Clinical trial results:
Single Arm Study to Assess Comprehensive Infusion Guidance for the Management of the Infusion Associated Reaction (IARs) in Relapsing-Remitting Multiple Sclerosis (RRMS) Patients Treated with LEMTRADA

Summary

EudraCT number	2014-000092-62
Trial protocol	BE NL ES FR
Global end of trial date	01 April 2016

Results information

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

Trial information

Trial identification

Sponsor protocol code	LPS13650

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02205489
WHO universal trial number (UTN)	U1111-1153-3922
Other trial identifiers	Study Name: EMERALD

Notes:

Sponsors

Sponsor organisation name	Genzyme Corporation
Sponsor organisation address	500 Kendall Street, Cambridge, MA, United States, 02142
Public contact	Trial Transparency Team, Sanofi aventis recherche & développement, Contact-US@sanofi.com
Scientific contact	Trial Transparency Team, Sanofi aventis recherche & développement, Contact-US@sanofi.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	10 June 2016
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	01 April 2016
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To assess the distribution of infusion associated reactions (IARs) by severity grade when alemtuzumab is administered to relapsing-remitting multiple sclerosis (RRMS) subjects who will be medicated according to a specified algorithm designed to manage IARs.

Protection of trial subjects:

Subjects were fully informed of all pertinent aspects of the clinical trial as well as the possibility to discontinue at any time in language and terms appropriate for the subject and considering the local culture. During the course of the trial, subjects were provided with individual subject cards indicating the nature of the trial the subject is participating, contact details and any information needed in the event of a medical emergency.
Collected personal data and human biological samples were processed in compliance with the Sanofi-Aventis Group Personal Data Protection Charter ensuring that the Group abides by the laws governing personal data protection in force in all countries in which it operates.

Background therapy:

The following alemtuzumab-associated medications were to be administered to all study subjects: cetirizine 10 mg tablet or equivalent on Day 0 of both periods and post each infusion; ranitidine or esomeprazole, or equivalents, on Day 0 of both periods and pre- and post each infusion; methylprednisolone 1000 mg tablet on Day 0 of both periods; paracetamol 500 mg tablet or equivalent prior to each infusion; acyclovir 200 mg tablet or equivalent pre- and post each infusion, and daily through Day 30 of both periods; diphenhydramine 25 mg intravenously or equivalent prior to each infusion; methylprednisolone 1000 mg intravenously prior to each infusion (dose reduced after Day 1 and 2 of each period). During and post infusion, subjects could also receive as needed: diphenhydramine or equivalent, paracetamol or equivalent, ondansetron or equivalent, esomeprazole or equivalent, ibuprofen or equivalent (post infusion only).

Evidence for comparator: -

Actual start date of recruitment	20 October 2014
Long term follow-up planned	Yes
Long term follow-up rationale	Safety
Long term follow-up duration	48 Months
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Netherlands: 7
Country: Number of subjects enrolled	Spain: 12
Country: Number of subjects enrolled	Belgium: 8
Country: Number of subjects enrolled	France: 31
Worldwide total number of subjects	58
EEA total number of subjects	58

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)	58
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

The study was conducted at 19 sites in 4 countries from 20 October 2014 to 01 April 2016. A total of 61 subjects were screened, of whom 58 subjects were enrolled in the study. Screen failures were mainly due to the subjects falling under exclusion criteria.

Pre-assignment

Screening details:

The study consisted of 2 Periods: Period 1 (30 days) and Period 2 (30 days). Period 2 began 12 months after the start of Period 1. Safety was assessed monthly in interval between Period 1 and 2.

Period 1

Period 1 title	Study Period 1
Is this the baseline period?	Yes
Allocation method	Not applicable
Blinding used	Not blinded

Arms

Arm title	Alemtuzumab: Period 1

Arm description:

Alemtuzumab 12 mg per day administered as intravenous (IV) infusion, once a day for 5 consecutive days (from Day 1 to Day 5) along with alemtuzumab-associated medications (described under "Trial Information/Background Therapy").

Arm type	Experimental
Investigational medicinal product name	Alemtuzumab
Investigational medicinal product code	GZ402673
Other name	Lemtrada
Pharmaceutical forms	Concentrate for solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Alemtuzumab was administered as IV infusion over approximately 4 hours.

Number of subjects in period 1	Alemtuzumab: Period 1
Started	58
Completed	52
Not completed	6
Physician decision	1
Consent withdrawn by subject	1
Adverse event	3
Lost to follow-up	1

Period 2

Period 2 title	Study Period 2
Is this the baseline period?	No
Allocation method	Not applicable
Blinding used	Not blinded

Arms

Arm title	Alemtuzumab: Period 2

Arm description:

Alemtuzumab 12 mg per day administered as IV infusion, once a day for 3 consecutive days (from Day 1 to Day 3) along with alemtuzumab-associated medications (described under "Trial Information/Background Therapy").

Arm type	Experimental
Investigational medicinal product name	Alemtuzumab
Investigational medicinal product code	GZ402673
Other name	Lemtrada
Pharmaceutical forms	Concentrate for solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Alemtuzumab was administered as IV infusion over approximately 4 hours.

Number of subjects in period 2	Alemtuzumab: Period 2
Started	52
Completed	54

Joined	2
Subjects not completed Period1 but entered Period2	2

Baseline characteristics

Reporting groups	
Reporting group title	Alemtuzumab: Period 1
Reporting group description:	
Alemtuzumab 12 mg per day administered as intravenous (IV) infusion, once a day for 5 consecutive days (from Day 1 to Day 5) along with alemtuzumab-associated medications (described under "Trial Information/Background Therapy").	

Reporting group values	Alemtuzumab: Period 1	Total	
Number of subjects	58	58	
Age categorical Units: Subjects			
Age continuous Units: years arithmetic mean standard deviation	 36.42 ± 8.11	 -	
Gender categorical Units: Subjects			
Female	35	35	
Male	23	23	

End points

End points reporting groups

Reporting group title	Alemtuzumab: Period 1

Reporting group description:

Alemtuzumab 12 mg per day administered as intravenous (IV) infusion, once a day for 5 consecutive days (from Day 1 to Day 5) along with alemtuzumab-associated medications (described under "Trial Information/Background Therapy").

Reporting group title	Alemtuzumab: Period 2

Reporting group description:

Alemtuzumab 12 mg per day administered as IV infusion, once a day for 3 consecutive days (from Day 1 to Day 3) along with alemtuzumab-associated medications (described under "Trial Information/Background Therapy").

Subject analysis set title	Alemtuzumab: Overall Study (with Monthly Safety Monitoring)
Subject analysis set type	Full analysis

Subject analysis set description:

Alemtuzumab 12 mg per day administered as IV infusion, once a day for 5 consecutive days (from Day 1 to Day 5) in Period 1 and for 3 consecutive days (from Day 1 to Day 3) during Period 2, along with alemtuzumab-associated medications (described under "Trial Information/Background Therapy"). Period 2 began 12 months after the start of Period 1. Safety was assessed monthly in interval between Period 1 and 2.

Primary: Percentage of Subjects with IARs by Severity Grade

End point title	Percentage of Subjects with IARs by Severity Grade[1]

End point description:

An IAR was defined as any treatment emergent adverse event (TEAE) that occurred during or within 24 hours after alemtuzumab infusion. This summary includes events occurring during Period 1 and/or Period 2. Toxicity grade (severity) of adverse events was based on Common Terminology Criteria for Adverse Events (CTCAE) version 4.03: Grade 1 (mild), Grade 2 (moderate), Grade 3 (severe), Grade 4 (life-threatening) and Grade 5 (death). Analysis was performed on safety set defined as all enrolled subjects who received at least part of a dose of the investigational medicinal product (IMP) during Period 1 or 2. Only those grade categories, in which at least 1 subject had event, were reported.

End point type	Primary

End point timeframe:

From the first administration of IMP (Day 1) to 24 hours after each infusion of Period 1 and Period 2

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: As there was no comparator arm and no hypothesis to be tested, no statistical analysis was performed.

End point values	Alemtuzumab: Overall Study (with Monthly Safety Monitoring)			
Subject group type	Subject analysis set			
Number of subjects analysed	58			
Units: percentage of subjects				
number (confidence interval 95%)				
Grade 1 - Mild	87.9 (76.7 to 95)			
Grade 2 - Moderate	62.1 (48.4 to 74.5)			
Grade 3 - Severe	10.3 (3.9 to 21.2)			

Statistical analyses

No statistical analyses for this end point

Primary: Percentage of Subjects with Individual IARs Occurring with >5% Incidence

End point title	Percentage of Subjects with Individual IARs Occurring with >5% Incidence[2]

End point description:

An IAR was defined as any TEAE that occurred during or within 24 hours after alemtuzumab infusion. This summary includes events occurring during Period 1 and/or Period 2. Analysis was performed on safety set.

End point type	Primary

End point timeframe:

From the first administration of IMP (Day 1) to 24 hours after each infusion of Period 1 and Period 2

Notes:

[2] - 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: As there was no comparator arm and no hypothesis to be tested, no statistical analysis was performed.

End point values	Alemtuzumab: Overall Study (with Monthly Safety Monitoring)			
Subject group type	Subject analysis set			
Number of subjects analysed	58			
Units: percentage of subjects				
number (confidence interval 95%)				
Headache	58.6 (44.9 to 71.4)			
Dizziness	8.6 (2.9 to 19)			
Presyncope	5.2 (1.1 to 14.4)			
Pyrexia	29.3 (18.1 to 42.7)			
Fatigue	12.1 (5 to 23.3)			
Chest Discomfort	8.6 (2.9 to 19)			
Malaise	5.2 (1.1 to 14.4)			
Rash	22.4 (12.5 to 35.3)			
Pruritus	17.2 (8.6 to 29.4)			
Erythema	15.5 (7.4 to 27.4)			
Urticaria	10.3 (3.9 to 21.2)			

Pruritus Generalised	5.2 (1.1 to 14.4)			
Nausea	17.2 (8.6 to 29.4)			
Abdominal Pain Upper	15.5 (7.4 to 27.4)			
Diarrhoea	10.3 (3.9 to 21.2)			
Abdominal Pain	6.9 (1.9 to 16.7)			
Constipation	6.9 (1.9 to 16.7)			
Bradycardia	15.5 (7.4 to 27.4)			
Palpitations	5.2 (1.1 to 14.4)			
Insomnia	19 (9.9 to 31.4)			
Flushing	10.3 (3.9 to 21.2)			
Hot Flush	6.9 (1.9 to 16.7)			
Musculoskeletal Stiffness	5.2 (1.1 to 14.4)			
Myalgia	5.2 (1.1 to 14.4)			
Dyspnoea	6.9 (1.9 to 16.7)			

Statistical analyses

No statistical analyses for this end point

Primary: Percentage of Subjects with Serious IARs by Severity Grade

End point title	Percentage of Subjects with Serious IARs by Severity Grade[3]

End point description:

A serious IAR was defined as any serious TEAE that occurred during or within 24 hours after alemtuzumab infusion. This summary includes events occurring during Period 1 and/or Period 2. A serious TEAE was a TEAE that resulted in death, was life-threatening, required inpatient hospitalization or caused prolongation of existing hospitalization, resulted in persistent or significant disability/incapacity, was a congenital anomaly/birth defect, or was an important medical event. Toxicity grade (severity) of adverse events was based on CTCAE version 4.03: Grade 1 (mild), Grade 2 (moderate), Grade 3 (severe), Grade 4 (life-threatening) and Grade 5 (death). Analysis was performed on safety set. Only those grade categories, in which at least 1 subject had event, were reported.

End point type	Primary

End point timeframe:

From the first administration of IMP (Day 1) to 24 hours after each infusion of Period 1 and Period 2

Notes:

[3] - 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: As there was no comparator arm and no hypothesis to be tested, no statistical analysis was performed.

End point values	Alemtuzumab: Overall Study (with Monthly Safety Monitoring)			
Subject group type	Subject analysis set			
Number of subjects analysed	58			
Units: percentage of subjects				
number (confidence interval 95%)				
Grade 1 - Mild	6.9 (1.9 to 16.7)			
Grade 2 - Moderate	6.9 (1.9 to 16.7)			
Grade 3 - Severe	3.4 (0.4 to 11.9)			

Statistical analyses

No statistical analyses for this end point

Primary: Percentage of Subjects with Individual Serious IARs

End point title	Percentage of Subjects with Individual Serious IARs [4]

End point description:

A serious IAR was defined as any serious TEAE that occurred during or within 24 hours after alemtuzumab infusion. This summary includes events occurring during Period 1 and/or Period 2. A serious TEAE was a TEAE that resulted in death, was life-threatening, required inpatient hospitalization or caused prolongation of existing hospitalization, results in persistent or significant disability/incapacity, was a congenital anomaly/birth defect, or was an important medical event. Analysis was performed on safety set.

End point type	Primary

End point timeframe:

From the first administration of IMP (Day 1) to 24 hours after each infusion of Period 1 and Period 2

Notes:

[4] - 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: As there was no comparator arm and no hypothesis to be tested, no statistical analysis was performed.

End point values	Alemtuzumab: Overall Study (with Monthly Safety Monitoring)			
Subject group type	Subject analysis set			
Number of subjects analysed	58			
Units: percentage of subjects				
number (confidence interval 95%)				
Bradycardia	5.2 (1.1 to 14.4)			
Tachycardia	1.7 (0 to 9.2)			
Hyperthermia	1.7 (0 to 9.2)			
Pyrexia	1.7 (0 to 9.2)			
Fibrin D Dimer Increased	1.7 (0 to 9.2)			
Gammaglutamyl Transferase Increased	1.7 (0 to 9.2)			
Erythema	1.7 (0 to 9.2)			

Urticaria	1.7 (0 to 9.2)			
Hepatocellular Injury	1.7 (0 to 9.2)			
Hypersensitivity	1.7 (0 to 9.2)			
Hepatitis Viral	1.7 (0 to 9.2)			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

All AEs were collected from signature of the informed consent form up to the final visit (Month 13) regardless of seriousness or relationship to investigational product. Month 13 visit was scheduled to occur at Day 30 of Period 2.

Adverse event reporting additional description:

Reported AEs are TEAE that is AEs that developed/worsened during the period from first administration of the IMP (Day 1 of Period 1) to the end of study (Month 13).

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	19.0

Reporting groups

Reporting group title	Alemtuzumab: Overall Study (with Monthly Safety Monitoring)

Reporting group description:

Alemtuzumab 12 mg per day administered as IV infusion, once a day for 5 consecutive days (from Day 1 to Day 5) in Period 1 and for 3 consecutive days (from Day 1 to Day 3) during Period 2, along with alemtuzumab-associated medications (described under "Trial Information/Background Therapy"). Period 2 began 12 months after start of Period 1. Safety was assessed monthly in interval between Period 1 and 2.

Serious adverse events	Alemtuzumab: Overall Study (with Monthly Safety Monitoring)		
Total subjects affected by serious adverse events			
subjects affected / exposed	19 / 58 (32.76%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events			
General disorders and administration site conditions			
Hyperthermia			
subjects affected / exposed	1 / 58 (1.72%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Pyrexia			
subjects affected / exposed	1 / 58 (1.72%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Immune system disorders			
Hypersensitivity			

subjects affected / exposed	1 / 58 (1.72%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Psychiatric disorders			
Affective Disorder			
subjects affected / exposed	1 / 58 (1.72%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Depression			
subjects affected / exposed	1 / 58 (1.72%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Psychotic Disorder			
subjects affected / exposed	1 / 58 (1.72%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Suicidal Ideation			
subjects affected / exposed	1 / 58 (1.72%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Investigations			
Fibrin D Dimer Increased			
subjects affected / exposed	1 / 58 (1.72%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Gamma-Glutamyltransferase Increased			
subjects affected / exposed	1 / 58 (1.72%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Human Papilloma Virus Test Positive			
subjects affected / exposed	1 / 58 (1.72%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		

Injury, poisoning and procedural complications			
Spinal Column Injury			
subjects affected / exposed	1 / 58 (1.72%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Cardiac disorders			
Bradycardia			
subjects affected / exposed	3 / 58 (5.17%)		
occurrences causally related to treatment / all	3 / 3		
deaths causally related to treatment / all	0 / 0		
Tachycardia			
subjects affected / exposed	1 / 58 (1.72%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Nervous system disorders			
Epilepsy			
subjects affected / exposed	1 / 58 (1.72%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Monoplegia			
subjects affected / exposed	1 / 58 (1.72%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Multiple Sclerosis Relapse			
subjects affected / exposed	3 / 58 (5.17%)		
occurrences causally related to treatment / all	0 / 4		
deaths causally related to treatment / all	0 / 0		
Blood and lymphatic system disorders			
Immune Thrombocytopenic Purpura			
subjects affected / exposed	1 / 58 (1.72%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Hepatobiliary disorders			
Hepatocellular Injury			

subjects affected / exposed	1 / 58 (1.72%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Skin and subcutaneous tissue disorders			
Erythema			
subjects affected / exposed	1 / 58 (1.72%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Urticaria			
subjects affected / exposed	1 / 58 (1.72%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Vascular Purpura			
subjects affected / exposed	1 / 58 (1.72%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Endocrine disorders			
Basedow's Disease			
subjects affected / exposed	1 / 58 (1.72%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Musculoskeletal and connective tissue disorders			
Back Pain			
subjects affected / exposed	1 / 58 (1.72%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Infections and infestations			
Hepatitis Viral			
subjects affected / exposed	1 / 58 (1.72%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Herpes Zoster			

subjects affected / exposed	1 / 58 (1.72%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Influenza			
subjects affected / exposed	1 / 58 (1.72%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Upper Respiratory Tract Infection			
subjects affected / exposed	1 / 58 (1.72%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Varicella Zoster Virus Infection			
subjects affected / exposed	1 / 58 (1.72%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		

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

Non-serious adverse events	Alemtuzumab: Overall Study (with Monthly Safety Monitoring)		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	57 / 58 (98.28%)		
Vascular disorders			
Flushing			
subjects affected / exposed	6 / 58 (10.34%)		
occurrences (all)	6		
Hot Flush			
subjects affected / exposed	6 / 58 (10.34%)		
occurrences (all)	6		
Hypertension			
subjects affected / exposed	3 / 58 (5.17%)		
occurrences (all)	3		
General disorders and administration site conditions			

Asthenia subjects affected / exposed occurrences (all)	3 / 58 (5.17%) 3		
Chest Discomfort subjects affected / exposed occurrences (all)	5 / 58 (8.62%) 7		
Chills subjects affected / exposed occurrences (all)	4 / 58 (6.90%) 5		
Fatigue subjects affected / exposed occurrences (all)	12 / 58 (20.69%) 13		
Influenza Like Illness subjects affected / exposed occurrences (all)	4 / 58 (6.90%) 5		
Malaise subjects affected / exposed occurrences (all)	4 / 58 (6.90%) 4		
Pain subjects affected / exposed occurrences (all)	5 / 58 (8.62%) 5		
Pyrexia subjects affected / exposed occurrences (all)	18 / 58 (31.03%) 21		
Respiratory, thoracic and mediastinal disorders			
Cough subjects affected / exposed occurrences (all)	4 / 58 (6.90%) 4		
Dysphonia subjects affected / exposed occurrences (all)	3 / 58 (5.17%) 3		
Dyspnoea subjects affected / exposed occurrences (all)	4 / 58 (6.90%) 4		
Epistaxis			

subjects affected / exposed	4 / 58 (6.90%)		
occurrences (all)	4		
Oropharyngeal Pain			
subjects affected / exposed	6 / 58 (10.34%)		
occurrences (all)	6		
Psychiatric disorders			
Anxiety			
subjects affected / exposed	4 / 58 (6.90%)		
occurrences (all)	4		
Depression			
subjects affected / exposed	3 / 58 (5.17%)		
occurrences (all)	3		
Insomnia			
subjects affected / exposed	14 / 58 (24.14%)		
occurrences (all)	14		
Sleep Disorder			
subjects affected / exposed	5 / 58 (8.62%)		
occurrences (all)	5		
Injury, poisoning and procedural complications			
Fall			
subjects affected / exposed	3 / 58 (5.17%)		
occurrences (all)	3		
Cardiac disorders			
Bradycardia			
subjects affected / exposed	8 / 58 (13.79%)		
occurrences (all)	8		
Palpitations			
subjects affected / exposed	5 / 58 (8.62%)		
occurrences (all)	5		
Nervous system disorders			
Dizziness			
subjects affected / exposed	10 / 58 (17.24%)		
occurrences (all)	10		
Headache			
subjects affected / exposed	39 / 58 (67.24%)		
occurrences (all)	62		

Multiple Sclerosis Relapse subjects affected / exposed occurrences (all)	10 / 58 (17.24%) 10		
Muscle Spasticity subjects affected / exposed occurrences (all)	4 / 58 (6.90%) 5		
Presyncope subjects affected / exposed occurrences (all)	4 / 58 (6.90%) 4		
Tremor subjects affected / exposed occurrences (all)	3 / 58 (5.17%) 3		
Uhthoff's Phenomenon subjects affected / exposed occurrences (all)	3 / 58 (5.17%) 3		
Blood and lymphatic system disorders Lymphopenia subjects affected / exposed occurrences (all)	4 / 58 (6.90%) 5		
Ear and labyrinth disorders Ear Pain subjects affected / exposed occurrences (all)	3 / 58 (5.17%) 3		
Eye disorders Vision Blurred subjects affected / exposed occurrences (all)	4 / 58 (6.90%) 4		
Gastrointestinal disorders Abdominal Pain subjects affected / exposed occurrences (all)	4 / 58 (6.90%) 4		
Abdominal Pain Upper subjects affected / exposed occurrences (all)	13 / 58 (22.41%) 13		
Constipation subjects affected / exposed occurrences (all)	8 / 58 (13.79%) 8		

Diarrhoea subjects affected / exposed occurrences (all)	7 / 58 (12.07%) 7			
Gingival Bleeding subjects affected / exposed occurrences (all)	4 / 58 (6.90%) 4			
Nausea subjects affected / exposed occurrences (all)	17 / 58 (29.31%) 18			
Toothache subjects affected / exposed occurrences (all)	4 / 58 (6.90%) 4			
Vomiting subjects affected / exposed occurrences (all)	6 / 58 (10.34%) 6			
Skin and subcutaneous tissue disorders Acne subjects affected / exposed occurrences (all)	11 / 58 (18.97%) 11			
Alopecia subjects affected / exposed occurrences (all)	3 / 58 (5.17%) 3			
Erythema subjects affected / exposed occurrences (all)	10 / 58 (17.24%) 10			
Pruritus subjects affected / exposed occurrences (all)	14 / 58 (24.14%) 16			
Pruritus Generalised subjects affected / exposed occurrences (all)	6 / 58 (10.34%) 6			
Rash subjects affected / exposed occurrences (all)	22 / 58 (37.93%) 29			
Rash Generalised				

subjects affected / exposed	5 / 58 (8.62%)		
occurrences (all)	5		
Urticaria			
subjects affected / exposed	9 / 58 (15.52%)		
occurrences (all)	10		
Musculoskeletal and connective tissue disorders			
Back Pain			
subjects affected / exposed	3 / 58 (5.17%)		
occurrences (all)	3		
Muscle Spasms			
subjects affected / exposed	3 / 58 (5.17%)		
occurrences (all)	4		
Musculoskeletal Stiffness			
subjects affected / exposed	3 / 58 (5.17%)		
occurrences (all)	3		
Myalgia			
subjects affected / exposed	6 / 58 (10.34%)		
occurrences (all)	6		
Neck Pain			
subjects affected / exposed	4 / 58 (6.90%)		
occurrences (all)	5		
Infections and infestations			
Bronchitis			
subjects affected / exposed	8 / 58 (13.79%)		
occurrences (all)	8		
Gastroenteritis			
subjects affected / exposed	6 / 58 (10.34%)		
occurrences (all)	6		
Gastroenteritis Viral			
subjects affected / exposed	3 / 58 (5.17%)		
occurrences (all)	3		
Nasopharyngitis			
subjects affected / exposed	15 / 58 (25.86%)		
occurrences (all)	16		
Oral Herpes			

subjects affected / exposed	6 / 58 (10.34%)		
occurrences (all)	6		
Rhinitis			
subjects affected / exposed	3 / 58 (5.17%)		
occurrences (all)	3		
Sinusitis			
subjects affected / exposed	4 / 58 (6.90%)		
occurrences (all)	4		
Tonsillitis			
subjects affected / exposed	5 / 58 (8.62%)		
occurrences (all)	5		
Upper Respiratory Tract Infection			
subjects affected / exposed	3 / 58 (5.17%)		
occurrences (all)	3		
Urinary Tract Infection			
subjects affected / exposed	13 / 58 (22.41%)		
occurrences (all)	14		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
07 September 2015	The principal changes were: Added Kurtzke Expanded Disability Status Scale (EDSS) score; included other equivalent antisecretory drugs such as Proton Pump Inhibitors (PPIs) in addition to H2 receptors antagonists as alemtuzumab-associated medications; clarified recording and review process of the subject diary.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported