



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	v2 (current)
This version publication date	31 December 2020
First version publication date	30 July 2017
Version creation reason	• Correction of full data set Updated for Consistency with ClinicalTrials.gov Results posting

Trial information

Trial identification

Sponsor protocol code	7264-010
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Additional study identifiers

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

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., 1 8006726372, ClinicalTrialsDisclosure@merck.com
Scientific contact	Senior Vice President, Global Clinical Development, Merck Sharp & Dohme Corp., 1 8006726372, 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:

29 participants were enrolled, randomized and treated with study drug in Cohort 1 and 30 participants in Cohort 2. Of the 30 participants in Cohort 2, 18 of them were from Cohort 1 and they re-consented, were given new randomization numbers and treated with study drug.

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:

Gefapixant 50, 100, 150, and 200 mg, tablet(s) administered by mouth, twice daily, for 4 days each in Period 1 and placebo to gefapixant 50, 100, 150, and 200 mg, tablet(s) administered by mouth, twice daily, for 4 days each 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
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Arm description:

Placebo to gefapixant 50, 100, 150, and 200 mg, tablet(s) administered by mouth, twice daily, for 4 days each in Period 1 and gefapixant 50, 100, 150, and 200 mg, tablet(s) administered by mouth, twice daily, for 4 days each in Period 2. For Cohort 1, there was a 3 to 7 day washout period between treatment periods.

Arm type	Experimental
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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
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Arm description:

Gefapixant 7.5, 15, 30, and 50 mg, tablet(s) administered by mouth, twice daily, for 4 days each in Period 1 and placebo to gefapixant 7.5, 15, 30, and 50 mg, tablet(s) administered by mouth twice daily for 4 days each in Period 2. For Cohort 2 there was a 14-21 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
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Arm description:

Placebo to gefapixant 7.5, 15, 30, and 50 mg, tablet(s) administered by mouth twice daily for 4 days each in Period 1 and gefapixant 7.5, 15, 30, and 50 mg, tablet(s) administered by mouth, twice daily, for 4 days each in Period 2. For Cohort 2 there was a 14-21 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:

Gefapixant 50, 100, 150, and 200 mg, tablet(s) administered by mouth, twice daily, for 4 days each in Period 1 and placebo to gefapixant 50, 100, 150, and 200 mg, tablet(s) administered by mouth, twice daily, for 4 days each 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	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

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	
Arm title	Cohort 1: Placebo>Gefapixant
Arm description:	
Placebo to gefapixant 50, 100, 150, and 200 mg, tablet(s) administered by mouth, twice daily, for 4 days each in Period 1 and gefapixant 50, 100, 150, and 200 mg, tablet(s) administered by mouth, twice daily, for 4 days each 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:	
Gefapixant 7.5, 15, 30, and 50 mg, tablet(s) administered by mouth, twice daily, for 4 days each in Period 1 and placebo to gefapixant 7.5, 15, 30, and 50 mg, tablet(s) administered by mouth twice daily for 4 days each in Period 2. For Cohort 2 there was a 14-21 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 to gefapixant 7.5, 15, 30, and 50 mg, tablet(s) administered by mouth twice daily for 4 days each in Period 1 and gefapixant 7.5, 15, 30, and 50 mg, tablet(s) administered by mouth, twice daily, for 4 days each in Period 2. For Cohort 2 there was a 14-21 day washout period between treatment periods.

Arm type	Experimental
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

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

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	Cohort 1: Gefapixant>Placebo
Reporting group description: Gefapixant 50, 100, 150, and 200 mg, tablet(s) administered by mouth, twice daily, for 4 days each in Period 1 and placebo to gefapixant 50, 100, 150, and 200 mg, tablet(s) administered by mouth, twice daily, for 4 days each 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 to gefapixant 50, 100, 150, and 200 mg, tablet(s) administered by mouth, twice daily, for 4 days each in Period 1 and gefapixant 50, 100, 150, and 200 mg, tablet(s) administered by mouth, twice daily, for 4 days each 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: Gefapixant 7.5, 15, 30, and 50 mg, tablet(s) administered by mouth, twice daily, for 4 days each in Period 1 and placebo to gefapixant 7.5, 15, 30, and 50 mg, tablet(s) administered by mouth twice daily for 4 days each in Period 2. For Cohort 2 there was a 14-21 day washout period between treatment periods.	
Reporting group title	Cohort 2: Placebo>Gefapixant
Reporting group description: Placebo to gefapixant 7.5, 15, 30, and 50 mg, tablet(s) administered by mouth twice daily for 4 days each in Period 1 and gefapixant 7.5, 15, 30, and 50 mg, tablet(s) administered by mouth, twice daily, for 4 days each in Period 2. For Cohort 2 there was a 14-21 day washout period between treatment periods.	

Reporting group values	Cohort 1: Gefapixant>Placebo	Cohort 1: Placebo>Gefapixant	Cohort 2: Gefapixant>Placebo
Number of subjects	15	14	15
Age categorical Units: Subjects			
In utero	0	0	0
Preterm newborn infants (gestational age < 37 wks)	0	0	0
Newborns (0-27 days)	0	0	0
Infants and toddlers (28 days-23 months)	0	0	0
Children (2-11 years)	0	0	0
Adolescents (12-17 years)	0	0	0
Adults (18-64 years)	6	9	8
From 65-84 years	9	5	7
85 years and over	0	0	0
Age Continuous Units: Years			
arithmetic mean	64.5	61.7	60.7
standard deviation	± 6.92	± 7.77	± 9.42
Sex: Female, Male Units: Participants			
Female	13	12	12
Male	2	2	3

Race (NIH/OMB)			
Units: Subjects			
American Indian or Alaska Native	0	0	0
Asian	0	1	1
Native Hawaiian or Other Pacific Islander	0	0	0
Black or African American	0	0	1
White	15	13	13
More than one race	0	0	0
Unknown or Not Reported	0	0	0
Ethnicity (NIH/OMB)			
Units: Subjects			
Hispanic or Latino	1	0	1
Not Hispanic or Latino	14	14	14
Unknown or Not Reported	0	0	0

Reporting group values	Cohort 2: Placebo>Gefapixant	Total	
Number of subjects	15	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)	8	31	
From 65-84 years	7	28	
85 years and over	0	0	
Age Continuous			
Units: Years			
arithmetic mean	59.8		
standard deviation	± 12.8	-	
Sex: Female, Male			
Units: Participants			
Female	12	49	
Male	3	10	
Race (NIH/OMB)			
Units: Subjects			
American Indian or Alaska Native	0	0	
Asian	0	2	
Native Hawaiian or Other Pacific Islander	0	0	
Black or African American	0	1	
White	15	56	
More than one race	0	0	
Unknown or Not Reported	0	0	
Ethnicity (NIH/OMB)			
Units: Subjects			
Hispanic or Latino	1	3	

Not Hispanic or Latino	14	56	
Unknown or Not Reported	0	0	

End points

End points reporting groups

Reporting group title	Cohort 1: Gefapixant>Placebo
Reporting group description: Gefapixant 50, 100, 150, and 200 mg, tablet(s) administered by mouth, twice daily, for 4 days each in Period 1 and placebo to gefapixant 50, 100, 150, and 200 mg, tablet(s) administered by mouth, twice daily, for 4 days each 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 to gefapixant 50, 100, 150, and 200 mg, tablet(s) administered by mouth, twice daily, for 4 days each in Period 1 and gefapixant 50, 100, 150, and 200 mg, tablet(s) administered by mouth, twice daily, for 4 days each 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: Gefapixant 7.5, 15, 30, and 50 mg, tablet(s) administered by mouth, twice daily, for 4 days each in Period 1 and placebo to gefapixant 7.5, 15, 30, and 50 mg, tablet(s) administered by mouth twice daily for 4 days each in Period 2. For Cohort 2 there was a 14-21 day washout period between treatment periods.	
Reporting group title	Cohort 2: Placebo>Gefapixant
Reporting group description: Placebo to gefapixant 7.5, 15, 30, and 50 mg, tablet(s) administered by mouth twice daily for 4 days each in Period 1 and gefapixant 7.5, 15, 30, and 50 mg, tablet(s) administered by mouth, twice daily, for 4 days each in Period 2. For Cohort 2 there was a 14-21 day washout period between treatment periods.	
Reporting group title	Cohort 1: Gefapixant>Placebo
Reporting group description: Gefapixant 50, 100, 150, and 200 mg, tablet(s) administered by mouth, twice daily, for 4 days each in Period 1 and placebo to gefapixant 50, 100, 150, and 200 mg, tablet(s) administered by mouth, twice daily, for 4 days each 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 to gefapixant 50, 100, 150, and 200 mg, tablet(s) administered by mouth, twice daily, for 4 days each in Period 1 and gefapixant 50, 100, 150, and 200 mg, tablet(s) administered by mouth, twice daily, for 4 days each 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: Gefapixant 7.5, 15, 30, and 50 mg, tablet(s) administered by mouth, twice daily, for 4 days each in Period 1 and placebo to gefapixant 7.5, 15, 30, and 50 mg, tablet(s) administered by mouth twice daily for 4 days each in Period 2. For Cohort 2 there was a 14-21 day washout period between treatment periods.	
Reporting group title	Cohort 2: Placebo>Gefapixant
Reporting group description: Placebo to gefapixant 7.5, 15, 30, and 50 mg, tablet(s) administered by mouth twice daily for 4 days each in Period 1 and gefapixant 7.5, 15, 30, and 50 mg, tablet(s) administered by mouth, twice daily, for 4 days each in Period 2. For Cohort 2 there was a 14-21 day washout period between treatment periods.	
Subject analysis set title	Cohort 1 – Gefapixant>Placebo
Subject analysis set type	Full analysis
Subject analysis set description: Gefapixant 50, 100, 150, and 200 mg, tablet(s) administered by mouth, twice daily, for 4 days each in Period 1 and placebo to gefapixant 50, 100, 150, and 200 mg, tablet(s) administered by mouth, twice daily, for 4 days each in Period 2. For Cohort 1, there was a 3 to 7-day washout period between treatment periods.	

Subject analysis set title	Cohort 1 - Placebo>Gefapixant
Subject analysis set type	Full analysis
Subject analysis set description: Placebo to gefapixant 50, 100, 150, and 200 mg, tablet(s) administered by mouth, twice daily, for 4 days each in Period 1 and gefapixant 50, 100, 150, and 200 mg, tablet(s) administered by mouth, twice daily, for 4 days each in Period 2. For Cohort 1, there was a 3 to 7 day washout period between treatment periods.	
Subject analysis set title	Cohort 2 - Gefapixant>Placebo
Subject analysis set type	Full analysis
Subject analysis set description: Gefapixant 7.5, 15, 30 and 50 mg, tablet(s) administered by mouth, twice daily, for 4 days each in Period 1 and placebo to gefapixant 7.5, 15, 30 and 50 mg, tablet(s) administered by mouth, twice daily, for 4 days each in Period 2. For Cohort 2, there was a 14 to 21-day washout period between treatment periods.	
Subject analysis set title	Cohort 2 - Placebo>Gefapixant
Subject analysis set type	Full analysis
Subject analysis set description: Placebo to gefapixant 7.5, 15, 30 and 50 mg, tablet(s) administered by mouth, twice daily, for 4 days each in Period 1 and gefapixant 7.5, 15, 30 and 50 mg, tablet(s) administered by mouth, twice daily, for 4 days each 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 tablet administered by mouth BID for 4 days.	
Subject analysis set title	Cohort 1 - Placebo for Gefapixant 50 mg
Subject analysis set type	Full analysis
Subject analysis set description: Placebo tablet administered by mouth BID for 4 days.	
Subject analysis set title	Cohort 1 - Gefapixant 100 mg
Subject analysis set type	Full analysis
Subject analysis set description: Gefapixant 100 mg tablet administered by mouth BID for 4 days.	
Subject analysis set title	Cohort 1 - Placebo for Gefapixant 100 mg
Subject analysis set type	Full analysis
Subject analysis set description: Placebo tablet administered by mouth BID for 4 days.	
Subject analysis set title	Cohort 1 - Gefapixant 150 mg
Subject analysis set type	Full analysis
Subject analysis set description: Gefapixant 150 mg tablet administered by mouth BID for 4 days.	
Subject analysis set title	Cohort 1 - Placebo for Gefapixant 150 mg
Subject analysis set type	Full analysis
Subject analysis set description: Placebo tablet administered by mouth BID for 4 days.	
Subject analysis set title	Cohort 1 - Gefapixant 200 mg
Subject analysis set type	Full analysis
Subject analysis set description: Gefapixant 200 mg tablet administered by mouth BID for 4 days.	
Subject analysis set title	Cohort 1 - Placebo for Gefapixant 200 mg
Subject analysis set type	Full analysis
Subject analysis set description: Placebo tablet administered by mouth BID for 4 days.	
Subject analysis set title	Cohort 2 - Gefapixant 7.5 mg

Subject analysis set type	Full analysis
Subject analysis set description: Gefapixant 7.5 mg tablet administered by mouth BID for 4 days.	
Subject analysis set title	Cohort 2 - Placebo for Gefapixant 7.5 mg
Subject analysis set type	Full analysis
Subject analysis set description: Placebo tablet administered by mouth BID for 4 days.	
Subject analysis set title	Cohort 2 - Gefapixant 15 mg
Subject analysis set type	Full analysis
Subject analysis set description: Gefapixant 15 mg tablet administered by mouth BID for 4 days.	
Subject analysis set title	Cohort 2 - Placebo for Gefapixant 15 mg
Subject analysis set type	Full analysis
Subject analysis set description: Placebo tablet administered by mouth BID for 4 days.	
Subject analysis set title	Cohort 2 - Gefapixant 30 mg
Subject analysis set type	Full analysis
Subject analysis set description: Gefapixant 30 mg tablet administered by mouth BID for 4 days.	
Subject analysis set title	Cohort 2 - Placebo for Gefapixant 30 mg
Subject analysis set type	Full analysis
Subject analysis set description: Placebo tablet administered by mouth BID for 4 days.	
Subject analysis set title	Cohort 2 - Gefapixant 50 mg
Subject analysis set type	Full analysis
Subject analysis set description: Gefapixant 50 mg tablet administered by mouth BID for 4 days.	
Subject analysis set title	Cohort 2 - Gefapixant 50 mg
Subject analysis set type	Full analysis
Subject analysis set description: Gefapixant 50 mg tablet administered by mouth BID for 4 days	
Subject analysis set title	Cohort 2 - Placebo for Gefapixant 50 mg
Subject analysis set type	Full analysis
Subject analysis set description: Placebo tablet administered by mouth BID for 4 days.	
Subject analysis set title	Cohort 1 - Gefapixant
Subject analysis set type	Full analysis
Subject analysis set description: Gefapixant 50, 100, 150, and 200 mg tablet(s) administered by mouth BID for 4 days each.	
Subject analysis set title	Cohort 1 - Placebo
Subject analysis set type	Full analysis
Subject analysis set description: Placebo tablet administered by mouth BID for 4 days.	
Subject analysis set title	Cohort 2 - Gefapixant
Subject analysis set type	Full analysis
Subject analysis set description: Gefapixant 7.5, 15, 30, and 50 mg tablet(s) administered by mouth BID for 4 days each.	
Subject analysis set title	Cohort 2 - Placebo
Subject analysis set type	Full analysis
Subject analysis set description: Placebo tablet administered by mouth BID for 4 days each.	
Subject analysis set title	Cohort 1 - Gefapixant 50 mg

Subject analysis set type	Full analysis
Subject analysis set description:	
Gefapixant 50 mg tablet administered by mouth BID for 4 days	
Subject analysis set title	Cohort 1 - Placebo for Gefapixant 50 mg
Subject analysis set type	Full analysis
Subject analysis set description:	
Placebo tablet administered by mouth BID for 4 days.	
Subject analysis set title	Cohort 1 - Gefapixant 100 mg
Subject analysis set type	Full analysis
Subject analysis set description:	
Gefapixant 100 mg tablet administered by mouth BID for 4 days	
Subject analysis set title	Cohort 1 - Placebo for Gefapixant 100 mg
Subject analysis set type	Full analysis
Subject analysis set description:	
Placebo tablet administered by mouth BID for 4 days	
Subject analysis set title	Cohort 1 - Gefapixant 150 mg
Subject analysis set type	Full analysis
Subject analysis set description:	
Gefapixant 150 mg tablet administered by mouth BID for 4 days	
Subject analysis set title	Cohort 1 - Placebo for Gefapixant 150 mg
Subject analysis set type	Full analysis
Subject analysis set description:	
Placebo tablet administered by mouth BID for 4 days	
Subject analysis set title	Cohort 1 - Gefapixant 200 mg
Subject analysis set type	Full analysis
Subject analysis set description:	
Gefapixant 200 mg tablet administered by mouth BID for 4 days	
Subject analysis set title	Cohort 1 - Placebo for Gefapixant 200 mg
Subject analysis set type	Full analysis
Subject analysis set description:	
Placebo tablet administered by mouth BID for 4 days	
Subject analysis set title	Cohort 2 - Gefapixant 50 mg
Subject analysis set type	Full analysis
Subject analysis set description:	
Gefapixant 50 mg tablet administered by mouth BID for 4 days	
Subject analysis set title	Cohort 2 - Placebo for Gefapixant 50 mg
Subject analysis set type	Full analysis
Subject analysis set description:	
Placebo tablet administered by mouth BID for 4 days	
Subject analysis set title	Cohort 1 - Gefapixant 50 mg
Subject analysis set type	Full analysis
Subject analysis set description:	
Gefapixant 50 mg tablet administered by mouth BID for 4 days	
Subject analysis set title	Cohort 1 - Placebo for Gefapixant 50 mg
Subject analysis set type	Full analysis
Subject analysis set description:	
Placebo tablet administered by mouth BID for 4 days	
Subject analysis set title	Cohort 1 - Gefapixant 100 mg
Subject analysis set type	Full analysis
Subject analysis set description:	
Gefapixant 100 mg tablet administered by mouth BID for 4 days	
Subject analysis set title	Cohort 1 - Placebo for Gefapixant 100 mg

Subject analysis set type	Full analysis
Subject analysis set description:	
Placebo tablet administered by mouth BID for 4 days	
Subject analysis set title	Cohort 1 - Gefapixant 150 mg
Subject analysis set type	Full analysis
Subject analysis set description:	
Gefapixant 150 mg tablet administered by mouth BID for 4 days	
Subject analysis set title	Cohort 1 - Placebo for Gefapixant 150 mg
Subject analysis set type	Full analysis
Subject analysis set description:	
Placebo tablet administered by mouth BID for 4 days	
Subject analysis set title	Cohort 1 - Gefapixant 200 mg
Subject analysis set type	Full analysis
Subject analysis set description:	
Gefapixant 200 mg tablet administered by mouth BID for 4 days	
Subject analysis set title	Cohort 1 - Placebo for Gefapixant 200 mg
Subject analysis set type	Full analysis
Subject analysis set description:	
Placebo tablet administered by mouth BID for 4 days	
Subject analysis set title	Cohort 2 - Gefapixant 7.5 mg
Subject analysis set type	Full analysis
Subject analysis set description:	
Gefapixant 7.5 mg tablet administered by mouth BID for 4 days	
Subject analysis set title	Cohort 2 - Placebo for Gefapixant 7.5 mg
Subject analysis set type	Full analysis
Subject analysis set description:	
Placebo tablet administered by mouth BID for 4 days	
Subject analysis set title	Cohort 2 - Gefapixant 15 mg
Subject analysis set type	Full analysis
Subject analysis set description:	
Gefapixant 15 mg tablet administered by mouth BID for 4 days	
Subject analysis set title	Cohort 2 - Placebo for Gefapixant 15 mg
Subject analysis set type	Full analysis
Subject analysis set description:	
Placebo tablet administered by mouth BID for 4 days.	
Subject analysis set title	Cohort 2 - Gefapixant 30 mg
Subject analysis set type	Full analysis
Subject analysis set description:	
Gefapixant 30 mg tablet administered by mouth BID for 4 days	
Subject analysis set title	Cohort 2 - Placebo for Gefapixant 30 mg
Subject analysis set type	Full analysis
Subject analysis set description:	
Placebo tablet administered by mouth BID for 4 days	
Subject analysis set title	Cohort 2 - Gefapixant 50 mg
Subject analysis set type	Full analysis
Subject analysis set description:	
Gefapixant 50 mg tablet administered by mouth BID for 4 days.	
Subject analysis set title	Cohort 2 - Placebo for Gefapixant 50 mg
Subject analysis set type	Full analysis
Subject analysis set description:	
Placebo tablet administered by mouth BID for 4 days	
Subject analysis set title	Cohort 1 - Gefapixant 50 mg

Subject analysis set type	Full analysis
Subject analysis set description: Gefapixant 50 mg tablet administered by mouth BID for 4 days.	
Subject analysis set title	Cohort 1 - Placebo for Gefapixant 50 mg
Subject analysis set type	Full analysis
Subject analysis set description: Placebo tablet administered by mouth BID for 4 days	
Subject analysis set title	Cohort 1 - Gefapixant 100 mg
Subject analysis set type	Full analysis
Subject analysis set description: Gefapixant 100 mg tablet administered by mouth BID for 4 days	
Subject analysis set title	Cohort 1 - Placebo for Gefapixant 100 mg
Subject analysis set type	Full analysis
Subject analysis set description: Placebo tablet administered by mouth BID for 4 days	
Subject analysis set title	Cohort 1 - Gefapixant 150 mg
Subject analysis set type	Full analysis
Subject analysis set description: Gefapixant 150 mg tablet administered by mouth BID for 4 days	
Subject analysis set title	Cohort 1 - Placebo for Gefapixant 150 mg
Subject analysis set type	Full analysis
Subject analysis set description: Placebo tablet administered by mouth BID for 4 days	
Subject analysis set title	Cohort 1 - Gefapixant 200 mg
Subject analysis set type	Full analysis
Subject analysis set description: Gefapixant 200 mg tablet administered by mouth BID for 4 days	
Subject analysis set title	Cohort 1 - Placebo for Gefapixant 200 mg
Subject analysis set type	Full analysis
Subject analysis set description: Placebo tablet administered by mouth BID for 4 days	
Subject analysis set title	Cohort 1 - Gefapixant
Subject analysis set type	Full analysis
Subject analysis set description: Gefapixant 50, 100, 150, and 200 mg tablet(s) administered by mouth BID for 4 days each.	
Subject analysis set title	Cohort 1 - Placebo
Subject analysis set type	Full analysis
Subject analysis set description: Placebo tablet administered by mouth BID for 4 days	
Subject analysis set title	Cohort 2 - Gefapixant
Subject analysis set type	Full analysis
Subject analysis set description: Gefapixant 7.5, 15, 30, and 50 mg tablet(s) administered by mouth BID for 4 days each	
Subject analysis set title	Cohort 2 - Placebo
Subject analysis set type	Full analysis
Subject analysis set description: Placebo tablet administered by mouth BID for 4 days each	
Subject analysis set title	Cohort 1 - Gefapixant
Subject analysis set type	Full analysis
Subject analysis set description: Gefapixant 50, 100, 150, and 200 mg tablet(s) administered by mouth BID for 4 days each.	
Subject analysis set title	Cohort 1 - Placebo

Subject analysis set type	Full analysis
Subject analysis set description:	
Placebo tablet administered by mouth BID for 4 days	
Subject analysis set title	Cohort 2 - Gefapixant
Subject analysis set type	Full analysis
Subject analysis set description:	
Gefapixant 7.5, 15, 30, and 50 mg tablet(s) administered by mouth BID for 4 days each	
Subject analysis set title	Cohort 2 - Placebo
Subject analysis set type	Full analysis
Subject analysis set description:	
Placebo tablet administered by mouth BID for 4 days each	
Subject analysis set title	Cohort 1 - Gefapixant
Subject analysis set type	Full analysis
Subject analysis set description:	
Gefapixant 50, 100, 150, and 200 mg tablet(s) administered by mouth BID for 4 days each	
Subject analysis set title	Cohort 1 - Placebo
Subject analysis set type	Full analysis
Subject analysis set description:	
Placebo tablet administered by mouth BID for 4 days each	
Subject analysis set title	Cohort 2 - Gefapixant
Subject analysis set type	Full analysis
Subject analysis set description:	
Gefapixant 7.5, 15, 30, and 50 mg tablet(s) administered by mouth BID for 4 days each	
Subject analysis set title	Cohort 2 - Placebo
Subject analysis set type	Full analysis
Subject analysis set description:	
Placebo tablet administered by mouth BID for 4 days each	
Subject analysis set title	Cohort 2 - Placebo
Subject analysis set type	Full analysis
Subject analysis set description:	
Placebo tablet administered by mouth BID for 4 days each	

Primary: Change in Awake Objective Cough Frequency on Log-transformed Scale - Cohort 1

End point title	Change in Awake Objective Cough Frequency on Log-transformed Scale - Cohort 1
End point description:	
Awake Objective Frequency (per hour) is 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.	
End point type	Primary
End point timeframe:	
Period 1 (while awake): baseline (Day 0) and 24 hours after Day 4, 8, 12 & 16 doses; Period 2 (while awake): baseline (Day 22) and 24 hours after Day 26, 30, 34 and 38 doses	

End point values	Cohort 1 - Gefapixant 50 mg	Cohort 1 - Placebo for Gefapixant 50 mg	Cohort 1 - Gefapixant 100 mg	Cohort 1 - Placebo for 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: Log coughs/hour				
geometric mean (confidence interval 95%)	0.56 (0.43 to 0.72)	0.95 (0.73 to 1.23)	0.46 (0.34 to 0.61)	0.95 (0.71 to 1.28)

End point values	Cohort 1 - Gefapixant 150 mg	Cohort 1 - Placebo for Gefapixant 150 mg	Cohort 1 - Gefapixant 200 mg	Cohort 1 - Placebo for 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: Log coughs/hour				
geometric mean (confidence interval 95%)	0.48 (0.35 to 0.65)	0.90 (0.65 to 1.24)	0.45 (0.33 to 0.63)	1.06 (0.75 to 1.48)

Statistical analyses

Statistical analysis title	Gefapixant 50 mg vs. Placebo
Comparison groups	Cohort 1 - Gefapixant 50 mg v Cohort 1 - Placebo for Gefapixant 50 mg
Number of subjects included in analysis	51
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0055
Method	Mixed models analysis
Parameter estimate	Estimated percent change
Point estimate	-41.222
Confidence interval	
level	95 %
sides	2-sided
lower limit	-59.294
upper limit	-15.127

Statistical analysis title	Gefapixant 100 mg vs. Placebo
Comparison groups	Cohort 1 - Gefapixant 100 mg v Cohort 1 - Placebo for Gefapixant 100 mg

Number of subjects included in analysis	49
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0008
Method	Mixed models analysis
Parameter estimate	Estimated percent change
Point estimate	-51.973
Confidence interval	
level	95 %
sides	2-sided
lower limit	-68.23
upper limit	-27.397

Statistical analysis title	Gefapixant 150 mg vs. Placebo
Comparison groups	Cohort 1 - Gefapixant 150 mg v Cohort 1 - Placebo for Gefapixant 150 mg
Number of subjects included in analysis	45
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0075
Method	Mixed models analysis
Parameter estimate	Estimated percent change
Point estimate	-46.853
Confidence interval	
level	95 %
sides	2-sided
lower limit	-66.291
upper limit	-16.206

Statistical analysis title	Gefapixant 200 mg vs. Placebo
Comparison groups	Cohort 1 - Gefapixant 200 mg v Cohort 1 - Placebo for Gefapixant 200 mg
Number of subjects included in analysis	50
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0009
Method	Mixed models analysis
Parameter estimate	Estimated percent change
Point estimate	-57.067
Confidence interval	
level	95 %
sides	2-sided
lower limit	-73.375
upper limit	-30.771

Primary: Change in Awake Objective Cough Frequency on Log-transformed Scale - Cohort 2

End point title	Change in Awake Objective Cough Frequency on Log-transformed Scale - Cohort 2
End point description: Awake Objective Frequency (per hour) is 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.	
End point type	Primary
End point timeframe: Period 1 (while awake): baseline (Day 0) and 24 hours after Day 4, 8, 12 & 16 doses; Period 2 (while awake): baseline (Day 22) and 24 hours after Day 26, 30, 34 and 38 doses	

End point values	Cohort 2 - Gefapixant 7.5 mg	Cohort 2 - Placebo for Gefapixant 7.5 mg	Cohort 2 - Gefapixant 15 mg	Cohort 2 - Placebo for 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: Log coughs/hour				
geometric mean (confidence interval 95%)	0.80 (0.66 to 0.96)	0.93 (0.77 to 1.13)	0.67 (0.57 to 0.80)	0.90 (0.75 to 1.08)

End point values	Cohort 2 - Gefapixant 30 mg	Cohort 2 - Placebo for Gefapixant 30 mg	Cohort 2 - Gefapixant 50 mg	Cohort 2 - Placebo for 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: Log coughs/hour				
geometric mean (confidence interval 95%)	0.53 (0.40 to 0.69)	0.84 (0.64 to 1.10)	0.44 (0.32 to 0.60)	1.00 (0.72 to 1.38)

Statistical analyses

Statistical analysis title	Gefapixant 7.5 mg vs. Placebo
Comparison groups	Cohort 2 - Gefapixant 7.5 mg v Cohort 2 - Placebo for Gefapixant 7.5 mg
Number of subjects included in analysis	57
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.2542
Method	Mixed models analysis
Parameter estimate	Estimated percent change
Point estimate	-14.691

Confidence interval	
level	95 %
sides	2-sided
lower limit	-35.307
upper limit	12.493

Statistical analysis title	Gefapixant 15 mg vs. Placebo
Comparison groups	Cohort 2 - Gefapixant 15 mg v Cohort 2 - Placebo for Gefapixant 15 mg
Number of subjects included in analysis	59
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0267
Method	Mixed models analysis
Parameter estimate	Estimated percent change
Point estimate	-25.165
Confidence interval	
level	95 %
sides	2-sided
lower limit	-42.014
upper limit	-3.421

Statistical analysis title	Gefapixant 30 mg vs. Placebo
Comparison groups	Cohort 2 - Gefapixant 30 mg v Cohort 2 - Placebo for Gefapixant 30 mg
Number of subjects included in analysis	58
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0198
Method	Mixed models analysis
Parameter estimate	Estimated percent change
Point estimate	-37.146
Confidence interval	
level	95 %
sides	2-sided
lower limit	-57.345
upper limit	-7.3821

Statistical analysis title	gefapixant 50 mg vs. Placebo
Comparison groups	Cohort 2 - Gefapixant 50 mg v Cohort 2 - Placebo for Gefapixant 50 mg

Number of subjects included in analysis	56
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0006
Method	Mixed models analysis
Parameter estimate	Estimated percent change
Point estimate	-55.92
Confidence interval	
level	95 %
sides	2-sided
lower limit	-71.923
upper limit	-30.797

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 ^[1]
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End point description:

Awake Objective Cough Frequency (per hour) is 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. Percent Change in Awake Cough Frequency is the change from baseline in awake cough frequency x 100, divided by baseline awake cough frequency. A negative result indicates a decrease in cough frequency, while a positive result indicates an increase in cough frequency.

End point type	Primary
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End point timeframe:

Period 1 (while awake): baseline (Day 0) and 24 hours after Day 4, 8, 12 & 16 doses; Period 2 (while awake): baseline (Day 22) and 24 hours after Day 26, 30, 34 and 38 doses

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 analyses were performed for this endpoint.

End point values	Cohort 1 - Gefapixant 50 mg	Cohort 1 - Placebo for Gefapixant 50 mg	Cohort 1 - Gefapixant 100 mg	Cohort 1 - Placebo for 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 for Gefapixant 150 mg	Cohort 1 - Gefapixant 200 mg	Cohort 1 - Placebo for 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)	-22.0 (± 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 for Cohort 2

End point title	Percent Change from Baseline in Awake Cough Frequency for Cohort 2 ^[2]
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End point description:

Awake Objective Cough Frequency (per hour) is 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. Percent Change in Awake Cough Frequency is the change from baseline in awake cough frequency x 100, divided by baseline awake cough frequency. A negative result indicates a decrease in cough frequency, while a positive result indicates an increase in cough frequency.

End point type	Primary
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End point timeframe:

Period 1 (while awake): baseline (Day 0) and 24 hours after Day 4, 8, 12 & 16 doses; Period 2 (while awake): baseline (Day 22) and 24 hours after Day 26, 30, 34 and 38 doses

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 analyses were performed for this endpoint.

End point values	Cohort 2 - Gefapixant 7.5 mg	Cohort 2 - Placebo for Gefapixant 7.5 mg	Cohort 2 - Gefapixant 15 mg	Cohort 2 - Placebo for 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)	5.0 (± 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 for Gefapixant 30 mg	Cohort 2 - Gefapixant 50 mg	Cohort 2 - Placebo for 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 (± 74.90)	23.1 (± 92.60)

Statistical analyses

Primary: Responder Analysis of Awake Cough Frequency for Cohort 1

End point title	Responder Analysis of Awake Cough Frequency for Cohort 1 ^[3]
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End point description:

Participants were classified as responders based on the magnitude of the percent change from baseline in Awake Objective cough frequency: 1. $\geq 70\%$ Reduction=1 if Percent Change from Baseline in cough frequency at the end of the dosing interval $\leq -70.0\%$; 0 Otherwise; 2. $\geq 50\%$ Reduction=1 if Percent Change from Baseline in cough frequency at the end of the dosing interval $\leq -50.0\%$; 0 Otherwise; 3. $\geq 30\%$ Reduction=1 if Percent Change from Baseline in cough frequency at the end of the dosing interval $\leq -30.0\%$; 0 Otherwise. These responder definitions were not mutually exclusive. A participant who achieved a 1 for $\geq 70\%$ Reduction for a particular period and dosing interval, were by definition, classified as $\geq 50\%$ Reduction and $\geq 30\%$ Reduction.

End point type	Primary
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End point timeframe:

Period 1 (while awake): baseline (Day 0) and 24 hours after Day 4, 8, 12 & 16 doses; Period 2 (while awake): baseline (Day 22) and 24 hours after Day 26, 30, 34 and 38 doses

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 analyses were performed for this endpoint.

End point values	Cohort 1 - Gefapixant 50 mg	Cohort 1 - Placebo for Gefapixant 50 mg	Cohort 1 - Gefapixant 100 mg	Cohort 1 - Placebo for 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 Responders				
number (not applicable)				
% Reduction ≥ 70	34.6	0	33.3	0
% Reduction ≥ 50	46.2	0	50.0	4.0
% Reduction ≥ 30	53.8	12.0	66.7	16.0

End point values	Cohort 1 - Gefapixant 150 mg	Cohort 1 - Placebo for Gefapixant 150 mg	Cohort 1 - Gefapixant 200 mg	Cohort 1 - Placebo for 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 Responders				
number (not applicable)				
% Reduction ≥ 70	34.8	4.5	32.0	0
% Reduction ≥ 50	47.8	4.5	44.0	0
% Reduction ≥ 30	65.2	22.7	56.0	16.0

Statistical analyses

No statistical analyses for this end point

Primary: Responder Analysis of Awake Cough Frequency for Cohort 2

End point title	Responder Analysis of Awake Cough Frequency for Cohort 2 ^[4]
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End point description:

Participants were classified as responders based on the magnitude of the percent change from baseline in Awake Objective cough frequency: 1. $\geq 70\%$ Reduction=1 if Percent Change from Baseline in cough frequency at the end of the dosing interval $\leq -70.0\%$; 0 Otherwise; 2. $\geq 50\%$ Reduction=1 if Percent Change from Baseline in cough frequency at the end of the dosing interval $\leq -50.0\%$; 0 Otherwise; 3. $\geq 30\%$ Reduction=1 if Percent Change from Baseline in cough frequency at the end of the dosing interval $\leq -30.0\%$; 0 Otherwise. These responder definitions were not mutually exclusive. A participant who achieved a 1 for $\geq 70\%$ Reduction for a particular period and dosing interval, were by definition, classified as $\geq 50\%$ Reduction and $\geq 30\%$ Reduction.

End point type	Primary
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End point timeframe:

Period 1 (while awake): baseline (Day 0) and 24 hours after Day 4, 8, 12 & 16 doses; Period 2 (while awake): baseline (Day 22) and 24 hours after Day 26, 30, 34 and 38 doses

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 analyses were performed for this endpoint.

End point values	Cohort 2 - Gefapixant 7.5 mg	Cohort 2 - Placebo for Gefapixant 7.5 mg	Cohort 2 - Gefapixant 15 mg	Cohort 2 - Placebo for 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 Responders				
number (not applicable)				
% Reduction ≥ 70	3.4	3.6	10.0	0
% Reduction ≥ 50	13.8	7.1	20.0	6.9
% Reduction ≥ 30	37.9	14.3	46.7	20.7

End point values	Cohort 2 - Gefapixant 30 mg	Cohort 2 - Placebo for Gefapixant 30 mg	Cohort 2 - Gefapixant 50 mg	Cohort 2 - Placebo for 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 Responders				
number (not applicable)				
% Reduction ≥ 70	20.7	3.4	31.0	3.7
% Reduction ≥ 50	31.0	17.2	41.4	11.1
% Reduction ≥ 30	62.1	31.0	55.2	22.2

Statistical analyses

No statistical analyses for this end point

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

End point title	Change from Baseline in Awake (0-8 Hours) Objective Cough
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End point description:

Awake (0-8 hours) Objective Cough Frequency is the 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 using a digital recording device. Results are change from baseline: a negative result indicates a decrease in cough frequency, while a positive result indicates an increase in cough frequency.

Cough frequency was analyzed using a mixed model repeated measures (MMRM) to evaluate the results of the 2-period cross-over study. The derived change measured at each dose were the repeated measures.

End point type	Secondary
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End point timeframe:

Period 1 (while awake): baseline (Day 0) and 0-8 hours after Day 4, 8, 12 & 16 doses; Period 2 (while awake): baseline (Day 22) and 0-8 hours after Day 26, 30, 34 and 38 doses

End point values	Cohort 1 - Gefapixant 50 mg	Cohort 1 - Placebo for Gefapixant 50 mg	Cohort 1 - Gefapixant 100 mg	Cohort 1 - Placebo for 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				
least squares mean (confidence interval 95%)	-24.5 (-33.0 to -15.9)	-5.5 (-14.2 to 3.3)	-24.5 (-33.1 to -15.8)	-0.1 (-8.8 to 8.7)

End point values	Cohort 1 - Gefapixant 150 mg	Cohort 1 - Placebo for Gefapixant 150 mg	Cohort 1 - Gefapixant 200 mg	Cohort 1 - Placebo for 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				
least squares mean (confidence interval 95%)	-26.5 (-40.3 to -12.8)	2.7 (-11.4 to 16.9)	-27.5 (-37.9 to -17.0)	2.2 (-8.5 to 12.8)

Statistical analyses

Statistical analysis title	Gefapixant 50 mg vs. Placebo
Comparison groups	Cohort 1 - Gefapixant 50 mg v Cohort 1 - Placebo for Gefapixant 50 mg
Number of subjects included in analysis	51
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.003
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)
Point estimate	-19

Confidence interval	
level	95 %
sides	2-sided
lower limit	-31.2
upper limit	-6.8

Statistical analysis title	Gefapixant 100 mg vs. Placebo
Comparison groups	Cohort 1 - Gefapixant 100 mg v Cohort 1 - Placebo for Gefapixant 100 mg
Number of subjects included in analysis	49
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)
Point estimate	-24.4
Confidence interval	
level	95 %
sides	2-sided
lower limit	-36.7
upper limit	-12.1

Statistical analysis title	Gefapixant 150 mg vs. Placebo
Comparison groups	Cohort 1 - Gefapixant 150 mg v Cohort 1 - Placebo for Gefapixant 150 mg
Number of subjects included in analysis	45
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.005
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)
Point estimate	-29.3
Confidence interval	
level	95 %
sides	2-sided
lower limit	-49
upper limit	-9.5

Statistical analysis title	Gefapixant 200 mg vs. Placebo
Comparison groups	Cohort 1 - Gefapixant 200 mg v Cohort 1 - Placebo for Gefapixant 200 mg

Number of subjects included in analysis	50
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)
Point estimate	-29.6
Confidence interval	
level	95 %
sides	2-sided
lower limit	-44.6
upper limit	-14.7

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

End point title	Change from Baseline in Awake (0-8 Hours) Objective Cough Frequency for Cohort 2
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End point description:

Awake (0-8 hours) Objective Cough Frequency is the 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 using a digital recording device. Results are change from baseline: a negative result indicates a decrease in cough frequency, while a positive result indicates an increase in cough frequency.

Cough frequency was analyzed using a mixed model repeated measures (MMRM) to evaluate the results of the 2-period cross-over study. The derived change measured at each dose were the repeated measures.

End point type	Secondary
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End point timeframe:

Period 1 (while awake): baseline (Day 0) and 0-8 hours after Day 4, 8, 12 & 16 doses; Period 2 (while awake): baseline (Day 22) and 0-8 hours after Day 26, 30, 34 and 38 doses

End point values	Cohort 2 - Gefapixant 7.5 mg	Cohort 2 - Placebo for Gefapixant 7.5 mg	Cohort 2 - Gefapixant 15 mg	Cohort 2 - Placebo for 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				
least squares mean (confidence interval 95%)	-8.0 (-17.9 to 1.9)	-1.1 (-11.1 to 9.0)	-15.2 (-22.1 to -8.3)	-1.7 (-8.8 to 5.3)

End point values	Cohort 2 - Gefapixant 30 mg	Cohort 2 - Placebo for Gefapixant 30 mg	Cohort 2 - Gefapixant 50 mg	Cohort 2 - Placebo for 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				
least squares mean (confidence interval 95%)	-21.7 (-31.9 to -11.5)	8.5 (-1.8 to 18.8)	-21.9 (-32.8 to -11.0)	4.7 (-6.5 to 16.0)

Statistical analyses

Statistical analysis title	Gefapixant 7.5 mg vs. Placebo
Comparison groups	Cohort 2 - Gefapixant 7.5 mg v Cohort 2 - Placebo for Gefapixant 7.5 mg
Number of subjects included in analysis	57
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.332
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)
Point estimate	-6.9
Confidence interval	
level	95 %
sides	2-sided
lower limit	-21
upper limit	7.2

Statistical analysis title	Gefapixant 15 mg vs. Placebo
Comparison groups	Cohort 2 - Gefapixant 15 mg v Cohort 2 - Placebo for Gefapixant 15 mg
Number of subjects included in analysis	59
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.008
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)
Point estimate	-13.5
Confidence interval	
level	95 %
sides	2-sided
lower limit	-23.3
upper limit	-3.6

Statistical analysis title	Gefapixant 30 mg vs. Placebo
Comparison groups	Cohort 2 - Gefapixant 30 mg v Cohort 2 - Placebo for Gefapixant 30 mg

Number of subjects included in analysis	58
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)
Point estimate	-30.2
Confidence interval	
level	95 %
sides	2-sided
lower limit	-44.7
upper limit	-15.7

Statistical analysis title	Gefapixant 50 mg vs. Placebo
Comparison groups	Cohort 2 - Gefapixant 50 mg v Cohort 2 - Placebo for Gefapixant 50 mg
Number of subjects included in analysis	56
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.001
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)
Point estimate	-26.7
Confidence interval	
level	95 %
sides	2-sided
lower limit	-42.3
upper limit	-11

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

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

Total (0-24 hours) Objective Cough Frequency is the total number of cough events during the monitoring period divided by the total duration (in hours, i.e., 24 hours mostly) for the monitoring period. 24-hour sound recordings were collected using a digital recording device. Results are change from baseline: a negative result indicates a decrease in cough frequency, while a positive result indicates an increase in cough frequency.

Cough frequency was analyzed using MMRM to evaluate the results of the 2-period cross-over study. The derived change measured at each dose were the repeated measures.

End point type	Secondary
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End point timeframe:

Period 1: baseline (Day 0) and 0-24 hours after Day 4, 8, 12 & 16 doses; Period 2: baseline (Day 22) and 0-24 hours after Day 26, 30, 34 and 38 doses

End point values	Cohort 1 - Gefapixant 50 mg	Cohort 1 - Placebo for Gefapixant 50 mg	Cohort 1 - Gefapixant 100 mg	Cohort 1 - Placebo for 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				
least squares mean (confidence interval 95%)	-16.6 (-22.4 to -10.9)	-1.5 (-7.5 to 4.5)	-17.6 (-24.1 to -11.0)	-0.9 (-7.5 to 5.8)

End point values	Cohort 1 - Gefapixant 150 mg	Cohort 1 - Placebo for Gefapixant 150 mg	Cohort 1 - Gefapixant 200 mg	Cohort 1 - Placebo for 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				
least squares mean (confidence interval 95%)	-18.0 (-26.1 to -9.9)	1.5 (-6.8 to 9.8)	-17.4 (-25.2 to -9.5)	3.1 (-4.9 to 11.2)

Statistical analyses

Statistical analysis title	Gefapixant 50 mg vs. Placebo
Comparison groups	Cohort 1 - Gefapixant 50 mg v Cohort 1 - Placebo for Gefapixant 50 mg
Number of subjects included in analysis	51
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)
Point estimate	-15.2
Confidence interval	
level	95 %
sides	2-sided
lower limit	-23.5
upper limit	-6.8

Statistical analysis title	Gefapixant 100 mg vs. Placebo
Comparison groups	Cohort 1 - Gefapixant 100 mg v Cohort 1 - Placebo for Gefapixant 100 mg

Number of subjects included in analysis	49
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)
Point estimate	-16.7
Confidence interval	
level	95 %
sides	2-sided
lower limit	-26.1
upper limit	-7.4

Statistical analysis title	Gefapixant 150 mg vs. Placebo
Comparison groups	Cohort 1 - Gefapixant 150 mg v Cohort 1 - Placebo for Gefapixant 150 mg
Number of subjects included in analysis	45
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.002
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)
Point estimate	-19.5
Confidence interval	
level	95 %
sides	2-sided
lower limit	-31.1
upper limit	-7.8

Statistical analysis title	Gefapixant 200 mg vs. Placebo
Comparison groups	Cohort 1 - Gefapixant 200 mg v Cohort 1 - Placebo for Gefapixant 200 mg
Number of subjects included in analysis	50
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)
Point estimate	-20.5
Confidence interval	
level	95 %
sides	2-sided
lower limit	-31.8
upper limit	-9.3

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

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

Total (0-24 hours) Objective Cough Frequency is the total number of cough events during the monitoring period divided by the total duration (in hours, i.e., 24 hours mostly) for the monitoring period. 24-hour sound recordings were collected using a digital recording device. Results are change from baseline: a negative result indicates a decrease in cough frequency, while a positive result indicates an increase in cough frequency.

Cough frequency was analyzed using MMRM to evaluate the results of the 2-period cross-over study. The derived change measured at each dose were the repeated measures.

End point type	Secondary
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End point timeframe:

Period 1: baseline (Day 0) and 0-24 hours after Day 4, 8, 12 & 16 doses; Period 2: baseline (Day 22) and 0-24 hours after Day 26, 30, 34 and 38 doses

End point values	Cohort 2 - Gefapixant 7.5 mg	Cohort 2 - Placebo for Gefapixant 7.5 mg	Cohort 2 - Gefapixant 15 mg	Cohort 2 - Placebo for 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				
least squares mean (confidence interval 95%)	-6.9 (-12.6 to -1.1)	-2.7 (-8.6 to 3.1)	-11.0 (-15.5 to -6.4)	-3.8 (-8.4 to 0.9)

End point values	Cohort 2 - Gefapixant 30 mg	Cohort 2 - Placebo for Gefapixant 30 mg	Cohort 2 - Gefapixant 50 mg	Cohort 2 - Placebo for 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				
least squares mean (confidence interval 95%)	-16.9 (-23.3 to -10.4)	1.4 (-5.2 to 7.9)	-15.9 (-21.0 to -9.9)	1.8 (-4.4 to 7.9)

Statistical analyses

Statistical analysis title	Gefapixant 7.5 mg vs. Placebo
Comparison groups	Cohort 2 - Gefapixant 7.5 mg v Cohort 2 - Placebo for Gefapixant 7.5 mg
Number of subjects included in analysis	57
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.315
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)
Point estimate	-4.1

Confidence interval	
level	95 %
sides	2-sided
lower limit	-12.3
upper limit	4

Statistical analysis title	Gefapixant 15 mg vs. Placebo
Comparison groups	Cohort 2 - Gefapixant 15 mg v Cohort 2 - Placebo for Gefapixant 15 mg
Number of subjects included in analysis	59
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.03
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)
Point estimate	-7.2
Confidence interval	
level	95 %
sides	2-sided
lower limit	-13.7
upper limit	-0.7

Statistical analysis title	Gefapixant 30 mg vs. Placebo
Comparison groups	Cohort 2 - Gefapixant 30 mg v Cohort 2 - Placebo for Gefapixant 30 mg
Number of subjects included in analysis	58
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)
Point estimate	-18.2
Confidence interval	
level	95 %
sides	2-sided
lower limit	-27.4
upper limit	-9.1

Statistical analysis title	Gefapixant 50 mg vs. Placebo
Comparison groups	Cohort 2 - Gefapixant 50 mg v Cohort 2 - Placebo for Gefapixant 50 mg

Number of subjects included in analysis	56
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)
Point estimate	-17.6
Confidence interval	
level	95 %
sides	2-sided
lower limit	-26.3
upper limit	-9

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

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

Sleep Objective Cough Frequency is the 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. Results are change from baseline: a negative result indicates a decrease in cough frequency, while a positive result indicates an increase in cough frequency.

Cough frequency was analyzed using MMRM to evaluate the results of the 2-period cross-over study. The derived change measured at each dose were the repeated measures.

End point type	Secondary
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End point timeframe:

Period 1 (while asleep): baseline (Day 0) and 24 hours after Day 4, 8, 12 & 16 doses; Period 2 (while asleep): baseline (Day 22) and 24 hours after Day 26, 30, 34 and 38 doses

End point values	Cohort 1 - Gefapixant 50 mg	Cohort 1 - Placebo for Gefapixant 50 mg	Cohort 1 - Gefapixant 100 mg	Cohort 1 - Placebo for 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				
least squares mean (confidence interval 95%)	-3.5 (-7.0 to 0.1)	0.1 (-3.5 to 3.7)	-3.1 (-6.8 to 0.6)	-0.7 (-4.2 to 2.8)

End point values	Cohort 1 - Gefapixant 150 mg	Cohort 1 - Placebo for Gefapixant 150 mg	Cohort 1 - Gefapixant 200 mg	Cohort 1 - Placebo for 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				
least squares mean (confidence interval 95%)	-2.0 (-4.8 to 0.7)	-0.1 (-2.8 to 2.6)	-3.6 (-7.0 to 0.1)	0.2 (-3.2 to 3.6)

Statistical analyses

Statistical analysis title	Gefapixant 50 mg vs. Placebo
Comparison groups	Cohort 1 - Gefapixant 50 mg v Cohort 1 - Placebo for Gefapixant 50 mg
Number of subjects included in analysis	48
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.169
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)
Point estimate	-3.5
Confidence interval	
level	95 %
sides	2-sided
lower limit	-8.6
upper limit	1.6

Statistical analysis title	Gefapixant 100 mg vs. Placebo
Comparison groups	Cohort 1 - Gefapixant 100 mg v Cohort 1 - Placebo for Gefapixant 100 mg
Number of subjects included in analysis	45
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.341
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)
Point estimate	-2.4
Confidence interval	
level	95 %
sides	2-sided
lower limit	-7.5
upper limit	2.6

Statistical analysis title	Gefapixant 150 mg vs. Placebo
Comparison groups	Cohort 1 - Gefapixant 150 mg v Cohort 1 - Placebo for Gefapixant 150 mg

Number of subjects included in analysis	44
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.311
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)
Point estimate	-2
Confidence interval	
level	95 %
sides	2-sided
lower limit	-5.8
upper limit	1.9

Statistical analysis title	Gefapixant 200 mg vs. Placebo
Comparison groups	Cohort 1 - Gefapixant 200 mg v Cohort 1 - Placebo for Gefapixant 200 mg
Number of subjects included in analysis	49
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.128
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)
Point estimate	-3.7
Confidence interval	
level	95 %
sides	2-sided
lower limit	-8.6
upper limit	1.1

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 is the 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. Results are change from baseline: a negative result indicates a decrease in cough frequency, while a positive result indicates an increase in cough frequency.	
Cough frequency was analyzed using MMRM to evaluate the results of the 2-period cross-over study. The derived change measured at each dose were the repeated measures.	
End point type	Secondary
End point timeframe:	
Period 1 (while asleep): baseline (Day 0) and 24 hours after Day 4, 8, 12 & 16 doses; Period 2 (while asleep): baseline (Day 22) and 24 hours after Day 26, 30, 34 and 38 doses	

End point values	Cohort 2 - Gefapixant 7.5 mg	Cohort 2 - Placebo for Gefapixant 7.5 mg	Cohort 2 - Gefapixant 15 mg	Cohort 2 - Placebo for 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				
least squares mean (confidence interval 95%)	0.6 (-2.7 to 3.9)	-0.6 (-3.9 to 2.8)	-3.1 (-5.6 to -0.5)	-2.5 (-5.1 to 0.2)

End point values	Cohort 2 - Gefapixant 30 mg	Cohort 2 - Placebo for Gefapixant 30 mg	Cohort 2 - Gefapixant 50 mg	Cohort 2 - Placebo for 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				
least squares mean (confidence interval 95%)	-2.4 (-4.7 to -0.2)	-1.6 (-3.8 to 0.7)	-3.0 (-8.7 to 2.6)	2.1 (-3.6 to 7.9)

Statistical analyses

Statistical analysis title	Gefapixant 7.5 mg vs. Placebo
Comparison groups	Cohort 2 - Gefapixant 7.5 mg v Cohort 2 - Placebo for Gefapixant 7.5 mg
Number of subjects included in analysis	57
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.613
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)
Point estimate	1.2
Confidence interval	
level	95 %
sides	2-sided
lower limit	-3.5
upper limit	5.9

Statistical analysis title	Gefapixant 15 mg vs. Placebo
Comparison groups	Cohort 2 - Gefapixant 15 mg v Cohort 2 - Placebo for Gefapixant 15 mg

Number of subjects included in analysis	59
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.743
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)
Point estimate	-0.6
Confidence interval	
level	95 %
sides	2-sided
lower limit	-4.3
upper limit	3.1

Statistical analysis title	Gefapixant 30 mg vs. Placebo
Comparison groups	Cohort 2 - Gefapixant 30 mg v Cohort 2 - Placebo for Gefapixant 30 mg
Number of subjects included in analysis	58
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.589
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)
Point estimate	-0.9
Confidence interval	
level	95 %
sides	2-sided
lower limit	-4.1
upper limit	2.3

Statistical analysis title	Gefapixant 50 mg vs. Placebo
Comparison groups	Cohort 2 - Gefapixant 50 mg v Cohort 2 - Placebo for Gefapixant 50 mg
Number of subjects included in analysis	55
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.205
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)
Point estimate	-5.1
Confidence interval	
level	95 %
sides	2-sided
lower limit	-13.2
upper limit	2.9

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
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End point description:

The daily CSD Score is calculated using the daily CSD instrument, a 7-item, disease specific, patient-reported outcome measure with a recall period of "today" (the current day). The measure evaluates frequency of cough (3 items); intensity of cough (2 items); and sleep disruption due to cough (2 items). Each of these 7 items is rated on an 11-point scale, ranging from 0 (best) to 10 (worst), with higher scores indicating greater severity. The total daily CSD score is the sum of these 7 item scores (Min=0, Max=70). Baseline CSD score = average of CSD scores at screening and baseline. Results are change from baseline: a negative result indicates a decrease in cough severity, while a positive result indicates an increase in cough severity.

CSD was analyzed using MMRM to evaluate the results of the 2-period cross-over study. The derived change measured at each dose were the repeated measures.

End point type	Secondary
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End point timeframe:

Screening; Period 1: baseline (Day 0) and Days 1-17; Period 2: baseline (Day 22) and Days 23-39

End point values	Cohort 1 - Gefapixant 50 mg	Cohort 1 - Placebo for Gefapixant 50 mg	Cohort 1 - Gefapixant 100 mg	Cohort 1 - Placebo for Gefapixant 100 mg
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	27	27	26	27
Units: Score on a scale				
least squares mean (confidence interval 95%)	-0.6 (-1.2 to -0.1)	0.0 (-0.5 to 0.5)	-1.1 (-1.8 to -0.5)	0.1 (-0.5 to 0.8)

End point values	Cohort 1 - Gefapixant 150 mg	Cohort 1 - Placebo for Gefapixant 150 mg	Cohort 1 - Gefapixant 200 mg	Cohort 1 - Placebo for Gefapixant 200 mg
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	26	27	28	28
Units: Score on a scale				
least squares mean (confidence interval 95%)	-1.5 (-2.2 to -0.8)	0.1 (-0.6 to 0.8)	-1.6 (-2.4 to -0.8)	0.1 (-0.7 to 0.9)

Statistical analyses

Statistical analysis title	Gefapixant 50 mg vs. Placebo
Comparison groups	Cohort 1 - Gefapixant 50 mg v Cohort 1 - Placebo for Gefapixant 50 mg

Number of subjects included in analysis	54
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0811
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)
Point estimate	-0.6
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.4
upper limit	0.1

Statistical analysis title	Gefapixant 100 mg vs. Placebo
Comparison groups	Cohort 1 - Gefapixant 100 mg v Cohort 1 - Placebo for Gefapixant 100 mg
Number of subjects included in analysis	53
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0097
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)
Point estimate	-1.3
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.2
upper limit	-0.3

Statistical analysis title	Gefapixant 150 mg vs. Placebo
Comparison groups	Cohort 1 - Gefapixant 150 mg v Cohort 1 - Placebo for Gefapixant 150 mg
Number of subjects included in analysis	53
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0025
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)
Point estimate	-1.6
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.6
upper limit	-0.6

Statistical analysis title	Gefapixant 200 mg vs. Placebo
Comparison groups	Cohort 1 - Gefapixant 200 mg v Cohort 1 - Placebo for Gefapixant 200 mg
Number of subjects included in analysis	56
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.005
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)
Point estimate	-1.7
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.8
upper limit	-0.5

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
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End point description:

The daily CSD Score is calculated using the daily CSD instrument, a 7-item, disease specific, patient-reported outcome measure with a recall period of "today" (the current day). The measure evaluates frequency of cough (3 items); intensity of cough (2 items); and sleep disruption due to cough (2 items). Each of these 7 items is rated on an 11-point scale, ranging from 0 (best) to 10 (worst), with higher scores indicating greater severity. The total daily CSD score is the sum of these 7 item scores (Min=0, Max=70). Baseline CSD score = average of CSD scores at screening and baseline. Results are change from baseline: a negative result indicates a decrease in cough severity, while a positive result indicates an increase in cough severity.

CSD was analyzed using MMRM to evaluate the results of the 2-period cross-over study. The derived change measured at each dose were the repeated measures.

End point type	Secondary
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End point timeframe:

Screening; Period 1: baseline (Day 0) and Days 1-17; Period 2: baseline (Day 22) and Days 23-39

End point values	Cohort 2 - Gefapixant 7.5 mg	Cohort 2 - Placebo for Gefapixant 7.5 mg	Cohort 2 - Gefapixant 15 mg	Cohort 2 - Placebo for 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: Score on a scale				
least squares mean (confidence interval 95%)	-1.0 (-1.5 to -0.5)	-0.3 (-0.8 to 0.2)	-1.2 (-1.8 to -0.6)	-0.3 (-0.9 to 0.3)

End point values	Cohort 2 - Gefapixant 30 mg	Cohort 2 - Placebo for Gefapixant 30	Cohort 2 - Gefapixant 50 mg	Cohort 2 - Placebo for Gefapixant 50
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		mg		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: Score on a scale				
least squares mean (confidence interval 95%)	-1.7 (-2.3 to -1.1)	-0.3 (-1.0 to 0.3)	-1.6 (-2.4 to -0.9)	-0.5 (-1.3 to 0.2)

Statistical analyses

Statistical analysis title	Gefapixant 7.5 mg vs. Placebo
Comparison groups	Cohort 2 - Gefapixant 7.5 mg v Cohort 2 - Placebo for Gefapixant 7.5 mg
Number of subjects included in analysis	59
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0506
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)
Point estimate	-0.7
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.4
upper limit	0

Statistical analysis title	Gefapixant 15 mg vs. Placebo
Comparison groups	Cohort 2 - Gefapixant 15 mg v Cohort 2 - Placebo for Gefapixant 15 mg
Number of subjects included in analysis	59
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0447
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)
Point estimate	-0.9
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.7
upper limit	0

Statistical analysis title	Gefapixant 30 mg vs. Placebo
Comparison groups	Cohort 2 - Gefapixant 30 mg v Cohort 2 - Placebo for Gefapixant 30 mg

Number of subjects included in analysis	59
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0026
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)
Point estimate	-1.3
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.2
upper limit	-0.5

Statistical analysis title	Gefapixant 50 mg vs. Placebo
Comparison groups	Cohort 2 - Gefapixant 50 mg v Cohort 2 - Placebo for Gefapixant 50 mg
Number of subjects included in analysis	58
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0405
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)
Point estimate	-1.1
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.2
upper limit	0

Secondary: Change from Baseline at End of Treatment Period Leicester Cough Questionnaire (LCQ): individual Domain and Total Scores for Cohort 1 and 2

End point title	Change from Baseline at End of Treatment Period Leicester Cough Questionnaire (LCQ): individual Domain and Total Scores for Cohort 1 and 2
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End point description:

The LCQ-Acute is a 19-item health-related quality-of-life (HRQoL) questionnaire specific for acute cough which contains three domains (i.e., physical, psychological, and social). It is calculated as a mean score for each domain ranging from 1 (worst) to 7 (best), and total score ranging from 3 (worst) to 21 (best). Each item on the LCQ-acute assesses symptoms or the impact of symptoms on HRQoL in the last 24 hours using a 7-point Likert scale ranging from 1 to 7. Higher scores indicate better HRQoL. Participants' perception of their cough severity was assessed, based on the LCQ-Acute score, at Baseline and last day of dose.

LCQ was analyzed using MMRM to evaluate the results of the 2-period cross-over study. The derived change measured at each dose were the repeated measures.

End point type	Secondary
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End point timeframe:

Period 1: Day 0 (baseline) and Day 17; Period 2: Day 22 (baseline) and Day 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: Score on a scale				
least squares mean (confidence interval 95%)	3.02 (1.61 to 4.42)	-0.82 (-2.19 to 0.55)	3.57 (2.27 to 4.87)	0.05 (-1.28 to 1.37)

Statistical analyses

Statistical analysis title	Gefapixant Vs. Placebo Cohort 1
Comparison groups	Cohort 1 - Gefapixant v Cohort 1 - Placebo
Number of subjects included in analysis	55
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)
Point estimate	3.84
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.88
upper limit	5.8

Statistical analysis title	Gefapixant vs. Placebo Cohort 2
Comparison groups	Cohort 2 - Gefapixant v Cohort 2 - Placebo
Number of subjects included in analysis	59
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)
Point estimate	3.52
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.66
upper limit	5.38

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
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End point description:

Cough VAS is scored from 0 to 100 using a 10 mm visual analogue scale with 0 at 0mm and 100 at 10mm with 0 (no cough) and 100 (most severe cough). Baseline cough VAS is defined as average of screening and baseline cough VAS. Results are change from baseline: a negative result indicates a decrease in cough severity, while a positive result indicates an increase in cough severity.

Cough VAS was analyzed using MMRM to evaluate the results of the 2-period cross-over study. The derived change measured at each dose were the repeated measures.

End point type	Secondary
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End point timeframe:

Screening; Period 1: baseline (Day 0) and Day 4, 8, 12 & 16; Period 2: baseline (Day 22) and Day 26, 30, 34, 38 and 39

End point values	Cohort 1 - Gefapixant 50 mg	Cohort 1 - Placebo for Gefapixant 50 mg	Cohort 1 - Gefapixant 100 mg	Cohort 1 - Placebo for 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: Score on a scale				
least squares mean (confidence interval 95%)	-14.4 (-23.4 to -5.5)	-3.8 (-12.6 to 5.0)	-26.3 (-36.0 to -16.6)	-6.3 (-15.9 to 3.2)

End point values	Cohort 1 - Gefapixant 150 mg	Cohort 1 - Placebo for Gefapixant 150 mg	Cohort 1 - Gefapixant 200 mg	Cohort 1 - Placebo for 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: Score on a scale				
least squares mean (confidence interval 95%)	-28.8 (-39.1 to -18.4)	-2.6 (-12.8 to 7.6)	-31.5 (-41.9 to -21.0)	2.3 (-8.0 to 12.6)

Statistical analyses

Statistical analysis title	Gefapixant 50 mg vs. Placebo
Comparison groups	Cohort 1 - Gefapixant 50 mg v Cohort 1 - Placebo for Gefapixant 50 mg
Number of subjects included in analysis	55
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.096
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)
Point estimate	-10.6

Confidence interval	
level	95 %
sides	2-sided
lower limit	-23.2
upper limit	1.9

Statistical analysis title	Gefapixant 100 mg vs. Placebo
Comparison groups	Cohort 1 - Gefapixant 100 mg v Cohort 1 - Placebo for Gefapixant 100 mg
Number of subjects included in analysis	54
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.005
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)
Point estimate	-20
Confidence interval	
level	95 %
sides	2-sided
lower limit	-33.6
upper limit	-6.3

Statistical analysis title	Gefapixant 150 mg vs. Placebo
Comparison groups	Cohort 1 - Gefapixant 150 mg v Cohort 1 - Placebo for Gefapixant 150 mg
Number of subjects included in analysis	53
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)
Point estimate	-26.1
Confidence interval	
level	95 %
sides	2-sided
lower limit	-40.7
upper limit	-11.6

Statistical analysis title	Gefapixant 200 mg vs. Placebo
Comparison groups	Cohort 1 - Gefapixant 200 mg v Cohort 1 - Placebo for Gefapixant 200 mg

Number of subjects included in analysis	53
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)
Point estimate	-33.8
Confidence interval	
level	95 %
sides	2-sided
lower limit	-48.4
upper limit	-19.1

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
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End point description:

Cough VAS is scored from 0 to 100 using a 10 mm visual analogue scale with 0 at 0mm and 100 at 10mm with 0 (no cough) and 100 (most severe cough). Baseline cough VAS is defined as average of screening and baseline cough VAS. Results are change from baseline: a negative result indicates a decrease in cough severity, while a positive result indicates an increase in cough severity.

Cough VAS was analyzed using MMRM to evaluate the results of the 2-period cross-over study. The derived change measured at each dose were the repeated measures.

End point type	Secondary
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End point timeframe:

Screening; Period 1: baseline (Day 0) and Day 4, 8, 12 & 16; Period 2: baseline (Day 22) and Day 26, 30, 34, 38 and 39

End point values	Cohort 2 - Gefapixant 7.5 mg	Cohort 2 - Placebo for Gefapixant 7.5 mg	Cohort 2 - Gefapixant 15 mg	Cohort 2 - Placebo for 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: Score on a scale				
least squares mean (confidence interval 95%)	-12.6 (-21.5 to -3.8)	-6.2 (-15.2 to 2.9)	-17.4 (-26.0 to -8.7)	-10.0 (-18.7 to -1.2)

End point values	Cohort 2 - Gefapixant 30 mg	Cohort 2 - Placebo for Gefapixant 30 mg	Cohort 2 - Gefapixant 50 mg	Cohort 2 - Placebo for 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: Score on a scale				
least squares mean (confidence interval 95%)	-23.3 (-31.7 to -14.9)	-7.7 (-16.2 to 0.8)	-24.7 (-35.2 to -14.2)	-9.3 (-19.9 to 1.3)

95%)	-14.9)	0.9)	-14.2)	1.4)
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Statistical analyses

Statistical analysis title	Gefapixant 7.5 mg vs. Placebo
Comparison groups	Cohort 2 - Gefapixant 7.5 mg v Cohort 2 - Placebo for Gefapixant 7.5 mg
Number of subjects included in analysis	59
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.311
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)
Point estimate	-6.4
Confidence interval	
level	95 %
sides	2-sided
lower limit	-19.1
upper limit	6.2

Statistical analysis title	Gefapixant 15 mg vs. Placebo
Comparison groups	Cohort 2 - Gefapixant 15 mg v Cohort 2 - Placebo for Gefapixant 15 mg
Number of subjects included in analysis	59
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.232
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)
Point estimate	-7.4
Confidence interval	
level	95 %
sides	2-sided
lower limit	-19.7
upper limit	4.9

Statistical analysis title	Gefapixant 30 mg vs. Placebo
Comparison groups	Cohort 2 - Gefapixant 30 mg v Cohort 2 - Placebo for Gefapixant 30 mg

Number of subjects included in analysis	59
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.012
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)
Point estimate	-15.6
Confidence interval	
level	95 %
sides	2-sided
lower limit	-27.6
upper limit	-3.6

Statistical analysis title	Gefapixant 50 mg vs. Placebo
Comparison groups	Cohort 2 - Gefapixant 50 mg v Cohort 2 - Placebo for Gefapixant 50 mg
Number of subjects included in analysis	58
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.043
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)
Point estimate	-15.4
Confidence interval	
level	95 %
sides	2-sided
lower limit	-30.4
upper limit	-0.5

Other pre-specified: Baseline (Predose) Awake Objective Cough Frequency for Cohort 1 and Cohort 2

End point title	Baseline (Predose) Awake Objective Cough Frequency for Cohort 1 and Cohort 2
End point description: Awake Objective Cough Frequency (per hour) is 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. Baseline measurements were not available by individual arm because baseline cough frequencies were measured before participants received the first dose of study drug. Baseline summaries were evaluated based on the participant's randomized group (gefapixant or placebo).	
End point type	Other pre-specified
End point timeframe: 24 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)	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

Other pre-specified: 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
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End point description:

Awake (0 - 8 hours) Objective Cough Frequency is the 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. Baseline measurements were not available by individual arm because baseline cough frequencies were measured before participants received the first dose of study drug. Baseline summaries were evaluated based on the participant's randomized group (gefapixant or placebo).

End point type	Other pre-specified
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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 (± 42.30)	47.2 (± 42.09)	42.2 (± 39.42)

Statistical analyses

No statistical analyses for this end point

Other pre-specified: 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
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End point description:

Total (0 - 24 hours) Objective Cough Frequency is the 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. Baseline measurements were not available by individual arm because baseline cough frequencies were measured before participants received the first dose of study drug. Baseline summaries were evaluated based on the participant's randomized group

(gefapixant or placebo).

End point type	Other pre-specified
End point timeframe:	
24 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)	39.7 (\pm 28.38)	37.9 (\pm 27.46)	36.3 (\pm 32.28)	32.2 (\pm 27.97)

Statistical analyses

No statistical analyses for this end point

Other pre-specified: 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
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End point description:

Sleep Objective Cough Frequency is the 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. Baseline measurements were not available by individual arm because baseline cough frequencies were measured before participants received the first dose of study drug. Baseline summaries were evaluated based on the participant's randomized group (gefapixant or placebo).

End point type	Other pre-specified
End point timeframe:	
First 8 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 (\pm 9.30)	7.8 (\pm 9.80)	10.1 (\pm 26.77)	5.6 (\pm 7.58)

Statistical analyses

No statistical analyses for this end point

Other pre-specified: 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 Score is calculated using the daily CSD instrument, a 7-item, disease specific, patient-reported outcome measure with a recall period of "today" (the current day). The measure evaluates frequency of cough (3 items); intensity of cough (2 items); and sleep disruption due to cough (2 items). Each of these 7 items is rated on an 11-point scale, ranging from 0 (best) to 10 (worst), with higher scores indicating greater severity. The total daily CSD score is the sum of these 7 item scores (Min=0, Max=70). Baseline CSD score = average of CSD scores at screening and baseline. A negative result indicates a decrease in cough frequency, while a positive result indicates an increase in cough frequency. Baseline measurements were not available by individual arm because baseline cough frequencies were measured before participants received the first dose of study drug. Baseline summaries were evaluated based on the participant's randomized group (gefaxipant or placebo).	
End point type	Other pre-specified
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: Score 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

Other pre-specified: 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-Acute is a 19-item health-related quality-of-life (HRQoL) questionnaire specific for acute cough which contains three domains (i.e., physical, psychological, and social). It is calculated as a mean score for each domain ranging from 1 (worst) to 7 (best), and total score ranging from 3 (worst) to 21 (best). Each item on the LCQ-acute assesses symptoms or the impact of symptoms on HRQoL in the last 24 hours using a 7-point Likert scale ranging from 1 to 7. Higher scores indicate better HRQoL. As per the Statistical Analysis Plan, each domain and total LCQ score change from baseline were analyzed without the treatment by dose interaction. Baseline summaries were evaluated based on the participant's randomized group (gefaxipant or placebo).	
End point type	Other pre-specified
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: Score on a scale				
arithmetic mean (standard deviation)				
Psychological Domain Score	3.8 (± 1.21)	4.1 (± 1.45)	3.9 (± 1.58)	4.1 (± 1.56)
Physical Domain Score	4.4 (± 0.99)	4.7 (± 1.06)	4.8 (± 1.19)	5.0 (± 1.00)
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

Other pre-specified: 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
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End point description:

Cough VAS: scored from 0 to 100 using a 10 mm visual analogue scale with 0 (no cough) and 100 (most severe cough) mm. Baseline cough VAS is defined as average of screening and baseline cough VAS. Baseline measurements were not available by individual arm because baseline cough frequencies were measured before participants received the first dose of study drug. Baseline summaries were evaluated based on the participant's randomized group (gefapixant or placebo).

End point type	Other pre-specified
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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: Score 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:

Adverse event data collection is up to 11 weeks

All-cause mortality is up to 22 weeks

Adverse event reporting additional description:

Analysis population consisted of all randomized participants who received at least 1 dose of study drug

Assessment type	Systematic
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Dictionary used

Dictionary name	MedDRA
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Dictionary version	17.1
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Reporting groups

Reporting group title	Cohort 1: Gefapixant 50 mg
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Reporting group description:

Gefapixant 50 mg tablet administered by mouth twice daily (BID) for 4 days.

Reporting group title	Cohort 1: Gefapixant 100 mg
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Reporting group description:

Gefapixant 100 mg tablet administered by mouth BID or 4 days.

Reporting group title	Cohort 1 - Gefapixant 150 mg
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Reporting group description:

Gefapixant 150 mg tablet administered by mouth BID for 4 days.

Reporting group title	Cohort 1: Gefapixant 200 mg
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Reporting group description:

Gefapixant 200 mg tablet administered by mouth BID for 4 days.

Reporting group title	Cohort 1 - Placebo
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Reporting group description:

Placebo tablet administered by mouth BID for 4 days each.

Reporting group title	Cohort 2 - Gefapixant 7.5 mg
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Reporting group description:

Gefapixant 7.5 mg tablet administered by mouth BID for 4 days.

Reporting group title	Cohort 2 - Gefapixant 15 mg
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Reporting group description:

Gefapixant 15 mg tablet administered by mouth BID for 4 days.

Reporting group title	Cohort 2 - Gefapixant 30 mg
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Reporting group description:

Gefapixant 30 mg tablet administered by mouth BID for 4 days.

Reporting group title	Cohort 2 - Gefapixant 50 mg
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Reporting group description:

Gefapixant 50 mg tablet administered by mouth BID for 4 days.

Reporting group title	Cohort 2- Placebo
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Reporting group description:

Placebo tablet administered by mouth BID for 4 days each.

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 occurrences (all)	1 / 28 (3.57%) 1	0 / 28 (0.00%) 0	0 / 26 (0.00%) 0
Hypoaesthesia oral subjects affected / exposed occurrences (all)	1 / 28 (3.57%) 1	2 / 28 (7.14%) 2	0 / 26 (0.00%) 0
Paraesthesia oral subjects affected / exposed occurrences (all)	2 / 28 (7.14%) 2	1 / 28 (3.57%) 1	0 / 26 (0.00%) 0
Respiratory, thoracic and mediastinal disorders Nasal dryness subjects affected / exposed occurrences (all)	0 / 28 (0.00%) 0	0 / 28 (0.00%) 0	0 / 26 (0.00%) 0
Musculoskeletal and connective tissue disorders Flank pain subjects affected / exposed occurrences (all)	1 / 28 (3.57%) 1	0 / 28 (0.00%) 0	0 / 26 (0.00%) 0
Infections and infestations Rhinitis subjects affected / exposed occurrences (all)	0 / 28 (0.00%) 0	0 / 28 (0.00%) 0	0 / 26 (0.00%) 0
Upper respiratory tract infection subjects affected / exposed occurrences (all)	0 / 28 (0.00%) 0	0 / 28 (0.00%) 0	0 / 26 (0.00%) 0
Viral upper respiratory tract infection subjects affected / exposed occurrences (all)	0 / 28 (0.00%) 0	0 / 28 (0.00%) 0	0 / 26 (0.00%) 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 occurrences (all)	0 / 26 (0.00%) 0	0 / 28 (0.00%) 0	0 / 30 (0.00%) 0
Nervous system disorders			

Ageusia subjects affected / exposed occurrences (all)	1 / 26 (3.85%) 1	0 / 28 (0.00%) 0	0 / 30 (0.00%) 0
Dysgeusia subjects affected / exposed occurrences (all)	1 / 26 (3.85%) 1	1 / 28 (3.57%) 1	2 / 30 (6.67%) 2
Hypogeusia subjects affected / exposed occurrences (all)	0 / 26 (0.00%) 0	0 / 28 (0.00%) 0	0 / 30 (0.00%) 0
Gastrointestinal disorders			
Dry mouth subjects affected / exposed occurrences (all)	0 / 26 (0.00%) 0	0 / 28 (0.00%) 0	0 / 30 (0.00%) 0
Hypoaesthesia oral subjects affected / exposed occurrences (all)	1 / 26 (3.85%) 1	0 / 28 (0.00%) 0	0 / 30 (0.00%) 0
Paraesthesia oral subjects affected / exposed occurrences (all)	1 / 26 (3.85%) 1	0 / 28 (0.00%) 0	0 / 30 (0.00%) 0
Respiratory, thoracic and mediastinal disorders			
Nasal dryness subjects affected / exposed occurrences (all)	0 / 26 (0.00%) 0	0 / 28 (0.00%) 0	2 / 30 (6.67%) 2
Musculoskeletal and connective tissue disorders			
Flank pain subjects affected / exposed occurrences (all)	2 / 26 (7.69%) 2	0 / 28 (0.00%) 0	0 / 30 (0.00%) 0
Infections and infestations			
Rhinitis subjects affected / exposed occurrences (all)	0 / 26 (0.00%) 0	1 / 28 (3.57%) 1	2 / 30 (6.67%) 2
Upper respiratory tract infection subjects affected / exposed occurrences (all)	0 / 26 (0.00%) 0	1 / 28 (3.57%) 1	0 / 30 (0.00%) 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 occurrences (all)	0 / 30 (0.00%) 0	0 / 30 (0.00%) 0	0 / 30 (0.00%) 0
Infections and infestations			
Rhinitis subjects affected / exposed occurrences (all)	0 / 30 (0.00%) 0	0 / 30 (0.00%) 0	0 / 30 (0.00%) 0
Upper respiratory tract infection subjects affected / exposed occurrences (all)	0 / 30 (0.00%) 0	0 / 30 (0.00%) 0	4 / 30 (13.33%) 4
Viral upper respiratory tract infection subjects affected / exposed occurrences (all)	0 / 30 (0.00%) 0	0 / 30 (0.00%) 0	0 / 30 (0.00%) 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 occurrences (all)	0 / 29 (0.00%) 0		
Nervous system disorders			
Ageusia subjects affected / exposed occurrences (all)	0 / 29 (0.00%) 0		
Dysgeusia subjects affected / exposed occurrences (all)	0 / 29 (0.00%) 0		
Hypogeusia subjects affected / exposed occurrences (all)	0 / 29 (0.00%) 0		
Gastrointestinal disorders			
Dry mouth subjects affected / exposed occurrences (all)	2 / 29 (6.90%) 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