



Clinical trial results:

A Phase 2, Randomized, Double-blind, Placebo-controlled Study to Evaluate the Efficacy and Safety of AMG 334 in Migraine Prevention Summary

EudraCT number	2012-005331-90
Trial protocol	DE SE FI NO DK
Global end of trial date	12 November 2019

Results information

Result version number	v1 (current)
This version publication date	26 November 2020
First version publication date	26 November 2020

Trial information

Trial identification

Sponsor protocol code	20120178
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Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01952574
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Amgen Inc.
Sponsor organisation address	One Amgen Center Drive, Thousand Oaks, CA, United States, 91320
Public contact	IHQ Medical Info-Clinical Trials, Amgen (EUROPE) GmbH, MedInfoInternational@amgen.com
Scientific contact	IHQ Medical Info-Clinical Trials, Amgen (EUROPE) GmbH, MedInfoInternational@amgen.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	12 November 2019
Is this the analysis of the primary completion data?	No
Global end of trial reached?	Yes
Global end of trial date	12 November 2019
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The primary objective was to evaluate the effect of erenumab (AMG 334) compared to placebo on the change from baseline in monthly migraine days, in subjects with episodic migraine.

Protection of trial subjects:

This study was conducted in accordance with relevant country regulations and International Conference on Harmonisation (ICH) Good Clinical Practice (GCP) regulations/guidelines.

A copy of the protocol, proposed informed consent form, other written subject information, and any proposed advertising materials were submitted to the Independent Ethics Committee (IEC)/Institutional Review Board (IRB) for written approval. A copy of the written approval of the protocol and informed consent form must have been received by Amgen before recruitment of subjects into the study and shipment of investigational product.

Before a subject's participation in the clinical study, the investigator obtained written informed consent from the subject or the subject's legally acceptable representative after adequate explanation of the aims, methods, anticipated benefits, and potential hazards of the study and before any protocol-specific screening procedures or any investigational product was administered.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	06 August 2013
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	Canada: 6
Country: Number of subjects enrolled	Germany: 58
Country: Number of subjects enrolled	Denmark: 26
Country: Number of subjects enrolled	Finland: 42
Country: Number of subjects enrolled	Norway: 56
Country: Number of subjects enrolled	Sweden: 42
Country: Number of subjects enrolled	United States: 253
Worldwide total number of subjects	483
EEA total number of subjects	224

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)	483
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

This study was conducted at 59 centers in North America (Canada, USA) and Europe (Denmark, Finland, Germany, Norway, Sweden, and Portugal).

The study consisted of a 12-week double-blind treatment phase (DBTP) and a 256-week open-label treatment phase (OLTP) followed by a safety follow-up of 8 to 12 weeks (12 -16 weeks after last dose).

Pre-assignment

Screening details:

Participants were randomized 3:2:2:2 to receive placebo, erenumab 7 mg, erenumab 21 mg, or erenumab 70 mg once a month (QM) in the double-blind phase. Randomization was stratified by region (North America vs. Europe).

During the open-label treatment phase, participants in the US could participate in an optional Clinical Home Use (CHU) substudy.

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	DBTP: Placebo QM

Arm description:

Participants received placebo on day 1 and at weeks 4 and 8 by subcutaneous injection in the double-blind treatment phase.

Arm type	Placebo
Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Administered once a month (QM) by subcutaneous injection

Arm title	DBTP: Erenumab 7 mg QM
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Arm description:

Participants received erenumab 7 mg on day 1 and at weeks 4 and 8 by subcutaneous injection in the double-blind treatment phase.

Arm type	Experimental
Investigational medicinal product name	Erenumab
Investigational medicinal product code	AMG 334
Other name	Aimovig™
Pharmaceutical forms	Solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Administered once a month (QM) by subcutaneous injection

Arm title	DBTP: Erenumab 21 mg QM
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Arm description:

Participants received erenumab 21 mg on day 1 and at weeks 4 and 8 by subcutaneous injection in the double-blind treatment phase.

Arm type	Experimental
Investigational medicinal product name	Erenumab
Investigational medicinal product code	AMG 334
Other name	Aimovig™
Pharmaceutical forms	Solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Administered once a month (QM) by subcutaneous injection

Arm title	DBTP: Erenumab 70 mg QM
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Arm description:

Participants received erenumab 70 mg on day 1 and at weeks 4 and 8 by subcutaneous injection in the double-blind treatment phase.

Arm type	Experimental
Investigational medicinal product name	Erenumab
Investigational medicinal product code	AMG 334
Other name	Aimovig™
Pharmaceutical forms	Solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Administered once a month (QM) by subcutaneous injection

Number of subjects in period 1	DBTP: Placebo QM	DBTP: Erenumab 7 mg QM	DBTP: Erenumab 21 mg QM
Started	160	108	108
Received Study Drug	153	108	105
Completed	143	105	99
Not completed	17	3	9
Consent withdrawn by subject	9	3	3
Sponsor Decision	6	-	5
Lost to follow-up	2	-	1

Number of subjects in period 1	DBTP: Erenumab 70 mg QM
Started	107
Received Study Drug	106
Completed	101
Not completed	6
Consent withdrawn by subject	4
Sponsor Decision	2
Lost to follow-up	-

Period 2

Period 2 title	Open-label Treatment Phase
Is this the baseline period?	No
Allocation method	Not applicable
Blinding used	Not blinded

Arms

Arm title	OLTP: Erenumab 70/140 mg QM
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Arm description:

Participants received 70 mg erenumab QM from the beginning of the OLTP (week 12). After Protocol Amendment 3, participants still on study had their dose increased to 140 mg QM.

Arm type	Experimental
Investigational medicinal product name	Erenumab
Investigational medicinal product code	AMG 334
Other name	Aimovig™
Pharmaceutical forms	Solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Administered once a month (QM) by subcutaneous injection

Number of subjects in period 2^[1]	OLTP: Erenumab 70/140 mg QM
Started	383
Received 70 mg Erenumab	383
Received 140 mg Erenumab	250
Completed	221
Not completed	162
Adverse event, serious fatal	1
Consent withdrawn by subject	121
Decision by Sponsor	17
Lost to follow-up	19
Missing	4

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: Participants who were enrolled in Norway did not participate in the OLTP. In addition, 12 subjects who completed the DBTP did not enter the OLTP.

Period 3

Period 3 title	Clinical Home Use Substudy
Is this the baseline period?	No
Allocation method	Randomised - controlled
Blinding used	Not blinded

Arms

Are arms mutually exclusive?	Yes
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Arm title	CHU Substudy: Erenumab 140 mg by Prefilled Syringe
Arm description:	
Participants in the open-label treatment phase in the United States randomized to self-administer 140 mg erenumab via two 70 mg injections using a prefilled syringe (PFS) on CHU substudy day 1 (under study site supervision), and at home on day 29 (week 4) and day 57 (week 8).	
Arm type	Experimental
Investigational medicinal product name	Erenumab
Investigational medicinal product code	AMG 334
Other name	Aimovig™
Pharmaceutical forms	Solution for injection in pre-filled syringe
Routes of administration	Subcutaneous use

Dosage and administration details:

Administered once a month (QM) by subcutaneous injection

Arm title	CHU Substudy: Erenumab 140 mg Autoinjector/Pen
Arm description:	
Participants in the open-label treatment phase in the United States randomized to self-administer 140 mg erenumab via two 70 mg injections using an autoinjector (AI)/pen on CHU substudy day 1 (under study site supervision), and at home on day 29 (week 4) and day 57 (week 8).	
Arm type	Experimental
Investigational medicinal product name	Erenumab
Investigational medicinal product code	AMG 334
Other name	Aimovig™
Pharmaceutical forms	Solution for injection in needle-free injector, Solution for injection in pre-filled pen
Routes of administration	Subcutaneous use

Dosage and administration details:

Administered once a month (QM) by subcutaneous injection

Number of subjects in period 3^[2]	CHU Substudy: Erenumab 140 mg by Prefilled Syringe	CHU Substudy: Erenumab 140 mg Autoinjector/Pen
Started	42	41
Completed	39	40
Not completed	3	1
Consent withdrawn by subject	1	-
Decision by Sponsor	2	1

Notes:

[2] - 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: Only participants enrolled in the open-label treatment phase in the United States were eligible to participate in the clinical home use substudy

Baseline characteristics

Reporting groups

Reporting group title	DBTP: Placebo QM
Reporting group description:	
Participants received placebo on day 1 and at weeks 4 and 8 by subcutaneous injection in the double-blind treatment phase.	
Reporting group title	DBTP: Erenumab 7 mg QM
Reporting group description:	
Participants received erenumab 7 mg on day 1 and at weeks 4 and 8 by subcutaneous injection in the double-blind treatment phase.	
Reporting group title	DBTP: Erenumab 21 mg QM
Reporting group description:	
Participants received erenumab 21 mg on day 1 and at weeks 4 and 8 by subcutaneous injection in the double-blind treatment phase.	
Reporting group title	DBTP: Erenumab 70 mg QM
Reporting group description:	
Participants received erenumab 70 mg on day 1 and at weeks 4 and 8 by subcutaneous injection in the double-blind treatment phase.	

Reporting group values	DBTP: Placebo QM	DBTP: Erenumab 7 mg QM	DBTP: Erenumab 21 mg QM
Number of subjects	160	108	108
Age categorical			
Units: Subjects			
Adults (18-64 years)	160	108	108
From 65-84 years	0	0	0
85 years and over	0	0	0
Age Continuous			
Units: years			
arithmetic mean	41.4	40.3	39.9
standard deviation	± 10.0	± 10.9	± 12.3
Sex: Female, Male			
Units: participants			
Female	132	88	87
Male	28	20	21
Race/Ethnicity, Customized			
Units: Subjects			
American Indian or Alaska Native	0	0	0
Asian	2	0	1
Black or African American	13	10	7
Native Hawaiian or other Pacific Islander	1	0	0
White	142	97	100
Multiple	0	0	0
Other	2	1	0
Ethnicity (NIH/OMB)			
Units: Subjects			
Hispanic or Latino	11	9	9
Not Hispanic or Latino	149	99	99
Region			

Region is based on actual data collected at study baseline instead of randomization stratification.			
Units: Subjects			
North America	85	58	58
Europe	75	50	50
Monthly Migraine Days			
A migraine day was any calendar day in which the participant experienced a qualified migraine headache (onset, continuation, or recurrence of the migraine headache). A qualified migraine headache was defined as a migraine without aura or a migraine with aura. Monthly migraine days were calculated as the number of migraine days in the 4-week baseline phase.			
Units: migraine days/month			
arithmetic mean	8.77	8.62	8.93
standard deviation	± 2.72	± 2.79	± 2.88

Reporting group values	DBTP: Erenumab 70 mg QM	Total	
Number of subjects	107	483	
Age categorical			
Units: Subjects			
Adults (18-64 years)	107	483	
From 65-84 years	0	0	
85 years and over	0	0	
Age Continuous			
Units: years			
arithmetic mean	42.6	-	
standard deviation	± 9.9		
Sex: Female, Male			
Units: participants			
Female	82	389	
Male	25	94	
Race/Ethnicity, Customized			
Units: Subjects			
American Indian or Alaska Native	0	0	
Asian	1	4	
Black or African American	2	32	
Native Hawaiian or other Pacific Islander	0	1	
White	103	442	
Multiple	1	1	
Other	0	3	
Ethnicity (NIH/OMB)			
Units: Subjects			
Hispanic or Latino	1	30	
Not Hispanic or Latino	106	453	
Region			

Region is based on actual data collected at study baseline instead of randomization stratification.			
Units: Subjects			
North America	58	259	
Europe	49	224	
Monthly Migraine Days			
A migraine day was any calendar day in which the participant experienced a qualified migraine headache (onset, continuation, or recurrence of the migraine headache). A qualified migraine headache was defined as a migraine without aura or a migraine with aura. Monthly migraine days were calculated as the number of migraine days in the 4-week baseline phase.			
Units: migraine days/month			

arithmetic mean	8.58		
standard deviation	± 2.49	-	

End points

End points reporting groups

Reporting group title	DBTP: Placebo QM
Reporting group description: Participants received placebo on day 1 and at weeks 4 and 8 by subcutaneous injection in the double-blind treatment phase.	
Reporting group title	DBTP: Erenumab 7 mg QM
Reporting group description: Participants received erenumab 7 mg on day 1 and at weeks 4 and 8 by subcutaneous injection in the double-blind treatment phase.	
Reporting group title	DBTP: Erenumab 21 mg QM
Reporting group description: Participants received erenumab 21 mg on day 1 and at weeks 4 and 8 by subcutaneous injection in the double-blind treatment phase.	
Reporting group title	DBTP: Erenumab 70 mg QM
Reporting group description: Participants received erenumab 70 mg on day 1 and at weeks 4 and 8 by subcutaneous injection in the double-blind treatment phase.	
Reporting group title	OLTP: Erenumab 70/140 mg QM
Reporting group description: Participants received 70 mg erenumab QM from the beginning of the OLTP (week 12). After Protocol Amendment 3, participants still on study had their dose increased to 140 mg QM.	
Reporting group title	CHU Substudy: Erenumab 140 mg by Prefilled Syringe
Reporting group description: Participants in the open-label treatment phase in the United States randomized to self-administer 140 mg erenumab via two 70 mg injections using a prefilled syringe (PFS) on CHU substudy day 1 (under study site supervision), and at home on day 29 (week 4) and day 57 (week 8).	
Reporting group title	CHU Substudy: Erenumab 140 mg Autoinjector/Pen
Reporting group description: Participants in the open-label treatment phase in the United States randomized to self-administer 140 mg erenumab via two 70 mg injections using an autoinjector (AI)/pen on CHU substudy day 1 (under study site supervision), and at home on day 29 (week 4) and day 57 (week 8).	
Subject analysis set title	OLTP: Erenumab 70 mg QM
Subject analysis set type	Safety analysis
Subject analysis set description: Participants received 70 mg erenumab QM from week 12 until implementation of Protocol Amendment 3 (07 April 2016) in the open-label treatment phase; median duration of exposure was 104 weeks.	
Subject analysis set title	OLTP: Erenumab 140 mg QM
Subject analysis set type	Safety analysis
Subject analysis set description: After implementation of Protocol Amendment 3 (07 April 2016), participants still on study received erenumab 140 mg QM up to week 264 in the open-label treatment phase; median duration of exposure was 141 weeks.	
Subject analysis set title	Placebo / Erenumab 70/140 mg QM
Subject analysis set type	Safety analysis
Subject analysis set description: Participants randomized to placebo in the double-blind treatment phase received 70 mg erenumab QM from week 12 in the open-label treatment phase. After Protocol Amendment 3, participants still on study had their dose increased to 140 mg QM.	
Subject analysis set title	Erenumab 7 mg QM / Erenumab 70/140 mg QM
Subject analysis set type	Safety analysis
Subject analysis set description: Participants randomized to erenumab 7 mg in the double-blind treatment phase received 70 mg erenumab QM from week 12 in the open-label treatment phase. After Protocol Amendment 3,	

participants still on study had their dose increased to 140 mg QM.

Subject analysis set title	Erenumab 21 mg QM / Erenumab 70/140 mg QM
Subject analysis set type	Safety analysis

Subject analysis set description:

Participants randomized to erenumab 21 mg in the double-blind treatment phase received 70 mg erenumab QM from week 12 in the open-label treatment phase. After Protocol Amendment 3, participants still on study had their dose increased to 140 mg QM.

Subject analysis set title	Erenumab 70 mg QM / Erenumab 70/140 mg QM
Subject analysis set type	Safety analysis

Subject analysis set description:

Participants randomized to erenumab 70 mg in the double-blind treatment phase received 70 mg erenumab QM from week 12 in the open-label treatment phase. After Protocol Amendment 3, participants still on study had their dose increased to 140 mg QM.

Primary: Change From Baseline in Monthly Migraine Days at Week 12

End point title	Change From Baseline in Monthly Migraine Days at Week 12
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End point description:

A migraine day was any calendar day in which the participant experienced a qualified migraine headache (onset, continuation, or recurrence of the migraine headache). A qualified migraine headache was defined as a migraine with or without aura. The change from baseline in monthly migraine days was calculated as the number of migraine days during the last 4 weeks of the 12-week double-blind treatment phase – the number of migraine days during the 4-week baseline phase.

Data were analyzed in participants who received at least 1 dose of investigational product (IP) and had ≥ 4 migraine days during the 4-week baseline phase (efficacy analysis set), and with at least one change from baseline value in monthly migraine days.

End point type	Primary
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End point timeframe:

4-week baseline phase and the last 4 weeks of the 12-week double-blind treatment phase

End point values	DBTP: Placebo QM	DBTP: Erenumab 7 mg QM	DBTP: Erenumab 21 mg QM	DBTP: Erenumab 70 mg QM
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	152	107	99	104
Units: migraine days / month				
least squares mean (standard error)	-2.28 (\pm 0.31)	-2.18 (\pm 0.36)	-2.39 (\pm 0.38)	-3.40 (\pm 0.37)

Statistical analyses

Statistical analysis title	Analysis of Change in Monthly Migraine Days
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Statistical analysis description:

The primary analysis utilized a generalized linear mixed model which included treatment, visit, treatment by visit, the stratification factor region, and baseline value as covariates.

Comparison groups	DBTP: Placebo QM v DBTP: Erenumab 70 mg QM
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Number of subjects included in analysis	256
Analysis specification	Pre-specified
Analysis type	superiority ^[1]
P-value	= 0.021
Method	Generalized Linear Mixed Model
Parameter estimate	LS Mean Difference
Point estimate	-1.12
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.06
upper limit	-0.17

Notes:

[1] - To maintain the type I error at ≤ 0.05 , the pairwise comparison was tested in a sequential testing procedure in the order of erenumab 70 mg vs placebo, 21 mg vs placebo, and 7 mg vs placebo. The lower dose group was only to be tested when the higher dose group was tested as significant.

Statistical analysis title	Analysis of Change in Monthly Migraine Days
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Statistical analysis description:

The primary analysis utilized a generalized linear mixed model which included treatment, visit, treatment by visit, the stratification factor region, and baseline value as covariates.

Comparison groups	DBTP: Placebo QM v DBTP: Erenumab 21 mg QM
Number of subjects included in analysis	251
Analysis specification	Pre-specified
Analysis type	superiority ^[2]
P-value	= 0.83
Method	Generalized Linear Mixed Model
Parameter estimate	LS Mean Difference
Point estimate	-0.1
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.07
upper limit	0.86

Notes:

[2] - To maintain the type I error at ≤ 0.05 , the pairwise comparison was tested in a sequential testing procedure in the order of erenumab 70 mg vs placebo, 21 mg vs placebo, and 7 mg vs placebo. The lower dose group was only to be tested when the higher dose group was tested as significant.

Statistical analysis title	Analysis of Change in Monthly Migraine Days
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Statistical analysis description:

The primary analysis utilized a generalized linear mixed model which included treatment, visit, treatment by visit, the stratification factor region, and baseline value as covariates.

Comparison groups	DBTP: Placebo QM v DBTP: Erenumab 7 mg QM
Number of subjects included in analysis	259
Analysis specification	Pre-specified
Analysis type	superiority ^[3]
P-value	= 0.82
Method	Generalized Linear Mixed Model
Parameter estimate	LS Mean Difference
Point estimate	0.11

Confidence interval	
level	Other: 92 %
sides	2-sided
lower limit	-0.83
upper limit	1.05

Notes:

[3] - To maintain the type I error at ≤ 0.05 , the pairwise comparison was tested in a sequential testing procedure in the order of erenumab 70 mg vs placebo, 21 mg vs placebo, and 7 mg vs placebo. The lower dose group was only to be tested when the higher dose group was tested as significant.

Primary: CHU Substudy: Percentage of Participants Who Self-administered a Full Dose, Partial Dose, or No Dose of Erenumab

End point title	CHU Substudy: Percentage of Participants Who Self-administered a Full Dose, Partial Dose, or No Dose of Erenumab ^[4]
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End point description:

To assess participants ability to administer a full dose of erenumab in home-use at day 29 (week 4) and day 57 (week 8), site staff called participants and asked whether the participant administered a full, partial, or no dose of erenumab. A full dose means that the entire volume of both prefilled syringes or autoinjector/pens were injected. Discontinued prior to dosing day indicates participants who had discontinued the investigational product and did not attempt to self-administer on day 29 or 57.

End point type	Primary
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End point timeframe:

CHU substudy day 29 (week 4) and day 57 (week 8)

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: In the CHU substudy it was hypothesized that users were able to administer a full dose of erenumab comparably using either the prefilled syringe or autoinjector/pen. No formal hypotheses were tested.

End point values	CHU Substudy: Erenumab 140 mg by Prefilled Syringe	CHU Substudy: Erenumab 140 mg Autoinjector/Pen		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	42 ^[5]	41 ^[6]		
Units: participants				
Day 29 (week 4): Full dose	39	41		
Day 29 (week 4): Partial dose	1	0		
Day 29 (week 4): Discontinued prior to dosing day	2	0		
Day 57 (week 8): Full dose	39	39		
Day 57 (week 8): Partial dose	0	1		
Day 57 (week 8): Discontinued prior to dosing day	3	1		

Notes:

[5] - Participants enrolled in the CHU substudy who received at least 1 dose of IP in the substudy.

[6] - Participants enrolled in the CHU substudy who received at least 1 dose of IP in the substudy.

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants with at Least a 50% Reduction From Baseline in Monthly Migraine Days at Week 12

End point title	Percentage of Participants with at Least a 50% Reduction From
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End point description:

A migraine day was any calendar day in which the participant experienced a qualified migraine headache (onset, continuation, or recurrence of the migraine headache). A qualified migraine headache was defined either as a migraine without aura or a migraine with aura. Monthly migraine days were calculated as the number of migraine days in the 4-week baseline phase and during the last 4 weeks of double-blind treatment. At least a 50% reduction from baseline in monthly migraine days was determined if the change in monthly migraine days from the 4-week baseline phase to the last 4 weeks of the 12-week double-blind treatment phase * 100 / baseline monthly migraine days was less than or equal to -50%.

Analyzed in participants who received at least 1 dose of investigational product and had ≥ 4 migraine days during the 4-week baseline phase (efficacy analysis set) with available data at week 12.

End point type	Secondary
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End point timeframe:

4-week baseline phase and the last 4 weeks of the 12-week double-blind treatment phase

End point values	DBTP: Placebo QM	DBTP: Erenumab 7 mg QM	DBTP: Erenumab 21 mg QM	DBTP: Erenumab 70 mg QM
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	144	104	93	99
Units: percentage of participants				
number (not applicable)	22.9	28.8	34.4	46.5

Statistical analyses

Statistical analysis title	Analysis of Responder Rate
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Statistical analysis description:

The generalized linear mixed model includes data for all participants in the efficacy analysis set with at least one percent change from baseline value in monthly migraine days (152 participants in the placebo group and 104 in the erenumab 70 mg group)

Comparison groups	DBTP: Placebo QM v DBTP: Erenumab 70 mg QM
Number of subjects included in analysis	243
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.011 ^[7]
Method	Generalised Linear Mixed Model
Parameter estimate	Odds ratio (OR)
Point estimate	2
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.17
upper limit	3.42

Notes:

[7] - Generalized linear mixed model including treatment, visit, treatment by visit, stratification factor region, and baseline value as covariates.

Statistical analysis title	Analysis of Responder Rate
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Statistical analysis description:

The generalized linear mixed model includes data for all participants in the efficacy analysis set with at least one change from baseline value in monthly migraine days (152 participants in the placebo group and 99 in the erenumab 21 mg group)

Comparison groups	DBTP: Placebo QM v DBTP: Erenumab 21 mg QM
Number of subjects included in analysis	237
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.44 ^[8]
Method	Generalized Linear Mixed Model
Parameter estimate	Odds ratio (OR)
Point estimate	1.25
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.71
upper limit	2.18

Notes:

[8] - Generalized linear mixed model including treatment, visit, treatment by visit, stratification factor region, and baseline value as covariates.

Statistical analysis title	Analysis of Responder Rate
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Statistical analysis description:

The generalized linear mixed model includes data for all participants in the efficacy analysis set with at least one change from baseline value in monthly migraine days (152 participants in the placebo group and 107 in the erenumab 7 mg group)

Comparison groups	DBTP: Placebo QM v DBTP: Erenumab 7 mg QM
Number of subjects included in analysis	248
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.8 ^[9]
Method	Generalized Linear Mixed Model
Parameter estimate	Odds ratio (OR)
Point estimate	0.93
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.53
upper limit	1.63

Notes:

[9] - Generalized linear mixed model including treatment, visit, treatment by visit, stratification factor region, and baseline value as covariates.

Secondary: Change From Baseline in Monthly Migraine Attacks at Week 12

End point title	Change From Baseline in Monthly Migraine Attacks at Week 12
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End point description:

A migraine attack is an episode of any qualified migraine headache or migraine specific medication intakes for aura only. A migraine attack that was interrupted by sleep or that temporarily remits and then recurs within 48 hours or an attack treated successfully with medication but that relapses within 48 hours was considered to be one attack.

The change from baseline in monthly migraine attacks was calculated as the number of migraine attacks during the last 4 weeks of the 12-week double-blind treatment phase – the number of migraine attacks during the 4-week baseline phase.

Analyzed in participants who received at least 1 dose of investigational product and had ≥ 4 migraine days during the 4-week baseline phase (efficacy analysis set), and with at least one change from baseline value in monthly migraine attacks.

End point type	Secondary
End point timeframe:	
4-week baseline phase and the last 4 weeks of the 12-week double-blind treatment phase	

End point values	DBTP: Placebo QM	DBTP: Erenumab 7 mg QM	DBTP: Erenumab 21 mg QM	DBTP: Erenumab 70 mg QM
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	152	107	99	104
Units: migraine attacks/month				
least squares mean (standard error)	-1.44 (± 0.17)	-1.07 (± 0.20)	-1.42 (± 0.21)	-1.84 (± 0.20)

Statistical analyses

Statistical analysis title	Analysis of Change in Monthly Migraine Attacks
Comparison groups	DBTP: Placebo QM v DBTP: Erenumab 70 mg QM
Number of subjects included in analysis	256
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.13 ^[10]
Method	Generalized Linear Mixed Model
Parameter estimate	LS Mean Difference
Point estimate	-0.4
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.92
upper limit	0.12

Notes:

[10] - Generalized linear mixed model including treatment, visit, treatment by visit, the stratification factor region, and baseline value as covariates.

Statistical analysis title	Analysis of Change in Monthly Migraine Attacks
Comparison groups	DBTP: Placebo QM v DBTP: Erenumab 21 mg QM
Number of subjects included in analysis	251
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.95 ^[11]
Method	Generalized Linear Mixed Model
Parameter estimate	LS Mean Difference
Point estimate	0.02
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.51
upper limit	0.54

Notes:

[11] - Generalized linear mixed model including treatment, visit, treatment by visit, the stratification factor region, and baseline value as covariates.

Statistical analysis title	Analysis of Change in Monthly Migraine Attacks
Comparison groups	DBTP: Placebo QM v DBTP: Erenumab 7 mg QM
Number of subjects included in analysis	259
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.16 ^[12]
Method	Generalized Linear Mixed Model
Parameter estimate	LS Mean Difference
Point estimate	0.37
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.14
upper limit	0.87

Notes:

[12] - Generalized linear mixed model including treatment, visit, treatment by visit, the stratification factor region, and baseline value as covariates.

Secondary: Number of Participants with Treatment-emergent Adverse Events in the Double-blind Treatment Phase

End point title	Number of Participants with Treatment-emergent Adverse Events in the Double-blind Treatment Phase
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End point description:

An adverse event (AE) is any untoward medical occurrence in a clinical trial subject, including worsening of a pre-existing medical condition and laboratory value changes that require treatment or adjustment in current therapy.

AEs were graded using the Common Terminology Criteria for Adverse Events (CTCAE) version 4.03:

- 1 Mild; asymptomatic or mild symptoms
- 2 Moderate; minimal, local or noninvasive intervention indicated; limiting daily activities
- 3 Severe or medically significant but not immediately life-threatening; hospitalization indicated; disabling; limiting self-care
- 4 Life-threatening consequences; urgent intervention indicated
- 5 Death related to AE

A serious adverse event is an AE that meets at least 1 of the following criteria:

- fatal
- life threatening
- requires in-patient hospitalization or prolongation of existing hospitalization
- results in persistent or significant disability/incapacity
- congenital anomaly/birth defect
- other medically important serious event

End point type	Secondary
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End point timeframe:

From first dose of study drug in the double-blind treatment phase until the first dose of study drug in the open-label treatment phase (12 weeks) or up to 12 weeks after last dose for participants who did not enter the open-label treatment phase.

End point values	DBTP: Placebo QM	DBTP: Erenumab 7 mg QM	DBTP: Erenumab 21 mg QM	DBTP: Erenumab 70 mg QM
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	153 ^[13]	108 ^[14]	105 ^[15]	106 ^[16]
Units: participants				
Any adverse event (AE)	81	57	55	57
Serious adverse events (SAEs)	1	1	0	1
AE leading to discontinuation of IP	2	2	2	3
AE Grade \geq 2	36	31	25	23
AE Grade \geq 3	3	3	3	3
AE Grade \geq 4	0	0	0	0
Fatal adverse events	0	0	0	0

Notes:

[13] - Safety analysis set

[14] - Safety analysis set

[15] - Safety analysis set

[16] - Safety analysis set

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants with Treatment-emergent Adverse Events in the Open-label Treatment Phase

End point title	Number of Participants with Treatment-emergent Adverse Events in the Open-label Treatment Phase
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End point description:

An adverse event (AE) is any untoward medical occurrence in a clinical trial subject, including worsening of a pre-existing medical condition and laboratory value changes that require treatment or adjustment in current therapy.

AEs were graded using the Common Terminology Criteria for Adverse Events (CTCAE) version 4.03:

- 1 Mild; asymptomatic or mild symptoms
- 2 Moderate; minimal, local or noninvasive intervention indicated; limiting daily activities
- 3 Severe or medically significant but not immediately life-threatening; hospitalization indicated; disabling; limiting self-care
- 4 Life-threatening consequences; urgent intervention indicated
- 5 Death related to AE

A serious adverse event is an AE that meets at least 1 of the following criteria:

- fatal
- life threatening
- requires in-patient hospitalization or prolongation of existing hospitalization
- results in persistent or significant disability/incapacity
- congenital anomaly/birth defect
- other medically important serious event

End point type	Secondary
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End point timeframe:

From first dose in the open-label treatment phase up to 12 weeks (participants receiving 70 mg only) or 16 weeks (participants with dose increased to 140 mg) after the last dose; a maximum of 268 weeks.

End point values	OLTP: Erenumab 70/140 mg QM	OLTP: Erenumab 70 mg QM	OLTP: Erenumab 140 mg QM	
Subject group type	Reporting group	Subject analysis set	Subject analysis set	
Number of subjects analysed	383	383	250	
Units: participants				
Any adverse event (AE)	340	323	216	
Serious adverse events (SAEs)	49	30	25	
AE leading to discontinuation of IP	18	16	2	
AE Grade ≥ 2	286	249	180	
AE Grade ≥ 3	83	55	40	
AE Grade ≥ 4	4	1	3	
Fatal adverse events	2	1	1	

Statistical analyses

No statistical analyses for this end point

Secondary: CHU Substudy: Number of Participants with Treatment-emergent Adverse Events During the CHU Substudy

End point title	CHU Substudy: Number of Participants with Treatment-emergent Adverse Events During the CHU Substudy
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End point description:

AEs were graded using the CTCAE version 4.03:

- 1 Mild; asymptomatic or mild symptoms
- 2 Moderate; minimal, local or noninvasive intervention indicated; limiting daily activities
- 3 Severe or medically significant but not immediately life-threatening; hospitalization indicated; disabling; limiting self-care
- 4 Life-threatening consequences; urgent intervention indicated
- 5 Death related to AE

A serious adverse event is an AE that meets at least 1 of the following criteria:

- fatal
- life threatening
- requires in-patient hospitalization or prolongation of existing hospitalization
- results in persistent or significant disability/incapacity
- congenital anomaly/birth defect
- other medically important serious event

An adverse device effect is any AE related to the use of a medical device, including AEs resulting from insufficient or inadequate instructions for use, any malfunction of the device, or use error or from intentional misuse of the device.

End point type	Secondary
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End point timeframe:

From first dose in the CHU substudy to end of substudy (up to 12 weeks)

End point values	CHU Substudy: Erenumab 140 mg by Prefilled Syringe	CHU Substudy: Erenumab 140 mg Autoinjector/Pe n		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	42 ^[17]	41 ^[18]		
Units: participants				
Any adverse event	13	17		

AE Grade ≥ 2	7	10		
AE Grade ≥ 3	1	2		
AE Grade ≥ 4	0	0		
Serious adverse events	0	0		
Leading to discontinuation of IP	0	0		
Fatal adverse events	0	0		
Injection site reactions	4	2		
Adverse device effects	2	2		

Notes:

[17] - Participants enrolled in the CHU substudy who received at least 1 dose of IP in the substudy

[18] - Participants enrolled in the CHU substudy who received at least 1 dose of IP in the substudy

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants who Developed Anti-erenumab Antibodies During the Double-blind Treatment Phase

End point title	Number of Participants who Developed Anti-erenumab Antibodies During the Double-blind Treatment Phase
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End point description:

Two validated assays were used to detect the presence of anti-erenumab antibodies. First, an electrochemiluminescent bridging immunoassay was used to detect binding antibodies (screening assay) and confirm antibodies (confirmatory assay) capable of binding erenumab. Second, a cell-based bioassay was used to test positive binding antibody samples for neutralizing activity against erenumab. Participants who developed anti-erenumab antibodies are participants who were negative or had no result at baseline but positive at any time postbaseline during the DBTP.

If a sample was positive for binding antibodies and demonstrated neutralizing activity at the same time point, the participant was defined as positive for neutralizing antibodies.

End point type	Secondary
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End point timeframe:

12 weeks

End point values	DBTP: Placebo QM	DBTP: Erenumab 7 mg QM	DBTP: Erenumab 21 mg QM	DBTP: Erenumab 70 mg QM
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	149 ^[19]	107 ^[20]	104 ^[21]	106 ^[22]
Units: participants				
Developed binding antibodies	0	13	12	8
Developed neutralizing antibodies	0	5	3	1

Notes:

[19] - Participants who received at least 1 dose of IP and with valid postbaseline antibody testing results

[20] - Participants who received at least 1 dose of IP and with valid postbaseline antibody testing results

[21] - Participants who received at least 1 dose of IP and with valid postbaseline antibody testing results

[22] - Participants who received at least 1 dose of IP and with valid postbaseline antibody testing results

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants who Developed Anti-erenumab Antibodies

During the Open-label Treatment Phase

End point title	Number of Participants who Developed Anti-erenumab Antibodies During the Open-label Treatment Phase
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End point description:

Two validated assays were used to detect the presence of anti-erenumab antibodies. First, an electrochemiluminescent bridging immunoassay was used to detect binding antibodies (screening assay) and confirm antibodies (confirmatory assay) capable of binding erenumab. Second, a cell-based bioassay was used to test positive binding antibody samples for neutralizing activity against erenumab. Participants who developed anti-erenumab antibodies are participants who were negative prior to the first OLTP dose but positive at any time during the OLTP, or participants with no data prior to first dose in OLTP with any post-baseline positive results.

If a sample was positive for binding antibodies and demonstrated neutralizing activity at the same time point, the participant was defined as positive for neutralizing antibodies.

End point type	Secondary
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End point timeframe:

From week 12 up to 12 weeks (participants receiving 70 mg only) or 16 weeks (participants with dose increased to 140 mg) after the last dose; maximum 268 weeks.

End point values	Placebo / Erenumab 70/140 mg QM	Erenumab 7 mg QM / Erenumab 70/140 mg QM	Erenumab 21 mg QM / Erenumab 70/140 mg QM	Erenumab 70 mg QM / Erenumab 70/140 mg QM
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	119 ^[23]	88 ^[24]	87 ^[25]	86 ^[26]
Units: participants				
Developed binding antibodies	12	8	6	5
Developed neutralizing antibodies	1	0	1	0

Notes:

[23] - Subjects who received at least 1 dose of IP in the OLTP with valid antibody results during the OLTP

[24] - Subjects who received at least 1 dose of IP in the OLTP with valid antibody results during the OLTP

[25] - Subjects who received at least 1 dose of IP in the OLTP with valid antibody results during the OLTP

[26] - Subjects who received at least 1 dose of IP in the OLTP with valid antibody results during the OLTP

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

DBTP: From first dose of IP in the DBTP until the first dose of IP in the OLTP (12 weeks).

OLTP: From first dose in the OLTP up to 12 weeks or 16 weeks (70 mg and 140 mg doses respectively) after the last dose; up to 268 weeks.

CHU substudy: 12 weeks

Adverse event reporting additional description:

Participants who did not enter the OLTP were followed for up to 12 weeks after last dose in the DBTP.

In the OLTP participants were followed for up to 12 weeks (participants receiving 70 mg only) or 16 weeks (participants with dose increased to 140 mg) after last dose.

Assessment type	Systematic
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Dictionary used

Dictionary name	MedDRA
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Dictionary version	22.1
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Reporting groups

Reporting group title	DBTP: Placebo QM
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Reporting group description:

Participants received placebo on day 1 and at weeks 4 and 8 by subcutaneous injection in the double-blind treatment phase.

Reporting group title	DBTP: Erenumab 7 mg QM
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Reporting group description:

Participants received erenumab 7 mg on day 1 and at weeks 4 and 8 by subcutaneous injection in the double-blind treatment phase.

Reporting group title	DBTP: Erenumab 21 mg QM
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Reporting group description:

Participants received erenumab 21 mg on day 1 and at weeks 4 and 8 by subcutaneous injection in the double-blind treatment phase.

Reporting group title	DBTP: Erenumab 70 mg QM
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Reporting group description:

Participants received erenumab 70 mg on day 1 and at weeks 4 and 8 by subcutaneous injection in the double-blind treatment phase.

Reporting group title	OpLTP: Erenumab 70 mg QM
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Reporting group description:

Participants received 70 mg erenumab QM from week 12 until implementation of Protocol Amendment 3 (07 April 2016) in the open-label treatment phase; median duration of exposure was 104 weeks.

Reporting group title	OLTP: Erenumab 140 mg QM
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Reporting group description:

After implementation of Protocol Amendment 3 (07 April 2016), participants still on study received erenumab 140 mg QM up to week 264 in the open-label treatment phase; median duration of exposure was 141 weeks.

Reporting group title	OLTP: Erenumab 70/140 mg QM
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Reporting group description:

Participants received 70 mg erenumab QM from week 12 to week 264 (last dose). After Protocol Amendment 3, participants still on study had their dose increased to 140 mg QM. The overall median duration of exposure was 255 weeks.

Reporting group title	CHU Substudy: Erenumab 140 mg PFS
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Reporting group description:

Participants in the open-label treatment phase in the United States self-administered 140 mg erenumab via two 70 mg injections using a prefilled syringe (PFS) on CHU substudy day 1 (under study site supervision), and at home on day 29 (week 4) and day 57 (week 8).

Reporting group title	CHU Substudy: Erenumab 140 mg AI/Pen
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Reporting group description:

Participants in the open-label treatment phase in the United States self-administered 140 mg erenumab

via two 70 mg injections using an autoinjector/pen (AI)/pen) on CHU substudy day 1 (under study site supervision), and at home on day 29 (week 4) and day 57 (week 8).

Reporting group title	CHU Substudy: Total
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Reporting group description:

Participants in the open-label treatment phase in the United States self-administered 140 mg erenumab via two 70 mg injections using a prefilled syringe or autoinjector/pen on CHU substudy day 1 (under study site supervision), and at home on day 29 (week 4) and day 57 (week 8).

Serious adverse events	DBTP: Placebo QM	DBTP: Erenumab 7 mg QM	DBTP: Erenumab 21 mg QM
Total subjects affected by serious adverse events			
subjects affected / exposed	1 / 153 (0.65%)	1 / 108 (0.93%)	0 / 105 (0.00%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events			
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Adenocarcinoma of the cervix			
subjects affected / exposed	0 / 153 (0.00%)	0 / 108 (0.00%)	0 / 105 (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
Breast cancer			
subjects affected / exposed	0 / 153 (0.00%)	0 / 108 (0.00%)	0 / 105 (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
Invasive lobular breast carcinoma			
subjects affected / exposed	0 / 153 (0.00%)	0 / 108 (0.00%)	0 / 105 (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
Lipoma			
subjects affected / exposed	0 / 153 (0.00%)	0 / 108 (0.00%)	0 / 105 (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 adenocarcinoma stage III			
subjects affected / exposed	0 / 153 (0.00%)	0 / 108 (0.00%)	0 / 105 (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
Prostate cancer			

subjects affected / exposed	0 / 153 (0.00%)	0 / 108 (0.00%)	0 / 105 (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
Uterine leiomyoma			
subjects affected / exposed	0 / 153 (0.00%)	0 / 108 (0.00%)	0 / 105 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vascular disorders			
Arteriosclerosis			
subjects affected / exposed	0 / 153 (0.00%)	0 / 108 (0.00%)	0 / 105 (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
Deep vein thrombosis			
subjects affected / exposed	0 / 153 (0.00%)	0 / 108 (0.00%)	0 / 105 (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
Thrombosis			
subjects affected / exposed	0 / 153 (0.00%)	0 / 108 (0.00%)	0 / 105 (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			
Death			
subjects affected / exposed	0 / 153 (0.00%)	0 / 108 (0.00%)	0 / 105 (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
Non-cardiac chest pain			
subjects affected / exposed	0 / 153 (0.00%)	0 / 108 (0.00%)	0 / 105 (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
Reproductive system and breast disorders			
Ovarian cyst ruptured			

subjects affected / exposed	0 / 153 (0.00%)	1 / 108 (0.93%)	0 / 105 (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
Adnexa uteri cyst			
subjects affected / exposed	0 / 153 (0.00%)	0 / 108 (0.00%)	0 / 105 (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
Menorrhagia			
subjects affected / exposed	0 / 153 (0.00%)	0 / 108 (0.00%)	0 / 105 (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
Ovarian cyst			
subjects affected / exposed	0 / 153 (0.00%)	0 / 108 (0.00%)	0 / 105 (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
Respiratory, thoracic and mediastinal disorders			
Pleural effusion			
subjects affected / exposed	0 / 153 (0.00%)	0 / 108 (0.00%)	0 / 105 (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
Pulmonary embolism			
subjects affected / exposed	0 / 153 (0.00%)	0 / 108 (0.00%)	0 / 105 (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
Psychiatric disorders			
Adjustment disorder			
subjects affected / exposed	0 / 153 (0.00%)	0 / 108 (0.00%)	0 / 105 (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
Suicide attempt			
subjects affected / exposed	0 / 153 (0.00%)	0 / 108 (0.00%)	0 / 105 (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

Investigations			
Aspartate aminotransferase increased			
subjects affected / exposed	0 / 153 (0.00%)	0 / 108 (0.00%)	0 / 105 (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
Injury, poisoning and procedural complications			
Ligament rupture			
subjects affected / exposed	0 / 153 (0.00%)	0 / 108 (0.00%)	0 / 105 (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
Spinal compression fracture			
subjects affected / exposed	0 / 153 (0.00%)	0 / 108 (0.00%)	0 / 105 (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			
Developmental hip dysplasia			
subjects affected / exposed	0 / 153 (0.00%)	0 / 108 (0.00%)	0 / 105 (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
Cardiac disorders			
Coronary artery stenosis			
subjects affected / exposed	0 / 153 (0.00%)	0 / 108 (0.00%)	0 / 105 (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
Hypertensive heart disease			
subjects affected / exposed	0 / 153 (0.00%)	0 / 108 (0.00%)	0 / 105 (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
Myocardial ischaemia			
subjects affected / exposed	0 / 153 (0.00%)	0 / 108 (0.00%)	0 / 105 (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
Nervous system disorders			

Migraine			
subjects affected / exposed	0 / 153 (0.00%)	0 / 108 (0.00%)	0 / 105 (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
Cauda equina syndrome			
subjects affected / exposed	0 / 153 (0.00%)	0 / 108 (0.00%)	0 / 105 (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
Cervicobrachial syndrome			
subjects affected / exposed	0 / 153 (0.00%)	0 / 108 (0.00%)	0 / 105 (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
Headache			
subjects affected / exposed	0 / 153 (0.00%)	0 / 108 (0.00%)	0 / 105 (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
Lumbar radiculopathy			
subjects affected / exposed	0 / 153 (0.00%)	0 / 108 (0.00%)	0 / 105 (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
Optic neuritis			
subjects affected / exposed	0 / 153 (0.00%)	0 / 108 (0.00%)	0 / 105 (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
Syncope			
subjects affected / exposed	0 / 153 (0.00%)	0 / 108 (0.00%)	0 / 105 (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
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	0 / 153 (0.00%)	0 / 108 (0.00%)	0 / 105 (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
Ear and labyrinth disorders			

Vertigo			
subjects affected / exposed	0 / 153 (0.00%)	0 / 108 (0.00%)	0 / 105 (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
Eye disorders			
Visual impairment			
subjects affected / exposed	0 / 153 (0.00%)	0 / 108 (0.00%)	0 / 105 (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			
Abdominal adhesions			
subjects affected / exposed	0 / 153 (0.00%)	0 / 108 (0.00%)	0 / 105 (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
Abdominal hernia			
subjects affected / exposed	0 / 153 (0.00%)	0 / 108 (0.00%)	0 / 105 (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
Appendicitis noninfective			
subjects affected / exposed	0 / 153 (0.00%)	0 / 108 (0.00%)	0 / 105 (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
Colitis ischaemic			
subjects affected / exposed	0 / 153 (0.00%)	0 / 108 (0.00%)	0 / 105 (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
Crohn's disease			
subjects affected / exposed	0 / 153 (0.00%)	0 / 108 (0.00%)	0 / 105 (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
Diverticulum			
subjects affected / exposed	0 / 153 (0.00%)	0 / 108 (0.00%)	0 / 105 (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

Faecaloma			
subjects affected / exposed	0 / 153 (0.00%)	0 / 108 (0.00%)	0 / 105 (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 haemorrhage			
subjects affected / exposed	0 / 153 (0.00%)	0 / 108 (0.00%)	0 / 105 (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
Intra-abdominal haematoma			
subjects affected / exposed	0 / 153 (0.00%)	0 / 108 (0.00%)	0 / 105 (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
Pancreatic cyst			
subjects affected / exposed	0 / 153 (0.00%)	0 / 108 (0.00%)	0 / 105 (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
Peritoneal haemorrhage			
subjects affected / exposed	0 / 153 (0.00%)	0 / 108 (0.00%)	0 / 105 (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
Rectal prolapse			
subjects affected / exposed	0 / 153 (0.00%)	0 / 108 (0.00%)	0 / 105 (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
Hepatobiliary disorders			
Cholecystitis			
subjects affected / exposed	0 / 153 (0.00%)	0 / 108 (0.00%)	0 / 105 (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
Hepatic cyst			
subjects affected / exposed	0 / 153 (0.00%)	0 / 108 (0.00%)	0 / 105 (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			

Bladder prolapse			
subjects affected / exposed	0 / 153 (0.00%)	0 / 108 (0.00%)	0 / 105 (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
Pelvi-ureteric obstruction			
subjects affected / exposed	0 / 153 (0.00%)	0 / 108 (0.00%)	0 / 105 (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
Endocrine disorders			
Primary hyperaldosteronism			
subjects affected / exposed	0 / 153 (0.00%)	0 / 108 (0.00%)	0 / 105 (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
Musculoskeletal and connective tissue disorders			
Intervertebral disc protrusion			
subjects affected / exposed	0 / 153 (0.00%)	0 / 108 (0.00%)	0 / 105 (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
Lumbar spinal stenosis			
subjects affected / exposed	0 / 153 (0.00%)	0 / 108 (0.00%)	0 / 105 (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
Metatarsalgia			
subjects affected / exposed	0 / 153 (0.00%)	0 / 108 (0.00%)	0 / 105 (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
Musculoskeletal chest pain			
subjects affected / exposed	0 / 153 (0.00%)	0 / 108 (0.00%)	0 / 105 (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 / 153 (0.00%)	0 / 108 (0.00%)	0 / 105 (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 Abdominal abscess subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all	0 / 153 (0.00%) 0 / 0 0 / 0	0 / 108 (0.00%) 0 / 0 0 / 0	0 / 105 (0.00%) 0 / 0 0 / 0
Appendicitis subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all	0 / 153 (0.00%) 0 / 0 0 / 0	0 / 108 (0.00%) 0 / 0 0 / 0	0 / 105 (0.00%) 0 / 0 0 / 0
Cellulitis subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all	0 / 153 (0.00%) 0 / 0 0 / 0	0 / 108 (0.00%) 0 / 0 0 / 0	0 / 105 (0.00%) 0 / 0 0 / 0
Diverticulitis subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all	0 / 153 (0.00%) 0 / 0 0 / 0	0 / 108 (0.00%) 0 / 0 0 / 0	0 / 105 (0.00%) 0 / 0 0 / 0
Gastroenteritis subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all	0 / 153 (0.00%) 0 / 0 0 / 0	0 / 108 (0.00%) 0 / 0 0 / 0	0 / 105 (0.00%) 0 / 0 0 / 0
Pneumonia klebsiella subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all	0 / 153 (0.00%) 0 / 0 0 / 0	0 / 108 (0.00%) 0 / 0 0 / 0	0 / 105 (0.00%) 0 / 0 0 / 0
Tubo-ovarian abscess subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all	0 / 153 (0.00%) 0 / 0 0 / 0	0 / 108 (0.00%) 0 / 0 0 / 0	0 / 105 (0.00%) 0 / 0 0 / 0
Urinary tract infection subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all	1 / 153 (0.65%) 0 / 1 0 / 0	0 / 108 (0.00%) 0 / 0 0 / 0	0 / 105 (0.00%) 0 / 0 0 / 0
Metabolism and nutrition disorders			

Hypoglycaemia			
subjects affected / exposed	0 / 153 (0.00%)	0 / 108 (0.00%)	0 / 105 (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	DBTP: Erenumab 70 mg QM	OpLTP: Erenumab 70 mg QM	OLTP: Erenumab 140 mg QM
Total subjects affected by serious adverse events			
subjects affected / exposed	1 / 106 (0.94%)	30 / 383 (7.83%)	25 / 250 (10.00%)
number of deaths (all causes)	0	1	1
number of deaths resulting from adverse events			
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Adenocarcinoma of the cervix			
subjects affected / exposed	0 / 106 (0.00%)	0 / 383 (0.00%)	1 / 250 (0.40%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Breast cancer			
subjects affected / exposed	0 / 106 (0.00%)	2 / 383 (0.52%)	0 / 250 (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
Invasive lobular breast carcinoma			
subjects affected / exposed	0 / 106 (0.00%)	1 / 383 (0.26%)	0 / 250 (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
Lipoma			
subjects affected / exposed	0 / 106 (0.00%)	0 / 383 (0.00%)	1 / 250 (0.40%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lung adenocarcinoma stage III			
subjects affected / exposed	0 / 106 (0.00%)	1 / 383 (0.26%)	0 / 250 (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
Prostate cancer			

subjects affected / exposed	0 / 106 (0.00%)	0 / 383 (0.00%)	1 / 250 (0.40%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Uterine leiomyoma			
subjects affected / exposed	0 / 106 (0.00%)	1 / 383 (0.26%)	1 / 250 (0.40%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vascular disorders			
Arteriosclerosis			
subjects affected / exposed	0 / 106 (0.00%)	1 / 383 (0.26%)	0 / 250 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
Deep vein thrombosis			
subjects affected / exposed	0 / 106 (0.00%)	1 / 383 (0.26%)	1 / 250 (0.40%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Thrombosis			
subjects affected / exposed	0 / 106 (0.00%)	1 / 383 (0.26%)	0 / 250 (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
General disorders and administration site conditions			
Death			
subjects affected / exposed	0 / 106 (0.00%)	0 / 383 (0.00%)	1 / 250 (0.40%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Non-cardiac chest pain			
subjects affected / exposed	0 / 106 (0.00%)	1 / 383 (0.26%)	0 / 250 (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
Reproductive system and breast disorders			
Ovarian cyst ruptured			

subjects affected / exposed	0 / 106 (0.00%)	0 / 383 (0.00%)	0 / 250 (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
Adnexa uteri cyst			
subjects affected / exposed	0 / 106 (0.00%)	1 / 383 (0.26%)	0 / 250 (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
Menorrhagia			
subjects affected / exposed	0 / 106 (0.00%)	1 / 383 (0.26%)	0 / 250 (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
Ovarian cyst			
subjects affected / exposed	0 / 106 (0.00%)	1 / 383 (0.26%)	0 / 250 (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
Respiratory, thoracic and mediastinal disorders			
Pleural effusion			
subjects affected / exposed	0 / 106 (0.00%)	0 / 383 (0.00%)	1 / 250 (0.40%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pulmonary embolism			
subjects affected / exposed	0 / 106 (0.00%)	1 / 383 (0.26%)	0 / 250 (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
Psychiatric disorders			
Adjustment disorder			
subjects affected / exposed	0 / 106 (0.00%)	1 / 383 (0.26%)	1 / 250 (0.40%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Suicide attempt			
subjects affected / exposed	0 / 106 (0.00%)	0 / 383 (0.00%)	1 / 250 (0.40%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Investigations			
Aspartate aminotransferase increased			
subjects affected / exposed	0 / 106 (0.00%)	0 / 383 (0.00%)	1 / 250 (0.40%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Injury, poisoning and procedural complications			
Ligament rupture			
subjects affected / exposed	0 / 106 (0.00%)	1 / 383 (0.26%)	2 / 250 (0.80%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Spinal compression fracture			
subjects affected / exposed	0 / 106 (0.00%)	0 / 383 (0.00%)	1 / 250 (0.40%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Congenital, familial and genetic disorders			
Developmental hip dysplasia			
subjects affected / exposed	0 / 106 (0.00%)	0 / 383 (0.00%)	1 / 250 (0.40%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac disorders			
Coronary artery stenosis			
subjects affected / exposed	0 / 106 (0.00%)	0 / 383 (0.00%)	1 / 250 (0.40%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypertensive heart disease			
subjects affected / exposed	0 / 106 (0.00%)	1 / 383 (0.26%)	0 / 250 (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
Myocardial ischaemia			
subjects affected / exposed	0 / 106 (0.00%)	1 / 383 (0.26%)	0 / 250 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nervous system disorders			

Migraine			
subjects affected / exposed	1 / 106 (0.94%)	0 / 383 (0.00%)	0 / 250 (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
Cauda equina syndrome			
subjects affected / exposed	0 / 106 (0.00%)	0 / 383 (0.00%)	1 / 250 (0.40%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cervicobrachial syndrome			
subjects affected / exposed	0 / 106 (0.00%)	0 / 383 (0.00%)	1 / 250 (0.40%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Headache			
subjects affected / exposed	0 / 106 (0.00%)	0 / 383 (0.00%)	1 / 250 (0.40%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lumbar radiculopathy			
subjects affected / exposed	0 / 106 (0.00%)	1 / 383 (0.26%)	0 / 250 (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
Optic neuritis			
subjects affected / exposed	0 / 106 (0.00%)	1 / 383 (0.26%)	0 / 250 (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
Syncope			
subjects affected / exposed	0 / 106 (0.00%)	2 / 383 (0.52%)	0 / 250 (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
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	0 / 106 (0.00%)	0 / 383 (0.00%)	1 / 250 (0.40%)
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			

Vertigo			
subjects affected / exposed	1 / 106 (0.94%)	0 / 383 (0.00%)	1 / 250 (0.40%)
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			
Visual impairment			
subjects affected / exposed	0 / 106 (0.00%)	1 / 383 (0.26%)	0 / 250 (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 adhesions			
subjects affected / exposed	0 / 106 (0.00%)	1 / 383 (0.26%)	0 / 250 (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
Abdominal hernia			
subjects affected / exposed	0 / 106 (0.00%)	1 / 383 (0.26%)	0 / 250 (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
Appendicitis noninfective			
subjects affected / exposed	0 / 106 (0.00%)	0 / 383 (0.00%)	1 / 250 (0.40%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Colitis ischaemic			
subjects affected / exposed	0 / 106 (0.00%)	1 / 383 (0.26%)	0 / 250 (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
Crohn's disease			
subjects affected / exposed	0 / 106 (0.00%)	1 / 383 (0.26%)	0 / 250 (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
Diverticulum			
subjects affected / exposed	0 / 106 (0.00%)	1 / 383 (0.26%)	0 / 250 (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

Faecaloma			
subjects affected / exposed	0 / 106 (0.00%)	1 / 383 (0.26%)	0 / 250 (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 haemorrhage			
subjects affected / exposed	0 / 106 (0.00%)	1 / 383 (0.26%)	0 / 250 (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
Intra-abdominal haematoma			
subjects affected / exposed	0 / 106 (0.00%)	0 / 383 (0.00%)	1 / 250 (0.40%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pancreatic cyst			
subjects affected / exposed	0 / 106 (0.00%)	1 / 383 (0.26%)	0 / 250 (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
Peritoneal haemorrhage			
subjects affected / exposed	0 / 106 (0.00%)	1 / 383 (0.26%)	0 / 250 (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 prolapse			
subjects affected / exposed	0 / 106 (0.00%)	0 / 383 (0.00%)	1 / 250 (0.40%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatobiliary disorders			
Cholecystitis			
subjects affected / exposed	0 / 106 (0.00%)	1 / 383 (0.26%)	0 / 250 (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
Hepatic cyst			
subjects affected / exposed	0 / 106 (0.00%)	1 / 383 (0.26%)	0 / 250 (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
Renal and urinary disorders			

Bladder prolapse			
subjects affected / exposed	0 / 106 (0.00%)	0 / 383 (0.00%)	1 / 250 (0.40%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pelvi-ureteric obstruction			
subjects affected / exposed	0 / 106 (0.00%)	0 / 383 (0.00%)	1 / 250 (0.40%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Endocrine disorders			
Primary hyperaldosteronism			
subjects affected / exposed	0 / 106 (0.00%)	0 / 383 (0.00%)	1 / 250 (0.40%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Musculoskeletal and connective tissue disorders			
Intervertebral disc protrusion			
subjects affected / exposed	0 / 106 (0.00%)	0 / 383 (0.00%)	1 / 250 (0.40%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lumbar spinal stenosis			
subjects affected / exposed	0 / 106 (0.00%)	0 / 383 (0.00%)	1 / 250 (0.40%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metatarsalgia			
subjects affected / exposed	0 / 106 (0.00%)	1 / 383 (0.26%)	0 / 250 (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
Musculoskeletal chest pain			
subjects affected / exposed	0 / 106 (0.00%)	1 / 383 (0.26%)	0 / 250 (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
Osteoarthritis			
subjects affected / exposed	0 / 106 (0.00%)	1 / 383 (0.26%)	1 / 250 (0.40%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Infections and infestations Abdominal abscess subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all	0 / 106 (0.00%) 0 / 0 0 / 0	0 / 383 (0.00%) 0 / 0 0 / 0	1 / 250 (0.40%) 0 / 1 0 / 0
Appendicitis subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all	0 / 106 (0.00%) 0 / 0 0 / 0	0 / 383 (0.00%) 0 / 0 0 / 0	2 / 250 (0.80%) 0 / 2 0 / 0
Cellulitis subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all	0 / 106 (0.00%) 0 / 0 0 / 0	1 / 383 (0.26%) 0 / 1 0 / 0	0 / 250 (0.00%) 0 / 0 0 / 0
Diverticulitis subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all	0 / 106 (0.00%) 0 / 0 0 / 0	0 / 383 (0.00%) 0 / 0 0 / 0	1 / 250 (0.40%) 0 / 1 0 / 0
Gastroenteritis subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all	0 / 106 (0.00%) 0 / 0 0 / 0	1 / 383 (0.26%) 0 / 1 0 / 0	0 / 250 (0.00%) 0 / 0 0 / 0
Pneumonia klebsiella subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all	0 / 106 (0.00%) 0 / 0 0 / 0	0 / 383 (0.00%) 0 / 0 0 / 0	1 / 250 (0.40%) 0 / 1 0 / 0
Tubo-ovarian abscess subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all	0 / 106 (0.00%) 0 / 0 0 / 0	0 / 383 (0.00%) 0 / 0 0 / 0	1 / 250 (0.40%) 0 / 1 0 / 0
Urinary tract infection subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all	0 / 106 (0.00%) 0 / 0 0 / 0	0 / 383 (0.00%) 0 / 0 0 / 0	0 / 250 (0.00%) 0 / 0 0 / 0
Metabolism and nutrition disorders			

Hypoglycaemia			
subjects affected / exposed	0 / 106 (0.00%)	0 / 383 (0.00%)	1 / 250 (0.40%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	OLTP: Erenumab 70/140 mg QM	CHU Substudy: Erenumab 140 mg PFS	CHU Substudy: Erenumab 140 mg AI/Pen
Total subjects affected by serious adverse events			
subjects affected / exposed	49 / 383 (12.79%)	0 / 42 (0.00%)	0 / 41 (0.00%)
number of deaths (all causes)	2	0	0
number of deaths resulting from adverse events			
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Adenocarcinoma of the cervix			
subjects affected / exposed	1 / 383 (0.26%)	0 / 42 (0.00%)	0 / 41 (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
Breast cancer			
subjects affected / exposed	2 / 383 (0.52%)	0 / 42 (0.00%)	0 / 41 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Invasive lobular breast carcinoma			
subjects affected / exposed	1 / 383 (0.26%)	0 / 42 (0.00%)	0 / 41 (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
Lipoma			
subjects affected / exposed	1 / 383 (0.26%)	0 / 42 (0.00%)	0 / 41 (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
Lung adenocarcinoma stage III			
subjects affected / exposed	1 / 383 (0.26%)	0 / 42 (0.00%)	0 / 41 (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
Prostate cancer			

subjects affected / exposed	1 / 383 (0.26%)	0 / 42 (0.00%)	0 / 41 (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
Uterine leiomyoma			
subjects affected / exposed	2 / 383 (0.52%)	0 / 42 (0.00%)	0 / 41 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vascular disorders			
Arteriosclerosis			
subjects affected / exposed	1 / 383 (0.26%)	0 / 42 (0.00%)	0 / 41 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Deep vein thrombosis			
subjects affected / exposed	2 / 383 (0.52%)	0 / 42 (0.00%)	0 / 41 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Thrombosis			
subjects affected / exposed	1 / 383 (0.26%)	0 / 42 (0.00%)	0 / 41 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General disorders and administration site conditions			
Death			
subjects affected / exposed	1 / 383 (0.26%)	0 / 42 (0.00%)	0 / 41 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Non-cardiac chest pain			
subjects affected / exposed	1 / 383 (0.26%)	0 / 42 (0.00%)	0 / 41 (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
Reproductive system and breast disorders			
Ovarian cyst ruptured			

subjects affected / exposed	0 / 383 (0.00%)	0 / 42 (0.00%)	0 / 41 (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
Adnexa uteri cyst			
subjects affected / exposed	1 / 383 (0.26%)	0 / 42 (0.00%)	0 / 41 (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
Menorrhagia			
subjects affected / exposed	1 / 383 (0.26%)	0 / 42 (0.00%)	0 / 41 (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
Ovarian cyst			
subjects affected / exposed	1 / 383 (0.26%)	0 / 42 (0.00%)	0 / 41 (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
Respiratory, thoracic and mediastinal disorders			
Pleural effusion			
subjects affected / exposed	1 / 383 (0.26%)	0 / 42 (0.00%)	0 / 41 (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
Pulmonary embolism			
subjects affected / exposed	1 / 383 (0.26%)	0 / 42 (0.00%)	0 / 41 (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
Psychiatric disorders			
Adjustment disorder			
subjects affected / exposed	2 / 383 (0.52%)	0 / 42 (0.00%)	0 / 41 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Suicide attempt			
subjects affected / exposed	1 / 383 (0.26%)	0 / 42 (0.00%)	0 / 41 (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

Investigations			
Aspartate aminotransferase increased			
subjects affected / exposed	1 / 383 (0.26%)	0 / 42 (0.00%)	0 / 41 (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
Injury, poisoning and procedural complications			
Ligament rupture			
subjects affected / exposed	3 / 383 (0.78%)	0 / 42 (0.00%)	0 / 41 (0.00%)
occurrences causally related to treatment / all	0 / 3	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Spinal compression fracture			
subjects affected / exposed	1 / 383 (0.26%)	0 / 42 (0.00%)	0 / 41 (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
Congenital, familial and genetic disorders			
Developmental hip dysplasia			
subjects affected / exposed	1 / 383 (0.26%)	0 / 42 (0.00%)	0 / 41 (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
Cardiac disorders			
Coronary artery stenosis			
subjects affected / exposed	1 / 383 (0.26%)	0 / 42 (0.00%)	0 / 41 (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
Hypertensive heart disease			
subjects affected / exposed	1 / 383 (0.26%)	0 / 42 (0.00%)	0 / 41 (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
Myocardial ischaemia			
subjects affected / exposed	1 / 383 (0.26%)	0 / 42 (0.00%)	0 / 41 (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
Nervous system disorders			

Migraine			
subjects affected / exposed	0 / 383 (0.00%)	0 / 42 (0.00%)	0 / 41 (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
Cauda equina syndrome			
subjects affected / exposed	1 / 383 (0.26%)	0 / 42 (0.00%)	0 / 41 (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
Cervicobrachial syndrome			
subjects affected / exposed	1 / 383 (0.26%)	0 / 42 (0.00%)	0 / 41 (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
Headache			
subjects affected / exposed	1 / 383 (0.26%)	0 / 42 (0.00%)	0 / 41 (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
Lumbar radiculopathy			
subjects affected / exposed	1 / 383 (0.26%)	0 / 42 (0.00%)	0 / 41 (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
Optic neuritis			
subjects affected / exposed	1 / 383 (0.26%)	0 / 42 (0.00%)	0 / 41 (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
Syncope			
subjects affected / exposed	2 / 383 (0.52%)	0 / 42 (0.00%)	0 / 41 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	1 / 383 (0.26%)	0 / 42 (0.00%)	0 / 41 (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
Ear and labyrinth disorders			

Vertigo			
subjects affected / exposed	1 / 383 (0.26%)	0 / 42 (0.00%)	0 / 41 (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
Eye disorders			
Visual impairment			
subjects affected / exposed	1 / 383 (0.26%)	0 / 42 (0.00%)	0 / 41 (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
Gastrointestinal disorders			
Abdominal adhesions			
subjects affected / exposed	1 / 383 (0.26%)	0 / 42 (0.00%)	0 / 41 (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
Abdominal hernia			
subjects affected / exposed	1 / 383 (0.26%)	0 / 42 (0.00%)	0 / 41 (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
Appendicitis noninfective			
subjects affected / exposed	1 / 383 (0.26%)	0 / 42 (0.00%)	0 / 41 (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
Colitis ischaemic			
subjects affected / exposed	1 / 383 (0.26%)	0 / 42 (0.00%)	0 / 41 (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
Crohn's disease			
subjects affected / exposed	1 / 383 (0.26%)	0 / 42 (0.00%)	0 / 41 (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
Diverticulum			
subjects affected / exposed	1 / 383 (0.26%)	0 / 42 (0.00%)	0 / 41 (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

Faecaloma			
subjects affected / exposed	1 / 383 (0.26%)	0 / 42 (0.00%)	0 / 41 (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
Gastrointestinal haemorrhage			
subjects affected / exposed	1 / 383 (0.26%)	0 / 42 (0.00%)	0 / 41 (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
Intra-abdominal haematoma			
subjects affected / exposed	1 / 383 (0.26%)	0 / 42 (0.00%)	0 / 41 (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
Pancreatic cyst			
subjects affected / exposed	1 / 383 (0.26%)	0 / 42 (0.00%)	0 / 41 (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
Peritoneal haemorrhage			
subjects affected / exposed	1 / 383 (0.26%)	0 / 42 (0.00%)	0 / 41 (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
Rectal prolapse			
subjects affected / exposed	1 / 383 (0.26%)	0 / 42 (0.00%)	0 / 41 (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
Hepatobiliary disorders			
Cholecystitis			
subjects affected / exposed	1 / 383 (0.26%)	0 / 42 (0.00%)	0 / 41 (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
Hepatic cyst			
subjects affected / exposed	1 / 383 (0.26%)	0 / 42 (0.00%)	0 / 41 (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
Renal and urinary disorders			

Bladder prolapse			
subjects affected / exposed	1 / 383 (0.26%)	0 / 42 (0.00%)	0 / 41 (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
Pelvi-ureteric obstruction			
subjects affected / exposed	1 / 383 (0.26%)	0 / 42 (0.00%)	0 / 41 (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
Endocrine disorders			
Primary hyperaldosteronism			
subjects affected / exposed	1 / 383 (0.26%)	0 / 42 (0.00%)	0 / 41 (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
Musculoskeletal and connective tissue disorders			
Intervertebral disc protrusion			
subjects affected / exposed	1 / 383 (0.26%)	0 / 42 (0.00%)	0 / 41 (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
Lumbar spinal stenosis			
subjects affected / exposed	1 / 383 (0.26%)	0 / 42 (0.00%)	0 / 41 (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
Metatarsalgia			
subjects affected / exposed	1 / 383 (0.26%)	0 / 42 (0.00%)	0 / 41 (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
Musculoskeletal chest pain			
subjects affected / exposed	1 / 383 (0.26%)	0 / 42 (0.00%)	0 / 41 (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
Osteoarthritis			
subjects affected / exposed	2 / 383 (0.52%)	0 / 42 (0.00%)	0 / 41 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Infections and infestations Abdominal abscess subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all	1 / 383 (0.26%) 0 / 1 0 / 0	0 / 42 (0.00%) 0 / 0 0 / 0	0 / 41 (0.00%) 0 / 0 0 / 0
Appendicitis subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all	2 / 383 (0.52%) 0 / 2 0 / 0	0 / 42 (0.00%) 0 / 0 0 / 0	0 / 41 (0.00%) 0 / 0 0 / 0
Cellulitis subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all	1 / 383 (0.26%) 0 / 1 0 / 0	0 / 42 (0.00%) 0 / 0 0 / 0	0 / 41 (0.00%) 0 / 0 0 / 0
Diverticulitis subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all	1 / 383 (0.26%) 0 / 1 0 / 0	0 / 42 (0.00%) 0 / 0 0 / 0	0 / 41 (0.00%) 0 / 0 0 / 0
Gastroenteritis subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all	1 / 383 (0.26%) 0 / 1 0 / 0	0 / 42 (0.00%) 0 / 0 0 / 0	0 / 41 (0.00%) 0 / 0 0 / 0
Pneumonia klebsiella subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all	1 / 383 (0.26%) 0 / 1 0 / 0	0 / 42 (0.00%) 0 / 0 0 / 0	0 / 41 (0.00%) 0 / 0 0 / 0
Tubo-ovarian abscess subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all	1 / 383 (0.26%) 0 / 1 0 / 0	0 / 42 (0.00%) 0 / 0 0 / 0	0 / 41 (0.00%) 0 / 0 0 / 0
Urinary tract infection subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all	0 / 383 (0.00%) 0 / 0 0 / 0	0 / 42 (0.00%) 0 / 0 0 / 0	0 / 41 (0.00%) 0 / 0 0 / 0
Metabolism and nutrition disorders			

Hypoglycaemia			
subjects affected / exposed	1 / 383 (0.26%)	0 / 42 (0.00%)	0 / 41 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	CHU Substudy: Total		
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 83 (0.00%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events			
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Adenocarcinoma of the cervix			
subjects affected / exposed	0 / 83 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Breast cancer			
subjects affected / exposed	0 / 83 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Invasive lobular breast carcinoma			
subjects affected / exposed	0 / 83 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Lipoma			
subjects affected / exposed	0 / 83 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Lung adenocarcinoma stage III			
subjects affected / exposed	0 / 83 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Prostate cancer			

subjects affected / exposed	0 / 83 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Uterine leiomyoma			
subjects affected / exposed	0 / 83 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Vascular disorders			
Arteriosclerosis			
subjects affected / exposed	0 / 83 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Deep vein thrombosis			
subjects affected / exposed	0 / 83 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Thrombosis			
subjects affected / exposed	0 / 83 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
General disorders and administration site conditions			
Death			
subjects affected / exposed	0 / 83 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Non-cardiac chest pain			
subjects affected / exposed	0 / 83 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Reproductive system and breast disorders			
Ovarian cyst ruptured			

subjects affected / exposed	0 / 83 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Adnexa uteri cyst			
subjects affected / exposed	0 / 83 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Menorrhagia			
subjects affected / exposed	0 / 83 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Ovarian cyst			
subjects affected / exposed	0 / 83 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Respiratory, thoracic and mediastinal disorders			
Pleural effusion			
subjects affected / exposed	0 / 83 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Pulmonary embolism			
subjects affected / exposed	0 / 83 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Psychiatric disorders			
Adjustment disorder			
subjects affected / exposed	0 / 83 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Suicide attempt			
subjects affected / exposed	0 / 83 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		

Investigations			
Aspartate aminotransferase increased			
subjects affected / exposed	0 / 83 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Injury, poisoning and procedural complications			
Ligament rupture			
subjects affected / exposed	0 / 83 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Spinal compression fracture			
subjects affected / exposed	0 / 83 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Congenital, familial and genetic disorders			
Developmental hip dysplasia			
subjects affected / exposed	0 / 83 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Cardiac disorders			
Coronary artery stenosis			
subjects affected / exposed	0 / 83 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Hypertensive heart disease			
subjects affected / exposed	0 / 83 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Myocardial ischaemia			
subjects affected / exposed	0 / 83 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Nervous system disorders			

Migraine			
subjects affected / exposed	0 / 83 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Cauda equina syndrome			
subjects affected / exposed	0 / 83 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Cervicobrachial syndrome			
subjects affected / exposed	0 / 83 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Headache			
subjects affected / exposed	0 / 83 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Lumbar radiculopathy			
subjects affected / exposed	0 / 83 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Optic neuritis			
subjects affected / exposed	0 / 83 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Syncope			
subjects affected / exposed	0 / 83 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	0 / 83 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Ear and labyrinth disorders			

Vertigo			
subjects affected / exposed	0 / 83 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Eye disorders			
Visual impairment			
subjects affected / exposed	0 / 83 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Gastrointestinal disorders			
Abdominal adhesions			
subjects affected / exposed	0 / 83 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Abdominal hernia			
subjects affected / exposed	0 / 83 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Appendicitis noninfective			
subjects affected / exposed	0 / 83 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Colitis ischaemic			
subjects affected / exposed	0 / 83 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Crohn's disease			
subjects affected / exposed	0 / 83 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Diverticulum			
subjects affected / exposed	0 / 83 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		

Faecaloma			
subjects affected / exposed	0 / 83 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Gastrointestinal haemorrhage			
subjects affected / exposed	0 / 83 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Intra-abdominal haematoma			
subjects affected / exposed	0 / 83 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Pancreatic cyst			
subjects affected / exposed	0 / 83 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Peritoneal haemorrhage			
subjects affected / exposed	0 / 83 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Rectal prolapse			
subjects affected / exposed	0 / 83 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Hepatobiliary disorders			
Cholecystitis			
subjects affected / exposed	0 / 83 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Hepatic cyst			
subjects affected / exposed	0 / 83 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Renal and urinary disorders			

Bladder prolapse			
subjects affected / exposed	0 / 83 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Pelvi-ureteric obstruction			
subjects affected / exposed	0 / 83 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Endocrine disorders			
Primary hyperaldosteronism			
subjects affected / exposed	0 / 83 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Musculoskeletal and connective tissue disorders			
Intervertebral disc protrusion			
subjects affected / exposed	0 / 83 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Lumbar spinal stenosis			
subjects affected / exposed	0 / 83 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Metatarsalgia			
subjects affected / exposed	0 / 83 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Musculoskeletal chest pain			
subjects affected / exposed	0 / 83 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Osteoarthritis			
subjects affected / exposed	0 / 83 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		

Infections and infestations Abdominal abscess subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all	0 / 83 (0.00%) 0 / 0 0 / 0		
Appendicitis subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all	0 / 83 (0.00%) 0 / 0 0 / 0		
Cellulitis subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all	0 / 83 (0.00%) 0 / 0 0 / 0		
Diverticulitis subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all	0 / 83 (0.00%) 0 / 0 0 / 0		
Gastroenteritis subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all	0 / 83 (0.00%) 0 / 0 0 / 0		
Pneumonia klebsiella subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all	0 / 83 (0.00%) 0 / 0 0 / 0		
Tubo-ovarian abscess subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all	0 / 83 (0.00%) 0 / 0 0 / 0		
Urinary tract infection subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all	0 / 83 (0.00%) 0 / 0 0 / 0		
Metabolism and nutrition disorders			

Hypoglycaemia			
subjects affected / exposed	0 / 83 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		

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

Non-serious adverse events	DBTP: Placebo QM	DBTP: Erenumab 7 mg QM	DBTP: Erenumab 21 mg QM
Total subjects affected by non-serious adverse events			
subjects affected / exposed	45 / 153 (29.41%)	27 / 108 (25.00%)	24 / 105 (22.86%)
Vascular disorders			
Hypertension			
subjects affected / exposed	2 / 153 (1.31%)	1 / 108 (0.93%)	0 / 105 (0.00%)
occurrences (all)	2	1	0
Nervous system disorders			
Headache			
subjects affected / exposed	1 / 153 (0.65%)	4 / 108 (3.70%)	1 / 105 (0.95%)
occurrences (all)	1	5	1
General disorders and administration site conditions			
Fatigue			
subjects affected / exposed	3 / 153 (1.96%)	5 / 108 (4.63%)	2 / 105 (1.90%)
occurrences (all)	3	8	3
Gastrointestinal disorders			
Constipation			
subjects affected / exposed	1 / 153 (0.65%)	0 / 108 (0.00%)	1 / 105 (0.95%)
occurrences (all)	1	0	1
Nausea			
subjects affected / exposed	2 / 153 (1.31%)	3 / 108 (2.78%)	1 / 105 (0.95%)
occurrences (all)	2	4	1
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	3 / 153 (1.96%)	2 / 108 (1.85%)	1 / 105 (0.95%)
occurrences (all)	3	2	1
Oropharyngeal pain			
subjects affected / exposed	1 / 153 (0.65%)	1 / 108 (0.93%)	2 / 105 (1.90%)
occurrences (all)	1	1	2

Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	5 / 153 (3.27%)	1 / 108 (0.93%)	0 / 105 (0.00%)
occurrences (all)	6	1	0
Back pain			
subjects affected / exposed	4 / 153 (2.61%)	2 / 108 (1.85%)	4 / 105 (3.81%)
occurrences (all)	4	2	4
Pain in extremity			
subjects affected / exposed	1 / 153 (0.65%)	1 / 108 (0.93%)	2 / 105 (1.90%)
occurrences (all)	1	1	2
Infections and infestations			
Nasopharyngitis			
subjects affected / exposed	12 / 153 (7.84%)	10 / 108 (9.26%)	6 / 105 (5.71%)
occurrences (all)	13	10	8
Bronchitis			
subjects affected / exposed	1 / 153 (0.65%)	0 / 108 (0.00%)	0 / 105 (0.00%)
occurrences (all)	1	0	0
Influenza			
subjects affected / exposed	5 / 153 (3.27%)	1 / 108 (0.93%)	4 / 105 (3.81%)
occurrences (all)	5	1	4
Pneumonia			
subjects affected / exposed	1 / 153 (0.65%)	0 / 108 (0.00%)	0 / 105 (0.00%)
occurrences (all)	1	0	0
Sinusitis			
subjects affected / exposed	2 / 153 (1.31%)	2 / 108 (1.85%)	1 / 105 (0.95%)
occurrences (all)	2	2	1
Upper respiratory tract infection			
subjects affected / exposed	3 / 153 (1.96%)	1 / 108 (0.93%)	2 / 105 (1.90%)
occurrences (all)	3	1	2
Urinary tract infection			
subjects affected / exposed	1 / 153 (0.65%)	0 / 108 (0.00%)	1 / 105 (0.95%)
occurrences (all)	1	0	1

Non-serious adverse events	DBTP: Erenumab 70 mg QM	OpLTP: Erenumab 70 mg QM	OLTP: Erenumab 140 mg QM
Total subjects affected by non-serious adverse events			
subjects affected / exposed	31 / 106 (29.25%)	220 / 383 (57.44%)	172 / 250 (68.80%)

Vascular disorders Hypertension subjects affected / exposed occurrences (all)	2 / 106 (1.89%) 2	14 / 383 (3.66%) 14	11 / 250 (4.40%) 12
Nervous system disorders Headache subjects affected / exposed occurrences (all)	3 / 106 (2.83%) 5	10 / 383 (2.61%) 11	11 / 250 (4.40%) 13
General disorders and administration site conditions Fatigue subjects affected / exposed occurrences (all)	4 / 106 (3.77%) 4	19 / 383 (4.96%) 25	11 / 250 (4.40%) 12
Gastrointestinal disorders Constipation subjects affected / exposed occurrences (all) Nausea subjects affected / exposed occurrences (all)	3 / 106 (2.83%) 3 3 / 106 (2.83%) 3	9 / 383 (2.35%) 9 13 / 383 (3.39%) 14	15 / 250 (6.00%) 16 18 / 250 (7.20%) 18
Respiratory, thoracic and mediastinal disorders Cough subjects affected / exposed occurrences (all) Oropharyngeal pain subjects affected / exposed occurrences (all)	0 / 106 (0.00%) 0 2 / 106 (1.89%) 2	15 / 383 (3.92%) 17 15 / 383 (3.92%) 18	14 / 250 (5.60%) 18 7 / 250 (2.80%) 7
Musculoskeletal and connective tissue disorders Arthralgia subjects affected / exposed occurrences (all) Back pain subjects affected / exposed occurrences (all) Pain in extremity subjects affected / exposed occurrences (all)	1 / 106 (0.94%) 1 2 / 106 (1.89%) 2 2 / 106 (1.89%) 3	26 / 383 (6.79%) 35 30 / 383 (7.83%) 40 16 / 383 (4.18%) 18	13 / 250 (5.20%) 15 21 / 250 (8.40%) 24 11 / 250 (4.40%) 11

Infections and infestations Nasopharyngitis subjects affected / exposed occurrences (all)	6 / 106 (5.66%) 6	82 / 383 (21.41%) 145	59 / 250 (23.60%) 106
Bronchitis subjects affected / exposed occurrences (all)	1 / 106 (0.94%) 1	17 / 383 (4.44%) 18	14 / 250 (5.60%) 15
Influenza subjects affected / exposed occurrences (all)	1 / 106 (0.94%) 1	36 / 383 (9.40%) 46	31 / 250 (12.40%) 39
Pneumonia subjects affected / exposed occurrences (all)	1 / 106 (0.94%) 1	11 / 383 (2.87%) 13	11 / 250 (4.40%) 12
Sinusitis subjects affected / exposed occurrences (all)	2 / 106 (1.89%) 2	30 / 383 (7.83%) 40	26 / 250 (10.40%) 33
Upper respiratory tract infection subjects affected / exposed occurrences (all)	2 / 106 (1.89%) 2	52 / 383 (13.58%) 81	53 / 250 (21.20%) 98
Urinary tract infection subjects affected / exposed occurrences (all)	1 / 106 (0.94%) 2	23 / 383 (6.01%) 25	23 / 250 (9.20%) 32

Non-serious adverse events	OLTP: Erenumab 70/140 mg QM	CHU Substudy: Erenumab 140 mg PFS	CHU Substudy: Erenumab 140 mg AI/Pen
Total subjects affected by non-serious adverse events subjects affected / exposed	264 / 383 (68.93%)	7 / 42 (16.67%)	9 / 41 (21.95%)
Vascular disorders Hypertension subjects affected / exposed occurrences (all)	25 / 383 (6.53%) 26	0 / 42 (0.00%) 0	0 / 41 (0.00%) 0
Nervous system disorders Headache subjects affected / exposed occurrences (all)	21 / 383 (5.48%) 24	1 / 42 (2.38%) 1	0 / 41 (0.00%) 0
General disorders and administration site conditions			

Fatigue subjects affected / exposed occurrences (all)	29 / 383 (7.57%) 37	0 / 42 (0.00%) 0	0 / 41 (0.00%) 0
Gastrointestinal disorders			
Constipation subjects affected / exposed occurrences (all)	24 / 383 (6.27%) 25	1 / 42 (2.38%) 1	0 / 41 (0.00%) 0
Nausea subjects affected / exposed occurrences (all)	29 / 383 (7.57%) 32	0 / 42 (0.00%) 0	0 / 41 (0.00%) 0
Respiratory, thoracic and mediastinal disorders			
Cough subjects affected / exposed occurrences (all)	27 / 383 (7.05%) 35	0 / 42 (0.00%) 0	0 / 41 (0.00%) 0
Oropharyngeal pain subjects affected / exposed occurrences (all)	20 / 383 (5.22%) 25	1 / 42 (2.38%) 1	0 / 41 (0.00%) 0
Musculoskeletal and connective tissue disorders			
Arthralgia subjects affected / exposed occurrences (all)	37 / 383 (9.66%) 50	0 / 42 (0.00%) 0	1 / 41 (2.44%) 1
Back pain subjects affected / exposed occurrences (all)	48 / 383 (12.53%) 64	0 / 42 (0.00%) 0	1 / 41 (2.44%) 1
Pain in extremity subjects affected / exposed occurrences (all)	25 / 383 (6.53%) 29	0 / 42 (0.00%) 0	0 / 41 (0.00%) 0
Infections and infestations			
Nasopharyngitis subjects affected / exposed occurrences (all)	111 / 383 (28.98%) 251	0 / 42 (0.00%) 0	2 / 41 (4.88%) 2
Bronchitis subjects affected / exposed occurrences (all)	31 / 383 (8.09%) 33	0 / 42 (0.00%) 0	0 / 41 (0.00%) 0
Influenza			

subjects affected / exposed	56 / 383 (14.62%)	0 / 42 (0.00%)	1 / 41 (2.44%)
occurrences (all)	85	0	1
Pneumonia			
subjects affected / exposed	22 / 383 (5.74%)	0 / 42 (0.00%)	0 / 41 (0.00%)
occurrences (all)	25	0	0
Sinusitis			
subjects affected / exposed	53 / 383 (13.84%)	1 / 42 (2.38%)	1 / 41 (2.44%)
occurrences (all)	73	1	1
Upper respiratory tract infection			
subjects affected / exposed	78 / 383 (20.37%)	3 / 42 (7.14%)	2 / 41 (4.88%)
occurrences (all)	179	3	2
Urinary tract infection			
subjects affected / exposed	41 / 383 (10.70%)	0 / 42 (0.00%)	1 / 41 (2.44%)
occurrences (all)	57	0	1

Non-serious adverse events	CHU Substudy: Total		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	16 / 83 (19.28%)		
Vascular disorders			
Hypertension			
subjects affected / exposed	0 / 83 (0.00%)		
occurrences (all)	0		
Nervous system disorders			
Headache			
subjects affected / exposed	1 / 83 (1.20%)		
occurrences (all)	1		
General disorders and administration site conditions			
Fatigue			
subjects affected / exposed	0 / 83 (0.00%)		
occurrences (all)	0		
Gastrointestinal disorders			
Constipation			
subjects affected / exposed	1 / 83 (1.20%)		
occurrences (all)	1		
Nausea			
subjects affected / exposed	0 / 83 (0.00%)		
occurrences (all)	0		

Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	0 / 83 (0.00%)		
occurrences (all)	0		
Oropharyngeal pain			
subjects affected / exposed	1 / 83 (1.20%)		
occurrences (all)	1		
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	1 / 83 (1.20%)		
occurrences (all)	1		
Back pain			
subjects affected / exposed	1 / 83 (1.20%)		
occurrences (all)	1		
Pain in extremity			
subjects affected / exposed	0 / 83 (0.00%)		
occurrences (all)	0		
Infections and infestations			
Nasopharyngitis			
subjects affected / exposed	2 / 83 (2.41%)		
occurrences (all)	2		
Bronchitis			
subjects affected / exposed	0 / 83 (0.00%)		
occurrences (all)	0		
Influenza			
subjects affected / exposed	1 / 83 (1.20%)		
occurrences (all)	1		
Pneumonia			
subjects affected / exposed	0 / 83 (0.00%)		
occurrences (all)	0		
Sinusitis			
subjects affected / exposed	2 / 83 (2.41%)		
occurrences (all)	2		
Upper respiratory tract infection			
subjects affected / exposed	5 / 83 (6.02%)		
occurrences (all)	5		

Urinary tract infection subjects affected / exposed occurrences (all)	1 / 83 (1.20%) 1		
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More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
15 November 2013	<ul style="list-style-type: none">- Exploratory objective and endpoint regarding change from baseline in monthly average severity of migraine-related symptoms was added.- Removed saliva collection procedures and the associated objective and endpoint.- Modified inclusion and exclusion criteria to remove the exclusion of basilar-type migraine, modified contraception eligibility criterion, adjusted the definition of poorly controlled hypertension, and removed the exception for Gilberti's syndrome in the exclusion criteria.- Added hepatitis reflexive polymerase chain reaction to confirm viral status for hepatitis B and C.- Added chemistry and hematology laboratory assessments at the week 2 study visit.- Added anti-AMG 334 antibody sampling (and associated PK testing) at weeks 2, 4, 8, and 36 study visits and clarified the communication process for antibody results to maintain blinding.- Modified the list of medications excluded during the study and modified the list of medications for which eligible subjects must not have failed due to lack of efficacy in migraine prophylaxis.- Updated AMG 334 background information.- Changed the visit window for the day 1 study visit from ± 3 days to $+ 7$ days.- Removed several limitations for re-screening subjects.- Added details from the Investigational Product Instruction Manual related to the number of investigational product injections and acceptable injection locations.- A closed testing procedure was incorporated to control the family-wise error rate at 0.05 for the primary endpoint.- Implemented minor text clarifications and corrections.
09 July 2014	<ul style="list-style-type: none">- To allow for the collection of long-term safety, tolerability, and efficacy data beyond 1 year, the open-label treatment phase was extended from 40 weeks to up to 256 weeks. Appropriate changes were made throughout the protocol to reflect this change in duration of the open-label treatment phase.- ECG and laboratory assessments were added in the open-label treatment phase.- A formal interim analysis was added at week 64, to occur once all subjects completed the week 64 study visit.- An Event Adjudication Committee was added for the overall AMG 334 clinical development program to provide a thorough and systematic review and classification of all cardiovascular and cerebrovascular events that may have occurred during the study.- Clarified the testing procedure to be utilized (ie, sequential) to control the family-wise error rate at 0.05 for the primary endpoint.- Certain protocol text was clarified and minor text errors were corrected.
07 April 2016	<ul style="list-style-type: none">- Increased the dose of erenumab to 140 mg during the open-label phase.- Added a 12-week safety follow-up (16 weeks after the last dose of investigational product).- Added that HIT-6 will be collected every 4 weeks for 52 weeks after dose increase.- Added that laboratory, vital sign, and anti-erenumab antibody data would be collected 12 weeks after the dose increase.
23 May 2017	<ul style="list-style-type: none">- Allowed subjects at all sites globally to participate in a single-injection clinical home use substudy.

19 September 2017	<ul style="list-style-type: none"> - Removed the clinical home use substudy as the substudy was no longer necessary. - Added collection of clinical outcomes assessments and patient-reported outcomes up to week 268 to evaluate long-term efficacy. Previously eDiary collection stopped at week 64. Monthly clinical outcome assessments were collected every 24 weeks beginning at the week 188 visit. - Added new packaging of erenumab as prefilled syringes containing 1 mL of 70 mg/mL or 140 mg/mL erenumab. - Added serum pregnancy testing to the safety follow-up visit in the Schedule of Assessment to be consistent with the rest of the protocol. - Clarified language in Section 10.4.4 Final Analysis and Section 10.5.4 Safety Analyses.
08 March 2019	<ul style="list-style-type: none"> - Clarified that commercial erenumab may be used during the safety follow-up period. - Aligned end of study and primary completion language with the current template. - Removed retired language related to self-evident corrections.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported