ClinicalTrials.gov Protocol Registration and Results System (PRS) Receipt
Release Date: 01/26/2014

ClinicalTrials.gov ID: NCT01142466

Study Identification

Unique Protocol ID:	IMP 25874
Brief Title:	A Phase IV Study of Rebif ® 44mcg Administered Three Times Per Week by Subcutaneous Injection Compared With no Treatment in the Therapy of Relapsing Multiple Sclerosis After Mitoxantrone (REMAIN)
Official Title:	Phase IV, Multicenter, Open Label, Randomized Study of Rebif® 44mcg Administered Three Times Per Week by Subcutaneous Injection Compared With no Treatment in the Therapy of Relapsing Multiple Sclerosis After Mitoxantrone
Secondary IDs:	

Study Status

Record Verification:	January 2014
Overall Status:	Completed
Study Start:	December 2005
Primary Completion:	December 2009 [Actual]
Study Completion:	January 2010 [Actual]

Sponsor/Collaborators

Sponsor:	Merck KGaA
Responsible Party:	Sponsor
Collaborators:	Gesellschaft für Therapieforschung mbH

Oversight

FDA Regulated?:	No

IND/IDE Protocol?:	No
Review Board:	Approval Status: Approved Approval Number: 05051 Board Name: LAEK Bavaria Board Affiliation: Ethic Commission of the Regional Authority Munich Phone: +49 89 4147 Email: ethikkommission@blaek.de
Data Monitoring?:	No
Plan to Share Data?:	
Oversight Authorities:	Germany: Federal Ministry of Food, Agriculture and Consumer Protection

Study Description

Brief Summary: In the course of therapy escalation, the multiple sclerosis (MS) subjects with high activity of disease receive mainly mitoxantrone. The duration of therapy is limited because of a cumulative dose for life (140 mg/m^2 body surface area). In practice lower doses of mitoxantrone (60-120 mg/m^2 body surface area) are being used. The specific reason for this limited total dose are potential cardiotoxic side effects of mitoxantrone. Once this cumulative dose of mitoxantrone is reached and the subject becomes stable, there is the question for subsequent therapy. A possibility at this time, is the so-called "de-escalation", therefore reducing the subject back to immunomodulating basic treatment.

The target of this open-label, randomised, multicentric, comparative, parallel-group study was to inquire systematically into the use and course of basic therapy with Rebif 44 mcg thrice weekly (tiw) for a larger number of subjects.

Detailed Description: Multiple sclerosis is a chronic, inflammatory, demyelinating disease of the central nervous system (CNS) and is one of the most common causes of neurological disability in young adults. It is characterised by multi-focal recurrent attacks of neurological symptoms and signs with variable recovery. Eventually, the majority of subjects develop a progressive clinical course. The exact cause of MS is unknown, although an autoimmune process has been implicated. Genetic susceptibility plays a role in disease initiation but unidentified environmental factors may also be involved. Three clinical forms of MS are recognized: primary progressive multiple sclerosis (PPMS), secondary progressive multiple sclerosis (SPMS) and relapsing remitting multiple sclerosis (RRMS). Primary progressive subjects are characterised by slow and steady accumulation of neurological deficits from onset without superimposed attacks. Subjects with RRMS have exacerbations or relapses with subsequent variable recovery (remission). Secondary progressive multiple sclerosis is characterised by the steady accumulation of significant and persistent neurological deficit with or without superimposed relapses.

Rebif [recombinant interferon (IFN) beta-1a] has been tested in a series of studies in MS subjects at doses ranging from 22 mcg to 132 mcg weekly with a dose frequency ranging from weekly (qw) to tiw. Rebif has been found to be well tolerated in all clinical pharmacology studies, even at high doses (up to 66 mcg/m^2). In later phase trials, Rebif has been tested across a broad range of doses, for varying duration, and in different stages of MS disease. Dose testing has ranged from 22 mcg to 132 mcg weekly with frequency of administration being qw to tiw.

OBJECTIVES

Primary objective:

- To asses if treatment with Rebif 44 mcg tiw compared with subjects not treated during 96 weeks can maintain or prolong clinical or magnetic resonance imaging (MRI) stability after previous treatment with mitoxantrone

Secondary objectives:

- To compare the mean number of T2 active lesions, defined as new or enlarging T2 lesions, per subject per scan during 96 weeks of treatment with Rebif 44 mcg three times per week with subjects not treated
- To assess the safety and efficacy of Rebif 44 mcg

This was an open-label, randomised, multicentric, comparative, parallel-group study with a neurologist blinded to treatment for performing neurologic exams and a neuro-radiologist blinded to treatment for assessing central MRI scans. The study was divided into a screening phase (up to 28 days before the start of IFN-beta-1a treatment), a treatment phase of 96 weeks as well as a follow-up period of 4 weeks for subjects with ongoing serious adverse events (SAEs) at week 96. The study consisted of 2 groups to compare the therapeutic effect of high dose, high frequency IFN beta-1a therapy (Rebif 44 mcg) to subjects who will not be treated with Rebif 44 mcg. Subjects of both groups were previously treated with mitoxantrone in the < 3 months prior to study inclusion. Subjects assigned to no treatment were switched to Rebif 44 mcg x 3 after reaching the primary endpoint or defined stopping criteria. The treatment period of this study begun with the completion of all baseline evaluations and the initiation of study drug treatment on Study Day 1 (baseline visit) and continues through until completion of the treatment period at the Week 96 visit.

Conditions

Conditions:	Multiple Sclerosis, Relapsing-Remitting
Keywords:	Multiple sclerosis Expanded Disability Status Scale Multiple Sclerosis, Relapsing-Remitting Rebif Beta-1, interferon

Study Design

Study Type:	Interventional
Primary Purpose:	Treatment
Study Phase:	Phase 4
Intervention Model:	Parallel Assignment
Number of Arms:	2
Masking:	Open Label
Allocation:	Randomized
Endpoint Classification:	Safety/Efficacy Study

Enrollment: 30 [Actual]

Arms and Interventions

Arms	Assigned Interventions
Experimental: Rebif (3x44 mcg) Group	Drug: Interferon beta-1a (Rebif) The dosage of IFN-beta-1a , following initial dose titration, was 44 mcg injected subcutaneously (s.c.) tiw. An auto-injector device, Rebiject, was available as an optional aid for the administration of IFN-beta-1a . IFN-beta-1a was administered, if possible, at the same time (preferably in the late afternoon or evening) on the same three days at least 48 hours apart each week. Other Names: • Rebif
No Intervention: No treatment Group	

Outcome Measures

[See Results Section.]

Eligibility

Minimum Age: 18 Years

Maximum Age: 60 Years

Gender: Both

Accepts Healthy Volunteers?: No

Criteria: Inclusion Criteria:

- Subject who had given written informed consent.
- Subjects with definite RRMS or SPMS with relapses
- Subjects with EDSS 1-6
- Subjects aged between 18-60 years
- Subjects who were escalated to mitoxantrone due to high relapse activity or MRI activity (not due to EDSS progression exclusively)
- Subjects who may not have a confirmed 1 point EDSS progression (0.5 points for EDSS >5.5) within the last 9 months
- Subjects free of relapses over the last 6 months
- Subjects with last mitoxantrone treatment between 1 and 6 months prior to screening
- Subjects treated with mitoxantrone for minimum 9 months and maximum 36 months, total cumulative dose being 40-120 mg/m^2

- Female subjects who must be neither pregnant nor breast-feeding and must lack childbearing potential, as defined by either:

    a. Being post-menopausal or surgically sterile,or
    b. Using a hormonal contraceptive, intra-uterine device, diaphragm with spermicide or condom with spermicide for the duration of the study. Confirmation that the subject is not pregnant must be established by a negative serum or urinary human chorionic gonadotropin (hCG) test within 7 days prior to start of study treatment. A pregnancy test is not required if the subject is post menopausal or surgically sterile.

Exclusion Criteria:

- Subject who has received any cytokine or anti-cytokine therapy within the 3 months prior to study Day 1
- Subject who has been escalated to mitoxantrone due to EDSS progression
- Subject with an ongoing MS relapse
- Subject with PPMS
- Subject with SPMS without superimposed relapses
- Subject who has received immunomodulatory treatment other than IFN-beta or glatiramer acetate before mitoxantrone
- Subject who has previously received total lymphoid irradiation
- Subject who has received oral or systemic corticosteroids or adrenocorticotrophic hormone ACTH within 30 days of study Day 1
- Subject who has received intravenous immunoglobulins or underwent plasmapheresis within the 6 months prior to study day 1
- Subject who has received immunomodulatory or immunosuppressive therapy (including but not limited to cyclophosphamide, cyclosporin, methotrexate, azathioprine, linomide, teriflunomide, natalizumab, laquinimod, Campath) within the 12 months prior to study Day 1
- Subject who requires chronic or monthly pulse corticosteroids during the study
- Subject who has received any investigational drug or experimental procedure within 12 month of study Day 1
- Subject who has inadequate liver function, defined by a total bilirubin, aspartate aminotransferase (AST) or alanine aminotransferase (ALT) or alkaline phosphatase greater than 2.5 times the upper limit of the normal values.
- Subject who has inadequate bone marrow reserve, defined as a white blood cell count less than 0.5 times the lower limit of normal
- Subject who suffers from current autoimmune disease
- Subject with known allergy to IFN or the excipient(s)
- Subject who suffers from major medical or psychiatric illness that in the opinion of the investigator creates undue risk to the subject or could affect compliance with the study protocol
- Subject treated with drugs other than IFN-beta or glatiramer acetate within 2 years before mitoxantrone
- Subject with known cardiac or other systemic diseases
- Subjects who are pregnant.

Contacts/Locations

Study Officials: Sigbert Jahn, PD Dr. med
Study Director
Merck Serono GmbH Germany

Locations:

References

Citations:

Links:

Study Data/Documents:

Study Results

Participant Flow

Recruitment Details	Participants were enrolled at multiple centres in Germany.
Pre-Assignment Details	A total of 36 participants were screened and 30 were randomized to the study treatment. 6 participants were not treated (4 participants were screening failures and 2 participants did not meet the inclusion and exclusion criteria).

Reporting Groups

	Description
Rebif 44 mcg	Rebif was administered subcutaneously (s.c.) at a dose of 44 microgram (mcg), three times a week.
No Treatment	Participants in this group did not receive any treatment.

Overall Study

	Rebif 44 mcg	No Treatment
Started	15	15
Completed	12	13
Not Completed	3	2
Adverse Event	2	1
Withdrawal by Subject	1	1

Baseline Characteristics

Reporting Groups

	Description
Rebif 44 mcg	Rebif was administered subcutaneously (s.c.) at a dose of 44 microgram (mcg), three times a week.
No Treatment	Participants in this group did not receive any treatment.

Baseline Measures

	Rebif 44 mcg	No Treatment	Total
Number of Participants	14	15	29
Age, Continuous [1] [units: years] Mean (Standard Deviation)	43.8 (7.0)	44.3 (6.5)	44.1 (6.6)
Gender, Male/Female [1] [units: participants]			
Female	11	9	20
Male	3	6	9
Expanded Disability Status Scale (EDSS) [2] [units: Units on Scale] Mean (Standard Deviation)	4.1 (1.4)	4.3 (1.0)	4.2 (1.2)

[1] One participant of the safety population discontinued the study after 25 days due to an adverse event (AE) without providing any baseline data and hence was not included in this analysis.

[2] EDSS assesses disability in 8 functional systems. An overall score ranging from 0 (normal) to 10 (death due to MS) was calculated. One participant of the safety population discontinued the study after 25 days due to an adverse event (AE) without providing any baseline data and hence was not included in this analysis.

Outcome Measures

1. Primary Outcome Measure:

Measure Title	Time From Baseline to First Multiple Sclerosis Relapse (in Weeks)
Measure Description	A qualifying relapse was defined as a new or worsening neurological symptom, in the absence of fever, lasting for >= 48 hours, and accompanied by an objective change in the relevant (i.e. symptomatic) Kurtzke Functional Systems (KFS).

Time Frame	Baseline through Week 96
Safety Issue?	No

Analysis Population Description

Intent-to-treat (ITT) population included all participants who received at least 1 treatment dose (only for Rebif group) and had at least 1 post-baseline efficacy endpoint assessment. Time to relapse was documented for participants who had at least 1 relapse during the study period.

Reporting Groups

	Description
Rebif 44 mcg	Rebif was administered subcutaneously (s.c.) at a dose of 44 microgram (mcg), three times a week.
No Treatment	Participants in this group did not receive any treatment.

Measured Values

	Rebif 44 mcg	No Treatment
Number of Participants Analyzed	4	8
Time From Baseline to First Multiple Sclerosis Relapse (in Weeks) [units: weeks] Mean (Standard Deviation)	35.5 (40.8)	40.9 (28.7)

Statistical Analysis 1 for Time From Baseline to First Multiple Sclerosis Relapse (in Weeks)

Statistical Analysis Overview	Comparison Groups	Rebif 44 mcg, No Treatment
	Comments	Two-sided log rank test with alpha equal to 0.05 was used as the appropriate nonparametric method to compare the two groups.
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]

Statistical Test of Hypothesis	P-Value	0.1384
	Comments	[Not specified]
	Method	Log Rank
	Comments	[Not specified]

2. Secondary Outcome Measure:

Measure Title	Number of Relapse-free Participants
Measure Description	A qualifying relapse was defined as a new or worsening neurological symptom, in the absence of fever, lasting for >= 48 hours, and accompanied by an objective change in the relevant (i.e. symptomatic) Kurtzke Functional Systems (KFS).
Time Frame	Baseline through Week 96
Safety Issue?	No

Analysis Population Description

ITT population included all participants who received at least 1 treatment dose (only for Rebif group) and had at least 1 post-baseline efficacy endpoint assessment.

Reporting Groups

	Description
Rebif 44 mcg	Rebif was administered subcutaneously (s.c.) at a dose of 44 microgram (mcg), three times a week.
No Treatment	Participants in this group did not receive any treatment.

Measured Values

	Rebif 44 mcg	No Treatment
Number of Participants Analyzed	14	15
Number of Relapse-free Participants [units: participants]	10	7

Statistical Analysis 1 for Number of Relapse-free Participants

Statistical Analysis Overview	Comparison Groups	Rebif 44 mcg, No Treatment
	Comments	[Not specified]
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]

Statistical Test of Hypothesis	P-Value	0.2635
	Comments	[Not specified]
	Method	Fisher Exact
	Comments	[Not specified]

3. Secondary Outcome Measure:

Measure Title	Absolute Changes in the Number of T1 Lesions From Baseline to Week 24, 48, 72 and 96
Measure Description	Analysis of T1 lesions was done using magnetic resonance imaging (MRI) scans.
Time Frame	Baseline to Week 24, 48, 72, and 96
Safety Issue?	No

Analysis Population Description

ITT population included all participants who received at least 1 treatment dose (only for Rebif group) and had at least 1 post-baseline efficacy endpoint assessment. The 'n' is signifying those participants who received study drug and were evaluated for this measure at the time point for each group respectively.

Reporting Groups

	Description
Rebif 44 mcg	Rebif was administered subcutaneously (s.c.) at a dose of 44 microgram (mcg), three times a week.
No Treatment	Participants in this group did not receive any treatment.

Measured Values

	Rebif 44 mcg	No Treatment
Number of Participants Analyzed	14	15
Absolute Changes in the Number of T1 Lesions From Baseline to Week 24, 48, 72 and 96 [units: T1 lesions] Mean (Standard Deviation)		
Week 24 (n= 13,15)	-0.5 (4.4)	-0.9 (8.9)
Week 48 (n= 13,13)	-0.8 (4.3)	1.5 (11.2)
Week 72 (n= 12,12)	-0.8 (9.2)	-3.6 (12.0)
Week 96 (n= 12,12)	-1.8 (5.5)	-2.3 (11.6)

4. Secondary Outcome Measure:

Measure Title	Absolute Changes in the Number of T1-Gadolinium (T1-Gd) Lesions From Baseline to Week 24, 48, 72 and 96
Measure Description	Analysis of T1-Gadolinium enhancing lesions was done using magnetic resonance imaging (MRI) scans.

Time Frame	Baseline to Week 24, 48, 72, and 96
Safety Issue?	No

Analysis Population Description

The data was not evaluated due to the small sample size available for this parameter.

Reporting Groups

	Description
Rebif 44 mcg	Rebif was administered subcutaneously (s.c.) at a dose of 44 microgram (mcg), three times a week.
No Treatment	Participants in this group did not receive any treatment.

Measured Values

	Rebif 44 mcg	No Treatment
Number of Participants Analyzed	0	0

No data displayed because Outcome Measure has zero total participants analyzed.

5. Secondary Outcome Measure:

Measure Title	Absolute Changes in the Number of T2 Lesions From Baseline to Week 24, 48, 72 and 96
Measure Description	Analysis of T2 lesions was done using magnetic resonance imaging (MRI) scans.
Time Frame	Baseline to Week 24, 48, 72, and 96
Safety Issue?	No

Analysis Population Description

ITT population included all participants who received at least 1 treatment dose (only for Rebif group) and had at least 1 post-baseline efficacy endpoint assessment. The 'n' is signifying those participants who received study drug and were evaluated for this measure at the time point for each group respectively.

Reporting Groups

	Description
Rebif 44 mcg	Rebif was administered subcutaneously (s.c.) at a dose of 44 microgram (mcg), three times a week.
No Treatment	Participants in this group did not receive any treatment.

Measured Values

	Rebif 44 mcg	No Treatment
Number of Participants Analyzed	14	15
Absolute Changes in the Number of T2 Lesions From Baseline to Week 24, 48, 72 and 96 [units: T2 lesions] Mean (Standard Deviation)		
Week 24 (n= 13,15)	-1.2 (4.0)	1.0 (6.0)
Week 48 (n= 13,13)	0.2 (8.5)	3.2 (10.1)
Week 72 (n= 12,13)	-1.8 (3.3)	3.1 (14.1)
Week 96 (n= 12,12)	-3.1 (7.6)	2.1 (15.4)

6. Secondary Outcome Measure:

Measure Title	Mean Changes in Expanded Disability Status Scale (EDSS) Score From Baseline to Week 12, 24, 36, 48, 60, 72, 84, and 96
Measure Description	EDSS assesses disability in 8 functional systems. An overall score ranging from 0 (normal) to 10 (death due to MS) was calculated. EDSS progression was defined as increase by at least 1 point if last value of EDSS was equal to 5.5, and by at least 0.5 points if last EDSS was more than 5.5.
Time Frame	Baseline to Week 12, 24, 36, 48, 60, 72, 84, and 96
Safety Issue?	No

Analysis Population Description

ITT population included all participants who received at least 1 treatment dose (only for Rebif group) and had at least 1 post-baseline efficacy endpoint assessment. The 'n' is signifying those participants who received study drug and were evaluated for this measure at the time point for each group respectively.

Reporting Groups

	Description
Rebif 44 mcg	Rebif was administered subcutaneously (s.c.) at a dose of 44 microgram (mcg), three times a week.
No Treatment	Participants in this group did not receive any treatment.

Measured Values

	Rebif 44 mcg	No Treatment
Number of Participants Analyzed	14	15
Mean Changes in Expanded Disability Status Scale (EDSS) Score From Baseline to Week 12, 24, 36, 48, 60, 72, 84, and 96 [units: Units on a Scale] Mean (Standard Deviation)		
Week 12 (n= 14, 15)	-0.1 (0.5)	-0.1 (0.4)
Week 24 (n= 14, 15)	0.3 (0.6)	0.1 (0.4)
Week 36 (n= 13, 14)	0.5 (0.8)	-0.2 (0.4)
Week 48 (n= 14, 14)	0.5 (0.8)	0.2 (0.7)
Week 60 (n= 10, 11)	0.4 (0.8)	0.0 (1.0)
Week 72 (n= 12, 13)	0.3 (0.6)	0.2 (0.9)
Week 84 (n= 12, 13)	0.5 (0.9)	0.2 (0.9)
Week 96 (n= 12, 13)	0.1 (0.8)	0.3 (1.0)

7. Secondary Outcome Measure:

Measure Title	Number of Participants With Adverse Events (AE) and Serious Adverse Events (SAE)
Measure Description	AE: any new untoward medical occurrence/worsening of pre-existing medical condition, whether or not related to study drug. SAE: any AE that resulted in death; was life threatening; resulted in persistent/significant disability/incapacity; resulted in/prolonged an existing in-patient hospitalization; was a congenital anomaly/birth defect; or was a medically important condition.
Time Frame	Baseline to Week 96
Safety Issue?	Yes

Analysis Population Description

Safety population included all participants all randomized participants of the active treatment group who received at least 1 injection and all randomized participants of the 'No Treatment' group, provided that any post-baseline data was available.

Reporting Groups

	Description
Rebif 44 mcg	Rebif was administered subcutaneously (s.c.) at a dose of 44 microgram (mcg), three times a week.

	Description
No Treatment	Participants in this group did not receive any treatment.

Measured Values

	Rebif 44 mcg	No Treatment
Number of Participants Analyzed	15	15
Number of Participants With Adverse Events (AE) and Serious Adverse Events (SAE) [units: participants]		
Adverse Events	15	14
Serious Adverse Events	5	1

Reported Adverse Events

Time Frame	Baseline to Week 96 or premature termination or unscheduled visit.
Additional Description	An adverse event (AE) was defined as any untoward medical occurrence in the form of signs, symptoms, abnormal laboratory findings, or diseases that emerges or worsens relative to baseline during a clinical study with an Investigational Medicinal Product (IMP), regardless of causal relationship and even if no IMP has been administered.

Reporting Groups

	Description
Rebif 44 mcg	Rebif was administered subcutaneously (s.c.) at a dose of 44 microgram (mcg), three times a week.
No Treatment	Participants in this group did not receive any treatment.

Serious Adverse Events

	Rebif 44 mcg		No Treatment	
	Affected/At Risk (%)	# Events	Affected/At Risk (%)	# Events
Total	5/15 (33.33%)		1/15 (6.67%)	
Eye disorders				
Angle Closure Glaucoma [A] *	1/15 (6.67%)	1	0/15 (0%)	0

	Rebif 44 mcg		No Treatment	
	Affected/At Risk (%)	# Events	Affected/At Risk (%)	# Events
Gastrointestinal disorders				
Gastroenteritis salmonella [A] *	1/15 (6.67%)	1	0/15 (0%)	0
Haemorrhoid Operation [A] *	1/15 (6.67%)	1	0/15 (0%)	0
Hepatobiliary disorders				
Cholecystitis chronic [A] *	1/15 (6.67%)	1	0/15 (0%)	0
Cholelithiasis [A] *	1/15 (6.67%)	1	0/15 (0%)	0
Nervous system disorders				
Convulsion [A] *	1/15 (6.67%)	1	0/15 (0%)	0
Depression [A] *	0/15 (0%)	0	1/15 (6.67%)	1
Status Epilepticus [A] *	1/15 (6.67%)	1	0/15 (0%)	0

* Indicates events were collected by non-systematic methods.
A Term from vocabulary, MedDRA (11.1)

Other Adverse Events

Frequency Threshold Above Which Other Adverse Events are Reported: 5%

	Rebif 44 mcg		No Treatment	
	Affected/At Risk (%)	# Events	Affected/At Risk (%)	# Events
Total	15/15 (100%)		14/15 (93.33%)	
Ear and labyrinth disorders				
Vertigo [A] *	1/15 (6.67%)	1	1/15 (6.67%)	1
Gastrointestinal disorders				
Diarrhoea [A] *	0/15 (0%)	0	3/15 (20%)	4
Nausea [A] *	0/15 (0%)	0	2/15 (13.33%)	2
Oral herpes [A] *	1/15 (6.67%)	1	1/15 (6.67%)	1
Vomiting [A] *	1/15 (6.67%)	2	2/15 (13.33%)	2

	Rebif 44 mcg		No Treatment	
	Affected/At Risk (%)	# Events	Affected/At Risk (%)	# Events
General disorders				
Fatigue [A] *	1/15 (6.67%)	1	1/15 (6.67%)	1
Influenza like illness [A] *	3/15 (20%)	3	2/15 (13.33%)	2
Injection site erythema [A] *	2/15 (13.33%)	4	1/15 (6.67%)	1
Injection site pain [A] *	2/15 (13.33%)	2	0/15 (0%)	0
Pyrexia [A] *	2/15 (13.33%)	3	0/15 (0%)	0
Infections and infestations				
Bronchitis [A] *	0/15 (0%)	0	2/15 (13.33%)	2
Infection [A] *	3/15 (20%)	5	0/15 (0%)	0
Nasopharyngitis [A] *	6/15 (40%)	9	4/15 (26.67%)	5
Rhinitis [A] *	3/15 (20%)	5	0/15 (0%)	0
Skin reaction [A] *	2/15 (13.33%)	2	0/15 (0%)	0
Injury, poisoning and procedural complications				
Fall [A] *	2/15 (13.33%)	2	1/15 (6.67%)	1
Wound [A] *	1/15 (6.67%)	1	1/15 (6.67%)	1
Investigations				
Blood bilirubin increased [A] *	1/15 (6.67%)	1	1/15 (6.67%)	1
Musculoskeletal and connective tissue disorders				
Arthralgia [A] *	2/15 (13.33%)	2	1/15 (6.67%)	1
Back Pain [A] *	2/15 (13.33%)	2	1/15 (6.67%)	1
Pain in extremity [A] *	1/15 (6.67%)	1	1/15 (6.67%)	1
Nervous system disorders				
Headache [A] *	4/15 (26.67%)	4	2/15 (13.33%)	3

	Rebif 44 mcg		No Treatment	
	Affected/At Risk (%)	# Events	Affected/At Risk (%)	# Events
Muscle Spasticity [A] *	2/15 (13.33%)	2	1/15 (6.67%)	1
Paresthesia [A] *	1/15 (6.67%)	1	1/15 (6.67%)	1
Renal and urinary disorders				
Urinary tract infection [A] *	2/15 (13.33%)	6	2/15 (13.33%)	4
Respiratory, thoracic and mediastinal disorders				
Cough [A] *	2/15 (13.33%)	5	1/15 (6.67%)	1
Upper respiratory tract infection [A] *	2/15 (13.33%)	3	1/15 (6.67%)	1

* Indicates events were collected by non-systematic methods.
A Term from vocabulary, MedDRA (11.1)

Limitations and Caveats

[Not specified]

More Information

Certain Agreements:

Principal Investigators are NOT employed by the organization sponsoring the study.

There IS an agreement between the Principal Investigator and the Sponsor (or its agents) that restricts the PI's rights to discuss or publish trial results after the trial is completed.

Results Point of Contact:

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