<1)	2 (<1)
鼻漏	1 (<1)	3 (<1)	2 (<1)	1 (<1)	3 (<1)
血中ブドウ糖増加	0	1 (<1)	0	1 (<1)	2 (<1)
尿中血陽性	0	2 (<1)	1 (<1)	0	1 (<1)
抑うつ気分	4 (<1)	0	1 (<1)	0	1 (<1)
高血圧	2 (<1)	1 (<1)	0	0	1 (<1)
インフルエンザ様疾患	1 (<1)	1 (<1)	1 (<1)	2 (<1)	1 (<1)
アレルギー性皮膚炎	3 (<1)	0	1 (<1)	1 (<1)	1 (<1)
蕁麻疹	4 (<1)	1 (<1)	0	0	0
異常感覚	5 (1)	3 (<1)	1 (<1)	0	1 (<1)
眼痛	0	1 (<1)	0	0	1 (<1)
腹部膨満	3 (<1)	0	1 (<1)	0	0
排尿困難	1 (<1)	0	1 (<1)	0	0
振戦	5 (1)	1 (<1)	0	2 (<1)	0
腟感染	0	2 (<1)	2 (<1)	2 (<1)	2 (<1)
脱毛症	4 (<1)	1 (<1)	0	0	1 (<1)
関節捻挫	0	1 (<1)	0	1 (<1)	2 (<1)
筋肉痛	2 (<1)	2 (<1)	0	0	1 (<1)

NOTE 1: Numbers in parentheses are percentages.
2: Data after subjects switched to alternative MS treatment are excluded.
3: A subject was counted only once within each interval for each preferred term.
4: Preferred terms are presented by decreasing order of incidence in overall Total BG00012.

SOURCE: BG12MS/JAPAN/ISS/T-AE-PT-2PCT-3MON-301.SAS DATE: 02DEC2015

Incidence of adverse events at least 2% higher for any treatment group and the entire study period by preferred term and 3-months interval: Study 109MS301
Page 22 of 48

	BG00012 240 mg BID			
	>15-18 months	>18-21 months	>21-24 months	>24 months
平衡障害	0	2 (<1)	0	0
血中副甲状腺ホルモン増加	0	0	0	4 (2)
過敏症	0	1 (<1)	0	0
ケトン尿	2 (<1)	1 (<1)	1 (<1)	0
鼻漏	0	0	0	0
血中ブドウ糖増加	1 (<1)	2 (<1)	0	0
尿中血陽性	1 (<1)	0	1 (<1)	0
抑うつ気分	2 (<1)	0	0	1 (<1)
高血圧	1 (<1)	1 (<1)	0	1 (<1)
インフルエンザ様疾患	1 (<1)	1 (<1)	0	0
アレルギー性皮膚炎	1 (<1)	1 (<1)	1 (<1)	0
蕁麻疹	1 (<1)	0	0	0
異常感覚	0	1 (<1)	1 (<1)	0
眼痛	3 (<1)	0	1 (<1)	0
腹部膨満	0	1 (<1)	0	0
排尿困難	1 (<1)	1 (<1)	0	0
振戦	1 (<1)	1 (<1)	0	0
腟感染	0	0	1 (<1)	0
脱毛症	0	1 (<1)	0	0
関節捻挫	1 (<1)	0	0	0
筋肉痛	0	0	1 (<1)	0

NOTE 1: Numbers in parentheses are percentages.
2: Data after subjects switched to alternative MS treatment are excluded.
3: A subject was counted only once within each interval for each preferred term.
4: Preferred terms are presented by decreasing order of incidence in overall Total BG00012.

SOURCE: BG12MS/JAPAN/ISS/T-AE-PT-2PCT-3MON-301.SAS DATE: 02DEC2015

Incidence of adverse events at least 2% higher for any treatment group and the entire study period by preferred term and 3-months interval: Study 109MS301
Page 23 of 48

	BG00012 240 mg BID				
	0-3 months	>3-6 months	>6-9 months	>9-12 months	>12-15 months
耳感染	0	0	1 (<1)	0	2 (<1)
多発性硬化症	0	1 (<1)	1 (<1)	0	1 (<1)
末梢性浮腫	0	0	1 (<1)	0	1 (<1)
頻尿	1 (<1)	0	0	1 (<1)	2 (<1)
白血球数増加	1 (<1)	1 (<1)	0	0	0

NOTE 1: Numbers in parentheses are percentages.
2: Data after subjects switched to alternative MS treatment are excluded.
3: A subject was counted only once within each interval for each preferred term.
4: Preferred terms are presented by decreasing order of incidence in overall Total BG00012.

SOURCE: BG12MS/JAPAN/ISS/T-AE-PT-2PCT-3MON-301.SAS DATE: 02DEC2015

Incidence of adverse events at least 2% higher for any treatment group and the entire study period by preferred term and 3-months interval: Study 109MS301
Page 24 of 48

	BG00012 240 mg BID			
	>15-18 months	>18-21 months	>21-24 months	>24 months
耳感染	1 (<1)	0	0	0
多発性硬化症	0	1 (<1)	0	0
末梢性浮腫	1 (<1)	0	0	0
頻尿	1 (<1)	1 (<1)	0	0
白血球数増加	0	0	0	0

NOTE 1: Numbers in parentheses are percentages.
2: Data after subjects switched to alternative MS treatment are excluded.
3: A subject was counted only once within each interval for each preferred term.
4: Preferred terms are presented by decreasing order of incidence in overall Total BG00012.

SOURCE: BG12MS/JAPAN/ISS/T-AE-PT-2PCT-3MON-301.SAS DATE: 02DEC2015

Incidence of adverse events at least 2% higher for any treatment group and the entire study period by preferred term and 3-months interval: Study 109MS301
Page 25 of 48

	BG00012 240 mg TID				
	0-3 months	>3-6 months	>6-9 months	>9-12 months	>12-15 months
Number of subjects followed in the interval	416 (100)	379 (100)	365 (100)	349 (100)	341 (100)
Number of subjects with an event	352 (85)	237 (63)	215 (59)	202 (58)	183 (54)
Number of subjects with deaths	1 (<1)	0	0	0	0
Number of subjects with SAEs other than deaths	16 (4)	14 (4)	10 (3)	3 (<1)	7 (2)
Number of subjects who discontinued	29 (7)	2 (<1)	3 (<1)	2 (<1)	4 (1)
潮紅	117 (28)	19 (5)	18 (5)	8 (2)	7 (2)
多発性硬化症再発	34 (8)	24 (6)	24 (7)	22 (6)	12 (4)
鼻咽頭炎	36 (9)	32 (8)	26 (7)	25 (7)	19 (6)
頭痛	39 (9)	18 (5)	9 (2)	13 (4)	11 (3)
下痢	57 (14)	11 (3)	9 (2)	9 (3)	5 (1)
疲労	21 (5)	12 (3)	12 (3)	6 (2)	9 (3)
上気道感染	20 (5)	7 (2)	7 (2)	9 (3)	10 (3)
尿路感染	15 (4)	14 (4)	14 (4)	9 (3)	3 (<1)
悪心	41 (10)	5 (1)	3 (<1)	1 (<1)	3 (<1)

NOTE 1: Numbers in parentheses are percentages.
2: Data after subjects switched to alternative MS treatment are excluded.
3: A subject was counted only once within each interval for each preferred term.
4: Preferred terms are presented by decreasing order of incidence in overall Total BG00012.

SOURCE: BG12MS/JAPAN/ISS/T-AE-PT-2PCT-3MON-301.SAS DATE: 02DEC2015

Incidence of adverse events at least 2% higher for any treatment group and the entire study period by preferred term and 3-months interval: Study 109MS301
Page 26 of 48

	BG00012 240 mg TID			
	>15-18 months	>18-21 months	>21-24 months	>24 months
Number of subjects followed in the interval	328 (100)	319 (100)	312 (100)	228 (100)
Number of subjects with an event	186 (57)	168 (53)	147 (47)	34 (15)
Number of subjects with deaths	0	0	0	0
Number of subjects with SAEs other than deaths	15 (5)	7 (2)	8 (3)	3 (1)
Number of subjects who discontinued	0	0	0	0
潮紅	8 (2)	7 (2)	3 (<1)	1 (<1)
多発性硬化症再発	22 (7)	13 (4)	14 (4)	4 (2)
鼻咽頭炎	26 (8)	17 (5)	21 (7)	0
頭痛	5 (2)	4 (1)	8 (3)	1 (<1)
下痢	5 (2)	3 (<1)	2 (<1)	0
疲労	5 (2)	6 (2)	7 (2)	0
上気道感染	7 (2)	5 (2)	8 (3)	1 (<1)
尿路感染	5 (2)	12 (4)	7 (2)	2 (<1)
悪心	2 (<1)	2 (<1)	3 (<1)	1 (<1)

NOTE 1: Numbers in parentheses are percentages.
2: Data after subjects switched to alternative MS treatment are excluded.
3: A subject was counted only once within each interval for each preferred term.
4: Preferred terms are presented by decreasing order of incidence in overall Total BG00012.

SOURCE: BG12MS/JAPAN/ISS/T-AE-PT-2PCT-3MON-301.SAS DATE: 02DEC2015

Incidence of adverse events at least 2% higher for any treatment group and the entire study period by preferred term and 3-months interval: Study 109MS301
Page 27 of 48

	BG00012 240 mg TID				
	0-3 months	>3-6 months	>6-9 months	>9-12 months	>12-15 months
背部痛	9 (2)	11 (3)	4 (1)	7 (2)	4 (1)
上腹部痛	32 (8)	5 (1)	5 (1)	5 (1)	7 (2)
蛋白尿	19 (5)	10 (3)	10 (3)	8 (2)	8 (2)
腹痛	23 (6)	3 (<1)	1 (<1)	5 (1)	3 (<1)
関節痛	9 (2)	6 (2)	6 (2)	9 (3)	3 (<1)
インフルエンザ	14 (3)	3 (<1)	9 (2)	7 (2)	7 (2)
そう痒症	23 (6)	3 (<1)	4 (1)	3 (<1)	1 (<1)
錯感覚	8 (2)	11 (3)	7 (2)	6 (2)	4 (1)
嘔吐	21 (5)	1 (<1)	3 (<1)	4 (1)	3 (<1)
四肢痛	8 (2)	7 (2)	7 (2)	7 (2)	1 (<1)
うつ病	6 (1)	5 (1)	6 (2)	10 (3)	2 (<1)
発疹	15 (4)	5 (1)	6 (2)	2 (<1)	2 (<1)
ほてり	22 (5)	3 (<1)	2 (<1)	2 (<1)	2 (<1)
アラニン・アミノトランスフェラーゼ増加	16 (4)	2 (<1)	1 (<1)	3 (<1)	4 (1)
紅斑	24 (6)	6 (2)	1 (<1)	3 (<1)	1 (<1)
血尿	12 (3)	5 (1)	6 (2)	5 (1)	3 (<1)
副鼻腔炎	6 (1)	3 (<1)	8 (2)	8 (2)	9 (3)
胃腸炎	7 (2)	1 (<1)	3 (<1)	2 (<1)	3 (<1)
気管支炎	7 (2)	4 (1)	4 (1)	1 (<1)	4 (1)
消化不良	14 (3)	6 (2)	2 (<1)	2 (<1)	0
尿中アルブミン陽性	8 (2)	5 (1)	2 (<1)	5 (1)	2 (<1)

NOTE 1: Numbers in parentheses are percentages.
2: Data after subjects switched to alternative MS treatment are excluded.
3: A subject was counted only once within each interval for each preferred term.
4: Preferred terms are presented by decreasing order of incidence in overall Total BG00012.

SOURCE: BG12MS/JAPAN/ISS/T-AE-PT-2PCT-3MON-301.SAS DATE: 02DEC2015

Incidence of adverse events at least 2% higher for any treatment group and the entire study period by preferred term and 3-months interval: Study 109MS301
Page 28 of 48

	BG00012 240 mg TID			
	>15-18 months	>18-21 months	>21-24 months	>24 months
背部痛	7 (2)	3 (<1)	6 (2)	3 (1)
上腹部痛	3 (<1)	2 (<1)	3 (<1)	0
蛋白尿	5 (2)	3 (<1)	5 (2)	2 (<1)
腹痛	1 (<1)	2 (<1)	1 (<1)	0
関節痛	2 (<1)	2 (<1)	3 (<1)	1 (<1)
インフルエンザ	4 (1)	5 (2)	7 (2)	1 (<1)
そう痒症	0	1 (<1)	3 (<1)	0
錯感覚	5 (2)	6 (2)	2 (<1)	0
嘔吐	1 (<1)	1 (<1)	0	0
四肢痛	2 (<1)	1 (<1)	3 (<1)	0
うつ病	2 (<1)	4 (1)	5 (2)	0
発疹	0	0	2 (<1)	0
ほてり	1 (<1)	1 (<1)	1 (<1)	0
アラニン・アミノトランスフェラーゼ増加	2 (<1)	1 (<1)	1 (<1)	1 (<1)
紅斑	2 (<1)	1 (<1)	2 (<1)	0
血尿	2 (<1)	0	1 (<1)	1 (<1)
副鼻腔炎	10 (3)	4 (1)	5 (2)	0
胃腸炎	3 (<1)	3 (<1)	1 (<1)	0
気管支炎	2 (<1)	4 (1)	4 (1)	1 (<1)
消化不良	5 (2)	0	2 (<1)	0
尿中アルブミン陽性	3 (<1)	5 (2)	2 (<1)	2 (<1)

NOTE 1: Numbers in parentheses are percentages.
2: Data after subjects switched to alternative MS treatment are excluded.
3: A subject was counted only once within each interval for each preferred term.
4: Preferred terms are presented by decreasing order of incidence in overall Total BG00012.

SOURCE: BG12MS/JAPAN/ISS/T-AE-PT-2PCT-3MON-301.SAS DATE: 02DEC2015

Incidence of adverse events at least 2% higher for any treatment group and the entire study period by preferred term and 3-months interval: Study 109MS301
Page 29 of 48

	BG00012 240 mg TID				
	0-3 months	>3-6 months	>6-9 months	>9-12 months	>12-15 months
口腔咽頭痛	3 (<1)	7 (2)	2 (<1)	3 (<1)	4 (1)
感覚鈍麻	3 (<1)	3 (<1)	9 (2)	5 (1)	2 (<1)
回転性めまい	3 (<1)	3 (<1)	4 (1)	6 (2)	6 (2)
咳嗽	3 (<1)	2 (<1)	3 (<1)	5 (1)	2 (<1)
浮動性めまい	7 (2)	2 (<1)	7 (2)	1 (<1)	3 (<1)
不眠症	6 (1)	3 (<1)	1 (<1)	3 (<1)	5 (1)
筋痙縮	6 (1)	3 (<1)	4 (1)	3 (<1)	7 (2)
ミクロアルブミン尿	4 (<1)	1 (<1)	2 (<1)	1 (<1)	5 (1)
発熱	7 (2)	2 (<1)	1 (<1)	0	3 (<1)
アスパラギン酸アミノトランスフェラーゼ増加	11 (3)	0	0	1 (<1)	3 (<1)
咽頭炎	3 (<1)	1 (<1)	2 (<1)	3 (<1)	5 (1)
便秘	9 (2)	4 (1)	1 (<1)	2 (<1)	0
不安	5 (1)	5 (1)	2 (<1)	3 (<1)	0
灼熱感	7 (2)	1 (<1)	1 (<1)	1 (<1)	1 (<1)
片頭痛	7 (2)	2 (<1)	1 (<1)	2 (<1)	3 (<1)
挫傷	2 (<1)	4 (1)	5 (1)	3 (<1)	1 (<1)
胃腸障害	18 (4)	1 (<1)	1 (<1)	0	0
鼻炎	6 (1)	1 (<1)	2 (<1)	2 (<1)	0
多汗症	8 (2)	3 (<1)	1 (<1)	1 (<1)	1 (<1)
リンパ球減少症	4 (<1)	0	4 (1)	2 (<1)	2 (<1)
歯痛	4 (<1)	2 (<1)	2 (<1)	0	2 (<1)

NOTE 1: Numbers in parentheses are percentages.
2: Data after subjects switched to alternative MS treatment are excluded.
3: A subject was counted only once within each interval for each preferred term.
4: Preferred terms are presented by decreasing order of incidence in overall Total BG00012.

SOURCE: BG12MS/JAPAN/ISS/T-AE-PT-2PCT-3MON-301.SAS DATE: 02DEC2015

Incidence of adverse events at least 2% higher for any treatment group and the entire study period by preferred term and 3-months interval: Study 109MS301
Page 30 of 48

	BG00012 240 mg TID			
	>15-18 months	>18-21 months	>21-24 months	>24 months
口腔咽頭痛	2 (<1)	2 (<1)	2 (<1)	0
感覚鈍麻	5 (2)	2 (<1)	1 (<1)	0
回転性めまい	6 (2)	4 (1)	0	0
咳嗽	2 (<1)	3 (<1)	2 (<1)	0
浮動性めまい	4 (1)	3 (<1)	3 (<1)	0
不眠症	2 (<1)	2 (<1)	0	0
筋痙縮	1 (<1)	7 (2)	3 (<1)	0
ミクロアルブミン尿	3 (<1)	1 (<1)	3 (<1)	1 (<1)
発熱	4 (1)	2 (<1)	1 (<1)	0
アスパラギン酸アミノトランスフェラーゼ増加	1 (<1)	0	0	2 (<1)
咽頭炎	4 (1)	2 (<1)	0	0
便秘	1 (<1)	0	1 (<1)	0
不安	1 (<1)	2 (<1)	0	0
灼熱感	3 (<1)	2 (<1)	0	0
片頭痛	1 (<1)	4 (1)	1 (<1)	0
挫傷	4 (1)	0	1 (<1)	0
胃腸障害	0	0	0	0
鼻炎	4 (1)	3 (<1)	0	0
多汗症	1 (<1)	3 (<1)	0	0
リンパ球減少症	1 (<1)	2 (<1)	1 (<1)	1 (<1)
歯痛	0	2 (<1)	2 (<1)	1 (<1)

NOTE 1: Numbers in parentheses are percentages.
2: Data after subjects switched to alternative MS treatment are excluded.
3: A subject was counted only once within each interval for each preferred term.
4: Preferred terms are presented by decreasing order of incidence in overall Total BG00012.

SOURCE: BG12MS/JAPAN/ISS/T-AE-PT-2PCT-3MON-301.SAS DATE: 02DEC2015

Incidence of adverse events at least 2% higher for any treatment group and the entire study period by preferred term and 3-months interval: Study 109MS301
Page 31 of 48

	BG00012 240 mg TID				
	0-3 months	>3-6 months	>6-9 months	>9-12 months	>12-15 months
ウイルス感染	4 (<1)	3 (<1)	0	3 (<1)	2 (<1)
筋力低下	4 (<1)	2 (<1)	3 (<1)	4 (1)	1 (<1)
胃食道逆流性疾患	5 (1)	3 (<1)	2 (<1)	4 (1)	1 (<1)
寝汗	6 (1)	1 (<1)	3 (<1)	0	3 (<1)
胃炎	4 (<1)	1 (<1)	1 (<1)	0	1 (<1)
尿中蛋白陽性	4 (<1)	4 (1)	2 (<1)	0	3 (<1)
膀胱炎	5 (1)	1 (<1)	1 (<1)	1 (<1)	3 (<1)
転倒	1 (<1)	2 (<1)	2 (<1)	1 (<1)	3 (<1)
口腔ヘルペス	0	1 (<1)	2 (<1)	1 (<1)	2 (<1)
尿中白血球陽性	4 (<1)	0	2 (<1)	1 (<1)	2 (<1)
無力症	5 (1)	2 (<1)	1 (<1)	2 (<1)	0
γ－グルタミルトランスフェラーゼ増加	3 (<1)	1 (<1)	0	1 (<1)	1 (<1)
筋骨格痛	3 (<1)	4 (1)	2 (<1)	2 (<1)	1 (<1)
気道感染	3 (<1)	1 (<1)	2 (<1)	2 (<1)	0
腹部不快感	7 (2)	0	1 (<1)	1 (<1)	0
食欲減退	5 (1)	3 (<1)	0	1 (<1)	0
霧視	3 (<1)	4 (1)	1 (<1)	2 (<1)	1 (<1)
胸痛	4 (<1)	2 (<1)	1 (<1)	1 (<1)	1 (<1)
口内乾燥	4 (<1)	0	0	1 (<1)	0
筋痙直	1 (<1)	2 (<1)	0	2 (<1)	1 (<1)
頚部痛	3 (<1)	1 (<1)	2 (<1)	3 (<1)	0

NOTE 1: Numbers in parentheses are percentages.
2: Data after subjects switched to alternative MS treatment are excluded.
3: A subject was counted only once within each interval for each preferred term.
4: Preferred terms are presented by decreasing order of incidence in overall Total BG00012.

SOURCE: BG12MS/JAPAN/ISS/T-AE-PT-2PCT-3MON-301.SAS DATE: 02DEC2015

Incidence of adverse events at least 2% higher for any treatment group and the entire study period by preferred term and 3-months interval: Study 109MS301
Page 32 of 48

	BG00012 240 mg TID			
	>15-18 months	>18-21 months	>21-24 months	>24 months
ウイルス感染	2 (<1)	0	0	0
筋力低下	2 (<1)	1 (<1)	1 (<1)	0
胃食道逆流性疾患	1 (<1)	0	0	1 (<1)
寝汗	1 (<1)	1 (<1)	1 (<1)	0
胃炎	2 (<1)	3 (<1)	0	0
尿中蛋白陽性	2 (<1)	0	2 (<1)	0
膀胱炎	4 (1)	0	1 (<1)	1 (<1)
転倒	2 (<1)	1 (<1)	0	0
口腔ヘルペス	4 (1)	3 (<1)	0	0
尿中白血球陽性	2 (<1)	0	2 (<1)	0
無力症	1 (<1)	1 (<1)	0	0
γ－グルタミルトランスフェラーゼ増加	0	0	1 (<1)	0
筋骨格痛	3 (<1)	1 (<1)	1 (<1)	0
気道感染	1 (<1)	1 (<1)	1 (<1)	0
腹部不快感	0	0	0	0
食欲減退	1 (<1)	0	0	0
霧視	1 (<1)	0	0	0
胸痛	0	1 (<1)	2 (<1)	0
口内乾燥	0	0	0	0
筋痙直	0	2 (<1)	1 (<1)	0
頚部痛	1 (<1)	1 (<1)	1 (<1)	0

NOTE 1: Numbers in parentheses are percentages.
2: Data after subjects switched to alternative MS treatment are excluded.
3: A subject was counted only once within each interval for each preferred term.
4: Preferred terms are presented by decreasing order of incidence in overall Total BG00012.

SOURCE: BG12MS/JAPAN/ISS/T-AE-PT-2PCT-3MON-301.SAS DATE: 02DEC2015

Incidence of adverse events at least 2% higher for any treatment group and the entire study period by preferred term and 3-months interval: Study 109MS301
Page 33 of 48

	BG00012 240 mg TID				
	0-3 months	>3-6 months	>6-9 months	>9-12 months	>12-15 months
平衡障害	4 (<1)	0	1 (<1)	3 (<1)	0
血中副甲状腺ホルモン増加	2 (<1)	0	0	1 (<1)	4 (1)
過敏症	4 (<1)	2 (<1)	0	0	1 (<1)
ケトン尿	5 (1)	4 (1)	2 (<1)	1 (<1)	2 (<1)
鼻漏	3 (<1)	1 (<1)	0	0	1 (<1)
血中ブドウ糖増加	1 (<1)	2 (<1)	1 (<1)	2 (<1)	1 (<1)
尿中血陽性	3 (<1)	1 (<1)	2 (<1)	1 (<1)	4 (1)
抑うつ気分	3 (<1)	1 (<1)	0	1 (<1)	2 (<1)
高血圧	1 (<1)	2 (<1)	2 (<1)	0	1 (<1)
インフルエンザ様疾患	1 (<1)	0	0	3 (<1)	0
アレルギー性皮膚炎	2 (<1)	0	1 (<1)	1 (<1)	0
蕁麻疹	6 (1)	1 (<1)	0	2 (<1)	0
異常感覚	1 (<1)	0	0	0	1 (<1)
眼痛	2 (<1)	3 (<1)	1 (<1)	2 (<1)	1 (<1)
腹部膨満	6 (1)	2 (<1)	0	0	1 (<1)
排尿困難	2 (<1)	1 (<1)	2 (<1)	1 (<1)	1 (<1)
振戦	0	2 (<1)	1 (<1)	0	1 (<1)
腟感染	0	0	0	1 (<1)	3 (<1)
脱毛症	1 (<1)	1 (<1)	1 (<1)	2 (<1)	0
関節捻挫	1 (<1)	1 (<1)	0	1 (<1)	0
筋肉痛	5 (1)	1 (<1)	0	0	0

NOTE 1: Numbers in parentheses are percentages.
2: Data after subjects switched to alternative MS treatment are excluded.
3: A subject was counted only once within each interval for each preferred term.
4: Preferred terms are presented by decreasing order of incidence in overall Total BG00012.

SOURCE: BG12MS/JAPAN/ISS/T-AE-PT-2PCT-3MON-301.SAS DATE: 02DEC2015

Incidence of adverse events at least 2% higher for any treatment group and the entire study period by preferred term and 3-months interval: Study 109MS301
Page 34 of 48

	BG00012 240 mg TID			
	>15-18 months	>18-21 months	>21-24 months	>24 months
平衡障害	0	0	1 (<1)	0
血中副甲状腺ホルモン増加	0	0	2 (<1)	1 (<1)
過敏症	0	0	0	0
ケトン尿	1 (<1)	0	1 (<1)	0
鼻漏	1 (<1)	1 (<1)	2 (<1)	0
血中ブドウ糖増加	2 (<1)	3 (<1)	1 (<1)	1 (<1)
尿中血陽性	1 (<1)	1 (<1)	1 (<1)	0
抑うつ気分	0	1 (<1)	0	0
高血圧	3 (<1)	1 (<1)	0	0
インフルエンザ様疾患	2 (<1)	2 (<1)	0	0
アレルギー性皮膚炎	1 (<1)	1 (<1)	0	0
蕁麻疹	1 (<1)	0	0	0
異常感覚	1 (<1)	1 (<1)	0	0
眼痛	1 (<1)	0	1 (<1)	0
腹部膨満	0	0	0	0
排尿困難	0	3 (<1)	0	0
振戦	0	0	0	0
腟感染	1 (<1)	1 (<1)	0	0
脱毛症	0	0	0	0
関節捻挫	2 (<1)	1 (<1)	0	1 (<1)
筋肉痛	0	0	0	0

NOTE 1: Numbers in parentheses are percentages.
2: Data after subjects switched to alternative MS treatment are excluded.
3: A subject was counted only once within each interval for each preferred term.
4: Preferred terms are presented by decreasing order of incidence in overall Total BG00012.

SOURCE: BG12MS/JAPAN/ISS/T-AE-PT-2PCT-3MON-301.SAS DATE: 02DEC2015

Incidence of adverse events at least 2% higher for any treatment group and the entire study period by preferred term and 3-months interval: Study 109MS301
Page 35 of 48

	BG00012 240 mg TID				
	0-3 months	>3-6 months	>6-9 months	>9-12 months	>12-15 months
耳感染	2 (<1)	3 (<1)	2 (<1)	0	1 (<1)
多発性硬化症	1 (<1)	0	1 (<1)	3 (<1)	1 (<1)
末梢性浮腫	3 (<1)	2 (<1)	0	1 (<1)	0
頻尿	1 (<1)	1 (<1)	0	1 (<1)	2 (<1)
白血球数増加	0	0	1 (<1)	1 (<1)	0

NOTE 1: Numbers in parentheses are percentages.
2: Data after subjects switched to alternative MS treatment are excluded.
3: A subject was counted only once within each interval for each preferred term.
4: Preferred terms are presented by decreasing order of incidence in overall Total BG00012.

SOURCE: BG12MS/JAPAN/ISS/T-AE-PT-2PCT-3MON-301.SAS DATE: 02DEC2015

Incidence of adverse events at least 2% higher for any treatment group and the entire study period by preferred term and 3-months interval: Study 109MS301
Page 36 of 48

	BG00012 240 mg TID			
	>15-18 months	>18-21 months	>21-24 months	>24 months
耳感染	3 (<1)	1 (<1)	0	0
多発性硬化症	2 (<1)	1 (<1)	1 (<1)	0
末梢性浮腫	1 (<1)	0	0	0
頻尿	0	0	0	0
白血球数増加	0	0	0	0

NOTE 1: Numbers in parentheses are percentages.
2: Data after subjects switched to alternative MS treatment are excluded.
3: A subject was counted only once within each interval for each preferred term.
4: Preferred terms are presented by decreasing order of incidence in overall Total BG00012.

SOURCE: BG12MS/JAPAN/ISS/T-AE-PT-2PCT-3MON-301.SAS DATE: 02DEC2015

Incidence of adverse events at least 2% higher for any treatment group and the entire study period by preferred term and 3-months interval: Study 109MS301
Page 37 of 48

	Total BG00012				
	0-3 months	>3-6 months	>6-9 months	>9-12 months	>12-15 months
Number of subjects followed in the interval	826 (100)	760 (100)	729 (100)	698 (100)	675 (100)
Number of subjects with an event	691 (84)	466 (61)	430 (59)	389 (56)	375 (56)
Number of subjects with deaths	1 (<1)	1 (<1)	0	0	0
Number of subjects with SAEs other than deaths	35 (4)	28 (4)	18 (2)	17 (2)	17 (3)
Number of subjects who discontinued	59 (7)	3 (<1)	7 (<1)	2 (<1)	5 (<1)
潮紅	239 (29)	49 (6)	32 (4)	27 (4)	21 (3)
多発性硬化症再発	58 (7)	53 (7)	45 (6)	39 (6)	32 (5)
鼻咽頭炎	63 (8)	55 (7)	54 (7)	51 (7)	38 (6)
頭痛	80 (10)	32 (4)	19 (3)	27 (4)	23 (3)
下痢	98 (12)	20 (3)	14 (2)	17 (2)	8 (1)
疲労	48 (6)	20 (3)	20 (3)	12 (2)	15 (2)
上気道感染	42 (5)	17 (2)	22 (3)	22 (3)	27 (4)
尿路感染	32 (4)	32 (4)	23 (3)	19 (3)	10 (1)
悪心	81 (10)	9 (1)	9 (1)	7 (1)	5 (<1)

NOTE 1: Numbers in parentheses are percentages.
2: Data after subjects switched to alternative MS treatment are excluded.
3: A subject was counted only once within each interval for each preferred term.
4: Preferred terms are presented by decreasing order of incidence in overall Total BG00012.

SOURCE: BG12MS/JAPAN/ISS/T-AE-PT-2PCT-3MON-301.SAS DATE: 02DEC2015

Incidence of adverse events at least 2% higher for any treatment group and the entire study period by preferred term and 3-months interval: Study 109MS301
Page 38 of 48

	Total BG00012			
	>15-18 months	>18-21 months	>21-24 months	>24 months
Number of subjects followed in the interval	651 (100)	636 (100)	622 (100)	448 (100)
Number of subjects with an event	366 (56)	314 (49)	296 (48)	67 (15)
Number of subjects with deaths	0	0	0	0
Number of subjects with SAEs other than deaths	23 (4)	19 (3)	19 (3)	4 (<1)
Number of subjects who discontinued	2 (<1)	1 (<1)	1 (<1)	0
潮紅	18 (3)	11 (2)	5 (<1)	1 (<1)
多発性硬化症再発	36 (6)	28 (4)	31 (5)	7 (2)
鼻咽頭炎	46 (7)	32 (5)	43 (7)	0
頭痛	19 (3)	14 (2)	16 (3)	4 (<1)
下痢	7 (1)	7 (1)	5 (<1)	0
疲労	12 (2)	11 (2)	9 (1)	0
上気道感染	14 (2)	15 (2)	16 (3)	1 (<1)
尿路感染	13 (2)	19 (3)	12 (2)	4 (<1)
悪心	4 (<1)	5 (<1)	6 (<1)	2 (<1)

NOTE 1: Numbers in parentheses are percentages.
2: Data after subjects switched to alternative MS treatment are excluded.
3: A subject was counted only once within each interval for each preferred term.
4: Preferred terms are presented by decreasing order of incidence in overall Total BG00012.

SOURCE: BG12MS/JAPAN/ISS/T-AE-PT-2PCT-3MON-301.SAS DATE: 02DEC2015

Incidence of adverse events at least 2% higher for any treatment group and the entire study period by preferred term and 3-months interval: Study 109MS301
Page 39 of 48

	Total BG00012				
	0-3 months	>3-6 months	>6-9 months	>9-12 months	>12-15 months
背部痛	24 (3)	23 (3)	14 (2)	16 (2)	16 (2)
上腹部痛	61 (7)	11 (1)	11 (2)	10 (1)	11 (2)
蛋白尿	27 (3)	20 (3)	21 (3)	13 (2)	16 (2)
腹痛	52 (6)	8 (1)	7 (<1)	13 (2)	5 (<1)
関節痛	23 (3)	12 (2)	12 (2)	13 (2)	9 (1)
インフルエンザ	21 (3)	11 (1)	14 (2)	12 (2)	11 (2)
そう痒症	47 (6)	10 (1)	12 (2)	9 (1)	4 (<1)
錯感覚	21 (3)	16 (2)	12 (2)	11 (2)	7 (1)
嘔吐	44 (5)	4 (<1)	7 (<1)	10 (1)	5 (<1)
四肢痛	15 (2)	16 (2)	14 (2)	13 (2)	3 (<1)
うつ病	11 (1)	8 (1)	13 (2)	15 (2)	7 (1)
発疹	33 (4)	13 (2)	12 (2)	6 (<1)	6 (<1)
ほてり	46 (6)	7 (<1)	3 (<1)	5 (<1)	2 (<1)
アラニン・アミノトランスフェラーゼ増加	29 (4)	10 (1)	2 (<1)	5 (<1)	5 (<1)
紅斑	35 (4)	8 (1)	1 (<1)	3 (<1)	1 (<1)
血尿	16 (2)	12 (2)	8 (1)	10 (1)	8 (1)
副鼻腔炎	10 (1)	4 (<1)	13 (2)	8 (1)	10 (1)
胃腸炎	17 (2)	5 (<1)	4 (<1)	6 (<1)	11 (2)
気管支炎	13 (2)	10 (1)	7 (<1)	3 (<1)	6 (<1)
消化不良	26 (3)	9 (1)	4 (<1)	7 (1)	2 (<1)
尿中アルブミン陽性	11 (1)	12 (2)	10 (1)	6 (<1)	4 (<1)

NOTE 1: Numbers in parentheses are percentages.
2: Data after subjects switched to alternative MS treatment are excluded.
3: A subject was counted only once within each interval for each preferred term.
4: Preferred terms are presented by decreasing order of incidence in overall Total BG00012.

SOURCE: BG12MS/JAPAN/ISS/T-AE-PT-2PCT-3MON-301.SAS DATE: 02DEC2015

Incidence of adverse events at least 2% higher for any treatment group and the entire study period by preferred term and 3-months interval: Study 109MS301
Page 40 of 48

	Total BG00012			
	>15-18 months	>18-21 months	>21-24 months	>24 months
背部痛	16 (2)	8 (1)	13 (2)	3 (<1)
上腹部痛	3 (<1)	3 (<1)	3 (<1)	0
蛋白尿	11 (2)	7 (1)	8 (1)	3 (<1)
腹痛	2 (<1)	3 (<1)	3 (<1)	0
関節痛	9 (1)	8 (1)	7 (1)	1 (<1)
インフルエンザ	10 (2)	8 (1)	13 (2)	1 (<1)
そう痒症	3 (<1)	2 (<1)	6 (<1)	0
錯感覚	9 (1)	9 (1)	4 (<1)	0
嘔吐	3 (<1)	1 (<1)	3 (<1)	2 (<1)
四肢痛	8 (1)	5 (<1)	7 (1)	0
うつ病	4 (<1)	6 (<1)	8 (1)	2 (<1)
発疹	3 (<1)	0	4 (<1)	0
ほてり	2 (<1)	1 (<1)	1 (<1)	0
アラニン・アミノトランスフェラーゼ増加	6 (<1)	2 (<1)	5 (<1)	2 (<1)
紅斑	6 (<1)	4 (<1)	3 (<1)	0
血尿	5 (<1)	6 (<1)	9 (1)	2 (<1)
副鼻腔炎	11 (2)	7 (1)	7 (1)	0
胃腸炎	5 (<1)	5 (<1)	1 (<1)	0
気管支炎	4 (<1)	7 (1)	6 (<1)	1 (<1)
消化不良	6 (<1)	1 (<1)	3 (<1)	0
尿中アルブミン陽性	4 (<1)	7 (1)	4 (<1)	3 (<1)

NOTE 1: Numbers in parentheses are percentages.
2: Data after subjects switched to alternative MS treatment are excluded.
3: A subject was counted only once within each interval for each preferred term.
4: Preferred terms are presented by decreasing order of incidence in overall Total BG00012.

SOURCE: BG12MS/JAPAN/ISS/T-AE-PT-2PCT-3MON-301.SAS DATE: 02DEC2015

Incidence of adverse events at least 2% higher for any treatment group and the entire study period by preferred term and 3-months interval: Study 109MS301
Page 41 of 48

	Total BG00012				
	0-3 months	>3-6 months	>6-9 months	>9-12 months	>12-15 months
口腔咽頭痛	8 (<1)	11 (1)	4 (<1)	8 (1)	6 (<1)
感覚鈍麻	8 (<1)	7 (<1)	13 (2)	10 (1)	5 (<1)
回転性めまい	6 (<1)	7 (<1)	6 (<1)	6 (<1)	8 (1)
咳嗽	8 (<1)	6 (<1)	4 (<1)	7 (1)	5 (<1)
浮動性めまい	12 (1)	4 (<1)	11 (2)	4 (<1)	6 (<1)
不眠症	10 (1)	5 (<1)	7 (<1)	8 (1)	7 (1)
筋痙縮	9 (1)	4 (<1)	5 (<1)	6 (<1)	10 (1)
ミクロアルブミン尿	7 (<1)	7 (<1)	4 (<1)	2 (<1)	14 (2)
発熱	10 (1)	5 (<1)	1 (<1)	2 (<1)	6 (<1)
アスパラギン酸アミノトランスフェラーゼ増加	18 (2)	4 (<1)	1 (<1)	2 (<1)	4 (<1)
咽頭炎	7 (<1)	4 (<1)	3 (<1)	6 (<1)	9 (1)
便秘	14 (2)	6 (<1)	2 (<1)	2 (<1)	6 (<1)
不安	10 (1)	10 (1)	6 (<1)	5 (<1)	2 (<1)
灼熱感	17 (2)	1 (<1)	2 (<1)	4 (<1)	1 (<1)
片頭痛	11 (1)	6 (<1)	5 (<1)	4 (<1)	5 (<1)
挫傷	3 (<1)	6 (<1)	7 (<1)	6 (<1)	3 (<1)
胃腸障害	27 (3)	2 (<1)	1 (<1)	1 (<1)	0
鼻炎	9 (1)	4 (<1)	2 (<1)	3 (<1)	2 (<1)
多汗症	11 (1)	5 (<1)	3 (<1)	4 (<1)	1 (<1)
リンパ球減少症	6 (<1)	3 (<1)	6 (<1)	3 (<1)	3 (<1)
歯痛	5 (<1)	4 (<1)	3 (<1)	2 (<1)	4 (<1)

NOTE 1: Numbers in parentheses are percentages.
2: Data after subjects switched to alternative MS treatment are excluded.
3: A subject was counted only once within each interval for each preferred term.
4: Preferred terms are presented by decreasing order of incidence in overall Total BG00012.

SOURCE: BG12MS/JAPAN/ISS/T-AE-PT-2PCT-3MON-301.SAS DATE: 02DEC2015

Incidence of adverse events at least 2% higher for any treatment group and the entire study period by preferred term and 3-months interval: Study 109MS301
Page 42 of 48

	Total BG00012			
	>15-18 months	>18-21 months	>21-24 months	>24 months
口腔咽頭痛	6 (<1)	6 (<1)	4 (<1)	0
感覚鈍麻	6 (<1)	3 (<1)	1 (<1)	0
回転性めまい	7 (1)	4 (<1)	2 (<1)	0
咳嗽	7 (1)	5 (<1)	5 (<1)	0
浮動性めまい	5 (<1)	4 (<1)	5 (<1)	1 (<1)
不眠症	4 (<1)	4 (<1)	1 (<1)	0
筋痙縮	4 (<1)	8 (1)	6 (<1)	1 (<1)
ミクロアルブミン尿	4 (<1)	4 (<1)	4 (<1)	4 (<1)
発熱	6 (<1)	6 (<1)	2 (<1)	1 (<1)
アスパラギン酸アミノトランスフェラーゼ増加	4 (<1)	0	1 (<1)	2 (<1)
咽頭炎	8 (1)	4 (<1)	3 (<1)	0
便秘	1 (<1)	0	2 (<1)	0
不安	1 (<1)	2 (<1)	0	0
灼熱感	4 (<1)	2 (<1)	1 (<1)	0
片頭痛	2 (<1)	5 (<1)	2 (<1)	0
挫傷	4 (<1)	2 (<1)	2 (<1)	0
胃腸障害	0	0	0	0
鼻炎	6 (<1)	5 (<1)	0	0
多汗症	1 (<1)	3 (<1)	2 (<1)	0
リンパ球減少症	4 (<1)	4 (<1)	4 (<1)	1 (<1)
歯痛	2 (<1)	3 (<1)	4 (<1)	1 (<1)

NOTE 1: Numbers in parentheses are percentages.
2: Data after subjects switched to alternative MS treatment are excluded.
3: A subject was counted only once within each interval for each preferred term.
4: Preferred terms are presented by decreasing order of incidence in overall Total BG00012.

SOURCE: BG12MS/JAPAN/ISS/T-AE-PT-2PCT-3MON-301.SAS DATE: 02DEC2015

Incidence of adverse events at least 2% higher for any treatment group and the entire study period by preferred term and 3-months interval: Study 109MS301
Page 43 of 48

	Total BG00012				
	0-3 months	>3-6 months	>6-9 months	>9-12 months	>12-15 months
ウイルス感染	7 (<1)	5 (<1)	0	4 (<1)	3 (<1)
筋力低下	6 (<1)	4 (<1)	6 (<1)	4 (<1)	4 (<1)
胃食道逆流性疾患	10 (1)	4 (<1)	3 (<1)	5 (<1)	2 (<1)
寝汗	12 (1)	2 (<1)	6 (<1)	1 (<1)	3 (<1)
胃炎	8 (<1)	4 (<1)	1 (<1)	2 (<1)	2 (<1)
尿中蛋白陽性	9 (1)	5 (<1)	3 (<1)	1 (<1)	5 (<1)
膀胱炎	6 (<1)	4 (<1)	1 (<1)	1 (<1)	3 (<1)
転倒	1 (<1)	5 (<1)	6 (<1)	2 (<1)	6 (<1)
口腔ヘルペス	4 (<1)	5 (<1)	4 (<1)	3 (<1)	3 (<1)
尿中白血球陽性	4 (<1)	3 (<1)	4 (<1)	3 (<1)	4 (<1)
無力症	13 (2)	2 (<1)	2 (<1)	3 (<1)	0
γ－グルタミルトランスフェラーゼ増加	5 (<1)	4 (<1)	2 (<1)	1 (<1)	3 (<1)
筋骨格痛	5 (<1)	5 (<1)	3 (<1)	5 (<1)	3 (<1)
気道感染	6 (<1)	3 (<1)	4 (<1)	3 (<1)	1 (<1)
腹部不快感	14 (2)	0	2 (<1)	3 (<1)	2 (<1)
食欲減退	9 (1)	5 (<1)	0	2 (<1)	1 (<1)
霧視	6 (<1)	5 (<1)	2 (<1)	3 (<1)	1 (<1)
胸痛	6 (<1)	4 (<1)	1 (<1)	3 (<1)	1 (<1)
口内乾燥	17 (2)	1 (<1)	0	2 (<1)	0
筋痙直	2 (<1)	7 (<1)	0	2 (<1)	2 (<1)
頚部痛	3 (<1)	5 (<1)	4 (<1)	4 (<1)	1 (<1)

NOTE 1: Numbers in parentheses are percentages.
2: Data after subjects switched to alternative MS treatment are excluded.
3: A subject was counted only once within each interval for each preferred term.
4: Preferred terms are presented by decreasing order of incidence in overall Total BG00012.

SOURCE: BG12MS/JAPAN/ISS/T-AE-PT-2PCT-3MON-301.SAS DATE: 02DEC2015

Incidence of adverse events at least 2% higher for any treatment group and the entire study period by preferred term and 3-months interval: Study 109MS301
Page 44 of 48

	Total BG00012			
	>15-18 months	>18-21 months	>21-24 months	>24 months
ウイルス感染	3 (<1)	6 (<1)	2 (<1)	0
筋力低下	4 (<1)	1 (<1)	3 (<1)	0
胃食道逆流性疾患	1 (<1)	0	1 (<1)	1 (<1)
寝汗	1 (<1)	1 (<1)	1 (<1)	0
胃炎	4 (<1)	3 (<1)	0	0
尿中蛋白陽性	2 (<1)	1 (<1)	3 (<1)	1 (<1)
膀胱炎	5 (<1)	0	3 (<1)	1 (<1)
転倒	3 (<1)	2 (<1)	1 (<1)	0
口腔ヘルペス	6 (<1)	4 (<1)	2 (<1)	0
尿中白血球陽性	3 (<1)	2 (<1)	3 (<1)	0
無力症	1 (<1)	2 (<1)	0	0
γ－グルタミルトランスフェラーゼ増加	1 (<1)	2 (<1)	5 (<1)	0
筋骨格痛	5 (<1)	2 (<1)	3 (<1)	0
気道感染	2 (<1)	1 (<1)	2 (<1)	0
腹部不快感	1 (<1)	0	1 (<1)	0
食欲減退	2 (<1)	0	2 (<1)	0
霧視	4 (<1)	1 (<1)	0	0
胸痛	0	3 (<1)	2 (<1)	0
口内乾燥	0	0	0	0
筋痙直	2 (<1)	3 (<1)	2 (<1)	0
頚部痛	4 (<1)	1 (<1)	2 (<1)	0

NOTE 1: Numbers in parentheses are percentages.
2: Data after subjects switched to alternative MS treatment are excluded.
3: A subject was counted only once within each interval for each preferred term.
4: Preferred terms are presented by decreasing order of incidence in overall Total BG00012.

SOURCE: BG12MS/JAPAN/ISS/T-AE-PT-2PCT-3MON-301.SAS DATE: 02DEC2015

Incidence of adverse events at least 2% higher for any treatment group and the entire study period by preferred term and 3-months interval: Study 109MS301
Page 45 of 48

	Total BG00012				
	0-3 months	>3-6 months	>6-9 months	>9-12 months	>12-15 months
平衡障害	4 (<1)	1 (<1)	2 (<1)	6 (<1)	1 (<1)
血中副甲状腺ホルモン増加	3 (<1)	1 (<1)	0	2 (<1)	5 (<1)
過敏症	11 (1)	2 (<1)	0	0	4 (<1)
ケトン尿	6 (<1)	6 (<1)	3 (<1)	2 (<1)	4 (<1)
鼻漏	4 (<1)	4 (<1)	2 (<1)	1 (<1)	4 (<1)
血中ブドウ糖増加	1 (<1)	3 (<1)	1 (<1)	3 (<1)	3 (<1)
尿中血陽性	3 (<1)	3 (<1)	3 (<1)	1 (<1)	5 (<1)
抑うつ気分	7 (<1)	1 (<1)	1 (<1)	1 (<1)	3 (<1)
高血圧	3 (<1)	3 (<1)	2 (<1)	0	2 (<1)
インフルエンザ様疾患	2 (<1)	1 (<1)	1 (<1)	5 (<1)	1 (<1)
アレルギー性皮膚炎	5 (<1)	0	2 (<1)	2 (<1)	1 (<1)
蕁麻疹	10 (1)	2 (<1)	0	2 (<1)	0
異常感覚	6 (<1)	3 (<1)	1 (<1)	0	2 (<1)
眼痛	2 (<1)	4 (<1)	1 (<1)	2 (<1)	2 (<1)
腹部膨満	9 (1)	2 (<1)	1 (<1)	0	1 (<1)
排尿困難	3 (<1)	1 (<1)	3 (<1)	1 (<1)	1 (<1)
振戦	5 (<1)	3 (<1)	1 (<1)	2 (<1)	1 (<1)
腟感染	0	2 (<1)	2 (<1)	3 (<1)	5 (<1)
脱毛症	5 (<1)	2 (<1)	1 (<1)	2 (<1)	1 (<1)
関節捻挫	1 (<1)	2 (<1)	0	2 (<1)	2 (<1)
筋肉痛	7 (<1)	3 (<1)	0	0	1 (<1)

NOTE 1: Numbers in parentheses are percentages.
2: Data after subjects switched to alternative MS treatment are excluded.
3: A subject was counted only once within each interval for each preferred term.
4: Preferred terms are presented by decreasing order of incidence in overall Total BG00012.

SOURCE: BG12MS/JAPAN/ISS/T-AE-PT-2PCT-3MON-301.SAS DATE: 02DEC2015

Incidence of adverse events at least 2% higher for any treatment group and the entire study period by preferred term and 3-months interval: Study 109MS301
Page 46 of 48

	Total BG00012			
	>15-18 months	>18-21 months	>21-24 months	>24 months
平衡障害	0	2 (<1)	1 (<1)	0
血中副甲状腺ホルモン増加	0	0	2 (<1)	5 (1)
過敏症	0	1 (<1)	0	0
ケトン尿	3 (<1)	1 (<1)	2 (<1)	0
鼻漏	1 (<1)	1 (<1)	2 (<1)	0
血中ブドウ糖増加	3 (<1)	5 (<1)	1 (<1)	1 (<1)
尿中血陽性	2 (<1)	1 (<1)	2 (<1)	0
抑うつ気分	2 (<1)	1 (<1)	0	1 (<1)
高血圧	4 (<1)	2 (<1)	0	1 (<1)
インフルエンザ様疾患	3 (<1)	3 (<1)	0	0
アレルギー性皮膚炎	2 (<1)	2 (<1)	1 (<1)	0
蕁麻疹	2 (<1)	0	0	0
異常感覚	1 (<1)	2 (<1)	1 (<1)	0
眼痛	4 (<1)	0	2 (<1)	0
腹部膨満	0	1 (<1)	0	0
排尿困難	1 (<1)	4 (<1)	0	0
振戦	1 (<1)	1 (<1)	0	0
腟感染	1 (<1)	1 (<1)	1 (<1)	0
脱毛症	0	1 (<1)	0	0
関節捻挫	3 (<1)	1 (<1)	0	1 (<1)
筋肉痛	0	0	1 (<1)	0

NOTE 1: Numbers in parentheses are percentages.
2: Data after subjects switched to alternative MS treatment are excluded.
3: A subject was counted only once within each interval for each preferred term.
4: Preferred terms are presented by decreasing order of incidence in overall Total BG00012.

SOURCE: BG12MS/JAPAN/ISS/T-AE-PT-2PCT-3MON-301.SAS DATE: 02DEC2015

Incidence of adverse events at least 2% higher for any treatment group and the entire study period by preferred term and 3-months interval: Study 109MS301
Page 47 of 48

	Total BG00012				
	0-3 months	>3-6 months	>6-9 months	>9-12 months	>12-15 months
耳感染	2 (<1)	3 (<1)	3 (<1)	0	3 (<1)
多発性硬化症	1 (<1)	1 (<1)	2 (<1)	3 (<1)	2 (<1)
末梢性浮腫	3 (<1)	2 (<1)	1 (<1)	1 (<1)	1 (<1)
頻尿	2 (<1)	1 (<1)	0	2 (<1)	4 (<1)
白血球数増加	1 (<1)	1 (<1)	1 (<1)	1 (<1)	0

NOTE 1: Numbers in parentheses are percentages.
2: Data after subjects switched to alternative MS treatment are excluded.
3: A subject was counted only once within each interval for each preferred term.
4: Preferred terms are presented by decreasing order of incidence in overall Total BG00012.

SOURCE: BG12MS/JAPAN/ISS/T-AE-PT-2PCT-3MON-301.SAS DATE: 02DEC2015

Incidence of adverse events at least 2% higher for any treatment group and the entire study period by preferred term and 3-months interval: Study 109MS301
Page 48 of 48

	Total BG00012			
	>15-18 months	>18-21 months	>21-24 months	>24 months
耳感染	4 (<1)	1 (<1)	0	0
多発性硬化症	2 (<1)	2 (<1)	1 (<1)	0
末梢性浮腫	2 (<1)	0	0	0
頻尿	1 (<1)	1 (<1)	0	0
白血球数増加	0	0	0	0

NOTE 1: Numbers in parentheses are percentages.
2: Data after subjects switched to alternative MS treatment are excluded.
3: A subject was counted only once within each interval for each preferred term.
4: Preferred terms are presented by decreasing order of incidence in overall Total BG00012.

SOURCE: BG12MS/JAPAN/ISS/T-AE-PT-2PCT-3MON-301.SAS DATE: 02DEC2015

Table 321: Incidence of Adverse Events At Least 2% Higher for Any Treatment Group and the Entire Study Period by Preferred Term and 3-Months Interval: Study 109MS302

Incidence of adverse events at least 2% higher for any treatment group and the entire study period by preferred term and 3-months interval:
Study 109MS302
Page 1 of 50

	Placebo				
	0-3 months	>3-6 months	>6-9 months	>9-12 months	>12-15 months
Number of subjects followed in the interval	363 (100)	357 (100)	341 (100)	323 (100)	305 (100)
Number of subjects with an event	220 (61)	196 (55)	160 (47)	147 (46)	126 (41)
Number of subjects with deaths	0	0	0	0	1 (<1)
Number of subjects with SAEs other than deaths	21 (6)	20 (6)	21 (6)	9 (3)	11 (4)
Number of subjects who discontinued	6 (2)	0	2 (<1)	0	1 (<1)
多発性硬化症再発	49 (13)	49 (14)	39 (11)	26 (8)	26 (9)
潮紅	7 (2)	3 (<1)	1 (<1)	0	0
鼻咽頭炎	14 (4)	13 (4)	13 (4)	14 (4)	4 (1)
頭痛	29 (8)	9 (3)	14 (4)	8 (2)	5 (2)
下痢	11 (3)	6 (2)	3 (<1)	2 (<1)	3 (<1)
尿路感染	10 (3)	9 (3)	8 (2)	9 (3)	6 (2)
悪心	14 (4)	8 (2)	2 (<1)	1 (<1)	1 (<1)
上気道感染	9 (2)	10 (3)	5 (1)	5 (2)	2 (<1)
背部痛	5 (1)	12 (3)	7 (2)	4 (1)	3 (<1)

NOTE 1: Numbers in parentheses are percentages.
2: Data after subjects switched to alternative MS treatment are excluded.
3: A subject was counted only once within each interval for each preferred term.
4: Preferred terms are presented by decreasing order of incidence in overall Total BG00012.

SOURCE: BG12MS/JAPAN/ISS/T-AE-PT-2PCT-3MON-302.SAS DATE: 02DEC2015

Incidence of adverse events at least 2% higher for any treatment group and the entire study period by preferred term and 3-months interval:
Study 109MS302
Page 2 of 50

	Placebo			
	>15-18 months	>18-21 months	>21-24 months	>24 months
Number of subjects followed in the interval	281 (100)	268 (100)	260 (100)	178 (100)
Number of subjects with an event	116 (41)	119 (44)	98 (38)	21 (12)
Number of subjects with deaths	0	0	0	0
Number of subjects with SAEs other than deaths	9 (3)	10 (4)	6 (2)	2 (1)
Number of subjects who discontinued	0	1 (<1)	0	0
多発性硬化症再発	12 (4)	20 (7)	17 (7)	2 (1)
潮紅	0	1 (<1)	1 (<1)	0
鼻咽頭炎	7 (2)	8 (3)	10 (4)	0
頭痛	4 (1)	2 (<1)	4 (2)	0
下痢	3 (1)	2 (<1)	2 (<1)	1 (<1)
尿路感染	11 (4)	4 (1)	3 (1)	0
悪心	2 (<1)	1 (<1)	2 (<1)	0
上気道感染	5 (2)	4 (1)	4 (2)	0
背部痛	2 (<1)	5 (2)	1 (<1)	0

NOTE 1: Numbers in parentheses are percentages.
2: Data after subjects switched to alternative MS treatment are excluded.
3: A subject was counted only once within each interval for each preferred term.
4: Preferred terms are presented by decreasing order of incidence in overall Total BG00012.

SOURCE: BG12MS/JAPAN/ISS/T-AE-PT-2PCT-3MON-302.SAS DATE: 02DEC2015

Incidence of adverse events at least 2% higher for any treatment group and the entire study period by preferred term and 3-months interval:
Study 109MS302
Page 3 of 50

	Placebo				
	0-3 months	>3-6 months	>6-9 months	>9-12 months	>12-15 months
疲労	5 (1)	10 (3)	5 (1)	4 (1)	9 (3)
上腹部痛	10 (3)	1 (<1)	3 (<1)	2 (<1)	1 (<1)
蛋白尿	4 (1)	7 (2)	4 (1)	4 (1)	3 (<1)
腹痛	9 (2)	0	1 (<1)	3 (<1)	1 (<1)
発疹	4 (1)	2 (<1)	0	4 (1)	0
嘔吐	3 (<1)	1 (<1)	0	3 (<1)	2 (<1)
関節痛	6 (2)	1 (<1)	3 (<1)	8 (2)	4 (1)
四肢痛	6 (2)	7 (2)	5 (1)	6 (2)	4 (1)
インフルエンザ	8 (2)	4 (1)	4 (1)	0	3 (<1)
そう痒症	7 (2)	1 (<1)	1 (<1)	0	1 (<1)
錯感覚	9 (2)	4 (1)	3 (<1)	7 (2)	4 (1)
うつ病	7 (2)	11 (3)	2 (<1)	8 (2)	2 (<1)
アラニン・アミノトランスフェラーゼ増加	2 (<1)	5 (1)	5 (1)	4 (1)	2 (<1)
紅斑	1 (<1)	0	2 (<1)	0	0
ほてり	5 (1)	0	2 (<1)	0	0
尿中アルブミン陽性	3 (<1)	1 (<1)	0	3 (<1)	3 (<1)
気管支炎	1 (<1)	4 (1)	2 (<1)	4 (1)	3 (<1)
発熱	2 (<1)	4 (1)	5 (1)	1 (<1)	4 (1)
副鼻腔炎	0	2 (<1)	2 (<1)	3 (<1)	4 (1)
咳嗽	6 (2)	5 (1)	1 (<1)	5 (2)	1 (<1)
筋痙縮	3 (<1)	6 (2)	1 (<1)	3 (<1)	1 (<1)

NOTE 1: Numbers in parentheses are percentages.
2: Data after subjects switched to alternative MS treatment are excluded.
3: A subject was counted only once within each interval for each preferred term.
4: Preferred terms are presented by decreasing order of incidence in overall Total BG00012.

SOURCE: BG12MS/JAPAN/ISS/T-AE-PT-2PCT-3MON-302.SAS DATE: 02DEC2015

Incidence of adverse events at least 2% higher for any treatment group and the entire study period by preferred term and 3-months interval:
Study 109MS302
Page 4 of 50

	Placebo			
	>15-18 months	>18-21 months	>21-24 months	>24 months
疲労	2 (<1)	4 (1)	3 (1)	0
上腹部痛	0	3 (1)	1 (<1)	0
蛋白尿	4 (1)	5 (2)	4 (2)	2 (1)
腹痛	0	1 (<1)	0	1 (<1)
発疹	0	2 (<1)	0	1 (<1)
嘔吐	1 (<1)	3 (1)	0	1 (<1)
関節痛	3 (1)	3 (1)	3 (1)	0
四肢痛	1 (<1)	5 (2)	3 (1)	0
インフルエンザ	1 (<1)	2 (<1)	4 (2)	0
そう痒症	1 (<1)	2 (<1)	0	0
錯感覚	3 (1)	5 (2)	4 (2)	0
うつ病	2 (<1)	4 (1)	2 (<1)	0
アラニン・アミノトランスフェラーゼ増加	2 (<1)	4 (1)	2 (<1)	0
紅斑	0	0	2 (<1)	0
ほてり	0	1 (<1)	0	0
尿中アルブミン陽性	2 (<1)	1 (<1)	4 (2)	2 (1)
気管支炎	2 (<1)	3 (1)	1 (<1)	0
発熱	2 (<1)	3 (1)	2 (<1)	1 (<1)
副鼻腔炎	2 (<1)	2 (<1)	2 (<1)	0
咳嗽	2 (<1)	2 (<1)	1 (<1)	0
筋痙縮	1 (<1)	1 (<1)	0	0

NOTE 1: Numbers in parentheses are percentages.
2: Data after subjects switched to alternative MS treatment are excluded.
3: A subject was counted only once within each interval for each preferred term.
4: Preferred terms are presented by decreasing order of incidence in overall Total BG00012.

SOURCE: BG12MS/JAPAN/ISS/T-AE-PT-2PCT-3MON-302.SAS DATE: 02DEC2015

Incidence of adverse events at least 2% higher for any treatment group and the entire study period by preferred term and 3-months interval:
Study 109MS302
Page 5 of 50

	Placebo				
	0-3 months	>3-6 months	>6-9 months	>9-12 months	>12-15 months
ミクロアルブミン尿	3 (<1)	2 (<1)	2 (<1)	0	3 (<1)
口腔咽頭痛	4 (1)	4 (1)	4 (1)	0	0
感覚鈍麻	4 (1)	1 (<1)	4 (1)	6 (2)	2 (<1)
アスパラギン酸アミノトランスフェラーゼ増加	2 (<1)	1 (<1)	1 (<1)	2 (<1)	1 (<1)
消化不良	3 (<1)	3 (<1)	2 (<1)	1 (<1)	0
頚部痛	4 (1)	0	0	1 (<1)	1 (<1)
胃腸炎	1 (<1)	2 (<1)	2 (<1)	2 (<1)	0
不安	6 (2)	4 (1)	1 (<1)	3 (<1)	0
不眠症	3 (<1)	8 (2)	4 (1)	3 (<1)	1 (<1)
尿中蛋白陽性	2 (<1)	1 (<1)	0	3 (<1)	2 (<1)
咽頭炎	1 (<1)	3 (<1)	2 (<1)	3 (<1)	3 (<1)
胃腸障害	1 (<1)	1 (<1)	0	1 (<1)	0
浮動性めまい	3 (<1)	2 (<1)	2 (<1)	1 (<1)	3 (<1)
転倒	3 (<1)	2 (<1)	2 (<1)	3 (<1)	1 (<1)
ウイルス性胃腸炎	2 (<1)	0	1 (<1)	3 (<1)	0
血尿	7 (2)	2 (<1)	3 (<1)	2 (<1)	2 (<1)
回転性めまい	9 (2)	6 (2)	1 (<1)	2 (<1)	1 (<1)
鼻炎	0	1 (<1)	2 (<1)	1 (<1)	0
貧血	1 (<1)	1 (<1)	2 (<1)	1 (<1)	2 (<1)
無力症	3 (<1)	3 (<1)	0	1 (<1)	2 (<1)
便秘	5 (1)	2 (<1)	2 (<1)	0	1 (<1)

NOTE 1: Numbers in parentheses are percentages.
2: Data after subjects switched to alternative MS treatment are excluded.
3: A subject was counted only once within each interval for each preferred term.
4: Preferred terms are presented by decreasing order of incidence in overall Total BG00012.

SOURCE: BG12MS/JAPAN/ISS/T-AE-PT-2PCT-3MON-302.SAS DATE: 02DEC2015

Incidence of adverse events at least 2% higher for any treatment group and the entire study period by preferred term and 3-months interval:
Study 109MS302
Page 6 of 50

	Placebo			
	>15-18 months	>18-21 months	>21-24 months	>24 months
ミクロアルブミン尿	2 (<1)	1 (<1)	0	2 (1)
口腔咽頭痛	3 (1)	0	1 (<1)	1 (<1)
感覚鈍麻	2 (<1)	4 (1)	0	2 (1)
アスパラギン酸アミノトランスフェラーゼ増加	3 (1)	1 (<1)	0	0
消化不良	0	0	0	0
頚部痛	2 (<1)	1 (<1)	1 (<1)	0
胃腸炎	1 (<1)	0	0	0
不安	1 (<1)	0	1 (<1)	0
不眠症	0	1 (<1)	2 (<1)	0
尿中蛋白陽性	2 (<1)	0	2 (<1)	0
咽頭炎	4 (1)	2 (<1)	1 (<1)	0
胃腸障害	0	0	0	0
浮動性めまい	1 (<1)	3 (1)	2 (<1)	0
転倒	1 (<1)	0	1 (<1)	0
ウイルス性胃腸炎	1 (<1)	1 (<1)	0	0
血尿	2 (<1)	2 (<1)	2 (<1)	0
回転性めまい	3 (1)	5 (2)	1 (<1)	0
鼻炎	2 (<1)	2 (<1)	0	0
貧血	1 (<1)	0	1 (<1)	0
無力症	3 (1)	2 (<1)	1 (<1)	0
便秘	2 (<1)	1 (<1)	1 (<1)	0

NOTE 1: Numbers in parentheses are percentages.
2: Data after subjects switched to alternative MS treatment are excluded.
3: A subject was counted only once within each interval for each preferred term.
4: Preferred terms are presented by decreasing order of incidence in overall Total BG00012.

SOURCE: BG12MS/JAPAN/ISS/T-AE-PT-2PCT-3MON-302.SAS DATE: 02DEC2015

Incidence of adverse events at least 2% higher for any treatment group and the entire study period by preferred term and 3-months interval:
Study 109MS302
Page 7 of 50

	Placebo				
	0-3 months	>3-6 months	>6-9 months	>9-12 months	>12-15 months
胃炎	2 (<1)	2 (<1)	1 (<1)	1 (<1)	0
尿中血陽性	0	0	1 (<1)	0	3 (<1)
挫傷	4 (1)	0	1 (<1)	2 (<1)	1 (<1)
歯痛	0	1 (<1)	1 (<1)	0	2 (<1)
脱毛症	1 (<1)	2 (<1)	0	2 (<1)	0
尿中β２ミクログロブリン増加	0	2 (<1)	1 (<1)	2 (<1)	1 (<1)
灼熱感	2 (<1)	1 (<1)	2 (<1)	0	1 (<1)
多汗症	1 (<1)	1 (<1)	1 (<1)	0	0
高血圧	1 (<1)	1 (<1)	3 (<1)	2 (<1)	0
筋力低下	2 (<1)	1 (<1)	1 (<1)	2 (<1)	0
気道感染	0	3 (<1)	1 (<1)	2 (<1)	3 (<1)
血中副甲状腺ホルモン増加	1 (<1)	0	0	0	0
眼痛	1 (<1)	0	0	1 (<1)	0
疼痛	0	0	1 (<1)	0	0
関節捻挫	1 (<1)	0	1 (<1)	0	0
筋痙直	5 (1)	1 (<1)	4 (1)	0	1 (<1)
筋骨格痛	1 (<1)	0	1 (<1)	1 (<1)	0
筋肉痛	4 (1)	1 (<1)	1 (<1)	1 (<1)	1 (<1)
末梢性浮腫	4 (1)	1 (<1)	2 (<1)	1 (<1)	1 (<1)
口腔ヘルペス	3 (<1)	1 (<1)	3 (<1)	0	1 (<1)
結膜炎	1 (<1)	0	0	1 (<1)	1 (<1)

NOTE 1: Numbers in parentheses are percentages.
2: Data after subjects switched to alternative MS treatment are excluded.
3: A subject was counted only once within each interval for each preferred term.
4: Preferred terms are presented by decreasing order of incidence in overall Total BG00012.

SOURCE: BG12MS/JAPAN/ISS/T-AE-PT-2PCT-3MON-302.SAS DATE: 02DEC2015

Incidence of adverse events at least 2% higher for any treatment group and the entire study period by preferred term and 3-months interval:
Study 109MS302
Page 8 of 50

	Placebo			
	>15-18 months	>18-21 months	>21-24 months	>24 months
胃炎	0	0	1 (<1)	0
尿中血陽性	0	0	0	0
挫傷	0	1 (<1)	0	0
歯痛	1 (<1)	0	0	0
脱毛症	1 (<1)	0	0	0
尿中β２ミクログロブリン増加	5 (2)	2 (<1)	3 (1)	1 (<1)
灼熱感	0	1 (<1)	1 (<1)	0
多汗症	0	0	0	0
高血圧	2 (<1)	0	3 (1)	0
筋力低下	2 (<1)	1 (<1)	1 (<1)	0
気道感染	1 (<1)	1 (<1)	0	0
血中副甲状腺ホルモン増加	0	0	0	1 (<1)
眼痛	1 (<1)	0	1 (<1)	0
疼痛	1 (<1)	0	2 (<1)	0
関節捻挫	1 (<1)	0	0	0
筋痙直	2 (<1)	0	0	0
筋骨格痛	1 (<1)	1 (<1)	0	0
筋肉痛	2 (<1)	2 (<1)	1 (<1)	0
末梢性浮腫	0	0	0	0
口腔ヘルペス	2 (<1)	4 (1)	1 (<1)	0
結膜炎	1 (<1)	0	0	0

NOTE 1: Numbers in parentheses are percentages.
2: Data after subjects switched to alternative MS treatment are excluded.
3: A subject was counted only once within each interval for each preferred term.
4: Preferred terms are presented by decreasing order of incidence in overall Total BG00012.

SOURCE: BG12MS/JAPAN/ISS/T-AE-PT-2PCT-3MON-302.SAS DATE: 02DEC2015

Incidence of adverse events at least 2% higher for any treatment group and the entire study period by preferred term and 3-months interval:
Study 109MS302
Page 9 of 50

	Placebo				
	0-3 months	>3-6 months	>6-9 months	>9-12 months	>12-15 months
血中ブドウ糖増加	1 (<1)	0	0	1 (<1)	0
耳感染	1 (<1)	1 (<1)	0	1 (<1)	1 (<1)
γ－グルタミルトランスフェラーゼ増加	1 (<1)	1 (<1)	2 (<1)	2 (<1)	2 (<1)
霧視	1 (<1)	3 (<1)	0	1 (<1)	2 (<1)
外陰腟真菌感染	1 (<1)	2 (<1)	1 (<1)	1 (<1)	1 (<1)
膀胱炎	2 (<1)	1 (<1)	1 (<1)	0	0
尿中白血球陽性	4 (1)	1 (<1)	0	0	0
視力低下	3 (<1)	1 (<1)	2 (<1)	2 (<1)	1 (<1)
筋骨格硬直	1 (<1)	2 (<1)	1 (<1)	0	0

NOTE 1: Numbers in parentheses are percentages.
2: Data after subjects switched to alternative MS treatment are excluded.
3: A subject was counted only once within each interval for each preferred term.
4: Preferred terms are presented by decreasing order of incidence in overall Total BG00012.

SOURCE: BG12MS/JAPAN/ISS/T-AE-PT-2PCT-3MON-302.SAS DATE: 02DEC2015

Incidence of adverse events at least 2% higher for any treatment group and the entire study period by preferred term and 3-months interval:
Study 109MS302
Page 10 of 50

	Placebo			
	>15-18 months	>18-21 months	>21-24 months	>24 months
血中ブドウ糖増加	0	2 (<1)	1 (<1)	0
耳感染	1 (<1)	0	0	0
γ－グルタミルトランスフェラーゼ増加	0	0	0	1 (<1)
霧視	1 (<1)	0	0	0
外陰腟真菌感染	0	0	2 (<1)	0
膀胱炎	1 (<1)	1 (<1)	2 (<1)	0
尿中白血球陽性	0	0	1 (<1)	0
視力低下	0	1 (<1)	1 (<1)	0
筋骨格硬直	1 (<1)	0	0	0

NOTE 1: Numbers in parentheses are percentages.
2: Data after subjects switched to alternative MS treatment are excluded.
3: A subject was counted only once within each interval for each preferred term.
4: Preferred terms are presented by decreasing order of incidence in overall Total BG00012.

SOURCE: BG12MS/JAPAN/ISS/T-AE-PT-2PCT-3MON-302.SAS DATE: 02DEC2015

Incidence of adverse events at least 2% higher for any treatment group and the entire study period by preferred term and 3-months interval:
Study 109MS302
Page 11 of 50

	BG00012 240 mg BID				
	0-3 months	>3-6 months	>6-9 months	>9-12 months	>12-15 months
Number of subjects followed in the interval	359 (100)	338 (100)	318 (100)	303 (100)	294 (100)
Number of subjects with an event	257 (72)	172 (51)	150 (47)	135 (45)	121 (41)
Number of subjects with deaths	0	0	0	0	0
Number of subjects with SAEs other than deaths	18 (5)	9 (3)	12 (4)	10 (3)	9 (3)
Number of subjects who discontinued	15 (4)	2 (<1)	0	0	0
多発性硬化症再発	39 (11)	22 (7)	17 (5)	17 (6)	16 (5)
潮紅	90 (25)	10 (3)	9 (3)	9 (3)	4 (1)
鼻咽頭炎	13 (4)	14 (4)	9 (3)	8 (3)	11 (4)
頭痛	26 (7)	13 (4)	8 (3)	7 (2)	11 (4)
下痢	28 (8)	5 (1)	5 (2)	1 (<1)	3 (1)
尿路感染	14 (4)	14 (4)	7 (2)	5 (2)	6 (2)
悪心	30 (8)	3 (<1)	6 (2)	3 (<1)	0
上気道感染	8 (2)	10 (3)	5 (2)	9 (3)	4 (1)
背部痛	11 (3)	7 (2)	11 (3)	4 (1)	3 (1)

NOTE 1: Numbers in parentheses are percentages.
2: Data after subjects switched to alternative MS treatment are excluded.
3: A subject was counted only once within each interval for each preferred term.
4: Preferred terms are presented by decreasing order of incidence in overall Total BG00012.

SOURCE: BG12MS/JAPAN/ISS/T-AE-PT-2PCT-3MON-302.SAS DATE: 02DEC2015

Incidence of adverse events at least 2% higher for any treatment group and the entire study period by preferred term and 3-months interval:
Study 109MS302
Page 12 of 50

	BG00012 240 mg BID			
	>15-18 months	>18-21 months	>21-24 months	>24 months
Number of subjects followed in the interval	288 (100)	279 (100)	275 (100)	184 (100)
Number of subjects with an event	115 (40)	113 (41)	105 (38)	29 (16)
Number of subjects with deaths	0	0	0	0
Number of subjects with SAEs other than deaths	4 (1)	10 (4)	2 (<1)	0
Number of subjects who discontinued	1 (<1)	1 (<1)	2 (<1)	0
多発性硬化症再発	11 (4)	17 (6)	10 (4)	1 (<1)
潮紅	7 (2)	4 (1)	4 (1)	1 (<1)
鼻咽頭炎	17 (6)	9 (3)	10 (4)	1 (<1)
頭痛	4 (1)	5 (2)	5 (2)	2 (1)
下痢	2 (<1)	2 (<1)	4 (1)	1 (<1)
尿路感染	9 (3)	8 (3)	9 (3)	0
悪心	1 (<1)	3 (1)	2 (<1)	0
上気道感染	3 (1)	7 (3)	6 (2)	0
背部痛	0	4 (1)	2 (<1)	0

NOTE 1: Numbers in parentheses are percentages.
2: Data after subjects switched to alternative MS treatment are excluded.
3: A subject was counted only once within each interval for each preferred term.
4: Preferred terms are presented by decreasing order of incidence in overall Total BG00012.

SOURCE: BG12MS/JAPAN/ISS/T-AE-PT-2PCT-3MON-302.SAS DATE: 02DEC2015

Incidence of adverse events at least 2% higher for any treatment group and the entire study period by preferred term and 3-months interval:
Study 109MS302
Page 13 of 50

	BG00012 240 mg BID				
	0-3 months	>3-6 months	>6-9 months	>9-12 months	>12-15 months
疲労	14 (4)	5 (1)	10 (3)	5 (2)	2 (<1)
上腹部痛	25 (7)	3 (<1)	5 (2)	2 (<1)	3 (1)
蛋白尿	9 (3)	4 (1)	7 (2)	3 (<1)	7 (2)
腹痛	21 (6)	2 (<1)	2 (<1)	3 (<1)	0
発疹	15 (4)	5 (1)	2 (<1)	2 (<1)	2 (<1)
嘔吐	16 (4)	2 (<1)	6 (2)	1 (<1)	2 (<1)
関節痛	5 (1)	3 (<1)	4 (1)	6 (2)	4 (1)
四肢痛	7 (2)	4 (1)	2 (<1)	7 (2)	4 (1)
インフルエンザ	5 (1)	8 (2)	2 (<1)	4 (1)	1 (<1)
そう痒症	14 (4)	3 (<1)	4 (1)	0	0
錯感覚	7 (2)	4 (1)	5 (2)	2 (<1)	0
うつ病	9 (3)	5 (1)	4 (1)	2 (<1)	2 (<1)
アラニン・アミノトランスフェラーゼ増加	11 (3)	2 (<1)	3 (<1)	3 (<1)	1 (<1)
紅斑	10 (3)	4 (1)	2 (<1)	0	3 (1)
ほてり	11 (3)	1 (<1)	1 (<1)	0	2 (<1)
尿中アルブミン陽性	5 (1)	3 (<1)	4 (1)	3 (<1)	5 (2)
気管支炎	2 (<1)	3 (<1)	2 (<1)	3 (<1)	3 (1)
発熱	2 (<1)	3 (<1)	1 (<1)	1 (<1)	1 (<1)
副鼻腔炎	2 (<1)	4 (1)	3 (<1)	4 (1)	3 (1)
咳嗽	6 (2)	3 (<1)	3 (<1)	1 (<1)	1 (<1)
筋痙縮	4 (1)	0	0	3 (<1)	3 (1)

NOTE 1: Numbers in parentheses are percentages.
2: Data after subjects switched to alternative MS treatment are excluded.
3: A subject was counted only once within each interval for each preferred term.
4: Preferred terms are presented by decreasing order of incidence in overall Total BG00012.

SOURCE: BG12MS/JAPAN/ISS/T-AE-PT-2PCT-3MON-302.SAS DATE: 02DEC2015

Incidence of adverse events at least 2% higher for any treatment group and the entire study period by preferred term and 3-months interval:
Study 109MS302
Page 14 of 50

	BG00012 240 mg BID			
	>15-18 months	>18-21 months	>21-24 months	>24 months
疲労	5 (2)	1 (<1)	1 (<1)	1 (<1)
上腹部痛	0	5 (2)	2 (<1)	0
蛋白尿	3 (1)	4 (1)	4 (1)	3 (2)
腹痛	1 (<1)	2 (<1)	0	0
発疹	1 (<1)	0	0	0
嘔吐	0	1 (<1)	0	0
関節痛	0	1 (<1)	4 (1)	0
四肢痛	1 (<1)	1 (<1)	3 (1)	0
インフルエンザ	0	4 (1)	0	1 (<1)
そう痒症	0	0	0	0
錯感覚	3 (1)	1 (<1)	4 (1)	0
うつ病	1 (<1)	4 (1)	2 (<1)	0
アラニン・アミノトランスフェラーゼ増加	0	1 (<1)	2 (<1)	0
紅斑	1 (<1)	1 (<1)	0	0
ほてり	3 (1)	1 (<1)	0	0
尿中アルブミン陽性	4 (1)	2 (<1)	2 (<1)	3 (2)
気管支炎	0	1 (<1)	0	1 (<1)
発熱	2 (<1)	2 (<1)	1 (<1)	0
副鼻腔炎	3 (1)	4 (1)	1 (<1)	0
咳嗽	1 (<1)	2 (<1)	1 (<1)	0
筋痙縮	1 (<1)	1 (<1)	1 (<1)	0

NOTE 1: Numbers in parentheses are percentages.
2: Data after subjects switched to alternative MS treatment are excluded.
3: A subject was counted only once within each interval for each preferred term.
4: Preferred terms are presented by decreasing order of incidence in overall Total BG00012.

SOURCE: BG12MS/JAPAN/ISS/T-AE-PT-2PCT-3MON-302.SAS DATE: 02DEC2015

Incidence of adverse events at least 2% higher for any treatment group and the entire study period by preferred term and 3-months interval:
Study 109MS302
Page 15 of 50

	BG00012 240 mg BID				
	0-3 months	>3-6 months	>6-9 months	>9-12 months	>12-15 months
ミクロアルブミン尿	0	2 (<1)	1 (<1)	3 (<1)	1 (<1)
口腔咽頭痛	2 (<1)	4 (1)	2 (<1)	1 (<1)	2 (<1)
感覚鈍麻	6 (2)	0	1 (<1)	0	0
アスパラギン酸アミノトランスフェラーゼ増加	10 (3)	1 (<1)	3 (<1)	2 (<1)	1 (<1)
消化不良	6 (2)	3 (<1)	3 (<1)	0	0
頚部痛	1 (<1)	3 (<1)	2 (<1)	3 (<1)	1 (<1)
胃腸炎	4 (1)	1 (<1)	1 (<1)	2 (<1)	1 (<1)
不安	4 (1)	3 (<1)	7 (2)	1 (<1)	0
不眠症	5 (1)	0	1 (<1)	2 (<1)	1 (<1)
尿中蛋白陽性	3 (<1)	5 (1)	1 (<1)	2 (<1)	2 (<1)
咽頭炎	6 (2)	3 (<1)	2 (<1)	2 (<1)	2 (<1)
胃腸障害	8 (2)	0	0	1 (<1)	0
浮動性めまい	6 (2)	1 (<1)	2 (<1)	2 (<1)	2 (<1)
転倒	0	2 (<1)	2 (<1)	2 (<1)	0
ウイルス性胃腸炎	3 (<1)	0	1 (<1)	0	0
血尿	1 (<1)	2 (<1)	3 (<1)	1 (<1)	0
回転性めまい	3 (<1)	3 (<1)	2 (<1)	1 (<1)	0
鼻炎	2 (<1)	4 (1)	3 (<1)	2 (<1)	1 (<1)
貧血	1 (<1)	2 (<1)	0	0	1 (<1)
無力症	8 (2)	1 (<1)	0	1 (<1)	1 (<1)
便秘	8 (2)	1 (<1)	1 (<1)	0	0

NOTE 1: Numbers in parentheses are percentages.
2: Data after subjects switched to alternative MS treatment are excluded.
3: A subject was counted only once within each interval for each preferred term.
4: Preferred terms are presented by decreasing order of incidence in overall Total BG00012.

SOURCE: BG12MS/JAPAN/ISS/T-AE-PT-2PCT-3MON-302.SAS DATE: 02DEC2015

Incidence of adverse events at least 2% higher for any treatment group and the entire study period by preferred term and 3-months interval:
Study 109MS302
Page 16 of 50

	BG00012 240 mg BID			
	>15-18 months	>18-21 months	>21-24 months	>24 months
ミクロアルブミン尿	3 (1)	1 (<1)	3 (1)	3 (2)
口腔咽頭痛	2 (<1)	1 (<1)	1 (<1)	0
感覚鈍麻	0	1 (<1)	3 (1)	0
アスパラギン酸アミノトランスフェラーゼ増加	1 (<1)	0	1 (<1)	0
消化不良	0	1 (<1)	0	0
頚部痛	2 (<1)	1 (<1)	3 (1)	0
胃腸炎	1 (<1)	2 (<1)	3 (1)	0
不安	1 (<1)	0	0	1 (<1)
不眠症	2 (<1)	4 (1)	1 (<1)	0
尿中蛋白陽性	5 (2)	0	3 (1)	1 (<1)
咽頭炎	3 (1)	1 (<1)	3 (1)	0
胃腸障害	1 (<1)	0	0	0
浮動性めまい	3 (1)	1 (<1)	2 (<1)	0
転倒	0	1 (<1)	2 (<1)	0
ウイルス性胃腸炎	4 (1)	1 (<1)	2 (<1)	0
血尿	2 (<1)	1 (<1)	3 (1)	2 (1)
回転性めまい	2 (<1)	0	0	0
鼻炎	2 (<1)	0	1 (<1)	0
貧血	1 (<1)	1 (<1)	1 (<1)	0
無力症	1 (<1)	1 (<1)	1 (<1)	0
便秘	0	0	0	0

NOTE 1: Numbers in parentheses are percentages.
2: Data after subjects switched to alternative MS treatment are excluded.
3: A subject was counted only once within each interval for each preferred term.
4: Preferred terms are presented by decreasing order of incidence in overall Total BG00012.

SOURCE: BG12MS/JAPAN/ISS/T-AE-PT-2PCT-3MON-302.SAS DATE: 02DEC2015

Incidence of adverse events at least 2% higher for any treatment group and the entire study period by preferred term and 3-months interval:
Study 109MS302
Page 17 of 50

	BG00012 240 mg BID				
	0-3 months	>3-6 months	>6-9 months	>9-12 months	>12-15 months
胃炎	2 (<1)	2 (<1)	1 (<1)	2 (<1)	0
尿中血陽性	3 (<1)	2 (<1)	0	1 (<1)	2 (<1)
挫傷	1 (<1)	0	3 (<1)	1 (<1)	2 (<1)
歯痛	4 (1)	1 (<1)	0	1 (<1)	0
脱毛症	5 (1)	3 (<1)	0	1 (<1)	1 (<1)
尿中β２ミクログロブリン増加	2 (<1)	4 (1)	2 (<1)	0	2 (<1)
灼熱感	4 (1)	0	1 (<1)	0	1 (<1)
多汗症	4 (1)	0	2 (<1)	1 (<1)	0
高血圧	2 (<1)	0	0	1 (<1)	0
筋力低下	1 (<1)	1 (<1)	1 (<1)	0	1 (<1)
気道感染	1 (<1)	1 (<1)	1 (<1)	2 (<1)	0
白血球数減少	1 (<1)	2 (<1)	0	1 (<1)	2 (<1)
血中副甲状腺ホルモン増加	0	0	0	5 (2)	1 (<1)
眼痛	0	0	3 (<1)	4 (1)	0
疼痛	4 (1)	1 (<1)	0	0	2 (<1)
関節捻挫	1 (<1)	1 (<1)	1 (<1)	3 (<1)	0
筋痙直	1 (<1)	0	2 (<1)	0	1 (<1)
筋骨格痛	1 (<1)	1 (<1)	1 (<1)	0	0
筋肉痛	2 (<1)	1 (<1)	3 (<1)	0	1 (<1)
末梢性浮腫	3 (<1)	0	0	0	0
口腔ヘルペス	3 (<1)	0	3 (<1)	2 (<1)	2 (<1)

NOTE 1: Numbers in parentheses are percentages.
2: Data after subjects switched to alternative MS treatment are excluded.
3: A subject was counted only once within each interval for each preferred term.
4: Preferred terms are presented by decreasing order of incidence in overall Total BG00012.

SOURCE: BG12MS/JAPAN/ISS/T-AE-PT-2PCT-3MON-302.SAS DATE: 02DEC2015

Incidence of adverse events at least 2% higher for any treatment group and the entire study period by preferred term and 3-months interval:
Study 109MS302
Page 18 of 50

	BG00012 240 mg BID			
	>15-18 months	>18-21 months	>21-24 months	>24 months
胃炎	1 (<1)	2 (<1)	1 (<1)	0
尿中血陽性	1 (<1)	4 (1)	1 (<1)	0
挫傷	2 (<1)	1 (<1)	0	1 (<1)
歯痛	0	0	0	0
脱毛症	0	0	0	0
尿中β２ミクログロブリン増加	0	1 (<1)	0	0
灼熱感	0	0	1 (<1)	0
多汗症	0	0	0	0
高血圧	0	2 (<1)	0	0
筋力低下	0	1 (<1)	1 (<1)	0
気道感染	1 (<1)	0	1 (<1)	0
白血球数減少	2 (<1)	0	0	2 (1)
血中副甲状腺ホルモン増加	0	0	1 (<1)	1 (<1)
眼痛	2 (<1)	1 (<1)	0	0
疼痛	0	1 (<1)	0	0
関節捻挫	0	1 (<1)	1 (<1)	0
筋痙直	1 (<1)	2 (<1)	0	0
筋骨格痛	0	0	0	0
筋肉痛	0	0	0	0
末梢性浮腫	1 (<1)	0	1 (<1)	0
口腔ヘルペス	2 (<1)	0	1 (<1)	0

NOTE 1: Numbers in parentheses are percentages.
2: Data after subjects switched to alternative MS treatment are excluded.
3: A subject was counted only once within each interval for each preferred term.
4: Preferred terms are presented by decreasing order of incidence in overall Total BG00012.

SOURCE: BG12MS/JAPAN/ISS/T-AE-PT-2PCT-3MON-302.SAS DATE: 02DEC2015

Incidence of adverse events at least 2% higher for any treatment group and the entire study period by preferred term and 3-months interval:
Study 109MS302
Page 19 of 50

	BG00012 240 mg BID				
	0-3 months	>3-6 months	>6-9 months	>9-12 months	>12-15 months
結膜炎	1 (<1)	0	2 (<1)	3 (<1)	0
血中ブドウ糖増加	2 (<1)	3 (<1)	1 (<1)	0	1 (<1)
耳感染	0	0	0	0	1 (<1)
γ－グルタミルトランスフェラーゼ増加	2 (<1)	0	1 (<1)	0	1 (<1)
霧視	2 (<1)	0	0	1 (<1)	0
外陰腟真菌感染	0	1 (<1)	1 (<1)	0	0
インフルエンザ様疾患	0	0	0	2 (<1)	0
膀胱炎	0	2 (<1)	1 (<1)	0	1 (<1)
尿中白血球陽性	0	1 (<1)	2 (<1)	1 (<1)	0
視力低下	0	0	0	0	0
筋骨格硬直	0	1 (<1)	0	0	0

NOTE 1: Numbers in parentheses are percentages.
2: Data after subjects switched to alternative MS treatment are excluded.
3: A subject was counted only once within each interval for each preferred term.
4: Preferred terms are presented by decreasing order of incidence in overall Total BG00012.

SOURCE: BG12MS/JAPAN/ISS/T-AE-PT-2PCT-3MON-302.SAS DATE: 02DEC2015

Incidence of adverse events at least 2% higher for any treatment group and the entire study period by preferred term and 3-months interval:
Study 109MS302
Page 20 of 50

	BG00012 240 mg BID			
	>15-18 months	>18-21 months	>21-24 months	>24 months
結膜炎	1 (<1)	0	2 (<1)	0
血中ブドウ糖増加	0	0	0	0
耳感染	1 (<1)	0	1 (<1)	0
γ－グルタミルトランスフェラーゼ増加	0	0	2 (<1)	0
霧視	0	0	0	0
外陰腟真菌感染	0	0	0	0
インフルエンザ様疾患	0	0	0	0
膀胱炎	0	1 (<1)	0	0
尿中白血球陽性	0	0	1 (<1)	0
視力低下	0	0	0	1 (<1)
筋骨格硬直	0	0	0	0

NOTE 1: Numbers in parentheses are percentages.
2: Data after subjects switched to alternative MS treatment are excluded.
3: A subject was counted only once within each interval for each preferred term.
4: Preferred terms are presented by decreasing order of incidence in overall Total BG00012.

SOURCE: BG12MS/JAPAN/ISS/T-AE-PT-2PCT-3MON-302.SAS DATE: 02DEC2015

Incidence of adverse events at least 2% higher for any treatment group and the entire study period by preferred term and 3-months interval:
Study 109MS302
Page 21 of 50

	BG00012 240 mg TID				
	0-3 months	>3-6 months	>6-9 months	>9-12 months	>12-15 months
Number of subjects followed in the interval	344 (100)	316 (100)	300 (100)	289 (100)	284 (100)
Number of subjects with an event	253 (74)	159 (50)	151 (50)	138 (48)	119 (42)
Number of subjects with deaths	0	0	1 (<1)	0	0
Number of subjects with SAEs other than deaths	13 (4)	8 (3)	8 (3)	9 (3)	6 (2)
Number of subjects who discontinued	17 (5)	2 (<1)	1 (<1)	0	3 (1)
多発性硬化症再発	27 (8)	19 (6)	17 (6)	19 (7)	10 (4)
潮紅	68 (20)	12 (4)	5 (2)	6 (2)	4 (1)
鼻咽頭炎	13 (4)	12 (4)	17 (6)	10 (3)	8 (3)
頭痛	19 (6)	12 (4)	10 (3)	5 (2)	11 (4)
下痢	37 (11)	8 (3)	4 (1)	3 (1)	2 (<1)
尿路感染	9 (3)	11 (3)	3 (1)	8 (3)	6 (2)
悪心	33 (10)	6 (2)	5 (2)	2 (<1)	1 (<1)
上気道感染	11 (3)	12 (4)	12 (4)	8 (3)	6 (2)
背部痛	7 (2)	7 (2)	9 (3)	4 (1)	5 (2)

NOTE 1: Numbers in parentheses are percentages.
2: Data after subjects switched to alternative MS treatment are excluded.
3: A subject was counted only once within each interval for each preferred term.
4: Preferred terms are presented by decreasing order of incidence in overall Total BG00012.

SOURCE: BG12MS/JAPAN/ISS/T-AE-PT-2PCT-3MON-302.SAS DATE: 02DEC2015

Incidence of adverse events at least 2% higher for any treatment group and the entire study period by preferred term and 3-months interval:
Study 109MS302
Page 22 of 50

	BG00012 240 mg TID			
	>15-18 months	>18-21 months	>21-24 months	>24 months
Number of subjects followed in the interval	280 (100)	267 (100)	261 (100)	184 (100)
Number of subjects with an event	113 (40)	114 (43)	105 (40)	21 (11)
Number of subjects with deaths	0	0	0	0
Number of subjects with SAEs other than deaths	6 (2)	9 (3)	8 (3)	0
Number of subjects who discontinued	1 (<1)	2 (<1)	0	0
多発性硬化症再発	9 (3)	10 (4)	6 (2)	4 (2)
潮紅	5 (2)	3 (1)	4 (2)	0
鼻咽頭炎	16 (6)	9 (3)	6 (2)	0
頭痛	5 (2)	2 (<1)	5 (2)	0
下痢	2 (<1)	3 (1)	0	0
尿路感染	5 (2)	6 (2)	10 (4)	0
悪心	1 (<1)	5 (2)	2 (<1)	0
上気道感染	4 (1)	14 (5)	3 (1)	0
背部痛	8 (3)	3 (1)	3 (1)	1 (<1)

NOTE 1: Numbers in parentheses are percentages.
2: Data after subjects switched to alternative MS treatment are excluded.
3: A subject was counted only once within each interval for each preferred term.
4: Preferred terms are presented by decreasing order of incidence in overall Total BG00012.

SOURCE: BG12MS/JAPAN/ISS/T-AE-PT-2PCT-3MON-302.SAS DATE: 02DEC2015

Incidence of adverse events at least 2% higher for any treatment group and the entire study period by preferred term and 3-months interval:
Study 109MS302
Page 23 of 50

	BG00012 240 mg TID				
	0-3 months	>3-6 months	>6-9 months	>9-12 months	>12-15 months
疲労	16 (5)	7 (2)	3 (1)	3 (1)	2 (<1)
上腹部痛	22 (6)	3 (<1)	1 (<1)	5 (2)	2 (<1)
蛋白尿	13 (4)	3 (<1)	10 (3)	8 (3)	5 (2)
腹痛	15 (4)	4 (1)	1 (<1)	2 (<1)	2 (<1)
発疹	18 (5)	2 (<1)	1 (<1)	3 (1)	0
嘔吐	14 (4)	0	3 (1)	1 (<1)	1 (<1)
関節痛	6 (2)	2 (<1)	8 (3)	6 (2)	3 (1)
四肢痛	5 (1)	4 (1)	2 (<1)	6 (2)	4 (1)
インフルエンザ	10 (3)	3 (<1)	4 (1)	1 (<1)	2 (<1)
そう痒症	14 (4)	2 (<1)	0	2 (<1)	2 (<1)
錯感覚	10 (3)	2 (<1)	3 (1)	2 (<1)	0
うつ病	6 (2)	2 (<1)	1 (<1)	0	2 (<1)
アラニン・アミノトランスフェラーゼ増加	10 (3)	3 (<1)	3 (1)	1 (<1)	2 (<1)
紅斑	10 (3)	3 (<1)	1 (<1)	2 (<1)	2 (<1)
ほてり	13 (4)	4 (1)	1 (<1)	1 (<1)	0
尿中アルブミン陽性	0	3 (<1)	0	2 (<1)	3 (1)
気管支炎	5 (1)	3 (<1)	0	3 (1)	5 (2)
発熱	9 (3)	5 (2)	2 (<1)	4 (1)	4 (1)
副鼻腔炎	5 (1)	2 (<1)	4 (1)	2 (<1)	4 (1)
咳嗽	3 (<1)	3 (<1)	4 (1)	2 (<1)	6 (2)
筋痙縮	5 (1)	4 (1)	2 (<1)	1 (<1)	4 (1)

NOTE 1: Numbers in parentheses are percentages.
2: Data after subjects switched to alternative MS treatment are excluded.
3: A subject was counted only once within each interval for each preferred term.
4: Preferred terms are presented by decreasing order of incidence in overall Total BG00012.

SOURCE: BG12MS/JAPAN/ISS/T-AE-PT-2PCT-3MON-302.SAS DATE: 02DEC2015

Incidence of adverse events at least 2% higher for any treatment group and the entire study period by preferred term and 3-months interval:
Study 109MS302
Page 24 of 50

	BG00012 240 mg TID			
	>15-18 months	>18-21 months	>21-24 months	>24 months
疲労	3 (1)	3 (1)	1 (<1)	0
上腹部痛	2 (<1)	0	3 (1)	0
蛋白尿	4 (1)	5 (2)	3 (1)	1 (<1)
腹痛	2 (<1)	1 (<1)	2 (<1)	0
発疹	1 (<1)	5 (2)	1 (<1)	1 (<1)
嘔吐	1 (<1)	2 (<1)	2 (<1)	0
関節痛	1 (<1)	2 (<1)	2 (<1)	0
四肢痛	1 (<1)	4 (1)	4 (2)	2 (1)
インフルエンザ	5 (2)	4 (1)	3 (1)	0
そう痒症	1 (<1)	2 (<1)	4 (2)	0
錯感覚	0	3 (1)	3 (1)	0
うつ病	0	3 (1)	2 (<1)	0
アラニン・アミノトランスフェラーゼ増加	1 (<1)	3 (1)	4 (2)	0
紅斑	1 (<1)	2 (<1)	2 (<1)	0
ほてり	0	2 (<1)	1 (<1)	0
尿中アルブミン陽性	1 (<1)	2 (<1)	4 (2)	0
気管支炎	2 (<1)	3 (1)	1 (<1)	0
発熱	2 (<1)	1 (<1)	3 (1)	0
副鼻腔炎	1 (<1)	4 (1)	2 (<1)	0
咳嗽	3 (1)	1 (<1)	0	0
筋痙縮	2 (<1)	3 (1)	2 (<1)	0

NOTE 1: Numbers in parentheses are percentages.
2: Data after subjects switched to alternative MS treatment are excluded.
3: A subject was counted only once within each interval for each preferred term.
4: Preferred terms are presented by decreasing order of incidence in overall Total BG00012.

SOURCE: BG12MS/JAPAN/ISS/T-AE-PT-2PCT-3MON-302.SAS DATE: 02DEC2015

Incidence of adverse events at least 2% higher for any treatment group and the entire study period by preferred term and 3-months interval:
Study 109MS302
Page 25 of 50

	BG00012 240 mg TID				
	0-3 months	>3-6 months	>6-9 months	>9-12 months	>12-15 months
ミクロアルブミン尿	2 (<1)	3 (<1)	8 (3)	2 (<1)	2 (<1)
口腔咽頭痛	4 (1)	5 (2)	2 (<1)	4 (1)	2 (<1)
感覚鈍麻	5 (1)	5 (2)	4 (1)	1 (<1)	3 (1)
アスパラギン酸アミノトランスフェラーゼ増加	5 (1)	3 (<1)	2 (<1)	0	1 (<1)
消化不良	8 (2)	4 (1)	3 (1)	0	1 (<1)
頚部痛	1 (<1)	2 (<1)	1 (<1)	4 (1)	0
胃腸炎	4 (1)	1 (<1)	2 (<1)	3 (1)	0
不安	2 (<1)	2 (<1)	2 (<1)	1 (<1)	1 (<1)
不眠症	3 (<1)	1 (<1)	1 (<1)	2 (<1)	0
尿中蛋白陽性	1 (<1)	2 (<1)	2 (<1)	1 (<1)	1 (<1)
咽頭炎	4 (1)	1 (<1)	3 (1)	1 (<1)	3 (1)
胃腸障害	10 (3)	1 (<1)	1 (<1)	1 (<1)	0
浮動性めまい	5 (1)	2 (<1)	0	2 (<1)	1 (<1)
転倒	1 (<1)	5 (2)	3 (1)	4 (1)	0
ウイルス性胃腸炎	4 (1)	3 (<1)	3 (1)	2 (<1)	0
血尿	4 (1)	3 (<1)	5 (2)	3 (1)	0
回転性めまい	5 (1)	3 (<1)	2 (<1)	3 (1)	0
鼻炎	1 (<1)	0	0	1 (<1)	3 (1)
貧血	3 (<1)	1 (<1)	2 (<1)	3 (1)	1 (<1)
無力症	2 (<1)	1 (<1)	3 (1)	0	1 (<1)
便秘	5 (1)	1 (<1)	1 (<1)	2 (<1)	1 (<1)

NOTE 1: Numbers in parentheses are percentages.
2: Data after subjects switched to alternative MS treatment are excluded.
3: A subject was counted only once within each interval for each preferred term.
4: Preferred terms are presented by decreasing order of incidence in overall Total BG00012.

SOURCE: BG12MS/JAPAN/ISS/T-AE-PT-2PCT-3MON-302.SAS DATE: 02DEC2015

Incidence of adverse events at least 2% higher for any treatment group and the entire study period by preferred term and 3-months interval:
Study 109MS302
Page 26 of 50

	BG00012 240 mg TID			
	>15-18 months	>18-21 months	>21-24 months	>24 months
ミクロアルブミン尿	2 (<1)	4 (1)	3 (1)	0
口腔咽頭痛	0	4 (1)	2 (<1)	0
感覚鈍麻	3 (1)	3 (1)	2 (<1)	0
アスパラギン酸アミノトランスフェラーゼ増加	0	1 (<1)	2 (<1)	0
消化不良	2 (<1)	2 (<1)	1 (<1)	0
頚部痛	3 (1)	1 (<1)	1 (<1)	0
胃腸炎	2 (<1)	0	1 (<1)	0
不安	1 (<1)	1 (<1)	2 (<1)	0
不眠症	1 (<1)	2 (<1)	0	0
尿中蛋白陽性	2 (<1)	1 (<1)	0	0
咽頭炎	2 (<1)	2 (<1)	0	0
胃腸障害	1 (<1)	0	0	0
浮動性めまい	0	0	1 (<1)	0
転倒	3 (1)	1 (<1)	0	0
ウイルス性胃腸炎	2 (<1)	0	1 (<1)	0
血尿	0	2 (<1)	1 (<1)	0
回転性めまい	0	2 (<1)	0	0
鼻炎	2 (<1)	1 (<1)	0	0
貧血	0	1 (<1)	1 (<1)	1 (<1)
無力症	1 (<1)	0	0	0
便秘	0	1 (<1)	0	0

NOTE 1: Numbers in parentheses are percentages.
2: Data after subjects switched to alternative MS treatment are excluded.
3: A subject was counted only once within each interval for each preferred term.
4: Preferred terms are presented by decreasing order of incidence in overall Total BG00012.

SOURCE: BG12MS/JAPAN/ISS/T-AE-PT-2PCT-3MON-302.SAS DATE: 02DEC2015

Incidence of adverse events at least 2% higher for any treatment group and the entire study period by preferred term and 3-months interval:
Study 109MS302
Page 27 of 50

	BG00012 240 mg TID				
	0-3 months	>3-6 months	>6-9 months	>9-12 months	>12-15 months
胃炎	5 (1)	3 (<1)	0	0	1 (<1)
尿中血陽性	1 (<1)	1 (<1)	1 (<1)	1 (<1)	1 (<1)
挫傷	1 (<1)	0	0	2 (<1)	2 (<1)
歯痛	2 (<1)	3 (<1)	1 (<1)	0	1 (<1)
脱毛症	3 (<1)	2 (<1)	0	0	0
尿中β２ミクログロブリン増加	0	1 (<1)	2 (<1)	3 (1)	0
灼熱感	5 (1)	1 (<1)	2 (<1)	0	0
多汗症	4 (1)	0	2 (<1)	0	3 (1)
高血圧	4 (1)	3 (<1)	2 (<1)	0	1 (<1)
筋力低下	3 (<1)	1 (<1)	3 (1)	2 (<1)	0
気道感染	3 (<1)	2 (<1)	3 (1)	3 (1)	0
白血球数減少	2 (<1)	0	2 (<1)	1 (<1)	0
血中副甲状腺ホルモン増加	0	0	0	1 (<1)	4 (1)
眼痛	1 (<1)	4 (1)	0	1 (<1)	0
疼痛	3 (<1)	0	0	1 (<1)	0
関節捻挫	0	1 (<1)	1 (<1)	0	2 (<1)
筋痙直	2 (<1)	0	1 (<1)	0	0
筋骨格痛	1 (<1)	2 (<1)	1 (<1)	1 (<1)	1 (<1)
筋肉痛	3 (<1)	1 (<1)	0	1 (<1)	1 (<1)
末梢性浮腫	2 (<1)	2 (<1)	2 (<1)	3 (1)	0
口腔ヘルペス	2 (<1)	1 (<1)	0	2 (<1)	0

NOTE 1: Numbers in parentheses are percentages.
2: Data after subjects switched to alternative MS treatment are excluded.
3: A subject was counted only once within each interval for each preferred term.
4: Preferred terms are presented by decreasing order of incidence in overall Total BG00012.

SOURCE: BG12MS/JAPAN/ISS/T-AE-PT-2PCT-3MON-302.SAS DATE: 02DEC2015

Incidence of adverse events at least 2% higher for any treatment group and the entire study period by preferred term and 3-months interval:
Study 109MS302
Page 28 of 50

	BG00012 240 mg TID			
	>15-18 months	>18-21 months	>21-24 months	>24 months
胃炎	0	1 (<1)	1 (<1)	0
尿中血陽性	3 (1)	2 (<1)	1 (<1)	0
挫傷	2 (<1)	0	1 (<1)	0
歯痛	3 (1)	1 (<1)	1 (<1)	0
脱毛症	1 (<1)	0	0	0
尿中β２ミクログロブリン増加	2 (<1)	1 (<1)	2 (<1)	1 (<1)
灼熱感	0	2 (<1)	0	0
多汗症	0	1 (<1)	0	0
高血圧	0	0	1 (<1)	1 (<1)
筋力低下	2 (<1)	2 (<1)	0	0
気道感染	0	1 (<1)	1 (<1)	0
白血球数減少	2 (<1)	0	2 (<1)	0
血中副甲状腺ホルモン増加	0	0	0	2 (1)
眼痛	0	1 (<1)	0	0
疼痛	0	1 (<1)	2 (<1)	0
関節捻挫	1 (<1)	1 (<1)	1 (<1)	0
筋痙直	0	2 (<1)	2 (<1)	0
筋骨格痛	0	2 (<1)	3 (1)	0
筋肉痛	0	2 (<1)	0	0
末梢性浮腫	1 (<1)	1 (<1)	2 (<1)	0
口腔ヘルペス	0	0	0	0

NOTE 1: Numbers in parentheses are percentages.
2: Data after subjects switched to alternative MS treatment are excluded.
3: A subject was counted only once within each interval for each preferred term.
4: Preferred terms are presented by decreasing order of incidence in overall Total BG00012.

SOURCE: BG12MS/JAPAN/ISS/T-AE-PT-2PCT-3MON-302.SAS DATE: 02DEC2015

Incidence of adverse events at least 2% higher for any treatment group and the entire study period by preferred term and 3-months interval:
Study 109MS302
Page 29 of 50

	BG00012 240 mg TID				
	0-3 months	>3-6 months	>6-9 months	>9-12 months	>12-15 months
結膜炎	2 (<1)	0	2 (<1)	0	0
血中ブドウ糖増加	0	3 (<1)	3 (1)	0	1 (<1)
耳感染	3 (<1)	2 (<1)	0	2 (<1)	1 (<1)
γ－グルタミルトランスフェラーゼ増加	3 (<1)	0	0	0	0
霧視	0	2 (<1)	0	1 (<1)	0
外陰腟真菌感染	1 (<1)	2 (<1)	2 (<1)	1 (<1)	0
インフルエンザ様疾患	3 (<1)	0	1 (<1)	2 (<1)	0
膀胱炎	0	0	0	0	0
尿中白血球陽性	0	1 (<1)	0	1 (<1)	2 (<1)
視力低下	0	0	1 (<1)	0	0

NOTE 1: Numbers in parentheses are percentages.
2: Data after subjects switched to alternative MS treatment are excluded.
3: A subject was counted only once within each interval for each preferred term.
4: Preferred terms are presented by decreasing order of incidence in overall Total BG00012.

SOURCE: BG12MS/JAPAN/ISS/T-AE-PT-2PCT-3MON-302.SAS DATE: 02DEC2015

Incidence of adverse events at least 2% higher for any treatment group and the entire study period by preferred term and 3-months interval:
Study 109MS302
Page 30 of 50

	BG00012 240 mg TID			
	>15-18 months	>18-21 months	>21-24 months	>24 months
結膜炎	0	0	0	1 (<1)
血中ブドウ糖増加	3 (1)	2 (<1)	1 (<1)	0
耳感染	1 (<1)	1 (<1)	1 (<1)	0
γ－グルタミルトランスフェラーゼ増加	2 (<1)	0	1 (<1)	0
霧視	3 (1)	2 (<1)	0	0
外陰腟真菌感染	2 (<1)	0	1 (<1)	0
インフルエンザ様疾患	1 (<1)	0	0	0
膀胱炎	0	0	3 (1)	0
尿中白血球陽性	0	0	0	0
視力低下	0	0	0	0

NOTE 1: Numbers in parentheses are percentages.
2: Data after subjects switched to alternative MS treatment are excluded.
3: A subject was counted only once within each interval for each preferred term.
4: Preferred terms are presented by decreasing order of incidence in overall Total BG00012.

SOURCE: BG12MS/JAPAN/ISS/T-AE-PT-2PCT-3MON-302.SAS DATE: 02DEC2015

Incidence of adverse events at least 2% higher for any treatment group and the entire study period by preferred term and 3-months interval:
Study 109MS302
Page 31 of 50

	Total BG00012				
	0-3 months	>3-6 months	>6-9 months	>9-12 months	>12-15 months
Number of subjects followed in the interval	703 (100)	654 (100)	618 (100)	592 (100)	578 (100)
Number of subjects with an event	510 (73)	331 (51)	301 (49)	273 (46)	240 (42)
Number of subjects with deaths	0	0	1 (<1)	0	0
Number of subjects with SAEs other than deaths	31 (4)	17 (3)	20 (3)	19 (3)	15 (3)
Number of subjects who discontinued	32 (5)	4 (<1)	1 (<1)	0	3 (<1)
多発性硬化症再発	66 (9)	41 (6)	34 (6)	36 (6)	26 (4)
潮紅	158 (22)	22 (3)	14 (2)	15 (3)	8 (1)
鼻咽頭炎	26 (4)	26 (4)	26 (4)	18 (3)	19 (3)
頭痛	45 (6)	25 (4)	18 (3)	12 (2)	22 (4)
下痢	65 (9)	13 (2)	9 (1)	4 (<1)	5 (<1)
尿路感染	23 (3)	25 (4)	10 (2)	13 (2)	12 (2)
悪心	63 (9)	9 (1)	11 (2)	5 (<1)	1 (<1)
上気道感染	19 (3)	22 (3)	17 (3)	17 (3)	10 (2)
背部痛	18 (3)	14 (2)	20 (3)	8 (1)	8 (1)

NOTE 1: Numbers in parentheses are percentages.
2: Data after subjects switched to alternative MS treatment are excluded.
3: A subject was counted only once within each interval for each preferred term.
4: Preferred terms are presented by decreasing order of incidence in overall Total BG00012.

SOURCE: BG12MS/JAPAN/ISS/T-AE-PT-2PCT-3MON-302.SAS DATE: 02DEC2015

Incidence of adverse events at least 2% higher for any treatment group and the entire study period by preferred term and 3-months interval:
Study 109MS302
Page 32 of 50

	Total BG00012			
	>15-18 months	>18-21 months	>21-24 months	>24 months
Number of subjects followed in the interval	568 (100)	546 (100)	536 (100)	368 (100)
Number of subjects with an event	228 (40)	227 (42)	210 (39)	50 (14)
Number of subjects with deaths	0	0	0	0
Number of subjects with SAEs other than deaths	10 (2)	19 (3)	10 (2)	0
Number of subjects who discontinued	2 (<1)	3 (<1)	2 (<1)	0
多発性硬化症再発	20 (4)	27 (5)	16 (3)	5 (1)
潮紅	12 (2)	7 (1)	8 (1)	1 (<1)
鼻咽頭炎	33 (6)	18 (3)	16 (3)	1 (<1)
頭痛	9 (2)	7 (1)	10 (2)	2 (<1)
下痢	4 (<1)	5 (<1)	4 (<1)	1 (<1)
尿路感染	14 (2)	14 (3)	19 (4)	0
悪心	2 (<1)	8 (1)	4 (<1)	0
上気道感染	7 (1)	21 (4)	9 (2)	0
背部痛	8 (1)	7 (1)	5 (<1)	1 (<1)

NOTE 1: Numbers in parentheses are percentages.
2: Data after subjects switched to alternative MS treatment are excluded.
3: A subject was counted only once within each interval for each preferred term.
4: Preferred terms are presented by decreasing order of incidence in overall Total BG00012.

SOURCE: BG12MS/JAPAN/ISS/T-AE-PT-2PCT-3MON-302.SAS DATE: 02DEC2015

Incidence of adverse events at least 2% higher for any treatment group and the entire study period by preferred term and 3-months interval:
Study 109MS302
Page 33 of 50

	Total BG00012				
	0-3 months	>3-6 months	>6-9 months	>9-12 months	>12-15 months
疲労	30 (4)	12 (2)	13 (2)	8 (1)	4 (<1)
上腹部痛	47 (7)	6 (<1)	6 (<1)	7 (1)	5 (<1)
蛋白尿	22 (3)	7 (1)	17 (3)	11 (2)	12 (2)
腹痛	36 (5)	6 (<1)	3 (<1)	5 (<1)	2 (<1)
発疹	33 (5)	7 (1)	3 (<1)	5 (<1)	2 (<1)
嘔吐	30 (4)	2 (<1)	9 (1)	2 (<1)	3 (<1)
関節痛	11 (2)	5 (<1)	12 (2)	12 (2)	7 (1)
四肢痛	12 (2)	8 (1)	4 (<1)	13 (2)	8 (1)
インフルエンザ	15 (2)	11 (2)	6 (<1)	5 (<1)	3 (<1)
そう痒症	28 (4)	5 (<1)	4 (<1)	2 (<1)	2 (<1)
錯感覚	17 (2)	6 (<1)	8 (1)	4 (<1)	0
うつ病	15 (2)	7 (1)	5 (<1)	2 (<1)	4 (<1)
アラニン・アミノトランスフェラーゼ増加	21 (3)	5 (<1)	6 (<1)	4 (<1)	3 (<1)
紅斑	20 (3)	7 (1)	3 (<1)	2 (<1)	5 (<1)
ほてり	24 (3)	5 (<1)	2 (<1)	1 (<1)	2 (<1)
尿中アルブミン陽性	5 (<1)	6 (<1)	4 (<1)	5 (<1)	8 (1)
気管支炎	7 (<1)	6 (<1)	2 (<1)	6 (1)	8 (1)
発熱	11 (2)	8 (1)	3 (<1)	5 (<1)	5 (<1)
副鼻腔炎	7 (<1)	6 (<1)	7 (1)	6 (1)	7 (1)
咳嗽	9 (1)	6 (<1)	7 (1)	3 (<1)	7 (1)
筋痙縮	9 (1)	4 (<1)	2 (<1)	4 (<1)	7 (1)

NOTE 1: Numbers in parentheses are percentages.
2: Data after subjects switched to alternative MS treatment are excluded.
3: A subject was counted only once within each interval for each preferred term.
4: Preferred terms are presented by decreasing order of incidence in overall Total BG00012.

SOURCE: BG12MS/JAPAN/ISS/T-AE-PT-2PCT-3MON-302.SAS DATE: 02DEC2015

Incidence of adverse events at least 2% higher for any treatment group and the entire study period by preferred term and 3-months interval:
Study 109MS302
Page 34 of 50

	Total BG00012			
	>15-18 months	>18-21 months	>21-24 months	>24 months
疲労	8 (1)	4 (<1)	2 (<1)	1 (<1)
上腹部痛	2 (<1)	5 (<1)	5 (<1)	0
蛋白尿	7 (1)	9 (2)	7 (1)	4 (1)
腹痛	3 (<1)	3 (<1)	2 (<1)	0
発疹	2 (<1)	5 (<1)	1 (<1)	1 (<1)
嘔吐	1 (<1)	3 (<1)	2 (<1)	0
関節痛	1 (<1)	3 (<1)	6 (1)	0
四肢痛	2 (<1)	5 (<1)	7 (1)	2 (<1)
インフルエンザ	5 (<1)	8 (1)	3 (<1)	1 (<1)
そう痒症	1 (<1)	2 (<1)	4 (<1)	0
錯感覚	3 (<1)	4 (<1)	7 (1)	0
うつ病	1 (<1)	7 (1)	4 (<1)	0
アラニン・アミノトランスフェラーゼ増加	1 (<1)	4 (<1)	6 (1)	0
紅斑	2 (<1)	3 (<1)	2 (<1)	0
ほてり	3 (<1)	3 (<1)	1 (<1)	0
尿中アルブミン陽性	5 (<1)	4 (<1)	6 (1)	3 (<1)
気管支炎	2 (<1)	4 (<1)	1 (<1)	1 (<1)
発熱	4 (<1)	3 (<1)	4 (<1)	0
副鼻腔炎	4 (<1)	8 (1)	3 (<1)	0
咳嗽	4 (<1)	3 (<1)	1 (<1)	0
筋痙縮	3 (<1)	4 (<1)	3 (<1)	0

NOTE 1: Numbers in parentheses are percentages.
2: Data after subjects switched to alternative MS treatment are excluded.
3: A subject was counted only once within each interval for each preferred term.
4: Preferred terms are presented by decreasing order of incidence in overall Total BG00012.

SOURCE: BG12MS/JAPAN/ISS/T-AE-PT-2PCT-3MON-302.SAS DATE: 02DEC2015

Incidence of adverse events at least 2% higher for any treatment group and the entire study period by preferred term and 3-months interval:
Study 109MS302
Page 35 of 50

	Total BG00012				
	0-3 months	>3-6 months	>6-9 months	>9-12 months	>12-15 months
ミクロアルブミン尿	2 (<1)	5 (<1)	9 (1)	5 (<1)	3 (<1)
口腔咽頭痛	6 (<1)	9 (1)	4 (<1)	5 (<1)	4 (<1)
感覚鈍麻	11 (2)	5 (<1)	5 (<1)	1 (<1)	3 (<1)
アスパラギン酸アミノトランスフェラーゼ増加	15 (2)	4 (<1)	5 (<1)	2 (<1)	2 (<1)
消化不良	14 (2)	7 (1)	6 (<1)	0	1 (<1)
頚部痛	2 (<1)	5 (<1)	3 (<1)	7 (1)	1 (<1)
胃腸炎	8 (1)	2 (<1)	3 (<1)	5 (<1)	1 (<1)
不安	6 (<1)	5 (<1)	9 (1)	2 (<1)	1 (<1)
不眠症	8 (1)	1 (<1)	2 (<1)	4 (<1)	1 (<1)
尿中蛋白陽性	4 (<1)	7 (1)	3 (<1)	3 (<1)	3 (<1)
咽頭炎	10 (1)	4 (<1)	5 (<1)	3 (<1)	5 (<1)
胃腸障害	18 (3)	1 (<1)	1 (<1)	2 (<1)	0
浮動性めまい	11 (2)	3 (<1)	2 (<1)	4 (<1)	3 (<1)
転倒	1 (<1)	7 (1)	5 (<1)	6 (1)	0
ウイルス性胃腸炎	7 (<1)	3 (<1)	4 (<1)	2 (<1)	0
血尿	5 (<1)	5 (<1)	8 (1)	4 (<1)	0
回転性めまい	8 (1)	6 (<1)	4 (<1)	4 (<1)	0
鼻炎	3 (<1)	4 (<1)	3 (<1)	3 (<1)	4 (<1)
貧血	4 (<1)	3 (<1)	2 (<1)	3 (<1)	2 (<1)
無力症	10 (1)	2 (<1)	3 (<1)	1 (<1)	2 (<1)
便秘	13 (2)	2 (<1)	2 (<1)	2 (<1)	1 (<1)

NOTE 1: Numbers in parentheses are percentages.
2: Data after subjects switched to alternative MS treatment are excluded.
3: A subject was counted only once within each interval for each preferred term.
4: Preferred terms are presented by decreasing order of incidence in overall Total BG00012.

SOURCE: BG12MS/JAPAN/ISS/T-AE-PT-2PCT-3MON-302.SAS DATE: 02DEC2015

Incidence of adverse events at least 2% higher for any treatment group and the entire study period by preferred term and 3-months interval:
Study 109MS302
Page 36 of 50

	Total BG00012			
	>15-18 months	>18-21 months	>21-24 months	>24 months
ミクロアルブミン尿	5 (<1)	5 (<1)	6 (1)	3 (<1)
口腔咽頭痛	2 (<1)	5 (<1)	3 (<1)	0
感覚鈍麻	3 (<1)	4 (<1)	5 (<1)	0
アスパラギン酸アミノトランスフェラーゼ増加	1 (<1)	1 (<1)	3 (<1)	0
消化不良	2 (<1)	3 (<1)	1 (<1)	0
頚部痛	5 (<1)	2 (<1)	4 (<1)	0
胃腸炎	3 (<1)	2 (<1)	4 (<1)	0
不安	2 (<1)	1 (<1)	2 (<1)	1 (<1)
不眠症	3 (<1)	6 (1)	1 (<1)	0
尿中蛋白陽性	7 (1)	1 (<1)	3 (<1)	1 (<1)
咽頭炎	5 (<1)	3 (<1)	3 (<1)	0
胃腸障害	2 (<1)	0	0	0
浮動性めまい	3 (<1)	1 (<1)	3 (<1)	0
転倒	3 (<1)	2 (<1)	2 (<1)	0
ウイルス性胃腸炎	6 (1)	1 (<1)	3 (<1)	0
血尿	2 (<1)	3 (<1)	4 (<1)	2 (<1)
回転性めまい	2 (<1)	2 (<1)	0	0
鼻炎	4 (<1)	1 (<1)	1 (<1)	0
貧血	1 (<1)	2 (<1)	2 (<1)	1 (<1)
無力症	2 (<1)	1 (<1)	1 (<1)	0
便秘	0	1 (<1)	0	0

NOTE 1: Numbers in parentheses are percentages.
2: Data after subjects switched to alternative MS treatment are excluded.
3: A subject was counted only once within each interval for each preferred term.
4: Preferred terms are presented by decreasing order of incidence in overall Total BG00012.

SOURCE: BG12MS/JAPAN/ISS/T-AE-PT-2PCT-3MON-302.SAS DATE: 02DEC2015

Incidence of adverse events at least 2% higher for any treatment group and the entire study period by preferred term and 3-months interval:
Study 109MS302
Page 37 of 50

	Total BG00012				
	0-3 months	>3-6 months	>6-9 months	>9-12 months	>12-15 months
胃炎	7 (<1)	5 (<1)	1 (<1)	2 (<1)	1 (<1)
尿中血陽性	4 (<1)	3 (<1)	1 (<1)	2 (<1)	3 (<1)
挫傷	2 (<1)	0	3 (<1)	3 (<1)	4 (<1)
歯痛	6 (<1)	4 (<1)	1 (<1)	1 (<1)	1 (<1)
脱毛症	8 (1)	5 (<1)	0	1 (<1)	1 (<1)
尿中β２ミクログロブリン増加	2 (<1)	5 (<1)	4 (<1)	3 (<1)	2 (<1)
灼熱感	9 (1)	1 (<1)	3 (<1)	0	1 (<1)
多汗症	8 (1)	0	4 (<1)	1 (<1)	3 (<1)
高血圧	6 (<1)	3 (<1)	2 (<1)	1 (<1)	1 (<1)
筋力低下	4 (<1)	2 (<1)	4 (<1)	2 (<1)	1 (<1)
気道感染	4 (<1)	3 (<1)	4 (<1)	5 (<1)	0
白血球数減少	3 (<1)	2 (<1)	2 (<1)	2 (<1)	2 (<1)
血中副甲状腺ホルモン増加	0	0	0	6 (1)	5 (<1)
眼痛	1 (<1)	4 (<1)	3 (<1)	5 (<1)	0
疼痛	7 (<1)	1 (<1)	0	1 (<1)	2 (<1)
関節捻挫	1 (<1)	2 (<1)	2 (<1)	3 (<1)	2 (<1)
筋痙直	3 (<1)	0	3 (<1)	0	1 (<1)
筋骨格痛	2 (<1)	3 (<1)	2 (<1)	1 (<1)	1 (<1)
筋肉痛	5 (<1)	2 (<1)	3 (<1)	1 (<1)	2 (<1)
末梢性浮腫	5 (<1)	2 (<1)	2 (<1)	3 (<1)	0
口腔ヘルペス	5 (<1)	1 (<1)	3 (<1)	4 (<1)	2 (<1)

NOTE 1: Numbers in parentheses are percentages.
2: Data after subjects switched to alternative MS treatment are excluded.
3: A subject was counted only once within each interval for each preferred term.
4: Preferred terms are presented by decreasing order of incidence in overall Total BG00012.

SOURCE: BG12MS/JAPAN/ISS/T-AE-PT-2PCT-3MON-302.SAS DATE: 02DEC2015

Incidence of adverse events at least 2% higher for any treatment group and the entire study period by preferred term and 3-months interval:
Study 109MS302
Page 38 of 50

	Total BG00012			
	>15-18 months	>18-21 months	>21-24 months	>24 months
胃炎	1 (<1)	3 (<1)	2 (<1)	0
尿中血陽性	4 (<1)	6 (1)	2 (<1)	0
挫傷	4 (<1)	1 (<1)	1 (<1)	1 (<1)
歯痛	3 (<1)	1 (<1)	1 (<1)	0
脱毛症	1 (<1)	0	0	0
尿中β２ミクログロブリン増加	2 (<1)	2 (<1)	2 (<1)	1 (<1)
灼熱感	0	2 (<1)	1 (<1)	0
多汗症	0	1 (<1)	0	0
高血圧	0	2 (<1)	1 (<1)	1 (<1)
筋力低下	2 (<1)	3 (<1)	1 (<1)	0
気道感染	1 (<1)	1 (<1)	2 (<1)	0
白血球数減少	4 (<1)	0	2 (<1)	2 (<1)
血中副甲状腺ホルモン増加	0	0	1 (<1)	3 (<1)
眼痛	2 (<1)	2 (<1)	0	0
疼痛	0	2 (<1)	2 (<1)	0
関節捻挫	1 (<1)	2 (<1)	2 (<1)	0
筋痙直	1 (<1)	4 (<1)	2 (<1)	0
筋骨格痛	0	2 (<1)	3 (<1)	0
筋肉痛	0	2 (<1)	0	0
末梢性浮腫	2 (<1)	1 (<1)	3 (<1)	0
口腔ヘルペス	2 (<1)	0	1 (<1)	0

NOTE 1: Numbers in parentheses are percentages.
2: Data after subjects switched to alternative MS treatment are excluded.
3: A subject was counted only once within each interval for each preferred term.
4: Preferred terms are presented by decreasing order of incidence in overall Total BG00012.

SOURCE: BG12MS/JAPAN/ISS/T-AE-PT-2PCT-3MON-302.SAS DATE: 02DEC2015

Incidence of adverse events at least 2% higher for any treatment group and the entire study period by preferred term and 3-months interval:
Study 109MS302
Page 39 of 50

	Total BG00012				
	0-3 months	>3-6 months	>6-9 months	>9-12 months	>12-15 months
結膜炎	3 (<1)	0	4 (<1)	3 (<1)	0
血中ブドウ糖増加	2 (<1)	6 (<1)	4 (<1)	0	2 (<1)
耳感染	3 (<1)	2 (<1)	0	2 (<1)	2 (<1)
γ－グルタミルトランスフェラーゼ増加	5 (<1)	0	1 (<1)	0	1 (<1)
霧視	2 (<1)	2 (<1)	0	2 (<1)	0
外陰腟真菌感染	1 (<1)	3 (<1)	3 (<1)	1 (<1)	0
インフルエンザ様疾患	3 (<1)	0	1 (<1)	4 (<1)	0
膀胱炎	0	2 (<1)	1 (<1)	0	1 (<1)
尿中白血球陽性	0	2 (<1)	2 (<1)	2 (<1)	2 (<1)
視力低下	0	0	1 (<1)	0	0
筋骨格硬直	0	1 (<1)	0	0	0

NOTE 1: Numbers in parentheses are percentages.
2: Data after subjects switched to alternative MS treatment are excluded.
3: A subject was counted only once within each interval for each preferred term.
4: Preferred terms are presented by decreasing order of incidence in overall Total BG00012.

SOURCE: BG12MS/JAPAN/ISS/T-AE-PT-2PCT-3MON-302.SAS DATE: 02DEC2015

Incidence of adverse events at least 2% higher for any treatment group and the entire study period by preferred term and 3-months interval:
Study 109MS302
Page 40 of 50

	Total BG00012			
	>15-18 months	>18-21 months	>21-24 months	>24 months
結膜炎	1 (<1)	0	2 (<1)	1 (<1)
血中ブドウ糖増加	3 (<1)	2 (<1)	1 (<1)	0
耳感染	2 (<1)	1 (<1)	2 (<1)	0
γ－グルタミルトランスフェラーゼ増加	2 (<1)	0	3 (<1)	0
霧視	3 (<1)	2 (<1)	0	0
外陰腟真菌感染	2 (<1)	0	1 (<1)	0
インフルエンザ様疾患	1 (<1)	0	0	0
膀胱炎	0	1 (<1)	3 (<1)	0
尿中白血球陽性	0	0	1 (<1)	0
視力低下	0	0	0	1 (<1)
筋骨格硬直	0	0	0	0

NOTE 1: Numbers in parentheses are percentages.
2: Data after subjects switched to alternative MS treatment are excluded.
3: A subject was counted only once within each interval for each preferred term.
4: Preferred terms are presented by decreasing order of incidence in overall Total BG00012.

SOURCE: BG12MS/JAPAN/ISS/T-AE-PT-2PCT-3MON-302.SAS DATE: 02DEC2015

Incidence of adverse events at least 2% higher for any treatment group and the entire study period by preferred term and 3-months interval:
Study 109MS302
Page 41 of 50

	GA				
	0-3 months	>3-6 months	>6-9 months	>9-12 months	>12-15 months
Number of subjects followed in the interval	351 (100)	338 (100)	327 (100)	322 (100)	307 (100)
Number of subjects with an event	197 (56)	163 (48)	138 (42)	131 (41)	120 (39)
Number of subjects with deaths	0	0	0	0	0
Number of subjects with SAEs other than deaths	14 (4)	14 (4)	12 (4)	8 (2)	6 (2)
Number of subjects who discontinued	6 (2)	0	3 (<1)	0	0
多発性硬化症再発	33 (9)	30 (9)	32 (10)	22 (7)	17 (6)
潮紅	1 (<1)	2 (<1)	2 (<1)	1 (<1)	0
鼻咽頭炎	9 (3)	16 (5)	13 (4)	7 (2)	7 (2)
頭痛	21 (6)	15 (4)	7 (2)	5 (2)	3 (<1)
下痢	3 (<1)	1 (<1)	1 (<1)	2 (<1)	2 (<1)
尿路感染	16 (5)	10 (3)	9 (3)	10 (3)	5 (2)
悪心	8 (2)	1 (<1)	3 (<1)	1 (<1)	1 (<1)
上気道感染	7 (2)	2 (<1)	3 (<1)	5 (2)	1 (<1)
背部痛	9 (3)	5 (1)	7 (2)	3 (<1)	5 (2)

NOTE 1: Numbers in parentheses are percentages.
2: Data after subjects switched to alternative MS treatment are excluded.
3: A subject was counted only once within each interval for each preferred term.
4: Preferred terms are presented by decreasing order of incidence in overall Total BG00012.

SOURCE: BG12MS/JAPAN/ISS/T-AE-PT-2PCT-3MON-302.SAS DATE: 02DEC2015

Incidence of adverse events at least 2% higher for any treatment group and the entire study period by preferred term and 3-months interval:
Study 109MS302
Page 42 of 50

	GA			
	>15-18 months	>18-21 months	>21-24 months	>24 months
Number of subjects followed in the interval	298 (100)	291 (100)	282 (100)	217 (100)
Number of subjects with an event	108 (36)	115 (40)	91 (32)	18 (8)
Number of subjects with deaths	0	1 (<1)	0	0
Number of subjects with SAEs other than deaths	2 (<1)	6 (2)	10 (4)	0
Number of subjects who discontinued	1 (<1)	2 (<1)	0	0
多発性硬化症再発	17 (6)	17 (6)	12 (4)	2 (<1)
潮紅	1 (<1)	1 (<1)	0	0
鼻咽頭炎	6 (2)	8 (3)	8 (3)	3 (1)
頭痛	6 (2)	4 (1)	2 (<1)	0
下痢	0	4 (1)	1 (<1)	0
尿路感染	5 (2)	6 (2)	5 (2)	1 (<1)
悪心	2 (<1)	1 (<1)	0	0
上気道感染	5 (2)	8 (3)	3 (1)	0
背部痛	4 (1)	2 (<1)	2 (<1)	0

NOTE 1: Numbers in parentheses are percentages.
2: Data after subjects switched to alternative MS treatment are excluded.
3: A subject was counted only once within each interval for each preferred term.
4: Preferred terms are presented by decreasing order of incidence in overall Total BG00012.

SOURCE: BG12MS/JAPAN/ISS/T-AE-PT-2PCT-3MON-302.SAS DATE: 02DEC2015

Incidence of adverse events at least 2% higher for any treatment group and the entire study period by preferred term and 3-months interval:
Study 109MS302
Page 43 of 50

	GA				
	0-3 months	>3-6 months	>6-9 months	>9-12 months	>12-15 months
疲労	9 (3)	11 (3)	6 (2)	3 (<1)	4 (1)
上腹部痛	1 (<1)	1 (<1)	0	2 (<1)	0
蛋白尿	8 (2)	4 (1)	7 (2)	10 (3)	5 (2)
腹痛	1 (<1)	0	1 (<1)	1 (<1)	0
発疹	3 (<1)	1 (<1)	1 (<1)	0	1 (<1)
嘔吐	1 (<1)	0	1 (<1)	2 (<1)	3 (<1)
関節痛	3 (<1)	2 (<1)	3 (<1)	3 (<1)	1 (<1)
四肢痛	6 (2)	5 (1)	3 (<1)	3 (<1)	4 (1)
インフルエンザ	1 (<1)	1 (<1)	4 (1)	3 (<1)	3 (<1)
そう痒症	2 (<1)	0	0	1 (<1)	1 (<1)
錯感覚	0	4 (1)	5 (2)	2 (<1)	1 (<1)
うつ病	9 (3)	4 (1)	4 (1)	2 (<1)	3 (<1)
アラニン・アミノトランスフェラーゼ増加	5 (1)	5 (1)	3 (<1)	2 (<1)	5 (2)
紅斑	3 (<1)	1 (<1)	1 (<1)	0	0
ほてり	4 (1)	0	0	0	0
尿中アルブミン陽性	1 (<1)	3 (<1)	1 (<1)	5 (2)	5 (2)
気管支炎	2 (<1)	5 (1)	2 (<1)	1 (<1)	0
発熱	6 (2)	1 (<1)	2 (<1)	1 (<1)	3 (<1)
副鼻腔炎	1 (<1)	1 (<1)	0	3 (<1)	2 (<1)
咳嗽	0	3 (<1)	2 (<1)	3 (<1)	0
筋痙縮	2 (<1)	2 (<1)	2 (<1)	0	1 (<1)

NOTE 1: Numbers in parentheses are percentages.
2: Data after subjects switched to alternative MS treatment are excluded.
3: A subject was counted only once within each interval for each preferred term.
4: Preferred terms are presented by decreasing order of incidence in overall Total BG00012.

SOURCE: BG12MS/JAPAN/ISS/T-AE-PT-2PCT-3MON-302.SAS DATE: 02DEC2015

Incidence of adverse events at least 2% higher for any treatment group and the entire study period by preferred term and 3-months interval:
Study 109MS302
Page 44 of 50

	GA			
	>15-18 months	>18-21 months	>21-24 months	>24 months
疲労	2 (<1)	1 (<1)	0	0
上腹部痛	0	0	0	0
蛋白尿	1 (<1)	4 (1)	4 (1)	2 (<1)
腹痛	1 (<1)	0	0	0
発疹	1 (<1)	0	2 (<1)	0
嘔吐	0	1 (<1)	0	0
関節痛	0	1 (<1)	6 (2)	0
四肢痛	5 (2)	4 (1)	2 (<1)	0
インフルエンザ	3 (1)	2 (<1)	1 (<1)	0
そう痒症	1 (<1)	0	2 (<1)	0
錯感覚	1 (<1)	4 (1)	0	0
うつ病	4 (1)	4 (1)	1 (<1)	1 (<1)
アラニン・アミノトランスフェラーゼ増加	1 (<1)	1 (<1)	3 (1)	0
紅斑	0	0	1 (<1)	0
ほてり	0	0	0	0
尿中アルブミン陽性	4 (1)	2 (<1)	3 (1)	1 (<1)
気管支炎	3 (1)	2 (<1)	2 (<1)	0
発熱	3 (1)	2 (<1)	1 (<1)	0
副鼻腔炎	6 (2)	1 (<1)	0	0
咳嗽	2 (<1)	0	1 (<1)	0
筋痙縮	1 (<1)	1 (<1)	0	0

NOTE 1: Numbers in parentheses are percentages.
2: Data after subjects switched to alternative MS treatment are excluded.
3: A subject was counted only once within each interval for each preferred term.
4: Preferred terms are presented by decreasing order of incidence in overall Total BG00012.

SOURCE: BG12MS/JAPAN/ISS/T-AE-PT-2PCT-3MON-302.SAS DATE: 02DEC2015

Incidence of adverse events at least 2% higher for any treatment group and the entire study period by preferred term and 3-months interval:
Study 109MS302
Page 45 of 50

	GA				
	0-3 months	>3-6 months	>6-9 months	>9-12 months	>12-15 months
ミクロアルブミン尿	3 (<1)	2 (<1)	2 (<1)	3 (<1)	3 (<1)
口腔咽頭痛	4 (1)	1 (<1)	2 (<1)	1 (<1)	0
感覚鈍麻	3 (<1)	5 (1)	2 (<1)	3 (<1)	3 (<1)
アスパラギン酸アミノトランスフェラーゼ増加	2 (<1)	4 (1)	2 (<1)	1 (<1)	3 (<1)
消化不良	1 (<1)	2 (<1)	1 (<1)	1 (<1)	0
頚部痛	0	2 (<1)	1 (<1)	1 (<1)	1 (<1)
胃腸炎	0	1 (<1)	1 (<1)	0	1 (<1)
不安	3 (<1)	1 (<1)	0	2 (<1)	0
不眠症	4 (1)	2 (<1)	4 (1)	0	1 (<1)
尿中蛋白陽性	3 (<1)	6 (2)	1 (<1)	3 (<1)	2 (<1)
咽頭炎	2 (<1)	4 (1)	1 (<1)	3 (<1)	2 (<1)
胃腸障害	0	1 (<1)	0	0	0
浮動性めまい	7 (2)	0	0	0	0
転倒	4 (1)	3 (<1)	2 (<1)	4 (1)	1 (<1)
ウイルス性胃腸炎	1 (<1)	0	1 (<1)	2 (<1)	1 (<1)
血尿	2 (<1)	3 (<1)	0	3 (<1)	3 (<1)
回転性めまい	2 (<1)	4 (1)	1 (<1)	4 (1)	1 (<1)
鼻炎	1 (<1)	1 (<1)	4 (1)	1 (<1)	0
貧血	2 (<1)	0	1 (<1)	1 (<1)	1 (<1)
無力症	5 (1)	2 (<1)	2 (<1)	1 (<1)	2 (<1)
便秘	2 (<1)	1 (<1)	2 (<1)	2 (<1)	0

NOTE 1: Numbers in parentheses are percentages.
2: Data after subjects switched to alternative MS treatment are excluded.
3: A subject was counted only once within each interval for each preferred term.
4: Preferred terms are presented by decreasing order of incidence in overall Total BG00012.

SOURCE: BG12MS/JAPAN/ISS/T-AE-PT-2PCT-3MON-302.SAS DATE: 02DEC2015

Incidence of adverse events at least 2% higher for any treatment group and the entire study period by preferred term and 3-months interval:
Study 109MS302
Page 46 of 50

	GA			
	>15-18 months	>18-21 months	>21-24 months	>24 months
ミクロアルブミン尿	0	5 (2)	1 (<1)	0
口腔咽頭痛	5 (2)	1 (<1)	1 (<1)	0
感覚鈍麻	0	2 (<1)	2 (<1)	0
アスパラギン酸アミノトランスフェラーゼ増加	1 (<1)	1 (<1)	1 (<1)	0
消化不良	0	1 (<1)	0	0
頚部痛	1 (<1)	1 (<1)	0	0
胃腸炎	0	2 (<1)	1 (<1)	0
不安	0	1 (<1)	1 (<1)	0
不眠症	2 (<1)	0	1 (<1)	0
尿中蛋白陽性	2 (<1)	1 (<1)	1 (<1)	1 (<1)
咽頭炎	2 (<1)	0	2 (<1)	0
胃腸障害	1 (<1)	0	0	0
浮動性めまい	0	1 (<1)	1 (<1)	0
転倒	3 (1)	1 (<1)	1 (<1)	0
ウイルス性胃腸炎	1 (<1)	0	0	0
血尿	2 (<1)	0	3 (1)	0
回転性めまい	2 (<1)	2 (<1)	1 (<1)	0
鼻炎	1 (<1)	0	3 (1)	0
貧血	0	1 (<1)	1 (<1)	0
無力症	1 (<1)	1 (<1)	1 (<1)	1 (<1)
便秘	2 (<1)	0	0	0

NOTE 1: Numbers in parentheses are percentages.
2: Data after subjects switched to alternative MS treatment are excluded.
3: A subject was counted only once within each interval for each preferred term.
4: Preferred terms are presented by decreasing order of incidence in overall Total BG00012.

SOURCE: BG12MS/JAPAN/ISS/T-AE-PT-2PCT-3MON-302.SAS DATE: 02DEC2015

Incidence of adverse events at least 2% higher for any treatment group and the entire study period by preferred term and 3-months interval:
Study 109MS302
Page 47 of 50

	GA				
	0-3 months	>3-6 months	>6-9 months	>9-12 months	>12-15 months
胃炎	0	0	1 (<1)	0	1 (<1)
尿中血陽性	3 (<1)	1 (<1)	0	0	0
挫傷	2 (<1)	2 (<1)	1 (<1)	1 (<1)	0
歯痛	1 (<1)	1 (<1)	1 (<1)	1 (<1)	1 (<1)
脱毛症	5 (1)	0	1 (<1)	0	0
尿中β２ミクログロブリン増加	0	1 (<1)	0	2 (<1)	1 (<1)
多汗症	0	3 (<1)	1 (<1)	1 (<1)	0
高血圧	3 (<1)	3 (<1)	2 (<1)	1 (<1)	1 (<1)
筋力低下	3 (<1)	2 (<1)	2 (<1)	1 (<1)	1 (<1)
気道感染	1 (<1)	1 (<1)	2 (<1)	3 (<1)	1 (<1)
白血球数減少	0	0	0	0	1 (<1)
血中副甲状腺ホルモン増加	0	0	0	0	1 (<1)
眼痛	1 (<1)	2 (<1)	3 (<1)	1 (<1)	0
疼痛	1 (<1)	1 (<1)	1 (<1)	2 (<1)	0
関節捻挫	1 (<1)	0	1 (<1)	0	0
筋痙直	2 (<1)	1 (<1)	2 (<1)	0	0
筋骨格痛	0	3 (<1)	2 (<1)	1 (<1)	2 (<1)
筋肉痛	3 (<1)	0	1 (<1)	0	0
末梢性浮腫	1 (<1)	1 (<1)	2 (<1)	1 (<1)	0
口腔ヘルペス	1 (<1)	2 (<1)	2 (<1)	1 (<1)	1 (<1)
結膜炎	0	0	1 (<1)	1 (<1)	1 (<1)

NOTE 1: Numbers in parentheses are percentages.
2: Data after subjects switched to alternative MS treatment are excluded.
3: A subject was counted only once within each interval for each preferred term.
4: Preferred terms are presented by decreasing order of incidence in overall Total BG00012.

SOURCE: BG12MS/JAPAN/ISS/T-AE-PT-2PCT-3MON-302.SAS DATE: 02DEC2015

Incidence of adverse events at least 2% higher for any treatment group and the entire study period by preferred term and 3-months interval:
Study 109MS302
Page 48 of 50

	GA			
	>15-18 months	>18-21 months	>21-24 months	>24 months
胃炎	0	0	2 (<1)	0
尿中血陽性	0	0	0	0
挫傷	0	0	0	0
歯痛	0	0	0	0
脱毛症	0	1 (<1)	0	0
尿中β２ミクログロブリン増加	0	0	0	1 (<1)
多汗症	0	0	0	0
高血圧	3 (1)	2 (<1)	0	0
筋力低下	0	0	0	0
気道感染	0	1 (<1)	2 (<1)	0
白血球数減少	0	0	0	0
血中副甲状腺ホルモン増加	0	0	0	1 (<1)
眼痛	0	1 (<1)	0	0
疼痛	0	0	0	0
関節捻挫	1 (<1)	0	0	0
筋痙直	1 (<1)	1 (<1)	0	0
筋骨格痛	0	1 (<1)	0	0
筋肉痛	0	0	0	0
末梢性浮腫	1 (<1)	0	0	0
口腔ヘルペス	0	1 (<1)	0	0
結膜炎	0	0	0	0

NOTE 1: Numbers in parentheses are percentages.
2: Data after subjects switched to alternative MS treatment are excluded.
3: A subject was counted only once within each interval for each preferred term.
4: Preferred terms are presented by decreasing order of incidence in overall Total BG00012.

SOURCE: BG12MS/JAPAN/ISS/T-AE-PT-2PCT-3MON-302.SAS DATE: 02DEC2015

Incidence of adverse events at least 2% higher for any treatment group and the entire study period by preferred term and 3-months interval:
Study 109MS302
Page 49 of 50

	GA				
	0-3 months	>3-6 months	>6-9 months	>9-12 months	>12-15 months
血中ブドウ糖増加	1 (<1)	1 (<1)	0	2 (<1)	1 (<1)
耳感染	0	0	0	0	1 (<1)
γ－グルタミルトランスフェラーゼ増加	3 (<1)	1 (<1)	0	1 (<1)	1 (<1)
霧視	3 (<1)	0	0	0	1 (<1)
外陰腟真菌感染	1 (<1)	1 (<1)	0	1 (<1)	2 (<1)
インフルエンザ様疾患	1 (<1)	2 (<1)	0	0	0
膀胱炎	0	1 (<1)	0	0	3 (<1)
尿中白血球陽性	3 (<1)	5 (1)	3 (<1)	0	1 (<1)
視力低下	1 (<1)	0	0	3 (<1)	0
筋骨格硬直	1 (<1)	3 (<1)	2 (<1)	2 (<1)	2 (<1)
注射部位紅斑	29 (8)	2 (<1)	0	1 (<1)	0
注射部位疼痛	27 (8)	3 (<1)	1 (<1)	0	0
注射部位そう痒感	12 (3)	0	0	0	1 (<1)
注射部位腫脹	9 (3)	0	1 (<1)	0	0

NOTE 1: Numbers in parentheses are percentages.
2: Data after subjects switched to alternative MS treatment are excluded.
3: A subject was counted only once within each interval for each preferred term.
4: Preferred terms are presented by decreasing order of incidence in overall Total BG00012.

SOURCE: BG12MS/JAPAN/ISS/T-AE-PT-2PCT-3MON-302.SAS DATE: 02DEC2015

Incidence of adverse events at least 2% higher for any treatment group and the entire study period by preferred term and 3-months interval:
Study 109MS302
Page 50 of 50

	GA			
	>15-18 months	>18-21 months	>21-24 months	>24 months
血中ブドウ糖増加	1 (<1)	2 (<1)	0	0
耳感染	0	0	1 (<1)	0
γ－グルタミルトランスフェラーゼ増加	2 (<1)	0	1 (<1)	0
霧視	0	1 (<1)	1 (<1)	0
外陰腟真菌感染	0	1 (<1)	1 (<1)	0
インフルエンザ様疾患	0	0	0	0
膀胱炎	0	1 (<1)	1 (<1)	0
尿中白血球陽性	2 (<1)	0	0	0
視力低下	0	0	0	0
筋骨格硬直	0	0	0	0
注射部位紅斑	0	0	0	0
注射部位疼痛	1 (<1)	0	0	0
注射部位そう痒感	0	0	0	0
注射部位腫脹	0	0	0	0

NOTE 1: Numbers in parentheses are percentages.
2: Data after subjects switched to alternative MS treatment are excluded.
3: A subject was counted only once within each interval for each preferred term.
4: Preferred terms are presented by decreasing order of incidence in overall Total BG00012.

SOURCE: BG12MS/JAPAN/ISS/T-AE-PT-2PCT-3MON-302.SAS DATE: 02DEC2015

Table 323: BG00012 Exposure – for safety update

BG00012 Exposure - for safety update

	BG00012 + IFNBeta	BG00012 + GA	Total
Number of subjects dosed with BG00012	57 (100)	47 (100)	104 (100)
Number of subjects exposed to BG00012 for			
Less than 6 months	12 (21)	9 (19)	21 (20)
6 or more months	45 (79)	38 (81)	83 (80)

NOTE 1: Numbers in parentheses are percentages.
2: Less than 6 months: <154 days; 6 or more months: >=154 days.

SOURCE: BG12MS/109MS201/CSR/T-EXPOSURE.SAS DATE: 07MAY2012

Table 324: Extent of Exposure by Duration: Studies of 109MS301, 109MS302, and 109MS303

Extent of exposure by duration: Studies 109MS301, 109MS302, and 109MS303
Page 1 of 2

Study	Treatment	Exposure						
		Single	>= 6 months	>= 1 year	>= 2 years	>= 3 years	>= 4 years	>= 5 years
109MS301	BG00012 240 mg BID	410	346	317	285			
	BG00012 240 mg TID	416	348	330	287			
109MS302	BG00012 240 mg BID	359	309	286	253			
	BG00012 240 mg TID	344	291	276	247			
109MS303								
Newly Exposed Subjects	BG00012 240 mg BID	367	316	306	274	247	232	80
	BG00012 240 mg TID	367	296	280	259	229	219	66
109MS301/302 and 109MS303 Combined								
Continuers	BG00012 240 mg BID	501	501	501	497	459	440	392
	BG00012 240 mg TID	501	501	501	499	456	423	373
All Subjects	BG00012 240 mg BID	1136	971	914	823	706	672	472
	BG00012 240 mg TID	1127	936	888	806	685	642	439

NOTE: >=6 months: >= 154 days; >=1 years: >=322 days; >=2 years: >=658 days; >=3 years: >=994 days; >=4 years: >=1330 days; >=5 years: >=1666 days; >=6 years: >=2002 days; >=7 years: >=2338 days.

SOURCE: BG12MS/ISS/INTERIM6/T-EXP-INT.SAS DATE: 23JUL2015

Extent of exposure by duration: Studies 109MS301, 109MS302, and 109MS303
Page 2 of 2

Study	Treatment	Exposure >= 6 years	Exposure >= 7 years
109MS301	BG00012 240 mg BID		
	BG00012 240 mg TID		
109MS302	BG00012 240 mg BID		
	BG00012 240 mg TID		
109MS303			
Newly Exposed Subjects	BG00012 240 mg BID	8	
	BG00012 240 mg TID	11	
109MS301/302 and 109MS303 Combined			
Continuers	BG00012 240 mg BID	356	128
	BG00012 240 mg TID	346	136
All Subjects	BG00012 240 mg BID	364	128
	BG00012 240 mg TID	357	136

NOTE: >=6 months: >= 154 days; >=1 years: >=322 days; >=2 years: >=658 days; >=3 years: >=994 days; >=4 years: >=1330 days; >=5 years: >=1666 days; >=6 years: >=2002 days; >=7 years: >=2338 days.

SOURCE: BG12MS/ISS/INTERIM6/T-EXP-INT.SAS DATE: 23JUL2015

Table 325: Incidence of Adverse Events with an Incidence of ≥2% by System Organ Class and Preferred Term and Causal Association to Study Drug – Total – BG00012 240 240 mg BID (PMDA specific requirements)

Incidence of adverse events with an incidence of >=2% by system organ class
and preferred term and causal association to study drug
- Total - BG00012 240 mg BID(PMDA specific requirements)
Page 1 of 5

	Irrespective of causal association	Causal association cannot be ruled out
	Total - BG00012 240 mg BID	Total - BG00012 240 mg BID
Number of subjects with an event	197 (90)	137 (63)
感染症および寄生虫症	109 (50)	6 (3)
鼻咽頭炎	76 (35)	4 (2)
上気道感染	18 (8)	0
インフルエンザ	11 (5)	0
膀胱炎	7 (3)	0
尿路感染	6 (3)	2 (<1)
胃腸炎	6 (3)	1 (<1)
咽頭炎	6 (3)	0
副鼻腔炎	5 (2)	1 (<1)
血液およびリンパ系障害	12 (5)	6 (3)
リンパ球減少症	6 (3)	5 (2)
鉄欠乏性貧血	6 (3)	1 (<1)
精神障害	14 (6)	0
不眠症	9 (4)	0

NOTE 1: Total - BG00012 240 mg BID includes Study 305 Part I and II data for subjects who were randomized to BG00012 in Part I, and data for subjects who switched from placebo to BG00012 in Part II.
2: Numbers in parentheses are percentages.
3: Data after subjects switched to alternative MS medications are excluded.
4: A subject was counted only once within each system organ class or preferred term.

SOURCE: BG12MS/109MS305/PART2/T-AE-SOCPT-CAUS2-ALL.SAS DATE: 29APR2016

Incidence of adverse events with an incidence of >=2% by system organ class
and preferred term and causal association to study drug
- Total - BG00012 240 mg BID(PMDA specific requirements)
Page 2 of 5

	Irrespective of causal association	Causal association cannot be ruled out
	Total - BG00012 240 mg BID	Total - BG00012 240 mg BID
うつ病	5 (2)	0
神経系障害	76 (35)	7 (3)
多発性硬化症再発	61 (28)	2 (<1)
頭痛	14 (6)	1 (<1)
感覚鈍麻	8 (4)	1 (<1)
浮動性めまい	6 (3)	3 (1)
錯感覚	5 (2)	0
眼障害	7 (3)	1 (<1)
眼乾燥	7 (3)	1 (<1)
耳および迷路障害	7 (3)	1 (<1)
回転性めまい	7 (3)	1 (<1)
血管障害	70 (32)	66 (30)
潮紅	60 (27)	57 (26)
ほてり	12 (5)	11 (5)

NOTE 1: Total - BG00012 240 mg BID includes Study 305 Part I and II data for subjects who were randomized to BG00012 in Part I, and data for subjects who switched from placebo to BG00012 in Part II.
2: Numbers in parentheses are percentages.
3: Data after subjects switched to alternative MS medications are excluded.
4: A subject was counted only once within each system organ class or preferred term.

SOURCE: BG12MS/109MS305/PART2/T-AE-SOCPT-CAUS2-ALL.SAS DATE: 29APR2016

Incidence of adverse events with an incidence of >=2% by system organ class
and preferred term and causal association to study drug
- Total - BG00012 240 mg BID(PMDA specific requirements)
Page 3 of 5

	Irrespective of causal association	Causal association cannot be ruled out
	Total - BG00012 240 mg BID	Total - BG00012 240 mg BID
呼吸器、胸郭および縦隔障害	5 (2)	0
上気道の炎症	5 (2)	0
胃腸障害	74 (34)	55 (25)
下痢	28 (13)	18 (8)
悪心	22 (10)	15 (7)
上腹部痛	19 (9)	16 (7)
嘔吐	16 (7)	11 (5)
腹痛	15 (7)	12 (5)
消化不良	7 (3)	6 (3)
胃炎	6 (3)	1 (<1)
胃腸障害	5 (2)	4 (2)
便秘	5 (2)	1 (<1)
皮膚および皮下組織障害	40 (18)	22 (10)
そう痒症	20 (9)	13 (6)
発疹	11 (5)	9 (4)
紅斑	7 (3)	4 (2)

NOTE 1: Total - BG00012 240 mg BID includes Study 305 Part I and II data for subjects who were randomized to BG00012 in Part I, and data for subjects who switched from placebo to BG00012 in Part II.
2: Numbers in parentheses are percentages.
3: Data after subjects switched to alternative MS medications are excluded.
4: A subject was counted only once within each system organ class or preferred term.

SOURCE: BG12MS/109MS305/PART2/T-AE-SOCPT-CAUS2-ALL.SAS DATE: 29APR2016

Incidence of adverse events with an incidence of >=2% by system organ class
and preferred term and causal association to study drug
- Total - BG00012 240 mg BID(PMDA specific requirements)
Page 4 of 5

	Irrespective of causal association	Causal association cannot be ruled out
	Total - BG00012 240 mg BID	Total - BG00012 240 mg BID
蕁麻疹	7 (3)	1 (<1)
湿疹	5 (2)	1 (<1)
筋骨格系および結合組織障害	30 (14)	0
関節痛	14 (6)	0
四肢痛	10 (5)	0
背部痛	9 (4)	0
腎および尿路障害	12 (5)	5 (2)
ミクロアルブミン尿	11 (5)	5 (2)
蛋白尿	6 (3)	1 (<1)
一般・全身障害および投与部位の状態	18 (8)	5 (2)
疲労	7 (3)	3 (1)
発熱	7 (3)	2 (<1)
末梢性浮腫	5 (2)	0
臨床検査	20 (9)	15 (7)

NOTE 1: Total - BG00012 240 mg BID includes Study 305 Part I and II data for subjects who were randomized to BG00012 in Part I, and data for subjects who switched from placebo to BG00012 in Part II.
2: Numbers in parentheses are percentages.
3: Data after subjects switched to alternative MS medications are excluded.
4: A subject was counted only once within each system organ class or preferred term.

SOURCE: BG12MS/109MS305/PART2/T-AE-SOCPT-CAUS2-ALL.SAS DATE: 29APR2016

Incidence of adverse events with an incidence of >=2% by system organ class
and preferred term and causal association to study drug
- Total - BG00012 240 mg BID(PMDA specific requirements)
Page 5 of 5

	Irrespective of causal association	Causal association cannot be ruled out
	Total - BG00012 240 mg BID	Total - BG00012 240 mg BID
アラニン・アミノトランスフェラーゼ増加	11 (5)	10 (5)
リンパ球数減少	9 (4)	5 (2)
アスパラギン酸アミノトランスフェラーゼ増加	8 (4)	8 (4)
白血球数減少	5 (2)	3 (1)

NOTE 1: Total - BG00012 240 mg BID includes Study 305 Part I and II data for subjects who were randomized to BG00012 in Part I, and data for subjects who switched from placebo to BG00012 in Part II.
2: Numbers in parentheses are percentages.
3: Data after subjects switched to alternative MS medications are excluded.
4: A subject was counted only once within each system organ class or preferred term.

SOURCE: BG12MS/109MS305/PART2/T-AE-SOCPT-CAUS2-ALL.SAS DATE: 29APR2016

Table 326: Incidence of Adverse Events with an Incidence of ≥2% by System Organ Class and Preferred Term and Causal Association to Study Drug – Total – BG00012 240 mg BID (PMDA specific requirements) – Subjects from Japan

Incidence of adverse events with an incidence of >=2% by system organ class and preferred term and causal association to study drug - Total - BG00012 240 mg BID (PMDA specific requirements) - Subjects from Japan
Page 1 of 5

	Irrespective of causal association	Causal association cannot be ruled out
	Total - BG00012 240 mg BID	Total - BG00012 240 mg BID
Number of subjects from Japan with an event	104 (95)	75 (69)
感染症および寄生虫症	71 (65)	5 (5)
鼻咽頭炎	60 (55)	4 (4)
インフルエンザ	8 (7)	0
胃腸炎	5 (5)	1 (<1)
膀胱炎	5 (5)	0
咽頭炎	5 (5)	0
副鼻腔炎	4 (4)	1 (<1)
麦粒腫	3 (3)	0
血液およびリンパ系障害	5 (5)	1 (<1)
鉄欠乏性貧血	5 (5)	1 (<1)
精神障害	9 (8)	0
不眠症	7 (6)	0
不安	3 (3)	0
神経系障害	42 (39)	6 (6)

NOTE 1: Total - BG00012 240 mg BID includes Study 305 Part I and II data for subjects who were randomized to BG00012 in Part I, and data for subjects who switched from placebo to BG00012 in Part II.
2: Numbers in parentheses are percentages.
3: Data after subjects switched to alternative MS medications are excluded.
4: A subject was counted only once within each system organ class or preferred term.

SOURCE: BG12MS/109MS305/PART2/T-AE-SOCPT-CAUS2-ALL.SAS DATE: 29APR2016

Incidence of adverse events with an incidence of >=2% by system organ class and preferred term and causal association to study drug - Total - BG00012 240 mg BID (PMDA specific requirements) - Subjects from Japan
Page 2 of 5

	Irrespective of causal association	Causal association cannot be ruled out
	Total - BG00012 240 mg BID	Total - BG00012 240 mg BID
多発性硬化症再発	36 (33)	1 (<1)
頭痛	11 (10)	1 (<1)
浮動性めまい	4 (4)	3 (3)
感覚鈍麻	4 (4)	1 (<1)
眼障害	9 (8)	1 (<1)
眼乾燥	7 (6)	1 (<1)
眼精疲労	3 (3)	0
耳および迷路障害	5 (5)	0
回転性めまい	5 (5)	0
血管障害	27 (25)	26 (24)
潮紅	18 (17)	17 (16)
ほてり	11 (10)	11 (10)
呼吸器、胸郭および縦隔障害	8 (7)	0
上気道の炎症	5 (5)	0

NOTE 1: Total - BG00012 240 mg BID includes Study 305 Part I and II data for subjects who were randomized to BG00012 in Part I, and data for subjects who switched from placebo to BG00012 in Part II.
2: Numbers in parentheses are percentages.
3: Data after subjects switched to alternative MS medications are excluded.
4: A subject was counted only once within each system organ class or preferred term.

SOURCE: BG12MS/109MS305/PART2/T-AE-SOCPT-CAUS2-ALL.SAS DATE: 29APR2016

Incidence of adverse events with an incidence of >=2% by system organ class and preferred term and causal association to study drug - Total - BG00012 240 mg BID (PMDA specific requirements) - Subjects from Japan
Page 3 of 5

	Irrespective of causal association	Causal association cannot be ruled out
	Total - BG00012 240 mg BID	Total - BG00012 240 mg BID
鼻漏	3 (3)	0
胃腸障害	44 (40)	30 (28)
下痢	15 (14)	10 (9)
悪心	13 (12)	9 (8)
上腹部痛	12 (11)	10 (9)
嘔吐	10 (9)	5 (5)
腹痛	7 (6)	5 (5)
便秘	4 (4)	1 (<1)
齲歯	4 (4)	0
胃腸障害	3 (3)	3 (3)
胃炎	3 (3)	1 (<1)
肝胆道系障害	3 (3)	0
肝障害	3 (3)	0
皮膚および皮下組織障害	27 (25)	17 (16)
そう痒症	15 (14)	11 (10)
発疹	10 (9)	8 (7)

NOTE 1: Total - BG00012 240 mg BID includes Study 305 Part I and II data for subjects who were randomized to BG00012 in Part I, and data for subjects who switched from placebo to BG00012 in Part II.
2: Numbers in parentheses are percentages.
3: Data after subjects switched to alternative MS medications are excluded.
4: A subject was counted only once within each system organ class or preferred term.

SOURCE: BG12MS/109MS305/PART2/T-AE-SOCPT-CAUS2-ALL.SAS DATE: 29APR2016

Incidence of adverse events with an incidence of >=2% by system organ class and preferred term and causal association to study drug - Total - BG00012 240 mg BID (PMDA specific requirements) - Subjects from Japan
Page 4 of 5

	Irrespective of causal association	Causal association cannot be ruled out
	Total - BG00012 240 mg BID	Total - BG00012 240 mg BID
紅斑	4 (4)	3 (3)
湿疹	4 (4)	1 (<1)
蕁麻疹	3 (3)	0
筋骨格系および結合組織障害	19 (17)	2 (2)
関節痛	8 (7)	0
背部痛	6 (6)	0
四肢痛	5 (5)	0
筋痙縮	3 (3)	2 (2)
一般・全身障害および投与部位の状態	12 (11)	4 (4)
発熱	5 (5)	2 (2)
疲労	4 (4)	2 (2)
末梢性浮腫	4 (4)	0
臨床検査	16 (15)	15 (14)
アラニン・アミノトランスフェラーゼ増加	10 (9)	10 (9)

NOTE 1: Total - BG00012 240 mg BID includes Study 305 Part I and II data for subjects who were randomized to BG00012 in Part I, and data for subjects who switched from placebo to BG00012 in Part II.
2: Numbers in parentheses are percentages.
3: Data after subjects switched to alternative MS medications are excluded.
4: A subject was counted only once within each system organ class or preferred term.

SOURCE: BG12MS/109MS305/PART2/T-AE-SOCPT-CAUS2-ALL.SAS DATE: 29APR2016

Incidence of adverse events with an incidence of >=2% by system organ class and preferred term and causal association to study drug - Total - BG00012 240 mg BID (PMDA specific requirements) - Subjects from Japan
Page 5 of 5

	Irrespective of causal association	Causal association cannot be ruled out
	Total - BG00012 240 mg BID	Total - BG00012 240 mg BID
アスパラギン酸アミノトランスフェラーゼ増加	8 (7)	8 (7)
リンパ球数減少	5 (5)	4 (4)
γ－グルタミルトランスフェラーゼ増加	3 (3)	3 (3)
白血球数減少	3 (3)	3 (3)
傷害、中毒および処置合併症	3 (3)	0
転倒	3 (3)	0

NOTE 1: Total - BG00012 240 mg BID includes Study 305 Part I and II data for subjects who were randomized to BG00012 in Part I, and data for subjects who switched from placebo to BG00012 in Part II.
2: Numbers in parentheses are percentages.
3: Data after subjects switched to alternative MS medications are excluded.
4: A subject was counted only once within each system organ class or preferred term.

SOURCE: BG12MS/109MS305/PART2/T-AE-SOCPT-CAUS2-ALL.SAS DATE: 29APR2016

テクフィデラカプセル 120 mg
テクフィデラカプセル 240 mg

第 2 部 CTD の概要
2.7 臨床概要
2.7.5 参考文献

バイオジェン・ジャパン株式会社

目次

頁
2.7.5 参考文献 3
2.7.5.1 2.7.1 生物薬剤学及び関連する分析法の概要で引用した参考文献 3
2.7.5.2 2.7.2 臨床薬理試験で引用した参考文献 4
2.7.5.3 2.7.3 臨床的有効性で引用した参考文献 5
2.7.5.4 2.7.4 臨床的安全性で引用した文献 12

2.7.5 参考文献

2.7.5.1 2.7.1 生物薬剤学及び関連する分析法の概要で引用した参考文献

1) Litjens NH, Rademaker M, Ravensbergen B, et al. Monomethylfumarate affects polarization of monocyte-derived dendritic cells resulting in down-regulated Th1 lymphocyte responses. European Journal of Immunology. 2004;34(2):565-75. [M5.4-68]

2) Werdenberg D. Stability, permeability and pharmacokinetics of perorally administered fumarates [dissertation]. [Zürich (Switzerland)]: Swiss Federal Institute of Technology; 2003. [M5.4-127]

3) Linker RA, Lee DH, Ryan S, et al. Fumaric acid esters exert neuroprotective effects in neuroinflammation via activation of the Nrf2 antioxidant pathway. Brain. 2011;134(Pt 3):678- 92. [M5.4-67]

2.7.5.2 2.7.2 臨床薬理試験で引用した参考文献

1) Bjornsson TD, Callaghan JT, Einolf HJ, et al. The conduct of *in vitro* and *in vivo* drug-drug interaction studies: a Pharmaceutical Research and Manufacturers of America (PhRMA) perspective. Drug Metab Dispos. 2003;31(7):815-32. [M5.4-13]

2) Henderson R. Carbon dioxide measures up as a real hazard. Occup Health Staf. 2006;75(7):64, 68-9. [M5.4-136]

3) Watkins PB. Breath tests as noninvasive assays of P450s. Methods Enzymol. 1991;206:517-22. [M5.4-137]

4) Rostami-Yazdi M, Clement B, Schmidt TJ, et al. Detection of metabolites of fumaric acid esters in human urine: implications for their mode of action. J Invest Dermatol. 2009;129(1):231-4. [M5.4-96]

5) Litjens NH, Rademaker M, Ravensbergen B, et al. Monomethylfumarate affects polarization of monocyte-derived dendritic cells resulting in down-regulated Th1 lymphocyte responses. European Journal of Immunology. 2004;34(2):565-75. [M5.4-68]

6) Werdenberg D. Stability, permeability and pharmacokinetics of perorally administered fumarates [dissertation]. [Zürich (Switzerland)]: Swiss Federal Institute of Technology; 2003. [M5.4-127]

2.7.5.3 2.7.3 臨床的有効性で引用した参考文献

1) De Stefano N, Narayanan S, Matthews PM, et al. In vivo evidence for axonal dysfunction remote from focal cerebral demyelination of the type seen in multiple sclerosis. Brain. 1999;122(Pt 10):1933-9. [M5.4-32]

2) Ferguson B, Matyszak MK, Esiri MM, et al. Axonal damage in acute multiple sclerosis lesions. Brain. 1997;120(Pt 3):393-9. [M5.4-38]

3) Silber E, Sharief MK. Axonal degeneration in the pathogenesis of multiple sclerosis. J Neurol Sci. 1999;170(1):11-8. [M5.4-104]

4) Trapp BD, Peterson J, Ransohoff RM, et al. Axonal transection in the lesions of multiple sclerosis. N Engl J Med. 1998;338(5):278-85. [M5.4-115]

5) Noseworthy JH, Lucchinetti C, Rodriguez M, et al. Multiple sclerosis. N Engl J Med. 2000;343(13):938-52. [M5.4-84]

6) Rosati G. The prevalence of multiple sclerosis in the world: an update. Neurol Sci. 2001;22(2):117-39. [M5.4-95]

7) Kira J. Multiple sclerosis in the Japanese population. Lancet Neurol. 2003;2(2):117-27. [M5.4-63]

8) Horiuchi I, Kira J. Multiple sclerosis. In: Tamura A, Matsutani M, Shimizu T, editors. Evidence-based basic guidelines for treatment of cerebrospinal diseases. Tokyo: Medical View; 2004;276-279.

9) Kinoshita M, Obata K, Tanaka M. Latitude has more significant impact on prevalence of multiple sclerosis than ultraviolet level or sunshine duration in Japanese population. Neurol Sci. 2015. [M5.4-62]

10) Kim NH, Kim HJ, Cheong HK, et al. Prevalence of multiple sclerosis in Korea. Neurology. 2010;75(16):1432-8. [M5.4-61]

11) Makhani N, Morrow SA, Fisk J, et al. MS incidence and prevalence in Africa, Asia, Australia and New Zealand: A systematic review. Mult Scler Relat Disord. 2014;3(1):48-60. [M5.4-71]

12) Kasteng F, Kobelt G. Access to innovative treatments in multiple sclerosis in Europe. European Pharmaceutical Industry Associations (EFPIA); 2009. [M5.4-34]

13) Lublin FD, Reingold SC. Defining the clinical course of multiple sclerosis: results of an international survey. National Multiple Sclerosis Society (USA) Advisory Committee on Clinical Trials of New Agents in Multiple Sclerosis. Neurology. 1996;46(4):907-911. [M5.4-69]

14) Isaac C, Li DK, Genton M, et al. Multiple sclerosis: a serial study using MRI in relapsing patients. Neurology. 1988;38(10):1511-5. [M5.4-53]

15) Thompson AJ, Kermode AG, Wicks D, et al. Major differences in the dynamics of primary and secondary progressive multiple sclerosis. Annals of Neurology. 1991;29(1):53-62. [M5.4-113]

16) Thompson AJ, Miller D, Youl B, et al. Serial gadolinium-enhanced MRI in relapsing/remitting multiple sclerosis of varying disease duration. Neurology. 1992;42(1):60-3. [M5.4-114]

17) Ron MA, Callanan MM, Warrington EK. Cognitive abnormalities in multiple sclerosis: a psychometric and MRI study. Psychological Medicine. 1991;21(1):59-68. [M5.4-94]

18) Chen XL, Dodd G, Thomas S, et al. Activation of Nrf2/ARE pathway protects endothelial cells from oxidant injury and inhibits inflammatory gene expression. Am J Physiol Heart Circ Physiol. 2006;290(5):H1862-70. [M5.4-23]

19) Itoh K, Ishii T, Wakabayashi N, et al. Regulatory mechanisms of cellular response to oxidative stress. Free Radic Res. 1999;31(4):319-24. [M5.4-54]

20) Venugopal R, Jaiswal AK. Nrf2 and Nrf1 in association with Jun proteins regulate antioxidant response element-mediated expression and coordinated induction of genes encoding detoxifying enzymes. Oncogene. 1998;17(24):3145-56. Epub 1999/01/01. [M5.4-121]

21) Linker RA, Lee DH, Ryan S, et al. Fumaric acid esters exert neuroprotective effects in neuroinflammation via activation of the Nrf2 antioxidant pathway. Brain. 2011;134(Pt 3):678-92. Epub 2011/03/01. [M5.4-67]

22) Satoh T, Okamoto SI, Cui J, et al. Activation of the Keap1/Nrf2 pathway for neuroprotection by electrophilic [correction of electrophillic] phase II inducers. Proc Natl Acad Sci U S A. 2006;103(3):768-73. [M5.4-100]

23) Vargas MR, Pehar M, Cassina P, et al. Fibroblast growth factor-1 induces heme oxygenase-1 via nuclear factor erythroid 2-related factor 2 (Nrf2) in spinal cord astrocytes: consequences for motor neuron survival. J Biol Chem. 2005;280(27):25571-9. Epub 2005/05/05. [M5.4-117]

24) Zhao J, Moore AN, Redell JB, et al. Enhancing expression of Nrf2-driven genes protects the blood brain barrier after brain injury. J Neurosci. 2007;27(38):10240-8. Epub 2007/09/21. [M5.4-131]

25) Hubbs AF, Benkovic SA, Miller DB, et al. Vacuolar leukoencephalopathy with widespread astrogliosis in mice lacking transcription factor Nrf2. Am J Pathol. 2007;170(6):2068-76. [M5.4-51]

26) Wierinckx A, Brevé J, Mercier D, et al. Detoxication enzyme inducers modify cytokine production in rat mixed glial cells. J Neuroimmunol. 2005;166(1-2):132-43. [M5.4-129]

27) Schilling S, Goelz S, Linker R, et al. Fumaric acid esters are effective in chronic experimental autoimmune encephalomyelitis and suppress macrophage infiltration. Clin Exp Immunol. 2006;145(1):101-7. [M5.4-102]

28) Ellrichmann G, Petrasch-Parwez E, Lee DH, et al. Efficacy of fumaric acid esters in the R6/2 and YAC128 models of Huntington's disease. PLoS One. 2011;6(1):e16172. [M5.4-35]

29) Lublin FD, Baier M, Cutter G. Effect of relapses on development of residual deficit in multiple sclerosis. Neurology. 2003;61(11):1528-32. [M5.4-70]

30) O'Neill G, Polman C, Kappos L, et al. Relapse efficacy endpoints for the evaluation of disease-modifying therapies in clinical studies of multiple sclerosis [poster]. Presented at: 59th Annual Meeting of the American Academy of Neurology; 2007 April 28-May 5; Boston, MA. [M5.4-86]

31) Kurtzke JF. Rating neurologic impairment in multiple sclerosis: an expanded disability status scale (EDSS). Neurology. 1983;33(11):1444-52. Epub 1983 Nov 01. [M5.4-64]

32) Fischer JS, Rudick RA, Cutter GR, et al. The Multiple Sclerosis Functional Composite Measure (MSFC): an integrated approach to MS clinical outcome assessment. National MS Society Clinical Outcomes Assessment Task Force. Mult Scler. 1999;5(4):244-50. [M5.4-40]

33) Cohen JA, Fischer JS, Bolibrush DM, et al. Intrarater and interrater reliability of the MS functional composite outcome measure. Neurology. 2000;54(4):802-6. [M5.4-27]

34) Cutter GR, Baier ML, Rudick RA, et al. Development of a multiple sclerosis functional composite as a clinical trial outcome measure. Brain. 1999;122:871-882. [M5.4-30]

35) Fisher E, Rudick RA, Cutter G, et al. Relationship between brain atrophy and disability: an 8-year follow-up study of multiple sclerosis patients. Mult Scler. 2000;6(6):373-7. Epub 2001/02/24. [M5.4-41]

36) Polman CH, Reingold SC, Edan G, et al. Diagnostic criteria for multiple sclerosis: 2005 revisions to the "McDonald Criteria". Ann Neurol. 2005;58(6):840-6. Epub 2005/11/12. [M5.4-90]

37) McFarland HF, Barkhof F, Antel J, et al. The role of MRI as a surrogate outcome measure in multiple sclerosis. Mult Scler. 2002;8(1):40-51. Epub 2002/04/09. [M5.4-75]

38) Cotton F, Weiner HL, Jolesz FA, et al. MRI contrast uptake in new lesions in relapsing-remitting MS followed at weekly intervals. Neurology. 2003;60(4):640-6. Epub 2003/02/26. [M5.4-29]

39) Kappos L, Moeri D, Radue EW, et al. Predictive value of gadolinium-enhanced magnetic resonance imaging for relapse rate and changes in disability or impairment in multiple sclerosis: a meta-analysis. Gadolinium MRI Meta-analysis Group. Lancet. 1999;353(9157):964-9. Epub 1999/08/25. [M5.4-57]

40) Miller DH. Biomarkers and surrogate outcomes in neurodegenerative disease: lessons from multiple sclerosis. NeuroRx. 2004;1(2):284-94. Epub 2005/02/18. [M5.4-78]

41) Sormani MP, Bonzano L, Roccatagliata L, et al. Magnetic resonance imaging as a potential surrogate for relapses in multiple sclerosis: a meta-analytic approach. Ann Neurol. 2009;65(3):268-75. Epub 2009/04/01. [M5.4-108]

42) Sormani MP, Bonzano L, Roccatagliata L, et al. Surrogate endpoints for EDSS worsening in multiple sclerosis. A meta-analytic approach. Neurology. 2010;75(4):302-9. Epub 2010/06/25. [M5.4-109]

43) Frank JA, Stone LA, Smith ME, et al. Serial contrast-enhanced magnetic resonance imaging in patients with early relapsing-remitting multiple sclerosis: implications for treatment trials. Ann Neurol. 1994;36 Suppl:S86-90. Epub 1994/01/01. [M5.4-43]

44) Miller DH, Rudge P, Johnson G, et al. Serial gadolinium enhanced magnetic resonance imaging in multiple sclerosis. Brain. 1988;111(Pt 4):927-39. Epub 1988/08/01. [M5.4-77]

45) Barkhof F, Filippi M, Miller DH, et al. Comparison of MRI criteria at first presentation to predict conversion to clinically definite multiple sclerosis. Brain. 1997;120 (Pt 11):2059-69. Epub 1997/12/16. [M5.4-6]

46) Rudick RA, Lee JC, Simon J, et al. Significance of T2 lesions in multiple sclerosis: A 13-year longitudinal study. Ann Neurol. 2006;60(2):236-42. Epub 2006/06/21. [M5.4-97]

47) Bagnato F, Jeffries N, Richert ND, et al. Evolution of T1 black holes in patients with multiple sclerosis imaged monthly for 4 years. Brain. 2003;126(Pt 8):1782-9. Epub 2003/06/25. [M5.4-4]

48) Barkhof F. MRI in multiple sclerosis: correlation with expanded disability status scale (EDSS). Mult Scler. 1999;5(4):283-6. Epub 1999/09/01. [M5.4-7]

49) Bitsch A, Kuhlmann T, Stadelmann C, et al. A longitudinal MRI study of histopathologically defined hypointense multiple sclerosis lesions. Ann Neurol. 2001;49(6):793-6. Epub 2001/06/21. [M5.4-12]

50) Truyen L, van Waesberghe JH, van Walderveen MA, et al. Accumulation of hypointense lesions ("black holes") on T1 spin-echo MRI correlates with disease progression in multiple sclerosis. Neurology. 1996;47(6):1469-76. Epub 1996/12/01. [M5.4-116]

51) van Walderveen MA, Kamphorst W, Scheltens P, et al. Histopathologic correlate of hypointense lesions on T1-weighted spin-echo MRI in multiple sclerosis. Neurology. 1998;50(5):1282-8. Epub 1998/05/22. [M5.4-120]

52) Naismith RT, Xu J, Tutlam NT, et al. Increased diffusivity in acute multiple sclerosis lesions predicts risk of black hole. Neurology. 2010;74(21):1694-701. Epub 2010/05/26. [M5.4-82]

53) Bruck W, Bitsch A, Kolenda H, et al. Inflammatory central nervous system demyelination: correlation of magnetic resonance imaging findings with lesion pathology. Ann Neurol. 1997;42(5):783-93. Epub 1997/12/10. [M5.4-16]

54) Cabanillas F, Grillo-López AJ, McLaughlin P, et al. Anti-CD20 antibody, IDEC-C2B8: clearance of bcl-2 t(14;18) positive cells from peripheral blood and bone marrow in patients with relapsed low-grade or follicular lymphoma. Blood. 1996;88(10):91a, #351. [M5.4-17]

55) van Waesberghe JH, Kamphorst W, De Groot CJ, et al. Axonal loss in multiple sclerosis lesions: magnetic resonance imaging insights into substrates of disability. Ann Neurol. 1999;46(5):747-54. Epub 1999/11/30. [M5.4-119]

56) Barkhof F, Calabresi PA, Miller DH, et al. Imaging outcomes for neuroprotection and repair in multiple sclerosis trials. Nat Rev Neurol. 2009;5(5):256-66. Epub 2009/06/03. [M5.4-9]

57) Bermel RA, Bakshi R. The measurement and clinical relevance of brain atrophy in multiple sclerosis. Lancet Neurol. 2006;5(2):158-70. Epub 2006/01/24. [M5.4-10]

58) Zivadinov R, Reder AT, Filippi M, et al. Mechanisms of action of disease-modifying agents and brain volume changes in multiple sclerosis. Neurology. 2008;71(2):136-44. Epub 2008/07/09. [M5.4-132]

59) Fischer JS, Priore RL, Jacobs LD, et al. Neuropsychological effects of interferon beta-1a in relapsing multiple sclerosis. Multiple Sclerosis Collaborative Research Group. Annals of Neurology. 2000;48(6):885-892. [M5.4-39]

60) Fisher E, Rudick RA, Simon JH, et al. Eight-year follow-up study of brain atrophy in patients with MS. Neurology. 2002;59(9):1412-20. Epub 2002/11/13. [M5.4-42]

61) Simon JH. Brain atrophy in multiple sclerosis: what we know and would like to know. Mult Scler. 2006;12(6):679-87. [M5.4-105]

62) Smith SM, Zhang Y, Jenkinson M, et al. Accurate, robust, and automated longitudinal and cross-sectional brain change analysis. Neuroimage. 2002;17(1):479-89. [M5.4-106]

63) Schmierer K, Scaravilli F, Altmann DR, et al. Magnetization transfer ratio and myelin in postmortem multiple sclerosis brain. Ann Neurol. 2004;56(3):407-15. Epub 2004/09/07. [M5.4-103]

64) Barkhof F, Bruck W, De Groot CJ, et al. Remyelinated lesions in multiple sclerosis: magnetic resonance image appearance. Arch Neurol. 2003;60(8):1073-81. Epub 2003/08/20. [M5.4-8]

65) Chen JT, Kuhlmann T, Jansen GH, et al. Voxel-based analysis of the evolution of magnetization transfer ratio to quantify remyelination and demyelination with histopathological validation in a multiple sclerosis lesion. Neuroimage. 2007;36(4):1152-8. [M5.4-24]

66) Ware J, Kosinski M, Gandek B. SF-36 health survey: manual and interpretation guide. Lincoln (RI): QualityMetric Incorporated; 2005.

67) Hobart J, Lamping D, Fitzpatrick R, et al. The Multiple Sclerosis Impact Scale (MSIS-29): a new patient-based outcome measure. Brain. 2001;124(Pt 5):962-73. [M5.4-49]

68) Glanz BI, Dégano IR, Rintell DJ, et al. Work productivity in relapsing multiple sclerosis: associations with disability, depression, fatigue, anxiety, cognition, and health-related quality of life. Value Health. 2012;15(8):1029-35. [M5.4-47]

69) McDonald WI, Compston A, Edan G, et al. Recommended diagnostic criteria for multiple sclerosis: guidelines from the International panel on the diagnosis of multiple sclerosis. Ann Neurol. 2001;50(1):121-127. [M5.4-74]

70) Milo R, Miller A. Revised diagnostic criteria of multiple sclerosis. Autoimmun Rev. 2014;13(4-5):518-24. [M5.4-79]

71) Sormani MP, Rovaris M, Valsasina P, et al. Measurement error of two different techniques for brain atrophy assessment in multiple sclerosis. Neurology. 2004;62(8):1432-4. [M5.4-107]

72) Johnson KP, Brooks BR, Cohen JA, et al. Copolymer 1 reduces relapse rate and improves disability in relapsing-remitting multiple sclerosis: results of a phase III multicenter, double-blind placebo-controlled trial. The Copolymer 1 Multiple Sclerosis Study Group. Neurology. 1995;45(7):1268-76. [M5.4-56]

73) Mikol DD, Barkhof F, Chang P, et al. Comparison of subcutaneous interferon beta-1a with glatiramer acetate in patients with relapsing multiple sclerosis (the REbif vs Glatiramer Acetate in Relapsing MS

Disease [REGARD] study): a multicentre, randomised, parallel, open-label trial. Lancet Neurol. 2008;7(10):903-14. [M5.4-76]

74) O'Connor P, Filippi M, Arnason B, et al. 250 µg or 500 µg interferon beta-1b versus 20 mg glatiramer acetate in relapsing-remitting multiple sclerosis: a prospective, randomised, multicentre study. Lancet Neurol. 2009;8(10):889-97. [M5.4-85]

75) Kappos L, Gold R, Miller DH, et al. Effect of BG-12 on contrast-enhancing lesions in patients with relapsing-remitting multiple sclerosis: subgroup analyses from the phase 2b study. Mult Scler. 2011. [M5.4-59]

2.7.5.4 2.7.4 臨床的安全性で引用した文献

1) Agarwal R, Panesar A, Lewis RR. Dipstick proteinuria: can it guide hypertension management? Am J Kidney Dis. 2002;39(6):1190-5. [M5.4-1]

2) Arnett PA, Strober LB. Cognitive and neurobehavioral features in multiple sclerosis. Expert Rev Neurother. 2011;11(3):411-24. [M5.4-3]

3) Dahl OP, Stordal E, Lydersen S, et al. Anxiety and depression in multiple sclerosis. A comparative population-based study in Nord-Trøndelag County, Norway. Mult Scler. 2009;15(12):1495-501. [M5.4-31]

4) Feinstein A. Multiple sclerosis and depression. Mult Scler. 2011;17(11):1276-81. [M5.4-37]

5) Patten SB, Beck CA, Williams JV, et al. Major depression in multiple sclerosis: a population-based perspective. Neurology. 2003;61(11):1524-7. [M5.4-87]

6) Brønnum-Hansen H, Stenager E, Hansen T, et al. Survival and mortality rates among Danes with MS. Int MS J. 2006;13(2):66-71. [M5.4-15]

7) Sadovnick AD, Eisen K, Ebers GC, et al. Cause of death in patients attending multiple sclerosis clinics. Neurology. 1991;41(8):1193-6. [M5.4-98]

8) Stenager EN, Stenager E, Koch-Henriksen N, et al. Suicide and multiple sclerosis: an epidemiological investigation. J Neurol Neurosurg Psychiatry. 1992;55(7):542-5. [M5.4-111]

9) Gheuens S, Wüthrich C, Koralnik IJ. Progressive multifocal leukoencephalopathy: why gray and white matter. Annu Rev Pathol. 2013;8:189-215. [M5.4-45]

10) Glassock RJ. Is the presence of microalbuminuria a relevant marker of kidney disease? Curr Hypertens Rep. 2010;12(5):364-8. [M5.4-48]

11) Khan E, Batuman V, Lertora JJ. Emergence of biomarkers in nephropharmacology. Biomark Med. 2010;4(6):805-14. [M5.4-60]

12) Peterson PA, Evrin PE, Berggård I. Differentiation of glomerular, tubular, and normal proteinuria: determinations of urinary excretion of beta-2-macroglobulin, albumin, and total protein. J Clin Invest. 1969;48(7):1189-98. [M5.4-89]

13) Waring WS, Moonie A. Earlier recognition of nephrotoxicity using novel biomarkers of acute kidney injury. Clin Toxicol (Phila). 2011;49(8):720-8. [M5.4-124]

14) BfArM. BfArM Risk Information. Federal Institute for Drugs and Medical Devices. Published 2015 [Accessed 08 Jan 2016]. Available from: www.bfarm.de/SharedDocs/Risikoinformationen/Pharmakovigilanz/EN/RI/2015/RIdimethylfumarat.html [M5.4-11]

15) Nieuwkamp DJ, Murk JL, van Oosten BW, et al. PML in a patient without severe lymphocytopenia receiving dimethyl fumarate. N Engl J Med. 2015;372(15):1474-6. [M5.4-83]

16) Control CfD. Vital Statistics Report. Centers for Disease Control and Prevention. Published 2013 [Accessed 20 Feb 2015]. [M5.4-28]

17) Eurostat. Eurostat Statistics Explained: Mortality and Life Expectancy Statistics. Published 2012 [Accessed 20 May 2015]. Available from: http://ec.europa.eu/eurostat/statistics_explained/index.php/Mortality_and_life_expectancy_statistics#Main_statistical_findings [M5.4-36]

18) Brass D, McKay P, Scott F. Investigating an incidental finding of lymphopenia. BMJ. 2014;348:g1721. [M5.4-14]

19) Castelino DJ, McNair P, Kay TW. Lymphocytopenia in a hospital population--what does it signify? Aust N Z J Med. 1997;27(2):170-4. [M5.4-19]

20) Molloy ES, Calabrese LH. Progressive multifocal leukoencephalopathy associated with immunosuppressive therapy in rheumatic diseases: evolving role of biologic therapies. Arthritis Rheum. 2012;64(9):3043-51. [M5.4-80]

21) Zonios D, Sheikh V, Sereti I. Idiopathic CD4 lymphocytopenia: a case of missing, wandering or ineffective T cells. Arthritis Res Ther. 2012;14(4):222. [M5.4-134]

22) Zonios DI, Falloon J, Bennett JE, et al. Idiopathic CD4+ lymphocytopenia: natural history and prognostic factors. Blood. 2008;112(2):287-94. [M5.4-133]

23) Ammon Avalos L, Galindo C, Li DK. A systematic review to calculate background miscarriage rates using life table analysis. Birth Defects Res A Clin Mol Teratol. 2012;94(6):417-23. [M5.4-2]

24) Garcia-Enguidanos A, Calle ME, Valero J, et al. Risk factors in miscarriage: a review. Eur J Obstet Gynecol Reprod Biol. 2002;102(2):111-19. [M5.4-44]

25) CDC. Update on overall prevalence of major birth defects--Atlanta, Georgia, 1978-2005. MMWR Morb Mortal Wkly Rep. 2008;57(1):1-5. [M5.4-20]

26) Springett A, Budd J, Draper ES, et al. Congenital Anomaly Statistics 2012 England and Wales. London: British Isles Network of Congenital Anomaly Registers; 2014. [M5.4-110]