Clinical trial results:
A Multicenter, Randomized, Double-blind, Placebo-controlled, Parallel-group Study of the Safety and Efficacy of a Single Treatment of AGN-214868 in Patients With Postherpetic Neuralgia

Summary

EudraCT number	2012-002240-24
Trial protocol	DE AT PL
Global end of trial date	30 September 2015

Results information

Result version number	v1 (current)
This version publication date	10 November 2016
First version publication date	10 November 2016

Trial information

Trial identification

Sponsor protocol code	214868-007

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01678924
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Allergan plc
Sponsor organisation address	2525 Dupont Drive, Irvine, United States, 92623-9534
Public contact	Therapeutic Area Head, Allergan plc, +1 714-246-4500, clinicaltrials@allergan.com
Scientific contact	Allergan Ltd. EU Regulatory Affairs, Allergan Ltd., +44 1628494 444, ml-eu_reg_affairs@allergan.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	22 December 2015
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	30 September 2015
Was the trial ended prematurely?	Yes

Notes:

General information about the trial

Main objective of the trial:

To evaluate the safety, tolerability, and efficacy of AGN-214868 compared with placebo in the treatment of postherpetic neuralgia (PHN).

Protection of trial subjects:

This trial had investigator meetings at the outset to review all protocol procedures and investigator responsibilities under Good Clinical Practice (GCP). At the meeting, the conduct of the trial was explained and instructions were provided to ensure accuracy and consistency in data collection. This trial was conducted in conformance with GCP standards and applicable country and/or local statutes and regulations regarding ethical committee review, informed consent, and the protection of human subjects participating in biomedical research.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	16 January 2013
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	Poland: 75
Country: Number of subjects enrolled	Austria: 7
Country: Number of subjects enrolled	Germany: 141
Country: Number of subjects enrolled	United States: 57
Worldwide total number of subjects	280
EEA total number of subjects	223

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)	102
From 65 to 84 years	178
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

This was a multicenter, randomized, double-blind, placebo-controlled, parallel-group, 2 sequential dose cohort study. Patients in cohort 1 were randomized (1:2:2 ratio) to receive a two treatment sessions of AGN 214868 (total dose of either 32.5 or 65 µg) or placebo. Cohort 2 patients randomized (1:1 ratio) to receive a single treatment session

Pre-assignment

Screening details:

Patients had to be male or female, 18 to 80 years of age at screening with persistent Postherpetic Neuralgia (PHN) with pain present for ≥ 9 months (36 weeks) after the onset of a herpes zoster skin rash affecting the cervical, thoracic, lumbar, or sacral dermatomes.

Period 1

Period 1 title	Overall Study (overall period)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Investigator, Subject

Arms

Are arms mutually exclusive?	Yes
Arm title	AGN 214868 130µg

Arm description:

Single treatment session; total dose given as 65 injections into the area of pain on Day 1

Arm type	Experimental
Investigational medicinal product name	AGN 214868
Investigational medicinal product code	
Other name	Senrebotase
Pharmaceutical forms	Injection
Routes of administration	Intradermal use

Dosage and administration details:

65 injections of 2.0 micrograms/0.1ml into the area of pain on Day 1, for a total dose of 130 micrograms.

Arm title	AGN 214868 65µg

Arm description:

Single treatment session; total dose given as 65 injections into the area of pain on Day 1

Arm type	Experimental
Investigational medicinal product name	AGN 214868
Investigational medicinal product code	
Other name	Senrebotase
Pharmaceutical forms	Injection
Routes of administration	Intradermal use

Dosage and administration details:

65 injections of 1.0 micrograms/0.1ml into the area of pain on Day 1 for a total dose of 65 micrograms

Arm title	AGN 214868 32.5µg

Arm description:

Single treatment session; total dose given as 65 injections into the area of pain on Day 1

Arm type	Experimental

Investigational medicinal product name	AGN 214868
Investigational medicinal product code	
Other name	Senrebotase
Pharmaceutical forms	Injection
Routes of administration	Intradermal use

Dosage and administration details:

65 injections of 0.5 micrograms/0.1ml into the area of pain on Day 1 for a total dose of 32.5 micrograms

Arm title	Placebo

Arm description:

Single treatment session; placebo given as 65 injections into the area of pain on Day 1

Arm type	Placebo
Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Injection
Routes of administration	Intradermal use

Dosage and administration details:

65 injections of placebo/0.1ml into the area of pain on Day 1.

Number of subjects in period 1	AGN 214868 130µg	AGN 214868 65µg	AGN 214868 32.5µg
Started	64	63	30
Completed	54	51	28
Not completed	10	12	2
Consent withdrawn by subject	-	3	-
Adverse event, non-fatal	1	1	-
Unable to attend scheduled visits	-	-	-
Personal Reasons	2	2	2
Lost to follow-up	-	4	-
Lack of efficacy	7	2	-

Number of subjects in period 1	Placebo
Started	123
Completed	105
Not completed	18
Consent withdrawn by subject	2
Adverse event, non-fatal	1
Unable to attend scheduled visits	1
Personal Reasons	7
Lost to follow-up	2
Lack of efficacy	5

Baseline characteristics

Reporting groups	
Reporting group title	AGN 214868 130µg
Reporting group description:	
Single treatment session; total dose given as 65 injections into the area of pain on Day 1	
Reporting group title	AGN 214868 65µg
Reporting group description:	
Single treatment session; total dose given as 65 injections into the area of pain on Day 1	
Reporting group title	AGN 214868 32.5µg
Reporting group description:	
Single treatment session; total dose given as 65 injections into the area of pain on Day 1	
Reporting group title	Placebo
Reporting group description:	
Single treatment session; placebo given as 65 injections into the area of pain on Day 1	

Reporting group values	AGN 214868 130µg	AGN 214868 65µg	AGN 214868 32.5µg
Number of subjects	64	63	30
Age categorical Units: Subjects			
Adults (18 to less than 40 years)	1	3	1
Adults (40 to less than 65 years)	20	19	12
Adults (65 years and over)	43	41	17
Age continuous Units: years			
arithmetic mean	66.6	65.3	65
standard deviation	± 10.47	± 12.82	± 11.99
Gender categorical Units: Subjects			
Male	37	34	13
Female	27	29	17
Race and Ethnicity Units: Subjects			
Caucasian	56	52	26
Black	3	4	1
Asian	0	2	2
Hispanic	5	4	1
Other	0	1	0
Weight Units: Kilograms			
arithmetic mean	84.9	82.3	80
standard deviation	± 19.15	± 17.67	± 14.48
Height Units: Centimeters			
arithmetic mean	169.8	167.7	169.1
standard deviation	± 10.22	± 10.98	± 8.91

Reporting group values	Placebo	Total	
Number of subjects	123	280	

Age categorical Units: Subjects			
Adults (18 to less than 40 years)	0	5	
Adults (40 to less than 65 years)	46	97	
Adults (65 years and over)	77	178	
Age continuous Units: years			
arithmetic mean	67		
standard deviation	± 8.13	-	
Gender categorical Units: Subjects			
Male	50	134	
Female	73	146	
Race and Ethnicity Units: Subjects			
Caucasian	112	246	
Black	7	15	
Asian	1	5	
Hispanic	2	12	
Other	1	2	
Weight Units: Kilograms			
arithmetic mean	78.8		
standard deviation	± 17.83	-	
Height Units: Centimeters			
arithmetic mean	166.4		
standard deviation	± 9.07	-	

End points

End points reporting groups

Reporting group title	AGN 214868 130µg
Reporting group description:	
Single treatment session; total dose given as 65 injections into the area of pain on Day 1	
Reporting group title	AGN 214868 65µg
Reporting group description:	
Single treatment session; total dose given as 65 injections into the area of pain on Day 1	
Reporting group title	AGN 214868 32.5µg
Reporting group description:	
Single treatment session; total dose given as 65 injections into the area of pain on Day 1	
Reporting group title	Placebo
Reporting group description:	
Single treatment session; placebo given as 65 injections into the area of pain on Day 1	
Subject analysis set title	Intent to Treat population - Cohort 1
Subject analysis set type	Intention-to-treat
Subject analysis set description:	
The total modified intent to treat (mITT) population of 279 patients, consists of all randomized patients who received treatment and at least 1 postbaseline weekly average pain intensity score. Cohort 1 includes 154 patients from the mITT population	
Subject analysis set title	Intent to Treat population - Cohort 2
Subject analysis set type	Intention-to-treat
Subject analysis set description:	
The total modified intent to treat (mITT) population of 279 patients, consists of all randomized patients who received treatment and at least 1 postbaseline weekly average pain intensity score. Cohort 2 includes 125 patients from the mITT population	

Primary: Change from Baseline in Average Pain Intensity Score - Cohort 1

End point title	Change from Baseline in Average Pain Intensity Score - Cohort 1[1]
End point description:	
The average pain intensity score at each week was the mean of the daily average pain intensity scores reported in the patient's eDiary during each 7-day period, starting with the day of study treatment injection. patients used the 11-point Likert scale, with anchors at 0 = "no pain" and 10 = "pain as bad as you can imagine" Baseline was defined as the mean of the daily average pain intensity scores reported during the baseline period for the 7 days immediately prior to the treatment.	
End point type	Primary
End point timeframe:	
Baseline to Week 12	

Notes:

[1] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: No Statistical Analysis is reported for this outcome measure

End point values	AGN 214868 65µg	AGN 214868 32.5µg	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	63	30	123	
Units: units on a scale				
least squares mean (confidence interval 95%)				
Week 1	-0.88 (-1.249 to -0.538)	-1.02 (-1.38 to -0.587)	-1.11 (-1.425 to -0.808)	

Week 2	-1.33 (-1.746 to -0.968)	-1.56 (-1.963 to -1.017)	-1.57 (-1.97 to -1.174)	
Week 3	-1.66 (-2.143 to -1.203)	-1.93 (-2.426 to -1.227)	-1.84 (-2.248 to -1.388)	
Week 4	-1.78 (-2.277 to -1.31)	-2.2 (-2.721 to -1.432)	-1.98 (-2.423 to -1.482)	
Week 5	-1.83 (-2.321 to -1.384)	-2.19 (-2.675 to -1.379)	-2.1 (-2.557 to -1.554)	
Week 6	-1.97 (-2.442 to -1.495)	-2.07 (-2.597 to -1.297)	-2.34 (-2.755 to -1.697)	
Week 7	-2 (-2.481 to -1.506)	-2.08 (-2.572 to -1.328)	-2.32 (-2.746 to -1.673)	
Week 8	-2.11 (-2.591 to -1.618)	-2.02 (-2.53 to -1.263)	-2.4 (-2.825 to -1.745)	
Week 9	-2.21 (-2.66 to -1.701)	-2.15 (-2.682 to -1.352)	-2.52 (-2.805 to -1.733)	
Week 10	-2.28 (-2.679 to -1.674)	-2.29 (-2.812 to -1.481)	-2.48 (-2.743 to -1.634)	
Week 11	-2.27 (-2.684 to -1.672)	-2.46 (-2.996 to -1.57)	-2.56 (-2.807 to -1.724)	
Week 12	-2.2 (-2.626 to -1.6)	-2.53 (-3.061 to -1.605)	-2.65 (-2.886 to -1.783)	

Statistical analyses

Statistical analysis title	65ug vs. 32.5ug - Week 1
Comparison groups	AGN 214868 65µg v AGN 214868 32.5µg
Number of subjects included in analysis	93
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.633 [2]
Method	Type 3 sum of squares
Parameter estimate	Mean difference (final values)
Point estimate	0.14
Confidence interval	
level	90 %
sides	2-sided
lower limit	-0.343
upper limit	0.623

Notes:

[2] - Obtained from analysis of covariance model including treatment as fixed effect, and baseline maximal area of spontaneous pain and corresponding baseline average pain intensity score as covariates, with the type 3 sum of squares.

Statistical analysis title	65ug vs. Placebo - Week 1
Comparison groups	AGN 214868 65µg v Placebo
Number of subjects included in analysis	186
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.307 [3]
Method	Type 3 sum of squares
Parameter estimate	Mean difference (final values)
Point estimate	0.23

Confidence interval	
level	90 %
sides	2-sided
lower limit	-0.144
upper limit	0.613

Notes:

[3] - Obtained from analysis of covariance model including treatment as fixed effect, and baseline maximal area of spontaneous pain and corresponding baseline average pain intensity score as covariates, with the type 3 sum of squares.

Statistical analysis title	32.5ug vs. Placebo - Week 1
Comparison groups	AGN 214868 32.5µg v Placebo
Number of subjects included in analysis	153
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.744 [4]
Method	Type 3 sum of squares
Parameter estimate	Mean difference (final values)
Point estimate	0.09
Confidence interval	
level	90 %
sides	2-sided
lower limit	-0.384
upper limit	0.574

Notes:

[4] - Obtained from analysis of covariance model including treatment as fixed effect, and baseline maximal area of spontaneous pain and corresponding baseline average pain intensity score as covariates, with the type 3 sum of squares.

Statistical analysis title	65ug vs. 32.5ug - week 12
Comparison groups	AGN 214868 65µg v AGN 214868 32.5µg
Number of subjects included in analysis	93
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.495 [5]
Method	Type 3 sum of squares
Parameter estimate	Mean difference (final values)
Point estimate	0.33
Confidence interval	
level	90 %
sides	2-sided
lower limit	-0.473
upper limit	1.139

Notes:

[5] - Obtained from analysis of covariance model including treatment as fixed effect, and baseline maximal area of spontaneous pain and corresponding baseline average pain intensity score as covariates, with the type 3 sum of squares.

Statistical analysis title	65ug vs. Placebo - week 12
Comparison groups	AGN 214868 65µg v Placebo

Number of subjects included in analysis	186
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.25 [6]
Method	Type 3 sum of squares
Parameter estimate	Mean difference (final values)
Point estimate	0.45
Confidence interval	
level	90 %
sides	2-sided
lower limit	-0.196
upper limit	1.101

Notes:

[6] - Obtained from analysis of covariance model including treatment as fixed effect, and baseline maximal area of spontaneous pain and corresponding baseline average pain intensity score as covariates, with the type 3 sum of squares.

Statistical analysis title	32.5ug vs. Placebo - week 12
Comparison groups	AGN 214868 32.5µg v Placebo
Number of subjects included in analysis	153
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.806 [7]
Method	Type 3 sum of squares
Parameter estimate	Mean difference (final values)
Point estimate	0.12
Confidence interval	
level	90 %
sides	2-sided
lower limit	-0.684
upper limit	0.922

Notes:

[7] - Obtained from analysis of covariance model including treatment as fixed effect, and baseline maximal area of spontaneous pain and corresponding baseline average pain intensity score as covariates, with the type 3 sum of squares.

Primary: Change From Baseline in Average Pain Intensity Score - Cohort 2

End point title	Change From Baseline in Average Pain Intensity Score - Cohort 2[8]

End point description:

The average pain intensity score at each week was the mean of the daily average pain intensity scores reported in the patient's eDiary during each 7-day period, starting with the day of study treatment injection. patients used the 11-point Likert scale, with anchors at 0 = "no pain" and 10 = "pain as bad as you can imagine" Baseline was defined as the mean of the daily average pain intensity scores reported during the baseline period for the 7 days immediately prior to the treatment.

End point type	Primary

End point timeframe:

Baseline to Week 12

Notes:

[8] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: No Statistical Analysis is reported for this outcome measure

End point values	AGN 214868 130µg	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	64	61		
Units: units on a scale				
least squares mean (confidence interval 95%)				
Week 1	-0.78 (-1.093 to -0.451)	-0.88 (-1.19 to -0.492)		
Week 2	-1.12 (-1.508 to -0.701)	-1.37 (-1.791 to -0.799)		
Week 3	-1.45 (-1.788 to -0.952)	-1.65 (-2.064 to -1.057)		
Week 4	-1.62 (-1.934 to -1.072)	-1.9 (-2.344 to -1.269)		
Week 5	-1.88 (-2.202 to -1.301)	-1.88 (-2.366 to -1.257)		
Week 6	-2.04 (-2.226 to -1.305)	-1.9 (-2.339 to -1.235)		
Week 7	-2.14 (-2.345 to -1.352)	-1.9 (-2.352 to -1.225)		
Week 8	-2.29 (-2.405 to -1.404)	-1.96 (-2.412 to -1.27)		
Week 9	-2.35 (-2.493 to -1.497)	-2 (-2.457 to -1.293)		
Week 10	-2.44 (-2.584 to -1.557)	-2.04 (-2.515 to -1.311)		
Week 11	-2.49 (-2.647 to -1.581)	-2.03 (-2.489 to -1.314)		
Week 12	-2.49 (-2.659 to -1.632)	-2.03 (-2.538 to -1.354)		

Statistical analyses

Statistical analysis title	130ug vs. Placebo - Week 1
Comparison groups	AGN 214868 130µg v Placebo
Number of subjects included in analysis	125
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.683 [9]
Method	Type 3 sum of squares
Parameter estimate	Mean difference (final values)
Point estimate	0.1
Confidence interval	
level	90 %
sides	2-sided
lower limit	-0.293
upper limit	0.485

Notes:

[9] - Obtained from analysis of covariance model including treatment as fixed effect, and baseline maximal area of spontaneous pain and corresponding baseline average pain intensity score as covariates, with the type 3 sum of squares.

Statistical analysis title	130ug vs. Placebo - Week 12
Comparison groups	AGN 214868 130µg v Placebo

Number of subjects included in analysis	125
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.271 [10]
Method	Type 3 sum of squares
Parameter estimate	Mean difference (final values)
Point estimate	-0.47
Confidence interval	
level	90 %
sides	2-sided
lower limit	-1.166
upper limit	0.233

Notes:

[10] - Obtained from analysis of covariance model including treatment as fixed effect, and baseline maximal area of spontaneous pain and corresponding baseline average pain intensity score as covariates, with the type 3 sum of squares.

Secondary: Percentage of Average Pain Intensity Score Responders - Cohort 1 - Week 1

End point title	Percentage of Average Pain Intensity Score Responders - Cohort 1 - Week 1[11]

End point description:

The total modified intent to treat (mITT) population of 279 patients, consists of all randomized patients who received treatment and at least 1 postbaseline weekly average pain intensity score. Cohort 1 includes 154 patients from the mITT population

End point type	Secondary

End point timeframe:

Baseline to Week 1

Notes:

[11] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: No Statistical Analysis is reported for this outcome measure

End point values	AGN 214868 65µg	AGN 214868 32.5µg	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	61	30	61	
Units: percentage of patients				
number (not applicable)	18	33.3	21.3	

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Average Pain Intensity Score Responders - Cohort 1 - Week 2

End point title	Percentage of Average Pain Intensity Score Responders - Cohort 1 - Week 2[12]

End point description:

Average Pain Intensity Score Responder is defined as a patient who had at least a 30% improvement (decrease) in average pain intensity score at each week compared with baseline

End point type	Secondary

End point timeframe:

The total modified intent to treat (mITT) population of 279 patients, consists of all randomized patients who received treatment and at least 1 postbaseline weekly average pain intensity score. Cohort 1 includes 154 patients from the mITT population

Notes:

[12] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: No Statistical Analysis is reported for this outcome measure

End point values	AGN 214868 65µg	AGN 214868 32.5µg	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	63	30	60	
Units: percentage of patients				
number (not applicable)	27	40	36.7	

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Average Pain Intensity Score Responders - Cohort 1 - Week 3

End point title	Percentage of Average Pain Intensity Score Responders - Cohort 1 - Week 3[13]

End point description:

Average Pain Intensity Score Responder is defined as a patient who had at least a 30% improvement (decrease) in average pain intensity score at each week compared with baseline

End point type	Secondary

End point timeframe:

Baseline to Week 3

Notes:

[13] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: No Statistical Analysis is reported for this outcome measure

End point values	AGN 214868 65µg	AGN 214868 32.5µg	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	60	30	60	
Units: percentage of patients				
number (not applicable)	35	50	50	

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Average Pain Intensity Score Responders - Cohort 1 - Week 4

End point title	Percentage of Average Pain Intensity Score Responders - Cohort 1 - Week 4[14]

End point description:

Average Pain Intensity Score Responder is defined as a patient who had at least a 30% improvement (decrease), and in 10% increments, up to 100% improvement, in average pain intensity score at each week compared with baseline

End point type	Secondary

End point timeframe:

Baseline to Week 4

Notes:

[14] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: No Statistical Analysis is reported for this outcome measure

End point values	AGN 214868 65µg	AGN 214868 32.5µg	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	61	30	57	
Units: percentage of patients				
number (not applicable)	40	53.3	52.6	

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Average Pain Intensity Score Responders - Cohort 1 - Week 5

End point title	Percentage of Average Pain Intensity Score Responders - Cohort 1 - Week 5[15]

End point description:

Average Pain Intensity Score Responder is defined as a patient who had at least a 30% improvement (decrease) in average pain intensity score at each week compared with baseline

End point type	Secondary

End point timeframe:

Baseline to Week 5

Notes:

[15] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: No Statistical Analysis is reported for this outcome measure

End point values	AGN 214868 65µg	AGN 214868 32.5µg	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	59	30	57	
Units: percentage of patients				
number (not applicable)	40.7	53.3	52.6	

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Average Pain Intensity Score Responders - Cohort 1 - Week 6

End point title	Percentage of Average Pain Intensity Score Responders - Cohort 1 - Week 6[16]

End point description:

Average Pain Intensity Score Responder is defined as a patient who had at least a 30% improvement (decrease) in average pain intensity score at each week compared with baseline

End point type	Secondary

End point timeframe:

Baseline to Week 6

Notes:

[16] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: No Statistical Analysis is reported for this outcome measure

End point values	AGN 214868 65µg	AGN 214868 32.5µg	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	58	30	55	
Units: percentage of patients				
number (not applicable)	41.4	50	54.5	

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Average Pain Intensity Score Responders - Cohort 1 - Week 7

End point title	Percentage of Average Pain Intensity Score Responders - Cohort 1 - Week 7[17]

End point description:

Average Pain Intensity Score Responder is defined as a patient who had at least a 30% improvement (decrease) in average pain intensity score at each week compared with baseline

End point type	Secondary

End point timeframe:

Baseline to Week 7

Notes:

[17] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: No Statistical Analysis is reported for this outcome measure

End point values	AGN 214868 65µg	AGN 214868 32.5µg	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	60	30	57	
Units: percentage of patients				
number (not applicable)	43.3	56.7	50.9	

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Average Pain Intensity Score Responders - Cohort 1 - Week 8

End point title	Percentage of Average Pain Intensity Score Responders - Cohort 1 - Week 8[18]

End point description:

Average Pain Intensity Score Responder is defined as a patient who had at least a 30% improvement (decrease) in average pain intensity score at each week compared with baseline

End point type	Secondary

End point timeframe:

Baseline to Week 8

Notes:

[18] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: No Statistical Analysis is reported for this outcome measure

End point values	AGN 214868 65µg	AGN 214868 32.5µg	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	58	30	56	
Units: percentage of patients				
number (not applicable)	43.1	50	55.4	

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Average Pain Intensity Score Responders - Cohort 1 - Week 9

End point title	Percentage of Average Pain Intensity Score Responders - Cohort 1 - Week 9[19]

End point description:

Average Pain Intensity Score Responder is defined as a patient who had at least a 30% improvement (decrease) in average pain intensity score at each week compared with baseline

End point type	Secondary

End point timeframe:

Baseline to Week 9

Notes:

[19] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: No Statistical Analysis is reported for this outcome measure

End point values	AGN 214868 65µg	AGN 214868 32.5µg	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	55	27	52	
Units: percentage of patients				
number (not applicable)	43.6	51.9	51.9	

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Average Pain Intensity Score Responders - Cohort 1 - Week 10

End point title	Percentage of Average Pain Intensity Score Responders - Cohort 1 - Week 10[20]

End point description:

Average Pain Intensity Score Responder is defined as a patient who had at least a 30% improvement (decrease) in average pain intensity score at each week compared with baseline

End point type	Secondary

End point timeframe:

Baseline to Week 10

Notes:

[20] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: No Statistical Analysis is reported for this outcome measure

End point values	AGN 214868 65µg	AGN 214868 32.5µg	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	56	28	52	
Units: percentage of patients				
number (not applicable)	46.4	53.6	55.8	

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Average Pain Intensity Score Responders - Cohort 1 - Week 11

End point title	Percentage of Average Pain Intensity Score Responders - Cohort 1 - Week 11[21]

End point description:

Average Pain Intensity Score Responder is defined as a patient who had at least a 30% improvement (decrease) in average pain intensity score at each week compared with baseline

End point type	Secondary

End point timeframe:

Baseline to Week 11

Notes:

[21] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: No Statistical Analysis is reported for this outcome measure

End point values	AGN 214868 65µg	AGN 214868 32.5µg	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	53	28	52	
Units: percentage of patients				
number (not applicable)	47.2	53.6	59.6	

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Average Pain Intensity Score Responders - Cohort 1 - Week 12

End point title	Percentage of Average Pain Intensity Score Responders - Cohort 1 - Week 12[22]

End point description:

Average Pain Intensity Score Responder is defined as a patient who had at least a 30% improvement (decrease) in average pain intensity score at each week compared with baseline

End point type	Secondary

End point timeframe:

Baseline to Week 12

Notes:

[22] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: No Statistical Analysis is reported for this outcome measure

End point values	AGN 214868 65µg	AGN 214868 32.5µg	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	50	27	49	
Units: percentage of patients				
number (not applicable)	48	63	63.3	

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Average Pain Intensity Score Responders - Cohort 2 - Week 1

End point title	Percentage of Average Pain Intensity Score Responders - Cohort 2 - Week 1[23]

End point description:

Average Pain Intensity Score Responder is defined as a patient who had at least a 30% improvement

(decrease) in average pain intensity score at each week compared with baseline

End point type	Secondary

End point timeframe:

Baseline to Week 1

Notes:

[23] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: No Statistical Analysis is reported for this outcome measure

End point values	AGN 214868 130µg	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	63	59		
Units: percentage of patients				
number (not applicable)	14.3	20.3		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Average Pain Intensity Score Responders - Cohort 2 - Week 2

End point title	Percentage of Average Pain Intensity Score Responders - Cohort 2 - Week 2[24]

End point description:

Average Pain Intensity Score Responder is defined as a patient who had at least a 30% improvement (decrease) in average pain intensity score at each week compared with baseline

End point type	Secondary

End point timeframe:

Baseline to Week 2

Notes:

[24] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: No Statistical Analysis is reported for this outcome measure

End point values	AGN 214868 130µg	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	62	58		
Units: percentage of patients				
number (not applicable)	25.8	27.6		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Average Pain Intensity Score Responders - Cohort 2 -

Week 3

End point title	Percentage of Average Pain Intensity Score Responders - Cohort 2 - Week 3[25]

End point description:

Average Pain Intensity Score Responder is defined as a patient who had at least a 30% improvement (decrease) in average pain intensity score at each week compared with baseline

End point type	Secondary

End point timeframe:

Baseline to Week 3

Notes:

[25] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: No Statistical Analysis is reported for this outcome measure

End point values	AGN 214868 130µg	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	59	58		
Units: percentage of patients				
number (not applicable)	30.5	39.7		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Average Pain Intensity Score Responders - Cohort 2 - Week 4

End point title	Percentage of Average Pain Intensity Score Responders - Cohort 2 - Week 4[26]

End point description:

Average Pain Intensity Score Responder is defined as a patient who had at least a 30% improvement (decrease) in average pain intensity score at each week compared with baseline

End point type	Secondary

End point timeframe:

Baseline to Week 4

Notes:

[26] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: No Statistical Analysis is reported for this outcome measure

End point values	AGN 214868 130µg	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	60	58		
Units: percentage of patients				
number (not applicable)	35	43.1		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Average Pain Intensity Score Responders - Cohort 2 - Week 5

End point title	Percentage of Average Pain Intensity Score Responders - Cohort 2 - Week 5[27]

End point description:

Average Pain Intensity Score Responder is defined as a patient who had at least a 30% improvement (decrease) in average pain intensity score at each week compared with baseline

End point type	Secondary

End point timeframe:

Baseline to Week 5

Notes:

[27] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: No Statistical Analysis is reported for this outcome measure

End point values	AGN 214868 130µg	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	57	57		
Units: Baseline to Week 5				
number (not applicable)	42.1	45.6		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Average Pain Intensity Score Responders - Cohort 2 - Week 6

End point title	Percentage of Average Pain Intensity Score Responders - Cohort 2 - Week 6[28]

End point description:

Average Pain Intensity Score Responder is defined as a patient who had at least a 30% improvement (decrease) in average pain intensity score at each week compared with baseline

End point type	Secondary

End point timeframe:

Baseline to Week 6

Notes:

[28] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: No Statistical Analysis is reported for this outcome measure

End point values	AGN 214868 130µg	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	53	57		
Units: percentage of patients				
number (not applicable)	45.3	45.6		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Average Pain Intensity Score Responders - Cohort 2 - Week 7

End point title	Percentage of Average Pain Intensity Score Responders - Cohort 2 - Week 7[29]

End point description:

Average Pain Intensity Score Responder is defined as a patient who had at least a 30% improvement (decrease) in average pain intensity score at each week compared with baseline

End point type	Secondary

End point timeframe:

Baseline to Week 7

Notes:

[29] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: No Statistical Analysis is reported for this outcome measure

End point values	AGN 214868 130µg	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	50	56		
Units: percentage of patients				
number (not applicable)	50	48.2		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Average Pain Intensity Score Responders - Cohort 2 - Week 8

End point title	Percentage of Average Pain Intensity Score Responders - Cohort 2 - Week 8[30]

End point description:

Average Pain Intensity Score Responder is defined as a patient who had at least a 30% improvement (decrease) in average pain intensity score at each week compared with baseline

End point type	Secondary

End point timeframe:

Baseline to Week 8

Notes:

[30] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: No Statistical Analysis is reported for this outcome measure

End point values	AGN 214868 130µg	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	51	55		
Units: percentage of patients				
number (not applicable)	54.9	49.1		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Average Pain Intensity Score Responders - Cohort 2 - Week 9

End point title	Percentage of Average Pain Intensity Score Responders - Cohort 2 - Week 9[31]

End point description:

Average Pain Intensity Score Responder is defined as a patient who had at least a 30% improvement (decrease) in average pain intensity score at each week compared with baseline

End point type	Secondary

End point timeframe:

Baseline to Week 9

Notes:

[31] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: No Statistical Analysis is reported for this outcome measure

End point values	AGN 214868 130µg	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	51	55		
Units: percentage of patients				
number (not applicable)	58.8	45.5		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Average Pain Intensity Score Responders - Cohort 2 - Week 10

End point title	Percentage of Average Pain Intensity Score Responders - Cohort 2 - Week 10[32]

End point description:

Average Pain Intensity Score Responder is defined as a patient who had at least a 30% improvement

(decrease) in average pain intensity score at each week compared with baseline

End point type	Secondary

End point timeframe:

Baseline to Week 10

Notes:

[32] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: No Statistical Analysis is reported for this outcome measure

End point values	AGN 214868 130µg	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	51	55		
Units: percentage of patients				
number (not applicable)	64.7	47.3		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Average Pain Intensity Score Responders - Cohort 2 - Week 11

End point title	Percentage of Average Pain Intensity Score Responders - Cohort 2 - Week 11[33]

End point description:

Average Pain Intensity Score Responder is defined as a patient who had at least a 30% improvement (decrease) in average pain intensity score at each week compared with baseline

End point type	Secondary

End point timeframe:

Baseline to Week 11

Notes:

[33] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: No Statistical Analysis is reported for this outcome measure

End point values	AGN 214868 130µg	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	50	54		
Units: percentage of patients				
number (not applicable)	64	42.6		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Average Pain Intensity Score Responders - Cohort 2 -

Week 12

End point title	Percentage of Average Pain Intensity Score Responders - Cohort 2 - Week 12[34]

End point description:

Average Pain Intensity Score Responder is defined as a patient who had at least a 30% improvement (decrease) in average pain intensity score at each week compared with baseline

End point type	Secondary

End point timeframe:

Baseline to Week 12

Notes:

[34] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: No Statistical Analysis is reported for this outcome measure

End point values	AGN 214868 130µg	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	44	50		
Units: percentage of patients				
number (not applicable)	61.4	40		

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Maximal Area of Spontaneous Pain - Cohort 1 - Week 2

End point title	Change From Baseline in Maximal Area of Spontaneous Pain - Cohort 1 - Week 2[35]

End point description:

The assessment of maximal area of spontaneous pain was conducted by a qualified and trained investigator or designee (eg, physician, physician's assistant, nurse practitioner, and nurse). Areas of pain were quantified at a central reading center.

End point type	Secondary

End point timeframe:

Baseline to Week 2

Notes:

[35] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: No Statistical Analysis is reported for this outcome measure

End point values	AGN 214868 65µg	AGN 214868 32.5µg	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	61	27	60	
Units: Square Centimeters (cm2)				
least squares mean (confidence interval 95%)	-25.07 (-37.544 to -13.564)	-34.07 (-60.871 to -4.114)	-26.1 (-38.58 to -14.053)	

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Maximal Area of Spontaneous Pain - Cohort 1 - Week 4

End point title	Change From Baseline in Maximal Area of Spontaneous Pain - Cohort 1 - Week 4[36]

End point description:

The assessment of maximal area of spontaneous pain was conducted by a qualified and trained investigator or designee (eg, physician, physician's assistant, nurse practitioner, and nurse). Areas of pain were quantified at a central reading center.

End point type	Secondary

End point timeframe:

Baseline to Week 4

Notes:

[36] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: No Statistical Analysis is reported for this outcome measure

End point values	AGN 214868 65µg	AGN 214868 32.5µg	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	62	29	60	
Units: Square Centimeters (cm2)				
least squares mean (confidence interval 95%)	-27.65 (-40.978 to -15.412)	-25.96 (-49.316 to 0.309)	-32.23 (-48.543 to -16.214)	

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Maximal Area of Spontaneous Pain - Cohort 1 - Week 8

End point title	Change From Baseline in Maximal Area of Spontaneous Pain - Cohort 1 - Week 8[37]

End point description:

The assessment of maximal area of spontaneous pain was conducted by a qualified and trained investigator or designee (eg, physician, physician's assistant, nurse practitioner, and nurse). Areas of pain were quantified at a central reading center.

End point type	Secondary

End point timeframe:

Baseline to Week 8

Notes:

[37] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: No Statistical Analysis is reported for this outcome measure

End point values	AGN 214868 65µg	AGN 214868 32.5µg	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	56	28	55	
Units: Square Centimeters (cm2)				
least squares mean (confidence interval 95%)	-29.86 (-45.876 to -15.566)	-37.18 (-64.825 to -1.989)	-34.04 (-48.026 to -22.134)	

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Maximal Area of Spontaneous Pain - Cohort 1 - Week 12

End point title	Change From Baseline in Maximal Area of Spontaneous Pain - Cohort 1 - Week 12[38]

End point description:

The assessment of maximal area of spontaneous pain was conducted by a qualified and trained investigator or designee (eg, physician, physician's assistant, nurse practitioner, and nurse). Areas of pain were quantified at a central reading center.

End point type	Secondary

End point timeframe:

Baseline to Week 12

Notes:

[38] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: No Statistical Analysis is reported for this outcome measure

End point values	AGN 214868 65µg	AGN 214868 32.5µg	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	57	29	54	
Units: Square Centimeters (cm2)				
least squares mean (confidence interval 95%)	-30.99 (-46.118 to -17.138)	-31.4 (-61.185 to 3.853)	-35.03 (-53.242 to -18.425)	

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Maximal Area of Spontaneous Pain - Cohort 2 - Week 2

End point title	Change From Baseline in Maximal Area of Spontaneous Pain - Cohort 2 - Week 2[39]

End point description:

The assessment of maximal area of spontaneous pain was conducted by a qualified and trained investigator or designee (eg, physician, physician's assistant, nurse practitioner, and nurse). Areas of pain were quantified at a central reading center.

End point type	Secondary

End point timeframe:

Baseline to Week 2

Notes:

[39] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: No Statistical Analysis is reported for this outcome measure

End point values	AGN 214868 130µg	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	57	57		
Units: Square Centimeters (cm2)				
least squares mean (confidence interval 95%)	-9.86 (-38.087 to 18.02)	-27.52 (-43.841 to -10.854)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Maximal Area of Spontaneous Pain - Cohort 2 - Week 4

End point title	Change From Baseline in Maximal Area of Spontaneous Pain - Cohort 2 - Week 4[40]

End point description:

The assessment of maximal area of spontaneous pain was conducted by a qualified and trained investigator or designee (eg, physician, physician's assistant, nurse practitioner, and nurse). Areas of pain were quantified at a central reading center.

End point type	Secondary

End point timeframe:

Baseline to Week 4

Notes:

[40] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: No Statistical Analysis is reported for this outcome measure

End point values	AGN 214868 130µg	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	58	59		
Units: Square Centimeters (cm2)				
least squares mean (confidence interval 95%)	-22.23 (-48.893 to 3.903)	-25.67 (-42.901 to -7.909)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Maximal Area of Spontaneous Pain - Cohort 2 - Week 8

End point title	Change From Baseline in Maximal Area of Spontaneous Pain - Cohort 2 - Week 8[41]

End point description:

The assessment of maximal area of spontaneous pain was conducted by a qualified and trained investigator or designee (eg, physician, physician's assistant, nurse practitioner, and nurse). Areas of pain were quantified at a central reading center.

End point type	Secondary

End point timeframe:

Baseline to Week 8

Notes:

[41] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: No Statistical Analysis is reported for this outcome measure

End point values	AGN 214868 130µg	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	53	57		
Units: Square Centimeters (cm2)				
least squares mean (confidence interval 95%)	-42.92 (-65.58 to -23.08)	-31.95 (-47.299 to -13.978)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Maximal Area of Spontaneous Pain - Cohort 2 - Week 12

End point title	Change From Baseline in Maximal Area of Spontaneous Pain - Cohort 2 - Week 12[42]

End point description:

The assessment of maximal area of spontaneous pain was conducted by a qualified and trained investigator or designee (eg, physician, physician's assistant, nurse practitioner, and nurse). Areas of pain were quantified at a central reading center.

End point type	Secondary

End point timeframe:

Baseline to Week 12

Notes:

[42] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: No Statistical Analysis is reported for this outcome measure

End point values	AGN 214868 130µg	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	54	57		
Units: Square Centimeters (cm2)				
least squares mean (confidence interval 95%)	-36.73 (-67.719 to -8.696)	-32.6 (-49.823 to -12.574)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Area of Allodynia - Cohort 1 - Week 2

End point title	Change From Baseline in Area of Allodynia - Cohort 1 - Week

End point description:

The assessment of maximal area of allodynia was conducted by a qualified and trained investigator or designee (eg, physician, physician's assistant, nurse practitioner, and nurse). Areas of allodynia were quantified at a central reading center.

End point type	Secondary

End point timeframe:

Baseline to Week 2

Notes:

[43] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: No Statistical Analysis is reported for this outcome measure

End point values	AGN 214868 65µg	AGN 214868 32.5µg	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	61	27	60	
Units: Square Centimeters (cm2)				
least squares mean (confidence interval 95%)	-40.06 (-89.75 to -12.158)	-14.42 (-34.431 to 23.824)	-52.73 (-67.258 to -24.248)	

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Area of Allodynia - Cohort 1 - Week 4

End point title	Change From Baseline in Area of Allodynia - Cohort 1 - Week

End point description:

The assessment of maximal area of allodynia was conducted by a qualified and trained investigator or designee (eg, physician, physician's assistant, nurse practitioner, and nurse). Areas of allodynia were quantified at a central reading center.

End point type	Secondary

End point timeframe:

Baseline to Week 4

Notes:

[44] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: No Statistical Analysis is reported for this outcome measure

End point values	AGN 214868 65µg	AGN 214868 32.5µg	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	62	29	60	
Units: Square Centimeters (cm2)				
least squares mean (confidence interval 95%)	-54.12 (-118.867 to -19.566)	-23.07 (-41.985 to 19.468)	-58.14 (-70.452 to -26.048)	

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Area of Allodynia - Cohort 1 - Week 8

End point title	Change From Baseline in Area of Allodynia - Cohort 1 - Week

End point description:

The assessment of maximal area of allodynia was conducted by a qualified and trained investigator or designee (eg, physician, physician's assistant, nurse practitioner, and nurse). Areas of allodynia were quantified at a central reading center.

End point type	Secondary

End point timeframe:

Baseline to Week 8

Notes:

[45] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: No Statistical Analysis is reported for this outcome measure

End point values	AGN 214868 65µg	AGN 214868 32.5µg	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	56	28	55	
Units: Square Centimeters (cm2)				
least squares mean (confidence interval 95%)	-74.46 (-136.541 to -43.526)	-50.47 (-75.433 to -4.124)	-71.54 (-85.155 to -37.104)	

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Area of Allodynia - Cohort 1 - Week 12

End point title	Change From Baseline in Area of Allodynia - Cohort 1 - Week 12[46]

End point description:

The assessment of maximal area of allodynia was conducted by a qualified and trained investigator or designee (eg, physician, physician's assistant, nurse practitioner, and nurse). Areas of allodynia were quantified at a central reading center.

End point type	Secondary

End point timeframe:

Baseline to Week 12

Notes:

[46] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: No Statistical Analysis is reported for this outcome measure

End point values	AGN 214868 65µg	AGN 214868 32.5µg	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	57	29	54	
Units: Square Centimeters (cm2)				
least squares mean (confidence interval 95%)	-67.71 (-130.695 to -35.611)	-39.96 (-62.646 to 8.446)	-70.46 (-92.167 to -29.97)	

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Area of Allodynia - Cohort 2 - Week 2

End point title	Change From Baseline in Area of Allodynia - Cohort 2 - Week

End point description:

The assessment of maximal area of allodynia was conducted by a qualified and trained investigator or designee (eg, physician, physician's assistant, nurse practitioner, and nurse). Areas of allodynia were quantified at a central reading center.

End point type	Secondary

End point timeframe:

Baseline to Week 2

Notes:

[47] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: No Statistical Analysis is reported for this outcome measure

End point values	AGN 214868 130µg	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	57	57		
Units: Square Centimeters (cm2)				
least squares mean (confidence interval 95%)	-36.66 (-59.461 to -0.328)	-60.71 (-98.564 to -36.369)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Area of Allodynia - Cohort 2 - Week 4

End point title	Change From Baseline in Area of Allodynia - Cohort 2 - Week

End point description:

The assessment of maximal area of allodynia was conducted by a qualified and trained investigator or designee (eg, physician, physician's assistant, nurse practitioner, and nurse). Areas of allodynia were quantified at a central reading center.

End point type	Secondary

End point timeframe:

Baseline to Week 4

Notes:

[48] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: No Statistical Analysis is reported for this outcome measure

End point values	AGN 214868 130µg	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	58	59		
Units: Square Centimeters (cm2)				
least squares mean (confidence interval 95%)	-54.33 (-72.041 to -13.677)	-69.39 (-116.234 to -45.112)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Area of Allodynia - Cohort 2 - Week 8

End point title	Change From Baseline in Area of Allodynia - Cohort 2 - Week

End point description:

The assessment of maximal area of allodynia was conducted by a qualified and trained investigator or designee (eg, physician, physician's assistant, nurse practitioner, and nurse). Areas of allodynia were quantified at a central reading center.

End point type	Secondary

End point timeframe:

Baseline to Week 8

Notes:

[49] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: No Statistical Analysis is reported for this outcome measure

End point values	AGN 214868 130µg	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	53	57		
Units: Square Centimeters (cm2)				
least squares mean (confidence interval 95%)	-78.78 (-99.958 to -43.748)	-75.58 (-113.401 to -50.634)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Area of Allodynia - Cohort 2 - Week 12

End point title	Change From Baseline in Area of Allodynia - Cohort 2 - Week 12[50]

End point description:

The assessment of maximal area of allodynia was conducted by a qualified and trained investigator or designee (eg, physician, physician's assistant, nurse practitioner, and nurse). Areas of allodynia were quantified at a central reading center.

End point type	Secondary

End point timeframe:

Baseline to Week 12

Notes:

[50] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: No Statistical Analysis is reported for this outcome measure

End point values	AGN 214868 130µg	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	54	57		
Units: Square Centimeters (cm2)				
least squares mean (confidence interval 95%)	-77.98 (-99.148 to -36.515)	-79.99 (-129.775 to -49.428)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Evoked Pain Score in the Area of Allodynia

Cohort 1 - Week 2

End point title	Change From Baseline in Evoked Pain Score in the Area of Allodynia Cohort 1 - Week 2[51]

End point description:

Assessment of evoked pain were conducted by a qualified and trained investigator or designee (eg, physician, physician's assistant, nurse practitioner, and nurse). Evoked pain was scored using a visual analog scale (VAS; 0 to100 mm scale with anchors of 0 = No pain and 100 = Worst pain imaginable). The patient was asked to use the VAS to rate the unpleasantness of 3 brush strokes within the center of the area of allodynia and pain.

End point type	Secondary

End point timeframe:

Baseline to Week 2

Notes:

[51] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: No Statistical Analysis is reported for this outcome measure

End point values	AGN 214868 65µg	AGN 214868 32.5µg	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	48	21	50	
Units: units on a scale				
least squares mean (confidence interval 95%)	-17.4 (-25.67 to -10.68)	-21.2 (-30.01 to -10.09)	-15.3 (-22.76 to -7.32)	

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Evoked Pain Score in the Area of Allodynia Cohort 1 - Week 4

End point title	Change From Baseline in Evoked Pain Score in the Area of Allodynia Cohort 1 - Week 4[52]

End point description:

Assessment of evoked pain were conducted by a qualified and trained investigator or designee (eg, physician, physician's assistant, nurse practitioner, and nurse). Evoked pain was scored using a visual analog scale (VAS; 0 to100 mm scale with anchors of 0 = No pain and 100 = Worst pain imaginable). The patient was asked to use the VAS to rate the unpleasantness of 3 brush strokes within the center of the area of allodynia and pain.

End point type	Secondary

End point timeframe:

Baseline to Week 4

Notes:

[52] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: No Statistical Analysis is reported for this outcome measure

End point values	AGN 214868 65µg	AGN 214868 32.5µg	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	50	25	51	
Units: units on a scale				
least squares mean (confidence interval 95%)	-21.9 (-29.67 to -15.57)	-20.5 (-28.34 to -11.34)	-12.3 (-19.02 to -5.01)	

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Evoked Pain Score in the Area of Allodynia Cohort 1 - Week 8

End point title	Change From Baseline in Evoked Pain Score in the Area of Allodynia Cohort 1 - Week 8[53]

End point description:

Assessment of evoked pain were conducted by a qualified and trained investigator or designee (eg, physician, physician's assistant, nurse practitioner, and nurse). Evoked pain was scored using a visual analog scale (VAS; 0 to100 mm scale with anchors of 0 = No pain and 100 = Worst pain imaginable). The patient was asked to use the VAS to rate the unpleasantness of 3 brush strokes within the center of the area of allodynia and pain.

End point type	Secondary

End point timeframe:

Baseline to Week 8

Notes:

[53] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: No Statistical Analysis is reported for this outcome measure

End point values	AGN 214868 65µg	AGN 214868 32.5µg	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	51	22	49	
Units: units on a scale				
least squares mean (confidence interval 95%)	-22.7 (-31.18 to -15.8)	-24.8 (-34.73 to -14.45)	-19.4 (-27.27 to -10.15)	

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Evoked Pain Score in the Area of Allodynia Cohort 1 - Week 12

End point title	Change From Baseline in Evoked Pain Score in the Area of Allodynia Cohort 1 - Week 12[54]

End point description:

Assessment of evoked pain were conducted by a qualified and trained investigator or designee (eg, physician, physician's assistant, nurse practitioner, and nurse). Evoked pain was scored using a visual analog scale (VAS; 0 to100 mm scale with anchors of 0 = No pain and 100 = Worst pain imaginable). The patient was asked to use the VAS to rate the unpleasantness of 3 brush strokes within the center of

the area of allodynia and pain.

End point type	Secondary

End point timeframe:

Baseline to Week 12

Notes:

[54] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: No Statistical Analysis is reported for this outcome measure

End point values	AGN 214868 65µg	AGN 214868 32.5µg	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	51	23	46	
Units: units on a scale				
least squares mean (confidence interval 95%)	-19.2 (-27.51 to -12.14)	-21.6 (-33.46 to -9.41)	-21.5 (-28.99 to -12.79)	

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Evoked Pain Score in the Area of Allodynia - Cohort 2 - Week 2

End point title	Change From Baseline in Evoked Pain Score in the Area of Allodynia - Cohort 2 - Week 2[55]

End point description:

Assessment of evoked pain were conducted by a qualified and trained investigator or designee (eg, physician, physician's assistant, nurse practitioner, and nurse). Evoked pain was scored using a visual analog scale (VAS; 0 to100 mm scale with anchors of 0 = No pain and 100 = Worst pain imaginable). The patient was asked to use the VAS to rate the unpleasantness of 3 brush strokes within the center of the area of allodynia and pain.

End point type	Secondary

End point timeframe:

Baseline to Week 2

Notes:

[55] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: No Statistical Analysis is reported for this outcome measure

End point values	AGN 214868 130µg	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	53	55		
Units: units on a scale				
least squares mean (confidence interval 95%)	-19 (-26.102 to -11.03)	-16.2 (-23.4 to -9.691)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Evoked Pain Score in the Area of Allodynia - Cohort 2 - Week 4

End point title	Change From Baseline in Evoked Pain Score in the Area of Allodynia - Cohort 2 - Week 4[56]

End point description:

Assessment of evoked pain were conducted by a qualified and trained investigator or designee (eg, physician, physician's assistant, nurse practitioner, and nurse). Evoked pain was scored using a visual analog scale (VAS; 0 to100 mm scale with anchors of 0 = No pain and 100 = Worst pain imaginable). The patient was asked to use the VAS to rate the unpleasantness of 3 brush strokes within the center of the area of allodynia and pain.

End point type	Secondary

End point timeframe:

Baseline to Week 4

Notes:

[56] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: No Statistical Analysis is reported for this outcome measure

End point values	AGN 214868 130µg	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	52	55		
Units: units on a scale				
least squares mean (confidence interval 95%)	-20.6 (-27.941 to -10.867)	-20.5 (-29.487 to -13.64)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Evoked Pain Score in the Area of Allodynia - Cohort 2 - Week 8

End point title	Change From Baseline in Evoked Pain Score in the Area of Allodynia - Cohort 2 - Week 8[57]

End point description:

Assessment of evoked pain were conducted by a qualified and trained investigator or designee (eg, physician, physician's assistant, nurse practitioner, and nurse). Evoked pain was scored using a visual analog scale (VAS; 0 to100 mm scale with anchors of 0 = No pain and 100 = Worst pain imaginable). The patient was asked to use the VAS to rate the unpleasantness of 3 brush strokes within the center of the area of allodynia and pain.

End point type	Secondary

End point timeframe:

Baseline to Week 8

Notes:

[57] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: No Statistical Analysis is reported for this outcome measure

End point values	AGN 214868 130µg	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	48	52		
Units: units on a scale				
least squares mean (confidence interval 95%)	-28.7 (-35.924 to -21.285)	-19.7 (-27.721 to -11.895)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Evoked Pain Score in the Area of Allodynia - Cohort 2 - Week 12

End point title	Change From Baseline in Evoked Pain Score in the Area of Allodynia - Cohort 2 - Week 12[58]

End point description:

Assessment of evoked pain were conducted by a qualified and trained investigator or designee (eg, physician, physician's assistant, nurse practitioner, and nurse). Evoked pain was scored using a visual analog scale (VAS; 0 to100 mm scale with anchors of 0 = No pain and 100 = Worst pain imaginable). The patient was asked to use the VAS to rate the unpleasantness of 3 brush strokes within the center of the area of allodynia and pain.

End point type	Secondary

End point timeframe:

Baseline to Week 12

Notes:

[58] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: No Statistical Analysis is reported for this outcome measure

End point values	AGN 214868 130µg	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	47	51		
Units: units on a scale				
least squares mean (confidence interval 95%)	-26.9 (-37.75 to -16.548)	-19.1 (-26.996 to -10.612)		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information	
Timeframe for reporting adverse events:	
Adverse Event reporting occurred over a 6 month period from May to October of 2015	
Assessment type	Systematic
Dictionary used	
Dictionary name	MedDRA
Dictionary version	18.1
Reporting groups	
Reporting group title	AGN 214868 130µg
Reporting group description:	
Single treatment session of AGN-214868, total dose given as injections into the area of pain on Day 1	
Reporting group title	AGN 214868 65µg
Reporting group description:	
Single treatment session of AGN-214868, total dose given as injections into the area of pain on Day 1	
Reporting group title	AGN 214868 32.5µg
Reporting group description:	
Single treatment session of AGN-214868, total dose given as injections into the area of pain on Day 1	
Reporting group title	Placebo
Reporting group description:	
Single treatment session of AGN-214868 placebo, given as injections into the area of pain on Day 1	

Serious adverse events	AGN 214868 130µg	AGN 214868 65µg	AGN 214868 32.5µg
Total subjects affected by serious adverse events			
subjects affected / exposed	2 / 64 (3.13%)	8 / 63 (12.70%)	2 / 30 (6.67%)
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)			
Basal cell carcinoma			
subjects affected / exposed	0 / 64 (0.00%)	1 / 63 (1.59%)	1 / 30 (3.33%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Breast cancer			
subjects affected / exposed	0 / 64 (0.00%)	1 / 63 (1.59%)	0 / 30 (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
Squamous cell carcinoma			

subjects affected / exposed	0 / 64 (0.00%)	1 / 63 (1.59%)	0 / 30 (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
Adenocarcinoma of colon			
subjects affected / exposed	0 / 64 (0.00%)	0 / 63 (0.00%)	1 / 30 (3.33%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Malignant melanoma			
subjects affected / exposed	0 / 64 (0.00%)	0 / 63 (0.00%)	1 / 30 (3.33%)
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			
Fractured sacrum			
subjects affected / exposed	0 / 64 (0.00%)	0 / 63 (0.00%)	0 / 30 (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
Pubis fracture			
subjects affected / exposed	0 / 64 (0.00%)	0 / 63 (0.00%)	0 / 30 (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
Rib fracture			
subjects affected / exposed	0 / 64 (0.00%)	0 / 63 (0.00%)	0 / 30 (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
Urethral injury			
subjects affected / exposed	0 / 64 (0.00%)	0 / 63 (0.00%)	0 / 30 (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			
Aortic aneurysm			
subjects affected / exposed	0 / 64 (0.00%)	1 / 63 (1.59%)	0 / 30 (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

Cardiac disorders			
Atrial fibrillation			
subjects affected / exposed	1 / 64 (1.56%)	0 / 63 (0.00%)	0 / 30 (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 infarction			
subjects affected / exposed	1 / 64 (1.56%)	0 / 63 (0.00%)	0 / 30 (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
Angina unstable			
subjects affected / exposed	0 / 64 (0.00%)	1 / 63 (1.59%)	0 / 30 (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			
Thalamic infarction			
subjects affected / exposed	0 / 64 (0.00%)	1 / 63 (1.59%)	0 / 30 (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
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	0 / 64 (0.00%)	0 / 63 (0.00%)	0 / 30 (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			
Oedema peripheral			
subjects affected / exposed	0 / 64 (0.00%)	0 / 63 (0.00%)	0 / 30 (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			
Gastrooesophageal reflux disease			
subjects affected / exposed	0 / 64 (0.00%)	0 / 63 (0.00%)	0 / 30 (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 / 64 (0.00%)	2 / 63 (3.17%)	0 / 30 (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
Respiratory, thoracic and mediastinal disorders			
Haemothorax			
subjects affected / exposed	0 / 64 (0.00%)	0 / 63 (0.00%)	0 / 30 (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
Pneumothorax			
subjects affected / exposed	0 / 64 (0.00%)	0 / 63 (0.00%)	0 / 30 (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 failure			
subjects affected / exposed	0 / 64 (0.00%)	0 / 63 (0.00%)	0 / 30 (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			
Joint crepitation			
subjects affected / exposed	0 / 64 (0.00%)	0 / 63 (0.00%)	0 / 30 (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 / 64 (0.00%)	0 / 63 (0.00%)	0 / 30 (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			
Pyelonephritis			
subjects affected / exposed	0 / 64 (0.00%)	1 / 63 (1.59%)	0 / 30 (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
Erysipelas			

subjects affected / exposed	0 / 64 (0.00%)	0 / 63 (0.00%)	0 / 30 (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
Furuncle			
subjects affected / exposed	0 / 64 (0.00%)	0 / 63 (0.00%)	0 / 30 (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
Labyrinthitis			
subjects affected / exposed	0 / 64 (0.00%)	0 / 63 (0.00%)	0 / 30 (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	Placebo		
Total subjects affected by serious adverse events			
subjects affected / exposed	10 / 123 (8.13%)		
number of deaths (all causes)	1		
number of deaths resulting from adverse events	0		
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Basal cell carcinoma			
subjects affected / exposed	0 / 123 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Breast cancer			
subjects affected / exposed	1 / 123 (0.81%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Squamous cell carcinoma			
subjects affected / exposed	0 / 123 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Adenocarcinoma of colon			
subjects affected / exposed	0 / 123 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		

Malignant melanoma				
subjects affected / exposed	0 / 123 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Injury, poisoning and procedural complications				
Fractured sacrum				
subjects affected / exposed	1 / 123 (0.81%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Pubis fracture				
subjects affected / exposed	1 / 123 (0.81%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Rib fracture				
subjects affected / exposed	1 / 123 (0.81%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Urethral injury				
subjects affected / exposed	1 / 123 (0.81%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Vascular disorders				
Aortic aneurysm				
subjects affected / exposed	1 / 123 (0.81%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Cardiac disorders				
Atrial fibrillation				
subjects affected / exposed	0 / 123 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Myocardial infarction				

subjects affected / exposed	0 / 123 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Angina unstable			
subjects affected / exposed	0 / 123 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Nervous system disorders			
Thalamic infarction			
subjects affected / exposed	0 / 123 (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	1 / 123 (0.81%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
General disorders and administration site conditions			
Oedema peripheral			
subjects affected / exposed	1 / 123 (0.81%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Gastrointestinal disorders			
Gastrooesophageal reflux disease			
subjects affected / exposed	1 / 123 (0.81%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Hepatobiliary disorders			
Cholecystitis			
subjects affected / exposed	0 / 123 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Respiratory, thoracic and mediastinal disorders			
Haemothorax			

subjects affected / exposed	1 / 123 (0.81%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Pneumothorax			
subjects affected / exposed	1 / 123 (0.81%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Respiratory failure			
subjects affected / exposed	1 / 123 (0.81%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 1		
Musculoskeletal and connective tissue disorders			
Joint crepitation			
subjects affected / exposed	1 / 123 (0.81%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Osteoarthritis			
subjects affected / exposed	1 / 123 (0.81%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Infections and infestations			
Pyelonephritis			
subjects affected / exposed	0 / 123 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Erysipelas			
subjects affected / exposed	1 / 123 (0.81%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Furuncle			
subjects affected / exposed	1 / 123 (0.81%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		

Labyrinthitis			
subjects affected / exposed	1 / 123 (0.81%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		

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

Non-serious adverse events	AGN 214868 130µg	AGN 214868 65µg	AGN 214868 32.5µg
Total subjects affected by non-serious adverse events			
subjects affected / exposed	38 / 64 (59.38%)	39 / 63 (61.90%)	20 / 30 (66.67%)
Nervous system disorders			
Dizziness			
subjects affected / exposed	1 / 64 (1.56%)	2 / 63 (3.17%)	3 / 30 (10.00%)
occurrences (all)	1	2	3
General disorders and administration site conditions			
Injection site pain			
subjects affected / exposed	6 / 64 (9.38%)	1 / 63 (1.59%)	0 / 30 (0.00%)
occurrences (all)	6	1	0
Infections and infestations			
Upper respiratory tract infection			
subjects affected / exposed	4 / 64 (6.25%)	5 / 63 (7.94%)	1 / 30 (3.33%)
occurrences (all)	4	5	1
Nasopharyngitis			
subjects affected / exposed	3 / 64 (4.69%)	5 / 63 (7.94%)	2 / 30 (6.67%)
occurrences (all)	3	5	2
Urinary tract infection			
subjects affected / exposed	1 / 64 (1.56%)	2 / 63 (3.17%)	2 / 30 (6.67%)
occurrences (all)	1	2	2

Non-serious adverse events	Placebo		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	70 / 123 (56.91%)		
Nervous system disorders			
Dizziness			
subjects affected / exposed	2 / 123 (1.63%)		
occurrences (all)	2		
General disorders and administration site conditions			

Injection site pain subjects affected / exposed occurrences (all)	6 / 123 (4.88%) 6		
Infections and infestations Upper respiratory tract infection subjects affected / exposed occurrences (all) Nasopharyngitis subjects affected / exposed occurrences (all) Urinary tract infection subjects affected / exposed occurrences (all)	8 / 123 (6.50%) 8 9 / 123 (7.32%) 9 7 / 123 (5.69%) 7		

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