Clinical trial results:
Multicentre interventional Phase IV study for the assessment of the effects on patient's satisfaction of Plegridy® (pre-filled pen) in subjects with relapsing-remitting multiple sclerosis unsatisfied with other injectable subcutaneous Interferons

Summary

EudraCT number	2015-002201-11
Trial protocol	IT
Global end of trial date	21 December 2017

Results information

Result version number	v1 (current)
This version publication date	02 November 2019
First version publication date	02 November 2019

Trial information

Trial identification

Sponsor protocol code	ITA-PEG-14-10779

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02587065
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Biogen
Sponsor organisation address	225 Binney Street, Cambridge, Massachusetts,, United States, 02142
Public contact	Biogen Study Medical Director, Biogen, clinicaltrials@biogen.com
Scientific contact	Biogen 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 December 2017
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	21 December 2017
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The primary objective of this study was to investigate whether Peg-IFN beta-1a improves the satisfaction of relapsing-remitting multiple sclerosis (RRMS) subjects unsatisfied with injectable subcutaneous interferons.

Protection of trial subjects:

Written informed consent was obtained from each subject prior to evaluations performed for eligibility. Subjects were given adequate time to review the information in the informed consent 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	03 February 2016
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	Italy: 193
Worldwide total number of subjects	193
EEA total number of subjects	193

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)	193
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Subjects were recruited from 32 sites in Italy.

Pre-assignment

Screening details:

A total of 193 subjects with relapsing remitting multiple sclerosis (RRMS) were enrolled into the study.

Period 1

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

Arms

Arm title	Peg-interferon Beta-1a 125 µg

Arm description:

Subjects received peg-interferon beta-1a 63 µg on Day 1 followed by peg-interferon beta-1a 94 µg on Day 14 in the titration phase. Subjects received per-interferon beta-1a on Day 28 and then every 2 weeks for up to 12 months.

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

Dosage and administration details:

Single 125 µg Peg-interferon beta-1a subcutaneously every two weeks.

Number of subjects in period 1	Peg-interferon Beta-1a 125 µg
Started	193
Completed	166
Not completed	27
tWithdrawal of Informed Consent (IC)	5
Adverse Event	14
Non-adherence to the protocol	3
Discontinuation of study medication	2
Reasons not Specified	3

Baseline characteristics

Reporting groups	
Reporting group title	Peg-interferon Beta-1a 125 µg
Reporting group description:	
Subjects received peg-interferon beta-1a 63 µg on Day 1 followed by peg-interferon beta-1a 94 µg on Day 14 in the titration phase. Subjects received per-interferon beta-1a on Day 28 and then every 2 weeks for up to 12 months.	

Reporting group values	Peg-interferon Beta-1a 125 µg	Total	
Number of subjects	193	193	
Age Categorical Units: Subjects			
Age Continuous Units: years arithmetic mean standard deviation	 42.0 ± 10.6	 -	
Sex: Female, Male Units: Subjects			
Female Male	135 58	135 58	
Race/Ethnicity Units: Subjects			
Caucasian Other	192 1	192 1	

End points

End points reporting groups

Reporting group title	Peg-interferon Beta-1a 125 µg

Reporting group description:

Subjects received peg-interferon beta-1a 63 µg on Day 1 followed by peg-interferon beta-1a 94 µg on Day 14 in the titration phase. Subjects received per-interferon beta-1a on Day 28 and then every 2 weeks for up to 12 months.

Primary: Change from Baseline in Convenience Satisfaction Score of Treatment Satisfaction Questionnaire to Medication (TSQM-9) at Week 12

End point title	Change from Baseline in Convenience Satisfaction Score of Treatment Satisfaction Questionnaire to Medication (TSQM-9) at Week 12[1]

End point description:

TSQM: 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 global satisfaction scale (questions 12 to 14). In TSQM-9, five items related to side effects of medication were not included. The scores were computed by adding items for each domain. 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. Questionnaires were completed electronically by subjects, by means of a subject i-PAD at each study visit. Full analysis set (FAS) population included all enrolled subjects who took at least one dose of the study medication. 'n' indicates the number of subjects who were evaluated at a specified time point.

End point type	Primary

End point timeframe:

Baseline, Week 12

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 was planned to be reported for this endpoint.

End point values	Peg-interferon Beta-1a 125 µg			
Subject group type	Reporting group			
Number of subjects analysed	192[2]			
Units: score on a scale				
arithmetic mean (standard deviation)				
Baseline (n= 192)	38.5 (± 13.9)			
Change at Week 12 (n=188)	38.5 (± 23.3)			

Notes:

[2] - Number of subjects analysed are the subjects who were evaluated for this endpoint.

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in the Score of All Domains of TSQM-9 at Week 24

End point title	Change from Baseline in the Score of All Domains of TSQM-9 at Week 24

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 global 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. Questionnaires were completed electronically by subjects, by means of a subject i-PAD at each study visit. FAS population included all enrolled subjects who took at least one dose of the study medication. 'n' indicates the number of subjects who were evaluated at a specified time point.

End point type	Secondary

End point timeframe:

Baseline, Week 24

End point values	Peg-interferon Beta-1a 125 µg			
Subject group type	Reporting group			
Number of subjects analysed	192[3]			
Units: score on a scale				
arithmetic mean (standard deviation)				
Baseline: Convenience satisfaction (n=192)	38.5 (± 13.9)			
Change at Week 24: Convenience satisfaction(n=176)	41.9 (± 22.5)			
Baseline: Effectiveness (n=192)	47.0 (± 17.5)			
Change at Week 24: Effectiveness(n=176)	21.2 (± 26.9)			
Baseline: Global satisfaction (n=192)	41.4 (± 17.3)			
Change at Week 24: Global satisfaction (n=176)	27.9 (± 26.1)			

Notes:

[3] - Number of subjects analysed are the subjects who were evaluated for this endpoint.

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in Number of Subjects with Adherence to Study Treatment at Weeks 12 and 24

End point title	Change from Baseline in Number of Subjects with Adherence to Study Treatment at Weeks 12 and 24

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. Subjects who had taken the prescribed doses of treatment in the previous 28 days were evaluated. FAS population included all enrolled subjects who took at least one dose of the study medication.

End point type	Secondary

End point timeframe:

Baseline, Weeks 12 and 24

End point values	Peg-interferon Beta-1a 125 µg			
Subject group type	Reporting group			
Number of subjects analysed	113[4]			
Units: subjects				
Baseline	113			
Change at Week 12	65			
Change at Week 24	53			

Notes:

[4] - Number of subjects analysed are the subjects who were evaluated for this endpoint.

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in Fatigue Status Scale (FSS) Score at Week 12 and 24

End point title	Change from Baseline in Fatigue Status Scale (FSS) Score at Week 12 and 24

End point description:

FSS is a questionnaire composed of nine statements on the state of fatigue experienced during the previous week. The answers are within a scale of agreement ranging from 1 to 7, where 1 represents less fatigue and 7 indicates highest fatigue. The total score was obtained summing the number given at each item and it ranges from 7 to 63. An overall score of ≥36 indicates a state of fatigue. Questionnaires were completed electronically by subjects, by means of a subject i-PAD at each study visit. Here negative values indicate improvement in FSS score from baseline. FAS population included all enrolled subjects who took at least one dose of the study medication. 'n' indicates the number of subjects who were evaluated at a specified time points.

End point type	Secondary

End point timeframe:

Baseline, Weeks 12 and 24

End point values	Peg-interferon Beta-1a 125 µg			
Subject group type	Reporting group			
Number of subjects analysed	193			
Units: score on a scale				
arithmetic mean (standard deviation)				
Baseline (n= 193)	40.1 (± 15.6)			
Change at Week 12 (n= 191)	-4.6 (± 13.1)			
Change at Week 24 (n= 176)	-3.8 (± 13.1)			

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in Adapted Sclerosis Treatment Concerns Questionnaire (MSTCQ) Score at Weeks 12 and 24

End point title	Change from Baseline in Adapted Sclerosis Treatment Concerns

	Questionnaire (MSTCQ) Score at Weeks 12 and 24

End point description:

MSTCQ is a 20-item questionnaire containing two domains: injection-system satisfaction and side effects. The side-effects domain comprises of three subscales: injection site reaction (ISRs) and global side effects. All questions in the MSTCQ have a five-point response choice, with lower total scores indicating better outcomes. Questionnaires were completed electronically by subjects, by means of a subject i-PAD at each study visit. Here negative values indicate improvement in MSTCQ score from baseline. Here negative sign indicates improvement in MSTCQ score as compared to baseline. FAS population included all enrolled subjects who took at least one dose of the study medication. 'n' indicates the number of subjects who were evaluated at a specified time points.

End point type	Secondary

End point timeframe:

Baseline, Weeks 12 and 24

End point values	Peg-interferon Beta-1a 125 µg			
Subject group type	Reporting group			
Number of subjects analysed	193			
Units: score on a scale				
arithmetic mean (standard deviation)				
Baseline (n= 193)	71.9 (± 14.0)			
Change at Week 12 (n= 191)	-16.8 (± 16.9)			
Change at Week 24 (n= 176)	-19.4 (± 17.1)			

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in Multiple Sclerosis International Quality of Life questionnaire (MusiQoL) Score at Weeks 12 and 24

End point title	Change from Baseline in Multiple Sclerosis International Quality of Life questionnaire (MusiQoL) Score at Weeks 12 and 24

End point description:

MusiQoL is a self-administered questionnaire consisting of 31 items describing nine dimensions of health-related quality of life (QoL): activities of daily living, psychological wellbeing, symptoms, relationship with friends, relationship with family, sentimental and sexual life, coping rejection, relationship with healthcare system). All items are scored based on frequency/extent of an event on a five-point scale ranging from never/not at all (option 1) to always/very much (option 5). Total score is obtained by linearly transforming and standardizing on a 0-100 scale. Higher scores indicate a better level of health-related QoL for each dimension and for the global index score. Here, negative values indicate improvement in MusiQoL score from baseline. FAS population included all enrolled subjects who took at least one dose of the study medication. 'n' indicates the number of subjects who were evaluated at a specified time points.

End point type	Secondary

End point timeframe:

Baseline, Weeks 12 and 24

End point values	Peg-interferon Beta-1a 125 µg			
Subject group type	Reporting group			
Number of subjects analysed	193			
Units: score on a scale				
arithmetic mean (standard deviation)				
Baseline (n=193)	67.8 (± 16.5)			
Change at Week 12 (n= 191)	4.6 (± 14.89)			
Change at Week 24 (n= 176)	5.0 (± 14.2)			

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in Annualized Relapse Rate (ARR) at Week 24

End point title	Change from Baseline in Annualized Relapse Rate (ARR) at Week 24

End point description:

Relapses are defined as neurologic symptoms lasting more than 24 hours which occur at least 30 days after the onset of a preceding event. ARR was calculated as the total number of relapses for all subjects divided by the total subject-years of exposure to that treatment. Here negative sign indicates decrease in annual relapse rate as compared to baseline. FAS population included all enrolled subjects who took at least one dose of the study medication. 'n' indicates the number of subjects who were evaluated at a specified time points.

End point type	Secondary

End point timeframe:

Baseline, Week 24

End point values	Peg-interferon Beta-1a 125 µg			
Subject group type	Reporting group			
Number of subjects analysed	193			
Units: relapse per year				
number (not applicable)				
Baseline (n= 193)	0.15			
Change at Week 24 (n= 176)	-0.03			

Statistical analyses

No statistical analyses for this end point

Secondary: Percent Change in Relapse-Free Subjects at Week 24

End point title	Percent Change in Relapse-Free Subjects at Week 24

End point description:

Relapses are defined as neurologic symptoms lasting more than 24 hours which occur at least 30 days after the onset of a preceding event. Percent change in relapse-free subjects had been calculated with respect to the number of relapse-free subjects at baseline. Here, negative sign indicates decrease in

number of relapse-free subjects at specified timepoint as compared to baseline. FAS population included all enrolled subjects who took at least one dose of the study medication.

End point type	Secondary

End point timeframe:

Baseline, Week 24

End point values	Peg-interferon Beta-1a 125 µg			
Subject group type	Reporting group			
Number of subjects analysed	189[5]			
Units: percent change				
number (not applicable)	-7.94			

Notes:

[5] - Number of subjects analysed is the subjects who were evaluated for this endpoint.

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects With Adverse Events (AE)

End point title	Number of Subjects With Adverse Events (AE)

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 herefore 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. FAS population included all enrolled subjects who took at least one dose of the study medication.

End point type	Secondary

End point timeframe:

Baseline up to Week 24

End point values	Peg-interferon Beta-1a 125 µg			
Subject group type	Reporting group			
Number of subjects analysed	193			
Units: subjects	82			

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects with AE Stratified by Severity

End point title	Number of Subjects with AE Stratified by Severity

End point description:

Severity of AEs was evaluated based on the following criteria- Mild: Symptoms barely noticeable to subject or does not make subject uncomfortable; does not influence performance or functioning; prescription drug not ordinarily needed for relief of symptom(s) but may be given because of personality of subject. Moderate: Symptoms of a sufficient severity to make subject uncomfortable; performance of daily activity is influenced; subject is able to continue in study; treatment for symptom(s) may be needed. Severe: Symptoms cause severe discomfort; symptoms cause incapacitation or significant impact on subject's daily life; severity may cause cessation of treatment with study treatment; treatment for symptom(s) may be given and/or subject hospitalized. FAS population included all enrolled subjects who took at least one dose of the study medication.

End point type	Secondary

End point timeframe:

Baseline up to Week 24

End point values	Peg-interferon Beta-1a 125 µg			
Subject group type	Reporting group			
Number of subjects analysed	193			
Units: subjects				
Mild	55			
Moderate	27			

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects With Clinical Abnormal in Laboratory Values

End point title	Number of Subjects With Clinical Abnormal in Laboratory Values

End point description:

Subjects with clinical abnormal laboratory values were reported throughout the studies. FAS population included all enrolled subjects who took at least one dose of the study medication. 'n' indicates the number of subjects who were evaluated at a specified time point.

End point type	Secondary

End point timeframe:

Baseline up to Week 24

End point values	Peg-interferon Beta-1a 125 µg			
Subject group type	Reporting group			
Number of subjects analysed	193			
Units: subjects				
Baseline (n= 193)	4			
Week 12 (n= 191)	3			
Week 24 (n= 176)	3			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information	
Timeframe for reporting adverse events:	
Baseline up to Week 24	
Adverse event reporting additional description:	
FAS population included all enrolled subjects who took at least one dose of the study medication.	
Assessment type	Systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	20.1

Reporting groups	
Reporting group title	Peg INF Beta-1a 125 µg
Reporting group description:	
Subjects received peg-interferon beta-1a 63 µg on Day 1 followed by peg-interferon beta-1a 94 µg on Day 14 in the titration phase. Subjects received per-interferon beta-1a on Day 28 and then every 2 weeks for up to 12 months.	

Serious adverse events	Peg INF Beta-1a 125 µg		
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 193 (0.00%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events	0		

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

Non-serious adverse events	Peg INF Beta-1a 125 µg		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	44 / 193 (22.80%)		
General disorders and administration site conditions			
Influenza like illness			
subjects affected / exposed	28 / 193 (14.51%)		
occurrences (all)	42		
Injection site reactions			
subjects affected / exposed	10 / 193 (5.18%)		
occurrences (all)	12		
Pyrexia			

subjects affected / exposed occurrences (all)	10 / 193 (5.18%) 16		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? No

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported