# 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 |

**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 |

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 |

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 |
|---|---|

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 |

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 |

| **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<br>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<br>Units: years | | | |
| arithmetic mean | 41.4 | 40.3 | 39.9 |
| standard deviation | ± 10.0 | ± 10.9 | ± 12.3 |
| Sex: Female, Male<br>Units: participants | | | |
| Female | 132 | 88 | 87 |
| Male | 28 | 20 | 21 |
| Race/Ethnicity, Customized<br>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)<br>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 |

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 |

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 (± 0.31) | -2.18 (± 0.36) | -2.39 (± 0.38) | -3.40 (± 0.37) |

## Statistical analyses

| Statistical analysis title | Analysis of Change in Monthly Migraine Days |
|---|---|

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 |

| | |
|---|---|
| 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 |
|---|---|

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 |
|---|---|

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] |
|---|---|

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 |
|---|---|

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 |
|---|---|

| | |
|---|---|
| | Baseline in Monthly Migraine Days at Week 12 |

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 |

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 |
|---|---|

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 |
|---|---|

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 |
|---|---|

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 |
|---|---|

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 |
|---|---|

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 |
|---|---|

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 ≥ 2 | 36 | 31 | 25 | 23 |
| AE Grade ≥ 3 | 3 | 3 | 3 | 3 |
| AE Grade ≥ 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 |
|---|---|

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 |
|---|---|

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 |
|---|---|

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 |
|---|---|

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/Pen | | |
|---|---|---|---|---|
| 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 |
|---|---|

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 |
|---|---|

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 |
|---|---|

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 |
|---|---|

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 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 |

## Dictionary used

| | |
|---|---|
| Dictionary name | MedDRA |
| Dictionary version | 22.1 |

## 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 | OpLTP: Erenumab 70 mg QM |

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 |

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 |

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 |

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 |

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 |
|---|---|

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 | 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 | | | |
| 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 |
| Cellulitis | | | |
| 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 |
| Diverticulitis | | | |
| 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 |
| Gastroenteritis | | | |
| 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 |
| Pneumonia klebsiella | | | |
| 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 |
| Tubo-ovarian abscess | | | |
| 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 |
| Urinary tract infection | | | |
| subjects affected / exposed | 1 / 153 (0.65%) | 0 / 108 (0.00%) | 0 / 105 (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 |
| 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 | 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 |
| Appendicitis | | | |
| subjects affected / exposed | 0 / 106 (0.00%) | 0 / 383 (0.00%) | 2 / 250 (0.80%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Cellulitis | | | |
| 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 |
| Diverticulitis | | | |
| 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 |
| Gastroenteritis | | | |
| 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 |
| Pneumonia klebsiella | | | |
| 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 |
| Tubo-ovarian abscess | | | |
| 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 |
| Urinary tract infection | | | |
| 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 |
| 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 | 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 | | | |
| 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 |
| Cellulitis | | | |
| 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 |
| Diverticulitis | | | |
| 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 |
| Gastroenteritis | | | |
| 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 |
| Pneumonia klebsiella | | | |
| 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 |
| Tubo-ovarian abscess | | | |
| 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 |
| Urinary tract infection | | | |
| 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 |
| 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 | | | |

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|---|---|---|---|
| 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 | | | |

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|---|---|---|---|---|
| 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 | | | | |

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|---|---|---|---|---|
| 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 | 0 / 83 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Appendicitis | | | |
| subjects affected / exposed | 0 / 83 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Cellulitis | | | |
| subjects affected / exposed | 0 / 83 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Diverticulitis | | | |
| subjects affected / exposed | 0 / 83 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Gastroenteritis | | | |
| subjects affected / exposed | 0 / 83 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Pneumonia klebsiella | | | |
| subjects affected / exposed | 0 / 83 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Tubo-ovarian abscess | | | |
| subjects affected / exposed | 0 / 83 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Urinary tract infection | | | |
| subjects affected / exposed | 0 / 83 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 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 | 2 / 106 (1.89%) | 14 / 383 (3.66%) | 11 / 250 (4.40%) |
| occurrences (all) | 2 | 14 | 12 |
| Nervous system disorders | | | |
| Headache | | | |
| subjects affected / exposed | 3 / 106 (2.83%) | 10 / 383 (2.61%) | 11 / 250 (4.40%) |
| occurrences (all) | 5 | 11 | 13 |
| General disorders and administration site conditions | | | |
| Fatigue | | | |
| subjects affected / exposed | 4 / 106 (3.77%) | 19 / 383 (4.96%) | 11 / 250 (4.40%) |
| occurrences (all) | 4 | 25 | 12 |
| Gastrointestinal disorders | | | |
| Constipation | | | |
| subjects affected / exposed | 3 / 106 (2.83%) | 9 / 383 (2.35%) | 15 / 250 (6.00%) |
| occurrences (all) | 3 | 9 | 16 |
| Nausea | | | |
| subjects affected / exposed | 3 / 106 (2.83%) | 13 / 383 (3.39%) | 18 / 250 (7.20%) |
| occurrences (all) | 3 | 14 | 18 |
| Respiratory, thoracic and mediastinal disorders | | | |
| Cough | | | |
| subjects affected / exposed | 0 / 106 (0.00%) | 15 / 383 (3.92%) | 14 / 250 (5.60%) |
| occurrences (all) | 0 | 17 | 18 |
| Oropharyngeal pain | | | |
| subjects affected / exposed | 2 / 106 (1.89%) | 15 / 383 (3.92%) | 7 / 250 (2.80%) |
| occurrences (all) | 2 | 18 | 7 |
| Musculoskeletal and connective tissue disorders | | | |
| Arthralgia | | | |
| subjects affected / exposed | 1 / 106 (0.94%) | 26 / 383 (6.79%) | 13 / 250 (5.20%) |
| occurrences (all) | 1 | 35 | 15 |
| Back pain | | | |
| subjects affected / exposed | 2 / 106 (1.89%) | 30 / 383 (7.83%) | 21 / 250 (8.40%) |
| occurrences (all) | 2 | 40 | 24 |
| Pain in extremity | | | |
| subjects affected / exposed | 2 / 106 (1.89%) | 16 / 383 (4.18%) | 11 / 250 (4.40%) |
| occurrences (all) | 3 | 18 | 11 |

| | | | |
|---|---|---|---|
| Infections and infestations | | | |
| Nasopharyngitis | | | |
| subjects affected / exposed | 6 / 106 (5.66%) | 82 / 383 (21.41%) | 59 / 250 (23.60%) |
| occurrences (all) | 6 | 145 | 106 |
| Bronchitis | | | |
| subjects affected / exposed | 1 / 106 (0.94%) | 17 / 383 (4.44%) | 14 / 250 (5.60%) |
| occurrences (all) | 1 | 18 | 15 |
| Influenza | | | |
| subjects affected / exposed | 1 / 106 (0.94%) | 36 / 383 (9.40%) | 31 / 250 (12.40%) |
| occurrences (all) | 1 | 46 | 39 |
| Pneumonia | | | |
| subjects affected / exposed | 1 / 106 (0.94%) | 11 / 383 (2.87%) | 11 / 250 (4.40%) |
| occurrences (all) | 1 | 13 | 12 |
| Sinusitis | | | |
| subjects affected / exposed | 2 / 106 (1.89%) | 30 / 383 (7.83%) | 26 / 250 (10.40%) |
| occurrences (all) | 2 | 40 | 33 |
| Upper respiratory tract infection | | | |
| subjects affected / exposed | 2 / 106 (1.89%) | 52 / 383 (13.58%) | 53 / 250 (21.20%) |
| occurrences (all) | 2 | 81 | 98 |
| Urinary tract infection | | | |
| subjects affected / exposed | 1 / 106 (0.94%) | 23 / 383 (6.01%) | 23 / 250 (9.20%) |
| occurrences (all) | 2 | 25 | 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 | 25 / 383 (6.53%) | 0 / 42 (0.00%) | 0 / 41 (0.00%) |
| occurrences (all) | 26 | 0 | 0 |
| Nervous system disorders | | | |
| Headache | | | |
| subjects affected / exposed | 21 / 383 (5.48%) | 1 / 42 (2.38%) | 0 / 41 (0.00%) |
| occurrences (all) | 24 | 1 | 0 |
| General disorders and administration site conditions | | | |

| | | | |
|---|---|---|---|
| Fatigue | | | |
| subjects affected / exposed | 29 / 383 (7.57%) | 0 / 42 (0.00%) | 0 / 41 (0.00%) |
| occurrences (all) | 37 | 0 | 0 |
| Gastrointestinal disorders | | | |
| Constipation | | | |
| subjects affected / exposed | 24 / 383 (6.27%) | 1 / 42 (2.38%) | 0 / 41 (0.00%) |
| occurrences (all) | 25 | 1 | 0 |
| Nausea | | | |
| subjects affected / exposed | 29 / 383 (7.57%) | 0 / 42 (0.00%) | 0 / 41 (0.00%) |
| occurrences (all) | 32 | 0 | 0 |
| Respiratory, thoracic and mediastinal disorders | | | |
| Cough | | | |
| subjects affected / exposed | 27 / 383 (7.05%) | 0 / 42 (0.00%) | 0 / 41 (0.00%) |
| occurrences (all) | 35 | 0 | 0 |
| Oropharyngeal pain | | | |
| subjects affected / exposed | 20 / 383 (5.22%) | 1 / 42 (2.38%) | 0 / 41 (0.00%) |
| occurrences (all) | 25 | 1 | 0 |
| Musculoskeletal and connective tissue disorders | | | |
| Arthralgia | | | |
| subjects affected / exposed | 37 / 383 (9.66%) | 0 / 42 (0.00%) | 1 / 41 (2.44%) |
| occurrences (all) | 50 | 0 | 1 |
| Back pain | | | |
| subjects affected / exposed | 48 / 383 (12.53%) | 0 / 42 (0.00%) | 1 / 41 (2.44%) |
| occurrences (all) | 64 | 0 | 1 |
| Pain in extremity | | | |
| subjects affected / exposed | 25 / 383 (6.53%) | 0 / 42 (0.00%) | 0 / 41 (0.00%) |
| occurrences (all) | 29 | 0 | 0 |
| Infections and infestations | | | |
| Nasopharyngitis | | | |
| subjects affected / exposed | 111 / 383 (28.98%) | 0 / 42 (0.00%) | 2 / 41 (4.88%) |
| occurrences (all) | 251 | 0 | 2 |
| Bronchitis | | | |
| subjects affected / exposed | 31 / 383 (8.09%) | 0 / 42 (0.00%) | 0 / 41 (0.00%) |
| occurrences (all) | 33 | 0 | 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<br>subjects affected / exposed<br>occurrences (all) | 1 / 83 (1.20%)<br>1 | | |

## More information

## Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

| Date | Amendment |
|---|---|
| 15 November 2013 | - Exploratory objective and endpoint regarding change from baseline in monthly average severity of migraine-related symptoms was added.<br>- Removed saliva collection procedures and the associated objective and endpoint.<br>- 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.<br>- Added hepatitis reflexive polymerase chain reaction to confirm viral status for hepatitis B and C.<br>- Added chemistry and hematology laboratory assessments at the week 2 study visit.<br>- 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.<br>- 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.<br>- Updated AMG 334 background information.<br>- Changed the visit window for the day 1 study visit from ± 3 days to + 7 days.<br>- Removed several limitations for re-screening subjects.<br>- Added details from the Investigational Product Instruction Manual related to the number of investigational product injections and acceptable injection locations.<br>- A closed testing procedure was incorporated to control the family-wise error rate at 0.05 for the primary endpoint.<br>- Implemented minor text clarifications and corrections. |
| 09 July 2014 | - 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.<br>- ECG and laboratory assessments were added in the open-label treatment phase.<br>- A formal interim analysis was added at week 64, to occur once all subjects completed the week 64 study visit.<br>- 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.<br>- Clarified the testing procedure to be utilized (ie, sequential) to control the family-wise error rate at 0.05 for the primary endpoint.<br>- Certain protocol text was clarified and minor text errors were corrected. |
| 07 April 2016 | - Increased the dose of erenumab to 140 mg during the open-label phase.<br>- Added a 12-week safety follow-up (16 weeks after the last dose of investigational product).<br>- Added that HIT-6 will be collected every 4 weeks for 52 weeks after dose increase.<br>- Added that laboratory, vital sign, and anti-erenumab antibody data would be collected 12 weeks after the dose increase. |
| 23 May 2017 | - Allowed subjects at all sites globally to participate in a single-injection clinical home use substudy. |

| | |
|---|---|
| 19 September 2017 | - Removed the clinical home use substudy as the substudy was no longer necessary.<br>- 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.<br>- Added new packaging of erenumab as prefilled syringes containing 1 mL of 70 mg/mL or 140 mg/mL erenumab.<br>- Added serum pregnancy testing to the safety follow-up visit in the Schedule of Assessment to be consistent with the rest of the protocol.<br>- Clarified language in Section 10.4.4 Final Analysis and Section 10.5.4 Safety Analyses. |
| 08 March 2019 | - Clarified that commercial erenumab may be used during the safety follow-up period.<br>- Aligned end of study and primary completion language with the current template.<br>- 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