Clinical trial results:
A phase II, multicentre study to evaluate the long-term safety and efficacy of MT-1303 in subjects with relapsing-remitting multiple sclerosis who have completed the MT-1303-E04 study

Summary

EudraCT number	2012-002639-27
Trial protocol	GB HU ES FI BE LT CZ PL BG IT
Global end of trial date	15 March 2016

Results information

Result version number	v1 (current)
This version publication date	16 March 2017
First version publication date	16 March 2017

Trial information

Trial identification

Sponsor protocol code	MT-1303-E05

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01890655
WHO universal trial number (UTN)	-
Other trial identifiers	MOMENTUM extention study: MT-1303-E05

Notes:

Sponsors

Sponsor organisation name	Mitsubishi Tanabe Pharma Corporation
Sponsor organisation address	17-10, Nihonbashi-Koamicho, Chuo-ku, Tokyo, Japan, 103-8405
Public contact	General Information , Mitsubishi Tanabe Pharma Europe Ltd. , regulatory@mt-pharma-eu.com
Scientific contact	General Information , Mitsubishi Tanabe Pharma Europe Ltd. , regulatory@mt-pharma-eu.com

Notes:

Paediatric regulatory details

Is trial part of an agreed paediatric investigation plan (PIP)	No
Does article 45 of REGULATION (EC) No 1901/2006 apply to this trial?	No
Does article 46 of REGULATION (EC) No 1901/2006 apply to this trial?	No

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	02 August 2016
Is this the analysis of the primary completion data?	Yes
Primary completion date	15 March 2016
Global end of trial reached?	Yes
Global end of trial date	15 March 2016
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The primary objective of the trial was to evaluate the long-term safety and tolerability of MT-1303 in subjects with relapsing-remitting multiple sclerosis (RRMS).

Protection of trial subjects:

Subjects will be permanently withdrawn from study medication in the following circumstances:
• Confirmed absolute lymphocyte count values <200/µL, on 2 consecutive occasions
• Documented relapse of MS symptoms; or new or exacerbation of pre-existing conditions requiring treatment with one or more prohibited medications
• Development of any clinically significant abnormalities on ECG, including but not limited to: Symptomatic bradycardia; New onset 2nd degree AV block, Mobitz Type II; New onset 3rd degree AV block; Confirmed QTcF interval prolongation >500msec and/or QTcF interval increase from baseline >60msec
• Development of any clinically significant liver dysfunction as follows:
  o ALT or AST > 8 × ULN, or
  o ALT or AST >5 × ULN and persists for more than 2 consecutive visits, or
  o ALT or AST >3 × ULN in conjunction with elevated total bilirubin >2 × ULN or
  o ALT or AST >3 × ULN with appearance of fatigue, nausea, vomiting, right upper quadrant pain or tenderness, fever, rash and/or eosinophilia (>5%)
• Development of macular oedema during the study
• Recurrence of the abnormality at re-challenge

In addition, a subject may voluntarily withdraw or be permanently withdrawn from the study at any time for reasons including, but not limited to, the following:
• The subject wishes to withdraw from further participation
• The subject is non-compliant with the protocol
• The treatment blind is broken for the subject for the reasons other than regulatory reporting (during Part 1 only)
• Continuation in the study would be detrimental to the subject's safety in the opinion of the Investigator
• Pregnancy
• The Investigator or the Sponsor, for any reason, stops the study

Background therapy:

Not applicable

Evidence for comparator:

Not applicable

Actual start date of recruitment	31 January 2013
Long term follow-up planned	Yes
Long term follow-up rationale	Safety, Efficacy
Long term follow-up duration	21 Months
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Poland: 78
Country: Number of subjects enrolled	Spain: 19
Country: Number of subjects enrolled	United Kingdom: 15
Country: Number of subjects enrolled	Belgium: 9
Country: Number of subjects enrolled	Bulgaria: 54
Country: Number of subjects enrolled	Czech Republic: 54
Country: Number of subjects enrolled	Finland: 6
Country: Number of subjects enrolled	Germany: 3
Country: Number of subjects enrolled	Hungary: 22
Country: Number of subjects enrolled	Italy: 9
Country: Number of subjects enrolled	Lithuania: 2
Country: Number of subjects enrolled	Canada: 4
Country: Number of subjects enrolled	Croatia: 3
Country: Number of subjects enrolled	Russian Federation: 22
Country: Number of subjects enrolled	Serbia: 25
Country: Number of subjects enrolled	Turkey: 17
Country: Number of subjects enrolled	Ukraine: 25
Worldwide total number of subjects	367
EEA total number of subjects	274

Notes:

Subjects enrolled per age group

In utero	0
Preterm newborn - gestational age < 37 wk	0
Newborns (0-27 days)	0
Infants and toddlers (28 days-23 months)	0
Children (2-11 years)	0
Adolescents (12-17 years)	0
Adults (18-64 years)	367
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Part 1-Double Blind: subjects were randomised to receive 0.1mg, 0.2mg or 0.4mg of MT-1303. Part 2-Open Label: subjects with a minimum of 12 weeks left in the DB Period received OL treatment with the effective dose(s) for the remainder of the 18-month treatment period. Safety Follow Up: subjects then entered a 12-week Safety Follow Up Period

Pre-assignment

Screening details:

After providing the informed consent former MT-1303-E04 subjects could enter the MT-1303-E05 Double Blind period once all eligibility criteria were validated. There was no screening period.

Period 1

Period 1 title	Double-Blind Period
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator, Monitor, Data analyst, Assessor

Blinding implementation details:

During the double-blind part (part 1/2) of the E05 study lymphocyte counts, subsets and WBC were not provided to any site/study personnel to maintain the study medication blind. Also all subjects underwent recommended monitoring of cardiovascular safety within the clinic for at least 6 h following the first dose of study medication at E05 Visit 1. All 3 doses of MT-1303 capsules were identical in appearance, taste and smell and the same number of capsules were given.

Arms

Are arms mutually exclusive?	No
Arm title	MT-1303 0.1 mg (Safety Population)

Arm description:

MT-1303 0.1 mg (oral capsules) taken from Wk 0 up to Wk 24 in MT-1303-E04 and during double-blind period of MT-1303-E05 or taken only from Wk 0 in MT-1303-E05 after switching from placebo and during the double-blind period of MT-1303-E05. (Overall Summary all Treatments)

Arm type	Experimental
Investigational medicinal product name	MT-1303
Investigational medicinal product code	MT-1303
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

1 capsule, containing MT-1303 0.1mg, taken orally daily for 18 months.

Arm title	MT-1303 0.2 mg (Safety Population)

Arm description:

MT-1303 0.2 mg (oral capsules) taken from Wk 0 up to Wk 24 in MT-1303-E04 and during both double-blind and open-label periods of MT-1303-E05 or taken only from Wk 0 in MT-1303-E05 after switching from placebo then throughout the MT-1303-E05 treatment periods. (Overall Summary all Treatments)

Arm type	Experimental

Investigational medicinal product name	MT-1303
Investigational medicinal product code	MT-1303
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

1 capsule, containing MT-1303 0.2mg, taken orally daily for 18 months.

Arm title	MT-1303 0.4 mg (Safety Population)

Arm description:

MT-1303 0.4 mg (oral capsules) taken from Wk 0 up to Wk 24 in MT-1303-E04 and during both double-blind and open-label periods of MT-1303-E05 or taken only from Wk 0 in MT-1303-E05 after switching from placebo then throughout the MT-1303-E05 treatment periods. (Overall Summary all Treatments)

Arm type	Experimental
Investigational medicinal product name	MT-1303
Investigational medicinal product code	MT-1303
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

1 capsule, containing MT-1303 0.4mg, taken orally daily for 18 months.

Number of subjects in period 1	MT-1303 0.1 mg (Safety Population)	MT-1303 0.2 mg (Safety Population)	MT-1303 0.4 mg (Safety Population)
Started	123	123	121
Completed	108	115	107
Not completed	15	8	14
Protocol Specific	2	-	3
Consent withdrawn by subject	6	1	1
Protocol-specific reason	-	2	-
Adverse event, non-fatal	1	-	1
Other	-	2	5
Completed during E05 DB period	6	3	4

Period 2

Period 2 title	Open-Label Treatment Period
Is this the baseline period?	No
Allocation method	Randomised - controlled
Blinding used	Not blinded

Arms

Are arms mutually exclusive?	No

Arm title	MT-1303 0.2 mg (Safety Population)

Arm description:

MT-1303 0.2 mg (oral capsules) taken from Wk 0 up to Wk 24 in MT-1303-E04 and during both double-blind and open-label periods of MT-1303-E05 or taken only from Wk 0 in MT-1303-E05 after switching from placebo then throughout the MT-1303-E05 treatment periods or taken only from start of open-label period in MT-1303-E05 after switching from MT-1303 0.1 mg then throughout the MT-1303-E05 open label treatment period. (Overall Summary all Treatments)

Arm type	Experimental
Investigational medicinal product name	MT-1303
Investigational medicinal product code	MT-1303
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

1 capsule, containing MT-1303 0.2mg, taken orally daily for 18 months.

Arm title	MT-1303 0.4 mg (Safety Population)

Arm description:

MT-1303 0.4 mg (oral capsules) taken from Wk 0 up to Wk 24 in MT-1303-E04 and during both double-blind and open-label periods of MT-1303-E05 or taken only from Wk 0 in MT-1303-E05 after switching from placebo then throughout the MT-1303-E05 treatment periods or taken only from start of open-label period in MT-1303-E05 after switching from MT-1303 0.1 mg then throughout the MT-1303-E05 open label treatment period. (Overall Summary all Treatments)

Arm type	Experimental
Investigational medicinal product name	MT-1303
Investigational medicinal product code	MT-1303
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

1 capsule, containing MT-1303 0.4mg, taken orally daily for 18 months.

Number of subjects in period 2	MT-1303 0.2 mg (Safety Population)	MT-1303 0.4 mg (Safety Population)
Started	169	161
Completed	157	152
Not completed	12	9
Protocol Specific	2	1
Adverse event, serious fatal	-	1
Consent withdrawn by subject	4	2
Adverse event, non-fatal	3	4
Other	2	1
Pregnancy	1	-

Period 3	
Period 3 title	Safety Follow-up Period
Is this the baseline period?	No
Allocation method	Non-randomised - controlled
Blinding used	Not blinded

Arms	
Are arms mutually exclusive?	No
Arm title	MT-1303 0.1 mg (Safety Population)

Arm description:

MT-1303 0.1 mg (oral capsules) taken from Wk 0 up to Wk 24 in MT-1303-E04 and during double-blind period of MT-1303-E05 or taken only from Wk 0 in MT-1303-E05 after switching from placebo and during the double-blind period of MT-1303-E05. (Overall Summary all Treatments)

Arm type	No intervention

No investigational medicinal product assigned in this arm

Arm title	MT-1303 0.2 mg (Safety Population)

Arm description:

MT-1303 0.2 mg (oral capsules) taken from Wk 0 up to Wk 24 in MT-1303-E04 and during both double-blind and open-label periods of MT-1303-E05 or taken only from Wk 0 in MT-1303-E05 after switching from placebo then throughout the MT-1303-E05 treatment periods. (Overall Summary all Treatments)

Arm type	No intervention

No investigational medicinal product assigned in this arm

Arm title	MT-1303 0.4 mg (Safety Population)

Arm description:

MT-1303 0.4 mg (oral capsules) taken from Wk 0 up to Wk 24 in MT-1303-E04 and during both double-blind and open-label periods of MT-1303-E05 or taken only from Wk 0 in MT-1303-E05 after switching from placebo then throughout the MT-1303-E05 treatment periods. (Overall Summary all Treatments)

Arm type	No intervention

No investigational medicinal product assigned in this arm

Number of subjects in period 3	MT-1303 0.1 mg (Safety Population)	MT-1303 0.2 mg (Safety Population)	MT-1303 0.4 mg (Safety Population)
Started	121	119	117
Completed	116	116	114
Not completed	5	3	3
Consent withdrawn by subject	2	1	1
Other	2	2	2
Lost to follow-up	1	-	-

Baseline characteristics

Reporting groups

Reporting group title	MT-1303 0.1 mg (Safety Population)

Reporting group description:

MT-1303 0.1 mg (oral capsules) taken from Wk 0 up to Wk 24 in MT-1303-E04 and during double-blind period of MT-1303-E05 or taken only from Wk 0 in MT-1303-E05 after switching from placebo and during the double-blind period of MT-1303-E05. (Overall Summary all Treatments)

Reporting group title	MT-1303 0.2 mg (Safety Population)

Reporting group description:

MT-1303 0.2 mg (oral capsules) taken from Wk 0 up to Wk 24 in MT-1303-E04 and during both double-blind and open-label periods of MT-1303-E05 or taken only from Wk 0 in MT-1303-E05 after switching from placebo then throughout the MT-1303-E05 treatment periods. (Overall Summary all Treatments)

Reporting group title	MT-1303 0.4 mg (Safety Population)

Reporting group description:

MT-1303 0.4 mg (oral capsules) taken from Wk 0 up to Wk 24 in MT-1303-E04 and during both double-blind and open-label periods of MT-1303-E05 or taken only from Wk 0 in MT-1303-E05 after switching from placebo then throughout the MT-1303-E05 treatment periods. (Overall Summary all Treatments)

Reporting group values	MT-1303 0.1 mg (Safety Population)	MT-1303 0.2 mg (Safety Population)	MT-1303 0.4 mg (Safety Population)
Number of subjects	123	123	121
Age categorical			
Units: Subjects			
In utero	0	0	0
Preterm newborn infants (gestational age < 37 wks)	0	0	0
Newborns (0-27 days)	0	0	0
Infants and toddlers (28 days-23 months)	0	0	0
Children (2-11 years)	0	0	0
Adolescents (12-17 years)	0	0	0
Adults (18-64 years)	123	123	121
From 65-84 years	0	0	0
85 years and over	0	0	0
Age continuous			
Units: years			
arithmetic mean	37	38.1	37.5
standard deviation	± 9.27	± 9.56	± 8.53
Gender categorical			
Units: Subjects			
Female	83	87	82
Male	40	36	39
Baseline EDSS Score			
Expanded Disability Status Scale (EDSS) score taken during enrollment into the MT-1303-E05 study			
Units: No units			
arithmetic mean	2.8	2.7	2.5
standard deviation	± 1.3	± 1.3	± 1.3

Reporting group values	Total		
Number of subjects	367		
Age categorical Units: Subjects			
In utero	0		
Preterm newborn infants (gestational age < 37 wks)	0		
Newborns (0-27 days)	0		
Infants and toddlers (28 days-23 months)	0		
Children (2-11 years)	0		
Adolescents (12-17 years)	0		
Adults (18-64 years)	367		
From 65-84 years	0		
85 years and over	0		
Age continuous Units: years			
arithmetic mean			
standard deviation	-		
Gender categorical Units: Subjects			
Female	252		
Male	115		
Baseline EDSS Score			
Expanded Disability Status Scale (EDSS) score taken during enrollment into the MT-1303-E05 study			
Units: No units			
arithmetic mean			
standard deviation	-		

End points

End points reporting groups

Reporting group title	MT-1303 0.1 mg (Safety Population)

Reporting group description:

MT-1303 0.1 mg (oral capsules) taken from Wk 0 up to Wk 24 in MT-1303-E04 and during double-blind period of MT-1303-E05 or taken only from Wk 0 in MT-1303-E05 after switching from placebo and during the double-blind period of MT-1303-E05. (Overall Summary all Treatments)

Reporting group title	MT-1303 0.2 mg (Safety Population)

Reporting group description:

MT-1303 0.2 mg (oral capsules) taken from Wk 0 up to Wk 24 in MT-1303-E04 and during both double-blind and open-label periods of MT-1303-E05 or taken only from Wk 0 in MT-1303-E05 after switching from placebo then throughout the MT-1303-E05 treatment periods. (Overall Summary all Treatments)

Reporting group title	MT-1303 0.4 mg (Safety Population)

Reporting group description:

MT-1303 0.4 mg (oral capsules) taken from Wk 0 up to Wk 24 in MT-1303-E04 and during both double-blind and open-label periods of MT-1303-E05 or taken only from Wk 0 in MT-1303-E05 after switching from placebo then throughout the MT-1303-E05 treatment periods. (Overall Summary all Treatments)

Reporting group title	MT-1303 0.2 mg (Safety Population)

Reporting group description:

MT-1303 0.2 mg (oral capsules) taken from Wk 0 up to Wk 24 in MT-1303-E04 and during both double-blind and open-label periods of MT-1303-E05 or taken only from Wk 0 in MT-1303-E05 after switching from placebo then throughout the MT-1303-E05 treatment periods or taken only from start of open-label period in MT-1303-E05 after switching from MT-1303 0.1 mg then throughout the MT-1303-E05 open label treatment period. (Overall Summary all Treatments)

Reporting group title	MT-1303 0.4 mg (Safety Population)

Reporting group description:

MT-1303 0.4 mg (oral capsules) taken from Wk 0 up to Wk 24 in MT-1303-E04 and during both double-blind and open-label periods of MT-1303-E05 or taken only from Wk 0 in MT-1303-E05 after switching from placebo then throughout the MT-1303-E05 treatment periods or taken only from start of open-label period in MT-1303-E05 after switching from MT-1303 0.1 mg then throughout the MT-1303-E05 open label treatment period. (Overall Summary all Treatments)

Reporting group title	MT-1303 0.1 mg (Safety Population)

Reporting group description:

MT-1303 0.1 mg (oral capsules) taken from Wk 0 up to Wk 24 in MT-1303-E04 and during double-blind period of MT-1303-E05 or taken only from Wk 0 in MT-1303-E05 after switching from placebo and during the double-blind period of MT-1303-E05. (Overall Summary all Treatments)

Reporting group title	MT-1303 0.2 mg (Safety Population)

Reporting group description:

MT-1303 0.2 mg (oral capsules) taken from Wk 0 up to Wk 24 in MT-1303-E04 and during both double-blind and open-label periods of MT-1303-E05 or taken only from Wk 0 in MT-1303-E05 after switching from placebo then throughout the MT-1303-E05 treatment periods. (Overall Summary all Treatments)

Reporting group title	MT-1303 0.4 mg (Safety Population)

Reporting group description:

MT-1303 0.4 mg (oral capsules) taken from Wk 0 up to Wk 24 in MT-1303-E04 and during both double-blind and open-label periods of MT-1303-E05 or taken only from Wk 0 in MT-1303-E05 after switching from placebo then throughout the MT-1303-E05 treatment periods. (Overall Summary all Treatments)

Primary: Not Applicable - none reported as safety is primary endpoint

End point title	Not Applicable - none reported as safety is primary endpoint[1]

End point description:

No primary endpoints were defined for efficacy or PD variables. Safety was the only primary endpoint.

End point type	Primary

End point timeframe:

Not applicable

Notes:

[1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: There was no formal statistical analysis performed as safety was the primary endpoint

End point values	MT-1303 0.1 mg (Safety Population)	MT-1303 0.2 mg (Safety Population)	MT-1303 0.4 mg (Safety Population)	MT-1303 0.2 mg (Safety Population)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	0[2]	0[3]	0[4]	0[5]
Units: n/a				

Notes:

[2] - There are no pre-defined study endpoints. Safety was the only parameter measured

[3] - There are no pre-defined study endpoints. Safety was the only parameter measured

[4] - There are no pre-defined study endpoints. Safety was the only parameter measured

[5] - There are no pre-defined study endpoints. Safety was the only parameter measured

End point values	MT-1303 0.4 mg (Safety Population)			
Subject group type	Reporting group			
Number of subjects analysed	0[6]			
Units: n/a				

Notes:

[6] - There are no pre-defined study endpoints. Safety was the only parameter measured

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Adverse events were considered to be treatment-emergent if they started or worsened on or after the first dose of MT-1303-E04 or MT-1303-E05 study medication.

Adverse event reporting additional description:

For summaries by treatment period (E04 study period, E05 study periods, overall), data for AEs were assigned to the treatment period (and therefore study treatment) they started in each period. Subjects were carefully monitored by the Investigator for AEs, including regular questioning of the subject, although no leading questions were asked.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	17

Reporting groups

Reporting group title	MT-1303 0.2 mg only (Selected Treatment Sequences)

Reporting group description:

MT-1303 0.2 mg (oral capsules) taken from Wk 0 in MT-1303-E04 study and throughout both treatment periods of MT-1303-E05 (Overall for Selected Treatment Sequences)

Reporting group title	MT-1303 0.4 mg only (Selected Treatment Sequences)

Reporting group description:

MT-1303 0.4 mg (oral capsules) taken from Wk 0 in MT-1303-E04 study and throughout both treatment periods of MT-1303-E05 (Overall for Selected Treatment Sequences)

Reporting group title	Placebo to MT-1303 0.2 mg (Selected Treatment Sequences)

Reporting group description:

MT-1303 0.2 mg (oral capsules) taken throughout both treatment periods in MT-1303-E05 after switching from Placebo administered during the complete treatment period of MT-1303-E04 (Overall for Selected Treatment Sequences)

Reporting group title	Placebo to MT-1303 0.4 mg (Selected Treatment Sequences)

Reporting group description:

MT-1303 0.4 mg (oral capsules) taken throughout both treatment periods in MT-1303-E05 after switching from Placebo administered during the complete treatment period of MT-1303-E04 (Overall for Selected Treatment Sequences)

Serious adverse events	MT-1303 0.2 mg only (Selected Treatment Sequences)	MT-1303 0.4 mg only (Selected Treatment Sequences)	Placebo to MT-1303 0.2 mg (Selected Treatment Sequences)
Total subjects affected by serious adverse events			
subjects affected / exposed	21 / 90 (23.33%)	11 / 92 (11.96%)	9 / 33 (27.27%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events			
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Uterine leiomyoma			

subjects affected / exposed	0 / 90 (0.00%)	1 / 92 (1.09%)	0 / 33 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	3 / 90 (3.33%)	0 / 92 (0.00%)	0 / 33 (0.00%)
occurrences causally related to treatment / all	3 / 3	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Aspartate aminortransferase increased			
subjects affected / exposed	2 / 90 (2.22%)	0 / 92 (0.00%)	0 / 33 (0.00%)
occurrences causally related to treatment / all	2 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lymphocyte count decreased			
subjects affected / exposed	1 / 90 (1.11%)	0 / 92 (0.00%)	0 / 33 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
White blood cell count decreased			
subjects affected / exposed	0 / 90 (0.00%)	1 / 92 (1.09%)	0 / 33 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Injury, poisoning and procedural complications			
Exposure via father			
subjects affected / exposed	0 / 90 (0.00%)	0 / 92 (0.00%)	1 / 33 (3.03%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Fibula fracture			
subjects affected / exposed	1 / 90 (1.11%)	0 / 92 (0.00%)	0 / 33 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Joint injury			
subjects affected / exposed	0 / 90 (0.00%)	1 / 92 (1.09%)	0 / 33 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Meniscus injury			
subjects affected / exposed	0 / 90 (0.00%)	0 / 92 (0.00%)	0 / 33 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Upper limb fracture			
subjects affected / exposed	1 / 90 (1.11%)	0 / 92 (0.00%)	0 / 33 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Wrist fracture			
subjects affected / exposed	0 / 90 (0.00%)	1 / 92 (1.09%)	0 / 33 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Surgical and medical procedures			
Finger amputation			
subjects affected / exposed	1 / 90 (1.11%)	0 / 92 (0.00%)	0 / 33 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hysterectomy			
subjects affected / exposed	0 / 90 (0.00%)	1 / 92 (1.09%)	0 / 33 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Mammoplasty			
subjects affected / exposed	0 / 90 (0.00%)	0 / 92 (0.00%)	1 / 33 (3.03%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nervous system disorders			
Grand mal convulsion			
subjects affected / exposed	1 / 90 (1.11%)	0 / 92 (0.00%)	0 / 33 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lumbar radiculopathy			
subjects affected / exposed	0 / 90 (0.00%)	1 / 92 (1.09%)	0 / 33 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Multiple sclerosis relapse			
subjects affected / exposed	11 / 90 (12.22%)	3 / 92 (3.26%)	6 / 33 (18.18%)
occurrences causally related to treatment / all	0 / 15	0 / 3	0 / 10
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Radiculitis lumbosacral			
subjects affected / exposed	1 / 90 (1.11%)	0 / 92 (0.00%)	0 / 33 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Enteritis			
subjects affected / exposed	1 / 90 (1.11%)	0 / 92 (0.00%)	0 / 33 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Reproductive system and breast disorders			
Cervical dysplasia			
subjects affected / exposed	1 / 90 (1.11%)	0 / 92 (0.00%)	0 / 33 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ovarian cyst			
subjects affected / exposed	1 / 90 (1.11%)	1 / 92 (1.09%)	0 / 33 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Uterine enlargement			
subjects affected / exposed	0 / 90 (0.00%)	1 / 92 (1.09%)	0 / 33 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Psychiatric disorders			
Alcohol abuse			
subjects affected / exposed	0 / 90 (0.00%)	0 / 92 (0.00%)	0 / 33 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Confusional state			

subjects affected / exposed	0 / 90 (0.00%)	0 / 92 (0.00%)	1 / 33 (3.03%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Mood disorder due to a general medical condition			
subjects affected / exposed	0 / 90 (0.00%)	0 / 92 (0.00%)	0 / 33 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal and urinary disorders			
Calculus ureteric			
subjects affected / exposed	2 / 90 (2.22%)	0 / 92 (0.00%)	0 / 33 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	0 / 90 (0.00%)	0 / 92 (0.00%)	1 / 33 (3.03%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Intervertebral disc protrusion			
subjects affected / exposed	0 / 90 (0.00%)	0 / 92 (0.00%)	1 / 33 (3.03%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Spinal osteoarthritis			
subjects affected / exposed	0 / 90 (0.00%)	0 / 92 (0.00%)	1 / 33 (3.03%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Campylobacter gastroenteritis			
subjects affected / exposed	0 / 90 (0.00%)	1 / 92 (1.09%)	0 / 33 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Urinary tract infection			

subjects affected / exposed	0 / 90 (0.00%)	1 / 92 (1.09%)	0 / 33 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	Placebo to MT-1303 0.4 mg (Selected Treatment Sequences)		
Total subjects affected by serious adverse events			
subjects affected / exposed	7 / 28 (25.00%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events			
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Uterine leiomyoma			
subjects affected / exposed	0 / 28 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	1 / 28 (3.57%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Aspartate aminortransferase increased			
subjects affected / exposed	1 / 28 (3.57%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Lymphocyte count decreased			
subjects affected / exposed	0 / 28 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
White blood cell count decreased			
subjects affected / exposed	0 / 28 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Injury, poisoning and procedural complications			

Exposure via father				
subjects affected / exposed	0 / 28 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Fibula fracture				
subjects affected / exposed	0 / 28 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Joint injury				
subjects affected / exposed	0 / 28 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Meniscus injury				
subjects affected / exposed	1 / 28 (3.57%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Upper limb fracture				
subjects affected / exposed	0 / 28 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Wrist fracture				
subjects affected / exposed	0 / 28 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Surgical and medical procedures				
Finger amputation				
subjects affected / exposed	0 / 28 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Hysterectomy				
subjects affected / exposed	0 / 28 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Mammoplasty				

subjects affected / exposed	0 / 28 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Nervous system disorders			
Grand mal convulsion			
subjects affected / exposed	1 / 28 (3.57%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Lumbar radiculopathy			
subjects affected / exposed	0 / 28 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Multiple sclerosis relapse			
subjects affected / exposed	5 / 28 (17.86%)		
occurrences causally related to treatment / all	0 / 7		
deaths causally related to treatment / all	0 / 0		
Radiculitis lumbosacral			
subjects affected / exposed	0 / 28 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Gastrointestinal disorders			
Enteritis			
subjects affected / exposed	0 / 28 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Reproductive system and breast disorders			
Cervical dysplasia			
subjects affected / exposed	0 / 28 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Ovarian cyst			
subjects affected / exposed	0 / 28 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		

Uterine enlargement				
subjects affected / exposed	0 / 28 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Psychiatric disorders				
Alcohol abuse				
subjects affected / exposed	1 / 28 (3.57%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Confusional state				
subjects affected / exposed	0 / 28 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Mood disorder due to a general medical condition				
subjects affected / exposed	1 / 28 (3.57%)			
occurrences causally related to treatment / all	0 / 3			
deaths causally related to treatment / all	0 / 0			
Renal and urinary disorders				
Calculus ureteric				
subjects affected / exposed	0 / 28 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Musculoskeletal and connective tissue disorders				
Back pain				
subjects affected / exposed	0 / 28 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Intervertebral disc protrusion				
subjects affected / exposed	0 / 28 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Spinal osteoarthritis				

subjects affected / exposed	0 / 28 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Infections and infestations			
Campylobacter gastroenteritis			
subjects affected / exposed	0 / 28 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Urinary tract infection			
subjects affected / exposed	0 / 28 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		

Frequency threshold for reporting non-serious adverse events: 5 %

Non-serious adverse events	MT-1303 0.2 mg only (Selected Treatment Sequences)	MT-1303 0.4 mg only (Selected Treatment Sequences)	Placebo to MT-1303 0.2 mg (Selected Treatment Sequences)
Total subjects affected by non-serious adverse events			
subjects affected / exposed	71 / 90 (78.89%)	75 / 92 (81.52%)	30 / 33 (90.91%)
Investigations			
Lymphocyte count decreased			
subjects affected / exposed	15 / 90 (16.67%)	24 / 92 (26.09%)	6 / 33 (18.18%)
occurrences (all)	16	26	7
Gamma glutamyltransferase increased			
subjects affected / exposed	8 / 90 (8.89%)	6 / 92 (6.52%)	2 / 33 (6.06%)
occurrences (all)	9	6	2
Alanine aminotransferase increased			
subjects affected / exposed	4 / 90 (4.44%)	6 / 92 (6.52%)	2 / 33 (6.06%)
occurrences (all)	4	6	2
Aspartate aminotransferase increased			
subjects affected / exposed	2 / 90 (2.22%)	3 / 92 (3.26%)	2 / 33 (6.06%)
occurrences (all)	2	3	2
Blood creatine phosphokinase increased			

subjects affected / exposed	1 / 90 (1.11%)	1 / 92 (1.09%)	0 / 33 (0.00%)
occurrences (all)	1	3	0
Blood triglycerides increased			
subjects affected / exposed	3 / 90 (3.33%)	1 / 92 (1.09%)	1 / 33 (3.03%)
occurrences (all)	3	1	1
Neutrophil count decreased			
subjects affected / exposed	4 / 90 (4.44%)	2 / 92 (2.17%)	1 / 33 (3.03%)
occurrences (all)	4	3	1
White blood cell count decreased			
subjects affected / exposed	1 / 90 (1.11%)	4 / 92 (4.35%)	3 / 33 (9.09%)
occurrences (all)	1	5	5
Vascular disorders			
Hypertension			
subjects affected / exposed	5 / 90 (5.56%)	2 / 92 (2.17%)	1 / 33 (3.03%)
occurrences (all)	5	2	1
Nervous system disorders			
Headache			
subjects affected / exposed	18 / 90 (20.00%)	15 / 92 (16.30%)	5 / 33 (15.15%)
occurrences (all)	40	91	12
Multiple sclerosis relapse			
subjects affected / exposed	4 / 90 (4.44%)	3 / 92 (3.26%)	2 / 33 (6.06%)
occurrences (all)	6	3	2
Dizziness			
subjects affected / exposed	4 / 90 (4.44%)	6 / 92 (6.52%)	4 / 33 (12.12%)
occurrences (all)	10	7	4
Paraesthesia			
subjects affected / exposed	2 / 90 (2.22%)	7 / 92 (7.61%)	2 / 33 (6.06%)
occurrences (all)	2	7	2
Sciatica			
subjects affected / exposed	0 / 90 (0.00%)	2 / 92 (2.17%)	2 / 33 (6.06%)
occurrences (all)	0	2	2
General disorders and administration site conditions			
Fatigue			
subjects affected / exposed	4 / 90 (4.44%)	2 / 92 (2.17%)	1 / 33 (3.03%)
occurrences (all)	6	2	1
Pain			

subjects affected / exposed	1 / 90 (1.11%)	1 / 92 (1.09%)	2 / 33 (6.06%)
occurrences (all)	1	2	2
Pyrexia			
subjects affected / exposed	2 / 90 (2.22%)	5 / 92 (5.43%)	0 / 33 (0.00%)
occurrences (all)	2	6	0
Blood and lymphatic system disorders			
Iron deficiency anaemia			
subjects affected / exposed	1 / 90 (1.11%)	0 / 92 (0.00%)	2 / 33 (6.06%)
occurrences (all)	1	0	2
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	4 / 90 (4.44%)	7 / 92 (7.61%)	1 / 33 (3.03%)
occurrences (all)	5	11	1
Vomiting			
subjects affected / exposed	0 / 90 (0.00%)	5 / 92 (5.43%)	3 / 33 (9.09%)
occurrences (all)	0	6	5
Nausea			
subjects affected / exposed	5 / 90 (5.56%)	3 / 92 (3.26%)	1 / 33 (3.03%)
occurrences (all)	5	3	3
Respiratory, thoracic and mediastinal disorders			
Oropharyngeal pain			
subjects affected / exposed	4 / 90 (4.44%)	9 / 92 (9.78%)	1 / 33 (3.03%)
occurrences (all)	6	15	1
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	8 / 90 (8.89%)	1 / 92 (1.09%)	2 / 33 (6.06%)
occurrences (all)	8	1	3
Arthralgia			
subjects affected / exposed	4 / 90 (4.44%)	5 / 92 (5.43%)	3 / 33 (9.09%)
occurrences (all)	4	9	3
Intervertebral disc protrusion			
subjects affected / exposed	0 / 90 (0.00%)	0 / 92 (0.00%)	2 / 33 (6.06%)
occurrences (all)	0	0	4
Neck pain			
subjects affected / exposed	2 / 90 (2.22%)	0 / 92 (0.00%)	0 / 33 (0.00%)
occurrences (all)	2	0	0

Pain in extremity			
subjects affected / exposed	5 / 90 (5.56%)	1 / 92 (1.09%)	0 / 33 (0.00%)
occurrences (all)	6	4	0
Infections and infestations			
Nasopharyngitis			
subjects affected / exposed	14 / 90 (15.56%)	13 / 92 (14.13%)	5 / 33 (15.15%)
occurrences (all)	18	16	10
Urinary tract infection			
subjects affected / exposed	8 / 90 (8.89%)	9 / 92 (9.78%)	6 / 33 (18.18%)
occurrences (all)	14	13	8
Upper respiratory tract infection			
subjects affected / exposed	4 / 90 (4.44%)	5 / 92 (5.43%)	4 / 33 (12.12%)
occurrences (all)	8	6	9
Influenza			
subjects affected / exposed	6 / 90 (6.67%)	10 / 92 (10.87%)	1 / 33 (3.03%)
occurrences (all)	12	12	1
Bronchitis			
subjects affected / exposed	4 / 90 (4.44%)	1 / 92 (1.09%)	2 / 33 (6.06%)
occurrences (all)	4	1	2
Cystitis			
subjects affected / exposed	5 / 90 (5.56%)	2 / 92 (2.17%)	2 / 33 (6.06%)
occurrences (all)	8	3	2
Gastroenteritis			
subjects affected / exposed	6 / 90 (6.67%)	2 / 92 (2.17%)	2 / 33 (6.06%)
occurrences (all)	6	2	2
Oral herpes			
subjects affected / exposed	2 / 90 (2.22%)	5 / 92 (5.43%)	0 / 33 (0.00%)
occurrences (all)	5	10	0
Sinusitis			
subjects affected / exposed	1 / 90 (1.11%)	5 / 92 (5.43%)	0 / 33 (0.00%)
occurrences (all)	1	8	0
Tonsillitis			
subjects affected / exposed	1 / 90 (1.11%)	2 / 92 (2.17%)	2 / 33 (6.06%)
occurrences (all)	1	3	2
Viral upper respiratory tract infection			

subjects affected / exposed	0 / 90 (0.00%)	6 / 92 (6.52%)	1 / 33 (3.03%)
occurrences (all)	0	7	1

Non-serious adverse events	Placebo to MT-1303 0.4 mg (Selected Treatment Sequences)		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	22 / 28 (78.57%)		
Investigations			
Lymphocyte count decreased			
subjects affected / exposed	1 / 28 (3.57%)		
occurrences (all)	1		
Gamma glutamyltransferase increased			
subjects affected / exposed	2 / 28 (7.14%)		
occurrences (all)	3		
Alanine aminotransferase increased			
subjects affected / exposed	3 / 28 (10.71%)		
occurrences (all)	4		
Aspartate aminotransferase increased			
subjects affected / exposed	3 / 28 (10.71%)		
occurrences (all)	4		
Blood creatine phosphokinase increased			
subjects affected / exposed	2 / 28 (7.14%)		
occurrences (all)	2		
Blood triglycerides increased			
subjects affected / exposed	2 / 28 (7.14%)		
occurrences (all)	2		
Neutrophil count decreased			
subjects affected / exposed	2 / 28 (7.14%)		
occurrences (all)	2		
White blood cell count decreased			
subjects affected / exposed	0 / 28 (0.00%)		
occurrences (all)	0		
Vascular disorders			
Hypertension			

subjects affected / exposed occurrences (all)	2 / 28 (7.14%) 2		
Nervous system disorders Headache subjects affected / exposed occurrences (all) Multiple sclerosis relapse subjects affected / exposed occurrences (all) Dizziness subjects affected / exposed occurrences (all) Paraesthesia subjects affected / exposed occurrences (all) Sciatica subjects affected / exposed occurrences (all)	 3 / 28 (10.71%) 4 0 / 28 (0.00%) 0 1 / 28 (3.57%) 2 1 / 28 (3.57%) 1 1 / 28 (3.57%) 1		
General disorders and administration site conditions Fatigue subjects affected / exposed occurrences (all) Pain subjects affected / exposed occurrences (all) Pyrexia subjects affected / exposed occurrences (all)	 2 / 28 (7.14%) 3 0 / 28 (0.00%) 0 1 / 28 (3.57%) 1		
Blood and lymphatic system disorders Iron deficiency anaemia subjects affected / exposed occurrences (all)	 1 / 28 (3.57%) 1		
Gastrointestinal disorders Diarrhoea subjects affected / exposed occurrences (all)	 1 / 28 (3.57%) 1		

Vomiting			
subjects affected / exposed	0 / 28 (0.00%)		
occurrences (all)	0		
Nausea			
subjects affected / exposed	1 / 28 (3.57%)		
occurrences (all)	1		
Respiratory, thoracic and mediastinal disorders			
Oropharyngeal pain			
subjects affected / exposed	0 / 28 (0.00%)		
occurrences (all)	0		
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	1 / 28 (3.57%)		
occurrences (all)	2		
Arthralgia			
subjects affected / exposed	1 / 28 (3.57%)		
occurrences (all)	1		
Intervertebral disc protrusion			
subjects affected / exposed	0 / 28 (0.00%)		
occurrences (all)	0		
Neck pain			
subjects affected / exposed	2 / 28 (7.14%)		
occurrences (all)	2		
Pain in extremity			
subjects affected / exposed	2 / 28 (7.14%)		
occurrences (all)	3		
Infections and infestations			
Nasopharyngitis			
subjects affected / exposed	2 / 28 (7.14%)		
occurrences (all)	2		
Urinary tract infection			
subjects affected / exposed	2 / 28 (7.14%)		
occurrences (all)	3		
Upper respiratory tract infection			
subjects affected / exposed	2 / 28 (7.14%)		
occurrences (all)	3		

Influenza			
subjects affected / exposed	1 / 28 (3.57%)		
occurrences (all)	2		
Bronchitis			
subjects affected / exposed	0 / 28 (0.00%)		
occurrences (all)	0		
Cystitis			
subjects affected / exposed	0 / 28 (0.00%)		
occurrences (all)	0		
Gastroenteritis			
subjects affected / exposed	1 / 28 (3.57%)		
occurrences (all)	1		
Oral herpes			
subjects affected / exposed	1 / 28 (3.57%)		
occurrences (all)	2		
Sinusitis			
subjects affected / exposed	0 / 28 (0.00%)		
occurrences (all)	0		
Tonsillitis			
subjects affected / exposed	0 / 28 (0.00%)		
occurrences (all)	0		
Viral upper respiratory tract infection			
subjects affected / exposed	0 / 28 (0.00%)		
occurrences (all)	0		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
12 August 2013	Inclusion of two additional safety monitoring visits, between Visit 1 (Week 0) and Visit 2 (Week 12) to ensure consistent review of safety parameters for all patients in transit from the MT-1303-E04 study to the MT-1303-E05 study. Visit 1a and 1b at Week 4 and Week 8 respectively.
24 March 2015	In light of the increasing evidence from recent research for other disease-modifying therapies (DMTs) in MS, an amendment was made to allow patients to receive DMT during the Safety Follow-up Period if this was considered appropriate.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported