



Clinical trial results:

A Phase II, Randomized, Multi-center, Parallel-group, Rater-blinded Study to Evaluate the Efficacy, Safety and Tolerability of 0.5 mg, 3 mg, 10 mg and 20 mg Plovamer Acetate Doses Compared to Copaxone in Patients with Relapsing Remitting Multiple Sclerosis

Due to the EudraCT – Results system being out of service between 31 July 2015 and 12 January 2016, these results have been published in compliance with revised timelines.

Summary

EudraCT number	2013-002283-25
Trial protocol	CZ HU IT GB FI GR ES BG PL HR
Global end of trial date	03 March 2015

Results information

Result version number	v1 (current)
This version publication date	10 July 2016
First version publication date	10 July 2016

Trial information

Trial identification

Sponsor protocol code	EMR200575-001
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Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01963611
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Merck KGaA
Sponsor organisation address	Frankfurter Strasse 250, Darmstadt, Germany, 64293
Public contact	Communication Center, Merck KGaA, +49 6151725200, service@merckgroup.com
Scientific contact	Communication Center, Merck KGaA, +49 6151725200, service@merckgroup.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	03 March 2015
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	03 March 2015
Was the trial ended prematurely?	Yes

Notes:

General information about the trial

Main objective of the trial:

This was a Phase 2, randomized, rater-blinded, 5-arm, parallel-group trial that had 4 doses of plovamer acetate against the active comparator Copaxone in subjects with Relapsing Remitting Multiple Sclerosis (RRMS). The trial was conducted on an outpatient basis for minimum treatment duration of 40 weeks.

Protection of trial subjects:

Subject protection was ensured by following high medical and ethical standards in accordance with the principles laid down in the Declaration of Helsinki, and that are consistent with Good Clinical Practice and applicable regulations.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	03 February 2014
Long term follow-up planned	Yes
Long term follow-up rationale	Safety, Efficacy
Long term follow-up duration	4 Months
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects**Subjects enrolled per country**

Country: Number of subjects enrolled	Bulgaria: 47
Country: Number of subjects enrolled	Czech Republic: 63
Country: Number of subjects enrolled	Spain: 3
Country: Number of subjects enrolled	Croatia: 27
Country: Number of subjects enrolled	Hungary: 6
Country: Number of subjects enrolled	Italy: 8
Country: Number of subjects enrolled	Mexico: 1
Country: Number of subjects enrolled	Poland: 32
Country: Number of subjects enrolled	Serbia: 17
Country: Number of subjects enrolled	Turkey: 1
Country: Number of subjects enrolled	Ukraine: 19
Country: Number of subjects enrolled	United States: 25
Country: Number of subjects enrolled	South Africa: 6
Worldwide total number of subjects	255
EEA total number of subjects	186

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)	255
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

Of the 550 patients planned for enrollment, a total of 255 subjects were randomized and 254 were included in safety analysis set.

Period 1

Period 1 title	Overall Study (overall period)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Single blind
Roles blinded	Subject

Arms

Are arms mutually exclusive?	Yes
Arm title	Plovamer acetate 0.5 milligram (mg)

Arm description:

Plovamer acetate was administered at a dose of 0.5 mg as weekly subcutaneous injection for 40 weeks up to a maximum of 14 months.

Arm type	Experimental
Investigational medicinal product name	Plovamer acetate
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Plovamer acetate was administered at a dose of 0.5 mg as subcutaneous injection.

Arm title	Plovamer acetate 3 mg
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Arm description:

Plovamer acetate was administered at a dose of 3 mg as weekly subcutaneous injection for 40 weeks up to a maximum of 14 months.

Arm type	Experimental
Investigational medicinal product name	Plovamer acetate
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Plovamer acetate was administered at a dose of 3 mg as subcutaneous injection.

Arm title	Plovamer acetate 10 mg
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Arm description:

Plovamer acetate was administered at a dose of 10 mg as weekly subcutaneous injection for 40 weeks up to a maximum of 14 months.

Arm type	Experimental
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Investigational medicinal product name	Plovamer acetate
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Injection
Routes of administration	Subcutaneous use
Dosage and administration details:	
Plovamer acetate was administered at a dose of 10 mg as subcutaneous injection.	
Arm title	Plovamer acetate 20 mg

Arm description:

Plovamer acetate was administered as two subcutaneous injection of 10 mg weekly for 40 weeks up to a maximum of 14 months.

Arm type	Experimental
Investigational medicinal product name	Plovamer acetate
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Injection
Routes of administration	Subcutaneous use
Dosage and administration details:	
Plovamer acetate was administered as two subcutaneous injection of 10 mg.	
Arm title	Copaxone 20 mg

Arm description:

Copaxone was administered at a dose of 20 mg as subcutaneous injection once daily for 40 weeks up to a maximum of 14 months.

Arm type	Active comparator
Investigational medicinal product name	Copaxone 20 mg
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Injection
Routes of administration	Subcutaneous use
Dosage and administration details:	
Copaxone was administered at a dose of 20 mg as subcutaneous injection.	

Number of subjects in period 1^[1]	Plovamer acetate 0.5 milligram (mg)	Plovamer acetate 3 mg	Plovamer acetate 10 mg
Started	51	49	52
Safety Analysis Set	51	49	52
Completed	0	0	0
Not completed	51	49	52
Consent withdrawn by subject	3	2	1
Adverse event, non-fatal	1	1	3
Unspecified	47	46	48
Protocol deviation	-	-	-
Lack of efficacy	-	-	-

Number of subjects in period 1^[1]	Plovamer acetate 20 mg	Copaxone 20 mg
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Started	52	50
Safety Analysis Set	52	50
Completed	0	0
Not completed	52	50
Consent withdrawn by subject	1	2
Adverse event, non-fatal	4	3
Unspecified	45	45
Protocol deviation	1	-
Lack of efficacy	1	-

Notes:

[1] - The number of subjects reported to be in the baseline period are not the same as the worldwide number enrolled in the trial. It is expected that these numbers will be the same.

Justification: One subject in the Copaxone 20 mg arm was randomized but not treated due to withdrawal of consent.

Baseline characteristics

Reporting groups

Reporting group title	Plovamer acetate 0.5 milligram (mg)
Reporting group description: Plovamer acetate was administered at a dose of 0.5 mg as weekly subcutaneous injection for 40 weeks up to a maximum of 14 months.	
Reporting group title	Plovamer acetate 3 mg
Reporting group description: Plovamer acetate was administered at a dose of 3 mg as weekly subcutaneous injection for 40 weeks up to a maximum of 14 months.	
Reporting group title	Plovamer acetate 10 mg
Reporting group description: Plovamer acetate was administered at a dose of 10 mg as weekly subcutaneous injection for 40 weeks up to a maximum of 14 months.	
Reporting group title	Plovamer acetate 20 mg
Reporting group description: Plovamer acetate was administered as two subcutaneous injection of 10 mg weekly for 40 weeks up to a maximum of 14 months.	
Reporting group title	Copaxone 20 mg
Reporting group description: Copaxone was administered at a dose of 20 mg as subcutaneous injection once daily for 40 weeks up to a maximum of 14 months.	

Reporting group values	Plovamer acetate 0.5 milligram (mg)	Plovamer acetate 3 mg	Plovamer acetate 10 mg
Number of subjects	51	49	52
Age categorical Units: Subjects			

Age Continuous Units: years arithmetic mean standard deviation	39.2 ± 10.73	40.7 ± 9.54	41.1 ± 10.83
Gender, Male/Female Units: subjects			
Female	38	37	39
Male	13	12	13

Reporting group values	Plovamer acetate 20 mg	Copaxone 20 mg	Total
Number of subjects	52	50	254
Age categorical Units: Subjects			

Age Continuous Units: years arithmetic mean standard deviation	40.4 ± 9.53	41.8 ± 11.61	-
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Gender, Male/Female			
Units: subjects			
Female	37	26	177
Male	15	24	77

End points

End points reporting groups

Reporting group title	Plovamer acetate 0.5 milligram (mg)
Reporting group description: Plovamer acetate was administered at a dose of 0.5 mg as weekly subcutaneous injection for 40 weeks up to a maximum of 14 months.	
Reporting group title	Plovamer acetate 3 mg
Reporting group description: Plovamer acetate was administered at a dose of 3 mg as weekly subcutaneous injection for 40 weeks up to a maximum of 14 months.	
Reporting group title	Plovamer acetate 10 mg
Reporting group description: Plovamer acetate was administered at a dose of 10 mg as weekly subcutaneous injection for 40 weeks up to a maximum of 14 months.	
Reporting group title	Plovamer acetate 20 mg
Reporting group description: Plovamer acetate was administered as two subcutaneous injection of 10 mg weekly for 40 weeks up to a maximum of 14 months.	
Reporting group title	Copaxone 20 mg
Reporting group description: Copaxone was administered at a dose of 20 mg as subcutaneous injection once daily for 40 weeks up to a maximum of 14 months.	

Primary: Mean Number of Time Constant 1 (T1) Gadolinium (Gd)-Enhancing Lesions per Subject and Scan

End point title	Mean Number of Time Constant 1 (T1) Gadolinium (Gd)-Enhancing Lesions per Subject and Scan ^[1]
End point description: Time Constant 1 (T1) Gadolinium (Gd)-Enhancing Lesions per Subject and Scan was calculated using 5 serial magnetic resonance imaging (MRI) scans. Intent to Treat (ITT) analysis set included all randomised subjects with at least 1 post-baseline efficacy (MRI) assessment. Here 'n' signifies those subjects who were evaluated for this measure at the specified time point for each arm group respectively and "99999" for standard deviation signifies data not reported as number of subject was 1 while for both arithmetic mean and standard deviation '99999' signifies data not applicable as there was no evaluable subject.	
End point type	Primary
End point timeframe: Baseline , Week 12, 24, 28, 32, 36, 40	

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 the descriptive data was planned to be presented for the outcome measure.

End point values	Plovamer acetate 0.5 milligram (mg)	Plovamer acetate 3 mg	Plovamer acetate 10 mg	Plovamer acetate 20 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	45	45	43	41
Units: lesions per subjects per scan				
arithmetic mean (standard deviation)				
Baseline (n=44,45,42,41,44)	1.5 (± 2.93)	1.6 (± 4.12)	1 (± 2.43)	2.3 (± 5.65)
Week 12: (n=44,45,43,41,44)	1.7 (± 3.28)	1.3 (± 3.55)	1.2 (± 2.4)	1.5 (± 3.7)

Week 24: (n=17,17,21,18,19)	1.5 (± 2.53)	0.9 (± 2.33)	1.5 (± 4.14)	1.1 (± 1.92)
Week 28: (n=10,11,13,12,13)	1.7 (± 2.75)	0.4 (± 0.92)	0.5 (± 1.2)	2 (± 4)
Week 32: (n=5,6,9,10,9)	1 (± 1.41)	0.2 (± 0.41)	0.8 (± 1.72)	1.8 (± 3.33)
Week 36: (n=1,0,2,3,3)	0 (± 99999)	99999 (± 99999)	1 (± 1.41)	1.3 (± 2.31)
Week 40: (n=1,0,1,1,1)	0 (± 99999)	99999 (± 99999)	0 (± 99999)	0 (± 99999)

End point values	Copaxone 20 mg			
Subject group type	Reporting group			
Number of subjects analysed	44			
Units: lesions per subjects per scan				
arithmetic mean (standard deviation)				
Baseline (n=44,45,42,41,44)	2.5 (± 5.12)			
Week 12: (n=44,45,43,41,44)	1.7 (± 4.51)			
Week 24: (n=17,17,21,18,19)	0.6 (± 1.46)			
Week 28: (n=10,11,13,12,13)	0.9 (± 1.89)			
Week 32: (n=5,6,9,10,9)	1.2 (± 3.67)			
Week 36: (n=1,0,2,3,3)	7.3 (± 12.7)			
Week 40: (n=1,0,1,1,1)	16 (± 99999)			

Statistical analyses

No statistical analyses for this end point

Secondary: Mean Annualized Relapse Rate (ARR)

End point title	Mean Annualized Relapse Rate (ARR)
End point description:	
Relapse was defined as new, worsening or recurrent neurological symptoms attributed to multiple sclerosis that last for at least 24 hours without fever or infection, or adverse reaction to prescribed medication, preceded by a stable or improving neurological status of at least 30 days. These new or worsening symptoms should be noted by the patient and must be accompanied by at least one of the following: An increase of greater than or equal to (\geq) 1 grade in ≥ 2 functional scales of the Expanded Disability Status Scale (EDSS) or an increase of ≥ 2 grades in 1 functional scale of the EDSS or an increase of ≥ 0.5 or an increase of ≥ 1.0 in EDSS if the previous EDSS was 0. Annualized Relapse Rate was calculated as = $365.25 \times (\text{Number of relapses during Treatment Period}) / (\text{Number of days on treatment during Treatment Period})$. Safety Analysis Set (SAF) includes all randomised subjects who had received at least 1 dose of investigational medicinal product (IMP).	
End point type	Secondary
End point timeframe:	
Baseline up to Week 40	

End point values	Plovamer acetate 0.5 milligram (mg)	Plovamer acetate 3 mg	Plovamer acetate 10 mg	Plovamer acetate 20 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	51	49	52	52
Units: percent relapse				
arithmetic mean (standard deviation)	0.3 (± 0.88)	0.2 (± 0.62)	0.2 (± 0.76)	0.2 (± 0.88)

End point values	Copaxone 20 mg			
Subject group type	Reporting group			
Number of subjects analysed	50			
Units: percent relapse				
arithmetic mean (standard deviation)	0.2 (± 0.92)			

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects Remaining Relapse-Free

End point title	Percentage of Subjects Remaining Relapse-Free
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End point description:

Relapse was defined as new, worsening or recurrent neurological symptoms attributed to multiple sclerosis that last for at least 24 hours without fever or infection, or adverse reaction to prescribed medication, preceded by a stable or improving neurological status of at least 30 days. These new or worsening symptoms should be noted by the patient and must be accompanied by at least one of the following: An increase of greater than or equal to (\geq) 1 grade in ≥ 2 functional scales of the EDSS or an increase of ≥ 2 grades in 1 functional scale of the EDSS or an increase of ≥ 0.5 or an increase of ≥ 1.0 in EDSS if the previous EDSS was 0. SAF includes all randomized subjects who had received at least 1 dose of investigational medicinal product (IMP).

End point type	Secondary
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End point timeframe:

Baseline up to Week 40

End point values	Plovamer acetate 0.5 milligram (mg)	Plovamer acetate 3 mg	Plovamer acetate 10 mg	Plovamer acetate 20 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	51	49	52	52
Units: percent subjects				
number (not applicable)	86.3	89.8	94.2	94.2

End point values	Copaxone 20 mg			
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Subject group type	Reporting group			
Number of subjects analysed	50			
Units: percent subjects				
number (not applicable)	90			

Statistical analyses

No statistical analyses for this end point

Secondary: Mean number of new T1 Gadolinium (Gd)-enhancing lesions per subject and scan

End point title	Mean number of new T1 Gadolinium (Gd)-enhancing lesions per subject and scan
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End point description:

T1 Gd-enhancing lesions per subject and scan was measured using 5 serial MRI scans. ITT analysis set included all randomized subjects with at least 1 post-baseline efficacy (MRI) assessment. Here "n" signifies those subjects who were evaluated for this measure at the specified time point for each arm group respectively and "99999" for standard deviation signifies data not reported as number of subject was 1 while for both arithmetic mean and standard deviation '99999' signifies data not applicable as there was no evaluable subject.

End point type	Secondary
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End point timeframe:

Weeks 12, 24, 28, 32, 36, 40

End point values	Plovamer acetate 0.5 milligram (mg)	Plovamer acetate 3 mg	Plovamer acetate 10 mg	Plovamer acetate 20 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	45	45	43	41
Units: lesions/subject/scan				
arithmetic mean (standard deviation)				
Week 12: (n=44,45,43,41,44)	1.7 (± 3.26)	1.2 (± 3.54)	1.2 (± 2.26)	1.3 (± 2.99)
Week 24: (n=17,17,21,18,19)	1.5 (± 2.53)	0.9 (± 2.33)	1.4 (± 3.56)	1 (± 1.94)
Week 28: (n=10,11,13,12,13)	1.2 (± 2.15)	0.1 (± 0.3)	0.5 (± 1.13)	1.8 (± 3.83)
Week 32: (n=5,6,9,10,9)	0.8 (± 1.1)	0.2 (± 0.41)	0.4 (± 1.33)	1.5 (± 2.95)
Week 36: (n=1,0,2,3,3)	0 (± 99999)	99999 (± 99999)	0.5 (± 0.71)	1 (± 1.73)
Week 40: (n=1,0,1,1,1)	0 (± 99999)	99999 (± 99999)	0 (± 99999)	0 (± 99999)

End point values	Copaxone 20 mg			
Subject group type	Reporting group			
Number of subjects analysed	44			
Units: lesions/subject/scan				
arithmetic mean (standard deviation)				
Week 12: (n=44,45,43,41,44)	1.6 (± 4.31)			

Week 24: (n=17,17,21,18,19)	0.5 (± 1.26)			
Week 28: (n=10,11,13,12,13)	0.5 (± 1.33)			
Week 32: (n=5,6,9,10,9)	0.6 (± 1.67)			
Week 36: (n=1,0,2,3,3)	5.7 (± 9.81)			
Week 40: (n=1,0,1,1,1)	16 (± 99999)			

Statistical analyses

No statistical analyses for this end point

Secondary: Mean Number of New or Enlarging Time Constant 2 (T2) Lesions per Subject and Scan

End point title	Mean Number of New or Enlarging Time Constant 2 (T2) Lesions per Subject and Scan
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End point description:

New or enlarging Time Constant 2 (T2) lesions per subject and scan was calculated using 5 serial MRI scans. ITT analysis set included all randomized subjects with at least 1 post-baseline efficacy (MRI) assessment. Here 'n' signifies those subjects who were evaluated for this measure at the specified time point for each arm group respectively and "99999" for standard deviation signifies data not reported as number of subject was 1 while for both arithmetic mean and standard deviation '99999' signifies data not applicable as there was no evaluable subject.

End point type	Secondary
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End point timeframe:

Weeks 12, 24, 28, 32, 36,40

End point values	Plovamer acetate 0.5 milligram (mg)	Plovamer acetate 3 mg	Plovamer acetate 10 mg	Plovamer acetate 20 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	45	45	43	41
Units: lesions/subject/scan				
arithmetic mean (standard deviation)				
Week 12: (n=44,45,43,41,44)	4.5 (± 7.41)	2.6 (± 4.99)	2.7 (± 4.5)	4.1 (± 7.45)
Week 24: (n=17,17,21,18,19)	3.1 (± 5.61)	1.8 (± 3.35)	2.3 (± 4.91)	3.4 (± 6.03)
Week 28: (n=10,11,13,12,13)	1.3 (± 2.45)	0.2 (± 0.4)	0.8 (± 1.69)	2.5 (± 5.05)
Week 32: (n=5,6,9,10,9)	1.4 (± 2.19)	0.2 (± 0.41)	0.3 (± 0.71)	2.4 (± 4.12)
Week 36: (n=1,0,2,3,3)	0 (± 99999)	99999 (± 99999)	0.5 (± 0.71)	1.7 (± 2.89)
Week 40: (n=1,0,1,1,1)	0 (± 99999)	99999 (± 99999)	0 (± 99999)	0 (± 99999)

End point values	Copaxone 20 mg			
Subject group type	Reporting group			
Number of subjects analysed	44			
Units: lesions/subject/scan				
arithmetic mean (standard deviation)				

Week 12: (n=44,45,43,41,44)	4 (± 8.59)			
Week 24: (n=17,17,21,18,19)	1.7 (± 3.45)			
Week 28: (n=10,11,13,12,13)	0.8 (± 2.15)			
Week 32: (n=5,6,9,10,9)	0.9 (± 2.32)			
Week 36: (n=1,0,2,3,3)	4.3 (± 7.51)			
Week 40: (n=1,0,1,1,1)	13 (± 99999)			

Statistical analyses

No statistical analyses for this end point

Secondary: Mean Number of New, Unenhancing T1 Lesions (Black Holes) per Subject and Scan

End point title	Mean Number of New, Unenhancing T1 Lesions (Black Holes) per Subject and Scan
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End point description:

New, unenhancing T1 lesions (Black Holes) per subject and scan was calculated using 5 Serial MRIs. ITT analysis set included all randomized subjects with at least 1 post-baseline efficacy (MRI) assessment. Here 'n' signifies those subjects who were evaluated for this measure at the specified time point for each arm group respectively and "99999" for standard deviation signifies data not reported as number of subject was 1 while for both arithmetic mean and standard deviation '99999' signifies data not applicable as there was no evaluable subject.

End point type	Secondary
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End point timeframe:

Weeks 12, 24, 28, 32, 36, 40

End point values	Plovamer acetate 0.5 milligram (mg)	Plovamer acetate 3 mg	Plovamer acetate 10 mg	Plovamer acetate 20 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	45	45	43	41
Units: lesions/subject/scan				
arithmetic mean (standard deviation)				
Week 12: (n=44,45,43,41,44)	2.8 (± 6.48)	1.8 (± 3.97)	1.4 (± 2.21)	2.6 (± 5.24)
Week 24: (n=17,17,21,18,19)	2 (± 4.8)	0.8 (± 1.55)	0.8 (± 1.83)	1.3 (± 2.89)
Week 28: (n=10,11,13,12,13)	0.6 (± 1.26)	0.2 (± 0.6)	0.6 (± 1.56)	0.5 (± 1)
Week 32: (n=5,6,9,10,9)	2 (± 3.39)	0.2 (± 0.41)	0.8 (± 1.3)	0.7 (± 1.25)
Week 36: (n=1,0,2,3,3)	0 (± 99999)	99999 (± 99999)	0 (± 0)	0.7 (± 1.15)
Week 40: (n=1,0,1,1,1)	0 (± 99999)	99999 (± 99999)	0 (± 99999)	0 (± 99999)

End point values	Copaxone 20 mg			
Subject group type	Reporting group			
Number of subjects analysed	44			
Units: lesions/subject/scan				

arithmetic mean (standard deviation)				
Week 12: (n=44,45,43,41,44)	2.6 (± 5.13)			
Week 24: (n=17,17,21,18,19)	0.8 (± 1.75)			
Week 28: (n=10,11,13,12,13)	0.4 (± 1.39)			
Week 32: (n=5,6,9,10,9)	0.3 (± 0.71)			
Week 36: (n=1,0,2,3,3)	1.7 (± 2.89)			
Week 40: (n=1,0,1,1,1)	11 (± 99999)			

Statistical analyses

No statistical analyses for this end point

Secondary: Mean Change From Baseline in Volume of T1 Gadolinium (Gd)-Enhancing Lesions per Subject and Scan

End point title	Mean Change From Baseline in Volume of T1 Gadolinium (Gd)-Enhancing Lesions per Subject and Scan
End point description:	
Change from baseline in volume of T1 Gd-enhancing lesions per subject was calculated using 5 Serial MRI Scans. ITT analysis set included all randomized subjects with at least 1 post-baseline efficacy (MRI) assessment. Here 'n' signifies those subjects who were evaluated for this measure at the specified time point for each arm group respectively and "99999" for standard deviation signifies data not reported as number of subject was 1 while for both arithmetic mean and standard deviation '99999' signifies data not applicable as there was no evaluable subject.	
End point type	Secondary
End point timeframe:	
Baseline, Weeks 12, 24, 28, 32, 36, 40	

End point values	Plovamer acetate 0.5 milligram (mg)	Plovamer acetate 3 mg	Plovamer acetate 10 mg	Plovamer acetate 20 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	45	45	43	41
Units: cubic millimeter (mm ³)				
arithmetic mean (standard deviation)				
Baseline: (n=44,45,42,41,44)	0.182 (± 0.4212)	0.209 (± 0.6325)	0.138 (± 0.3577)	0.508 (± 1.1981)
Change at Week 12: (n=44,45,42,41,44)	0.037 (± 0.3982)	-0.007 (± 0.6019)	0.189 (± 0.8406)	-0.19 (± 1.0389)
Change at Week 24: (n=16,17,20,18,19)	0.053 (± 0.1705)	0.352 (± 1.4308)	0.06 (± 0.4858)	-0.591 (± 1.491)
Change at Week 28: (n=9,11,12,12,13)	0.224 (± 0.2948)	0.067 (± 0.464)	0.057 (± 0.5728)	-0.796 (± 1.7779)
Change at Week 32: (n=4,6,8,10,9)	-0.085 (± 0.2765)	-0.102 (± 0.2691)	-0.135 (± 0.6305)	-0.988 (± 1.98)
Change at Week 36: (n=0,0,1,3,3)	99999 (± 99999)	99999 (± 99999)	0.321 (± 99999)	-1.881 (± 3.4679)
Change at Week 40: (n=0,0,0,1,1)	99999 (± 99999)	99999 (± 99999)	99999 (± 99999)	0 (± 99999)

End point values	Copaxone 20 mg			
Subject group type	Reporting group			
Number of subjects analysed	44			
Units: cubic millimeter (mm ³)				
arithmetic mean (standard deviation)				
Baseline: (n=44,45,42,41,44)	0.264 (± 0.5707)			
Change at Week 12: (n=44,45,42,41,44)	0.023 (± 0.5794)			
Change at Week 24: (n=16,17,20,18,19)	-0.25 (± 0.5393)			
Change at Week 28: (n=9,11,12,12,13)	-0.257 (± 0.698)			
Change at Week 32: (n=4,6,8,10,9)	0.031 (± 0.8312)			
Change at Week 36: (n=0,0,1,3,3)	0.834 (± 2.1816)			
Change at Week 40: (n=0,0,0,1,1)	2.18 (± 99999)			

Statistical analyses

No statistical analyses for this end point

Secondary: Mean Change From Baseline in Volume of T2 Gadolinium (Gd)-Enhancing Lesions per Subject and Scan

End point title	Mean Change From Baseline in Volume of T2 Gadolinium (Gd)-Enhancing Lesions per Subject and Scan
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End point description:

Change from baseline per subjects in volume of T2 Gd-enhancing lesions was calculated using 5 series MRI scan. ITT analysis set included all randomized subjects with at least 1 post-baseline efficacy (MRI) assessment. Here 'n' signifies those subjects who were evaluated for this measure at the specified time point for each arm group respectively and "99999" for standard deviation signifies data not reported as number of subject was 1 while for both arithmetic mean and standard deviation '99999' signifies data not applicable as there was no evaluable subject.

End point type	Secondary
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End point timeframe:

Baseline, Weeks 12, 24, 28, 32, 36, 40

End point values	Plovamer acetate 0.5 milligram (mg)	Plovamer acetate 3 mg	Plovamer acetate 10 mg	Plovamer acetate 20 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	45	45	43	41
Units: cubic millimeter (mm ³)				
arithmetic mean (standard deviation)				
Baseline (n=44,45,42,41,44)	12.24 (± 14.6956)	13.482 (± 19.0522)	11.364 (± 16.0282)	9.518 (± 13.2248)
Change at Week 12: (n=44,45,42,41,44)	0.443 (± 2.2414)	0.397 (± 1.0399)	0.686 (± 2.4894)	-0.2 (± 4.5312)
Change at Week 24: (n=16,17,20,18,19)	-0.179 (± 2.2741)	0.871 (± 2.7803)	0.113 (± 1.2011)	-1.734 (± 6.8085)

Change at Week 28: (n=9,11,12,12,13)	0.016 (± 3.2248)	0.858 (± 3.0417)	0.306 (± 1.1945)	-2.61 (± 8.3108)
Change at Week 32: (n=4,6,8,10,9)	0.874 (± 2.4859)	0.163 (± 1.2524)	-0.106 (± 1.3423)	-3.246 (± 9.3533)
Change at Week 36: (n=0,0,1,3,3)	99999 (± 99999)	99999 (± 99999)	1.236 (± 99999)	-10.324 (± 17.2227)
Change at Week 40: (n=0,0,0,1,1)	99999 (± 99999)	99999 (± 99999)	99999 (± 99999)	-29.965 (± 99999)

End point values	Copaxone 20 mg			
Subject group type	Reporting group			
Number of subjects analysed	44			
Units: cubic millimeter (mm ³)				
arithmetic mean (standard deviation)				
Baseline (n=44,45,42,41,44)	11.616 (± 15.496)			
Change at Week 12: (n=44,45,42,41,44)	0.06 (± 1.3886)			
Change at Week 24: (n=16,17,20,18,19)	-0.907 (± 2.5627)			
Change at Week 28: (n=9,11,12,12,13)	-1.379 (± 3.4251)			
Change at Week 32: (n=4,6,8,10,9)	-1.867 (± 3.6432)			
Change at Week 36: (n=0,0,1,3,3)	-4.433 (± 4.6895)			
Change at Week 40: (n=0,0,0,1,1)	-10.661 (± 99999)			

Statistical analyses

No statistical analyses for this end point

Secondary: Time to First Relapse

End point title	Time to First Relapse
End point description:	
Relapse was defined as new, worsening or recurrent neurological symptoms attributed to multiple sclerosis that last for at least 24 hours without fever or infection, or adverse reaction to prescribed medication, preceded by a stable or improving neurological status of at least 30 days. These new or worsening symptoms should be noted by the patient and must be accompanied by at least one of the following: An increase of greater than or equal to (≥) 1 grade in ≥2 functional scales of the Expanded Disability Status Scale (EDSS) or an increase of ≥2 grades in 1 functional scale of the EDSS or an increase of ≥ 0.5 or an increase of ≥1.0 in EDSS if the previous EDSS was 0.	
End point type	Secondary
End point timeframe:	
Baseline up to Week 40	

End point values	Plovamer acetate 0.5 milligram (mg)	Plovamer acetate 3 mg	Plovamer acetate 10 mg	Plovamer acetate 20 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	0 ^[2]	0 ^[3]	0 ^[4]	0 ^[5]
Units: rate				
arithmetic mean (standard deviation)	()	()	()	()

Notes:

[2] - The Outcome Measure was not derived due to early termination of the study.

[3] - The Outcome Measure was not derived due to early termination of the study.

[4] - The Outcome Measure was not derived due to early termination of the study.

[5] - The Outcome Measure was not derived due to early termination of the study.

End point values	Copaxone 20 mg			
Subject group type	Reporting group			
Number of subjects analysed	0 ^[6]			
Units: rate				
arithmetic mean (standard deviation)	()			

Notes:

[6] - The Outcome Measure was not derived due to early termination of the study.

Statistical analyses

No statistical analyses for this end point

Secondary: Mean Change From Baseline in Brain Volume per Subject

End point title	Mean Change From Baseline in Brain Volume per Subject
End point description:	Change from baseline in brain volume per subject was calculated using 5 series MRI scan.
End point type	Secondary
End point timeframe:	Baseline, Weeks 24, 28, 32, 36, 40

End point values	Plovamer acetate 0.5 milligram (mg)	Plovamer acetate 3 mg	Plovamer acetate 10 mg	Plovamer acetate 20 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	0 ^[7]	0 ^[8]	0 ^[9]	0 ^[10]
Units: cubic millimeter (mm ³)				
arithmetic mean (standard deviation)	()	()	()	()

Notes:

[7] - The Outcome Measure was not derived due to early termination of the study.

[8] - The Outcome Measure was not derived due to early termination of the study.

[9] - The Outcome Measure was not derived due to early termination of the study.

[10] - The Outcome Measure was not derived due to early termination of the study.

End point values	Copaxone 20 mg			
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Subject group type	Reporting group			
Number of subjects analysed	0 ^[11]			
Units: cubic millimeter (mm ³)				
arithmetic mean (standard deviation)	()			

Notes:

[11] - The Outcome Measure was not derived due to early termination of the study.

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Baseline up to end of treatment (week 40)

Assessment type	Non-systematic
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Dictionary used

Dictionary name	MedDRA
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Dictionary version	18.0
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Reporting groups

Reporting group title	Plovamer acetate 0.5 milligram (mg)
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Reporting group description:

Plovamer acetate was administered at a dose of 0.5 mg as weekly subcutaneous injection for 40 weeks up to a maximum of 14 months.

Reporting group title	Plovamer acetate 3 mg
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Reporting group description:

Plovamer acetate was administered at a dose of 3 mg as weekly subcutaneous injection for 40 weeks up to a maximum of 14 months.

Reporting group title	Plovamer acetate 10 mg
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Reporting group description:

Plovamer acetate was administered at a dose of 10 mg as weekly subcutaneous injection for 40 weeks up to a maximum of 14 months.

Reporting group title	Plovamer acetate 20 mg
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Reporting group description:

Plovamer acetate was administered as two subcutaneous injection of 10 mg weekly for 40 weeks up to a maximum of 14 months.

Reporting group title	Copaxone 20 mg
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Reporting group description:

Copaxone was administered at a dose of 20 mg as subcutaneous injection once daily for 40 weeks up to a maximum of 14 months.

Serious adverse events	Plovamer acetate 0.5 milligram (mg)	Plovamer acetate 3 mg	Plovamer acetate 10 mg
Total subjects affected by serious adverse events			
subjects affected / exposed	2 / 51 (3.92%)	0 / 49 (0.00%)	2 / 52 (3.85%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Injury, poisoning and procedural complications			
Alcohol poisoning			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 51 (0.00%)	0 / 49 (0.00%)	0 / 52 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vascular disorders			

Venous thrombosis alternative assessment type: Systematic			
subjects affected / exposed	1 / 51 (1.96%)	0 / 49 (0.00%)	0 / 52 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General disorders and administration site conditions			
Influenza like illness alternative assessment type: Systematic			
subjects affected / exposed	0 / 51 (0.00%)	0 / 49 (0.00%)	0 / 52 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Immune system disorders			
Drug hypersensitivity alternative assessment type: Systematic			
subjects affected / exposed	0 / 51 (0.00%)	0 / 49 (0.00%)	0 / 52 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Constipation alternative assessment type: Systematic			
subjects affected / exposed	1 / 51 (1.96%)	0 / 49 (0.00%)	0 / 52 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pancreatitis acute alternative assessment type: Systematic			
subjects affected / exposed	0 / 51 (0.00%)	0 / 49 (0.00%)	1 / 52 (1.92%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Psychiatric disorders			
Major depression alternative assessment type: Systematic			
subjects affected / exposed	0 / 51 (0.00%)	0 / 49 (0.00%)	0 / 52 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Suicidal ideation alternative assessment type: Systematic			
subjects affected / exposed	0 / 51 (0.00%)	0 / 49 (0.00%)	0 / 52 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Cellulitis			
subjects affected / exposed	1 / 51 (1.96%)	0 / 49 (0.00%)	0 / 52 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pyelonephritis			
subjects affected / exposed	0 / 51 (0.00%)	0 / 49 (0.00%)	1 / 52 (1.92%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Urinary tract infection			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 51 (1.96%)	0 / 49 (0.00%)	0 / 52 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	Plovamer acetate 20 mg	Copaxone 20 mg	
Total subjects affected by serious adverse events			
subjects affected / exposed	3 / 52 (5.77%)	0 / 50 (0.00%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events	0	0	
Injury, poisoning and procedural complications			
Alcohol poisoning			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 52 (1.92%)	0 / 50 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vascular disorders			
Venous thrombosis			
alternative assessment type: Systematic			

subjects affected / exposed	0 / 52 (0.00%)	0 / 50 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
General disorders and administration site conditions			
Influenza like illness			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 52 (1.92%)	0 / 50 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Immune system disorders			
Drug hypersensitivity			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 52 (1.92%)	0 / 50 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
Constipation			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 52 (0.00%)	0 / 50 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pancreatitis acute			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 52 (0.00%)	0 / 50 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Psychiatric disorders			
Major depression			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 52 (1.92%)	0 / 50 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Suicidal ideation			
alternative assessment type: Systematic			

subjects affected / exposed	1 / 52 (1.92%)	0 / 50 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Cellulitis			
subjects affected / exposed	0 / 52 (0.00%)	0 / 50 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pyelonephritis			
subjects affected / exposed	0 / 52 (0.00%)	0 / 50 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urinary tract infection			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 52 (0.00%)	0 / 50 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Frequency threshold for reporting non-serious adverse events: 0 %

Non-serious adverse events	Plovamer acetate 0.5 milligram (mg)	Plovamer acetate 3 mg	Plovamer acetate 10 mg
Total subjects affected by non-serious adverse events			
subjects affected / exposed	28 / 51 (54.90%)	34 / 49 (69.39%)	38 / 52 (73.08%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Fibroadenoma of breast			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 51 (0.00%)	1 / 49 (2.04%)	0 / 52 (0.00%)
occurrences (all)	0	1	0
Skin papilloma			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 51 (0.00%)	0 / 49 (0.00%)	0 / 52 (0.00%)
occurrences (all)	0	0	0
Vascular disorders			

Hypertension alternative assessment type: Systematic subjects affected / exposed occurrences (all)	0 / 51 (0.00%) 0	1 / 49 (2.04%) 1	0 / 52 (0.00%) 0
General disorders and administration site conditions			
Injection site pain alternative assessment type: Systematic subjects affected / exposed occurrences (all)	8 / 51 (15.69%) 8	20 / 49 (40.82%) 20	26 / 52 (50.00%) 26
Injection site erythema alternative assessment type: Systematic subjects affected / exposed occurrences (all)	10 / 51 (19.61%) 10	16 / 49 (32.65%) 16	14 / 52 (26.92%) 14
Injection site pruritus alternative assessment type: Systematic subjects affected / exposed occurrences (all)	3 / 51 (5.88%) 3	6 / 49 (12.24%) 6	10 / 52 (19.23%) 10
Injection site induration alternative assessment type: Systematic subjects affected / exposed occurrences (all)	1 / 51 (1.96%) 1	2 / 49 (4.08%) 2	5 / 52 (9.62%) 5
Injection site oedema alternative assessment type: Systematic subjects affected / exposed occurrences (all)	1 / 51 (1.96%) 1	1 / 49 (2.04%) 1	2 / 52 (3.85%) 2
Injection site bruising alternative assessment type: Systematic subjects affected / exposed occurrences (all)	3 / 51 (5.88%) 3	1 / 49 (2.04%) 1	0 / 52 (0.00%) 0
Influenza like illness alternative assessment type: Systematic subjects affected / exposed occurrences (all)	1 / 51 (1.96%) 1	1 / 49 (2.04%) 1	1 / 52 (1.92%) 1
Injection site haematoma alternative assessment type:			

Systematic			
subjects affected / exposed	1 / 51 (1.96%)	0 / 49 (0.00%)	0 / 52 (0.00%)
occurrences (all)	1	0	0
Injection site laceration			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 51 (0.00%)	1 / 49 (2.04%)	1 / 52 (1.92%)
occurrences (all)	0	1	1
Injection site nodule			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 51 (0.00%)	1 / 49 (2.04%)	2 / 52 (3.85%)
occurrences (all)	0	1	2
Injection site rash			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 51 (1.96%)	0 / 49 (0.00%)	1 / 52 (1.92%)
occurrences (all)	1	0	1
Pyrexia			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 51 (0.00%)	1 / 49 (2.04%)	0 / 52 (0.00%)
occurrences (all)	0	1	0
Asthenia			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 51 (0.00%)	1 / 49 (2.04%)	1 / 52 (1.92%)
occurrences (all)	0	1	1
Chest discomfort			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 51 (0.00%)	1 / 49 (2.04%)	0 / 52 (0.00%)
occurrences (all)	0	1	0
Chills			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 51 (0.00%)	1 / 49 (2.04%)	1 / 52 (1.92%)
occurrences (all)	0	1	1
Fatigue			
alternative assessment type: Systematic			

subjects affected / exposed	1 / 51 (1.96%)	1 / 49 (2.04%)	0 / 52 (0.00%)
occurrences (all)	1	1	0
Injection site haemorrhage			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 51 (0.00%)	0 / 49 (0.00%)	0 / 52 (0.00%)
occurrences (all)	0	0	0
Injection site paraesthesia			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 51 (1.96%)	0 / 49 (0.00%)	1 / 52 (1.92%)
occurrences (all)	1	0	1
Injection site swelling			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 51 (0.00%)	0 / 49 (0.00%)	1 / 52 (1.92%)
occurrences (all)	0	0	1
Oedema peripheral			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 51 (0.00%)	1 / 49 (2.04%)	0 / 52 (0.00%)
occurrences (all)	0	1	0
Chest pain			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 51 (0.00%)	1 / 49 (2.04%)	0 / 52 (0.00%)
occurrences (all)	0	1	0
Inflammation			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 51 (0.00%)	0 / 49 (0.00%)	1 / 52 (1.92%)
occurrences (all)	0	0	1
Injection site cyst			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 51 (0.00%)	0 / 49 (0.00%)	0 / 52 (0.00%)
occurrences (all)	0	0	0
Injection site mass			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 51 (0.00%)	0 / 49 (0.00%)	0 / 52 (0.00%)
occurrences (all)	0	0	0

Peripheral swelling alternative assessment type: Systematic subjects affected / exposed occurrences (all)	0 / 51 (0.00%) 0	0 / 49 (0.00%) 0	1 / 52 (1.92%) 1
Cyst alternative assessment type: Systematic subjects affected / exposed occurrences (all)	0 / 51 (0.00%) 0	0 / 49 (0.00%) 0	0 / 52 (0.00%) 0
Hyperthermia alternative assessment type: Systematic subjects affected / exposed occurrences (all)	0 / 51 (0.00%) 0	0 / 49 (0.00%) 0	0 / 52 (0.00%) 0
Injection site discolouration alternative assessment type: Systematic subjects affected / exposed occurrences (all)	0 / 51 (0.00%) 0	0 / 49 (0.00%) 0	0 / 52 (0.00%) 0
Injection site granuloma alternative assessment type: Systematic subjects affected / exposed occurrences (all)	0 / 51 (0.00%) 0	0 / 49 (0.00%) 0	0 / 52 (0.00%) 0
Pain alternative assessment type: Systematic subjects affected / exposed occurrences (all)	0 / 51 (0.00%) 0	0 / 49 (0.00%) 0	0 / 52 (0.00%) 0
Reproductive system and breast disorders Epididymal cyst alternative assessment type: Systematic subjects affected / exposed occurrences (all)	0 / 51 (0.00%) 0	0 / 49 (0.00%) 0	1 / 52 (1.92%) 1
Erectile dysfunction alternative assessment type: Systematic subjects affected / exposed occurrences (all)	0 / 51 (0.00%) 0	0 / 49 (0.00%) 0	1 / 52 (1.92%) 1
Benign prostatic hyperplasia alternative assessment type:			

Systematic subjects affected / exposed occurrences (all)	0 / 51 (0.00%) 0	0 / 49 (0.00%) 0	0 / 52 (0.00%) 0
Respiratory, thoracic and mediastinal disorders			
Bronchospasm alternative assessment type: Systematic subjects affected / exposed occurrences (all)	0 / 51 (0.00%) 0	0 / 49 (0.00%) 0	1 / 52 (1.92%) 1
Cough alternative assessment type: Systematic subjects affected / exposed occurrences (all)	0 / 51 (0.00%) 0	1 / 49 (2.04%) 1	0 / 52 (0.00%) 0
Dysphonia alternative assessment type: Systematic subjects affected / exposed occurrences (all)	1 / 51 (1.96%) 1	0 / 49 (0.00%) 0	0 / 52 (0.00%) 0
Dyspnoea alternative assessment type: Systematic subjects affected / exposed occurrences (all)	0 / 51 (0.00%) 0	1 / 49 (2.04%) 1	0 / 52 (0.00%) 0
Psychiatric disorders			
Depression alternative assessment type: Systematic subjects affected / exposed occurrences (all)	1 / 51 (1.96%) 1	1 / 49 (2.04%) 1	2 / 52 (3.85%) 2
Depressive symptom alternative assessment type: Systematic subjects affected / exposed occurrences (all)	0 / 51 (0.00%) 0	2 / 49 (4.08%) 2	1 / 52 (1.92%) 1
Anxiety alternative assessment type: Systematic subjects affected / exposed occurrences (all)	1 / 51 (1.96%) 1	1 / 49 (2.04%) 1	0 / 52 (0.00%) 0
Panic attack alternative assessment type: Systematic			

subjects affected / exposed	0 / 51 (0.00%)	2 / 49 (4.08%)	0 / 52 (0.00%)
occurrences (all)	0	2	0
Adjustment disorder			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 51 (0.00%)	0 / 49 (0.00%)	1 / 52 (1.92%)
occurrences (all)	0	0	1
Affective disorder			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 51 (0.00%)	0 / 49 (0.00%)	0 / 52 (0.00%)
occurrences (all)	0	0	0
Depressed mood			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 51 (0.00%)	0 / 49 (0.00%)	1 / 52 (1.92%)
occurrences (all)	0	0	1
Emotional disorder			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 51 (0.00%)	1 / 49 (2.04%)	0 / 52 (0.00%)
occurrences (all)	0	1	0
Insomnia			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 51 (0.00%)	1 / 49 (2.04%)	0 / 52 (0.00%)
occurrences (all)	0	1	0
Mood altered			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 51 (1.96%)	0 / 49 (0.00%)	0 / 52 (0.00%)
occurrences (all)	1	0	0
Nightmare			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 51 (0.00%)	1 / 49 (2.04%)	0 / 52 (0.00%)
occurrences (all)	0	1	0
Investigations			
Alanine aminotransferase increased			
alternative assessment type: Systematic			

subjects affected / exposed	0 / 51 (0.00%)	0 / 49 (0.00%)	0 / 52 (0.00%)
occurrences (all)	0	0	0
Gamma-glutamyltransferase increased			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 51 (0.00%)	0 / 49 (0.00%)	1 / 52 (1.92%)
occurrences (all)	0	0	1
Aspartate aminotransferase increased			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 51 (0.00%)	0 / 49 (0.00%)	0 / 52 (0.00%)
occurrences (all)	0	0	0
Electrocardiogram PR shortened			
subjects affected / exposed	0 / 51 (0.00%)	1 / 49 (2.04%)	0 / 52 (0.00%)
occurrences (all)	0	1	0
Liver function test abnormal			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 51 (0.00%)	0 / 49 (0.00%)	0 / 52 (0.00%)
occurrences (all)	0	0	0
Injury, poisoning and procedural complications			
Head injury			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 51 (1.96%)	0 / 49 (0.00%)	0 / 52 (0.00%)
occurrences (all)	1	0	0
Ligament sprain			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 51 (0.00%)	0 / 49 (0.00%)	1 / 52 (1.92%)
occurrences (all)	0	0	1
Sunburn			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 51 (0.00%)	1 / 49 (2.04%)	0 / 52 (0.00%)
occurrences (all)	0	1	0
Wound			
alternative assessment type: Systematic			

subjects affected / exposed	0 / 51 (0.00%)	0 / 49 (0.00%)	1 / 52 (1.92%)
occurrences (all)	0	0	1
Arthropod sting			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 51 (0.00%)	0 / 49 (0.00%)	0 / 52 (0.00%)
occurrences (all)	0	0	0
Cardiac disorders			
Hypertensive heart disease			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 51 (0.00%)	1 / 49 (2.04%)	0 / 52 (0.00%)
occurrences (all)	0	1	0
Palpitations			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 51 (0.00%)	0 / 49 (0.00%)	1 / 52 (1.92%)
occurrences (all)	0	0	1
Supraventricular tachycardia			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 51 (1.96%)	0 / 49 (0.00%)	0 / 52 (0.00%)
occurrences (all)	1	0	0
Nervous system disorders			
Headache			
alternative assessment type: Systematic			
subjects affected / exposed	4 / 51 (7.84%)	0 / 49 (0.00%)	1 / 52 (1.92%)
occurrences (all)	4	0	1
Dizziness			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 51 (0.00%)	1 / 49 (2.04%)	1 / 52 (1.92%)
occurrences (all)	0	1	1
Carpal tunnel syndrome			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 51 (0.00%)	0 / 49 (0.00%)	0 / 52 (0.00%)
occurrences (all)	0	0	0
Essential tremor			
alternative assessment type: Systematic			

subjects affected / exposed	0 / 51 (0.00%)	0 / 49 (0.00%)	0 / 52 (0.00%)
occurrences (all)	0	0	0
Muscle spasticity			
subjects affected / exposed	0 / 51 (0.00%)	0 / 49 (0.00%)	1 / 52 (1.92%)
occurrences (all)	0	0	1
Paraesthesia			
subjects affected / exposed	1 / 51 (1.96%)	0 / 49 (0.00%)	0 / 52 (0.00%)
occurrences (all)	1	0	0
Radicular pain			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 51 (0.00%)	0 / 49 (0.00%)	0 / 52 (0.00%)
occurrences (all)	0	0	0
Restless legs syndrome			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 51 (0.00%)	0 / 49 (0.00%)	1 / 52 (1.92%)
occurrences (all)	0	0	1
Loss of consciousness			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 51 (0.00%)	0 / 49 (0.00%)	0 / 52 (0.00%)
occurrences (all)	0	0	0
Perineurial cyst			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 51 (0.00%)	0 / 49 (0.00%)	0 / 52 (0.00%)
occurrences (all)	0	0	0
Peripheral sensory neuropathy			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 51 (0.00%)	0 / 49 (0.00%)	0 / 52 (0.00%)
occurrences (all)	0	0	0
Blood and lymphatic system disorders			
Increased tendency to bruise			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 51 (0.00%)	1 / 49 (2.04%)	0 / 52 (0.00%)
occurrences (all)	0	1	0
Ear and labyrinth disorders			

Tinnitus alternative assessment type: Systematic subjects affected / exposed occurrences (all)	0 / 51 (0.00%) 0	0 / 49 (0.00%) 0	0 / 52 (0.00%) 0
Vertigo alternative assessment type: Systematic subjects affected / exposed occurrences (all)	1 / 51 (1.96%) 1	0 / 49 (0.00%) 0	0 / 52 (0.00%) 0
Eye disorders Eyelid skin dryness alternative assessment type: Systematic subjects affected / exposed occurrences (all)	0 / 51 (0.00%) 0	0 / 49 (0.00%) 0	0 / 52 (0.00%) 0
Iritis alternative assessment type: Systematic subjects affected / exposed occurrences (all)	0 / 51 (0.00%) 0	1 / 49 (2.04%) 1	0 / 52 (0.00%) 0
Vision blurred alternative assessment type: Systematic subjects affected / exposed occurrences (all)	1 / 51 (1.96%) 1	0 / 49 (0.00%) 0	0 / 52 (0.00%) 0
Gastrointestinal disorders Nausea alternative assessment type: Systematic subjects affected / exposed occurrences (all)	2 / 51 (3.92%) 2	0 / 49 (0.00%) 0	2 / 52 (3.85%) 2
Constipation alternative assessment type: Systematic subjects affected / exposed occurrences (all)	0 / 51 (0.00%) 0	0 / 49 (0.00%) 0	1 / 52 (1.92%) 1
Diarrhoea alternative assessment type: Systematic subjects affected / exposed occurrences (all)	0 / 51 (0.00%) 0	2 / 49 (4.08%) 2	0 / 52 (0.00%) 0
Abdominal pain lower			

<p>alternative assessment type: Systematic</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p>	<p>0 / 51 (0.00%)</p> <p>0</p>	<p>0 / 49 (0.00%)</p> <p>0</p>	<p>1 / 52 (1.92%)</p> <p>1</p>
<p>Abdominal pain upper</p> <p>alternative assessment type: Systematic</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p>	<p>0 / 51 (0.00%)</p> <p>0</p>	<p>0 / 49 (0.00%)</p> <p>0</p>	<p>0 / 52 (0.00%)</p> <p>0</p>
<p>Melanositis coli</p> <p>alternative assessment type: Systematic</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p>	<p>1 / 51 (1.96%)</p> <p>1</p>	<p>0 / 49 (0.00%)</p> <p>0</p>	<p>0 / 52 (0.00%)</p> <p>0</p>
<p>Abdominal rigidity</p> <p>alternative assessment type: Systematic</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p>	<p>0 / 51 (0.00%)</p> <p>0</p>	<p>0 / 49 (0.00%)</p> <p>0</p>	<p>0 / 52 (0.00%)</p> <p>0</p>
<p>Hepatobiliary disorders</p> <p>Cholecystitis acute</p> <p>alternative assessment type: Systematic</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p>	<p>0 / 51 (0.00%)</p> <p>0</p>	<p>0 / 49 (0.00%)</p> <p>0</p>	<p>1 / 52 (1.92%)</p> <p>1</p>
<p>Cholelithiasis</p> <p>alternative assessment type: Systematic</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p>	<p>0 / 51 (0.00%)</p> <p>0</p>	<p>0 / 49 (0.00%)</p> <p>0</p>	<p>1 / 52 (1.92%)</p> <p>1</p>
<p>Hepatomegaly</p> <p>alternative assessment type: Systematic</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p>	<p>0 / 51 (0.00%)</p> <p>0</p>	<p>0 / 49 (0.00%)</p> <p>0</p>	<p>0 / 52 (0.00%)</p> <p>0</p>
<p>Skin and subcutaneous tissue disorders</p> <p>Alopecia</p> <p>alternative assessment type: Systematic</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p>	<p>1 / 51 (1.96%)</p> <p>1</p>	<p>0 / 49 (0.00%)</p> <p>0</p>	<p>1 / 52 (1.92%)</p> <p>1</p>
<p>Acne</p> <p>alternative assessment type: Systematic</p>			

<p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>Ecchymosis</p> <p>alternative assessment type: Systematic</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>Erythema</p> <p>alternative assessment type: Systematic</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p>	<p>1 / 51 (1.96%)</p> <p>1</p> <p>0 / 51 (0.00%)</p> <p>0</p> <p>0 / 51 (0.00%)</p> <p>0</p>	<p>0 / 49 (0.00%)</p> <p>0</p> <p>0 / 49 (0.00%)</p> <p>0</p> <p>1 / 49 (2.04%)</p> <p>1</p>	<p>0 / 52 (0.00%)</p> <p>0</p> <p>0 / 52 (0.00%)</p> <p>0</p> <p>0 / 52 (0.00%)</p> <p>0</p>
<p>Renal and urinary disorders</p> <p>Urinary hesitation</p> <p>alternative assessment type: Systematic</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>Urinary incontinence</p> <p>alternative assessment type: Systematic</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p>	<p>0 / 51 (0.00%)</p> <p>0</p> <p>1 / 51 (1.96%)</p> <p>1</p>	<p>0 / 49 (0.00%)</p> <p>0</p> <p>0 / 49 (0.00%)</p> <p>0</p>	<p>1 / 52 (1.92%)</p> <p>1</p> <p>0 / 52 (0.00%)</p> <p>0</p>
<p>Musculoskeletal and connective tissue disorders</p> <p>Back pain</p> <p>alternative assessment type: Systematic</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>Pain in extremity</p> <p>alternative assessment type: Systematic</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>Muscular weakness</p> <p>alternative assessment type: Systematic</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>Neck pain</p> <p>alternative assessment type: Systematic</p>	<p>3 / 51 (5.88%)</p> <p>3</p> <p>1 / 51 (1.96%)</p> <p>1</p> <p>1 / 51 (1.96%)</p> <p>1</p>	<p>0 / 49 (0.00%)</p> <p>0</p> <p>0 / 49 (0.00%)</p> <p>0</p> <p>0 / 49 (0.00%)</p> <p>0</p>	<p>1 / 52 (1.92%)</p> <p>1</p> <p>1 / 52 (1.92%)</p> <p>1</p> <p>1 / 52 (1.92%)</p> <p>1</p>

subjects affected / exposed	1 / 51 (1.96%)	1 / 49 (2.04%)	0 / 52 (0.00%)
occurrences (all)	1	1	0
Joint stiffness			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 51 (0.00%)	0 / 49 (0.00%)	0 / 52 (0.00%)
occurrences (all)	0	0	0
Muscle spasms			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 51 (1.96%)	0 / 49 (0.00%)	0 / 52 (0.00%)
occurrences (all)	1	0	0
Myalgia			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 51 (1.96%)	0 / 49 (0.00%)	0 / 52 (0.00%)
occurrences (all)	1	0	0
Myokymia			
subjects affected / exposed	0 / 51 (0.00%)	1 / 49 (2.04%)	0 / 52 (0.00%)
occurrences (all)	0	1	0
Osteoarthritis			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 51 (0.00%)	0 / 49 (0.00%)	0 / 52 (0.00%)
occurrences (all)	0	0	0
Infections and infestations			
Nasopharyngitis			
subjects affected / exposed	1 / 51 (1.96%)	0 / 49 (0.00%)	1 / 52 (1.92%)
occurrences (all)	1	0	1
Upper respiratory tract infection			
subjects affected / exposed	1 / 51 (1.96%)	0 / 49 (0.00%)	1 / 52 (1.92%)
occurrences (all)	1	0	1
Urinary tract infection			
alternative assessment type: Systematic			
subjects affected / exposed	2 / 51 (3.92%)	0 / 49 (0.00%)	1 / 52 (1.92%)
occurrences (all)	2	0	1
Bronchitis			
alternative assessment type: Systematic			

subjects affected / exposed	1 / 51 (1.96%)	1 / 49 (2.04%)	1 / 52 (1.92%)
occurrences (all)	1	1	1
Cystitis			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 51 (0.00%)	1 / 49 (2.04%)	2 / 52 (3.85%)
occurrences (all)	0	1	2
Tonsillitis			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 51 (0.00%)	0 / 49 (0.00%)	2 / 52 (3.85%)
occurrences (all)	0	0	2
Gastroenteritis			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 51 (0.00%)	2 / 49 (4.08%)	1 / 52 (1.92%)
occurrences (all)	0	2	1
Conjunctivitis			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 51 (0.00%)	1 / 49 (2.04%)	1 / 52 (1.92%)
occurrences (all)	0	1	1
Erythema migrans			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 51 (0.00%)	0 / 49 (0.00%)	0 / 52 (0.00%)
occurrences (all)	0	0	0
Herpes simplex			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 51 (0.00%)	1 / 49 (2.04%)	1 / 52 (1.92%)
occurrences (all)	0	1	1
Chronic tonsillitis			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 51 (0.00%)	0 / 49 (0.00%)	1 / 52 (1.92%)
occurrences (all)	0	0	1
Gastroenteritis viral			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 51 (0.00%)	1 / 49 (2.04%)	0 / 52 (0.00%)
occurrences (all)	0	1	0

Ear infection			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 51 (0.00%)	1 / 49 (2.04%)	0 / 52 (0.00%)
occurrences (all)	0	1	0
Herpes zoster			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 51 (1.96%)	0 / 49 (0.00%)	0 / 52 (0.00%)
occurrences (all)	1	0	0
Influenza			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 51 (0.00%)	0 / 49 (0.00%)	0 / 52 (0.00%)
occurrences (all)	0	0	0
Laryngitis			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 51 (0.00%)	0 / 49 (0.00%)	0 / 52 (0.00%)
occurrences (all)	0	0	0
Pneumonia			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 51 (0.00%)	0 / 49 (0.00%)	0 / 52 (0.00%)
occurrences (all)	0	0	0
Tracheitis			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 51 (0.00%)	0 / 49 (0.00%)	1 / 52 (1.92%)
occurrences (all)	0	0	1
Urethritis			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 51 (0.00%)	0 / 49 (0.00%)	0 / 52 (0.00%)
occurrences (all)	0	0	0
Sinusitis			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 51 (0.00%)	0 / 49 (0.00%)	0 / 52 (0.00%)
occurrences (all)	0	0	0
Metabolism and nutrition disorders			

Hypertriglyceridaemia alternative assessment type: Systematic subjects affected / exposed occurrences (all)	0 / 51 (0.00%) 0	0 / 49 (0.00%) 0	0 / 52 (0.00%) 0
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Non-serious adverse events	Plovamer acetate 20 mg	Copaxone 20 mg	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	41 / 52 (78.85%)	42 / 50 (84.00%)	
Neoplasms benign, malignant and unspecified (incl cysts and polyps) Fibroadenoma of breast alternative assessment type: Systematic subjects affected / exposed occurrences (all)	0 / 52 (0.00%) 0	0 / 50 (0.00%) 0	
Skin papilloma alternative assessment type: Systematic subjects affected / exposed occurrences (all)	0 / 52 (0.00%) 0	1 / 50 (2.00%) 1	
Vascular disorders Hypertension alternative assessment type: Systematic subjects affected / exposed occurrences (all)	1 / 52 (1.92%) 1	0 / 50 (0.00%) 0	
General disorders and administration site conditions Injection site pain alternative assessment type: Systematic subjects affected / exposed occurrences (all)	26 / 52 (50.00%) 26	28 / 50 (56.00%) 28	
Injection site erythema alternative assessment type: Systematic subjects affected / exposed occurrences (all)	19 / 52 (36.54%) 19	18 / 50 (36.00%) 18	
Injection site pruritus alternative assessment type: Systematic subjects affected / exposed occurrences (all)	4 / 52 (7.69%) 4	15 / 50 (30.00%) 15	

Injection site induration			
alternative assessment type:			
Systematic			
subjects affected / exposed	6 / 52 (11.54%)	4 / 50 (8.00%)	
occurrences (all)	6	4	
Injection site oedema			
alternative assessment type:			
Systematic			
subjects affected / exposed	2 / 52 (3.85%)	2 / 50 (4.00%)	
occurrences (all)	2	2	
Injection site bruising			
alternative assessment type:			
Systematic			
subjects affected / exposed	1 / 52 (1.92%)	3 / 50 (6.00%)	
occurrences (all)	1	3	
Influenza like illness			
alternative assessment type:			
Systematic			
subjects affected / exposed	0 / 52 (0.00%)	1 / 50 (2.00%)	
occurrences (all)	0	1	
Injection site haematoma			
alternative assessment type:			
Systematic			
subjects affected / exposed	2 / 52 (3.85%)	4 / 50 (8.00%)	
occurrences (all)	2	4	
Injection site laceration			
alternative assessment type:			
Systematic			
subjects affected / exposed	1 / 52 (1.92%)	0 / 50 (0.00%)	
occurrences (all)	1	0	
Injection site nodule			
alternative assessment type:			
Systematic			
subjects affected / exposed	0 / 52 (0.00%)	0 / 50 (0.00%)	
occurrences (all)	0	0	
Injection site rash			
alternative assessment type:			
Systematic			
subjects affected / exposed	1 / 52 (1.92%)	0 / 50 (0.00%)	
occurrences (all)	1	0	
Pyrexia			
alternative assessment type:			
Systematic			

subjects affected / exposed	2 / 52 (3.85%)	0 / 50 (0.00%)
occurrences (all)	2	0
Asthenia		
alternative assessment type: Systematic		
subjects affected / exposed	0 / 52 (0.00%)	0 / 50 (0.00%)
occurrences (all)	0	0
Chest discomfort		
alternative assessment type: Systematic		
subjects affected / exposed	1 / 52 (1.92%)	0 / 50 (0.00%)
occurrences (all)	1	0
Chills		
alternative assessment type: Systematic		
subjects affected / exposed	0 / 52 (0.00%)	0 / 50 (0.00%)
occurrences (all)	0	0
Fatigue		
alternative assessment type: Systematic		
subjects affected / exposed	0 / 52 (0.00%)	1 / 50 (2.00%)
occurrences (all)	0	1
Injection site haemorrhage		
alternative assessment type: Systematic		
subjects affected / exposed	2 / 52 (3.85%)	0 / 50 (0.00%)
occurrences (all)	2	0
Injection site paraesthesia		
alternative assessment type: Systematic		
subjects affected / exposed	0 / 52 (0.00%)	0 / 50 (0.00%)
occurrences (all)	0	0
Injection site swelling		
alternative assessment type: Systematic		
subjects affected / exposed	1 / 52 (1.92%)	1 / 50 (2.00%)
occurrences (all)	1	1
Oedema peripheral		
alternative assessment type: Systematic		
subjects affected / exposed	1 / 52 (1.92%)	0 / 50 (0.00%)
occurrences (all)	1	0

Chest pain			
alternative assessment type:			
Systematic			
subjects affected / exposed	0 / 52 (0.00%)	0 / 50 (0.00%)	
occurrences (all)	0	0	
Inflammation			
alternative assessment type:			
Systematic			
subjects affected / exposed	0 / 52 (0.00%)	0 / 50 (0.00%)	
occurrences (all)	0	0	
Injection site cyst			
alternative assessment type:			
Systematic			
subjects affected / exposed	1 / 52 (1.92%)	0 / 50 (0.00%)	
occurrences (all)	1	0	
Injection site mass			
alternative assessment type:			
Systematic			
subjects affected / exposed	1 / 52 (1.92%)	0 / 50 (0.00%)	
occurrences (all)	1	0	
Peripheral swelling			
alternative assessment type:			
Systematic			
subjects affected / exposed	0 / 52 (0.00%)	0 / 50 (0.00%)	
occurrences (all)	0	0	
Cyst			
alternative assessment type:			
Systematic			
subjects affected / exposed	0 / 52 (0.00%)	1 / 50 (2.00%)	
occurrences (all)	0	1	
Hyperthermia			
alternative assessment type:			
Systematic			
subjects affected / exposed	0 / 52 (0.00%)	1 / 50 (2.00%)	
occurrences (all)	0	1	
Injection site discolouration			
alternative assessment type:			
Systematic			
subjects affected / exposed	0 / 52 (0.00%)	1 / 50 (2.00%)	
occurrences (all)	0	1	
Injection site granuloma			
alternative assessment type:			
Systematic			

<p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>Pain</p> <p>alternative assessment type: Systematic</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p>	<p>0 / 52 (0.00%)</p> <p>0</p> <p>0 / 52 (0.00%)</p> <p>0</p>	<p>1 / 50 (2.00%)</p> <p>1</p> <p>1 / 50 (2.00%)</p> <p>1</p>	
<p>Reproductive system and breast disorders</p> <p>Epididymal cyst</p> <p>alternative assessment type: Systematic</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>Erectile dysfunction</p> <p>alternative assessment type: Systematic</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>Benign prostatic hyperplasia</p> <p>alternative assessment type: Systematic</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p>	<p>0 / 52 (0.00%)</p> <p>0</p> <p>0 / 52 (0.00%)</p> <p>0</p> <p>0 / 52 (0.00%)</p> <p>0</p> <p>0 / 52 (0.00%)</p> <p>0</p>	<p>0 / 50 (0.00%)</p> <p>0</p> <p>0 / 50 (0.00%)</p> <p>0</p> <p>1 / 50 (2.00%)</p> <p>1</p>	
<p>Respiratory, thoracic and mediastinal disorders</p> <p>Bronchospasm</p> <p>alternative assessment type: Systematic</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>Cough</p> <p>alternative assessment type: Systematic</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>Dysphonia</p> <p>alternative assessment type: Systematic</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>Dyspnoea</p> <p>alternative assessment type: Systematic</p>	<p>0 / 52 (0.00%)</p> <p>0</p> <p>0 / 52 (0.00%)</p> <p>0</p> <p>0 / 52 (0.00%)</p> <p>0</p> <p>0 / 52 (0.00%)</p> <p>0</p>	<p>0 / 50 (0.00%)</p> <p>0</p> <p>0 / 50 (0.00%)</p> <p>0</p> <p>0 / 50 (0.00%)</p> <p>0</p>	

subjects affected / exposed	0 / 52 (0.00%)	0 / 50 (0.00%)	
occurrences (all)	0	0	
Psychiatric disorders			
Depression			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 52 (0.00%)	0 / 50 (0.00%)	
occurrences (all)	0	0	
Depressive symptom			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 52 (0.00%)	0 / 50 (0.00%)	
occurrences (all)	0	0	
Anxiety			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 52 (0.00%)	1 / 50 (2.00%)	
occurrences (all)	0	1	
Panic attack			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 52 (0.00%)	0 / 50 (0.00%)	
occurrences (all)	0	0	
Adjustment disorder			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 52 (0.00%)	0 / 50 (0.00%)	
occurrences (all)	0	0	
Affective disorder			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 52 (1.92%)	0 / 50 (0.00%)	
occurrences (all)	1	0	
Depressed mood			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 52 (0.00%)	1 / 50 (2.00%)	
occurrences (all)	0	1	
Emotional disorder			
alternative assessment type: Systematic			

subjects affected / exposed	0 / 52 (0.00%)	0 / 50 (0.00%)	
occurrences (all)	0	0	
Insomnia			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 52 (0.00%)	0 / 50 (0.00%)	
occurrences (all)	0	0	
Mood altered			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 52 (0.00%)	0 / 50 (0.00%)	
occurrences (all)	0	0	
Nightmare			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 52 (0.00%)	0 / 50 (0.00%)	
occurrences (all)	0	0	
Investigations			
Alanine aminotransferase increased			
alternative assessment type: Systematic			
subjects affected / exposed	2 / 52 (3.85%)	0 / 50 (0.00%)	
occurrences (all)	2	0	
Gamma-glutamyltransferase increased			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 52 (1.92%)	2 / 50 (4.00%)	
occurrences (all)	1	2	
Aspartate aminotransferase increased			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 52 (1.92%)	0 / 50 (0.00%)	
occurrences (all)	1	0	
Electrocardiogram PR shortened			
subjects affected / exposed	0 / 52 (0.00%)	0 / 50 (0.00%)	
occurrences (all)	0	0	
Liver function test abnormal			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 52 (1.92%)	0 / 50 (0.00%)	
occurrences (all)	1	0	

Injury, poisoning and procedural complications Head injury alternative assessment type: Systematic subjects affected / exposed occurrences (all) Ligament sprain alternative assessment type: Systematic subjects affected / exposed occurrences (all) Sunburn alternative assessment type: Systematic subjects affected / exposed occurrences (all) Wound alternative assessment type: Systematic subjects affected / exposed occurrences (all) Arthropod sting alternative assessment type: Systematic subjects affected / exposed occurrences (all)	 0 / 52 (0.00%) 0 0 / 52 (0.00%) 0 0 / 52 (0.00%) 0 0 / 52 (0.00%) 0 0 / 52 (0.00%) 0 0 / 52 (0.00%) 0 0 / 52 (0.00%) 0	 0 / 50 (0.00%) 0 0 / 50 (0.00%) 0 0 / 50 (0.00%) 0 0 / 50 (0.00%) 0 0 / 50 (0.00%) 0 1 / 50 (2.00%) 1	
Cardiac disorders Hypertensive heart disease alternative assessment type: Systematic subjects affected / exposed occurrences (all) Palpitations alternative assessment type: Systematic subjects affected / exposed occurrences (all) Supraventricular tachycardia alternative assessment type: Systematic subjects affected / exposed occurrences (all)	 0 / 52 (0.00%) 0 0 / 52 (0.00%) 0 0 / 52 (0.00%) 0	 0 / 50 (0.00%) 0 0 / 50 (0.00%) 0 0 / 50 (0.00%) 0	
Nervous system disorders			

Headache		
alternative assessment type: Systematic		
subjects affected / exposed	4 / 52 (7.69%)	0 / 50 (0.00%)
occurrences (all)	4	0
Dizziness		
alternative assessment type: Systematic		
subjects affected / exposed	2 / 52 (3.85%)	1 / 50 (2.00%)
occurrences (all)	2	1
Carpal tunnel syndrome		
alternative assessment type: Systematic		
subjects affected / exposed	1 / 52 (1.92%)	0 / 50 (0.00%)
occurrences (all)	1	0
Essential tremor		
alternative assessment type: Systematic		
subjects affected / exposed	1 / 52 (1.92%)	0 / 50 (0.00%)
occurrences (all)	1	0
Muscle spasticity		
subjects affected / exposed	0 / 52 (0.00%)	0 / 50 (0.00%)
occurrences (all)	0	0
Paraesthesia		
subjects affected / exposed	0 / 52 (0.00%)	0 / 50 (0.00%)
occurrences (all)	0	0
Radicular pain		
alternative assessment type: Systematic		
subjects affected / exposed	1 / 52 (1.92%)	0 / 50 (0.00%)
occurrences (all)	1	0
Restless legs syndrome		
alternative assessment type: Systematic		
subjects affected / exposed	0 / 52 (0.00%)	0 / 50 (0.00%)
occurrences (all)	0	0
Loss of consciousness		
alternative assessment type: Systematic		
subjects affected / exposed	0 / 52 (0.00%)	1 / 50 (2.00%)
occurrences (all)	0	1
Perineurial cyst		

alternative assessment type: Systematic subjects affected / exposed occurrences (all)	0 / 52 (0.00%) 0	1 / 50 (2.00%) 1	
Peripheral sensory neuropathy alternative assessment type: Systematic subjects affected / exposed occurrences (all)	0 / 52 (0.00%) 0	1 / 50 (2.00%) 1	
Blood and lymphatic system disorders Increased tendency to bruise alternative assessment type: Systematic subjects affected / exposed occurrences (all)	0 / 52 (0.00%) 0	0 / 50 (0.00%) 0	
Ear and labyrinth disorders Tinnitus alternative assessment type: Systematic subjects affected / exposed occurrences (all) Vertigo alternative assessment type: Systematic subjects affected / exposed occurrences (all)	1 / 52 (1.92%) 1 0 / 52 (0.00%) 0	0 / 50 (0.00%) 0 0 / 50 (0.00%) 0	
Eye disorders Eyelid skin dryness alternative assessment type: Systematic subjects affected / exposed occurrences (all) Iritis alternative assessment type: Systematic subjects affected / exposed occurrences (all) Vision blurred alternative assessment type: Systematic subjects affected / exposed occurrences (all)	1 / 52 (1.92%) 1 0 / 52 (0.00%) 0 0 / 52 (0.00%) 0	0 / 50 (0.00%) 0 0 / 50 (0.00%) 0 0 / 50 (0.00%) 0	
Gastrointestinal disorders			

Nausea			
alternative assessment type: Systematic			
subjects affected / exposed	2 / 52 (3.85%)	2 / 50 (4.00%)	
occurrences (all)	2	2	
Constipation			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 52 (0.00%)	0 / 50 (0.00%)	
occurrences (all)	0	0	
Diarrhoea			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 52 (0.00%)	0 / 50 (0.00%)	
occurrences (all)	0	0	
Abdominal pain lower			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 52 (0.00%)	0 / 50 (0.00%)	
occurrences (all)	0	0	
Abdominal pain upper			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 52 (1.92%)	0 / 50 (0.00%)	
occurrences (all)	1	0	
Melanosis coli			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 52 (0.00%)	0 / 50 (0.00%)	
occurrences (all)	0	0	
Abdominal rigidity			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 52 (0.00%)	1 / 50 (2.00%)	
occurrences (all)	0	1	
Hepatobiliary disorders			
Cholecystitis acute			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 52 (0.00%)	0 / 50 (0.00%)	
occurrences (all)	0	0	
Cholelithiasis			
alternative assessment type: Systematic			

<p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>Hepatomegaly</p> <p>alternative assessment type: Systematic</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p>	<p>0 / 52 (0.00%)</p> <p>0</p> <p>1 / 52 (1.92%)</p> <p>1</p>	<p>0 / 50 (0.00%)</p> <p>0</p> <p>0 / 50 (0.00%)</p> <p>0</p>	
<p>Skin and subcutaneous tissue disorders</p> <p>Alopecia</p> <p>alternative assessment type: Systematic</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>Acne</p> <p>alternative assessment type: Systematic</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>Ecchymosis</p> <p>alternative assessment type: Systematic</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>Erythema</p> <p>alternative assessment type: Systematic</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p>	<p>0 / 52 (0.00%)</p> <p>0</p> <p>0 / 52 (0.00%)</p> <p>0</p> <p>1 / 52 (1.92%)</p> <p>1</p> <p>0 / 52 (0.00%)</p> <p>0</p>	<p>0 / 50 (0.00%)</p> <p>0</p> <p>0 / 50 (0.00%)</p> <p>0</p> <p>0 / 50 (0.00%)</p> <p>0</p>	
<p>Renal and urinary disorders</p> <p>Urinary hesitation</p> <p>alternative assessment type: Systematic</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>Urinary incontinence</p> <p>alternative assessment type: Systematic</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p>	<p>0 / 52 (0.00%)</p> <p>0</p> <p>0 / 52 (0.00%)</p> <p>0</p>	<p>0 / 50 (0.00%)</p> <p>0</p> <p>0 / 50 (0.00%)</p> <p>0</p>	
<p>Musculoskeletal and connective tissue disorders</p>			

Back pain			
alternative assessment type:			
Systematic			
subjects affected / exposed	0 / 52 (0.00%)	0 / 50 (0.00%)	
occurrences (all)	0	0	
Pain in extremity			
alternative assessment type:			
Systematic			
subjects affected / exposed	1 / 52 (1.92%)	0 / 50 (0.00%)	
occurrences (all)	1	0	
Muscular weakness			
alternative assessment type:			
Systematic			
subjects affected / exposed	0 / 52 (0.00%)	0 / 50 (0.00%)	
occurrences (all)	0	0	
Neck pain			
alternative assessment type:			
Systematic			
subjects affected / exposed	0 / 52 (0.00%)	0 / 50 (0.00%)	
occurrences (all)	0	0	
Joint stiffness			
alternative assessment type:			
Systematic			
subjects affected / exposed	1 / 52 (1.92%)	0 / 50 (0.00%)	
occurrences (all)	1	0	
Muscle spasms			
alternative assessment type:			
Systematic			
subjects affected / exposed	0 / 52 (0.00%)	0 / 50 (0.00%)	
occurrences (all)	0	0	
Myalgia			
alternative assessment type:			
Systematic			
subjects affected / exposed	0 / 52 (0.00%)	0 / 50 (0.00%)	
occurrences (all)	0	0	
Myokymia			
subjects affected / exposed	0 / 52 (0.00%)	0 / 50 (0.00%)	
occurrences (all)	0	0	
Osteoarthritis			
alternative assessment type:			
Systematic			

subjects affected / exposed occurrences (all)	0 / 52 (0.00%) 0	1 / 50 (2.00%) 1	
Infections and infestations			
Nasopharyngitis			
subjects affected / exposed	6 / 52 (11.54%)	0 / 50 (0.00%)	
occurrences (all)	6	0	
Upper respiratory tract infection			
subjects affected / exposed	3 / 52 (5.77%)	4 / 50 (8.00%)	
occurrences (all)	3	4	
Urinary tract infection			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 52 (0.00%)	1 / 50 (2.00%)	
occurrences (all)	0	1	
Bronchitis			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 52 (0.00%)	0 / 50 (0.00%)	
occurrences (all)	0	0	
Cystitis			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 52 (0.00%)	0 / 50 (0.00%)	
occurrences (all)	0	0	
Tonsillitis			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 52 (1.92%)	0 / 50 (0.00%)	
occurrences (all)	1	0	
Gastroenteritis			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 52 (0.00%)	0 / 50 (0.00%)	
occurrences (all)	0	0	
Conjunctivitis			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 52 (0.00%)	0 / 50 (0.00%)	
occurrences (all)	0	0	
Erythema migrans			
alternative assessment type: Systematic			

subjects affected / exposed	2 / 52 (3.85%)	0 / 50 (0.00%)
occurrences (all)	2	0
Herpes simplex		
alternative assessment type: Systematic		
subjects affected / exposed	0 / 52 (0.00%)	0 / 50 (0.00%)
occurrences (all)	0	0
Chronic tonsillitis		
alternative assessment type: Systematic		
subjects affected / exposed	0 / 52 (0.00%)	0 / 50 (0.00%)
occurrences (all)	0	0
Gastroenteritis viral		
alternative assessment type: Systematic		
subjects affected / exposed	0 / 52 (0.00%)	0 / 50 (0.00%)
occurrences (all)	0	0
Ear infection		
alternative assessment type: Systematic		
subjects affected / exposed	0 / 52 (0.00%)	1 / 50 (2.00%)
occurrences (all)	0	1
Herpes zoster		
alternative assessment type: Systematic		
subjects affected / exposed	0 / 52 (0.00%)	0 / 50 (0.00%)
occurrences (all)	0	0
Influenza		
alternative assessment type: Systematic		
subjects affected / exposed	1 / 52 (1.92%)	0 / 50 (0.00%)
occurrences (all)	1	0
Laryngitis		
alternative assessment type: Systematic		
subjects affected / exposed	1 / 52 (1.92%)	0 / 50 (0.00%)
occurrences (all)	1	0
Pneumonia		
alternative assessment type: Systematic		
subjects affected / exposed	1 / 52 (1.92%)	0 / 50 (0.00%)
occurrences (all)	1	0

Tracheitis alternative assessment type: Systematic subjects affected / exposed occurrences (all)	0 / 52 (0.00%) 0	0 / 50 (0.00%) 0	
Urethritis alternative assessment type: Systematic subjects affected / exposed occurrences (all)	1 / 52 (1.92%) 1	0 / 50 (0.00%) 0	
Sinusitis alternative assessment type: Systematic subjects affected / exposed occurrences (all)	0 / 52 (0.00%) 0	1 / 50 (2.00%) 1	
Metabolism and nutrition disorders Hypertriglyceridaemia alternative assessment type: Systematic subjects affected / exposed occurrences (all)	0 / 52 (0.00%) 0	1 / 50 (2.00%) 1	

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? Yes

Date	Interruption	Restart date
29 October 2014	In late 2014, Merck KGaA made the business decision to discontinue the clinical development program of its investigational plovamer acetate therapy for multiple sclerosis. This decision was not related to any new safety or efficacy findings. The study was discontinued before all patients could be enrolled; of the 550 patients planned for enrollment, a total of 255 patients were randomized and 254 were included in the safety analysis set.	-

Notes:

Limitations and caveats

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

Based on Sponsor decision to discontinue the clinical development program of plovamer acetate therapy for multiple sclerosis the trial was prematurely terminated.
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Notes: