Clinical trial results:
A Dose Escalation Study to Assess the Efficacy and Tolerance of AF-219 in Subjects with Refractory Chronic Cough

Summary

EudraCT number	2015-000474-35
Trial protocol	GB
Global end of trial date	09 February 2016

Results information

Result version number	v1
This version publication date	30 July 2017
First version publication date	30 July 2017

Trial information

Trial identification

Sponsor protocol code	7264-010

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02349425
WHO universal trial number (UTN)	-
Other trial identifiers	Afferent study number: AF219-010, Merck study number: MK-7264-010

Notes:

Sponsors

Sponsor organisation name	Afferent Pharmaceuticals, Inc.
Sponsor organisation address	2929 Campus Dr #230, San Mateo, CA, United States, 94403
Public contact	Clinical Trials Disclosure, Merck Sharp & Dohme Corp., ClinicalTrialsDisclosure@merck.com
Scientific contact	Clinical Trials Disclosure, Merck Sharp & Dohme Corp., ClinicalTrialsDisclosure@merck.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	09 February 2016
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	09 February 2016
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To evaluate the dose-response of Gefapixant (AF-219) in reducing Awake Objective Cough Frequency and to identify tolerable dose(s) of Gefapixant that reduce Awake Objective Cough Frequency.

Protection of trial subjects:

This study was conducted in conformance with Good Clinical Practice 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	09 March 2015
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	United States: 59
Worldwide total number of subjects	59
EEA total number of subjects	0

Notes:

Subjects enrolled per age group

In utero	0
Preterm newborn - gestational age < 37 wk	0
Newborns (0-27 days)	0
Infants and toddlers (28 days-23 months)	0
Children (2-11 years)	0
Adolescents (12-17 years)	0
Adults (18-64 years)	31
From 65 to 84 years	28
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Participants were recruited at 12 clinical trial sites in the United States.

Pre-assignment

Screening details:

Participants were women and men between 18 and 80 years of age inclusive who had refractory chronic cough for at least one year without any abnormality considered to be significantly contributing to the chronic cough in chest radiograph or computed tomography thorax.

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	Cohort 1: Gefapixant > Placebo

Arm description:

50, 100, 150, or 200 mg Gefapixant BID for 4 days in Period 1 and placebo BID for 16 days in Period 2. For Cohort 1, there was a 3 to 7 day washout period between treatment periods.

Arm type	Experimental
Investigational medicinal product name	Gefapixant
Investigational medicinal product code	
Other name	AF-219
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Gefapixant: 50 mg, 100 mg, 150 mg, or 200 mg oral, administered as 1, 2, 3, or 4 50-mg tablets BID for 4 days

Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Placebo to Gefapixant, oral, administered BID for 16 days

Arm title	Cohort 1: Placebo > Gefapixant

Arm description:

Placebo BID for 16 days in Period 1 and Gefapixant 50, 100, 150, or 200 mg BID for 4 days in Period 2. For Cohort 1, there was a 3 to 7 day washout period between treatment periods.

Arm type	Experimental
Investigational medicinal product name	Gefapixant
Investigational medicinal product code	
Other name	AF-219
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Gefapixant: 50 mg, 100 mg, 150 mg, or 200 mg oral, administered as 1, 2, 3, or 4 50-mg tablets BID

for 4 days

Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Placebo to Gefapixant, oral, administered BID for 16 days

Arm title	Cohort 2: Gefapixant > Placebo

Arm description:

7.5, 15, 30, or 50 mg Gefapixant BID for 4 days in Period 1 and placebo BID for 16 days in Period 2. For Cohort 2, there was a 14 to 21 day washout period between treatment periods.

Arm type	Experimental
Investigational medicinal product name	Gefapixant
Investigational medicinal product code	
Other name	AF-219
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Gefapixant: 7.5 mg, 15 mg, 30 mg, or 50 mg oral, administered as 1, 2, or 4 7.5-mg tablets or 1 50-mg tablet BID for 4 days

Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Placebo to Gefapixant, oral, administered BID for 16 days

Arm title	Cohort 2: Placebo > Gefapixant

Arm description:

Placebo BID for 16 days in Period 1 and Gefapixant 7.5, 15, 30, or 50 mg BID for 4 days in Period 2. For Cohort 2, there was a 14 to 21 day washout period between treatment periods.

Arm type	Experimental
Investigational medicinal product name	Gefapixant
Investigational medicinal product code	
Other name	AF-219
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Gefapixant: 7.5 mg, 15 mg, 30 mg, or 50 mg oral, administered as 1, 2, or 4 7.5-mg tablets or 1 50-mg tablet BID for 4 days

Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Placebo to Gefapixant, oral, administered BID for 16 days

Number of subjects in period 1	Cohort 1: Gefapixant > Placebo	Cohort 1: Placebo > Gefapixant	Cohort 2: Gefapixant > Placebo
Started	15	14	15
Completed	14	13	15
Not completed	1	1	0
Adverse event, non-fatal	1	1	-

Number of subjects in period 1	Cohort 2: Placebo > Gefapixant
Started	15
Completed	15
Not completed	0
Adverse event, non-fatal	-

Period 2

Period 2 title	Period 2
Is this the baseline period?	No
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator

Arms

Are arms mutually exclusive?	Yes
Arm title	Cohort 1: Gefapixant > Placebo

Arm description:

50, 100, 150, or 200 mg Gefapixant BID for 4 days in Period 1 and placebo BID for 16 days in Period 2. For Cohort 1, there was a 3 to 7 day washout period between treatment periods.

Arm type	Experimental
Investigational medicinal product name	Gefapixant
Investigational medicinal product code	
Other name	AF-219
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Gefapixant: 50 mg, 100 mg, 150 mg, or 200 mg oral, administered as 1, 2, 3, or 4 50-mg tablets BID for 4 days

Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Placebo to Gefapixant, oral, administered BID for 16 days

Arm title	Cohort 1: Placebo > Gefapixant

Arm description:

Placebo BID for 16 days in Period 1 and Gefapixant 50, 100, 150, or 200 mg BID for 4 days in Period 2. For Cohort 1, there was a 3 to 7 day washout period between treatment periods.

Arm type	Experimental
Investigational medicinal product name	Gefapixant
Investigational medicinal product code	
Other name	AF-219
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Gefapixant: 50 mg, 100 mg, 150 mg, or 200 mg oral, administered as 1, 2, 3, or 4 50-mg tablets BID for 4 days

Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Placebo to Gefapixant, oral, administered BID for 16 days

Arm title	Cohort 2: Gefapixant > Placebo

Arm description:

7.5, 15, 30, or 50 mg Gefapixant BID for 4 days in Period 1 and placebo BID for 16 days in Period 2. For Cohort 2, there was a 14 to 21 day washout period between treatment periods.

Arm type	Experimental
Investigational medicinal product name	Gefapixant
Investigational medicinal product code	
Other name	AF-219
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Gefapixant: 7.5 mg, 15 mg, 30 mg, or 50 mg oral, administered as 1, 2, or 4 7.5-mg tablets or 1 50-mg tablet BID for 4 days

Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Placebo to Gefapixant, oral, administered BID for 16 days

Arm title	Cohort 2: Placebo > Gefapixant

Arm description:

Placebo BID for 16 days in Period 1 and Gefapixant 7.5, 15, 30, or 50 mg BID for 4 days in Period 2. For Cohort 2, there was a 14 to 21 day washout period between treatment periods.

Arm type	Experimental
Investigational medicinal product name	Gefapixant
Investigational medicinal product code	
Other name	AF-219
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Gefapixant: 7.5 mg, 15 mg, 30 mg, or 50 mg oral, administered as 1, 2, or 4 7.5-mg tablets or 1 50-mg tablet BID for 4 days

Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet

Routes of administration	Oral use

Dosage and administration details:

Placebo to Gefapixant, oral, administered BID for 16 days

Number of subjects in period 2	Cohort 1: Gefapixant > Placebo	Cohort 1: Placebo > Gefapixant	Cohort 2: Gefapixant > Placebo
Started	14	13	15
Completed	14	12	14
Not completed	0	1	1
Adverse event, non-fatal	-	1	1

Number of subjects in period 2	Cohort 2: Placebo > Gefapixant
Started	15
Completed	15
Not completed	0
Adverse event, non-fatal	-

Baseline characteristics

Reporting groups	
Reporting group title	Period 1

Reporting group description: -

Reporting group values	Period 1	Total	
Number of subjects	59	59	
Age Categorical Units: Subjects			
In utero	0	0	
Preterm newborn infants (gestational age < 37 wks)	0	0	
Newborns (0-27 days)	0	0	
Infants and toddlers (28 days-23 months)	0	0	
Children (2-11 years)	0	0	
Adolescents (12-17 years)	0	0	
Adults (18-64 years)	31	31	
From 65-84 years	28	28	
85 years and over	0	0	
Age Continuous Units: years			
arithmetic mean	61.7		
standard deviation	± 9.5	-	
Gender Categorical Units: Subjects			
Female	49	49	
Male	10	10	

End points

End points reporting groups

Reporting group title	Cohort 1: Gefapixant > Placebo
Reporting group description:	
50, 100, 150, or 200 mg Gefapixant BID for 4 days in Period 1 and placebo BID for 16 days in Period 2. For Cohort 1, there was a 3 to 7 day washout period between treatment periods.	
Reporting group title	Cohort 1: Placebo > Gefapixant
Reporting group description:	
Placebo BID for 16 days in Period 1 and Gefapixant 50, 100, 150, or 200 mg BID for 4 days in Period 2. For Cohort 1, there was a 3 to 7 day washout period between treatment periods.	
Reporting group title	Cohort 2: Gefapixant > Placebo
Reporting group description:	
7.5, 15, 30, or 50 mg Gefapixant BID for 4 days in Period 1 and placebo BID for 16 days in Period 2. For Cohort 2, there was a 14 to 21 day washout period between treatment periods.	
Reporting group title	Cohort 2: Placebo > Gefapixant
Reporting group description:	
Placebo BID for 16 days in Period 1 and Gefapixant 7.5, 15, 30, or 50 mg BID for 4 days in Period 2. For Cohort 2, there was a 14 to 21 day washout period between treatment periods.	
Reporting group title	Cohort 1: Gefapixant > Placebo
Reporting group description:	
50, 100, 150, or 200 mg Gefapixant BID for 4 days in Period 1 and placebo BID for 16 days in Period 2. For Cohort 1, there was a 3 to 7 day washout period between treatment periods.	
Reporting group title	Cohort 1: Placebo > Gefapixant
Reporting group description:	
Placebo BID for 16 days in Period 1 and Gefapixant 50, 100, 150, or 200 mg BID for 4 days in Period 2. For Cohort 1, there was a 3 to 7 day washout period between treatment periods.	
Reporting group title	Cohort 2: Gefapixant > Placebo
Reporting group description:	
7.5, 15, 30, or 50 mg Gefapixant BID for 4 days in Period 1 and placebo BID for 16 days in Period 2. For Cohort 2, there was a 14 to 21 day washout period between treatment periods.	
Reporting group title	Cohort 2: Placebo > Gefapixant
Reporting group description:	
Placebo BID for 16 days in Period 1 and Gefapixant 7.5, 15, 30, or 50 mg BID for 4 days in Period 2. For Cohort 2, there was a 14 to 21 day washout period between treatment periods.	
Subject analysis set title	Cohort 1: Gefapixant 50 mg
Subject analysis set type	Full analysis
Subject analysis set description:	
Gefapixant: 50 mg BID for 4 days in Period 1 or Period 2.	
Subject analysis set title	Cohort 1: Placebo to Gefapixant 50 mg
Subject analysis set type	Full analysis
Subject analysis set description:	
Placebo to Gefapixant 50 mg BID for 4 days in Period 1 or Period 2	
Subject analysis set title	Cohort 1: Gefapixant 100 mg
Subject analysis set type	Full analysis
Subject analysis set description:	
Gefapixant: 100 mg BID for 4 days in Period 1 or Period 2.	
Subject analysis set title	Cohort 1: Placebo to Gefapixant 100 mg
Subject analysis set type	Full analysis
Subject analysis set description:	
Placebo to Gefapixant 100 mg BID for 4 days in Period 1 or Period 2.	
Subject analysis set title	Cohort 1: Gefapixant 150 mg
Subject analysis set type	Full analysis

Subject analysis set description:

Gefapixant 150 mg BID for 4 days in Period 1 or Period 2.

Subject analysis set title	Cohort 1: Placebo to AF-219 150 mg
Subject analysis set type	Full analysis

Subject analysis set description:

Placebo to AF-219 150 mg BID for 4 days in Period 1 or Period 2.

Subject analysis set title	Cohort 1: Gefapixant 200 mg
Subject analysis set type	Full analysis

Subject analysis set description:

Gefapixant 200 mg BID for 4 days in Period 1 or Period 2.

Subject analysis set title	Cohort 1: Placebo to Gefapixant 200 mg
Subject analysis set type	Full analysis

Subject analysis set description:

Placebo to Gefapixant 200 mg BID for 4 days in Period 1 or Period 2.

Subject analysis set title	Cohort 2: Gefapixant 7.5 mg
Subject analysis set type	Full analysis

Subject analysis set description:

Gefapixant 7.5 mg BID for 4 days in Period 1 or Period 2.

Subject analysis set title	Cohort 2: Placebo to Gefapixant 7.5 mg
Subject analysis set type	Full analysis

Subject analysis set description:

Placebo to Gefapixant 7.5 mg BID for 4 days in Period 1 or Period 2.

Subject analysis set title	Cohort 2: Gefapixant 15 mg
Subject analysis set type	Full analysis

Subject analysis set description:

Gefapixant 15 mg BID for 4 days in Period 1 or Period 2.

Subject analysis set title	Cohort 2: Placebo to Gefapixant 15 mg
Subject analysis set type	Full analysis

Subject analysis set description:

Placebo to Gefapixant 15 mg BID for 4 days in Period 1 or Period 2.

Subject analysis set title	Cohort 2: Gefapixant 30 mg
Subject analysis set type	Full analysis

Subject analysis set description:

Gefapixant 30 mg BID for 4 days in Period 1 or Period 2.

Subject analysis set title	Cohort 2: Placebo to Gefapixant 30 mg
Subject analysis set type	Full analysis

Subject analysis set description:

Placebo to Gefapixant 30 mg BID for 4 days in Period 1 or Period 2.

Subject analysis set title	Cohort 2: Gefapixant 50 mg
Subject analysis set type	Full analysis

Subject analysis set description:

Gefapixant: 50 mg BID for 4 days in Period 1 or Period 2.

Subject analysis set title	Cohort 2: Placebo to Gefapixant 50 mg
Subject analysis set type	Full analysis

Subject analysis set description:

Placebo to Gefapixant 50 mg BID for 4 days in Period 1 or Period 2.

Subject analysis set title	Cohort 1
Subject analysis set type	Full analysis

Subject analysis set description:

50, 100, 150, or 200 mg Gefapixant BID for 4 days in Period 1 and placebo BID for 16 days in Period 2.
For Cohort 1, there was a 3 to 7 day washout period between treatment periods.
Placebo BID for 16 days in Period 1 and Gefapixant 50, 100, 150, or 200 mg BID for 4 days in Period 2.

For Cohort 1, there was a 3 to 7 day washout period between treatment periods.

Subject analysis set title	Cohort 2
Subject analysis set type	Full analysis

Subject analysis set description:

7.5, 15, 30, or 50 mg Gefapixant BID for 4 days in Period 1 and placebo BID for 16 days in Period 2. For Cohort 2, there was a 14 to 21 day washout period between treatment periods.
Placebo BID for 16 days in Period 1 and Gefapixant 7.5, 15, 30, or 50 mg BID for 4 days in Period 2. For Cohort 2, there was a 14 to 21 day washout period between treatment periods.

Subject analysis set title	Gefapixant
Subject analysis set type	Full analysis

Subject analysis set description:

Gefapixant: 50 mg/100 mg/150 mg/200 mg (all BID for 4 days in Period 1 or Period 2). For Cohort 1, there was a 3 to 7 day washout period between treatment periods. Gefapixant: 7.5 mg/15 mg/30 mg/50 mg (all BID for 4 days in Period 1 or Period 2). For Cohort 2, there was a 14 to 21 day washout period between treatment periods.

Subject analysis set title	Placebo
Subject analysis set type	Full analysis

Subject analysis set description:

Placebo to Gefapixant (BID for 16 days). For Cohort 1, there was a 3 to 7 day washout period between treatment periods. Placebo to Gefapixant (BID for 16 days). For Cohort 2, there was a 14 to 21 day washout period between treatment periods.

Subject analysis set title	Cohort 1 - Gefapixant
Subject analysis set type	Full analysis

Subject analysis set description:

Participants randomized to receive Gefapixant: 50 mg/100 mg/150 mg/200 mg (all BID for 4 days in Period 1 or Period 2). For Cohort 1, there was a 3 to 7 day washout period between treatment periods.

Subject analysis set title	Cohort 1 - Placebo
Subject analysis set type	Full analysis

Subject analysis set description:

Participants randomized to receive Placebo to Gefapixant (BID for 16 days). For Cohort 1, there was a 3 to 7 day washout period between treatment periods.

Subject analysis set title	Cohort 2 - Gefapixant
Subject analysis set type	Full analysis

Subject analysis set description:

Participants randomized to receive Gefapixant: 7.5 mg/15 mg/30 mg/50 mg (all BID for 4 days in Period 1 or Period 2). For Cohort 2, there was a 14 to 21 day washout period between treatment periods.

Subject analysis set title	Cohort 2- Placebo
Subject analysis set type	Full analysis

Subject analysis set description:

Participants randomized to receive Placebo to Gefapixant (BID for 16 days). For Cohort 2, there was a 14 to 21 day washout period between treatment periods.

Primary: Change from Baseline in Awake Cough Frequency for Cohort 1

End point title	Change from Baseline in Awake Cough Frequency for Cohort

End point description:

Awake Objective Frequency (per hour) = The total number of cough events during the monitoring period (in general, 24-hr interval) the participant is awake divided by the total duration (in hours) for the monitoring period the participant is awake. 24 hour sound recordings were collected using a digital recording device. The analysis population consisted of all randomized participants who took at least 1 dose of study medication and provided at least 1 baseline and at least 1 post baseline endpoint observation for the awake objective cough frequency endpoint for Cohort 1.

End point type	Primary

End point timeframe:

24 hours (while awake) on Days 0 and 22 (Baseline) and 24 hours (while awake) after dosing on Days 4, 8, 12, 16, 26, 30, 34, and 38

Notes:

[1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: No statistical analysis was planned or performed for this endpoint.

End point values	Cohort 1: Gefapixant 50 mg	Cohort 1: Placebo to Gefapixant 50 mg	Cohort 1: Gefapixant 100 mg	Cohort 1: Placebo to Gefapixant 100 mg
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	26	25	24	25
Units: Coughs/hour				
arithmetic mean (standard deviation)	-26.5 (± 37.79)	-0.4 (± 12.53)	-29.2 (± 39.11)	-0.4 (± 15.51)

End point values	Cohort 1: Gefapixant 150 mg	Cohort 1: Placebo to AF-219 150 mg	Cohort 1: Gefapixant 200 mg	Cohort 1: Placebo to Gefapixant 200 mg
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	23	22	25	25
Units: Coughs/hour				
arithmetic mean (standard deviation)	-25.2 (± 38.39)	4.3 (± 20.37)	-26.2 (± 40.75)	4 (± 22.56)

Statistical analyses

No statistical analyses for this end point

Primary: Change from Baseline in Awake Cough Frequency for Cohort 2

End point title	Change from Baseline in Awake Cough Frequency for Cohort

End point description:

Awake Objective Frequency (per hour) = The total number of cough events during the monitoring period (in general, 24-hr interval) the participant is awake divided by the total duration (in hours) for the monitoring period the participant is awake. 24 hour sound recordings were collected using a digital recording device. The analysis population consisted of all randomized subjects who took at least 1 dose of study medication and provided at least 1 baseline and at least 1 post baseline primary endpoint observation for the awake objective cough frequency endpoint for Cohort 2.

End point type	Primary

End point timeframe:

24 hours (while awake) on Days 0 and 22 (Baseline) and 24 hours (while awake) after dosing on Days 4, 8, 12, 16, 26, 30, 34, and 38

Notes:

[2] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: No statistical analysis was planned or performed for this endpoint.

End point values	Cohort 2: Gefapixant 7.5 mg	Cohort 2: Placebo to Gefapixant 7.5 mg	Cohort 2: Gefapixant 15 mg	Cohort 2: Placebo to Gefapixant 15 mg
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	29	28	30	29
Units: Coughs/hour				
arithmetic mean (standard deviation)	-11 (± 31.62)	-2.6 (± 16.47)	-14.9 (± 30.59)	-4.7 (± 12.24)

End point values	Cohort 2: Gefapixant 30 mg	Cohort 2: Placebo to Gefapixant 30 mg	Cohort 2: Gefapixant 50 mg	Cohort 2: Placebo to Gefapixant 50 mg
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	29	29	29	27
Units: Coughs/hour				
arithmetic mean (standard deviation)	-23.9 (± 37.99)	2.1 (± 16.71)	-24.3 (± 35.48)	1.1 (± 23.39)

Statistical analyses

No statistical analyses for this end point

Primary: Percent Change from Baseline in Awake Cough Frequency for Cohort 1

End point title	Percent Change from Baseline in Awake Cough Frequency for Cohort 1[3]

End point description:

Awake Objective Frequency (per hour) = The total number of cough events during the monitoring period (in general, 24-hr interval) the participant is awake divided by the total duration (in hours) for the monitoring period the participant is awake. 24 hour sound recordings were collected using a digital recording device. The analysis population consisted of all randomized participants who took at least 1 dose of study medication and provided at least 1 baseline and at least 1 post baseline endpoint observation for the awake objective cough frequency endpoint for Cohort 1.

End point type	Primary

End point timeframe:

24 hours (while awake) on Days 0 and 22 (Baseline) and 24 hours (while awake) after dosing on Days 4, 8, 12, 16, 26, 30, 34, and 38

Notes:

[3] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: No statistical analysis was planned or performed for this endpoint.

End point values	Cohort 1: Gefapixant 50 mg	Cohort 1: Placebo to Gefapixant 50 mg	Cohort 1: Gefapixant 100 mg	Cohort 1: Placebo to Gefapixant 100 mg
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	26	25	24	25
Units: Percent Change				
arithmetic mean (standard deviation)	-20.6 (± 84.29)	-0.1 (± 33.75)	-31.7 (± 70.27)	1.9 (± 35.18)

End point values	Cohort 1: Gefapixant 150 mg	Cohort 1: Placebo to AF-219 150 mg	Cohort 1: Gefapixant 200 mg	Cohort 1: Placebo to Gefapixant 200 mg
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	23	22	25	25
Units: Percent Change				
arithmetic mean (standard deviation)	-22 (± 82.84)	-0.1 (± 39.55)	-27.9 (± 57.03)	15.1 (± 48.38)

Statistical analyses

No statistical analyses for this end point

Primary: Percent Change from Baseline in Awake Cough Frequency - Cohort 2

End point title	Percent Change from Baseline in Awake Cough Frequency - Cohort 2[4]

End point description:

Awake Objective Frequency (per hour) = The total number of cough events during the monitoring period (in general, 24-hr interval) the participant is awake divided by the total duration (in hours) for the monitoring period the participant is awake. 24 hour sound recordings were collected using a digital recording device. The analysis population consisted of all randomized participants who took at least 1 dose of study medication and provided at least 1 baseline and at least 1 post baseline endpoint observation for the awake objective cough frequency endpoint for Cohort 2.

End point type	Primary

End point timeframe:

24 hours (while awake) on Days 0 and 22 (Baseline) and 24 hours (while awake) after dosing on Days 4, 8, 12, 16, 26, 30, 34, and 38

Notes:

[4] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: No statistical analysis was planned or performed for this endpoint.

End point values	Cohort 2: Gefapixant 7.5 mg	Cohort 2: Placebo to Gefapixant 7.5 mg	Cohort 2: Gefapixant 15 mg	Cohort 2: Placebo to Gefapixant 15 mg
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	29	28	30	29
Units: Percent Change				
arithmetic mean (standard deviation)	5 (± 125.05)	-3.8 (± 36.13)	-21.4 (± 39.32)	-6.4 (± 33.78)

End point values	Cohort 2: Gefapixant 30 mg	Cohort 2: Placebo to Gefapixant 30 mg	Cohort 2: Gefapixant 50 mg	Cohort 2: Placebo to Gefapixant 50 mg
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	29	29	29	27

Units: Percent Change				
arithmetic mean (standard deviation)	-26.3 (± 61.01)	-1.1 (± 64.38)	-28.1 (± 74.9)	23.1 (± 92.6)

Statistical analyses

No statistical analyses for this end point

Primary: Baseline (Predose) Awake Cough Frequency for Cohort 1 and Cohort 2

End point title	Baseline (Predose) Awake Cough Frequency for Cohort 1 and Cohort 2[5]

End point description:

Awake Objective Frequency (per hour) = The total number of cough events during the monitoring period (in general, 24-hr interval) the participant is awake divided by the total duration (in hours) for the monitoring period the participant is awake. 24 hour sound recordings were collected using a digital recording device. The analysis population consisted of all randomized participants who took at least 1 dose of study medication and provided at least 1 baseline observation for the awake objective cough frequency endpoint for Cohort 1.

End point type	Primary

End point timeframe:

24 hours (while awake) on Days 0 and 22 (Baseline)

Notes:

[5] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: No statistical analysis was planned or performed for this endpoint.

End point values	Cohort 1 - Gefapixant	Cohort 1 - Placebo	Cohort 2 - Gefapixant	Cohort 2- Placebo
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	28	26	30	29
Units: Coughs/hour				
arithmetic mean (standard deviation)	54.5 (± 41.09)	52.8 (± 40.44)	49.6 (± 44.01)	46.1 (± 39.82)

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in Total (24-hour) Cough Frequency - Cohort 1

End point title	Change from Baseline in Total (24-hour) Cough Frequency - Cohort 1

End point description:

Total (0 - 24 hours) Objective Cough Frequency = Total number of cough events during the monitoring period divided by the total duration (in hours) for the monitoring period. 24 hour sound recordings were collected using a digital recording device. The analysis population consisted of all randomized participants who took at least 1 dose of study medication and provided at least 1 baseline and at least 1 post baseline endpoint observation for the cough frequency endpoint for Cohort 1.

End point type	Secondary

End point timeframe:

24 hours on Days 0 and 22 (Baseline) and 24 hours after dosing on Days 4, 8, 12, 16, 26, 30, 34, and 38

End point values	Cohort 1: Gefapixant 50 mg	Cohort 1: Placebo to Gefapixant 50 mg	Cohort 1: Gefapixant 100 mg	Cohort 1: Placebo to Gefapixant 100 mg
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	26	25	24	25
Units: Coughs/hour				
arithmetic mean (standard deviation)	-18.4 (± 25.77)	-0.7 (± 10.76)	-19.3 (± 27.83)	-0.1 (± 10.5)

End point values	Cohort 1: Gefapixant 150 mg	Cohort 1: Placebo to AF-219 150 mg	Cohort 1: Gefapixant 200 mg	Cohort 1: Placebo to Gefapixant 200 mg
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	23	22	25	25
Units: Coughs/hour				
arithmetic mean (standard deviation)	-17.2 (± 26.27)	3.2 (± 16.21)	-18.1 (± 29.98)	4 (± 17.03)

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in Awake (0 - 8 hours) Cough Frequency - Cohort 1

End point title	Change from Baseline in Awake (0 - 8 hours) Cough Frequency - Cohort 1

End point description:

Awake (0 - 8 hours) Objective Cough Frequency = Total number of cough events during the monitoring period the participant was awake for the first 8 hours after the participant took their study medication divided by 8 or the total duration (in hours) for the monitoring period the participant was awake whichever is less. 24 hour sound recordings were collected with a digital recording device. The analysis population consisted of all randomized participants who took at least 1 dose of study medication and provided at least 1 baseline and at least 1 post baseline endpoint observation for the awake cough frequency endpoint for Cohort 1.

End point type	Secondary

End point timeframe:

First 8 hours (while awake) on Days 0 and 22 (Baseline) and the first 8 hours (while awake) after dosing on Days 4, 8, 12, 16, 26, 30, 34, and 38

End point values	Cohort 1: Gefapixant 50 mg	Cohort 1: Placebo to Gefapixant 50 mg	Cohort 1: Gefapixant 100 mg	Cohort 1: Placebo to Gefapixant 100 mg
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	26	25	24	25
Units: Coughs/hour				
arithmetic mean (standard deviation)	-25.8 (± 38.89)	-5.1 (± 17.55)	-27 (± 35.85)	0.5 (± 15.16)

End point values	Cohort 1: Gefapixant 150 mg	Cohort 1: Placebo to AF-219 150 mg	Cohort 1: Gefapixant 200 mg	Cohort 1: Placebo to Gefapixant 200 mg
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	23	22	25	25
Units: Coughs/hour				
arithmetic mean (standard deviation)	-23.3 (± 37.95)	4.8 (± 28.43)	-28.4 (± 39.76)	2.9 (± 23.02)

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in Sleep Cough Frequency - Cohort 1

End point title	Change from Baseline in Sleep Cough Frequency - Cohort 1

End point description:

Sleep Objective Cough Frequency = Total number of cough events during the monitoring period the participant is asleep divided by the total duration (in hours) for the monitoring period the participant is asleep. 24 hour sound recording were collected with a digital recording device. The analysis population consisted of all randomized participants who took at least 1 dose of study medication and provided at least 1 baseline and at least 1 post baseline endpoint observation for the sleep cough frequency endpoint for Cohort 1.

End point type	Secondary

End point timeframe:

24 hours (while asleep) on Days 0 and 22 (Baseline) and 24 hours (while asleep) after dosing on Days 4, 8, 12, 16, 26, 30, 34, and 38

End point values	Cohort 1: Gefapixant 50 mg	Cohort 1: Placebo to Gefapixant 50 mg	Cohort 1: Gefapixant 100 mg	Cohort 1: Placebo to Gefapixant 100 mg
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	24	24	21	24
Units: Coughs/hour				
arithmetic mean (standard deviation)	-3.8 (± 8.66)	-0.2 (± 13.23)	-3.3 (± 11.86)	-1.1 (± 8.6)

End point values	Cohort 1: Gefapixant 150 mg	Cohort 1: Placebo to AF-219 150 mg	Cohort 1: Gefapixant 200 mg	Cohort 1: Placebo to Gefapixant 200 mg
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	22	22	24	25
Units: Coughs/hour				
arithmetic mean (standard deviation)	-1.6 (± 6.54)	0.1 (± 6.96)	-3.2 (± 9.62)	0.2 (± 10.17)

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline of the Mean Total Daily Cough Severity Diary (CSD) Score for Cohort 1

End point title	Change from Baseline of the Mean Total Daily Cough Severity Diary (CSD) Score for Cohort 1

End point description:

The daily CSD instrument has a total of 7 items (daily cough frequency, daily number of coughing fits or episodes, daily number of urges to cough, daily cough harshness score, daily cough physical discomfort score, daily level of disruption of activities due to cough, daily level of sleep disruption due to cough, in the instrument, each with scores ranging from 0 (best) to 10 (worst). The total daily CSD score is the sum of these 7 item scores. Mean total daily CSD score for each dose period is defined as the average of the total daily scores for the corresponding dose period. Baseline CSD score is defined as the average of CSD scores at screening and baseline. The analysis population consisted of all randomized participants who took at least 1 dose of study medication and provided at least 1 baseline and at least 1 post baseline endpoint observation for the cough severity diary endpoint for Cohort 1.

End point type	Secondary

End point timeframe:

Baseline (Days 0 and 22) and daily during the treatment period (up to Day 39)

End point values	Cohort 1: Gefapixant 50 mg	Cohort 1: Placebo to Gefapixant 50 mg	Cohort 1: Gefapixant 100 mg	Cohort 1: Placebo to Gefapixant 100 mg
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	28	28	27	27
Units: Scores on a scale				
arithmetic mean (standard deviation)	-0.7 (± 1.56)	0 (± 1.1)	-1.1 (± 2.21)	0.2 (± 1.35)

End point values	Cohort 1: Gefapixant 150 mg	Cohort 1: Placebo to AF-219 150 mg	Cohort 1: Gefapixant 200 mg	Cohort 1: Placebo to Gefapixant 200 mg

Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	26	27	26	27
Units: Scores on a scale				
arithmetic mean (standard deviation)	-1.5 (± 2.38)	0.1 (± 1.49)	-1.6 (± 2.7)	0.1 (± 1.54)

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in the Acute Leicester Cough Questionnaire (LCQ) Instrument for Cohort 1 and Cohort 2

End point title	Change from Baseline in the Acute Leicester Cough Questionnaire (LCQ) Instrument for Cohort 1 and Cohort 2

End point description:

The LCQ instrument has 3 domains in the LCQ instrument: Physical (items 1, 2, 3, 9, 10, 11, 14 and 15), Psychological (4, 5, 6, 12, 13, 16, and 17), and Social (7, 8, 18, and 19). For each domain, the domain score (range 1 - 7) is the sum of individual item score within the domain divided by the number of items in the domain; total LCQ score (range 3-21) is the sum of the 3 domain scores. The analysis population consisted of all randomized participants who took at least 1 dose of study medication and provided at least 1 baseline and at least 1 post baseline endpoint observation for LCQ instrument endpoint.

End point type	Secondary

End point timeframe:

Days 0 and 22 (Baseline) and Days 17 and 39

End point values	Cohort 1 - Gefapixant	Cohort 1 - Placebo	Cohort 2 - Gefapixant	Cohort 2- Placebo
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	27	28	30	29
Units: Scores on a scale				
arithmetic mean (standard deviation)				
Psychological Domain Score	1.2 (± 1.63)	-0.2 (± 1.13)	1.2 (± 1.7)	0.1 (± 1.01)
Physical Domain Score	0.9 (± 1.45)	-0.4 (± 0.91)	1 (± 1.35)	0.1 (± 1)
Social Domain Score	0.9 (± 1.69)	-0.3 (± 1.21)	1.4 (± 1.69)	-0.1 (± 0.94)
Total Acute Leicester Score	3 (± 4.35)	-0.8 (± 2.74)	3.6 (± 4.44)	0.1 (± 2.48)

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline of Cough Visual Analogue Scale (VAS) Score for Cohort 1

End point title	Change from Baseline of Cough Visual Analogue Scale (VAS) Score for Cohort 1

End point description:

Cough VAS: scored from 0 to 100 using a 10 mm visual analogue scale with 0 at 0mm and 100 at 10mm. Baseline cough VAS is defined as average of screening and baseline cough VAS. The analysis

population consisted of all randomized participants who took at least 1 dose of study medication and provided at least 1 baseline and at least 1 post baseline endpoint observation for the cough VAS scores for Cohort 1.

End point type	Secondary

End point timeframe:

Screening, Days 0 and 22 (Baseline), and Days 4, 8, 12, 16, 26, 30, 34, and 38

End point values	Cohort 1: Gefapixant 50 mg	Cohort 1: Placebo to Gefapixant 50 mg	Cohort 1: Gefapixant 100 mg	Cohort 1: Placebo to Gefapixant 100 mg
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	27	28	27	27
Units: Scores on a scale				
arithmetic mean (standard deviation)	-14.5 (± 27.53)	-3.8 (± 16.14)	-26.3 (± 31.36)	-6 (± 17.37)

End point values	Cohort 1: Gefapixant 150 mg	Cohort 1: Placebo to AF-219 150 mg	Cohort 1: Gefapixant 200 mg	Cohort 1: Placebo to Gefapixant 200 mg
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	26	27	26	27
Units: Scores on a scale				
arithmetic mean (standard deviation)	-28.2 (± 31.93)	-2.1 (± 23.26)	-30.8 (± 32.15)	2.7 (± 22.03)

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in Total (24-hour) Cough Frequency - Cohort 2

End point title	Change from Baseline in Total (24-hour) Cough Frequency - Cohort 2

End point description:

Total (0 - 24 hours) Objective Cough Frequency = Total number of cough events during the monitoring period divided by the total duration (in hours) for the monitoring period. 24 hour sound recordings were collected at Baseline (Day 0) and on Days 4, 8, 12, 16, 22, 26, 30, 34, and 38 using a digital recording device. The analysis population consisted of all randomized participants who took at least 1 dose of study medication and provided at least 1 baseline and at least 1 post baseline endpoint observation for the cough frequency endpoint for Cohort 2.

End point type	Secondary

End point timeframe:

24 hours on Days 0 and 22 (Baseline) and 24 hours after dosing on Days 4, 8, 12, 16, 26, 30, 34, and 38

End point values	Cohort 2: Gefapixant 7.5 mg	Cohort 2: Placebo to Gefapixant 7.5 mg	Cohort 2: Gefapixant 15 mg	Cohort 2: Placebo to Gefapixant 15 mg
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	29	28	30	29
Units: Coughs/hour				
arithmetic mean (standard deviation)	-7.6 (± 23.55)	-1.6 (± 11.88)	-11.4 (± 21.15)	-2.8 (± 10.43)

End point values	Cohort 2: Gefapixant 30 mg	Cohort 2: Placebo to Gefapixant 30 mg	Cohort 2: Gefapixant 50 mg	Cohort 2: Placebo to Gefapixant 50 mg
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	29	29	29	27
Units: Coughs/hour				
arithmetic mean (standard deviation)	-17.5 (± 27.88)	2.3 (± 10.56)	-16.7 (± 24.84)	2.7 (± 16.48)

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in Awake (0 - 8 hours) Cough Frequency - Cohort 2

End point title	Change from Baseline in Awake (0 - 8 hours) Cough Frequency - Cohort 2

End point description:

Awake (0 - 8 hours) Objective Cough Frequency = Total number of cough events during the monitoring period the participant was awake for the first 8 hours after the participant took their study medication divided by 8 or the total duration (in hours) for the monitoring period the participant was awake whichever is less. The analysis population consisted of all randomized participants who took at least 1 dose of study medication and provided at least 1 baseline and at least 1 post baseline endpoint observation for the awake cough frequency endpoint for Cohort 2.

End point type	Secondary

End point timeframe:

First 8 hours (while awake) on Days 0 and 22 (Baseline) and the first 8 hours (while awake) after dosing on Days 4, 8, 12, 16, 26, 30, 34, and 38

End point values	Cohort 2: Gefapixant 7.5 mg	Cohort 2: Placebo to Gefapixant 7.5 mg	Cohort 2: Gefapixant 15 mg	Cohort 2: Placebo to Gefapixant 15 mg
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	29	28	30	29
Units: Coughs/hour				
arithmetic mean (standard deviation)	-8.5 (± 34.52)	0.2 (± 24.54)	-15.7 (± 29.03)	-0.5 (± 17.07)

End point values	Cohort 2: Gefapixant 30 mg	Cohort 2: Placebo to Gefapixant 30 mg	Cohort 2: Gefapixant 50 mg	Cohort 2: Placebo to Gefapixant 50 mg
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	29	29	29	27
Units: Coughs/hour				
arithmetic mean (standard deviation)	-22.4 (± 37.68)	9.5 (± 23.58)	-22.8 (± 38.88)	6.3 (± 30.58)

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in Sleep Cough Frequency - Cohort 2

End point title	Change from Baseline in Sleep Cough Frequency - Cohort 2

End point description:

Sleep Objective Cough Frequency = Total number of cough events during the monitoring period the participant is asleep divided by the total duration (in hours) for the monitoring period the participant is asleep. The analysis population consisted of all randomized participants who took at least 1 dose of study medication and provided at least 1 baseline and at least 1 post baseline endpoint observation for the sleep cough frequency endpoint for Cohort 2.

End point type	Secondary

End point timeframe:

24 hours (while asleep) on Days 0 and 22 (Baseline) and 24 hours (while asleep) after dosing on Days 4, 8, 12, 16, 26, 30, 34, and 38

End point values	Cohort 2: Gefapixant 7.5 mg	Cohort 2: Placebo to Gefapixant 7.5 mg	Cohort 2: Gefapixant 15 mg	Cohort 2: Placebo to Gefapixant 15 mg
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	29	28	30	29
Units: Coughs/hour				
arithmetic mean (standard deviation)	-1.2 (± 22.56)	1.2 (± 8.44)	-4.6 (± 25.04)	-0.6 (± 4.61)

End point values	Cohort 2: Gefapixant 30 mg	Cohort 2: Placebo to Gefapixant 30 mg	Cohort 2: Gefapixant 50 mg	Cohort 2: Placebo to Gefapixant 50 mg
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	29	29	28	27
Units: Coughs/hour				
arithmetic mean (standard deviation)	-4.2 (± 21.38)	0.2 (± 5.14)	-4.4 (± 24.38)	4.1 (± 17.08)

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline of the Mean Total Daily Cough Severity Diary (CSD) Score for Cohort 2

End point title	Change from Baseline of the Mean Total Daily Cough Severity Diary (CSD) Score for Cohort 2

End point description:

The daily CSD instrument has a total of 7 items (daily cough frequency, daily number of coughing fits or episodes, daily number of urges to cough, daily cough harshness score, daily cough physical discomfort score, daily level of disruption of activities due to cough, daily level of sleep disruption due to cough, in the instrument, each with scores ranging from 0 (best) to 10 (worst). The total daily CSD score is the sum of these 7 item scores. Mean total daily CSD score for each dose period is defined as the average of the total daily scores for the corresponding dose period. Baseline CSD score is defined as the average of CSD scores at screening and baseline. The analysis population consisted of all randomized participants who took at least 1 dose of study medication and provided at least 1 baseline and at least 1 post baseline endpoint observation for the cough severity diary endpoint for Cohort 2.

End point type	Secondary

End point timeframe:

Baseline (Days 0 and 22) and daily during the treatment period (up to Day 39)

End point values	Cohort 2: Gefapixant 7.5 mg	Cohort 2: Placebo to Gefapixant 7.5 mg	Cohort 2: Gefapixant 15 mg	Cohort 2: Placebo to Gefapixant 15 mg
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	30	28	30	28
Units: Scores on a scale				
arithmetic mean (standard deviation)	-1 (± 1.41)	-0.3 (± 1.13)	-1.2 (± 1.78)	-0.3 (± 1.4)

End point values	Cohort 2: Gefapixant 30 mg	Cohort 2: Placebo to Gefapixant 30 mg	Cohort 2: Gefapixant 50 mg	Cohort 2: Placebo to Gefapixant 50 mg
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	30	28	29	28
Units: Scores on a scale				
arithmetic mean (standard deviation)	-1.7 (± 2.12)	-0.4 (± 0.88)	-1.6 (± 2.55)	-0.6 (± 1.22)

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline of Cough Visual Analogue Scale (VAS) Score for Cohort 2

End point title	Change from Baseline of Cough Visual Analogue Scale (VAS) Score for Cohort 2

End point description:

Cough VAS: scored from 0 to 100 using a 10 mm visual analogue scale with 0 at 0mm and 100 at 10mm. Baseline cough VAS is defined as average of screening and baseline cough VAS. The analysis population consisted of all randomized participants who took at least 1 dose of study medication and provided at least 1 baseline and at least 1 post baseline endpoint observation for the cough VAS scores for Cohort 2.

End point type	Secondary

End point timeframe:

Screening, Days 0 and 22 (Baseline), and Days 4, 8, 12, 16, 26, 30, 34, and 38

End point values	Cohort 2: Gefapixant 7.5 mg	Cohort 2: Placebo to Gefapixant 7.5 mg	Cohort 2: Gefapixant 15 mg	Cohort 2: Placebo to Gefapixant 15 mg
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	30	29	30	29
Units: Scores on a scale				
arithmetic mean (standard deviation)	-12.6 (± 23.49)	-6.4 (± 23.07)	-17.4 (± 26.32)	-9.9 (± 20.01)

End point values	Cohort 2: Gefapixant 30 mg	Cohort 2: Placebo to Gefapixant 30 mg	Cohort 2: Gefapixant 50 mg	Cohort 2: Placebo to Gefapixant 50 mg
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	30	29	29	29
Units: Scores on a scale				
arithmetic mean (standard deviation)	-23.3 (± 29.81)	-7.7 (± 12.91)	-24.9 (± 35.69)	-9.3 (± 19.04)

Statistical analyses

No statistical analyses for this end point

Secondary: Baseline (Predose) Total (24-hour) Cough Frequency for Cohort 1 and Cohort 2

End point title	Baseline (Predose) Total (24-hour) Cough Frequency for Cohort 1 and Cohort 2

End point description:

Total (0 - 24 hours) Objective Cough Frequency = Total number of cough events during the monitoring period divided by the total duration (in hours) for the monitoring period. 24 hour sound recordings were collected using a digital recording device. The analysis population consisted of all randomized participants who took at least 1 dose of study medication and provided at least 1 baseline endpoint

observation for the cough frequency endpoint for Cohort 1 and for Cohort 2.

End point type	Secondary

End point timeframe:

24 hours on Days 0 and 22 (Baseline)

End point values	Cohort 1 - Gefapixant	Cohort 1 - Placebo	Cohort 2 - Gefapixant	Cohort 2- Placebo
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	28	26	30	29
Units: Coughs/hour				
arithmetic mean (standard deviation)	39.7 (± 28.38)	37.9 (± 27.46)	36.3 (± 32.28)	32.2 (± 27.97)

Statistical analyses

No statistical analyses for this end point

Secondary: Baseline (Predose) Awake (0 - 8 hours) Cough Frequency for Cohort 1 and Cohort 2

End point title	Baseline (Predose) Awake (0 - 8 hours) Cough Frequency for Cohort 1 and Cohort 2

End point description:

Awake (0 - 8 hours) Objective Cough Frequency = Total number of cough events during the monitoring period the participant was awake for the first 8 hours after the participant took their study medication divided by 8 or the total duration (in hours) for the monitoring period the participant was awake whichever is less. 24 hour sound recordings were collected with a digital recording device. The analysis population consisted of all randomized participants who took at least 1 dose of study medication and provided at least 1 baseline for the awake cough frequency endpoint for Cohort 1 and Cohort 2.

End point type	Secondary

End point timeframe:

First 8 hours (while awake) on Days 0 and 22 (Baseline)

End point values	Cohort 1 - Gefapixant	Cohort 1 - Placebo	Cohort 2 - Gefapixant	Cohort 2- Placebo
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	28	26	30	29
Units: Coughs/hour				
arithmetic mean (standard deviation)	51.8 (± 41.09)	53.3 (± 42.3)	47.2 (± 42.09)	42.2 (± 39.42)

Statistical analyses

No statistical analyses for this end point

Secondary: Baseline (Predose) for Sleep Cough Frequency for Cohort 1 and Cohort 2

End point title	Baseline (Predose) for Sleep Cough Frequency for Cohort 1 and Cohort 2

End point description:

Sleep Objective Cough Frequency = Total number of cough events during the monitoring period the participant is asleep divided by the total duration (in hours) for the monitoring period the participant is asleep. 24 hour sound recording were collected with a digital recording device. The analysis population consisted of all randomized participants who took at least 1 dose of study medication and provided at least 1 baseline for the sleep cough frequency endpoint for Cohort 1 and Cohort 2

End point type	Secondary

End point timeframe:

24 hours (while asleep) on Days 0 and 22 (Baseline)

End point values	Cohort 1 - Gefapixant	Cohort 1 - Placebo	Cohort 2 - Gefapixant	Cohort 2- Placebo
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	27	26	30	29
Units: Coughs/hour				
arithmetic mean (standard deviation)	8.3 (± 9.3)	7.8 (± 9.8)	10.1 (± 26.77)	5.6 (± 7.58)

Statistical analyses

No statistical analyses for this end point

Secondary: Baseline (Predose) for the Mean Total Daily Cough Severity Diary (CSD) Score for Cohort 1 and Cohort 2

End point title	Baseline (Predose) for the Mean Total Daily Cough Severity Diary (CSD) Score for Cohort 1 and Cohort 2

End point description:

The daily CSD instrument has a total of 7 items (daily cough frequency, daily number of coughing fits or episodes, daily number of urges to cough, daily cough harshness score, daily cough physical discomfort score, daily level of disruption of activities due to cough, daily level of sleep disruption due to cough, in the instrument, each with scores ranging from 0 (best) to 10 (worst). The total daily CSD score is the sum of these 7 item scores. Mean total daily CSD score for each dose period is defined as the average of the total daily scores for the corresponding dose period. Baseline CSD score is defined as the average of CSD scores at screening and baseline. The analysis population consisted of all randomized participants who took at least 1 dose of study medication and provided at least 1 baseline for the cough severity diary endpoint for Cohort 1 and Cohort 2.

End point type	Secondary

End point timeframe:

Baseline (Days 0 and 22)

End point values	Cohort 1 - Gefapixant	Cohort 1 - Placebo	Cohort 2 - Gefapixant	Cohort 2- Placebo
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	28	28	30	28
Units: Scores on a scale				
arithmetic mean (standard deviation)	4.2 (± 1.89)	3.7 (± 1.61)	4.5 (± 1.98)	4.5 (± 1.93)

Statistical analyses

No statistical analyses for this end point

Secondary: Baseline (Predose) for the Acute Leicester Cough Questionnaire (LCQ) Instrument for Cohort 1 and Cohort 2

End point title	Baseline (Predose) for the Acute Leicester Cough Questionnaire (LCQ) Instrument for Cohort 1 and Cohort 2

End point description:

The LCQ instrument has 3 domains in the LCQ instrument: Physical (items 1, 2, 3, 9, 10, 11, 14 and 15), Psychological (4, 5, 6, 12, 13, 16, and 17), and Social (7, 8, 18, and 19). For each domain, the domain score (range 1 - 7) is the sum of individual item score within the domain divided by the number of items in the domain; total LCQ score (range 3-21) is the sum of the 3 domain scores. The analysis population consisted of all randomized participants who took at least 1 dose of study medication and provided at least 1 baseline observation for the LCQ instrument endpoint for Cohort 1 and Cohort 2.

End point type	Secondary

End point timeframe:

Days 0 and 22 (Baseline)

End point values	Cohort 1 - Gefapixant	Cohort 1 - Placebo	Cohort 2 - Gefapixant	Cohort 2- Placebo
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	28	28	30	29
Units: Scores on a scale				
arithmetic mean (standard deviation)				
Psychological Domain Score	3.8 (± 1.21)	4.1 (± 1.45)	3.9 (± 1.57)	4.1 (± 1.56)
Physical Domain Score	4.4 (± 0.99)	4.7 (± 1.06)	4.8 (± 1.19)	5 (± 1)
Social Domain Score	4.2 (± 1.22)	4.3 (± 1.21)	3.9 (± 1.57)	4.2 (± 1.57)
Total Acute Leicester Score	12.3 (± 3.13)	13.1 (± 3.41)	12.6 (± 4.04)	13.3 (± 3.81)

Statistical analyses

No statistical analyses for this end point

Secondary: Baseline (Predose) for Cough Visual analogue Scale (VAS) for Cohort 1 and Cohort 2

End point title	Baseline (Predose) for Cough Visual analogue Scale (VAS) for Cohort 1 and Cohort 2

End point description:

Cough VAS: scored from 0 to 100 using a 10 mm visual analogue scale with 0 at 0mm and 100 at 10mm. Baseline cough VAS is defined as average of screening and baseline cough VAS. The analysis population consisted of all randomized participants who took at least 1 dose of study medication and provided at least 1 baseline observation for the cough VAS score for Cohort 1 and Cohort 2.

End point type	Secondary

End point timeframe:

Screening, Days 0 and 22 (Baseline)

End point values	Cohort 1 - Gefapixant	Cohort 1 - Placebo	Cohort 2 - Gefapixant	Cohort 2- Placebo
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	28	28	30	29
Units: Scores on a scale				
arithmetic mean (standard deviation)	58.4 (± 18.66)	52.2 (± 19.21)	54.5 (± 24.26)	57.2 (± 23.71)

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Up to 52 days

Adverse event reporting additional description:

Adverse events (AE) are attributed to the treatment that a participant was receiving at the onset of the AE. Adverse events were attributed only to the treatment that the participant was receiving at the time of onset of the AE.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	17.1

Reporting groups

Reporting group title	Cohort 1 Gefapixant 50 mg

Reporting group description:

Gefapixant: 50 mg BID for 4 days in Period 1 or Period 2.

Reporting group title	Cohort 1 Gefapixant 100 mg

Reporting group description:

Gefapixant: 100 mg BID for 4 days in Period 1 or Period 2.

Reporting group title	Cohort 1 Gefapixant 150 mg

Reporting group description:

Gefapixant 150 mg BID for 4 days in Period 1 or Period 2.

Reporting group title	Cohort 1 Gefapixant 200 mg

Reporting group description:

Gefapixant 200 mg BID for 4 days in Period 1 or Period 2.

Reporting group title	Cohort 1 Placebo

Reporting group description:

Participants randomized to receive Placebo to Gefapixant (BID for 16 days) in Period 1 or Period 2.

Reporting group title	Cohort 2 Gefapixant 7.5 mg

Reporting group description:

Gefapixant 7.5 mg BID for 4 days in Period 1 or Period 2.

Reporting group title	Cohort 2 Gefapixant 15 mg

Reporting group description:

Gefapixant 15 mg BID for 4 days in Period 1 or Period 2.

Reporting group title	Cohort 2 Gefapixant 30 mg

Reporting group description:

Gefapixant 30 mg BID for 4 days in Period 1 or Period 2.

Reporting group title	Cohort 2 Gefapixant 50 mg

Reporting group description:

Gefapixant: 50 mg BID for 4 days in Period 1 or Period 2.

Reporting group title	Cohort 2 Placebo

Reporting group description:

Participants randomized to receive Placebo to Gefapixant (BID for 16 days) in Period 1 or Period 2.

Serious adverse events	Cohort 1 Gefapixant 50 mg	Cohort 1 Gefapixant 100 mg	Cohort 1 Gefapixant 150 mg
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 28 (0.00%)	1 / 28 (3.57%)	0 / 26 (0.00%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Investigations			
Blood creatinine increased			
subjects affected / exposed	0 / 28 (0.00%)	1 / 28 (3.57%)	0 / 26 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Invasive ductal breast carcinoma			
subjects affected / exposed	0 / 28 (0.00%)	0 / 28 (0.00%)	0 / 26 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nervous system disorders			
Cerebrovascular accident			
subjects affected / exposed	0 / 28 (0.00%)	0 / 28 (0.00%)	0 / 26 (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
Presyncope			
subjects affected / exposed	0 / 28 (0.00%)	1 / 28 (3.57%)	0 / 26 (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
Metabolism and nutrition disorders			
Dehydration			
subjects affected / exposed	0 / 28 (0.00%)	1 / 28 (3.57%)	0 / 26 (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	Cohort 1 Gefapixant 200 mg	Cohort 1 Placebo	Cohort 2 Gefapixant 7.5 mg
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 26 (0.00%)	1 / 28 (3.57%)	0 / 30 (0.00%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0

Investigations			
Blood creatinine increased			
subjects affected / exposed	0 / 26 (0.00%)	0 / 28 (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
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Invasive ductal breast carcinoma			
subjects affected / exposed	0 / 26 (0.00%)	1 / 28 (3.57%)	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			
Cerebrovascular accident			
subjects affected / exposed	0 / 26 (0.00%)	0 / 28 (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
Presyncope			
subjects affected / exposed	0 / 26 (0.00%)	0 / 28 (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
Metabolism and nutrition disorders			
Dehydration			
subjects affected / exposed	0 / 26 (0.00%)	0 / 28 (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	Cohort 2 Gefapixant 15 mg	Cohort 2 Gefapixant 30 mg	Cohort 2 Gefapixant 50 mg
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 30 (0.00%)	0 / 30 (0.00%)	1 / 30 (3.33%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Investigations			
Blood creatinine increased			
subjects affected / exposed	0 / 30 (0.00%)	0 / 30 (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
Neoplasms benign, malignant and			

unspecified (incl cysts and polyps)			
Invasive ductal breast carcinoma			
subjects affected / exposed	0 / 30 (0.00%)	0 / 30 (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
Nervous system disorders			
Cerebrovascular accident			
subjects affected / exposed	0 / 30 (0.00%)	0 / 30 (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
Presyncope			
subjects affected / exposed	0 / 30 (0.00%)	0 / 30 (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
Metabolism and nutrition disorders			
Dehydration			
subjects affected / exposed	0 / 30 (0.00%)	0 / 30 (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	Cohort 2 Placebo		
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 29 (0.00%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events	0		
Investigations			
Blood creatinine increased			
subjects affected / exposed	0 / 29 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Invasive ductal breast carcinoma			
subjects affected / exposed	0 / 29 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Nervous system disorders			

Cerebrovascular accident			
subjects affected / exposed	0 / 29 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Presyncope			
subjects affected / exposed	0 / 29 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Metabolism and nutrition disorders			
Dehydration			
subjects affected / exposed	0 / 29 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		

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

Non-serious adverse events	Cohort 1 Gefapixant 50 mg	Cohort 1 Gefapixant 100 mg	Cohort 1 Gefapixant 150 mg
Total subjects affected by non-serious adverse events			
subjects affected / exposed	17 / 28 (60.71%)	8 / 28 (28.57%)	4 / 26 (15.38%)
Investigations			
Urine output decreased			
subjects affected / exposed	2 / 28 (7.14%)	0 / 28 (0.00%)	0 / 26 (0.00%)
occurrences (all)	3	0	0
Nervous system disorders			
Ageusia			
subjects affected / exposed	2 / 28 (7.14%)	0 / 28 (0.00%)	0 / 26 (0.00%)
occurrences (all)	2	0	0
Dysgeusia			
subjects affected / exposed	13 / 28 (46.43%)	6 / 28 (21.43%)	4 / 26 (15.38%)
occurrences (all)	13	6	4
Hypogeusia			
subjects affected / exposed	2 / 28 (7.14%)	2 / 28 (7.14%)	0 / 26 (0.00%)
occurrences (all)	2	2	0
Gastrointestinal disorders			
Dry mouth			

subjects affected / exposed	1 / 28 (3.57%)	0 / 28 (0.00%)	0 / 26 (0.00%)
occurrences (all)	1	0	0
Hypoaesthesia oral			
subjects affected / exposed	1 / 28 (3.57%)	2 / 28 (7.14%)	0 / 26 (0.00%)
occurrences (all)	1	2	0
Paraesthesia oral			
subjects affected / exposed	2 / 28 (7.14%)	1 / 28 (3.57%)	0 / 26 (0.00%)
occurrences (all)	2	1	0
Respiratory, thoracic and mediastinal disorders			
Nasal dryness			
subjects affected / exposed	0 / 28 (0.00%)	0 / 28 (0.00%)	0 / 26 (0.00%)
occurrences (all)	0	0	0
Musculoskeletal and connective tissue disorders			
Flank pain			
subjects affected / exposed	1 / 28 (3.57%)	0 / 28 (0.00%)	0 / 26 (0.00%)
occurrences (all)	1	0	0
Infections and infestations			
Rhinitis			
subjects affected / exposed	0 / 28 (0.00%)	0 / 28 (0.00%)	0 / 26 (0.00%)
occurrences (all)	0	0	0
Upper respiratory tract infection			
subjects affected / exposed	0 / 28 (0.00%)	0 / 28 (0.00%)	0 / 26 (0.00%)
occurrences (all)	0	0	0
Viral upper respiratory tract infection			
subjects affected / exposed	0 / 28 (0.00%)	0 / 28 (0.00%)	0 / 26 (0.00%)
occurrences (all)	0	0	0

Non-serious adverse events	Cohort 1 Gefapixant 200 mg	Cohort 1 Placebo	Cohort 2 Gefapixant 7.5 mg
Total subjects affected by non-serious adverse events			
subjects affected / exposed	6 / 26 (23.08%)	4 / 28 (14.29%)	6 / 30 (20.00%)
Investigations			
Urine output decreased			
subjects affected / exposed	0 / 26 (0.00%)	0 / 28 (0.00%)	0 / 30 (0.00%)
occurrences (all)	0	0	0
Nervous system disorders			

Ageusia			
subjects affected / exposed	1 / 26 (3.85%)	0 / 28 (0.00%)	0 / 30 (0.00%)
occurrences (all)	1	0	0
Dysgeusia			
subjects affected / exposed	1 / 26 (3.85%)	1 / 28 (3.57%)	2 / 30 (6.67%)
occurrences (all)	1	1	2
Hypogeusia			
subjects affected / exposed	0 / 26 (0.00%)	0 / 28 (0.00%)	0 / 30 (0.00%)
occurrences (all)	0	0	0
Gastrointestinal disorders			
Dry mouth			
subjects affected / exposed	0 / 26 (0.00%)	0 / 28 (0.00%)	0 / 30 (0.00%)
occurrences (all)	0	0	0
Hypoaesthesia oral			
subjects affected / exposed	1 / 26 (3.85%)	0 / 28 (0.00%)	0 / 30 (0.00%)
occurrences (all)	1	0	0
Paraesthesia oral			
subjects affected / exposed	1 / 26 (3.85%)	0 / 28 (0.00%)	0 / 30 (0.00%)
occurrences (all)	1	0	0
Respiratory, thoracic and mediastinal disorders			
Nasal dryness			
subjects affected / exposed	0 / 26 (0.00%)	0 / 28 (0.00%)	2 / 30 (6.67%)
occurrences (all)	0	0	2
Musculoskeletal and connective tissue disorders			
Flank pain			
subjects affected / exposed	2 / 26 (7.69%)	0 / 28 (0.00%)	0 / 30 (0.00%)
occurrences (all)	2	0	0
Infections and infestations			
Rhinitis			
subjects affected / exposed	0 / 26 (0.00%)	1 / 28 (3.57%)	2 / 30 (6.67%)
occurrences (all)	0	1	2
Upper respiratory tract infection			
subjects affected / exposed	0 / 26 (0.00%)	1 / 28 (3.57%)	0 / 30 (0.00%)
occurrences (all)	0	1	0
Viral upper respiratory tract infection			

subjects affected / exposed	0 / 26 (0.00%)	2 / 28 (7.14%)	0 / 30 (0.00%)
occurrences (all)	0	2	0

Non-serious adverse events	Cohort 2 Gefapixant 15 mg	Cohort 2 Gefapixant 30 mg	Cohort 2 Gefapixant 50 mg
Total subjects affected by non-serious adverse events			
subjects affected / exposed	1 / 30 (3.33%)	13 / 30 (43.33%)	9 / 30 (30.00%)
Investigations			
Urine output decreased			
subjects affected / exposed	0 / 30 (0.00%)	0 / 30 (0.00%)	0 / 30 (0.00%)
occurrences (all)	0	0	0
Nervous system disorders			
Ageusia			
subjects affected / exposed	0 / 30 (0.00%)	0 / 30 (0.00%)	2 / 30 (6.67%)
occurrences (all)	0	0	2
Dysgeusia			
subjects affected / exposed	1 / 30 (3.33%)	12 / 30 (40.00%)	4 / 30 (13.33%)
occurrences (all)	1	12	4
Hypogeusia			
subjects affected / exposed	0 / 30 (0.00%)	0 / 30 (0.00%)	0 / 30 (0.00%)
occurrences (all)	0	0	0
Gastrointestinal disorders			
Dry mouth			
subjects affected / exposed	0 / 30 (0.00%)	1 / 30 (3.33%)	0 / 30 (0.00%)
occurrences (all)	0	1	0
Hypoaesthesia oral			
subjects affected / exposed	0 / 30 (0.00%)	1 / 30 (3.33%)	0 / 30 (0.00%)
occurrences (all)	0	1	0
Paraesthesia oral			
subjects affected / exposed	0 / 30 (0.00%)	2 / 30 (6.67%)	1 / 30 (3.33%)
occurrences (all)	0	2	1
Respiratory, thoracic and mediastinal disorders			
Nasal dryness			
subjects affected / exposed	0 / 30 (0.00%)	0 / 30 (0.00%)	0 / 30 (0.00%)
occurrences (all)	0	0	0
Musculoskeletal and connective tissue disorders			

Flank pain			
subjects affected / exposed	0 / 30 (0.00%)	0 / 30 (0.00%)	0 / 30 (0.00%)
occurrences (all)	0	0	0
Infections and infestations			
Rhinitis			
subjects affected / exposed	0 / 30 (0.00%)	0 / 30 (0.00%)	0 / 30 (0.00%)
occurrences (all)	0	0	0
Upper respiratory tract infection			
subjects affected / exposed	0 / 30 (0.00%)	0 / 30 (0.00%)	4 / 30 (13.33%)
occurrences (all)	0	0	4
Viral upper respiratory tract infection			
subjects affected / exposed	0 / 30 (0.00%)	0 / 30 (0.00%)	0 / 30 (0.00%)
occurrences (all)	0	0	0

Non-serious adverse events	Cohort 2 Placebo		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	2 / 29 (6.90%)		
Investigations			
Urine output decreased			
subjects affected / exposed	0 / 29 (0.00%)		
occurrences (all)	0		
Nervous system disorders			
Ageusia			
subjects affected / exposed	0 / 29 (0.00%)		
occurrences (all)	0		
Dysgeusia			
subjects affected / exposed	0 / 29 (0.00%)		
occurrences (all)	0		
Hypogeusia			
subjects affected / exposed	0 / 29 (0.00%)		
occurrences (all)	0		
Gastrointestinal disorders			
Dry mouth			
subjects affected / exposed	2 / 29 (6.90%)		
occurrences (all)	2		
Hypoaesthesia oral			

subjects affected / exposed occurrences (all) Paraesthesia oral subjects affected / exposed occurrences (all)	0 / 29 (0.00%) 0 0 / 29 (0.00%) 0		
Respiratory, thoracic and mediastinal disorders Nasal dryness subjects affected / exposed occurrences (all)	 0 / 29 (0.00%) 0		
Musculoskeletal and connective tissue disorders Flank pain subjects affected / exposed occurrences (all)	 0 / 29 (0.00%) 0		
Infections and infestations Rhinitis subjects affected / exposed occurrences (all) Upper respiratory tract infection subjects affected / exposed occurrences (all) Viral upper respiratory tract infection subjects affected / exposed occurrences (all)	 0 / 29 (0.00%) 0 0 / 29 (0.00%) 0 0 / 29 (0.00%) 0		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
08 July 2015	Amendment 1: Low-Dose Cohort 2 with an additional 30 subjects was added to the trial.
03 September 2015	Amendment 2: Changes in study objectives and endpoints and elimination of study sites in the United Kingdom.
02 October 2015	Amendment 3: Changes made to Renal/Urologic Symptom Inventory assessments, wash-out periods, and the follow-up of adverse events.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported