Clinical trial results:
A Phase 3, Long-Term, Open-Label Safety Study of LY2951742 in Patients with Migraine

Summary

EudraCT number	2015-001884-38
Trial protocol	HU BE FR
Global end of trial date	14 August 2018

Results information

Result version number	v1 (current)
This version publication date	25 August 2019
First version publication date	25 August 2019

Trial information

Trial identification

Sponsor protocol code	I5Q-MC-CGAJ

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02614287
WHO universal trial number (UTN)	-
Other trial identifiers	Trial Number: 15770

Notes:

Sponsors

Sponsor organisation name	Eli Lilly and Company
Sponsor organisation address	Lilly Corporate Center, Indianapolis, IN, United States, 46285
Public contact	Available Mon Fri 9 AM 5 PM EST, Eli Lilly and Company, 1 877CTLilly,
Scientific contact	Available Mon Fri 9 AM 5 PM EST, Eli Lilly and Company, 1 8772854559,

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	14 August 2018
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	14 August 2018
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The main purpose of this study is to evaluate the longer term safety of the study drug known as galcanezumab in participants with episodic or chronic migraine.

Protection of trial subjects:

"This study was conducted in accordance with International Conference on Harmonization (ICH) Good Clinical Practice, and the principles of the Declaration of Helsinki, in addition to following the laws and regulations of the country or countries in which a study is conducted."

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	30 November 2015
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Belgium: 37
Country: Number of subjects enrolled	Canada: 25
Country: Number of subjects enrolled	Hungary: 47
Country: Number of subjects enrolled	France: 28
Country: Number of subjects enrolled	United States: 133
Worldwide total number of subjects	270
EEA total number of subjects	112

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)	270

From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

At first visit subjects had undergone full clinical assessment, including a comprehensive medical evaluation documenting medical history, and a physical and neurological examination.

Period 1

Period 1 title	Open label (OL) treatment phase
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Not blinded

Arms

Are arms mutually exclusive?	Yes
Arm title	Galcanezumab 120 mg

Arm description:

Participants received a loading dose of 240 milligram (mg) galcanezumab at first dosing visit followed by120 mg galcanezumab once a month by subcutaneous injection during open label treatment phase.

Arm type	Experimental
Investigational medicinal product name	Galcanezumab
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection in pre-filled syringe, Solution for injection in pre-filled injector
Routes of administration	Subcutaneous use

Dosage and administration details:

Participants received a loading dose of 240 milligram (mg) galcanezumab at first dosing visit followed by120 mg galcanezumab once a month by subcutaneous injection.

Arm title	Galcanezumab 240 mg

Arm description:

Participants received 240 mg of galcanezumab once a month by subcutaneous injection during open label treatment phase.

Arm type	Experimental
Investigational medicinal product name	Galcanezumab
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection in pre-filled injector, Solution for injection in pre-filled syringe
Routes of administration	Subcutaneous use

Dosage and administration details:

Participants received 240 milligram (mg) galcanezumab once a month by subcutaneous injection.

Number of subjects in period 1	Galcanezumab 120 mg	Galcanezumab 240 mg
Started	135	135
Received at least one dose of study drug	135	135
Completed	97	113
Not completed	38	22
Physician decision	1	-
Consent withdrawn by subject	10	7
Adverse event, non-fatal	7	6
Lost to follow-up	7	4
Lack of efficacy	13	5

Period 2

Period 2 title	Post Treatment Follow-up Phase
Is this the baseline period?	No
Allocation method	Randomised - controlled
Blinding used	Not blinded

Arms

Are arms mutually exclusive?	Yes
Arm title	Galcanezumab 120 mg

Arm description:

Participants did not receive any intervention during post treatment follow-up phase.

Arm type	No intervention

No investigational medicinal product assigned in this arm

Arm title	Galcanezumab 240 mg

Arm description:

Participants did not receive any intervention during post treatment follow-up phase.

Arm type	No intervention

No investigational medicinal product assigned in this arm

Number of subjects in period 2	Galcanezumab 120 mg	Galcanezumab 240 mg
Started	97	113
Completed	103	119
Not completed	9	5
Consent withdrawn by subject	6	3
Adverse event, non-fatal	1	-
Lost to follow-up	2	2
Joined	15	11

Open Label Discontinued Subjects	15	11

Baseline characteristics

Reporting groups	
Reporting group title	Galcanezumab 120 mg
Reporting group description:	
Participants received a loading dose of 240 milligram (mg) galcanezumab at first dosing visit followed by120 mg galcanezumab once a month by subcutaneous injection during open label treatment phase.	
Reporting group title	Galcanezumab 240 mg
Reporting group description:	
Participants received 240 mg of galcanezumab once a month by subcutaneous injection during open label treatment phase.	

Reporting group values	Galcanezumab 120 mg	Galcanezumab 240 mg	Total
Number of subjects	135	135	270
Age categorical Units: Subjects			
In utero			0
Preterm newborn infants (gestational age < 37 wks)			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)			0
From 65-84 years			0
85 years and over			0
Age Continuous Units: years			
arithmetic mean	40.21	43.69	
standard deviation	± 11.68	± 10.99	-
Gender categorical Units: Subjects			
Female	110	113	223
Male	25	22	47
Sex: Female, Male Units: Subjects			
Female	110	113	223
Male	25	22	47
Ethnicity (NIH/OMB) Units: Subjects			
Hispanic or Latino	12	20	32
Not Hispanic or Latino	115	108	223
Unknown or Not Reported	8	7	15
Race (NIH/OMB) Units: Subjects			
American Indian or Alaska Native	0	0	0
Asian	2	0	2
Native Hawaiian or Other Pacific Islander	1	0	1

Black or African American	6	8	14
White	103	108	211
More than one race	23	19	42
Unknown or Not Reported	0	0	0

End points

End points reporting groups

Reporting group title	Galcanezumab 120 mg
Reporting group description:	
Participants received a loading dose of 240 milligram (mg) galcanezumab at first dosing visit followed by120 mg galcanezumab once a month by subcutaneous injection during open label treatment phase.	
Reporting group title	Galcanezumab 240 mg
Reporting group description:	
Participants received 240 mg of galcanezumab once a month by subcutaneous injection during open label treatment phase.	
Reporting group title	Galcanezumab 120 mg
Reporting group description:	
Participants did not receive any intervention during post treatment follow-up phase.	
Reporting group title	Galcanezumab 240 mg
Reporting group description:	
Participants did not receive any intervention during post treatment follow-up phase.	

Primary: Percentage of Participants who Discontinued due to Adverse Event

End point title	Percentage of Participants who Discontinued due to Adverse Event

End point description:

Adverse Event: Any untoward medical occurrence in a participant or clinical investigation participant administered a pharmaceutical product that does not necessarily have a causal relationship with this treatment. An adverse event can therefore be any unfavorable and unintended sign (including an abnormal laboratory finding), symptom, or disease temporally associated with the use of a medicinal (investigational) product, whether or not related to the medicinal (investigational) product.
A summary of other non-serious AEs, and all SAE's, regardless of causality, is reported in the Adverse Events section.

Analysis Population Description (APD): All randomized participants who received at least one dose of study drug. There were 6 participants in the 120 mg group who discontinued after receiving loading dose of 240mg, these participants were moved to 240mg group for AE analysis.

End point type	Primary

End point timeframe:

Baseline through Month 12

End point values	Galcanezumab 120 mg	Galcanezumab 240 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	129	135[1]		
Units: Percentage of Participants				
number (not applicable)	4.65	4.96		

Notes:

[1] - N=141;
6 subjects in 120mg who received initial dose of 240mg & discontinued were moved to 240mg.

Statistical analyses

Statistical analysis title	Statistical Analysis 1
Comparison groups	Galcanezumab 120 mg v Galcanezumab 240 mg
Number of subjects included in analysis	264
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 1
Method	Fisher exact

Secondary: Pharmacokinetics (PK): Area Under the Concentration Time Curve (AUC) of Galcanezumab

End point title	Pharmacokinetics (PK): Area Under the Concentration Time Curve (AUC) of Galcanezumab

End point description:

Pharmacokinetics (PK): Area Under the Concentration Time Curve (AUC) of Galcanezumab.

Zero participants analyzed. AUC data was not collected as AUC was not pre-specified in protocol.

End point type	Secondary

End point timeframe:

Baseline through Month 12

End point values	Galcanezumab 120 mg	Galcanezumab 240 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	0[2]	0[3]		
Units: NA				

Notes:

[2] - Zero participants analyzed. AUC data was not collected as AUC was not pre-specified in protocol.

[3] - Zero participants analyzed. AUC data was not collected as AUC was not pre-specified in protocol.

Statistical analyses

No statistical analyses for this end point

Secondary: Serum Concentrations of Galcanezumab

End point title	Serum Concentrations of Galcanezumab

End point description:

Serum Concentrations of Galcanezumab.

APD: All randomized participants with measurable serum concentrations at month 12.

End point type	Secondary

End point timeframe:

Month 12

End point values	Galcanezumab 120 mg	Galcanezumab 240 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	61	78		
Units: Nanogram per milliliter (ng/mL)				
arithmetic mean (standard deviation)	16500 (± 8370)	31600 (± 15900)		

Statistical analyses

No statistical analyses for this end point

Secondary: Plasma Concentration of Calcitonin Gene-Related Peptide (CGRP)

End point title	Plasma Concentration of Calcitonin Gene-Related Peptide (CGRP)

End point description:

Plasma Concentration of Calcitonin Gene-Related Peptide (CGRP)

APD: All randomized participants with measurable plasma concentration.

End point type	Secondary

End point timeframe:

Month 12

End point values	Galcanezumab 120 mg	Galcanezumab 240 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	87	103		
Units: ng/mL				
arithmetic mean (standard deviation)	2.74 (± 1.07)	3.85 (± 1.85)		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants Developing Anti-Drug Antibodies to Galcanezumab

End point title	Percentage of Participants Developing Anti-Drug Antibodies to Galcanezumab

End point description:

A Treatment Emergent Anti-drug Antibody (TE ADA) evaluable participant is considered to be TE ADA+ if the participant has at least one post-baseline titer that is a 4-fold or
greater increase in titer from baseline measurement. If baseline result is ADA Not Present, then the participant is TE ADA+ if there is at least one post-baseline result of ADA Present with titer >= 1: 20 (treatment-induced).
There were 6 participants in the 120 mg group Open Label who discontinued after receiving loading dose of 240mg, these participants were moved to 240mg group for safety analysis.
APD: All randomized participants who received at least one dose of study drug and had baseline and at least one post baseline evaluable data for TE ADA.

End point type	Secondary

End point timeframe:

Month 1 through Month 12

End point values	Galcanezumab 120 mg	Galcanezumab 240 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	129	135[4]		
Units: Percentage of Participants				
number (not applicable)	12.40	7.30		

Notes:

[4] - N=137;
6 subjects in 120mg who received initial dose of 240mg & discontinued were moved to 240mg.

Statistical analyses

Statistical analysis title	Statistical Analysis 1

Statistical analysis description:

Neutralizing Antibodies

Comparison groups	Galcanezumab 120 mg v Galcanezumab 240 mg
Number of subjects included in analysis	264
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.215
Method	Fisher exact

Statistical analysis title	Statistical Analysis 2

Statistical analysis description:

TE ADA Positive (TE ADA+)

Comparison groups	Galcanezumab 120 mg v Galcanezumab 240 mg
Number of subjects included in analysis	264
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.215
Method	Fisher exact

Secondary: Overall Mean Change from Baseline in the Number of Migraine Headache Days (MHD)

End point title	Overall Mean Change from Baseline in the Number of Migraine Headache Days (MHD)

End point description:

MHD: A calendar day on which a migraine headache or probable migraine headache occurred. Overall mean is derived from the average of months 1 to 12 from MMRM model. Least squares mean (LSMean) was calculated using mixed model repeated measures (MMRM) model with treatment, pooled investigative site, month, and treatment by month, baseline, and baseline by month as fixed effects.

APD: All randomized participants who received at least one dose of study drug and had baseline & at least one post baseline value.

End point type	Secondary

End point timeframe:

Baseline, Month 1 through Month 12

End point values	Galcanezumab 120 mg	Galcanezumab 240 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	132	135		
Units: Migraine Headache Days per Month				
least squares mean (standard error)	-5.61 (± 0.34)	-6.47 (± 0.33)		

Statistical analyses

Statistical analysis title	Statistical Analysis 1
Comparison groups	Galcanezumab 120 mg v Galcanezumab 240 mg
Number of subjects included in analysis	267
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.6
Method	Mixed models analysis
Parameter estimate	LSMean Difference
Point estimate	-0.86
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.76
upper limit	0.04
Variability estimate	Standard error of the mean
Dispersion value	0.46

Secondary: Overall Mean Change from Baseline in the Number of Headache Days

End point title	Overall Mean Change from Baseline in the Number of Headache Days

End point description:

Headache Day: A calendar day on which any type of headache occurred (including migraine, probable migraine, and non-migraine headache).
Overall mean is derived from the average of months 1 to 12 from MMRM model. LSMean was calculated using MMRM model with treatment, pooled investigative site, month, and treatment by month, baseline, and baseline by month as fixed effects.

APD: All randomized participants who received at least one dose of study drug and had baseline & at least one post baseline Value.

End point type	Secondary

End point timeframe:

Baseline, Month 1 through Month 12

End point values	Galcanezumab 120 mg	Galcanezumab 240 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	132	135		
Units: Headache Days per Month				
least squares mean (standard error)	-2.17 (± 0.30)	-2.09 (± 0.30)		

Statistical analyses

Statistical analysis title	Statistical Analysis 1
Comparison groups	Galcanezumab 120 mg v Galcanezumab 240 mg
Number of subjects included in analysis	267
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.835
Method	Mixed models analysis
Parameter estimate	LSMean Difference
Point estimate	0.09
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.72
upper limit	0.89
Variability estimate	Standard error of the mean
Dispersion value	0.41

Secondary: Percentage of Participants with Overall Reduction from Baseline ≥50% in Monthly Migraine Headache Days

End point title	Percentage of Participants with Overall Reduction from Baseline ≥50% in Monthly Migraine Headache Days

End point description:

Migraine Headache Day: A calendar day on which a migraine headache or probable migraine headache occurred.

The overall percentage of patients with a given response rate were estimated from the GLIMMIX model.

APD: All randomized participants who received at least one dose of study drug and had baseline & at least one post baseline value.

End point type	Secondary

End point timeframe:

Baseline, Month 1 through Month 12

End point values	Galcanezumab 120 mg	Galcanezumab 240 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	132	135		
Units: percentage of Participants				
number (not applicable)	65.6	73.7		

Statistical analyses

Statistical analysis title	Statistical Analysis 1
Comparison groups	Galcanezumab 120 mg v Galcanezumab 240 mg
Number of subjects included in analysis	267
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.063
Method	CPLRM
Parameter estimate	Odds ratio (OR)
Point estimate	1.467
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.979
upper limit	2.197

Secondary: Overall Mean Change from Baseline in the Frequency of Medication Use for the Acute Treatment of Migraines or Headaches

End point title	Overall Mean Change from Baseline in the Frequency of Medication Use for the Acute Treatment of Migraines or Headaches

End point description:

Overall mean is derived from the average of months 1 to 12 from MMRM model. LSMean was calculated using MMRM model with treatment, pooled investigative site, month, and treatment by month, baseline, and baseline by month as fixed effects.

APD: All randomized participants who received at least one dose of study drug and had baseline and at least one post baseline value.

End point type	Secondary

End point timeframe:

Baseline, Month 1 through Month 12

End point values	Galcanezumab 120 mg	Galcanezumab 240 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	132	135		
Units: Medication Used Days per Month				
least squares mean (standard error)	-5.09 (± 0.38)	-5.05 (± 0.37)		

Statistical analyses

Statistical analysis title	Statistical Analysis 1
Comparison groups	Galcanezumab 120 mg v Galcanezumab 240 mg
Number of subjects included in analysis	267
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.937
Method	Mixed models analysis
Parameter estimate	LSMean Difference
Point estimate	0.04
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.96
upper limit	1.04
Variability estimate	Standard error of the mean
Dispersion value	0.51

Secondary: Overall Mean Patient Global Impression-Improvement (PGI-I) Score

End point title	Overall Mean Patient Global Impression-Improvement (PGI-I) Score

End point description:

The Patient Global Impression of Improvement (PGI -I) scale is a participant-rated instrument that measures the participants own global impression of their symptom improvement. The participant was instructed as follows: “Mark the box that best describes your migraine headache condition since you started taking this medicine.” Response options were on a 7-point scale in which a score of 1 indicates that the participant's condition is "very much better," a score of 4 indicates that the participant has experienced "no change," and a score of 7 indicates that the participant is "very much worse." Overall mean is derived from the average of months 1 to 12 from MMRM model. LSMean was calculated using MMRM model with treatment, pooled investigative site, month, and treatment by month, baseline PGI-S, and baseline PGI-S by month as fixed effects.

End point type	Secondary

End point timeframe:

Month 1 through Month 12

APD: All randomized participants who received at least one dose of study drug and had at least one post baseline value.

End point values	Galcanezumab 120 mg	Galcanezumab 240 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	130	135		
Units: units on a scale				
least squares mean (standard error)	2.18 (± 0.08)	1.99 (± 0.08)		

Statistical analyses

Statistical analysis title	Statistical Analysis 1
Comparison groups	Galcanezumab 120 mg v Galcanezumab 240 mg
Number of subjects included in analysis	265
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.073
Method	Mixed models analysis
Parameter estimate	LSMean Difference
Point estimate	-0.19
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.4
upper limit	0.02
Variability estimate	Standard error of the mean
Dispersion value	0.1

Secondary: Overall Mean Change from Baseline on the Migraine Disability Assessment Test (MIDAS) Total Score

End point title	Overall Mean Change from Baseline on the Migraine Disability Assessment Test (MIDAS) Total Score

End point description:

The MIDAS is a participant-rated scale which was designed to quantify headache-related disability over a 3-month period. This instrument consists of five items that reflect the number of days reported as missing or with reduced productivity at work or home, and the number of days of missed social events. Each item has a numeric response range from 0 to 90 days, if days are missed from work or home they are not counted as days with reduced productivity at work or home. The numeric responses are summed to produce a total score ranging from 0 to 270, in which a higher value is indicative of more disability. Overall mean is derived from the average of months 1 to 12 from MMRM model. LSMean was calculated using MMRM model with treatment, pooled investigative site, month, and treatment by month, baseline, and baseline by month.

APD: All randomized participants who received at least one dose of study drug and had baseline and at least one post baseline value.

End point type	Secondary

End point timeframe:

Baseline, Month 1 through Month 12

End point values	Galcanezumab 120 mg	Galcanezumab 240 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	124	130		
Units: units on a scale				
least squares mean (standard error)	-33.58 (± 2.11)	-32.67 (± 2.04)		

Statistical analyses

Statistical analysis title	Statistical Analysis 1
Comparison groups	Galcanezumab 120 mg v Galcanezumab 240 mg
Number of subjects included in analysis	254
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.747
Method	Mixed models analysis
Parameter estimate	LSMean Difference
Point estimate	0.91
Confidence interval	
level	95 %
sides	2-sided
lower limit	-4.65
upper limit	6.47
Variability estimate	Standard error of the mean
Dispersion value	2.82

Secondary: Overall Mean Change from Baseline on the Migraine-Specific Quality of Life Questionnaire (MSQ) version 2.1

End point title	Overall Mean Change from Baseline on the Migraine-Specific Quality of Life Questionnaire (MSQ) version 2.1

End point description:

MSQ v2.1 is a health status instrument, with a 4-week recall period, developed to address physical & emotional limitations of specific concern to individuals with migraine. Addressing the impact of migraine on work or daily activities, relationships with family & friends, leisure time, productivity, concentration, energy, tiredness & feelings. It consists of 14 items that address 3 domains:(1) Role Function-Restrictive (items 1-7);(2) Role Function- Preventive (items 8-11);&(3) Emotional Function (items 12-14).Response options range from "none of the time" (value 1) to "all of the time" (value 6), & are reverse-recoded (value 6 to 1) before domain scores are calculated. Total raw scores for each domain is the sum of the final item value for all the items in that domain. After total raw score is computed for each domain & total score, they are transformed to a 0-100 scale with higher scores indicating a better health status & positive change in scores reflecting functional improvement.

End point type	Secondary

End point timeframe:

Baseline, Month 1 through Month 12

APD: All randomized participants who received at least one dose of study drug and had baseline and at least one post baseline value.

End point values	Galcanezumab 120 mg	Galcanezumab 240 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	130	135		
Units: units on a scale				
least squares mean (standard error)				
Total Score	28.27 (± 1.16)	30.25 (± 1.13)		
Role Function-Restrictive Domain	31.55 (± 1.20)	33.40 (± 1.16)		
Role Function-Preventive Domain	22.08 (± 1.11)	23.33 (± 1.08)		
Emotional Function Domain	28.92 (± 1.35)	32.01 (± 1.31)		

Statistical analyses

Statistical analysis title	Statistical Analysis 1
Statistical analysis description: Total Score	
Comparison groups	Galcanezumab 120 mg v Galcanezumab 240 mg
Number of subjects included in analysis	265
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.203
Method	Mixed models analysis
Parameter estimate	LSMean Difference
Point estimate	1.98
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.07
upper limit	5.03
Variability estimate	Standard error of the mean
Dispersion value	1.55

Statistical analysis title	Statistical Analysis 2
Statistical analysis description: Role Function-Restrictive Domain Score	
Comparison groups	Galcanezumab 120 mg v Galcanezumab 240 mg
Number of subjects included in analysis	265
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.247
Method	Mixed models analysis
Parameter estimate	LSMean Difference
Point estimate	1.85

Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.29
upper limit	4.98
Variability estimate	Standard error of the mean
Dispersion value	1.59

Statistical analysis title	Statistical Analysis 3
Statistical analysis description: Role Function-Preventive Domain Score	
Comparison groups	Galcanezumab 120 mg v Galcanezumab 240 mg
Number of subjects included in analysis	265
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.399
Method	Mixed models analysis
Parameter estimate	LSMean Difference
Point estimate	1.26
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.67
upper limit	4.19
Variability estimate	Standard error of the mean
Dispersion value	1.49

Statistical analysis title	Statistical Analysis 4
Statistical analysis description: Emotional Function Domain Score	
Comparison groups	Galcanezumab 120 mg v Galcanezumab 240 mg
Number of subjects included in analysis	265
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.88
Method	Mixed models analysis
Parameter estimate	LSMean Difference
Point estimate	3.09
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.46
upper limit	6.64
Variability estimate	Standard error of the mean
Dispersion value	1.8

Secondary: Percentage of participant Visits with positive responses on Patient Satisfaction with Medication Questionnaire-Modified (PSMQ-M)

End point title	Percentage of participant Visits with positive responses on Patient Satisfaction with Medication Questionnaire-Modified (PSMQ-M)

End point description:

The PSMQ-M is a self-rated scale which measures participants level of satisfaction with study medication.The scale has been modified for use in this study, assessing 3 items related to the clinical trial treatment over the past 4 weeks: satisfaction, preference, and side effects. Satisfaction responses range from "very unsatisfied" to "very satisfied" with the current treatment. Preference compares the current study medication to previous medications, with responses from "much rather prefer my previous medication" to "much rather prefer the medication administered to me during the study".

APD: All randomized participants who received at least one dose of study drug and had month 12 PSMQ-M measurement.

End point type	Secondary

End point timeframe:

Month 1 through Month 12

End point values	Galcanezumab 120 mg	Galcanezumab 240 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	131	133		
Units: percentage of Participants				
number (not applicable)				
Satisfaction: Very satisfied	57.78	58.04		
Satisfaction: Somewhat satisfied	18.89	15.18		
Preference: Much prefer study medication	66.67	63.39		
Preference: Prefer study medication	22.22	17.86		
Side effects: Much less side effects	66.67	50.89		
Side effects: Less side effects	14.44	30.36		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants with Positive Reponses by Device Type Subcutaneous Administration Assessment Questionnaire Q1, Q3-Q12

End point title	Number of Participants with Positive Reponses by Device Type Subcutaneous Administration Assessment Questionnaire Q1, Q3-Q12

End point description:

The SQAAQ is a self-administered questionnaire that provides an assessment of ease of use and confidence with using a device to administer a subcutaneous injection of study drug. Participants will respond to questionnaire items using a 7-point Likert scale (from "Strongly Disagree" to "Strongly Agree") shortly after the injection. If a caregiver administers the injection, the participants should be prepared to provide the caregiver's ratings of the questions.strongly agree & agree are considered as

positive responses.

APD: All randomized participants who switched from pre-filled syringe and received at least one dose of study drug by autoinjector.

End point type	Secondary

End point timeframe:

Month 1 through Month 12

End point values	Galcanezumab 120 mg	Galcanezumab 240 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	84	95		
Units: Number of participant visits				
number (not applicable)				
Pre-filled Syringe : Easy to learn how to use	611	688		
Pre-filled Syringe : Easy to hold in hand	589	660		
Pre-filled Syringe : Easy to inject my dose	580	659		
Pre-filled Syringe : Easy to know dose is complete	615	703		
Pre-filled Syringe: Easy to store device in fridge	536	630		
Pre-filled Syringe : Easy to remove needle shield	610	699		
Pre-filled Syringe : Easy to pickup	610	693		
Pre-filled Syringe : overall, easy to use	600	663		
Pre-filled Syringe:Dvc is stable against skin	590	652		
Pre-filled Syringe:Confident in ability to use	580	654		
Pre-filled Syringe : Confident my dose is complete	618	708		
Autoinjector : Easy to learn how to use	250	265		
Autoinjector : Easy to hold in hand	247	267		
Autoinjector : Easy to inject my dose	245	265		
Autoinjector : Easy to know dose is complete	241	261		
Autoinjector : Easy store device in fridge	230	256		
Autoinjector : Easy to remove needle shield	250	268		
Autoinjector : Easy to pickup	251	271		
Autoinjector : Overall, easy to use	251	262		
Autoinjector : Dvc is stable against skin	244	264		
Autoinjector : Confident in ability to use	247	260		
Autoinjector : Confident my dose is complete	244	263		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Entire Study

Adverse event reporting additional description:

All randomized participants. There were 6 participants in the 120 mg group Open Label who discontinued after receiving loading dose of 240mg, these participants were moved to 240mg group for AE analysis.

Per protocol, AE analysis was planned per treatment regimen received.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	20.0

Reporting groups

Reporting group title	Galcanezumab 120mg - Open-Label Phase
Reporting group description: -	
Reporting group title	Galcanezumab 240mg - Open-Label Phase
Reporting group description: -	
Reporting group title	Galcanezumab 120mg - Post-treatment Phase
Reporting group description: -	
Reporting group title	Galcanezumab 240mg - Post-treatment Phase

Reporting group description: -

Serious adverse events	Galcanezumab 120mg - Open-Label Phase	Galcanezumab 240mg - Open-Label Phase	Galcanezumab 120mg - Post-treatment Phase
Total subjects affected by serious adverse events			
subjects affected / exposed	3 / 129 (2.33%)	7 / 141 (4.96%)	3 / 112 (2.68%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
lung neoplasm malignant			
alternative dictionary used: MedDRA 20.0			
subjects affected / exposed	0 / 129 (0.00%)	0 / 141 (0.00%)	1 / 112 (0.89%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
malignant melanoma			
alternative dictionary used: MedDRA 20.0			

subjects affected / exposed	0 / 129 (0.00%)	0 / 141 (0.00%)	0 / 112 (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			
subarachnoid haemorrhage			
alternative dictionary used: MedDRA 20.0			
subjects affected / exposed	0 / 129 (0.00%)	0 / 141 (0.00%)	1 / 112 (0.89%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Surgical and medical procedures			
uterine leiomyoma embolisation			
alternative dictionary used: MedDRA 20.0			
subjects affected / exposed[1]	0 / 104 (0.00%)	1 / 119 (0.84%)	0 / 91 (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
Nervous system disorders			
lumbar radiculopathy			
alternative dictionary used: MedDRA 20.0			
subjects affected / exposed	1 / 129 (0.78%)	0 / 141 (0.00%)	0 / 112 (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
migraine			
alternative dictionary used: MedDRA 20.0			
subjects affected / exposed	1 / 129 (0.78%)	0 / 141 (0.00%)	0 / 112 (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
pineal gland cyst			
alternative dictionary used: MedDRA 20.0			
subjects affected / exposed	0 / 129 (0.00%)	0 / 141 (0.00%)	0 / 112 (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			
non-cardiac chest pain			

alternative dictionary used: MedDRA 20.0			
subjects affected / exposed	0 / 129 (0.00%)	1 / 141 (0.71%)	0 / 112 (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			
diverticulum intestinal			
alternative dictionary used: MedDRA 20.0			
subjects affected / exposed	0 / 129 (0.00%)	1 / 141 (0.71%)	0 / 112 (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			
haemorrhagic ovarian cyst			
alternative dictionary used: MedDRA 20.0			
subjects affected / exposed[2]	0 / 104 (0.00%)	0 / 119 (0.00%)	1 / 91 (1.10%)
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			
alternative dictionary used: MedDRA 20.0			
subjects affected / exposed	0 / 129 (0.00%)	1 / 141 (0.71%)	0 / 112 (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 and connective tissue disorders			
intervertebral disc protrusion			
alternative dictionary used: MedDRA 20.0			
subjects affected / exposed	0 / 129 (0.00%)	1 / 141 (0.71%)	0 / 112 (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			
alternative dictionary used: MedDRA 20.0			
subjects affected / exposed	1 / 129 (0.78%)	0 / 141 (0.00%)	0 / 112 (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

pain in extremity			
alternative dictionary used: MedDRA 20.0			
subjects affected / exposed	0 / 129 (0.00%)	1 / 141 (0.71%)	0 / 112 (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
Infections and infestations			
endocarditis			
alternative dictionary used: MedDRA 20.0			
subjects affected / exposed	0 / 129 (0.00%)	0 / 141 (0.00%)	1 / 112 (0.89%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
infective aneurysm			
alternative dictionary used: MedDRA 20.0			
subjects affected / exposed	0 / 129 (0.00%)	0 / 141 (0.00%)	1 / 112 (0.89%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
pneumonia			
alternative dictionary used: MedDRA 20.0			
subjects affected / exposed	0 / 129 (0.00%)	1 / 141 (0.71%)	0 / 112 (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

Serious adverse events	Galcanezumab 240mg - Post-treatment Phase		
Total subjects affected by serious adverse events			
subjects affected / exposed	2 / 124 (1.61%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events	0		
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
lung neoplasm malignant			
alternative dictionary used: MedDRA 20.0			
subjects affected / exposed	0 / 124 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
malignant melanoma			

alternative dictionary used: MedDRA 20.0				
subjects affected / exposed	1 / 124 (0.81%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Injury, poisoning and procedural complications				
subarachnoid haemorrhage				
alternative dictionary used: MedDRA 20.0				
subjects affected / exposed	0 / 124 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Surgical and medical procedures				
uterine leiomyoma embolisation				
alternative dictionary used: MedDRA 20.0				
subjects affected / exposed[1]	0 / 106 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Nervous system disorders				
lumbar radiculopathy				
alternative dictionary used: MedDRA 20.0				
subjects affected / exposed	0 / 124 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
migraine				
alternative dictionary used: MedDRA 20.0				
subjects affected / exposed	0 / 124 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
pineal gland cyst				
alternative dictionary used: MedDRA 20.0				
subjects affected / exposed	1 / 124 (0.81%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
General disorders and administration site conditions				

non-cardiac chest pain				
alternative dictionary used: MedDRA 20.0				
subjects affected / exposed	0 / 124 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Gastrointestinal disorders				
diverticulum intestinal				
alternative dictionary used: MedDRA 20.0				
subjects affected / exposed	0 / 124 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Reproductive system and breast disorders				
haemorrhagic ovarian cyst				
alternative dictionary used: MedDRA 20.0				
subjects affected / exposed[2]	0 / 106 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Hepatobiliary disorders				
cholecystitis				
alternative dictionary used: MedDRA 20.0				
subjects affected / exposed	0 / 124 (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				
alternative dictionary used: MedDRA 20.0				
subjects affected / exposed	0 / 124 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
osteoarthritis				
alternative dictionary used: MedDRA 20.0				

subjects affected / exposed	0 / 124 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
pain in extremity			
alternative dictionary used: MedDRA 20.0			
subjects affected / exposed	0 / 124 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Infections and infestations			
endocarditis			
alternative dictionary used: MedDRA 20.0			
subjects affected / exposed	0 / 124 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
infective aneurysm			
alternative dictionary used: MedDRA 20.0			
subjects affected / exposed	0 / 124 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
pneumonia			
alternative dictionary used: MedDRA 20.0			
subjects affected / exposed	0 / 124 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		

Notes:

[1] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed to this adverse event. These numbers are expected to be equal.
Justification: Gender based adverse event, analyzed in female subjects.

[2] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed to this adverse event. These numbers are expected to be equal.
Justification: Gender based adverse event, analyzed in female subjects.

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

Non-serious adverse events	Galcanezumab 120mg - Open-Label Phase	Galcanezumab 240mg - Open-Label Phase	Galcanezumab 120mg - Post-treatment Phase
Total subjects affected by non-serious adverse events			
subjects affected / exposed	76 / 129 (58.91%)	83 / 141 (58.87%)	6 / 112 (5.36%)

Investigations weight increased alternative dictionary used: MedDRA 20.0 subjects affected / exposed occurrences (all)	7 / 129 (5.43%) 7	4 / 141 (2.84%) 4	0 / 112 (0.00%) 0
Nervous system disorders dizziness alternative dictionary used: MedDRA 20.0 subjects affected / exposed occurrences (all)	5 / 129 (3.88%) 7	9 / 141 (6.38%) 11	0 / 112 (0.00%) 0
General disorders and administration site conditions injection site bruising alternative dictionary used: MedDRA 20.0 subjects affected / exposed occurrences (all)	5 / 129 (3.88%) 5	8 / 141 (5.67%) 10	0 / 112 (0.00%) 0
injection site erythema alternative dictionary used: MedDRA 20.0 subjects affected / exposed occurrences (all)	9 / 129 (6.98%) 20	9 / 141 (6.38%) 19	0 / 112 (0.00%) 0
injection site pain alternative dictionary used: MedDRA 20.0 subjects affected / exposed occurrences (all)	22 / 129 (17.05%) 148	28 / 141 (19.86%) 272	0 / 112 (0.00%) 0
injection site reaction alternative dictionary used: MedDRA 20.0 subjects affected / exposed occurrences (all)	15 / 129 (11.63%) 48	13 / 141 (9.22%) 32	0 / 112 (0.00%) 0
Gastrointestinal disorders nausea alternative dictionary used: MedDRA 20.0 subjects affected / exposed occurrences (all)	10 / 129 (7.75%) 11	9 / 141 (6.38%) 15	1 / 112 (0.89%) 1
Reproductive system and breast disorders prostatitis alternative dictionary used: MedDRA 20.0			

subjects affected / exposed[3]	0 / 25 (0.00%)	0 / 22 (0.00%)	0 / 21 (0.00%)
occurrences (all)	0	0	0
Musculoskeletal and connective tissue disorders			
arthralgia			
alternative dictionary used: MedDRA 20.0			
subjects affected / exposed	8 / 129 (6.20%)	8 / 141 (5.67%)	1 / 112 (0.89%)
occurrences (all)	12	10	1
back pain			
alternative dictionary used: MedDRA 20.0			
subjects affected / exposed	12 / 129 (9.30%)	15 / 141 (10.64%)	2 / 112 (1.79%)
occurrences (all)	15	18	2
myalgia			
alternative dictionary used: MedDRA 20.0			
subjects affected / exposed	8 / 129 (6.20%)	3 / 141 (2.13%)	1 / 112 (0.89%)
occurrences (all)	9	4	1
Infections and infestations			
influenza			
alternative dictionary used: MedDRA 20.0			
subjects affected / exposed	8 / 129 (6.20%)	8 / 141 (5.67%)	1 / 112 (0.89%)
occurrences (all)	9	8	1
sinusitis			
alternative dictionary used: MedDRA 20.0			
subjects affected / exposed	14 / 129 (10.85%)	13 / 141 (9.22%)	0 / 112 (0.00%)
occurrences (all)	16	17	0
upper respiratory tract infection			
alternative dictionary used: MedDRA 20.0			
subjects affected / exposed	9 / 129 (6.98%)	21 / 141 (14.89%)	0 / 112 (0.00%)
occurrences (all)	10	23	0
viral upper respiratory tract infection			
alternative dictionary used: MedDRA 20.0			
subjects affected / exposed	21 / 129 (16.28%)	16 / 141 (11.35%)	0 / 112 (0.00%)
occurrences (all)	27	19	0

Non-serious adverse events	Galcanezumab 240mg - Post-treatment Phase		

Total subjects affected by non-serious adverse events subjects affected / exposed	8 / 124 (6.45%)		
Investigations weight increased alternative dictionary used: MedDRA 20.0 subjects affected / exposed occurrences (all)	0 / 124 (0.00%) 0		
Nervous system disorders dizziness alternative dictionary used: MedDRA 20.0 subjects affected / exposed occurrences (all)	0 / 124 (0.00%) 0		
General disorders and administration site conditions injection site bruising alternative dictionary used: MedDRA 20.0 subjects affected / exposed occurrences (all) injection site erythema alternative dictionary used: MedDRA 20.0 subjects affected / exposed occurrences (all) injection site pain alternative dictionary used: MedDRA 20.0 subjects affected / exposed occurrences (all) injection site reaction alternative dictionary used: MedDRA 20.0 subjects affected / exposed occurrences (all)	0 / 124 (0.00%) 0 0 / 124 (0.00%) 0 0 / 124 (0.00%) 0 0 / 124 (0.00%) 0		
Gastrointestinal disorders nausea alternative dictionary used: MedDRA 20.0 subjects affected / exposed occurrences (all)	0 / 124 (0.00%) 0		
Reproductive system and breast disorders			

prostatitis			
alternative dictionary used: MedDRA 20.0			
subjects affected / exposed[3]	1 / 18 (5.56%)		
occurrences (all)	1		
Musculoskeletal and connective tissue disorders			
arthralgia			
alternative dictionary used: MedDRA 20.0			
subjects affected / exposed	1 / 124 (0.81%)		
occurrences (all)	1		
back pain			
alternative dictionary used: MedDRA 20.0			
subjects affected / exposed	3 / 124 (2.42%)		
occurrences (all)	3		
myalgia			
alternative dictionary used: MedDRA 20.0			
subjects affected / exposed	0 / 124 (0.00%)		
occurrences (all)	0		
Infections and infestations			
influenza			
alternative dictionary used: MedDRA 20.0			
subjects affected / exposed	1 / 124 (0.81%)		
occurrences (all)	1		
sinusitis			
alternative dictionary used: MedDRA 20.0			
subjects affected / exposed	0 / 124 (0.00%)		
occurrences (all)	0		
upper respiratory tract infection			
alternative dictionary used: MedDRA 20.0			
subjects affected / exposed	1 / 124 (0.81%)		
occurrences (all)	2		
viral upper respiratory tract infection			
alternative dictionary used: MedDRA 20.0			
subjects affected / exposed	2 / 124 (1.61%)		
occurrences (all)	2		

Notes:

[3] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed for the reporting group. These numbers are expected to be equal.
Justification: Gender based adverse event, analyzed in male subjects.

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? No

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported