Clinical trial results:
A Randomized, Double-Blind, Double-Dummy, Placebo-Controlled, 3-Arm, Parallel-Group Study in Pediatric Subjects Aged 10 Through 17 Years to Evaluate the Efficacy and Safety of BG00012 and BIIB017 for the Treatment of Relapsing-Remitting Multiple Sclerosis

Summary

EudraCT number	2018-000516-22
Trial protocol	PT EE HU
Global end of trial date	21 July 2022

Results information

Result version number	v1 (current)
This version publication date	19 April 2023
First version publication date	06 February 2023

Trial information

Trial identification

Sponsor protocol code	800MS301

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT03870763
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Biogen
Sponsor organisation address	250 Binney Street, Cambridge, United States, 02142
Public contact	Study Medical Director, Biogen, clinicaltrials@biogen.com
Scientific contact	Study Medical Director, Biogen, clinicaltrials@biogen.com

Notes:

Paediatric regulatory details

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

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	21 July 2022
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	21 July 2022
Was the trial ended prematurely?	Yes

Notes:

General information about the trial

Main objective of the trial:

The objective of the study is to evaluate the efficacy and safety of Dimethyl Fumarate (BG00012) and Peginterferon Beta-1a (BIIB017), both compared with placebo, in paediatric subjects with relapsing-remitting multiple sclerosis (RRMS).

Protection of trial subjects:

Written informed consent was obtained from each subject or subject's legally authorized representative (e.g., legal guardian), as applicable, prior to evaluations performed for eligibility. Subjects or the subject's legally authorized representative were given adequate time to review the information in the informed consent/assent and were allowed to ask, and have answered, questions concerning all portions of the conduct of the study.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	19 March 2019
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Estonia: 4
Country: Number of subjects enrolled	Tunisia: 2
Country: Number of subjects enrolled	Turkey: 2
Country: Number of subjects enrolled	Jordan: 2
Country: Number of subjects enrolled	Taiwan: 1
Worldwide total number of subjects	11
EEA total number of subjects	4

Notes:

Subjects enrolled per age group

In utero	0
Preterm newborn - gestational age < 37 wk	0
Newborns (0-27 days)	0
Infants and toddlers (28 days-23 months)	0
Children (2-11 years)	0

Adolescents (12-17 years)	11
Adults (18-64 years)	0
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Subjects were enrolled at the investigative sites in Estonia, Tunisia, Turkey, Jordan and Taiwan from 19 March 2019 to 21 July 2022.

Pre-assignment

Screening details:

A total of 11 subjects were enrolled and treated in the study.

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	Dimethyl Fumarate 240 mg

Arm description:

Subjects received dimethyl fumarate 120 milligrams (mg) capsules twice daily (BID), orally for 7 days followed by 240 mg capsules, BID, orally for 95 weeks and peginterferon beta-1a matching placebo subcutaneous (SC) injection once every 2 weeks (Q2W) for up to 96 weeks.

Arm type	Experimental
Investigational medicinal product name	Dimethyl Fumarate
Investigational medicinal product code	
Other name	BG00012
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

Dimethyl fumarate 120 mg capsules, BID, orally for 7 days followed by 240 mg capsules, BID, orally for 95 weeks.

Investigational medicinal product name	Peginterferon beta-1a matching placebo
Investigational medicinal product code	
Other name	BIIB017
Pharmaceutical forms	Injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Peginterferon beta-1a matching placebo Q2W for up to 96 weeks.

Arm title	Peginterferon Beta-1a 125 µg

Arm description:

Subjects received peginterferon beta-1a, 63 micrograms (µg) on Day 1, 94 µg at Week 2, 125 µg SC injection Q2W from Week 4 up to 96 weeks and peginterferon beta-1a matching placebo SC injection, Q2W for up to 96 weeks.

Arm type	Experimental
Investigational medicinal product name	Peginterferon beta-1a matching placebo
Investigational medicinal product code	
Other name	BIIB017
Pharmaceutical forms	Injection
Routes of administration	Subcutaneous use

Dosage and administration details:	
Peginterferon beta-1a matching placebo Q2W for up to 96 weeks.	
Investigational medicinal product name	peginterferon beta-1a
Investigational medicinal product code	
Other name	BIIB017
Pharmaceutical forms	Injection
Routes of administration	Subcutaneous use
Dosage and administration details:	
Peginterferon beta-1a, 63 µg on Day 1, 94 µg at Week 2, 125 µg SC injection Q2W from Week 4 up to 96 weeks.	
Arm title	Placebo
Arm description:	
Subjects received peginterferon beta-1a matching placebo SC injection Q2W and dimethyl fumarate matching placebo capsules BID, orally for up to 96 weeks.	
Arm type	Placebo
Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Injection, Capsule
Routes of administration	Subcutaneous use, Oral use
Dosage and administration details:	
Peginterferon beta-1a matching placebo SC injection, Q2W and dimethyl fumarate matching placebo capsules, BID, orally for up to 96 weeks.	

Number of subjects in period 1	Dimethyl Fumarate 240 mg	Peginterferon Beta-1a 125 µg	Placebo
Started	2	6	3
Completed	2	3	2
Not completed	0	3	1
Consent withdrawn by subject	-	1	-
Worsening of multiple sclerosis attack	-	-	1
Study terminated by sponsor	-	2	-

Baseline characteristics

Reporting groups	
Reporting group title	Dimethyl Fumarate 240 mg
Reporting group description:	
Subjects received dimethyl fumarate 120 milligrams (mg) capsules twice daily (BID), orally for 7 days followed by 240 mg capsules, BID, orally for 95 weeks and peginterferon beta-1a matching placebo subcutaneous (SC) injection once every 2 weeks (Q2W) for up to 96 weeks.	
Reporting group title	Peginterferon Beta-1a 125 µg
Reporting group description:	
Subjects received peginterferon beta-1a, 63 micrograms (µg) on Day 1, 94 µg at Week 2, 125 µg SC injection Q2W from Week 4 up to 96 weeks and peginterferon beta-1a matching placebo SC injection, Q2W for up to 96 weeks.	
Reporting group title	Placebo
Reporting group description:	
Subjects received peginterferon beta-1a matching placebo SC injection Q2W and dimethyl fumarate matching placebo capsules BID, orally for up to 96 weeks.	

Reporting group values	Dimethyl Fumarate 240 mg	Peginterferon Beta-1a 125 µg	Placebo
Number of subjects	2	6	3
Age Categorical Units: Subjects			
Age continuous Units: years			
arithmetic mean	15.5	15.7	15.7
standard deviation	± 2.12	± 1.51	± 1.15
Gender categorical Units: Subjects			
Female	1	5	2
Male	1	1	1
Race Units: Subjects			
White	2	5	3
Asian	0	1	0
Ethnicity Units: Subjects			
Not Hispanic or Latino	2	6	3

Reporting group values	Total		
Number of subjects	11		
Age Categorical Units: Subjects			
Age continuous Units: years			
arithmetic mean			
standard deviation	-		

Gender categorical Units: Subjects			
Female	8		
Male	3		
Race Units: Subjects			
White	10		
Asian	1		
Ethnicity Units: Subjects			
Not Hispanic or Latino	11		

End points

End points reporting groups

Reporting group title	Dimethyl Fumarate 240 mg
Reporting group description:	
Subjects received dimethyl fumarate 120 milligrams (mg) capsules twice daily (BID), orally for 7 days followed by 240 mg capsules, BID, orally for 95 weeks and peginterferon beta-1a matching placebo subcutaneous (SC) injection once every 2 weeks (Q2W) for up to 96 weeks.	
Reporting group title	Peginterferon Beta-1a 125 µg
Reporting group description:	
Subjects received peginterferon beta-1a, 63 micrograms (µg) on Day 1, 94 µg at Week 2, 125 µg SC injection Q2W from Week 4 up to 96 weeks and peginterferon beta-1a matching placebo SC injection, Q2W for up to 96 weeks.	
Reporting group title	Placebo
Reporting group description:	
Subjects received peginterferon beta-1a matching placebo SC injection Q2W and dimethyl fumarate matching placebo capsules BID, orally for up to 96 weeks.	

Primary: Time to First Relapse

End point title	Time to First Relapse[1]
End point description:	
A clinical relapse is defined as new or recurrent neurological symptoms, not associated with fever, lasting for at least 24 hours, and followed by a period of 30 days of stability or improvement. Time to First Relapse is estimated by Kaplan Mayer method. "99999" signifies data is not available as no participant in this arm group had a relapse. ITT population included all subjects who were randomised and received at least 1 dose of study treatment (BG00012, BIIB017, or placebo). The overall number of subjects analysed signifies the number of subjects with relapse.	
End point type	Primary
End point timeframe:	
Baseline up to Week 96	

Notes:

[1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Only descriptive analysis is planned to be analysed.

End point values	Dimethyl Fumarate 240 mg	Peginterferon Beta-1a 125 µg	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	2	6	3	
Units: Days				
median (inter-quartile range (Q1-Q3))	413 (413 to 413)	99999 (99999 to 99999)	166.5 (113 to 220)	

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects With Adverse Events (AEs) and Serious Adverse Events (SAEs)

End point title	Number of Subjects With Adverse Events (AEs) and Serious Adverse Events (SAEs)

End point description:

An AE was any untoward medical occurrence in a subject who received study drug without regard to possibility of causal relationship. An SAE is an AE resulting in any of the following outcomes or deemed significant for any other reason: death; Initial or prolonged inpatient hospitalization; life threatening experience (immediate risk of dying); persistent or significant disability/incapacity; congenital anomaly. Safety population included all subjects who had received at least 1 dose of study treatment.

End point type	Secondary

End point timeframe:

Baseline up to Week 100

End point values	Dimethyl Fumarate 240 mg	Peginterferon Beta-1a 125 µg	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	2	6	3	
Units: subjects				
AEs	2	6	3	
SAEs	1	0	1	

Statistical analyses

No statistical analyses for this end point

Secondary: Number of New or Newly Enlarging T2 Hyperintense Lesions on Brain Magnetic Resonance Imaging (MRI) Scans at Weeks 48 and 96

End point title	Number of New or Newly Enlarging T2 Hyperintense Lesions on Brain Magnetic Resonance Imaging (MRI) Scans at Weeks 48 and 96

End point description:

The number of new or newly enlarging T2 hyperintense lesions that developed in each subject assessed on magnetic resonance imaging (MRI) scans. The overall number of subjects analysed signifies number of subjects analysed in this endpoint and the number analysed 'n' signifies number of subjects analysed at a given timepoint. ITT population included all subjects who were randomised and received at least 1 dose of study treatment (BG00012, BIIB017, or placebo).

End point type	Secondary

End point timeframe:

Weeks 48 and 96

End point values	Dimethyl Fumarate 240 mg	Peginterferon Beta-1a 125 µg	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	2	5	3	
Units: number of lesions				
arithmetic mean (full range (min-max))				
Week 48	0.5 (0 to 1)	1.0 (0 to 3)	3.3 (2 to 4)	

Week 96 (n= 2, 4, 2)	2.5 (0 to 5)	1.3 (0 to 3)	3.5 (2 to 5)	

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Galdolinium(Gd)-Enhancing Lesions at Weeks 48 and 96

End point title	Number of Galdolinium(Gd)-Enhancing Lesions at Weeks 48 and 96

End point description:

The number of Gd-enhancing lesions was assessed by using MRI scans. The overall number of subjects analysed signifies number of subjects analysed in this endpoint and the number analysed 'n' signifies number of subjects analysed at a given timepoint. ITT population included all subjects who were randomised and received at least 1 dose of study treatment (BG00012, BIIB017, or placebo).

End point type	Secondary

End point timeframe:

Weeks 48 and 96

End point values	Dimethyl Fumarate 240 mg	Peginterferon Beta-1a 125 µg	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	2	5	2	
Units: number of lesions				
arithmetic mean (full range (min-max))				
Week 48	0 (0 to 0)	0 (0 to 0)	1.5 (0 to 3)	
Week 96 (n= 2, 4, 2)	0 (0 to 0)	0.25 (0 to 1)	0.5 (0 to 1)	

Statistical analyses

No statistical analyses for this end point

Secondary: Annualized Relapse Rate

End point title	Annualized Relapse Rate

End point description:

A clinical relapse was defined as new or recurrent neurological symptoms, not associated with fever, lasting for at least 24 hours, and followed by a period of 30 days of stability or improvement. The relapse rate for an individual participant was calculated as the number of relapses for that participant divided by the number of participant-years followed. The ARR for each enrolment group was calculated as the total number of relapses experienced in the group divided by the total number of participant-years on the study. An unadjusted relapse rate is reported. ITT population included all subjects who were randomised and received at least 1 dose of study treatment (BG00012, BIIB017, or placebo).

End point type	Secondary

End point timeframe:

up to Week 96

End point values	Dimethyl Fumarate 240 mg	Peginterferon Beta-1a 125 µg	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	2	6	3	
Units: relapses per subject year				
number (not applicable)	0.26	0.00	0.46	

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information	
Timeframe for reporting adverse events:	
Baseline up to Week 100	
Adverse event reporting additional description:	
Safety population included all subjects who had received at least 1 dose of study treatment.	
Assessment type	Systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	24.1

Reporting groups	
Reporting group title	Dimethyl Fumarate 240 mg
Reporting group description:	
Subjects received dimethyl fumarate 120 mg capsules BID, orally for 7 days followed by 240 mg capsules, BID, orally for 95 weeks and peginterferon beta-1a matching placebo SC injection Q2W for up to 96 weeks.	
Reporting group title	Placebo
Reporting group description:	
Subjects received peginterferon beta-1a matching placebo SC injection, Q2W and dimethyl fumarate matching placebo capsules, BID, orally for up to 96 weeks.	
Reporting group title	Peginterferon Beta-1a 125 µg
Reporting group description:	
Subjects received peginterferon beta-1a, 63 µg on Day 1, 94 µg at Week 2, 125 µg SC injection Q2W from Week 4 up to 96 weeks and peginterferon beta-1a matching placebo SC injection, Q2W for up to 96 weeks.	

Serious adverse events	Dimethyl Fumarate 240 mg	Placebo	Peginterferon Beta-1a 125 µg
Total subjects affected by serious adverse events			
subjects affected / exposed	1 / 2 (50.00%)	1 / 3 (33.33%)	0 / 6 (0.00%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Nervous system disorders			
Multiple sclerosis relapse			
subjects affected / exposed	1 / 2 (50.00%)	1 / 3 (33.33%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

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

Non-serious adverse events	Dimethyl Fumarate 240 mg	Placebo	Peginterferon Beta-1a 125 µg
Total subjects affected by non-serious adverse events			
subjects affected / exposed	2 / 2 (100.00%)	3 / 3 (100.00%)	6 / 6 (100.00%)
Investigations			
Parasite stool test positive			
subjects affected / exposed	0 / 2 (0.00%)	0 / 3 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
Vitamin D decreased			
subjects affected / exposed	0 / 2 (0.00%)	0 / 3 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
Injury, poisoning and procedural complications			
Arthropod sting			
subjects affected / exposed	0 / 2 (0.00%)	1 / 3 (33.33%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Cardiac disorders			
Tachycardia			
subjects affected / exposed	0 / 2 (0.00%)	0 / 3 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
Nervous system disorders			
Dysgeusia			
subjects affected / exposed	0 / 2 (0.00%)	1 / 3 (33.33%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Headache			
subjects affected / exposed	1 / 2 (50.00%)	1 / 3 (33.33%)	4 / 6 (66.67%)
occurrences (all)	1	7	14
Multiple sclerosis relapse			
subjects affected / exposed	1 / 2 (50.00%)	2 / 3 (66.67%)	0 / 6 (0.00%)
occurrences (all)	1	3	0
Blood and lymphatic system disorders			
Iron deficiency anaemia			
subjects affected / exposed	0 / 2 (0.00%)	1 / 3 (33.33%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Lymphadenopathy			
subjects affected / exposed	0 / 2 (0.00%)	0 / 3 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
General disorders and administration site conditions			

Asthenia			
subjects affected / exposed	0 / 2 (0.00%)	0 / 3 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	2
Chills			
subjects affected / exposed	0 / 2 (0.00%)	0 / 3 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	2
Fatigue			
subjects affected / exposed	0 / 2 (0.00%)	1 / 3 (33.33%)	1 / 6 (16.67%)
occurrences (all)	0	1	1
Feeling cold			
subjects affected / exposed	0 / 2 (0.00%)	0 / 3 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
Influenza like illness			
subjects affected / exposed	0 / 2 (0.00%)	0 / 3 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	2
Injection site bruising			
subjects affected / exposed	0 / 2 (0.00%)	0 / 3 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
Injection site erythema			
subjects affected / exposed	0 / 2 (0.00%)	0 / 3 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
Non-cardiac chest pain			
subjects affected / exposed	0 / 2 (0.00%)	0 / 3 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	2
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	0 / 2 (0.00%)	0 / 3 (0.00%)	2 / 6 (33.33%)
occurrences (all)	0	0	3
Diarrhoea			
subjects affected / exposed	0 / 2 (0.00%)	1 / 3 (33.33%)	0 / 6 (0.00%)
occurrences (all)	0	2	0
Gastrointestinal disorder			
subjects affected / exposed	0 / 2 (0.00%)	1 / 3 (33.33%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Respiratory, thoracic and mediastinal disorders			

Cough			
subjects affected / exposed	1 / 2 (50.00%)	0 / 3 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Dyspnoea exertional			
subjects affected / exposed	0 / 2 (0.00%)	0 / 3 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
Epistaxis			
subjects affected / exposed	0 / 2 (0.00%)	1 / 3 (33.33%)	0 / 6 (0.00%)
occurrences (all)	0	7	0
Oropharyngeal pain			
subjects affected / exposed	0 / 2 (0.00%)	0 / 3 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
Skin and subcutaneous tissue disorders			
Erythema			
subjects affected / exposed	1 / 2 (50.00%)	0 / 3 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Sensitive skin			
subjects affected / exposed	0 / 2 (0.00%)	0 / 3 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
Psychiatric disorders			
Anxiety			
subjects affected / exposed	0 / 2 (0.00%)	0 / 3 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
Musculoskeletal and connective tissue disorders			
Muscle spasms			
subjects affected / exposed	0 / 2 (0.00%)	1 / 3 (33.33%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Musculoskeletal chest pain			
subjects affected / exposed	0 / 2 (0.00%)	0 / 3 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
Myalgia			
subjects affected / exposed	0 / 2 (0.00%)	1 / 3 (33.33%)	0 / 6 (0.00%)
occurrences (all)	0	2	0
Neck pain			
subjects affected / exposed	0 / 2 (0.00%)	0 / 3 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1

Pain in extremity			
subjects affected / exposed	0 / 2 (0.00%)	1 / 3 (33.33%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Infections and infestations			
Asymptomatic COVID-19			
subjects affected / exposed	0 / 2 (0.00%)	0 / 3 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
COVID-19			
subjects affected / exposed	0 / 2 (0.00%)	1 / 3 (33.33%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Upper respiratory tract infection			
subjects affected / exposed	0 / 2 (0.00%)	0 / 3 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
Urinary tract infection			
subjects affected / exposed	0 / 2 (0.00%)	1 / 3 (33.33%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Vaginal infection			
subjects affected / exposed	1 / 2 (50.00%)	0 / 3 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
15 June 2018	a) Excluded the subjects who had a low lymphocyte count following study withdrawal/completion from further follow-up, should they be initiated on appropriate MS treatment, according to local standard of care. b) Provision of open-label access to BG00012 (Tecfidera) for subjects who experienced a confirmed relapse at any point during the study or who had a high lesion burden on MRI at Week 48 until the end of their scheduled participation in the study if considered suitable by the treating neurologist.
09 August 2018	Clarified the level of detail and purpose of date-of-birth (DOB) information collected for the subjects enrolled in the study.
06 November 2019	Adjusted the sample sizes of the study populations.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

Limitations of the trial such as small numbers of subjects analysed or technical problems leading to unreliable data.

The study was terminated because of long-term difficulties in fulfilling the enrolment commitments and changes in paediatric MS landscape which no longer support placebo-controlled trials. Decision to stop study was not based on safety concerns.

Notes: