Clinical trial results:

A Single-Dose, Open-Label Study to Characterize the Pharmacokinetics, Safety and Tolerability of Subcutaneous Administration of Fremanezumab in Pediatric Migraine Patients (6 to 11 Years of Age Inclusive)

Summary

EudraCT number	2018-000734-35
Trial protocol	Outside EU/EEA
Global end of trial date	07 June 2019

Results information

Result version number	v1 (current)
This version publication date	19 December 2019
First version publication date	19 December 2019

Trial information

Trial identification

Sponsor protocol code	TV48125-CNS-10141

Additional study identifiers

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

Notes:

Sponsors

Sponsor organisation name	Teva Branded Pharmaceutical Products, R&D Inc.
Sponsor organisation address	41 Moores Road, Frazer, United States, 19355
Public contact	Director, Clinical Research, Teva Branded Pharmaceutical Products, R&D Inc, 001 8884838279, info.eraclinical@teva.de
Scientific contact	Director, Clinical Research, Teva Branded Pharmaceutical Products, R&D Inc., 001 8884838279, info.eraclinical@teva.de

Notes:

Paediatric regulatory details

Is trial part of an agreed paediatric investigation plan (PIP)	Yes
EMA paediatric investigation plan number(s)	EMEA-001877-PIP01-15
Does article 45 of REGULATION (EC) No 1901/2006 apply to this trial?	No
Does article 46 of REGULATION (EC) No 1901/2006 apply to this trial?	Yes

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	21 July 2019
Is this the analysis of the primary completion data?	Yes
Primary completion date	07 June 2019
Global end of trial reached?	Yes
Global end of trial date	07 June 2019
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The primary objective of this study was to characterize the pharmacokinetic profile of fremanezumab following administration of a single subcutaneous (SC) dose in pediatric participants with migraine (6 to 11 years of age inclusive).

Protection of trial subjects:

This study was conducted in full accordance with the International Council for Harmonisation (ICH) Good Clinical Practice (GCP) Consolidated Guideline (E6) and any applicable national and local laws and regulations (for example; Code of Federal Regulations Title 21, Parts 11, 50, 54, 56, 312, and 314; European Union (EU) Directive 2001/20/EC on the approximation of the laws, regulations and administrative provisions of the Member States relating to the implementation of GCP in the conduct of clinical studies on medicinal products for human use).

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	19 June 2018
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	United States: 15
Worldwide total number of subjects	15
EEA total number of subjects	0

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)	15
Adolescents (12-17 years)	0
Adults (18-64 years)	0
From 65 to 84 years	0

85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

A total of 17 pediatric participants with migraine were screened for enrollment into this study. Of the 17 participants screened, 15 participants who met entry criteria were enrolled into the study.

Period 1

Period 1 title	Overall Study (overall period)
Is this the baseline period?	Yes
Allocation method	Not applicable
Blinding used	Not blinded

Arms

Arm title	Fremanezumab

Arm description:

Participants received a single 75 milligrams (mg) dose of fremanezumab administered SC in the abdomen on Day 1.

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

Dosage and administration details:

Fremanezumab was administered per dose and schedule specified in the arm description.

Number of subjects in period 1	Fremanezumab
Started	15
Completed	15

Baseline characteristics

Reporting groups

Reporting group title	Fremanezumab

Reporting group description:

Participants received a single 75 milligrams (mg) dose of fremanezumab administered SC in the abdomen on Day 1.

Reporting group values	Fremanezumab	Total	
Number of subjects	15	15	
Age Categorical			
Units: Subjects			
Children (2-11 years)	15	15	
Age Continuous			
Units: years			
arithmetic mean	9.3		
standard deviation	± 1.58	-	
Gender Categorical			
Units: Subjects			
Female	7	7	
Male	8	8	

End points

End points reporting groups

Reporting group title	Fremanezumab
Reporting group description:	
Participants received a single 75 milligrams (mg) dose of fremanezumab administered SC in the abdomen on Day 1.	

Primary: Maximum Observed Plasma Drug Concentration (Cmax)

End point title	Maximum Observed Plasma Drug Concentration (Cmax)[1]
End point description:	
Observed peak plasma concentration was obtained directly from the experimental data without interpolation. Pharmacokinetic (PK) analysis set included all participants who received fremanezumab and had sufficient data to calculate at least 1 PK parameter for fremanezumab and participants who had no significant leakage at the injection site, other events, or deviations that could affect the calculation of PK parameters.	
End point type	Primary
End point timeframe:	
Day 1 (pre-dose), Day 2 (24 hours [hrs] post-dose), Day 11 (240 hrs post-dose), Day 29 (672 hrs post-dose), Day 85 (2016 hrs post-dose), and Day 113 (2688 hrs post-dose)	

Notes:

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

End point values	Fremanezumab			
Subject group type	Reporting group			
Number of subjects analysed	15			
Units: micrograms/milliliter (µg/mL)				
geometric mean (geometric coefficient of variation)	20.742 (± 54.78)			

Statistical analyses

No statistical analyses for this end point

Primary: Area Under the Plasma Concentration-Time Curve (AUC) From Time 0 to the Time of the Last Measurable Study Drug Concentration (AUC0-t)

End point title	Area Under the Plasma Concentration-Time Curve (AUC) From Time 0 to the Time of the Last Measurable Study Drug Concentration (AUC0-t)[2]
End point description:	
AUC0-t was calculated by linear trapezoidal summation. PK analysis set included all participants who received fremanezumab and had sufficient data to calculate at least 1 PK parameter for fremanezumab and participants who had no significant leakage at the injection site, other events, or deviations that could affect the calculation of PK parameters.	
End point type	Primary
End point timeframe:	
Day 1 (pre-dose), Day 2 (24 hrs post-dose), Day 11 (240 hrs post-dose), Day 29 (672 hrs post-dose), Day 85 (2016 hrs post-dose), and Day 113 (2688 hrs post-dose)	

Notes:

[2] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: PK analyses were descriptive in nature.

End point values	Fremanezumab			
Subject group type	Reporting group			
Number of subjects analysed	15			
Units: hrs*µg/mL				
geometric mean (geometric coefficient of variation)	21726.5 (± 47.14)			

Statistical analyses

No statistical analyses for this end point

Primary: AUC From Time 0 to 28 Days After Study Drug Administration (AUC0-28d)

End point title	AUC From Time 0 to 28 Days After Study Drug Administration (AUC0-28d)[3]

End point description:

AUC0-28d was calculated by linear trapezoidal summation. PK analysis set included all participants who received fremanezumab and had sufficient data to calculate at least 1 PK parameter for fremanezumab and participants who had no significant leakage at the injection site, other events, or deviations that could affect the calculation of PK parameters.

End point type	Primary

End point timeframe:

Day 1 (pre-dose), Day 2 (24 hrs post-dose), Day 11 (240 hrs post-dose), Day 29 (672 hrs post-dose), Day 85 (2016 hrs post-dose), and Day 113 (2688 hrs post-dose)

Notes:

[3] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: PK analyses were descriptive in nature.

End point values	Fremanezumab			
Subject group type	Reporting group			
Number of subjects analysed	15			
Units: hrs*µg/mL				
geometric mean (geometric coefficient of variation)	10659.7 (± 50.17)			

Statistical analyses

No statistical analyses for this end point

Primary: AUC From Time 0 to 84 Days After Study Drug Administration (AUC0-84d)

End point title	AUC From Time 0 to 84 Days After Study Drug Administration (AUC0-84d)[4]

End point description:

AUC084d was calculated by linear trapezoidal summation. PK analysis set included all participants who

received fremanezumab and had sufficient data to calculate at least 1 PK parameter for fremanezumab and participants who had no significant leakage at the injection site, other events, or deviations that could affect the calculation of PK parameters.

End point type	Primary

End point timeframe:

Day 1 (pre-dose), Day 2 (24 hrs post-dose), Day 11 (240 hrs post-dose), Day 29 (672 hrs post-dose), Day 85 (2016 hrs post-dose), and Day 113 (2688 hrs post-dose)

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: PK analyses were descriptive in nature.

End point values	Fremanezumab			
Subject group type	Reporting group			
Number of subjects analysed	15			
Units: hrs*µg/mL				
geometric mean (geometric coefficient of variation)	20220.9 (± 47.08)			

Statistical analyses

No statistical analyses for this end point

Primary: Time to Reach Cmax (Tmax)

End point title	Time to Reach Cmax (Tmax)[5]

End point description:

Time corresponding to Cmax was obtained directly from the experimental data. PK analysis set included all participants who received fremanezumab and had sufficient data to calculate at least 1 PK parameter for fremanezumab and participants who had no significant leakage at the injection site, other events, or deviations that could affect the calculation of PK parameters.

End point type	Primary

End point timeframe:

Day 1 (pre-dose), Day 2 (24 hrs post-dose), Day 11 (240 hrs post-dose), Day 29 (672 hrs post-dose), Day 85 (2016 hrs post-dose), and Day 113 (2688 hrs post-dose)

Notes:

[5] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: PK analyses were descriptive in nature.

End point values	Fremanezumab			
Subject group type	Reporting group			
Number of subjects analysed	15			
Units: days				
median (full range (min-max))	7.990 (1.00 to 12.30)			

Statistical analyses

No statistical analyses for this end point

Primary: AUC From Time 0 to Infinity (AUC0-∞)

End point title	AUC From Time 0 to Infinity (AUC0-∞)[6]

End point description:

AUC0-∞ was calculated as AUC0-t + the area extrapolated from the time of the last quantifiable concentration to infinity (Clast/λz). PK analysis set included all participants who received fremanezumab and had sufficient data to calculate at least 1 PK parameter for fremanezumab and participants who had no significant leakage at the injection site, other events, or deviations that could affect the calculation of PK parameters.

End point type	Primary

End point timeframe:

Day 1 (pre-dose), Day 2 (24 hrs post-dose), Day 11 (240 hrs post-dose), Day 29 (672 hrs post-dose), Day 85 (2016 hrs post-dose), and Day 113 (2688 hrs post-dose)

Notes:

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

Justification: PK analyses were descriptive in nature.

End point values	Fremanezumab			
Subject group type	Reporting group			
Number of subjects analysed	15			
Units: hrs*µg/mL				
geometric mean (geometric coefficient of variation)	23259.9 (± 47.93)			

Statistical analyses

No statistical analyses for this end point

Primary: Percentage Extrapolated AUC (%AUCext)

End point title	Percentage Extrapolated AUC (%AUCext)[7]

End point description:

%AUCext was calculated as: ([AUC0-∞ −AUC0-t]/AUC0-∞) * 100. PK analysis set included all participants who received fremanezumab and had sufficient data to calculate at least 1 PK parameter for fremanezumab and participants who had no significant leakage at the injection site, other events, or deviations that could affect the calculation of PK parameters.

End point type	Primary

End point timeframe:

Day 1 (pre-dose), Day 2 (24 hrs post-dose), Day 11 (240 hrs post-dose), Day 29 (672 hrs post-dose), Day 85 (2016 hrs post-dose), and Day 113 (2688 hrs post-dose)

Notes:

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

Justification: PK analyses were descriptive in nature.

End point values	Fremanezumab			
Subject group type	Reporting group			
Number of subjects analysed	15			
Units: percentage of AUC				
geometric mean (geometric coefficient of variation)	5.666 (± 59.98)			

Statistical analyses

No statistical analyses for this end point

Primary: Apparent Plasma Terminal Elimination Rate Constant (λz)

End point title	Apparent Plasma Terminal Elimination Rate Constant (λz)[8]

End point description:

λz was calculated by linear regression of the terminal semi-log portion of the concentration-time curve. PK analysis set included all participants who received fremanezumab and had sufficient data to calculate at least 1 PK parameter for fremanezumab and participants who had no significant leakage at the injection site, other events, or deviations that could affect the calculation of PK parameters.

End point type	Primary

End point timeframe:

Day 1 (pre-dose), Day 2 (24 hrs post-dose), Day 11 (240 hrs post-dose), Day 29 (672 hrs post-dose), Day 85 (2016 hrs post-dose), and Day 113 (2688 hrs post-dose)

Notes:

[8] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: PK analyses were descriptive in nature.

End point values	Fremanezumab			
Subject group type	Reporting group			
Number of subjects analysed	15			
Units: per day				
arithmetic mean (standard deviation)	0.02525 (± 0.004837)			

Statistical analyses

No statistical analyses for this end point

Primary: Apparent Terminal Elimination Half-Life (t1/2)

End point title	Apparent Terminal Elimination Half-Life (t1/2)[9]

End point description:

t1/2 was calculated as: $\ln(2)/\lambda z$. PK analysis set included all participants who received fremanezumab and had sufficient data to calculate at least 1 PK parameter for fremanezumab and participants who had no significant leakage at the injection site, other events, or deviations that could affect the calculation of PK parameters.

End point type	Primary

End point timeframe:

Day 1 (pre-dose), Day 2 (24 hrs post-dose), Day 11 (240 hrs post-dose), Day 29 (672 hrs post-dose), Day 85 (2016 hrs post-dose), and Day 113 (2688 hrs post-dose)

Notes:

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

Justification: PK analyses were descriptive in nature.

End point values	Fremanezumab			
Subject group type	Reporting group			
Number of subjects analysed	15			
Units: days				
arithmetic mean (standard deviation)	28.45 (± 5.506)			

Statistical analyses

No statistical analyses for this end point

Primary: Apparent Volume of Distribution (Vz/F)

End point title	Apparent Volume of Distribution (Vz/F)[10]

End point description:

Apparent volume of distribution during the terminal phase was calculated as: $Vz/F = Dose/\lambda z * AUCinf$. PK analysis set included all participants who received fremanezumab and had sufficient data to calculate at least 1 PK parameter for fremanezumab and participants who had no significant leakage at the injection site, other events, or deviations that could affect the calculation of PK parameters.

End point type	Primary

End point timeframe:

Day 1 (pre-dose), Day 2 (24 hrs post-dose), Day 11 (240 hrs post-dose), Day 29 (672 hrs post-dose), Day 85 (2016 hrs post-dose), and Day 113 (2688 hrs post-dose)

Notes:

[10] - 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: PK analyses were descriptive in nature.

End point values	Fremanezumab			
Subject group type	Reporting group			
Number of subjects analysed	15			
Units: liters				
arithmetic mean (standard deviation)	3.433 (± 1.5691)			

Statistical analyses

No statistical analyses for this end point

Primary: Apparent Clearance (CL/F)

End point title	Apparent Clearance (CL/F)[11]

End point description:

CL/F was calculated as: $Dose/AUC0-\infty$. PK analysis set included all participants who received fremanezumab and had sufficient data to calculate at least 1 PK parameter for fremanezumab and participants who had no significant leakage at the injection site, other events, or deviations that could

affect the calculation of PK parameters.

End point type	Primary

End point timeframe:

Day 1 (pre-dose), Day 2 (24 hrs post-dose), Day 11 (240 hrs post-dose), Day 29 (672 hrs post-dose), Day 85 (2016 hrs post-dose), and Day 113 (2688 hrs post-dose)

Notes:

[11] - 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: PK analyses were descriptive in nature.

End point values	Fremanezumab			
Subject group type	Reporting group			
Number of subjects analysed	15			
Units: milliliters/minute (mL/min)				
arithmetic mean (standard deviation)	0.05981 (± 0.031688)			

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants With Adverse Events (AEs)

End point title	Number of Participants With Adverse Events (AEs)

End point description:

An AE was defined as any untoward medical occurrence in a participant who received study drug without regard to possibility of causal relationship. Severe AE was defined as inability to carry out usual activities. Treatment-related AEs were defined as AEs with possible, probable, definite, or missing relationship to study drug. Serious AEs were defined as death, a life-threatening AE, inpatient hospitalization or prolongation of existing hospitalization, persistent or significant disability or incapacity, a congenital anomaly or birth defect, or an important medical event that jeopardized participant and required medical intervention to prevent 1 of the outcomes listed in this definition. A summary of other non-serious AEs and all serious AEs, regardless of causality is located in Reported AE section. Safety analysis set included all participants who received fremanezumab.

End point type	Secondary

End point timeframe:

Baseline up to end of study (Week 17)

End point values	Fremanezumab			
Subject group type	Reporting group			
Number of subjects analysed	15			
Units: participants	7			

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants With Potentially Clinically Significant Abnormal Vital Signs Values

End point title	Number of Participants With Potentially Clinically Significant Abnormal Vital Signs Values

End point description:

Criteria for potentially clinically significant abnormal vital signs values included: pulse: greater than (>)130 millimeters of mercury (mmHg) and less than (<)60 mmHg (in participants of age greater than or equal to [≥] 6 to less than or equal to [≤] 8 years), >110 mmHg and <60 mmHg (in participants of age ≥9 to <12 years), and change of ≥20 mmHg; systolic blood pressure: >120 mmHg and <80 mmHg (in participants of age ≥6 to ≤8 years), >130 mmHg and <80 mmHg (in participants of age ≥9 to <12 years), and change of ≥20 mmHg; diastolic blood pressure: >80 mmHg and <50 mmHg (in participants of age ≥6 to <12 years), and and change of ≥15 mmHg; and body temperature >38.2 degrees Celsius and <35.5 degrees celsius and change of ≥1.1 degrees celsius. A summary of other non-serious AEs and all serious AEs, regardless of causality is located in Reported AE section. Safety analysis set included all participants who received fremanezumab.

End point type	Secondary

End point timeframe:

Baseline up to end of study (Week 17)

End point values	Fremanezumab			
Subject group type	Reporting group			
Number of subjects analysed	15			
Units: participants	4			

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants With Potentially Clinically Significant Abnormal Electrocardiogram (ECG) Values

End point title	Number of Participants With Potentially Clinically Significant Abnormal Electrocardiogram (ECG) Values

End point description:

Criteria for potentially clinically significant abnormal ECG values included: heart rate: <60 beats/min and >100 beats/min (in participants of age ≥6 to <12 years); PR interval: <90 millisecond (msec) and >170 msec (in participants of age ≥6 to <12 years); QRS interval: <40 msec and >80 msec (in participants of age ≥6 to ≤7 years), <40 msec and >90 msec (in participants of age ≥8 to <12 years); QT interval: <268 msec and >356 msec (in participants of age ≥6 to ≤7 years), <297 msec and >397 msec (in participants of age ≥8 to <12 years); and RR interval <600 msec and >1000 msec (in participants of age ≥6 to <12 years). A summary of other non-serious AEs and all serious AEs, regardless of causality is located in Reported AE section. Safety analysis set included all participants who received fremanezumab.

End point type	Secondary

End point timeframe:

Baseline up to end of study (Week 17)

End point values	Fremanezumab			
Subject group type	Reporting group			
Number of subjects analysed	15			
Units: participants	13			

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants With Potentially Clinically Significant Abnormal Physical Examination Findings

End point title	Number of Participants With Potentially Clinically Significant Abnormal Physical Examination Findings

End point description:

Physical examination included assessments of the lungs, cardiovascular system, abdomen, and any system or organ that was of interest and/or indicated by symptoms. A summary of other non-serious AEs and all serious AEs, regardless of causality is located in Reported AE section. Safety analysis set included all participants who received fremanezumab.

End point type	Secondary

End point timeframe:

Baseline up to end of study (Week 17)

End point values	Fremanezumab			
Subject group type	Reporting group			
Number of subjects analysed	15			
Units: participants	0			

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants With Potentially Clinically Significant Abnormal Clinical Laboratory Values

End point title	Number of Participants With Potentially Clinically Significant Abnormal Clinical Laboratory Values

End point description:

Criteria for clinically significant abnormal clinical laboratory values: serum chemistry (albumin: ≤0.9*lower limit of normal[LLN];alanine aminotransferase, aspartate aminotransferase, alkaline phosphatase, gamma-glutamyl transpeptidase, lactate dehydrogenase: ≥3*upper limit of normal[ULN]; international normalized ratio: ≥1.5*ULN; creatine phosphokinase: ≥3.1*ULN; blood urea nitrogen: ≥10.71 millimoles/liter[mmol/L]; creatinine: ≥2*ULN; uric acid: ≥625 micromoles/L[µmol/L] [men], ≥506 µmol/L[women]; bilirubin: ≥34.2 µmol/L), hematology (hematocrit: <0.37 L/L[men], <0.32 L/L[women]; haemoglobin[Hb]: ≤115 grams/L [g/L] [men], ≤95 g/L[women]; leukocytes: ≤3*10^9/L, ≥20*10^9/L; eosinophils: ≥10%; absolute neutrophil counts: ≤1*10^9/L; platelets: ≤75*10^9/L, ≥700*10^9/L), and urinalysis (Hb,glucose,ketones,total proteins: ≥2 unit increase from baseline). A summary of other non-serious AEs and all serious AEs, regardless of causality is located in Reported AE section. Safety analysis set.

End point type	Secondary

End point timeframe:

Baseline up to end of study (Week 17)

End point values	Fremanezumab			
Subject group type	Reporting group			
Number of subjects analysed	15			
Units: participants				
Abnormal serum chemistry	0			
Abnormal hematology	4			
Abnormal urinalysis	0			

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants Who Received Concomitant Medications

End point title	Number of Participants Who Received Concomitant Medications

End point description:

Concomitant medications included all medications taken during study participation. Concomitant medications included: analgesics; antiemetics and antinauseants; antihistamines for systemic use; antiinflammatory and antirheumatic products; antipruritics including antihistamines, anesthetics, etc.; drugs for obstructive airway diseases; psychoanaleptics; psycholeptics; and vitamins. Safety analysis set included all participants who received fremanezumab.

End point type	Secondary

End point timeframe:

Baseline up to end of study (Week 17)

End point values	Fremanezumab			
Subject group type	Reporting group			
Number of subjects analysed	15			
Units: participants	14			

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants who Failed to Complete the Study Due to any Reason and Due to AEs

End point title	Number of Participants who Failed to Complete the Study Due to any Reason and Due to AEs

End point description:

End point type	Secondary

End point timeframe:

Baseline up to end of study (Week 17)

End point values	Fremanezumab			
Subject group type	Reporting group			
Number of subjects analysed	15			
Units: participants				
Due to any reason	0			
Due to AEs	0			

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants With Injection Site Reactions and Pain

End point title	Number of Participants With Injection Site Reactions and Pain

End point description:

Injection site reactions included erythema, induration, and ecchymosis. Injection site erythema, injection site ecchymosis, and injection site induration were considered only if they reached a diameter of at least 5 millimeters (mm). Induration was assessed by careful superficial palpation, avoiding pressuring or squeezing the injection site. Safety analysis set included all participants who received fremanezumab.

End point type	Secondary

End point timeframe:

Day 1 (20 minutes and 1, 2, and 4 hrs post-dose) and on Day 2 (24 hrs after study drug administration)

End point values	Fremanezumab			
Subject group type	Reporting group			
Number of subjects analysed	15			
Units: participants				
Erythema	5			
Induration	1			
Ecchymosis	0			
Pain	0			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:	
Baseline up to end of study (Week 17)	
Adverse event reporting additional description:	
Safety analysis set included all participants who received fremanezumab.	
Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	21.0

Reporting groups

Reporting group title	Fremanezumab
Reporting group description:	
Participants received a single 75 mg dose of fremanezumab administered SC in the abdomen on Day 1.	

Serious adverse events	Fremanezumab		
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 15 (0.00%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events			

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

Non-serious adverse events	Fremanezumab		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	7 / 15 (46.67%)		
Investigations			
International normalised ratio increased			
subjects affected / exposed	2 / 15 (13.33%)		
occurrences (all)	2		
Neutrophil count decreased			
subjects affected / exposed	1 / 15 (6.67%)		
occurrences (all)	1		
Prothrombin time prolonged			
subjects affected / exposed	1 / 15 (6.67%)		
occurrences (all)	1		

Injury, poisoning and procedural complications			
Laceration			
subjects affected / exposed	1 / 15 (6.67%)		
occurrences (all)	1		
General disorders and administration site conditions			
Injection site erythema			
subjects affected / exposed	5 / 15 (33.33%)		
occurrences (all)	5		
Injection site induration			
subjects affected / exposed	1 / 15 (6.67%)		
occurrences (all)	1		
Gastrointestinal disorders			
Abdominal pain upper			
subjects affected / exposed	1 / 15 (6.67%)		
occurrences (all)	1		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
27 September 2018	The following major procedural changes (not all-inclusive) were made to the protocol: - Shortened the screening period which allowed the use of the screening visit procedures to determine initial eligibility for the study; - Changed the general study design to provide participants the option to remain overnight at the investigational center for 2 nights (Day −1 to Day 2) so as to facilitate the conduct of multiple intensive and time sensitive study procedures; - Changes to the visit, week, or day due to the new timing of procedures and assessments; - Removed cotinine testing at screening or check-in for exclusion criteria; - Changed where the clinical laboratory test will be performed from site local laboratory to the central laboratory; - Changed the storage temperature range of the plasma samples.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

 None reported