ClinicalTrials.gov Protocol Registration and Results System (PRS) Receipt
Release Date: 01/10/2014

ClinicalTrials.gov ID: NCT00641537

Study Identification

Unique Protocol ID:	27820
Brief Title:	CLARITY Extension Study
Official Title:	A Phase IIIb, Double-Blind, Placebo-Controlled, Multicenter, Parallel Group, Extension Trial to Evaluate the Safety and Tolerability of Oral Cladribine in Subjects With Relapsing-Remitting Multiple Sclerosis Who Have Completed Trial 25643 (CLARITY)
Secondary IDs:	

Study Status

Record Verification:	January 2014
Overall Status:	Completed
Study Start:	February 2008
Primary Completion:	December 2011 [Actual]
Study Completion:	December 2011 [Actual]

Sponsor/Collaborators

Sponsor:	EMD Serono
Responsible Party:	Sponsor
Collaborators:	

Oversight

FDA Regulated?:	Yes

Applicable Trial?:	Section 801 Clinical Trial? No Delayed Posting? No
IND/IDE Protocol?:	Yes
IND/IDE Information:	Grantor: CDER IND/IDE Number: 74,634 Serial Number: 075 Has Expanded Access? No
Review Board:	Approval Status: Approved Approval Number: 9/24/07 Board Name: Coast Independent Review Board Board Affiliation: United States Food and Drug Administration Phone: 719.325.8817 Email: srego@coastirb.com
Data Monitoring?:	
Plan to Share Data?:	
Oversight Authorities:	United States: Food and Drug Administration

Study Description

Brief Summary:	The purpose of this extension trial is to further evaluate the safety and tolerability of oral cladribine in subjects who have previously completed treatment within Trial 25643 (CLARITY). This trial also explored clinical benefit of prolonged 192-week versus 96-week treatment.
Detailed Description:	

Conditions

Conditions:	Relapsing-Remitting Multiple Sclerosis
Keywords:	

Study Design

Study Type:	Interventional
Primary Purpose:	Treatment
Study Phase:	Phase 3
Intervention Model:	Parallel Assignment

Number of Arms: 5

Masking: Double Blind (Subject, Caregiver, Investigator, Outcomes Assessor)

Allocation: Randomized

Endpoint Classification:

Enrollment: 867 [Actual]

Arms and Interventions

Arms	Assigned Interventions
Placebo Comparator: Cladribine Low/Placebo (LLPP)	Drug: Placebo Participants who received Cladribine 3.5 mg/kg in the previous study 25643 (NCT00213135) and completed will be re-randomized in this extension study and receive placebo matched to cladribine tablet 0.875 mg/kg orally administered over a course of 4 or 5 consecutive days of 28-day period at Week 1, 5, 48, and 52 during the treatment period of 96 weeks.
Placebo Comparator: Cladribine High Dose/Placebo (HLPP)	Drug: Placebo Participants who received Cladribine 5.25 mg/kg in the previous study 25643 (NCT00213135) and completed will be re-randomized in this extension study and receive placebo matched to cladribine tablet 0.875 mg/kg orally administered over a course of 4 or 5 consecutive days of 28-day period at Week 1, 5, 48, and 52 during the treatment period of 96 weeks.
Experimental: Cladribine Low/Low Dose (LLLL)	Drug: Cladribine Participants who received Cladribine 3.5 mg/kg in the previous study 25643 (NCT00213135) and completed will be re-randomized in this extension study and receive cladribine tablet orally as cumulative dose of 0.875 mg/kg over a course of 4 or 5 consecutive days of 28-day period at Week 1, 5, 48, and 52 resulting in total cladribine dose of 3.5 mg/kg during the treatment period of 96 weeks.
Experimental: Cladribine High/Low Dose (HLLL)	Drug: Cladribine Participants who received Cladribine 5.25 mg/kg in the previous study 25643 (NCT00213135) and completed will be re-randomized in this extension study and receive cladribine tablet orally as cumulative dose of 0.875 mg/kg over a course of 4 or 5 consecutive days of 28-day period at Week 1, 5, 48, and 52 resulting in total cladribine dose of 3.5 mg/kg during the treatment period of 96 weeks.
Experimental: Placebo/Cladribine Low Dose (PPLL)	Drug: Cladribine Participants who received placebo in the previous study 25643 (NCT00213135) and completed will be re-randomized in this extension study and receive cladribine tablet orally as cumulative dose of 0.875 mg/

Arms	Assigned Interventions
	kg over a course of 4 or 5 consecutive days of 28-day period at Week 1, 5, 48, and 52 resulting in total cladribine dose of 3.5 mg/kg during the treatment period of 96 weeks.

Outcome Measures

[See Results Section.]

Eligibility

Minimum Age: 18 Years

Maximum Age: 65 Years

Gender: Both

Accepts Healthy Volunteers?: No

Criteria: Inclusion Criteria:

- Randomized in Trial 25643 and satisfied one of the following:
  - Completed randomized treatment course and scheduled visits for the full 96 weeks; or
  - Did not complete the randomized treatment course in Trial 25643 but elected to receive rescue treatment with Rebif®, another beta-interferon, or glatiramer acetate and completed scheduled clinic visits for the full 96 weeks; or
  - Did not complete the randomized treatment course in Trial 25643, declined rescue with Rebif®, another beta-interferon, or glatiramer acetate and still completed scheduled clinic visits for the full 96 weeks; or
  - Did not complete the randomized treatment course in Trial 25643, were not eligible for rescue option with Rebif®, and still completed scheduled clinic visits for the full 96 weeks
- Male or female, between 18 and 65 years of age (inclusive, at time of informed consent for Trial 25643)
- No medical history or evidence of latent tuberculosis infection (LTBI) or tuberculosis (TB), as evidenced by TB skin test or chest X-ray
- All of the following laboratory hematologic parameters evaluated as normal (as define below, inclusively) within 28 days of first dosing of blinded study medication at study Day 1:
  - Hemoglobin = 11.6 to 16.2 gram per deciliter (g/dL)
  - Leukocytes (total white blood cell) = 4.1 to 12.3*10^3 per microliter
  - Absolute lymphocyte count (ALC) = 1.02 to 3.36*10^3 per microliter
  - Absolute neutrophil count (ANC) = 2.03 to 8.36*10^3 per microliter
  - Platelet count = 140 to 450*10^3 per microliter
- Other protocol-defined inclusion/exclusion criteria may apply

Exclusion Criteria:

- Subjects who were not enrolled in Trial 25643
- Subject has moderate to severe renal impairment

- Use of mitoxantrone, total lymphoid irradiation, myelosuppressive therapy, campath-1h, cyclophosphamide, azathioprine, methotrexate or natalizumab at any time during and since Trial 25643
- Use of cytokine or anti-cytokine therapy, intravenous immunoglobulin (IVIG) or plasmapheresis at any time during and since Trial 25643
- Treatment with oral or systemic corticosteroids or adrenocorticotropic hormone within 28 days before Study Day 1

Contacts/Locations

Study Officials:

Locations:

Australia
Research Site
Melbourne, Australia

Austria
Research Site
Linz, Austria

Bulgaria
Research Site
Pleven, Bulgaria

Croatia
Research Site
Sisak, Croatia

Czech Republic
Research Site
Praha, Czech Republic

Denmark
Research Site
Copenhagen, Denmark

Estonia
Research Site
Tallinn, Estonia

Finland
Research Site
Oulu, Finland

France
Research Site
Paris, France

Germany
Research Site
Frankfurt, Germany

Greece
Research Site
Athens, Greece

Italy
Research Site
Roma, Italy

Latvia
Research Site
Riga, Latvia

Lebanon
Research Site
Beyrouth, Lebanon

Lithuania
Research Site
Kaunas, Lithuania

Morocco
Research Site
Rabat, Morocco

Netherlands
Research Site
Sittard- Geleen, Netherlands

Poland
Research Site
Warszawy, Poland

Russian Federation
Research Site
Tomsk, Russian Federation

Saudi Arabia
Research Site
Riyadh, Saudi Arabia

Serbia
Research Site

Belgrade, Serbia

Switzerland
Research Site
Lausanne, Switzerland

United Kingdom
Research Site
London, United Kingdom

Ukraine
Research Site
Kiev, Ukraine

Brazil
Research Site
Recife, Brazil

Canada
Research Site
Greenfield Park, Canada

Portugal
Research Site
Lisboa, Portugal

Australia
Research Site
Camperdown, Australia

Research Site
Victoria, Australia

Belgium
Research Site
Esneux, Belgium

Research Site
Diepenbeek, Belgium

Bulgaria
Research Site
Varna, Bulgaria

Research Site
Sofia, Bulgaria

Research Site
Plovdiv, Bulgaria

Research Site
Zagora, Bulgaria

Research Site
Ruse, Bulgaria

Research Site
Shuman, Bulgaria

Croatia
Research Site
Karlovac, Croatia

Research Site
Split, Croatia

Czech Republic
Research Site
Hradec Králové, Czech Republic

Estonia
Research Site
Tartu, Estonia

Czech Republic
Research Site
Olomouc, Czech Republic

Finland
Research Site
Turku, Finland

France
Research Site
Clermont-Ferrand, France

Research Site
Nancy, France

Research Site
Rennes, France

Research Site

Lille, France

Research Site
Saint Herblain, France

Research Site
Nimes, France

Germany
Research Site
Hannover, Germany

Research Site
Bochum, Germany

Research Site
Regensburg, Germany

Research Site
Rostock, Germany

Research Site
Giessen, Germany

Italy
Research Site
Milano, Italy

Research Site
Firenze, Italy

Research Site
Napoli, Italy

Research Site
Padova, Italy

Research Site
Cagliari, Italy

Research Site
Catania, Italy

Research Site
Bari, Italy

Research Site
Genova, Italy

Lebanon
Research Site
Beirut, Lebanon

Morocco
Research Site
Casablanca, Morocco

Research Site
Fes, Morocco

Poland
Research Site
Poznan, Poland

Research Site
Gdansk, Poland

Research Site
Lodz, Poland

Research Site
Krakow, Poland

Russian Federation
Research Site
Rostov-on-Don, Russian Federation

Research Site
Kemerovo, Russian Federation

Research Site
Nizhny Novgorod, Russian Federation

Research Site
Moscow, Russian Federation

Research Site
St-Petersburg, Russian Federation

Research Site
Kazan, Russian Federation

Research Site
Ekaterinburg, Russian Federation

Research Site
Kaluga, Russian Federation

Research Site
Samara, Russian Federation

Research Site
Yaroslavl, Russian Federation

Research Site
Novosibirsk, Russian Federation

Research Site
Vladimir, Russian Federation

Research Site
Kursk, Russian Federation

Switzerland
Research Site
St. Gallen, Switzerland

Tunisia
Research Site
Sfax, Tunisia

Research Site
Tunis, Tunisia

Research Site
Monastir, Tunisia

Turkey
Research Site
Izmir, Turkey

Research Site
Bursa, Turkey

United Kingdom
Research Site
Nottingham, United Kingdom

Research Site
Stoke-on-Trent, United Kingdom

Research Site
Oxford, United Kingdom

Research Site
Sheffield, United Kingdom

Research Site
Hull, United Kingdom

Ukraine
Research Site
Lviv, Ukraine

Research Site
Vinnitsa, Ukraine

Research Site
Vinnitsa, Ukraine

Research Site
Kharkov, Ukraine

Canada
Research Site
Ottawa, Canada

Research Site
Quebec, Canada

Research Site
Burnaby, Canada

United States, New Jersey
Research Site
Newark, New Jersey, United States

United States, North Carolina
Research Site
Durham, North Carolina, United States

United States, Maryland
Research Site
Baltimore, Maryland, United States

United States, West Virginia
Research Site
Charleston, West Virginia, United States

United States, Oklahoma
Research Site
Oklahoma City, Oklahoma, United States

United States, Colorado
Research Site
Boulder, Colorado, United States

United States, Michigan
Research Site
Ann Arbor, Michigan, United States

United States, North Carolina
Research Site
Charlotte, North Carolina, United States

United States, Illinois
Research Site
Chicago, Illinois, United States

United States, Washington
Research Site
Seattle, Washington, United States

United States, Georgia
Research Site
Atlanta, Georgia, United States

United States, Ohio
Research Site
Columbus, Ohio, United States

United States, Oklahoma
Research Site
Tulsa, Oklahoma, United States

United States, Washington
Research Site
Tacoma, Washington, United States

United States, Illinois
Research Site

Northbrook, Illinois, United States

United States, Oregon
Research Site
Medford, Oregon, United States

United States, Nevada
Research Site
Henderson, Nevada, United States

Russian Federation
Reseach Site
Saratov, Russian Federation

References

Citations:

Links:

Study Data/Documents:

Study Results

Participant Flow

Reporting Groups

	Description
Cladribine Low/Placebo (LLPP)	Participants who received cladribine 3.5 milligram/kilogram (mg/kg) in previous study 25643 (NCT00213135) and completed were re-randomized in this extension study and received placebo matched to cladribine tablet 0.875 mg/kg orally over a course of 4 or 5 consecutive days of 28-day period at Week 1, 5, 48, and 52 resulting in total dose of 3.5 mg/kg during the treatment period of 96 weeks. Participants were followed up for 24 weeks in supplemental follow-up period.
Cladribine High Dose/Placebo (HLPP)	Participants who received Cladribine 5.25 mg/kg in previous study 25643 (NCT00213135) and completed were re-randomized in this extension study and received placebo matched to cladribine tablet 0.875 mg/kg orally over a course of 4 or 5 consecutive days of 28-day period at Week 1, 5, 48, and 52 resulting in total dose of 3.5 mg/kg during the treatment period of 96 weeks. Participants were followed up for 24 weeks in supplemental follow-up period.

	Description
Cladribine Low/Low Dose (LLLL)	Participants who received Cladribine 3.5 mg/kg in previous study 25643 (NCT00213135) and completed were re-randomized in this extension study and received cladribine tablet orally as cumulative dose of 0.875 mg/kg over a course of 4 or 5 consecutive days of 28-day period at Week 1, 5, 48, and 52 resulting in total cladribine dose of 3.5 mg/kg during the treatment period of 96 weeks. Participants were followed up for 24 weeks in supplemental follow-up period.
Cladribine High/Low Dose (HLLL)	Participants who received Cladribine 5.25 mg/kg in previous study 25643 (NCT00213135) and completed were re-randomized in this extension study and received cladribine tablet orally as cumulative dose of 0.875 mg/kg over a course of 4 or 5 consecutive days of 28-day period at Week 1, 5, 48, and 52 resulting in total cladribine dose of 3.5 mg/kg during the treatment period of 96 weeks. Participants were followed up for 24 weeks in supplemental follow-up period.
Placebo/Cladribine Low Dose (PPLL)	Participants who received placebo matched to cladribine in previous study 25643 (NCT00213135) and completed were re-randomized in this extension study and received Cladribine tablet orally as cumulative dose of 0.875 mg/kg over a course of 4 or 5 consecutive days of 28-day period at Week 1, 5, 48, and 52 resulting in total cladribine dose of 3.5 mg/kg during the treatment period of 96 weeks. Participants were followed up for 24 weeks in supplemental follow-up period.
Placebo/No Treatment	Participants who received placebo matched to cladribine in previous study 25643 (NCT00213135) and were enrolled in this extension study and received no cladribine treatment and were followed up for safety assessment for 96 weeks (during the treatment period) and followed up for 24 weeks (during supplemental follow-up period).
Cladribine 3.5 mg/kg/No Treatment	Participants who received Cladribine 3.5 mg/kg in previous study 25643 (NCT00213135) and completed were enrolled in this extension study and received no cladribine treatment and were followed up for safety assessment for 96 weeks (during the treatment period) and followed up for 24 weeks (during supplemental follow-up period).
Cladribine 5.25 mg/kg/No Treatment	Participants who received Cladribine 5.25 mg/kg in previous study 25643 (NCT00213135) and completed were enrolled in this extension study and received no cladribine treatment and were followed up for safety assessment for 96 weeks (during the treatment period) and followed up for 24 weeks (during supplemental follow-up period).

96-week Period

	Cladribine Low/Placebo (LLPP)	Cladribine High Dose/ Placebo (HLPP)	Cladribine Low/Low Dose (LLLL)	Cladribine High/Low Dose (HLLL)	Placebo/ Cladribine Low Dose (PPLL)	Placebo/No Treatment
Started	98	92	186	186	244	22
Completed	89	82	166	174	226	15
Not Completed	9	10	20	12	18	7
Adverse Event	0	1	3	0	2	0

	Cladribine Low/Placebo (LLPP)	Cladribine High Dose/ Placebo (HLPP)	Cladribine Low/Low Dose (LLLL)	Cladribine High/Low Dose (HLLL)	Placebo/ Cladribine Low Dose (PPLL)	Placebo/No Treatment
Lost to Follow-up	3	1	2	2	4	0
Protocol Violation	0	1	0	1	0	1
Death	2	0	1	0	0	0
Unspecified	4	7	14	9	12	6

	Cladribine 3.5 mg/kg/No Treatment	Cladribine 5.25 mg/ kg/No Treatment
Started	17	22
Completed	12	16
Not Completed	5	6
Adverse Event	0	0
Lost to Follow-up	1	0
Protocol Violation	0	0
Death	0	0
Unspecified	4	6

24-Week Supplemental Follow-up Period

	Cladribine Low/Placebo (LLPP)	Cladribine High Dose/ Placebo (HLPP)	Cladribine Low/Low Dose (LLLL)	Cladribine High/Low Dose (HLLL)	Placebo/ Cladribine Low Dose (PPLL)	Placebo/No Treatment
Started	75	69	143	151	198	15
Completed	75	66	140	147	193	14
Not Completed	0	3	3	4	5	1
Lost to Follow-up	0	1	1	3	2	1
Unspecified	0	2	2	1	3	0

	Cladribine 3.5 mg/kg/No Treatment	Cladribine 5.25 mg/kg/No Treatment
Started	9	11
Completed	8	10
Not Completed	1	1
Lost to Follow-up	0	0
Unspecified	1	1

Baseline Characteristics

Analysis Population Description

Intention-to-treat (ITT) population included all participants who were randomized in the study.

Reporting Groups

	Description
Cladribine Low/Placebo (LLPP)	Participants who received cladribine 3.5 milligram/kilogram (mg/kg) in previous study 25643 (NCT00213135) and completed were re-randomized in this extension study and received placebo matched to cladribine tablet 0.875 mg/kg orally over a course of 4 or 5 consecutive days of 28-day period at Week 1, 5, 48, and 52 resulting in total dose of 3.5 mg/kg during the treatment period of 96 weeks. Participants were followed up for 24 weeks in supplemental follow-up period.
Cladribine High Dose/Placebo (HLPP)	Participants who received Cladribine 5.25 mg/kg in previous study 25643 (NCT00213135) and completed were re-randomized in this extension study and received placebo matched to cladribine tablet 0.875 mg/kg orally over a course of 4 or 5 consecutive days of 28-day period at Week 1, 5, 48, and 52 resulting in total dose of 3.5 mg/kg during the treatment period of 96 weeks. Participants were followed up for 24 weeks in supplemental follow-up period.
Cladribine Low/Low Dose (LLLL)	Participants who received Cladribine 3.5 mg/kg in previous study 25643 (NCT00213135) and completed were re-randomized in this extension study and received cladribine tablet orally as cumulative dose of 0.875 mg/kg over a course of 4 or 5 consecutive days of 28-day period at Week 1, 5, 48, and 52 resulting in total cladribine dose of 3.5 mg/kg during the treatment period of 96 weeks. Participants were followed up for 24 weeks in supplemental follow-up period.

	Description
Cladribine High/Low Dose (HLLL)	Participants who received Cladribine 5.25 mg/kg in previous study 25643 (NCT00213135) and completed were re-randomized in this extension study and received cladribine tablet orally as cumulative dose of 0.875 mg/kg over a course of 4 or 5 consecutive days of 28-day period at Week 1, 5, 48, and 52 resulting in total cladribine dose of 3.5 mg/kg during the treatment period of 96 weeks. Participants were followed up for 24 weeks in supplemental follow-up period.
Placebo/Cladribine Low Dose (PPLL)	Participants who received placebo matched to cladribine in previous study 25643 (NCT00213135) and completed were re-randomized in this extension study and received Cladribine tablet orally as cumulative dose of 0.875 mg/kg over a course of 4 or 5 consecutive days of 28-day period at Week 1, 5, 48, and 52 resulting in total cladribine dose of 3.5 mg/kg during the treatment period of 96 weeks. Participants were followed up for 24 weeks in supplemental follow-up period.

Baseline Measures

	Cladribine Low/ Placebo (LLPP)	Cladribine High Dose/ Placebo (HLPP)	Cladribine Low/ Low Dose (LLLL)	Cladribine High/ Low Dose (HLLL)	Placebo/Cladribine Low Dose (PPLL)	Total
Number of Participants	98	92	186	186	244	806
Age, Continuous [units: years] Mean (Standard Deviation)	40.7 (10.7)	40.8 (9.6)	40.6 (10.5)	41.4 (10.1)	41.6 (9.6)	41.1 (10.1)
Gender, Male/Female [units: participants]						
Female	67	59	124	125	156	531
Male	31	33	62	61	88	275

Outcome Measures

1. Primary Outcome Measure:

Measure Title	Percentage of Participants With at Least 1 Common Terminology Criteria for Adverse Events (CTCAE) Grade 3 or 4 Lymphocyte Toxicity
Measure Description	Lymphocyte toxicity was assessed using Common Terminology Criteria for Adverse Events (CTCAE). CTCAE grade for absolute lymphocyte counts included: Grade 1 = less than lower limit of normal; Grade 2 = less than 800 per cubic millimeter (/mm^3); Grade 3 = less than 500/mm^3; Grade 4 = less than 200/mm^3.
Time Frame	Baseline up to Week 120
Safety Issue?	Yes

Analysis Population Description

Safety population included all the randomized participants who had received at least 1 dose of study medication and had follow-up safety data.

Reporting Groups

	Description
Cladribine Low/Placebo (LLPP)	Participants who received cladribine 3.5 milligram/kilogram (mg/kg) in previous study 25643 (NCT00213135) and completed were re-randomized in this extension study and received placebo matched to cladribine tablet 0.875 mg/kg orally over a course of 4 or 5 consecutive days of 28-day period at Week 1, 5, 48, and 52 resulting in total dose of 3.5 mg/kg during the treatment period of 96 weeks. Participants were followed up for 24 weeks in supplemental follow-up period.
Cladribine High Dose/Placebo (HLPP)	Participants who received Cladribine 5.25 mg/kg in previous study 25643 (NCT00213135) and completed were re-randomized in this extension study and received placebo matched to cladribine tablet 0.875 mg/kg orally over a course of 4 or 5 consecutive days of 28-day period at Week 1, 5, 48, and 52 resulting in total dose of 3.5 mg/kg during the treatment period of 96 weeks. Participants were followed up for 24 weeks in supplemental follow-up period.
Cladribine Low/Low Dose (LLLL)	Participants who received Cladribine 3.5 mg/kg in previous study 25643 (NCT00213135) and completed were re-randomized in this extension study and received cladribine tablet orally as cumulative dose of 0.875 mg/kg over a course of 4 or 5 consecutive days of 28-day period at Week 1, 5, 48, and 52 resulting in total cladribine dose of 3.5 mg/kg during the treatment period of 96 weeks. Participants were followed up for 24 weeks in supplemental follow-up period.
Cladribine High/Low Dose (HLLL)	Participants who received Cladribine 5.25 mg/kg in previous study 25643 (NCT00213135) and completed were re-randomized in this extension study and received cladribine tablet orally as cumulative dose of 0.875 mg/kg over a course of 4 or 5 consecutive days of 28-day period at Week 1, 5, 48, and 52 resulting in total cladribine dose of 3.5 mg/kg during the treatment period of 96 weeks. Participants were followed up for 24 weeks in supplemental follow-up period.
Placebo/Cladribine Low Dose (PPLL)	Participants who received placebo matched to cladribine in previous study 25643 (NCT00213135) and completed were re-randomized in this extension study and received Cladribine tablet orally as cumulative dose of 0.875 mg/kg over a course of 4 or 5 consecutive days of 28-day period at Week 1, 5, 48, and 52 resulting in total cladribine dose of 3.5 mg/kg during the treatment period of 96 weeks. Participants were followed up for 24 weeks in supplemental follow-up period.

Measured Values

	Cladribine Low/ Placebo (LLPP)	Cladribine High Dose/ Placebo (HLPP)	Cladribine Low/Low Dose (LLLL)	Cladribine High/Low Dose (HLLL)	Placebo/ Cladribine Low Dose (PPLL)
Number of Participants Analyzed	98	92	186	186	244
Percentage of Participants With at Least 1 Common Terminology Criteria for Adverse Events (CTCAE) Grade 3 or 4 Lymphocyte Toxicity [units: percentage of participants]					

	Cladribine Low/ Placebo (LLPP)	Cladribine High Dose/ Placebo (HLPP)	Cladribine Low/Low Dose (LLLL)	Cladribine High/Low Dose (HLLL)	Placebo/ Cladribine Low Dose (PPLL)
Grade 3 Lymphocyte toxicity	5.1	6.5	38.1	50.0	24.6
Grade 4 Lymphocyte toxicity	0	0	2.7	3.2	0.4

2. Primary 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.
Time Frame	Baseline up to week 120
Safety Issue?	Yes

Analysis Population Description

Safety population included all the randomized participants who had received at least 1 dose of study medication and had follow-up safety data.

Reporting Groups

	Description
Cladribine Low/Placebo (LLPP)	Participants who received cladribine 3.5 milligram/kilogram (mg/kg) in previous study 25643 (NCT00213135) and completed were re-randomized in this extension study and received placebo matched to cladribine tablet 0.875 mg/kg orally over a course of 4 or 5 consecutive days of 28-day period at Week 1, 5, 48, and 52 resulting in total dose of 3.5 mg/kg during the treatment period of 96 weeks. Participants were followed up for 24 weeks in supplemental follow-up period.
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Measured Values

	Cladribine Low/ Placebo (LLPP)	Cladribine High Dose/ Placebo (HLPP)	Cladribine Low/Low Dose (LLLL)	Cladribine High/Low Dose (HLLL)	Placebo/ Cladribine Low Dose (PPLL)
Number of Participants Analyzed	98	92	186	186	244
Number of Participants With Adverse Events (AEs) and Serious Adverse Events (SAEs) [units: participants]					
AEs	74	71	149	149	194
SAEs	16	8	25	23	22

3. Primary Outcome Measure:

Measure Title	Median Time to Recovery From Grade 3 or 4 Lymphocyte Toxicity
Measure Description	Lymphocyte toxicity was assessed using Common Terminology Criteria for Adverse Events (CTCAE). CTCAE grade for absolute lymphocyte counts included: Grade 1 = less than lower limit of normal; Grade 2 = less than 800 per cubic millimeter (/mm^3); Grade 3 = less than 500/mm^3; Grade 4 = less than 200/mm^3. Recovery from a Grade 3 or 4 toxicity is defined as a return to a Grade 0 or 1 during the CLARITY Extension Study.
Time Frame	Baseline up to Week 120
Safety Issue?	Yes

Analysis Population Description

Safety population included all the randomized participants who had received at least 1 dose of study medication and had follow-up safety data. 'N' signifies number of participants who were evaluable for this outcome measure.

Reporting Groups

	Description
Cladribine Low/Placebo (LLPP)	Participants who received cladribine 3.5 milligram/kilogram (mg/kg) in previous study 25643 (NCT00213135) and completed were re-randomized in this extension study and received placebo matched to cladribine tablet 0.875 mg/kg orally over a course of 4 or 5 consecutive days of 28-day period at Week 1, 5, 48, and 52 resulting in total dose of 3.5 mg/kg during the treatment period of 96 weeks. Participants were followed up for 24 weeks in supplemental follow-up period.
Cladribine High Dose/Placebo (HLPP)	Participants who received Cladribine 5.25 mg/kg in previous study 25643 (NCT00213135) and completed were re-randomized in this extension study and received placebo matched to cladribine tablet 0.875 mg/kg orally over a course of 4 or 5 consecutive days of 28-day period at Week 1, 5, 48, and 52 resulting in total dose of 3.5 mg/kg during the treatment period of 96 weeks. Participants were followed up for 24 weeks in supplemental follow-up period.
Cladribine Low/Low Dose (LLLL)	Participants who received Cladribine 3.5 mg/kg in previous study 25643 (NCT00213135) and completed were re-randomized in this extension study and received cladribine tablet orally as cumulative dose of 0.875 mg/kg over a course of 4 or 5 consecutive days of 28-day period at Week 1, 5, 48, and 52 resulting in total cladribine dose of 3.5 mg/kg during the treatment period of 96 weeks. Participants were followed up for 24 weeks in supplemental follow-up period.
Cladribine High/Low Dose (HLLL)	Participants who received Cladribine 5.25 mg/kg in previous study 25643 (NCT00213135) and completed were re-randomized in this extension study and received cladribine tablet orally as cumulative dose of 0.875 mg/kg over a course of 4 or 5 consecutive days of 28-day period at Week 1, 5, 48, and 52 resulting in total cladribine dose of 3.5 mg/kg during the treatment period of 96 weeks. Participants were followed up for 24 weeks in supplemental follow-up period.
Placebo/Cladribine Low Dose (PPLL)	Participants who received placebo matched to cladribine in previous study 25643 (NCT00213135) and completed were re-randomized in this extension study and received Cladribine tablet orally as cumulative dose of 0.875 mg/kg over a course of 4 or 5 consecutive days of 28-day period at Week 1, 5, 48, and 52 resulting in total cladribine dose of 3.5 mg/kg during the treatment period of 96 weeks. Participants were followed up for 24 weeks in supplemental follow-up period.

Measured Values

	Cladribine Low/ Placebo (LLPP)	Cladribine High Dose/ Placebo (HLPP)	Cladribine Low/Low Dose (LLLL)	Cladribine High/Low Dose (HLLL)	Placebo/ Cladribine Low Dose (PPLL)
Number of Participants Analyzed	5	4	69	89	50
Median Time to Recovery From Grade 3 or 4 Lymphocyte Toxicity [units: days] Median (Full Range)	21 (13 to 84)	30.5 (24.5 to 50)	211 (7 to 1183)	167 (6 to 798)	110.3 (4 to 700)

4. Primary Outcome Measure:

Measure Title	Number of Participants Who Developed Herpes Zoster Infections and Malignancies
Measure Description	Herpes zoster infection is defined as having at least one adverse event coded to medical dictionary for regulatory activities (MedDRA) preferred terms herpes zoster, herpes zoster iridocyclitis, herpes zoster ophthalmic, herpes zoster multi-dermatomal, herpes zoster infection neurological, herpes zoster oticus. Malignancy is defined as having at least one adverse event coded to MedDRA preferred terms under the pre_specified grouping Malignant and unspecified tumors.
Time Frame	Baseline up to Week 120
Safety Issue?	Yes

Analysis Population Description

Safety population included all the randomized participants who had received at least 1 dose of study medication and had follow-up safety data.

Reporting Groups

	Description
Cladribine Low/Placebo (LLPP)	Participants who received cladribine 3.5 milligram/kilogram (mg/kg) in previous study 25643 (NCT00213135) and completed were re-randomized in this extension study and received placebo matched to cladribine tablet 0.875 mg/kg orally over a course of 4 or 5 consecutive days of 28-day period at Week 1, 5, 48, and 52 resulting in total dose of 3.5 mg/kg during the treatment period of 96 weeks. Participants were followed up for 24 weeks in supplemental follow-up period.
Cladribine High Dose/Placebo (HLPP)	Participants who received Cladribine 5.25 mg/kg in previous study 25643 (NCT00213135) and completed were re-randomized in this extension study and received placebo matched to cladribine tablet 0.875 mg/kg orally over a course of 4 or 5 consecutive days of 28-day period at Week 1, 5, 48, and 52 resulting in total dose of 3.5 mg/kg during the treatment period of 96 weeks. Participants were followed up for 24 weeks in supplemental follow-up period.
Cladribine Low/Low Dose (LLLL)	Participants who received Cladribine 3.5 mg/kg in previous study 25643 (NCT00213135) and completed were re-randomized in this extension study and received cladribine tablet orally as cumulative dose of 0.875 mg/kg over a course of 4 or 5 consecutive days of 28-day period at Week 1, 5, 48, and 52 resulting in total cladribine dose of 3.5 mg/kg during the treatment period of 96 weeks. Participants were followed up for 24 weeks in supplemental follow-up period.
Cladribine High/Low Dose (HLLL)	Participants who received Cladribine 5.25 mg/kg in previous study 25643 (NCT00213135) and completed were re-randomized in this extension study and received cladribine tablet orally as cumulative dose of 0.875 mg/kg over a course of 4 or 5 consecutive days of 28-day period at Week 1, 5, 48, and 52 resulting in total cladribine dose of 3.5 mg/kg during the treatment period of 96 weeks. Participants were followed up for 24 weeks in supplemental follow-up period.

	Description
Placebo/Cladribine Low Dose (PPLL)	Participants who received placebo matched to cladribine in previous study 25643 (NCT00213135) and completed were re-randomized in this extension study and received Cladribine tablet orally as cumulative dose of 0.875 mg/kg over a course of 4 or 5 consecutive days of 28-day period at Week 1, 5, 48, and 52 resulting in total cladribine dose of 3.5 mg/kg during the treatment period of 96 weeks. Participants were followed up for 24 weeks in supplemental follow-up period.

Measured Values

	Cladribine Low/ Placebo (LLPP)	Cladribine High Dose/ Placebo (HLPP)	Cladribine Low/Low Dose (LLLL)	Cladribine High/Low Dose (HLLL)	Placebo/ Cladribine Low Dose (PPLL)
Number of Participants Analyzed	98	92	186	186	244
Number of Participants Who Developed Herpes Zoster Infections and Malignancies [units: Participants]					
Herpes Zoster Infections	2	1	2	9	5
Malignancies	2	1	7	2	2

5. Secondary Outcome Measure:

Measure Title	Annualized Qualifying Relapse Rate
Measure Description	A qualifying relapse was defined as an increase of 2 points in at least one functional system of the expanded disability status scale (EDSS) or an increase of 1 point in at least two functional systems (excluding changes in bowel or bladder function or cognition) in the absence of fever, lasting for at least 24 hours and to have been preceded by at least 30 days of clinical stability or improvement. Expanded disability status scale (EDSS) assesses disability in 8 functional systems. An overall score ranging from 0 (normal) to 10 (death due to multiple sclerosis [MS]) was calculated. The annualized relapse rate for each treatment group was calculated as the total number of confirmed relapses divided by the total number of days on study multiplied by 365.25.
Time Frame	Week 96
Safety Issue?	No

Analysis Population Description

Intention-to-treat (ITT) population included all participants who were randomized in the study.

Reporting Groups

	Description
Cladribine Low/Placebo (LLPP)	Participants who received cladribine 3.5 milligram/kilogram (mg/kg) in previous study 25643 (NCT00213135) and completed were re-randomized in this extension study and received placebo matched to cladribine tablet 0.875 mg/kg orally over a course of 4 or 5 consecutive days of 28-day period at Week 1, 5, 48, and 52 resulting in total dose of 3.5 mg/kg during the treatment period of 96 weeks. Participants were followed up for 24 weeks in supplemental follow-up period.
Cladribine High Dose/Placebo (HLPP)	Participants who received Cladribine 5.25 mg/kg in previous study 25643 (NCT00213135) and completed were re-randomized in this extension study and received placebo matched to cladribine tablet 0.875 mg/kg orally over a course of 4 or 5 consecutive days of 28-day period at Week 1, 5, 48, and 52 resulting in total dose of 3.5 mg/kg during the treatment period of 96 weeks. Participants were followed up for 24 weeks in supplemental follow-up period.
Cladribine Low/Low Dose (LLLL)	Participants who received Cladribine 3.5 mg/kg in previous study 25643 (NCT00213135) and completed were re-randomized in this extension study and received cladribine tablet orally as cumulative dose of 0.875 mg/kg over a course of 4 or 5 consecutive days of 28-day period at Week 1, 5, 48, and 52 resulting in total cladribine dose of 3.5 mg/kg during the treatment period of 96 weeks. Participants were followed up for 24 weeks in supplemental follow-up period.
Cladribine High/Low Dose (HLLL)	Participants who received Cladribine 5.25 mg/kg in previous study 25643 (NCT00213135) and completed were re-randomized in this extension study and received cladribine tablet orally as cumulative dose of 0.875 mg/kg over a course of 4 or 5 consecutive days of 28-day period at Week 1, 5, 48, and 52 resulting in total cladribine dose of 3.5 mg/kg during the treatment period of 96 weeks. Participants were followed up for 24 weeks in supplemental follow-up period.
Placebo/Cladribine Low Dose (PPLL)	Participants who received placebo matched to cladribine in previous study 25643 (NCT00213135) and completed were re-randomized in this extension study and received Cladribine tablet orally as cumulative dose of 0.875 mg/kg over a course of 4 or 5 consecutive days of 28-day period at Week 1, 5, 48, and 52 resulting in total cladribine dose of 3.5 mg/kg during the treatment period of 96 weeks. Participants were followed up for 24 weeks in supplemental follow-up period.

Measured Values

	Cladribine Low/ Placebo (LLPP)	Cladribine High Dose/ Placebo (HLPP)	Cladribine Low/Low Dose (LLLL)	Cladribine High/Low Dose (HLLL)	Placebo/ Cladribine Low Dose (PPLL)
Number of Participants Analyzed	98	92	186	186	244
Annualized Qualifying Relapse Rate [units: relapses per year] Number (95% Confidence Interval)	0.15 (0.08 to 0.22)	0.16 (0.09 to 0.23)	0.10 (0.06 to 0.14)	0.11 (0.07 to 0.15)	0.10 (0.07 to 0.13)

6. Secondary Outcome Measure:

Measure Title	Mean Number of Combined Unique (CU) Lesions
Measure Description	Mean Number of CU lesions were measured by using magnetic resonance imaging (MRI) scans.
Time Frame	Week 96
Safety Issue?	No

Analysis Population Description

ITT population included all participants who were randomized in the study.

Reporting Groups

	Description
Cladribine Low/Placebo (LLPP)	Participants who received cladribine 3.5 milligram/kilogram (mg/kg) in previous study 25643 (NCT00213135) and completed were re-randomized in this extension study and received placebo matched to cladribine tablet 0.875 mg/kg orally over a course of 4 or 5 consecutive days of 28-day period at Week 1, 5, 48, and 52 resulting in total dose of 3.5 mg/kg during the treatment period of 96 weeks. Participants were followed up for 24 weeks in supplemental follow-up period.
Cladribine High Dose/Placebo (HLPP)	Participants who received Cladribine 5.25 mg/kg in previous study 25643 (NCT00213135) and completed were re-randomized in this extension study and received placebo matched to cladribine tablet 0.875 mg/kg orally over a course of 4 or 5 consecutive days of 28-day period at Week 1, 5, 48, and 52 resulting in total dose of 3.5 mg/kg during the treatment period of 96 weeks. Participants were followed up for 24 weeks in supplemental follow-up period.
Cladribine Low/Low Dose (LLLL)	Participants who received Cladribine 3.5 mg/kg in previous study 25643 (NCT00213135) and completed were re-randomized in this extension study and received cladribine tablet orally as cumulative dose of 0.875 mg/kg over a course of 4 or 5 consecutive days of 28-day period at Week 1, 5, 48, and 52 resulting in total cladribine dose of 3.5 mg/kg during the treatment period of 96 weeks. Participants were followed up for 24 weeks in supplemental follow-up period.
Cladribine High/Low Dose (HLLL)	Participants who received Cladribine 5.25 mg/kg in previous study 25643 (NCT00213135) and completed were re-randomized in this extension study and received cladribine tablet orally as cumulative dose of 0.875 mg/kg over a course of 4 or 5 consecutive days of 28-day period at Week 1, 5, 48, and 52 resulting in total cladribine dose of 3.5 mg/kg during the treatment period of 96 weeks. Participants were followed up for 24 weeks in supplemental follow-up period.
Placebo/Cladribine Low Dose (PPLL)	Participants who received placebo matched to cladribine in previous study 25643 (NCT00213135) and completed were re-randomized in this extension study and received Cladribine tablet orally as cumulative dose of 0.875 mg/kg over a course of 4 or 5 consecutive days of 28-day period at Week 1, 5, 48, and 52 resulting in total cladribine dose of 3.5 mg/kg during the treatment period of 96 weeks. Participants were followed up for 24 weeks in supplemental follow-up period.

Measured Values

	Cladribine Low/ Placebo (LLPP)	Cladribine High Dose/ Placebo (HLPP)	Cladribine Low/Low Dose (LLLL)	Cladribine High/Low Dose (HLLL)	Placebo/ Cladribine Low Dose (PPLL)
Number of Participants Analyzed	98	92	186	186	244
Mean Number of Combined Unique (CU) Lesions [units: lesions] Mean (Standard Deviation)	5.88 (15.31)	6.02 (9.22)	3.97 (7.18)	5.53 (14.79)	5.10 (9.08)

7. Secondary Outcome Measure:

Measure Title	Time to Disability Progression (Confirmed After 3 Months)
Measure Description	Time to disability progression was defined as the time to a sustained increase in EDSS score of at least 1 point if baseline EDSS score between 0.5 and 4.5 inclusively, or at least 1.5 points if the baseline EDSS score was 0, or at least 0.5 point if the baseline EDSS score was at least 5, over a period of at least three months. 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. As few participants have reached EDSS progression, fourth Percentile of time to sustained increase in EDSS score was reported using Kaplan-Meier survival curve.
Time Frame	Baseline up to Week 96
Safety Issue?	No

Analysis Population Description

ITT population included all participants who were randomized in the study.

Reporting Groups

	Description
Cladribine Low/Placebo (LLPP)	Participants who received cladribine 3.5 milligram/kilogram (mg/kg) in previous study 25643 (NCT00213135) and completed were re-randomized in this extension study and received placebo matched to cladribine tablet 0.875 mg/kg orally over a course of 4 or 5 consecutive days of 28-day period at Week 1, 5, 48, and 52 resulting in total dose of 3.5 mg/kg during the treatment period of 96 weeks. Participants were followed up for 24 weeks in supplemental follow-up period.
Cladribine High Dose/Placebo (HLPP)	Participants who received Cladribine 5.25 mg/kg in previous study 25643 (NCT00213135) and completed were re-randomized in this extension study and received placebo matched to cladribine tablet 0.875 mg/kg orally over a course of 4 or 5 consecutive days of 28-day period at Week 1, 5, 48, and 52 resulting in total dose of 3.5 mg/kg during the treatment period of 96 weeks. Participants were followed up for 24 weeks in supplemental follow-up period.

	Description
Cladribine Low/Low Dose (LLLL)	Participants who received Cladribine 3.5 mg/kg in previous study 25643 (NCT00213135) and completed were re-randomized in this extension study and received cladribine tablet orally as cumulative dose of 0.875 mg/kg over a course of 4 or 5 consecutive days of 28-day period at Week 1, 5, 48, and 52 resulting in total cladribine dose of 3.5 mg/kg during the treatment period of 96 weeks. Participants were followed up for 24 weeks in supplemental follow-up period.
Cladribine High/Low Dose (HLLL)	Participants who received Cladribine 5.25 mg/kg in previous study 25643 (NCT00213135) and completed were re-randomized in this extension study and received cladribine tablet orally as cumulative dose of 0.875 mg/kg over a course of 4 or 5 consecutive days of 28-day period at Week 1, 5, 48, and 52 resulting in total cladribine dose of 3.5 mg/kg during the treatment period of 96 weeks. Participants were followed up for 24 weeks in supplemental follow-up period.
Placebo/Cladribine Low Dose (PPLL)	Participants who received placebo matched to cladribine in previous study 25643 (NCT00213135) and completed were re-randomized in this extension study and received Cladribine tablet orally as cumulative dose of 0.875 mg/kg over a course of 4 or 5 consecutive days of 28-day period at Week 1, 5, 48, and 52 resulting in total cladribine dose of 3.5 mg/kg during the treatment period of 96 weeks. Participants were followed up for 24 weeks in supplemental follow-up period.

Measured Values

	Cladribine Low/ Placebo (LLPP)	Cladribine High Dose/ Placebo (HLPP)	Cladribine Low/Low Dose (LLLL)	Cladribine High/Low Dose (HLLL)	Placebo/ Cladribine Low Dose (PPLL)
Number of Participants Analyzed	98	92	186	186	244
Time to Disability Progression (Confirmed After 3 Months) [units: months]	5.6	5.5	8.2	5.5	5.4

Reported Adverse Events

Time Frame	Adverse events collected from baseline up to Week 96 and 24-Week supplemental follow-up period.
Additional Description	[Not specified]

Reporting Groups

	Description
Cladribine Low/Placebo (LLPP)	Participants who received cladribine 3.5 milligram/kilogram (mg/kg) in previous study 25643 (NCT00213135) and completed were re-randomized in this extension study and received placebo matched to cladribine tablet 0.875 mg/kg orally over a course of 4 or 5 consecutive days of 28-day period at Week 1, 5, 48, and 52 resulting in total dose of 3.5 mg/kg during the treatment period of 96 weeks. Participants were followed up for 24 weeks in supplemental follow-up period.
Cladribine High Dose/Placebo (HLPP)	Participants who received Cladribine 5.25 mg/kg in previous study 25643 (NCT00213135) and completed were re-randomized in this extension study and received placebo matched to cladribine tablet 0.875 mg/kg orally over a course of 4 or 5 consecutive days of 28-day period at Week 1, 5, 48, and 52 resulting in total dose of 3.5 mg/kg during the treatment period of 96 weeks. Participants were followed up for 24 weeks in supplemental follow-up period.
Cladribine Low/Low Dose (LLLL)	Participants who received Cladribine 3.5 mg/kg in previous study 25643 (NCT00213135) and completed were re-randomized in this extension study and received cladribine tablet orally as cumulative dose of 0.875 mg/kg over a course of 4 or 5 consecutive days of 28-day period at Week 1, 5, 48, and 52 resulting in total cladribine dose of 3.5 mg/kg during the treatment period of 96 weeks. Participants were followed up for 24 weeks in supplemental follow-up period.
Cladribine High/Low Dose (HLLL)	Participants who received Cladribine 5.25 mg/kg in previous study 25643 (NCT00213135) and completed were re-randomized in this extension study and received cladribine tablet orally as cumulative dose of 0.875 mg/kg over a course of 4 or 5 consecutive days of 28-day period at Week 1, 5, 48, and 52 resulting in total cladribine dose of 3.5 mg/kg during the treatment period of 96 weeks. Participants were followed up for 24 weeks in supplemental follow-up period.
Placebo/Cladribine Low Dose (PPLL)	Participants who received placebo matched to cladribine in previous study 25643 (NCT00213135) and completed were re-randomized in this extension study and received Cladribine tablet orally as cumulative dose of 0.875 mg/kg over a course of 4 or 5 consecutive days of 28-day period at Week 1, 5, 48, and 52 resulting in total cladribine dose of 3.5 mg/kg during the treatment period of 96 weeks. Participants were followed up for 24 weeks in supplemental follow-up period.
Placebo/No Treatment	Participants who received placebo matched to cladribine in previous study 25643 (NCT00213135) and were enrolled in this extension study and received no cladribine treatment and were followed up for safety assessment for 96 weeks (during the treatment period) and followed up for 24 weeks (during supplemental follow-up period).
Cladribine 3.5 mg/kg/No Treatment	Participants who received Cladribine 3.5 mg/kg in previous study 25643 (NCT00213135) and completed were enrolled in this extension study and received no cladribine treatment and were followed up for safety assessment for 96 weeks (during the treatment period) and followed up for 24 weeks (during supplemental follow-up period).
Cladribine 5.25 mg/kg/No Treatment	Participants who received Cladribine 5.25 mg/kg in previous study 25643 (NCT00213135) and completed were enrolled in this extension study and received no cladribine treatment and were followed up for safety assessment for 96 weeks (during the treatment period) and followed up for 24 weeks (during supplemental follow-up period).

	Description
Cladribine Low/Placebo (LLPP) (24-week Follow-up Period)	Participants who received placebo matched to cladribine tablet during the treatment period of 96 weeks were followed up for 24 weeks in supplemental follow-up period.
Cladribine High Dose/Placebo (HLPP) (24-week Follow-up Period	Participants who received placebo matched to cladribine tablet during the treatment period of 96 weeks were followed up for 24 weeks in supplemental follow-up period.
Cladribine Low/Low Dose (LLLL) (24-week Follow-up Period)	Participants who received cladribine 3.5 mg/kg during the treatment period of 96 weeks were followed up for 24 weeks in supplemental follow-up period.
Cladribine High/Low Dose (HLLL) (24-week Follow-up Period)	Participants who received cladribine 3.5 mg/kg during the treatment period of 96 weeks were followed up for 24 weeks in supplemental follow-up period.
Placebo/Cladribine Low Dose (PPLL) (24-week Follow-up Period)	Participants who received cladribine 3.5 mg/kg during the treatment period of 96 weeks were followed up for 24 weeks in supplemental follow-up period.
Placebo/No Treatment (24-week Follow-up Period)	Participants who received no cladribine treatment during 96 weeks were followed up for 24-Week supplemental follow-up period.
Cladribine 3.5 mg/kg/No Treatment (24-week Follow-up Period)	Participants who received no cladribine treatment during 96 weeks were followed up for 24 weeks in supplemental follow-up period.
Cladribine 5.25 mg/kg/No Treatment (24-week Follow-up Period)	Participants who received no cladribine treatment during 96 weeks were followed up for 24 weeks in supplemental follow-up period.

Serious Adverse Events

	Cladribine Low/ Placebo (LLPP)	Cladribine High Dose/ Placebo (HLPP)	Cladribine Low/Low Dose (LLLL)	Cladribine High/Low Dose (HLLL)	Placebo/ Cladribine Low Dose (PPLL)	Placebo/No Treatment
	Affected/ At Risk (%)	Affected/ At Risk (%)	Affected/ At Risk (%)	Affected/ At Risk (%)	Affected/ At Risk (%)	Affected/ At Risk (%)
Total	14/98 (14.29%)	7/92 (7.61%)	23/186 (12.37%)	21/186 (11.29%)	21/244 (8.61%)	1/22 (4.55%)
Blood and lymphatic system disorders						
Iron deficiency anaemia [A] *	0/98 (0%)	0/92 (0%)	1/186 (0.54%)	0/186 (0%)	0/244 (0%)	0/22 (0%)
Lymphopenia [A] *	0/98 (0%)	0/92 (0%)	0/186 (0%)	1/186 (0.54%)	1/244 (0.41%)	0/22 (0%)
Thrombocytopenia [A] *	0/98 (0%)	0/92 (0%)	0/186 (0%)	0/186 (0%)	0/244 (0%)	0/22 (0%)
Cardiac disorders						
Adams-Stokes syndrome [A] *	0/98 (0%)	0/92 (0%)	0/186 (0%)	1/186 (0.54%)	0/244 (0%)	0/22 (0%)
Atrial fibrillation [A] *	0/98 (0%)	0/92 (0%)	0/186 (0%)	0/186 (0%)	1/244 (0.41%)	0/22 (0%)

	Cladribine Low/ Placebo (LLPP)	Cladribine High Dose/ Placebo (HLPP)	Cladribine Low/Low Dose (LLLL)	Cladribine High/Low Dose (HLLL)	Placebo/ Cladribine Low Dose (PPLL)	Placebo/No Treatment
	Affected/ At Risk (%)	Affected/ At Risk (%)	Affected/ At Risk (%)	Affected/ At Risk (%)	Affected/ At Risk (%)	Affected/ At Risk (%)
Myocardial infarction [A] *	0/98 (0%)	0/92 (0%)	0/186 (0%)	0/186 (0%)	1/244 (0.41%)	0/22 (0%)
Tachycardia [A] *	1/98 (1.02%)	0/92 (0%)	0/186 (0%)	0/186 (0%)	0/244 (0%)	0/22 (0%)
Ear and labyrinth disorders						
Vertigo positional [A] *	0/98 (0%)	0/92 (0%)	0/186 (0%)	1/186 (0.54%)	0/244 (0%)	0/22 (0%)
Endocrine disorders						
Autoimmune thyroiditis [A] *	0/98 (0%)	0/92 (0%)	0/186 (0%)	0/186 (0%)	0/244 (0%)	0/22 (0%)
Basedow's disease [A] *	1/98 (1.02%)	0/92 (0%)	0/186 (0%)	0/186 (0%)	0/244 (0%)	0/22 (0%)
Thyroiditis [A] *	0/98 (0%)	0/92 (0%)	0/186 (0%)	1/186 (0.54%)	0/244 (0%)	0/22 (0%)
Eye disorders						
Iridocyclitis [A] *	1/98 (1.02%)	0/92 (0%)	0/186 (0%)	0/186 (0%)	0/244 (0%)	0/22 (0%)
Macular degeneration [A] *	1/98 (1.02%)	0/92 (0%)	0/186 (0%)	0/186 (0%)	0/244 (0%)	0/22 (0%)
Gastrointestinal disorders						
Abdominal pain [A] *	0/98 (0%)	0/92 (0%)	1/186 (0.54%)	0/186 (0%)	1/244 (0.41%)	0/22 (0%)
Colonic polyp [A] *	0/98 (0%)	0/92 (0%)	0/186 (0%)	1/186 (0.54%)	0/244 (0%)	0/22 (0%)
Crohn's disease [A] *	0/98 (0%)	0/92 (0%)	0/186 (0%)	0/186 (0%)	0/244 (0%)	0/22 (0%)
Duodenal ulcer [A] *	1/98 (1.02%)	0/92 (0%)	0/186 (0%)	0/186 (0%)	0/244 (0%)	0/22 (0%)
Duodenal ulcer perforation [A] *	0/98 (0%)	1/92 (1.09%)	0/186 (0%)	0/186 (0%)	0/244 (0%)	0/22 (0%)
Gastric haemorrhage [A] *	1/98 (1.02%)	0/92 (0%)	0/186 (0%)	0/186 (0%)	0/244 (0%)	0/22 (0%)
Gastritis [A] *	0/98 (0%)	0/92 (0%)	0/186 (0%)	0/186 (0%)	1/244 (0.41%)	0/22 (0%)
Gastrooesophageal reflux disease [A] *	0/98 (0%)	0/92 (0%)	0/186 (0%)	0/186 (0%)	1/244 (0.41%)	0/22 (0%)
Ileus paralytic [A] *	0/98 (0%)	0/92 (0%)	1/186 (0.54%)	0/186 (0%)	0/244 (0%)	0/22 (0%)

	Cladribine Low/ Placebo (LLPP)	Cladribine High Dose/ Placebo (HLPP)	Cladribine Low/Low Dose (LLLL)	Cladribine High/Low Dose (HLLL)	Placebo/ Cladribine Low Dose (PPLL)	Placebo/No Treatment
	Affected/ At Risk (%)	Affected/ At Risk (%)	Affected/ At Risk (%)	Affected/ At Risk (%)	Affected/ At Risk (%)	Affected/ At Risk (%)
Irritable bowel syndrome [A] *	0/98 (0%)	0/92 (0%)	0/186 (0%)	0/186 (0%)	1/244 (0.41%)	0/22 (0%)
Peritonitis [A] *	0/98 (0%)	0/92 (0%)	0/186 (0%)	1/186 (0.54%)	0/244 (0%)	0/22 (0%)
General disorders						
Chest pain [A] *	0/98 (0%)	0/92 (0%)	0/186 (0%)	1/186 (0.54%)	0/244 (0%)	0/22 (0%)
Death [A] *	1/98 (1.02%)	0/92 (0%)	0/186 (0%)	0/186 (0%)	0/244 (0%)	0/22 (0%)
Drowning [A] *	1/98 (1.02%)	0/92 (0%)	0/186 (0%)	0/186 (0%)	0/244 (0%)	0/22 (0%)
Influenza like illness [A] *	0/98 (0%)	0/92 (0%)	0/186 (0%)	0/186 (0%)	1/244 (0.41%)	0/22 (0%)
Hepatobiliary disorders						
Biliary colic [A] *	0/98 (0%)	0/92 (0%)	0/186 (0%)	1/186 (0.54%)	0/244 (0%)	0/22 (0%)
Biliary tract disorder [A] *	0/98 (0%)	0/92 (0%)	0/186 (0%)	1/186 (0.54%)	0/244 (0%)	0/22 (0%)
Cholecystitis [A] *	1/98 (1.02%)	0/92 (0%)	0/186 (0%)	1/186 (0.54%)	0/244 (0%)	0/22 (0%)
Cholelithiasis [A] *	1/98 (1.02%)	0/92 (0%)	2/186 (1.08%)	1/186 (0.54%)	0/244 (0%)	0/22 (0%)
Immune system disorders						
Secondary immunodeficiency [A] *	0/98 (0%)	0/92 (0%)	1/186 (0.54%)	0/186 (0%)	0/244 (0%)	0/22 (0%)
Infections and infestations						
Abscess oral [A] *	0/98 (0%)	0/92 (0%)	1/186 (0.54%)	0/186 (0%)	0/244 (0%)	0/22 (0%)
Appendicitis [A] *	1/98 (1.02%)	0/92 (0%)	0/186 (0%)	0/186 (0%)	0/244 (0%)	0/22 (0%)
Bacterial sepsis [A] *	0/98 (0%)	0/92 (0%)	0/186 (0%)	1/186 (0.54%)	0/244 (0%)	0/22 (0%)
Breast abscess [A] *	0/98 (0%)	0/92 (0%)	0/186 (0%)	0/186 (0%)	1/244 (0.41%)	0/22 (0%)
Gastroenteritis [A] *	0/98 (0%)	0/92 (0%)	0/186 (0%)	0/186 (0%)	1/244 (0.41%)	0/22 (0%)
Herpes zoster [A] *	0/98 (0%)	0/92 (0%)	0/186 (0%)	2/186 (1.08%)	1/244 (0.41%)	0/22 (0%)

	Cladribine Low/ Placebo (LLPP)	Cladribine High Dose/ Placebo (HLPP)	Cladribine Low/Low Dose (LLLL)	Cladribine High/Low Dose (HLLL)	Placebo/ Cladribine Low Dose (PPLL)	Placebo/No Treatment
	Affected/ At Risk (%)	Affected/ At Risk (%)	Affected/ At Risk (%)	Affected/ At Risk (%)	Affected/ At Risk (%)	Affected/ At Risk (%)
Infection [A] *	1/98 (1.02%)	0/92 (0%)	0/186 (0%)	0/186 (0%)	0/244 (0%)	0/22 (0%)
Influenza [A] *	0/98 (0%)	0/92 (0%)	1/186 (0.54%)	0/186 (0%)	0/244 (0%)	0/22 (0%)
Pneumonia [A] *	0/98 (0%)	0/92 (0%)	0/186 (0%)	0/186 (0%)	2/244 (0.82%)	0/22 (0%)
Pulmonary tuberculosis [A] *	0/98 (0%)	0/92 (0%)	0/186 (0%)	1/186 (0.54%)	0/244 (0%)	0/22 (0%)
Pyelonephritis [A] *	0/98 (0%)	1/92 (1.09%)	0/186 (0%)	0/186 (0%)	0/244 (0%)	0/22 (0%)
Pyelonephritis chronic [A] *	0/98 (0%)	1/92 (1.09%)	0/186 (0%)	0/186 (0%)	0/244 (0%)	0/22 (0%)
Tuberculosis [A] *	1/98 (1.02%)	0/92 (0%)	0/186 (0%)	0/186 (0%)	0/244 (0%)	0/22 (0%)
Urethral abscess [A] *	0/98 (0%)	0/92 (0%)	0/186 (0%)	0/186 (0%)	1/244 (0.41%)	0/22 (0%)
Urinary tract infection [A] *	0/98 (0%)	0/92 (0%)	0/186 (0%)	0/186 (0%)	1/244 (0.41%)	0/22 (0%)
Injury, poisoning and procedural complications						
Femoral neck fracture [A] *	0/98 (0%)	0/92 (0%)	0/186 (0%)	0/186 (0%)	1/244 (0.41%)	0/22 (0%)
Humerus fracture [A] *	0/98 (0%)	0/92 (0%)	0/186 (0%)	1/186 (0.54%)	0/244 (0%)	0/22 (0%)
Intentional overdose [A] *	0/98 (0%)	0/92 (0%)	0/186 (0%)	0/186 (0%)	1/244 (0.41%)	0/22 (0%)
Limb injury [A] *	0/98 (0%)	0/92 (0%)	1/186 (0.54%)	0/186 (0%)	0/244 (0%)	0/22 (0%)
Radius fracture [A] *	0/98 (0%)	0/92 (0%)	0/186 (0%)	0/186 (0%)	0/244 (0%)	0/22 (0%)
Road traffic accident [A] *	0/98 (0%)	0/92 (0%)	0/186 (0%)	1/186 (0.54%)	0/244 (0%)	0/22 (0%)
Subdural haematoma [A] *	0/98 (0%)	0/92 (0%)	1/186 (0.54%)	0/186 (0%)	0/244 (0%)	0/22 (0%)
Investigations						
Blood culture positive [A] *	1/98 (1.02%)	0/92 (0%)	0/186 (0%)	0/186 (0%)	0/244 (0%)	0/22 (0%)
Pregnancy test positive [A] *	0/98 (0%)	0/92 (0%)	0/186 (0%)	0/186 (0%)	1/244 (0.41%)	0/22 (0%)
Tuberculin test positive [A] *	0/98 (0%)	0/92 (0%)	0/186 (0%)	0/186 (0%)	1/244 (0.41%)	0/22 (0%)

	Cladribine Low/ Placebo (LLPP)	Cladribine High Dose/ Placebo (HLPP)	Cladribine Low/Low Dose (LLLL)	Cladribine High/Low Dose (HLLL)	Placebo/ Cladribine Low Dose (PPLL)	Placebo/No Treatment
	Affected/ At Risk (%)	Affected/ At Risk (%)	Affected/ At Risk (%)	Affected/ At Risk (%)	Affected/ At Risk (%)	Affected/ At Risk (%)
Weight decreased [A] *	0/98 (0%)	0/92 (0%)	1/186 (0.54%)	0/186 (0%)	0/244 (0%)	0/22 (0%)
Metabolism and nutrition disorders						
Diabetic ketoacidosis [A] *	0/98 (0%)	0/92 (0%)	0/186 (0%)	0/186 (0%)	1/244 (0.41%)	0/22 (0%)
Hypokalaemia [A] *	0/98 (0%)	0/92 (0%)	1/186 (0.54%)	0/186 (0%)	0/244 (0%)	0/22 (0%)
Type 2 diabetes mellitus [A] *	0/98 (0%)	0/92 (0%)	1/186 (0.54%)	0/186 (0%)	0/244 (0%)	0/22 (0%)
Musculoskeletal and connective tissue disorders						
Intervertebral disc protrusion [A] *	1/98 (1.02%)	1/92 (1.09%)	0/186 (0%)	0/186 (0%)	0/244 (0%)	0/22 (0%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)						
Adrenal adenoma [A] *	0/98 (0%)	0/92 (0%)	0/186 (0%)	1/186 (0.54%)	0/244 (0%)	0/22 (0%)
Basal cell carcinoma [A] *	1/98 (1.02%)	0/92 (0%)	0/186 (0%)	0/186 (0%)	0/244 (0%)	1/22 (4.55%)
Bile duct cancer [A] *	0/98 (0%)	0/92 (0%)	0/186 (0%)	0/186 (0%)	0/244 (0%)	0/22 (0%)
Breast cancer [A] *	0/98 (0%)	0/92 (0%)	1/186 (0.54%)	0/186 (0%)	0/244 (0%)	0/22 (0%)
Breast fibroma [A] *	0/98 (0%)	0/92 (0%)	0/186 (0%)	1/186 (0.54%)	0/244 (0%)	0/22 (0%)
Colorectal cancer metastatic [A] *	0/98 (0%)	0/92 (0%)	1/186 (0.54%)	0/186 (0%)	0/244 (0%)	0/22 (0%)
Fibrous histiocytoma [A] *	1/98 (1.02%)	0/92 (0%)	0/186 (0%)	0/186 (0%)	0/244 (0%)	0/22 (0%)
Haemangioma of liver [A] *	0/98 (0%)	0/92 (0%)	0/186 (0%)	1/186 (0.54%)	0/244 (0%)	0/22 (0%)
Juvenile melanoma benign [A] *	0/98 (0%)	0/92 (0%)	0/186 (0%)	0/186 (0%)	1/244 (0.41%)	0/22 (0%)
Lipoma [A] *	0/98 (0%)	1/92 (1.09%)	0/186 (0%)	0/186 (0%)	1/244 (0.41%)	0/22 (0%)
Lung neoplasm [A] *	0/98 (0%)	0/92 (0%)	0/186 (0%)	0/186 (0%)	0/244 (0%)	0/22 (0%)
Malignant melanoma [A] *	1/98 (1.02%)	0/92 (0%)	0/186 (0%)	1/186 (0.54%)	0/244 (0%)	0/22 (0%)
Melanocytic naevus [A] *	0/98 (0%)	0/92 (0%)	0/186 (0%)	1/186 (0.54%)	0/244 (0%)	0/22 (0%)

	Cladribine Low/ Placebo (LLPP)	Cladribine High Dose/ Placebo (HLPP)	Cladribine Low/Low Dose (LLLL)	Cladribine High/Low Dose (HLLL)	Placebo/ Cladribine Low Dose (PPLL)	Placebo/No Treatment
	Affected/ At Risk (%)	Affected/ At Risk (%)	Affected/ At Risk (%)	Affected/ At Risk (%)	Affected/ At Risk (%)	Affected/ At Risk (%)
Metastases to lung [A] *	0/98 (0%)	0/92 (0%)	0/186 (0%)	0/186 (0%)	0/244 (0%)	0/22 (0%)
Metastases to lymph nodes [A] *	0/98 (0%)	0/92 (0%)	0/186 (0%)	0/186 (0%)	0/244 (0%)	0/22 (0%)
Neurilemmoma benign [A] *	0/98 (0%)	0/92 (0%)	0/186 (0%)	0/186 (0%)	1/244 (0.41%)	0/22 (0%)
Ovarian cancer [A] *	0/98 (0%)	0/92 (0%)	1/186 (0.54%)	0/186 (0%)	0/244 (0%)	0/22 (0%)
Prostatic adenoma [A] *	0/98 (0%)	0/92 (0%)	0/186 (0%)	1/186 (0.54%)	0/244 (0%)	0/22 (0%)
Rectal cancer [A] *	0/98 (0%)	0/92 (0%)	1/186 (0.54%)	0/186 (0%)	0/244 (0%)	0/22 (0%)
Renal cell carcinoma [A] *	0/98 (0%)	0/92 (0%)	0/186 (0%)	1/186 (0.54%)	0/244 (0%)	0/22 (0%)
Seborrhoeic keratosis [A] *	0/98 (0%)	0/92 (0%)	1/186 (0.54%)	0/186 (0%)	0/244 (0%)	0/22 (0%)
Skin papilloma [A] *	0/98 (0%)	0/92 (0%)	0/186 (0%)	1/186 (0.54%)	0/244 (0%)	0/22 (0%)
Squamous cell carcinoma [A] *	0/98 (0%)	0/92 (0%)	1/186 (0.54%)	0/186 (0%)	0/244 (0%)	0/22 (0%)
Thyroid adenoma [A] *	0/98 (0%)	0/92 (0%)	1/186 (0.54%)	0/186 (0%)	0/244 (0%)	0/22 (0%)
Thyroid cancer [A] *	0/98 (0%)	1/92 (1.09%)	0/186 (0%)	0/186 (0%)	0/244 (0%)	0/22 (0%)
Uterine leiomyoma [A] *	0/98 (0%)	0/92 (0%)	1/186 (0.54%)	2/186 (1.08%)	0/244 (0%)	0/22 (0%)
Nervous system disorders						
Brain injury [A] *	0/98 (0%)	0/92 (0%)	1/186 (0.54%)	0/186 (0%)	0/244 (0%)	0/22 (0%)
Cauda equina syndrome [A] *	0/98 (0%)	0/92 (0%)	0/186 (0%)	1/186 (0.54%)	0/244 (0%)	0/22 (0%)
Radicular syndrome [A] *	1/98 (1.02%)	0/92 (0%)	0/186 (0%)	0/186 (0%)	0/244 (0%)	0/22 (0%)
Sciatica [A] *	1/98 (1.02%)	0/92 (0%)	0/186 (0%)	0/186 (0%)	0/244 (0%)	0/22 (0%)
Status epilepticus [A] *	0/98 (0%)	0/92 (0%)	1/186 (0.54%)	0/186 (0%)	0/244 (0%)	0/22 (0%)
Pregnancy, puerperium and perinatal conditions						
Abortion missed [A] *	0/98 (0%)	0/92 (0%)	0/186 (0%)	0/186 (0%)	0/244 (0%)	0/22 (0%)

	Cladribine Low/ Placebo (LLPP)	Cladribine High Dose/ Placebo (HLPP)	Cladribine Low/Low Dose (LLLL)	Cladribine High/Low Dose (HLLL)	Placebo/ Cladribine Low Dose (PPLL)	Placebo/No Treatment
	Affected/ At Risk (%)	Affected/ At Risk (%)	Affected/ At Risk (%)	Affected/ At Risk (%)	Affected/ At Risk (%)	Affected/ At Risk (%)
Abortion threatened [A] *	0/98 (0%)	0/92 (0%)	0/186 (0%)	0/186 (0%)	0/244 (0%)	0/22 (0%)
Psychiatric disorders						
Mental disorder [A] *	0/98 (0%)	0/92 (0%)	0/186 (0%)	0/186 (0%)	1/244 (0.41%)	0/22 (0%)
Suicidal ideation [A] *	1/98 (1.02%)	0/92 (0%)	0/186 (0%)	0/186 (0%)	0/244 (0%)	0/22 (0%)
Suicide attempt [A] *	0/98 (0%)	0/92 (0%)	0/186 (0%)	0/186 (0%)	1/244 (0.41%)	0/22 (0%)
Renal and urinary disorders						
Cystitis noninfective [A] *	0/98 (0%)	0/92 (0%)	0/186 (0%)	1/186 (0.54%)	0/244 (0%)	0/22 (0%)
Dysuria [A] *	0/98 (0%)	0/92 (0%)	0/186 (0%)	1/186 (0.54%)	0/244 (0%)	0/22 (0%)
Nephrolithiasis [A] *	0/98 (0%)	0/92 (0%)	0/186 (0%)	0/186 (0%)	0/244 (0%)	0/22 (0%)
Renal failure acute [A] *	0/98 (0%)	0/92 (0%)	1/186 (0.54%)	0/186 (0%)	0/244 (0%)	0/22 (0%)
Renal failure chronic [A] *	0/98 (0%)	0/92 (0%)	1/186 (0.54%)	0/186 (0%)	0/244 (0%)	0/22 (0%)
Reproductive system and breast disorders						
Menorrhagia [A] *	0/98 (0%)	0/92 (0%)	1/186 (0.54%)	0/186 (0%)	1/244 (0.41%)	0/22 (0%)
Ovarian cyst [A] *	0/98 (0%)	0/92 (0%)	1/186 (0.54%)	0/186 (0%)	1/244 (0.41%)	0/22 (0%)
Ovarian cyst ruptured [A] *	0/98 (0%)	0/92 (0%)	0/186 (0%)	1/186 (0.54%)	0/244 (0%)	0/22 (0%)
Respiratory, thoracic and mediastinal disorders						
Asthma [A] *	1/98 (1.02%)	0/92 (0%)	0/186 (0%)	0/186 (0%)	0/244 (0%)	0/22 (0%)
Bronchitis chronic [A] *	0/98 (0%)	0/92 (0%)	1/186 (0.54%)	0/186 (0%)	0/244 (0%)	0/22 (0%)
Pneumothorax [A] *	0/98 (0%)	0/92 (0%)	1/186 (0.54%)	0/186 (0%)	0/244 (0%)	0/22 (0%)
Respiratory failure [A] *	0/98 (0%)	0/92 (0%)	0/186 (0%)	0/186 (0%)	1/244 (0.41%)	0/22 (0%)
Skin and subcutaneous tissue disorders						

	Cladribine Low/ Placebo (LLPP)	Cladribine High Dose/ Placebo (HLPP)	Cladribine Low/Low Dose (LLLL)	Cladribine High/Low Dose (HLLL)	Placebo/ Cladribine Low Dose (PPLL)	Placebo/No Treatment
	Affected/ At Risk (%)	Affected/ At Risk (%)	Affected/ At Risk (%)	Affected/ At Risk (%)	Affected/ At Risk (%)	Affected/ At Risk (%)
Pain of skin [A] *	0/98 (0%)	0/92 (0%)	0/186 (0%)	0/186 (0%)	0/244 (0%)	0/22 (0%)
Surgical and medical procedures						
Abortion induced [A] *	0/98 (0%)	0/92 (0%)	0/186 (0%)	1/186 (0.54%)	0/244 (0%)	0/22 (0%)
Vascular disorders						
Varicose vein [A] *	0/98 (0%)	1/92 (1.09%)	0/186 (0%)	0/186 (0%)	0/244 (0%)	0/22 (0%)

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

	Cladribine 3.5 mg/kg/ No Treatment	Cladribine 5.25 mg/kg/ No Treatment	Cladribine Low/Placebo (LLPP) (24-week Follow-up Period)	Cladribine High Dose/Placebo (HLPP) (24-week Follow-up Period	Cladribine Low/Low Dose (LLLL) (24-week Follow-up Period)	Cladribine High/Low Dose (HLLL) (24-week Follow-up Period)
	Affected/ At Risk (%)	Affected/ At Risk (%)	Affected/ At Risk (%)	Affected/ At Risk (%)	Affected/ At Risk (%)	Affected/ At Risk (%)
Total	1/17 (5.88%)	3/22 (13.64%)	2/75 (2.67%)	0/69 (0%)	2/143 (1.4%)	1/151 (0.66%)
Blood and lymphatic system disorders						
Iron deficiency anaemia [A] *	0/17 (0%)	0/22 (0%)	0/75 (0%)	0/69 (0%)	0/143 (0%)	0/151 (0%)
Lymphopenia [A] *	0/17 (0%)	0/22 (0%)	0/75 (0%)	0/69 (0%)	0/143 (0%)	0/151 (0%)
Thrombocytopenia [A] *	0/17 (0%)	0/22 (0%)	1/75 (1.33%)	0/69 (0%)	0/143 (0%)	0/151 (0%)
Cardiac disorders						
Adams-Stokes syndrome [A] *	0/17 (0%)	0/22 (0%)	0/75 (0%)	0/69 (0%)	0/143 (0%)	0/151 (0%)
Atrial fibrillation [A] *	0/17 (0%)	0/22 (0%)	0/75 (0%)	0/69 (0%)	0/143 (0%)	0/151 (0%)
Myocardial infarction [A] *	0/17 (0%)	0/22 (0%)	0/75 (0%)	0/69 (0%)	0/143 (0%)	0/151 (0%)
Tachycardia [A] *	0/17 (0%)	0/22 (0%)	0/75 (0%)	0/69 (0%)	0/143 (0%)	0/151 (0%)

	Cladribine 3.5 mg/kg/ No Treatment	Cladribine 5.25 mg/kg/ No Treatment	Cladribine Low/Placebo (LLPP) (24-week Follow-up Period)	Cladribine High Dose/Placebo (HLPP) (24-week Follow-up Period	Cladribine Low/Low Dose (LLLL) (24-week Follow-up Period)	Cladribine High/Low Dose (HLLL) (24-week Follow-up Period)
	Affected/ At Risk (%)	Affected/ At Risk (%)	Affected/ At Risk (%)	Affected/ At Risk (%)	Affected/ At Risk (%)	Affected/ At Risk (%)
Ear and labyrinth disorders						
Vertigo positional [A] *	0/17 (0%)	0/22 (0%)	0/75 (0%)	0/69 (0%)	0/143 (0%)	0/151 (0%)
Endocrine disorders						
Autoimmune thyroiditis [A] *	0/17 (0%)	1/22 (4.55%)	0/75 (0%)	0/69 (0%)	0/143 (0%)	0/151 (0%)
Basedow's disease [A] *	0/17 (0%)	0/22 (0%)	0/75 (0%)	0/69 (0%)	0/143 (0%)	0/151 (0%)
Thyroiditis [A] *	0/17 (0%)	0/22 (0%)	0/75 (0%)	0/69 (0%)	0/143 (0%)	0/151 (0%)
Eye disorders						
Iridocyclitis [A] *	0/17 (0%)	0/22 (0%)	1/75 (1.33%)	0/69 (0%)	0/143 (0%)	0/151 (0%)
Macular degeneration [A] *	0/17 (0%)	0/22 (0%)	0/75 (0%)	0/69 (0%)	0/143 (0%)	0/151 (0%)
Gastrointestinal disorders						
Abdominal pain [A] *	0/17 (0%)	0/22 (0%)	0/75 (0%)	0/69 (0%)	0/143 (0%)	0/151 (0%)
Colonic polyp [A] *	0/17 (0%)	0/22 (0%)	0/75 (0%)	0/69 (0%)	0/143 (0%)	0/151 (0%)
Crohn's disease [A] *	0/17 (0%)	1/22 (4.55%)	0/75 (0%)	0/69 (0%)	0/143 (0%)	0/151 (0%)
Duodenal ulcer [A] *	0/17 (0%)	0/22 (0%)	0/75 (0%)	0/69 (0%)	0/143 (0%)	0/151 (0%)
Duodenal ulcer perforation [A] *	0/17 (0%)	0/22 (0%)	0/75 (0%)	0/69 (0%)	0/143 (0%)	0/151 (0%)
Gastric haemorrhage [A] *	0/17 (0%)	0/22 (0%)	0/75 (0%)	0/69 (0%)	0/143 (0%)	0/151 (0%)
Gastritis [A] *	0/17 (0%)	0/22 (0%)	0/75 (0%)	0/69 (0%)	0/143 (0%)	0/151 (0%)
Gastrooesophageal reflux disease [A] *	0/17 (0%)	0/22 (0%)	0/75 (0%)	0/69 (0%)	0/143 (0%)	0/151 (0%)
Ileus paralytic [A] *	0/17 (0%)	0/22 (0%)	0/75 (0%)	0/69 (0%)	0/143 (0%)	0/151 (0%)
Irritable bowel syndrome [A] *	0/17 (0%)	0/22 (0%)	0/75 (0%)	0/69 (0%)	0/143 (0%)	0/151 (0%)

	Cladribine 3.5 mg/kg/ No Treatment	Cladribine 5.25 mg/kg/ No Treatment	Cladribine Low/Placebo (LLPP) (24-week Follow-up Period)	Cladribine High Dose/Placebo (HLPP) (24-week Follow-up Period	Cladribine Low/Low Dose (LLLL) (24-week Follow-up Period)	Cladribine High/Low Dose (HLLL) (24-week Follow-up Period)
	Affected/ At Risk (%)	Affected/ At Risk (%)	Affected/ At Risk (%)	Affected/ At Risk (%)	Affected/ At Risk (%)	Affected/ At Risk (%)
Peritonitis [A] *	0/17 (0%)	0/22 (0%)	0/75 (0%)	0/69 (0%)	0/143 (0%)	0/151 (0%)
General disorders						
Chest pain [A] *	0/17 (0%)	0/22 (0%)	0/75 (0%)	0/69 (0%)	0/143 (0%)	0/151 (0%)
Death [A] *	0/17 (0%)	0/22 (0%)	0/75 (0%)	0/69 (0%)	0/143 (0%)	0/151 (0%)
Drowning [A] *	0/17 (0%)	0/22 (0%)	0/75 (0%)	0/69 (0%)	0/143 (0%)	0/151 (0%)
Influenza like illness [A] *	0/17 (0%)	0/22 (0%)	0/75 (0%)	0/69 (0%)	0/143 (0%)	0/151 (0%)
Hepatobiliary disorders						
Biliary colic [A] *	0/17 (0%)	0/22 (0%)	0/75 (0%)	0/69 (0%)	0/143 (0%)	0/151 (0%)
Biliary tract disorder [A] *	0/17 (0%)	0/22 (0%)	0/75 (0%)	0/69 (0%)	0/143 (0%)	0/151 (0%)
Cholecystitis [A] *	0/17 (0%)	0/22 (0%)	0/75 (0%)	0/69 (0%)	0/143 (0%)	0/151 (0%)
Cholelithiasis [A] *	0/17 (0%)	0/22 (0%)	0/75 (0%)	0/69 (0%)	0/143 (0%)	0/151 (0%)
Immune system disorders						
Secondary immunodeficiency [A] *	0/17 (0%)	0/22 (0%)	0/75 (0%)	0/69 (0%)	0/143 (0%)	0/151 (0%)
Infections and infestations						
Abscess oral [A] *	0/17 (0%)	0/22 (0%)	0/75 (0%)	0/69 (0%)	0/143 (0%)	0/151 (0%)
Appendicitis [A] *	0/17 (0%)	0/22 (0%)	0/75 (0%)	0/69 (0%)	0/143 (0%)	0/151 (0%)
Bacterial sepsis [A] *	0/17 (0%)	0/22 (0%)	0/75 (0%)	0/69 (0%)	0/143 (0%)	0/151 (0%)
Breast abscess [A] *	0/17 (0%)	0/22 (0%)	0/75 (0%)	0/69 (0%)	0/143 (0%)	0/151 (0%)
Gastroenteritis [A] *	0/17 (0%)	0/22 (0%)	0/75 (0%)	0/69 (0%)	0/143 (0%)	0/151 (0%)
Herpes zoster [A] *	0/17 (0%)	0/22 (0%)	0/75 (0%)	0/69 (0%)	0/143 (0%)	0/151 (0%)

	Cladribine 3.5 mg/kg/ No Treatment	Cladribine 5.25 mg/kg/ No Treatment	Cladribine Low/Placebo (LLPP) (24-week Follow-up Period)	Cladribine High Dose/Placebo (HLPP) (24-week Follow-up Period	Cladribine Low/Low Dose (LLLL) (24-week Follow-up Period)	Cladribine High/Low Dose (HLLL) (24-week Follow-up Period)
	Affected/ At Risk (%)	Affected/ At Risk (%)	Affected/ At Risk (%)	Affected/ At Risk (%)	Affected/ At Risk (%)	Affected/ At Risk (%)
Infection [A] *	0/17 (0%)	0/22 (0%)	0/75 (0%)	0/69 (0%)	0/143 (0%)	0/151 (0%)
Influenza [A] *	0/17 (0%)	0/22 (0%)	0/75 (0%)	0/69 (0%)	0/143 (0%)	0/151 (0%)
Pneumonia [A] *	0/17 (0%)	1/22 (4.55%)	0/75 (0%)	0/69 (0%)	0/143 (0%)	0/151 (0%)
Pulmonary tuberculosis [A] *	0/17 (0%)	0/22 (0%)	0/75 (0%)	0/69 (0%)	0/143 (0%)	0/151 (0%)
Pyelonephritis [A] *	0/17 (0%)	0/22 (0%)	0/75 (0%)	0/69 (0%)	0/143 (0%)	0/151 (0%)
Pyelonephritis chronic [A] *	0/17 (0%)	0/22 (0%)	0/75 (0%)	0/69 (0%)	0/143 (0%)	0/151 (0%)
Tuberculosis [A] *	0/17 (0%)	0/22 (0%)	0/75 (0%)	0/69 (0%)	0/143 (0%)	0/151 (0%)
Urethral abscess [A] *	0/17 (0%)	0/22 (0%)	0/75 (0%)	0/69 (0%)	0/143 (0%)	0/151 (0%)
Urinary tract infection [A] *	0/17 (0%)	0/22 (0%)	0/75 (0%)	0/69 (0%)	0/143 (0%)	0/151 (0%)
Injury, poisoning and procedural complications						
Femoral neck fracture [A] *	0/17 (0%)	0/22 (0%)	0/75 (0%)	0/69 (0%)	0/143 (0%)	0/151 (0%)
Humerus fracture [A] *	0/17 (0%)	0/22 (0%)	0/75 (0%)	0/69 (0%)	0/143 (0%)	0/151 (0%)
Intentional overdose [A] *	0/17 (0%)	0/22 (0%)	0/75 (0%)	0/69 (0%)	0/143 (0%)	0/151 (0%)
Limb injury [A] *	0/17 (0%)	0/22 (0%)	0/75 (0%)	0/69 (0%)	0/143 (0%)	0/151 (0%)
Radius fracture [A] *	0/17 (0%)	0/22 (0%)	0/75 (0%)	0/69 (0%)	0/143 (0%)	1/151 (0.66%)
Road traffic accident [A] *	0/17 (0%)	0/22 (0%)	0/75 (0%)	0/69 (0%)	0/143 (0%)	0/151 (0%)
Subdural haematoma [A] *	0/17 (0%)	0/22 (0%)	0/75 (0%)	0/69 (0%)	0/143 (0%)	0/151 (0%)
Investigations						
Blood culture positive [A] *	0/17 (0%)	0/22 (0%)	0/75 (0%)	0/69 (0%)	0/143 (0%)	0/151 (0%)
Pregnancy test positive [A] *	0/17 (0%)	0/22 (0%)	0/75 (0%)	0/69 (0%)	0/143 (0%)	0/151 (0%)

	Cladribine 3.5 mg/kg/ No Treatment	Cladribine 5.25 mg/kg/ No Treatment	Cladribine Low/Placebo (LLPP) (24-week Follow-up Period)	Cladribine High Dose/Placebo (HLPP) (24-week Follow-up Period	Cladribine Low/Low Dose (LLLL) (24-week Follow-up Period)	Cladribine High/Low Dose (HLLL) (24-week Follow-up Period)
	Affected/ At Risk (%)	Affected/ At Risk (%)	Affected/ At Risk (%)	Affected/ At Risk (%)	Affected/ At Risk (%)	Affected/ At Risk (%)
Tuberculin test positive [A] *	0/17 (0%)	0/22 (0%)	0/75 (0%)	0/69 (0%)	0/143 (0%)	0/151 (0%)
Weight decreased [A] *	0/17 (0%)	0/22 (0%)	0/75 (0%)	0/69 (0%)	0/143 (0%)	0/151 (0%)
Metabolism and nutrition disorders						
Diabetic ketoacidosis [A] *	0/17 (0%)	0/22 (0%)	0/75 (0%)	0/69 (0%)	0/143 (0%)	0/151 (0%)
Hypokalaemia [A] *	0/17 (0%)	0/22 (0%)	0/75 (0%)	0/69 (0%)	0/143 (0%)	0/151 (0%)
Type 2 diabetes mellitus [A] *	0/17 (0%)	0/22 (0%)	0/75 (0%)	0/69 (0%)	0/143 (0%)	0/151 (0%)
Musculoskeletal and connective tissue disorders						
Intervertebral disc protrusion [A] *	0/17 (0%)	0/22 (0%)	0/75 (0%)	0/69 (0%)	0/143 (0%)	0/151 (0%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)						
Adrenal adenoma [A] *	0/17 (0%)	0/22 (0%)	0/75 (0%)	0/69 (0%)	0/143 (0%)	0/151 (0%)
Basal cell carcinoma [A] *	0/17 (0%)	1/22 (4.55%)	0/75 (0%)	0/69 (0%)	0/143 (0%)	0/151 (0%)
Bile duct cancer [A] *	0/17 (0%)	0/22 (0%)	0/75 (0%)	0/69 (0%)	0/143 (0%)	0/151 (0%)
Breast cancer [A] *	0/17 (0%)	0/22 (0%)	0/75 (0%)	0/69 (0%)	0/143 (0%)	0/151 (0%)
Breast fibroma [A] *	0/17 (0%)	0/22 (0%)	0/75 (0%)	0/69 (0%)	0/143 (0%)	0/151 (0%)
Colorectal cancer metastatic [A] *	0/17 (0%)	0/22 (0%)	0/75 (0%)	0/69 (0%)	0/143 (0%)	0/151 (0%)
Fibrous histiocytoma [A] *	0/17 (0%)	0/22 (0%)	0/75 (0%)	0/69 (0%)	0/143 (0%)	0/151 (0%)
Haemangioma of liver [A] *	0/17 (0%)	0/22 (0%)	0/75 (0%)	0/69 (0%)	0/143 (0%)	0/151 (0%)
Juvenile melanoma benign [A] *	0/17 (0%)	0/22 (0%)	0/75 (0%)	0/69 (0%)	0/143 (0%)	0/151 (0%)
Lipoma [A] *	0/17 (0%)	0/22 (0%)	0/75 (0%)	0/69 (0%)	0/143 (0%)	0/151 (0%)
Lung neoplasm [A] *	0/17 (0%)	0/22 (0%)	0/75 (0%)	0/69 (0%)	0/143 (0%)	0/151 (0%)

	Cladribine 3.5 mg/kg/ No Treatment	Cladribine 5.25 mg/kg/ No Treatment	Cladribine Low/Placebo (LLPP) (24-week Follow-up Period)	Cladribine High Dose/Placebo (HLPP) (24-week Follow-up Period	Cladribine Low/Low Dose (LLLL) (24-week Follow-up Period)	Cladribine High/Low Dose (HLLL) (24-week Follow-up Period)
	Affected/ At Risk (%)	Affected/ At Risk (%)	Affected/ At Risk (%)	Affected/ At Risk (%)	Affected/ At Risk (%)	Affected/ At Risk (%)
Malignant melanoma [A] *	0/17 (0%)	0/22 (0%)	0/75 (0%)	0/69 (0%)	0/143 (0%)	0/151 (0%)
Melanocytic naevus [A] *	0/17 (0%)	0/22 (0%)	0/75 (0%)	0/69 (0%)	0/143 (0%)	0/151 (0%)
Metastases to lung [A] *	0/17 (0%)	0/22 (0%)	0/75 (0%)	0/69 (0%)	1/143 (0.7%)	0/151 (0%)
Metastases to lymph nodes [A] *	0/17 (0%)	0/22 (0%)	0/75 (0%)	0/69 (0%)	0/143 (0%)	0/151 (0%)
Neurilemmoma benign [A] *	0/17 (0%)	0/22 (0%)	0/75 (0%)	0/69 (0%)	0/143 (0%)	0/151 (0%)
Ovarian cancer [A] *	0/17 (0%)	0/22 (0%)	0/75 (0%)	0/69 (0%)	0/143 (0%)	0/151 (0%)
Prostatic adenoma [A] *	0/17 (0%)	0/22 (0%)	0/75 (0%)	0/69 (0%)	0/143 (0%)	0/151 (0%)
Rectal cancer [A] *	0/17 (0%)	0/22 (0%)	0/75 (0%)	0/69 (0%)	0/143 (0%)	0/151 (0%)
Renal cell carcinoma [A] *	0/17 (0%)	0/22 (0%)	0/75 (0%)	0/69 (0%)	0/143 (0%)	0/151 (0%)
Seborrhoeic keratosis [A] *	0/17 (0%)	0/22 (0%)	0/75 (0%)	0/69 (0%)	0/143 (0%)	0/151 (0%)
Skin papilloma [A] *	0/17 (0%)	0/22 (0%)	0/75 (0%)	0/69 (0%)	0/143 (0%)	0/151 (0%)
Squamous cell carcinoma [A] *	0/17 (0%)	0/22 (0%)	0/75 (0%)	0/69 (0%)	0/143 (0%)	0/151 (0%)
Thyroid adenoma [A] *	0/17 (0%)	0/22 (0%)	0/75 (0%)	0/69 (0%)	0/143 (0%)	0/151 (0%)
Thyroid cancer [A] *	0/17 (0%)	0/22 (0%)	0/75 (0%)	0/69 (0%)	0/143 (0%)	0/151 (0%)
Uterine leiomyoma [A] *	1/17 (5.88%)	0/22 (0%)	0/75 (0%)	0/69 (0%)	0/143 (0%)	0/151 (0%)
Nervous system disorders						
Brain injury [A] *	0/17 (0%)	0/22 (0%)	0/75 (0%)	0/69 (0%)	0/143 (0%)	0/151 (0%)
Cauda equina syndrome [A] *	0/17 (0%)	0/22 (0%)	0/75 (0%)	0/69 (0%)	0/143 (0%)	0/151 (0%)
Radicular syndrome [A] *	0/17 (0%)	0/22 (0%)	0/75 (0%)	0/69 (0%)	0/143 (0%)	0/151 (0%)

	Cladribine 3.5 mg/kg/ No Treatment	Cladribine 5.25 mg/kg/ No Treatment	Cladribine Low/Placebo (LLPP) (24-week Follow-up Period)	Cladribine High Dose/Placebo (HLPP) (24-week Follow-up Period	Cladribine Low/Low Dose (LLLL) (24-week Follow-up Period)	Cladribine High/Low Dose (HLLL) (24-week Follow-up Period)
	Affected/ At Risk (%)	Affected/ At Risk (%)	Affected/ At Risk (%)	Affected/ At Risk (%)	Affected/ At Risk (%)	Affected/ At Risk (%)
Sciatica [A] *	0/17 (0%)	0/22 (0%)	0/75 (0%)	0/69 (0%)	0/143 (0%)	0/151 (0%)
Status epilepticus [A] *	0/17 (0%)	0/22 (0%)	0/75 (0%)	0/69 (0%)	0/143 (0%)	0/151 (0%)
Pregnancy, puerperium and perinatal conditions						
Abortion missed [A] *	0/17 (0%)	0/22 (0%)	0/75 (0%)	0/69 (0%)	1/143 (0.7%)	0/151 (0%)
Abortion threatened [A] *	1/17 (5.88%)	0/22 (0%)	0/75 (0%)	0/69 (0%)	0/143 (0%)	0/151 (0%)
Psychiatric disorders						
Mental disorder [A] *	0/17 (0%)	0/22 (0%)	0/75 (0%)	0/69 (0%)	0/143 (0%)	0/151 (0%)
Suicidal ideation [A] *	0/17 (0%)	0/22 (0%)	0/75 (0%)	0/69 (0%)	0/143 (0%)	0/151 (0%)
Suicide attempt [A] *	0/17 (0%)	0/22 (0%)	0/75 (0%)	0/69 (0%)	0/143 (0%)	0/151 (0%)
Renal and urinary disorders						
Cystitis noninfective [A] *	0/17 (0%)	0/22 (0%)	0/75 (0%)	0/69 (0%)	0/143 (0%)	0/151 (0%)
Dysuria [A] *	0/17 (0%)	0/22 (0%)	0/75 (0%)	0/69 (0%)	0/143 (0%)	0/151 (0%)
Nephrolithiasis [A] *	0/17 (0%)	1/22 (4.55%)	0/75 (0%)	0/69 (0%)	0/143 (0%)	0/151 (0%)
Renal failure acute [A] *	0/17 (0%)	0/22 (0%)	0/75 (0%)	0/69 (0%)	0/143 (0%)	0/151 (0%)
Renal failure chronic [A] *	0/17 (0%)	0/22 (0%)	0/75 (0%)	0/69 (0%)	0/143 (0%)	0/151 (0%)
Reproductive system and breast disorders						
Menorrhagia [A] *	0/17 (0%)	0/22 (0%)	0/75 (0%)	0/69 (0%)	0/143 (0%)	0/151 (0%)
Ovarian cyst [A] *	0/17 (0%)	0/22 (0%)	0/75 (0%)	0/69 (0%)	0/143 (0%)	0/151 (0%)
Ovarian cyst ruptured [A] *	0/17 (0%)	0/22 (0%)	0/75 (0%)	0/69 (0%)	0/143 (0%)	0/151 (0%)
Respiratory, thoracic and mediastinal disorders						

	Cladribine 3.5 mg/kg/ No Treatment	Cladribine 5.25 mg/kg/ No Treatment	Cladribine Low/Placebo (LLPP) (24-week Follow-up Period)	Cladribine High Dose/Placebo (HLPP) (24-week Follow-up Period	Cladribine Low/Low Dose (LLLL) (24-week Follow-up Period)	Cladribine High/Low Dose (HLLL) (24-week Follow-up Period)
	Affected/ At Risk (%)	Affected/ At Risk (%)	Affected/ At Risk (%)	Affected/ At Risk (%)	Affected/ At Risk (%)	Affected/ At Risk (%)
Asthma [A] *	0/17 (0%)	1/22 (4.55%)	0/75 (0%)	0/69 (0%)	0/143 (0%)	0/151 (0%)
Bronchitis chronic [A] *	0/17 (0%)	0/22 (0%)	0/75 (0%)	0/69 (0%)	0/143 (0%)	0/151 (0%)
Pneumothorax [A] *	0/17 (0%)	0/22 (0%)	0/75 (0%)	0/69 (0%)	0/143 (0%)	0/151 (0%)
Respiratory failure [A] *	0/17 (0%)	0/22 (0%)	0/75 (0%)	0/69 (0%)	0/143 (0%)	0/151 (0%)
Skin and subcutaneous tissue disorders						
Pain of skin [A] *	0/17 (0%)	0/22 (0%)	0/75 (0%)	0/69 (0%)	0/143 (0%)	0/151 (0%)
Surgical and medical procedures						
Abortion induced [A] *	0/17 (0%)	0/22 (0%)	0/75 (0%)	0/69 (0%)	0/143 (0%)	0/151 (0%)
Vascular disorders						
Varicose vein [A] *	0/17 (0%)	0/22 (0%)	0/75 (0%)	0/69 (0%)	0/143 (0%)	0/151 (0%)

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

	Placebo/Cladribine Low Dose (PPLL) (24-week Follow-up Period)	Placebo/No Treatment (24-week Follow-up Period)	Cladribine 3.5 mg/kg/ No Treatment (24-week Follow-up Period)	Cladribine 5.25 mg/ kg/No Treatment (24-week Follow-up Period)
	Affected/At Risk (%)	Affected/At Risk (%)	Affected/At Risk (%)	Affected/At Risk (%)
Total	4/198 (2.02%)	0/15 (0%)	0/9 (0%)	0/11 (0%)
Blood and lymphatic system disorders				
Iron deficiency anaemia [A] *	0/198 (0%)	0/15 (0%)	0/9 (0%)	0/11 (0%)
Lymphopenia [A] *	0/198 (0%)	0/15 (0%)	0/9 (0%)	0/11 (0%)
Thrombocytopenia [A] *	0/198 (0%)	0/15 (0%)	0/9 (0%)	0/11 (0%)
Cardiac disorders				

	Placebo/Cladribine Low Dose (PPLL) (24-week Follow-up Period)	Placebo/No Treatment (24-week Follow-up Period)	Cladribine 3.5 mg/kg/ No Treatment (24-week Follow-up Period)	Cladribine 5.25 mg/ kg/No Treatment (24-week Follow-up Period)
	Affected/At Risk (%)	Affected/At Risk (%)	Affected/At Risk (%)	Affected/At Risk (%)
Adams-Stokes syndrome [A] *	0/198 (0%)	0/15 (0%)	0/9 (0%)	0/11 (0%)
Atrial fibrillation [A] *	0/198 (0%)	0/15 (0%)	0/9 (0%)	0/11 (0%)
Myocardial infarction [A] *	0/198 (0%)	0/15 (0%)	0/9 (0%)	0/11 (0%)
Tachycardia [A] *	0/198 (0%)	0/15 (0%)	0/9 (0%)	0/11 (0%)
Ear and labyrinth disorders				
Vertigo positional [A] *	0/198 (0%)	0/15 (0%)	0/9 (0%)	0/11 (0%)
Endocrine disorders				
Autoimmune thyroiditis [A] *	0/198 (0%)	0/15 (0%)	0/9 (0%)	0/11 (0%)
Basedow's disease [A] *	0/198 (0%)	0/15 (0%)	0/9 (0%)	0/11 (0%)
Thyroiditis [A] *	0/198 (0%)	0/15 (0%)	0/9 (0%)	0/11 (0%)
Eye disorders				
Iridocyclitis [A] *	0/198 (0%)	0/15 (0%)	0/9 (0%)	0/11 (0%)
Macular degeneration [A] *	0/198 (0%)	0/15 (0%)	0/9 (0%)	0/11 (0%)
Gastrointestinal disorders				
Abdominal pain [A] *	0/198 (0%)	0/15 (0%)	0/9 (0%)	0/11 (0%)
Colonic polyp [A] *	0/198 (0%)	0/15 (0%)	0/9 (0%)	0/11 (0%)
Crohn's disease [A] *	0/198 (0%)	0/15 (0%)	0/9 (0%)	0/11 (0%)
Duodenal ulcer [A] *	0/198 (0%)	0/15 (0%)	0/9 (0%)	0/11 (0%)
Duodenal ulcer perforation [A] *	0/198 (0%)	0/15 (0%)	0/9 (0%)	0/11 (0%)
Gastric haemorrhage [A] *	0/198 (0%)	0/15 (0%)	0/9 (0%)	0/11 (0%)
Gastritis [A] *	0/198 (0%)	0/15 (0%)	0/9 (0%)	0/11 (0%)

	Placebo/Cladribine Low Dose (PPLL) (24-week Follow-up Period)	Placebo/No Treatment (24-week Follow-up Period)	Cladribine 3.5 mg/kg/ No Treatment (24-week Follow-up Period)	Cladribine 5.25 mg/ kg/No Treatment (24-week Follow-up Period)
	Affected/At Risk (%)	Affected/At Risk (%)	Affected/At Risk (%)	Affected/At Risk (%)
Gastrooesophageal reflux disease [A] *	0/198 (0%)	0/15 (0%)	0/9 (0%)	0/11 (0%)
Ileus paralytic [A] *	0/198 (0%)	0/15 (0%)	0/9 (0%)	0/11 (0%)
Irritable bowel syndrome [A] *	0/198 (0%)	0/15 (0%)	0/9 (0%)	0/11 (0%)
Peritonitis [A] *	0/198 (0%)	0/15 (0%)	0/9 (0%)	0/11 (0%)
General disorders				
Chest pain [A] *	0/198 (0%)	0/15 (0%)	0/9 (0%)	0/11 (0%)
Death [A] *	0/198 (0%)	0/15 (0%)	0/9 (0%)	0/11 (0%)
Drowning [A] *	0/198 (0%)	0/15 (0%)	0/9 (0%)	0/11 (0%)
Influenza like illness [A] *	0/198 (0%)	0/15 (0%)	0/9 (0%)	0/11 (0%)
Hepatobiliary disorders				
Biliary colic [A] *	0/198 (0%)	0/15 (0%)	0/9 (0%)	0/11 (0%)
Biliary tract disorder [A] *	0/198 (0%)	0/15 (0%)	0/9 (0%)	0/11 (0%)
Cholecystitis [A] *	0/198 (0%)	0/15 (0%)	0/9 (0%)	0/11 (0%)
Cholelithiasis [A] *	0/198 (0%)	0/15 (0%)	0/9 (0%)	0/11 (0%)
Immune system disorders				
Secondary immunodeficiency [A] *	0/198 (0%)	0/15 (0%)	0/9 (0%)	0/11 (0%)
Infections and infestations				
Abscess oral [A] *	0/198 (0%)	0/15 (0%)	0/9 (0%)	0/11 (0%)
Appendicitis [A] *	0/198 (0%)	0/15 (0%)	0/9 (0%)	0/11 (0%)
Bacterial sepsis [A] *	0/198 (0%)	0/15 (0%)	0/9 (0%)	0/11 (0%)
Breast abscess [A] *	0/198 (0%)	0/15 (0%)	0/9 (0%)	0/11 (0%)

	Placebo/Cladribine Low Dose (PPLL) (24-week Follow-up Period)	Placebo/No Treatment (24-week Follow-up Period)	Cladribine 3.5 mg/kg/ No Treatment (24-week Follow-up Period)	Cladribine 5.25 mg/ kg/No Treatment (24-week Follow-up Period)
	Affected/At Risk (%)	Affected/At Risk (%)	Affected/At Risk (%)	Affected/At Risk (%)
Gastroenteritis [A] *	0/198 (0%)	0/15 (0%)	0/9 (0%)	0/11 (0%)
Herpes zoster [A] *	1/198 (0.51%)	0/15 (0%)	0/9 (0%)	0/11 (0%)
Infection [A] *	0/198 (0%)	0/15 (0%)	0/9 (0%)	0/11 (0%)
Influenza [A] *	0/198 (0%)	0/15 (0%)	0/9 (0%)	0/11 (0%)
Pneumonia [A] *	1/198 (0.51%)	0/15 (0%)	0/9 (0%)	0/11 (0%)
Pulmonary tuberculosis [A] *	0/198 (0%)	0/15 (0%)	0/9 (0%)	0/11 (0%)
Pyelonephritis [A] *	0/198 (0%)	0/15 (0%)	0/9 (0%)	0/11 (0%)
Pyelonephritis chronic [A] *	0/198 (0%)	0/15 (0%)	0/9 (0%)	0/11 (0%)
Tuberculosis [A] *	0/198 (0%)	0/15 (0%)	0/9 (0%)	0/11 (0%)
Urethral abscess [A] *	0/198 (0%)	0/15 (0%)	0/9 (0%)	0/11 (0%)
Urinary tract infection [A] *	1/198 (0.51%)	0/15 (0%)	0/9 (0%)	0/11 (0%)
Injury, poisoning and procedural complications				
Femoral neck fracture [A] *	0/198 (0%)	0/15 (0%)	0/9 (0%)	0/11 (0%)
Humerus fracture [A] *	0/198 (0%)	0/15 (0%)	0/9 (0%)	0/11 (0%)
Intentional overdose [A] *	0/198 (0%)	0/15 (0%)	0/9 (0%)	0/11 (0%)
Limb injury [A] *	0/198 (0%)	0/15 (0%)	0/9 (0%)	0/11 (0%)
Radius fracture [A] *	0/198 (0%)	0/15 (0%)	0/9 (0%)	0/11 (0%)
Road traffic accident [A] *	0/198 (0%)	0/15 (0%)	0/9 (0%)	0/11 (0%)
Subdural haematoma [A] *	0/198 (0%)	0/15 (0%)	0/9 (0%)	0/11 (0%)
Investigations				
Blood culture positive [A] *	0/198 (0%)	0/15 (0%)	0/9 (0%)	0/11 (0%)

	Placebo/Cladribine Low Dose (PPLL) (24-week Follow-up Period)	Placebo/No Treatment (24-week Follow-up Period)	Cladribine 3.5 mg/kg/ No Treatment (24-week Follow-up Period)	Cladribine 5.25 mg/ kg/No Treatment (24-week Follow-up Period)
	Affected/At Risk (%)	Affected/At Risk (%)	Affected/At Risk (%)	Affected/At Risk (%)
Pregnancy test positive [A] *	0/198 (0%)	0/15 (0%)	0/9 (0%)	0/11 (0%)
Tuberculin test positive [A] *	0/198 (0%)	0/15 (0%)	0/9 (0%)	0/11 (0%)
Weight decreased [A] *	0/198 (0%)	0/15 (0%)	0/9 (0%)	0/11 (0%)
Metabolism and nutrition disorders				
Diabetic ketoacidosis [A] *	1/198 (0.51%)	0/15 (0%)	0/9 (0%)	0/11 (0%)
Hypokalaemia [A] *	0/198 (0%)	0/15 (0%)	0/9 (0%)	0/11 (0%)
Type 2 diabetes mellitus [A] *	0/198 (0%)	0/15 (0%)	0/9 (0%)	0/11 (0%)
Musculoskeletal and connective tissue disorders				
Intervertebral disc protrusion [A] *	0/198 (0%)	0/15 (0%)	0/9 (0%)	0/11 (0%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)				
Adrenal adenoma [A] *	0/198 (0%)	0/15 (0%)	0/9 (0%)	0/11 (0%)
Basal cell carcinoma [A] *	0/198 (0%)	0/15 (0%)	0/9 (0%)	0/11 (0%)
Bile duct cancer [A] *	1/198 (0.51%)	0/15 (0%)	0/9 (0%)	0/11 (0%)
Breast cancer [A] *	0/198 (0%)	0/15 (0%)	0/9 (0%)	0/11 (0%)
Breast fibroma [A] *	0/198 (0%)	0/15 (0%)	0/9 (0%)	0/11 (0%)
Colorectal cancer metastatic [A] *	0/198 (0%)	0/15 (0%)	0/9 (0%)	0/11 (0%)
Fibrous histiocytoma [A] *	0/198 (0%)	0/15 (0%)	0/9 (0%)	0/11 (0%)
Haemangioma of liver [A] *	0/198 (0%)	0/15 (0%)	0/9 (0%)	0/11 (0%)
Juvenile melanoma benign [A] *	0/198 (0%)	0/15 (0%)	0/9 (0%)	0/11 (0%)
Lipoma [A] *	0/198 (0%)	0/15 (0%)	0/9 (0%)	0/11 (0%)
Lung neoplasm [A] *	1/198 (0.51%)	0/15 (0%)	0/9 (0%)	0/11 (0%)

	Placebo/Cladribine Low Dose (PPLL) (24-week Follow-up Period)	Placebo/No Treatment (24-week Follow-up Period)	Cladribine 3.5 mg/kg/ No Treatment (24-week Follow-up Period)	Cladribine 5.25 mg/ kg/No Treatment (24-week Follow-up Period)
	Affected/At Risk (%)	Affected/At Risk (%)	Affected/At Risk (%)	Affected/At Risk (%)
Malignant melanoma [A] *	0/198 (0%)	0/15 (0%)	0/9 (0%)	0/11 (0%)
Melanocytic naevus [A] *	0/198 (0%)	0/15 (0%)	0/9 (0%)	0/11 (0%)
Metastases to lung [A] *	0/198 (0%)	0/15 (0%)	0/9 (0%)	0/11 (0%)
Metastases to lymph nodes [A] *	1/198 (0.51%)	0/15 (0%)	0/9 (0%)	0/11 (0%)
Neurilemmoma benign [A] *	0/198 (0%)	0/15 (0%)	0/9 (0%)	0/11 (0%)
Ovarian cancer [A] *	0/198 (0%)	0/15 (0%)	0/9 (0%)	0/11 (0%)
Prostatic adenoma [A] *	0/198 (0%)	0/15 (0%)	0/9 (0%)	0/11 (0%)
Rectal cancer [A] *	0/198 (0%)	0/15 (0%)	0/9 (0%)	0/11 (0%)
Renal cell carcinoma [A] *	0/198 (0%)	0/15 (0%)	0/9 (0%)	0/11 (0%)
Seborrhoeic keratosis [A] *	0/198 (0%)	0/15 (0%)	0/9 (0%)	0/11 (0%)
Skin papilloma [A] *	0/198 (0%)	0/15 (0%)	0/9 (0%)	0/11 (0%)
Squamous cell carcinoma [A] *	0/198 (0%)	0/15 (0%)	0/9 (0%)	0/11 (0%)
Thyroid adenoma [A] *	0/198 (0%)	0/15 (0%)	0/9 (0%)	0/11 (0%)
Thyroid cancer [A] *	0/198 (0%)	0/15 (0%)	0/9 (0%)	0/11 (0%)
Uterine leiomyoma [A] *	0/198 (0%)	0/15 (0%)	0/9 (0%)	0/11 (0%)
Nervous system disorders				
Brain injury [A] *	0/198 (0%)	0/15 (0%)	0/9 (0%)	0/11 (0%)
Cauda equina syndrome [A] *	0/198 (0%)	0/15 (0%)	0/9 (0%)	0/11 (0%)
Radicular syndrome [A] *	0/198 (0%)	0/15 (0%)	0/9 (0%)	0/11 (0%)
Sciatica [A] *	0/198 (0%)	0/15 (0%)	0/9 (0%)	0/11 (0%)
Status epilepticus [A] *	0/198 (0%)	0/15 (0%)	0/9 (0%)	0/11 (0%)

	Placebo/Cladribine Low Dose (PPLL) (24-week Follow-up Period)	Placebo/No Treatment (24-week Follow-up Period)	Cladribine 3.5 mg/kg/ No Treatment (24-week Follow-up Period)	Cladribine 5.25 mg/ kg/No Treatment (24-week Follow-up Period)
	Affected/At Risk (%)	Affected/At Risk (%)	Affected/At Risk (%)	Affected/At Risk (%)
Pregnancy, puerperium and perinatal conditions				
Abortion missed [A] *	0/198 (0%)	0/15 (0%)	0/9 (0%)	0/11 (0%)
Abortion threatened [A] *	0/198 (0%)	0/15 (0%)	0/9 (0%)	0/11 (0%)
Psychiatric disorders				
Mental disorder [A] *	0/198 (0%)	0/15 (0%)	0/9 (0%)	0/11 (0%)
Suicidal ideation [A] *	0/198 (0%)	0/15 (0%)	0/9 (0%)	0/11 (0%)
Suicide attempt [A] *	0/198 (0%)	0/15 (0%)	0/9 (0%)	0/11 (0%)
Renal and urinary disorders				
Cystitis noninfective [A] *	0/198 (0%)	0/15 (0%)	0/9 (0%)	0/11 (0%)
Dysuria [A] *	0/198 (0%)	0/15 (0%)	0/9 (0%)	0/11 (0%)
Nephrolithiasis [A] *	0/198 (0%)	0/15 (0%)	0/9 (0%)	0/11 (0%)
Renal failure acute [A] *	0/198 (0%)	0/15 (0%)	0/9 (0%)	0/11 (0%)
Renal failure chronic [A] *	0/198 (0%)	0/15 (0%)	0/9 (0%)	0/11 (0%)
Reproductive system and breast disorders				
Menorrhagia [A] *	0/198 (0%)	0/15 (0%)	0/9 (0%)	0/11 (0%)
Ovarian cyst [A] *	0/198 (0%)	0/15 (0%)	0/9 (0%)	0/11 (0%)
Ovarian cyst ruptured [A] *	0/198 (0%)	0/15 (0%)	0/9 (0%)	0/11 (0%)
Respiratory, thoracic and mediastinal disorders				
Asthma [A] *	0/198 (0%)	0/15 (0%)	0/9 (0%)	0/11 (0%)
Bronchitis chronic [A] *	0/198 (0%)	0/15 (0%)	0/9 (0%)	0/11 (0%)
Pneumothorax [A] *	0/198 (0%)	0/15 (0%)	0/9 (0%)	0/11 (0%)
Respiratory failure [A] *	0/198 (0%)	0/15 (0%)	0/9 (0%)	0/11 (0%)

	Placebo/Cladribine Low Dose (PPLL) (24-week Follow-up Period)	Placebo/No Treatment (24-week Follow-up Period)	Cladribine 3.5 mg/kg/ No Treatment (24-week Follow-up Period)	Cladribine 5.25 mg/ kg/No Treatment (24-week Follow-up Period)
	Affected/At Risk (%)	Affected/At Risk (%)	Affected/At Risk (%)	Affected/At Risk (%)
Skin and subcutaneous tissue disorders				
Pain of skin [A] *	1/198 (0.51%)	0/15 (0%)	0/9 (0%)	0/11 (0%)
Surgical and medical procedures				
Abortion induced [A] *	0/198 (0%)	0/15 (0%)	0/9 (0%)	0/11 (0%)
Vascular disorders				
Varicose vein [A] *	0/198 (0%)	0/15 (0%)	0/9 (0%)	0/11 (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 Low/ Placebo (LLPP)	Cladribine High Dose/ Placebo (HLPP)	Cladribine Low/Low Dose (LLLL)	Cladribine High/Low Dose (HLLL)	Placebo/ Cladribine Low Dose (PPLL)	Placebo/No Treatment
	Affected/ At Risk (%)	Affected/ At Risk (%)	Affected/ At Risk (%)	Affected/ At Risk (%)	Affected/ At Risk (%)	Affected/ At Risk (%)
Total	59/98 (60.2%)	53/92 (57.61%)	124/186 (66.67%)	123/186 (66.13%)	163/244 (66.8%)	15/22 (68.18%)
Blood and lymphatic system disorders						
Anaemia of pregnancy [A] *	0/98 (0%)	0/92 (0%)	0/186 (0%)	0/186 (0%)	0/244 (0%)	0/22 (0%)
Iron deficiency anaemia [A] *	0/98 (0%)	0/92 (0%)	0/186 (0%)	0/186 (0%)	0/244 (0%)	0/22 (0%)
Leukopenia [A] *	1/98 (1.02%)	2/92 (2.17%)	19/186 (10.22%)	20/186 (10.75%)	12/244 (4.92%)	2/22 (9.09%)
Lymphopenia [A] *	9/98 (9.18%)	7/92 (7.61%)	68/186 (36.56%)	75/186 (40.32%)	69/244 (28.28%)	2/22 (9.09%)
Neutropenia [A] *	2/98 (2.04%)	2/92 (2.17%)	7/186 (3.76%)	10/186 (5.38%)	7/244 (2.87%)	1/22 (4.55%)
Thrombocytopenia [A] *	0/98 (0%)	0/92 (0%)	0/186 (0%)	0/186 (0%)	0/244 (0%)	2/22 (9.09%)

	Cladribine Low/ Placebo (LLPP)	Cladribine High Dose/ Placebo (HLPP)	Cladribine Low/Low Dose (LLLL)	Cladribine High/Low Dose (HLLL)	Placebo/ Cladribine Low Dose (PPLL)	Placebo/No Treatment
	Affected/ At Risk (%)	Affected/ At Risk (%)	Affected/ At Risk (%)	Affected/ At Risk (%)	Affected/ At Risk (%)	Affected/ At Risk (%)
Ear and labyrinth disorders						
Ear pain [A] *	0/98 (0%)	0/92 (0%)	0/186 (0%)	0/186 (0%)	0/244 (0%)	0/22 (0%)
Vertigo [A] *	5/98 (5.1%)	1/92 (1.09%)	6/186 (3.23%)	5/186 (2.69%)	5/244 (2.05%)	0/22 (0%)
Eye disorders						
Eye irritation [A] *	0/98 (0%)	0/92 (0%)	0/186 (0%)	0/186 (0%)	0/244 (0%)	0/22 (0%)
Eye pruritus [A] *	0/98 (0%)	0/92 (0%)	0/186 (0%)	0/186 (0%)	0/244 (0%)	0/22 (0%)
Gastrointestinal disorders						
Diarrhoea [A] *	7/98 (7.14%)	6/92 (6.52%)	6/186 (3.23%)	9/186 (4.84%)	14/244 (5.74%)	0/22 (0%)
Faecal incontinence [A] *	0/98 (0%)	0/92 (0%)	0/186 (0%)	0/186 (0%)	0/244 (0%)	0/22 (0%)
Gastrooesophageal reflux disease [A] *	0/98 (0%)	0/92 (0%)	0/186 (0%)	0/186 (0%)	0/244 (0%)	0/22 (0%)
Mouth ulceration [A] *	0/98 (0%)	0/92 (0%)	0/186 (0%)	0/186 (0%)	0/244 (0%)	0/22 (0%)
Nausea [A] *	8/98 (8.16%)	4/92 (4.35%)	11/186 (5.91%)	7/186 (3.76%)	10/244 (4.1%)	0/22 (0%)
Tooth disorder [A] *	0/98 (0%)	0/92 (0%)	0/186 (0%)	0/186 (0%)	0/244 (0%)	1/22 (4.55%)
Toothache [A] *	4/98 (4.08%)	6/92 (6.52%)	5/186 (2.69%)	3/186 (1.61%)	4/244 (1.64%)	0/22 (0%)
Vomiting [A] *	1/98 (1.02%)	5/92 (5.43%)	5/186 (2.69%)	0/186 (0%)	4/244 (1.64%)	0/22 (0%)
General disorders						
Asthenia [A] *	0/98 (0%)	0/92 (0%)	0/186 (0%)	0/186 (0%)	0/244 (0%)	2/22 (9.09%)
Fatigue [A] *	5/98 (5.1%)	5/92 (5.43%)	8/186 (4.3%)	10/186 (5.38%)	12/244 (4.92%)	1/22 (4.55%)
Hyperthermia [A] *	0/98 (0%)	0/92 (0%)	0/186 (0%)	0/186 (0%)	0/244 (0%)	0/22 (0%)
Influenza like illness [A] *	5/98 (5.1%)	2/92 (2.17%)	14/186 (7.53%)	9/186 (4.84%)	10/244 (4.1%)	1/22 (4.55%)

	Cladribine Low/ Placebo (LLPP)	Cladribine High Dose/ Placebo (HLPP)	Cladribine Low/Low Dose (LLLL)	Cladribine High/Low Dose (HLLL)	Placebo/ Cladribine Low Dose (PPLL)	Placebo/No Treatment
	Affected/ At Risk (%)	Affected/ At Risk (%)	Affected/ At Risk (%)	Affected/ At Risk (%)	Affected/ At Risk (%)	Affected/ At Risk (%)
Immune system disorders						
Hypersensitivity [A] *	0/98 (0%)	0/92 (0%)	0/186 (0%)	0/186 (0%)	0/244 (0%)	0/22 (0%)
Infections and infestations						
Bronchitis [A] *	6/98 (6.12%)	7/92 (7.61%)	1/186 (0.54%)	12/186 (6.45%)	17/244 (6.97%)	0/22 (0%)
Erythema infectiosum [A] *	0/98 (0%)	0/92 (0%)	0/186 (0%)	0/186 (0%)	0/244 (0%)	0/22 (0%)
Furuncle [A] *	0/98 (0%)	0/92 (0%)	0/186 (0%)	0/186 (0%)	0/244 (0%)	0/22 (0%)
Herpes zoster [A] *	0/98 (0%)	0/92 (0%)	0/186 (0%)	0/186 (0%)	0/244 (0%)	0/22 (0%)
Hordeolum [A] *	0/98 (0%)	0/92 (0%)	0/186 (0%)	0/186 (0%)	0/244 (0%)	0/22 (0%)
Infected insect bite [A] *	0/98 (0%)	0/92 (0%)	0/186 (0%)	0/186 (0%)	0/244 (0%)	0/22 (0%)
Influenza [A] *	11/98 (11.22%)	10/92 (10.87%)	15/186 (8.06%)	23/186 (12.37%)	17/244 (6.97%)	4/22 (18.18%)
Injection site abscess [A] *	0/98 (0%)	0/92 (0%)	0/186 (0%)	0/186 (0%)	0/244 (0%)	0/22 (0%)
Nasopharyngitis [A] *	19/98 (19.39%)	15/92 (16.3%)	22/186 (11.83%)	28/186 (15.05%)	45/244 (18.44%)	1/22 (4.55%)
Oral herpes [A] *	0/98 (0%)	0/92 (0%)	0/186 (0%)	0/186 (0%)	0/244 (0%)	0/22 (0%)
Pneumonia [A] *	0/98 (0%)	0/92 (0%)	0/186 (0%)	0/186 (0%)	0/244 (0%)	0/22 (0%)
Respiratory tract infection viral [A] *	0/98 (0%)	0/92 (0%)	0/186 (0%)	0/186 (0%)	0/244 (0%)	2/22 (9.09%)
Sinusitis [A] *	0/98 (0%)	0/92 (0%)	0/186 (0%)	0/186 (0%)	0/244 (0%)	0/22 (0%)
Skin bacterial infection [A] *	0/98 (0%)	0/92 (0%)	0/186 (0%)	0/186 (0%)	0/244 (0%)	0/22 (0%)
Upper respiratory tract infection [A] *	8/98 (8.16%)	9/92 (9.78%)	17/186 (9.14%)	20/186 (10.75%)	19/244 (7.79%)	1/22 (4.55%)
Urinary tract infection [A] *	6/98 (6.12%)	4/92 (4.35%)	17/186 (9.14%)	16/186 (8.6%)	16/244 (6.56%)	0/22 (0%)

	Cladribine Low/ Placebo (LLPP)	Cladribine High Dose/ Placebo (HLPP)	Cladribine Low/Low Dose (LLLL)	Cladribine High/Low Dose (HLLL)	Placebo/ Cladribine Low Dose (PPLL)	Placebo/No Treatment
	Affected/ At Risk (%)	Affected/ At Risk (%)	Affected/ At Risk (%)	Affected/ At Risk (%)	Affected/ At Risk (%)	Affected/ At Risk (%)
Viral infection [A] *	0/98 (0%)	0/92 (0%)	0/186 (0%)	0/186 (0%)	0/244 (0%)	1/22 (4.55%)
Viral upper respiratory tract infection [A] *	0/98 (0%)	0/92 (0%)	0/186 (0%)	0/186 (0%)	0/244 (0%)	1/22 (4.55%)
Injury, poisoning and procedural complications						
Contusion [A] *	0/98 (0%)	0/92 (0%)	0/186 (0%)	0/186 (0%)	0/244 (0%)	0/22 (0%)
Fall [A] *	0/98 (0%)	0/92 (0%)	0/186 (0%)	0/186 (0%)	0/244 (0%)	0/22 (0%)
Joint sprain [A] *	0/98 (0%)	0/92 (0%)	0/186 (0%)	0/186 (0%)	0/244 (0%)	1/22 (4.55%)
Investigations						
Alanine aminotransferase increased [A] *	0/98 (0%)	0/92 (0%)	0/186 (0%)	0/186 (0%)	0/244 (0%)	2/22 (9.09%)
Blood creatine phosphokinase increased [A] *	0/98 (0%)	0/92 (0%)	0/186 (0%)	0/186 (0%)	0/244 (0%)	0/22 (0%)
Blood potassium decreased [A] *	0/98 (0%)	0/92 (0%)	0/186 (0%)	0/186 (0%)	0/244 (0%)	0/22 (0%)
Blood urea increased [A] *	0/98 (0%)	0/92 (0%)	0/186 (0%)	0/186 (0%)	0/244 (0%)	0/22 (0%)
Liver function test abnormal [A] *	0/98 (0%)	0/92 (0%)	0/186 (0%)	0/186 (0%)	0/244 (0%)	0/22 (0%)
Red blood cell burr cells present [A] *	0/98 (0%)	0/92 (0%)	0/186 (0%)	0/186 (0%)	0/244 (0%)	0/22 (0%)
Thyroid function test abnormal [A] *	0/98 (0%)	0/92 (0%)	0/186 (0%)	0/186 (0%)	0/244 (0%)	0/22 (0%)
Weight decreased [A] *	0/98 (0%)	0/92 (0%)	0/186 (0%)	0/186 (0%)	0/244 (0%)	0/22 (0%)
Weight increased [A] *	0/98 (0%)	0/92 (0%)	0/186 (0%)	0/186 (0%)	0/244 (0%)	0/22 (0%)
White blood cell count decreased [A] *	0/98 (0%)	0/92 (0%)	0/186 (0%)	0/186 (0%)	0/244 (0%)	0/22 (0%)
White blood cell count increased [A] *	0/98 (0%)	0/92 (0%)	0/186 (0%)	0/186 (0%)	0/244 (0%)	0/22 (0%)
Musculoskeletal and connective tissue disorders						
Arthralgia [A] *	5/98 (5.1%)	4/92 (4.35%)	5/186 (2.69%)	8/186 (4.3%)	13/244 (5.33%)	0/22 (0%)

	Cladribine Low/ Placebo (LLPP)	Cladribine High Dose/ Placebo (HLPP)	Cladribine Low/Low Dose (LLLL)	Cladribine High/Low Dose (HLLL)	Placebo/ Cladribine Low Dose (PPLL)	Placebo/No Treatment
	Affected/ At Risk (%)	Affected/ At Risk (%)	Affected/ At Risk (%)	Affected/ At Risk (%)	Affected/ At Risk (%)	Affected/ At Risk (%)
Back pain [A] *	9/98 (9.18%)	9/92 (9.78%)	16/186 (8.6%)	18/186 (9.68%)	28/244 (11.48%)	1/22 (4.55%)
Joint swelling [A] *	0/98 (0%)	0/92 (0%)	0/186 (0%)	0/186 (0%)	0/244 (0%)	0/22 (0%)
Musculoskeletal pain [A] *	0/98 (0%)	0/92 (0%)	0/186 (0%)	0/186 (0%)	0/244 (0%)	2/22 (9.09%)
Pain in extremity [A] *	8/98 (8.16%)	6/92 (6.52%)	10/186 (5.38%)	10/186 (5.38%)	11/244 (4.51%)	2/22 (9.09%)
Sensation of heaviness [A] *	0/98 (0%)	0/92 (0%)	0/186 (0%)	0/186 (0%)	0/244 (0%)	0/22 (0%)
Tendonitis [A] *	0/98 (0%)	0/92 (0%)	0/186 (0%)	0/186 (0%)	0/244 (0%)	0/22 (0%)
Nervous system disorders						
Carpal tunnel syndrome [A] *	0/98 (0%)	0/92 (0%)	0/186 (0%)	0/186 (0%)	0/244 (0%)	0/22 (0%)
Dizziness [A] *	0/98 (0%)	0/92 (0%)	0/186 (0%)	0/186 (0%)	0/244 (0%)	1/22 (4.55%)
Headache [A] *	20/98 (20.41%)	16/92 (17.39%)	21/186 (11.29%)	25/186 (13.44%)	38/244 (15.57%)	3/22 (13.64%)
Paraesthesia [A] *	0/98 (0%)	0/92 (0%)	0/186 (0%)	0/186 (0%)	0/244 (0%)	0/22 (0%)
Restless legs syndrome [A] *	0/98 (0%)	0/92 (0%)	0/186 (0%)	0/186 (0%)	0/244 (0%)	0/22 (0%)
Syncope [A] *	0/98 (0%)	0/92 (0%)	0/186 (0%)	0/186 (0%)	0/244 (0%)	0/22 (0%)
Pregnancy, puerperium and perinatal conditions						
Pregnancy [A] *	0/98 (0%)	0/92 (0%)	0/186 (0%)	0/186 (0%)	0/244 (0%)	0/22 (0%)
Psychiatric disorders						
Anxiety [A] *	5/98 (5.1%)	2/92 (2.17%)	4/186 (2.15%)	5/186 (2.69%)	7/244 (2.87%)	0/22 (0%)
Depressed mood [A] *	0/98 (0%)	0/92 (0%)	0/186 (0%)	0/186 (0%)	0/244 (0%)	0/22 (0%)
Depression [A] *	6/98 (6.12%)	1/92 (1.09%)	6/186 (3.23%)	5/186 (2.69%)	9/244 (3.69%)	1/22 (4.55%)
Respiratory, thoracic and mediastinal disorders						

	Cladribine Low/ Placebo (LLPP)	Cladribine High Dose/ Placebo (HLPP)	Cladribine Low/Low Dose (LLLL)	Cladribine High/Low Dose (HLLL)	Placebo/ Cladribine Low Dose (PPLL)	Placebo/No Treatment
	Affected/ At Risk (%)	Affected/ At Risk (%)	Affected/ At Risk (%)	Affected/ At Risk (%)	Affected/ At Risk (%)	Affected/ At Risk (%)
Cough [A] *	0/98 (0%)	0/92 (0%)	0/186 (0%)	0/186 (0%)	0/244 (0%)	0/22 (0%)
Pharyngolaryngeal pain [A] *	0/98 (0%)	0/92 (0%)	0/186 (0%)	0/186 (0%)	0/244 (0%)	0/22 (0%)
Vascular disorders						
Hypertension [A] *	4/98 (4.08%)	5/92 (5.43%)	5/186 (2.69%)	2/186 (1.08%)	7/244 (2.87%)	1/22 (4.55%)

* Indicates events were collected by non-systematic methods.

A Term from vocabulary, MedDRA (11.0)

	Cladribine 3.5 mg/kg/ No Treatment	Cladribine 5.25 mg/kg/ No Treatment	Cladribine Low/Placebo (LLPP) (24-week Follow-up Period)	Cladribine High Dose/Placebo (HLPP) (24-week Follow-up Period	Cladribine Low/Low Dose (LLLL) (24-week Follow-up Period)	Cladribine High/Low Dose (HLLL) (24-week Follow-up Period)
	Affected/ At Risk (%)	Affected/ At Risk (%)	Affected/ At Risk (%)	Affected/ At Risk (%)	Affected/ At Risk (%)	Affected/ At Risk (%)
Total	13/17 (76.47%)	18/22 (81.82%)	1/75 (1.33%)	3/69 (4.35%)	3/143 (2.1%)	9/151 (5.96%)
Blood and lymphatic system disorders						
Anaemia of pregnancy [A] *	1/17 (5.88%)	0/22 (0%)	0/75 (0%)	0/69 (0%)	0/143 (0%)	0/151 (0%)
Iron deficiency anaemia [A] *	1/17 (5.88%)	0/22 (0%)	0/75 (0%)	0/69 (0%)	0/143 (0%)	0/151 (0%)
Leukopenia [A] *	0/17 (0%)	3/22 (13.64%)	0/75 (0%)	0/69 (0%)	0/143 (0%)	0/151 (0%)
Lymphopenia [A] *	2/17 (11.76%)	5/22 (22.73%)	0/75 (0%)	0/69 (0%)	0/143 (0%)	0/151 (0%)
Neutropenia [A] *	1/5 (20%)	5/22 (22.73%)	0/75 (0%)	0/69 (0%)	0/143 (0%)	0/151 (0%)
Thrombocytopenia [A] *	0/17 (0%)	1/22 (4.55%)	0/75 (0%)	0/69 (0%)	0/143 (0%)	0/151 (0%)
Ear and labyrinth disorders						
Ear pain [A] *	0/17 (0%)	2/22 (9.09%)	0/75 (0%)	0/69 (0%)	0/143 (0%)	0/151 (0%)
Vertigo [A] *	0/17 (0%)	0/22 (0%)	0/75 (0%)	0/69 (0%)	0/143 (0%)	0/151 (0%)

	Cladribine 3.5 mg/kg/ No Treatment	Cladribine 5.25 mg/kg/ No Treatment	Cladribine Low/Placebo (LLPP) (24-week Follow-up Period)	Cladribine High Dose/Placebo (HLPP) (24-week Follow-up Period	Cladribine Low/Low Dose (LLLL) (24-week Follow-up Period)	Cladribine High/Low Dose (HLLL) (24-week Follow-up Period)
	Affected/ At Risk (%)	Affected/ At Risk (%)	Affected/ At Risk (%)	Affected/ At Risk (%)	Affected/ At Risk (%)	Affected/ At Risk (%)
Eye disorders						
Eye irritation [A] *	1/17 (5.88%)	0/22 (0%)	0/75 (0%)	0/69 (0%)	0/143 (0%)	0/151 (0%)
Eye pruritus [A] *	1/17 (5.88%)	0/22 (0%)	0/75 (0%)	0/69 (0%)	0/143 (0%)	0/151 (0%)
Gastrointestinal disorders						
Diarrhoea [A] *	0/17 (0%)	0/22 (0%)	0/75 (0%)	0/69 (0%)	0/143 (0%)	0/151 (0%)
Faecal incontinence [A] *	1/17 (5.88%)	0/22 (0%)	0/75 (0%)	0/69 (0%)	0/143 (0%)	0/151 (0%)
Gastrooesophageal reflux disease [A] *	1/17 (5.88%)	0/22 (0%)	0/75 (0%)	0/69 (0%)	0/143 (0%)	0/151 (0%)
Mouth ulceration [A] *	0/17 (0%)	0/22 (0%)	0/75 (0%)	0/69 (0%)	0/143 (0%)	0/151 (0%)
Nausea [A] *	0/17 (0%)	2/22 (9.09%)	0/75 (0%)	0/69 (0%)	0/143 (0%)	0/151 (0%)
Tooth disorder [A] *	1/17 (5.88%)	0/22 (0%)	0/75 (0%)	0/69 (0%)	0/143 (0%)	0/151 (0%)
Toothache [A] *	0/17 (0%)	3/22 (13.64%)	0/75 (0%)	0/69 (0%)	0/143 (0%)	0/151 (0%)
Vomiting [A] *	0/17 (0%)	0/22 (0%)	0/75 (0%)	0/69 (0%)	0/143 (0%)	0/151 (0%)
General disorders						
Asthenia [A] *	0/17 (0%)	2/22 (9.09%)	0/75 (0%)	0/69 (0%)	0/143 (0%)	0/151 (0%)
Fatigue [A] *	2/17 (11.76%)	1/22 (4.55%)	0/75 (0%)	0/69 (0%)	0/143 (0%)	0/151 (0%)
Hyperthermia [A] *	2/17 (11.76%)	0/22 (0%)	0/75 (0%)	0/69 (0%)	0/143 (0%)	0/151 (0%)
Influenza like illness [A] *	2/17 (11.76%)	2/22 (9.09%)	0/75 (0%)	0/69 (0%)	0/143 (0%)	0/151 (0%)
Immune system disorders						
Hypersensitivity [A] *	1/17 (5.88%)	0/22 (0%)	0/75 (0%)	0/69 (0%)	0/143 (0%)	0/151 (0%)
Infections and infestations						

	Cladribine 3.5 mg/kg/ No Treatment	Cladribine 5.25 mg/kg/ No Treatment	Cladribine Low/Placebo (LLPP) (24-week Follow-up Period)	Cladribine High Dose/Placebo (HLPP) (24-week Follow-up Period	Cladribine Low/Low Dose (LLLL) (24-week Follow-up Period)	Cladribine High/Low Dose (HLLL) (24-week Follow-up Period)
	Affected/ At Risk (%)	Affected/ At Risk (%)	Affected/ At Risk (%)	Affected/ At Risk (%)	Affected/ At Risk (%)	Affected/ At Risk (%)
Bronchitis [A] *	0/17 (0%)	0/22 (0%)	0/75 (0%)	0/69 (0%)	0/143 (0%)	0/151 (0%)
Erythema infectiosum [A] *	1/17 (5.88%)	0/22 (0%)	0/75 (0%)	0/69 (0%)	0/143 (0%)	0/151 (0%)
Furuncle [A] *	0/17 (0%)	0/22 (0%)	0/75 (0%)	0/69 (0%)	0/143 (0%)	0/151 (0%)
Herpes zoster [A] *	1/17 (5.88%)	0/22 (0%)	0/75 (0%)	0/69 (0%)	0/143 (0%)	0/151 (0%)
Hordeolum [A] *	0/17 (0%)	0/22 (0%)	0/75 (0%)	0/69 (0%)	0/143 (0%)	0/151 (0%)
Infected insect bite [A] *	1/17 (5.88%)	0/22 (0%)	0/75 (0%)	0/69 (0%)	0/143 (0%)	0/151 (0%)
Influenza [A] *	2/17 (11.76%)	2/22 (9.09%)	0/75 (0%)	0/69 (0%)	0/143 (0%)	0/151 (0%)
Injection site abscess [A] *	1/17 (5.88%)	0/22 (0%)	0/75 (0%)	0/69 (0%)	0/143 (0%)	0/151 (0%)
Nasopharyngitis [A] *	0/17 (0%)	6/22 (27.27%)	1/75 (1.33%)	3/69 (4.35%)	3/143 (2.1%)	9/151 (5.96%)
Oral herpes [A] *	0/17 (0%)	0/22 (0%)	0/75 (0%)	0/69 (0%)	0/143 (0%)	0/151 (0%)
Pneumonia [A] *	0/17 (0%)	2/22 (9.09%)	0/75 (0%)	0/69 (0%)	0/143 (0%)	0/151 (0%)
Respiratory tract infection viral [A] *	1/17 (5.88%)	0/22 (0%)	0/75 (0%)	0/69 (0%)	0/143 (0%)	0/151 (0%)
Sinusitis [A] *	1/17 (5.88%)	1/22 (4.55%)	0/75 (0%)	0/69 (0%)	0/143 (0%)	0/151 (0%)
Skin bacterial infection [A] *	1/17 (5.88%)	0/22 (0%)	0/75 (0%)	0/69 (0%)	0/143 (0%)	0/151 (0%)
Upper respiratory tract infection [A] *	1/17 (5.88%)	2/22 (9.09%)	0/75 (0%)	0/69 (0%)	0/143 (0%)	0/151 (0%)
Urinary tract infection [A] *	0/17 (0%)	0/22 (0%)	0/75 (0%)	0/69 (0%)	0/143 (0%)	0/151 (0%)
Viral infection [A] *	1/17 (5.88%)	0/22 (0%)	0/75 (0%)	0/69 (0%)	0/143 (0%)	0/151 (0%)
Viral upper respiratory tract infection [A] *	1/17 (5.88%)	0/22 (0%)	0/75 (0%)	0/69 (0%)	0/143 (0%)	0/151 (0%)
Injury, poisoning and procedural complications						

	Cladribine 3.5 mg/kg/ No Treatment	Cladribine 5.25 mg/kg/ No Treatment	Cladribine Low/Placebo (LLPP) (24-week Follow-up Period)	Cladribine High Dose/Placebo (HLPP) (24-week Follow-up Period	Cladribine Low/Low Dose (LLLL) (24-week Follow-up Period)	Cladribine High/Low Dose (HLLL) (24-week Follow-up Period)
	Affected/ At Risk (%)	Affected/ At Risk (%)	Affected/ At Risk (%)	Affected/ At Risk (%)	Affected/ At Risk (%)	Affected/ At Risk (%)
Contusion [A] *	1/17 (5.88%)	1/22 (4.55%)	0/75 (0%)	0/69 (0%)	0/143 (0%)	0/151 (0%)
Fall [A] *	0/17 (0%)	0/22 (0%)	0/75 (0%)	0/69 (0%)	0/143 (0%)	0/151 (0%)
Joint sprain [A] *	1/17 (5.88%)	0/22 (0%)	0/75 (0%)	0/69 (0%)	0/143 (0%)	0/151 (0%)
Investigations						
Alanine aminotransferase increased [A] *	0/17 (0%)	0/22 (0%)	0/75 (0%)	0/69 (0%)	0/143 (0%)	0/151 (0%)
Blood creatine phosphokinase increased [A] *	0/17 (0%)	2/22 (9.09%)	0/75 (0%)	0/69 (0%)	0/143 (0%)	0/151 (0%)
Blood potassium decreased [A] *	0/17 (0%)	0/22 (0%)	0/75 (0%)	0/69 (0%)	0/143 (0%)	0/151 (0%)
Blood urea increased [A] *	0/17 (0%)	0/22 (0%)	0/75 (0%)	0/69 (0%)	0/143 (0%)	0/151 (0%)
Liver function test abnormal [A] *	1/17 (5.88%)	0/22 (0%)	0/75 (0%)	0/69 (0%)	0/143 (0%)	0/151 (0%)
Red blood cell burr cells present [A] *	0/17 (0%)	2/22 (9.09%)	0/75 (0%)	0/69 (0%)	0/143 (0%)	0/151 (0%)
Thyroid function test abnormal [A] *	0/17 (0%)	0/22 (0%)	0/75 (0%)	0/69 (0%)	0/143 (0%)	0/151 (0%)
Weight decreased [A] *	1/17 (5.88%)	0/22 (0%)	0/75 (0%)	0/69 (0%)	0/143 (0%)	0/151 (0%)
Weight increased [A] *	0/17 (0%)	0/22 (0%)	0/75 (0%)	0/69 (0%)	0/143 (0%)	0/151 (0%)
White blood cell count decreased [A] *	1/17 (5.88%)	2/22 (9.09%)	0/75 (0%)	0/69 (0%)	0/143 (0%)	0/151 (0%)
White blood cell count increased [A] *	0/17 (0%)	0/22 (0%)	0/75 (0%)	0/69 (0%)	0/143 (0%)	0/151 (0%)
Musculoskeletal and connective tissue disorders						
Arthralgia [A] *	1/17 (5.88%)	3/22 (13.64%)	0/75 (0%)	0/69 (0%)	0/143 (0%)	0/151 (0%)
Back pain [A] *	4/17 (23.53%)	2/22 (9.09%)	0/75 (0%)	0/69 (0%)	0/143 (0%)	0/151 (0%)
Joint swelling [A] *	1/17 (5.88%)	0/22 (0%)	0/75 (0%)	0/69 (0%)	0/143 (0%)	0/151 (0%)
Musculoskeletal pain [A] *	0/17 (0%)	1/22 (4.55%)	0/75 (0%)	0/69 (0%)	0/143 (0%)	0/151 (0%)

	Cladribine 3.5 mg/kg/ No Treatment	Cladribine 5.25 mg/kg/ No Treatment	Cladribine Low/Placebo (LLPP) (24-week Follow-up Period)	Cladribine High Dose/Placebo (HLPP) (24-week Follow-up Period	Cladribine Low/Low Dose (LLLL) (24-week Follow-up Period)	Cladribine High/Low Dose (HLLL) (24-week Follow-up Period)
	Affected/ At Risk (%)	Affected/ At Risk (%)	Affected/ At Risk (%)	Affected/ At Risk (%)	Affected/ At Risk (%)	Affected/ At Risk (%)
Pain in extremity [A] *	1/17 (5.88%)	1/22 (4.55%)	0/75 (0%)	0/69 (0%)	0/143 (0%)	0/151 (0%)
Sensation of heaviness [A] *	1/17 (5.88%)	0/22 (0%)	0/75 (0%)	0/69 (0%)	0/143 (0%)	0/151 (0%)
Tendonitis [A] *	0/17 (0%)	0/22 (0%)	0/75 (0%)	0/69 (0%)	0/143 (0%)	0/151 (0%)
Nervous system disorders						
Carpal tunnel syndrome [A] *	1/17 (5.88%)	0/22 (0%)	0/75 (0%)	0/69 (0%)	0/143 (0%)	0/151 (0%)
Dizziness [A] *	1/17 (5.88%)	2/22 (9.09%)	0/75 (0%)	0/69 (0%)	0/143 (0%)	0/151 (0%)
Headache [A] *	1/17 (5.88%)	4/22 (18.18%)	0/75 (0%)	0/69 (0%)	0/143 (0%)	0/151 (0%)
Paraesthesia [A] *	0/17 (0%)	0/22 (0%)	0/75 (0%)	0/69 (0%)	0/143 (0%)	0/151 (0%)
Restless legs syndrome [A] *	1/17 (5.88%)	0/22 (0%)	0/75 (0%)	0/69 (0%)	0/143 (0%)	0/151 (0%)
Syncope [A] *	1/17 (5.88%)	0/22 (0%)	0/75 (0%)	0/69 (0%)	0/143 (0%)	0/151 (0%)
Pregnancy, puerperium and perinatal conditions						
Pregnancy [A] *	1/17 (5.88%)	0/22 (0%)	0/75 (0%)	0/69 (0%)	0/143 (0%)	0/151 (0%)
Psychiatric disorders						
Anxiety [A] *	1/17 (5.88%)	2/22 (9.09%)	0/75 (0%)	0/69 (0%)	0/143 (0%)	0/151 (0%)
Depressed mood [A] *	1/17 (5.88%)	0/22 (0%)	0/75 (0%)	0/69 (0%)	0/143 (0%)	0/151 (0%)
Depression [A] *	1/17 (5.88%)	1/22 (4.55%)	0/75 (0%)	0/69 (0%)	0/143 (0%)	0/151 (0%)
Respiratory, thoracic and mediastinal disorders						
Cough [A] *	1/17 (5.88%)	1/22 (4.55%)	0/75 (0%)	0/69 (0%)	0/143 (0%)	0/151 (0%)
Pharyngolaryngeal pain [A] *	1/17 (5.88%)	2/22 (9.09%)	0/75 (0%)	0/69 (0%)	0/143 (0%)	0/151 (0%)
Vascular disorders						

	Cladribine 3.5 mg/kg/ No Treatment	Cladribine 5.25 mg/kg/ No Treatment	Cladribine Low/Placebo (LLPP) (24-week Follow-up Period)	Cladribine High Dose/Placebo (HLPP) (24-week Follow-up Period	Cladribine Low/Low Dose (LLLL) (24-week Follow-up Period)	Cladribine High/Low Dose (HLLL) (24-week Follow-up Period)
	Affected/ At Risk (%)	Affected/ At Risk (%)	Affected/ At Risk (%)	Affected/ At Risk (%)	Affected/ At Risk (%)	Affected/ At Risk (%)
Hypertension [A] *	1/17 (5.88%)	0/22 (0%)	0/75 (0%)	0/69 (0%)	0/143 (0%)	0/151 (0%)

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

	Placebo/Cladribine Low Dose (PPLL) (24-week Follow-up Period)	Placebo/No Treatment (24-week Follow-up Period)	Cladribine 3.5 mg/kg/ No Treatment (24-week Follow-up Period)	Cladribine 5.25 mg/ kg/No Treatment (24-week Follow-up Period)
	Affected/At Risk (%)	Affected/At Risk (%)	Affected/At Risk (%)	Affected/At Risk (%)
Total	9/198 (4.55%)	7/15 (46.67%)	3/9 (33.33%)	6/11 (54.55%)
Blood and lymphatic system disorders				
Anaemia of pregnancy [A] *	0/198 (0%)	0/15 (0%)	0/9 (0%)	0/11 (0%)
Iron deficiency anaemia [A] *	0/198 (0%)	0/15 (0%)	0/9 (0%)	0/11 (0%)
Leukopenia [A] *	0/198 (0%)	0/15 (0%)	0/9 (0%)	0/11 (0%)
Lymphopenia [A] *	0/198 (0%)	1/15 (6.67%)	0/9 (0%)	0/11 (0%)
Neutropenia [A] *	0/198 (0%)	0/15 (0%)	0/9 (0%)	0/11 (0%)
Thrombocytopenia [A] *	0/198 (0%)	0/15 (0%)	0/9 (0%)	0/11 (0%)
Ear and labyrinth disorders				
Ear pain [A] *	0/198 (0%)	0/15 (0%)	0/9 (0%)	0/11 (0%)
Vertigo [A] *	0/198 (0%)	0/15 (0%)	0/9 (0%)	0/11 (0%)
Eye disorders				
Eye irritation [A] *	0/198 (0%)	0/15 (0%)	0/9 (0%)	0/11 (0%)
Eye pruritus [A] *	0/198 (0%)	0/15 (0%)	0/9 (0%)	0/11 (0%)
Gastrointestinal disorders				

	Placebo/Cladribine Low Dose (PPLL) (24-week Follow-up Period)	Placebo/No Treatment (24-week Follow-up Period)	Cladribine 3.5 mg/kg/ No Treatment (24-week Follow-up Period)	Cladribine 5.25 mg/ kg/No Treatment (24-week Follow-up Period)
	Affected/At Risk (%)	Affected/At Risk (%)	Affected/At Risk (%)	Affected/At Risk (%)
Diarrhoea [A] *	0/198 (0%)	0/15 (0%)	0/9 (0%)	0/11 (0%)
Faecal incontinence [A] *	0/198 (0%)	0/15 (0%)	0/9 (0%)	0/11 (0%)
Gastrooesophageal reflux disease [A] *	0/198 (0%)	0/15 (0%)	0/9 (0%)	0/11 (0%)
Mouth ulceration [A] *	0/198 (0%)	0/15 (0%)	0/9 (0%)	1/11 (9.09%)
Nausea [A] *	0/198 (0%)	0/15 (0%)	0/9 (0%)	0/11 (0%)
Tooth disorder [A] *	0/198 (0%)	0/15 (0%)	0/9 (0%)	0/11 (0%)
Toothache [A] *	0/198 (0%)	0/15 (0%)	0/9 (0%)	0/11 (0%)
Vomiting [A] *	0/198 (0%)	0/15 (0%)	0/9 (0%)	0/11 (0%)
General disorders				
Asthenia [A] *	0/198 (0%)	0/15 (0%)	0/9 (0%)	1/11 (9.09%)
Fatigue [A] *	0/198 (0%)	0/15 (0%)	1/9 (11.11%)	0/11 (0%)
Hyperthermia [A] *	0/198 (0%)	0/15 (0%)	0/9 (0%)	0/11 (0%)
Influenza like illness [A] *	0/198 (0%)	0/15 (0%)	0/9 (0%)	0/11 (0%)
Immune system disorders				
Hypersensitivity [A] *	0/198 (0%)	0/15 (0%)	0/9 (0%)	0/11 (0%)
Infections and infestations				
Bronchitis [A] *	0/198 (0%)	0/15 (0%)	0/9 (0%)	0/11 (0%)
Erythema infectiosum [A] *	0/198 (0%)	0/15 (0%)	0/9 (0%)	0/11 (0%)
Furuncle [A] *	0/198 (0%)	1/15 (6.67%)	0/9 (0%)	0/11 (0%)
Herpes zoster [A] *	0/198 (0%)	0/15 (0%)	1/9 (11.11%)	0/11 (0%)
Hordeolum [A] *	0/198 (0%)	0/15 (0%)	0/9 (0%)	1/11 (9.09%)

	Placebo/Cladribine Low Dose (PPLL) (24-week Follow-up Period)	Placebo/No Treatment (24-week Follow-up Period)	Cladribine 3.5 mg/kg/ No Treatment (24-week Follow-up Period)	Cladribine 5.25 mg/ kg/No Treatment (24-week Follow-up Period)
	Affected/At Risk (%)	Affected/At Risk (%)	Affected/At Risk (%)	Affected/At Risk (%)
Infected insect bite [A] *	0/198 (0%)	0/15 (0%)	0/9 (0%)	0/11 (0%)
Influenza [A] *	0/198 (0%)	2/15 (13.33%)	0/9 (0%)	0/11 (0%)
Injection site abscess [A] *	0/198 (0%)	0/15 (0%)	0/9 (0%)	0/11 (0%)
Nasopharyngitis [A] *	9/198 (4.55%)	0/15 (0%)	0/9 (0%)	3/11 (27.27%)
Oral herpes [A] *	0/198 (0%)	0/15 (0%)	0/9 (0%)	1/11 (9.09%)
Pneumonia [A] *	0/198 (0%)	0/15 (0%)	0/9 (0%)	0/11 (0%)
Respiratory tract infection viral [A] *	0/198 (0%)	0/15 (0%)	0/9 (0%)	0/11 (0%)
Sinusitis [A] *	0/198 (0%)	0/15 (0%)	0/9 (0%)	1/11 (9.09%)
Skin bacterial infection [A] *	0/198 (0%)	0/15 (0%)	0/9 (0%)	0/11 (0%)
Upper respiratory tract infection [A] *	0/198 (0%)	0/15 (0%)	0/9 (0%)	0/11 (0%)
Urinary tract infection [A] *	0/198 (0%)	0/15 (0%)	0/9 (0%)	0/11 (0%)
Viral infection [A] *	0/198 (0%)	0/15 (0%)	0/9 (0%)	0/11 (0%)
Viral upper respiratory tract infection [A] *	0/198 (0%)	0/15 (0%)	0/9 (0%)	0/11 (0%)
Injury, poisoning and procedural complications				
Contusion [A] *	0/198 (0%)	0/15 (0%)	0/9 (0%)	0/11 (0%)
Fall [A] *	0/198 (0%)	0/15 (0%)	0/9 (0%)	1/11 (9.09%)
Joint sprain [A] *	0/198 (0%)	0/15 (0%)	0/9 (0%)	0/11 (0%)
Investigations				
Alanine aminotransferase increased [A] *	0/198 (0%)	0/15 (0%)	0/9 (0%)	0/11 (0%)
Blood creatine phosphokinase increased [A] *	0/198 (0%)	0/15 (0%)	0/9 (0%)	1/11 (9.09%)
Blood potassium decreased [A] *	0/198 (0%)	0/15 (0%)	0/9 (0%)	1/11 (9.09%)

	Placebo/Cladribine Low Dose (PPLL) (24-week Follow-up Period)	Placebo/No Treatment (24-week Follow-up Period)	Cladribine 3.5 mg/kg/ No Treatment (24-week Follow-up Period)	Cladribine 5.25 mg/ kg/No Treatment (24-week Follow-up Period)
	Affected/At Risk (%)	Affected/At Risk (%)	Affected/At Risk (%)	Affected/At Risk (%)
Blood urea increased [A] *	0/198 (0%)	1/15 (6.67%)	0/9 (0%)	0/11 (0%)
Liver function test abnormal [A] *	0/198 (0%)	0/15 (0%)	0/9 (0%)	0/11 (0%)
Red blood cell burr cells present [A] *	0/198 (0%)	0/15 (0%)	0/9 (0%)	0/11 (0%)
Thyroid function test abnormal [A] *	0/198 (0%)	0/15 (0%)	0/9 (0%)	1/11 (9.09%)
Weight decreased [A] *	0/198 (0%)	0/15 (0%)	0/9 (0%)	0/11 (0%)
Weight increased [A] *	0/198 (0%)	1/15 (6.67%)	0/9 (0%)	0/11 (0%)
White blood cell count decreased [A] *	0/198 (0%)	0/15 (0%)	0/9 (0%)	0/11 (0%)
White blood cell count increased [A] *	0/198 (0%)	0/15 (0%)	0/9 (0%)	1/11 (9.09%)
Musculoskeletal and connective tissue disorders				
Arthralgia [A] *	0/198 (0%)	0/15 (0%)	0/9 (0%)	0/11 (0%)
Back pain [A] *	0/198 (0%)	0/15 (0%)	0/9 (0%)	0/11 (0%)
Joint swelling [A] *	0/198 (0%)	0/15 (0%)	0/9 (0%)	0/11 (0%)
Musculoskeletal pain [A] *	0/198 (0%)	0/15 (0%)	0/9 (0%)	0/11 (0%)
Pain in extremity [A] *	0/198 (0%)	0/15 (0%)	1/9 (11.11%)	0/11 (0%)
Sensation of heaviness [A] *	0/198 (0%)	0/15 (0%)	0/9 (0%)	0/11 (0%)
Tendonitis [A] *	0/198 (0%)	1/15 (6.67%)	0/9 (0%)	0/11 (0%)
Nervous system disorders				
Carpal tunnel syndrome [A] *	0/198 (0%)	0/15 (0%)	0/9 (0%)	0/11 (0%)
Dizziness [A] *	0/198 (0%)	0/15 (0%)	0/9 (0%)	0/11 (0%)
Headache [A] *	0/198 (0%)	0/15 (0%)	0/9 (0%)	1/11 (9.09%)
Paraesthesia [A] *	0/198 (0%)	0/15 (0%)	0/9 (0%)	1/11 (9.09%)

	Placebo/Cladribine Low Dose (PPLL) (24-week Follow-up Period)	Placebo/No Treatment (24-week Follow-up Period)	Cladribine 3.5 mg/kg/ No Treatment (24-week Follow-up Period)	Cladribine 5.25 mg/ kg/No Treatment (24-week Follow-up Period)
	Affected/At Risk (%)	Affected/At Risk (%)	Affected/At Risk (%)	Affected/At Risk (%)
Restless legs syndrome [A] *	0/198 (0%)	0/15 (0%)	0/9 (0%)	0/11 (0%)
Syncope [A] *	0/198 (0%)	0/15 (0%)	0/9 (0%)	0/11 (0%)
Pregnancy, puerperium and perinatal conditions				
Pregnancy [A] *	0/198 (0%)	0/15 (0%)	0/9 (0%)	0/11 (0%)
Psychiatric disorders				
Anxiety [A] *	0/198 (0%)	0/15 (0%)	0/9 (0%)	0/11 (0%)
Depressed mood [A] *	0/198 (0%)	0/15 (0%)	0/9 (0%)	0/11 (0%)
Depression [A] *	0/198 (0%)	0/15 (0%)	0/9 (0%)	0/11 (0%)
Respiratory, thoracic and mediastinal disorders				
Cough [A] *	0/198 (0%)	0/15 (0%)	0/9 (0%)	1/11 (9.09%)
Pharyngolaryngeal pain [A] *	0/198 (0%)	0/15 (0%)	0/9 (0%)	0/11 (0%)
Vascular disorders				
Hypertension [A] *	0/198 (0%)	0/15 (0%)	0/9 (0%)	0/11 (0%)

* Indicates events were collected by non-systematic methods.

A Term from vocabulary, MedDRA (11.0)

Limitations and Caveats

[Not specified]

More Information

Certain Agreements:

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

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

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