Clinical trial results:
Open-label, Randomized, 2-arm, Active Comparator Study to Evaluate Safety and Tolerability in Portuguese Patients With Relapsing Remitting Multiple Sclerosis (MS) Transitioning From Current Subcutaneous Interferon Therapy to Peginterferon Beta 1a (PLEGRIDY™)

Summary

EudraCT number	2016-000434-21
Trial protocol	PT
Global end of trial date	25 October 2020

Results information

Result version number	v1
This version publication date	10 February 2023
First version publication date	10 February 2023

Trial information

Trial identification

Sponsor protocol code	PRT-PEG-15-10880

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT03177083
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Biogen
Sponsor organisation address	225 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	25 October 2020
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	25 October 2020
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The primary objective of the study was to evaluate safety and tolerability as defined by the frequency of the adverse events (AEs) of flu-like symptoms (FLS) [chills, pyrexia, myalgia, and asthenia], injection site reactions (ISRs), and injection site reaction pain (ISR-P), over 24 weeks of treatment (the active comparator period) with Plegridy (peginterferon beta-1a) 125 microgram (µg) subcutaneous (SC) every 2 weeks versus current SC interferon beta (IFN-β) therapy in subjects with Relapsing Remitting Multiple Sclerosis (RRMS).

Protection of trial subjects:

Written informed consent was obtained from each subject or subject's legally authorised representative (e.g., legal guardian), as applicable, prior to evaluations performed for eligibility. Subjects or the subject's legally authorised 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	30 January 2017
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Portugal: 77
Worldwide total number of subjects	77
EEA total number of subjects	77

Notes:

Subjects enrolled per age group

In utero	0
Preterm newborn - gestational age < 37 wk	0
Newborns (0-27 days)	0
Infants and toddlers (28 days-23 months)	0
Children (2-11 years)	0
Adolescents (12-17 years)	0

Adults (18-64 years)	76
From 65 to 84 years	1
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Subjects receiving prior IFN-β therapy took part in the study at 14 investigative sites in Portugal from 30 January 2017 to 26 October 2020.

Pre-assignment

Screening details:

A total of 91 subjects were screened of which 77 were randomised to receive either Plegridy or continue on IFN-β therapy.

Period 1

Period 1 title	Overall Study (overall period)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Not blinded

Arms

Are arms mutually exclusive?	Yes
Arm title	Plegridy

Arm description:

Subjects were administered Plegridy 125 µg as a SC injection, once every 2 weeks during the 24-week active comparator period. During the 48-week extension period, subjects self-administered Plegridy 125 µg, SC injection, once every 2 weeks.

Arm type	Experimental
Investigational medicinal product name	Peginterferon beta-1a
Investigational medicinal product code	
Other name	Plegridy™
Pharmaceutical forms	Solution for injection in pre-filled pen
Routes of administration	Subcutaneous use

Dosage and administration details:

Subjects were administered Plegridy as specified in treatment arm.

Arm title	Current IFN-β Therapy

Arm description:

Subjects continued to receive IFN-β-1b 0.25 mg, SC injection, every other day or IFN-β-1a 22µg or 44 µg, SC injection, 3 times a week during the 24-week active comparator period. During the 48-week extension period, subjects self-administered SC injection of Plegridy 63 µg in Week 1, 94 µg in Week 3 and 125 µg thereafter once every 2 weeks

Arm type	Experimental
Investigational medicinal product name	Peginterferon beta-1a
Investigational medicinal product code	
Other name	Plegridy™
Pharmaceutical forms	Solution for injection in pre-filled pen
Routes of administration	Subcutaneous use

Dosage and administration details:

Subjects were administered Plegridy as specified in treatment arm.

Investigational medicinal product name	Interferon beta-1a
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection in pre-filled pen
Routes of administration	Subcutaneous use

Dosage and administration details:

Subjects were administered Interferon beta-1a as specified in treatment arm.

Number of subjects in period 1	Plegridy	Current IFN-β Therapy
Started	38	39
Completed	32	32
Not completed	6	7
Other - Withdrawal of consent	1	-
Adverse event, serious fatal	-	1
Other - Lack of effectiveness	1	-
Physician decision	-	3
Adverse event, non-fatal	2	1
Other - Subject wishes to discontinue treatment	2	-
Other - Sponsor's decision	-	1
Other - Foot fracture; Compliance	-	1

Baseline characteristics

Reporting groups	
Reporting group title	Plegridy
Reporting group description:	
Subjects were administered Plegridy 125 µg as a SC injection, once every 2 weeks during the 24-week active comparator period. During the 48-week extension period, subjects self-administered Plegridy 125 µg, SC injection, once every 2 weeks.	
Reporting group title	Current IFN-β Therapy
Reporting group description:	
Subjects continued to receive IFN-β-1b 0.25 mg, SC injection, every other day or IFN-β-1a 22µg or 44 µg, SC injection, 3 times a week during the 24-week active comparator period. During the 48-week extension period, subjects self-administered SC injection of Plegridy 63 µg in Week 1, 94 µg in Week 3 and 125 µg thereafter once every 2 weeks	

Reporting group values	Plegridy	Current IFN-β Therapy	Total
Number of subjects	38	39	77
Age Categorical			
Units: Subjects			
Age continuous			
Units: years			
arithmetic mean	45.18	47.82	
standard deviation	± 10.30	± 10.43	-
Gender categorical			
Units: Subjects			
Male	13	16	29
Female	25	23	48

End points

End points reporting groups

Reporting group title	Plegridy

Reporting group description:

Subjects were administered Plegridy 125 µg as a SC injection, once every 2 weeks during the 24-week active comparator period. During the 48-week extension period, subjects self-administered Plegridy 125 µg, SC injection, once every 2 weeks.

Reporting group title	Current IFN-β Therapy

Reporting group description:

Subjects continued to receive IFN-β-1b 0.25 mg, SC injection, every other day or IFN-β-1a 22µg or 44 µg, SC injection, 3 times a week during the 24-week active comparator period. During the 48-week extension period, subjects self-administered SC injection of Plegridy 63 µg in Week 1, 94 µg in Week 3 and 125 µg thereafter once every 2 weeks

Subject analysis set title	All Subjects
Subject analysis set type	Safety analysis

Subject analysis set description:

This group included all subjects who received either Plegridy 125 µg, once every 2 weeks or IFN-β-1b 0.25 mg, every other day or IFN-β-1a 22µg or 44 µg, SC injection, 3 times a week during the 24-week active comparator period and received Plegridy up to 125 µg, SC injection, once every 2 weeks during the 48-week extension period.

Primary: Number of Combined Adverse Event (AE) Counts of Flu-like Symptoms (FLS), Injection Site Reactions (ISRs), and Injection Site Reaction Pain (ISR-P)

End point title	Number of Combined Adverse Event (AE) Counts of Flu-like Symptoms (FLS), Injection Site Reactions (ISRs), and Injection Site Reaction Pain (ISR-P)[1]

End point description:

Combined counts of AEs of FLS, ISRs and ISR-P were reported. FLS included chills, pyrexia, myalgia, and asthenia. ISR is defined as a post-application assessment score ≥2 in subject and clinician assessments using Patient's Erythema Self-Assessment 1 (PSA) and Clinician Erythema Assessment (CEA) scales respectively. PSA assesses erythema severity (skin redness) on 5-point scale where 0=clear of unwanted redness and 4=completely unacceptable redness. CEA evaluated subject`s erythema severity on 5-point scale where 0=clear skin with no signs of erythema and 4=severe erythema/fiery redness. ISR-P is defined as a visual analog scale (VAS) associated with ISR ≥1 immediately after injection/30 minutes post-injection. Safety population included all the subjects who received at least one dose of the study treatment. Number of subjects analysed=subjects with AEs of FLS, ISRs and ISR-P over 24 weeks of treatment.

End point type	Primary

End point timeframe:

Up to end of comparator period (Week 24)

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: No statistical analysis was planned or performed for this endpoint.

End point values	Plegridy	Current IFN-β Therapy		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	25	31		
Units: Number of combined AEs				
arithmetic mean (standard deviation)	3.67 (± 1.53)	52.67 (± 76.51)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change in Subject-reported Treatment Satisfaction Using the Treatment Satisfaction Questionnaire for Medication (TSQM-9) From Baseline to Week 24 in Subjects Treated With Plegridy Versus Current SC IFN-β

End point title	Change in Subject-reported Treatment Satisfaction Using the Treatment Satisfaction Questionnaire for Medication (TSQM-9) From Baseline to Week 24 in Subjects Treated With Plegridy Versus Current SC IFN-β

End point description:

TSQM is a 14-item instrument consisting of four scales: Effectiveness scale (questions 1 to 3), side effects scale (questions 4 to 8), convenience scale (questions 9 to 11) and overall satisfaction scale (questions 12 to 14). In TSQM-9, the five items related to side effects of medication were not included. The scores were computed by adding items for each domain. The lowest possible score was subtracted from this composite score and divided by the greatest possible score minus the lowest possible score. This provided a transformed score between 0 and 1 that was then multiplied by 100. TSQM-9 domain scores range from 0 to 100 with higher scores representing higher satisfaction on that domain. Efficacy population included all enrolled subjects who had at least one post-baseline efficacy assessment. Number of subjects analysed=number of subjects with available data for analysis. Number analysed (n) signifies number of subjects analysed for the specified measurement.

End point type	Secondary

End point timeframe:

Baseline up to end of comparator period (Week 24)

End point values	Plegridy	Current IFN-β Therapy		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	35	35		
Units: score on a scale				
arithmetic mean (standard deviation)				
Effectiveness Score (n=33,35)	2.02 (± 11.79)	0.54 (± 29.73)		
Convenience Score	13.33 (± 15.49)	1.50 (± 12.43)		
Overall Satisfaction	2.35 (± 15.64)	0.17 (± 12.48)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change in Subject-reported Treatment Satisfaction Using the TSQM-9 From Week 24 Through 48 in Subjects who Switched From Current SC IFN-β Therapy to Plegridy at the End of the Comparator Period

End point title	Change in Subject-reported Treatment Satisfaction Using the TSQM-9 From Week 24 Through 48 in Subjects who Switched From Current SC IFN-β Therapy to Plegridy at the End of the Comparator Period

End point description:

TSQM is a 14-item instrument consisting of four scales: Effectiveness scale (questions 1 to 3), side effects scale (questions 4 to 8), convenience scale (questions 9 to 11) and overall satisfaction scale (questions 12 to 14). In TSQM-9, the five items related to side effects of medication were not included. The scores were computed by adding items for each domain. The lowest possible score was subtracted

from this composite score and divided by the greatest possible score minus the lowest possible score. This provided a transformed score between 0 and 1 that was then multiplied by 100. TSQM-9 domain scores range from 0 to 100 with higher scores representing higher satisfaction on that domain. Efficacy population included all enrolled subjects who had at least one post-baseline efficacy assessment. Number of subjects analysed=number of subjects with available data for analysis. Number analysed (n) signifies number of subjects analysed for the specified measurement.

End point type	Secondary

End point timeframe:

End of comparator period (Week 24) up to Week 48

End point values	Plegridy	Current IFN-β Therapy		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	32	34		
Units: score on a scale				
arithmetic mean (standard deviation)				
Effectiveness score (n=30,34)	-2.54 (± 19.04)	12.46 (± 24.98)		
Convenience score (n=32, 33)	-3.72 (± 11.65)	8.51 (± 13.77)		
Overall satisfaction	0.55 (± 11.41)	6.06 (± 15.70)		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Pain-free Subjects Immediately After Injection at End of the Comparator Period in Subjects Treated With Plegridy Versus Current SC IFN-β

End point title	Percentage of Pain-free Subjects Immediately After Injection at End of the Comparator Period in Subjects Treated With Plegridy Versus Current SC IFN-β

End point description:

Subjects were asked to indicate their pain immediately after the injection on the VAS scale ranging from 0 (no pain) to 100 millimetres (mm) (intense pain). Pain-free injection is defined as 0 mm for all full-dose injections on the VAS of subject-reported pain. Safety population included all the subjects who received at least one dose of the study treatment. Number analysed (n) signifies number of subjects with available data for analysis.

End point type	Secondary

End point timeframe:

End of comparator period (Week 24)

End point values	Plegridy	Current IFN-β Therapy		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	35	17		
Units: percentage of subjects				
number (not applicable)	42.9	17.6		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Pain-free Subjects 30 Minutes After Injection at End of the Comparator Period in Subjects Treated With Plegridy Versus Current SC IFN-β

End point title	Percentage of Pain-free Subjects 30 Minutes After Injection at End of the Comparator Period in Subjects Treated With Plegridy Versus Current SC IFN-β

End point description:

Subjects were asked to indicate their pain 30 minutes after the injection on the VAS scale ranging from 0 (no pain) to 100 mm (intense pain). Pain-free injection is defined as 0 mm for all full-dose injections on the VAS of subject-reported pain. Safety population included all the subjects who received at least one dose of the study treatment. Number analysed (n) signifies number of subjects with available data for analysis.

End point type	Secondary

End point timeframe:

End of comparator period (Week 24)

End point values	Plegridy	Current IFN-β Therapy		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	36	17		
Units: percentage of subjects				
number (not applicable)	47.2	41.2		

Statistical analyses

No statistical analyses for this end point

Secondary: Average Change in Subject-reported VAS Pain Score From Pre-injection to 30 Minutes Post-injection at the End of the Comparator Period in Subjects Treated With Plegridy Versus Current SC IFN-β

End point title	Average Change in Subject-reported VAS Pain Score From Pre-injection to 30 Minutes Post-injection at the End of the Comparator Period in Subjects Treated With Plegridy Versus Current SC IFN-β

End point description:

Subjects were asked to indicate their pain before and 30 minutes after the injection on the VAS scale ranging from 0 (no pain) to 100 mm (intense pain). The change between the 2 timepoints was calculated. Safety population included all the subjects who received at least one dose of the study treatment. Number of subjects analysed=number of subjects with available data for analysis.

End point type	Secondary

End point timeframe:

End of comparator period (Week 24)

End point values	Plegridy	Current IFN-β Therapy		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	35	17		
Units: mm				
arithmetic mean (standard deviation)	3.66 (± 10.07)	0.65 (± 11.98)		

Statistical analyses

No statistical analyses for this end point

Secondary: Average Change in Subject-reported VAS Pain Score From Pre-injection to Immediate Post-injection at the End of the Comparator Period in Subjects Treated With Plegridy Versus Current SC IFN-β

End point title	Average Change in Subject-reported VAS Pain Score From Pre-injection to Immediate Post-injection at the End of the Comparator Period in Subjects Treated With Plegridy Versus Current SC IFN-β

End point description:

Subjects were asked to indicate their pain before and immediately after the injection on the VAS scale ranging from 0 (no pain) to 100 mm (intense pain). The change between the 2 timepoints was calculated. Safety population included all the subjects who received at least one dose of the study treatment. Number of subjects analysed=number of subjects with available data for analysis.

End point type	Secondary

End point timeframe:

End of comparator period (Week 24)

End point values	Plegridy	Current IFN-β Therapy		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	34	17		
Units: mm				
arithmetic mean (standard deviation)	3.85 (± 11.59)	10.18 (± 18.53)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change in Patient-reported Outcome (PRO) Measure: 12-item Short Form Survey (SF-12) Score From Baseline to Week 24 in Subjects Treated With

Plegridy Versus Current SC IFN-β

End point title	Change in Patient-reported Outcome (PRO) Measure: 12-item Short Form Survey (SF-12) Score From Baseline to Week 24 in Subjects Treated With Plegridy Versus Current SC IFN-β

End point description:

The SF-12 is a short survey with 12 questions to measure functional health and well-being from the study subject`s perspective across eight domains: Physical functioning, role, bodily pain, general health perceptions, vitality, social functioning, emotional role, and mental health. Mental and physical composite scores (MCS & PCS) are computed using the scores of twelve questions and range from 0 to 100, where a higher score indicates better health. Positive change from baseline indicates improved health. Efficacy Population included all enrolled subjects who had at least one post-baseline efficacy assessment. Number of subjects analysed=number of subjects with available data for analysis.

End point type	Secondary

End point timeframe:

Baseline up to end of comparator period (Week 24)

End point values	Plegridy	Current IFN-β Therapy		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	34	34		
Units: score on a scale				
arithmetic mean (standard deviation)				
PCS	-1.45 (± 4.38)	-1.81 (± 6.54)		
MCS	0.23 (± 8.45)	-0.07 (± 8.20)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change in PRO Measure: EuroQol Group 5-dimension 3-level Version (EQ-5D-3L) Index From Baseline to Week 24 in Subjects Treated With Plegridy Versus Current SC IFN-β

End point title	Change in PRO Measure: EuroQol Group 5-dimension 3-level Version (EQ-5D-3L) Index From Baseline to Week 24 in Subjects Treated With Plegridy Versus Current SC IFN-β

End point description:

The EQ-5D-3L is a standardised instrument for use as a measure of health outcome. It is a health questionnaire that consists of the EQ-5D descriptive system and the EQ VAS. The descriptive system consists of 5 dimensions (mobility, self-care, usual activities, pain/discomfort, anxiety/depression), each dimension has 3 severity levels: No problems, some or moderate problems, extreme problems. The EQ-VAS records the respondent's self-rated health on a VAS ranging from 0 (worst imaginable health state) to 100 (best imaginable health state). The index score is transformed into a utility score between 0 (worst health state) and 1 (best health state). Higher scores indicate good health. Negative change from baseline indicates deteriorated health. Efficacy Population included all enrolled subjects who had at least one post-baseline efficacy assessment. Number of subjects analysed=number of subjects with available data for analysis.

End point type	Secondary

End point timeframe:

Baseline up to end of comparator period (Week 24)

End point values	Plegridy	Current IFN-β Therapy		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	34	35		
Units: score on a scale				
arithmetic mean (standard deviation)	-2.82 (± 21.71)	0.49 (± 20.10)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change in PRO Measure: Work Productivity and Activity Impairment Questionnaire: Multiple Sclerosis (WPAI: MS) From Baseline to Week 24 in Subjects Treated With Plegridy Versus Current SC IFN-β

End point title	Change in PRO Measure: Work Productivity and Activity Impairment Questionnaire: Multiple Sclerosis (WPAI: MS) From Baseline to Week 24 in Subjects Treated With Plegridy Versus Current SC IFN-β

End point description:

The WPAI questionnaire is a validated instrument to measure impairments in work and activities. The WPAI yields four types of scores: Absenteeism (percent work time missed), presenteeism (percent impairment at work/ reduced on-the-job effectiveness), work productivity loss (percent overall work impairment/absenteeism plus presenteeism), and activity impairment (percent) over the previous 7 days. WPAI outcomes are expressed as impairment percentages, with higher numbers indicating greater impairment and less productivity. Efficacy population included all enrolled subjects who had at least one post-baseline efficacy assessment. Number of subjects analysed=number of subjects with available data for analysis. Number analysed (n) signifies number of subjects analysed for the specified measurement.

End point type	Secondary

End point timeframe:

Baseline up to end of comparator period (Week 24)

End point values	Plegridy	Current IFN-β Therapy		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	34	33		
Units: percentage of impairment				
arithmetic mean (standard deviation)				
Percent Work Time Missed (n=18,16)	3.34 (± 9.06)	-0.17 (± 10.85)		
Percent Impairment While Working (n=20,16)	-2.00 (± 17.65)	-4.38 (± 15.04)		
Percent Overall Work Impairment (n=18,16)	0.76 (± 20.26)	-3.49 (± 15.73)		
Percent Activity Impairment	-0.29 (± 21.39)	-0.91 (± 24.29)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change in PRO Measure: Fatigue Severity Scale (FSS) Score From Baseline to Week 24 in Subjects Treated With Plegridy Versus Current SC IFN-β

End point title	Change in PRO Measure: Fatigue Severity Scale (FSS) Score From Baseline to Week 24 in Subjects Treated With Plegridy Versus Current SC IFN-β

End point description:

The FSS is a self-reported 9-item questionnaire with questions on the state of fatigue experienced during the previous week. The items are scored on a 7-point scale ranging from 1 (less fatigue) to 7 (greater fatigue severity). The total score was obtained summing the number given at each item and it ranges from 9 (less fatigue) to 63 (greater fatigue severity). The mean of all the scores is calculated and reported in this endpoint ranging from 1 (less fatigue) to 7 (greater fatigue severity). Positive change from baseline indicates greater fatigue. Efficacy population included all enrolled subjects who had at least one post-baseline efficacy assessment. Number of subjects analysed=number of subjects with available data for analysis.

End point type	Secondary

End point timeframe:

Baseline up to end of comparator period (Week 24)

End point values	Plegridy	Current IFN-β Therapy		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	33	33		
Units: score on a scale				
arithmetic mean (standard deviation)	1.03 (± 9.44)	0.97 (± 10.17)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change in PRO Measure: Hospital Anxiety and Depression Scale (HADS) Score From Baseline to Week 24 in Subjects Treated With Plegridy Versus Current SC IFN-β

End point title	Change in PRO Measure: Hospital Anxiety and Depression Scale (HADS) Score From Baseline to Week 24 in Subjects Treated With Plegridy Versus Current SC IFN-β

End point description:

The HADS is a self-rating scale that measures anxiety and depression in both hospital and community settings. Responses are based on the relative frequency of symptoms over the past week, recorded on a four-point Likert scale ranging from 0 (not at all) to 3 (very often indeed). Responses are summed to provide separate scores for anxiety and depression symptomology; Each of anxiety or depression scale has a score range of 0-21. Higher scores indicate severe symptoms (higher levels of anxiety and

depression). Negative change from baseline indicates improved symptoms (less anxiety and depression). Efficacy population included all enrolled subjects who had at least one post-baseline efficacy assessment. Number of subjects analysed=number of subjects with available data for analysis. Number analysed (n) signifies number of subjects analysed for the specified measurement.

End point type	Secondary

End point timeframe:

Baseline up to end of comparator period (Week 24)

End point values	Plegridy	Current IFN-β Therapy		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	34	35		
Units: score on a scale				
arithmetic mean (standard deviation)				
Depression Score	0.29 (± 2.41)	-0.23 (± 1.93)		
Anxiety Score (n=32,35)	-0.09 (± 2.40)	0.37 (± 3.31)		

Statistical analyses

No statistical analyses for this end point

Secondary: PRO Measure: SF-12 Score at Week 24 in Subjects Treated With Plegridy Versus Current SC IFN-β

End point title	PRO Measure: SF-12 Score at Week 24 in Subjects Treated With Plegridy Versus Current SC IFN-β

End point description:

The SF-12 is a short survey with 12 questions to measure functional health and well-being from the study subject`s perspective across eight domains: Physical functioning, role, bodily pain, general health perceptions, vitality, social functioning, emotional role, and mental health. MCS & PCS are computed using the scores of twelve questions and range from 0 to 100, where a higher score indicates better health. Efficacy population included all enrolled subjects who had at least one post-baseline efficacy assessment. Number of subjects analysed=number of subjects with available data for analysis.

End point type	Secondary

End point timeframe:

End of comparator period (Week 24)

End point values	Plegridy	Current IFN-β Therapy		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	35	35		
Units: score on a scale				
arithmetic mean (standard deviation)				
PCS	46.77 (± 8.93)	45.31 (± 8.10)		
MCS	51.55 (± 7.85)	48.05 (± 9.81)		

Statistical analyses

No statistical analyses for this end point

Secondary: PRO Measure: WPAI: MS Score at Week 24 in Subjects Treated With Plegridy Versus Current SC IFN-β

End point title	PRO Measure: WPAI: MS Score at Week 24 in Subjects Treated With Plegridy Versus Current SC IFN-β

End point description:

The WPAI questionnaire is a validated instrument to measure impairments in work and activities. The WPAI yields four types of scores: Absenteeism (percent work time missed), presenteeism (percent impairment at work/ reduced on-the-job effectiveness), work productivity loss (percent overall work impairment/absenteeism plus presenteeism), and activity impairment (percent) over the previous 7 days. WPAI outcomes are expressed as impairment percentages, with higher numbers indicating greater impairment and less productivity. Efficacy population included all enrolled subjects who had at least one post-baseline efficacy assessment. Number of subjects analysed=number of subjects with available data for analysis. Number analysed (n) signifies number of subjects analysed for the specified measurement.

End point type	Secondary

End point timeframe:

End of comparator period (Week 24)

End point values	Plegridy	Current IFN-β Therapy		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	35	35		
Units: percentage of impairment				
arithmetic mean (standard deviation)				
Percent Work Time Missed (n=21,16)	3.96 (± 12.04)	2.08 (± 8.33)		
Percent Impairment While Working (n=22,16)	12.27 (± 19.74)	11.88 (± 18.70)		
Percent Overall Work Impairment (n=21,16)	15.88 (± 22.49)	13.96 (± 19.14)		
Percent Activity Impairment	21.71 (± 26.95)	27.71 (± 28.19)		

Statistical analyses

No statistical analyses for this end point

Secondary: PRO Measure: EQ-5D-3L Index at Week 24 in Subjects Treated With Plegridy Versus Current SC IFN-β

End point title	PRO Measure: EQ-5D-3L Index at Week 24 in Subjects Treated With Plegridy Versus Current SC IFN-β

End point description:

The EQ-5D-3L is a standardised instrument for use as a measure of health outcome. It is a health questionnaire that consists of the EQ-5D descriptive system and the EQ VAS. The descriptive system consists of 5 dimensions (mobility, self-care, usual activities, pain/discomfort, anxiety/depression), each dimension has 3 severity levels: No problems, some or moderate problems, extreme problems. The EQ-VAS records the respondent's self-rated health on a VAS ranging from 0 (worst imaginable health state) to 100 (best imaginable health state). The index score is transformed into a utility score between 0 (worst health state) and 1 (best health state). Higher scores indicate good health. Efficacy population included all enrolled subjects who had at least one post-baseline efficacy assessment. Number of subjects analysed=number of subjects with available data for analysis.

End point type	Secondary

End point timeframe:

End of comparator period (Week 24)

End point values	Plegridy	Current IFN-β Therapy		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	35	35		
Units: score on a scale				
arithmetic mean (standard deviation)	76.06 (± 21.42)	77.00 (± 18.07)		

Statistical analyses

No statistical analyses for this end point

Secondary: PRO Measure: FSS score at Week 24 in Subjects Treated With Plegridy Versus Current SC IFN-β

End point title	PRO Measure: FSS score at Week 24 in Subjects Treated With Plegridy Versus Current SC IFN-β

End point description:

The FSS is a self-reported 9-item questionnaire with questions on the state of fatigue experienced during the previous week. The items are scored on a 7-point scale ranging from 1 (less fatigue) to 7 (greater fatigue severity). The total score was obtained summing the number given at each item and it ranges from 9 (less fatigue) to 63 (greater fatigue severity). The mean of all the scores is calculated and reported in this endpoint ranging from 1 (less fatigue) to 7 (greater fatigue severity). Efficacy population included all enrolled subjects who had at least one post-baseline efficacy assessment. Number of subjects analysed=number of subjects with available data for analysis.

End point type	Secondary

End point timeframe:

End of comparator period (Week 24)

End point values	Plegridy	Current IFN-β Therapy		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	34	34		
Units: score on a scale				
arithmetic mean (standard deviation)	37.38 (± 13.50)	40.85 (± 12.91)		

Statistical analyses

No statistical analyses for this end point

Secondary: PRO Measure: HADS score at Week 24 in Subjects Treated With Plegridy Versus Current SC IFN-β

End point title	PRO Measure: HADS score at Week 24 in Subjects Treated With Plegridy Versus Current SC IFN-β

End point description:

The HADS is a self-rating scale that measures anxiety and depression in both hospital and community settings. Responses are based on the relative frequency of symptoms over the past week, recorded on a four-point Likert scale ranging from 0 (not at all) to 3 (very often indeed). Responses are summed to provide separate scores for anxiety and depression symptomology; Each of anxiety or depression scale has a score range of 0-21. Higher scores indicate severe symptoms (higher levels of anxiety and depression). Efficacy population included all enrolled subjects who had at least one post-baseline efficacy assessment. Number of subjects analysed=number of subjects with available data for analysis

End point type	Secondary

End point timeframe:

End of comparator period (Week 24)

End point values	Plegridy	Current IFN-β Therapy		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	35	35		
Units: score on a scale				
arithmetic mean (standard deviation)				
Depression Score	4.51 (± 3.21)	5.23 (± 3.43)		
Anxiety Score	5.37 (± 3.80)	6.49 (± 4.15)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change in PRO Measure: SF-12 Score From Week 24 Through 48 in Subjects Continuously Treated With Plegridy Versus Subjects Who Switched From Current SC IFN- β Therapy to Plegridy at the End of the Comparator Period

End point title	Change in PRO Measure: SF-12 Score From Week 24 Through 48 in Subjects Continuously Treated With Plegridy Versus Subjects Who Switched From Current SC IFN- β Therapy to Plegridy at the End of the Comparator Period

End point description:

The SF-12 is a short survey with 12 questions to measure functional health and well-being from the study subject`s perspective across eight domains: Physical functioning, role, bodily pain, general health perceptions, vitality, social functioning, emotional role, and mental health. MCS & PCS are computed

using the scores of twelve questions and range from 0 to 100, where a higher score indicates better health. Positive change from baseline indicates improved health. Efficacy Population included all enrolled subjects who had at least one post-baseline efficacy assessment. Number of subjects analysed=number of subjects with available data for analysis.

End point type	Secondary

End point timeframe:

End of comparator period (Week 24) up to Week 48

End point values	Plegridy	Current IFN-β Therapy		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	32	34		
Units: score on a scale				
arithmetic mean (standard deviation)				
PCS	1.02 (± 4.81)	1.39 (± 5.03)		
MCS	-1.37 (± 7.66)	2.17 (± 9.96)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change in PRO Measure: EQ-5D-3L Index From Week 24 Through 48 in Subjects Continuously Treated With Plegridy Versus Subjects Who Switched From Current SC IFN- β Therapy to Plegridy at the End of the Comparator Period

End point title	Change in PRO Measure: EQ-5D-3L Index From Week 24 Through 48 in Subjects Continuously Treated With Plegridy Versus Subjects Who Switched From Current SC IFN- β Therapy to Plegridy at the End of the Comparator Period

End point description:

The EQ-5D-3L is a standardised instrument for use as a measure of health outcome. It is a health questionnaire that consists of the EQ-5D descriptive system and the EQ VAS. The descriptive system consists of 5 dimensions (mobility, self-care, usual activities, pain/discomfort, anxiety/depression), each dimension has 3 severity levels: No problems, some or moderate problems, extreme problems. The EQ-VAS records the respondent's self-rated health on a VAS ranging from 0 (worst imaginable health state) to 100 (best imaginable health state). The index score is transformed into a utility score between 0 (worst health state) and 1 (best health state). Higher scores indicate good health. Negative change from baseline indicates deteriorated health. Efficacy population included all enrolled subjects who had at least one post-baseline efficacy assessment. Number of subjects analysed=number of subjects with available data for analysis.

End point type	Secondary

End point timeframe:

End of comparator period (Week 24) up to Week 48

End point values	Plegridy	Current IFN-β Therapy		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	30	33		
Units: score on a scale				
arithmetic mean (standard deviation)	1.63 (± 26.96)	-1.09 (± 21.69)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change in PRO Measure: WPAI: MS Score From Week 24 Through 48 in Subjects Continuously Treated With Plegridy Versus Subjects Who Switched From Current SC IFN-β Therapy to Plegridy at the End of the Comparator Period

End point title	Change in PRO Measure: WPAI: MS Score From Week 24 Through 48 in Subjects Continuously Treated With Plegridy Versus Subjects Who Switched From Current SC IFN-β Therapy to Plegridy at the End of the Comparator Period

End point description:

The WPAI questionnaire is a validated instrument to measure impairments in work and activities. The WPAI yields four types of scores: Absenteeism (percent work time missed), presenteeism (percent impairment at work/ reduced on-the-job effectiveness), work productivity loss (percent overall work impairment/absenteeism plus presenteeism), and activity impairment (percent) over the previous 7 days. WPAI outcomes are expressed as impairment percentages, with higher numbers indicating greater impairment and less productivity. Efficacy population included all enrolled subjects who had at least one post-baseline efficacy assessment. Number of subjects analysed=number of subjects with available data for analysis. Number analysed (n) signifies number of subjects analysed for the specified measurement.

End point type	Secondary

End point timeframe:

End of comparator period (Week 24) up to Week 48

End point values	Plegridy	Current IFN-β Therapy		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	31	33		
Units: percentage of impairment				
arithmetic mean (standard deviation)				
Percent Work Time Missed (n=17,16)	1.00 (± 22.35)	-1.61 (± 6.46)		
Percent Impairment While Working (n=19,13)	8.42 (± 18.34)	0.00 (± 18.71)		
Percent Overall Work Impairment (n=16,13)	5.28 (± 21.83)	-2.10 (± 17.79)		
Percent Activity Impairment	1.29 (± 20.29)	-0.30 (± 53.12)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change in PRO Measure: FSS Score From Week 24 Through 48 in Subjects Continuously Treated With Plegridy Versus Subjects Who Switched From Current SC IFN-β Therapy to Plegridy at the End of the Comparator Period

End point title	Change in PRO Measure: FSS Score From Week 24 Through 48 in Subjects Continuously Treated With Plegridy Versus Subjects Who Switched From Current SC IFN-β Therapy to Plegridy at the End of the Comparator Period

End point description:

The FSS is a self-reported 9-item questionnaire with questions on the state of fatigue experienced during the previous week. The items are scored on a 7-point scale ranging from 1 (less fatigue) to 7 (greater fatigue severity). The total score was obtained summing the number given at each item and it ranges from 9 (less fatigue) to 63 (greater fatigue severity). The mean of all the scores is calculated and reported in this endpoint ranging from 1 (less fatigue) to 7 (greater fatigue severity). Positive change from baseline indicates greater fatigue. Efficacy population included all enrolled subjects who had at least one post-baseline efficacy assessment. Number of subjects analysed=number of subjects with available data for analysis.

End point type	Secondary

End point timeframe:

End of comparator period (Week 24) up to Week 48

End point values	Plegridy	Current IFN-β Therapy		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	31	33		
Units: score on a scale				
arithmetic mean (standard deviation)	-1.61 (± 8.22)	-1.30 (± 11.31)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change in PRO Measure: HADS Score From Week 24 Through 48 in Subjects Continuously Treated With Plegridy Versus Subjects Who Switched From Current SC IFN-β Therapy to Plegridy at the End of the Comparator Period

End point title	Change in PRO Measure: HADS Score From Week 24 Through 48 in Subjects Continuously Treated With Plegridy Versus Subjects Who Switched From Current SC IFN-β Therapy to Plegridy at the End of the Comparator Period

End point description:

The HADS is a self-rating scale that measures anxiety and depression in both hospital and community settings. Responses are based on the relative frequency of symptoms over the past week, recorded on a four-point Likert scale ranging from 0 (not at all) to 3 (very often indeed). Responses are summed to provide separate scores for anxiety and depression symptomology; Each of anxiety or depression scale has a score range of 0-21. Higher scores indicate severe symptoms (higher levels of anxiety and depression). Negative change from baseline indicates improved symptoms (less anxiety and depression). Efficacy population included all enrolled subjects who had at least one post-baseline efficacy assessment. Number of subjects analysed=number of subjects with available data for analysis. Number analysed (n) signifies number of subjects analysed for the specified measurement.

End point type	Secondary

End point timeframe:

End of comparator period (Week 24) up to Week 48

End point values	Plegridy	Current IFN-β Therapy		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	32	34		
Units: score on a scale				
arithmetic mean (standard deviation)				
Depression Score (n=32, 33)	0.19 (± 2.90)	-0.18 (± 2.67)		
Anxiety Score (n=31, 34)	-0.26 (± 2.61)	-0.09 (± 3.59)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change in PRO Measure: SF-12 Score From Week 24 Through 72 in Subjects Continuously Treated With Plegridy Versus Subjects Who Switched From Current SC IFN-β Therapy to Plegridy at the End of the Comparator Period

End point title	Change in PRO Measure: SF-12 Score From Week 24 Through 72 in Subjects Continuously Treated With Plegridy Versus Subjects Who Switched From Current SC IFN-β Therapy to Plegridy at the End of the Comparator Period

End point description:

The SF-12 is a short survey with 12 questions to measure functional health and well-being from the study subject`s perspective across eight domains: Physical functioning, role, bodily pain, general health perceptions, vitality, social functioning, emotional role, and mental health. MCS & PCS are computed using the scores of twelve questions and range from 0 to 100, where a higher score indicates better health. Positive change from baseline indicates improved health. Efficacy Population included all enrolled subjects who had at least one post-baseline efficacy assessment. Number of subjects analysed=number of subjects with available data for analysis.

End point type	Secondary

End point timeframe:

End of comparator period (Week 24) up to end of study (Week 72)

End point values	Plegridy	Current IFN-β Therapy		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	32	31		
Units: score on a scale				
arithmetic mean (standard deviation)				
PCS	1.78 (± 6.90)	1.84 (± 5.02)		
MCS	-0.83 (± 8.06)	1.36 (± 7.63)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change in PRO Measure: EQ-5D-3L Index From Week 24 Through 72 in Subjects Continuously Treated With Plegridy Versus Subjects Who Switched From Current SC IFN-β Therapy to Plegridy at the End of the Comparator Period

End point title	Change in PRO Measure: EQ-5D-3L Index From Week 24 Through 72 in Subjects Continuously Treated With Plegridy Versus Subjects Who Switched From Current SC IFN-β Therapy to Plegridy at the End of the Comparator Period

End point description:

The EQ-5D-3L is a standardised instrument for use as a measure of health outcome. It is a health questionnaire that consists of the EQ-5D descriptive system and the EQ VAS. The descriptive system consists of 5 dimensions (mobility, self-care, usual activities, pain/discomfort, anxiety/depression), each dimension has 3 severity levels: No problems, some or moderate problems, extreme problems. The EQ-VAS records the respondent's self-rated health on a VAS ranging from 0 (worst imaginable health state) to 100 (best imaginable health state). The index score is transformed into a utility score between 0 (worst health state) and 1 (best health state). Higher scores indicate good health. Negative change from baseline indicates deteriorated health. Efficacy population included all enrolled subjects who had at least one post-baseline efficacy assessment. Number of subjects analysed=number of subjects with available data for analysis.

End point type	Secondary

End point timeframe:

End of comparator period (Week 24) up to end of study (Week 72)

End point values	Plegridy	Current IFN-β Therapy		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	32	31		
Units: score on a scale				
arithmetic mean (standard deviation)	-0.81 (± 33.01)	-4.10 (± 17.31)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change in PRO Measure: WPAI: MS Score From Week 24 Through 72 in Subjects Continuously Treated With Plegridy Versus Subjects Who Switched From Current SC IFN-β Therapy to Plegridy at the End of the Comparator Period

End point title	Change in PRO Measure: WPAI: MS Score From Week 24 Through 72 in Subjects Continuously Treated With Plegridy Versus Subjects Who Switched From Current SC IFN-β Therapy to Plegridy at the End of the Comparator Period

End point description:

The WPAI questionnaire is a validated instrument to measure impairments in work and activities. The WPAI yields four types of scores: Absenteeism (percent work time missed), presenteeism (percent impairment at work/ reduced on-the-job effectiveness), work productivity loss (percent overall work impairment/absenteeism plus presenteeism), and activity impairment (percent) over the previous 7 days. WPAI outcomes are expressed as impairment percentages, with higher numbers indicating greater impairment and less productivity. Efficacy population included all enrolled subjects who had at least one post-baseline efficacy assessment. Number of subjects analysed=number of with available data for analysis. Number analysed (n) signifies number of subjects analysed for the specified measurement.

End point type	Secondary

End point timeframe:

End of comparator period (Week 24) up to end of study (Week 72)

End point values	Plegridy	Current IFN-β Therapy		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	28	30		
Units: percentage of impairment				
arithmetic mean (standard deviation)				
Percent Work Time Missed (n=16,15)	-5.19 (± 13.66)	-2.22 (± 8.61)		
Percent Impairment While Working (n=18,15)	1.67 (± 16.18)	-7.33 (± 15.80)		
Percent Overall Work Impairment (n=16,15)	-2.09 (± 18.82)	-9.56 (± 16.99)		
Percent Activity Impairment	3.93 (± 18.73)	-0.67 (± 14.84)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change in PRO Measure: FSS Score From Week 24 Through 72 in Subjects Continuously Treated With Plegridy Versus Subjects Who Switched From Current SC IFN-β Therapy to Plegridy at the End of the Comparator Period

End point title	Change in PRO Measure: FSS Score From Week 24 Through 72 in Subjects Continuously Treated With Plegridy Versus Subjects Who Switched From Current SC IFN-β Therapy to Plegridy at the End of the Comparator Period

End point description:

The FSS is a self-reported 9-item questionnaire with questions on the state of fatigue experienced during the previous week. The items are scored on a 7-point scale ranging from 1 (less fatigue) to 7 (greater fatigue severity). The total score was obtained summing the number given at each item and it ranges from 9 (less fatigue) to 63 (greater fatigue severity). The mean of all the scores is calculated and reported in this endpoint ranging from 1 (less fatigue) to 7 (greater fatigue severity). Positive change from baseline indicates greater fatigue. Efficacy population included all enrolled subjects who had at least one post-baseline efficacy assessment. Number of subjects analysed=number of subjects with available data for analysis.

End point type	Secondary

End point timeframe:

End of comparator period (Week 24) up to end of study (Week 72)

End point values	Plegridy	Current IFN-β Therapy		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	30	30		
Units: score on a scale				
arithmetic mean (standard deviation)	-1.43 (± 9.31)	-3.40 (± 12.81)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change in PRO Measure: HADS Score From Week 24 Through 72 in Subjects Continuously Treated With Plegridy Versus Subjects Who Switched From Current SC IFN-β Therapy to Plegridy at the End of the Comparator Period

End point title	Change in PRO Measure: HADS Score From Week 24 Through 72 in Subjects Continuously Treated With Plegridy Versus Subjects Who Switched From Current SC IFN-β Therapy to Plegridy at the End of the Comparator Period

End point description:

The HADS is a self-rating scale that measures anxiety and depression in both hospital and community settings. Responses are based on the relative frequency of symptoms over the past week, recorded on a four-point Likert scale ranging from 0 (not at all) to 3 (very often indeed). Responses are summed to provide separate scores for anxiety and depression symptomology; Each of anxiety or depression scale has a score range of 0-21. Higher scores indicate severe symptoms (higher levels of anxiety and depression). Negative change from baseline indicates improved symptoms (less anxiety and depression). Efficacy population included all enrolled subjects who had at least one post-baseline efficacy assessment. Number of subjects analysed=number of subjects with available data for analysis. Number analysed (n) signifies number of subjects analysed for the specified measurement.

End point type	Secondary

End point timeframe:

End of comparator period (Week 24) up to end of study (Week 72)

End point values	Plegridy	Current IFN-β Therapy		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	32	31		
Units: score on a scale				
arithmetic mean (standard deviation)				
Depression Score (n=32, 30)	-0.06 (± 2.45)	0.57 (± 2.28)		
Anxiety Score	-0.38 (± 3.10)	-0.94 (± 3.92)		

Statistical analyses

No statistical analyses for this end point

Secondary: Subjects Adherence to Study Treatment Measured by Treatment Adherence Questionnaire as Adherence Percentage at Week 24 in Subjects Treated With Plegridy Versus Current SC IFN-β

End point title	Subjects Adherence to Study Treatment Measured by Treatment Adherence Questionnaire as Adherence Percentage at Week 24 in Subjects Treated With Plegridy Versus Current SC IFN-β

End point description:

Adherence to treatment was evaluated using a questionnaire assessing adherence and the reasons for not taking drug at the recommended frequency of administration. Adherence based on the treatment adherence questionnaire is calculated with formula: Adherence (%)=(Injections completed/Injections expected)*100. Safety population included all the subjects who received at least one dose of the study treatment. Number of subjects analysed=number of subjects with available data for analysis.

End point type	Secondary

End point timeframe:

End of comparator period (Week 24)

End point values	Plegridy	Current IFN-β Therapy		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	35	33		
Units: adherence percentage				
arithmetic mean (standard deviation)	97.38 (± 15.49)	89.33 (± 29.24)		

Statistical analyses

No statistical analyses for this end point

Secondary: Subjects Adherence to Study Treatment Measured by Returned Injection Pens as Adherence Percentage Through Week 24 in Subjects Treated With Plegridy Versus Current SC IFN-β

End point title	Subjects Adherence to Study Treatment Measured by Returned Injection Pens as Adherence Percentage Through Week 24 in Subjects Treated With Plegridy Versus Current SC IFN-β

End point description:

Adherence to treatment was evaluated by the investigator by counting the number of empty pens. The subjects were asked to return the injection pens given previously and the investigator would infer the number of injections taken after counting the number of empty pens using the formula: Adherence (%)=(Injections completed/Injections expected)*100. Safety population included all the subjects who received at least one dose of the study treatment. Number of subjects analysed=number of subjects with available data for analysis.

End point type	Secondary

End point timeframe:

Up to end of comparator period (Week 24)

End point values	Plegridy	Current IFN-β Therapy		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	23	23		
Units: adherence percentage				
arithmetic mean (standard deviation)	86.96 (± 25.48)	86.69 (± 23.95)		

Statistical analyses

No statistical analyses for this end point

Secondary: Subjects Adherence to Study Treatment Measured by Treatment Adherence Questionnaire as Adherence Percentage From Week 24 Through 72 in all Subjects

End point title	Subjects Adherence to Study Treatment Measured by Treatment Adherence Questionnaire as Adherence Percentage From Week 24 Through 72 in all Subjects

End point description:

Adherence to treatment was evaluated by the investigator by counting the number of empty pens. The subjects were asked to return the injection pens given previously and the investigator would infer the number of injections taken after counting the number of empty pens using the formula: Adherence (%)=(Injections completed/Injections expected)*100. Safety population included all the subjects who received at least one dose of the study treatment. Number of subjects analysed=number of subjects with available data for analysis.

End point type	Secondary

End point timeframe:

End of comparator period (Week 24) up to end of study (Week 72)

End point values	All Subjects			
Subject group type	Subject analysis set			
Number of subjects analysed	65			
Units: adherence percentage				
arithmetic mean (standard deviation)	94.87 (± 14.91)			

Statistical analyses

No statistical analyses for this end point

Secondary: Subjects Adherence to Study Treatment Measured by Returned Injection Pens as Adherence Percentage From Week 24 Through 72 in all Subjects

End point title	Subjects Adherence to Study Treatment Measured by Returned Injection Pens as Adherence Percentage From Week 24 Through 72 in all Subjects

End point description:

Adherence to treatment was evaluated by the investigator by counting the number of empty pens. The subjects were asked to return the injection pens given previously and the investigator would infer the

number of injections taken after counting the number of empty pens using the formula: Adherence (%)=(Injections completed/Injections expected)*100. Safety population included all the subjects who received at least one dose of the study treatment. Number of subjects analysed=number of subjects with available data for analysis.

End point type	Secondary

End point timeframe:

End of comparator period (Week 24) up to end of study (Week 72)

End point values	All Subjects			
Subject group type	Subject analysis set			
Number of subjects analysed	43			
Units: adherence percentage				
arithmetic mean (standard deviation)	87.79 (± 22.24)			

Statistical analyses

No statistical analyses for this end point

Secondary: Subjects Adherence to Study Treatment Measured by Treatment Adherence Questionnaire as Adherence Percentage From Week 24 Through 48 in Subjects Who Switched From Current SC IFN- β Therapy to Plegridy at the End of the Comparator Period

End point title	Subjects Adherence to Study Treatment Measured by Treatment Adherence Questionnaire as Adherence Percentage From Week 24 Through 48 in Subjects Who Switched From Current SC IFN- β Therapy to Plegridy at the End of the Comparator Period[2]

End point description:

Adherence to treatment was evaluated by the investigator by counting the number of empty pens. The subjects were asked to return the injection pens given previously and the investigator would infer the number of injections taken after counting the number of empty pens using the formula: Adherence (%)=(Injections completed/Injections expected)*100. Safety population included all the subjects who received at least one dose of the study treatment. Number of subjects analysed=number of subjects with available data for analysis.

End point type	Secondary

End point timeframe:

End of comparator period (Week 24) up to Week 48

Notes:

[2] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: This endpoint was analyzed only for the subjects who switched from current SC IFN-β therapy to Plegridy at the end of the comparator period, hence data was reported only for the 'current IFN-β therapy' arm group.

End point values	Current IFN-β Therapy			
Subject group type	Reporting group			
Number of subjects analysed	34			
Units: adherence percentage				
arithmetic mean (standard deviation)	100 (± 0.00)			

Statistical analyses

No statistical analyses for this end point

Secondary: Subjects Adherence to Study Treatment Measured by Returned Injection Pens as Adherence Percentage From Week 24 Through 48 in Subjects Who Switched From Current SC IFN-β Therapy to Plegridy at the End of the Comparator Period

End point title	Subjects Adherence to Study Treatment Measured by Returned Injection Pens as Adherence Percentage From Week 24 Through 48 in Subjects Who Switched From Current SC IFN-β Therapy to Plegridy at the End of the Comparator Period[3]

End point description:

Adherence to treatment was evaluated by the investigator by counting the number of empty pens. The subjects were asked to return the injection pens given previously and the investigator would infer the number of injections taken after counting the number of empty pens using the formula: Adherence (%)=(Injections completed/Injections expected)*100. Safety population included all the subjects who received at least one dose of the study treatment. Number of subjects analysed=number of subjects with available data for analysis.

End point type	Secondary

End point timeframe:

End of comparator period (Week 24) up to Week 48

Notes:

[3] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period. Justification: This endpoint was analyzed only for the subjects who switched from current SC IFN-β therapy to Plegridy at the end of the comparator period, hence data was reported only for the 'current IFN-β therapy' arm group.

End point values	Current IFN-β Therapy			
Subject group type	Reporting group			
Number of subjects analysed	22			
Units: adherence percentage				
arithmetic mean (standard deviation)	87.12 (± 20.04)			

Statistical analyses

No statistical analyses for this end point

Secondary: Absolute Change in Expanded Disability Status Scale (EDSS) Score From Week 24 to 48

End point title	Absolute Change in Expanded Disability Status Scale (EDSS) Score From Week 24 to 48

End point description:

The EDSS is a method of quantifying disability in MS. The EDSS quantifies disability in 8 functional systems (pyramidal, cerebellar, brainstem, sensory, bowel and bladder, visual, cerebral [or mental]), and other). It is an ordinal clinical rating scale based on a standard neurological exam, with scores

ranging from 0 (normal neurological exam) to 10 (death due to MS) in half-point increments. Efficacy population included all enrolled subjects who had at least one post-baseline efficacy assessment. Number of subjects analysed=number of subjects with available data for analysis.

End point type	Secondary

End point timeframe:

End of comparator period (Week 24) up to Week 48

End point values	Plegridy	Current IFN-β Therapy		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	32	35		
Units: score on a scale				
arithmetic mean (standard deviation)	0.11 (± 0.77)	0.06 (± 0.63)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change of Annualised Relapse Rate (ARR) Pre-study to On-study ARR

End point title	Change of Annualised Relapse Rate (ARR) Pre-study to On-study ARR

End point description:

A clinical relapse is defined as new or recurrent neurological symptoms not associated with fever or infection, lasting for at least 24 hours, and accompanied by new objective neurologic findings on examination by a neurologist. New or recurrent neurologic symptoms that occur fewer than 30 days following the onset of a relapse should be considered part of the same relapse. The ARR is calculated by dividing the number of relapses the subject experiences by the total of subject-years. Safety population included all the subjects who received at least one dose of the study treatment.

End point type	Secondary

End point timeframe:

Up to end of study (Week 72)

End point values	Plegridy	Current IFN-β Therapy		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	38	39		
Units: relapses per subject-year				
arithmetic mean (standard deviation)				
Change of ARR From Prior 12-months to On-study	-0.061 (± 0.2299)	-0.042 (± 0.3927)		
Change of ARR From Prior 24-months to On-study	-0.048 (± 0.1602)	-0.042 (± 0.2744)		

Statistical analyses

No statistical analyses for this end point

Secondary: Annualised Relapse Rate (ARR)

End point title	Annualised Relapse Rate (ARR)

End point description:

A clinical relapse is defined as new or recurrent neurological symptoms not associated with fever or infection, lasting for at least 24 hours, and accompanied by new objective neurologic findings on examination by a neurologist. New or recurrent neurologic symptoms that occur fewer than 30 days following the onset of a relapse should be considered part of the same relapse. The ARR is calculated by dividing the number of relapses the subject experiences by the total of subject-years. Efficacy population included all enrolled subjects who had at least one post-baseline efficacy assessment.

End point type	Secondary

End point timeframe:

Up to end of study (Week 72)

End point values	Plegridy	Current IFN-β Therapy		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	37	39		
Units: relapses per subject-year				
number (not applicable)	0.021	0.040		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects Who Experienced at Least one Adverse Event (AE), Serious AE (SAE), and Study Treatment Discontinuations due to an AE Through Week 24 in Subjects Treated With Plegridy Versus Current SC IFN-β

End point title	Percentage of Subjects Who Experienced at Least one Adverse Event (AE), Serious AE (SAE), and Study Treatment Discontinuations due to an AE Through Week 24 in Subjects Treated With Plegridy Versus Current SC IFN-β

End point description:

An AE is any untoward medical occurrence in a subject or clinical investigation subject administered a pharmaceutical product and that does not necessarily have a causal relationship with this treatment. An AE can therefore be any unfavorable and unintended sign (including an abnormal laboratory finding), symptom, or disease temporally associated with the use of a medicinal (investigational) product, whether or not related to the medicinal (investigational) product. An SAE is any untoward medical occurrence that at any dose, results in death; in the view of the investigator places the subject at immediate risk of death; requires inpatient hospitalization or prolongation of existing hospitalization; results in persistent or significant disability/incapacity; results in a congenital anomaly/birth defect; is a medically important event. Safety population included all the subjects who received at least one dose of the study treatment.

End point type	Secondary

End point timeframe:

Up to end of comparator period (Week 24)

End point values	Plegridy	Current IFN-β Therapy		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	38	39		
Units: percentage of subjects				
number (not applicable)				
AEs	97.4	94.9		
SAEs	2.6	2.6		
Treatment Discontinuation due to AE	5.3	2.6		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Relapsed Subjects at the End of Study

End point title	Percentage of Relapsed Subjects at the End of Study

End point description:

A clinical relapse is defined as new or recurrent neurological symptoms not associated with fever or infection, lasting for at least 24 hours, and accompanied by new objective neurologic findings on examination by a neurologist. New or recurrent neurologic symptoms that occur fewer than 30 days following the onset of a relapse should be considered part of the same relapse. Safety population included all the subjects who received at least one dose of the study treatment.

End point type	Secondary

End point timeframe:

End of study (Week 72)

End point values	Plegridy	Current IFN-β Therapy		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	38	39		
Units: percentage of subjects				
number (not applicable)	0	2.6		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects who had at Least one AE, SAE, Treatment Discontinuations due to AE 24 Weeks up to 48, 72 Weeks in Subjects Continuously Treated With Plegridy Versus who Switched From Current SC IFN-β to Plegridy at End of Comparator Period

End point title	Percentage of Subjects who had at Least one AE, SAE, Treatment Discontinuations due to AE 24 Weeks up to 48, 72 Weeks in Subjects Continuously Treated With Plegridy Versus who Switched From Current SC IFN-β to Plegridy at End of Comparator Period

End point description:

An AE is any untoward medical occurrence in a subject or clinical investigation subject administered a pharmaceutical product and that does not necessarily have a causal relationship with this treatment. An AE can therefore be any unfavorable and unintended sign (including an abnormal laboratory finding), symptom, or disease temporally associated with the use of a medicinal (investigational) product, whether or not related to the medicinal (investigational) product. An SAE is any untoward medical occurrence that at any dose, results in death; in the view of the investigator places the subject at immediate risk of death; requires inpatient hospitalisation or prolongation of existing hospitalisation; results in persistent or significant disability/incapacity; results in a congenital anomaly/birth defect; is a medically important event. Safety population included all the subjects who received at least one dose of the study treatment

End point type	Secondary

End point timeframe:

End of comparator period [Week (Wk) 24] up to end of study (Week 72)

End point values	Plegridy	Current IFN-β Therapy		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	38	39		
Units: percentage of subjects				
number (not applicable)				
AEs: Wk 24 up to Wk 48	81.6	84.6		
SAEs: Wk 24 up to Wk 48	0.0	2.6		
Treatment Discontinuation due to AE:Wk 24 up to 48	0.0	2.6		
AEs: Wk 24 up to Wk 72	84.2	89.7		
SAEs: Wk 24 up to Wk 72	0.0	2.6		
Treatment Discontinuation due to AE:Wk 24 up to 72	0.0	2.6		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information	
Timeframe for reporting adverse events:	
Up to 76 weeks	
Adverse event reporting additional description:	
Safety population included all the subjects who received at least one dose of the study treatment.	
Assessment type	Systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	24.0

Reporting groups	
Reporting group title	Plegridy
Reporting group description:	
Subjects were administered Plegridy 125 µg as a SC injection, once every 2 weeks during the 24-week active comparator period. During the 48-week extension period, subjects self-administered Plegridy 125 µg, SC injection, once every 2 weeks.	
Reporting group title	Current IFN-β Therapy
Reporting group description:	
Subjects continued to receive IFN-β-1b 0.25 mg, SC injection, every other day or IFN-β-1a 22µg or 44 µg, SC injection, 3 times a week during the 24-week active comparator period. During the 48-week extension period, subjects self-administered SC injection of Plegridy 63 µg in Week1, 94 µg in Week 3 and 125 µg thereafter once every 2 weeks.	

Serious adverse events	Plegridy	Current IFN-β Therapy	
Total subjects affected by serious adverse events			
subjects affected / exposed	1 / 38 (2.63%)	2 / 39 (5.13%)	
number of deaths (all causes)	0	1	
number of deaths resulting from adverse events	0	0	
Injury, poisoning and procedural complications			
Foot fracture			
subjects affected / exposed	0 / 38 (0.00%)	1 / 39 (2.56%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
General disorders and administration site conditions			
Accidental death			
subjects affected / exposed	0 / 38 (0.00%)	1 / 39 (2.56%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Renal and urinary disorders			

Acute kidney injury			
subjects affected / exposed	1 / 38 (2.63%)	0 / 39 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

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

Non-serious adverse events	Plegridy	Current IFN-β Therapy	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	37 / 38 (97.37%)	39 / 39 (100.00%)	
Vascular disorders			
Hypertension			
subjects affected / exposed	2 / 38 (5.26%)	4 / 39 (10.26%)	
occurrences (all)	2	4	
General disorders and administration site conditions			
Chills			
subjects affected / exposed	17 / 38 (44.74%)	20 / 39 (51.28%)	
occurrences (all)	152	329	
Injection site pain			
subjects affected / exposed	15 / 38 (39.47%)	26 / 39 (66.67%)	
occurrences (all)	158	1713	
Pyrexia			
subjects affected / exposed	19 / 38 (50.00%)	16 / 39 (41.03%)	
occurrences (all)	78	143	
Oedema peripheral			
subjects affected / exposed	0 / 38 (0.00%)	2 / 39 (5.13%)	
occurrences (all)	0	2	
Injection site pruritus			
subjects affected / exposed	2 / 38 (5.26%)	0 / 39 (0.00%)	
occurrences (all)	4	0	
Gait disturbance			
subjects affected / exposed	1 / 38 (2.63%)	2 / 39 (5.13%)	
occurrences (all)	1	2	
Influenza like illness			

subjects affected / exposed	2 / 38 (5.26%)	3 / 39 (7.69%)	
occurrences (all)	4	4	
Asthenia			
subjects affected / exposed	17 / 38 (44.74%)	18 / 39 (46.15%)	
occurrences (all)	135	312	
Pain			
subjects affected / exposed	3 / 38 (7.89%)	9 / 39 (23.08%)	
occurrences (all)	4	290	
Injection site erythema			
subjects affected / exposed	31 / 38 (81.58%)	32 / 39 (82.05%)	
occurrences (all)	367	1143	
Fatigue			
subjects affected / exposed	7 / 38 (18.42%)	2 / 39 (5.13%)	
occurrences (all)	19	2	
Respiratory, thoracic and mediastinal disorders			
Nasal congestion			
subjects affected / exposed	1 / 38 (2.63%)	2 / 39 (5.13%)	
occurrences (all)	1	2	
Cough			
subjects affected / exposed	2 / 38 (5.26%)	0 / 39 (0.00%)	
occurrences (all)	2	0	
Psychiatric disorders			
Major depression			
subjects affected / exposed	0 / 38 (0.00%)	2 / 39 (5.13%)	
occurrences (all)	0	3	
Depression			
subjects affected / exposed	2 / 38 (5.26%)	0 / 39 (0.00%)	
occurrences (all)	2	0	
Anxiety			
subjects affected / exposed	6 / 38 (15.79%)	6 / 39 (15.38%)	
occurrences (all)	6	7	
Depressed mood			
subjects affected / exposed	0 / 38 (0.00%)	2 / 39 (5.13%)	
occurrences (all)	0	2	
Investigations			

Weight increased			
subjects affected / exposed	2 / 38 (5.26%)	0 / 39 (0.00%)	
occurrences (all)	2	0	
Urine leukocyte esterase positive			
subjects affected / exposed	0 / 38 (0.00%)	2 / 39 (5.13%)	
occurrences (all)	0	2	
Injury, poisoning and procedural complications			
Fall			
subjects affected / exposed	2 / 38 (5.26%)	1 / 39 (2.56%)	
occurrences (all)	2	1	
Contusion			
subjects affected / exposed	2 / 38 (5.26%)	1 / 39 (2.56%)	
occurrences (all)	10	1	
Nervous system disorders			
Hypoaesthesia			
subjects affected / exposed	2 / 38 (5.26%)	1 / 39 (2.56%)	
occurrences (all)	3	1	
Dizziness			
subjects affected / exposed	4 / 38 (10.53%)	2 / 39 (5.13%)	
occurrences (all)	5	3	
Muscle spasticity			
subjects affected / exposed	2 / 38 (5.26%)	0 / 39 (0.00%)	
occurrences (all)	23	0	
Balance disorder			
subjects affected / exposed	2 / 38 (5.26%)	1 / 39 (2.56%)	
occurrences (all)	2	2	
Paraesthesia			
subjects affected / exposed	1 / 38 (2.63%)	2 / 39 (5.13%)	
occurrences (all)	1	2	
Headache			
subjects affected / exposed	4 / 38 (10.53%)	10 / 39 (25.64%)	
occurrences (all)	15	44	
Blood and lymphatic system disorders			
Lymphopenia			
subjects affected / exposed	2 / 38 (5.26%)	1 / 39 (2.56%)	
occurrences (all)	2	1	

Lymphadenopathy			
subjects affected / exposed	3 / 38 (7.89%)	0 / 39 (0.00%)	
occurrences (all)	5	0	
Ear and labyrinth disorders			
Vertigo			
subjects affected / exposed	2 / 38 (5.26%)	1 / 39 (2.56%)	
occurrences (all)	5	1	
Eye disorders			
Vision blurred			
subjects affected / exposed	0 / 38 (0.00%)	2 / 39 (5.13%)	
occurrences (all)	0	2	
Gastrointestinal disorders			
Vomiting			
subjects affected / exposed	0 / 38 (0.00%)	2 / 39 (5.13%)	
occurrences (all)	0	3	
Toothache			
subjects affected / exposed	0 / 38 (0.00%)	2 / 39 (5.13%)	
occurrences (all)	0	2	
Nausea			
subjects affected / exposed	2 / 38 (5.26%)	2 / 39 (5.13%)	
occurrences (all)	2	3	
Skin and subcutaneous tissue disorders			
Erythema			
subjects affected / exposed	5 / 38 (13.16%)	8 / 39 (20.51%)	
occurrences (all)	26	50	
Musculoskeletal and connective tissue disorders			
Myalgia			
subjects affected / exposed	22 / 38 (57.89%)	26 / 39 (66.67%)	
occurrences (all)	233	735	
Arthralgia			
subjects affected / exposed	3 / 38 (7.89%)	3 / 39 (7.69%)	
occurrences (all)	4	4	
Back pain			
subjects affected / exposed	2 / 38 (5.26%)	4 / 39 (10.26%)	
occurrences (all)	4	4	
Pain in extremity			

subjects affected / exposed	3 / 38 (7.89%)	1 / 39 (2.56%)	
occurrences (all)	4	1	
Infections and infestations			
Adenoviral upper respiratory infection			
subjects affected / exposed	2 / 38 (5.26%)	0 / 39 (0.00%)	
occurrences (all)	2	0	
Urinary tract infection			
subjects affected / exposed	5 / 38 (13.16%)	3 / 39 (7.69%)	
occurrences (all)	5	3	
Upper respiratory tract infection			
subjects affected / exposed	2 / 38 (5.26%)	1 / 39 (2.56%)	
occurrences (all)	3	1	
Influenza			
subjects affected / exposed	4 / 38 (10.53%)	0 / 39 (0.00%)	
occurrences (all)	5	0	
Nasopharyngitis			
subjects affected / exposed	2 / 38 (5.26%)	1 / 39 (2.56%)	
occurrences (all)	2	1	
Metabolism and nutrition disorders			
Dyslipidaemia			
subjects affected / exposed	2 / 38 (5.26%)	0 / 39 (0.00%)	
occurrences (all)	2	0	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
27 February 2018	Removed the following from the list of required evaluations at Baseline Visit: Hematology; Blood chemistry (including thyroid function tests); Coagulation study; Urinalysis (including a urine pregnancy test for female subjects). • Removed "bicarbonate "from the list of laboratory safety assessments.
12 June 2018	Updated the reference of McDonald criteria (Polman 2011) to 2017.
22 October 2019	• Replaced 'current treatment' with 'PLEGRIDY™'. • Removed: for subjects who switch IFN β treatment to PLEGRIDY™ treatment at Week 24 in study visits. • Added text to sample size justification: Due to the small sample sizes of 37 & 38 in each group, primary endpoint of combined counts of narrow FLS and ISR events was presented in descriptive manner. • Removed:"2-sided 95% CIs for difference in means of combined counts of FLS and ISR/ISR-P events/subject over total study time of 24weeks of current SC IFN-β arm & PLEGRIDY™ every-2-weeks arm was provided. • If distribution of events did not follow normal distribution, Mann-Whitney test was used to test difference in combined counts of FLS & ISR/ISR-P events/subject for24 weeks between current SC IFN-β arm and PLEGRIDY™ every-2-weeks arm. • If over dispersion of data occurs, Poisson regression model and/or negative binomial model adjusted for certain demographic, baseline disease characteristics of interest was used to compare event rate between current SC IFN-β arm & PLEGRIDY™ every-2-weeks arm" from primary endpoint analysis. • Removed: "A t- test will be used to assess difference in means for current SC IFN-β arm & PLEGRIDY™ every-2-weeks arm. • For independent comparative analyses at 24 weeks for categorical additional endpoints, chi- square test/Fisher exact/2-sample proportion test was used to assess the distribution difference in these secondary endpoints between the current SC IFN-β arm & PLEGRIDY™ every-2-weeks arm. • For paired comparative analyses between 24, 48 weeks as well as 24 weeks and end of study for these additional endpoints, a paired t-test/Wilcoxon/a signed rank test was applied to compare continuous endpoints within same treatment arm at different time frames; McNemar test may be used to compare change of categories for those categorical endpoints within same treatment arm at different time frames" from additional endpoints analysis.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported