



Clinical trial results:

A Multicenter, Multinational, Extension Study to Evaluate the Long-Term Efficacy and Safety of BMN 110 in Patients with Mucopolysaccharidosis IVA (Morquio A Syndrome)

Summary

EudraCT number	2010-020199-45
Trial protocol	GB DE IT PT DK ES
Global end of trial date	16 June 2016

Results information

Result version number	v1 (current)
This version publication date	06 July 2018
First version publication date	06 July 2018

Trial information

Trial identification

Sponsor protocol code	MOR-005
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Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01415427
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	BioMarin Pharmaceutical Inc.
Sponsor organisation address	105 Digital Drive, Novato, United States, CA 94949
Public contact	Clinical Trials Information, BioMarin Pharmaceutical Inc., clinicaltrials@bmrn.com
Scientific contact	Clinical Trials Information, BioMarin Pharmaceutical Inc., clinicaltrials@bmrn.com

Notes:

Paediatric regulatory details

Is trial part of an agreed paediatric investigation plan (PIP)	Yes
EMA paediatric investigation plan number(s)	EMEA-000973-PIP01-10
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?	Yes

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	02 December 2016
Is this the analysis of the primary completion data?	Yes
Primary completion date	16 June 2016
Global end of trial reached?	Yes
Global end of trial date	16 June 2016
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To evaluate the long-term safety and efficacy of BMN 110 administration at 2.0 mg/kg/qw and 2.0 mg/kg/qow in patients with MPS IVA.

Protection of trial subjects:

This study was designed and monitored in accordance with sponsor procedures, which comply with the ethical principles of Good Clinical Practice, as required by the major regulatory authorities and in accordance with the Declaration of Helsinki.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	12 July 2011
Long term follow-up planned	Yes
Long term follow-up rationale	Safety, Efficacy
Long term follow-up duration	55 Months
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Argentina: 2
Country: Number of subjects enrolled	Brazil: 20
Country: Number of subjects enrolled	Canada: 14
Country: Number of subjects enrolled	Colombia: 6
Country: Number of subjects enrolled	Denmark: 1
Country: Number of subjects enrolled	France: 20
Country: Number of subjects enrolled	Germany: 10
Country: Number of subjects enrolled	Italy: 10
Country: Number of subjects enrolled	Japan: 6
Country: Number of subjects enrolled	Korea, Republic of: 7
Country: Number of subjects enrolled	Netherlands: 6
Country: Number of subjects enrolled	Portugal: 3
Country: Number of subjects enrolled	Qatar: 2
Country: Number of subjects enrolled	Saudi Arabia: 7
Country: Number of subjects enrolled	Taiwan: 5
Country: Number of subjects enrolled	United Kingdom: 23
Country: Number of subjects enrolled	United States: 33

Worldwide total number of subjects	175
EEA total number of subjects	73

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)	93
Adolescents (12-17 years)	43
Adults (18-64 years)	39
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

No screening was carried out in this study

Period 1

Period 1 title	MOR-005 Part 1
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator

Arms

Are arms mutually exclusive?	Yes
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Arm title	PBO-QOW
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Arm description:

Placebo-BMN 110 2.0 mg/kg/qow

Arm type	Placebo-BMN 110 2.0 mg/kg/qow
Investigational medicinal product name	placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Infusion
Routes of administration	Intravenous use

Dosage and administration details:

Patients randomized to the 2.0 mg/kg/qow arm will receive infusions of placebo on alternating weeks, to mask active drug weeks.

Arm title	PBO-QW
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Arm description:

Placebo-BMN 110 2.0 mg/kg/qw

Arm type	Placebo-BMN 110 2.0 mg/kg/qw
Investigational medicinal product name	placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Infusion
Routes of administration	Intravenous use

Dosage and administration details:

Patients randomized to the 2.0 mg/kg/qw arm will receive infusions of placebo on alternating weeks, to mask active drug weeks.

Arm title	QOW-QOW
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Arm description:

BMN 110-BMN 110 2.0 mg/kg/qow

Arm type	BMN 110-BMN 110 2.0 mg/kg/qow
Investigational medicinal product name	Elosulfase alfa
Investigational medicinal product code	BMN110
Other name	
Pharmaceutical forms	Infusion
Routes of administration	Intravenous use

Dosage and administration details:

During the double-blind phase of the study, patients will receive intravenous (IV) infusions of study drug at a dose of 2.0 mg/kg/qw or 2.0 mg/kg/qow.

Arm title	QW-QW
Arm description: BMN 110-BMN 110 2.0 mg/kg/qw	
Arm type	BMN 110-BMN 110 2.0 mg/kg/qw
Investigational medicinal product name	elosulfase alfa
Investigational medicinal product code	BMN110
Other name	
Pharmaceutical forms	Infusion
Routes of administration	Intravenous use

Dosage and administration details:

During the double-blind phase of the study, patients will receive intravenous (IV) infusions of study drug at a dose of 2.0 mg/kg/qw or 2.0 mg/kg/qow.

Number of subjects in period 1	PBO-QOW	PBO-QW	QOW-QOW
Started	29	29	59
Completed	29	28	58
Not completed	0	1	1
Consent withdrawn by subject	-	-	-
Subjects in Mor004 but not enrolled in Mor005	-	-	-
Lost to follow-up	-	1	1

Number of subjects in period 1	QW-QW
Started	58
Completed	55
Not completed	3
Consent withdrawn by subject	1
Subjects in Mor004 but not enrolled in Mor005	2
Lost to follow-up	-

Period 2

Period 2 title	MOR-005 Part 2
Is this the baseline period?	No
Allocation method	Non-randomised - controlled
Blinding used	Not blinded

Arms

Are arms mutually exclusive?	Yes
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Arm title	PBO-QOW
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Arm description:

Placebo-BMN 110 2.0 mg/kg/qow

Arm type	Placebo-BMN 110 2.0 mg/kg/qow
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Investigational medicinal product name	placebo
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Investigational medicinal product code	
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Other name	
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Pharmaceutical forms	Infusion
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Routes of administration	Intravenous use
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Dosage and administration details:

Patients randomized to the 2.0 mg/kg/qow arm will receive infusions of placebo on alternating weeks, to mask active drug weeks.

Arm title	PBO-QW
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Arm description:

Placebo-BMN 110 2.0 mg/kg/qw

Arm type	Placebo-BMN 110 2.0 mg/kg/qw
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Investigational medicinal product name	placebo
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Investigational medicinal product code	
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Other name	
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Pharmaceutical forms	Infusion
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Routes of administration	Intravenous use
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Dosage and administration details:

Patients randomized to the 2.0 mg/kg/qw arm will receive infusions of placebo on alternating weeks, to mask active drug weeks.

Arm title	QOW-QOW
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Arm description:

BMN 110-BMN 110 2.0 mg/kg/qow

Arm type	BMN 110-BMN 110 2.0 mg/kg/qow
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Investigational medicinal product name	elosulfase alfa
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Investigational medicinal product code	BMN110
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Other name	
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Pharmaceutical forms	Infusion
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Routes of administration	Intravenous use
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Dosage and administration details:

During the double-blind phase of the study, patients will receive intravenous (IV) infusions of study drug at a dose of 2.0 mg/kg/qw or 2.0 mg/kg/qow.

Arm title	QW-QW
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Arm description:

BMN 110-BMN 110 2.0 mg/kg/qw

Arm type	BMN 110-BMN 110 2.0 mg/kg/qw
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Investigational medicinal product name	elosulfase alfa
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Investigational medicinal product code	BMN110
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Other name	
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Pharmaceutical forms	Infusion
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Routes of administration	Intravenous use
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Dosage and administration details:

During the double-blind phase of the study, patients will receive intravenous (IV) infusions of study drug at a dose of 2.0 mg/kg/qw or 2.0 mg/kg/qow.

Number of subjects in period 2	PBO-QOW	PBO-QW	QOW-QOW
Started	29	28	58
Completed	0	0	1
Not completed	29	28	57
Adverse event, serious fatal	-	-	1
Consent withdrawn by subject	1	-	4
Adverse event, non-fatal	-	-	2
Other	-	-	1
Study Termination by Sponsor	28	28	49

Number of subjects in period 2	QW-QW
Started	55
Completed	0
Not completed	55
Adverse event, serious fatal	-
Consent withdrawn by subject	1
Adverse event, non-fatal	1
Other	-
Study Termination by Sponsor	53

Baseline characteristics

Reporting groups

Reporting group title	PBO-QOW
Reporting group description: Placebo-BMN 110 2.0 mg/kg/qow	
Reporting group title	PBO-QW
Reporting group description: Placebo-BMN 110 2.0 mg/kg/qw	
Reporting group title	QOW-QOW
Reporting group description: BMN 110-BMN 110 2.0 mg/kg/qow	
Reporting group title	QW-QW
Reporting group description: BMN 110-BMN 110 2.0 mg/kg/qw	

Reporting group values	PBO-QOW	PBO-QW	QOW-QOW
Number of subjects	29	29	59
Age categorical Units: Subjects			
5 - 11	15	15	31
12 - 18	7	7	16
>=19	7	7	12
Age continuous Units: Years			
arithmetic mean	16.7	13.5	15.3
standard deviation	± 13.66	± 8.5	± 10.79
Gender categorical Units: Subjects			
Female	14	18	25
Male	15	11	34

Reporting group values	QW-QW	Total	
Number of subjects	58	175	
Age categorical Units: Subjects			
5 - 11	32	93	
12 - 18	16	46	
>=19	10	36	
Age continuous Units: Years			
arithmetic mean	13.1	-	
standard deviation	± 8.1		
Gender categorical Units: Subjects			
Female	32	89	
Male	26	86	

End points

End points reporting groups

Reporting group title	PBO-QOW
Reporting group description: Placebo-BMN 110 2.0 mg/kg/qow	
Reporting group title	PBO-QW
Reporting group description: Placebo-BMN 110 2.0 mg/kg/qw	
Reporting group title	QOW-QOW
Reporting group description: BMN 110-BMN 110 2.0 mg/kg/qow	
Reporting group title	QW-QW
Reporting group description: BMN 110-BMN 110 2.0 mg/kg/qw	
Reporting group title	PBO-QOW
Reporting group description: Placebo-BMN 110 2.0 mg/kg/qow	
Reporting group title	PBO-QW
Reporting group description: Placebo-BMN 110 2.0 mg/kg/qw	
Reporting group title	QOW-QOW
Reporting group description: BMN 110-BMN 110 2.0 mg/kg/qow	
Reporting group title	QW-QW
Reporting group description: BMN 110-BMN 110 2.0 mg/kg/qw	
Subject analysis set title	Intent-to-Treat
Subject analysis set type	Intention-to-treat
Subject analysis set description: All subjects who were randomized into the parent MOR-004 study and received at least one dose of study drug.	

Subject analysis set title	Modified Per-Protocol
Subject analysis set type	Per protocol
Subject analysis set description: All subjects who were randomized into the parent MOR-004 study and received at least one dose of study drug with the exception of: 1. Subjects who underwent orthopaedic surgery in the first 120 weeks of MOR-004/005, based on medical monitor review. 2. Subjects who were administered less than 80% of dosing within the first 120 weeks of MOR-004/005.	

Primary: Baseline Distance Walked in Six Minutes - ITT Population

End point title	Baseline Distance Walked in Six Minutes - ITT Population ^[1]
End point description:	
End point type	Primary
End point timeframe: Baseline	

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: Justification: No statistical analysis performed for this endpoint as it is descriptive analysis

End point values	PBO-QOW	PBO-QW	QOW-QOW	QW-QW
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	29	29	59	58
Units: Metres				
arithmetic mean (standard deviation)	219.7 (± 74.22)	207.2 (± 64.87)	205.7 (± 81.19)	203.9 (± 76.32)

End point values	Intent-to-Treat			
Subject group type	Subject analysis set			
Number of subjects analysed	176			
Units: Metres				
arithmetic mean (standard deviation)	207.2 (± 75.58)			

Statistical analyses

No statistical analyses for this end point

Primary: Change from Baseline to Week 24 in Distance Walked in Six Minutes - ITT Population

End point title	Change from Baseline to Week 24 in Distance Walked in Six Minutes - ITT Population ^[2]
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End point description:

End point type	Primary
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End point timeframe:

Week 24 (MOR-005 Week 0)

Notes:

[2] - 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: Justification: No statistical analysis performed for this endpoint as it is descriptive analysis

End point values	PBO-QOW	PBO-QW	QOW-QOW	QW-QW
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	29	29	59	57
Units: Metres				
arithmetic mean (standard deviation)	23.8 (± 56.21)	5 (± 43.27)	11.1 (± 49.95)	36.5 (± 58.49)

End point values	Intent-to-Treat			
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Subject group type	Subject analysis set			
Number of subjects analysed	175			
Units: Metres				
arithmetic mean (standard deviation)	20.2 (± 54.02)			

Statistical analyses

No statistical analyses for this end point

Primary: Change from Baseline to Week 72 in Distance Walked in Six Minutes - ITT Population

End point title	Change from Baseline to Week 72 in Distance Walked in Six Minutes - ITT Population ^[3]
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End point description:

End point type	Primary
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End point timeframe:

Week 72 (MOR-005 Week 48)

Notes:

[3] - 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: Justification: No statistical analysis performed for this endpoint as it is descriptive analysis

End point values	PBO-QOW	PBO-QW	QOW-QOW	QW-QW
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	28	27	57	55
Units: Metres				
arithmetic mean (standard deviation)	41.5 (± 89.24)	-1.5 (± 112.07)	27.2 (± 56.66)	30.6 (± 73.66)

End point values	Intent-to-Treat			
Subject group type	Subject analysis set			
Number of subjects analysed	167			
Units: Metres				
arithmetic mean (standard deviation)	26.1 (± 79.26)			

Statistical analyses

No statistical analyses for this end point

Primary: Change from Baseline to Week 120 in Distance Walked in Six Minutes - ITT Population

End point title	Change from Baseline to Week 120 in Distance Walked in Six Minutes - ITT Population ^[4]
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End point description:

End point type	Primary
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End point timeframe:

Week 120 (MOR-005 Week 96)

Notes:

[4] - 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: Justification: No statistical analysis performed for this endpoint as it is descriptive analysis

End point values	PBO-QOW	PBO-QW	QOW-QOW	QW-QW
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	28	27	54	54
Units: Metres				
arithmetic mean (standard deviation)	32.3 (± 92.13)	-2.9 (± 95.69)	6 (± 86.28)	29.7 (± 81.37)

End point values	Intent-to-Treat			
Subject group type	Subject analysis set			
Number of subjects analysed	163			
Units: Metres				
arithmetic mean (standard deviation)	16.9 (± 87.67)			

Statistical analyses

No statistical analyses for this end point

Primary: Baseline Distance Walked in Six Minutes - MPP Population

End point title	Baseline Distance Walked in Six Minutes - MPP Population ^[5]
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End point description:

End point type	Primary
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End point timeframe:

Baseline

Notes:

[5] - 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: Justification: No statistical analysis performed for this endpoint as it is descriptive analysis

End point values	PBO-QOW	PBO-QW	QOW-QOW	QW-QW
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	20	19	42	43
Units: Metres				
arithmetic mean (standard deviation)	208.7 (± 78.12)	190.2 (± 65.54)	195.9 (± 80.4)	208.8 (± 73.24)

End point values	Modified Per-Protocol			
Subject group type	Subject analysis set			
Number of subjects analysed	124			
Units: Metres				
arithmetic mean (standard deviation)	201.6 (\pm 74.94)			

Statistical analyses

No statistical analyses for this end point

Primary: Change from Baseline to Week 24 in Distance Walked in Six Minutes - MPP Population

End point title	Change from Baseline to Week 24 in Distance Walked in Six Minutes - MPP Population ^[6]
End point description:	
End point type	Primary
End point timeframe:	
Week 24 (MOR-005 Week 0)	

Notes:

[6] - 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: Justification: No statistical analysis performed for this endpoint as it is descriptive analysis

End point values	PBO-QOW	PBO-QW	QOW-QOW	QW-QW
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	20	19	42	43
Units: Metres				
arithmetic mean (standard deviation)	30.3 (\pm 56.53)	9.6 (\pm 46.87)	13.6 (\pm 52.65)	41.5 (\pm 59.89)

End point values	Modified Per-Protocol			
Subject group type	Subject analysis set			
Number of subjects analysed	124			
Units: Metres				
arithmetic mean (standard deviation)	25.4 (\pm 56.08)			

Statistical analyses

No statistical analyses for this end point

Primary: Change from Baseline to Week 72 in Distance Walked in Six Minutes - MPP Population

End point title	Change from Baseline to Week 72 in Distance Walked in Six Minutes - MPP Population ^[7]
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End point description:

End point type	Primary
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End point timeframe:

Week 72 (MOR-005 Week 48)

Notes:

[7] - 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: Justification: No statistical analysis performed for this endpoint as it is descriptive analysis

End point values	PBO-QOW	PBO-QW	QOW-QOW	QW-QW
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	20	18	42	43
Units: Metres				
arithmetic mean (standard deviation)	54.5 (± 85.19)	37.7 (± 69.35)	35.3 (± 58.19)	37.5 (± 72.17)

End point values	Modified Per-Protocol			
Subject group type	Subject analysis set			
Number of subjects analysed	123			
Units: Metres				
arithmetic mean (standard deviation)	39.6 (± 69.11)			

Statistical analyses

No statistical analyses for this end point

Primary: Change from Baseline to Week 120 in Distance Walked in Six Minutes - MPP Population

End point title	Change from Baseline to Week 120 in Distance Walked in Six Minutes - MPP Population ^[8]
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End point description:

End point type	Primary
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End point timeframe:

Week 120 (MOR-005 Week 96)

Notes:

[8] - 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: Justification: No statistical analysis performed for this endpoint as it is descriptive analysis

End point values	PBO-QOW	PBO-QW	QOW-QOW	QW-QW
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	20	19	41	43
Units: Metres				
arithmetic mean (standard deviation)	60.8 (± 64.45)	19.8 (± 86.69)	19.7 (± 77.29)	38.6 (± 66.65)

End point values	Modified Per-Protocol			
Subject group type	Subject analysis set			
Number of subjects analysed	123			
Units: Metres				
arithmetic mean (standard deviation)	33 (± 73.94)			

Statistical analyses

No statistical analyses for this end point

Primary: Baseline Average Three Minute Stair Climb Rate - ITT Population

End point title	Baseline Average Three Minute Stair Climb Rate - ITT Population ^[9]
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End point description:

End point type	Primary
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End point timeframe:

Baseline

Notes:

[9] - 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: Justification: No statistical analysis performed for this endpoint as it is descriptive analysis

End point values	PBO-QOW	PBO-QW	QOW-QOW	QW-QW
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	29	29	59	58
Units: stairs/min				
arithmetic mean (standard deviation)	33.1 (± 15.6)	26.9 (± 12.08)	27.1 (± 15.8)	29.6 (± 16.44)

End point values	Intent-to-Treat			
Subject group type	Subject analysis set			
Number of subjects analysed	176			
Units: stairs/min				
arithmetic mean (standard deviation)	28.9 (± 15.42)			

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline to Week 24 in Average Three Minute Stair Climb Rate - ITT Population

End point title	Change from Baseline to Week 24 in Average Three Minute Stair Climb Rate - ITT Population
End point description:	
End point type	Secondary
End point timeframe:	
Week 24 (MOR-005 Week 0)	

End point values	PBO-QOW	PBO-QW	QOW-QOW	QW-QW
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	29	29	59	57
Units: stairs/min				
arithmetic mean (standard deviation)	4.7 (\pm 9.65)	2.9 (\pm 7.3)	2.9 (\pm 10.94)	4.8 (\pm 8.06)

End point values	Intent-to-Treat			
Subject group type	Subject analysis set			
Number of subjects analysed	173			
Units: stairs/min				
arithmetic mean (standard deviation)	3.8 (\pm 9.25)			

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline to Week 72 in Average Three Minute Stair Climb Rate - ITT Population

End point title	Change from Baseline to Week 72 in Average Three Minute Stair Climb Rate - ITT Population
End point description:	
End point type	Secondary

End point timeframe:

Week 72 (MOR-005 Week 48)

End point values	PBO-QOW	PBO-QW	QOW-QOW	QW-QW
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	28	26	56	54
Units: stairs/min				
arithmetic mean (standard deviation)	8.9 (± 15.44)	1.2 (± 14.95)	5.5 (± 11.96)	5.3 (± 9.88)

End point values	Intent-to-Treat			
Subject group type	Subject analysis set			
Number of subjects analysed	164			
Units: stairs/min				
arithmetic mean (standard deviation)	5.3 (± 12.6)			

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline to Week 120 in Average Three Minute Stair Climb Rate - ITT Population

End point title	Change from Baseline to Week 120 in Average Three Minute Stair Climb Rate - ITT Population
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End point description:

End point type	Secondary
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End point timeframe:

Week 120 (MOR-005 Week 96)

End point values	PBO-QOW	PBO-QW	QOW-QOW	QW-QW
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	28	27	54	53
Units: stairs/min				
arithmetic mean (standard deviation)	6 (± 17.05)	1.7 (± 14.8)	4.7 (± 14.6)	5.8 (± 13.42)

End point values	Intent-to-Treat			
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Subject group type	Subject analysis set			
Number of subjects analysed	162			
Units: stairs/min				
arithmetic mean (standard deviation)	4.8 (± 14.65)			

Statistical analyses

No statistical analyses for this end point

Secondary: Baseline Average Three Minute Stair Climb Rate - MPP Population

End point title	Baseline Average Three Minute Stair Climb Rate - MPP Population
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End point description:

End point type	Secondary
End point timeframe:	
Baseline	

End point values	PBO-QOW	PBO-QW	QOW-QOW	QW-QW
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	20	19	42	43
Units: stairs/min				
arithmetic mean (standard deviation)	33.1 (± 14.12)	24.8 (± 13.92)	25.6 (± 13.73)	31.3 (± 16.22)

End point values	Intent-to-Treat			
Subject group type	Subject analysis set			
Number of subjects analysed	124			
Units: stairs/min				
arithmetic mean (standard deviation)	28.7 (± 14.93)			

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline to Week 24 in Average Three Minute Stair Climb Rate - MPP Population

End point title	Change from Baseline to Week 24 in Average Three Minute Stair Climb Rate - MPP Population
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End point description:

End point type	Secondary
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End point timeframe:

Week 24 (MOR-005 Week 0)

End point values	PBO-QOW	PBO-QW	QOW-QOW	QW-QW
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	20	19	42	43
Units: stairs/min				
arithmetic mean (standard deviation)	3.4 (\pm 8.09)	3.6 (\pm 8.63)	5 (\pm 11.46)	3.9 (\pm 7.67)

End point values	Modified Per-Protocol			
Subject group type	Subject analysis set			
Number of subjects analysed	124			
Units: stairs/min				
arithmetic mean (standard deviation)	4.1 (\pm 9.23)			

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline to Week 72 in Average Three Minute Stair Climb Rate - MPP Population

End point title	Change from Baseline to Week 72 in Average Three Minute Stair Climb Rate - MPP Population
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End point description:

End point type	Secondary
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End point timeframe:

Week 72 (MOR-005 Week 48)

End point values	PBO-QOW	PBO-QW	QOW-QOW	QW-QW
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	20	18	42	43
Units: stairs/min				
arithmetic mean (standard deviation)	10.4 (\pm 13.77)	6.1 (\pm 10.56)	7.4 (\pm 12.53)	5.7 (\pm 9.98)

End point values	Modified Per-Protocol			
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Subject group type	Subject analysis set			
Number of subjects analysed	123			
Units: stairs/min				
arithmetic mean (standard deviation)	7.1 (\pm 11.61)			

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline to Week 120 in Average Three Minute Stair Climb Rate - MPP Population

End point title	Change from Baseline to Week 120 in Average Three Minute Stair Climb Rate - MPP Population
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End point description:

End point type	Secondary
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End point timeframe:

Week 120 (MOR-005 Week 96)

End point values	PBO-QOW	PBO-QW	QOW-QOW	QW-QW
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	20	19	41	42
Units: stairs/min				
arithmetic mean (standard deviation)	9.1 (\pm 13.38)	4.2 (\pm 12.49)	8.1 (\pm 13.83)	7.2 (\pm 12.58)

End point values	Modified Per-Protocol			
Subject group type	Subject analysis set			
Number of subjects analysed	122			
Units: stairs/min				
arithmetic mean (standard deviation)	7.4 (\pm 13.05)			

Statistical analyses

No statistical analyses for this end point

Secondary: Baseline Normalized Urine Keratan Sulfate - ITT Population

End point title	Baseline Normalized Urine Keratan Sulfate - ITT Population
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End point description:

End point type	Secondary
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End point timeframe:

Baseline

End point values	PBO-QOW	PBO-QW	QOW-QOW	QW-QW
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	28	29	59	58
Units: ug/mg				
arithmetic mean (standard deviation)	22.7 (± 15.27)	28.5 (± 14.89)	28.6 (± 21.17)	26.9 (± 14.11)

End point values	Intent-to-Treat			
Subject group type	Subject analysis set			
Number of subjects analysed	175			
Units: ug/mg				
arithmetic mean (standard deviation)	27.1 (± 17.05)			

Statistical analyses

No statistical analyses for this end point

Secondary: Percent Change from Baseline to Week 24 in Normalized Urine Keratan Sulfate - ITT Population

End point title	Percent Change from Baseline to Week 24 in Normalized Urine Keratan Sulfate - ITT Population
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End point description:

End point type	Secondary
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End point timeframe:

Week 24 (MOR-005 Week 0)

End point values	PBO-QOW	PBO-QW	QOW-QOW	QW-QW
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	26	28	57	54
Units: ug/mg				
arithmetic mean (standard deviation)	3.4 (± 29.15)	-11.3 (± 23.68)	-35.2 (± 20.7)	-45.1 (± 19.89)

End point values	Intent-to-Treat			
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Subject group type	Subject analysis set			
Number of subjects analysed	166			
Units: ug/mg				
arithmetic mean (standard deviation)	-28.2 (± 28.46)			

Statistical analyses

No statistical analyses for this end point

Secondary: Percent Change from Baseline to Week 72 in Normalized Urine Keratan Sulfate - ITT Population

End point title	Percent Change from Baseline to Week 72 in Normalized Urine Keratan Sulfate - ITT Population
End point description:	
End point type	Secondary
End point timeframe:	
Week 72 (MOR-005 Week 48)	

End point values	PBO-QOW	PBO-QW	QOW-QOW	QW-QW
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	26	28	57	51
Units: ug/mg				
arithmetic mean (standard deviation)	-54.1 (± 17.21)	-56.8 (± 13.69)	-55.6 (± 14.23)	-53.7 (± 17.45)

End point values	Intent-to-Treat			
Subject group type	Subject analysis set			
Number of subjects analysed	162			
Units: ug/mg				
arithmetic mean (standard deviation)	-55 (± 15.61)			

Statistical analyses

No statistical analyses for this end point

Secondary: Percent Change from Baseline to Week 120 in Normalized Urine Keratan Sulfate - ITT Population

End point title	Percent Change from Baseline to Week 120 in Normalized Urine Keratan Sulfate - ITT Population
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End point description:

End point type	Secondary
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End point timeframe:

Week 120 (MOR-005 Week 96)

End point values	PBO-QOW	PBO-QW	QOW-QOW	QW-QW
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	26	24	53	53
Units: ug/mg				
arithmetic mean (standard deviation)	-55.5 (± 18.6)	-62.2 (± 15.39)	-55.8 (± 26.56)	-61.5 (± 20.59)

End point values	Intent-to-Treat			
Subject group type	Subject analysis set			
Number of subjects analysed	156			
Units: ug/mg				
arithmetic mean (standard deviation)	-58.7 (± 21.88)			

Statistical analyses

No statistical analyses for this end point

Secondary: Baseline Normalized Urine Keratan Sulfate - MPP Population

End point title	Baseline Normalized Urine Keratan Sulfate - MPP Population
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End point description:

End point type	Secondary
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End point timeframe:

Baseline

End point values	PBO-QOW	PBO-QW	QOW-QOW	QW-QW
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	19	19	42	43
Units: ug/mg				
arithmetic mean (standard deviation)	21.2 (± 15.55)	27.5 (± 15.24)	27.2 (± 22.9)	24.9 (± 13.13)

End point values	Intent-to-Treat			
Subject group type	Subject analysis set			
Number of subjects analysed	123			
Units: ug/mg				
arithmetic mean (standard deviation)	25.5 (± 17.61)			

Statistical analyses

No statistical analyses for this end point

Secondary: Percent Change from Baseline to Week 24 in Normalized Urine Keratan Sulfate - MPP Population

End point title	Percent Change from Baseline to Week 24 in Normalized Urine Keratan Sulfate - MPP Population
End point description:	
End point type	Secondary
End point timeframe:	
Week 24 (MOR-005 Week 0)	

End point values	PBO-QOW	PBO-QW	QOW-QOW	QW-QW
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	17	19	41	40
Units: ug/mg				
arithmetic mean (standard deviation)	1.2 (± 24.34)	-12.9 (± 24.29)	-35.5 (± 22.62)	-44.9 (± 19.6)

End point values	Modified Per-Protocol			
Subject group type	Subject analysis set			
Number of subjects analysed	117			
Units: ug/mg				
arithmetic mean (standard deviation)	-29.7 (± 27.52)			

Statistical analyses

No statistical analyses for this end point

Secondary: Percent Change from Baseline to Week 72 in Normalized Urine Keratan Sulfate - MPP Population

End point title	Percent Change from Baseline to Week 72 in Normalized Urine
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End point description:

End point type Secondary

End point timeframe:

Week 72 (MOR-005 Week 48)

End point values	PBO-QOW	PBO-QW	QOW-QOW	QW-QW
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	18	19	41	41
Units: ug/mg				
arithmetic mean (standard deviation)	-51.7 (\pm 19.34)	-58.8 (\pm 14.6)	-56.9 (\pm 13.55)	-53.7 (\pm 17.87)

End point values	Modified Per-Protocol			
Subject group type	Subject analysis set			
Number of subjects analysed	119			
Units: ug/mg				
arithmetic mean (standard deviation)	-55.3 (\pm 16.21)			

Statistical analyses

No statistical analyses for this end point

Secondary: Percent Change from Baseline to Week 120 in Normalized Urine Keratan Sulfate - MPP Population

End point title Percent Change from Baseline to Week 120 in Normalized Urine Keratan Sulfate - MPP Population

End point description:

End point type Secondary

End point timeframe:

Week 120 (MOR-005 Week 96)

End point values	PBO-QOW	PBO-QW	QOW-QOW	QW-QW
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	18	17	40	42
Units: ug/mg				
arithmetic mean (standard deviation)	-58.3 (± 15.87)	-64.2 (± 16.58)	-62.1 (± 15.97)	-61.8 (± 21.28)

End point values	Modified Per-Protocol			
Subject group type	Subject analysis set			
Number of subjects analysed	117			
Units: ug/mg				
arithmetic mean (standard deviation)	-61.7 (± 17.98)			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Study Period

Assessment type	Systematic
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Dictionary used

Dictionary name	MedDRA
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Dictionary version	16.1
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Reporting groups

Reporting group title	PBO-QOW
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Reporting group description: -

Reporting group title	PBO-QW
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Reporting group description: -

Reporting group title	QOW-QOW
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Reporting group description: -

Reporting group title	QW-QW
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Reporting group description: -

Serious adverse events	PBO-QOW	PBO-QW	QOW-QOW
Total subjects affected by serious adverse events			
subjects affected / exposed	17 / 29 (58.62%)	15 / 29 (51.72%)	26 / 59 (44.07%)
number of deaths (all causes)	0	0	1
number of deaths resulting from adverse events			
Vascular disorders			
Poor venous access			
subjects affected / exposed	0 / 29 (0.00%)	2 / 29 (6.90%)	5 / 59 (8.47%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 5
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Surgical and medical procedures			
Central venous catheterisation			
subjects affected / exposed	1 / 29 (3.45%)	0 / 29 (0.00%)	3 / 59 (5.08%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Epiphyseal stapling			
subjects affected / exposed	0 / 29 (0.00%)	1 / 29 (3.45%)	0 / 59 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Knee operation			

subjects affected / exposed	1 / 29 (3.45%)	0 / 29 (0.00%)	0 / 59 (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
Medical device implantation			
subjects affected / exposed	0 / 29 (0.00%)	0 / 29 (0.00%)	1 / 59 (1.69%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Medical device removal			
subjects affected / exposed	1 / 29 (3.45%)	0 / 29 (0.00%)	0 / 59 (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
Spinal decompression			
subjects affected / exposed	0 / 29 (0.00%)	0 / 29 (0.00%)	1 / 59 (1.69%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pregnancy, puerperium and perinatal conditions			
Blighted ovum			
subjects affected / exposed	0 / 29 (0.00%)	0 / 29 (0.00%)	0 / 59 (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
Ectopic pregnancy			
subjects affected / exposed	0 / 29 (0.00%)	0 / 29 (0.00%)	0 / 59 (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
General disorders and administration site conditions			
Device dislocation			
subjects affected / exposed	0 / 29 (0.00%)	1 / 29 (3.45%)	1 / 59 (1.69%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Device occlusion			
subjects affected / exposed	0 / 29 (0.00%)	0 / 29 (0.00%)	1 / 59 (1.69%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Pyrexia			
subjects affected / exposed	0 / 29 (0.00%)	0 / 29 (0.00%)	1 / 59 (1.69%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Immune system disorders			
Anaphylactic reaction			
subjects affected / exposed	1 / 29 (3.45%)	0 / 29 (0.00%)	1 / 59 (1.69%)
occurrences causally related to treatment / all	1 / 1	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypersensitivity			
subjects affected / exposed	0 / 29 (0.00%)	0 / 29 (0.00%)	0 / 59 (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
Social circumstances			
Child abuse			
subjects affected / exposed	0 / 29 (0.00%)	0 / 29 (0.00%)	1 / 59 (1.69%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			
Asthma			
subjects affected / exposed	0 / 29 (0.00%)	0 / 29 (0.00%)	1 / 59 (1.69%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bronchopneumopathy			
subjects affected / exposed	0 / 29 (0.00%)	0 / 29 (0.00%)	1 / 59 (1.69%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bronchospasm			
subjects affected / exposed	0 / 29 (0.00%)	0 / 29 (0.00%)	0 / 59 (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
Lung disorder			

subjects affected / exposed	0 / 29 (0.00%)	0 / 29 (0.00%)	1 / 59 (1.69%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Sleep apnoea syndrome			
subjects affected / exposed	0 / 29 (0.00%)	1 / 29 (3.45%)	1 / 59 (1.69%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Status asthmaticus			
subjects affected / exposed	0 / 29 (0.00%)	0 / 29 (0.00%)	0 / 59 (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
Tonsillar hypertrophy			
subjects affected / exposed	1 / 29 (3.45%)	0 / 29 (0.00%)	0 / 59 (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
Tracheal disorder			
subjects affected / exposed	0 / 29 (0.00%)	1 / 29 (3.45%)	0 / 59 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Tracheal stenosis			
subjects affected / exposed	0 / 29 (0.00%)	0 / 29 (0.00%)	1 / 59 (1.69%)
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			
Somatoform disorder			
subjects affected / exposed	0 / 29 (0.00%)	0 / 29 (0.00%)	1 / 59 (1.69%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Injury, poisoning and procedural complications			
Fall			
subjects affected / exposed	0 / 29 (0.00%)	1 / 29 (3.45%)	0 / 59 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Joint dislocation			
subjects affected / exposed	0 / 29 (0.00%)	0 / 29 (0.00%)	1 / 59 (1.69%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lower limb fracture			
subjects affected / exposed	0 / 29 (0.00%)	1 / 29 (3.45%)	0 / 59 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Procedural pain			
subjects affected / exposed	0 / 29 (0.00%)	0 / 29 (0.00%)	0 / 59 (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
Pseudomeningocele			
subjects affected / exposed	0 / 29 (0.00%)	0 / 29 (0.00%)	0 / 59 (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
Congenital, familial and genetic disorders			
Congenital osteodystrophy			
subjects affected / exposed	0 / 29 (0.00%)	0 / 29 (0.00%)	0 / 59 (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
Developmental hip dysplasia			
subjects affected / exposed	1 / 29 (3.45%)	0 / 29 (0.00%)	1 / 59 (1.69%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac disorders			
Cardio-respiratory arrest			
subjects affected / exposed	0 / 29 (0.00%)	0 / 29 (0.00%)	1 / 59 (1.69%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nervous system disorders			
Cervical cord compression			

subjects affected / exposed	1 / 29 (3.45%)	1 / 29 (3.45%)	0 / 59 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cervical myelopathy			
subjects affected / exposed	1 / 29 (3.45%)	0 / 29 (0.00%)	0 / 59 (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
Convulsion			
subjects affected / exposed	0 / 29 (0.00%)	1 / 29 (3.45%)	0 / 59 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Myelopathy			
subjects affected / exposed	0 / 29 (0.00%)	0 / 29 (0.00%)	1 / 59 (1.69%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Paraplegia			
subjects affected / exposed	0 / 29 (0.00%)	0 / 29 (0.00%)	0 / 59 (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
Quadriplegia			
subjects affected / exposed	0 / 29 (0.00%)	1 / 29 (3.45%)	0 / 59 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Spinal cord compression			
subjects affected / exposed	1 / 29 (3.45%)	0 / 29 (0.00%)	0 / 59 (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
Spinal cord ischaemia			
subjects affected / exposed	0 / 29 (0.00%)	0 / 29 (0.00%)	1 / 59 (1.69%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ear and labyrinth disorders			
Deafness			

subjects affected / exposed	1 / 29 (3.45%)	0 / 29 (0.00%)	0 / 59 (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
Middle ear effusion			
subjects affected / exposed	1 / 29 (3.45%)	0 / 29 (0.00%)	1 / 59 (1.69%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Eye disorders			
Strabismus			
subjects affected / exposed	0 / 29 (0.00%)	1 / 29 (3.45%)	0 / 59 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	0 / 29 (0.00%)	0 / 29 (0.00%)	0 / 59 (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
Dyspepsia			
subjects affected / exposed	0 / 29 (0.00%)	1 / 29 (3.45%)	0 / 59 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Inguinal hernia			
subjects affected / exposed	0 / 29 (0.00%)	0 / 29 (0.00%)	1 / 59 (1.69%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Oesophageal spasm			
subjects affected / exposed	0 / 29 (0.00%)	1 / 29 (3.45%)	0 / 59 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Rectal haemorrhage			
subjects affected / exposed	0 / 29 (0.00%)	0 / 29 (0.00%)	1 / 59 (1.69%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vomiting			

subjects affected / exposed	0 / 29 (0.00%)	0 / 29 (0.00%)	1 / 59 (1.69%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Skin and subcutaneous tissue disorders			
Skin ulcer			
subjects affected / exposed	0 / 29 (0.00%)	0 / 29 (0.00%)	1 / 59 (1.69%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Urticaria			
subjects affected / exposed	0 / 29 (0.00%)	0 / 29 (0.00%)	0 / 59 (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
Renal and urinary disorders			
Haematuria			
subjects affected / exposed	1 / 29 (3.45%)	0 / 29 (0.00%)	0 / 59 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	0 / 29 (0.00%)	0 / 29 (0.00%)	1 / 59 (1.69%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Back pain			
subjects affected / exposed	0 / 29 (0.00%)	0 / 29 (0.00%)	2 / 59 (3.39%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Joint instability			
subjects affected / exposed	2 / 29 (6.90%)	0 / 29 (0.00%)	1 / 59 (1.69%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Knee deformity			
subjects affected / exposed	6 / 29 (20.69%)	8 / 29 (27.59%)	7 / 59 (11.86%)
occurrences causally related to treatment / all	0 / 8	0 / 9	0 / 7
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Limb deformity			
subjects affected / exposed	0 / 29 (0.00%)	0 / 29 (0.00%)	0 / 59 (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
Osteoarthritis			
subjects affected / exposed	0 / 29 (0.00%)	1 / 29 (3.45%)	0 / 59 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Osteochondrosis			
subjects affected / exposed	0 / 29 (0.00%)	0 / 29 (0.00%)	1 / 59 (1.69%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Appendicitis			
subjects affected / exposed	0 / 29 (0.00%)	0 / 29 (0.00%)	0 / 59 (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
Dengue fever			
subjects affected / exposed	0 / 29 (0.00%)	0 / 29 (0.00%)	1 / 59 (1.69%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Diverticulitis			
subjects affected / exposed	0 / 29 (0.00%)	0 / 29 (0.00%)	1 / 59 (1.69%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastroenteritis			
subjects affected / exposed	1 / 29 (3.45%)	0 / 29 (0.00%)	2 / 59 (3.39%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infected cyst			
subjects affected / exposed	0 / 29 (0.00%)	0 / 29 (0.00%)	0 / 59 (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
Influenza			

subjects affected / exposed	0 / 29 (0.00%)	0 / 29 (0.00%)	0 / 59 (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
Lower respiratory tract infection			
subjects affected / exposed	1 / 29 (3.45%)	0 / 29 (0.00%)	0 / 59 (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
Mononucleosis syndrome			
subjects affected / exposed	1 / 29 (3.45%)	0 / 29 (0.00%)	0 / 59 (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
Otitis media			
subjects affected / exposed	0 / 29 (0.00%)	0 / 29 (0.00%)	1 / 59 (1.69%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Otitis media chronic			
subjects affected / exposed	1 / 29 (3.45%)	0 / 29 (0.00%)	0 / 59 (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
Pilonidal cyst			
subjects affected / exposed	0 / 29 (0.00%)	0 / 29 (0.00%)	0 / 59 (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
Pneumonia			
subjects affected / exposed	0 / 29 (0.00%)	0 / 29 (0.00%)	0 / 59 (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
Tooth abscess			
subjects affected / exposed	0 / 29 (0.00%)	0 / 29 (0.00%)	1 / 59 (1.69%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Viral upper respiratory tract infection			

subjects affected / exposed	0 / 29 (0.00%)	0 / 29 (0.00%)	0 / 59 (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

Serious adverse events	QW-QW		
Total subjects affected by serious adverse events			
subjects affected / exposed	31 / 56 (55.36%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events			
Vascular disorders			
Poor venous access			
subjects affected / exposed	5 / 56 (8.93%)		
occurrences causally related to treatment / all	0 / 5		
deaths causally related to treatment / all	0 / 0		
Surgical and medical procedures			
Central venous catheterisation			
subjects affected / exposed	1 / 56 (1.79%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Epiphyseal stapling			
subjects affected / exposed	0 / 56 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Knee operation			
subjects affected / exposed	0 / 56 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Medical device implantation			
subjects affected / exposed	1 / 56 (1.79%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Medical device removal			
subjects affected / exposed	4 / 56 (7.14%)		
occurrences causally related to treatment / all	0 / 4		
deaths causally related to treatment / all	0 / 0		

Spinal decompression			
subjects affected / exposed	0 / 56 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Pregnancy, puerperium and perinatal conditions			
Blighted ovum			
subjects affected / exposed	1 / 56 (1.79%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Ectopic pregnancy			
subjects affected / exposed	1 / 56 (1.79%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
General disorders and administration site conditions			
Device dislocation			
subjects affected / exposed	1 / 56 (1.79%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Device occlusion			
subjects affected / exposed	0 / 56 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Pyrexia			
subjects affected / exposed	0 / 56 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Immune system disorders			
Anaphylactic reaction			
subjects affected / exposed	0 / 56 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Hypersensitivity			

subjects affected / exposed	1 / 56 (1.79%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Social circumstances			
Child abuse			
subjects affected / exposed	0 / 56 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Respiratory, thoracic and mediastinal disorders			
Asthma			
subjects affected / exposed	1 / 56 (1.79%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Bronchopneumopathy			
subjects affected / exposed	0 / 56 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Bronchospasm			
subjects affected / exposed	1 / 56 (1.79%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Lung disorder			
subjects affected / exposed	0 / 56 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Sleep apnoea syndrome			
subjects affected / exposed	0 / 56 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Status asthmaticus			
subjects affected / exposed	1 / 56 (1.79%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		

Tonsillar hypertrophy			
subjects affected / exposed	1 / 56 (1.79%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Tracheal disorder			
subjects affected / exposed	0 / 56 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Tracheal stenosis			
subjects affected / exposed	0 / 56 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Psychiatric disorders			
Somatoform disorder			
subjects affected / exposed	0 / 56 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Injury, poisoning and procedural complications			
Fall			
subjects affected / exposed	0 / 56 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Joint dislocation			
subjects affected / exposed	0 / 56 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Lower limb fracture			
subjects affected / exposed	0 / 56 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Procedural pain			
subjects affected / exposed	1 / 56 (1.79%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		

Pseudomeningocele			
subjects affected / exposed	1 / 56 (1.79%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Congenital, familial and genetic disorders			
Congenital osteodystrophy			
subjects affected / exposed	1 / 56 (1.79%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Developmental hip dysplasia			
subjects affected / exposed	1 / 56 (1.79%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Cardiac disorders			
Cardio-respiratory arrest			
subjects affected / exposed	0 / 56 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Nervous system disorders			
Cervical cord compression			
subjects affected / exposed	1 / 56 (1.79%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Cervical myelopathy			
subjects affected / exposed	0 / 56 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Convulsion			
subjects affected / exposed	0 / 56 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Myelopathy			

subjects affected / exposed	0 / 56 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Paraplegia			
subjects affected / exposed	1 / 56 (1.79%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Quadriplegia			
subjects affected / exposed	0 / 56 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Spinal cord compression			
subjects affected / exposed	3 / 56 (5.36%)		
occurrences causally related to treatment / all	0 / 3		
deaths causally related to treatment / all	0 / 0		
Spinal cord ischaemia			
subjects affected / exposed	0 / 56 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Ear and labyrinth disorders			
Deafness			
subjects affected / exposed	0 / 56 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Middle ear effusion			
subjects affected / exposed	0 / 56 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Eye disorders			
Strabismus			
subjects affected / exposed	0 / 56 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Gastrointestinal disorders			

Abdominal pain			
subjects affected / exposed	1 / 56 (1.79%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Dyspepsia			
subjects affected / exposed	0 / 56 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Inguinal hernia			
subjects affected / exposed	0 / 56 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Oesophageal spasm			
subjects affected / exposed	0 / 56 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Rectal haemorrhage			
subjects affected / exposed	0 / 56 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Vomiting			
subjects affected / exposed	3 / 56 (5.36%)		
occurrences causally related to treatment / all	1 / 5		
deaths causally related to treatment / all	0 / 0		
Skin and subcutaneous tissue disorders			
Skin ulcer			
subjects affected / exposed	0 / 56 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Urticaria			
subjects affected / exposed	1 / 56 (1.79%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Renal and urinary disorders			

Haematuria			
subjects affected / exposed	0 / 56 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	0 / 56 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Back pain			
subjects affected / exposed	0 / 56 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Joint instability			
subjects affected / exposed	2 / 56 (3.57%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Knee deformity			
subjects affected / exposed	8 / 56 (14.29%)		
occurrences causally related to treatment / all	0 / 8		
deaths causally related to treatment / all	0 / 0		
Limb deformity			
subjects affected / exposed	1 / 56 (1.79%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Osteoarthritis			
subjects affected / exposed	0 / 56 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Osteochondrosis			
subjects affected / exposed	0 / 56 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		

Infections and infestations Appendicitis subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all	1 / 56 (1.79%) 0 / 1 0 / 0		
Dengue fever subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all	0 / 56 (0.00%) 0 / 0 0 / 0		
Diverticulitis subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all	0 / 56 (0.00%) 0 / 0 0 / 0		
Gastroenteritis subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all	0 / 56 (0.00%) 0 / 0 0 / 0		
Infected cyst subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all	1 / 56 (1.79%) 0 / 2 0 / 0		
Influenza subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all	1 / 56 (1.79%) 0 / 1 0 / 0		
Lower respiratory tract infection subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all	3 / 56 (5.36%) 0 / 3 0 / 0		
Mononucleosis syndrome subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all	0 / 56 (0.00%) 0 / 0 0 / 0		
Otitis media			

subjects affected / exposed	1 / 56 (1.79%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Otitis media chronic			
subjects affected / exposed	0 / 56 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Pilonidal cyst			
subjects affected / exposed	1 / 56 (1.79%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Pneumonia			
subjects affected / exposed	3 / 56 (5.36%)		
occurrences causally related to treatment / all	0 / 3		
deaths causally related to treatment / all	0 / 0		
Tooth abscess			
subjects affected / exposed	0 / 56 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Viral upper respiratory tract infection			
subjects affected / exposed	1 / 56 (1.79%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		

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

Non-serious adverse events	PBO-QOW	PBO-QW	QOW-QOW
Total subjects affected by non-serious adverse events			
subjects affected / exposed	29 / 29 (100.00%)	29 / 29 (100.00%)	59 / 59 (100.00%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Skin papilloma			
subjects affected / exposed	0 / 29 (0.00%)	1 / 29 (3.45%)	3 / 59 (5.08%)
occurrences (all)	0	1	3
Vascular disorders			

Flushing subjects affected / exposed occurrences (all)	1 / 29 (3.45%) 3	2 / 29 (6.90%) 2	2 / 59 (3.39%) 2
Hot flush subjects affected / exposed occurrences (all)	0 / 29 (0.00%) 0	2 / 29 (6.90%) 6	3 / 59 (5.08%) 5
Hypertension subjects affected / exposed occurrences (all)	1 / 29 (3.45%) 1	4 / 29 (13.79%) 13	6 / 59 (10.17%) 28
Hypotension subjects affected / exposed occurrences (all)	2 / 29 (6.90%) 2	1 / 29 (3.45%) 1	3 / 59 (5.08%) 6
Pallor subjects affected / exposed occurrences (all)	2 / 29 (6.90%) 3	2 / 29 (6.90%) 2	2 / 59 (3.39%) 4
Poor venous access subjects affected / exposed occurrences (all)	6 / 29 (20.69%) 21	5 / 29 (17.24%) 10	6 / 59 (10.17%) 7
Surgical and medical procedures			
Central venous catheterisation subjects affected / exposed occurrences (all)	1 / 29 (3.45%) 1	1 / 29 (3.45%) 1	3 / 59 (5.08%) 3
Tooth extraction subjects affected / exposed occurrences (all)	1 / 29 (3.45%) 1	2 / 29 (6.90%) 2	4 / 59 (6.78%) 6
General disorders and administration site conditions			
Asthenia subjects affected / exposed occurrences (all)	1 / 29 (3.45%) 1	2 / 29 (6.90%) 2	1 / 59 (1.69%) 2
Catheter site pain subjects affected / exposed occurrences (all)	2 / 29 (6.90%) 6	0 / 29 (0.00%) 0	6 / 59 (10.17%) 6
Chest discomfort subjects affected / exposed occurrences (all)	3 / 29 (10.34%) 4	2 / 29 (6.90%) 3	2 / 59 (3.39%) 2
Chest pain			

subjects affected / exposed	1 / 29 (3.45%)	2 / 29 (6.90%)	3 / 59 (5.08%)
occurrences (all)	1	2	5
Chills			
subjects affected / exposed	4 / 29 (13.79%)	1 / 29 (3.45%)	8 / 59 (13.56%)
occurrences (all)	4	1	10
Device dislocation			
subjects affected / exposed	2 / 29 (6.90%)	0 / 29 (0.00%)	3 / 59 (5.08%)
occurrences (all)	2	0	4
Device occlusion			
subjects affected / exposed	1 / 29 (3.45%)	1 / 29 (3.45%)	2 / 59 (3.39%)
occurrences (all)	1	3	2
Effusion			
subjects affected / exposed	0 / 29 (0.00%)	2 / 29 (6.90%)	1 / 59 (1.69%)
occurrences (all)	0	2	1
Extravasation			
subjects affected / exposed	0 / 29 (0.00%)	3 / 29 (10.34%)	3 / 59 (5.08%)
occurrences (all)	0	3	6
Fatigue			
subjects affected / exposed	10 / 29 (34.48%)	13 / 29 (44.83%)	16 / 59 (27.12%)
occurrences (all)	17	45	32
Feeling hot			
subjects affected / exposed	0 / 29 (0.00%)	1 / 29 (3.45%)	4 / 59 (6.78%)
occurrences (all)	0	1	4
Gait disturbance			
subjects affected / exposed	0 / 29 (0.00%)	1 / 29 (3.45%)	3 / 59 (5.08%)
occurrences (all)	0	1	4
Hyperthermia			
subjects affected / exposed	0 / 29 (0.00%)	2 / 29 (6.90%)	0 / 59 (0.00%)
occurrences (all)	0	2	0
Influenza like illness			
subjects affected / exposed	3 / 29 (10.34%)	1 / 29 (3.45%)	1 / 59 (1.69%)
occurrences (all)	3	1	1
Infusion site extravasation			
subjects affected / exposed	3 / 29 (10.34%)	1 / 29 (3.45%)	9 / 59 (15.25%)
occurrences (all)	4	2	12
Infusion site pain			

subjects affected / exposed	2 / 29 (6.90%)	1 / 29 (3.45%)	6 / 59 (10.17%)
occurrences (all)	2	1	8
Infusion site rash			
subjects affected / exposed	2 / 29 (6.90%)	0 / 29 (0.00%)	2 / 59 (3.39%)
occurrences (all)	2	0	2
Infusion site swelling			
subjects affected / exposed	1 / 29 (3.45%)	0 / 29 (0.00%)	3 / 59 (5.08%)
occurrences (all)	1	0	3
Irritability			
subjects affected / exposed	0 / 29 (0.00%)	0 / 29 (0.00%)	0 / 59 (0.00%)
occurrences (all)	0	0	0
Local swelling			
subjects affected / exposed	3 / 29 (10.34%)	0 / 29 (0.00%)	5 / 59 (8.47%)
occurrences (all)	7	0	5
Malaise			
subjects affected / exposed	2 / 29 (6.90%)	3 / 29 (10.34%)	6 / 59 (10.17%)
occurrences (all)	2	5	7
Medical device complication			
subjects affected / exposed	2 / 29 (6.90%)	1 / 29 (3.45%)	5 / 59 (8.47%)
occurrences (all)	2	3	6
Non-cardiac chest pain			
subjects affected / exposed	1 / 29 (3.45%)	1 / 29 (3.45%)	4 / 59 (6.78%)
occurrences (all)	1	1	4
Oedema			
subjects affected / exposed	0 / 29 (0.00%)	2 / 29 (6.90%)	0 / 59 (0.00%)
occurrences (all)	0	2	0
Oedema peripheral			
subjects affected / exposed	1 / 29 (3.45%)	0 / 29 (0.00%)	4 / 59 (6.78%)
occurrences (all)	4	0	4
Pain			
subjects affected / exposed	5 / 29 (17.24%)	1 / 29 (3.45%)	6 / 59 (10.17%)
occurrences (all)	6	3	8
Puncture site pain			
subjects affected / exposed	1 / 29 (3.45%)	0 / 29 (0.00%)	4 / 59 (6.78%)
occurrences (all)	1	0	4
Pyrexia			

subjects affected / exposed occurrences (all)	22 / 29 (75.86%) 91	19 / 29 (65.52%) 62	38 / 59 (64.41%) 113
Immune system disorders			
Hypersensitivity			
subjects affected / exposed	1 / 29 (3.45%)	0 / 29 (0.00%)	5 / 59 (8.47%)
occurrences (all)	1	0	8
Seasonal allergy			
subjects affected / exposed	2 / 29 (6.90%)	2 / 29 (6.90%)	4 / 59 (6.78%)
occurrences (all)	2	4	6
Reproductive system and breast disorders			
Dysmenorrhoea			
subjects affected / exposed	3 / 29 (10.34%)	1 / 29 (3.45%)	5 / 59 (8.47%)
occurrences (all)	11	4	24
Respiratory, thoracic and mediastinal disorders			
Allergic cough			
subjects affected / exposed	1 / 29 (3.45%)	0 / 29 (0.00%)	3 / 59 (5.08%)
occurrences (all)	2	0	3
Asthma			
subjects affected / exposed	2 / 29 (6.90%)	2 / 29 (6.90%)	5 / 59 (8.47%)
occurrences (all)	2	3	12
Bronchospasm			
subjects affected / exposed	0 / 29 (0.00%)	1 / 29 (3.45%)	5 / 59 (8.47%)
occurrences (all)	0	1	6
Cough			
subjects affected / exposed	21 / 29 (72.41%)	14 / 29 (48.28%)	37 / 59 (62.71%)
occurrences (all)	62	49	85
Dyspnoea			
subjects affected / exposed	6 / 29 (20.69%)	5 / 29 (17.24%)	12 / 59 (20.34%)
occurrences (all)	8	7	33
Epistaxis			
subjects affected / exposed	3 / 29 (10.34%)	4 / 29 (13.79%)	5 / 59 (8.47%)
occurrences (all)	9	8	6
Nasal congestion			
subjects affected / exposed	10 / 29 (34.48%)	4 / 29 (13.79%)	15 / 59 (25.42%)
occurrences (all)	21	6	24
Nasal obstruction			

subjects affected / exposed	3 / 29 (10.34%)	3 / 29 (10.34%)	6 / 59 (10.17%)
occurrences (all)	10	3	7
Neonatal hypoxia			
subjects affected / exposed	0 / 29 (0.00%)	0 / 29 (0.00%)	2 / 59 (3.39%)
occurrences (all)	0	0	2
Obstructive airways disorder			
subjects affected / exposed	0 / 29 (0.00%)	1 / 29 (3.45%)	1 / 59 (1.69%)
occurrences (all)	0	1	1
Oropharyngeal pain			
subjects affected / exposed	13 / 29 (44.83%)	11 / 29 (37.93%)	23 / 59 (38.98%)
occurrences (all)	24	16	48
Pharyngeal disorder			
subjects affected / exposed	2 / 29 (6.90%)	0 / 29 (0.00%)	0 / 59 (0.00%)
occurrences (all)	2	0	0
Pharyngeal erythema			
subjects affected / exposed	0 / 29 (0.00%)	0 / 29 (0.00%)	0 / 59 (0.00%)
occurrences (all)	0	0	0
Productive cough			
subjects affected / exposed	1 / 29 (3.45%)	3 / 29 (10.34%)	2 / 59 (3.39%)
occurrences (all)	1	3	2
Respiratory tract congestion			
subjects affected / exposed	0 / 29 (0.00%)	0 / 29 (0.00%)	3 / 59 (5.08%)
occurrences (all)	0	0	5
Restrictive pulmonary disease			
subjects affected / exposed	2 / 29 (6.90%)	0 / 29 (0.00%)	1 / 59 (1.69%)
occurrences (all)	2	0	1
Rhinitis allergic			
subjects affected / exposed	3 / 29 (10.34%)	5 / 29 (17.24%)	9 / 59 (15.25%)
occurrences (all)	3	7	14
Rhinorrhoea			
subjects affected / exposed	5 / 29 (17.24%)	5 / 29 (17.24%)	7 / 59 (11.86%)
occurrences (all)	6	10	16
Sinus congestion			
subjects affected / exposed	2 / 29 (6.90%)	1 / 29 (3.45%)	0 / 59 (0.00%)
occurrences (all)	2	1	0
Sleep apnoea syndrome			

subjects affected / exposed occurrences (all)	1 / 29 (3.45%) 1	2 / 29 (6.90%) 2	4 / 59 (6.78%) 4
Sneezing subjects affected / exposed occurrences (all)	2 / 29 (6.90%) 2	1 / 29 (3.45%) 1	1 / 59 (1.69%) 1
Tachypnoea subjects affected / exposed occurrences (all)	3 / 29 (10.34%) 3	1 / 29 (3.45%) 1	3 / 59 (5.08%) 6
Throat irritation subjects affected / exposed occurrences (all)	3 / 29 (10.34%) 3	1 / 29 (3.45%) 1	0 / 59 (0.00%) 0
Tonsillar hypertrophy subjects affected / exposed occurrences (all)	2 / 29 (6.90%) 3	2 / 29 (6.90%) 2	2 / 59 (3.39%) 3
Wheezing subjects affected / exposed occurrences (all)	5 / 29 (17.24%) 10	5 / 29 (17.24%) 6	6 / 59 (10.17%) 8
Psychiatric disorders Agitation subjects affected / exposed occurrences (all)	1 / 29 (3.45%) 1	0 / 29 (0.00%) 0	2 / 59 (3.39%) 2
Anxiety subjects affected / exposed occurrences (all)	3 / 29 (10.34%) 4	3 / 29 (10.34%) 4	5 / 59 (8.47%) 7
Insomnia subjects affected / exposed occurrences (all)	2 / 29 (6.90%) 2	1 / 29 (3.45%) 1	2 / 59 (3.39%) 3
Investigations Blood cholesterol increased subjects affected / exposed occurrences (all)	2 / 29 (6.90%) 2	0 / 29 (0.00%) 0	0 / 59 (0.00%) 0
Blood pressure diastolic increased subjects affected / exposed occurrences (all)	0 / 29 (0.00%) 0	2 / 29 (6.90%) 4	3 / 59 (5.08%) 9
Blood pressure increased			

subjects affected / exposed	2 / 29 (6.90%)	0 / 29 (0.00%)	3 / 59 (5.08%)
occurrences (all)	6	0	3
Blood pressure systolic increased			
subjects affected / exposed	0 / 29 (0.00%)	2 / 29 (6.90%)	3 / 59 (5.08%)
occurrences (all)	0	7	28
Blood urine present			
subjects affected / exposed	2 / 29 (6.90%)	0 / 29 (0.00%)	1 / 59 (1.69%)
occurrences (all)	5	0	1
Heart rate decreased			
subjects affected / exposed	2 / 29 (6.90%)	0 / 29 (0.00%)	0 / 59 (0.00%)
occurrences (all)	2	0	0
Heart rate increased			
subjects affected / exposed	2 / 29 (6.90%)	1 / 29 (3.45%)	4 / 59 (6.78%)
occurrences (all)	3	1	4
Oxygen saturation decreased			
subjects affected / exposed	6 / 29 (20.69%)	3 / 29 (10.34%)	9 / 59 (15.25%)
occurrences (all)	17	15	16
Respiratory rate increased			
subjects affected / exposed	4 / 29 (13.79%)	1 / 29 (3.45%)	2 / 59 (3.39%)
occurrences (all)	5	1	2
Vital capacity decreased			
subjects affected / exposed	1 / 29 (3.45%)	0 / 29 (0.00%)	3 / 59 (5.08%)
occurrences (all)	1	0	3
Injury, poisoning and procedural complications			
Arthropod bite			
subjects affected / exposed	0 / 29 (0.00%)	1 / 29 (3.45%)	2 / 59 (3.39%)
occurrences (all)	0	1	2
Contusion			
subjects affected / exposed	3 / 29 (10.34%)	0 / 29 (0.00%)	2 / 59 (3.39%)
occurrences (all)	3	0	3
Excoriation			
subjects affected / exposed	0 / 29 (0.00%)	0 / 29 (0.00%)	4 / 59 (6.78%)
occurrences (all)	0	0	5
Fall			

subjects affected / exposed occurrences (all)	4 / 29 (13.79%) 5	3 / 29 (10.34%) 4	12 / 59 (20.34%) 20
Head injury subjects affected / exposed occurrences (all)	1 / 29 (3.45%) 1	0 / 29 (0.00%) 0	4 / 59 (6.78%) 8
Infusion related reaction subjects affected / exposed occurrences (all)	3 / 29 (10.34%) 5	0 / 29 (0.00%) 0	2 / 59 (3.39%) 4
Joint dislocation subjects affected / exposed occurrences (all)	0 / 29 (0.00%) 0	0 / 29 (0.00%) 0	4 / 59 (6.78%) 5
Joint injury subjects affected / exposed occurrences (all)	0 / 29 (0.00%) 0	0 / 29 (0.00%) 0	4 / 59 (6.78%) 4
Ligament sprain subjects affected / exposed occurrences (all)	2 / 29 (6.90%) 2	1 / 29 (3.45%) 1	1 / 59 (1.69%) 1
Limb injury subjects affected / exposed occurrences (all)	2 / 29 (6.90%) 2	0 / 29 (0.00%) 0	3 / 59 (5.08%) 3
Procedural pain subjects affected / exposed occurrences (all)	3 / 29 (10.34%) 9	2 / 29 (6.90%) 2	6 / 59 (10.17%) 7
Tooth fracture subjects affected / exposed occurrences (all)	2 / 29 (6.90%) 2	0 / 29 (0.00%) 0	1 / 59 (1.69%) 1
Cardiac disorders			
Aortic valve disease subjects affected / exposed occurrences (all)	1 / 29 (3.45%) 1	1 / 29 (3.45%) 1	5 / 59 (8.47%) 5
Aortic valve incompetence subjects affected / exposed occurrences (all)	1 / 29 (3.45%) 1	3 / 29 (10.34%) 3	8 / 59 (13.56%) 8
Left ventricular hypertrophy subjects affected / exposed occurrences (all)	0 / 29 (0.00%) 0	0 / 29 (0.00%) 0	1 / 59 (1.69%) 1

Mitral valve disease subjects affected / exposed occurrences (all)	1 / 29 (3.45%) 1	1 / 29 (3.45%) 1	6 / 59 (10.17%) 6
Mitral valve incompetence subjects affected / exposed occurrences (all)	4 / 29 (13.79%) 4	6 / 29 (20.69%) 6	12 / 59 (20.34%) 12
Palpitations subjects affected / exposed occurrences (all)	1 / 29 (3.45%) 1	2 / 29 (6.90%) 4	1 / 59 (1.69%) 1
Pulmonary valve incompetence subjects affected / exposed occurrences (all)	2 / 29 (6.90%) 2	3 / 29 (10.34%) 3	2 / 59 (3.39%) 2
Sinus arrhythmia subjects affected / exposed occurrences (all)	0 / 29 (0.00%) 0	0 / 29 (0.00%) 0	3 / 59 (5.08%) 3
Sinus tachycardia subjects affected / exposed occurrences (all)	1 / 29 (3.45%) 1	3 / 29 (10.34%) 4	1 / 59 (1.69%) 1
Tachycardia subjects affected / exposed occurrences (all)	8 / 29 (27.59%) 14	4 / 29 (13.79%) 15	8 / 59 (13.56%) 31
Tricuspid valve incompetence subjects affected / exposed occurrences (all)	6 / 29 (20.69%) 6	1 / 29 (3.45%) 1	11 / 59 (18.64%) 12
Nervous system disorders			
Cervical cord compression subjects affected / exposed occurrences (all)	2 / 29 (6.90%) 2	0 / 29 (0.00%) 0	0 / 59 (0.00%) 0
Dizziness subjects affected / exposed occurrences (all)	5 / 29 (17.24%) 6	6 / 29 (20.69%) 6	8 / 59 (13.56%) 20
Headache subjects affected / exposed occurrences (all)	23 / 29 (79.31%) 102	16 / 29 (55.17%) 67	39 / 59 (66.10%) 232
Hyperreflexia			

subjects affected / exposed occurrences (all)	2 / 29 (6.90%) 3	3 / 29 (10.34%) 4	1 / 59 (1.69%) 2
Hypoaesthesia subjects affected / exposed occurrences (all)	1 / 29 (3.45%) 1	1 / 29 (3.45%) 1	4 / 59 (6.78%) 5
Lethargy subjects affected / exposed occurrences (all)	1 / 29 (3.45%) 1	1 / 29 (3.45%) 1	3 / 59 (5.08%) 3
Paraesthesia subjects affected / exposed occurrences (all)	1 / 29 (3.45%) 1	1 / 29 (3.45%) 1	2 / 59 (3.39%) 2
Somnolence subjects affected / exposed occurrences (all)	2 / 29 (6.90%) 28	3 / 29 (10.34%) 3	1 / 59 (1.69%) 1
Syncope subjects affected / exposed occurrences (all)	0 / 29 (0.00%) 0	2 / 29 (6.90%) 9	0 / 59 (0.00%) 0
Blood and lymphatic system disorders Lymphadenopathy subjects affected / exposed occurrences (all)	3 / 29 (10.34%) 4	0 / 29 (0.00%) 0	1 / 59 (1.69%) 1
Ear and labyrinth disorders Ear discomfort subjects affected / exposed occurrences (all)	2 / 29 (6.90%) 3	0 / 29 (0.00%) 0	1 / 59 (1.69%) 1
Ear pain subjects affected / exposed occurrences (all)	10 / 29 (34.48%) 16	7 / 29 (24.14%) 8	19 / 59 (32.20%) 42
Hypoacusis subjects affected / exposed occurrences (all)	2 / 29 (6.90%) 3	0 / 29 (0.00%) 0	3 / 59 (5.08%) 3
Middle ear effusion subjects affected / exposed occurrences (all)	2 / 29 (6.90%) 2	0 / 29 (0.00%) 0	1 / 59 (1.69%) 1
Motion sickness			

subjects affected / exposed	1 / 29 (3.45%)	1 / 29 (3.45%)	0 / 59 (0.00%)
occurrences (all)	1	1	0
Tinnitus			
subjects affected / exposed	0 / 29 (0.00%)	0 / 29 (0.00%)	0 / 59 (0.00%)
occurrences (all)	0	0	0
Vertigo			
subjects affected / exposed	1 / 29 (3.45%)	2 / 29 (6.90%)	3 / 59 (5.08%)
occurrences (all)	4	2	7
Eye disorders			
Astigmatism			
subjects affected / exposed	0 / 29 (0.00%)	3 / 29 (10.34%)	0 / 59 (0.00%)
occurrences (all)	0	3	0
Conjunctivitis			
subjects affected / exposed	2 / 29 (6.90%)	2 / 29 (6.90%)	6 / 59 (10.17%)
occurrences (all)	2	2	9
Corneal opacity			
subjects affected / exposed	3 / 29 (10.34%)	5 / 29 (17.24%)	5 / 59 (8.47%)
occurrences (all)	3	5	5
Glaucoma			
subjects affected / exposed	0 / 29 (0.00%)	2 / 29 (6.90%)	0 / 59 (0.00%)
occurrences (all)	0	2	0
Myopia			
subjects affected / exposed	0 / 29 (0.00%)	2 / 29 (6.90%)	1 / 59 (1.69%)
occurrences (all)	0	2	1
Ocular hyperaemia			
subjects affected / exposed	0 / 29 (0.00%)	2 / 29 (6.90%)	3 / 59 (5.08%)
occurrences (all)	0	2	4
Visual impairment			
subjects affected / exposed	0 / 29 (0.00%)	0 / 29 (0.00%)	0 / 59 (0.00%)
occurrences (all)	0	0	0
Gastrointestinal disorders			
Abdominal discomfort			
subjects affected / exposed	3 / 29 (10.34%)	1 / 29 (3.45%)	5 / 59 (8.47%)
occurrences (all)	6	1	8
Abdominal distension			

subjects affected / exposed	3 / 29 (10.34%)	0 / 29 (0.00%)	0 / 59 (0.00%)
occurrences (all)	19	0	0
Abdominal pain			
subjects affected / exposed	12 / 29 (41.38%)	6 / 29 (20.69%)	22 / 59 (37.29%)
occurrences (all)	19	8	59
Abdominal pain lower			
subjects affected / exposed	0 / 29 (0.00%)	1 / 29 (3.45%)	3 / 59 (5.08%)
occurrences (all)	0	1	3
Abdominal pain upper			
subjects affected / exposed	8 / 29 (27.59%)	9 / 29 (31.03%)	9 / 59 (15.25%)
occurrences (all)	15	11	16
Anal pruritus			
subjects affected / exposed	2 / 29 (6.90%)	0 / 29 (0.00%)	1 / 59 (1.69%)
occurrences (all)	2	0	1
Breath odour			
subjects affected / exposed	0 / 29 (0.00%)	3 / 29 (10.34%)	0 / 59 (0.00%)
occurrences (all)	0	3	0
Constipation			
subjects affected / exposed	4 / 29 (13.79%)	4 / 29 (13.79%)	7 / 59 (11.86%)
occurrences (all)	5	4	7
Dental caries			
subjects affected / exposed	0 / 29 (0.00%)	3 / 29 (10.34%)	4 / 59 (6.78%)
occurrences (all)	0	3	4
Diarrhoea			
subjects affected / exposed	11 / 29 (37.93%)	11 / 29 (37.93%)	25 / 59 (42.37%)
occurrences (all)	26	27	71
Dyspepsia			
subjects affected / exposed	3 / 29 (10.34%)	5 / 29 (17.24%)	3 / 59 (5.08%)
occurrences (all)	26	5	5
Enterocolitis			
subjects affected / exposed	0 / 29 (0.00%)	0 / 29 (0.00%)	3 / 59 (5.08%)
occurrences (all)	0	0	3
Flatulence			
subjects affected / exposed	2 / 29 (6.90%)	1 / 29 (3.45%)	2 / 59 (3.39%)
occurrences (all)	6	1	2
Gastrooesophageal reflux disease			

subjects affected / exposed	1 / 29 (3.45%)	1 / 29 (3.45%)	2 / 59 (3.39%)
occurrences (all)	1	1	3
Haemorrhoids			
subjects affected / exposed	2 / 29 (6.90%)	0 / 29 (0.00%)	1 / 59 (1.69%)
occurrences (all)	2	0	1
Mouth ulceration			
subjects affected / exposed	2 / 29 (6.90%)	0 / 29 (0.00%)	2 / 59 (3.39%)
occurrences (all)	3	0	3
Nausea			
subjects affected / exposed	15 / 29 (51.72%)	10 / 29 (34.48%)	26 / 59 (44.07%)
occurrences (all)	34	18	65
Proctalgia			
subjects affected / exposed	2 / 29 (6.90%)	0 / 29 (0.00%)	0 / 59 (0.00%)
occurrences (all)	2	0	0
Stomatitis			
subjects affected / exposed	0 / 29 (0.00%)	1 / 29 (3.45%)	3 / 59 (5.08%)
occurrences (all)	0	1	3
Toothache			
subjects affected / exposed	3 / 29 (10.34%)	3 / 29 (10.34%)	8 / 59 (13.56%)
occurrences (all)	4	5	14
Vomiting			
subjects affected / exposed	20 / 29 (68.97%)	17 / 29 (58.62%)	39 / 59 (66.10%)
occurrences (all)	105	62	134
Skin and subcutaneous tissue disorders			
Acne			
subjects affected / exposed	2 / 29 (6.90%)	3 / 29 (10.34%)	2 / 59 (3.39%)
occurrences (all)	2	3	2
Blister			
subjects affected / exposed	0 / 29 (0.00%)	0 / 29 (0.00%)	3 / 59 (5.08%)
occurrences (all)	0	0	6
Dermatitis			
subjects affected / exposed	1 / 29 (3.45%)	0 / 29 (0.00%)	1 / 59 (1.69%)
occurrences (all)	1	0	1
Dermatitis allergic			
subjects affected / exposed	2 / 29 (6.90%)	0 / 29 (0.00%)	5 / 59 (8.47%)
occurrences (all)	2	0	5

Dry skin			
subjects affected / exposed	3 / 29 (10.34%)	0 / 29 (0.00%)	1 / 59 (1.69%)
occurrences (all)	3	0	1
Eczema			
subjects affected / exposed	2 / 29 (6.90%)	4 / 29 (13.79%)	8 / 59 (13.56%)
occurrences (all)	2	7	10
Erythema			
subjects affected / exposed	6 / 29 (20.69%)	3 / 29 (10.34%)	7 / 59 (11.86%)
occurrences (all)	12	4	7
Hyperhidrosis			
subjects affected / exposed	1 / 29 (3.45%)	4 / 29 (13.79%)	1 / 59 (1.69%)
occurrences (all)	1	6	1
Petechiae			
subjects affected / exposed	0 / 29 (0.00%)	0 / 29 (0.00%)	4 / 59 (6.78%)
occurrences (all)	0	0	4
Pruritus			
subjects affected / exposed	7 / 29 (24.14%)	3 / 29 (10.34%)	8 / 59 (13.56%)
occurrences (all)	18	6	28
Rash			
subjects affected / exposed	8 / 29 (27.59%)	8 / 29 (27.59%)	15 / 59 (25.42%)
occurrences (all)	13	30	61
Rash erythematous			
subjects affected / exposed	2 / 29 (6.90%)	0 / 29 (0.00%)	1 / 59 (1.69%)
occurrences (all)	3	0	3
Rash macular			
subjects affected / exposed	1 / 29 (3.45%)	1 / 29 (3.45%)	1 / 59 (1.69%)
occurrences (all)	5	1	1
Rash maculo-papular			
subjects affected / exposed	0 / 29 (0.00%)	0 / 29 (0.00%)	3 / 59 (5.08%)
occurrences (all)	0	0	59
Rash pruritic			
subjects affected / exposed	0 / 29 (0.00%)	0 / 29 (0.00%)	3 / 59 (5.08%)
occurrences (all)	0	0	3
Skin disorder			
subjects affected / exposed	0 / 29 (0.00%)	0 / 29 (0.00%)	0 / 59 (0.00%)
occurrences (all)	0	0	0

Skin lesion subjects affected / exposed occurrences (all)	2 / 29 (6.90%) 2	1 / 29 (3.45%) 1	3 / 59 (5.08%) 3
Urticaria subjects affected / exposed occurrences (all)	6 / 29 (20.69%) 38	1 / 29 (3.45%) 37	11 / 59 (18.64%) 53
Renal and urinary disorders			
Dysuria subjects affected / exposed occurrences (all)	2 / 29 (6.90%) 2	0 / 29 (0.00%) 0	3 / 59 (5.08%) 3
Haematuria subjects affected / exposed occurrences (all)	0 / 29 (0.00%) 0	0 / 29 (0.00%) 0	1 / 59 (1.69%) 2
Pollakiuria subjects affected / exposed occurrences (all)	0 / 29 (0.00%) 0	0 / 29 (0.00%) 0	4 / 59 (6.78%) 4
Proteinuria subjects affected / exposed occurrences (all)	2 / 29 (6.90%) 2	0 / 29 (0.00%) 0	3 / 59 (5.08%) 4
Musculoskeletal and connective tissue disorders			
Arthralgia subjects affected / exposed occurrences (all)	20 / 29 (68.97%) 90	16 / 29 (55.17%) 57	40 / 59 (67.80%) 93
Back pain subjects affected / exposed occurrences (all)	10 / 29 (34.48%) 17	4 / 29 (13.79%) 6	19 / 59 (32.20%) 45
Joint swelling subjects affected / exposed occurrences (all)	2 / 29 (6.90%) 2	0 / 29 (0.00%) 0	2 / 59 (3.39%) 2
Knee deformity subjects affected / exposed occurrences (all)	2 / 29 (6.90%) 2	5 / 29 (17.24%) 6	1 / 59 (1.69%) 1
Muscle spasms subjects affected / exposed occurrences (all)	2 / 29 (6.90%) 2	3 / 29 (10.34%) 4	1 / 59 (1.69%) 1
Musculoskeletal chest pain			

subjects affected / exposed	1 / 29 (3.45%)	1 / 29 (3.45%)	5 / 59 (8.47%)
occurrences (all)	3	2	5
Musculoskeletal pain			
subjects affected / exposed	7 / 29 (24.14%)	4 / 29 (13.79%)	10 / 59 (16.95%)
occurrences (all)	14	9	14
Musculoskeletal stiffness			
subjects affected / exposed	2 / 29 (6.90%)	1 / 29 (3.45%)	3 / 59 (5.08%)
occurrences (all)	2	2	4
Myalgia			
subjects affected / exposed	7 / 29 (24.14%)	1 / 29 (3.45%)	3 / 59 (5.08%)
occurrences (all)	11	1	3
Neck pain			
subjects affected / exposed	9 / 29 (31.03%)	3 / 29 (10.34%)	9 / 59 (15.25%)
occurrences (all)	9	3	14
Osteopenia			
subjects affected / exposed	2 / 29 (6.90%)	1 / 29 (3.45%)	4 / 59 (6.78%)
occurrences (all)	2	1	4
Pain in extremity			
subjects affected / exposed	16 / 29 (55.17%)	12 / 29 (41.38%)	27 / 59 (45.76%)
occurrences (all)	54	25	80
Spinal pain			
subjects affected / exposed	3 / 29 (10.34%)	0 / 29 (0.00%)	0 / 59 (0.00%)
occurrences (all)	3	0	0
Infections and infestations			
Bronchitis			
subjects affected / exposed	5 / 29 (17.24%)	3 / 29 (10.34%)	7 / 59 (11.86%)
occurrences (all)	7	4	8
Cellulitis			
subjects affected / exposed	2 / 29 (6.90%)	0 / 29 (0.00%)	0 / 59 (0.00%)
occurrences (all)	2	0	0
Ear infection			
subjects affected / exposed	7 / 29 (24.14%)	3 / 29 (10.34%)	5 / 59 (8.47%)
occurrences (all)	9	3	13
Fungal infection			
subjects affected / exposed	2 / 29 (6.90%)	0 / 29 (0.00%)	2 / 59 (3.39%)
occurrences (all)	2	0	2

Furuncle			
subjects affected / exposed	2 / 29 (6.90%)	0 / 29 (0.00%)	0 / 59 (0.00%)
occurrences (all)	4	0	0
Gastroenteritis			
subjects affected / exposed	5 / 29 (17.24%)	9 / 29 (31.03%)	24 / 59 (40.68%)
occurrences (all)	9	13	36
Gastroenteritis viral			
subjects affected / exposed	2 / 29 (6.90%)	1 / 29 (3.45%)	2 / 59 (3.39%)
occurrences (all)	2	1	2
Gingivitis			
subjects affected / exposed	0 / 29 (0.00%)	2 / 29 (6.90%)	3 / 59 (5.08%)
occurrences (all)	0	3	3
Hordeolum			
subjects affected / exposed	1 / 29 (3.45%)	1 / 29 (3.45%)	6 / 59 (10.17%)
occurrences (all)	2	1	14
Influenza			
subjects affected / exposed	3 / 29 (10.34%)	5 / 29 (17.24%)	11 / 59 (18.64%)
occurrences (all)	7	6	24
Laryngitis			
subjects affected / exposed	0 / 29 (0.00%)	0 / 29 (0.00%)	3 / 59 (5.08%)
occurrences (all)	0	0	4
Lice infestation			
subjects affected / exposed	0 / 29 (0.00%)	0 / 29 (0.00%)	1 / 59 (1.69%)
occurrences (all)	0	0	2
Lower respiratory tract infection			
subjects affected / exposed	1 / 29 (3.45%)	1 / 29 (3.45%)	2 / 59 (3.39%)
occurrences (all)	2	1	2
Nasopharyngitis			
subjects affected / exposed	13 / 29 (44.83%)	13 / 29 (44.83%)	29 / 59 (49.15%)
occurrences (all)	34	28	62
Oral candidiasis			
subjects affected / exposed	0 / 29 (0.00%)	1 / 29 (3.45%)	4 / 59 (6.78%)
occurrences (all)	0	1	7
Oral herpes			
subjects affected / exposed	1 / 29 (3.45%)	1 / 29 (3.45%)	4 / 59 (6.78%)
occurrences (all)	2	1	7

Otitis externa			
subjects affected / exposed	3 / 29 (10.34%)	1 / 29 (3.45%)	8 / 59 (13.56%)
occurrences (all)	4	1	15
Otitis media			
subjects affected / exposed	8 / 29 (27.59%)	5 / 29 (17.24%)	11 / 59 (18.64%)
occurrences (all)	10	5	29
Otitis media acute			
subjects affected / exposed	1 / 29 (3.45%)	2 / 29 (6.90%)	5 / 59 (8.47%)
occurrences (all)	2	2	11
Pharyngitis			
subjects affected / exposed	9 / 29 (31.03%)	6 / 29 (20.69%)	8 / 59 (13.56%)
occurrences (all)	12	7	10
Rash pustular			
subjects affected / exposed	2 / 29 (6.90%)	0 / 29 (0.00%)	0 / 59 (0.00%)
occurrences (all)	2	0	0
Respiratory tract infection viral			
subjects affected / exposed	1 / 29 (3.45%)	2 / 29 (6.90%)	3 / 59 (5.08%)
occurrences (all)	1	2	6
Rhinitis			
subjects affected / exposed	9 / 29 (31.03%)	6 / 29 (20.69%)	11 / 59 (18.64%)
occurrences (all)	21	17	30
Sinusitis			
subjects affected / exposed	5 / 29 (17.24%)	1 / 29 (3.45%)	4 / 59 (6.78%)
occurrences (all)	7	1	4
Tinea pedis			
subjects affected / exposed	2 / 29 (6.90%)	1 / 29 (3.45%)	0 / 59 (0.00%)
occurrences (all)	2	1	0
Tonsillitis			
subjects affected / exposed	2 / 29 (6.90%)	2 / 29 (6.90%)	5 / 59 (8.47%)
occurrences (all)	3	2	8
Tooth infection			
subjects affected / exposed	0 / 29 (0.00%)	2 / 29 (6.90%)	1 / 59 (1.69%)
occurrences (all)	0	2	1
Upper respiratory tract infection			
subjects affected / exposed	13 / 29 (44.83%)	8 / 29 (27.59%)	24 / 59 (40.68%)
occurrences (all)	53	25	82

Varicella			
subjects affected / exposed	1 / 29 (3.45%)	0 / 29 (0.00%)	3 / 59 (5.08%)
occurrences (all)	1	0	3
Viral infection			
subjects affected / exposed	1 / 29 (3.45%)	3 / 29 (10.34%)	9 / 59 (15.25%)
occurrences (all)	3	5	12
Viral pharyngitis			
subjects affected / exposed	2 / 29 (6.90%)	0 / 29 (0.00%)	0 / 59 (0.00%)
occurrences (all)	2	0	0
Viral upper respiratory tract infection			
subjects affected / exposed	6 / 29 (20.69%)	0 / 29 (0.00%)	5 / 59 (8.47%)
occurrences (all)	12	0	9
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	1 / 29 (3.45%)	2 / 29 (6.90%)	1 / 59 (1.69%)
occurrences (all)	1	3	1

Non-serious adverse events	QW-QW		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	56 / 56 (100.00%)		
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Skin papilloma			
subjects affected / exposed	0 / 56 (0.00%)		
occurrences (all)	0		
Vascular disorders			
Flushing			
subjects affected / exposed	5 / 56 (8.93%)		
occurrences (all)	8		
Hot flush			
subjects affected / exposed	2 / 56 (3.57%)		
occurrences (all)	2		
Hypertension			
subjects affected / exposed	6 / 56 (10.71%)		
occurrences (all)	16		
Hypotension			
subjects affected / exposed	6 / 56 (10.71%)		
occurrences (all)	7		

Pallor subjects affected / exposed occurrences (all)	7 / 56 (12.50%) 21		
Poor venous access subjects affected / exposed occurrences (all)	8 / 56 (14.29%) 16		
Surgical and medical procedures Central venous catheterisation subjects affected / exposed occurrences (all)	1 / 56 (1.79%) 1		
Tooth extraction subjects affected / exposed occurrences (all)	0 / 56 (0.00%) 0		
General disorders and administration site conditions Asthenia subjects affected / exposed occurrences (all)	4 / 56 (7.14%) 5		
Catheter site pain subjects affected / exposed occurrences (all)	5 / 56 (8.93%) 12		
Chest discomfort subjects affected / exposed occurrences (all)	3 / 56 (5.36%) 3		
Chest pain subjects affected / exposed occurrences (all)	4 / 56 (7.14%) 4		
Chills subjects affected / exposed occurrences (all)	9 / 56 (16.07%) 14		
Device dislocation subjects affected / exposed occurrences (all)	1 / 56 (1.79%) 1		
Device occlusion subjects affected / exposed occurrences (all)	4 / 56 (7.14%) 6		
Effusion			

subjects affected / exposed	1 / 56 (1.79%)		
occurrences (all)	2		
Extravasation			
subjects affected / exposed	5 / 56 (8.93%)		
occurrences (all)	5		
Fatigue			
subjects affected / exposed	19 / 56 (33.93%)		
occurrences (all)	50		
Feeling hot			
subjects affected / exposed	2 / 56 (3.57%)		
occurrences (all)	3		
Gait disturbance			
subjects affected / exposed	5 / 56 (8.93%)		
occurrences (all)	5		
Hyperthermia			
subjects affected / exposed	1 / 56 (1.79%)		
occurrences (all)	1		
Influenza like illness			
subjects affected / exposed	3 / 56 (5.36%)		
occurrences (all)	4		
Infusion site extravasation			
subjects affected / exposed	4 / 56 (7.14%)		
occurrences (all)	4		
Infusion site pain			
subjects affected / exposed	4 / 56 (7.14%)		
occurrences (all)	6		
Infusion site rash			
subjects affected / exposed	1 / 56 (1.79%)		
occurrences (all)	1		
Infusion site swelling			
subjects affected / exposed	2 / 56 (3.57%)		
occurrences (all)	2		
Irritability			
subjects affected / exposed	3 / 56 (5.36%)		
occurrences (all)	5		
Local swelling			

subjects affected / exposed	4 / 56 (7.14%)		
occurrences (all)	9		
Malaise			
subjects affected / exposed	3 / 56 (5.36%)		
occurrences (all)	5		
Medical device complication			
subjects affected / exposed	5 / 56 (8.93%)		
occurrences (all)	8		
Non-cardiac chest pain			
subjects affected / exposed	2 / 56 (3.57%)		
occurrences (all)	2		
Oedema			
subjects affected / exposed	0 / 56 (0.00%)		
occurrences (all)	0		
Oedema peripheral			
subjects affected / exposed	3 / 56 (5.36%)		
occurrences (all)	4		
Pain			
subjects affected / exposed	5 / 56 (8.93%)		
occurrences (all)	7		
Puncture site pain			
subjects affected / exposed	1 / 56 (1.79%)		
occurrences (all)	1		
Pyrexia			
subjects affected / exposed	39 / 56 (69.64%)		
occurrences (all)	231		
Immune system disorders			
Hypersensitivity			
subjects affected / exposed	3 / 56 (5.36%)		
occurrences (all)	3		
Seasonal allergy			
subjects affected / exposed	2 / 56 (3.57%)		
occurrences (all)	3		
Reproductive system and breast disorders			

Dysmenorrhoea subjects affected / exposed occurrences (all)	3 / 56 (5.36%) 9		
Respiratory, thoracic and mediastinal disorders			
Allergic cough subjects affected / exposed occurrences (all)	1 / 56 (1.79%) 1		
Asthma subjects affected / exposed occurrences (all)	3 / 56 (5.36%) 11		
Bronchospasm subjects affected / exposed occurrences (all)	2 / 56 (3.57%) 2		
Cough subjects affected / exposed occurrences (all)	28 / 56 (50.00%) 70		
Dyspnoea subjects affected / exposed occurrences (all)	11 / 56 (19.64%) 23		
Epistaxis subjects affected / exposed occurrences (all)	8 / 56 (14.29%) 19		
Nasal congestion subjects affected / exposed occurrences (all)	16 / 56 (28.57%) 38		
Nasal obstruction subjects affected / exposed occurrences (all)	3 / 56 (5.36%) 3		
Neonatal hypoxia subjects affected / exposed occurrences (all)	3 / 56 (5.36%) 4		
Obstructive airways disorder subjects affected / exposed occurrences (all)	3 / 56 (5.36%) 4		
Oropharyngeal pain			

subjects affected / exposed	27 / 56 (48.21%)		
occurrences (all)	63		
Pharyngeal disorder			
subjects affected / exposed	0 / 56 (0.00%)		
occurrences (all)	0		
Pharyngeal erythema			
subjects affected / exposed	3 / 56 (5.36%)		
occurrences (all)	5		
Productive cough			
subjects affected / exposed	0 / 56 (0.00%)		
occurrences (all)	0		
Respiratory tract congestion			
subjects affected / exposed	1 / 56 (1.79%)		
occurrences (all)	1		
Restrictive pulmonary disease			
subjects affected / exposed	1 / 56 (1.79%)		
occurrences (all)	2		
Rhinitis allergic			
subjects affected / exposed	2 / 56 (3.57%)		
occurrences (all)	2		
Rhinorrhoea			
subjects affected / exposed	14 / 56 (25.00%)		
occurrences (all)	24		
Sinus congestion			
subjects affected / exposed	3 / 56 (5.36%)		
occurrences (all)	4		
Sleep apnoea syndrome			
subjects affected / exposed	2 / 56 (3.57%)		
occurrences (all)	2		
Sneezing			
subjects affected / exposed	2 / 56 (3.57%)		
occurrences (all)	2		
Tachypnoea			
subjects affected / exposed	2 / 56 (3.57%)		
occurrences (all)	4		
Throat irritation			

<p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>Tonsillar hypertrophy</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>Wheezing</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p>	<p>4 / 56 (7.14%)</p> <p>5</p> <p>1 / 56 (1.79%)</p> <p>1</p> <p>4 / 56 (7.14%)</p> <p>6</p>		
<p>Psychiatric disorders</p> <p>Agitation</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>Anxiety</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>Insomnia</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p>	<p>4 / 56 (7.14%)</p> <p>6</p> <p>1 / 56 (1.79%)</p> <p>1</p> <p>0 / 56 (0.00%)</p> <p>0</p>		
<p>Investigations</p> <p>Blood cholesterol increased</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>Blood pressure diastolic increased</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>Blood pressure increased</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>Blood pressure systolic increased</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>Blood urine present</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>Heart rate decreased</p>	<p>2 / 56 (3.57%)</p> <p>2</p> <p>3 / 56 (5.36%)</p> <p>4</p> <p>1 / 56 (1.79%)</p> <p>1</p> <p>1 / 56 (1.79%)</p> <p>2</p> <p>0 / 56 (0.00%)</p> <p>0</p>		

subjects affected / exposed	0 / 56 (0.00%)		
occurrences (all)	0		
Heart rate increased			
subjects affected / exposed	7 / 56 (12.50%)		
occurrences (all)	13		
Oxygen saturation decreased			
subjects affected / exposed	10 / 56 (17.86%)		
occurrences (all)	26		
Respiratory rate increased			
subjects affected / exposed	3 / 56 (5.36%)		
occurrences (all)	3		
Vital capacity decreased			
subjects affected / exposed	0 / 56 (0.00%)		
occurrences (all)	0		
Injury, poisoning and procedural complications			
Arthropod bite			
subjects affected / exposed	6 / 56 (10.71%)		
occurrences (all)	7		
Contusion			
subjects affected / exposed	2 / 56 (3.57%)		
occurrences (all)	3		
Excoriation			
subjects affected / exposed	2 / 56 (3.57%)		
occurrences (all)	2		
Fall			
subjects affected / exposed	5 / 56 (8.93%)		
occurrences (all)	7		
Head injury			
subjects affected / exposed	2 / 56 (3.57%)		
occurrences (all)	2		
Infusion related reaction			
subjects affected / exposed	2 / 56 (3.57%)		
occurrences (all)	3		
Joint dislocation			

subjects affected / exposed	0 / 56 (0.00%)		
occurrences (all)	0		
Joint injury			
subjects affected / exposed	2 / 56 (3.57%)		
occurrences (all)	2		
Ligament sprain			
subjects affected / exposed	1 / 56 (1.79%)		
occurrences (all)	1		
Limb injury			
subjects affected / exposed	1 / 56 (1.79%)		
occurrences (all)	1		
Procedural pain			
subjects affected / exposed	7 / 56 (12.50%)		
occurrences (all)	9		
Tooth fracture			
subjects affected / exposed	0 / 56 (0.00%)		
occurrences (all)	0		
Cardiac disorders			
Aortic valve disease			
subjects affected / exposed	2 / 56 (3.57%)		
occurrences (all)	2		
Aortic valve incompetence			
subjects affected / exposed	4 / 56 (7.14%)		
occurrences (all)	4		
Left ventricular hypertrophy			
subjects affected / exposed	4 / 56 (7.14%)		
occurrences (all)	4		
Mitral valve disease			
subjects affected / exposed	3 / 56 (5.36%)		
occurrences (all)	4		
Mitral valve incompetence			
subjects affected / exposed	4 / 56 (7.14%)		
occurrences (all)	5		
Palpitations			
subjects affected / exposed	2 / 56 (3.57%)		
occurrences (all)	2		

Pulmonary valve incompetence subjects affected / exposed occurrences (all)	5 / 56 (8.93%) 5		
Sinus arrhythmia subjects affected / exposed occurrences (all)	1 / 56 (1.79%) 1		
Sinus tachycardia subjects affected / exposed occurrences (all)	1 / 56 (1.79%) 11		
Tachycardia subjects affected / exposed occurrences (all)	11 / 56 (19.64%) 29		
Tricuspid valve incompetence subjects affected / exposed occurrences (all)	7 / 56 (12.50%) 8		
Nervous system disorders			
Cervical cord compression subjects affected / exposed occurrences (all)	0 / 56 (0.00%) 0		
Dizziness subjects affected / exposed occurrences (all)	12 / 56 (21.43%) 30		
Headache subjects affected / exposed occurrences (all)	36 / 56 (64.29%) 271		
Hyperreflexia subjects affected / exposed occurrences (all)	0 / 56 (0.00%) 0		
Hypoaesthesia subjects affected / exposed occurrences (all)	1 / 56 (1.79%) 1		
Lethargy subjects affected / exposed occurrences (all)	3 / 56 (5.36%) 4		
Paraesthesia			

subjects affected / exposed	7 / 56 (12.50%)		
occurrences (all)	18		
Somnolence			
subjects affected / exposed	4 / 56 (7.14%)		
occurrences (all)	4		
Syncope			
subjects affected / exposed	1 / 56 (1.79%)		
occurrences (all)	1		
Blood and lymphatic system disorders			
Lymphadenopathy			
subjects affected / exposed	0 / 56 (0.00%)		
occurrences (all)	0		
Ear and labyrinth disorders			
Ear discomfort			
subjects affected / exposed	2 / 56 (3.57%)		
occurrences (all)	6		
Ear pain			
subjects affected / exposed	19 / 56 (33.93%)		
occurrences (all)	26		
Hypoacusis			
subjects affected / exposed	3 / 56 (5.36%)		
occurrences (all)	4		
Middle ear effusion			
subjects affected / exposed	2 / 56 (3.57%)		
occurrences (all)	2		
Motion sickness			
subjects affected / exposed	3 / 56 (5.36%)		
occurrences (all)	3		
Tinnitus			
subjects affected / exposed	3 / 56 (5.36%)		
occurrences (all)	6		
Vertigo			
subjects affected / exposed	3 / 56 (5.36%)		
occurrences (all)	4		
Eye disorders			

Astigmatism			
subjects affected / exposed	1 / 56 (1.79%)		
occurrences (all)	1		
Conjunctivitis			
subjects affected / exposed	8 / 56 (14.29%)		
occurrences (all)	9		
Corneal opacity			
subjects affected / exposed	12 / 56 (21.43%)		
occurrences (all)	13		
Glaucoma			
subjects affected / exposed	0 / 56 (0.00%)		
occurrences (all)	0		
Myopia			
subjects affected / exposed	1 / 56 (1.79%)		
occurrences (all)	1		
Ocular hyperaemia			
subjects affected / exposed	2 / 56 (3.57%)		
occurrences (all)	3		
Visual impairment			
subjects affected / exposed	3 / 56 (5.36%)		
occurrences (all)	5		
Gastrointestinal disorders			
Abdominal discomfort			
subjects affected / exposed	7 / 56 (12.50%)		
occurrences (all)	18		
Abdominal distension			
subjects affected / exposed	2 / 56 (3.57%)		
occurrences (all)	5		
Abdominal pain			
subjects affected / exposed	24 / 56 (42.86%)		
occurrences (all)	60		
Abdominal pain lower			
subjects affected / exposed	0 / 56 (0.00%)		
occurrences (all)	0		
Abdominal pain upper			

subjects affected / exposed	18 / 56 (32.14%)		
occurrences (all)	72		
Anal pruritus			
subjects affected / exposed	0 / 56 (0.00%)		
occurrences (all)	0		
Breath odour			
subjects affected / exposed	0 / 56 (0.00%)		
occurrences (all)	0		
Constipation			
subjects affected / exposed	8 / 56 (14.29%)		
occurrences (all)	9		
Dental caries			
subjects affected / exposed	3 / 56 (5.36%)		
occurrences (all)	4		
Diarrhoea			
subjects affected / exposed	23 / 56 (41.07%)		
occurrences (all)	43		
Dyspepsia			
subjects affected / exposed	2 / 56 (3.57%)		
occurrences (all)	2		
Enterocolitis			
subjects affected / exposed	1 / 56 (1.79%)		
occurrences (all)	1		
Flatulence			
subjects affected / exposed	1 / 56 (1.79%)		
occurrences (all)	1		
Gastrooesophageal reflux disease			
subjects affected / exposed	3 / 56 (5.36%)		
occurrences (all)	4		
Haemorrhoids			
subjects affected / exposed	0 / 56 (0.00%)		
occurrences (all)	0		
Mouth ulceration			
subjects affected / exposed	1 / 56 (1.79%)		
occurrences (all)	1		
Nausea			

subjects affected / exposed	28 / 56 (50.00%)		
occurrences (all)	91		
Proctalgia			
subjects affected / exposed	0 / 56 (0.00%)		
occurrences (all)	0		
Stomatitis			
subjects affected / exposed	1 / 56 (1.79%)		
occurrences (all)	1		
Toothache			
subjects affected / exposed	4 / 56 (7.14%)		
occurrences (all)	4		
Vomiting			
subjects affected / exposed	38 / 56 (67.86%)		
occurrences (all)	160		
Skin and subcutaneous tissue disorders			
Acne			
subjects affected / exposed	3 / 56 (5.36%)		
occurrences (all)	4		
Blister			
subjects affected / exposed	2 / 56 (3.57%)		
occurrences (all)	4		
Dermatitis			
subjects affected / exposed	3 / 56 (5.36%)		
occurrences (all)	4		
Dermatitis allergic			
subjects affected / exposed	0 / 56 (0.00%)		
occurrences (all)	0		
Dry skin			
subjects affected / exposed	2 / 56 (3.57%)		
occurrences (all)	3		
Eczema			
subjects affected / exposed	1 / 56 (1.79%)		
occurrences (all)	2		
Erythema			
subjects affected / exposed	10 / 56 (17.86%)		
occurrences (all)	29		

Hyperhidrosis			
subjects affected / exposed	3 / 56 (5.36%)		
occurrences (all)	3		
Petechiae			
subjects affected / exposed	0 / 56 (0.00%)		
occurrences (all)	0		
Pruritus			
subjects affected / exposed	19 / 56 (33.93%)		
occurrences (all)	32		
Rash			
subjects affected / exposed	19 / 56 (33.93%)		
occurrences (all)	103		
Rash erythematous			
subjects affected / exposed	1 / 56 (1.79%)		
occurrences (all)	1		
Rash macular			
subjects affected / exposed	3 / 56 (5.36%)		
occurrences (all)	3		
Rash maculo-papular			
subjects affected / exposed	2 / 56 (3.57%)		
occurrences (all)	28		
Rash pruritic			
subjects affected / exposed	0 / 56 (0.00%)		
occurrences (all)	0		
Skin disorder			
subjects affected / exposed	3 / 56 (5.36%)		
occurrences (all)	7		
Skin lesion			
subjects affected / exposed	3 / 56 (5.36%)		
occurrences (all)	3		
Urticaria			
subjects affected / exposed	12 / 56 (21.43%)		
occurrences (all)	33		
Renal and urinary disorders			
Dysuria			

subjects affected / exposed	2 / 56 (3.57%)		
occurrences (all)	2		
Haematuria			
subjects affected / exposed	4 / 56 (7.14%)		
occurrences (all)	4		
Pollakiuria			
subjects affected / exposed	3 / 56 (5.36%)		
occurrences (all)	3		
Proteinuria			
subjects affected / exposed	3 / 56 (5.36%)		
occurrences (all)	4		
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	29 / 56 (51.79%)		
occurrences (all)	94		
Back pain			
subjects affected / exposed	18 / 56 (32.14%)		
occurrences (all)	46		
Joint swelling			
subjects affected / exposed	1 / 56 (1.79%)		
occurrences (all)	1		
Knee deformity			
subjects affected / exposed	6 / 56 (10.71%)		
occurrences (all)	6		
Muscle spasms			
subjects affected / exposed	3 / 56 (5.36%)		
occurrences (all)	4		
Musculoskeletal chest pain			
subjects affected / exposed	2 / 56 (3.57%)		
occurrences (all)	2		
Musculoskeletal pain			
subjects affected / exposed	9 / 56 (16.07%)		
occurrences (all)	20		
Musculoskeletal stiffness			

subjects affected / exposed	1 / 56 (1.79%)		
occurrences (all)	1		
Myalgia			
subjects affected / exposed	5 / 56 (8.93%)		
occurrences (all)	9		
Neck pain			
subjects affected / exposed	10 / 56 (17.86%)		
occurrences (all)	24		
Osteopenia			
subjects affected / exposed	0 / 56 (0.00%)		
occurrences (all)	0		
Pain in extremity			
subjects affected / exposed	31 / 56 (55.36%)		
occurrences (all)	102		
Spinal pain			
subjects affected / exposed	5 / 56 (8.93%)		
occurrences (all)	6		
Infections and infestations			
Bronchitis			
subjects affected / exposed	6 / 56 (10.71%)		
occurrences (all)	8		
Cellulitis			
subjects affected / exposed	0 / 56 (0.00%)		
occurrences (all)	0		
Ear infection			
subjects affected / exposed	16 / 56 (28.57%)		
occurrences (all)	42		
Fungal infection			
subjects affected / exposed	3 / 56 (5.36%)		
occurrences (all)	3		
Furuncle			
subjects affected / exposed	1 / 56 (1.79%)		
occurrences (all)	3		
Gastroenteritis			
subjects affected / exposed	17 / 56 (30.36%)		
occurrences (all)	20		

Gastroenteritis viral			
subjects affected / exposed	2 / 56 (3.57%)		
occurrences (all)	2		
Gingivitis			
subjects affected / exposed	2 / 56 (3.57%)		
occurrences (all)	2		
Hordeolum			
subjects affected / exposed	0 / 56 (0.00%)		
occurrences (all)	0		
Influenza			
subjects affected / exposed	5 / 56 (8.93%)		
occurrences (all)	6		
Laryngitis			
subjects affected / exposed	0 / 56 (0.00%)		
occurrences (all)	0		
Lice infestation			
subjects affected / exposed	5 / 56 (8.93%)		
occurrences (all)	6		
Lower respiratory tract infection			
subjects affected / exposed	3 / 56 (5.36%)		
occurrences (all)	3		
Nasopharyngitis			
subjects affected / exposed	28 / 56 (50.00%)		
occurrences (all)	67		
Oral candidiasis			
subjects affected / exposed	1 / 56 (1.79%)		
occurrences (all)	1		
Oral herpes			
subjects affected / exposed	0 / 56 (0.00%)		
occurrences (all)	0		
Otitis externa			
subjects affected / exposed	6 / 56 (10.71%)		
occurrences (all)	8		
Otitis media			
subjects affected / exposed	10 / 56 (17.86%)		
occurrences (all)	18		

Otitis media acute			
subjects affected / exposed	4 / 56 (7.14%)		
occurrences (all)	6		
Pharyngitis			
subjects affected / exposed	11 / 56 (19.64%)		
occurrences (all)	18		
Rash pustular			
subjects affected / exposed	0 / 56 (0.00%)		
occurrences (all)	0		
Respiratory tract infection viral			
subjects affected / exposed	3 / 56 (5.36%)		
occurrences (all)	4		
Rhinitis			
subjects affected / exposed	9 / 56 (16.07%)		
occurrences (all)	19		
Sinusitis			
subjects affected / exposed	4 / 56 (7.14%)		
occurrences (all)	6		
Tinea pedis			
subjects affected / exposed	2 / 56 (3.57%)		
occurrences (all)	2		
Tonsillitis			
subjects affected / exposed	6 / 56 (10.71%)		
occurrences (all)	7		
Tooth infection			
subjects affected / exposed	1 / 56 (1.79%)		
occurrences (all)	2		
Upper respiratory tract infection			
subjects affected / exposed	24 / 56 (42.86%)		
occurrences (all)	81		
Varicella			
subjects affected / exposed	2 / 56 (3.57%)		
occurrences (all)	2		
Viral infection			
subjects affected / exposed	5 / 56 (8.93%)		
occurrences (all)	6		

Viral pharyngitis subjects affected / exposed occurrences (all)	0 / 56 (0.00%) 0		
Viral upper respiratory tract infection subjects affected / exposed occurrences (all)	5 / 56 (8.93%) 10		
Metabolism and nutrition disorders Decreased appetite subjects affected / exposed occurrences (all)	5 / 56 (8.93%) 5		

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

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

Notes: Efficacy analysis based on all patients randomized (pbo-QOW, pbo-QW, QOW-QOW, QW-QW(N=175)), meanwhile it is available for the first 24 weeks in MOR-004 (N=176).The safety evaluation is based on patients who entered MOR-005(N=173)

Notes: