ClinicalTrials.gov Protocol Registration and Results System (PRS) Receipt
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ClinicalTrials.gov ID: NCT00725985

Study Identification

Unique Protocol ID:	28821
Brief Title:	Oral Cladribine in Early Multiple Sclerosis (MS) (ORACLE MS)
Official Title:	A Phase III, Randomized, Double-blind, Placebo-controlled, Multi-center Clinical Trial of Oral Cladribine in Subjects With a First Clinical Event at High Risk of Converting to MS
Secondary IDs:	

Study Status

Record Verification:	August 2013
Overall Status:	Completed
Study Start:	December 2008
Primary Completion:	July 2011 [Actual]
Study Completion:	April 2012 [Actual]

Sponsor/Collaborators

Sponsor:	EMD Serono
Responsible Party:	Sponsor
Collaborators:	

Oversight

FDA Regulated?:	Yes
Applicable Trial?:	Section 801 Clinical Trial? Yes

	Delayed Posting? No
IND/IDE Protocol?:	Yes
IND/IDE Information:	Grantor: CDER IND/IDE Number: 74634 Serial Number: Has Expanded Access? No
Review Board:	Approval Status: Approved Approval Number: 9/21/08 Board Name: Schulman Associates IRB Board Affiliation: Independent Phone: +513-761-4100 Email:
Data Monitoring?:	Yes
Plan to Share Data?:	
Oversight Authorities:	United States: Food and Drug Administration Algeria: Ministry of Health Argentina: Administracion Nacional de Medicamentos, Alimentos y Tecnologia Medica Australia: Human Research Ethics Committee Austria: Agency for Health and Food Safety Belgium: Federal Agency for Medicinal Products and Health Products Bulgaria: Ministry of Health Canada: Health Canada Chile: Comisión Nacional de Investigación Científica y Tecnológica Croatia: Ministry of Health and Social Care Czech Republic: State Institute for Drug Control Estonia: The State Agency of Medicine Finland: Finnish Medicines Agency France: Ministry of Health Germany: Federal Institute for Drugs and Medical Devices Greece: National Organization of Medicines India: Ministry of Health Ireland: Ministry of Health Italy: National Institute of Health Korea: Food and Drug Administration Lebanon: Ministry of Public Health Lithuania: State Medicine Control Agency - Ministry of Health Macedonia: Ethics Committee Mexico: Ministry of Health Norway: Norwegian Medicines Agency Poland: Ministry of Health Portugal: National Pharmacy and Medicines Institute Romania: National Medicines Agency

Serbia and Montenegro: Agency for Drugs and Medicinal Devices
Singapore: Health Sciences Authority
Spain: Ministry of Health
Sweden: Medical Products Agency
Switzerland: Federal Office of Public Health
Taiwan: National Bureau of Controlled Drugs
Thailand: Food and Drug Administration
Turkey: Ministry of Health
United Kingdom: Medicines and Healthcare Products Regulatory Agency

Study Description

Brief Summary: A randomized, double-blind, clinical trial to assess the safety and efficacy of two doses of oral cladribine versus placebo in subjects who had a first clinical demyelinating event (clinically isolated syndrome). Subjects in either the cladribine or placebo group may also enter treatment periods with open-label interferon-beta or open-label cladribine depending upon the disease status. The primary objective of this study is to evaluate the effect of two dosage regimens of oral cladribine versus placebo on the time to conversion to multiple sclerosis (MS) (from randomization) according to the Poser criteria in subjects with first clinical demyelinating event at high risk of converting to MS.

Detailed Description: This will be a randomized, double blind, three-arm, placebo-controlled, multi-center trial to evaluate the safety and efficacy of oral cladribine versus placebo in the treatment of subjects who have sustained a first clinical demyelinating event within 75 days prior to the Screening. Subjects must have a minimum of 2 clinically silent lesions on the Screening magnetic resonance imaging (MRI).

The study will include a pre-study evaluation period (Screening period: between 10 and 28 days prior to the start of treatment with blinded study medication (oral cladribine or placebo).

Depending upon the clinical course of their MS, subjects will then proceed from the ITP to either the Maintenance Treatment Period (with open-label interferon-beta treatment) or LTFU period (with either open-label low-dose cladribine or no additional treatment (if no progression to MS has been noted after the initial treatment period). The single primary endpoint for the overall study, which will be determined during the ITP, is time to conversion to MS (from randomization), according to the Poser criteria.

For every subject, eligibility for study enrollment and entry into each of the study periods, and diagnosis of conversion to either McDonald MS or CDMS must be confirmed and approved by a Sponsor appointed study Adjudication Committee.

Conditions

Conditions: Multiple Sclerosis

Keywords: Clinically Isolated Syndrome (CIS)
Early MS
Multiple Sclerosis

Study Design

Study Type:	Interventional
Primary Purpose:	Treatment
Study Phase:	Phase 3
Intervention Model:	Parallel Assignment
Number of Arms:	3
Masking:	Double Blind (Subject, Caregiver, Investigator, Outcomes Assessor)
Allocation:	Randomized
Endpoint Classification:	Safety/Efficacy Study
Enrollment:	617 [Actual]

Arms and Interventions

Arms	Assigned Interventions
Experimental: Cladribine 5.25 mg/kg	Drug: Cladribine Cladribine tablets will be administered as cumulative dose of 0.875 milligram per kilogram (mg/kg) over a course of 5 consecutive days at Weeks 1, 5, 9, 13, 48, and 52 resulting in total cladribine dose of 5.25 mg/kg during the initial treatment period (ITP) of 96 weeks or until CDMS conversion, whichever occur first Drug: Rebif® new formulation (RNF) Participants who will convert to CDMS during ITP will enter in open-label maintenance period (OLMP) and receive RNF subcutaneously at a dose of 44 microgram (mcg) three times a week. Participants who will convert to CDMS during long-term follow-up (LTFU) period, will also receive RNF subcutaneously at a dose of 44 mcg three times a week
Experimental: Cladribine 3.5 mg/kg	Drug: Cladribine Cladribine tablets will be administered as cumulative dose of 0.875 mg/kg over a course of 5 consecutive days at Weeks 1, 5, 48, 52 and placebo matched to cladribine tablets will be administered at Week 9 and 13 resulting in total cladribine dose of 3.5 mg/kg during the ITP of 96 weeks or until CDMS conversion, whichever occur first Drug: Rebif® new formulation (RNF) Participants who will convert to CDMS during ITP will enter in open-label maintenance period (OLMP) and receive RNF subcutaneously at a dose of 44 microgram (mcg) three times a week. Participants who will convert to CDMS during long-term follow-up (LTFU) period, will also receive RNF subcutaneously at a dose of 44 mcg three times a week

Arms	Assigned Interventions
Placebo Comparator: Placebo	Drug: Placebo Placebo matched to cladribine tablets will be administered over a course of 5 consecutive days at Weeks 1, 5, 9, 13, 48 and 52 during the ITP of 96 weeks or until CDMS conversion, whichever occur first Drug: Rebif® new formulation (RNF) Participants who will convert to CDMS during ITP will enter in open-label maintenance period (OLMP) and receive RNF subcutaneously at a dose of 44 microgram (mcg) three times a week. Participants who will convert to CDMS during long-term follow-up (LTFU) period, will also receive RNF subcutaneously at a dose of 44 mcg three times a week

Outcome Measures

[See Results Section.]

Eligibility

Minimum Age: 18 Years

Maximum Age: 55 Years

Gender: Both

Accepts Healthy Volunteers?: No

Criteria: Inclusion Criteria:

- Male or female between 18 and 55 years old, inclusive
- Weighed between 40 to 120 kilogram (kg), inclusive
- Subject has experienced a single, first clinical event suggestive of MS within 75 days prior to the Screening visit, (clock starts 24 hours after onset). The event must be a new neurological abnormality present for at least 24 hours, either mono- or polysymptomatic
- Subject has at least two clinically silent lesions on the T2-weighted MRI scan, at screening, with a size of at least 3 millimeter (mm), at least one of which is ovoid or periventricular or infratentorial on screening MRI
- Subject has EDSS 0 - 5.0 at Screening
- Subject has no medical history or evidence of latent tuberculosis infection (LTBI) or active tubercular disease, as evidenced by the Mantoux tuberculosis (TB) skin test or a comparable sensitive test according to local regulations/guidelines (if the Mantoux test is not available), and/or a chest X-ray
- Subject has normal hematological parameters at Screening, as defined by the central laboratory that performed all the assessments
- If female, she must:
    - be neither pregnant nor breast-feeding, nor attempting to conceive and
    - use a highly effective method of contraception throughout the entire duration of the study and for 90 days following completion of the last dose of study medication. A highly effective method of contraception is defined as those which

result in a low failure rate (that is less than 1 percent per year) when used consistently and correctly such as implants, injectables, combined oral contraceptives, some intrauterine devices, sexual abstinence or vasectomized partner, or
    - be post-menopausal or surgically sterilized (Note: for Danish sites only, subjects should use a hormonal contraceptive or intrauterine device for the duration of the trial)
- Male subjects must be willing to use contraception to avoid impregnating partners throughout the study, and for 90 days following the last dose of study medication
- Be willing and able to comply with study procedures for the duration of the study
- Subject has to provide written informed consent voluntarily, including, for United states of America (USA), subject authorization under Health Insurance Portability and Accountability Act (HIPAA), prior to any study-related procedure that is not part of normal medical care
- Subject has refused any treatment already available for clinically isolated syndrome (CIS) such as interferons or glatiramer acetate, at the time of entry into the Initial Treatment Period of this study

Exclusion Criteria:

- Subject has a diagnosis of MS (per McDonald criteria, 2005)
- Subject has any other disease that could better explain the subject's signs and symptoms
- Subject has complete transverse myelitis or bilateral optic neuritis
- Subject using or has used any other approved MS disease modifying drug (DMD)
- Subject has used any investigational drug or undergone an experimental procedure within 12 weeks prior to Study day 1
- Subject received oral or systemic corticosteroids or adrenocorticotropic hormone (ACTH) within 30 days prior to screening MRI. The MRI had to be performed 30 days after the oral or systemic corticosteroids or ACTH treatment. In case this interfered with MRI timing the screening period could be extended accordingly.
- Subject has abnormal total bilirubin, or aspartate aminotransferase (AST) or alanine aminotransferase (ALT) or alkaline phosphatase greater than 2.5 times the upper limit of normal
- Subject suffered from current autoimmune disease other than MS
- Subject suffered from psychiatric illness (including history of, or concurrent, severe depressive disorders and/or suicidal ideation) that in the opinion of the investigator creates undue risk to the subject or could affect compliance with the study protocol
- Subject suffered from major medical illness such as cardiac (for example angina, congestive heart failure or arrhythmia), endocrinologic, hepatic, immunologic, metabolic, renal, pulmonary, gastrointestinal, dermatologic, or other major disease that would preclude the administration of oral cladribine
- Subject has a history of seizures not adequately controlled by medications
- Subject has a known allergy to cladribine, interferon-beta, the excipient(s) of the study medications, or to gadolinium-diethylenetriamine penta-acetic acid (DTPA)
- Subject has any renal condition that would preclude the administration of gadolinium (for example acute or chronic severe renal insufficiency (glomerular filtration rate [GFR] less than 30 milliliter per minute per 1.73 square meter [mL/min/1.73 m^2])
- Subject has a history of chronic or clinically significant hematological abnormalities
- Subject has a history of active or chronic infectious disease or any disease that compromises immune function (for example human immunodeficiency virus positive [HIV+], human T-lymphotrophic virus [HTLV-1], Lyme disease, latent tuberculosis infection [LTBI] or TB, insulin-dependent diabetes).
- Subject has previously been screened in this study (signed an informed consent) and then withdrawn
- Subject has received any immunomodulatory or immunosuppressive therapy) at any time prior to Study Day 1, including, but not limited to, the following products: any interferon, glatiramer acetate (Copolymer I), cyclophosphamide, cyclosporine, methotrexate, linomide, azathioprine, mitoxantrone, teriflunomide, laquinimod, cladribine, total lymphoid irradiation, anti-

lymphocyte monoclonal antibody treatment (for example natalizumab, alemtuzumab/Campath, anti-cluster of differentiation 4 [CD4]), intravenous immunoglobulin G (IVIG), cytokines or anti-cytokine therapy
- Subject has received experimental MS treatment
- Subject has a history of alcohol or drug abuse
- Subject has intolerance or any contraindication to both paracetamol (acetaminophen) and ibuprofen
- Subject has inability to administer subcutaneous injections either by self or by caregiver
- Subject has prior or current malignancy (with the exception of in situ basal or squamous cell skin cancer surgically removed without recurrence for at least five years)
- Subject has a positive stool hemoccult test at Screening

Contacts/Locations

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Saudi Arabia
King Abdullah International Medical Research Center, King Saud Ben Abdulazziz University for Health Sciences, and National Guard Health Affairs
Riyadh, Saudi Arabia

Russian Federation
Municipal Treatment Prophylactic Institution "City Hospital #33"
Nizhny Novgorod, Russian Federation

State Medical Institution "Republican Rehabilitation Clinic of Tatarstan Ministry of Health"
Kazan, Russian Federation

State Healthcare Institution "Kemerovo Regional Clinical Hospital"
Kemerovo, Russian Federation

State Medical Institution " Jursk Regional Clinical Hospital"
Kursk, Russian Federation

Federal State Institution " Siberian Reginal Medical Center of Roszdarv"
Novosibirsk, Russian Federation

State Educational Institution of Higher Professional Education "Military Medical Academy named after S. M. Korov of Dept of Defense of Russian Federation based on Clinic of Neurology of State Institution
Saint-Petersburg, Russian Federation

State Healthcare Institution "Kaluga Regional Hospital"
Laluga, Russian Federation

State Educational Institution of Higher Professional Education "Samara State Medical University of Roszdrav" on State Healthcare Institution "Samara Regional Clinical Hospital named after M. I. Kalinin"
Samara, Russian Federation

Closed joint-stock society Medical sanitary unit "Nephtaynik" based the hospital
Tyumen, Russian Federation

Non-State Healthcare Institution "Central Clinical Hospital #2 named after N.A. Semasko of Russian Railways"
Moscow, Russian Federation

State Educational Institution of Higher Professional Education "Saratov State Medical University of Roszdrav" based on Clincial Hosptial #3 of Saratov State Medical University
Saratov, Russian Federation

St. Petersburg State Healthcare Institution "Multifield City Hospital #2"
St. Petersburg, Russian Federation

State Educational Institute of Higher Professional Education "I.M. Sechenov Moscow Medical Academy of Roszdrav" Russia based on A. Ya. Kozhevnikov Nervous Disease Clinic
Moscow, Russian Federation

Municipal Healthcare Institution "City Clinical Hospital #3"
Chelyabinsk, Russian Federation

State Healthcare Institution "Sverdlovsk Regional Clinical Hospital #1"
Ekaterinburg, Russian Federation

Municipal Healthcare Institution "Yaroslavi Clinical Hospital #8"
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State Educational Institute of Higher Professional Education "Rostov State Medical University of Roszdrav"
Rostov-on-Don, Russian Federation

References

Citations:

Links:

Study Data/Documents:

Study Results

Participant Flow

Reporting Groups

	Description
Cladribine 5.25 mg/kg (ITP)	Cladribine tablets administered as cumulative dose of 0.875 milligram per kilogram (mg/kg) over a course of 5 consecutive days at Weeks 1, 5, 9, 13, 48, and 52 resulting in total cladribine dose of 5.25 mg/kg during the initial treatment period (ITP) of 96 weeks or until clinically definite multiple sclerosis (CDMS) conversion, whichever occurred first.
Cladribine 3.5 mg/kg (ITP)	Cladribine tablets administered as cumulative dose of 0.875 mg/kg over a course of 5 consecutive days at Weeks 1, 5, 48, 52 and placebo matched to cladribine tablets was administered at Week 9 and 13 resulting in total cladribine dose of 3.5 mg/kg during the ITP of 96 weeks or until CDMS conversion, whichever occurred first.
Placebo (ITP)	Placebo matched to cladribine tablets administered over a course of 5 consecutive days at Weeks 1, 5, 9, 13, 48 and 52 during the ITP of 96 weeks or until CDMS conversion, whichever occurred first.
Cladribine 5.25 mg/kg, Rebif (OLMP)	Participants who received cladribine 5.25 mg/kg and converted to CDMS during ITP entered in open-label maintenance period (OLMP) and received Rebif® new formulation (RNF) subcutaneously at a dose of 44 microgram (mcg) three times a week for up to 96 weeks. Due to trial termination, the OLMP duration was reduced for some participants.
Cladribine 3.5 mg/kg, Rebif (OLMP)	Participants who received cladribine 3.5 mg/kg and converted to CDMS during ITP entered in OLMP and received RNF subcutaneously at a dose of 44 mcg three times a week for up to 96 weeks. Due to trial termination, the OLMP duration was reduced for some participants.
Placebo, Rebif (OLMP)	Participants who received placebo and converted to CDMS during ITP entered in OLMP and received RNF subcutaneously at a dose of 44 mcg three times a week for up to 96 weeks. Due to trial termination, the OLMP duration was reduced for some participants.

	Description
Cladribine 5.25 mg/kg, Rebif, Cladribine 3.5 mg/kg (LTFU)	Participants who received cladribine 5.25 mg/kg and did not convert to CDMS during ITP, entered in long-term follow-up (LTFU) period. Participants who converted to McDonald multiple sclerosis (MS) during ITP or during LTFU period received open-label cladribine tablets (3.5 mg/kg) during LTFU period. Participants who converted to CDMS during LTFU received RNF subcutaneously at a dose of 44 mcg three times a week for the remaining LTFU period. Under the original study design, total duration of LTFU period was up to 96 weeks. The LTFU duration was reduced due to trial termination. Following the notice of trial termination, no further open label cladribine treatment was administered during the LTFU.
Cladribine 3.5 mg/kg, Rebif, Cladribine 3.5 mg/kg (LTFU)	Participants who received cladribine 3.5 mg/kg and did not convert to CDMS during ITP, entered in long-term follow-up (LTFU) period. Participants who converted to McDonald multiple sclerosis (MS) during ITP or during LTFU period received open-label cladribine tablets (3.5 mg/kg) during LTFU period. Participants who converted to CDMS during LTFU received RNF subcutaneously at a dose of 44 mcg three times a week for the remaining LTFU period. Under the original study design, total duration of LTFU period was up to 96 weeks. The LTFU duration was reduced due to trial termination. Following the notice of trial termination, no further open label cladribine treatment was administered during the LTFU.
Placebo, Rebif, Cladribine 3.5 mg/kg (LTFU)	Participants who received placebo and did not convert to CDMS during ITP, entered in long-term follow-up (LTFU) period. Participants who converted to McDonald multiple sclerosis (MS) during ITP or during LTFU period received open-label cladribine tablets (3.5 mg/kg) during LTFU period. Participants who converted to CDMS during LTFU received RNF subcutaneously at a dose of 44 mcg three times a week for the remaining LTFU period. Under the original study design, total duration of LTFU period was up to 96 weeks. The LTFU duration was reduced due to trial termination. Following the notice of trial termination, no further open label cladribine treatment was administered during the LTFU.
Cladribine 5.25 mg/kg, Rebif (LTFU)	Participants who received cladribine 5.25 mg/kg and did not convert to CDMS during ITP, entered in LTFU period. Participants who did not convert to McDonald MS during ITP did not receive any treatment during LTFU period. Participants who converted to CDMS during LTFU period received RNF subcutaneously at a dose of 44 mcg three times a week for the remaining LTFU period. Under the original study design, total duration of LTFU period was up to 96 weeks. The LTFU duration was reduced due to trial termination. Following the notice of trial termination, no further open label cladribine treatment was administered during the LTFU.
Cladribine 3.5 mg/kg, Rebif (LTFU)	Participants who received cladribine 3.5 mg/kg and did not convert to CDMS during ITP, entered in LTFU period. Participants who did not convert to McDonald MS during ITP did not receive any treatment during LTFU period. Participants who converted to CDMS during LTFU period received RNF subcutaneously at a dose of 44 mcg three times a week for the remaining LTFU period. Under the original study design, total duration of LTFU period was up to 96 weeks. The LTFU duration was reduced due to trial termination. Following the notice of trial termination, no further open label cladribine treatment was administered during the LTFU.
Placebo, Rebif (LTFU)	Participants who received placebo and did not convert to CDMS during ITP, entered in LTFU period. Participants who did not convert to McDonald MS during ITP did not receive any treatment during LTFU period. Participants who convert to CDMS during LTFU period received RNF subcutaneously at a dose of 44 mcg three times a week for the remaining LTFU period. Under the original study design, total duration of LTFU period was up to 96 weeks. The LTFU duration was reduced due to trial termination. Following the notice of trial termination, no further open label cladribine treatment was administered during the LTFU.

ITP (Up to 96 Weeks)

	Cladribine 5.25 mg/ kg (ITP)	Cladribine 3.5 mg/ kg (ITP)	Placebo (ITP)	Cladribine 5.25 mg/ kg, Rebif (OLMP)	Cladribine 3.5 mg/ kg, Rebif (OLMP)	Placebo, Rebif (OLMP)
Started	205	206	206	0	0	0
Treated	204	206	206	0	0	0
Completed	104	131	104	0	0	0
Not Completed	101	75	102	0	0	0
Adverse Event	20	10	5	0	0	0
Lost to Follow-up	0	0	2	0	0	0
Randomized but not treated	1	0	0	0	0	0
Converted to CDMS	30	27	71	0	0	0
Unspecified	50	38	24	0	0	0

	Cladribine 5.25 mg/ kg, Rebif, Cladribine 3.5 mg/ kg (LTFU)	Cladribine 3.5 mg/ kg, Rebif, Cladribine 3.5 mg/ kg (LTFU)	Placebo, Rebif, Cladribine 3.5 mg/ kg (LTFU)	Cladribine 5.25 mg/kg, Rebif (LTFU)	Cladribine 3.5 mg/kg, Rebif (LTFU)	Placebo, Rebif (LTFU)
Started	0	0	0	0	0	0
Treated	0	0	0	0	0	0
Completed	0	0	0	0	0	0
Not Completed	0	0	0	0	0	0
Adverse Event	0	0	0	0	0	0
Lost to Follow-up	0	0	0	0	0	0
Randomized but not treated	0	0	0	0	0	0
Converted to CDMS	0	0	0	0	0	0
Unspecified	0	0	0	0	0	0

OLMP

	Cladribine 5.25 mg/ kg (ITP)	Cladribine 3.5 mg/ kg (ITP)	Placebo (ITP)	Cladribine 5.25 mg/ kg, Rebif (OLMP)	Cladribine 3.5 mg/ kg, Rebif (OLMP)	Placebo, Rebif (OLMP)
Started	0	0	0	24	25	60
Completed	0	0	0	6	2	7
Not Completed	0	0	0	18	23	53
Adverse Event	0	0	0	2	2	5
Death	0	0	0	0	1	0
Lost to Follow-up	0	0	0	1	0	0
Disease progression	0	0	0	0	0	4
Unspecified	0	0	0	15	20	44

	Cladribine 5.25 mg/ kg, Rebif, Cladribine 3.5 mg/ kg (LTFU)	Cladribine 3.5 mg/ kg, Rebif, Cladribine 3.5 mg/ kg (LTFU)	Placebo, Rebif, Cladribine 3.5 mg/ kg (LTFU)	Cladribine 5.25 mg/kg, Rebif (LTFU)	Cladribine 3.5 mg/kg, Rebif (LTFU)	Placebo, Rebif (LTFU)
Started	0	0	0	0	0	0
Completed	0	0	0	0	0	0
Not Completed	0	0	0	0	0	0
Adverse Event	0	0	0	0	0	0
Death	0	0	0	0	0	0
Lost to Follow-up	0	0	0	0	0	0
Disease progression	0	0	0	0	0	0
Unspecified	0	0	0	0	0	0

LTFU (With Cladribine Treatment)

	Cladribine 5.25 mg/ kg (ITP)	Cladribine 3.5 mg/ kg (ITP)	Placebo (ITP)	Cladribine 5.25 mg/ kg, Rebif (OLMP)	Cladribine 3.5 mg/ kg, Rebif (OLMP)	Placebo, Rebif (OLMP)
Started	0	0	0	0	0	0
Completed	0	0	0	0	0	0
Not Completed	0	0	0	0	0	0
Adverse Event	0	0	0	0	0	0
Lost to Follow-up	0	0	0	0	0	0
Unspecified	0	0	0	0	0	0

	Cladribine 5.25 mg/ kg, Rebif, Cladribine 3.5 mg/ kg (LTFU)	Cladribine 3.5 mg/ kg, Rebif, Cladribine 3.5 mg/ kg (LTFU)	Placebo, Rebif, Cladribine 3.5 mg/ kg (LTFU)	Cladribine 5.25 mg/kg, Rebif (LTFU)	Cladribine 3.5 mg/kg, Rebif (LTFU)	Placebo, Rebif (LTFU)
Started	9	9	17	0	0	0
Completed	0	0	0	0	0	0
Not Completed	9	9	17	0	0	0
Adverse Event	0	1	0	0	0	0
Lost to Follow-up	0	0	1	0	0	0
Unspecified	9	8	16	0	0	0

LTFU (No Cladribine Treatment)

	Cladribine 5.25 mg/ kg (ITP)	Cladribine 3.5 mg/ kg (ITP)	Placebo (ITP)	Cladribine 5.25 mg/ kg, Rebif (OLMP)	Cladribine 3.5 mg/ kg, Rebif (OLMP)	Placebo, Rebif (OLMP)
Started	0	0	0	0	0	0
Completed	0	0	0	0	0	0
Not Completed	0	0	0	0	0	0

	Cladribine 5.25 mg/ kg (ITP)	Cladribine 3.5 mg/ kg (ITP)	Placebo (ITP)	Cladribine 5.25 mg/ kg, Rebif (OLMP)	Cladribine 3.5 mg/ kg, Rebif (OLMP)	Placebo, Rebif (OLMP)
Unspecified	0	0	0	0	0	0

	Cladribine 5.25 mg/ kg, Rebif, Cladribine 3.5 mg/ kg (LTFU)	Cladribine 3.5 mg/ kg, Rebif, Cladribine 3.5 mg/ kg (LTFU)	Placebo, Rebif, Cladribine 3.5 mg/ kg (LTFU)	Cladribine 5.25 mg/kg, Rebif (LTFU)	Cladribine 3.5 mg/kg, Rebif (LTFU)	Placebo, Rebif (LTFU)
Started	0	0	0	34	36	14
Completed	0	0	0	0	0	0
Not Completed	0	0	0	34	36	14
Unspecified	0	0	0	34	36	14

Baseline Characteristics

Analysis Population Description

The intent-to-treat (ITT) population included all randomized participants who received at least 1 dose of ITP study medication (cladribine or placebo).

Reporting Groups

	Description
Cladribine 5.25 mg/kg	Cladribine tablets administered as cumulative dose of 0.875 mg/kg over a course of 5 consecutive days at Weeks 1, 5, 9, 13, 48, and 52 resulting in total cladribine dose of 5.25 mg/kg during the ITP of 96 weeks or until CDMS conversion, whichever occurred first. Participants who converted to CDMS during ITP entered OLMP and received RNF subcutaneously at a dose of 44 mcg three times a week for up to 96 weeks. Participants who did not convert to CDMS during ITP, entered in (LTFU period. Participants who converted to McDonald MS during ITP or during LTFU period received open-label cladribine tablets (3.5 mg/kg) during LTFU period. Participants who did not convert to McDonald MS during ITP did not receive any treatment during LTFU period. Participants who converted to CDMS during LTFU received RNF subcutaneously at a dose of 44 mcg three times a week for the remaining LTFU period.

	Description
Cladribine 3.5 mg/kg	Cladribine tablets administered as cumulative dose of 0.875 mg/kg over a course of 5 consecutive days at Weeks 1, 5, 48, 52 and placebo matched to cladribine tablets was administered at Week 9 and 13 resulting in total cladribine dose of 3.5 mg/kg during the ITP of 96 weeks or until CDMS conversion, whichever occurred first. Participants who converted to CDMS during ITP entered OLMP and received RNF subcutaneously at a dose of 44 mcg three times a week for up to 96 weeks. Participants who did not convert to CDMS during ITP, entered in (LTFU period. Participants who converted to McDonald MS during ITP or during LTFU period received open-label cladribine tablets (3.5 mg/kg) during LTFU period. Participants who did not convert to McDonald MS during ITP did not receive any study treatment during LTFU period. Participants who converted to CDMS during LTFU received RNF subcutaneously at a dose of 44 mcg three times a week for the remaining LTFU period.
Placebo	Placebo matched to cladribine tablets administered over a course of 5 consecutive days at Weeks 1, 5, 9, 13, 48 and 52 during the ITP of 96 weeks or until CDMS conversion, whichever occurred first. Participants who converted to CDMS during ITP entered OLMP and received RNF subcutaneously at a dose of 44 mcg three times a week for up to 96 weeks. Participants who did not convert to CDMS during ITP, entered in LTFU period. Participants who converted to McDonald MS during ITP or during LTFU period received open-label cladribine tablets (3.5 mg/kg) during LTFU period. Participants who did not convert to McDonald MS during ITP did not receive any study treatment during LTFU period. Participants who converted to CDMS during LTFU received RNF subcutaneously at a dose of 44 mcg three times a week for the remaining LTFU period.

Baseline Measures

	Cladribine 5.25 mg/kg	Cladribine 3.5 mg/kg	Placebo	Total
Number of Participants	204	206	206	616
Age, Continuous [units: years] Mean (Standard Deviation)	31.9 (8.8)	31.7 (9.1)	32.2 (8.2)	31.9 (8.7)
Age, Customized [units: participants]				
Greater than or equal to 30 years	111	110	113	334
Less than 30 years	93	96	93	282
Gender, Male/Female [units: participants]				
Female	132	130	138	400
Male	72	76	68	216

	Cladribine 5.25 mg/kg	Cladribine 3.5 mg/kg	Placebo	Total
Expanded disability status scale (EDSS) score [1] [units: units on scale] Mean (Standard Deviation)	1.6 (0.9)	1.6 (0.9)	1.7 (0.9)	1.6 (0.9)
Number of Time Constant 1 (T1) Gadolinium Enhanced (Gd +) Lesions [units: lesions] Mean (Standard Deviation)	1.8 (5.8)	1.5 (4.5)	0.9 (2.5)	1.4 (4.5)
Number of Time constant 2 (T2) Lesions [units: lesions] Mean (Standard Deviation)	29.7 (29.6)	26.8 (28.3)	26.3 (27.4)	27.6 (28.4)
Number of T1 Hypointense Lesions [units: lesions] Mean (Standard Deviation)	8.0 (11.7)	7.3 (12.2)	7.0 (8.6)	7.4 (10.9)

[1] Expanded disability status scale (EDSS) assesses disability in 8 functional systems. An overall score ranging from 0 (normal) to 10 (death due to MS) was calculated.

Outcome Measures

1. Primary Outcome Measure:

Measure Title	Time to Clinically Definite Multiple Sclerosis (CDMS) Conversion Represented by Kaplan-Meier Estimates of the Cumulative Percentage of Participants With CDMS
Measure Description	Clinically definite multiple sclerosis (CDMS) according to the Poser criteria is defined as the occurrence of a second attack or a sustained increase in the expanded disability status scale (EDSS) Score. EDSS assesses disability in 8 functional systems. An overall score ranging from 0 (normal) to 10 (death due to MS) was calculated. Sustained EDSS progression was defined as an increase in the EDSS score of greater than or equal to (>=) 1 point if baseline EDSS was between >= 1.0 and less than or equal to (=<) 4.5; or >= 1.5 points if baseline EDSS was 0, or >= 0.5 if baseline EDSS >= 5.0 over a period of at least 3 months. Kaplan-Meier estimates were provided for of the cumulative (cum.) percentage (%) of participants with CDMS over time. The probability of patients remaining event-free over time (from randomization) in each of the three treatment groups was displayed in the form of survival curves estimated using the non-parametric Kaplan-Meier method.
Time Frame	Baseline up to Week 96
Safety Issue?	No

Analysis Population Description

The intent-to-treat (ITT) population included all randomized participants who received at least 1 dose of ITP study medication (cladribine or placebo).

Reporting Groups

	Description
Cladribine 5.25 mg/kg (ITP)	Cladribine tablets administered as cumulative dose of 0.875 mg/kg over a course of 5 consecutive days at Weeks 1, 5, 9, 13, 48, and 52 resulting in total cladribine dose of 5.25 mg/kg during the ITP of 96 weeks or until CDMS conversion, whichever occurred first.
Cladribine 3.5 mg/kg (ITP)	Cladribine tablets administered as cumulative dose of 0.875 mg/kg over a course of 5 consecutive days at Weeks 1, 5, 48, 52 and placebo matched to cladribine tablets was administered at Week 9 and 13 resulting in total cladribine dose of 3.5 mg/kg during the ITP of 96 weeks or until CDMS conversion, whichever occurred first.
Placebo (ITP)	Placebo matched to cladribine tablets administered over a course of 5 consecutive days at Weeks 1, 5, 9, 13, 48 and 52 during the ITP of 96 weeks or until CDMS conversion, whichever occurred first.

Measured Values

	Cladribine 5.25 mg/kg (ITP)	Cladribine 3.5 mg/kg (ITP)	Placebo (ITP)
Number of Participants Analyzed	204	206	206
Time to Clinically Definite Multiple Sclerosis (CDMS) Conversion Represented by Kaplan-Meier Estimates of the Cumulative Percentage of Participants With CDMS [units: Cum. % of participants with CDMS]	15.9	14.0	38.0

Statistical Analysis 1 for Time to Clinically Definite Multiple Sclerosis (CDMS) Conversion Represented by Kaplan-Meier Estimates of the Cumulative Percentage of Participants With CDMS

Statistical Analysis Overview	Comparison Groups	Cladribine 5.25 mg/kg (ITP), Placebo (ITP)
	Comments	[Not specified]
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]

Statistical Test of Hypothesis	P-Value	0.0001
	Comments	The treatment effect was also assessed by hazard ratios using the Cox's proportional hazards model.
	Method	Other [two-sided Wald test]

	Comments	[Not specified]

Method of Estimation	Estimation Parameter	Hazard Ratio (HR)
	Estimated Value	0.381
	Confidence Interval	(2-Sided) 95% 0.249 to 0.584
	Estimation Comments	[Not specified]

Statistical Analysis 2 for Time to Clinically Definite Multiple Sclerosis (CDMS) Conversion Represented by Kaplan-Meier Estimates of the Cumulative Percentage of Participants With CDMS

Statistical Analysis Overview	Comparison Groups	Cladribine 3.5 mg/kg (ITP), Placebo (ITP)
	Comments	[Not specified]
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]

Statistical Test of Hypothesis	P-Value	< 0.0001
	Comments	The treatment effect was also assessed by hazard ratios using the Cox's proportional hazards model.
	Method	Other [two-sided Wald test]
	Comments	[Not specified]

Method of Estimation	Estimation Parameter	Hazard Ratio (HR)
	Estimated Value	0.327
	Confidence Interval	(2-Sided) 95% 0.210 to 0.509
	Estimation Comments	[Not specified]

2. Secondary Outcome Measure:

Measure Title	Time to Develop Multiple Sclerosis (MS) Conversion According to the Revised McDonald Criteria (2005) Represented by Kaplan-Meier Estimates of the Cumulative Percentage of Participants With McDonald MS

Measure Description	The McDonald criteria use dissemination in time and space established by magnetic resonance imaging (MRI) findings to provide a clinical diagnosis for MS. Dissemination in time is established by a new time constant 2 (T2) or gadolinium enhanced (Gd+) lesion found on a repeat MRI. Dissemination in space is established by the presence of any 3 of the following: 1 Gd+ lesion or 9 T2 bright lesions if there is no enhancement; greater than or equal to 1 infratentorial lesion; greater than or equal to 1 juxtacortical lesion; greater than or equal to 3 periventricular lesions. Kaplan-Meier estimates were provided for the cum. % of participants with McDonald MS over time.
Time Frame	Baseline up to Week 96
Safety Issue?	No

Analysis Population Description

The ITT population included all randomized participants who received at least 1 dose of ITP study medication (cladribine or placebo).

Reporting Groups

	Description
Cladribine 5.25 mg/kg (ITP)	Cladribine tablets administered as cumulative dose of 0.875 mg/kg over a course of 5 consecutive days at Weeks 1, 5, 9, 13, 48, and 52 resulting in total cladribine dose of 5.25 mg/kg during the ITP of 96 weeks or until CDMS conversion, whichever occurred first.
Cladribine 3.5 mg/kg (ITP)	Cladribine tablets administered as cumulative dose of 0.875 mg/kg over a course of 5 consecutive days at Weeks 1, 5, 48, 52 and placebo matched to cladribine tablets was administered at Week 9 and 13 resulting in total cladribine dose of 3.5 mg/kg during the ITP of 96 weeks or until CDMS conversion, whichever occurred first.
Placebo (ITP)	Placebo matched to cladribine tablets administered over a course of 5 consecutive days at Weeks 1, 5, 9, 13, 48 and 52 during the ITP of 96 weeks or until CDMS conversion, whichever occurred first.

Measured Values

	Cladribine 5.25 mg/kg (ITP)	Cladribine 3.5 mg/kg (ITP)	Placebo (ITP)
Number of Participants Analyzed	204	206	206
Time to Develop Multiple Sclerosis (MS) Conversion According to the Revised McDonald Criteria (2005) Represented by Kaplan-Meier Estimates of the Cumulative Percentage of Participants With McDonald MS [units: Cum. % of participants with McDonald MS]	51.4	56.1	87.1

Statistical Analysis 1 for Time to Develop Multiple Sclerosis (MS) Conversion According to the Revised McDonald Criteria (2005) Represented by Kaplan-Meier Estimates of the Cumulative Percentage of Participants With McDonald MS

Statistical Analysis Overview	Comparison Groups	Cladribine 5.25 mg/kg (ITP), Placebo (ITP)
	Comments	[Not specified]
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]

Statistical Test of Hypothesis	P-Value	< 0.0001
	Comments	The treatment effect was also assessed by hazard ratios using the Cox's proportional hazards model.
	Method	Other [two-sided Wald test]
	Comments	[Not specified]

Method of Estimation	Estimation Parameter	Hazard Ratio (HR)
	Estimated Value	0.425
	Confidence Interval	(2-Sided) 95% 0.331 to 0.546
	Estimation Comments	[Not specified]

Statistical Analysis 2 for Time to Develop Multiple Sclerosis (MS) Conversion According to the Revised McDonald Criteria (2005) Represented by Kaplan-Meier Estimates of the Cumulative Percentage of Participants With McDonald MS

Statistical Analysis Overview	Comparison Groups	Cladribine 3.5 mg/kg (ITP), Placebo (ITP)
	Comments	[Not specified]
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]

Statistical Test of Hypothesis	P-Value	< 0.0001
	Comments	The treatment effect was also assessed by hazard ratios using the Cox's proportional hazards model.
	Method	Other [two-sided Wald test]
	Comments	[Not specified]

Method of Estimation	Estimation Parameter	Hazard Ratio (HR)
	Estimated Value	0.496
	Confidence Interval	(2-Sided) 95% 0.389 to 0.631
	Estimation Comments	[Not specified]

3. Secondary Outcome Measure:

Measure Title	Number of Combined Unique Active (CUA) Lesions, New or Enlarging Time Constant 2 (T2) Lesions, and New or Persisting Time Constant 1 (T1) Gadolinium Enhanced (Gd+) Lesions Per Participant Per Scan
Measure Description	Number of CUA lesions, new or enlarging T2 lesions, and new or persisting T1 Gd+ lesions were measured by using magnetic resonance imaging (MRI) scans.
Time Frame	Week 96
Safety Issue?	No

Analysis Population Description

The ITT population included all randomized participants who received at least 1 dose of ITP study medication (cladribine or placebo).

Reporting Groups

	Description
Cladribine 5.25 mg/kg (ITP)	Cladribine tablets administered as cumulative dose of 0.875 mg/kg over a course of 5 consecutive days at Weeks 1, 5, 9, 13, 48, and 52 resulting in total cladribine dose of 5.25 mg/kg during the ITP of 96 weeks or until CDMS conversion, whichever occurred first.
Cladribine 3.5 mg/kg (ITP)	Cladribine tablets administered as cumulative dose of 0.875 mg/kg over a course of 5 consecutive days at Weeks 1, 5, 48, 52 and placebo matched to cladribine tablets was administered at Week 9 and 13 resulting in total cladribine dose of 3.5 mg/kg during the ITP of 96 weeks or until CDMS conversion, whichever occurred first.
Placebo (ITP)	Placebo matched to cladribine tablets administered over a course of 5 consecutive days at Weeks 1, 5, 9, 13, 48 and 52 during the ITP of 96 weeks or until CDMS conversion, whichever occurred first.

Measured Values

	Cladribine 5.25 mg/kg (ITP)	Cladribine 3.5 mg/kg (ITP)	Placebo (ITP)
Number of Participants Analyzed	204	204	206
Number of Combined Unique Active (CUA) Lesions, New or Enlarging Time Constant 2 (T2) Lesions, and New or Persisting Time Constant 1 (T1) Gadolinium Enhanced (Gd+) Lesions Per Participant Per Scan			

	Cladribine 5.25 mg/kg (ITP)	Cladribine 3.5 mg/kg (ITP)	Placebo (ITP)
[units: Lesions] Mean (Standard Deviation)			
CUA lesions	1.20 (5.79)	0.65 (1.80)	2.13 (2.87)
New or persisting T1 Gd+ lesions	0.61 (5.33)	0.29 (0.97)	0.97 (1.62)
New or enlarging T2 lesions	0.62 (1.90)	0.40 (1.12)	1.19 (1.88)

4. Secondary Outcome Measure:

Measure Title	Number of Participants With Adverse Events (AEs) and Serious Adverse Events (SAEs)
Measure Description	An 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. 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. Number of participants with AEs includes number of participants with both serious adverse events (SAEs) and non-SAEs.
Time Frame	Baseline up to Week 96
Safety Issue?	Yes

Analysis Population Description

The ITT population included all randomized participants who received at least 1 dose of ITP study medication (cladribine or placebo) and had at least one safety assessment during the ITP.

Reporting Groups

	Description
Cladribine 5.25 mg/kg (ITP)	Cladribine tablets administered as cumulative dose of 0.875 mg/kg over a course of 5 consecutive days at Weeks 1, 5, 9, 13, 48, and 52 resulting in total cladribine dose of 5.25 mg/kg during the ITP of 96 weeks or until CDMS conversion, whichever occurred first.
Cladribine 3.5 mg/kg (ITP)	Cladribine tablets administered as cumulative dose of 0.875 mg/kg over a course of 5 consecutive days at Weeks 1, 5, 48, 52 and placebo matched to cladribine tablets was administered at Week 9 and 13 resulting in total cladribine dose of 3.5 mg/kg during the ITP of 96 weeks or until CDMS conversion, whichever occurred first.
Placebo (ITP)	Placebo matched to cladribine tablets administered over a course of 5 consecutive days at Weeks 1, 5, 9, 13, 48 and 52 during the ITP of 96 weeks or until CDMS conversion, whichever occurred first.

Measured Values

	Cladribine 5.25 mg/kg (ITP)	Cladribine 3.5 mg/kg (ITP)	Placebo (ITP)
Number of Participants Analyzed	204	206	206
Number of Participants With Adverse Events (AEs) and Serious Adverse Events (SAEs) [units: Participants]			
AEs	165	168	162
SAEs	10	23	21

Reported Adverse Events

Time Frame	Baseline up to 144 weeks (96 weeks [ITP] and 48 weeks [OLMP or LFTU])
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
Cladribine 5.25 mg/kg (ITP)	Cladribine tablets administered as cumulative dose of 0.875 milligram per kilogram (mg/kg) over a course of 5 consecutive days at Weeks 1, 5, 9, 13, 48, and 52 resulting in total cladribine dose of 5.25 mg/kg during the initial treatment period (ITP) of 96 weeks or until clinically definite multiple sclerosis (CDMS) conversion, whichever occurred first.
Cladribine 3.5 mg/kg (ITP)	Cladribine tablets administered as cumulative dose of 0.875 mg/kg over a course of 5 consecutive days at Weeks 1, 5, 48, 52 and placebo matched to cladribine tablets was administered at Week 9 and 13 resulting in total cladribine dose of 3.5 mg/kg during the ITP of 96 weeks or until CDMS conversion, whichever occurred first.
Placebo (ITP)	Placebo matched to cladribine tablets administered over a course of 5 consecutive days at Weeks 1, 5, 9, 13, 48 and 52 during the ITP of 96 weeks or until CDMS conversion, whichever occurred first.
Cladribine 5.25 mg/kg, Rebif (OLMP)	Participants who received cladribine 5.25 mg/kg and converted to CDMS during ITP entered in open-label maintenance period (OLMP) and received Rebif® new formulation (RNF) subcutaneously at a dose of 44 microgram (mcg) three times a week up to 96 weeks. Due to trial termination, the OLMP duration was reduced for some participants.

	Description
Cladribine 3.5 mg/kg, Rebif (OLMP)	Participants who received cladribine 3.5 mg/kg and converted to CDMS during ITP entered in OLMP and received RNF subcutaneously at a dose of 44 mcg three times a week up to 96 weeks. Due to trial termination, the OLMP duration was reduced for some participants.
Placebo, Rebif (OLMP)	Participants who received placebo and converted to CDMS during ITP entered in OLMP and received RNF subcutaneously at a dose of 44 mcg three times a week up to 96 weeks. Due to trial termination, the OLMP duration was reduced for some participants.
Cladribine 5.25 mg/kg, Rebif, Cladribine 3.5 mg/kg (LTFU)	Participants who received cladribine 5.25 mg/kg and did not convert to CDMS during ITP, entered in long-term follow-up (LTFU) period. Participants who converted to McDonald multiple sclerosis (MS) during ITP or during LTFU period received open-label cladribine tablets (3.5 mg/kg) during LTFU period . Participants who did not convert to McDonald MS during ITP did not receive any treatment during LTFU period. Participants who converted to CDMS during LTFU received RNF subcutaneously at a dose of 44 mcg three times a week for the remaining LTFU period. Under the original study design, total duration of LTFU period was up to 96 weeks. The LTFU duration was reduced due to trial termination. Following the notice of trial termination, no further open label cladribine treatment was administered during the LTFU.
Cladribine 3.5 mg/kg, Rebif, Cladribine 3.5 mg/kg (LTFU)	Participants who received cladribine 3.5 mg/kg and did not convert to CDMS during ITP, entered in long-term follow-up (LTFU) period. Participants who converted to McDonald multiple sclerosis (MS) during ITP or during LTFU period received open-label cladribine tablets (3.5 mg/kg) during LTFU period . Participants who did not convert to McDonald MS during ITP did not receive any treatment during LTFU period. Participants who converted to CDMS during LTFU received RNF subcutaneously at a dose of 44 mcg three times a week for the remaining LTFU period. Under the original study design, total duration of LTFU period was up to 96 weeks. The LTFU duration was reduced due to trial termination. Following the notice of trial termination, no further open label cladribine treatment was administered during the LTFU.
Placebo, Rebif, Cladribine 3.5 mg/kg (LTFU)	Participants who received placebo and did not convert to CDMS during ITP, entered in long-term follow-up (LTFU) period. Participants who converted to McDonald multiple sclerosis (MS) during ITP or during LTFU period received open-label cladribine tablets (3.5 mg/kg) during LTFU period . Participants who did not convert to McDonald MS during ITP did not receive any treatment during LTFU period. Participants who converted to CDMS during LTFU received RNF subcutaneously at a dose of 44 mcg three times a week for the remaining LTFU period. Under the original study design, total duration of LTFU period was up to 96 weeks. The LTFU duration was reduced due to trial termination. Following the notice of trial termination, no further open label cladribine treatment was administered during the LTFU.
Cladribine 5.25 mg/kg, Rebif (LTFU)	Participants who received cladribine 5.25 mg/kg and did not convert to CDMS during ITP, entered in LTFU period. Participants who did not convert to McDonald MS during ITP did not receive any treatment during LTFU period. Participants who converted to CDMS during LTFU period received RNF subcutaneously at a dose of 44 mcg three times a week for the remaining LTFU period. Under the original study design, total duration of LTFU period was up to 96 weeks. The LTFU duration was reduced due to trial termination. Following the notice of trial termination, no further open label cladribine treatment was administered during the LTFU.

	Description
Cladribine 3.5 mg/kg, Rebif (LTFU)	Participants who received cladribine 3.5 mg/kg and did not convert to CDMS during ITP, entered in LTFU period. Participants who did not convert to McDonald MS during ITP did not receive any treatment during LTFU period. Participants who converted to CDMS during LTFU period received RNF subcutaneously at a dose of 44 mcg three times a week for the remaining LTFU period. Under the original study design, total duration of LTFU period was up to 96 weeks. The LTFU duration was reduced due to trial termination. Following the notice of trial termination, no further open label cladribine treatment was administered during the LTFU.
Placebo, Rebif (LTFU)	Participants who received placebo and did not convert to CDMS during ITP, entered in LTFU period. Participants who did not convert to McDonald MS during ITP did not receive any treatment during LTFU period. Participants who convert to CDMS during LTFU period received RNF subcutaneously at a dose of 44 mcg three times a week for the remaining LTFU period. Under the original study design, total duration of LTFU period was up to 96 weeks. The LTFU duration was reduced due to trial termination. Following the notice of trial termination, no further open label cladribine treatment was administered during the LTFU.

Serious Adverse Events

	Cladribine 5.25 mg/kg (ITP)	Cladribine 3.5 mg/kg (ITP)	Placebo (ITP)	Cladribine 5.25 mg/kg, Rebif (OLMP)	Cladribine 3.5 mg/kg, Rebif (OLMP)	Placebo, Rebif (OLMP)
	Affected/ At Risk (%)	Affected/ At Risk (%)	Affected/ At Risk (%)	Affected/ At Risk (%)	Affected/ At Risk (%)	Affected/ At Risk (%)
Total	10/204 (4.9%)	23/206 (11.17%)	21/206 (10.19%)	1/24 (4.17%)	4/25 (16%)	4/60 (6.67%)
Blood and lymphatic system disorders						
Lymphopenia [A] *	1/204 (0.49%)	0/206 (0%)	0/206 (0%)	0/24 (0%)	0/25 (0%)	0/60 (0%)
Cardiac disorders						
Atrial fibrillation [A] *	1/204 (0.49%)	0/206 (0%)	0/206 (0%)	0/24 (0%)	0/25 (0%)	0/60 (0%)
Cardio-respiratory arrest [A] *	0/204 (0%)	0/206 (0%)	0/206 (0%)	0/24 (0%)	1/25 (4%)	0/60 (0%)
Myocarditis [A] *	1/204 (0.49%)	0/206 (0%)	0/206 (0%)	0/24 (0%)	0/25 (0%)	0/60 (0%)
Endocrine disorders						
Autoimmune thyroiditis [A] *	1/204 (0.49%)	0/206 (0%)	0/206 (0%)	0/24 (0%)	0/25 (0%)	0/60 (0%)
Hyperprolactinaemia [A] *	0/204 (0%)	0/206 (0%)	0/206 (0%)	0/24 (0%)	1/25 (4%)	0/60 (0%)
Hyperthyroidism [A] *	0/204 (0%)	0/206 (0%)	1/206 (0.49%)	0/24 (0%)	0/25 (0%)	0/60 (0%)
Eye disorders						

	Cladribine 5.25 mg/kg (ITP)	Cladribine 3.5 mg/kg (ITP)	Placebo (ITP)	Cladribine 5.25 mg/kg, Rebif (OLMP)	Cladribine 3.5 mg/kg, Rebif (OLMP)	Placebo, Rebif (OLMP)
	Affected/ At Risk (%)	Affected/ At Risk (%)	Affected/ At Risk (%)	Affected/ At Risk (%)	Affected/ At Risk (%)	Affected/ At Risk (%)
Retinal vein thrombosis [A] *	0/204 (0%)	0/206 (0%)	1/206 (0.49%)	0/24 (0%)	0/25 (0%)	0/60 (0%)
Gastrointestinal disorders						
Gastric ulcer perforation [A] *	0/204 (0%)	0/206 (0%)	0/206 (0%)	0/24 (0%)	1/25 (4%)	0/60 (0%)
Mechanical ileus [A] *	0/204 (0%)	0/206 (0%)	1/206 (0.49%)	0/24 (0%)	0/25 (0%)	0/60 (0%)
General disorders						
Injection site necrosis [A] *	0/204 (0%)	0/206 (0%)	0/206 (0%)	0/24 (0%)	0/25 (0%)	1/60 (1.67%)
Infections and infestations						
Anogenital warts [A] *	0/204 (0%)	0/206 (0%)	1/206 (0.49%)	0/24 (0%)	0/25 (0%)	0/60 (0%)
Erysipelas [A] *	0/204 (0%)	0/206 (0%)	0/206 (0%)	0/24 (0%)	0/25 (0%)	1/60 (1.67%)
Herpes zoster [A] *	1/204 (0.49%)	0/206 (0%)	0/206 (0%)	0/24 (0%)	0/25 (0%)	0/60 (0%)
Pilonidal cyst [A] *	0/204 (0%)	1/206 (0.49%)	0/206 (0%)	0/24 (0%)	0/25 (0%)	0/60 (0%)
Injury, poisoning and procedural complications						
Accidental overdose [A] *	1/204 (0.49%)	0/206 (0%)	0/206 (0%)	0/24 (0%)	0/25 (0%)	0/60 (0%)
Back injury [A] *	0/204 (0%)	0/206 (0%)	1/206 (0.49%)	0/24 (0%)	0/25 (0%)	0/60 (0%)
Clavicle fracture [A] *	0/204 (0%)	0/206 (0%)	1/206 (0.49%)	0/24 (0%)	0/25 (0%)	0/60 (0%)
Fall [A] *	0/204 (0%)	1/206 (0.49%)	0/206 (0%)	0/24 (0%)	0/25 (0%)	0/60 (0%)
Gun shot wound [A] *	0/204 (0%)	1/206 (0.49%)	0/206 (0%)	0/24 (0%)	0/25 (0%)	0/60 (0%)
Injury [A] *	0/204 (0%)	0/206 (0%)	1/206 (0.49%)	0/24 (0%)	0/25 (0%)	0/60 (0%)
Joint sprain [A] *	0/204 (0%)	0/206 (0%)	1/206 (0.49%)	0/24 (0%)	0/25 (0%)	0/60 (0%)
Ligament rupture [A] *	0/204 (0%)	0/206 (0%)	1/206 (0.49%)	0/24 (0%)	0/25 (0%)	0/60 (0%)
Road traffic accident [A] *	0/204 (0%)	0/206 (0%)	2/206 (0.97%)	0/24 (0%)	0/25 (0%)	0/60 (0%)

	Cladribine 5.25 mg/kg (ITP)	Cladribine 3.5 mg/kg (ITP)	Placebo (ITP)	Cladribine 5.25 mg/kg, Rebif (OLMP)	Cladribine 3.5 mg/kg, Rebif (OLMP)	Placebo, Rebif (OLMP)
	Affected/ At Risk (%)	Affected/ At Risk (%)	Affected/ At Risk (%)	Affected/ At Risk (%)	Affected/ At Risk (%)	Affected/ At Risk (%)
Skin injury [A] *	0/204 (0%)	0/206 (0%)	1/206 (0.49%)	0/24 (0%)	0/25 (0%)	0/60 (0%)
Thoracic vertebral fracture [A] *	0/204 (0%)	1/206 (0.49%)	0/206 (0%)	0/24 (0%)	0/25 (0%)	0/60 (0%)
Investigations						
Alanine aminotransferase increased [A] *	0/204 (0%)	1/206 (0.49%)	1/206 (0.49%)	0/24 (0%)	0/25 (0%)	0/60 (0%)
Aspartate aminotransferase increased [A] *	0/204 (0%)	0/206 (0%)	1/206 (0.49%)	0/24 (0%)	0/25 (0%)	0/60 (0%)
Blood amylase increased [A] *	0/204 (0%)	2/206 (0.97%)	0/206 (0%)	0/24 (0%)	0/25 (0%)	0/60 (0%)
Blood creatine phosphokinase increased [A] *	3/204 (1.47%)	11/206 (5.34%)	6/206 (2.91%)	1/24 (4.17%)	0/25 (0%)	0/60 (0%)
Blood potassium increased [A] *	0/204 (0%)	0/206 (0%)	1/206 (0.49%)	0/24 (0%)	0/25 (0%)	0/60 (0%)
Blood uric acid increased [A] *	0/204 (0%)	0/206 (0%)	1/206 (0.49%)	0/24 (0%)	0/25 (0%)	1/60 (1.67%)
Lipase increased [A] *	0/204 (0%)	2/206 (0.97%)	0/206 (0%)	0/24 (0%)	0/25 (0%)	0/60 (0%)
Platelet count decreased [A] *	0/204 (0%)	1/206 (0.49%)	0/206 (0%)	0/24 (0%)	0/25 (0%)	0/60 (0%)
Musculoskeletal and connective tissue disorders						
Arthralgia [A] *	0/204 (0%)	1/206 (0.49%)	0/206 (0%)	0/24 (0%)	0/25 (0%)	0/60 (0%)
Arthropathy [A] *	0/204 (0%)	1/206 (0.49%)	0/206 (0%)	0/24 (0%)	0/25 (0%)	0/60 (0%)
Neck pain [A] *	0/204 (0%)	0/206 (0%)	1/206 (0.49%)	0/24 (0%)	0/25 (0%)	0/60 (0%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)						
Melanocytic naevus [A] *	0/204 (0%)	0/206 (0%)	0/206 (0%)	0/24 (0%)	0/25 (0%)	0/60 (0%)
Papillary thyroid cancer [A] *	0/204 (0%)	1/206 (0.49%)	0/206 (0%)	0/24 (0%)	0/25 (0%)	0/60 (0%)
Pituitary tumour benign [A] *	0/204 (0%)	0/206 (0%)	0/206 (0%)	0/24 (0%)	1/25 (4%)	0/60 (0%)
Skin papilloma [A] *	0/204 (0%)	1/206 (0.49%)	0/206 (0%)	0/24 (0%)	0/25 (0%)	0/60 (0%)
Squamous cell carcinoma of skin [A] *	0/204 (0%)	1/206 (0.49%)	0/206 (0%)	0/24 (0%)	0/25 (0%)	0/60 (0%)

	Cladribine 5.25 mg/kg (ITP)	Cladribine 3.5 mg/kg (ITP)	Placebo (ITP)	Cladribine 5.25 mg/kg, Rebif (OLMP)	Cladribine 3.5 mg/kg, Rebif (OLMP)	Placebo, Rebif (OLMP)
	Affected/ At Risk (%)	Affected/ At Risk (%)	Affected/ At Risk (%)	Affected/ At Risk (%)	Affected/ At Risk (%)	Affected/ At Risk (%)
Thyroid neoplasm [A] *	0/204 (0%)	0/206 (0%)	3/206 (1.46%)	0/24 (0%)	0/25 (0%)	0/60 (0%)
Tonsillar neoplasm benign [A] *	0/204 (0%)	0/206 (0%)	1/206 (0.49%)	0/24 (0%)	0/25 (0%)	0/60 (0%)
Uterine leiomyoma [A] *	1/204 (0.49%)	0/206 (0%)	2/206 (0.97%)	0/24 (0%)	0/25 (0%)	0/60 (0%)
Nervous system disorders						
Cerebral haemorrhage [A] *	1/204 (0.49%)	0/206 (0%)	0/206 (0%)	0/24 (0%)	0/25 (0%)	0/60 (0%)
Pregnancy, puerperium and perinatal conditions						
Abortion spontaneous [A] *	0/204 (0%)	0/206 (0%)	1/206 (0.49%)	0/24 (0%)	0/25 (0%)	0/60 (0%)
Psychiatric disorders						
Delirium [A] *	0/204 (0%)	0/206 (0%)	1/206 (0.49%)	0/24 (0%)	0/25 (0%)	0/60 (0%)
Renal and urinary disorders						
Calculus ureteric [A] *	0/204 (0%)	0/206 (0%)	0/206 (0%)	0/24 (0%)	0/25 (0%)	0/60 (0%)
Calculus urinary [A] *	0/204 (0%)	0/206 (0%)	1/206 (0.49%)	0/24 (0%)	0/25 (0%)	0/60 (0%)
Renal colic [A] *	0/204 (0%)	0/206 (0%)	1/206 (0.49%)	0/24 (0%)	0/25 (0%)	0/60 (0%)
Reproductive system and breast disorders						
Bartholin's cyst [A] *	0/204 (0%)	1/206 (0.49%)	0/206 (0%)	0/24 (0%)	0/25 (0%)	0/60 (0%)
Fibrocystic breast disease [A] *	0/204 (0%)	1/206 (0.49%)	0/206 (0%)	0/24 (0%)	0/25 (0%)	0/60 (0%)
Ovarian cyst [A] *	1/204 (0.49%)	1/206 (0.49%)	1/206 (0.49%)	0/24 (0%)	0/25 (0%)	0/60 (0%)
Respiratory, thoracic and mediastinal disorders						
Nasal cyst [A] *	0/204 (0%)	0/206 (0%)	0/206 (0%)	0/24 (0%)	0/25 (0%)	1/60 (1.67%)
Pulmonary oedema [A] *	1/204 (0.49%)	0/206 (0%)	0/206 (0%)	0/24 (0%)	0/25 (0%)	0/60 (0%)
Tracheal mass [A] *	0/204 (0%)	0/206 (0%)	1/206 (0.49%)	0/24 (0%)	0/25 (0%)	0/60 (0%)
Skin and subcutaneous tissue disorders						

	Cladribine 5.25 mg/kg (ITP)	Cladribine 3.5 mg/kg (ITP)	Placebo (ITP)	Cladribine 5.25 mg/kg, Rebif (OLMP)	Cladribine 3.5 mg/kg, Rebif (OLMP)	Placebo, Rebif (OLMP)
	Affected/ At Risk (%)	Affected/ At Risk (%)	Affected/ At Risk (%)	Affected/ At Risk (%)	Affected/ At Risk (%)	Affected/ At Risk (%)
Psoriasis [A] *	0/204 (0%)	0/206 (0%)	0/206 (0%)	0/24 (0%)	0/25 (0%)	1/60 (1.67%)
Vascular disorders						
Hypertension [A] *	1/204 (0.49%)	0/206 (0%)	0/206 (0%)	0/24 (0%)	0/25 (0%)	0/60 (0%)

* Indicates events were collected by non-systematic methods.
A Term from vocabulary, MedDRA (11.0)

	Cladribine 5.25 mg/kg, Rebif, Cladribine 3.5 mg/kg (LTFU)	Cladribine 3.5 mg/kg, Rebif, Cladribine 3.5 mg/kg (LTFU)	Placebo, Rebif, Cladribine 3.5 mg/kg (LTFU)	Cladribine 5.25 mg/kg, Rebif (LTFU)	Cladribine 3.5 mg/kg, Rebif (LTFU)	Placebo, Rebif (LTFU)
	Affected/ At Risk (%)	Affected/ At Risk (%)	Affected/ At Risk (%)	Affected/ At Risk (%)	Affected/ At Risk (%)	Affected/ At Risk (%)
Total	0/9 (0%)	0/9 (0%)	1/16 (6.25%)	0/34 (0%)	1/36 (2.78%)	0/14 (0%)
Blood and lymphatic system disorders						
Lymphopenia [A] *	0/9 (0%)	0/9 (0%)	0/16 (0%)	0/34 (0%)	0/36 (0%)	0/14 (0%)
Cardiac disorders						
Atrial fibrillation [A] *	0/9 (0%)	0/9 (0%)	0/16 (0%)	0/34 (0%)	0/36 (0%)	0/14 (0%)
Cardio-respiratory arrest [A] *	0/9 (0%)	0/9 (0%)	0/16 (0%)	0/34 (0%)	0/36 (0%)	0/14 (0%)
Myocarditis [A] *	0/9 (0%)	0/9 (0%)	0/16 (0%)	0/34 (0%)	0/36 (0%)	0/14 (0%)
Endocrine disorders						
Autoimmune thyroiditis [A] *	0/9 (0%)	0/9 (0%)	0/16 (0%)	0/34 (0%)	0/36 (0%)	0/14 (0%)
Hyperprolactinaemia [A] *	0/9 (0%)	0/9 (0%)	0/16 (0%)	0/34 (0%)	0/36 (0%)	0/14 (0%)
Hyperthyroidism [A] *	0/9 (0%)	0/9 (0%)	0/16 (0%)	0/34 (0%)	0/36 (0%)	0/14 (0%)
Eye disorders						
Retinal vein thrombosis [A] *	0/9 (0%)	0/9 (0%)	0/16 (0%)	0/34 (0%)	0/36 (0%)	0/14 (0%)

	Cladribine 5.25 mg/kg, Rebif, Cladribine 3.5 mg/kg (LTFU)	Cladribine 3.5 mg/kg, Rebif, Cladribine 3.5 mg/kg (LTFU)	Placebo, Rebif, Cladribine 3.5 mg/kg (LTFU)	Cladribine 5.25 mg/kg, Rebif (LTFU)	Cladribine 3.5 mg/kg, Rebif (LTFU)	Placebo, Rebif (LTFU)
	Affected/ At Risk (%)	Affected/ At Risk (%)	Affected/ At Risk (%)	Affected/ At Risk (%)	Affected/ At Risk (%)	Affected/ At Risk (%)
Gastrointestinal disorders						
Gastric ulcer perforation [A] *	0/9 (0%)	0/9 (0%)	0/16 (0%)	0/34 (0%)	0/36 (0%)	0/14 (0%)
Mechanical ileus [A] *	0/9 (0%)	0/9 (0%)	0/16 (0%)	0/34 (0%)	0/36 (0%)	0/14 (0%)
General disorders						
Injection site necrosis [A] *	0/9 (0%)	0/9 (0%)	0/16 (0%)	0/34 (0%)	0/36 (0%)	0/14 (0%)
Infections and infestations						
Anogenital warts [A] *	0/9 (0%)	0/9 (0%)	0/16 (0%)	0/34 (0%)	0/36 (0%)	0/14 (0%)
Erysipelas [A] *	0/9 (0%)	0/9 (0%)	0/16 (0%)	0/34 (0%)	0/36 (0%)	0/14 (0%)
Herpes zoster [A] *	0/9 (0%)	0/9 (0%)	0/16 (0%)	0/34 (0%)	0/36 (0%)	0/14 (0%)
Pilonidal cyst [A] *	0/9 (0%)	0/9 (0%)	0/16 (0%)	0/34 (0%)	0/36 (0%)	0/14 (0%)
Injury, poisoning and procedural complications						
Accidental overdose [A] *	0/9 (0%)	0/9 (0%)	0/16 (0%)	0/34 (0%)	0/36 (0%)	0/14 (0%)
Back injury [A] *	0/9 (0%)	0/9 (0%)	0/16 (0%)	0/34 (0%)	0/36 (0%)	0/14 (0%)
Clavicle fracture [A] *	0/9 (0%)	0/9 (0%)	0/16 (0%)	0/34 (0%)	0/36 (0%)	0/14 (0%)
Fall [A] *	0/9 (0%)	0/9 (0%)	0/16 (0%)	0/34 (0%)	0/36 (0%)	0/14 (0%)
Gun shot wound [A] *	0/9 (0%)	0/9 (0%)	0/16 (0%)	0/34 (0%)	0/36 (0%)	0/14 (0%)
Injury [A] *	0/9 (0%)	0/9 (0%)	0/16 (0%)	0/34 (0%)	0/36 (0%)	0/14 (0%)
Joint sprain [A] *	0/9 (0%)	0/9 (0%)	0/16 (0%)	0/34 (0%)	0/36 (0%)	0/14 (0%)
Ligament rupture [A] *	0/9 (0%)	0/9 (0%)	0/16 (0%)	0/34 (0%)	0/36 (0%)	0/14 (0%)
Road traffic accident [A] *	0/9 (0%)	0/9 (0%)	0/16 (0%)	0/34 (0%)	0/36 (0%)	0/14 (0%)
Skin injury [A] *	0/9 (0%)	0/9 (0%)	0/16 (0%)	0/34 (0%)	0/36 (0%)	0/14 (0%)

	Cladribine 5.25 mg/kg, Rebif, Cladribine 3.5 mg/kg (LTFU)	Cladribine 3.5 mg/kg, Rebif, Cladribine 3.5 mg/kg (LTFU)	Placebo, Rebif, Cladribine 3.5 mg/kg (LTFU)	Cladribine 5.25 mg/kg, Rebif (LTFU)	Cladribine 3.5 mg/kg, Rebif (LTFU)	Placebo, Rebif (LTFU)
	Affected/ At Risk (%)	Affected/ At Risk (%)	Affected/ At Risk (%)	Affected/ At Risk (%)	Affected/ At Risk (%)	Affected/ At Risk (%)
Thoracic vertebral fracture [A] *	0/9 (0%)	0/9 (0%)	0/16 (0%)	0/34 (0%)	0/36 (0%)	0/14 (0%)
Investigations						
Alanine aminotransferase increased [A] *	0/9 (0%)	0/9 (0%)	0/16 (0%)	0/34 (0%)	0/36 (0%)	0/14 (0%)
Aspartate aminotransferase increased [A] *	0/9 (0%)	0/9 (0%)	0/16 (0%)	0/34 (0%)	0/36 (0%)	0/14 (0%)
Blood amylase increased [A] *	0/9 (0%)	0/9 (0%)	0/16 (0%)	0/34 (0%)	0/36 (0%)	0/14 (0%)
Blood creatine phosphokinase increased [A] *	0/9 (0%)	0/9 (0%)	1/16 (6.25%)	0/34 (0%)	0/36 (0%)	0/14 (0%)
Blood potassium increased [A] *	0/9 (0%)	0/9 (0%)	0/16 (0%)	0/34 (0%)	0/36 (0%)	0/14 (0%)
Blood uric acid increased [A] *	0/9 (0%)	0/9 (0%)	0/16 (0%)	0/34 (0%)	0/36 (0%)	0/14 (0%)
Lipase increased [A] *	0/9 (0%)	0/9 (0%)	0/16 (0%)	0/34 (0%)	0/36 (0%)	0/14 (0%)
Platelet count decreased [A] *	0/9 (0%)	0/9 (0%)	0/16 (0%)	0/34 (0%)	0/36 (0%)	0/14 (0%)
Musculoskeletal and connective tissue disorders						
Arthralgia [A] *	0/9 (0%)	0/9 (0%)	0/16 (0%)	0/34 (0%)	0/36 (0%)	0/14 (0%)
Arthropathy [A] *	0/9 (0%)	0/9 (0%)	0/16 (0%)	0/34 (0%)	0/36 (0%)	0/14 (0%)
Neck pain [A] *	0/9 (0%)	0/9 (0%)	0/16 (0%)	0/34 (0%)	0/36 (0%)	0/14 (0%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)						
Melanocytic naevus [A] *	0/9 (0%)	0/9 (0%)	0/16 (0%)	0/34 (0%)	1/36 (2.78%)	0/14 (0%)
Papillary thyroid cancer [A] *	0/9 (0%)	0/9 (0%)	0/16 (0%)	0/34 (0%)	0/36 (0%)	0/14 (0%)
Pituitary tumour benign [A] *	0/9 (0%)	0/9 (0%)	0/16 (0%)	0/34 (0%)	0/36 (0%)	0/14 (0%)
Skin papilloma [A] *	0/9 (0%)	0/9 (0%)	0/16 (0%)	0/34 (0%)	0/36 (0%)	0/14 (0%)
Squamous cell carcinoma of skin [A] *	0/9 (0%)	0/9 (0%)	0/16 (0%)	0/34 (0%)	0/36 (0%)	0/14 (0%)

	Cladribine 5.25 mg/kg, Rebif, Cladribine 3.5 mg/kg (LTFU)	Cladribine 3.5 mg/kg, Rebif, Cladribine 3.5 mg/kg (LTFU)	Placebo, Rebif, Cladribine 3.5 mg/kg (LTFU)	Cladribine 5.25 mg/kg, Rebif (LTFU)	Cladribine 3.5 mg/kg, Rebif (LTFU)	Placebo, Rebif (LTFU)
	Affected/ At Risk (%)	Affected/ At Risk (%)	Affected/ At Risk (%)	Affected/ At Risk (%)	Affected/ At Risk (%)	Affected/ At Risk (%)
Thyroid neoplasm [A] *	0/9 (0%)	0/9 (0%)	0/16 (0%)	0/34 (0%)	0/36 (0%)	0/14 (0%)
Tonsillar neoplasm benign [A] *	0/9 (0%)	0/9 (0%)	0/16 (0%)	0/34 (0%)	0/36 (0%)	0/14 (0%)
Uterine leiomyoma [A] *	0/9 (0%)	0/9 (0%)	0/16 (0%)	0/34 (0%)	0/36 (0%)	0/14 (0%)
Nervous system disorders						
Cerebral haemorrhage [A] *	0/9 (0%)	0/9 (0%)	0/16 (0%)	0/34 (0%)	0/36 (0%)	0/14 (0%)
Pregnancy, puerperium and perinatal conditions						
Abortion spontaneous [A] *	0/9 (0%)	0/9 (0%)	0/16 (0%)	0/34 (0%)	0/36 (0%)	0/14 (0%)
Psychiatric disorders						
Delirium [A] *	0/9 (0%)	0/9 (0%)	0/16 (0%)	0/34 (0%)	0/36 (0%)	0/14 (0%)
Renal and urinary disorders						
Calculus ureteric [A] *	0/9 (0%)	0/9 (0%)	0/16 (0%)	0/34 (0%)	0/36 (0%)	0/14 (0%)
Calculus urinary [A] *	0/9 (0%)	0/9 (0%)	0/16 (0%)	0/34 (0%)	0/36 (0%)	0/14 (0%)
Renal colic [A] *	0/9 (0%)	0/9 (0%)	0/16 (0%)	0/34 (0%)	0/36 (0%)	0/14 (0%)
Reproductive system and breast disorders						
Bartholin's cyst [A] *	0/9 (0%)	0/9 (0%)	0/16 (0%)	0/34 (0%)	0/36 (0%)	0/14 (0%)
Fibrocystic breast disease [A] *	0/9 (0%)	0/9 (0%)	0/16 (0%)	0/34 (0%)	0/36 (0%)	0/14 (0%)
Ovarian cyst [A] *	0/9 (0%)	0/9 (0%)	0/16 (0%)	0/34 (0%)	0/36 (0%)	0/14 (0%)
Respiratory, thoracic and mediastinal disorders						
Nasal cyst [A] *	0/9 (0%)	0/9 (0%)	0/16 (0%)	0/34 (0%)	0/36 (0%)	0/14 (0%)
Pulmonary oedema [A] *	0/9 (0%)	0/9 (0%)	0/16 (0%)	0/34 (0%)	0/36 (0%)	0/14 (0%)
Tracheal mass [A] *	0/9 (0%)	0/9 (0%)	0/16 (0%)	0/34 (0%)	0/36 (0%)	0/14 (0%)

	Cladribine 5.25 mg/kg, Rebif, Cladribine 3.5 mg/kg (LTFU)	Cladribine 3.5 mg/kg, Rebif, Cladribine 3.5 mg/kg (LTFU)	Placebo, Rebif, Cladribine 3.5 mg/kg (LTFU)	Cladribine 5.25 mg/kg, Rebif (LTFU)	Cladribine 3.5 mg/kg, Rebif (LTFU)	Placebo, Rebif (LTFU)
	Affected/ At Risk (%)	Affected/ At Risk (%)	Affected/ At Risk (%)	Affected/ At Risk (%)	Affected/ At Risk (%)	Affected/ At Risk (%)
Skin and subcutaneous tissue disorders						
Psoriasis [A] *	0/9 (0%)	0/9 (0%)	0/16 (0%)	0/34 (0%)	0/36 (0%)	0/14 (0%)
Vascular disorders						
Hypertension [A] *	0/9 (0%)	0/9 (0%)	0/16 (0%)	0/34 (0%)	0/36 (0%)	0/14 (0%)

* Indicates events were collected by non-systematic methods.
A Term from vocabulary, MedDRA (11.0)

Other Adverse Events

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

	Cladribine 5.25 mg/kg (ITP)	Cladribine 3.5 mg/kg (ITP)	Placebo (ITP)	Cladribine 5.25 mg/kg, Rebif (OLMP)	Cladribine 3.5 mg/kg, Rebif (OLMP)	Placebo, Rebif (OLMP)
	Affected/ At Risk (%)	Affected/ At Risk (%)	Affected/ At Risk (%)	Affected/ At Risk (%)	Affected/ At Risk (%)	Affected/ At Risk (%)
Total	133/204 (65.2%)	132/206 (64.08%)	116/206 (56.31%)	18/24 (75%)	19/25 (76%)	41/60 (68.33%)
Blood and lymphatic system disorders						
Leukopenia [A] *	0/204 (0%)	0/206 (0%)	0/206 (0%)	0/24 (0%)	2/25 (8%)	2/60 (3.33%)
Lymphopenia [A] *	47/204 (23.04%)	25/206 (12.14%)	0/206 (0%)	2/24 (8.33%)	1/25 (4%)	2/60 (3.33%)
Neutropenia [A] *	0/204 (0%)	0/206 (0%)	0/206 (0%)	0/24 (0%)	2/25 (8%)	1/60 (1.67%)
Ear and labyrinth disorders						
Vertigo [A] *	0/204 (0%)	0/206 (0%)	0/206 (0%)	1/24 (4.17%)	0/25 (0%)	3/60 (5%)
Eye disorders						
Eye pain [A] *	0/204 (0%)	0/206 (0%)	0/206 (0%)	0/24 (0%)	0/25 (0%)	3/60 (5%)
Gastrointestinal disorders						

	Cladribine 5.25 mg/kg (ITP)	Cladribine 3.5 mg/kg (ITP)	Placebo (ITP)	Cladribine 5.25 mg/kg, Rebif (OLMP)	Cladribine 3.5 mg/kg, Rebif (OLMP)	Placebo, Rebif (OLMP)
	Affected/ At Risk (%)	Affected/ At Risk (%)	Affected/ At Risk (%)	Affected/ At Risk (%)	Affected/ At Risk (%)	Affected/ At Risk (%)
Abdominal pain [A] *	7/204 (3.43%)	9/206 (4.37%)	12/206 (5.83%)	0/24 (0%)	0/25 (0%)	0/60 (0%)
Abdominal pain upper [A] *	10/204 (4.9%)	15/206 (7.28%)	4/206 (1.94%)	2/24 (8.33%)	0/25 (0%)	0/60 (0%)
Dental caries [A] *	0/204 (0%)	0/206 (0%)	0/206 (0%)	2/24 (8.33%)	0/25 (0%)	1/60 (1.67%)
Diarrhoea [A] *	11/204 (5.39%)	16/206 (7.77%)	13/206 (6.31%)	0/24 (0%)	0/25 (0%)	0/60 (0%)
Food poisoning [A] *	0/204 (0%)	0/206 (0%)	0/206 (0%)	0/24 (0%)	0/25 (0%)	0/60 (0%)
Gastrointestinal toxicity [A] *	0/204 (0%)	0/206 (0%)	0/206 (0%)	0/24 (0%)	0/25 (0%)	0/60 (0%)
Nausea [A] *	23/204 (11.27%)	24/206 (11.65%)	19/206 (9.22%)	1/24 (4.17%)	1/25 (4%)	3/60 (5%)
Radicular cyst [A] *	0/204 (0%)	0/206 (0%)	0/206 (0%)	0/24 (0%)	0/25 (0%)	0/60 (0%)
Toothache [A] *	6/204 (2.94%)	14/206 (6.8%)	8/206 (3.88%)	0/24 (0%)	0/25 (0%)	0/60 (0%)
General disorders						
Fatigue [A] *	15/204 (7.35%)	15/206 (7.28%)	19/206 (9.22%)	3/24 (12.5%)	0/25 (0%)	1/60 (1.67%)
Influenza like illness [A] *	0/204 (0%)	0/206 (0%)	0/206 (0%)	7/24 (29.17%)	9/25 (36%)	21/60 (35%)
Injection site erythema [A] *	0/204 (0%)	0/206 (0%)	0/206 (0%)	0/24 (0%)	2/25 (8%)	2/60 (3.33%)
Injection site pain [A] *	0/204 (0%)	0/206 (0%)	0/206 (0%)	2/24 (8.33%)	0/25 (0%)	3/60 (5%)
Injection site reaction [A] *	0/204 (0%)	0/206 (0%)	0/206 (0%)	2/24 (8.33%)	0/25 (0%)	4/60 (6.67%)
Pyrexia [A] *	0/204 (0%)	0/206 (0%)	0/206 (0%)	1/24 (4.17%)	5/25 (20%)	5/60 (8.33%)
Immune system disorders						
Drug hypersensitivity [A] *	0/204 (0%)	0/206 (0%)	0/206 (0%)	0/24 (0%)	0/25 (0%)	0/60 (0%)
Hypersensitivity [A] *	0/204 (0%)	0/206 (0%)	0/206 (0%)	0/24 (0%)	0/25 (0%)	0/60 (0%)

	Cladribine 5.25 mg/kg (ITP)	Cladribine 3.5 mg/kg (ITP)	Placebo (ITP)	Cladribine 5.25 mg/kg, Rebif (OLMP)	Cladribine 3.5 mg/kg, Rebif (OLMP)	Placebo, Rebif (OLMP)
	Affected/ At Risk (%)	Affected/ At Risk (%)	Affected/ At Risk (%)	Affected/ At Risk (%)	Affected/ At Risk (%)	Affected/ At Risk (%)
Infections and infestations						
Acute tonsillitis [A] *	0/204 (0%)	0/206 (0%)	0/206 (0%)	0/24 (0%)	0/25 (0%)	0/60 (0%)
Bronchitis [A] *	0/204 (0%)	0/206 (0%)	0/206 (0%)	0/24 (0%)	0/25 (0%)	0/60 (0%)
Hordeolum [A] *	0/204 (0%)	0/206 (0%)	0/206 (0%)	0/24 (0%)	0/25 (0%)	0/60 (0%)
Influenza [A] *	14/204 (6.86%)	21/206 (10.19%)	13/206 (6.31%)	2/24 (8.33%)	0/25 (0%)	6/60 (10%)
Nasopharyngitis [A] *	36/204 (17.65%)	35/206 (16.99%)	38/206 (18.45%)	2/24 (8.33%)	1/25 (4%)	5/60 (8.33%)
Pharyngitis [A] *	12/204 (5.88%)	10/206 (4.85%)	12/206 (5.83%)	2/24 (8.33%)	9/25 (36%)	3/60 (5%)
Respiratory tract infection viral [A] *	0/204 (0%)	0/206 (0%)	0/206 (0%)	0/24 (0%)	0/25 (0%)	0/60 (0%)
Upper respiratory tract infection [A] *	23/204 (11.27%)	21/206 (10.19%)	17/206 (8.25%)	0/24 (0%)	0/25 (0%)	0/60 (0%)
Vaginal candidiasis [A] *	0/204 (0%)	0/206 (0%)	0/206 (0%)	0/24 (0%)	0/25 (0%)	0/60 (0%)
Wound [A] *	0/204 (0%)	0/206 (0%)	0/206 (0%)	0/24 (0%)	0/25 (0%)	0/60 (0%)
Investigations						
Alanine aminotransferase increased [A] *	0/204 (0%)	0/206 (0%)	0/206 (0%)	0/24 (0%)	0/25 (0%)	3/60 (5%)
Aspartate aminotransferase increased [A] *	0/204 (0%)	0/206 (0%)	0/206 (0%)	1/24 (4.17%)	0/25 (0%)	4/60 (6.67%)
Musculoskeletal and connective tissue disorders						
Arthralgia [A] *	10/204 (4.9%)	13/206 (6.31%)	13/206 (6.31%)	0/24 (0%)	2/25 (8%)	2/60 (3.33%)
Back pain [A] *	14/204 (6.86%)	17/206 (8.25%)	13/206 (6.31%)	2/24 (8.33%)	0/25 (0%)	3/60 (5%)
Musculoskeletal pain [A] *	0/204 (0%)	0/206 (0%)	0/206 (0%)	0/24 (0%)	2/25 (8%)	3/60 (5%)
Myalgia [A] *	0/204 (0%)	0/206 (0%)	0/206 (0%)	3/24 (12.5%)	0/25 (0%)	7/60 (11.67%)

	Cladribine 5.25 mg/kg (ITP)	Cladribine 3.5 mg/kg (ITP)	Placebo (ITP)	Cladribine 5.25 mg/kg, Rebif (OLMP)	Cladribine 3.5 mg/kg, Rebif (OLMP)	Placebo, Rebif (OLMP)
	Affected/ At Risk (%)	Affected/ At Risk (%)	Affected/ At Risk (%)	Affected/ At Risk (%)	Affected/ At Risk (%)	Affected/ At Risk (%)
Pain in extremity [A] *	10/204 (4.9%)	11/206 (5.34%)	9/206 (4.37%)	0/24 (0%)	0/25 (0%)	0/60 (0%)
Nervous system disorders						
Dizziness [A] *	12/204 (5.88%)	16/206 (7.77%)	19/206 (9.22%)	0/24 (0%)	0/25 (0%)	0/60 (0%)
Headache [A] *	58/204 (28.43%)	64/206 (31.07%)	57/206 (27.67%)	5/24 (20.83%)	8/25 (32%)	10/60 (16.67%)
Hypoaesthesia [A] *	0/204 (0%)	0/206 (0%)	0/206 (0%)	0/24 (0%)	0/25 (0%)	0/60 (0%)
Nystagmus [A] *	0/204 (0%)	0/206 (0%)	0/206 (0%)	0/24 (0%)	0/25 (0%)	0/60 (0%)
Paraesthesia [A] *	9/204 (4.41%)	11/206 (5.34%)	10/206 (4.85%)	0/24 (0%)	0/25 (0%)	0/60 (0%)
Psychiatric disorders						
Insomnia [A] *	5/204 (2.45%)	9/206 (4.37%)	12/206 (5.83%)	1/24 (4.17%)	1/25 (4%)	4/60 (6.67%)
Neurosis [A] *	0/204 (0%)	0/206 (0%)	0/206 (0%)	0/24 (0%)	0/25 (0%)	0/60 (0%)
Reproductive system and breast disorders						
Bartholin's cyst [A] *	0/204 (0%)	0/206 (0%)	0/206 (0%)	0/24 (0%)	0/25 (0%)	0/60 (0%)
Dysmenorrhoea [A] *	0/204 (0%)	0/206 (0%)	0/206 (0%)	0/24 (0%)	0/25 (0%)	0/60 (0%)
Respiratory, thoracic and mediastinal disorders						
Cough [A] *	10/204 (4.9%)	8/206 (3.88%)	11/206 (5.34%)	2/24 (8.33%)	1/25 (4%)	1/60 (1.67%)
Pharyngolaryngeal pain [A] *	16/204 (7.84%)	10/206 (4.85%)	10/206 (4.85%)	0/24 (0%)	0/25 (0%)	0/60 (0%)
Skin and subcutaneous tissue disorders						
Hyperhidrosis [A] *	0/204 (0%)	0/206 (0%)	0/206 (0%)	0/24 (0%)	0/25 (0%)	0/60 (0%)

* Indicates events were collected by non-systematic methods.

A Term from vocabulary, MedDRA (11.0)

	Cladribine 5.25 mg/kg, Rebif, Cladribine 3.5 mg/kg (LTFU)	Cladribine 3.5 mg/kg, Rebif, Cladribine 3.5 mg/kg (LTFU)	Placebo, Rebif, Cladribine 3.5 mg/kg (LTFU)	Cladribine 5.25 mg/kg, Rebif (LTFU)	Cladribine 3.5 mg/kg, Rebif (LTFU)	Placebo, Rebif (LTFU)
	Affected/ At Risk (%)	Affected/ At Risk (%)	Affected/ At Risk (%)	Affected/ At Risk (%)	Affected/ At Risk (%)	Affected/ At Risk (%)
Total	3/9 (33.33%)	4/9 (44.44%)	7/16 (43.75%)	2/34 (5.88%)	0/36 (0%)	2/14 (14.29%)
Blood and lymphatic system disorders						
Leukopenia [A] *	0/9 (0%)	0/9 (0%)	0/16 (0%)	0/34 (0%)	0/36 (0%)	0/14 (0%)
Lymphopenia [A] *	0/9 (0%)	1/9 (11.11%)	0/16 (0%)	0/34 (0%)	0/36 (0%)	0/14 (0%)
Neutropenia [A] *	0/9 (0%)	0/9 (0%)	0/16 (0%)	0/34 (0%)	0/36 (0%)	0/14 (0%)
Ear and labyrinth disorders						
Vertigo [A] *	0/9 (0%)	0/9 (0%)	0/16 (0%)	0/34 (0%)	0/36 (0%)	0/14 (0%)
Eye disorders						
Eye pain [A] *	0/9 (0%)	0/9 (0%)	0/16 (0%)	0/34 (0%)	0/36 (0%)	0/14 (0%)
Gastrointestinal disorders						
Abdominal pain [A] *	0/9 (0%)	0/9 (0%)	0/16 (0%)	0/34 (0%)	0/36 (0%)	0/14 (0%)
Abdominal pain upper [A] *	0/9 (0%)	0/9 (0%)	0/16 (0%)	0/34 (0%)	0/36 (0%)	0/14 (0%)
Dental caries [A] *	0/9 (0%)	0/9 (0%)	0/16 (0%)	0/34 (0%)	0/36 (0%)	1/14 (7.14%)
Diarrhoea [A] *	0/9 (0%)	0/9 (0%)	0/16 (0%)	0/34 (0%)	0/36 (0%)	0/14 (0%)
Food poisoning [A] *	0/9 (0%)	1/9 (11.11%)	1/16 (6.25%)	0/34 (0%)	0/36 (0%)	0/14 (0%)
Gastrointestinal toxicity [A] *	0/9 (0%)	0/9 (0%)	1/16 (6.25%)	0/34 (0%)	0/36 (0%)	0/14 (0%)
Nausea [A] *	0/9 (0%)	0/9 (0%)	0/16 (0%)	0/34 (0%)	0/36 (0%)	0/14 (0%)
Radicular cyst [A] *	0/9 (0%)	0/9 (0%)	1/16 (6.25%)	0/34 (0%)	0/36 (0%)	0/14 (0%)
Toothache [A] *	0/9 (0%)	1/9 (11.11%)	0/16 (0%)	0/34 (0%)	0/36 (0%)	0/14 (0%)
General disorders						

	Cladribine 5.25 mg/kg, Rebif, Cladribine 3.5 mg/kg (LTFU)	Cladribine 3.5 mg/kg, Rebif, Cladribine 3.5 mg/kg (LTFU)	Placebo, Rebif, Cladribine 3.5 mg/kg (LTFU)	Cladribine 5.25 mg/kg, Rebif (LTFU)	Cladribine 3.5 mg/kg, Rebif (LTFU)	Placebo, Rebif (LTFU)
	Affected/ At Risk (%)	Affected/ At Risk (%)	Affected/ At Risk (%)	Affected/ At Risk (%)	Affected/ At Risk (%)	Affected/ At Risk (%)
Fatigue [A] *	0/9 (0%)	0/9 (0%)	0/16 (0%)	0/34 (0%)	0/36 (0%)	0/14 (0%)
Influenza like illness [A] *	0/9 (0%)	0/9 (0%)	0/16 (0%)	0/34 (0%)	0/36 (0%)	0/14 (0%)
Injection site erythema [A] *	0/9 (0%)	0/9 (0%)	0/16 (0%)	0/34 (0%)	0/36 (0%)	0/14 (0%)
Injection site pain [A] *	0/9 (0%)	0/9 (0%)	0/16 (0%)	0/34 (0%)	0/36 (0%)	0/14 (0%)
Injection site reaction [A] *	0/9 (0%)	0/9 (0%)	0/16 (0%)	0/34 (0%)	0/36 (0%)	0/14 (0%)
Pyrexia [A] *	0/9 (0%)	0/9 (0%)	0/16 (0%)	0/34 (0%)	0/36 (0%)	0/14 (0%)
Immune system disorders						
Drug hypersensitivity [A] *	0/9 (0%)	0/9 (0%)	1/16 (6.25%)	0/34 (0%)	0/36 (0%)	0/14 (0%)
Hypersensitivity [A] *	0/9 (0%)	0/9 (0%)	1/16 (6.25%)	0/34 (0%)	0/36 (0%)	0/14 (0%)
Infections and infestations						
Acute tonsillitis [A] *	0/9 (0%)	1/9 (11.11%)	0/16 (0%)	0/34 (0%)	0/36 (0%)	0/14 (0%)
Bronchitis [A] *	0/9 (0%)	1/9 (11.11%)	0/16 (0%)	0/34 (0%)	0/36 (0%)	0/14 (0%)
Hordeolum [A] *	0/9 (0%)	0/9 (0%)	1/16 (6.25%)	0/34 (0%)	0/36 (0%)	0/14 (0%)
Influenza [A] *	0/9 (0%)	0/9 (0%)	0/16 (0%)	0/34 (0%)	0/36 (0%)	0/14 (0%)
Nasopharyngitis [A] *	0/9 (0%)	1/9 (11.11%)	0/16 (0%)	0/34 (0%)	0/36 (0%)	0/14 (0%)
Pharyngitis [A] *	0/9 (0%)	0/9 (0%)	0/16 (0%)	0/34 (0%)	0/36 (0%)	0/14 (0%)
Respiratory tract infection viral [A] *	0/9 (0%)	0/9 (0%)	1/16 (6.25%)	0/34 (0%)	0/36 (0%)	0/14 (0%)
Upper respiratory tract infection [A] *	1/9 (11.11%)	0/9 (0%)	2/16 (12.5%)	0/34 (0%)	0/36 (0%)	0/14 (0%)
Vaginal candidiasis [A] *	0/9 (0%)	1/9 (11.11%)	1/16 (6.25%)	0/34 (0%)	0/36 (0%)	0/14 (0%)
Wound [A] *	0/9 (0%)	0/9 (0%)	1/16 (6.25%)	0/34 (0%)	0/36 (0%)	0/14 (0%)

	Cladribine 5.25 mg/kg, Rebif, Cladribine 3.5 mg/kg (LTFU)	Cladribine 3.5 mg/kg, Rebif, Cladribine 3.5 mg/kg (LTFU)	Placebo, Rebif, Cladribine 3.5 mg/kg (LTFU)	Cladribine 5.25 mg/kg, Rebif (LTFU)	Cladribine 3.5 mg/kg, Rebif (LTFU)	Placebo, Rebif (LTFU)
	Affected/ At Risk (%)	Affected/ At Risk (%)	Affected/ At Risk (%)	Affected/ At Risk (%)	Affected/ At Risk (%)	Affected/ At Risk (%)
Investigations						
Alanine aminotransferase increased [A] *	0/9 (0%)	0/9 (0%)	1/16 (6.25%)	0/34 (0%)	0/36 (0%)	0/14 (0%)
Aspartate aminotransferase increased [A] *	0/9 (0%)	0/9 (0%)	0/16 (0%)	0/34 (0%)	0/36 (0%)	0/14 (0%)
Musculoskeletal and connective tissue disorders						
Arthralgia [A] *	0/9 (0%)	0/9 (0%)	0/16 (0%)	0/34 (0%)	0/36 (0%)	0/14 (0%)
Back pain [A] *	0/9 (0%)	0/9 (0%)	0/16 (0%)	0/34 (0%)	0/36 (0%)	0/14 (0%)
Musculoskeletal pain [A] *	0/9 (0%)	0/9 (0%)	0/16 (0%)	0/34 (0%)	0/36 (0%)	0/14 (0%)
Myalgia [A] *	0/9 (0%)	0/9 (0%)	0/16 (0%)	0/34 (0%)	0/36 (0%)	0/14 (0%)
Pain in extremity [A] *	0/9 (0%)	0/9 (0%)	0/16 (0%)	0/34 (0%)	0/36 (0%)	0/14 (0%)
Nervous system disorders						
Dizziness [A] *	0/9 (0%)	0/9 (0%)	0/16 (0%)	0/34 (0%)	0/36 (0%)	0/14 (0%)
Headache [A] *	1/9 (11.11%)	0/9 (0%)	3/16 (18.75%)	2/34 (5.88%)	0/36 (0%)	0/14 (0%)
Hypoaesthesia [A] *	0/9 (0%)	0/9 (0%)	1/16 (6.25%)	0/34 (0%)	0/36 (0%)	0/14 (0%)
Nystagmus [A] *	0/9 (0%)	0/9 (0%)	1/16 (6.25%)	0/34 (0%)	0/36 (0%)	0/14 (0%)
Paraesthesia [A] *	0/9 (0%)	0/9 (0%)	1/16 (6.25%)	0/34 (0%)	0/36 (0%)	0/14 (0%)
Psychiatric disorders						
Insomnia [A] *	0/9 (0%)	0/9 (0%)	0/16 (0%)	0/34 (0%)	0/36 (0%)	0/14 (0%)
Neurosis [A] *	0/9 (0%)	1/9 (11.11%)	0/16 (0%)	0/34 (0%)	0/36 (0%)	0/14 (0%)
Reproductive system and breast disorders						
Bartholin's cyst [A] *	1/9 (11.11%)	0/9 (0%)	0/16 (0%)	0/34 (0%)	0/36 (0%)	0/14 (0%)
Dysmenorrhoea [A] *	0/9 (0%)	0/9 (0%)	0/16 (0%)	0/34 (0%)	0/36 (0%)	1/14 (7.14%)

	Cladribine 5.25 mg/kg, Rebif, Cladribine 3.5 mg/kg (LTFU)	Cladribine 3.5 mg/kg, Rebif, Cladribine 3.5 mg/kg (LTFU)	Placebo, Rebif, Cladribine 3.5 mg/kg (LTFU)	Cladribine 5.25 mg/kg, Rebif (LTFU)	Cladribine 3.5 mg/kg, Rebif (LTFU)	Placebo, Rebif (LTFU)
	Affected/ At Risk (%)	Affected/ At Risk (%)	Affected/ At Risk (%)	Affected/ At Risk (%)	Affected/ At Risk (%)	Affected/ At Risk (%)
Respiratory, thoracic and mediastinal disorders						
Cough [A] *	0/9 (0%)	0/9 (0%)	0/16 (0%)	0/34 (0%)	0/36 (0%)	0/14 (0%)
Pharyngolaryngeal pain [A] *	0/9 (0%)	0/9 (0%)	0/16 (0%)	0/34 (0%)	0/36 (0%)	0/14 (0%)
Skin and subcutaneous tissue disorders						
Hyperhidrosis [A] *	0/9 (0%)	0/9 (0%)	1/16 (6.25%)	0/34 (0%)	0/36 (0%)	0/14 (0%)

* Indicates events were collected by non-systematic methods.
A Term from vocabulary, MedDRA (11.0)

Limitations and Caveats

Due to early termination of trial, efficacy data presented from core double blind ITP only. Due to low number of participants entering OLMP and LTFU period and the reduced duration, only descriptive safety data from OLMP and LTFU are presented.

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.

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