Clinical trial results:
A Study to Assess the Effect of AF-219 on Cough Reflex Sensitivity in Both Healthy and Chronic Cough Subjects

Summary

EudraCT number	2015-000464-34
Trial protocol	GB
Global end of trial date	16 May 2016

Results information

Result version number	v2 (current)
This version publication date	30 June 2021
First version publication date	31 May 2017
Version creation reason	

Trial information

Trial identification

Sponsor protocol code	7264-015

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02397460
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Merck Sharp & Dohme Corp.
Sponsor organisation address	2000 Galloping Hill Road, Kenilworth, NJ, United States, 07033
Public contact	Clinical Trials Disclosure, Merck Sharp & Dohme Corp., ClinicalTrialsDisclosure@merck.com
Scientific contact	Clinical Trials Disclosure, Merck Sharp & Dohme Corp., ClinicalTrialsDisclosure@merck.com

Notes:

Paediatric regulatory details

Is trial part of an agreed paediatric investigation plan (PIP)	No
Does article 45 of REGULATION (EC) No 1901/2006 apply to this trial?	No
Does article 46 of REGULATION (EC) No 1901/2006 apply to this trial?	No

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	16 May 2016
Is this the analysis of the primary completion data?	Yes
Primary completion date	16 May 2016
Global end of trial reached?	Yes
Global end of trial date	16 May 2016
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The primary objective of this double-blind crossover study is to assess the effect of single doses of 50 mg and 300 mg gefapixant (AF-219/MK-7264) on cough reflex sensitivity to capsaicin in both healthy participants and participants with chronic cough. This study will also assess the effect of single doses of gefapixant on cough reflex sensitivity to adenosine triphosphate (ATP) in healthy participants and participants with chronic cough.

Protection of trial subjects:

The Investigators agreed to conduct the study in compliance with the study Protocol, with the International Standard of Good Clinical Practice (GCP) procedures, with all applicable local GCP standards and regulations, and with the principles of the Declaration of Helsinki (1964) and relevant amendments.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	29 April 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 Kingdom: 50
Worldwide total number of subjects	50
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)	42
From 65 to 84 years	8

85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

The main purpose of the 14-day Screening period (Day -14 to Day -1) was to ensure that each participant met all the specified eligibility criteria. In addition, cough sensitivity was measured at Screening by standard clinical methodology using cough challenge in response to capsaicin.

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	Cohort 1: PBOGefapixant 300 mgPBOGefapixant 300 mg/Healthy

Arm description:

Healthy participants in Cohort 1/Sequence A received single doses of placebo (PBO) on Day 1 of Periods 1 and 3 and single doses of gefapixant 300 mg on Day 1 of Periods 2 and 4. (Each treatment period consisted of Day 1 and Day 2.) There was a minimum 48-hour washout period between treatment periods.

Arm type	Experimental or placebo
Investigational medicinal product name	Placebo (PBO)
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Gefapixant matching placebo, administered as a single oral dose

Arm title	Cohort 1: Gefapixant 300 mgPBOGefapixant 300 mgPBO/Healthy

Arm description:

Healthy participants in Cohort 1/Sequence B received single doses of gefapixant 300 mg on Day 1 of Periods 1 and 3 and singles doses of placebo on Day 1 of Periods 2 and 4. (Each treatment period consisted of Day 1 and Day 2.) There was a minimum 48-hour washout period between treatment periods.

Arm type	Experimental or placebo
Investigational medicinal product name	Gefapixant
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Gefapixant 300 mg, administered as a single oral dose

Arm title	Cohort 1: PBOGefapixant 300 mgPBOGefapixant 300 mg/CC

Arm description:

Participants with chronic cough (CC) in Cohort 1/Sequence A received singles doses of placebo on Day 1 of Periods 1 and 3 and single doses of gefapixant 300 mg on Day 1 of Periods 2 and 4. (Each treatment period consisted of Day 1 and Day 2.) There was a minimum 48-hour washout period between

treatment periods.

Arm type	Experimental or placebo
Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Gefapixant matching placebo, administered as a single oral dose

Arm title	Cohort 1: Gefapixant 300 mgPBOGefapixant 300 mgPBO/CC

Arm description:

Participants with chronic cough in Cohort 1/Sequence B received singles doses of gefapixant 300 mg on Day 1 of Periods 1 and 3 and single doses of placebo on Day 1 of Periods 2 and 4. (Each treatment period consisted of Day 1 and Day 2.) There was a minimum 48-hour washout period between treatment periods.

Arm type	Experimental or placebo
Investigational medicinal product name	Gefapixant
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Gefapixant 300 mg, administered as a single oral dose

Arm title	Cohort 2: PBOGefapixant 50 mgPBOGefapixant 50 mg/Healthy

Arm description:

Healthy participants in Cohort 2/Sequence A received singles doses of placebo on Day 1 of Periods 1 and 3 and single doses of gefapixant 50 mg on Day 1 of Periods 2 and 4. (Each treatment period consisted of Day 1 and Day 2.) There was a minimum 48-hour washout period between treatment periods.

Arm type	Experimental or placebo
Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Gefapixant matching placebo, administered as a single oral dose

Arm title	Cohort 2: Gefapixant 50 mgPBOGefapixant 50 mgPBO/Healthy

Arm description:

Healthy participants in Cohort 2/Sequence B received single doses of gefapixant 50 mg on Day 1 of Periods 1 and 3 and single doses of placebo on Day 1 of Periods 2 and 4. (Each treatment period consisted of Day 1 and Day 2.) There was a minimum 48-hour washout period between treatment periods.

Arm type	Experimental or placebo
Investigational medicinal product name	Gefapixant
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Gefapixant 50 mg, administered as a single oral dose

Arm title	Cohort 2: PBOGefapixant 50 mgPBOGefapixant 50 mg/CC

Arm description:

Participants with chronic cough in Cohort 2/Sequence A received singles doses of placebo on Day of Periods 1 and 3 and singles doses of gefapixant 50 mg on Day 1 of Periods 2 and 4. (Each treatment period consisted of Day 1 and Day 2.) There was a minimum 48-hour washout period between treatment periods.

Arm type	Experimental or placebo
Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Gefapixant matching placebo, administered as a single oral dose

Arm title	Cohort 2: Gefapixant 50 mgPBOGefapixant 50 mgPBO/CC

Arm description:

Participants with chronic cough in Cohort 2/Sequence B received singles doses of gefapixant 50 mg on Day 1 of Periods 1 and 3 and singles doses of placebo on Day 1 of Periods 2 and 4. (Each treatment period
consisted of Day 1 and Day 2.) There was a minimum 48-hour washout period between treatment periods.

Arm type	Experimental or placebo
Investigational medicinal product name	Gefapixant
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Gefapixant 50 mg, administered as a single oral dose

Number of subjects in period 1	Cohort 1: PBOGefapixant 300 mgPBOGefapixant 300 mg/Healthy	Cohort 1: Gefapixant 300 mgPBOGefapixant 300 mgPBO/Healthy	Cohort 1: PBOGefapixant 300 mgPBOGefapixant 300 mg/CC
Started	7	7	6
Completed	7	7	6

Number of subjects in period 1	Cohort 1: Gefapixant 300 mgPBOGefapixant 300 mgPBO/CC	Cohort 2: PBOGefapixant 50 mgPBOGefapixant 50 mg/Healthy	Cohort 2: Gefapixant 50 mgPBOGefapixant 50 mgPBO/Healthy
Started	6	6	6
Completed	6	6	6

Number of subjects in period 1	Cohort 2: PBOGefapixant 50 mgPBOGefapixant 50 mg/CC	Cohort 2: Gefapixant 50 mgPBOGefapixant 50 mgPBO/CC
Started	6	6
Completed	6	6

Period 2

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

Arms

Are arms mutually exclusive?	Yes
Arm title	Cohort 1: PBOGefapixant 300 mgPBOGefapixant 300 mg/Healthy

Arm description:

Healthy participants in Cohort 1/Sequence A received single doses of placebo (PBO) on Day 1 of Periods 1 and 3 and single doses of gefapixant 300 mg on Day 1 of Periods 2 and 4. (Each treatment period consisted of Day 1 and Day 2.) There was a minimum 48-hour washout period between treatment periods.

Arm type	Experimental or placebo
Investigational medicinal product name	Gefapixant
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Gefapixant 300 mg, administered as a single oral dose

Arm title	Cohort 1: Gefapixant 300 mgPBOGefapixant 300 mgPBO/Healthy

Arm description:

Healthy participants in Cohort 1/Sequence B received single doses of gefapixant 300 mg on Day 1 of Periods 1 and 3 and singles doses of placebo on Day 1 of Periods 2 and 4. (Each treatment period consisted of Day 1 and Day 2.) There was a minimum 48-hour washout period between treatment periods

Arm type	Experimental or placebo
Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Gefapixant matching placebo, administered as a single oral dose

Arm title	Cohort 1: PBOGefapixant 300 mgPBOGefapixant 300 mg/CC

Arm description:

Participants with chronic cough (CC) in Cohort 1/Sequence A received singles doses of placebo on Day 1 of Periods 1 and 3 and single doses of gefapixant 300 mg on Day 1 of Periods 2 and 4. (Each treatment period consisted of Day 1 and Day 2.) There was a minimum 48-hour washout period between

treatment periods.

Arm type	Experimental or placebo
Investigational medicinal product name	Gefapixant
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Gefapixant 300 mg, administered as a single oral dose

Arm title	Cohort 1: Gefapixant 300 mgPBOGefapixant 300 mgPBO/CC

Arm description:

Participants with chronic cough in Cohort 1/Sequence B received singles doses of gefapixant 300 mg on Day 1 of Periods 1 and 3 and single doses of placebo on Day 1 of Periods 2 and 4. (Each treatment period consisted of Day 1 and Day 2.) There was a minimum 48-hour washout period between treatment periods.

Arm type	Experimental or placebo
Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Gefapixant matching placebo, administered as a single oral dose

Arm title	Cohort 2: PBOGefapixant 50 mgPBOGefapixant 50 mg/Healthy

Arm description:

Healthy participants in Cohort 2/Sequence A received singles doses of placebo on Day 1 of Periods 1 and 3 and single doses of gefapixant 50 mg on Day 1 of Periods 2 and 4. (Each treatment period consisted of Day 1 and Day 2.) There was a minimum 48-hour washout period between treatment periods.

Arm type	Experimental or placebo
Investigational medicinal product name	Gefapixant
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Gefapixant 50 mg, administered as a single oral dose

Arm title	Cohort 2: Gefapixant 50 mgPBOGefapixant 50 mgPBO/Healthy

Arm description:

Healthy participants in Cohort 2/Sequence B received single doses of gefapixant 50 mg on Day 1 of Periods 1 and 3 and single doses of placebo on Day 1 of Periods 2 and 4. (Each treatment period consisted of Day 1 and Day 2.) There was a minimum 48-hour washout period between treatment periods.

Arm type	Experimental or placebo
Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Gefapixant matching placebo, administered as a single oral dose

Arm title	Cohort 2: PBOGefapixant 50 mgPBOGefapixant 50 mg/CC

Arm description:

Participants with chronic cough in Cohort 2/Sequence A received singles doses of placebo on Day of Periods 1 and 3 and singles doses of gefapixant 50 mg on Day 1 of Periods 2 and 4. (Each treatment period consisted of Day 1 and Day 2.) There was a minimum 48-hour washout period between treatment periods.

Arm type	Experimental or placebo
Investigational medicinal product name	Gefapixant
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Gefapixant 50 mg, administered as a single oral dose

Arm title	Cohort 2: Gefapixant 50 mgPBOGefapixant 50 mgPBO/CC

Arm description:

Participants with chronic cough in Cohort 2/Sequence B received singles doses of gefapixant 50 mg on Day 1 of Periods 1 and 3 and singles doses of placebo on Day 1 of Periods 2 and 4. (Each treatment period consisted of Day 1 and Day 2.) There was a minimum 48-hour washout period between treatment periods.

Arm type	Experimental or placebo
Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Gefapixant matching placebo, administered as a single oral dose

Number of subjects in period 2	Cohort 1: PBOGefapixant 300 mgPBOGefapixant 300 mg/Healthy	Cohort 1: Gefapixant 300 mgPBOGefapixant 300 mgPBO/Healthy	Cohort 1: PBOGefapixant 300 mgPBOGefapixant 300 mg/CC
Started	7	7	6
Completed	7	7	6
Not completed	0	0	0
Adverse event, non-fatal	-	-	-

Number of subjects in period 2	Cohort 1: Gefapixant 300 mgPBOGefapixant 300 mgPBO/CC	Cohort 2: PBOGefapixant 50 mgPBOGefapixant 50 mg/Healthy	Cohort 2: Gefapixant 50 mgPBOGefapixant 50 mgPBO/Healthy
Started	6	6	6
Completed	6	6	6
Not completed	0	0	0
Adverse event, non-fatal	-	-	-

Number of subjects in period 2	Cohort 2: PBOGefapixant 50 mgPBOGefapixant 50 mg/CC	Cohort 2: Gefapixant 50 mgPBOGefapixant 50 mgPBO/CC
Started	6	6

Completed	6	5
Not completed	0	1
Adverse event, non-fatal	-	1

Period 3

Period 3 title	Treatment Period 3
Is this the baseline period?	No
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator, Monitor, Data analyst

Arms

Are arms mutually exclusive?	Yes
Arm title	Cohort 1: PBOGefapixant 300 mgPBOGefapixant 300 mg/Healthy

Arm description:

Healthy participants in Cohort 1/Sequence A received single doses of placebo (PBO) on Day 1 of Periods 1 and 3 and single doses of gefapixant 300 mg on Day 1 of Periods 2 and 4. (Each treatment period consisted of Day 1 and Day 2.) There was a minimum 48-hour washout period between treatment periods.

Arm type	Experimental or placebo
Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Gefapixant matching placebo, administered as a single oral dose

Arm title	Cohort 1: Gefapixant 300 mgPBOGefapixant 300 mgPBO/Healthy

Arm description:

Healthy participants in Cohort 1/Sequence B received single doses of gefapixant 300 mg on Day 1 of Periods 1 and 3 and singles doses of placebo on Day 1 of Periods 2 and 4. (Each treatment period consisted of Day 1 and Day 2.) There was a minimum 48-hour washout period between treatment periods

Arm type	Experimental or placebo
Investigational medicinal product name	Gefapixant
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Gefapixant 300 mg, administered as a single oral dose

Arm title	Cohort 1: PBOGefapixant 300 mgPBOGefapixant 300 mg/CC

Arm description:

Participants with chronic cough (CC) in Cohort 1/Sequence A received singles doses of placebo on Day 1 of Periods 1 and 3 and single doses of gefapixant 300 mg on Day 1 of Periods 2 and 4. (Each treatment period consisted of Day 1 and Day 2.) There was a minimum 48-hour washout period between

treatment periods.

Arm type	Experimental or placebo
Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Gefapixant matching placebo, administered as a single oral dose

Arm title	Cohort 1: Gefapixant 300 mgPBOGefapixant 300 mgPBO/CC

Arm description:

Participants with chronic cough in Cohort 1/Sequence B received singles doses of gefapixant 300 mg on Day 1 of Periods 1 and 3 and single doses of placebo on Day 1 of Periods 2 and 4. (Each treatment period consisted of Day 1 and Day 2.) There was a minimum 48-hour washout period between treatment periods.

Arm type	Experimental or placebo
Investigational medicinal product name	Gefapixant
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Gefapixant 300 mg, administered as a single oral dose

Arm title	Cohort 2: PBOGefapixant 50 mgPBOGefapixant 50 mg/Healthy

Arm description:

Healthy participants in Cohort 2/Sequence A received singles doses of placebo on Day 1 of Periods 1 and 3 and single doses of gefapixant 50 mg on Day 1 of Periods 2 and 4. (Each treatment period consisted of Day 1 and Day 2.) There was a minimum 48-hour washout period between treatment periods.

Arm type	Experimental or placebo
Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Gefapixant matching placebo, administered as a single oral dose

Arm title	Cohort 2: Gefapixant 50 mgPBOGefapixant 50 mgPBO/Healthy

Arm description:

Healthy participants in Cohort 2/Sequence B received single doses of gefapixant 50 mg on Day 1 of Periods 1 and 3 and single doses of placebo on Day 1 of Periods 2 and 4. (Each treatment period consisted of Day 1 and Day 2.) There was a minimum 48-hour washout period between treatment periods.

Arm type	Experimental or placebo
Investigational medicinal product name	Gefapixant
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Gefapixant 50 mg, administered as a single oral dose

Arm title	Cohort 2: PBOGefapixant 50 mgPBOGefapixant 50 mg/CC

Arm description:

Participants with chronic cough in Cohort 2/Sequence A received singles doses of placebo on Day of Periods 1 and 3 and singles doses of gefapixant 50 mg on Day 1 of Periods 2 and 4. (Each treatment period consisted of Day 1 and Day 2.) There was a minimum 48-hour washout period between treatment periods.

Arm type	Experimental or placebo
Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Gefapixant matching placebo, administered as a single oral dose

Arm title	Cohort 2: Gefapixant 50 mgPBOGefapixant 50 mgPBO/CC

Arm description:

Participants with chronic cough in Cohort 2/Sequence B received singles doses of gefapixant 50 mg on Day 1 of Periods 1 and 3 and singles doses of placebo on Day 1 of Periods 2 and 4. (Each treatment period consisted of Day 1 and Day 2.) There was a minimum 48-hour washout period between treatment periods.

Arm type	Experimental or placebo
Investigational medicinal product name	Gefapixant
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Gefapixant 50 mg, administered as a single oral dose

Number of subjects in period 3	Cohort 1: PBOGefapixant 300 mgPBOGefapixant 300 mg/Healthy	Cohort 1: Gefapixant 300 mgPBOGefapixant 300 mgPBO/Healthy	Cohort 1: PBOGefapixant 300 mgPBOGefapixant 300 mg/CC
Started	7	7	6
Completed	7	7	6

Number of subjects in period 3	Cohort 1: Gefapixant 300 mgPBOGefapixant 300 mgPBO/CC	Cohort 2: PBOGefapixant 50 mgPBOGefapixant 50 mg/Healthy	Cohort 2: Gefapixant 50 mgPBOGefapixant 50 mgPBO/Healthy
Started	6	6	6
Completed	6	6	6

Number of subjects in period 3	Cohort 2: PBOGefapixant 50 mgPBOGefapixant 50 mg/CC	Cohort 2: Gefapixant 50 mgPBOGefapixant 50 mgPBO/CC
Started	6	5
Completed	6	5

Period 4

Period 4 title	Treatment Period 4
Is this the baseline period?	No
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator, Monitor, Data analyst

Arms

Are arms mutually exclusive?	Yes
Arm title	Cohort 1: PBOGefapixant 300 mgPBOGefapixant 300 mg/Healthy

Arm description:

Healthy participants in Cohort 1/Sequence A received single doses of placebo (PBO) on Day 1 of Periods 1 and 3 and single doses of gefapixant 300 mg on Day 1 of Periods 2 and 4. (Each treatment period consisted of Day 1 and Day 2.) There was a minimum 48-hour washout period between treatment periods.

Arm type	Experimental or placebo
Investigational medicinal product name	Gefapixant
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Gefapixant 300 mg, administered as a single oral dose

Arm title	Cohort 1: Gefapixant 300 mgPBOGefapixant 300 mgPBO/Healthy

Arm description:

Healthy participants in Cohort 1/Sequence B received single doses of gefapixant 300 mg on Day 1 of Periods 1 and 3 and singles doses of placebo on Day 1 of Periods 2 and 4. (Each treatment period consisted of Day 1 and Day 2.) There was a minimum 48-hour washout period between treatment periods

Arm type	Experimental or placebo
Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Gefapixant matching placebo, administered as a single oral dose

Arm title	Cohort 1: PBOGefapixant 300 mgPBOGefapixant 300 mg/CC

Arm description:

Participants with chronic cough (CC) in Cohort 1/Sequence A received singles doses of placebo on Day 1 of Periods 1 and 3 and single doses of gefapixant 300 mg on Day 1 of Periods 2 and 4. (Each treatment period consisted of Day 1 and Day 2.) There was a minimum 48-hour washout period between

treatment periods.

Arm type	Experimental or placebo
Investigational medicinal product name	Gefapixant
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Gefapixant 300 mg, administered as a single oral dose

Arm title	Cohort 1: Gefapixant 300 mgPBOGefapixant 300 mgPBO/CC

Arm description:

Participants with chronic cough in Cohort 1/Sequence B received singles doses of gefapixant 300 mg on Day 1 of Periods 1 and 3 and single doses of placebo on Day 1 of Periods 2 and 4. (Each treatment period consisted of Day 1 and Day 2.) There was a minimum 48-hour washout period between treatment periods.

Arm type	Experimental or placebo
Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Gefapixant matching placebo, administered as a single oral dose

Arm title	Cohort 2: PBOGefapixant 50 mgPBOGefapixant 50 mg/Healthy

Arm description:

Healthy participants in Cohort 2/Sequence A received singles doses of placebo on Day 1 of Periods 1 and 3 and single doses of gefapixant 50 mg on Day 1 of Periods 2 and 4. (Each treatment period consisted of Day 1 and Day 2.) There was a minimum 48-hour washout period between treatment periods.

Arm type	Experimental or placebo
Investigational medicinal product name	Gefapixant
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Gefapixant 50 mg, administered as a single oral dose

Arm title	Cohort 2: Gefapixant 50 mgPBOGefapixant 50 mgPBO/Healthy

Arm description:

Healthy participants in Cohort 2/Sequence B received single doses of gefapixant 50 mg on Day 1 of Periods 1 and 3 and single doses of placebo on Day 1 of Periods 2 and 4. (Each treatment period consisted of Day 1 and Day 2.) There was a minimum 48-hour washout period between treatment periods.

Arm type	Experimental or placebo
Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Gefapixant matching placebo, administered as a single oral dose

Arm title	Cohort 2: PBOGefapixant 50 mgPBOGefapixant 50 mg/CC

Arm description:

Participants with chronic cough in Cohort 2/Sequence A received singles doses of placebo on Day of Periods 1 and 3 and singles doses of gefapixant 50 mg on Day 1 of Periods 2 and 4. (Each treatment period consisted of Day 1 and Day 2.) There was a minimum 48-hour washout period between treatment periods.

Arm type	Experimental or placebo
Investigational medicinal product name	Gefapixant
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Gefapixant 50 mg, administered as a single oral dose

Arm title	Cohort 2: Gefapixant 50 mgPBOGefapixant 50 mgPBO/CC

Arm description:

Participants with chronic cough in Cohort 2/Sequence B received singles doses of gefapixant 50 mg on Day 1 of Periods 1 and 3 and singles doses of placebo on Day 1 of Periods 2 and 4. (Each treatment period consisted of Day 1 and Day 2.) There was a minimum 48-hour washout period between treatment periods.

Arm type	Experimental or placebo
Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Gefapixant matching placebo, administered as a single oral dose

Number of subjects in period 4	Cohort 1: PBOGefapixant 300 mgPBOGefapixant 300 mg/Healthy	Cohort 1: Gefapixant 300 mgPBOGefapixant 300 mgPBO/Healthy	Cohort 1: PBOGefapixant 300 mgPBOGefapixant 300 mg/CC
Started	7	7	6
Completed	7	6	6
Not completed	0	1	0
Physician decision	-	-	-
Adverse event, non-fatal	-	1	-

Number of subjects in period 4	Cohort 1: Gefapixant 300 mgPBOGefapixant 300 mgPBO/CC	Cohort 2: PBOGefapixant 50 mgPBOGefapixant 50 mg/Healthy	Cohort 2: Gefapixant 50 mgPBOGefapixant 50 mgPBO/Healthy
Started	6	6	5
Completed	6	5	5
Not completed	0	1	0
Physician decision	-	1	-
Adverse event, non-fatal	-	-	-

Number of subjects in period 4	Cohort 2: PBOGefapixant 50 mgPBOGefapixant 50 mg/CC	Cohort 2: Gefapixant 50 mgPBOGefapixant 50 mgPBO/CC
Started	6	6
Completed	6	6
Not completed	0	0
Physician decision	-	-
Adverse event, non-fatal	-	-

Baseline characteristics

Reporting groups

Reporting group title	Cohort 1: PBOGefapixant 300 mgPBOGefapixant 300 mg/Healthy

Reporting group description:

Healthy participants in Cohort 1/Sequence A received single doses of placebo (PBO) on Day 1 of Periods 1 and 3 and single doses of gefapixant 300 mg on Day 1 of Periods 2 and 4. (Each treatment period consisted of Day 1 and Day 2.) There was a minimum 48-hour washout period between treatment periods.

Reporting group title	Cohort 1: Gefapixant 300 mgPBOGefapixant 300 mgPBO/Healthy

Reporting group description:

Healthy participants in Cohort 1/Sequence B received single doses of gefapixant 300 mg on Day 1 of Periods 1 and 3 and singles doses of placebo on Day 1 of Periods 2 and 4. (Each treatment period consisted of Day 1 and Day 2.) There was a minimum 48-hour washout period between treatment periods.

Reporting group title	Cohort 1: PBOGefapixant 300 mgPBOGefapixant 300 mg/CC

Reporting group description:

Participants with chronic cough (CC) in Cohort 1/Sequence A received singles doses of placebo on Day 1 of Periods 1 and 3 and single doses of gefapixant 300 mg on Day 1 of Periods 2 and 4. (Each treatment period consisted of Day 1 and Day 2.) There was a minimum 48-hour washout period between treatment periods.

Reporting group title	Cohort 1: Gefapixant 300 mgPBOGefapixant 300 mgPBO/CC

Reporting group description:

Participants with chronic cough in Cohort 1/Sequence B received singles doses of gefapixant 300 mg on Day 1 of Periods 1 and 3 and single doses of placebo on Day 1 of Periods 2 and 4. (Each treatment period consisted of Day 1 and Day 2.) There was a minimum 48-hour washout period between treatment periods.

Reporting group title	Cohort 2: PBOGefapixant 50 mgPBOGefapixant 50 mg/Healthy

Reporting group description:

Healthy participants in Cohort 2/Sequence A received singles doses of placebo on Day 1 of Periods 1 and 3 and single doses of gefapixant 50 mg on Day 1 of Periods 2 and 4. (Each treatment period consisted of Day 1 and Day 2.) There was a minimum 48-hour washout period between treatment periods.

Reporting group title	Cohort 2: Gefapixant 50 mgPBOGefapixant 50 mgPBO/Healthy

Reporting group description:

Healthy participants in Cohort 2/Sequence B received single doses of gefapixant 50 mg on Day 1 of Periods 1 and 3 and single doses of placebo on Day 1 of Periods 2 and 4. (Each treatment period consisted of Day 1 and Day 2.) There was a minimum 48-hour washout period between treatment periods.

Reporting group title	Cohort 2: PBOGefapixant 50 mgPBOGefapixant 50 mg/CC

Reporting group description:

Participants with chronic cough in Cohort 2/Sequence A received singles doses of placebo on Day of Periods 1 and 3 and singles doses of gefapixant 50 mg on Day 1 of Periods 2 and 4. (Each treatment period consisted of Day 1 and Day 2.) There was a minimum 48-hour washout period between treatment periods.

Reporting group title	Cohort 2: Gefapixant 50 mgPBOGefapixant 50 mgPBO/CC

Reporting group description:

Participants with chronic cough in Cohort 2/Sequence B received singles doses of gefapixant 50 mg on Day 1 of Periods 1 and 3 and singles doses of placebo on Day 1 of Periods 2 and 4. (Each treatment period
consisted of Day 1 and Day 2.) There was a minimum 48-hour washout period between treatment periods.

Reporting group values	Cohort 1: PBOGefapixant 300 mgPBOGefapixant 300 mg/Healthy	Cohort 1: Gefapixant 300 mgPBOGefapixant 300 mgPBO/Healthy	Cohort 1: PBOGefapixant 300 mgPBOGefapixant 300 mg/CC
Number of subjects	7	7	6
Age Categorical			
Participants who received AF-219 300 mg (Cohort 1), AF-219 50 mg (Cohort 2), or placebo (Cohorts 1 and 2)			
Units: Subjects			

Age Continuous			
Healthy participants who received AF-219 300 mg (Cohort 1), AF-219 50 mg (Cohort 2), or placebo (Cohorts 1 and 2)			
Units: years			
arithmetic mean	34.1	40.9	61.0
standard deviation	± 11.87	± 6.20	± 9.25
Gender Categorical			
Healthy participants who received AF-219 300 mg (Cohort 1), AF-219 50 mg (Cohort 2), or placebo (Cohorts 1 and 2)			
Units: Subjects			
Female	0	0	5
Male	7	7	1

Reporting group values	Cohort 1: Gefapixant 300 mgPBOGefapixant 300 mgPBO/CC	Cohort 2: PBOGefapixant 50 mgPBOGefapixant 50 mg/Healthy	Cohort 2: Gefapixant 50 mgPBOGefapixant 50 mgPBO/Healthy
Number of subjects	6	6	6
Age Categorical			
Participants who received AF-219 300 mg (Cohort 1), AF-219 50 mg (Cohort 2), or placebo (Cohorts 1 and 2)			
Units: Subjects			

Age Continuous			
Healthy participants who received AF-219 300 mg (Cohort 1), AF-219 50 mg (Cohort 2), or placebo (Cohorts 1 and 2)			
Units: years			
arithmetic mean	59.5	35.0	34.7
standard deviation	± 8.38	± 8.17	± 7.42
Gender Categorical			
Healthy participants who received AF-219 300 mg (Cohort 1), AF-219 50 mg (Cohort 2), or placebo (Cohorts 1 and 2)			
Units: Subjects			
Female	5	0	0
Male	1	6	6

Reporting group values	Cohort 2: PBOGefapixant 50 mgPBOGefapixant 50 mg/CC	Cohort 2: Gefapixant 50 mgPBOGefapixant 50 mgPBO/CC	Total
Number of subjects	6	6	50
Age Categorical			
Participants who received AF-219 300 mg (Cohort 1), AF-219 50 mg (Cohort 2), or placebo (Cohorts 1 and 2)			
Units: Subjects			

Age Continuous			
Healthy participants who received AF-219 300 mg (Cohort 1), AF-219 50 mg (Cohort 2), or placebo (Cohorts 1 and 2)			
Units: years			
arithmetic mean	60.5	55	
standard deviation	± 6.83	± 9.01	-
Gender Categorical			
Healthy participants who received AF-219 300 mg (Cohort 1), AF-219 50 mg (Cohort 2), or placebo (Cohorts 1 and 2)			
Units: Subjects			
Female	5	4	19
Male	1	2	31

End points

End points reporting groups

Reporting group title	Cohort 1: PBOGefapixant 300 mgPBOGefapixant 300 mg/Healthy

Reporting group description:

Healthy participants in Cohort 1/Sequence A received single doses of placebo (PBO) on Day 1 of Periods 1 and 3 and single doses of gefapixant 300 mg on Day 1 of Periods 2 and 4. (Each treatment period consisted of Day 1 and Day 2.) There was a minimum 48-hour washout period between treatment periods.

Reporting group title	Cohort 1: Gefapixant 300 mgPBOGefapixant 300 mgPBO/Healthy

Reporting group description:

Healthy participants in Cohort 1/Sequence B received single doses of gefapixant 300 mg on Day 1 of Periods 1 and 3 and singles doses of placebo on Day 1 of Periods 2 and 4. (Each treatment period consisted of Day 1 and Day 2.) There was a minimum 48-hour washout period between treatment periods.

Reporting group title	Cohort 1: PBOGefapixant 300 mgPBOGefapixant 300 mg/CC

Reporting group description:

Participants with chronic cough (CC) in Cohort 1/Sequence A received singles doses of placebo on Day 1 of Periods 1 and 3 and single doses of gefapixant 300 mg on Day 1 of Periods 2 and 4. (Each treatment period consisted of Day 1 and Day 2.) There was a minimum 48-hour washout period between treatment periods.

Reporting group title	Cohort 1: Gefapixant 300 mgPBOGefapixant 300 mgPBO/CC

Reporting group description:

Participants with chronic cough in Cohort 1/Sequence B received singles doses of gefapixant 300 mg on Day 1 of Periods 1 and 3 and single doses of placebo on Day 1 of Periods 2 and 4. (Each treatment period consisted of Day 1 and Day 2.) There was a minimum 48-hour washout period between treatment periods.

Reporting group title	Cohort 2: PBOGefapixant 50 mgPBOGefapixant 50 mg/Healthy

Reporting group description:

Healthy participants in Cohort 2/Sequence A received singles doses of placebo on Day 1 of Periods 1 and 3 and single doses of gefapixant 50 mg on Day 1 of Periods 2 and 4. (Each treatment period consisted of Day 1 and Day 2.) There was a minimum 48-hour washout period between treatment periods.

Reporting group title	Cohort 2: Gefapixant 50 mgPBOGefapixant 50 mgPBO/Healthy

Reporting group description:

Healthy participants in Cohort 2/Sequence B received single doses of gefapixant 50 mg on Day 1 of Periods 1 and 3 and single doses of placebo on Day 1 of Periods 2 and 4. (Each treatment period consisted of Day 1 and Day 2.) There was a minimum 48-hour washout period between treatment periods.

Reporting group title	Cohort 2: PBOGefapixant 50 mgPBOGefapixant 50 mg/CC

Reporting group description:

Participants with chronic cough in Cohort 2/Sequence A received singles doses of placebo on Day of Periods 1 and 3 and singles doses of gefapixant 50 mg on Day 1 of Periods 2 and 4. (Each treatment period consisted of Day 1 and Day 2.) There was a minimum 48-hour washout period between treatment periods.

Reporting group title	Cohort 2: Gefapixant 50 mgPBOGefapixant 50 mgPBO/CC

Reporting group description:

Participants with chronic cough in Cohort 2/Sequence B received singles doses of gefapixant 50 mg on Day 1 of Periods 1 and 3 and singles doses of placebo on Day 1 of Periods 2 and 4. (Each treatment period
consisted of Day 1 and Day 2.) There was a minimum 48-hour washout period between treatment periods.

Reporting group title	Cohort 1: PBOGefapixant 300 mgPBOGefapixant 300 mg/Healthy

Reporting group description:

Healthy participants in Cohort 1/Sequence A received single doses of placebo (PBO) on Day 1 of Periods 1 and 3 and single doses of gefapixant 300 mg on Day 1 of Periods 2 and 4. (Each treatment period consisted of Day 1 and Day 2.) There was a minimum 48-hour washout period between treatment periods.

Reporting group title	Cohort 1: Gefapixant 300 mgPBOGefapixant 300 mgPBO/Healthy

Reporting group description:

Healthy participants in Cohort 1/Sequence B received single doses of gefapixant 300 mg on Day 1 of Periods 1 and 3 and singles doses of placebo on Day 1 of Periods 2 and 4. (Each treatment period consisted of Day 1 and Day 2.) There was a minimum 48-hour washout period between treatment periods

Reporting group title	Cohort 1: PBOGefapixant 300 mgPBOGefapixant 300 mg/CC

Reporting group description:

Participants with chronic cough (CC) in Cohort 1/Sequence A received singles doses of placebo on Day 1 of Periods 1 and 3 and single doses of gefapixant 300 mg on Day 1 of Periods 2 and 4. (Each treatment period consisted of Day 1 and Day 2.) There was a minimum 48-hour washout period between treatment periods.

Reporting group title	Cohort 1: Gefapixant 300 mgPBOGefapixant 300 mgPBO/CC

Reporting group description:

Participants with chronic cough in Cohort 1/Sequence B received singles doses of gefapixant 300 mg on Day 1 of Periods 1 and 3 and single doses of placebo on Day 1 of Periods 2 and 4. (Each treatment period consisted of Day 1 and Day 2.) There was a minimum 48-hour washout period between treatment periods.

Reporting group title	Cohort 2: PBOGefapixant 50 mgPBOGefapixant 50 mg/Healthy

Reporting group description:

Healthy participants in Cohort 2/Sequence A received singles doses of placebo on Day 1 of Periods 1 and 3 and single doses of gefapixant 50 mg on Day 1 of Periods 2 and 4. (Each treatment period consisted of Day 1 and Day 2.) There was a minimum 48-hour washout period between treatment periods.

Reporting group title	Cohort 2: Gefapixant 50 mgPBOGefapixant 50 mgPBO/Healthy

Reporting group description:

Healthy participants in Cohort 2/Sequence B received single doses of gefapixant 50 mg on Day 1 of Periods 1 and 3 and single doses of placebo on Day 1 of Periods 2 and 4. (Each treatment period consisted of Day 1 and Day 2.) There was a minimum 48-hour washout period between treatment periods.

Reporting group title	Cohort 2: PBOGefapixant 50 mgPBOGefapixant 50 mg/CC

Reporting group description:

Participants with chronic cough in Cohort 2/Sequence A received singles doses of placebo on Day of Periods 1 and 3 and singles doses of gefapixant 50 mg on Day 1 of Periods 2 and 4. (Each treatment period consisted of Day 1 and Day 2.) There was a minimum 48-hour washout period between treatment periods.

Reporting group title	Cohort 2: Gefapixant 50 mgPBOGefapixant 50 mgPBO/CC

Reporting group description:

Participants with chronic cough in Cohort 2/Sequence B received singles doses of gefapixant 50 mg on Day 1 of Periods 1 and 3 and singles doses of placebo on Day 1 of Periods 2 and 4. (Each treatment period consisted of Day 1 and Day 2.) There was a minimum 48-hour washout period between treatment periods.

Reporting group title	Cohort 1: PBOGefapixant 300 mgPBOGefapixant 300 mg/Healthy

Reporting group description:

Healthy participants in Cohort 1/Sequence A received single doses of placebo (PBO) on Day 1 of Periods 1 and 3 and single doses of gefapixant 300 mg on Day 1 of Periods 2 and 4. (Each treatment period consisted of Day 1 and Day 2.) There was a minimum 48-hour washout period between treatment periods.

Reporting group title	Cohort 1: Gefapixant 300 mgPBOGefapixant 300 mgPBO/Healthy

Reporting group description:

Healthy participants in Cohort 1/Sequence B received single doses of gefapixant 300 mg on Day 1 of

Periods 1 and 3 and singles doses of placebo on Day 1 of Periods 2 and 4. (Each treatment period consisted of Day 1 and Day 2.) There was a minimum 48-hour washout period between treatment periods

Reporting group title	Cohort 1: PBOGefapixant 300 mgPBOGefapixant 300 mg/CC

Reporting group description:

Participants with chronic cough (CC) in Cohort 1/Sequence A received singles doses of placebo on Day 1 of Periods 1 and 3 and single doses of gefapixant 300 mg on Day 1 of Periods 2 and 4. (Each treatment period consisted of Day 1 and Day 2.) There was a minimum 48-hour washout period between treatment periods.

Reporting group title	Cohort 1: Gefapixant 300 mgPBOGefapixant 300 mgPBO/CC

Reporting group description:

Participants with chronic cough in Cohort 1/Sequence B received singles doses of gefapixant 300 mg on Day 1 of Periods 1 and 3 and single doses of placebo on Day 1 of Periods 2 and 4. (Each treatment period consisted of Day 1 and Day 2.) There was a minimum 48-hour washout period between treatment periods.

Reporting group title	Cohort 2: PBOGefapixant 50 mgPBOGefapixant 50 mg/Healthy

Reporting group description:

Healthy participants in Cohort 2/Sequence A received singles doses of placebo on Day 1 of Periods 1 and 3 and single doses of gefapixant 50 mg on Day 1 of Periods 2 and 4. (Each treatment period consisted of Day 1 and Day 2.) There was a minimum 48-hour washout period between treatment periods.

Reporting group title	Cohort 2: Gefapixant 50 mgPBOGefapixant 50 mgPBO/Healthy

Reporting group description:

Healthy participants in Cohort 2/Sequence B received single doses of gefapixant 50 mg on Day 1 of Periods 1 and 3 and single doses of placebo on Day 1 of Periods 2 and 4. (Each treatment period consisted of Day 1 and Day 2.) There was a minimum 48-hour washout period between treatment periods.

Reporting group title	Cohort 2: PBOGefapixant 50 mgPBOGefapixant 50 mg/CC

Reporting group description:

Participants with chronic cough in Cohort 2/Sequence A received singles doses of placebo on Day of Periods 1 and 3 and singles doses of gefapixant 50 mg on Day 1 of Periods 2 and 4. (Each treatment period consisted of Day 1 and Day 2.) There was a minimum 48-hour washout period between treatment periods.

Reporting group title	Cohort 2: Gefapixant 50 mgPBOGefapixant 50 mgPBO/CC

Reporting group description:

Participants with chronic cough in Cohort 2/Sequence B received singles doses of gefapixant 50 mg on Day 1 of Periods 1 and 3 and singles doses of placebo on Day 1 of Periods 2 and 4. (Each treatment period consisted of Day 1 and Day 2.) There was a minimum 48-hour washout period between treatment periods.

Reporting group title	Cohort 1: PBOGefapixant 300 mgPBOGefapixant 300 mg/Healthy

Reporting group description:

Healthy participants in Cohort 1/Sequence A received single doses of placebo (PBO) on Day 1 of Periods 1 and 3 and single doses of gefapixant 300 mg on Day 1 of Periods 2 and 4. (Each treatment period consisted of Day 1 and Day 2.) There was a minimum 48-hour washout period between treatment periods.

Reporting group title	Cohort 1: Gefapixant 300 mgPBOGefapixant 300 mgPBO/Healthy

Reporting group description:

Healthy participants in Cohort 1/Sequence B received single doses of gefapixant 300 mg on Day 1 of Periods 1 and 3 and singles doses of placebo on Day 1 of Periods 2 and 4. (Each treatment period consisted of Day 1 and Day 2.) There was a minimum 48-hour washout period between treatment periods

Reporting group title	Cohort 1: PBOGefapixant 300 mgPBOGefapixant 300 mg/CC

Reporting group description:

Participants with chronic cough (CC) in Cohort 1/Sequence A received singles doses of placebo on Day 1 of Periods 1 and 3 and single doses of gefapixant 300 mg on Day 1 of Periods 2 and 4. (Each treatment period consisted of Day 1 and Day 2.) There was a minimum 48-hour washout period between

treatment periods.

Reporting group title	Cohort 1: Gefapixant 300 mgPBOGefapixant 300 mgPBO/CC

Reporting group description:

Participants with chronic cough in Cohort 1/Sequence B received singles doses of gefapixant 300 mg on Day 1 of Periods 1 and 3 and single doses of placebo on Day 1 of Periods 2 and 4. (Each treatment period consisted of Day 1 and Day 2.) There was a minimum 48-hour washout period between treatment periods.

Reporting group title	Cohort 2: PBOGefapixant 50 mgPBOGefapixant 50 mg/Healthy

Reporting group description:

Healthy participants in Cohort 2/Sequence A received singles doses of placebo on Day 1 of Periods 1 and 3 and single doses of gefapixant 50 mg on Day 1 of Periods 2 and 4. (Each treatment period consisted of Day 1 and Day 2.) There was a minimum 48-hour washout period between treatment periods.

Reporting group title	Cohort 2: Gefapixant 50 mgPBOGefapixant 50 mgPBO/Healthy

Reporting group description:

Healthy participants in Cohort 2/Sequence B received single doses of gefapixant 50 mg on Day 1 of Periods 1 and 3 and single doses of placebo on Day 1 of Periods 2 and 4. (Each treatment period consisted of Day 1 and Day 2.) There was a minimum 48-hour washout period between treatment periods.

Reporting group title	Cohort 2: PBOGefapixant 50 mgPBOGefapixant 50 mg/CC

Reporting group description:

Participants with chronic cough in Cohort 2/Sequence A received singles doses of placebo on Day of Periods 1 and 3 and singles doses of gefapixant 50 mg on Day 1 of Periods 2 and 4. (Each treatment period consisted of Day 1 and Day 2.) There was a minimum 48-hour washout period between treatment periods.

Reporting group title	Cohort 2: Gefapixant 50 mgPBOGefapixant 50 mgPBO/CC

Reporting group description:

Participants with chronic cough in Cohort 2/Sequence B received singles doses of gefapixant 50 mg on Day 1 of Periods 1 and 3 and singles doses of placebo on Day 1 of Periods 2 and 4. (Each treatment period consisted of Day 1 and Day 2.) There was a minimum 48-hour washout period between treatment periods.

Subject analysis set title	Cohort 1: Gefapixant 300 mg/Healthy
Subject analysis set type	Full analysis

Subject analysis set description:

Healthy males and females in Cohort 1 who received single doses of gefapixant 300 mg in Periods 1 and 2 combined

Subject analysis set title	Cohort 1: Placebo/Healthy
Subject analysis set type	Full analysis

Subject analysis set description:

Healthy males and females in Cohort 1 who received single doses of placebo in Periods 1 and 2 combined

Subject analysis set title	Cohort 1: Gefapixant 300 mg/Chronic Cough
Subject analysis set type	Full analysis

Subject analysis set description:

Males and females with chronic cough in Cohort 1 who received single doses of gefapixant 300 mg in Periods 1 and 2 combined

Subject analysis set title	Cohort 1: Placebo/Chronic Cough
Subject analysis set type	Full analysis

Subject analysis set description:

Males and females in Cohort 1 with chronic cough who received single doses of placebo in Periods 1 and 2 combined

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

Subject analysis set description:

Healthy males and females who received single doses of gefapixant 50 mg in Periods 1 and 2 combined

Subject analysis set title	Cohort 2: Placebo/Healthy

Subject analysis set type	Full analysis
Subject analysis set description:	
Healthy males and females in Cohort 2 who received single doses of placebo in Periods 1 and 2 combined	
Subject analysis set title	Cohort 2: Gefapixant 50 mg/Chronic Cough
Subject analysis set type	Full analysis
Subject analysis set description:	
Males and females with chronic cough in Cohort 2 who received single doses of gefapixant 50 mg in Periods 1 and 2 combined	
Subject analysis set title	Cohort 2: Placebo/Chronic Cough
Subject analysis set type	Full analysis
Subject analysis set description:	
Males and females with chronic cough in Cohort 2 who received single doses of placebo in Periods 1 and 2 combined	
Subject analysis set title	Cohort 1: Gefapixant 300 mg/Chronic Cough
Subject analysis set type	Full analysis
Subject analysis set description:	
Participants with chronic cough in Cohort 1 who received single doses of gefapixant 300 mg in Periods 1 and 2 combined	
Subject analysis set title	Cohort 1: Placebo/Chronic Cough
Subject analysis set type	Full analysis
Subject analysis set description:	
Participants with chronic cough in Cohort 1 who received single doses of placebo in Periods 1 and 2 combined	
Subject analysis set title	Cohort 2: Gefapixant 50 mg/Chronic Cough
Subject analysis set type	Full analysis
Subject analysis set description:	
Participants with chronic cough in Cohort 2 who received single doses of gefapixant 50 mg in Periods 1 and 2 combined	
Subject analysis set title	Cohort 2: Placebo/Chronic Cough
Subject analysis set type	Full analysis
Subject analysis set description:	
Participants with chronic cough in Cohort 2 who received single doses of placebo in Periods 1 and 2 combined	
Subject analysis set title	Cohort 1: Gefapixant 300 mg/Healthy
Subject analysis set type	Safety analysis
Subject analysis set description:	
Healthy participants in Cohort 1 who received singles doses of gefapixant 300 mg	
Subject analysis set title	Cohort 1: Placebo/Healthy
Subject analysis set type	Safety analysis
Subject analysis set description:	
Healthy participants in Cohort 1 who received single doses of placebo	
Subject analysis set title	Cohort 1: Gefapixant 300 mg/Chronic Cough
Subject analysis set type	Safety analysis
Subject analysis set description:	
Participants with chronic cough in Cohort 1 who received single doses of gefapixant 300 mg	
Subject analysis set title	Cohort 1: Placebo/Chronic Cough
Subject analysis set type	Safety analysis
Subject analysis set description:	
Participants with chronic cough in Cohort 1 who received single doses of placebo	
Subject analysis set title	Cohort 2: Gefapixant 50 mg/Healthy
Subject analysis set type	Safety analysis
Subject analysis set description:	
Healthy participants in Cohort 2 who received single doses of gefapixant 50 mg	

Subject analysis set title	Cohort 2: Placebo/Healthy
Subject analysis set type	Safety analysis
Subject analysis set description: Healthy participants in Cohort 2 who received single doses of placebo	
Subject analysis set title	Cohort 2: Gefapixant 50 mg/Chronic Cough
Subject analysis set type	Safety analysis
Subject analysis set description: Participants with chronic cough in Cohort 2 who received single doses of gefapixant 50 mg	
Subject analysis set title	Cohort 2: Placebo/Chronic Cough
Subject analysis set type	Safety analysis
Subject analysis set description: Participants with chronic cough in Cohort 2 who received single doses of placebo	
Subject analysis set title	Placebo/Healthy Males
Subject analysis set type	Full analysis
Subject analysis set description: Healthy males who received single doses of placebo in Periods 1 and 2	
Subject analysis set title	Placebo/Chronic Cough Males
Subject analysis set type	Full analysis
Subject analysis set description: Males with chronic cough who received single doses of placebo in Periods 1 and 2	
Subject analysis set title	Placebo/Chronic Cough Females
Subject analysis set type	Full analysis
Subject analysis set description: Females with chronic cough who received single doses of placebo in Periods 1 and 2	
Subject analysis set title	Gefapixant 50 mg/Healthy Males
Subject analysis set type	Full analysis
Subject analysis set description: Healthy males who received single doses of gefapixant 50 mg in Periods 1 and 2	
Subject analysis set title	Gefapixant 50 mg/Chronic Cough Males
Subject analysis set type	Full analysis
Subject analysis set description: Males with chronic cough who received single doses of gefapixant 50 mg in Periods 1 and 2	
Subject analysis set title	Gefapixant 50 mg/Chronic Cough Females
Subject analysis set type	Full analysis
Subject analysis set description: Females with chronic cough who received single doses of gefapixant 50 mg in Periods 1 and 2	
Subject analysis set title	Gefapixant 300 mg/Healthy Males
Subject analysis set type	Full analysis
Subject analysis set description: Healthy males who received single doses of gefapixant 300 mg in Periods 1 and 2	
Subject analysis set title	Gefapixant 300 mg/Chronic Cough Males
Subject analysis set type	Full analysis
Subject analysis set description: Males with chronic cough who received single doses of gefapixant 300 mg in Periods 1 and 2	
Subject analysis set title	Gefapixant 300 mg/Chronic Cough Females
Subject analysis set type	Full analysis
Subject analysis set description: Females with chronic cough who received single doses of gefapixant 300 mg in Periods 1 and 2	

Primary: Cough Reflex Sensitivity to Capsaicin Measured by Maximal Cough Response (Emax)

End point title	Cough Reflex Sensitivity to Capsaicin Measured by Maximal Cough Response (Emax)

End point description:

The effect of single doses of 50 mg and 300 mg gefapixant on cough reflex sensitivity to challenge with capsaicin was assessed. Capsaicin-evoked cough challenge was performed 2 hours post-dose in Periods 1 and 2. For capsaicin challenge, doubling concentrations from 0.49 µM to 1000 µM were prepared by dilution of stock solutions with saline, and were administered by inhalation. The number of explosive cough sounds occurring within the first 15 seconds after inhalation were recorded. Nonlinear mixed-effects modeling was used to estimate the Emax. Population pharmacodynamic modeling was performed in NONMEM 7.3. Data exploration, goodness-of-fit plots, statistical analyses, and simulations were performed in Matlab R2015a. Note: All values presented are model-based. The analysis population included all randomized participants who received at least 1 dose of study medication and had at least 1 post-dose primary endpoint assessment of Emax in response to capsaicin challenge.

End point type	Primary

End point timeframe:

2 hours post-dose

End point values	Placebo/Healthy Males	Placebo/Chronic Cough Males	Placebo/Chronic Cough Females	Gefapixant 50 mg/Healthy Males
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	26	5	18	26
Units: Emax (Explosive coughs/15 sec)				
number (not applicable)	4.14	4.14	7.57	3.66

End point values	Gefapixant 50 mg/Chronic Cough Males	Gefapixant 50 mg/Chronic Cough Females	Gefapixant 300 mg/Healthy Males	Gefapixant 300 mg/Chronic Cough Males
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	5	18	26	5
Units: Emax (Explosive coughs/15 sec)				
number (not applicable)	3.37	6.17	3.66	3.37

End point values	Gefapixant 300 mg/Chronic Cough Females			
Subject group type	Subject analysis set			
Number of subjects analysed	18			
Units: Emax (Explosive coughs/15 sec)				
number (not applicable)	6.17			

Statistical analyses

Statistical analysis title	Emax Response: Gefapixant vs Placebo

Statistical analysis description:

Treatment effects on Emax following capsaicin challenge were modeled for dose dependence and were estimated on the basis of disease status for participants who were healthy or had chronic cough and received gefapixant 50 mg, gefapixant 300 mg, or placebo.

Comparison groups	Placebo/Healthy Males v Placebo/Chronic Cough Males v Placebo/Chronic Cough Females v Gefapixant 50 mg/Healthy Males v Gefapixant 50 mg/Chronic Cough Males v Gefapixant 50 mg/Chronic Cough Females v Gefapixant 300 mg/Healthy Males v Gefapixant 300 mg/Chronic Cough Males v Gefapixant 300 mg/Chronic Cough Females
Number of subjects included in analysis	147
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001
Method	Mixed models analysis

Primary: Cough Reflex Sensitivity to Capsaicin Measured by the Tussive Concentration Required to Achieve 50% of Emax (ED50)

End point title	Cough Reflex Sensitivity to Capsaicin Measured by the Tussive Concentration Required to Achieve 50% of Emax (ED50)

End point description:

The effect of single doses of 50 mg and 300 mg gefapixant on cough reflex sensitivity to challenge with capsaicin was assessed. Capsaicin-evoked cough challenge was performed 2 hours post-dose in Periods 1 and 2. The concentration of capsaicin required to induce 50% of the Emax (ED50) was assessed. For capsaicin challenge, doubling concentrations from 0.49 µM to 1000 µM were prepared by dilution of stock solutions with saline, and were administered by inhalation. Nonlinear mixed-effects modeling was used to estimate the ED50. Population pharmacodynamic modeling was performed in NONMEM 7.3 using Laplace estimation method. Data exploration, goodness-of-fit plots, statistical analyses, and simulations were performed in Matlab R2015a. Note: All values presented are model-based. The analysis population included all randomized participants who received at least 1 dose of study medication and had at least 1 post-dose primary endpoint assessment of ED50 in response to capsaicin challenge.

End point type	Primary

End point timeframe:

2 hours post-dose

End point values	Placebo/Healthy Males	Placebo/Chronic Cough Males	Placebo/Chronic Cough Females	Gefapixant 50 mg/Healthy Males
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	26	5	18	26
Units: µM				
number (not applicable)	33	33	9.56	33

End point values	Gefapixant 50 mg/Chronic Cough Males	Gefapixant 50 mg/Chronic Cough Females	Gefapixant 300 mg/Healthy Males	Gefapixant 300 mg/Chronic Cough Males
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	5	18	26	5

Units: µM				
number (not applicable)	33	9.56	33	33

End point values	Gefapixant 300 mg/Chronic Cough Females			
Subject group type	Subject analysis set			
Number of subjects analysed	18			
Units: µM				
number (not applicable)	9.56			

Statistical analyses

Statistical analysis title	ED50 Response: Gefapixant vs Placebo

Statistical analysis description:

Treatment effects following capsaicin challenge were modeled for dose dependence and were estimated on
the basis of disease status for participants who had chronic cough and received gefapixant 50 mg, gefapixant 300 mg, or placebo.

Comparison groups	Placebo/Healthy Males v Placebo/Chronic Cough Males v Placebo/Chronic Cough Females v Gefapixant 50 mg/Healthy Males v Gefapixant 50 mg/Chronic Cough Males v Gefapixant 50 mg/Chronic Cough Females v Gefapixant 300 mg/Healthy Males v Gefapixant 300 mg/Chronic Cough Males v Gefapixant 300 mg/Chronic Cough Females
Number of subjects included in analysis	147
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001
Method	Mixed models analysis

Secondary: Cough Reflex Sensitivity to Adenosine Triphosphate (ATP) Measured by Maximal Cough Response (Emax)

End point title	Cough Reflex Sensitivity to Adenosine Triphosphate (ATP) Measured by Maximal Cough Response (Emax)

End point description:

The effect of single doses of 50 mg and 300 mg gefapixant on cough reflex sensitivity to challenge with adenosine triphosphate (ATP) was assessed. ATP-evoked cough challenge was performed 2 hours post-dose in Periods 3 and 4. For ATP challenge, doubling concentrations from 0.227 µmol/mL to 929 µmol/mL were prepared from ATP powder dissolved in saline, and were administered by inhalation. The number of explosive cough sounds occurring within the first 15 seconds after inhalation were recorded. Nonlinear mixed-effects modeling was used to estimate the Emax. Population pharmacodynamic modeling was performed in NONMEM 7.3. Data exploration, goodness-of-fit plots, statistical analyses, and simulations were performed in Matlab R2015a. Note: All values presented are model-based. The analysis population included all randomized participants who received at least 1 dose of study medication and had at least 1 post-dose secondary endpoint assessment of Emax in response to ATP challenge.

End point type	Secondary

End point timeframe:

2 hours post-dose

End point values	Placebo/Healthy Males	Placebo/Chronic Cough Males	Placebo/Chronic Cough Females	Gefapixant 50 mg/Healthy Males
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	26	4	18	26
Units: Emax (Explosive coughs/15 sec)				
number (not applicable)	2.35	2.35	5.4	2.35

End point values	Gefapixant 50 mg/Chronic Cough Males	Gefapixant 50 mg/Chronic Cough Females	Gefapixant 300 mg/Healthy Males	Gefapixant 300 mg/Chronic Cough Males
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	4	18	26	4
Units: Emax (Explosive coughs/15 sec)				
number (not applicable)	2.35	5.4	2.35	2.35

End point values	Gefapixant 300 mg/Chronic Cough Females			
Subject group type	Subject analysis set			
Number of subjects analysed	18			
Units: Emax (Explosive coughs/15 sec)				
number (not applicable)	5.4			

Statistical analyses

No statistical analyses for this end point

Secondary: Cough Reflex Sensitivity to ATP Measured by the Tussive Concentration Required to Achieve 50% of Emax (E50)

End point title	Cough Reflex Sensitivity to ATP Measured by the Tussive Concentration Required to Achieve 50% of Emax (E50)

End point description:

The effect of single doses of 50 mg and 300 mg gefapixant on cough reflex sensitivity to challenge with ATP was assessed. ATP-evoked cough challenge was performed 2 hours post-dose in Periods 3 and 4. The concentration of ATP required to induce 50% of the Emax (ED50) was assessed. For ATP challenge, doubling concentrations from 0.227 µmol/mL to 929 µmol/mL were prepared by dilution of stock solutions with saline, and were administered by inhalation. Nonlinear mixed-effects modeling was used to estimate the ED50. Population pharmacodynamic modeling was performed in NONMEM 7.3 using Laplace estimation method. Data exploration, goodness-of-fit plots, statistical analyses, and simulations were performed in Matlab R2015a. Note: All values presented are model-based. The analysis population included all randomized participants who received at least 1 dose of study medication and had at least 1 post-dose secondary endpoint assessment of ED50 in response to ATP challenge.

End point type	Secondary

End point timeframe:

2 hours post-dose

End point values	Placebo/Healthy Males	Placebo/Chronic Cough Males	Placebo/Chronic Cough Females	Gefapixant 50 mg/Healthy Males
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	14	4	18	26
Units: µmol/mL				
number (not applicable)	54.9	54.9	8.63	119.13

End point values	Gefapixant 50 mg/Chronic Cough Males	Gefapixant 50 mg/Chronic Cough Females	Gefapixant 300 mg/Healthy Males	Gefapixant 300 mg/Chronic Cough Males
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	4	18	26	4
Units: µmol/mL				
number (not applicable)	155.92	24.51	119.13	192.7

End point values	Gefapixant 300 mg/Chronic Cough Females			
Subject group type	Subject analysis set			
Number of subjects analysed	18			
Units: µmol/mL				
number (not applicable)	30.29			

Statistical analyses

No statistical analyses for this end point

Secondary: Concentrations of Capsaicin Inducing 2 or More Coughs (C2)

End point title	Concentrations of Capsaicin Inducing 2 or More Coughs (C2)

End point description:

The concentrations of capsaicin inducing 2 or more coughs (C2) in participants were assessed in Periods 1 and 2. For capsaicin challenge, doubling concentrations from 0.49 µM to 1000 µM were prepared by dilution of stock solutions with saline, and were administered by inhalation. The analysis population for this endpoint included all randomized participants who received at least 1 dose of study medication and had at least 1 post-dose secondary endpoint assessment of C2 in response to capsaicin challenge.

End point type	Secondary

End point timeframe:

2 hours post-dose

End point values	Cohort 1: Gefapixant 300 mg/Healthy	Cohort 1: Placebo/Healthy	Cohort 1: Gefapixant 300 mg/Chronic Cough	Cohort 1: Placebo/Chronic Cough
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	12	14	10	10
Units: µM				
median (full range (min-max))	31.25 (4 to 1000)	31.25 (4 to 500)	3.90 (0 to 16)	7.81 (0 to 31)

End point values	Cohort 2: Gefapixant 50 mg/Healthy	Cohort 2: Placebo/Healthy	Cohort 2: Gefapixant 50 mg/Chronic Cough	Cohort 2: Placebo/Chronic Cough
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	12	12	10	12
Units: µM				
median (full range (min-max))	15.62 (2 to 63)	23.44 (8 to 125)	15.62 (0 to 125)	5.86 (0 to 250)

Statistical analyses

No statistical analyses for this end point

Secondary: Concentrations of Capsaicin Inducing 5 or More Coughs (C5)

End point title	Concentrations of Capsaicin Inducing 5 or More Coughs (C5)

End point description:

The concentrations of capsaicin inducing 5 or more coughs (C5) in participants were assessed in Periods 1 and 2. For capsaicin challenge, doubling concentrations from 0.49 µM to 1000 µM were prepared by dilution of stock solutions with saline, and were administered by inhalation. The analysis population for this endpoint included all randomized participants who received at least 1 dose of study medication and had at least 1 post-dose secondary endpoint assessment of C5 in response to capsaicin challenge.

End point type	Secondary

End point timeframe:

2 hours post-dose

End point values	Cohort 1: Gefapixant 300 mg/Healthy	Cohort 1: Placebo/Healthy	Cohort 1: Gefapixant 300 mg/Chronic Cough	Cohort 1: Placebo/Chronic Cough
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	5	6	10	10
Units: µM				
median (full range (min-max))	31.25 (16 to 250)	62.50 (16 to 1000)	3.90 (0 to 31)	11.72 (0 to 125)

End point values	Cohort 2: Gefapixant 50 mg/Healthy	Cohort 2: Placebo/Healthy	Cohort 2: Gefapixant 50 mg/Chronic Cough	Cohort 2: Placebo/Chronic Cough
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	6	7	7	10
Units: µM				
median (full range (min-max))	250.00 (63 to 500)	125.00 (63 to 500)	15.62 (2 to 63)	5.86 (0 to 31)

Statistical analyses

No statistical analyses for this end point

Secondary: Concentrations of ATP Inducing 2 or More Coughs (C2)

End point title	Concentrations of ATP Inducing 2 or More Coughs (C2)

End point description:

The concentrations of ATP inducing 2 or more coughs (C2) in participants were assessed in Periods 3 and 4. For ATP challenge, doubling concentrations from 0.227 to 929 µmol/mL were prepared from ATP powder, dissolved and diluted in saline, and administered by inhalation. The analysis population for this endpoint included all randomized participants who received at least 1 dose of study medication and had at least 1 post-dose secondary endpoint assessment of C2 in response to ATP challenge.

End point type	Secondary

End point timeframe:

2 hours post-dose

End point values	Cohort 1: Gefapixant 300 mg/Healthy	Cohort 1: Placebo/Healthy	Cohort 1: Gefapixant 300 mg/Chronic Cough	Cohort 1: Placebo/Chronic Cough
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	10	11	7	11
Units: mg/mL				
median (full range (min-max))	192.00 (8 to 256)	64.00 (1 to 512)	8.00 (0 to 64)	1.00 (0 to 64)

End point values	Cohort 2: Gefapixant 50 mg/Healthy	Cohort 2: Placebo/Healthy	Cohort 2: Gefapixant 50 mg/Chronic Cough	Cohort 2: Placebo/Chronic Cough
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	9	8	8	9
Units: mg/mL				
median (full range (min-max))	16.00 (8 to 256)	24.00 (2 to 512)	4.25 (0 to 512)	4.00 (0 to 256)

Statistical analyses

No statistical analyses for this end point

Secondary: Concentrations of ATP Inducing 5 or More Coughs (C5)

End point title	Concentrations of ATP Inducing 5 or More Coughs (C5)

End point description:

The concentrations of ATP inducing 5 or more coughs (C5) in participants were assessed in Periods 3 and 4. For ATP challenge, doubling concentrations from 0.227 to 929 µmol/mL were prepared from ATP powder, dissolved and diluted in saline, and administered by inhalation. The analysis population for this endpoint included all randomized participants who received at least 1 dose of study medication and had at least 1 post-dose secondary endpoint assessment of C5 in response to ATP challenge.

End point type	Secondary

End point timeframe:

2 hours post-dose

End point values	Cohort 1: Gefapixant 300 mg/Healthy	Cohort 1: Placebo/Healthy	Cohort 1: Gefapixant 300 mg/Chronic Cough	Cohort 1: Placebo/Chronic Cough
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	2	5	7	8
Units: mg/mL				
median (full range (min-max))	192.00 (128 to 256)	128.0 (64 to 256)	8.00 (0 to 64)	16.50 (0 to 512)

End point values	Cohort 2: Gefapixant 50 mg/Healthy	Cohort 2: Placebo/Healthy	Cohort 2: Gefapixant 50 mg/Chronic Cough	Cohort 2: Placebo/Chronic Cough
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	4	4	5	8
Units: mg/mL				
median (full range (min-max))	64.00 (32 to 256)	32.00 (2 to 32)	128.00 (8 to 512)	4.00 (0 to 128)

Statistical analyses

No statistical analyses for this end point

Secondary: Urge-to-Cough in Response to Capsaicin Challenge (Chronic Cough

Participants Only)

End point title	Urge-to-Cough in Response to Capsaicin Challenge (Chronic Cough Participants Only)

End point description:

In response to capsaicin challenges in Periods 1 and 2, participants with chronic cough completed a visual analogue scale (VAS) at the end of a 4-hour post-dose observation period on Day 1; and at end of 24-hour observation period on Day 2. For both periods, participants were asked to mark on a 100 mm VAS the severity of their urge to cough between 0 mm (no urge-to-cough) and 100 mm (worst urge-to-cough). The analysis population for this endpoint included all randomized participants with chronic cough who received at least 1 dose of study medication and had at least 1 post-dose secondary endpoint assessment of urge-to-cough in response to capsaicin challenge.

End point type	Secondary

End point timeframe:

At the end of a 4-hour post-dose observation period on Day 1; at the end of a 24-hour observation period on Day 2

End point values	Cohort 1: Gefapixant 300 mg/Chronic Cough	Cohort 1: Placebo/Chronic Cough	Cohort 2: Gefapixant 50 mg/Chronic Cough	Cohort 2: Placebo/Chronic Cough
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	12	12	12	11
Units: Score on a scale				
arithmetic mean (standard deviation)				
Day 1	28.9 (± 29.79)	38.6 (± 26.82)	36.6 (± 30.84)	20.5 (± 11.54)
Day 2	28.2 (± 32.72)	46.7 (± 29.20)	41.8 (± 31.02)	36.7 (± 23.28)

Statistical analyses

No statistical analyses for this end point

Secondary: Urge-to-Cough in Response to ATP Challenge (Chronic Cough Participants Only)

End point title	Urge-to-Cough in Response to ATP Challenge (Chronic Cough Participants Only)

End point description:

In response to ATP challenges in Periods 3 and 4, participants with chronic cough completed a VAS at the end of a 4-hour post-dose observation period on Day 1; and at end of 24-hour observation period on Day 2. For both periods, participants were asked to mark on a 100 mm VAS the severity of their urge to cough between 0 mm (no urge-to-cough) and 100 mm (worst urge-to-cough). The analysis population for this endpoint included all randomized participants with chronic cough who received at least 1 dose of study medication and had at least 1 post-dose secondary endpoint assessment of urge-to-cough in response to ATP challenge.

End point type	Secondary

End point timeframe:

At the end of a 4-hour post-dose observation period on Day 1; at the end of a 24-hour observation period on Day 2

End point values	Cohort 1: Gefapixant 300 mg/Chronic Cough	Cohort 1: Placebo/Chronic Cough	Cohort 2: Gefapixant 50 mg/Chronic Cough	Cohort 2: Placebo/Chronic Cough
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	12	12	11	11
Units: Score on a scale				
arithmetic mean (standard deviation)				
Day 1	19.8 (± 23.54)	34.4 (± 26.78)	21.5 (± 22.45)	25.3 (± 19.69)
Day 2	21.6 (± 20.65)	39.8 (± 26.51)	27.5 (± 29.54)	37.5 (± 27.33)

Statistical analyses

No statistical analyses for this end point

Secondary: Cough Severity in Response to Capsaicin Challenge (Chronic Cough Participants Only)

End point title	Cough Severity in Response to Capsaicin Challenge (Chronic Cough Participants Only)

End point description:

In response to capsaicin challenges in Periods 1 and 2, participants with chronic cough completed a VAS at the end of a 4-hour post-dose observation period on Day 1; and at end of 24-hour observation period on Day 2. For both periods, participants were asked to mark on a 100 mm VAS their cough severity between 0 mm (no cough) and 100 mm (worst cough). The analysis population for this endpoint included all randomized participants with chronic cough who received at least 1 dose of study medication and had at least 1 post-dose secondary endpoint assessment of cough severity in response to capsaicin challenge.

End point type	Secondary

End point timeframe:

At the end of a 4-hour post-dose observation period; at the end of a 24-hour observation period on Day 2

End point values	Cohort 1: Gefapixant 300 mg/Chronic Cough	Cohort 1: Placebo/Chronic Cough	Cohort 2: Gefapixant 50 mg/Chronic Cough	Cohort 2: Placebo/Chronic Cough
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	12	12	12	11
Units: Score on a scale				
arithmetic mean (standard deviation)				
Day 1	28.2 (± 30.71)	35.7 (± 24.32)	30.9 (± 27.22)	20.5 (± 12.75)
Day 2	25.8 (± 30.20)	44.3 (± 27.43)	39.8 (± 28.97)	35.5 (± 22.25)

Statistical analyses

No statistical analyses for this end point

Secondary: Cough Severity in Response to ATP Challenge (Chronic Cough

Participants Only)	
End point title	Cough Severity in Response to ATP Challenge (Chronic Cough Participants Only)

End point description:

In response to ATP challenge in Periods 3 and 4, participants with chronic cough completed a VAS at the end of a 4-hour post-dose observation period on Day 1; and at end of 24-hour observation period on Day 2. For both periods, participants were asked to mark on a 100 mm VAS their cough severity between 0 mm (no cough) and 100 mm (worst cough). The analysis population for this endpoint included all randomized participants with chronic cough who received at least 1 dose of study medication and had at least 1 post-dose secondary endpoint assessment of cough severity in response to ATP challenge.

End point type	Secondary

End point timeframe:

At the end of a 4-hour post-dose observation period on Day 1; at the end of a 24-hour observation period on Day 2

End point values	Cohort 1: Gefapixant 300 mg/Chronic Cough	Cohort 1: Placebo/Chronic Cough	Cohort 2: Gefapixant 50 mg/Chronic Cough	Cohort 2: Placebo/Chronic Cough
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	12	12	11	11
Units: Score on a scale				
arithmetic mean (standard deviation)				
Day 1	21.5 (± 27.06)	32.7 (± 24.23)	21.2 (± 21.04)	23.5 (± 16.02)
Day 2	18.9 (± 18.29)	36.8 (± 26.50)	27.5 (± 26.78)	35.5 (± 24.07)

Statistical analyses

No statistical analyses for this end point

Secondary: Daytime Cough Frequency in Participants With Chronic Cough Who Underwent Capsaicin Challenge

End point title	Daytime Cough Frequency in Participants With Chronic Cough Who Underwent Capsaicin Challenge

End point description:

Daily cough frequency monitoring was performed in participants with chronic cough, who were attached to a digital sound recorder with 2 microphones (a lapel air microphone attached to the participant's clothing and an adhesive chest wall microphone attached to the skin at the top of the sternum). Participants wore the sound recorder from the start of capsaicin challenge to bedtime on Day 1 in Periods 1 and 2. The resulting recording was processed by software which cut out the majority of speech and background noise but retained cough sounds. The investigator listened to the recording and documented the number of coughs per hour. The analysis population for this endpoint included all randomized participants with chronic cough who received at least 1 dose of study medication and had at least 1 post-dose secondary endpoint assessment of daytime cough frequency in response to capsaicin challenge.

End point type	Secondary

End point timeframe:

From start of challenge (2 hours post-dose) to bedtime; up to 12 hours

End point values	Cohort 1: Gefapixant 300 mg/Chronic Cough	Cohort 1: Placebo/Chronic Cough	Cohort 2: Gefapixant 50 mg/Chronic Cough	Cohort 2: Placebo/Chronic Cough
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	12	12	12	12
Units: coughs/hour				
arithmetic mean (standard deviation)	13.7 (± 13.85)	19.1 (± 16.76)	15.5 (± 16.92)	20.3 (± 13.27)

Statistical analyses

No statistical analyses for this end point

Secondary: Daytime Cough Frequency in Participants With Chronic Cough Who Underwent ATP Challenge

End point title	Daytime Cough Frequency in Participants With Chronic Cough Who Underwent ATP Challenge

End point description:

Daily cough frequency monitoring was performed in participants with chronic cough, who were attached to a digital sound recorder with 2 microphones (a lapel air microphone attached to the participant's clothing and an adhesive chest wall microphone attached to the skin at the top of the sternum). Participants wore the sound recorder from the start of ATP challenge to bedtime on Day 1 in Periods 3 and 4. The resulting recording was processed by software which cut out the majority of speech and background noise but retained cough sounds. The investigator listened to the recording and documented the number of coughs per hour. The analysis population for this endpoint included all treated participants with chronic cough who had at least 1 post-dose secondary endpoint assessment of daytime cough frequency in response to ATP challenge.

End point type	Secondary

End point timeframe:

From start of challenge (2 hours post-dose) to bedtime; up to 12 hours

End point values	Cohort 1: Gefapixant 300 mg/Chronic Cough	Cohort 1: Placebo/Chronic Cough	Cohort 2: Gefapixant 50 mg/Chronic Cough	Cohort 2: Placebo/Chronic Cough
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	12	12	11	11
Units: coughs/hour				
arithmetic mean (standard deviation)	10.3 (± 11.65)	22.3 (± 15.48)	15.6 (± 17.31)	26.4 (± 16.75)

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants Who Experienced at Least One Adverse Event

End point title	Percentage of Participants Who Experienced at Least One Adverse Event

End point description:

An adverse event (AE) is any untoward medical occurrence in a study participant administered a pharmaceutical product that does not necessarily have to have a causal relationship with this treatment. An AE can therefore be any unfavorable and unintended sign, symptom, or disease temporally associated with the use of a medicinal product, whether or not related to the medicinal product. The analysis population for this endpoint included all randomized participants who received at least 1 dose of study medication.

End point type	Secondary

End point timeframe:

Up to Day 41

End point values	Cohort 1: Gefapixant 300 mg/Healthy	Cohort 1: Placebo/Healthy	Cohort 1: Gefapixant 300 mg/Chronic Cough	Cohort 1: Placebo/Chronic Cough
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	14	14	12	12
Units: Percentage of participants				
number (not applicable)	100.0	35.7	100.0	58.3

End point values	Cohort 2: Gefapixant 50 mg/Healthy	Cohort 2: Placebo/Healthy	Cohort 2: Gefapixant 50 mg/Chronic Cough	Cohort 2: Placebo/Chronic Cough
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	12	12	12	11
Units: Percentage of participants				
number (not applicable)	75.0	33.3	50.0	27.3

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants Who Discontinued Study Treatment Due to an Adverse Event

End point title	Percentage of Participants Who Discontinued Study Treatment Due to an Adverse Event

End point description:

An adverse event (AE) is any untoward medical occurrence in a study participant administered a pharmaceutical product that does not necessarily have to have a causal relationship with this treatment. An AE can therefore be any unfavorable and unintended sign, symptom, or disease temporally associated with the use of a medicinal product, whether or not related to the medicinal product. The analysis population for this endpoint included all randomized participants who received at least 1 dose of study medication.

End point type	Secondary

End point timeframe:
Up to Day 24

End point values	Cohort 1: Gefapixant 300 mg/Healthy	Cohort 1: Placebo/Healthy	Cohort 1: Gefapixant 300 mg/Chronic Cough	Cohort 1: Placebo/Chronic Cough
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	14	14	12	12
Units: Percentage of participants				
number (not applicable)	0.0	0.0	0.0	0.0

End point values	Cohort 2: Gefapixant 50 mg/Healthy	Cohort 2: Placebo/Healthy	Cohort 2: Gefapixant 50 mg/Chronic Cough	Cohort 2: Placebo/Chronic Cough
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	12	12	12	11
Units: Percentage of participants				
number (not applicable)	0.0	0.0	0.0	0.0

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Up to Day 41

Adverse event reporting additional description:

The safety analysis population included all randomized participants who received at least 1 dose of study medication. The analysis population for number of deaths (all causes) included all randomized participants.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	17.0

Reporting groups

Reporting group title	Cohort 1: Gefapixant 300 mg/Healthy

Reporting group description:

Healthy participants in Cohort 1 who received single doses of gefapixant 300 mg

Reporting group title	Cohort 1: Placebo/Healthy

Reporting group description:

Healthy participants in Cohort 1 who received single doses of placebo

Reporting group title	Cohort 1: Gefapixant 300 mg/Chronic Cough

Reporting group description:

Participants with chronic cough in Cohort 1 who received singles doses

Reporting group title	Cohort 1: Placebo/Chronic Cough

Reporting group description:

Participants with chronic cough in Cohort 1 who received single doses of placebo

Reporting group title	Cohort 2: Gefapixant 50 mg/Healthy

Reporting group description:

Healthy participants in Cohort 2 who received single doses of gefapixant 50 mg

Reporting group title	Cohort 2: Placebo/Healthy

Reporting group description:

Healthy participants in Cohort 2 who received single doses of placebo

Reporting group title	Cohort 2: Gefapixant 50 mg/Chronic Cough

Reporting group description:

Participants with chronic cough in Cohort 2 who received single doses of gefapixant 50 mg

Reporting group title	Cohort 2: Placebo/Chronic Cough

Reporting group description:

Participants with chronic cough in Cohort 2 who received single doses of placebo

Serious adverse events	Cohort 1: Gefapixant 300 mg/Healthy	Cohort 1: Placebo/Healthy	Cohort 1: Gefapixant 300 mg/Chronic Cough
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 14 (0.00%)	0 / 14 (0.00%)	0 / 12 (0.00%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0

Serious adverse events	Cohort 1: Placebo/Chronic Cough	Cohort 2: Gefapixant 50 mg/Healthy	Cohort 2: Placebo/Healthy
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 12 (0.00%)	0 / 12 (0.00%)	0 / 12 (0.00%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0

Serious adverse events	Cohort 2: Gefapixant 50 mg/Chronic Cough	Cohort 2: Placebo/Chronic Cough	
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 12 (0.00%)	0 / 11 (0.00%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events	0	0	

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

Non-serious adverse events	Cohort 1: Gefapixant 300 mg/Healthy	Cohort 1: Placebo/Healthy	Cohort 1: Gefapixant 300 mg/Chronic Cough
Total subjects affected by non-serious adverse events			
subjects affected / exposed	14 / 14 (100.00%)	5 / 14 (35.71%)	12 / 12 (100.00%)
Injury, poisoning and procedural complications			
Arthropod bite			
subjects affected / exposed	0 / 14 (0.00%)	0 / 14 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Excoriation			
subjects affected / exposed	1 / 14 (7.14%)	0 / 14 (0.00%)	0 / 12 (0.00%)
occurrences (all)	1	0	0
Vascular disorders			
Hot flush			
subjects affected / exposed	0 / 14 (0.00%)	0 / 14 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Hypertension			
subjects affected / exposed	0 / 14 (0.00%)	0 / 14 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Nervous system disorders			

Ageusia			
subjects affected / exposed	0 / 14 (0.00%)	0 / 14 (0.00%)	3 / 12 (25.00%)
occurrences (all)	0	0	4
Dizziness			
subjects affected / exposed	0 / 14 (0.00%)	0 / 14 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Dysgeusia			
subjects affected / exposed	13 / 14 (92.86%)	1 / 14 (7.14%)	9 / 12 (75.00%)
occurrences (all)	20	1	15
Headache			
subjects affected / exposed	3 / 14 (21.43%)	2 / 14 (14.29%)	5 / 12 (41.67%)
occurrences (all)	3	2	5
Hypogeusia			
subjects affected / exposed	2 / 14 (14.29%)	0 / 14 (0.00%)	3 / 12 (25.00%)
occurrences (all)	2	0	3
VIIth Nerve Paralysis			
subjects affected / exposed	0 / 14 (0.00%)	0 / 14 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
General disorders and administration site conditions			
Chest discomfort			
subjects affected / exposed	0 / 14 (0.00%)	0 / 14 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Fatigue			
subjects affected / exposed	1 / 14 (7.14%)	0 / 14 (0.00%)	0 / 12 (0.00%)
occurrences (all)	1	0	0
Pain			
subjects affected / exposed	0 / 14 (0.00%)	0 / 14 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Ear and labyrinth disorders			
Ear pain			
subjects affected / exposed	0 / 14 (0.00%)	0 / 14 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	0 / 14 (0.00%)	0 / 14 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0

Dry mouth			
subjects affected / exposed	1 / 14 (7.14%)	0 / 14 (0.00%)	0 / 12 (0.00%)
occurrences (all)	1	0	0
Dyspepsia			
subjects affected / exposed	1 / 14 (7.14%)	0 / 14 (0.00%)	1 / 12 (8.33%)
occurrences (all)	1	0	1
Hypoaesthesia oral			
subjects affected / exposed	1 / 14 (7.14%)	0 / 14 (0.00%)	1 / 12 (8.33%)
occurrences (all)	1	0	1
Nausea			
subjects affected / exposed	1 / 14 (7.14%)	0 / 14 (0.00%)	0 / 12 (0.00%)
occurrences (all)	1	0	0
Paraesthesia oral			
subjects affected / exposed	4 / 14 (28.57%)	0 / 14 (0.00%)	4 / 12 (33.33%)
occurrences (all)	4	0	4
Reflux gastritis			
subjects affected / exposed	1 / 14 (7.14%)	0 / 14 (0.00%)	0 / 12 (0.00%)
occurrences (all)	1	0	0
Salivary hypersecretion			
subjects affected / exposed	0 / 14 (0.00%)	0 / 14 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Tongue coated			
subjects affected / exposed	1 / 14 (7.14%)	0 / 14 (0.00%)	0 / 12 (0.00%)
occurrences (all)	1	0	0
Tooth deposit			
subjects affected / exposed	0 / 14 (0.00%)	0 / 14 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Vomiting			
subjects affected / exposed	1 / 14 (7.14%)	0 / 14 (0.00%)	0 / 12 (0.00%)
occurrences (all)	1	0	0
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	0 / 14 (0.00%)	1 / 14 (7.14%)	0 / 12 (0.00%)
occurrences (all)	0	1	0
Dry throat			

subjects affected / exposed	1 / 14 (7.14%)	0 / 14 (0.00%)	1 / 12 (8.33%)
occurrences (all)	1	0	1
Oropharyngeal discomfort			
subjects affected / exposed	0 / 14 (0.00%)	0 / 14 (0.00%)	1 / 12 (8.33%)
occurrences (all)	0	0	1
Oropharyngeal pain			
subjects affected / exposed	0 / 14 (0.00%)	0 / 14 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Pharyngeal hypoaesthesia			
subjects affected / exposed	2 / 14 (14.29%)	0 / 14 (0.00%)	1 / 12 (8.33%)
occurrences (all)	2	0	1
Throat irritation			
subjects affected / exposed	0 / 14 (0.00%)	0 / 14 (0.00%)	1 / 12 (8.33%)
occurrences (all)	0	0	1
Wheezing			
subjects affected / exposed	0 / 14 (0.00%)	1 / 14 (7.14%)	0 / 12 (0.00%)
occurrences (all)	0	1	0
Skin and subcutaneous tissue disorders			
Erythema			
subjects affected / exposed	1 / 14 (7.14%)	0 / 14 (0.00%)	1 / 12 (8.33%)
occurrences (all)	1	0	1
Psychiatric disorders			
Anxiety			
subjects affected / exposed	1 / 14 (7.14%)	0 / 14 (0.00%)	0 / 12 (0.00%)
occurrences (all)	1	0	0
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	0 / 14 (0.00%)	0 / 14 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Musculoskeletal pain			
subjects affected / exposed	0 / 14 (0.00%)	0 / 14 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Spinal osteoarthritis			
subjects affected / exposed	0 / 14 (0.00%)	0 / 14 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Infections and infestations			

Gastroenteritis			
subjects affected / exposed	1 / 14 (7.14%)	1 / 14 (7.14%)	0 / 12 (0.00%)
occurrences (all)	1	1	0
Oral herpes			
subjects affected / exposed	0 / 14 (0.00%)	0 / 14 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Rhinitis			
subjects affected / exposed	0 / 14 (0.00%)	0 / 14 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Upper respiratory tract infection			
subjects affected / exposed	0 / 14 (0.00%)	0 / 14 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0

Non-serious adverse events	Cohort 1: Placebo/Chronic Cough	Cohort 2: Gefapixant 50 mg/Healthy	Cohort 2: Placebo/Healthy
Total subjects affected by non-serious adverse events			
subjects affected / exposed	7 / 12 (58.33%)	9 / 12 (75.00%)	4 / 12 (33.33%)
Injury, poisoning and procedural complications			
Arthropod bite			
subjects affected / exposed	1 / 12 (8.33%)	0 / 12 (0.00%)	0 / 12 (0.00%)
occurrences (all)	1	0	0
Excoriation			
subjects affected / exposed	0 / 12 (0.00%)	1 / 12 (8.33%)	0 / 12 (0.00%)
occurrences (all)	0	1	0
Vascular disorders			
Hot flush			
subjects affected / exposed	1 / 12 (8.33%)	0 / 12 (0.00%)	0 / 12 (0.00%)
occurrences (all)	1	0	0
Hypertension			
subjects affected / exposed	0 / 12 (0.00%)	0 / 12 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Nervous system disorders			
Ageusia			
subjects affected / exposed	0 / 12 (0.00%)	4 / 12 (33.33%)	0 / 12 (0.00%)
occurrences (all)	0	4	0
Dizziness			

subjects affected / exposed	0 / 12 (0.00%)	1 / 12 (8.33%)	0 / 12 (0.00%)
occurrences (all)	0	1	0
Dysgeusia			
subjects affected / exposed	1 / 12 (8.33%)	4 / 12 (33.33%)	0 / 12 (0.00%)
occurrences (all)	1	5	0
Headache			
subjects affected / exposed	2 / 12 (16.67%)	2 / 12 (16.67%)	1 / 12 (8.33%)
occurrences (all)	2	2	1
Hypogeusia			
subjects affected / exposed	0 / 12 (0.00%)	2 / 12 (16.67%)	0 / 12 (0.00%)
occurrences (all)	0	2	0
VIIth Nerve Paralysis			
subjects affected / exposed	1 / 12 (8.33%)	0 / 12 (0.00%)	0 / 12 (0.00%)
occurrences (all)	1	0	0
General disorders and administration site conditions			
Chest discomfort			
subjects affected / exposed	0 / 12 (0.00%)	0 / 12 (0.00%)	1 / 12 (8.33%)
occurrences (all)	0	0	1
Fatigue			
subjects affected / exposed	0 / 12 (0.00%)	0 / 12 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Pain			
subjects affected / exposed	1 / 12 (8.33%)	0 / 12 (0.00%)	0 / 12 (0.00%)
occurrences (all)	1	0	0
Ear and labyrinth disorders			
Ear pain			
subjects affected / exposed	1 / 12 (8.33%)	0 / 12 (0.00%)	0 / 12 (0.00%)
occurrences (all)	1	0	0
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	0 / 12 (0.00%)	0 / 12 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Dry mouth			
subjects affected / exposed	1 / 12 (8.33%)	0 / 12 (0.00%)	0 / 12 (0.00%)
occurrences (all)	1	0	0
Dyspepsia			

subjects affected / exposed	0 / 12 (0.00%)	0 / 12 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Hypoaesthesia oral			
subjects affected / exposed	0 / 12 (0.00%)	0 / 12 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Nausea			
subjects affected / exposed	0 / 12 (0.00%)	0 / 12 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Paraesthesia oral			
subjects affected / exposed	1 / 12 (8.33%)	0 / 12 (0.00%)	0 / 12 (0.00%)
occurrences (all)	1	0	0
Reflux gastritis			
subjects affected / exposed	0 / 12 (0.00%)	0 / 12 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Salivary hypersecretion			
subjects affected / exposed	1 / 12 (8.33%)	0 / 12 (0.00%)	0 / 12 (0.00%)
occurrences (all)	1	0	0
Tongue coated			
subjects affected / exposed	0 / 12 (0.00%)	0 / 12 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Tooth deposit			
subjects affected / exposed	0 / 12 (0.00%)	1 / 12 (8.33%)	0 / 12 (0.00%)
occurrences (all)	0	1	0
Vomiting			
subjects affected / exposed	0 / 12 (0.00%)	0 / 12 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	0 / 12 (0.00%)	2 / 12 (16.67%)	3 / 12 (25.00%)
occurrences (all)	0	2	3
Dry throat			
subjects affected / exposed	0 / 12 (0.00%)	0 / 12 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Oropharyngeal discomfort			

subjects affected / exposed	0 / 12 (0.00%)	0 / 12 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Oropharyngeal pain			
subjects affected / exposed	0 / 12 (0.00%)	1 / 12 (8.33%)	1 / 12 (8.33%)
occurrences (all)	0	1	1
Pharyngeal hypoaesthesia			
subjects affected / exposed	0 / 12 (0.00%)	1 / 12 (8.33%)	0 / 12 (0.00%)
occurrences (all)	0	1	0
Throat irritation			
subjects affected / exposed	0 / 12 (0.00%)	0 / 12 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Wheezing			
subjects affected / exposed	0 / 12 (0.00%)	0 / 12 (0.00%)	1 / 12 (8.33%)
occurrences (all)	0	0	1
Skin and subcutaneous tissue disorders			
Erythema			
subjects affected / exposed	0 / 12 (0.00%)	0 / 12 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Psychiatric disorders			
Anxiety			
subjects affected / exposed	0 / 12 (0.00%)	0 / 12 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	1 / 12 (8.33%)	0 / 12 (0.00%)	0 / 12 (0.00%)
occurrences (all)	1	0	0
Musculoskeletal pain			
subjects affected / exposed	0 / 12 (0.00%)	0 / 12 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Spinal osteoarthritis			
subjects affected / exposed	0 / 12 (0.00%)	0 / 12 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Infections and infestations			
Gastroenteritis			
subjects affected / exposed	0 / 12 (0.00%)	0 / 12 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0

Oral herpes			
subjects affected / exposed	1 / 12 (8.33%)	0 / 12 (0.00%)	0 / 12 (0.00%)
occurrences (all)	1	0	0
Rhinitis			
subjects affected / exposed	1 / 12 (8.33%)	0 / 12 (0.00%)	0 / 12 (0.00%)
occurrences (all)	1	0	0
Upper respiratory tract infection			
subjects affected / exposed	0 / 12 (0.00%)	0 / 12 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0

Non-serious adverse events	Cohort 2: Gefapixant 50 mg/Chronic Cough	Cohort 2: Placebo/Chronic Cough	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	6 / 12 (50.00%)	3 / 11 (27.27%)	
Injury, poisoning and procedural complications			
Arthropod bite			
subjects affected / exposed	0 / 12 (0.00%)	0 / 11 (0.00%)	
occurrences (all)	0	0	
Excoriation			
subjects affected / exposed	0 / 12 (0.00%)	0 / 11 (0.00%)	
occurrences (all)	0	0	
Vascular disorders			
Hot flush			
subjects affected / exposed	0 / 12 (0.00%)	1 / 11 (9.09%)	
occurrences (all)	0	1	
Hypertension			
subjects affected / exposed	0 / 12 (0.00%)	1 / 11 (9.09%)	
occurrences (all)	0	1	
Nervous system disorders			
Ageusia			
subjects affected / exposed	0 / 12 (0.00%)	0 / 11 (0.00%)	
occurrences (all)	0	0	
Dizziness			
subjects affected / exposed	0 / 12 (0.00%)	0 / 11 (0.00%)	
occurrences (all)	0	0	
Dysgeusia			

subjects affected / exposed	3 / 12 (25.00%)	1 / 11 (9.09%)	
occurrences (all)	5	1	
Headache			
subjects affected / exposed	1 / 12 (8.33%)	2 / 11 (18.18%)	
occurrences (all)	1	2	
Hypogeusia			
subjects affected / exposed	1 / 12 (8.33%)	0 / 11 (0.00%)	
occurrences (all)	1	0	
VIIth Nerve Paralysis			
subjects affected / exposed	0 / 12 (0.00%)	0 / 11 (0.00%)	
occurrences (all)	0	0	
General disorders and administration site conditions			
Chest discomfort			
subjects affected / exposed	0 / 12 (0.00%)	0 / 11 (0.00%)	
occurrences (all)	0	0	
Fatigue			
subjects affected / exposed	0 / 12 (0.00%)	0 / 11 (0.00%)	
occurrences (all)	0	0	
Pain			
subjects affected / exposed	0 / 12 (0.00%)	0 / 11 (0.00%)	
occurrences (all)	0	0	
Ear and labyrinth disorders			
Ear pain			
subjects affected / exposed	0 / 12 (0.00%)	0 / 11 (0.00%)	
occurrences (all)	0	0	
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	0 / 12 (0.00%)	1 / 11 (9.09%)	
occurrences (all)	0	2	
Dry mouth			
subjects affected / exposed	0 / 12 (0.00%)	0 / 11 (0.00%)	
occurrences (all)	0	0	
Dyspepsia			
subjects affected / exposed	0 / 12 (0.00%)	0 / 11 (0.00%)	
occurrences (all)	0	0	
Hypoaesthesia oral			

subjects affected / exposed	0 / 12 (0.00%)	0 / 11 (0.00%)	
occurrences (all)	0	0	
Nausea			
subjects affected / exposed	0 / 12 (0.00%)	1 / 11 (9.09%)	
occurrences (all)	0	1	
Paraesthesia oral			
subjects affected / exposed	1 / 12 (8.33%)	0 / 11 (0.00%)	
occurrences (all)	1	0	
Reflux gastritis			
subjects affected / exposed	0 / 12 (0.00%)	0 / 11 (0.00%)	
occurrences (all)	0	0	
Salivary hypersecretion			
subjects affected / exposed	0 / 12 (0.00%)	0 / 11 (0.00%)	
occurrences (all)	0	0	
Tongue coated			
subjects affected / exposed	0 / 12 (0.00%)	0 / 11 (0.00%)	
occurrences (all)	0	0	
Tooth deposit			
subjects affected / exposed	0 / 12 (0.00%)	0 / 11 (0.00%)	
occurrences (all)	0	0	
Vomiting			
subjects affected / exposed	0 / 12 (0.00%)	0 / 11 (0.00%)	
occurrences (all)	0	0	
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	3 / 12 (25.00%)	0 / 11 (0.00%)	
occurrences (all)	3	0	
Dry throat			
subjects affected / exposed	0 / 12 (0.00%)	1 / 11 (9.09%)	
occurrences (all)	0	1	
Oropharyngeal discomfort			
subjects affected / exposed	0 / 12 (0.00%)	0 / 11 (0.00%)	
occurrences (all)	0	0	
Oropharyngeal pain			

subjects affected / exposed	0 / 12 (0.00%)	0 / 11 (0.00%)	
occurrences (all)	0	0	
Pharyngeal hypoaesthesia			
subjects affected / exposed	0 / 12 (0.00%)	0 / 11 (0.00%)	
occurrences (all)	0	0	
Throat irritation			
subjects affected / exposed	0 / 12 (0.00%)	0 / 11 (0.00%)	
occurrences (all)	0	0	
Wheezing			
subjects affected / exposed	0 / 12 (0.00%)	0 / 11 (0.00%)	
occurrences (all)	0	0	
Skin and subcutaneous tissue disorders			
Erythema			
subjects affected / exposed	0 / 12 (0.00%)	0 / 11 (0.00%)	
occurrences (all)	0	0	
Psychiatric disorders			
Anxiety			
subjects affected / exposed	0 / 12 (0.00%)	0 / 11 (0.00%)	
occurrences (all)	0	0	
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	0 / 12 (0.00%)	0 / 11 (0.00%)	
occurrences (all)	0	0	
Musculoskeletal pain			
subjects affected / exposed	0 / 12 (0.00%)	1 / 11 (9.09%)	
occurrences (all)	0	1	
Spinal osteoarthritis			
subjects affected / exposed	0 / 12 (0.00%)	1 / 11 (9.09%)	
occurrences (all)	0	1	
Infections and infestations			
Gastroenteritis			
subjects affected / exposed	0 / 12 (0.00%)	0 / 11 (0.00%)	
occurrences (all)	0	0	
Oral herpes			
subjects affected / exposed	0 / 12 (0.00%)	0 / 11 (0.00%)	
occurrences (all)	0	0	

Rhinitis subjects affected / exposed occurrences (all)	0 / 12 (0.00%) 0	0 / 11 (0.00%) 0	
Upper respiratory tract infection subjects affected / exposed occurrences (all)	1 / 12 (8.33%) 1	0 / 11 (0.00%) 0	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
25 February 2015	Amendment 1: Added steps specifying when and for which treatment group the cough monitor was attached and removed
17 July 2015	Amendment 2: Clarified that an ambulatory cough recorder chest microphone (in addition to the lapel microphone) would be used for cough participants only
05 August 2015	Amendment 3: Removed spirometry from the Schedule of Assessments and Procedures
02 September 2015	Amendment 4: Low Dose Extension (AF-219 50 mg, Cohort 2) added to include up to an additional 24 participants
19 October 2015	Amendment 5: Time frame of the exclusion criteria for treatment with an investigational drug decreased to facilitate the enrollment of participants in Cohort 1 into Cohort 2

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported