Clinical trial results:
PHASE II, OPEN, RANDOMISED, PARALLEL GROUP, NONCOMPARATIVE MULTICENTRE STUDY TO ASSESS THE EFFICACY AND SAFETY OF REPEATED SUBCUTANEOUS (S.C.) ADMINISTRATION OF DIFFERENT DOSES OF BIM 23A760 IN ACROMEGALIC PATIENTS

Summary

EudraCT number	2009-010787-42
Trial protocol	SE BE NL GB LV DE FR LT CZ IT PL
Global end of trial date	11 February 2011

Results information

Result version number	v1 (current)
This version publication date	16 March 2016
First version publication date	16 March 2016

Trial information

Trial identification

Sponsor protocol code	2-55-52060-003

Additional study identifiers

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

Notes:

Sponsors

Sponsor organisation name	Ipsen Pharma
Sponsor organisation address	65 quai Georges Gorse, Boulogne-Billancourt, France, 92100
Public contact	Ipsen Pharma, Ipsen Pharma, 331 58335000, clinical.trials@ipsen.com
Scientific contact	Ipsen Pharma, Ipsen Pharma, 331 58335000, clinical.trials@ipsen.com

Notes:

Paediatric regulatory details

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

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	28 November 2011
Is this the analysis of the primary completion data?	Yes
Primary completion date	11 February 2011
Global end of trial reached?	Yes
Global end of trial date	11 February 2011
Was the trial ended prematurely?	Yes

Notes:

General information about the trial

Main objective of the trial:

Part A: To assess the efficacy of repeated s.c. injections at different doses of BIM 23A760 on growth hormone (GH) and insulin-like growth factor-1 (IGF-1) levels in acromegalic patients after 6 months of treatment.

Part B: To assess the long term safety of weekly injections of BIM 23A760 in patients with acromegaly.

Protection of trial subjects:

This clinical study was designed and implemented and reported in accordance with the International Conference on Harmonisation (ICH) Harmonized Tripartite Guidelines for Good Clinical Practice (GCP), with applicable local regulations (including European Directive 2001/20/EC, US Code of Federal Regulations Title 21, and Japanese Ministry of Health, Labor, and Welfare), and with the ethical principles laid down in the Declaration of Helsinki.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	09 November 2009
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Brazil: 10
Country: Number of subjects enrolled	Mexico: 11
Country: Number of subjects enrolled	Ukraine: 20
Country: Number of subjects enrolled	United States: 3
Country: Number of subjects enrolled	Poland: 2
Country: Number of subjects enrolled	Netherlands: 3
Country: Number of subjects enrolled	Romania: 12
Country: Number of subjects enrolled	Sweden: 1
Country: Number of subjects enrolled	Belgium: 2
Country: Number of subjects enrolled	Czech Republic: 3
Country: Number of subjects enrolled	France: 2
Country: Number of subjects enrolled	Latvia: 1
Country: Number of subjects enrolled	Lithuania: 6
Worldwide total number of subjects	76
EEA total number of subjects	32

Notes:

Subjects enrolled per age group	
In utero	0
Preterm newborn - gestational age < 37 wk	0
Newborns (0-27 days)	0
Infants and toddlers (28 days-23 months)	0
Children (2-11 years)	0
Adolescents (12-17 years)	0
Adults (18-64 years)	74
From 65 to 84 years	2
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

This was a multicentre study conducted at 36 investigational sites in 16 countries: Czech Republic, Lithuania, Poland, Romania, Ukraine, Latvia, USA, United Kingdom (UK), Italy, Mexico, Brazil, France, Belgium, Netherlands, Germany and Sweden.

Pre-assignment

Screening details:

Screened subjects were 109 and screen failures were 33. Subjects randomised and treated in part A were 76. Subjects completed part A were 21 and subjects entered Part B were 12, excluding 9 subjects, who chose not to continue in part B. No subjects completed the study.

Period 1

Period 1 title	ITT (Intention-to-Treat) - Part A
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Not blinded

Arms

Are arms mutually exclusive?	Yes
Arm title	Part A-Arm A: BIM 23A760 1 mg

Arm description:

BIM 23A760 1 mg subcutaneous 24 weekly injections.

Arm type	Experimental
Investigational medicinal product name	BIM 23A760 1 mg
Investigational medicinal product code	BIM 23A760 1 mg
Other name	
Pharmaceutical forms	Injection
Routes of administration	Subcutaneous use

Dosage and administration details:

1 mg

Arm title	Part A-Arm B: BIM 23A760 2 mg

Arm description:

BIM 23A760 2 mg subcutaneous 24 weekly injections.

Arm type	Experimental
Investigational medicinal product name	BIM 23A760 2 mg
Investigational medicinal product code	BIM 23A760 2 mg
Other name	
Pharmaceutical forms	Injection
Routes of administration	Subcutaneous use

Dosage and administration details:

2 mg

Arm title	Part A-Arm C: BIM 23A760 4 mg

Arm description:

BIM 23A760 4 mg subcutaneous 24 weekly injections.

Arm type	Experimental

Investigational medicinal product name	BIM 23A760 4 mg
Investigational medicinal product code	BIM 23A760 4 mg
Other name	
Pharmaceutical forms	Injection
Routes of administration	Subcutaneous use

Dosage and administration details:

4 mg

Arm title	Part A-Arm D: BIM 23A760 6 mg

Arm description:

BIM 23A760 6 mg subcutaneous 24 weekly injections.

Arm type	Experimental
Investigational medicinal product name	BIM 23A760 6 mg
Investigational medicinal product code	BIM 23A760 6 mg
Other name	
Pharmaceutical forms	Injection
Routes of administration	Subcutaneous use

Dosage and administration details:

6 mg

Number of subjects in period 1	Part A-Arm A: BIM 23A760 1 mg	Part A-Arm B: BIM 23A760 2 mg	Part A-Arm C: BIM 23A760 4 mg
Started	19	19	18
Completed	5	6	5
Not completed	14	13	13
Withdrawn - Study termination by sponsor	13	12	13
Consent withdrawn by subject	-	-	-
Adverse event, non-fatal	-	1	-
Lost to follow-up	1	-	-

Number of subjects in period 1	Part A-Arm D: BIM 23A760 6 mg
Started	20
Completed	5
Not completed	15
Withdrawn - Study termination by sponsor	14
Consent withdrawn by subject	1
Adverse event, non-fatal	-
Lost to follow-up	-

Period 2

Period 2 title	ITT (Intention-to-Treat) - Part B
Is this the baseline period?	No
Allocation method	Randomised - controlled
Blinding used	Not blinded

Arms

Are arms mutually exclusive?	Yes
Arm title	Part B-Arm A: BIM 23A760 1 mg

Arm description:

BIM 23A760 1 mg subcutaneous 24 weekly injections.

Arm type	Experimental
Investigational medicinal product name	BIM 23A760 1 mg
Investigational medicinal product code	BIM 23A760 1 mg
Other name	
Pharmaceutical forms	Injection
Routes of administration	Subcutaneous use

Dosage and administration details:

1 mg

Arm title	Part B-Arm B: BIM 23A760 2 mg

Arm description:

BIM 23A760 2 mg subcutaneous 24 weekly injections.

Arm type	Experimental
Investigational medicinal product name	BIM 23A760 2 mg
Investigational medicinal product code	BIM 23A760 2 mg
Other name	
Pharmaceutical forms	Injection
Routes of administration	Subcutaneous use

Dosage and administration details:

2 mg

Arm title	Part B-Arm C: BIM 23A760 4 mg

Arm description:

BIM 23A760 4 mg subcutaneous 24 weekly injections.

Arm type	Experimental
Investigational medicinal product name	BIM 23A760 4 mg
Investigational medicinal product code	BIM 23A760 4 mg
Other name	
Pharmaceutical forms	Injection
Routes of administration	Subcutaneous use

Dosage and administration details:

4 mg

Arm title	Part B-Arm D: BIM 23A760 6 mg

Arm description:

BIM 23A760 6 mg subcutaneous 24 weekly injections.

Arm type	Experimental
Investigational medicinal product name	BIM 23A760 6 mg
Investigational medicinal product code	BIM 23A760 6 mg
Other name	
Pharmaceutical forms	Injection
Routes of administration	Subcutaneous use

Dosage and administration details:

6 mg

Number of subjects in period 2[1]	Part B-Arm A: BIM 23A760 1 mg	Part B-Arm B: BIM 23A760 2 mg	Part B-Arm C: BIM 23A760 4 mg
Started	4	3	2
Received maximum dose of 1 mg	0	0	0
Received maximum dose of 2 mg	3	0	0
Received maximum dose of 4 mg	1	3	0
Received maximum dose of 6 mg	0	0	2
Completed	0	0	0
Not completed	4	3	2
Withdrawn - Study termination by sponsor	4	3	2
Consent withdrawn by subject	-	-	-

Number of subjects in period 2[1]	Part B-Arm D: BIM 23A760 6 mg
Started	3
Received maximum dose of 1 mg	0
Received maximum dose of 2 mg	0
Received maximum dose of 4 mg	0
Received maximum dose of 6 mg	3
Completed	0
Not completed	3
Withdrawn - Study termination by sponsor	2
Consent withdrawn by subject	1

Notes:

[1] - The number of subjects starting the period is not consistent with the number completing the preceding period. It is expected the number of subjects starting the subsequent period will be the same as the number completing the preceding period.
Justification: 1 subject did not enter Part B Arm A
3 subjects did not enter Part B Arm B
3 subjects did not enter Part B Arm C
2 subjects did not enter Part B Arm D

Baseline characteristics

Reporting groups	
Reporting group title	Part A-Arm A: BIM 23A760 1 mg
Reporting group description: BIM 23A760 1 mg subcutaneous 24 weekly injections.	
Reporting group title	Part A-Arm B: BIM 23A760 2 mg
Reporting group description: BIM 23A760 2 mg subcutaneous 24 weekly injections.	
Reporting group title	Part A-Arm C: BIM 23A760 4 mg
Reporting group description: BIM 23A760 4 mg subcutaneous 24 weekly injections.	
Reporting group title	Part A-Arm D: BIM 23A760 6 mg
Reporting group description: BIM 23A760 6 mg subcutaneous 24 weekly injections.	

Reporting group values	Part A-Arm A: BIM 23A760 1 mg	Part A-Arm B: BIM 23A760 2 mg	Part A-Arm C: BIM 23A760 4 mg
Number of subjects	19	19	18
Age categorical Units: Subjects			
Adults (20-74 Years)	19	19	18
Age continuous Units: years			
arithmetic mean	42.8	48.7	40.3
standard deviation	± 11.3	± 11.2	± 11.3
Gender categorical Units: Subjects			
Female	10	13	6
Male	9	6	12
Race/Ethnicity, Customized Units: Subjects			
Caucasian/White	17	14	13
Multiple race	2	5	5
Region of Enrollment			
ITT			
Units: Subjects			
Belgium	1	1	0
Brazil	1	1	3
Czech Republic	1	1	0
Lithuania	1	1	3
Mexico	2	4	4
Netherlands	2	0	0
Poland	1	1	0
Romania	4	3	1
Ukraine	6	4	4
France	0	1	0
United States	0	2	1
Latvia	0	0	1

Sweden	0	0	1
Diabetic status at entry Units: Subjects			
Diabetic	2	1	2
Non-diabetic	17	18	16
Height Units: Cm			
arithmetic mean	170.1	170.3	175
standard deviation	± 8.1	± 13.2	± 10.1
Insulin-like growth factor 1 (IGF-1) Units: Percentage of ULN			
median	307	315	382
full range (min-max)	146 to 690	176 to 508	168 to 549
Growth Hormone Units: ng/mL			
arithmetic mean	16.79	20.99	28.6
standard deviation	± 24.56	± 59.28	± 64.83
Baseline Prolactin (Males) Units: µg/L			
arithmetic mean	11.506	34.113	41.657
standard deviation	± 14.233	± 49.588	± 60.965
Baseline Prolactin (Pre-menopausal females) Units: µg/L			
arithmetic mean	19.838	26.158	35.608
standard deviation	± 15.247	± 19.798	± 25.536
Baseline Prolactin (Post-menopausal females) Units: µg/L			
arithmetic mean	8.42	16.409	7.87
standard deviation	± 3.167	± 24.232	± 0.693
Ring Finger Circumference			
Number of Patients Analysed at Baseline: Arm A: 4 Arm B: 4 Arm C: 3 Arm D: 4			
Units: mm			
arithmetic mean	70.2	68.5	71.2
standard deviation	± 5.6	± 6.2	± 4.7

Reporting group values	Part A-Arm D: BIM 23A760 6 mg	Total	
Number of subjects	20	76	
Age categorical Units: Subjects			
Adults (20-74 Years)	20	76	
Age continuous Units: years			
arithmetic mean	43.4		
standard deviation	± 12.9	-	

Gender categorical Units: Subjects			
Female	13	42	
Male	7	34	
Race/Ethnicity, Customized Units: Subjects			
Caucasian/White	18	62	
Multiple race	2	14	
Region of Enrollment			
ITT			
Units: Subjects			
Belgium	0	2	
Brazil	5	10	
Czech Republic	1	3	
Lithuania	1	6	
Mexico	1	11	
Netherlands	1	3	
Poland	0	2	
Romania	4	12	
Ukraine	6	20	
France	1	2	
United States	0	3	
Latvia	0	1	
Sweden	0	1	
Diabetic status at entry Units: Subjects			
Diabetic	2	7	
Non-diabetic	18	69	
Height Units: Cm			
arithmetic mean	166.4		
standard deviation	± 8.6	-	
Insulin-like growth factor 1 (IGF-1) Units: Percentage of ULN			
median	335		
full range (min-max)	157 to 539	-	
Growth Hormone Units: ng/mL			
arithmetic mean	26.59		
standard deviation	± 63.47	-	
Baseline Prolactin (Males) Units: µg/L			
arithmetic mean	83.036		
standard deviation	± 131.024	-	
Baseline Prolactin (Pre-menopausal females) Units: µg/L			
arithmetic mean	23.634		
standard deviation	± 23.778	-	
Baseline Prolactin (Post-menopausal females) Units: µg/L			

arithmetic mean	25.118		
standard deviation	± 39.986	-	
Ring Finger Circumference			
Number of Patients Analysed at Baseline: Arm A: 4 Arm B: 4 Arm C: 3 Arm D: 4			
Units: mm			
arithmetic mean	68.4		
standard deviation	± 6.3	-	

End points

End points reporting groups

Reporting group title	Part A-Arm A: BIM 23A760 1 mg
Reporting group description: BIM 23A760 1 mg subcutaneous 24 weekly injections.	
Reporting group title	Part A-Arm B: BIM 23A760 2 mg
Reporting group description: BIM 23A760 2 mg subcutaneous 24 weekly injections.	
Reporting group title	Part A-Arm C: BIM 23A760 4 mg
Reporting group description: BIM 23A760 4 mg subcutaneous 24 weekly injections.	
Reporting group title	Part A-Arm D: BIM 23A760 6 mg
Reporting group description: BIM 23A760 6 mg subcutaneous 24 weekly injections.	
Reporting group title	Part B-Arm A: BIM 23A760 1 mg
Reporting group description: BIM 23A760 1 mg subcutaneous 24 weekly injections.	
Reporting group title	Part B-Arm B: BIM 23A760 2 mg
Reporting group description: BIM 23A760 2 mg subcutaneous 24 weekly injections.	
Reporting group title	Part B-Arm C: BIM 23A760 4 mg
Reporting group description: BIM 23A760 4 mg subcutaneous 24 weekly injections.	
Reporting group title	Part B-Arm D: BIM 23A760 6 mg
Reporting group description: BIM 23A760 6 mg subcutaneous 24 weekly injections.	
Subject analysis set title	Overall - Part A
Subject analysis set type	Intention-to-treat
Subject analysis set description: Overall subjects in Part A (BIM 23A760 1 mg, 2 mg, 4 mg and 6 mg)	
Subject analysis set title	Overall - Part B
Subject analysis set type	Intention-to-treat
Subject analysis set description: Overall subjects in Part B (BIM 23A760 2 mg, 4 mg and 6 mg)	

Primary: Percentage of subjects with mean GH ≤2.5 ng/mL and normalised IGF-1

End point title	Percentage of subjects with mean GH ≤2.5 ng/mL and normalised IGF-1[1]
End point description: Intention-to-Treat (ITT) population: All randomized subjects who received at least one dose of study medication. N=Number of subjects attended Month 6 (visit 9).	
End point type	Primary
End point timeframe: At Month 6	

Notes:

[1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: No statistical analysis performed.

End point values	Part A-Arm A: BIM 23A760 1 mg	Part A-Arm B: BIM 23A760 2 mg	Part A-Arm C: BIM 23A760 4 mg	Part A-Arm D: BIM 23A760 6 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	6	7	5	5
Units: Percentage of subjects				
number (not applicable)				
Yes	0	0	0	0
No	8.3	100	100	100
Missing	16.7	0	0	0

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects With Mean GH≤2.5 ng/mL and Normalised IGF-1

End point title	Percentage of Subjects With Mean GH≤2.5 ng/mL and Normalised IGF-1

End point description:

ITT population. N=Number of subjects attended Month 3 (visit 7).

End point type	Secondary

End point timeframe:

At Month 3

End point values	Part A-Arm A: BIM 23A760 1 mg	Part A-Arm B: BIM 23A760 2 mg	Part A-Arm C: BIM 23A760 4 mg	Part A-Arm D: BIM 23A760 6 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	12	13	12	13
Units: Percentage of subjects				
number (not applicable)				
Yes	0	0	0	7.7
No	100	100	100	92.3
Missing	0	0	0	0

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects With Mean GH≤2.5 ng/mL and Normalised IGF-1

End point title	Percentage of Subjects With Mean GH≤2.5 ng/mL and Normalised IGF-1

End point description:

ITT population. N=Number of subjects attended Month 1 (visit 5).

End point type	Secondary

End point timeframe:

At Month 1

End point values	Part A-Arm A: BIM 23A760 1 mg	Part A-Arm B: BIM 23A760 2 mg	Part A-Arm C: BIM 23A760 4 mg	Part A-Arm D: BIM 23A760 6 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	19	18	18	20
Units: Percentage of subjects				
number (not applicable)				
Yes	5.3	0	0	5
No	94.7	100	100	95
Missing	0	0	0	0

Statistical analyses

No statistical analyses for this end point

Secondary: Percent Change From Baseline in the Mean GH From 0-3 Hours at Months 1, 3 and 6

End point title	Percent Change From Baseline in the Mean GH From 0-3 Hours at Months 1, 3 and 6

End point description:

Percentage change from Baseline at month X = (Mean GH at month X - Mean GH at baseline) x 100 / Mean GH at baseline

N=Number of patients randomized to treatment in IGF-1 <2.5 x upper limit of normal (ULN) stratum and IGF-1 ≥2.5 x ULN stratum.

End point type	Secondary

End point timeframe:

0-3 hr on Baseline (Day 1) and Months 1, 3 and 6

End point values	Part A-Arm A: BIM 23A760 1 mg	Part A-Arm B: BIM 23A760 2 mg	Part A-Arm C: BIM 23A760 4 mg	Part A-Arm D: BIM 23A760 6 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	15	15	15	16
Units: Percentage of change in mean GH				
arithmetic mean (standard deviation)				
At Month 1: IGF-1<2.5xULN	4.1 (± 53.03)	-0.55 (± 23.98)	-9.92 (± 71.51)	-17.59 (± 41.82)
At Month 3: IGF-1<2.5xULN	29.26 (± 45.97)	-18.99 (± 21.36)	17.48 (± 127.97)	-28.84 (± 43.25)
At Month 6: IGF-1<2.5xULN	71.44 (± 35.97)	3.32 (± 9.09)	82.45 (± 0)	-38.21 (± 27.27)
At Month 1: IGF-1≥2.5xUL	-39.2 (± 30.33)	-22.24 (± 34.72)	-10.64 (± 51.18)	-23.63 (± 39.57)

At Month 3: IGF-1≥2.5xUL	-26.14 (± 39.6)	-22.35 (± 31.71)	-7.64 (± 30.11)	-20.53 (± 42.23)
At Month 6: IGF-1≥2.5xUL	-36.15 (± 45.63)	15.28 (± 82.56)	-10.43 (± 28.9)	-19.47 (± 68.9)

Statistical analyses

No statistical analyses for this end point

Secondary: Changes in IGF-1

End point title	Changes in IGF-1
End point description:	
ITT population.	
End point type	Secondary
End point timeframe:	
Baseline (Day 1) and Month 6	

End point values	Part A-Arm A: BIM 23A760 1 mg	Part A-Arm B: BIM 23A760 2 mg	Part A-Arm C: BIM 23A760 4 mg	Part A-Arm D: BIM 23A760 6 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	19	19	18	20
Units: Percentage of change in IGF-1				
arithmetic mean (standard deviation)	-51.3 (± 136.66)	-53.31 (± 80.57)	-40.53 (± 56.65)	-85.91 (± 95.34)

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage Change in Ring Finger Circumference

End point title	Percentage Change in Ring Finger Circumference
End point description:	
Percentage change from Baseline at month X = (Ring finger circumference at month X - ring finger circumference at baseline) x 100 / ring finger circumference at baseline. ITT population. N=Number of subjects attended Month 6 (visit 9). Circ = Circumference	
End point type	Secondary
End point timeframe:	
Baseline (Day 1) and Month 6	

End point values	Part A-Arm A: BIM 23A760 1 mg	Part A-Arm B: BIM 23A760 2 mg	Part A-Arm C: BIM 23A760 4 mg	Part A-Arm D: BIM 23A760 6 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	6	7	5	5
Units: percentage of Change in Ring Finger circ				
arithmetic mean (standard deviation)	-3.518 (± 3.688)	-1.469 (± 2.12)	-0.678 (± 2.409)	-4.003 (± 3.367)

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects Reported Adverse Events During the Study

End point title	Number of Subjects Reported Adverse Events During the Study

End point description:

For summaries of intensity and causality, individual patients may be reported in more than one category. In the event of multiple episodes of AEs being reported by the same patient during the study, the maximum intensity (severe > moderate > mild) and the most serious causality (related > not related) have been chosen.

TEAE (Treatment emergent adverse event) are reported by Maximum Dose Received in Each Part of the Study.

Analysis Population Description: Safety Population

Number of subjects analysed:

Arm: Part B-Arm C: BIM 23A760 4 mg=4

Arm: Part B-Arm D: BIM 23A760 6 mg=5

End point type	Secondary

End point timeframe:

Up to Visit 10 (An average of 6.5 Months)

End point values	Part A-Arm A: BIM 23A760 1 mg	Part A-Arm B: BIM 23A760 2 mg	Part A-Arm C: BIM 23A760 4 mg	Part A-Arm D: BIM 23A760 6 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	19	19	18	20
Units: Number of subjects				
Severe	0	1	1	2
Moderate	3	8	4	7
Mild	11	9	12	15
Related	7	8	10	11
Not Related	8	9	6	11

End point values	Part B-Arm B: BIM 23A760 2	Part B-Arm C: BIM 23A760 4	Part B-Arm D: BIM 23A760 6	Overall - Part A

	mg	mg	mg	
Subject group type	Reporting group	Reporting group	Reporting group	Subject analysis set
Number of subjects analysed	3	2	3	76
Units: Number of subjects				
Severe	0	0	0	4
Moderate	0	0	3	22
Mild	0	1	1	47
Related	0	0	1	36
Not Related	0	1	3	34

End point values	Overall - Part B			
Subject group type	Subject analysis set			
Number of subjects analysed	12			
Units: Number of subjects				
Severe	0			
Moderate	3			
Mild	2			
Related	1			
Not Related	4			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Up to Visit 10 (An average of 6.5 Months)

Adverse event reporting additional description:

Included Serious Adverse Events (SAEs) and Adverse Events (AEs) during treatment phase for Safety Population

TEAE are reported by Maximum Dose Received in Each Part of the Study.

4 subjects from part B, Arm A were considered under other arms of part B based on the maximum dose received.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	13.1

Reporting groups

Reporting group title	Part A: Arm A: BIM 23A760 1 mg

Reporting group description:

BIM 23A760 1 mg subcutaneous 24 weekly injections.

Reporting group title	Part A: Arm B: BIM 23A760 2 mg

Reporting group description:

BIM 23A760 2 mg subcutaneous 24 weekly injections.

Reporting group title	Part A: Arm C: BIM 23A760 4 mg

Reporting group description:

BIM 23A760 4 mg subcutaneous 24 weekly injections.

Reporting group title	Part A: Arm D: BIM 23A760 6 mg

Reporting group description:

BIM 23A760 6 mg subcutaneous 24 weekly injections.

Reporting group title	Part B: Arm B: BIM 23A760 2 mg

Reporting group description: -

Reporting group title	Part B: Arm C: BIM 23A760 4 mg

Reporting group description:

BIM 23A760 4 mg subcutaneous 24 weekly injections.

Reporting group title	Part B: Arm D: BIM 23A760 6 mg

Reporting group description:

BIM 23A760 6 mg subcutaneous 24 weekly injections.

Reporting group title	Overall - Part A

Reporting group description: -

Reporting group title	Overall - Part B

Reporting group description: -

Serious adverse events	Part A: Arm A: BIM 23A760 1 mg	Part A: Arm B: BIM 23A760 2 mg	Part A: Arm C: BIM 23A760 4 mg
Total subjects affected by serious adverse events			
subjects affected / exposed	1 / 19 (5.26%)	2 / 19 (10.53%)	0 / 18 (0.00%)
number of deaths (all causes)	0	0	0
number of deaths resulting from	0	0	0

adverse events			
Ear and labyrinth disorders			
Vertigo			
subjects affected / exposed	0 / 19 (0.00%)	1 / 19 (5.26%)	0 / 18 (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			
Nausea			
subjects affected / exposed	1 / 19 (5.26%)	1 / 19 (5.26%)	0 / 18 (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
Gastritis			
subjects affected / exposed	0 / 19 (0.00%)	0 / 19 (0.00%)	0 / 18 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Sinusitis			
subjects affected / exposed	0 / 19 (0.00%)	0 / 19 (0.00%)	0 / 18 (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	Part A: Arm D: BIM 23A760 6 mg	Part B: Arm B: BIM 23A760 2 mg	Part B: Arm C: BIM 23A760 4 mg
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 20 (0.00%)	0 / 3 (0.00%)	0 / 4 (0.00%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Ear and labyrinth disorders			
Vertigo			
subjects affected / exposed	0 / 20 (0.00%)	0 / 3 (0.00%)	0 / 4 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Nausea			
subjects affected / exposed	0 / 20 (0.00%)	0 / 3 (0.00%)	0 / 4 (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

Gastritis			
subjects affected / exposed	0 / 20 (0.00%)	0 / 3 (0.00%)	0 / 4 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Sinusitis			
subjects affected / exposed	0 / 20 (0.00%)	0 / 3 (0.00%)	0 / 4 (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	Part B: Arm D: BIM 23A760 6 mg	Overall - Part A	Overall - Part B
Total subjects affected by serious adverse events			
subjects affected / exposed	2 / 5 (40.00%)	3 / 76 (3.95%)	2 / 12 (16.67%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Ear and labyrinth disorders			
Vertigo			
subjects affected / exposed	0 / 5 (0.00%)	1 / 76 (1.32%)	0 / 12 (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			
Nausea			
subjects affected / exposed	0 / 5 (0.00%)	2 / 76 (2.63%)	0 / 12 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastritis			
subjects affected / exposed	1 / 5 (20.00%)	0 / 76 (0.00%)	1 / 12 (8.33%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Sinusitis			
subjects affected / exposed	1 / 5 (20.00%)	0 / 76 (0.00%)	1 / 12 (8.33%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

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

Non-serious adverse events	Part A: Arm A: BIM 23A760 1 mg	Part A: Arm B: BIM 23A760 2 mg	Part A: Arm C: BIM 23A760 4 mg
Total subjects affected by non-serious adverse events			
subjects affected / exposed	11 / 19 (57.89%)	12 / 19 (63.16%)	12 / 18 (66.67%)
Vascular disorders			
Hypotension			
subjects affected / exposed	0 / 19 (0.00%)	1 / 19 (5.26%)	3 / 18 (16.67%)
occurrences (all)	0	1	4
Orthostatic hypotension			
subjects affected / exposed	0 / 19 (0.00%)	0 / 19 (0.00%)	1 / 18 (5.56%)
occurrences (all)	0	0	1
Peripheral coldness			
subjects affected / exposed	1 / 19 (5.26%)	0 / 19 (0.00%)	0 / 18 (0.00%)
occurrences (all)	1	0	0
Phlebitis			
subjects affected / exposed	0 / 19 (0.00%)	0 / 19 (0.00%)	1 / 18 (5.56%)
occurrences (all)	0	0	1
General disorders and administration site conditions			
Administration site reaction			
subjects affected / exposed	0 / 19 (0.00%)	0 / 19 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
Application site erythema			
subjects affected / exposed	0 / 19 (0.00%)	1 / 19 (5.26%)	0 / 18 (0.00%)
occurrences (all)	0	1	0
Application site induration			
subjects affected / exposed	0 / 19 (0.00%)	0 / 19 (0.00%)	1 / 18 (5.56%)
occurrences (all)	0	0	1
Asthenia			
subjects affected / exposed	0 / 19 (0.00%)	0 / 19 (0.00%)	1 / 18 (5.56%)
occurrences (all)	0	0	1
Fatigue			
subjects affected / exposed	0 / 19 (0.00%)	0 / 19 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
Hyperthermia			

subjects affected / exposed	0 / 19 (0.00%)	0 / 19 (0.00%)	1 / 18 (5.56%)
occurrences (all)	0	0	1
Injection site erythema			
subjects affected / exposed	0 / 19 (0.00%)	2 / 19 (10.53%)	1 / 18 (5.56%)
occurrences (all)	0	4	15
Injection site induration			
subjects affected / exposed	2 / 19 (10.53%)	2 / 19 (10.53%)	4 / 18 (22.22%)
occurrences (all)	2	4	5
Injection site inflammation			
subjects affected / exposed	1 / 19 (5.26%)	0 / 19 (0.00%)	0 / 18 (0.00%)
occurrences (all)	1	0	0
Injection site nodule			
subjects affected / exposed	1 / 19 (5.26%)	1 / 19 (5.26%)	2 / 18 (11.11%)
occurrences (all)	1	1	4
Injection site pain			
subjects affected / exposed	0 / 19 (0.00%)	0 / 19 (0.00%)	2 / 18 (11.11%)
occurrences (all)	0	0	6
Injection site pruritis			
subjects affected / exposed	0 / 19 (0.00%)	2 / 19 (10.53%)	3 / 18 (16.67%)
occurrences (all)	0	4	16
Injection site rash			
subjects affected / exposed	1 / 19 (5.26%)	0 / 19 (0.00%)	0 / 18 (0.00%)
occurrences (all)	1	0	0
Injection site reaction			
subjects affected / exposed	0 / 19 (0.00%)	2 / 19 (10.53%)	0 / 18 (0.00%)
occurrences (all)	0	4	0
Injection site swelling			
subjects affected / exposed	0 / 19 (0.00%)	1 / 19 (5.26%)	0 / 18 (0.00%)
occurrences (all)	0	2	0
Oedema peripheral			
subjects affected / exposed	0 / 19 (0.00%)	0 / 19 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
Reproductive system and breast disorders			
Menstruation delayed			

subjects affected / exposed	1 / 19 (5.26%)	0 / 19 (0.00%)	0 / 18 (0.00%)
occurrences (all)	1	0	0
Respiratory, thoracic and mediastinal disorders			
Oropharyngeal pain			
subjects affected / exposed	1 / 19 (5.26%)	0 / 19 (0.00%)	0 / 18 (0.00%)
occurrences (all)	1	0	0
Respiratory disorder			
subjects affected / exposed	0 / 19 (0.00%)	0 / 19 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
Psychiatric disorders			
Insomnia			
subjects affected / exposed	0 / 19 (0.00%)	0 / 19 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
Pollakiuria			
subjects affected / exposed	0 / 19 (0.00%)	0 / 19 (0.00%)	1 / 18 (5.56%)
occurrences (all)	0	0	1
Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	0 / 19 (0.00%)	2 / 19 (10.53%)	0 / 18 (0.00%)
occurrences (all)	0	2	0
Aspartate aminotransferase increased			
subjects affected / exposed	0 / 19 (0.00%)	2 / 19 (10.53%)	0 / 18 (0.00%)
occurrences (all)	0	2	0
Blood amylase increased			
subjects affected / exposed	0 / 19 (0.00%)	1 / 19 (5.26%)	0 / 18 (0.00%)
occurrences (all)	0	1	0
Blood glucose increased			
subjects affected / exposed	0 / 19 (0.00%)	0 / 19 (0.00%)	1 / 18 (5.56%)
occurrences (all)	0	0	1
Blood pressure decreased			
subjects affected / exposed	0 / 19 (0.00%)	0 / 19 (0.00%)	2 / 18 (11.11%)
occurrences (all)	0	0	3
Blood pressure diastolic decreased			
subjects affected / exposed	0 / 19 (0.00%)	1 / 19 (5.26%)	0 / 18 (0.00%)
occurrences (all)	0	1	0
Blood thyroid stimulating hormone			

decreased			
subjects affected / exposed	1 / 19 (5.26%)	0 / 19 (0.00%)	0 / 18 (0.00%)
occurrences (all)	1	0	0
Red blood cells urine positive			
subjects affected / exposed	0 / 19 (0.00%)	0 / 19 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
Tri-iodothyronine free increased			
subjects affected / exposed	1 / 19 (5.26%)	0 / 19 (0.00%)	0 / 18 (0.00%)
occurrences (all)	1	0	0
White blood cell count decreased			
subjects affected / exposed	0 / 19 (0.00%)	1 / 19 (5.26%)	0 / 18 (0.00%)
occurrences (all)	0	1	0
White blood cells urine positive			
subjects affected / exposed	0 / 19 (0.00%)	0 / 19 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
Blood pressure increased			
subjects affected / exposed	0 / 19 (0.00%)	0 / 19 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
Injury, poisoning and procedural complications			
Concussion			
subjects affected / exposed	0 / 19 (0.00%)	1 / 19 (5.26%)	0 / 18 (0.00%)
occurrences (all)	0	1	0
Wound			
subjects affected / exposed	0 / 19 (0.00%)	1 / 19 (5.26%)	0 / 18 (0.00%)
occurrences (all)	0	2	0
Nervous system disorders			
Acoustic neuritis			
subjects affected / exposed	0 / 19 (0.00%)	1 / 19 (5.26%)	0 / 18 (0.00%)
occurrences (all)	0	1	0
Carpal tunnel syndrome			
subjects affected / exposed	0 / 19 (0.00%)	1 / 19 (5.26%)	0 / 18 (0.00%)
occurrences (all)	0	1	0
Headache			
subjects affected / exposed	0 / 19 (0.00%)	0 / 19 (0.00%)	1 / 18 (5.56%)
occurrences (all)	0	0	2
Hypoaesthesia			

subjects affected / exposed	0 / 19 (0.00%)	1 / 19 (5.26%)	0 / 18 (0.00%)
occurrences (all)	0	1	0
Paraesthesia			
subjects affected / exposed	1 / 19 (5.26%)	0 / 19 (0.00%)	0 / 18 (0.00%)
occurrences (all)	1	0	0
Presyncope			
subjects affected / exposed	0 / 19 (0.00%)	1 / 19 (5.26%)	0 / 18 (0.00%)
occurrences (all)	0	1	0
Syncope			
subjects affected / exposed	0 / 19 (0.00%)	0 / 19 (0.00%)	1 / 18 (5.56%)
occurrences (all)	0	0	1
Trigeminal neuralgia			
subjects affected / exposed	1 / 19 (5.26%)	0 / 19 (0.00%)	0 / 18 (0.00%)
occurrences (all)	1	0	0
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	1 / 19 (5.26%)	0 / 19 (0.00%)	0 / 18 (0.00%)
occurrences (all)	1	0	0
Pancytopenia			
subjects affected / exposed	0 / 19 (0.00%)	1 / 19 (5.26%)	0 / 18 (0.00%)
occurrences (all)	0	1	0
Ear and labyrinth disorders			
Vertigo			
subjects affected / exposed	0 / 19 (0.00%)	1 / 19 (5.26%)	0 / 18 (0.00%)
occurrences (all)	0	1	0
Hyperthyroidism			
subjects affected / exposed	0 / 19 (0.00%)	0 / 19 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
Eye disorders			
Eye irritation			
subjects affected / exposed	0 / 19 (0.00%)	0 / 19 (0.00%)	1 / 18 (5.56%)
occurrences (all)	0	0	1
Lacrimation increased			
subjects affected / exposed	0 / 19 (0.00%)	0 / 19 (0.00%)	1 / 18 (5.56%)
occurrences (all)	0	0	1
Gastrointestinal disorders			

Abdominal pain			
subjects affected / exposed	1 / 19 (5.26%)	1 / 19 (5.26%)	1 / 18 (5.56%)
occurrences (all)	1	2	1
Abdominal pain upper			
subjects affected / exposed	0 / 19 (0.00%)	0 / 19 (0.00%)	1 / 18 (5.56%)
occurrences (all)	0	1	1
Constipation			
subjects affected / exposed	0 / 19 (0.00%)	1 / 19 (5.26%)	1 / 18 (5.56%)
occurrences (all)	0	1	1
Diarrhoea			
subjects affected / exposed	2 / 19 (10.53%)	1 / 19 (5.26%)	1 / 18 (5.56%)
occurrences (all)	3	1	10
Flatulence			
subjects affected / exposed	1 / 19 (5.26%)	1 / 19 (5.26%)	2 / 18 (11.11%)
occurrences (all)	1	1	2
Gastrointestinal pain			
subjects affected / exposed	1 / 19 (5.26%)	0 / 19 (0.00%)	0 / 18 (0.00%)
occurrences (all)	1	0	0
Nausea			
subjects affected / exposed	2 / 19 (10.53%)	2 / 19 (10.53%)	2 / 18 (11.11%)
occurrences (all)	2	3	3
Proctalgia			
subjects affected / exposed	0 / 19 (0.00%)	1 / 19 (5.26%)	0 / 18 (0.00%)
occurrences (all)	0	1	0
Vomiting			
subjects affected / exposed	0 / 19 (0.00%)	1 / 19 (5.26%)	1 / 18 (5.56%)
occurrences (all)	0	1	1
Gastritis			
subjects affected / exposed	0 / 19 (0.00%)	0 / 19 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
Hepatobiliary disorders			
Cholelithiasis			
subjects affected / exposed	0 / 19 (0.00%)	0 / 19 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
Cytolytic hepatitis			

subjects affected / exposed	0 / 19 (0.00%)	0 / 19 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
Skin and subcutaneous tissue disorders			
Erythema			
subjects affected / exposed	0 / 19 (0.00%)	0 / 19 (0.00%)	1 / 18 (5.56%)
occurrences (all)	0	0	2
Hyperhidrosis			
subjects affected / exposed	0 / 19 (0.00%)	1 / 19 (5.26%)	0 / 18 (0.00%)
occurrences (all)	0	1	0
Hyperkeratosis			
subjects affected / exposed	1 / 19 (5.26%)	0 / 19 (0.00%)	0 / 18 (0.00%)
occurrences (all)	1	0	0
Pruritus			
subjects affected / exposed	1 / 19 (5.26%)	0 / 19 (0.00%)	0 / 18 (0.00%)
occurrences (all)	2	0	0
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	0 / 19 (0.00%)	1 / 19 (5.26%)	0 / 18 (0.00%)
occurrences (all)	0	1	0
Back pain			
subjects affected / exposed	0 / 19 (0.00%)	0 / 19 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
Musculoskeletal chest pain			
subjects affected / exposed	1 / 19 (5.26%)	0 / 19 (0.00%)	0 / 18 (0.00%)
occurrences (all)	1	0	0
Myalgia			
subjects affected / exposed	0 / 19 (0.00%)	0 / 19 (0.00%)	1 / 18 (5.56%)
occurrences (all)	0	0	1
Pain in extremity			
subjects affected / exposed	0 / 19 (0.00%)	0 / 19 (0.00%)	1 / 18 (5.56%)
occurrences (all)	0	0	1
Rheumatoid arthritis			
subjects affected / exposed	0 / 19 (0.00%)	1 / 19 (5.26%)	0 / 18 (0.00%)
occurrences (all)	0	1	0
Synovitis			

subjects affected / exposed	0 / 19 (0.00%)	1 / 19 (5.26%)	0 / 18 (0.00%)
occurrences (all)	0	1	0
Dizziness			
subjects affected / exposed	2 / 19 (10.53%)	1 / 19 (5.26%)	1 / 18 (5.56%)
occurrences (all)	2	1	1
Infections and infestations			
Cystitis			
subjects affected / exposed	0 / 19 (0.00%)	1 / 19 (5.26%)	0 / 18 (0.00%)
occurrences (all)	0	1	0
Fungal skin infection			
subjects affected / exposed	0 / 19 (0.00%)	0 / 19 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
Nasopharyngitis			
subjects affected / exposed	1 / 19 (5.26%)	1 / 19 (5.26%)	0 / 18 (0.00%)
occurrences (all)	1	1	0
Sinusitis			
subjects affected / exposed	1 / 19 (5.26%)	0 / 19 (0.00%)	0 / 18 (0.00%)
occurrences (all)	1	0	0
Urinary tract infection			
subjects affected / exposed	0 / 19 (0.00%)	0 / 19 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
Metabolism and nutrition disorders			
Hypercholesterolaemia			
subjects affected / exposed	0 / 19 (0.00%)	0 / 19 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
Hyperglycaema			
subjects affected / exposed	1 / 19 (5.26%)	0 / 19 (0.00%)	0 / 18 (0.00%)
occurrences (all)	1	0	0
Impacted fasting glucose			
subjects affected / exposed	0 / 19 (0.00%)	1 / 19 (5.26%)	0 / 18 (0.00%)
occurrences (all)	0	1	0

Non-serious adverse events	Part A: Arm D: BIM 23A760 6 mg	Part B: Arm B: BIM 23A760 2 mg	Part B: Arm C: BIM 23A760 4 mg
Total subjects affected by non-serious adverse events			
subjects affected / exposed	15 / 20 (75.00%)	0 / 3 (0.00%)	1 / 4 (25.00%)
Vascular disorders			

Hypotension			
subjects affected / exposed	0 / 20 (0.00%)	0 / 3 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Orthostatic hypotension			
subjects affected / exposed	0 / 20 (0.00%)	0 / 3 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Peripheral coldness			
subjects affected / exposed	0 / 20 (0.00%)	0 / 3 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Phlebitis			
subjects affected / exposed	0 / 20 (0.00%)	0 / 3 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
General disorders and administration site conditions			
Administration site reaction			
subjects affected / exposed	1 / 20 (5.00%)	0 / 3 (0.00%)	0 / 4 (0.00%)
occurrences (all)	7	0	0
Application site erythema			
subjects affected / exposed	0 / 20 (0.00%)	0 / 3 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Application site induration			
subjects affected / exposed	1 / 20 (5.00%)	0 / 3 (0.00%)	0 / 4 (0.00%)
occurrences (all)	1	0	0
Asthenia			
subjects affected / exposed	1 / 20 (5.00%)	0 / 3 (0.00%)	0 / 4 (0.00%)
occurrences (all)	1	0	0
Fatigue			
subjects affected / exposed	1 / 20 (5.00%)	0 / 3 (0.00%)	0 / 4 (0.00%)
occurrences (all)	1	0	0
Hyperthermia			
subjects affected / exposed	0 / 20 (0.00%)	0 / 3 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Injection site erythema			
subjects affected / exposed	3 / 20 (15.00%)	0 / 3 (0.00%)	0 / 4 (0.00%)
occurrences (all)	10	0	0
Injection site induration			

subjects affected / exposed	1 / 20 (5.00%)	0 / 3 (0.00%)	0 / 4 (0.00%)
occurrences (all)	2	0	0
Injection site inflammation			
subjects affected / exposed	0 / 20 (0.00%)	0 / 3 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Injection site nodule			
subjects affected / exposed	2 / 20 (10.00%)	0 / 3 (0.00%)	0 / 4 (0.00%)
occurrences (all)	6	0	0
Injection site pain			
subjects affected / exposed	2 / 20 (10.00%)	0 / 3 (0.00%)	0 / 4 (0.00%)
occurrences (all)	5	0	0
Injection site pruritis			
subjects affected / exposed	3 / 20 (15.00%)	0 / 3 (0.00%)	0 / 4 (0.00%)
occurrences (all)	7	0	0
Injection site rash			
subjects affected / exposed	0 / 20 (0.00%)	0 / 3 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Injection site reaction			
subjects affected / exposed	2 / 20 (10.00%)	0 / 3 (0.00%)	0 / 4 (0.00%)
occurrences (all)	9	0	0
Injection site swelling			
subjects affected / exposed	0 / 20 (0.00%)	0 / 3 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Oedema peripheral			
subjects affected / exposed	1 / 20 (5.00%)	0 / 3 (0.00%)	0 / 4 (0.00%)
occurrences (all)	1	0	0
Reproductive system and breast disorders			
Menstruation delayed			
subjects affected / exposed	0 / 20 (0.00%)	0 / 3 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Respiratory, thoracic and mediastinal disorders			
Oropharyngeal pain			
subjects affected / exposed	0 / 20 (0.00%)	0 / 3 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Respiratory disorder			

subjects affected / exposed	1 / 20 (5.00%)	0 / 3 (0.00%)	0 / 4 (0.00%)
occurrences (all)	1	0	0
Psychiatric disorders			
Insomnia			
subjects affected / exposed	1 / 20 (5.00%)	0 / 3 (0.00%)	0 / 4 (0.00%)
occurrences (all)	1	0	0
Pollakiuria			
subjects affected / exposed	0 / 20 (0.00%)	0 / 3 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	0 / 20 (0.00%)	0 / 3 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Aspartate aminotransferase increased			
subjects affected / exposed	0 / 20 (0.00%)	0 / 3 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Blood amylase increased			
subjects affected / exposed	0 / 20 (0.00%)	0 / 3 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Blood glucose increased			
subjects affected / exposed	0 / 20 (0.00%)	0 / 3 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Blood pressure decreased			
subjects affected / exposed	0 / 20 (0.00%)	0 / 3 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Blood pressure diastolic decreased			
subjects affected / exposed	0 / 20 (0.00%)	0 / 3 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Blood thyroid stimulating hormone decreased			
subjects affected / exposed	1 / 20 (5.00%)	0 / 3 (0.00%)	0 / 4 (0.00%)
occurrences (all)	1	0	0
Red blood cells urine positive			
subjects affected / exposed	1 / 20 (5.00%)	0 / 3 (0.00%)	0 / 4 (0.00%)
occurrences (all)	1	0	0
Tri-iodothyronine free increased			

subjects affected / exposed	0 / 20 (0.00%)	0 / 3 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
White blood cell count decreased			
subjects affected / exposed	0 / 20 (0.00%)	0 / 3 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
White blood cells urine positive			
subjects affected / exposed	1 / 20 (5.00%)	0 / 3 (0.00%)	0 / 4 (0.00%)
occurrences (all)	1	0	0
Blood pressure increased			
subjects affected / exposed	0 / 20 (0.00%)	0 / 3 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Injury, poisoning and procedural complications			
Concussion			
subjects affected / exposed	0 / 20 (0.00%)	0 / 3 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Wound			
subjects affected / exposed	0 / 20 (0.00%)	0 / 3 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Nervous system disorders			
Acoustic neuritis			
subjects affected / exposed	0 / 20 (0.00%)	0 / 3 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Carpal tunnel syndrome			
subjects affected / exposed	0 / 20 (0.00%)	0 / 3 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Headache			
subjects affected / exposed	3 / 20 (15.00%)	0 / 3 (0.00%)	0 / 4 (0.00%)
occurrences (all)	4	0	0
Hypoaesthesia			
subjects affected / exposed	0 / 20 (0.00%)	0 / 3 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Paraesthesia			
subjects affected / exposed	0 / 20 (0.00%)	0 / 3 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Presyncope			

subjects affected / exposed	0 / 20 (0.00%)	0 / 3 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Syncope			
subjects affected / exposed	0 / 20 (0.00%)	0 / 3 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Trigeminal neuralgia			
subjects affected / exposed	0 / 20 (0.00%)	0 / 3 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	2 / 20 (10.00%)	0 / 3 (0.00%)	0 / 4 (0.00%)
occurrences (all)	2	0	0
Pancytopenia			
subjects affected / exposed	0 / 20 (0.00%)	0 / 3 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Ear and labyrinth disorders			
Vertigo			
subjects affected / exposed	0 / 20 (0.00%)	0 / 3 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Hyperthyroidism			
subjects affected / exposed	1 / 20 (5.00%)	0 / 3 (0.00%)	0 / 4 (0.00%)
occurrences (all)	1	0	0
Eye disorders			
Eye irritation			
subjects affected / exposed	0 / 20 (0.00%)	0 / 3 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Lacrimation increased			
subjects affected / exposed	0 / 20 (0.00%)	0 / 3 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	3 / 20 (15.00%)	0 / 3 (0.00%)	0 / 4 (0.00%)
occurrences (all)	5	0	0
Abdominal pain upper			
subjects affected / exposed	0 / 20 (0.00%)	0 / 3 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Constipation			

subjects affected / exposed	2 / 20 (10.00%)	0 / 3 (0.00%)	0 / 4 (0.00%)
occurrences (all)	2	0	0
Diarrhoea			
subjects affected / exposed	2 / 20 (10.00%)	0 / 3 (0.00%)	0 / 4 (0.00%)
occurrences (all)	7	0	0
Flatulence			
subjects affected / exposed	1 / 20 (5.00%)	0 / 3 (0.00%)	0 / 4 (0.00%)
occurrences (all)	1	0	0
Gastrointestinal pain			
subjects affected / exposed	0 / 20 (0.00%)	0 / 3 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Nausea			
subjects affected / exposed	2 / 20 (10.00%)	0 / 3 (0.00%)	0 / 4 (0.00%)
occurrences (all)	5	0	0
Proctalgia			
subjects affected / exposed	0 / 20 (0.00%)	0 / 3 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Vomiting			
subjects affected / exposed	1 / 20 (5.00%)	0 / 3 (0.00%)	0 / 4 (0.00%)
occurrences (all)	1	0	0
Gastritis			
subjects affected / exposed	0 / 20 (0.00%)	0 / 3 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Hepatobiliary disorders			
Cholelithiasis			
subjects affected / exposed	0 / 20 (0.00%)	0 / 3 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Cytolytic hepatitis			
subjects affected / exposed	0 / 20 (0.00%)	0 / 3 (0.00%)	1 / 4 (25.00%)
occurrences (all)	0	0	1
Skin and subcutaneous tissue disorders			
Erythema			
subjects affected / exposed	0 / 20 (0.00%)	0 / 3 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Hyperhidrosis			

subjects affected / exposed	1 / 20 (5.00%)	0 / 3 (0.00%)	0 / 4 (0.00%)
occurrences (all)	2	0	0
Hyperkeratosis			
subjects affected / exposed	0 / 20 (0.00%)	0 / 3 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Pruritus			
subjects affected / exposed	1 / 20 (5.00%)	0 / 3 (0.00%)	0 / 4 (0.00%)
occurrences (all)	1	0	0
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	1 / 20 (5.00%)	0 / 3 (0.00%)	0 / 4 (0.00%)
occurrences (all)	1	0	0
Back pain			
subjects affected / exposed	1 / 20 (5.00%)	0 / 3 (0.00%)	0 / 4 (0.00%)
occurrences (all)	1	0	0
Musculoskeletal chest pain			
subjects affected / exposed	0 / 20 (0.00%)	0 / 3 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Myalgia			
subjects affected / exposed	0 / 20 (0.00%)	0 / 3 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Pain in extremity			
subjects affected / exposed	0 / 20 (0.00%)	0 / 3 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Rheumatoid arthritis			
subjects affected / exposed	0 / 20 (0.00%)	0 / 3 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Synovitis			
subjects affected / exposed	0 / 20 (0.00%)	0 / 3 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Dizziness			
subjects affected / exposed	1 / 20 (5.00%)	0 / 3 (0.00%)	0 / 4 (0.00%)
occurrences (all)	2	0	0
Infections and infestations			

Cystitis			
subjects affected / exposed	0 / 20 (0.00%)	0 / 3 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Fungal skin infection			
subjects affected / exposed	1 / 20 (5.00%)	0 / 3 (0.00%)	0 / 4 (0.00%)
occurrences (all)	1	0	0
Nasopharyngitis			
subjects affected / exposed	1 / 20 (5.00%)	0 / 3 (0.00%)	0 / 4 (0.00%)
occurrences (all)	1	0	0
Sinusitis			
subjects affected / exposed	1 / 20 (5.00%)	0 / 3 (0.00%)	0 / 4 (0.00%)
occurrences (all)	1	0	0
Urinary tract infection			
subjects affected / exposed	1 / 20 (5.00%)	0 / 3 (0.00%)	0 / 4 (0.00%)
occurrences (all)	1	0	0
Metabolism and nutrition disorders			
Hypercholesterolaemia			
subjects affected / exposed	1 / 20 (5.00%)	0 / 3 (0.00%)	0 / 4 (0.00%)
occurrences (all)	1	0	0
Hyperglycaema			
subjects affected / exposed	0 / 20 (0.00%)	0 / 3 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Impacted fasting glucose			
subjects affected / exposed	1 / 20 (5.00%)	0 / 3 (0.00%)	0 / 4 (0.00%)
occurrences (all)	2	0	0

Non-serious adverse events	Part B: Arm D: BIM 23A760 6 mg	Overall - Part A	Overall - Part B
Total subjects affected by non-serious adverse events			
subjects affected / exposed	4 / 5 (80.00%)	50 / 76 (65.79%)	5 / 12 (41.67%)
Vascular disorders			
Hypotension			
subjects affected / exposed	0 / 5 (0.00%)	4 / 76 (5.26%)	0 / 12 (0.00%)
occurrences (all)	0	5	0
Orthostatic hypotension			
subjects affected / exposed	0 / 5 (0.00%)	1 / 76 (1.32%)	0 / 12 (0.00%)
occurrences (all)	0	1	0
Peripheral coldness			

subjects affected / exposed	0 / 5 (0.00%)	1 / 76 (1.32%)	0 / 12 (0.00%)
occurrences (all)	0	1	0
Phlebitis			
subjects affected / exposed	0 / 5 (0.00%)	1 / 76 (1.32%)	0 / 12 (0.00%)
occurrences (all)	0	1	0
General disorders and administration site conditions			
Administration site reaction			
subjects affected / exposed	0 / 5 (0.00%)	1 / 76 (1.32%)	0 / 12 (0.00%)
occurrences (all)	0	7	0
Application site erythema			
subjects affected / exposed	0 / 5 (0.00%)	1 / 76 (1.32%)	0 / 12 (0.00%)
occurrences (all)	0	1	0
Application site induration			
subjects affected / exposed	0 / 5 (0.00%)	2 / 76 (2.63%)	0 / 12 (0.00%)
occurrences (all)	0	2	0
Asthenia			
subjects affected / exposed	0 / 5 (0.00%)	2 / 76 (2.63%)	0 / 12 (0.00%)
occurrences (all)	0	2	0
Fatigue			
subjects affected / exposed	0 / 5 (0.00%)	1 / 76 (1.32%)	0 / 12 (0.00%)
occurrences (all)	0	1	0
Hyperthermia			
subjects affected / exposed	0 / 5 (0.00%)	1 / 76 (1.32%)	0 / 12 (0.00%)
occurrences (all)	0	1	0
Injection site erythema			
subjects affected / exposed	0 / 5 (0.00%)	6 / 76 (7.89%)	0 / 12 (0.00%)
occurrences (all)	0	29	0
Injection site induration			
subjects affected / exposed	0 / 5 (0.00%)	9 / 76 (11.84%)	0 / 12 (0.00%)
occurrences (all)	0	13	0
Injection site inflammation			
subjects affected / exposed	0 / 5 (0.00%)	1 / 76 (1.32%)	0 / 12 (0.00%)
occurrences (all)	0	1	0
Injection site nodule			

subjects affected / exposed	0 / 5 (0.00%)	6 / 76 (7.89%)	0 / 12 (0.00%)
occurrences (all)	0	12	0
Injection site pain			
subjects affected / exposed	0 / 5 (0.00%)	4 / 76 (5.26%)	0 / 12 (0.00%)
occurrences (all)	0	11	0
Injection site pruritis			
subjects affected / exposed	0 / 5 (0.00%)	8 / 76 (10.53%)	0 / 12 (0.00%)
occurrences (all)	0	27	0
Injection site rash			
subjects affected / exposed	0 / 5 (0.00%)	1 / 76 (1.32%)	0 / 12 (0.00%)
occurrences (all)	0	1	0
Injection site reaction			
subjects affected / exposed	0 / 5 (0.00%)	4 / 76 (5.26%)	0 / 12 (0.00%)
occurrences (all)	0	13	0
Injection site swelling			
subjects affected / exposed	0 / 5 (0.00%)	1 / 76 (1.32%)	0 / 12 (0.00%)
occurrences (all)	0	2	0
Oedema peripheral			
subjects affected / exposed	0 / 5 (0.00%)	1 / 76 (1.32%)	0 / 12 (0.00%)
occurrences (all)	0	1	0
Reproductive system and breast disorders			
Menstruation delayed			
subjects affected / exposed	0 / 5 (0.00%)	1 / 76 (1.32%)	0 / 12 (0.00%)
occurrences (all)	0	1	0
Respiratory, thoracic and mediastinal disorders			
Oropharyngeal pain			
subjects affected / exposed	0 / 5 (0.00%)	1 / 76 (1.32%)	0 / 12 (0.00%)
occurrences (all)	0	1	0
Respiratory disorder			
subjects affected / exposed	0 / 5 (0.00%)	1 / 76 (1.32%)	0 / 12 (0.00%)
occurrences (all)	0	1	0
Psychiatric disorders			
Insomnia			
subjects affected / exposed	0 / 5 (0.00%)	1 / 76 (1.32%)	0 / 12 (0.00%)
occurrences (all)	0	1	0
Pollakiuria			

subjects affected / exposed	0 / 5 (0.00%)	1 / 76 (1.32%)	0 / 12 (0.00%)
occurrences (all)	0	1	0
Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	0 / 5 (0.00%)	2 / 76 (2.63%)	0 / 12 (0.00%)
occurrences (all)	0	2	0
Aspartate aminotransferase increased			
subjects affected / exposed	0 / 5 (0.00%)	2 / 76 (2.63%)	0 / 12 (0.00%)
occurrences (all)	0	2	0
Blood amylase increased			
subjects affected / exposed	0 / 5 (0.00%)	1 / 76 (1.32%)	0 / 12 (0.00%)
occurrences (all)	0	1	0
Blood glucose increased			
subjects affected / exposed	0 / 5 (0.00%)	1 / 76 (1.32%)	0 / 12 (0.00%)
occurrences (all)	0	1	0
Blood pressure decreased			
subjects affected / exposed	0 / 5 (0.00%)	2 / 76 (2.63%)	0 / 12 (0.00%)
occurrences (all)	0	3	0
Blood pressure diastolic decreased			
subjects affected / exposed	0 / 5 (0.00%)	1 / 76 (1.32%)	0 / 12 (0.00%)
occurrences (all)	0	1	0
Blood thyroid stimulating hormone decreased			
subjects affected / exposed	0 / 5 (0.00%)	2 / 76 (2.63%)	0 / 12 (0.00%)
occurrences (all)	0	2	0
Red blood cells urine positive			
subjects affected / exposed	0 / 5 (0.00%)	1 / 76 (1.32%)	0 / 12 (0.00%)
occurrences (all)	0	1	0
Tri-iodothyronine free increased			
subjects affected / exposed	0 / 5 (0.00%)	1 / 76 (1.32%)	0 / 12 (0.00%)
occurrences (all)	0	1	0
White blood cell count decreased			
subjects affected / exposed	0 / 5 (0.00%)	1 / 76 (1.32%)	0 / 12 (0.00%)
occurrences (all)	0	1	0
White blood cells urine positive			

subjects affected / exposed	0 / 5 (0.00%)	1 / 76 (1.32%)	0 / 12 (0.00%)
occurrences (all)	0	1	0
Blood pressure increased			
subjects affected / exposed	1 / 5 (20.00%)	0 / 76 (0.00%)	1 / 12 (8.33%)
occurrences (all)	1	0	1
Injury, poisoning and procedural complications			
Concussion			
subjects affected / exposed	0 / 5 (0.00%)	1 / 76 (1.32%)	0 / 12 (0.00%)
occurrences (all)	0	1	0
Wound			
subjects affected / exposed	0 / 5 (0.00%)	1 / 76 (1.32%)	0 / 12 (0.00%)
occurrences (all)	0	2	0
Nervous system disorders			
Acoustic neuritis			
subjects affected / exposed	0 / 5 (0.00%)	1 / 76 (1.32%)	0 / 12 (0.00%)
occurrences (all)	0	1	0
Carpal tunnel syndrome			
subjects affected / exposed	0 / 5 (0.00%)	1 / 76 (1.32%)	0 / 12 (0.00%)
occurrences (all)	0	1	0
Headache			
subjects affected / exposed	0 / 5 (0.00%)	4 / 76 (5.26%)	0 / 12 (0.00%)
occurrences (all)	0	6	0
Hypoaesthesia			
subjects affected / exposed	0 / 5 (0.00%)	1 / 76 (1.32%)	0 / 12 (0.00%)
occurrences (all)	0	1	0
Paraesthesia			
subjects affected / exposed	0 / 5 (0.00%)	1 / 76 (1.32%)	0 / 12 (0.00%)
occurrences (all)	0	1	0
Presyncope			
subjects affected / exposed	0 / 5 (0.00%)	1 / 76 (1.32%)	0 / 12 (0.00%)
occurrences (all)	0	1	0
Syncope			
subjects affected / exposed	0 / 5 (0.00%)	1 / 76 (1.32%)	0 / 12 (0.00%)
occurrences (all)	0	1	0
Trigeminal neuralgia			

subjects affected / exposed	0 / 5 (0.00%)	1 / 76 (1.32%)	0 / 12 (0.00%)
occurrences (all)	0	1	0
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	0 / 5 (0.00%)	3 / 76 (3.95%)	0 / 12 (0.00%)
occurrences (all)	0	3	0
Pancytopenia			
subjects affected / exposed	0 / 5 (0.00%)	1 / 76 (1.32%)	0 / 12 (0.00%)
occurrences (all)	0	1	0
Ear and labyrinth disorders			
Vertigo			
subjects affected / exposed	0 / 5 (0.00%)	1 / 76 (1.32%)	0 / 12 (0.00%)
occurrences (all)	0	1	0
Hyperthyroidism			
subjects affected / exposed	0 / 5 (0.00%)	1 / 76 (1.32%)	0 / 12 (0.00%)
occurrences (all)	0	1	0
Eye disorders			
Eye irritation			
subjects affected / exposed	0 / 5 (0.00%)	1 / 76 (1.32%)	0 / 12 (0.00%)
occurrences (all)	0	1	0
Lacrimation increased			
subjects affected / exposed	0 / 5 (0.00%)	1 / 76 (1.32%)	0 / 12 (0.00%)
occurrences (all)	0	1	0
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	0 / 5 (0.00%)	6 / 76 (7.89%)	0 / 12 (0.00%)
occurrences (all)	0	9	0
Abdominal pain upper			
subjects affected / exposed	0 / 5 (0.00%)	1 / 76 (1.32%)	0 / 12 (0.00%)
occurrences (all)	0	1	0
Constipation			
subjects affected / exposed	0 / 5 (0.00%)	4 / 76 (5.26%)	0 / 12 (0.00%)
occurrences (all)	0	4	0
Diarrhoea			
subjects affected / exposed	0 / 5 (0.00%)	6 / 76 (7.89%)	0 / 12 (0.00%)
occurrences (all)	0	21	0
Flatulence			

subjects affected / exposed	0 / 5 (0.00%)	5 / 76 (6.58%)	0 / 12 (0.00%)
occurrences (all)	0	5	0
Gastrointestinal pain			
subjects affected / exposed	0 / 5 (0.00%)	1 / 76 (1.32%)	0 / 12 (0.00%)
occurrences (all)	0	1	0
Nausea			
subjects affected / exposed	0 / 5 (0.00%)	8 / 76 (10.53%)	0 / 12 (0.00%)
occurrences (all)	0	13	0
Proctalgia			
subjects affected / exposed	0 / 5 (0.00%)	1 / 76 (1.32%)	0 / 12 (0.00%)
occurrences (all)	0	1	0
Vomiting			
subjects affected / exposed	0 / 5 (0.00%)	3 / 76 (3.95%)	0 / 12 (0.00%)
occurrences (all)	0	3	0
Gastritis			
subjects affected / exposed	1 / 5 (20.00%)	0 / 76 (0.00%)	1 / 12 (8.33%)
occurrences (all)	1	0	1
Hepatobiliary disorders			
Cholelithiasis			
subjects affected / exposed	1 / 5 (20.00%)	0 / 76 (0.00%)	1 / 12 (8.33%)
occurrences (all)	1	0	1
Cytolytic hepatitis			
subjects affected / exposed	0 / 5 (0.00%)	0 / 76 (0.00%)	1 / 12 (8.33%)
occurrences (all)	0	0	1
Skin and subcutaneous tissue disorders			
Erythema			
subjects affected / exposed	0 / 5 (0.00%)	1 / 76 (1.32%)	0 / 12 (0.00%)
occurrences (all)	0	2	0
Hyperhidrosis			
subjects affected / exposed	0 / 5 (0.00%)	2 / 76 (2.63%)	0 / 12 (0.00%)
occurrences (all)	0	3	0
Hyperkeratosis			
subjects affected / exposed	0 / 5 (0.00%)	1 / 76 (1.32%)	0 / 12 (0.00%)
occurrences (all)	0	1	0
Pruritus			

subjects affected / exposed	0 / 5 (0.00%)	2 / 76 (2.63%)	0 / 12 (0.00%)
occurrences (all)	0	3	0
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	0 / 5 (0.00%)	2 / 76 (2.63%)	0 / 12 (0.00%)
occurrences (all)	0	2	0
Back pain			
subjects affected / exposed	0 / 5 (0.00%)	1 / 76 (1.32%)	0 / 12 (0.00%)
occurrences (all)	0	1	0
Musculoskeletal chest pain			
subjects affected / exposed	0 / 5 (0.00%)	1 / 76 (1.32%)	0 / 12 (0.00%)
occurrences (all)	0	1	0
Myalgia			
subjects affected / exposed	0 / 5 (0.00%)	1 / 76 (1.32%)	0 / 12 (0.00%)
occurrences (all)	0	1	0
Pain in extremity			
subjects affected / exposed	0 / 5 (0.00%)	1 / 76 (1.32%)	0 / 12 (0.00%)
occurrences (all)	0	1	0
Rheumatoid arthritis			
subjects affected / exposed	0 / 5 (0.00%)	1 / 76 (1.32%)	0 / 12 (0.00%)
occurrences (all)	0	1	0
Synovitis			
subjects affected / exposed	0 / 5 (0.00%)	1 / 76 (1.32%)	0 / 12 (0.00%)
occurrences (all)	0	1	0
Dizziness			
subjects affected / exposed	0 / 5 (0.00%)	5 / 76 (6.58%)	0 / 12 (0.00%)
occurrences (all)	0	6	0
Infections and infestations			
Cystitis			
subjects affected / exposed	0 / 5 (0.00%)	1 / 76 (1.32%)	0 / 12 (0.00%)
occurrences (all)	0	1	0
Fungal skin infection			
subjects affected / exposed	0 / 5 (0.00%)	1 / 76 (1.32%)	0 / 12 (0.00%)
occurrences (all)	0	1	0
Nasopharyngitis			

subjects affected / exposed	0 / 5 (0.00%)	3 / 76 (3.95%)	0 / 12 (0.00%)
occurrences (all)	0	3	0
Sinusitis			
subjects affected / exposed	1 / 5 (20.00%)	2 / 76 (2.63%)	1 / 12 (8.33%)
occurrences (all)	1	2	1
Urinary tract infection			
subjects affected / exposed	0 / 5 (0.00%)	1 / 76 (1.32%)	0 / 12 (0.00%)
occurrences (all)	0	1	0
Metabolism and nutrition disorders			
Hypercholesterolaemia			
subjects affected / exposed	0 / 5 (0.00%)	1 / 76 (1.32%)	0 / 12 (0.00%)
occurrences (all)	0	1	0
Hyperglycaema			
subjects affected / exposed	0 / 5 (0.00%)	1 / 76 (1.32%)	0 / 12 (0.00%)
occurrences (all)	0	1	0
Impacted fasting glucose			
subjects affected / exposed	0 / 5 (0.00%)	2 / 76 (2.63%)	0 / 12 (0.00%)
occurrences (all)	0	3	0

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
23 September 2009	Amendment 1 The following change was implemented to comply with French regulations: - The eligibility criteria were amended to exclude patients deprived of their freedom/rights and those unable to give consent.
09 October 2009	Amendment 2 The following changes were implemented: - The exclusion criterion regarding patients deprived of their freedom/rights and those unable to give consent was extended to apply to all countries to ensure homogeneity of the population. - More comprehensive guidance on when and how to withdraw patients was added, following a request by the German Competent Authorities to provide more information.
09 December 2009	Amendment 3 A dose titration schedule was added for patients in the 2, 4 and 6 mg groups, so that all patients in the study began treatment at 1 mg and then those in the 2, 4 and 6 mg groups had their dose titrated up to the randomised dose. This change was implemented as a result of new PK data in monkeys which showed a 2x higher first peak concentration for the solution formulation compared to the lyophilisate formulation used in previous studies.
28 April 2010	Amendment 4 An extension phase (Part B) was added.
09 September 2010	Amendment 5 An administrative change to the fax number for the US PV contact was implemented.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

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

The study was terminated prematurely due to lack of efficacy.

Notes: