Clinical trial results:
A 12-Week Study to Assess the Efficacy and Safety of AF 219 in Subjects With Refractory Chronic Cough

Summary

EudraCT number	2015-005064-42
Trial protocol	GB
Global end of trial date	04 November 2016

Results information

Result version number	v3 (current)
This version publication date	19 January 2019
First version publication date	12 November 2017
Version creation reason	

Trial information

Trial identification

Sponsor protocol code	7264-012

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02612610
WHO universal trial number (UTN)	-
Other trial identifiers	MK-7264-012: Merck Protocol Number

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, ClinicalTrialsDisclosure@merck.com, 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	04 November 2016
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	04 November 2016
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

This study is designed to evaluate the efficacy of three dose regimens of gefapixant ([MK-7264] 7.5 mg, 20 mg, and 50 mg) relative to placebo in reducing awake objective cough frequency. The primary hypothesis for this trial is that at least one dose regimen of gefapixant is superior to placebo with respect to the mean change from baseline in awake cough frequency (on the log scale).

Protection of trial subjects:

This study was conducted in conformance with Good Clinical Practice standards and applicable country and/or local statutes and regulations regarding ethical committee review, informed consent, and the protection of human subjects participating in biomedical research.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	15 December 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: 88
Country: Number of subjects enrolled	United States: 165
Worldwide total number of subjects	253
EEA total number of subjects	88

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)	152
From 65 to 84 years	101

85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

Of 367 screened, 253 were randomised to treatment with placebo or 7.5 mg, 20 mg, or 50 mg gefapixant. One participant randomised to receive 7.5 mg gefapixant was discontinued before receiving treatment.

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	Placebo

Arm description:

Participants received one matching placebo tablet administered by mouth twice daily for 12 weeks.

Arm type	Placebo
Investigational medicinal product name	Placebo to gefapixant
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Dose-matched placebo tablet to gefapixant administered twice daily.

Arm title	Gefapixant 7.5 mg

Arm description:

Participants received one 7.5 mg gefapixant tablet administered by mouth twice daily for 12 weeks.

Arm type	Experimental
Investigational medicinal product name	Gefapixant
Investigational medicinal product code	
Other name	MK-7264, AF-219
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Gefapixant administered as one 7.5 mg tablet twice daily.

Arm title	Gefapixant 20 mg

Arm description:

Participants received one 20 mg gefapixant tablet administered by mouth twice daily for 12 weeks.

Arm type	Experimental
Investigational medicinal product name	Gefapixant
Investigational medicinal product code	
Other name	MK-7264, AF-219
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:
Gefapixant administered as one 20 mg tablet twice daily.

Arm title	Gefapixant 50 mg

Arm description:
Participants received one 50 mg gefapixant tablet administered by mouth twice daily for 12 weeks.

Arm type	Experimental
Investigational medicinal product name	Gefapixant
Investigational medicinal product code	
Other name	MK-7264, AF-219
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:
Gefapixant administered as one 50 mg tablet twice daily.

Number of subjects in period 1	Placebo	Gefapixant 7.5 mg	Gefapixant 20 mg
Started	63	64	63
Treated	63	63	63
Completed	58	56	58
Not completed	5	8	5
Consent withdrawn by subject	1	1	-
Physician decision	-	1	-
Adverse event, non-fatal	2	2	3
Cough Improvement	-	-	1
Lost to follow-up	-	1	-
Lack of efficacy	1	2	-
Noncompliance	1	-	-
Protocol deviation	-	1	1

Number of subjects in period 1	Gefapixant 50 mg
Started	63
Treated	63
Completed	50
Not completed	13
Consent withdrawn by subject	2
Physician decision	-
Adverse event, non-fatal	10
Cough Improvement	-
Lost to follow-up	-

Lack of efficacy	1
Noncompliance	-
Protocol deviation	-

Baseline characteristics

Reporting groups	
Reporting group title	Placebo
Reporting group description:	
Participants received one matching placebo tablet administered by mouth twice daily for 12 weeks.	
Reporting group title	Gefapixant 7.5 mg
Reporting group description:	
Participants received one 7.5 mg gefapixant tablet administered by mouth twice daily for 12 weeks.	
Reporting group title	Gefapixant 20 mg
Reporting group description:	
Participants received one 20 mg gefapixant tablet administered by mouth twice daily for 12 weeks.	
Reporting group title	Gefapixant 50 mg
Reporting group description:	
Participants received one 50 mg gefapixant tablet administered by mouth twice daily for 12 weeks.	

Reporting group values	Placebo	Gefapixant 7.5 mg	Gefapixant 20 mg
Number of subjects	63	64	63
Age categorical Units: Subjects			
Age Continuous Units: years			
arithmetic mean	60.0	59.9	61.8
standard deviation	± 10.9	± 10.46	± 9.13
Gender, Male/Female Units: Subjects			
Female	47	48	48
Male	16	16	15

Reporting group values	Gefapixant 50 mg	Total	
Number of subjects	63	253	
Age categorical Units: Subjects			
Age Continuous Units: years			
arithmetic mean	59.3		
standard deviation	± 9.19	-	
Gender, Male/Female Units: Subjects			
Female	50	193	
Male	13	60	

End points

End points reporting groups

Reporting group title	Placebo
Reporting group description:	
Participants received one matching placebo tablet administered by mouth twice daily for 12 weeks.	
Reporting group title	Gefapixant 7.5 mg
Reporting group description:	
Participants received one 7.5 mg gefapixant tablet administered by mouth twice daily for 12 weeks.	
Reporting group title	Gefapixant 20 mg
Reporting group description:	
Participants received one 20 mg gefapixant tablet administered by mouth twice daily for 12 weeks.	
Reporting group title	Gefapixant 50 mg
Reporting group description:	
Participants received one 50 mg gefapixant tablet administered by mouth twice daily for 12 weeks.	

Primary: Change from Baseline in Awake Objective Cough Frequency after 12 Weeks of Treatment (Day 84)

End point title	Change from Baseline in Awake Objective Cough Frequency after 12 Weeks of Treatment (Day 84)

End point description:

Awake Objective Cough Frequency (per hour) was defined as the total number of cough events during the monitoring period while the participant was awake divided by the total duration for the monitoring period that the participant was awake. 24 hour sound recordings were made at Baseline ([BL], Study Day -1) and at Week 12 (Day 84) using a digital recording device. An independent cough monitoring center documented the time of each cough event over the 24 hour period, as well as the time when the participant went to sleep and the time the participant woke. Least-squares (LS) mean change from BL (in log scale) with associated standard error (SE) reported for each treatment group. Change from BL in Awake Objective Cough Frequency = (Post-Treatment Awake Cough Frequency minus BL Awake Cough Frequency). All randomized participants who had taken at least 1 dose of study medication and provided at least 1 BL and ≥1 post BL endpoint observation during the treatment period were analysed.

End point type	Primary

End point timeframe:

Baseline Visit (Day -1), Day 84

End point values	Placebo	Gefapixant 7.5 mg	Gefapixant 20 mg	Gefapixant 50 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	61	59	59	57
Units: log coughs/hour				
least squares mean (standard error)	-0.40 (± 0.11)	-0.64 (± 0.11)	-0.65 (± 0.11)	-0.86 (± 0.11)

Statistical analyses

Statistical analysis title	Day 84 Awake Cough Freq: 7.5 mg gefapixant v PBO

Statistical analysis description:

Estimated treatment differences (gefapixant vs. placebo [PBO]) and corresponding 95% confidence intervals (CIs) were estimated using a mixed effect repeated measures (MMRM) model, which included fixed effects for treatment group, visit, country, treatment-by-visit interaction, and Baseline value (on log scale) as a covariate.

Comparison groups	Placebo v Gefapixant 7.5 mg
Number of subjects included in analysis	120
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.0971
Method	Mixed Effect Repeated Measures model
Parameter estimate	LS Mean Difference
Point estimate	-0.25
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.54
upper limit	0.05

Statistical analysis title	Day 84 Awake Cough Freq: 20 mg gefapixant v PBO

Statistical analysis description:

Estimated treatment differences (gefapixant vs. placebo) and corresponding 95% CIs were estimated using a MMRM model, which included fixed effects for treatment group, visit, country, treatment-by-visit interaction, and Baseline value (on log scale) as a covariate.

Comparison groups	Placebo v Gefapixant 20 mg
Number of subjects included in analysis	120
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.0928
Method	Mixed Effect Repeated Measures model
Parameter estimate	LS Mean Difference
Point estimate	-0.25
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.54
upper limit	0.04

Statistical analysis title	Day 84 Awake Cough Freq: 50 mg gefapixant v PBO

Statistical analysis description:

Estimated treatment differences (gefapixant vs. placebo) and corresponding 95% CIs were estimated using a MMRM model, which included fixed effects for treatment group, visit, country, treatment-by-visit interaction, and Baseline value (on log scale) as a covariate.

Comparison groups	Placebo v Gefapixant 50 mg

Number of subjects included in analysis	118
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.0027
Method	Mixed Effect Repeated Measures model
Parameter estimate	LS Mean Difference
Point estimate	-0.46
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.76
upper limit	-0.16

Secondary: Change from Baseline in 24-Hour Objective Cough Frequency after 4 Weeks of Treatment (Day 28)

End point title	Change from Baseline in 24-Hour Objective Cough Frequency after 4 Weeks of Treatment (Day 28)

End point description:

24-hr Objective Cough Frequency was defined as the total number of cough events during the monitoring period divided by the total duration in hours for the monitoring period (generally 24 hours). 24 hour sound recordings were made at Baseline (Study Day -1) and at Week 4 (Day 28) using a digital recording device. An independent cough monitoring center documented the time of each cough event over the 24 hour period, as well as the time when the participant went to sleep and the time the participant woke. LS mean change from baseline (in log scale) with associated SE reported for each treatment group. Change from Baseline in 24-Hour Objective Cough Frequency = (Post-Treatment 24-Hour Cough Frequency minus Baseline 24-Hour Cough Frequency).

All randomized participants who had taken at least 1 dose of study medication and provided at least 1 baseline and at least one post baseline endpoint observation during the treatment period were analysed.

End point type	Secondary

End point timeframe:

Baseline (Study Day -1), Day 28

End point values	Placebo	Gefapixant 7.5 mg	Gefapixant 20 mg	Gefapixant 50 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	61	59	59	57
Units: log coughs/hour				
least squares mean (standard error)	-0.41 (± 0.10)	-0.59 (± 0.10)	-0.46 (± 0.10)	-0.93 (± 0.10)

Statistical analyses

Statistical analysis title	Day 28 Awake Cough Freq: 7.5 mg gefapixant v PBO

Statistical analysis description:

Day 28 estimated treatment differences (gefapixant vs. placebo) and corresponding 95% CIs were estimated using a MMRM model, which included fixed effects for treatment group, visit, country, treatment-by-visit interaction, and Baseline value (on log scale) as a covariate.

Comparison groups	Placebo v Gefapixant 7.5 mg

Number of subjects included in analysis	120
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.1914
Method	Mixed Effect Repeated Measures model
Parameter estimate	LS Mean Difference
Point estimate	-0.19
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.47
upper limit	0.09

Statistical analysis title	Day 28 Awake Cough Freq: 20 mg gefapixant v PBO

Statistical analysis description:

Day 28 estimated treatment differences (gefapixant vs. placebo) and corresponding 95% CIs were estimated using a MMRM model, which included fixed effects for treatment group, visit, country, treatment-by-visit interaction, and Baseline value (on log scale) as a covariate.

Comparison groups	Placebo v Gefapixant 20 mg
Number of subjects included in analysis	120
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.7099
Method	Mixed Effect Repeated Measures model
Parameter estimate	LS Mean Difference
Point estimate	-0.05
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.33
upper limit	0.23

Statistical analysis title	Day 28 Awake Cough Freq: 50 mg gefapixant v PBO

Statistical analysis description:

Day 28 estimated treatment differences (gefapixant vs. placebo) and corresponding 95% CIs were estimated using a MMRM model, which included fixed effects for treatment group, visit, country, treatment-by-visit interaction, and Baseline value (on log scale) as a covariate.

Comparison groups	Placebo v Gefapixant 50 mg
Number of subjects included in analysis	118
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.0003
Method	Mixed Effect Repeated Measures model
Parameter estimate	LS Mean Difference
Point estimate	-0.52

Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.8
upper limit	-0.24

Secondary: Change from Baseline in 24-Hour Objective Cough Frequency after 8 Weeks of Treatment (Day 56)

End point title	Change from Baseline in 24-Hour Objective Cough Frequency after 8 Weeks of Treatment (Day 56)

End point description:

24-hr Objective Cough Frequency was defined as the total number of cough events during the monitoring period divided by the total duration in hours for the monitoring period (generally 24 hours). 24 hour sound recordings were made at Baseline (Study Day -1) and at Week 8 (Day 56) using a digital recording device. An independent cough monitoring center documented the time of each cough event over the 24 hour period, as well as the time when the participant went to sleep and the time the participant woke. LS mean change from baseline (in log scale) with associated SE reported for each treatment group. Change from Baseline in 24-Hour Objective Cough Frequency = (Post-Treatment 24-Hour Cough Frequency minus Baseline 24-Hour Cough Frequency).

All randomised participants who had taken at least 1 dose of study medication and provided at least 1 baseline and at least one post baseline endpoint observation during the treatment period were analysed.

End point type	Secondary

End point timeframe:

Baseline (Study Day -1), Day 56

End point values	Placebo	Gefapixant 7.5 mg	Gefapixant 20 mg	Gefapixant 50 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	61	59	59	57
Units: log coughs/hour				
least squares mean (standard error)	-0.31 (± 0.11)	-0.71 (± 0.11)	-0.59 (± 0.11)	-0.93 (± 0.11)

Statistical analyses

Statistical analysis title	Day 56 24-hour Cough Freq: 7.5 mg gefapixant v PBO

Statistical analysis description:

Day 56 estimated treatment differences (gefapixant vs. placebo) and corresponding 95% CIs were estimated using a MMRM model, which included fixed effects for treatment group, visit, country, treatment-by-visit interaction, and Baseline value (on log scale) as a covariate.

Comparison groups	Placebo v Gefapixant 7.5 mg
Number of subjects included in analysis	120
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.0099
Method	Mixed Effect Repeated Measures model
Parameter estimate	LS Mean Difference
Point estimate	-0.4

Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.71
upper limit	-0.1

Statistical analysis title	Day 56 24-hour Cough Freq: 20 mg gefapixant v PBO

Statistical analysis description:

Day 56 estimated treatment differences (gefapixant vs. placebo) and corresponding 95% CIs were estimated using a MMRM model, which included fixed effects for treatment group, visit, country, treatment-by-visit interaction, and Baseline value (on log scale) as a covariate.

Comparison groups	Placebo v Gefapixant 20 mg
Number of subjects included in analysis	120
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.0695
Method	Mixed Effect Repeated Measures model
Parameter estimate	LS Mean Difference
Point estimate	-0.28
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.58
upper limit	0.02

Statistical analysis title	Day 56 24-hour Cough Freq: 50 mg gefapixant v PBO

Statistical analysis description:

Day 56 estimated treatment differences (gefapixant vs. placebo) and corresponding 95% CIs were estimated using a MMRM model, which included fixed effects for treatment group, visit, country, treatment-by-visit interaction, and Baseline value (on log scale) as a covariate.

Comparison groups	Placebo v Gefapixant 50 mg
Number of subjects included in analysis	118
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.0001
Method	Mixed Effect Repeated Measures model
Parameter estimate	LS Mean Difference
Point estimate	-0.62
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.93
upper limit	-0.31

Secondary: Change from Baseline in 24-Hour Objective Cough Frequency after 12

Weeks of Treatment (Day 84)

End point title	Change from Baseline in 24-Hour Objective Cough Frequency after 12 Weeks of Treatment (Day 84)

End point description:

24-hr Objective Cough Frequency was defined as the total number of cough events during the monitoring period divided by the total duration in hours for the monitoring period (generally 24 hours). 24 hour sound recordings were made at Baseline (Study Day -1) and at Week 12 (Day 84) using a digital recording device. An independent cough monitoring center documented the time of each cough event over the 24 hour period, as well as the time when the participant went to sleep and the time the participant woke. LS mean change from baseline (in log scale) with associated SE reported for each treatment group. Change from Baseline in 24-Hour Objective Cough Frequency = (Post-Treatment 24-Hour Cough Frequency minus Baseline 24-Hour Cough Frequency).

All randomised participants who had taken at least 1 dose of study medication and provided at least 1 baseline and at least one post baseline endpoint observation during the treatment period were analysed.

End point type	Secondary

End point timeframe:

Baseline (Study Day -1), Day 84

End point values	Placebo	Gefapixant 7.5 mg	Gefapixant 20 mg	Gefapixant 50 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	61	59	59	57
Units: log coughs/hour				
least squares mean (standard error)	-0.39 (± 0.10)	-0.62 (± 0.10)	-0.64 (± 0.10)	-0.86 (± 0.11)

Statistical analyses

Statistical analysis title	Day 84 24-hour Cough Freq: 7.5 mg gefapixant v PBO

Statistical analysis description:

Day 84 estimated treatment differences (gefapixant vs. placebo) and corresponding 95% CIs were estimated using a MMRM model, which included fixed effects for treatment group, visit, country, treatment-by-visit interaction, and Baseline value (on log scale) as a covariate.

Comparison groups	Placebo v Gefapixant 7.5 mg
Number of subjects included in analysis	120
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.0991
Method	Mixed Effect Repeated Measures model
Parameter estimate	LS Mean Difference
Point estimate	-0.24
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.52
upper limit	0.04

Statistical analysis title	Day 84 24-hour Cough Freq: 20 mg gefapixant v PBO

Statistical analysis description:

Day 84 estimated treatment differences (gefapixant vs. placebo) and corresponding 95% CIs were estimated using a MMRM model, which included fixed effects for treatment group, visit, country, treatment-by-visit interaction, and Baseline value (on log scale) as a covariate.

Comparison groups	Placebo v Gefapixant 20 mg
Number of subjects included in analysis	120
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.0811
Method	Mixed Effect Repeated Measures model
Parameter estimate	LS Mean Difference
Point estimate	-0.25
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.53
upper limit	0.03

Statistical analysis title	Day 84 24-hour Cough Freq: 50 mg gefapixant v PBO

Statistical analysis description:

Day 84 estimated treatment differences (gefapixant vs. placebo) and corresponding 95% CIs were estimated using a MMRM model, which included fixed effects for treatment group, visit, country, treatment-by-visit interaction, and Baseline value (on log scale) as a covariate.

Comparison groups	Placebo v Gefapixant 50 mg
Number of subjects included in analysis	118
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.0014
Method	Mixed Effect Repeated Measures model
Parameter estimate	LS Mean Difference
Point estimate	-0.47
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.76
upper limit	-0.19

Secondary: Change from Baseline in Awake Objective Cough Frequency after 4 Weeks of Treatment (Day 28)

End point title	Change from Baseline in Awake Objective Cough Frequency after 4 Weeks of Treatment (Day 28)

End point description:

Awake Objective Cough Frequency (per hour) was defined as the total number of cough events during the monitoring period while the participant was awake divided by the total duration for the monitoring period that the participant was awake. 24 hour sound recordings were made at Baseline (Study Day -1) and at Week 4 (Day 28) using a digital recording device. An independent cough monitoring center documented the time of each cough event over the 24 hour period, as well as the time when the participant went to sleep and the time the participant woke. LS mean change from baseline (in log

scale) with associated SE reported for each treatment group. Change from Baseline in Awake Objective Cough Frequency = (Post-Treatment Awake Cough Frequency minus Baseline Awake Cough Frequency).

All randomized participants who had taken at least 1 dose of study medication and provided at least 1 baseline and at least one post baseline endpoint observation during the treatment period were analysed.

End point type	Secondary

End point timeframe:

Baseline (Study Day -1), Day 28,

End point values	Placebo	Gefapixant 7.5 mg	Gefapixant 20 mg	Gefapixant 50 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	61	59	59	57
Units: log coughs/hour				
least squares mean (standard error)	-0.41 (± 0.10)	-0.62 (± 0.10)	-0.48 (± 0.10)	-0.90 (± 0.11)

Statistical analyses

Statistical analysis title	Day 28 Awake Cough Freq: 7.5 mg gefapixant v PBO

Statistical analysis description:

Day 28 estimated treatment differences (gefapixant vs. placebo) and corresponding 95% CIs were estimated using a MMRM model, which included fixed effects for treatment group, visit, country, treatment-by-visit interaction, and Baseline value (on log scale) as a covariate.

Comparison groups	Placebo v Gefapixant 7.5 mg
Number of subjects included in analysis	120
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.1468
Method	Mixed Effect Repeated Measures model
Parameter estimate	LS Mean Difference
Point estimate	-0.21
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.5
upper limit	0.07

Statistical analysis title	Day 28 Awake Cough Freq: 20 mg gefapixant v PBO

Statistical analysis description:

Day 28 estimated treatment differences (gefapixant vs. placebo) and corresponding 95% CIs were estimated using a MMRM model, which included fixed effects for treatment group, visit, country, treatment-by-visit interaction, and Baseline value (on log scale) as a covariate.

Comparison groups	Placebo v Gefapixant 20 mg

Number of subjects included in analysis	120
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.5874
Method	Mixed Effect Repeated Measures model
Parameter estimate	LS Mean Difference
Point estimate	-0.08
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.36
upper limit	0.2

Statistical analysis title	Day 28 Awake Cough Freq: 50 mg gefapixant v PBO

Statistical analysis description:

Day 28 estimated treatment differences (gefapixant vs. placebo) and corresponding 95% CIs were estimated using a MMRM model, which included fixed effects for treatment group, visit, country, treatment-by-visit interaction, and Baseline value (on log scale) as a covariate.

Comparison groups	Placebo v Gefapixant 50 mg
Number of subjects included in analysis	118
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.0008
Method	Mixed Effect Repeated Measures model
Parameter estimate	LS Mean Difference
Point estimate	-0.49
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.78
upper limit	-0.21

Secondary: Change from Baseline in Awake Objective Cough Frequency after 8 Weeks of Treatment (Day 56)

End point title	Change from Baseline in Awake Objective Cough Frequency after 8 Weeks of Treatment (Day 56)

End point description:

Awake Objective Cough Frequency (per hour) was defined as the total number of cough events during the monitoring period while the participant was awake divided by the total duration for the monitoring period that the participant was awake. 24 hour sound recordings were made at Baseline (Study Day -1) and at Week 8 (Day 56) using a digital recording device. An independent cough monitoring center documented the time of each cough event over the 24 hour period, as well as the time when the participant went to sleep and the time the participant woke. LS mean change from baseline (in log scale) with associated SE reported for each treatment group. Change from Baseline in Awake Objective Cough Frequency = (Post-Treatment Awake Cough Frequency minus Baseline Awake Cough Frequency).

All randomized participants who had taken at least 1 dose of study medication and provided at least 1 baseline and at least one post baseline endpoint observation during the treatment period were analysed.

End point type	Secondary

End point timeframe:

Baseline (Study Day -1), Day 56

End point values	Placebo	Gefapixant 7.5 mg	Gefapixant 20 mg	Gefapixant 50 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	61	59	59	57
Units: log coughs/hour				
least squares mean (standard error)	-0.31 (± 0.11)	-0.70 (± 0.12)	-0.63 (± 0.11)	-0.90 (± 0.12)

Statistical analyses

Statistical analysis title	Day 56 Awake Cough Freq: 7.5 mg gefapixant v PBO

Statistical analysis description:

Day 56 estimated treatment differences (gefapixant vs. placebo) and corresponding 95% CIs were estimated using a MMRM model, which included fixed effects for treatment group, visit, country, treatment-by-visit interaction, and Baseline value (on log scale) as a covariate.

Comparison groups	Placebo v Gefapixant 7.5 mg
Number of subjects included in analysis	120
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.0177
Method	Mixed Effect Repeated Measures model
Parameter estimate	Mixed Effect Repeated Measures model
Point estimate	-0.39
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.7
upper limit	-0.07

Statistical analysis title	Day 56 Awake Cough Freq: 20 mg gefapixant v PBO

Statistical analysis description:

Day 56 estimated treatment differences (gefapixant vs. placebo) and corresponding 95% CIs were estimated using a MMRM model, which included fixed effects for treatment group, visit, country, treatment-by-visit interaction, and Baseline value (on log scale) as a covariate.

Comparison groups	Placebo v Gefapixant 20 mg
Number of subjects included in analysis	120
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.0498
Method	Mixed Effect Repeated Measures model
Parameter estimate	LS Mean Difference
Point estimate	-0.32

Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.63
upper limit	0

Statistical analysis title	Day 56 Awake Cough Freq: 50 mg gefapixant v PBO

Statistical analysis description:

Day 56 estimated treatment differences (gefapixant vs. placebo) and corresponding 95% CIs were estimated using a MMRM model, which included fixed effects for treatment group, visit, country, treatment-by-visit interaction, and Baseline value (on log scale) as a covariate.

Comparison groups	Placebo v Gefapixant 50 mg
Number of subjects included in analysis	118
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.0004
Method	Mixed Effect Repeated Measures model
Parameter estimate	LS Mean Difference
Point estimate	-0.59
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.92
upper limit	-0.27

Secondary: Change from Baseline in Awake Objective Cough Frequency at the Follow-up Visit (Day 98)

End point title	Change from Baseline in Awake Objective Cough Frequency at the Follow-up Visit (Day 98)

End point description:

Awake Objective Cough Frequency (per hour) was defined as the total number of cough events during the monitoring period (in general, 24-hr interval) while the participant was awake divided by the total duration (in hours) for the monitoring period that the participant was awake. 24 hour sound recordings were made at Baseline (Study Day -1) and at the Follow-up visit (Day 98) using a digital recording device. An independent cough monitoring center documented the time of each cough event over the 24 hour period, as well as the time when the participant went to sleep and the time the participant woke. Change from Baseline in Awake Objective Cough Frequency = (Post-Treatment Awake Cough Frequency minus Baseline Awake Cough Frequency).

All randomised participants who had taken at least 1 dose of study medication and provided baseline and follow-up visit (Day 98) data during the treatment period were analysed.

End point type	Secondary

End point timeframe:

Baseline (Study Day -1), Day 98

End point values	Placebo	Gefapixant 7.5 mg	Gefapixant 20 mg	Gefapixant 50 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	58	55	56	51
Units: coughs/hour				
arithmetic mean (standard deviation)	-6.4 (± 22.72)	-9.3 (± 47.72)	-7.4 (± 29.24)	-16.2 (± 39.00)

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in Cough Severity Visual Analogue Scale (VAS) after 4 Weeks of Treatment (Day 28)

End point title	Change from Baseline in Cough Severity Visual Analogue Scale (VAS) after 4 Weeks of Treatment (Day 28)

End point description:

Cough VAS was scored from 0 to 100 using a 100 mm visual analogue scale. Participants were asked to mark on a 100 mm scale between 0 (no cough) and 100 (the worst cough severity). Cough VAS was evaluated at Baseline (Study Day -1) and at Week 4 (Day 28). Baseline cough VAS was defined as the cough VAS at Baseline (Study Day -1). LS mean change from baseline with associated SE reported for each treatment group.

All randomized participants who had taken at least 1 dose of study medication and provided at least 1 baseline and at least one post baseline endpoint observation during the treatment period were analysed.

End point type	Secondary

End point timeframe:

Baseline (Study Day -1), Day 28

End point values	Placebo	Gefapixant 7.5 mg	Gefapixant 20 mg	Gefapixant 50 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	61	59	59	57
Units: units on a scale				
least squares mean (standard error)	-15.2 (± 3.02)	-21.6 (± 3.05)	-18.1 (± 3.04)	-25. (± 3.09)

Statistical analyses

Statistical analysis title	Day 28 Cough Severity VAS: 7.5 mg gefapixant v PBO

Statistical analysis description:

Day 28 estimated treatment differences (gefapixant vs. placebo) and corresponding 95% CIs were estimated using a MMRM model, which included fixed effects for treatment group, visit, country, treatment-by-visit interaction, and Baseline value as a covariate.

Comparison groups	Placebo v Gefapixant 7.5 mg

Number of subjects included in analysis	120
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.1318
Method	Mixed Effect Repeated Measures model
Parameter estimate	LS Mean Difference
Point estimate	-6.4
Confidence interval	
level	95 %
sides	2-sided
lower limit	-14.8
upper limit	1.9

Statistical analysis title	Day 28 Cough Severity VAS: 20 mg gefapixant v PBO

Statistical analysis description:

Day 28 estimated treatment differences (gefapixant vs. placebo) and corresponding 95% CIs were estimated using a MMRM model, which included fixed effects for treatment group, visit, country, treatment-by-visit interaction, and Baseline value as a covariate.

Comparison groups	Placebo v Gefapixant 20 mg
Number of subjects included in analysis	120
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.4917
Method	Mixed Effect Repeated Measures model
Parameter estimate	LS Mean Difference
Point estimate	-2.9
Confidence interval	
level	95 %
sides	2-sided
lower limit	-11.3
upper limit	5.4

Statistical analysis title	Day 28 Cough Severity VAS: 50 mg gefapixant v PBO

Statistical analysis description:

Day 28 estimated treatment differences (gefapixant vs. placebo) and corresponding 95% CIs were estimated using a MMRM model, which included fixed effects for treatment group, visit, country, treatment-by-visit interaction, and Baseline value as a covariate.

Comparison groups	Placebo v Gefapixant 50 mg
Number of subjects included in analysis	118
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.0228
Method	Mixed Effect Repeated Measures model
Parameter estimate	LS Mean Difference
Point estimate	-9.8

Confidence interval	
level	95 %
sides	2-sided
lower limit	-18.2
upper limit	-1.4

Secondary: Change from Baseline in Cough Severity VAS after 8 Weeks of Treatment (Day 56)

End point title	Change from Baseline in Cough Severity VAS after 8 Weeks of Treatment (Day 56)

End point description:

Cough VAS was scored from 0 to 100 using a 100 mm visual analogue scale. Participants were asked to mark on a 100 mm scale between 0 (no cough) and 100 (the worst cough severity). Cough VAS was evaluated at Baseline (Study Day -1) and at Week 8 (Day 56). Baseline cough VAS was defined as the cough VAS at Baseline (Study Day -1). LS mean change from baseline with associated SE reported for each treatment group.

All randomized participants who had taken at least 1 dose of study medication and provided at least 1 baseline and at least one post baseline endpoint observation during the treatment period were analysed.

End point type	Secondary

End point timeframe:

Baseline (Study Day -1), Day 56

End point values	Placebo	Gefapixant 7.5 mg	Gefapixant 20 mg	Gefapixant 50 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	61	59	59	57
Units: units on a scale				
least squares mean (standard error)	-16.1 (± 3.18)	-18.8 (± 3.19)	-19.4 (± 3.18)	-26.9 (± 3.33)

Statistical analyses

Statistical analysis title	Day 56 Cough Severity VAS: 7.5 mg gefapixant v PBO

Statistical analysis description:

Day 56 estimated treatment differences (gefapixant vs. placebo) and corresponding 95% CIs were estimated using a MMRM model, which included fixed effects for treatment group, visit, country, treatment-by-visit interaction, and Baseline value as a covariate.

Comparison groups	Placebo v Gefapixant 7.5 mg
Number of subjects included in analysis	120
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.554
Method	Mixed Effect Repeated Measures model
Parameter estimate	LS Mean Difference
Point estimate	-2.6

Confidence interval	
level	95 %
sides	2-sided
lower limit	-11.5
upper limit	6.2

Statistical analysis title	Day 56 Cough Severity VAS: 20 mg gefapixant v PBO

Statistical analysis description:

Day 56 estimated treatment differences (gefapixant vs. placebo) and corresponding 95% CIs were estimated using a MMRM model, which included fixed effects for treatment group, visit, country, treatment-by-visit interaction, and Baseline value as a covariate.

Comparison groups	Placebo v Gefapixant 20 mg
Number of subjects included in analysis	120
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.4702
Method	Mixed Effect Repeated Measures model
Parameter estimate	LS Mean Difference
Point estimate	-3.2
Confidence interval	
level	95 %
sides	2-sided
lower limit	-12
upper limit	5.6

Statistical analysis title	Day 56 Cough Severity VAS: 50 mg gefapixant v PBO

Statistical analysis description:

Day 56 estimated treatment differences (gefapixant vs. placebo) and corresponding 95% CIs were estimated using a MMRM model, which included fixed effects for treatment group, visit, country, treatment-by-visit interaction, and Baseline value as a covariate.

Comparison groups	Placebo v Gefapixant 50 mg
Number of subjects included in analysis	118
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.0197
Method	Mixed Effect Repeated Measures model
Parameter estimate	LS Mean Difference
Point estimate	-10.7
Confidence interval	
level	95 %
sides	2-sided
lower limit	-19.8
upper limit	-1.7

Secondary: Change from Baseline in Cough Severity VAS after 12 Weeks of

Treatment (Day 84)

End point title	Change from Baseline in Cough Severity VAS after 12 Weeks of Treatment (Day 84)

End point description:

Cough VAS was scored from 0 to 100 using a 100 mm visual analogue scale. Participants were asked to mark on a 100 mm scale between 0 (no cough) and 100 (the worst cough severity). Cough VAS was evaluated at Baseline (Study Day -1) and at Week 12 (Day 84). Baseline cough VAS was defined as the cough VAS at Baseline (Study Day -1). LS mean change from baseline with associated SE reported for each treatment group.

All randomized participants who had taken at least 1 dose of study medication and provided at least 1 baseline and at least one post baseline endpoint observation during the treatment period were analysed.

End point type	Secondary

End point timeframe:

Baseline (Study Day -1), Day 84

End point values	Placebo	Gefapixant 7.5 mg	Gefapixant 20 mg	Gefapixant 50 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	61	59	59	57
Units: units on a scale				
least squares mean (standard error)	-16.7 (± 3.04)	-21.1 (± 3.08)	-23.1 (± 3.05)	-27.9 (± 3.16)

Statistical analyses

Statistical analysis title	Day 84 Cough Severity VAS: 7.5 mg gefapixant v PBO

Statistical analysis description:

Day 84 estimated treatment differences (gefapixant vs. placebo) and corresponding 95% CIs were estimated using a MMRM model, which included fixed effects for treatment group, visit, country, treatment-by-visit interaction, and Baseline value as a covariate.

Comparison groups	Placebo v Gefapixant 7.5 mg
Number of subjects included in analysis	120
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.302
Method	Mixed Effect Repeated Measures model
Parameter estimate	LS Mean Difference
Point estimate	-4.4
Confidence interval	
level	95 %
sides	2-sided
lower limit	-12.9
upper limit	4

Statistical analysis title	Day 84 Cough Severity VAS: 20 mg gefapixant v PBO

Statistical analysis description:

Day 84 estimated treatment differences (gefapixant vs. placebo) and corresponding 95% CIs were

estimated using a MMRM model, which included fixed effects for treatment group, visit, country, treatment-by-visit interaction, and Baseline value as a covariate.

Comparison groups	Placebo v Gefapixant 20 mg
Number of subjects included in analysis	120
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.1365
Method	Mixed Effect Repeated Measures model
Parameter estimate	LS Mean Difference
Point estimate	-6.4
Confidence interval	
level	95 %
sides	2-sided
lower limit	-14.8
upper limit	2

Statistical analysis title	Day 84 Cough Severity VAS: 50 mg gefapixant v PBO

Statistical analysis description:

Day 84 estimated treatment differences (gefapixant vs. placebo) and corresponding 95% CIs were estimated using a MMRM model, which included fixed effects for treatment group, visit, country, treatment-by-visit interaction, and Baseline value as a covariate.

Comparison groups	Placebo v Gefapixant 50 mg
Number of subjects included in analysis	118
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.0108
Method	Mixed Effect Repeated Measures model
Parameter estimate	LS Mean Difference
Point estimate	-11.2
Confidence interval	
level	95 %
sides	2-sided
lower limit	-19.7
upper limit	-2.6

Secondary: Change from Baseline in Cough Severity VAS At Day 85/Early Termination

End point title	Change from Baseline in Cough Severity VAS At Day 85/Early Termination

End point description:

Cough VAS was scored from 0 to 100 using a 100 mm visual analogue scale. Participants were asked to mark on a 100 mm scale between 0 (no cough) and 100 (the worst cough severity). Cough VAS was evaluated at Baseline (Study Day -1) and at Day 85/Early Termination. Baseline cough VAS was defined as the cough VAS at Baseline (Study Day -1). LS mean change from baseline with associated SE reported for each treatment group.

All randomized participants who had taken at least 1 dose of study medication and provided at least 1 baseline and at least one post baseline endpoint observation during the treatment period were analysed.

End point type	Secondary

End point timeframe:
Baseline (Study Day -1), Day 85

End point values	Placebo	Gefapixant 7.5 mg	Gefapixant 20 mg	Gefapixant 50 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	61	59	59	57
Units: unit on a scale				
least squares mean (standard error)	-15.2 (± 3.00)	-19.2 (± 3.04)	-23.4 (± 3.03)	-31.1 (± 3.09)

Statistical analyses

Statistical analysis title	Day 85 Cough Severity VAS: 7.5 mg gefapixant v PBO
Statistical analysis description:	
Day 85/Early Termination estimated treatment differences (gefapixant vs. placebo) and corresponding 95% CIs were estimated using a MMRM model, which included fixed effects for treatment group, visit, country, treatment-by-visit interaction, and Baseline value as a covariate.	
Comparison groups	Placebo v Gefapixant 7.5 mg
Number of subjects included in analysis	120
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.3509
Method	Mixed Effect Repeated Measures model
Parameter estimate	LS Mean Difference
Point estimate	-4
Confidence interval	
level	95 %
sides	2-sided
lower limit	-12.3
upper limit	4.4

Statistical analysis title	Day 85 Cough Severity VAS: 20 mg gefapixant v PBO
Statistical analysis description:	
Day 85/Early Termination estimated treatment differences (gefapixant vs. placebo) and corresponding 95% CIs were estimated using a MMRM model, which included fixed effects for treatment group, visit, country, treatment-by-visit interaction, and Baseline value as a covariate.	
Comparison groups	Placebo v Gefapixant 20 mg
Number of subjects included in analysis	120
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.0519
Method	Mixed Effect Repeated Measures model
Parameter estimate	LS Mean Difference
Point estimate	-8.2

Confidence interval	
level	95 %
sides	2-sided
lower limit	-16.6
upper limit	0.1

Statistical analysis title	Day 85 Cough Severity VAS: 50 mg gefapixant v PBO

Statistical analysis description:

Day 85/Early Termination estimated treatment differences (gefapixant vs. placebo) and corresponding 95% CIs were estimated using a MMRM model, which included fixed effects for treatment group, visit, country, treatment-by-visit interaction, and Baseline value as a covariate.

Comparison groups	Placebo v Gefapixant 50 mg
Number of subjects included in analysis	118
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.0003
Method	Mixed Effect Repeated Measures model
Parameter estimate	LS Mean Difference
Point estimate	-15.9
Confidence interval	
level	95 %
sides	2-sided
lower limit	-24.3
upper limit	-7.5

Secondary: Percentage of Participants with ≥70%, ≥50%, and ≥30% Change in Awake Objective Cough Frequency after 4 Weeks of Treatment (Day 28)

End point title	Percentage of Participants with ≥70%, ≥50%, and ≥30% Change in Awake Objective Cough Frequency after 4 Weeks of Treatment (Day 28)

End point description:

Awake Objective Cough Frequency (per hour) was defined as the total number of cough events during the monitoring period (in general, 24-hr interval) while the participant was awake divided by the total duration (in hours) for the monitoring period that the participant was awake. 24 hour sound recordings were made at Baseline (Study Day -1) and at Week 4 (Day 28) using a digital recording device. An independent cough monitoring center documented the time of each cough event over the 24 hour period, as well as the time when the participant went to sleep and the time the participant woke. The percentages of participants that met responder criteria for ≥70%, ≥50%, and ≥30% change (reduction) from baseline levels in Awake Objective Cough Frequency were reported for each treatment group at Day 28.

All randomised participants who had taken ≥1 dose of study medication and provided ≥1 baseline and ≥1 Day 28 endpoint observation during the treatment period were analysed.

End point type	Secondary

End point timeframe:

Baseline (Study Day -1), Day 28

End point values	Placebo	Gefapixant 7.5 mg	Gefapixant 20 mg	Gefapixant 50 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	60	55	59	55
Units: percentage of participants				
number (not applicable)				
≥70% Change	15.0	25.5	16.9	34.5
≥50% Change	23.3	38.2	30.5	47.3
≥30% Change	46.7	63.6	50.8	60.0

Statistical analyses

Statistical analysis title	Day 28: ≥70% Change: 7.5 mg gefapixant v PBO

Statistical analysis description:

Cough frequency responder endpoints were analyzed by a generalized linear mixed model (GLMM) with treatment, visit, and treatment by visit interaction, and country as fixed effects. Comparison of response rates between each gefapixant treatment group and placebo was conducted using the stratified Cochran Mantel Haenszel (CMH) test (stratified by country, unless stated otherwise). Missing data was categorised as discontinued or missing

Comparison groups	Placebo v Gefapixant 7.5 mg
Number of subjects included in analysis	115
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.1387
Method	Cochran-Mantel-Haenszel

Statistical analysis title	Day 28: ≥70% Change: 20 mg gefapixant v PBO

Statistical analysis description:

Cough frequency responder endpoints were analyzed by a GLMM with treatment, visit, and treatment by visit interaction, and country as fixed effects. Comparison of response rates between each gefapixant treatment group and placebo was conducted using the stratified CMH test (stratified by country, unless stated otherwise). Missing data was categorised as discontinued or missing

Comparison groups	Placebo v Gefapixant 20 mg
Number of subjects included in analysis	119
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.7238
Method	Cochran-Mantel-Haenszel

Statistical analysis title	Day 28: ≥70% Change: 50 mg gefapixant v PBO

Statistical analysis description:

Cough frequency responder endpoints were analyzed by a GLMM with treatment, visit, and treatment by visit interaction, and country as fixed effects. Comparison of response rates between each gefapixant treatment group and placebo was conducted using the stratified CMH test (stratified by country, unless stated otherwise). Missing data was categorised as discontinued or missing

Comparison groups	Placebo v Gefapixant 50 mg

Number of subjects included in analysis	115
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.0144
Method	Cochran-Mantel-Haenszel

Statistical analysis title	Day 28: ≥50% Change: 7.5 mg gefapixant v PBO

Statistical analysis description:

Cough frequency responder endpoints were analyzed by a GLMM with treatment, visit, and treatment by visit interaction, and country as fixed effects. Comparison of response rates between each gefapixant treatment group and placebo was conducted using the stratified CMH test (stratified by country, unless stated otherwise). Missing data was categorised as discontinued or missing

Comparison groups	Placebo v Gefapixant 7.5 mg
Number of subjects included in analysis	115
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.0922
Method	Cochran-Mantel-Haenszel

Statistical analysis title	Day 28: ≥50% Change: 20 mg gefapixant v PBO

Statistical analysis description:

Cough frequency responder endpoints were analyzed by a GLMM with treatment, visit, and treatment by visit interaction, and country as fixed effects. Comparison of response rates between each gefapixant treatment group and placebo was conducted using the stratified CMH test (stratified by country, unless stated otherwise). Missing data was categorised as discontinued or missing

Comparison groups	Placebo v Gefapixant 20 mg
Number of subjects included in analysis	119
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.3812
Method	Cochran-Mantel-Haenszel

Statistical analysis title	Day 28: ≥50% Change: 50 mg gefapixant v PBO

Statistical analysis description:

Cough frequency responder endpoints were analyzed by a GLMM with treatment, visit, and treatment by visit interaction, and country as fixed effects. Comparison of response rates between each gefapixant treatment group and placebo was conducted using the stratified CMH test (stratified by country, unless stated otherwise). Missing data was categorised as discontinued or missing

Comparison groups	Placebo v Gefapixant 50 mg
Number of subjects included in analysis	115
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.0088
Method	Cochran-Mantel-Haenszel

Statistical analysis title	Day 28: ≥30% Change: 7.5 mg gefapixant v PBO

Statistical analysis description:

Cough frequency responder endpoints were analyzed by a GLMM with treatment, visit, and treatment by visit interaction, and country as fixed effects. Comparison of response rates between each gefapixant treatment group and placebo was conducted using the stratified CMH test (stratified by country, unless stated otherwise). Missing data was categorised as discontinued or missing

Comparison groups	Placebo v Gefapixant 7.5 mg
Number of subjects included in analysis	115
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.0653
Method	Cochran-Mantel-Haenszel

Statistical analysis title	Day 28: ≥30% Change: 20 mg gefapixant v PBO

Statistical analysis description:

Cough frequency responder endpoints were analyzed by a GLMM with treatment, visit, and treatment by visit interaction, and country as fixed effects. Comparison of response rates between each gefapixant treatment group and placebo was conducted using the stratified CMH test (stratified by country, unless stated otherwise). Missing data was categorised as discontinued or missing

Comparison groups	Placebo v Gefapixant 20 mg
Number of subjects included in analysis	119
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.6443
Method	Cochran-Mantel-Haenszel

Statistical analysis title	Day 28: ≥30% Change: 50 mg gefapixant v PBO

Statistical analysis description:

Cough frequency responder endpoints were analyzed by a GLMM with treatment, visit, and treatment by visit interaction, and country as fixed effects. Comparison of response rates between each gefapixant treatment group and placebo was conducted using the stratified CMH test (stratified by country, unless stated otherwise). Missing data was categorised as discontinued or missing

Comparison groups	Placebo v Gefapixant 50 mg
Number of subjects included in analysis	115
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.1511
Method	Cochran-Mantel-Haenszel

Secondary: Percentage of Participants with ≥70%, ≥50%, and ≥30% Change in Awake Objective Cough Frequency after 8 Weeks of Treatment (Day 56)

End point title	Percentage of Participants with ≥70%, ≥50%, and ≥30% Change in Awake Objective Cough Frequency after 8 Weeks of

	Treatment (Day 56)

End point description:

Awake Objective Cough Frequency (per hour) was defined as the total number of cough events during the monitoring period (in general, 24-hr interval) while the participant was awake divided by the total duration (in hours) for the monitoring period that the participant was awake. 24 hour sound recordings were made at Baseline (Study Day -1) and at Week 8 (Day 56) using a digital recording device. An independent cough monitoring center documented the time of each cough event over the 24 hour period, as well as the time when the participant went to sleep and the time the participant woke. The percentages of participants that met responder criteria for ≥70%, ≥50%, and ≥30% change (reduction) from baseline levels in Awake Objective Cough Frequency were reported for each treatment group at Day 56.

All randomised participants who had taken ≥1 dose of study medication and provided ≥1 baseline and ≥1 Day 56 endpoint observation during the treatment period were analysed.

End point type	Secondary

End point timeframe:

Baseline (Study Day -1), Day 56

End point values	Placebo	Gefapixant 7.5 mg	Gefapixant 20 mg	Gefapixant 50 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	57	56	59	51
Units: percentage of participants				
number (not applicable)				
≥70% Change	10.5	32.1	22.0	31.4
≥50% Change	26.3	46.4	39.0	54.9
≥30% Change	47.4	64.3	55.9	72.5

Statistical analyses

Statistical analysis title	Day 56: ≥70% Change: 7.5 mg gefapixant v PBO

Statistical analysis description:

Cough frequency responder endpoints were analyzed by a generalized linear mixed model (GLMM) with treatment, visit, and treatment by visit interaction, and country as fixed effects. Comparison of response rates between each gefapixant treatment group and placebo was conducted using the stratified Cochran Mantel Haenszel (CMH) test (stratified by country, unless stated otherwise). Missing data was categorised as discontinued or missing

Comparison groups	Placebo v Gefapixant 7.5 mg
Number of subjects included in analysis	113
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.0045
Method	Cochran-Mantel-Haenszel

Statistical analysis title	Day 56: ≥70% Change: 20 mg gefapixant v PBO

Statistical analysis description:

Cough frequency responder endpoints were analyzed by a GLMM with treatment, visit, and treatment by visit interaction, and country as fixed effects. Comparison of response rates between each gefapixant treatment group and placebo was conducted using the stratified CMH test (stratified by country, unless

stated otherwise). Missing data was categorised as discontinued or missing

Comparison groups	Placebo v Gefapixant 20 mg
Number of subjects included in analysis	116
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.0947
Method	Cochran-Mantel-Haenszel

Statistical analysis title	Day 56: ≥70% Change: 50 mg gefapixant v PBO

Statistical analysis description:

Cough frequency responder endpoints were analyzed by a GLMM with treatment, visit, and treatment by visit interaction, and country as fixed effects. Comparison of response rates between each gefapixant treatment group and placebo was conducted using the stratified CMH test (stratified by country, unless stated otherwise). Missing data was categorised as discontinued or missing

Comparison groups	Placebo v Gefapixant 50 mg
Number of subjects included in analysis	108
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.008
Method	Cochran-Mantel-Haenszel

Statistical analysis title	Day 56: ≥50% Change: 7.5 mg gefapixant v PBO

Statistical analysis description:

Cough frequency responder endpoints were analyzed by a GLMM with treatment, visit, and treatment by visit interaction, and country as fixed effects. Comparison of response rates between each gefapixant treatment group and placebo was conducted using the stratified CMH test (stratified by country, unless stated otherwise). Missing data was categorised as discontinued or missing

Comparison groups	Placebo v Gefapixant 7.5 mg
Number of subjects included in analysis	113
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.0283
Method	Cochran-Mantel-Haenszel

Statistical analysis title	Day 56: ≥50% Change: 20 mg gefapixant v PBO

Statistical analysis description:

Cough frequency responder endpoints were analyzed by a GLMM with treatment, visit, and treatment by visit interaction, and country as fixed effects. Comparison of response rates between each gefapixant treatment group and placebo was conducted using the stratified CMH test (stratified by country, unless stated otherwise). Missing data was categorised as discontinued or missing

Comparison groups	Placebo v Gefapixant 20 mg

Number of subjects included in analysis	116
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.1493
Method	Cochran-Mantel-Haenszel

Statistical analysis title	Day 56: ≥50% Change: 50 mg gefapixant v PBO

Statistical analysis description:

Cough frequency responder endpoints were analyzed by a GLMM with treatment, visit, and treatment by visit interaction, and country as fixed effects. Comparison of response rates between each gefapixant treatment group and placebo was conducted using the stratified CMH test (stratified by country, unless stated otherwise). Missing data was categorised as discontinued or missing

Comparison groups	Placebo v Gefapixant 50 mg
Number of subjects included in analysis	108
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.0026
Method	Cochran-Mantel-Haenszel

Statistical analysis title	Day 56: ≥30% Change: 7.5 mg gefapixant v PBO

Statistical analysis description:

Cough frequency responder endpoints were analyzed by a GLMM with treatment, visit, and treatment by visit interaction, and country as fixed effects. Comparison of response rates between each gefapixant treatment group and placebo was conducted using the stratified CMH test (stratified by country, unless stated otherwise). Missing data was categorised as discontinued or missing

Comparison groups	Placebo v Gefapixant 7.5 mg
Number of subjects included in analysis	113
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.0652
Method	Cochran-Mantel-Haenszel

Statistical analysis title	Day 56: ≥30% Change: 20 mg gefapixant v PBO

Statistical analysis description:

Cough frequency responder endpoints were analyzed by a GLMM with treatment, visit, and treatment by visit interaction, and country as fixed effects. Comparison of response rates between each gefapixant treatment group and placebo was conducted using the stratified CMH test (stratified by country, unless stated otherwise). Missing data was categorised as discontinued or missing

Comparison groups	Placebo v Gefapixant 20 mg
Number of subjects included in analysis	116
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.3601
Method	Cochran-Mantel-Haenszel

Statistical analysis title	Day 56: ≥30% Change: 50 mg gefapixant v PBO

Statistical analysis description:

Cough frequency responder endpoints were analyzed by a GLMM with treatment, visit, and treatment by visit interaction, and country as fixed effects. Comparison of response rates between each gefapixant treatment group and placebo was conducted using the stratified CMH test (stratified by country, unless stated otherwise). Missing data was categorised as discontinued or missing

Comparison groups	Placebo v Gefapixant 50 mg
Number of subjects included in analysis	108
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.0086
Method	Cochran-Mantel-Haenszel

Secondary: Percentage of Participants with ≥70%, ≥50%, and ≥30% Change in Awake Objective Cough Frequency after 12 Weeks of Treatment (Day 84)

End point title	Percentage of Participants with ≥70%, ≥50%, and ≥30% Change in Awake Objective Cough Frequency after 12 Weeks of Treatment (Day 84)

End point description:

Awake Objective Cough Frequency (per hour) was defined as the total number of cough events during the monitoring period (in general, 24-hr interval) while the participant was awake divided by the total duration (in hours) for the monitoring period that the participant was awake. 24 hour sound recordings were made at Baseline (Study Day -1) and at Week 12 (Day 84) using a digital recording device. An independent cough monitoring center documented the time of each cough event over the 24 hour period, as well as the time when the participant went to sleep and the time the participant woke. The percentages of participants that met responder criteria for ≥70%, ≥50%, and ≥30% change (reduction) from baseline levels in Awake Objective Cough Frequency were reported for each treatment group at Day 84.

All randomised participants who had taken ≥1 dose of study medication and provided ≥1 baseline and ≥1 Day 84 endpoint observation during the treatment period were analysed.

End point type	Secondary

End point timeframe:

Baseline (Study Day -1), Day 84

End point values	Placebo	Gefapixant 7.5 mg	Gefapixant 20 mg	Gefapixant 50 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	57	56	56	51
Units: percentage of participants				
number (not applicable)				
≥70% Change	15.8	21.4	23.2	31.4
≥50% Change	24.6	44.6	32.1	51.0
≥30% Change	43.9	64.3	48.2	80.4

Statistical analyses

Statistical analysis title	Day 84: ≥70% Change: 7.5 mg gefapixant v PBO

Statistical analysis description:

Cough frequency responder endpoints were analyzed by a generalized linear mixed model (GLMM) with treatment, visit, and treatment by visit interaction, and country as fixed effects. Comparison of response rates between each gefapixant treatment group and placebo was conducted using the stratified Cochran Mantel Haenszel (CMH) test (stratified by country, unless stated otherwise). Missing data was categorised as discontinued or missing

Comparison groups	Placebo v Gefapixant 7.5 mg
Number of subjects included in analysis	113
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.3893
Method	Cochran-Mantel-Haenszel

Statistical analysis title	Day 84: ≥70% Change: 20 mg gefapixant v PBO

Statistical analysis description:

Cough frequency responder endpoints were analyzed by a GLMM with treatment, visit, and treatment by visit interaction, and country as fixed effects. Comparison of response rates between each gefapixant treatment group and placebo was conducted using the stratified CMH test (stratified by country, unless stated otherwise). Missing data was categorised as discontinued or missing

Comparison groups	Placebo v Gefapixant 20 mg
Number of subjects included in analysis	113
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.2803
Method	Cochran-Mantel-Haenszel

Statistical analysis title	Day 84: ≥70% Change: 50 mg gefapixant v PBO

Statistical analysis description:

Cough frequency responder endpoints were analyzed by a GLMM with treatment, visit, and treatment by visit interaction, and country as fixed effects. Comparison of response rates between each gefapixant treatment group and placebo was conducted using the stratified CMH test (stratified by country, unless stated otherwise). Missing data was categorised as discontinued or missing

Comparison groups	Placebo v Gefapixant 50 mg
Number of subjects included in analysis	108
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.0427
Method	Cochran-Mantel-Haenszel

Statistical analysis title	Day 84: ≥50% Change: 7.5 mg gefapixant v PBO

Statistical analysis description:

Cough frequency responder endpoints were analyzed by a GLMM with treatment, visit, and treatment by visit interaction, and country as fixed effects. Comparison of response rates between each gefapixant treatment group and placebo was conducted using the stratified CMH test (stratified by country, unless stated otherwise). Missing data was categorised as discontinued or missing

Comparison groups	Placebo v Gefapixant 7.5 mg
Number of subjects included in analysis	113
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.0209
Method	Cochran-Mantel-Haenszel

Statistical analysis title	Day 84: ≥50% Change: 20 mg gefapixant v PBO

Statistical analysis description:

Cough frequency responder endpoints were analyzed by a GLMM with treatment, visit, and treatment by visit interaction, and country as fixed effects. Comparison of response rates between each gefapixant treatment group and placebo was conducted using the stratified CMH test (stratified by country, unless stated otherwise). Missing data was categorised as discontinued or missing

Comparison groups	Placebo v Gefapixant 20 mg
Number of subjects included in analysis	113
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.3401
Method	Cochran-Mantel-Haenszel

Statistical analysis title	Day 84: ≥50% Change: 50 mg gefapixant v PBO

Statistical analysis description:

Cough frequency responder endpoints were analyzed by a GLMM with treatment, visit, and treatment by visit interaction, and country as fixed effects. Comparison of response rates between each gefapixant treatment group and placebo was conducted using the stratified CMH test (stratified by country, unless stated otherwise). Missing data was categorised as discontinued or missing

Comparison groups	Placebo v Gefapixant 50 mg
Number of subjects included in analysis	108
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.0031
Method	Cochran-Mantel-Haenszel

Statistical analysis title	Day 84: ≥30% Change: 7.5 mg gefapixant v PBO

Statistical analysis description:

Cough frequency responder endpoints were analyzed by a GLMM with treatment, visit, and treatment by visit interaction, and country as fixed effects. Comparison of response rates between each gefapixant treatment group and placebo was conducted using the stratified CMH test (stratified by country, unless stated otherwise). Missing data was categorised as discontinued or missing

Comparison groups	Placebo v Gefapixant 7.5 mg

Number of subjects included in analysis	113
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.0283
Method	Cochran-Mantel-Haenszel

Statistical analysis title	Day 84: ≥30% Change: 20 mg gefapixant v placebo

Statistical analysis description:

Cough frequency responder endpoints were analyzed by a GLMM with treatment, visit, and treatment by visit interaction, and country as fixed effects. Comparison of response rates between each gefapixant treatment group and placebo was conducted using the stratified CMH test (stratified by country, unless stated otherwise). Missing data was categorised as discontinued or missing

Comparison groups	Placebo v Gefapixant 20 mg
Number of subjects included in analysis	113
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.6233
Method	Cochran-Mantel-Haenszel

Statistical analysis title	Day 84: ≥30% Change: 50 mg gefapixant v PBO

Statistical analysis description:

Cough frequency responder endpoints were analyzed by a GLMM with treatment, visit, and treatment by visit interaction, and country as fixed effects. Comparison of response rates between each gefapixant treatment group and placebo was conducted using the stratified CMH test (stratified by country, unless stated otherwise). Missing data was categorised as discontinued or missing

Comparison groups	Placebo v Gefapixant 50 mg
Number of subjects included in analysis	108
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.0001
Method	Cochran-Mantel-Haenszel

Secondary: Percentage of Participants with ≥70%, ≥50%, and ≥30% Change in Awake Objective Cough Frequency at the Follow-up Visit (Day 98)

End point title	Percentage of Participants with ≥70%, ≥50%, and ≥30% Change in Awake Objective Cough Frequency at the Follow-up Visit (Day 98)

End point description:

Awake Objective Cough Frequency (per hour) was defined as the total number of cough events during the monitoring period (in general, 24-hr interval) while the participant was awake divided by the total duration (in hours) for the monitoring period that the participant was awake. 24 hour sound recordings were made at Baseline (Study Day -1) and at the Follow-up visit (Day 98) using a digital recording device. An independent cough monitoring center documented the time of each cough event over the 24 hour period, as well as the time when the participant went to sleep and the time the participant woke. The percentages of participants that met responder criteria for ≥70%, ≥50%, and ≥30% change (reduction) from baseline levels in Awake Objective Cough Frequency were reported for each treatment group at Day 98.

All randomised participants who had taken ≥1 dose of study medication and provided ≥1 baseline and

≥1 Day 98 endpoint observation during the treatment period were analysed.

End point type	Secondary

End point timeframe:

Baseline (Study Day -1), Day 98

End point values	Placebo	Gefapixant 7.5 mg	Gefapixant 20 mg	Gefapixant 50 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	58	55	56	51
Units: percentage of participants				
number (not applicable)				
≥70% Change	13.8	18.2	14.3	23.5
≥50% Change	25.9	32.7	25.0	39.2
≥30% Change	51.7	56.4	50.0	58.8

Statistical analyses

Statistical analysis title	Day 98: ≥70% Change: 7.5 mg gefapixant v PBO

Statistical analysis description:

Cough frequency responder endpoints were analyzed by a generalized linear mixed model (GLMM) with treatment, visit, and treatment by visit interaction, and country as fixed effects. Comparison of response rates between each gefapixant treatment group and placebo was conducted using the stratified Cochran Mantel Haenszel (CMH) test (stratified by country, unless stated otherwise). Missing data was categorised as discontinued or missing

Comparison groups	Placebo v Gefapixant 7.5 mg
Number of subjects included in analysis	113
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.4925
Method	Cochran-Mantel-Haenszel

Statistical analysis title	Day 98: ≥70% Change: 20 mg gefapixant v PBO

Statistical analysis description:

Cough frequency responder endpoints were analyzed by a GLMM with treatment, visit, and treatment by visit interaction, and country as fixed effects. Comparison of response rates between each gefapixant treatment group and placebo was conducted using the stratified CMH test (stratified by country, unless stated otherwise). Missing data was categorised as discontinued or missing

Comparison groups	Placebo v Gefapixant 20 mg
Number of subjects included in analysis	114
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.9007
Method	Cochran-Mantel-Haenszel

Statistical analysis title	Day 98: ≥70% Change: 50 mg gefapixant v PBO

Statistical analysis description:

Cough frequency responder endpoints were analyzed by a GLMM with treatment, visit, and treatment by visit interaction, and country as fixed effects. Comparison of response rates between each gefapixant treatment group and placebo was conducted using the stratified CMH test (stratified by country, unless stated otherwise). Missing data was categorised as discontinued or missing

Comparison groups	Placebo v Gefapixant 50 mg
Number of subjects included in analysis	109
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.1602
Method	Cochran-Mantel-Haenszel

Statistical analysis title	Day 98: ≥50% Change: 7.5 mg gefapixant v PBO

Statistical analysis description:

Cough frequency responder endpoints were analyzed by a GLMM with treatment, visit, and treatment by visit interaction, and country as fixed effects. Comparison of response rates between each gefapixant treatment group and placebo was conducted using the stratified CMH test (stratified by country, unless stated otherwise). Missing data was categorised as discontinued or missing

Comparison groups	Placebo v Gefapixant 7.5 mg
Number of subjects included in analysis	113
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.344
Method	Cochran-Mantel-Haenszel

Statistical analysis title	Day 98: ≥50% Change: 20 mg gefapixant v PBO

Statistical analysis description:

Cough frequency responder endpoints were analyzed by a GLMM with treatment, visit, and treatment by visit interaction, and country as fixed effects. Comparison of response rates between each gefapixant treatment group and placebo was conducted using the stratified CMH test (stratified by country, unless stated otherwise). Missing data was categorised as discontinued or missing

Comparison groups	Placebo v Gefapixant 20 mg
Number of subjects included in analysis	114
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.9876
Method	Cochran-Mantel-Haenszel

Statistical analysis title	Day 98: ≥50% Change: 50 mg gefapixant v PBO

Statistical analysis description:

Cough frequency responder endpoints were analyzed by a GLMM with treatment, visit, and treatment by visit interaction, and country as fixed effects. Comparison of response rates between each gefapixant treatment group and placebo was conducted using the stratified CMH test (stratified by country, unless stated otherwise). Missing data was categorised as discontinued or missing

Comparison groups	Placebo v Gefapixant 50 mg

Number of subjects included in analysis	109
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.0993
Method	Cochran-Mantel-Haenszel

Statistical analysis title	Day 98: ≥30% Change: 7.5 mg gefapixant v PBO

Statistical analysis description:

Cough frequency responder endpoints were analyzed by a GLMM with treatment, visit, and treatment by visit interaction, and country as fixed effects. Comparison of response rates between each gefapixant treatment group and placebo was conducted using the stratified CMH test (stratified by country, unless stated otherwise). Missing data was categorised as discontinued or missing

Comparison groups	Placebo v Gefapixant 7.5 mg
Number of subjects included in analysis	113
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.5968
Method	Cochran-Mantel-Haenszel

Statistical analysis title	Day 98: ≥30% Change: 20 mg gefapixant v PBO

Statistical analysis description:

Cough frequency responder endpoints were analyzed by a GLMM with treatment, visit, and treatment by visit interaction, and country as fixed effects. Comparison of response rates between each gefapixant treatment group and placebo was conducted using the stratified CMH test (stratified by country, unless stated otherwise). Missing data was categorised as discontinued or missing

Comparison groups	Placebo v Gefapixant 20 mg
Number of subjects included in analysis	114
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.8726
Method	Cochran-Mantel-Haenszel

Statistical analysis title	Day 98: ≥30% Change: 50 mg gefapixant v PBO

Statistical analysis description:

Cough frequency responder endpoints were analyzed by a GLMM with treatment, visit, and treatment by visit interaction, and country as fixed effects. Comparison of response rates between each gefapixant treatment group and placebo was conducted using the stratified CMH test (stratified by country, unless stated otherwise). Missing data was categorised as discontinued or missing

Comparison groups	Placebo v Gefapixant 50 mg
Number of subjects included in analysis	109
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.4092
Method	Cochran-Mantel-Haenszel

Secondary: Percentage of Participants with ≥70%, ≥50%, and ≥30% Change in 24-Hour Objective Cough Frequency after 4 Weeks of Treatment (Day 28)

End point title	Percentage of Participants with ≥70%, ≥50%, and ≥30% Change in 24-Hour Objective Cough Frequency after 4 Weeks of Treatment (Day 28)

End point description:

24-hr Objective Cough Frequency was defined as the total number of cough events during the monitoring period divided by the total duration in hours for the monitoring period (generally 24 hours). 24 hour sound recordings were made at Baseline (Study Day -1) and at Week 4 (Day 28) using a digital recording device. An independent cough monitoring center documented the time of each cough event over the 24 hour period, as well as the time when the participant went to sleep and the time the participant woke. The percentages of participants that met responder criteria for ≥70%, ≥50%, and ≥30% change (reduction) from baseline levels in 24-hr Objective Cough Frequency were reported for each treatment group at Day 28.

All randomised participants who had taken ≥1 dose of study medication and provided ≥1 baseline and ≥1 Day 28 endpoint observation during the treatment period were analysed.

End point type	Secondary

End point timeframe:

Baseline (Study Day -1), Day 28

End point values	Placebo	Gefapixant 7.5 mg	Gefapixant 20 mg	Gefapixant 50 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	60	55	59	55
Units: percentage of participants				
number (not applicable)				
≥70% Change	13.3	25.5	15.3	34.5
≥50% Change	21.7	34.5	30.5	50.9
≥30% Change	51.7	58.2	45.8	67.3

Statistical analyses

Statistical analysis title	Day 28: ≥70% Change: 7.5 mg gefapixant v PBO

Statistical analysis description:

Cough frequency responder endpoints were analyzed by a generalized linear mixed model (GLMM) with treatment, visit, and treatment by visit interaction, and country as fixed effects. Comparison of response rates between each gefapixant treatment group and placebo was conducted using the stratified Cochran Mantel Haenszel (CMH) test (stratified by country, unless stated otherwise). Missing data was categorised as discontinued or missing

Comparison groups	Placebo v Gefapixant 7.5 mg
Number of subjects included in analysis	115
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.0781
Method	Cochran-Mantel-Haenszel

Statistical analysis title	Day 28: ≥70% Change: 20 mg gefapixant v PBO

Statistical analysis description:

Cough frequency responder endpoints were analyzed by a GLMM with treatment, visit, and treatment by visit interaction, and country as fixed effects. Comparison of response rates between each gefapixant treatment group and placebo was conducted using the stratified CMH test (stratified by country, unless stated otherwise). Missing data was categorised as discontinued or missing

Comparison groups	Placebo v Gefapixant 20 mg
Number of subjects included in analysis	119
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.7098
Method	Cochran-Mantel-Haenszel

Statistical analysis title	Day 28: ≥70% Change: 50 mg gefapixant v PBO

Statistical analysis description:

Cough frequency responder endpoints were analyzed by a GLMM with treatment, visit, and treatment by visit interaction, and country as fixed effects. Comparison of response rates between each gefapixant treatment group and placebo was conducted using the stratified CMH test (stratified by country, unless stated otherwise). Missing data was categorised as discontinued or missing

Comparison groups	Placebo v Gefapixant 50 mg
Number of subjects included in analysis	115
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.0068
Method	Cochran-Mantel-Haenszel

Statistical analysis title	Day 28: ≥50% Change: 7.5 mg gefapixant v PBO

Statistical analysis description:

Cough frequency responder endpoints were analyzed by a GLMM with treatment, visit, and treatment by visit interaction, and country as fixed effects. Comparison of response rates between each gefapixant treatment group and placebo was conducted using the stratified CMH test (stratified by country, unless stated otherwise). Missing data was categorised as discontinued or missing

Comparison groups	Placebo v Gefapixant 7.5 mg
Number of subjects included in analysis	115
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.1284
Method	Cochran-Mantel-Haenszel

Statistical analysis title	Day 28: ≥50% Change: 20 mg gefapixant v PBO

Statistical analysis description:

Cough frequency responder endpoints were analyzed by a GLMM with treatment, visit, and treatment by visit interaction, and country as fixed effects. Comparison of response rates between each gefapixant

treatment group and placebo was conducted using the stratified CMH test (stratified by country, unless stated otherwise). Missing data was categorised as discontinued or missing

Comparison groups	Placebo v Gefapixant 20 mg
Number of subjects included in analysis	119
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.267
Method	Cochran-Mantel-Haenszel

Statistical analysis title	Day 28: ≥50% Change: 50 mg gefapixant v PBO

Statistical analysis description:

Cough frequency responder endpoints were analyzed by a GLMM with treatment, visit, and treatment by visit interaction, and country as fixed effects. Comparison of response rates between each gefapixant treatment group and placebo was conducted using the stratified CMH test (stratified by country, unless stated otherwise). Missing data was categorised as discontinued or missing

Comparison groups	Placebo v Gefapixant 50 mg
Number of subjects included in analysis	115
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.0013
Method	Cochran-Mantel-Haenszel

Statistical analysis title	Day 28: ≥30% Change: 7.5 mg gefapixant v PBO

Statistical analysis description:

Cough frequency responder endpoints were analyzed by a GLMM with treatment, visit, and treatment by visit interaction, and country as fixed effects. Comparison of response rates between each gefapixant treatment group and placebo was conducted using the stratified CMH test (stratified by country, unless stated otherwise). Missing data was categorised as discontinued or missing

Comparison groups	Placebo v Gefapixant 7.5 mg
Number of subjects included in analysis	115
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.4343
Method	Cochran-Mantel-Haenszel

Statistical analysis title	Day 28: ≥30% Change: 20 mg gefapixant v placebo

Statistical analysis description:

Cough frequency responder endpoints were analyzed by a GLMM with treatment, visit, and treatment by visit interaction, and country as fixed effects. Comparison of response rates between each gefapixant treatment group and placebo was conducted using the stratified CMH test (stratified by country, unless stated otherwise). Missing data was categorised as discontinued or missing

Comparison groups	Placebo v Gefapixant 20 mg

Number of subjects included in analysis	119
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.5384
Method	Cochran-Mantel-Haenszel

Statistical analysis title	Day 28: ≥30% Change: 50 mg gefapixant v placebo

Statistical analysis description:

Cough frequency responder endpoints were analyzed by a GLMM with treatment, visit, and treatment by visit interaction, and country as fixed effects. Comparison of response rates between each gefapixant treatment group and placebo was conducted using the stratified CMH test (stratified by country, unless stated otherwise). Missing data was categorised as discontinued or missing

Comparison groups	Placebo v Gefapixant 50 mg
Number of subjects included in analysis	115
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.0822
Method	Cochran-Mantel-Haenszel

Secondary: Percentage of Participants with ≥70%, ≥50%, and ≥30% Change in 24-Hour Objective Cough Frequency after 8 Weeks of Treatment (Day 56)

End point title	Percentage of Participants with ≥70%, ≥50%, and ≥30% Change in 24-Hour Objective Cough Frequency after 8 Weeks of Treatment (Day 56)

End point description:

24-hr Objective Cough Frequency was defined as the total number of cough events during the monitoring period divided by the total duration in hours for the monitoring period (generally 24 hours). 24 hour sound recordings were made at Baseline (Study Day -1) and at Week 8 (Day 56) using a digital recording device. An independent cough monitoring center documented the time of each cough event over the 24 hour period, as well as the time when the participant went to sleep and the time the participant woke. The percentages of participants that met responder criteria for ≥70%, ≥50%, and ≥30% change (reduction) from baseline levels in 24-hr Objective Cough Frequency were reported for each treatment group at Day 56.

All randomised participants who had taken ≥1 dose of study medication and provided ≥1 baseline and ≥1 Day 56 endpoint observation during the treatment period were analysed.

End point type	Secondary

End point timeframe:

Baseline (Study Day -1), Day 56

End point values	Placebo	Gefapixant 7.5 mg	Gefapixant 20 mg	Gefapixant 50 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	57	56	59	51
Units: percentage of participants				
number (not applicable)				
≥70% Change	7.0	32.1	22.0	37.3
≥50% Change	28.1	50.0	32.2	52.9

≥30% Change	45.6	62.5	54.2	78.4

Statistical analyses

Statistical analysis title	Day 56: ≥70% Change: 7.5 mg gefapixant v PBO

Statistical analysis description:

Cough frequency responder endpoints were analyzed by a generalized linear mixed model (GLMM) with treatment, visit, and treatment by visit interaction, and country as fixed effects. Comparison of response rates between each gefapixant treatment group and placebo was conducted using the stratified Cochran Mantel Haenszel (CMH) test (stratified by country, unless stated otherwise). Missing data was categorised as discontinued or missing

Comparison groups	Placebo v Gefapixant 7.5 mg
Number of subjects included in analysis	113
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.0006
Method	Cochran-Mantel-Haenszel

Statistical analysis title	Day 56: ≥70% Change: 20 mg gefapixant v PBO

Statistical analysis description:

Cough frequency responder endpoints were analyzed by a GLMM with treatment, visit, and treatment by visit interaction, and country as fixed effects. Comparison of response rates between each gefapixant treatment group and placebo was conducted using the stratified CMH test (stratified by country, unless stated otherwise). Missing data was categorised as discontinued or missing

Comparison groups	Placebo v Gefapixant 20 mg
Number of subjects included in analysis	116
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.0223
Method	Cochran-Mantel-Haenszel

Statistical analysis title	Day 56: ≥70% Change: 50 mg gefapixant v PBO

Statistical analysis description:

Cough frequency responder endpoints were analyzed by a GLMM with treatment, visit, and treatment by visit interaction, and country as fixed effects. Comparison of response rates between each gefapixant treatment group and placebo was conducted using the stratified CMH test (stratified by country, unless stated otherwise). Missing data was categorised as discontinued or missing

Comparison groups	Placebo v Gefapixant 50 mg
Number of subjects included in analysis	108
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.0001
Method	Cochran-Mantel-Haenszel

Statistical analysis title	Day 56: ≥50% Change: 7.5 mg gefapixant v PBO

Statistical analysis description:

Cough frequency responder endpoints were analyzed by a GLMM with treatment, visit, and treatment by visit interaction, and country as fixed effects. Comparison of response rates between each gefapixant treatment group and placebo was conducted using the stratified CMH test (stratified by country, unless stated otherwise). Missing data was categorised as discontinued or missing

Comparison groups	Placebo v Gefapixant 7.5 mg
Number of subjects included in analysis	113
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.0165
Method	Cochran-Mantel-Haenszel

Statistical analysis title	Day 56: ≥50% Change: 20 mg gefapixant v PBO

Statistical analysis description:

Cough frequency responder endpoints were analyzed by a GLMM with treatment, visit, and treatment by visit interaction, and country as fixed effects. Comparison of response rates between each gefapixant treatment group and placebo was conducted using the stratified CMH test (stratified by country, unless stated otherwise). Missing data was categorised as discontinued or missing

Comparison groups	Placebo v Gefapixant 20 mg
Number of subjects included in analysis	116
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.6255
Method	Cochran-Mantel-Haenszel

Statistical analysis title	Day 56: ≥50% Change: 50 mg gefapixant v PBO

Statistical analysis description:

Cough frequency responder endpoints were analyzed by a GLMM with treatment, visit, and treatment by visit interaction, and country as fixed effects. Comparison of response rates between each gefapixant treatment group and placebo was conducted using the stratified CMH test (stratified by country, unless stated otherwise). Missing data was categorised as discontinued or missing

Comparison groups	Placebo v Gefapixant 50 mg
Number of subjects included in analysis	108
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.0085
Method	Cochran-Mantel-Haenszel

Statistical analysis title	Day 56: ≥30% Change: 7.5 mg gefapixant v PBO

Statistical analysis description:

Cough frequency responder endpoints were analyzed by a GLMM with treatment, visit, and treatment by visit interaction, and country as fixed effects. Comparison of response rates between each gefapixant

treatment group and placebo was conducted using the stratified CMH test (stratified by country, unless stated otherwise). Missing data was categorised as discontinued or missing

Comparison groups	Placebo v Gefapixant 7.5 mg
Number of subjects included in analysis	113
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.0722
Method	Cochran-Mantel-Haenszel

Statistical analysis title	Day 56: ≥30% Change: 20 mg gefapixant v placebo

Statistical analysis description:

Cough frequency responder endpoints were analyzed by a GLMM with treatment, visit, and treatment by visit interaction, and country as fixed effects. Comparison of response rates between each gefapixant treatment group and placebo was conducted using the stratified CMH test (stratified by country, unless stated otherwise). Missing data was categorised as discontinued or missing

Comparison groups	Placebo v Gefapixant 20 mg
Number of subjects included in analysis	116
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.3577
Method	Cochran-Mantel-Haenszel

Statistical analysis title	Day 56: ≥30% Change: 50 mg gefapixant v PBO

Statistical analysis description:

Cough frequency responder endpoints were analyzed by a GLMM with treatment, visit, and treatment by visit interaction, and country as fixed effects. Comparison of response rates between each gefapixant treatment group and placebo was conducted using the stratified CMH test (stratified by country, unless stated otherwise). Missing data was categorised as discontinued or missing

Comparison groups	Placebo v Gefapixant 50 mg
Number of subjects included in analysis	108
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.0006
Method	Cochran-Mantel-Haenszel

Secondary: Percentage of Participants with ≥70%, ≥50%, and ≥30% Change in 24-Hour Objective Cough Frequency after 12 Weeks of Treatment (Day 84)

End point title	Percentage of Participants with ≥70%, ≥50%, and ≥30% Change in 24-Hour Objective Cough Frequency after 12 Weeks of Treatment (Day 84)

End point description:

24-hr Objective Cough Frequency was defined as the total number of cough events during the monitoring period divided by the total duration in hours for the monitoring period (generally 24 hours). 24 hour sound recordings were made at Baseline (Study Day -1) and at Week 12 (Day 84) using a digital recording device. An independent cough monitoring center documented the time of each cough event over the 24 hour period, as well as the time when the participant went to sleep and the time the participant woke. The percentages of participants that met responder criteria for ≥70%, ≥50%, and ≥30% change (reduction) from baseline levels in 24-hr Objective Cough Frequency were reported for

each treatment group at Day 84.

All randomised participants who had taken ≥1 dose of study medication and provided ≥1 baseline and ≥1 Day 84 endpoint observation during the treatment period were analysed.

End point type	Secondary

End point timeframe:

Baseline (Study Day -1), Day 84

End point values	Placebo	Gefapixant 7.5 mg	Gefapixant 20 mg	Gefapixant 50 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	57	56	56	51
Units: percentage of participants				
number (not applicable)				
≥70% Change	14.0	19.6	25.0	31.4
≥50% Change	24.6	44.6	32.1	54.9
≥30% Change	42.1	62.5	50.0	78.4

Statistical analyses

Statistical analysis title	Day 84: ≥70% Change: 7.5 mg gefapixant v PBO

Statistical analysis description:

Cough frequency responder endpoints were analyzed by a generalized linear mixed model (GLMM) with treatment, visit, and treatment by visit interaction, and country as fixed effects. Comparison of response rates between each gefapixant treatment group and placebo was conducted using the stratified Cochran Mantel Haenszel (CMH) test (stratified by country, unless stated otherwise). Missing data was categorised as discontinued or missing

Comparison groups	Placebo v Gefapixant 7.5 mg
Number of subjects included in analysis	113
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.3845
Method	Cochran-Mantel-Haenszel

Statistical analysis title	Day 84: ≥70% Change: 20 mg gefapixant v PBO

Statistical analysis description:

Cough frequency responder endpoints were analyzed by a GLMM with treatment, visit, and treatment by visit interaction, and country as fixed effects. Comparison of response rates between each gefapixant treatment group and placebo was conducted using the stratified CMH test (stratified by country, unless stated otherwise). Missing data was categorised as discontinued or missing

Comparison groups	Placebo v Gefapixant 20 mg

Number of subjects included in analysis	113
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.1177
Method	Cochran-Mantel-Haenszel

Statistical analysis title	Day 84: ≥70% Change: 50 mg gefapixant v PBO

Statistical analysis description:

Cough frequency responder endpoints were analyzed by a GLMM with treatment, visit, and treatment by visit interaction, and country as fixed effects. Comparison of response rates between each gefapixant treatment group and placebo was conducted using the stratified CMH test (stratified by country, unless stated otherwise). Missing data was categorised as discontinued or missing

Comparison groups	Placebo v Gefapixant 50 mg
Number of subjects included in analysis	108
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.0236
Method	Cochran-Mantel-Haenszel

Statistical analysis title	Day 84: ≥50% Change: 7.5 mg gefapixant v PBO

Statistical analysis description:

Cough frequency responder endpoints were analyzed by a GLMM with treatment, visit, and treatment by visit interaction, and country as fixed effects. Comparison of response rates between each gefapixant treatment group and placebo was conducted using the stratified CMH test (stratified by country, unless stated otherwise). Missing data was categorised as discontinued or missing

Comparison groups	Placebo v Gefapixant 7.5 mg
Number of subjects included in analysis	113
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.0192
Method	Cochran-Mantel-Haenszel

Statistical analysis title	Day 84: ≥50% Change: 20 mg gefapixant v PBO

Statistical analysis description:

Cough frequency responder endpoints were analyzed by a GLMM with treatment, visit, and treatment by visit interaction, and country as fixed effects. Comparison of response rates between each gefapixant treatment group and placebo was conducted using the stratified CMH test (stratified by country, unless stated otherwise). Missing data was categorised as discontinued or missing

Comparison groups	Placebo v Gefapixant 20 mg
Number of subjects included in analysis	113
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.3301
Method	Cochran-Mantel-Haenszel

Statistical analysis title	Day 84: ≥50% Change: 50 mg gefapixant v PBO

Statistical analysis description:

Cough frequency responder endpoints were analyzed by a GLMM with treatment, visit, and treatment by visit interaction, and country as fixed effects. Comparison of response rates between each gefapixant treatment group and placebo was conducted using the stratified CMH test (stratified by country, unless stated otherwise). Missing data was categorised as discontinued or missing

Comparison groups	Placebo v Gefapixant 50 mg
Number of subjects included in analysis	108
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.0008
Method	Cochran-Mantel-Haenszel

Statistical analysis title	Day 84: ≥30% Change: 7.5 mg gefapixant v PBO

Statistical analysis description:

Cough frequency responder endpoints were analyzed by a GLMM with treatment, visit, and treatment by visit interaction, and country as fixed effects. Comparison of response rates between each gefapixant treatment group and placebo was conducted using the stratified CMH test (stratified by country, unless stated otherwise). Missing data was categorised as discontinued or missing

Comparison groups	Placebo v Gefapixant 7.5 mg
Number of subjects included in analysis	113
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.0285
Method	Cochran-Mantel-Haenszel

Statistical analysis title	Day 84: ≥30% Change: 20 mg gefapixant v PBO

Statistical analysis description:

Cough frequency responder endpoints were analyzed by a GLMM with treatment, visit, and treatment by visit interaction, and country as fixed effects. Comparison of response rates between each gefapixant treatment group and placebo was conducted using the stratified CMH test (stratified by country, unless stated otherwise). Missing data was categorised as discontinued or missing

Comparison groups	Placebo v Gefapixant 20 mg
Number of subjects included in analysis	113
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.3856
Method	Cochran-Mantel-Haenszel

Statistical analysis title	Day 84: ≥30% Change: 50 mg gefapixant v PBO

Statistical analysis description:

Cough frequency responder endpoints were analyzed by a GLMM with treatment, visit, and treatment by visit interaction, and country as fixed effects. Comparison of response rates between each gefapixant

treatment group and placebo was conducted using the stratified CMH test (stratified by country, unless stated otherwise). Missing data was categorised as discontinued or missing

Comparison groups	Placebo v Gefapixant 50 mg
Number of subjects included in analysis	108
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.0001
Method	Cochran-Mantel-Haenszel

Secondary: Percentage of Participants with ≥70%, ≥50%, and ≥30% Change in 24-Hour Objective Cough Frequency at the Follow-up Visit (Day 98)

End point title	Percentage of Participants with ≥70%, ≥50%, and ≥30% Change in 24-Hour Objective Cough Frequency at the Follow-up Visit (Day 98)

End point description:

24-hr Objective Cough Frequency was defined as the total number of cough events during the monitoring period divided by the total duration in hours for the monitoring period (generally 24 hours). 24 hour sound recordings were made at Baseline (Study Day -1) and at Week 14 (Day 98) using a digital recording device. An independent cough monitoring center documented the time of each cough event over the 24 hour period, as well as the time when the participant went to sleep and the time the participant woke. The percentages of participants that met responder criteria for ≥70%, ≥50%, and ≥30% change (reduction) from baseline levels in 24-hr Objective Cough Frequency were reported for each treatment group at Day 98.

All randomised participants who had taken ≥1 dose of study medication and provided ≥1 baseline and ≥1 Day 98 endpoint observation during the treatment period were analysed.

End point type	Secondary

End point timeframe:

Baseline (Study Day -1), Day 98

End point values	Placebo	Gefapixant 7.5 mg	Gefapixant 20 mg	Gefapixant 50 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	58	55	56	51
Units: percentage of participants				
number (not applicable)				
≥70% Change	12.1	20.0	16.1	21.6
≥50% Change	25.9	34.5	25.0	39.2
≥30% Change	46.6	52.7	46.4	54.9

Statistical analyses

Statistical analysis title	Day 98: ≥70% Change: 7.5 mg gefapixant v PBO

Statistical analysis description:

Cough frequency responder endpoints were analyzed by a generalized linear mixed model (GLMM) with treatment, visit, and treatment by visit interaction, and country as fixed effects. Comparison of response rates between each gefapixant treatment group and placebo was conducted using the stratified Cochran Mantel Haenszel (CMH) test (stratified by country, unless stated otherwise). Missing data was categorised as discontinued or missing

Comparison groups	Placebo v Gefapixant 7.5 mg
Number of subjects included in analysis	113
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.2441
Method	Cochran-Mantel-Haenszel

Statistical analysis title	Day 98: ≥70% Change: 20 mg gefapixant v PBO

Statistical analysis description:

Cough frequency responder endpoints were analyzed by a GLMM with treatment, visit, and treatment by visit interaction, and country as fixed effects. Comparison of response rates between each gefapixant treatment group and placebo was conducted using the stratified CMH test (stratified by country, unless stated otherwise). Missing data was categorised as discontinued or missing

Comparison groups	Placebo v Gefapixant 20 mg
Number of subjects included in analysis	114
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.5055
Method	Cochran-Mantel-Haenszel

Statistical analysis title	Day 98: ≥70% Change: 50 mg gefapixant v PBO

Statistical analysis description:

Cough frequency responder endpoints were analyzed by a GLMM with treatment, visit, and treatment by visit interaction, and country as fixed effects. Comparison of response rates between each gefapixant treatment group and placebo was conducted using the stratified CMH test (stratified by country, unless stated otherwise). Missing data was categorised as discontinued or missing

Comparison groups	Placebo v Gefapixant 50 mg
Number of subjects included in analysis	109
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.1602
Method	Cochran-Mantel-Haenszel

Statistical analysis title	Day 98: ≥50% Change: 7.5 mg gefapixant v PBO

Statistical analysis description:

Cough frequency responder endpoints were analyzed by a GLMM with treatment, visit, and treatment by visit interaction, and country as fixed effects. Comparison of response rates between each gefapixant treatment group and placebo was conducted using the stratified CMH test (stratified by country, unless stated otherwise). Missing data was categorised as discontinued or missing

Comparison groups	Placebo v Gefapixant 7.5 mg

Number of subjects included in analysis	113
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.2721
Method	Cochran-Mantel-Haenszel

Statistical analysis title	Day 98: ≥50% Change: 20 mg gefapixant v PBO

Statistical analysis description:

Cough frequency responder endpoints were analyzed by a GLMM with treatment, visit, and treatment by visit interaction, and country as fixed effects. Comparison of response rates between each gefapixant treatment group and placebo was conducted using the stratified CMH test (stratified by country, unless stated otherwise). Missing data was categorised as discontinued or missing

Comparison groups	Placebo v Gefapixant 20 mg
Number of subjects included in analysis	114
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.9763
Method	Cochran-Mantel-Haenszel

Statistical analysis title	Day 98: ≥50% Change: 50 mg gefapixant v PBO

Statistical analysis description:

Cough frequency responder endpoints were analyzed by a GLMM with treatment, visit, and treatment by visit interaction, and country as fixed effects. Comparison of response rates between each gefapixant treatment group and placebo was conducted using the stratified CMH test (stratified by country, unless stated otherwise). Missing data was categorised as discontinued or missing

Comparison groups	Placebo v Gefapixant 50 mg
Number of subjects included in analysis	109
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.0993
Method	Cochran-Mantel-Haenszel

Statistical analysis title	Day 98: ≥30% Change: 7.5 mg gefapixant v PBO

Statistical analysis description:

Cough frequency responder endpoints were analyzed by a GLMM with treatment, visit, and treatment by visit interaction, and country as fixed effects. Comparison of response rates between each gefapixant treatment group and placebo was conducted using the stratified CMH test (stratified by country, unless stated otherwise). Missing data was categorised as discontinued or missing

Comparison groups	Placebo v Gefapixant 7.5 mg
Number of subjects included in analysis	113
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.4575
Method	Cochran-Mantel-Haenszel

Statistical analysis title	Day 98: ≥30% Change: 20 mg gefapixant v PBO

Statistical analysis description:

Cough frequency responder endpoints were analyzed by a GLMM with treatment, visit, and treatment by visit interaction, and country as fixed effects. Comparison of response rates between each gefapixant treatment group and placebo was conducted using the stratified CMH test (stratified by country, unless stated otherwise). Missing data was categorised as discontinued or missing

Comparison groups	Placebo v Gefapixant 20 mg
Number of subjects included in analysis	114
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.9706
Method	Cochran-Mantel-Haenszel

Statistical analysis title	Day 98: ≥30% Change: 50 mg gefapixant v PBO

Statistical analysis description:

Cough frequency responder endpoints were analyzed by a GLMM with treatment, visit, and treatment by visit interaction, and country as fixed effects. Comparison of response rates between each gefapixant treatment group and placebo was conducted using the stratified CMH test (stratified by country, unless stated otherwise). Missing data was categorised as discontinued or missing

Comparison groups	Placebo v Gefapixant 50 mg
Number of subjects included in analysis	109
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.3258
Method	Cochran-Mantel-Haenszel

Secondary: Change from Baseline in Sleep Objective Cough Frequency After 4 Weeks of Treatment (Day 28)

End point title	Change from Baseline in Sleep Objective Cough Frequency After 4 Weeks of Treatment (Day 28)

End point description:

Sleep Objective Cough Frequency was defined as the total number of cough events during the monitoring period while the participant was asleep divided by the total duration in hours for the monitoring period that the participant was asleep. 24 hour sound recordings were made at Baseline (Study Day -1) and at Week 4 (Day 28) using a digital recording device. An independent cough monitoring center documented the time of each cough event over the 24 hour period, as well as the time when the participant went to sleep and the time the participant woke. LS mean change from baseline (in log scale) with associated SE reported for each treatment group. Change from Baseline in Sleep Objective Cough Frequency = (Post-Treatment Objective Sleep Cough Frequency minus Baseline Sleep Cough Frequency).

All randomized participants who had taken ≥1 dose of study medication and provided ≥1 baseline and ≥1 post baseline endpoint observation during the treatment period were analysed.

End point type	Secondary

End point timeframe:

Baseline (Study Day -1), Day 28

End point values	Placebo	Gefapixant 7.5 mg	Gefapixant 20 mg	Gefapixant 50 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	61	59	59	57
Units: log coughs/hour				
least squares mean (standard error)	-0.37 (± 0.19)	-0.37 (± 0.20)	-0.38 (± 0.19)	-0.49 (± 0.20)

Statistical analyses

Statistical analysis title	Day 28 Sleep Cough Freq: 7.5 mg gefapixant v PBO
Statistical analysis description:	
Day 28 estimated treatment differences (gefapixant vs. placebo) and corresponding 95% CIs were estimated using a MMRM model, which included fixed effects for treatment group, visit, country, treatment-by-visit interaction, and Baseline value (on log scale) as a covariate.	
Comparison groups	Placebo v Gefapixant 7.5 mg
Number of subjects included in analysis	120
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.9858
Method	Mixed Effect Repeated Measures model
Parameter estimate	LS Mean Difference
Point estimate	0
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.53
upper limit	0.54

Statistical analysis title	Day 28 Sleep Cough Freq: 20 mg gefapixant v PBO
Statistical analysis description:	
Day 28 estimated treatment differences (gefapixant vs. placebo) and corresponding 95% CIs were estimated using a MMRM model, which included fixed effects for treatment group, visit, country, treatment-by-visit interaction, and Baseline value (on log scale) as a covariate.	
Comparison groups	Placebo v Gefapixant 20 mg
Number of subjects included in analysis	120
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.9813
Method	Mixed Effect Repeated Measures model
Parameter estimate	LS Mean Difference
Point estimate	-0.01

Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.53
upper limit	0.52

Statistical analysis title	Day 28 Sleep Cough Freq: 50 mg gefapixant v PBO

Statistical analysis description:

Day 28 estimated treatment differences (gefapixant vs. placebo) and corresponding 95% CIs were estimated using a MMRM model, which included fixed effects for treatment group, visit, country, treatment-by-visit interaction, and Baseline value (on log scale) as a covariate.

Comparison groups	Gefapixant 50 mg v Placebo
Number of subjects included in analysis	118
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.6746
Method	Mixed Effect Repeated Measures model
Parameter estimate	LS Mean Difference
Point estimate	-0.11
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.65
upper limit	0.42

Secondary: Change from Baseline in Sleep Objective Cough Frequency After 8 Weeks of Treatment (Day 56)

End point title	Change from Baseline in Sleep Objective Cough Frequency After 8 Weeks of Treatment (Day 56)

End point description:

Sleep Objective Cough Frequency was defined as the total number of cough events during the monitoring period while the participant was asleep divided by the total duration in hours for the monitoring period that the participant was asleep. 24 hour sound recordings were made at Baseline (Study Day -1) and at Week 8 (Day 56) using a digital recording device. An independent cough monitoring center documented the time of each cough event over the 24 hour period, as well as the time when the participant went to sleep and the time the participant woke. LS mean change from baseline (in log scale) with associated SE reported for each treatment group. Change from Baseline in Sleep Objective Cough Frequency = (Post-Treatment Objective Sleep Cough Frequency minus Baseline Sleep Cough Frequency).

All randomized participants who had taken ≥1 dose of study medication and provided ≥1 baseline and ≥1 post baseline endpoint observation during the treatment period were analysed.

End point type	Secondary

End point timeframe:

Baseline (Study Day -1), Day 56

End point values	Placebo	Gefapixant 7.5 mg	Gefapixant 20 mg	Gefapixant 50 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	61	59	59	57
Units: log coughs/hour				
least squares mean (standard error)	-0.40 (± 0.20)	-0.72 (± 0.20)	-0.40 (± 0.20)	-0.80 (± 0.21)

Statistical analyses

Statistical analysis title	Day 56 Sleep Cough Freq: 7.5 mg gefapixant v PBO

Statistical analysis description:

Day 56 estimated treatment differences (gefapixant vs. placebo) and corresponding 95% CIs were estimated using a MMRM model, which included fixed effects for treatment group, visit, country, treatment-by-visit interaction, and Baseline value (on log scale) as a covariate.

Comparison groups	Placebo v Gefapixant 7.5 mg
Number of subjects included in analysis	120
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.2583
Method	Mixed Effect Repeated Measures model
Parameter estimate	LS Mean Difference
Point estimate	-0.32
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.88
upper limit	0.24

Statistical analysis title	Day 56 Sleep Cough Freq: 20 mg gefapixant v PBO

Statistical analysis description:

Day 56 estimated treatment differences (gefapixant vs. placebo) and corresponding 95% CIs were estimated using a MMRM model, which included fixed effects for treatment group, visit, country, treatment-by-visit interaction, and Baseline value (on log scale) as a covariate.

Comparison groups	Placebo v Gefapixant 20 mg
Number of subjects included in analysis	120
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.9826
Method	Mixed Effect Repeated Measures model
Parameter estimate	LS Mean Difference
Point estimate	0.01
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.55
upper limit	0.56

Statistical analysis title	Day 56 Sleep Cough Freq: 50 mg gefapixant v PBO

Statistical analysis description:

Day 56 estimated treatment differences (gefapixant vs. placebo) and corresponding 95% CIs were estimated using a MMRM model, which included fixed effects for treatment group, visit, country, treatment-by-visit interaction, and Baseline value (on log scale) as a covariate.

Comparison groups	Placebo v Gefapixant 50 mg
Number of subjects included in analysis	118
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.1672
Method	Mixed Effect Repeated Measures model
Parameter estimate	LS Mean Difference
Point estimate	-0.4
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.98
upper limit	0.17

Secondary: Change from Baseline in Sleep Objective Cough Frequency After 12 Weeks of Treatment (Day 84)

End point title	Change from Baseline in Sleep Objective Cough Frequency After 12 Weeks of Treatment (Day 84)

End point description:

Sleep Objective Cough Frequency was defined as the total number of cough events during the monitoring period while the participant was asleep divided by the total duration in hours for the monitoring period that the participant was asleep. 24 hour sound recordings were made at Baseline (Study Day -1) and at Week 12 (Day 84) using a digital recording device. An independent cough monitoring center documented the time of each cough event over the 24 hour period, as well as the time when the participant went to sleep and the time the participant woke. LS mean change from baseline (in log scale) with associated SE reported for each treatment group. Change from Baseline in Sleep Objective Cough Frequency = (Post-Treatment Objective Sleep Cough Frequency minus Baseline Sleep Cough Frequency)

All randomized participants who had taken ≥1 dose of study medication and provided ≥1 baseline and ≥1 post baseline endpoint observation during the treatment period were analysed.

End point type	Secondary

End point timeframe:

Baseline (Study Day -1), Day 84

End point values	Placebo	Gefapixant 7.5 mg	Gefapixant 20 mg	Gefapixant 50 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	61	59	59	57
Units: log coughs/hour				
least squares mean (standard error)	-0.72 (± 0.19)	-0.58 (± 0.20)	-0.65 (± 0.19)	-0.44 (± 0.20)

Statistical analyses

Statistical analysis title	Day 84 Sleep Cough Freq: 7.5 mg gefapixant v PBO

Statistical analysis description:

Day 84 estimated treatment differences (gefapixant vs. placebo) and corresponding 95% CIs were estimated using a MMRM model, which included fixed effects for treatment group, visit, country, treatment-by-visit interaction, and Baseline value (on log scale) as a covariate.

Comparison groups	Placebo v Gefapixant 7.5 mg
Number of subjects included in analysis	120
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.6102
Method	Mixed Effect Repeated Measures model
Parameter estimate	LS Mean Difference
Point estimate	0.14
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.4
upper limit	0.68

Statistical analysis title	Day 84 Sleep Cough Freq: 20 mg gefapixant v PBO

Statistical analysis description:

Day 84 estimated treatment differences (gefapixant vs. placebo) and corresponding 95% CIs were estimated using a MMRM model, which included fixed effects for treatment group, visit, country, treatment-by-visit interaction, and Baseline value (on log scale) as a covariate.

Comparison groups	Placebo v Gefapixant 20 mg
Number of subjects included in analysis	120
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.7782
Method	Mixed Effect Repeated Measures model
Parameter estimate	LS Mean Difference
Point estimate	0.08
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.46
upper limit	0.61

Statistical analysis title	Day 84 Sleep Cough Freq: 50 mg gefapixant v PBO

Statistical analysis description:

Day 84 estimated treatment differences (gefapixant vs. placebo) and corresponding 95% CIs were estimated using a MMRM model, which included fixed effects for treatment group, visit, country, treatment-by-visit interaction, and Baseline value (on log scale) as a covariate.

Comparison groups	Placebo v Gefapixant 50 mg
Number of subjects included in analysis	118
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.3167
Method	Mixed Effect Repeated Measures model
Parameter estimate	LS Mean Difference
Point estimate	0.28
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.27
upper limit	0.83

Secondary: Change from Baseline in Weekly Mean Daily Cough Severity Diary (CSD) Total Score at Week 1

End point title	Change from Baseline in Weekly Mean Daily Cough Severity Diary (CSD) Total Score at Week 1

End point description:

The daily CSD instrument has a total of 7 items, each with scores ranging from 0 (best) to 10 (worst). The total daily CSD is the sum of these 7 item scores (Min=0, Max=70). Mean total daily score (the sum of 7 item scores divided by 7) was derived for each day. Weekly mean total daily score was defined as the average of the mean total daily scores for each week. LS mean change from baseline with associated SE reported for each treatment group. Baseline was defined as the average CSD scores collected during the week prior to Day 1 (Study Day -7 to Day -1).

All randomized participants who had taken at least 1 dose of study medication and provided at least 1 baseline and at least one post baseline endpoint observation during the treatment period were analysed.

End point type	Secondary

End point timeframe:

Baseline, Week 1

End point values	Placebo	Gefapixant 7.5 mg	Gefapixant 20 mg	Gefapixant 50 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	61	59	59	57
Units: score on a scale				
least squares mean (standard error)	-1.0 (± 0.15)	-0.7 (± 0.15)	-0.7 (± 0.15)	-1.10 (± 0.15)

Statistical analyses

Statistical analysis title	Week 1 CSD Total Score: 7.5 mg gefapixant v PBO

Statistical analysis description:

Week 1 estimated treatment differences (gefapixant vs. placebo) and corresponding 95% CIs were estimated using a MMRM model, which included fixed effects for treatment group, visit, country, treatment-by-visit interaction, and Baseline value as a covariate.

Comparison groups	Placebo v Gefapixant 7.5 mg
Number of subjects included in analysis	120
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.1545
Method	Mixed Effect Repeated Measures model
Parameter estimate	LS Mean Difference
Point estimate	0.3
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.1
upper limit	0.7

Statistical analysis title	Week 1 CSD Total Score: 20 mg gefapixant v PBO

Statistical analysis description:

Week 1 estimated treatment differences (gefapixant vs. placebo) and corresponding 95% CIs were estimated using a MMRM model, which included fixed effects for treatment group, visit, country, treatment-by-visit interaction, and Baseline value as a covariate.

Comparison groups	Placebo v Gefapixant 20 mg
Number of subjects included in analysis	120
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.2013
Method	Mixed Effect Repeated Measures model
Parameter estimate	LS Mean Difference
Point estimate	0.3
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.1
upper limit	0.7

Statistical analysis title	Week 1 CSD Total Score: 50 mg gefapixant v PBO

Statistical analysis description:

Week 1 estimated treatment differences (gefapixant vs. placebo) and corresponding 95% CIs were estimated using a MMRM model, which included fixed effects for treatment group, visit, country, treatment-by-visit interaction, and Baseline value as a covariate.

Comparison groups	Placebo v Gefapixant 50 mg

Number of subjects included in analysis	118
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.9962
Method	Mixed Effect Repeated Measures model
Parameter estimate	LS Mean Difference
Point estimate	0
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.4
upper limit	0.4

Secondary: Change from Baseline in Weekly Mean Daily CSD Total Score at Week 2

End point title	Change from Baseline in Weekly Mean Daily CSD Total Score at Week 2

End point description:

The daily CSD instrument has a total of 7 items, each with scores ranging from 0 (best) to 10 (worst). The total daily CSD is the sum of these 7 item scores (Min=0, Max=70). Mean total daily score (the sum of 7 item scores divided by 7) was derived for each day. Weekly mean total daily score was defined as the average of the mean total daily scores for each week. LS mean change from baseline with associated SE reported for each treatment group. Baseline was defined as the average CSD scores collected during the week prior to Day 1 (Study Day -7 to Day -1).

All randomized participants who had taken at least 1 dose of study medication and provided at least 1 baseline and at least one post baseline endpoint observation during the treatment period were analysed.

End point type	Secondary

End point timeframe:

Baseline, Week 2

End point values	Placebo	Gefapixant 7.5 mg	Gefapixant 20 mg	Gefapixant 50 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	61	59	59	57
Units: score on a scale				
least squares mean (standard error)	-1.0 (± 0.18)	-0.9 (± 0.19)	-1.0 (± 0.19)	-1.5 (± 0.19)

Statistical analyses

Statistical analysis title	Week 2 CSD Total Score: 7.5 mg gefapixant v PBO

Statistical analysis description:

Week 2 estimated treatment differences (gefapixant vs. placebo) and corresponding 95% CIs were estimated using a MMRM model, which included fixed effects for treatment group, visit, country, treatment-by-visit interaction, and Baseline value as a covariate.

Comparison groups	Placebo v Gefapixant 7.5 mg

Number of subjects included in analysis	120
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.7328
Method	Mixed Effect Repeated Measures model
Parameter estimate	LS Mean Difference
Point estimate	0.1
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.4
upper limit	0.6

Statistical analysis title	Week 2 CSD Total Score: 20 mg gefapixant v PBO

Statistical analysis description:

Week 2 estimated treatment differences (gefapixant vs. placebo) and corresponding 95% CIs were estimated using a MMRM model, which included fixed effects for treatment group, visit, country, treatment-by-visit interaction, and Baseline value as a covariate.

Comparison groups	Placebo v Gefapixant 20 mg
Number of subjects included in analysis	120
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.7635
Method	Mixed Effect Repeated Measures model
Parameter estimate	LS Mean Difference
Point estimate	0.1
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.4
upper limit	0.6

Statistical analysis title	Week 2 CSD Total Score: 50 mg gefapixant v PBO

Statistical analysis description:

Week 2 estimated treatment differences (gefapixant vs. placebo) and corresponding 95% CIs were estimated using a MMRM model, which included fixed effects for treatment group, visit, country, treatment-by-visit interaction, and Baseline value as a covariate.

Comparison groups	Placebo v Gefapixant 50 mg
Number of subjects included in analysis	118
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.0951
Method	Mixed Effect Repeated Measures model
Parameter estimate	LS Mean Difference
Point estimate	-0.4

Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.9
upper limit	0.1

Secondary: Change from Baseline in Weekly Mean Daily CSD Total Score at Week 3

End point title	Change from Baseline in Weekly Mean Daily CSD Total Score at Week 3

End point description:

The daily CSD instrument has a total of 7 items, each with scores ranging from 0 (best) to 10 (worst). The total daily CSD is the sum of these 7 item scores (Min=0, Max=70). Mean total daily score (the sum of 7 item scores divided by 7) was derived for each day. Weekly mean total daily score was defined as the average of the mean total daily scores for each week. LS mean change from baseline with associated SE reported for each treatment group. Baseline was defined as the average CSD scores collected during the week prior to Day 1 (Study Day -7 to Day -1).

All randomized participants who had taken at least 1 dose of study medication and provided at least 1 baseline and at least one post baseline endpoint observation during the treatment period were analysed.

End point type	Secondary

End point timeframe:

Baseline, Week 3

End point values	Placebo	Gefapixant 7.5 mg	Gefapixant 20 mg	Gefapixant 50 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	61	59	59	57
Units: score on a scale				
least squares mean (standard error)	-1.0 (± 0.20)	-1.2 (± 0.20)	-1.3 (± 0.20)	-1.5 (± 0.20)

Statistical analyses

Statistical analysis title	Week 3 CSD Total Score: 7.5 mg gefapixant v PBO

Statistical analysis description:

Week 3 estimated treatment differences (gefapixant vs. placebo) and corresponding 95% CIs were estimated using a MMRM model, which included fixed effects for treatment group, visit, country, treatment-by-visit interaction, and Baseline value as a covariate.

Comparison groups	Placebo v Gefapixant 7.5 mg
Number of subjects included in analysis	120
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.5797
Method	Mixed Effect Repeated Measures model
Parameter estimate	LS Mean Difference
Point estimate	-0.2

Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.7
upper limit	0.4

Statistical analysis title	Week 3 CSD Total Score: 20 mg gefapixant v PBO

Statistical analysis description:

Week 3 estimated treatment differences (gefapixant vs. placebo) and corresponding 95% CIs were estimated using a MMRM model, which included fixed effects for treatment group, visit, country, treatment-by-visit interaction, and Baseline value as a covariate.

Comparison groups	Placebo v Gefapixant 20 mg
Number of subjects included in analysis	120
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.2499
Method	Mixed Effect Repeated Measures model
Parameter estimate	LS Mean Difference
Point estimate	-0.3
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.9
upper limit	0.2

Statistical analysis title	Week 3 CSD Total Score: 50 mg gefapixant v PBO

Statistical analysis description:

Week 3 estimated treatment differences (gefapixant vs. placebo) and corresponding 95% CIs were estimated using a MMRM model, which included fixed effects for treatment group, visit, country, treatment-by-visit interaction, and Baseline value as a covariate.

Comparison groups	Placebo v Gefapixant 50 mg
Number of subjects included in analysis	118
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.0612
Method	Mixed Effect Repeated Measures model
Parameter estimate	LS Mean Difference
Point estimate	-0.5
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.1
upper limit	0

Secondary: Change from Baseline in Weekly Mean Daily CSD Total Score at Week 4

End point title	Change from Baseline in Weekly Mean Daily CSD Total Score at Week 4

End point description:

The daily CSD instrument has a total of 7 items, each with scores ranging from 0 (best) to 10 (worst). The total daily CSD is the sum of these 7 item scores (Min=0, Max=70). Mean total daily score (the sum of 7 item scores divided by 7) was derived for each day. Weekly mean total daily score was defined as the average of the mean total daily scores for each week. LS mean change from baseline with associated SE reported for each treatment group. Baseline was defined as the average CSD scores collected during the week prior to Day 1 (Study Day -7 to Day -1).

All randomized participants who had taken at least 1 dose of study medication and provided at least 1 baseline and at least one post baseline endpoint observation during the treatment period were analysed.

End point type	Secondary

End point timeframe:

Baseline, Week 4

End point values	Placebo	Gefapixant 7.5 mg	Gefapixant 20 mg	Gefapixant 50 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	61	59	59	57
Units: score on a scale				
least squares mean (standard error)	-1.2 (± 0.20)	-1.4 (± 0.20)	-1.5 (± 0.20)	-1.7 (± 0.20)

Statistical analyses

Statistical analysis title	Week 4 CSD Total Score: 7.5 mg gefapixant v PBO

Statistical analysis description:

Week 4 estimated treatment differences (gefapixant vs. placebo) and corresponding 95% CIs were estimated using a MMRM model, which included fixed effects for treatment group, visit, country, treatment-by-visit interaction, and Baseline value as a covariate.

Comparison groups	Placebo v Gefapixant 7.5 mg
Number of subjects included in analysis	120
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.5358
Method	Mixed Effect Repeated Measures model
Parameter estimate	LS Mean Difference
Point estimate	-0.2
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.7
upper limit	0.4

Statistical analysis title	Week 4 CSD Total Score: 20 mg gefapixant v PBO

Statistical analysis description:

Week 4 estimated treatment differences (gefapixant vs. placebo) and corresponding 95% CIs were estimated using a MMRM model, which included fixed effects for treatment group, visit, country,

treatment-by-visit interaction, and Baseline value as a covariate.

Comparison groups	Placebo v Gefapixant 20 mg
Number of subjects included in analysis	120
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.3129
Method	Mixed Effect Repeated Measures model
Parameter estimate	LS Mean Difference
Point estimate	-0.3
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.8
upper limit	0.3

Statistical analysis title	Week 4 CSD Total Score: 50 mg gefapixant v PBO

Statistical analysis description:

Week 4 estimated treatment differences (gefapixant vs. placebo) and corresponding 95% CIs were estimated using a MMRM model, which included fixed effects for treatment group, visit, country, treatment-by-visit interaction, and Baseline value as a covariate.

Comparison groups	Placebo v Gefapixant 50 mg
Number of subjects included in analysis	118
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.1046
Method	Mixed Effect Repeated Measures model
Parameter estimate	LS Mean Difference
Point estimate	-0.5
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1
upper limit	0.1

Secondary: Change from Baseline in Weekly Mean Daily CSD Total Score at Week 5

End point title	Change from Baseline in Weekly Mean Daily CSD Total Score at Week 5

End point description:

The daily CSD instrument has a total of 7 items, each with scores ranging from 0 (best) to 10 (worst). The total daily CSD is the sum of these 7 item scores (Min=0, Max=70). Mean total daily score (the sum of 7 item scores divided by 7) was derived for each day. Weekly mean total daily score was defined as the average of the mean total daily scores for each week. LS mean change from baseline with associated SE reported for each treatment group. Baseline was defined as the average CSD scores collected during the week prior to Day 1 (Study Day -7 to Day -1).

All randomized participants who had taken at least 1 dose of study medication and provided at least 1 baseline and at least one post baseline endpoint observation during the treatment period were analysed.

End point type	Secondary

End point timeframe:
Baseline, Week 5

End point values	Placebo	Gefapixant 7.5 mg	Gefapixant 20 mg	Gefapixant 50 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	61	59	59	57
Units: score on a scale				
least squares mean (standard error)	-1.1 (± 0.20)	-1.3 (± 0.20)	-1.5 (± 0.20)	-1.8 (± 0.21)

Statistical analyses

Statistical analysis title	Week 5 CSD Total Score: 7.5 mg gefapixant v PBO
Statistical analysis description:	
Week 5 estimated treatment differences (gefapixant vs. placebo) and corresponding 95% CIs were estimated using a MMRM model, which included fixed effects for treatment group, visit, country, treatment-by-visit interaction, and Baseline value as a covariate.	
Comparison groups	Placebo v Gefapixant 7.5 mg
Number of subjects included in analysis	120
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.5796
Method	Mixed Effect Repeated Measures model
Parameter estimate	LS Mean Difference
Point estimate	-0.2
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.7
upper limit	0.4

Statistical analysis title	Week 5 CSD Total Score: 20 mg gefapixant v PBO
Statistical analysis description:	
Week 5 estimated treatment differences (gefapixant vs. placebo) and corresponding 95% CIs were estimated using a MMRM model, which included fixed effects for treatment group, visit, country, treatment-by-visit interaction, and Baseline value as a covariate.	
Comparison groups	Placebo v Gefapixant 20 mg
Number of subjects included in analysis	120
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.143
Method	Mixed Effect Repeated Measures model
Parameter estimate	LS Mean Difference
Point estimate	-0.4

Confidence interval	
level	95 %
sides	2-sided
lower limit	-1
upper limit	0.1

Statistical analysis title	Week 5 CSD Total Score: 50 mg gefapixant v PBO

Statistical analysis description:

Week 5 estimated treatment differences (gefapixant vs. placebo) and corresponding 95% CIs were estimated using a MMRM model, which included fixed effects for treatment group, visit, country, treatment-by-visit interaction, and Baseline value as a covariate.

Comparison groups	Placebo v Gefapixant 50 mg
Number of subjects included in analysis	118
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.0221
Method	Mixed Effect Repeated Measures model
Parameter estimate	LS Mean Difference
Point estimate	-0.7
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.2
upper limit	-0.1

Secondary: Change from Baseline in Weekly Mean Daily CSD Total Score at Week 6

End point title	Change from Baseline in Weekly Mean Daily CSD Total Score at Week 6

End point description:

The daily CSD instrument has a total of 7 items, each with scores ranging from 0 (best) to 10 (worst). The total daily CSD is the sum of these 7 item scores (Min=0, Max=70). Mean total daily score (the sum of 7 item scores divided by 7) was derived for each day. Weekly mean total daily score was defined as the average of the mean total daily scores for each week. LS mean change from baseline with associated SE reported for each treatment group. Baseline was defined as the average CSD scores collected during the week prior to Day 1 (Study Day -7 to Day -1).

All randomized participants who had taken at least 1 dose of study medication and provided at least 1 baseline and at least one post baseline endpoint observation during the treatment period were analysed.

End point type	Secondary

End point timeframe:

Baseline, Week 6

End point values	Placebo	Gefapixant 7.5 mg	Gefapixant 20 mg	Gefapixant 50 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	61	59	59	57
Units: score on a scale				
least squares mean (standard error)	-1.0 (± 0.21)	-1.4 (± 0.21)	-1.5 (± 0.21)	-1.7 (± 0.21)

Statistical analyses

Statistical analysis title	Week 6 CSD Total Score: 7.5 mg gefapixant v PBO

Statistical analysis description:

Week 6 estimated treatment differences (gefapixant vs. placebo) and corresponding 95% CIs were estimated using a MMRM model, which included fixed effects for treatment group, visit, country, treatment-by-visit interaction, and Baseline value as a covariate.

Comparison groups	Placebo v Gefapixant 7.5 mg
Number of subjects included in analysis	120
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.1562
Method	Mixed Effect Repeated Measures model
Parameter estimate	LS Mean Difference
Point estimate	-0.4
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1
upper limit	0.2

Statistical analysis title	Week 6 CSD Total Score: 20 mg gefapixant v PBO

Statistical analysis description:

Week 6 estimated treatment differences (gefapixant vs. placebo) and corresponding 95% CIs were estimated using a MMRM model, which included fixed effects for treatment group, visit, country, treatment-by-visit interaction, and Baseline value as a covariate.

Comparison groups	Placebo v Gefapixant 20 mg
Number of subjects included in analysis	120
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.071
Method	Mixed Effect Repeated Measures model
Parameter estimate	LS Mean Difference
Point estimate	-0.5
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.1
upper limit	0

Statistical analysis title	Week 6 CSD Total Score: 50 mg gefapixant v PBO

Statistical analysis description:

Week 6 estimated treatment differences (gefapixant vs. placebo) and corresponding 95% CIs were estimated using a MMRM model, which included fixed effects for treatment group, visit, country, treatment-by-visit interaction, and Baseline value as a covariate.

Comparison groups	Placebo v Gefapixant 50 mg
Number of subjects included in analysis	118
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.0274
Method	Mixed Effect Repeated Measures model
Parameter estimate	LS Mean Difference
Point estimate	-0.7
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.2
upper limit	0.1

Secondary: Change from Baseline in Weekly Mean Daily CSD Total Score at Week 7

End point title	Change from Baseline in Weekly Mean Daily CSD Total Score at Week 7

End point description:

The daily CSD instrument has a total of 7 items, each with scores ranging from 0 (best) to 10 (worst). The total daily CSD is the sum of these 7 item scores (Min=0, Max=70). Mean total daily score (the sum of 7 item scores divided by 7) was derived for each day. Weekly mean total daily score was defined as the average of the mean total daily scores for each week. LS mean change from baseline with associated SE reported for each treatment group. Baseline was defined as the average CSD scores collected during the week prior to Day 1 (Study Day -7 to Day -1).

All randomized participants who had taken at least 1 dose of study medication and provided at least 1 baseline and at least one post baseline endpoint observation during the treatment period were analysed.

End point type	Secondary

End point timeframe:

Baseline, Week 7

End point values	Placebo	Gefapixant 7.5 mg	Gefapixant 20 mg	Gefapixant 50 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	61	59	59	57
Units: score on a scale				
least squares mean (standard error)	-1.2 (± 0.21)	-1.4 (± 0.22)	-1.5 (± 0.22)	-1.7 (± 0.22)

Statistical analyses

Statistical analysis title	Week 7 CSD Total Score: 7.5 mg gefapixant v PBO

Statistical analysis description:

Week 7 estimated treatment differences (gefapixant vs. placebo) and corresponding 95% CIs were estimated using a MMRM model, which included fixed effects for treatment group, visit, country, treatment-by-visit interaction, and Baseline value as a covariate.

Comparison groups	Placebo v Gefapixant 7.5 mg
Number of subjects included in analysis	120
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.4464
Method	Mixed Effect Repeated Measures model
Parameter estimate	LS Mean Difference
Point estimate	-0.2
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.8
upper limit	0.4

Statistical analysis title	Week 7 CSD Total Score: 20 mg gefapixant v PBO

Statistical analysis description:

Week 7 estimated treatment differences (gefapixant vs. placebo) and corresponding 95% CIs were estimated using a MMRM model, which included fixed effects for treatment group, visit, country, treatment-by-visit interaction, and Baseline value as a covariate.

Comparison groups	Placebo v Gefapixant 20 mg
Number of subjects included in analysis	120
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.332
Method	Mixed Effect Repeated Measures model
Parameter estimate	LS Mean Difference
Point estimate	-0.3
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.9
upper limit	0.3

Statistical analysis title	Week 7 CSD Total Score: 50 mg gefapixant v PBO

Statistical analysis description:

Week 7 estimated treatment differences (gefapixant vs. placebo) and corresponding 95% CIs were estimated using a MMRM model, which included fixed effects for treatment group, visit, country, treatment-by-visit interaction, and Baseline value as a covariate.

Comparison groups	Placebo v Gefapixant 50 mg

Number of subjects included in analysis	118
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.0792
Method	Mixed Effect Repeated Measures model
Parameter estimate	LS Mean Difference
Point estimate	-0.5
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.1
upper limit	0.1

Secondary: Change from Baseline in Weekly Mean Daily CSD Total Score at Week 8

End point title	Change from Baseline in Weekly Mean Daily CSD Total Score at Week 8

End point description:

The daily CSD instrument has a total of 7 items, each with scores ranging from 0 (best) to 10 (worst). The total daily CSD is the sum of these 7 item scores (Min=0, Max=70). Mean total daily score (the sum of 7 item scores divided by 7) was derived for each day. Weekly mean total daily score was defined as the average of the mean total daily scores for each week. LS mean change from baseline with associated SE reported for each treatment group. Baseline was defined as the average CSD scores collected during the week prior to Day 1 (Study Day -7 to Day -1).

All randomized participants who had taken at least 1 dose of study medication and provided at least 1 baseline and at least one post baseline endpoint observation during the treatment period were analysed.

End point type	Secondary

End point timeframe:

Baseline, Week 8

End point values	Placebo	Gefapixant 7.5 mg	Gefapixant 20 mg	Gefapixant 50 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	61	59	59	57
Units: score on a scale				
least squares mean (standard error)	-1.3 (± 0.22)	-1.5 (± 0.22)	-1.6 (± 0.22)	-1.7 (± 0.23)

Statistical analyses

Statistical analysis title	Week 8 CSD Total Score: 7.5 mg gefapixant v PBO

Statistical analysis description:

Week 8 estimated treatment differences (gefapixant vs. placebo) and corresponding 95% CIs were estimated using a MMRM model, which included fixed effects for treatment group, visit, country, treatment-by-visit interaction, and Baseline value as a covariate.

Comparison groups	Placebo v Gefapixant 7.5 mg

Number of subjects included in analysis	120
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.4716
Method	Mixed Effect Repeated Measures model
Parameter estimate	LS Mean Difference
Point estimate	-0.2
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.8
upper limit	0.4

Statistical analysis title	Week 8 CSD Total Score: 20 mg gefapixant v PBO

Statistical analysis description:

Week 8 estimated treatment differences (gefapixant vs. placebo) and corresponding 95% CIs were estimated using a MMRM model, which included fixed effects for treatment group, visit, country, treatment-by-visit interaction, and Baseline value as a covariate.

Comparison groups	Placebo v Gefapixant 20 mg
Number of subjects included in analysis	120
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.4371
Method	Mixed Effect Repeated Measures model
Parameter estimate	LS Mean Difference
Point estimate	-0.2
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.8
upper limit	0.4

Statistical analysis title	Week 8 CSD Total Score: 50 mg gefapixant v PBO

Statistical analysis description:

Week 8 estimated treatment differences (gefapixant vs. placebo) and corresponding 95% CIs were estimated using a MMRM model, which included fixed effects for treatment group, visit, country, treatment-by-visit interaction, and Baseline value as a covariate.

Comparison groups	Placebo v Gefapixant 50 mg
Number of subjects included in analysis	118
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.1907
Method	Mixed Effect Repeated Measures model
Parameter estimate	LS Mean Difference
Point estimate	-0.4

Confidence interval	
level	95 %
sides	2-sided
lower limit	-1
upper limit	0.2

Secondary: Change from Baseline in Weekly Mean Daily CSD Total Score at Week 9

End point title	Change from Baseline in Weekly Mean Daily CSD Total Score at Week 9

End point description:

The daily CSD instrument has a total of 7 items, each with scores ranging from 0 (best) to 10 (worst). The total daily CSD is the sum of these 7 item scores (Min=0, Max=70). Mean total daily score (the sum of 7 item scores divided by 7) was derived for each day. Weekly mean total daily score was defined as the average of the mean total daily scores for each week. LS mean change from baseline with associated SE reported for each treatment group. Baseline was defined as the average CSD scores collected during the week prior to Day 1 (Study Day -7 to Day -1).

All randomized participants who had taken at least 1 dose of study medication and provided at least 1 baseline and at least one post baseline endpoint observation during the treatment period were analysed.

End point type	Secondary

End point timeframe:

Baseline, Week 9

End point values	Placebo	Gefapixant 7.5 mg	Gefapixant 20 mg	Gefapixant 50 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	61	59	59	57
Units: score on a scale				
least squares mean (standard error)	-1.3 (± 0.21)	-1.6 (± 0.22)	-1.7 (± 0.22)	-1.8 (± 0.22)

Statistical analyses

Statistical analysis title	Week 9 CSD Total Score: 7.5 mg gefapixant v PBO

Statistical analysis description:

Week 9 estimated treatment differences (gefapixant vs. placebo) and corresponding 95% CIs were estimated using a MMRM model, which included fixed effects for treatment group, visit, country, treatment-by-visit interaction, and Baseline value as a covariate.

Comparison groups	Placebo v Gefapixant 7.5 mg
Number of subjects included in analysis	120
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.2772
Method	Mixed Effect Repeated Measures model
Parameter estimate	LS Mean Difference
Point estimate	-0.3

Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.9
upper limit	0.3

Statistical analysis title	Week 9 CSD Total Score: 20 mg gefapixant v PBO

Statistical analysis description:

Week 9 estimated treatment differences (gefapixant vs. placebo) and corresponding 95% CIs were estimated using a MMRM model, which included fixed effects for treatment group, visit, country, treatment-by-visit interaction, and Baseline value as a covariate.

Comparison groups	Placebo v Gefapixant 20 mg
Number of subjects included in analysis	120
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.1132
Method	Mixed Effect Repeated Measures model
Parameter estimate	LS Mean Difference
Point estimate	-0.5
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.1
upper limit	0.1

Statistical analysis title	Week 9 CSD Total Score: 50 mg gefapixant v PBO

Statistical analysis description:

Week 9 estimated treatment differences (gefapixant vs. placebo) and corresponding 95% CIs were estimated using a MMRM model, which included fixed effects for treatment group, visit, country, treatment-by-visit interaction, and Baseline value as a covariate.

Comparison groups	Placebo v Gefapixant 50 mg
Number of subjects included in analysis	118
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.0737
Method	Mixed Effect Repeated Measures model
Parameter estimate	LS Mean Difference
Point estimate	-0.6
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.2
upper limit	0.1

Secondary: Change from Baseline in Weekly Mean Daily CSD Total Score at Week 10

End point title	Change from Baseline in Weekly Mean Daily CSD Total Score at Week 10

End point description:

The daily CSD instrument has a total of 7 items, each with scores ranging from 0 (best) to 10 (worst). The total daily CSD is the sum of these 7 item scores (Min=0, Max=70). Mean total daily score (the sum of 7 item scores divided by 7) was derived for each day. Weekly mean total daily score was defined as the average of the mean total daily scores for each week. LS mean change from baseline with associated SE reported for each treatment group. Baseline was defined as the average CSD scores collected during the week prior to Day 1 (Study Day -7 to Day -1).

All randomized participants who had taken at least 1 dose of study medication and provided at least 1 baseline and at least one post baseline endpoint observation during the treatment period were analysed.

End point type	Secondary

End point timeframe:

Baseline, Week 10

End point values	Placebo	Gefapixant 7.5 mg	Gefapixant 20 mg	Gefapixant 50 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	61	59	59	57
Units: score on a scale				
least squares mean (standard error)	-1.2 (± 0.22)	-1.4 (± 0.22)	-1.6 (± 0.22)	-1.9 (± 0.22)

Statistical analyses

Statistical analysis title	Week 10 CSD Total Score: 7.5 mg gefapixant v PBO

Statistical analysis description:

Week 10 estimated treatment differences (gefapixant vs. placebo) and corresponding 95% CIs were estimated using a MMRM model, which included fixed effects for treatment group, visit, country, treatment-by-visit interaction, and Baseline value as a covariate.

Comparison groups	Placebo v Gefapixant 7.5 mg
Number of subjects included in analysis	120
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.6266
Method	Mixed Effect Repeated Measures model
Parameter estimate	LS Mean Difference
Point estimate	-0.1
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.8
upper limit	0.5

Statistical analysis title	Week 10 CSD Total Score: 20 mg gefapixant v PBO

Statistical analysis description:

Week 10 estimated treatment differences (gefapixant vs. placebo) and corresponding 95% CIs were estimated using a MMRM model, which included fixed effects for treatment group, visit, country,

treatment-by-visit interaction, and Baseline value as a covariate.

Comparison groups	Placebo v Gefapixant 20 mg
Number of subjects included in analysis	120
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.1769
Method	Mixed Effect Repeated Measures model
Parameter estimate	LS Mean Difference
Point estimate	-0.4
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1
upper limit	0.2

Statistical analysis title	Week 10 CSD Total Score: 50 mg gefapixant v PBO

Statistical analysis description:

Week 10 estimated treatment differences (gefapixant vs. placebo) and corresponding 95% CIs were estimated using a MMRM model, which included fixed effects for treatment group, visit, country, treatment-by-visit interaction, and Baseline value as a covariate.

Comparison groups	Placebo v Gefapixant 50 mg
Number of subjects included in analysis	118
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.0313
Method	Mixed Effect Repeated Measures model
Parameter estimate	LS Mean Difference
Point estimate	-0.7
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.3
upper limit	-0.1

Secondary: Change from Baseline in Weekly Mean Daily CSD Total Score at Week 11

End point title	Change from Baseline in Weekly Mean Daily CSD Total Score at Week 11

End point description:

The daily CSD instrument has a total of 7 items, each with scores ranging from 0 (best) to 10 (worst). The total daily CSD is the sum of these 7 item scores (Min=0, Max=70). Mean total daily score (the sum of 7 item scores divided by 7) was derived for each day. Weekly mean total daily score was defined as the average of the mean total daily scores for each week. LS mean change from baseline with associated SE reported for each treatment group. Baseline was defined as the average CSD scores collected during the week prior to Day 1 (Study Day -7 to Day -1).

All randomized participants who had taken at least 1 dose of study medication and provided at least 1 baseline and at least one post baseline endpoint observation during the treatment period were analysed.

End point type	Secondary

End point timeframe:
Baseline, Week 11

End point values	Placebo	Gefapixant 7.5 mg	Gefapixant 20 mg	Gefapixant 50 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	61	59	59	57
Units: score on a scale				
least squares mean (standard error)	-1.1 (± 0.22)	-1.5 (± 0.22)	-1.7 (± 0.22)	-1.9 (± 0.23)

Statistical analyses

Statistical analysis title	Week 10 CSD Total Score: 7.5 mg gefapixant v PBO
Statistical analysis description:	
Week 10 estimated treatment differences (gefapixant vs. placebo) and corresponding 95% CIs were estimated using a MMRM model, which included fixed effects for treatment group, visit, country, treatment-by-visit interaction, and Baseline value as a covariate.	
Comparison groups	Placebo v Gefapixant 7.5 mg
Number of subjects included in analysis	120
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.2058
Method	Mixed Effect Repeated Measures model
Parameter estimate	LS Mean Difference
Point estimate	-0.4
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1
upper limit	0.2

Statistical analysis title	Week 10 CSD Total Score: 20 mg gefapixant v PBO
Statistical analysis description:	
Week 10 estimated treatment differences (gefapixant vs. placebo) and corresponding 95% CIs were estimated using a MMRM model, which included fixed effects for treatment group, visit, country, treatment-by-visit interaction, and Baseline value as a covariate.	
Comparison groups	Placebo v Gefapixant 20 mg
Number of subjects included in analysis	120
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.0665
Method	Mixed Effect Repeated Measures model
Parameter estimate	LS Mean Difference
Point estimate	-0.6

Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.2
upper limit	0

Statistical analysis title	Week 10 CSD Total Score: 50 mg gefapixant v PBO

Statistical analysis description:

Week 10 estimated treatment differences (gefapixant vs. placebo) and corresponding 95% CIs were estimated using a MMRM model, which included fixed effects for treatment group, visit, country, treatment-by-visit interaction, and Baseline value as a covariate.

Comparison groups	Placebo v Gefapixant 50 mg
Number of subjects included in analysis	118
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.0155
Method	Mixed Effect Repeated Measures model
Parameter estimate	LS Mean Difference
Point estimate	-0.8
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.4
upper limit	-0.1

Secondary: Change from Baseline in Weekly Mean Daily CSD Total Score at Week 12

End point title	Change from Baseline in Weekly Mean Daily CSD Total Score at Week 12

End point description:

The daily CSD instrument has a total of 7 items, each with scores ranging from 0 (best) to 10 (worst). The total daily CSD is the sum of these 7 item scores (Min=0, Max=70). Mean total daily score (the sum of 7 item scores divided by 7) was derived for each day. Weekly mean total daily score was defined as the average of the mean total daily scores for each week. LS mean change from baseline with associated SE reported for each treatment group. Baseline was defined as the average CSD scores collected during the week prior to Day 1 (Study Day -7 to Day -1).

All randomized participants who had taken at least 1 dose of study medication and provided at least 1 baseline and at least one post baseline endpoint observation during the treatment period were analysed.

End point type	Secondary

End point timeframe:

Baseline, Week 12

End point values	Placebo	Gefapixant 7.5 mg	Gefapixant 20 mg	Gefapixant 50 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	61	59	59	57
Units: score on a scale				
least squares mean (standard error)	-1.2 (± 0.22)	-1.5 (± 0.22)	-1.7 (± 0.22)	-1.9 (± 0.23)

Statistical analyses

Statistical analysis title	Week 12 CSD Total Score: 7.5 mg gefapixant v PBO
Statistical analysis description:	
Week 12 estimated treatment differences (gefapixant vs. placebo) and corresponding 95% CIs were estimated using a MMRM model, which included fixed effects for treatment group, visit, country, treatment-by-visit interaction, and Baseline value as a covariate.	
Comparison groups	Placebo v Gefapixant 7.5 mg
Number of subjects included in analysis	120
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.2458
Method	Mixed Effect Repeated Measures model
Parameter estimate	LS Mean Difference
Point estimate	-0.4
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1
upper limit	0.3

Statistical analysis title	Week 12 CSD Total Score: 20 mg gefapixant v PBO
Statistical analysis description:	
Week 12 estimated treatment differences (gefapixant vs. placebo) and corresponding 95% CIs were estimated using a MMRM model, which included fixed effects for treatment group, visit, country, treatment-by-visit interaction, and Baseline value as a covariate.	
Comparison groups	Placebo v Gefapixant 20 mg
Number of subjects included in analysis	120
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.0662
Method	Mixed Effect Repeated Measures model
Parameter estimate	LS Mean Difference
Point estimate	-0.6
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.2
upper limit	0

Statistical analysis title	Week 12 CSD Total Score: 50 mg gefapixant v PBO

Statistical analysis description:

Week 12 estimated treatment differences (gefapixant vs. placebo) and corresponding 95% CIs were estimated using a MMRM model, which included fixed effects for treatment group, visit, country, treatment-by-visit interaction, and Baseline value as a covariate.

Comparison groups	Placebo v Gefapixant 50 mg
Number of subjects included in analysis	118
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.0197
Method	Mixed Effect Repeated Measures model
Parameter estimate	LS Mean Difference
Point estimate	-0.7
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.4
upper limit	-0.1

Secondary: Change from Baseline in Weekly Mean Daily Cough Score (DCS) at Week 1

End point title	Change from Baseline in Weekly Mean Daily Cough Score (DCS) at Week 1

End point description:

The DCS has a score ranging from 0 (best) to 10 (worst). Weekly mean daily score was defined as the average of the daily scores for each week. Baseline was defined as the average DCS score collected during the week prior to Day 1 (Day -7 to Day -1). Participants rated the severity of their cough using the DCS each day. LS mean change from baseline with associated SE reported for each treatment group.

All randomized participants who had taken at least 1 dose of study medication and provided at least 1 baseline and at least one post baseline endpoint observation during the treatment period were analysed.

End point type	Secondary

End point timeframe:

Baseline, Week 1

End point values	Placebo	Gefapixant 7.5 mg	Gefapixant 20 mg	Gefapixant 50 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	61	59	59	57
Units: score on a scale				
least squares mean (standard error)	-1.1 (± 0.18)	-0.7 (± 0.18)	-0.8 (± 0.19)	-1.1 (± 0.19)

Statistical analyses

Statistical analysis title	Week 1 DCS Total Score: 7.5 mg gefapixant v PBO

Statistical analysis description:

Week 1 estimated treatment differences (gefapixant vs. placebo) and corresponding 95% CIs were estimated using a MMRM model, which included fixed effects for treatment group, visit, country, treatment-by-visit interaction, and Baseline value as a covariate.

Comparison groups	Placebo v Gefapixant 7.5 mg
Number of subjects included in analysis	120
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.1921
Method	Mixed Effect Repeated Measures model
Parameter estimate	LS Mean Difference
Point estimate	0.3
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.2
upper limit	0.8

Statistical analysis title	Week 1 DCS Total Score: 20 mg gefapixant v PBO

Statistical analysis description:

Week 1 estimated treatment differences (gefapixant vs. placebo) and corresponding 95% CIs were estimated using a MMRM model, which included fixed effects for treatment group, visit, country, treatment-by-visit interaction, and Baseline value as a covariate.

Comparison groups	Placebo v Gefapixant 20 mg
Number of subjects included in analysis	120
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.2428
Method	Mixed Effect Repeated Measures model
Parameter estimate	LS Mean Difference
Point estimate	0.3
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.2
upper limit	0.8

Statistical analysis title	Week 1 DCS Total Score: 50 mg gefapixant v PBO

Statistical analysis description:

Week 1 estimated treatment differences (gefapixant vs. placebo) and corresponding 95% CIs were estimated using a MMRM model, which included fixed effects for treatment group, visit, country, treatment-by-visit interaction, and Baseline value as a covariate.

Comparison groups	Placebo v Gefapixant 50 mg

Number of subjects included in analysis	118
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.7383
Method	Mixed Effect Repeated Measures model
Parameter estimate	LS Mean Difference
Point estimate	-0.1
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.6
upper limit	0.4

Secondary: Change from Baseline in Weekly Mean DCS at Week 2

End point title	Change from Baseline in Weekly Mean DCS at Week 2

End point description:

The DCS has a score ranging from 0 (best) to 10 (worst). Weekly mean daily score was defined as the average of the daily scores for each week. Baseline was defined as the average DCS score collected during the week prior to Day 1 (Day -7 to Day -1). Participants rated the severity of their cough using the DCS each day. LS mean change from baseline with associated SE reported for each treatment group.

All randomized participants who had taken at least 1 dose of study medication and provided at least 1 baseline and at least one post baseline endpoint observation during the treatment period were analysed.

End point type	Secondary

End point timeframe:

Baseline, Week 2

End point values	Placebo	Gefapixant 7.5 mg	Gefapixant 20 mg	Gefapixant 50 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	61	59	59	57
Units: score on a scale				
least squares mean (standard error)	-1.4 (± 0.22)	-1.1 (± 0.23)	-1.1 (± 0.23)	-1.7 (± 0.23)

Statistical analyses

Statistical analysis title	Week 2 DCS Total Score: 7.5 mg gefapixant v PBO

Statistical analysis description:

Week 2 estimated treatment differences (gefapixant vs. placebo) and corresponding 95% CIs were estimated using a MMRM model, which included fixed effects for treatment group, visit, country, treatment-by-visit interaction, and Baseline value as a covariate.

Comparison groups	Placebo v Gefapixant 7.5 mg

Number of subjects included in analysis	120
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.4033
Method	Mixed Effect Repeated Measures model
Parameter estimate	LS Mean Difference
Point estimate	0.3
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.4
upper limit	0.9

Statistical analysis title	Week 2 DCS Total Score: 20 mg gefapixant v PBO

Statistical analysis description:

Week 2 estimated treatment differences (gefapixant vs. placebo) and corresponding 95% CIs were estimated using a MMRM model, which included fixed effects for treatment group, visit, country, treatment-by-visit interaction, and Baseline value as a covariate.

Comparison groups	Placebo v Gefapixant 20 mg
Number of subjects included in analysis	120
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.4599
Method	Mixed Effect Repeated Measures model
Parameter estimate	LS Mean Difference
Point estimate	0.2
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.4
upper limit	0.9

Statistical analysis title	Week 2 DCS Total Score: 50 mg gefapixant v PBO

Statistical analysis description:

Week 2 estimated treatment differences (gefapixant vs. placebo) and corresponding 95% CIs were estimated using a MMRM model, which included fixed effects for treatment group, visit, country, treatment-by-visit interaction, and Baseline value as a covariate.

Comparison groups	Placebo v Gefapixant 50 mg
Number of subjects included in analysis	118
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.2837
Method	Mixed Effect Repeated Measures model
Parameter estimate	LS Mean Difference
Point estimate	-0.3

Confidence interval	
level	95 %
sides	2-sided
lower limit	-1
upper limit	0.3

Secondary: Change from Baseline in Weekly Mean DCS at Week 3

End point title	Change from Baseline in Weekly Mean DCS at Week 3

End point description:

The DCS has a score ranging from 0 (best) to 10 (worst). Weekly mean daily score was defined as the average of the daily scores for each week. Baseline was defined as the average DCS score collected during the week prior to Day 1 (Day -7 to Day -1). Participants rated the severity of their cough using the DCS each day. LS mean change from baseline with associated SE reported for each treatment group.

All randomized participants who had taken at least 1 dose of study medication and provided at least 1 baseline and at least one post baseline endpoint observation during the treatment period were analysed.

End point type	Secondary

End point timeframe:

Baseline, Week 3

End point values	Placebo	Gefapixant 7.5 mg	Gefapixant 20 mg	Gefapixant 50 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	61	59	59	57
Units: score on a scale				
least squares mean (standard error)	-1.4 (± 0.24)	-1.3 (± 0.24)	-1.6 (± 0.25)	-1.7 (± 0.25)

Statistical analyses

Statistical analysis title	Week 3 DCS Total Score: 7.5 mg gefapixant v PBO

Statistical analysis description:

Week 3 estimated treatment differences (gefapixant vs. placebo) and corresponding 95% CIs were estimated using a MMRM model, which included fixed effects for treatment group, visit, country, treatment-by-visit interaction, and Baseline value as a covariate.

Comparison groups	Placebo v Gefapixant 7.5 mg
Number of subjects included in analysis	120
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.8084
Method	Mixed Effect Repeated Measures model
Parameter estimate	LS Mean Difference
Point estimate	0.1

Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.6
upper limit	0.8

Statistical analysis title	Week 3 DCS Total Score: 20 mg gefapixant v PBO

Statistical analysis description:

Week 3 estimated treatment differences (gefapixant vs. placebo) and corresponding 95% CIs were estimated using a MMRM model, which included fixed effects for treatment group, visit, country, treatment-by-visit interaction, and Baseline value as a covariate.

Comparison groups	Placebo v Gefapixant 20 mg
Number of subjects included in analysis	120
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.6108
Method	Mixed Effect Repeated Measures model
Parameter estimate	LS Mean Difference
Point estimate	-0.2
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.8
upper limit	0.5

Statistical analysis title	Week 3 DCS Total Score: 50 mg gefapixant v PBO

Statistical analysis description:

Week 3 estimated treatment differences (gefapixant vs. placebo) and corresponding 95% CIs were estimated using a MMRM model, which included fixed effects for treatment group, visit, country, treatment-by-visit interaction, and Baseline value as a covariate.

Comparison groups	Placebo v Gefapixant 50 mg
Number of subjects included in analysis	118
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.422
Method	Mixed Effect Repeated Measures model
Parameter estimate	LS Mean Difference
Point estimate	-0.3
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.9
upper limit	0.4

Secondary: Change from Baseline in Weekly Mean DCS at Week 4

End point title	Change from Baseline in Weekly Mean DCS at Week 4

End point description:

The DCS has a score ranging from 0 (best) to 10 (worst). Weekly mean daily score was defined as the average of the daily scores for each week. Baseline was defined as the average DCS score collected during the week prior to Day 1 (Day -7 to Day -1). Participants rated the severity of their cough using the DCS each day. LS mean change from baseline with associated SE reported for each treatment group.

All randomized participants who had taken at least 1 dose of study medication and provided at least 1 baseline and at least one post baseline endpoint observation during the treatment period were analysed.

End point type	Secondary

End point timeframe:

Baseline, Week 4

End point values	Placebo	Gefapixant 7.5 mg	Gefapixant 20 mg	Gefapixant 50 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	61	59	59	57
Units: score on a scale				
least squares mean (standard error)	-1.5 (± 0.24)	-1.6 (± 0.24)	-1.8 (± 0.24)	-1.9 (± 0.24)

Statistical analyses

Statistical analysis title	Week 4 DCS Total Score: 7.5 mg gefapixant v PBO

Statistical analysis description:

Week 4 estimated treatment differences (gefapixant vs. placebo) and corresponding 95% CIs were estimated using a MMRM model, which included fixed effects for treatment group, visit, country, treatment-by-visit interaction, and Baseline value as a covariate.

Comparison groups	Placebo v Gefapixant 7.5 mg
Number of subjects included in analysis	120
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.8457
Method	Mixed Effect Repeated Measures model
Parameter estimate	LS Mean Difference
Point estimate	-0.1
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.7
upper limit	0.6

Statistical analysis title	Week 4 DCS Total Score: 20 mg gefapixant v PBO

Statistical analysis description:

Week 4 estimated treatment differences (gefapixant vs. placebo) and corresponding 95% CIs were estimated using a MMRM model, which included fixed effects for treatment group, visit, country, treatment-by-visit interaction, and Baseline value as a covariate.

Comparison groups	Placebo v Gefapixant 20 mg
Number of subjects included in analysis	120
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.4044
Method	Mixed Effect Repeated Measures model
Parameter estimate	LS Mean Difference
Point estimate	-0.3
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.9
upper limit	0.4

Statistical analysis title	Week 4 DCS Total Score: 50 mg gefapixant v PBO

Statistical analysis description:

Week 4 estimated treatment differences (gefapixant vs. placebo) and corresponding 95% CIs were estimated using a MMRM model, which included fixed effects for treatment group, visit, country, treatment-by-visit interaction, and Baseline value as a covariate.

Comparison groups	Placebo v Gefapixant 50 mg
Number of subjects included in analysis	118
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.3031
Method	Mixed Effect Repeated Measures model
Parameter estimate	LS Mean Difference
Point estimate	-0.3
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1
upper limit	0.3

Secondary: Change from Baseline in Weekly Mean DCS at Week 5

End point title	Change from Baseline in Weekly Mean DCS at Week 5

End point description:

The DCS has a score ranging from 0 (best) to 10 (worst). Weekly mean daily score was defined as the average of the daily scores for each week. Baseline was defined as the average DCS score collected during the week prior to Day 1 (Day -7 to Day -1). Participants rated the severity of their cough using the DCS each day. LS mean change from baseline with associated SE reported for each treatment group.

All randomized participants who had taken at least 1 dose of study medication and provided at least 1 baseline and at least one post baseline endpoint observation during the treatment period were analysed.

End point type	Secondary

End point timeframe:

Baseline, Week 5

End point values	Placebo	Gefapixant 7.5 mg	Gefapixant 20 mg	Gefapixant 50 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	61	59	59	57
Units: score on a scale				
least squares mean (standard error)	-1.4 (± 0.23)	-1.4 (± 0.24)	-1.9 (± 0.24)	-2.1 (± 0.24)

Statistical analyses

Statistical analysis title	Week 5 DCS Total Score: 7.5 mg gefapixant v PBO

Statistical analysis description:

Week 5 estimated treatment differences (gefapixant vs. placebo) and corresponding 95% CIs were estimated using a MMRM model, which included fixed effects for treatment group, visit, country, treatment-by-visit interaction, and Baseline value as a covariate.

Comparison groups	Placebo v Gefapixant 7.5 mg
Number of subjects included in analysis	120
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.9126
Method	Mixed Effect Repeated Measures model
Parameter estimate	LS Mean Difference
Point estimate	0
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.7
upper limit	0.6

Statistical analysis title	Week 5 DCS Total Score: 20 mg gefapixant v PBO

Statistical analysis description:

Week 5 estimated treatment differences (gefapixant vs. placebo) and corresponding 95% CIs were estimated using a MMRM model, which included fixed effects for treatment group, visit, country, treatment-by-visit interaction, and Baseline value as a covariate.

Comparison groups	Placebo v Gefapixant 20 mg
Number of subjects included in analysis	120
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.1136
Method	Mixed Effect Repeated Measures model
Parameter estimate	LS Mean Difference
Point estimate	-0.5

Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.2
upper limit	0.1

Statistical analysis title	Week 5 DCS Total Score: 50 mg gefapixant v PBO

Statistical analysis description:

Week 5 estimated treatment differences (gefapixant vs. placebo) and corresponding 95% CIs were estimated using a MMRM model, which included fixed effects for treatment group, visit, country, treatment-by-visit interaction, and Baseline value as a covariate.

Comparison groups	Placebo v Gefapixant 50 mg
Number of subjects included in analysis	118
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.0352
Method	Mixed Effect Repeated Measures model
Parameter estimate	LS Mean Difference
Point estimate	-0.7
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.4
upper limit	0

Secondary: Change from Baseline in Weekly Mean DCS at Week 6

End point title	Change from Baseline in Weekly Mean DCS at Week 6

End point description:

The DCS has a score ranging from 0 (best) to 10 (worst). Weekly mean daily score was defined as the average of the daily scores for each week. Baseline was defined as the average DCS score collected during the week prior to Day 1 (Day -7 to Day -1). Participants rated the severity of their cough using the DCS each day. LS mean change from baseline with associated SE reported for each treatment group.

All randomized participants who had taken at least 1 dose of study medication and provided at least 1 baseline and at least one post baseline endpoint observation during the treatment period were analysed.

End point type	Secondary

End point timeframe:

Baseline, Week 6

End point values	Placebo	Gefapixant 7.5 mg	Gefapixant 20 mg	Gefapixant 50 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	61	59	59	57
Units: score on a scale				
least squares mean (standard error)	-1.2 (± 0.24)	-1.7 (± 0.24)	-1.9 (± 0.24)	-1.8 (± 0.24)

Statistical analyses

Statistical analysis title	Week 6 DCS Total Score: 7.5 mg gefapixant v PBO

Statistical analysis description:

Week 6 estimated treatment differences (gefapixant vs. placebo) and corresponding 95% CIs were estimated using a MMRM model, which included fixed effects for treatment group, visit, country, treatment-by-visit interaction, and Baseline value as a covariate.

Comparison groups	Placebo v Gefapixant 7.5 mg
Number of subjects included in analysis	120
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.1718
Method	Mixed Effect Repeated Measures model
Parameter estimate	LS Mean Difference
Point estimate	-0.5
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.1
upper limit	0.2

Statistical analysis title	Week 6 DCS Total Score: 20 mg gefapixant v PBO

Statistical analysis description:

Week 6 estimated treatment differences (gefapixant vs. placebo) and corresponding 95% CIs were estimated using a MMRM model, which included fixed effects for treatment group, visit, country, treatment-by-visit interaction, and Baseline value as a covariate.

Comparison groups	Placebo v Gefapixant 20 mg
Number of subjects included in analysis	120
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.0651
Method	Mixed Effect Repeated Measures model
Parameter estimate	LS Mean Difference
Point estimate	-0.6
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.3
upper limit	0

Statistical analysis title	Week 6 DCS Total Score: 50 mg gefapixant v PBO

Statistical analysis description:

Week 6 estimated treatment differences (gefapixant vs. placebo) and corresponding 95% CIs were estimated using a MMRM model, which included fixed effects for treatment group, visit, country, treatment-by-visit interaction, and Baseline value as a covariate.

Comparison groups	Placebo v Gefapixant 50 mg
Number of subjects included in analysis	118
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.0848
Method	Mixed Effect Repeated Measures model
Parameter estimate	LS Mean Difference
Point estimate	-0.6
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.2
upper limit	0.1

Secondary: Change from Baseline in Weekly Mean DCS at Week 7

End point title	Change from Baseline in Weekly Mean DCS at Week 7

End point description:

The DCS has a score ranging from 0 (best) to 10 (worst). Weekly mean daily score was defined as the average of the daily scores for each week. Baseline was defined as the average DCS score collected during the week prior to Day 1 (Day -7 to Day -1). Participants rated the severity of their cough using the DCS each day. LS mean change from baseline with associated SE reported for each treatment group.

All randomized participants who had taken at least 1 dose of study medication and provided at least 1 baseline and at least one post baseline endpoint observation during the treatment period were analysed.

End point type	Secondary

End point timeframe:

Baseline, Week 7

End point values	Placebo	Gefapixant 7.5 mg	Gefapixant 20 mg	Gefapixant 50 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	61	59	59	57
Units: score on a scale				
least squares mean (standard error)	-1.5 (± 0.25)	-1.7 (± 0.25)	-1.9 (± 0.25)	-1.9 (± 0.25)

Statistical analyses

Statistical analysis title	Week 7 DCS Total Score: 7.5 mg gefapixant v PBO
Statistical analysis description:	
Week 7 estimated treatment differences (gefapixant vs. placebo) and corresponding 95% CIs were estimated using a MMRM model, which included fixed effects for treatment group, visit, country, treatment-by-visit interaction, and Baseline value as a covariate.	
Comparison groups	Placebo v Gefapixant 7.5 mg
Number of subjects included in analysis	120
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.6715
Method	Mixed Effect Repeated Measures model
Parameter estimate	LS Mean Difference
Point estimate	-0.1
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.8
upper limit	0.5

Statistical analysis title	Week 7 DCS Total Score: 20 mg gefapixant v PBO
Statistical analysis description:	
Week 7 estimated treatment differences (gefapixant vs. placebo) and corresponding 95% CIs were estimated using a MMRM model, which included fixed effects for treatment group, visit, country, treatment-by-visit interaction, and Baseline value as a covariate.	
Comparison groups	Placebo v Gefapixant 20 mg
Number of subjects included in analysis	120
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.3514
Method	Mixed Effect Repeated Measures model
Parameter estimate	LS Mean Difference
Point estimate	-0.3
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1
upper limit	0.4

Statistical analysis title	Week 7 DCS Total Score: 50 mg gefapixant v PBO
Statistical analysis description:	
Week 7 estimated treatment differences (gefapixant vs. placebo) and corresponding 95% CIs were estimated using a MMRM model, which included fixed effects for treatment group, visit, country, treatment-by-visit interaction, and Baseline value as a covariate.	
Comparison groups	Placebo v Gefapixant 50 mg

Number of subjects included in analysis	118
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.2809
Method	Mixed Effect Repeated Measures model
Parameter estimate	LS Mean Difference
Point estimate	-0.4
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.1
upper limit	0.3

Secondary: Change from Baseline in Weekly Mean DCS at Week 8

End point title	Change from Baseline in Weekly Mean DCS at Week 8

End point description:

The DCS has a score ranging from 0 (best) to 10 (worst). Weekly mean daily score was defined as the average of the daily scores for each week. Baseline was defined as the average DCS score collected during the week prior to Day 1 (Day -7 to Day -1). Participants rated the severity of their cough using the DCS each day. LS mean change from baseline with associated SE reported for each treatment group.

All randomized participants who had taken at least 1 dose of study medication and provided at least 1 baseline and at least one post baseline endpoint observation during the treatment period were analysed.

End point type	Secondary

End point timeframe:

Baseline, Week 8

End point values	Placebo	Gefapixant 7.5 mg	Gefapixant 20 mg	Gefapixant 50 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	61	59	59	57
Units: score on a scale				
least squares mean (standard error)	-1.7 (± 0.25)	-1.8 (± 0.25)	-1.9 (± 0.25)	-1.9 (± 0.26)

Statistical analyses

Statistical analysis title	Week 8 DCS Total Score: 7.5 mg gefapixant v PBO

Statistical analysis description:

Week 8 estimated treatment differences (gefapixant vs. placebo) and corresponding 95% CIs were estimated using a MMRM model, which included fixed effects for treatment group, visit, country, treatment-by-visit interaction, and Baseline value as a covariate.

Comparison groups	Placebo v Gefapixant 7.5 mg

Number of subjects included in analysis	120
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.6022
Method	Mixed Effect Repeated Measures model
Parameter estimate	LS Mean Difference
Point estimate	-0.2
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.9
upper limit	0.5

Statistical analysis title	Week 8 DCS Total Score: 20 mg gefapixant v PBO

Statistical analysis description:

Week 8 estimated treatment differences (gefapixant vs. placebo) and corresponding 95% CIs were estimated using a MMRM model, which included fixed effects for treatment group, visit, country, treatment-by-visit interaction, and Baseline value as a covariate.

Comparison groups	Placebo v Gefapixant 20 mg
Number of subjects included in analysis	120
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.4456
Method	Mixed Effect Repeated Measures model
Parameter estimate	LS Mean Difference
Point estimate	-0.3
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1
upper limit	0.4

Statistical analysis title	Week 8 DCS Total Score: 50 mg gefapixant v PBO

Statistical analysis description:

Week 8 estimated treatment differences (gefapixant vs. placebo) and corresponding 95% CIs were estimated using a MMRM model, which included fixed effects for treatment group, visit, country, treatment-by-visit interaction, and Baseline value as a covariate.

Comparison groups	Placebo v Gefapixant 50 mg
Number of subjects included in analysis	118
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.4629
Method	Mixed Effect Repeated Measures model
Parameter estimate	LS Mean Difference
Point estimate	-0.3

Confidence interval	
level	95 %
sides	2-sided
lower limit	-1
upper limit	0.4

Secondary: Change from Baseline in Weekly Mean DCS at Week 9

End point title	Change from Baseline in Weekly Mean DCS at Week 9

End point description:

The DCS has a score ranging from 0 (best) to 10 (worst). Weekly mean daily score was defined as the average of the daily scores for each week. Baseline was defined as the average DCS score collected during the week prior to Day 1 (Day -7 to Day -1). Participants rated the severity of their cough using the DCS each day. LS mean change from baseline with associated SE reported for each treatment group.

All randomized participants who had taken at least 1 dose of study medication and provided at least 1 baseline and at least one post baseline endpoint observation during the treatment period were analysed.

End point type	Secondary

End point timeframe:

Baseline, Week 9

End point values	Placebo	Gefapixant 7.5 mg	Gefapixant 20 mg	Gefapixant 50 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	61	59	59	57
Units: score on a scale				
least squares mean (standard error)	-1.6 (± 0.25)	-1.9 (± 0.25)	-2.2 (± 0.25)	-2.0 (± 0.26)

Statistical analyses

Statistical analysis title	Week 9 DCS Total Score: 7.5 mg gefapixant v PBO

Statistical analysis description:

Week 9 estimated treatment differences (gefapixant vs. placebo) and corresponding 95% CIs were estimated using a MMRM model, which included fixed effects for treatment group, visit, country, treatment-by-visit interaction, and Baseline value as a covariate.

Comparison groups	Placebo v Gefapixant 7.5 mg
Number of subjects included in analysis	120
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.3749
Method	Mixed Effect Repeated Measures model
Parameter estimate	LS Mean Difference
Point estimate	-0.3

Confidence interval	
level	95 %
sides	2-sided
lower limit	-1
upper limit	0.4

Statistical analysis title	Week 9 DCS Total Score: 20 mg gefapixant v PBO

Statistical analysis description:

Week 9 estimated treatment differences (gefapixant vs. placebo) and corresponding 95% CIs were estimated using a MMRM model, which included fixed effects for treatment group, visit, country, treatment-by-visit interaction, and Baseline value as a covariate.

Comparison groups	Placebo v Gefapixant 20 mg
Number of subjects included in analysis	120
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.0854
Method	Mixed Effect Repeated Measures model
Parameter estimate	LS Mean Difference
Point estimate	-0.6
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.3
upper limit	0.1

Statistical analysis title	Week 9 DCS Total Score: 50 mg gefapixant v PBO

Statistical analysis description:

Week 9 estimated treatment differences (gefapixant vs. placebo) and corresponding 95% CIs were estimated using a MMRM model, which included fixed effects for treatment group, visit, country, treatment-by-visit interaction, and Baseline value as a covariate.

Comparison groups	Placebo v Gefapixant 50 mg
Number of subjects included in analysis	118
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.2672
Method	Mixed Effect Repeated Measures model
Parameter estimate	LS Mean Difference
Point estimate	-0.4
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.1
upper limit	0.3

Secondary: Change from Baseline in Weekly Mean DCS at Week 10

End point title	Change from Baseline in Weekly Mean DCS at Week 10

End point description:

The DCS has a score ranging from 0 (best) to 10 (worst). Weekly mean daily score was defined as the average of the daily scores for each week. Baseline was defined as the average DCS score collected during the week prior to Day 1 (Day -7 to Day -1). Participants rated the severity of their cough using the DCS each day. LS mean change from baseline with associated SE reported for each treatment group.

All randomized participants who had taken at least 1 dose of study medication and provided at least 1 baseline and at least one post baseline endpoint observation during the treatment period were analysed.

End point type	Secondary

End point timeframe:

Baseline, Week 10

End point values	Placebo	Gefapixant 7.5 mg	Gefapixant 20 mg	Gefapixant 50 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	61	59	59	57
Units: score on a scale				
least squares mean (standard error)	-1.5 (± 0.25)	-1.6 (± 0.25)	-2.1 (± 0.25)	-2.1 (± 0.26)

Statistical analyses

Statistical analysis title	Week 10 DCS Total Score: 7.5 mg gefapixant v PBO

Statistical analysis description:

Week 10 estimated treatment differences (gefapixant vs. placebo) and corresponding 95% CIs were estimated using a MMRM model, which included fixed effects for treatment group, visit, country, treatment-by-visit interaction, and Baseline value as a covariate.

Comparison groups	Placebo v Gefapixant 7.5 mg
Number of subjects included in analysis	120
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.7255
Method	Mixed Effect Repeated Measures model
Parameter estimate	LS Mean Difference
Point estimate	-0.1
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.8
upper limit	0.6

Statistical analysis title	Week 10 DCS Total Score: 20 mg gefapixant v PBO

Statistical analysis description:

Week 10 estimated treatment differences (gefapixant vs. placebo) and corresponding 95% CIs were estimated using a MMRM model, which included fixed effects for treatment group, visit, country, treatment-by-visit interaction, and Baseline value as a covariate.

Comparison groups	Placebo v Gefapixant 20 mg
Number of subjects included in analysis	120
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.0918
Method	Mixed Effect Repeated Measures model
Parameter estimate	LS Mean Difference
Point estimate	-0.6
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.3
upper limit	0.1

Statistical analysis title	Week 10 DCS Total Score: 50 mg gefapixant v PBO

Statistical analysis description:

Week 10 estimated treatment differences (gefapixant vs. placebo) and corresponding 95% CIs were estimated using a MMRM model, which included fixed effects for treatment group, visit, country, treatment-by-visit interaction, and Baseline value as a covariate.

Comparison groups	Placebo v Gefapixant 50 mg
Number of subjects included in analysis	118
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.1263
Method	Mixed Effect Repeated Measures model
Parameter estimate	LS Mean Difference
Point estimate	-0.5
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.2
upper limit	0.2

Secondary: Change from Baseline in Weekly Mean DCS at Week 11

End point title	Change from Baseline in Weekly Mean DCS at Week 11

End point description:

The DCS has a score ranging from 0 (best) to 10 (worst). Weekly mean daily score was defined as the average of the daily scores for each week. Baseline was defined as the average DCS score collected during the week prior to Day 1 (Day -7 to Day -1). Participants rated the severity of their cough using the DCS each day. LS mean change from baseline with associated SE reported for each treatment group.

All randomized participants who had taken at least 1 dose of study medication and provided at least 1 baseline and at least one post baseline endpoint observation during the treatment period were analysed.

End point type	Secondary

End point timeframe:

Baseline, Week 11

End point values	Placebo	Gefapixant 7.5 mg	Gefapixant 20 mg	Gefapixant 50 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	61	59	59	57
Units: score on a scale				
least squares mean (standard error)	-1.5 (± 0.25)	-1.8 (± 0.25)	-2.1 (± 0.25)	-2.2 (± 0.26)

Statistical analyses

Statistical analysis title	Week 11 DCS Total Score: 7.5 mg gefapixant v PBO

Statistical analysis description:

Week 11 estimated treatment differences (gefapixant vs. placebo) and corresponding 95% CIs were estimated using a MMRM model, which included fixed effects for treatment group, visit, country, treatment-by-visit interaction, and Baseline value as a covariate.

Comparison groups	Placebo v Gefapixant 7.5 mg
Number of subjects included in analysis	120
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.4058
Method	Mixed Effect Repeated Measures model
Parameter estimate	LS Mean Difference
Point estimate	-0.3
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1
upper limit	0.4

Statistical analysis title	Week 11 DCS Total Score: 20 mg gefapixant v PBO

Statistical analysis description:

Week 11 estimated treatment differences (gefapixant vs. placebo) and corresponding 95% CIs were estimated using a MMRM model, which included fixed effects for treatment group, visit, country, treatment-by-visit interaction, and Baseline value as a covariate.

Comparison groups	Placebo v Gefapixant 20 mg
Number of subjects included in analysis	120
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.0828
Method	Mixed Effect Repeated Measures model
Parameter estimate	LS Mean Difference
Point estimate	-0.6

Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.3
upper limit	0.1

Statistical analysis title	Week 11 DCS Total Score: 50 mg gefapixant v PBO

Statistical analysis description:

Week 11 estimated treatment differences (gefapixant vs. placebo) and corresponding 95% CIs were estimated using a MMRM model, which included fixed effects for treatment group, visit, country, treatment-by-visit interaction, and Baseline value as a covariate.

Comparison groups	Placebo v Gefapixant 50 mg
Number of subjects included in analysis	118
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.0575
Method	Mixed Effect Repeated Measures model
Parameter estimate	LS Mean Difference
Point estimate	-0.7
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.4
upper limit	0

Secondary: Change from Baseline in Weekly Mean DCS at Week 12

End point title	Change from Baseline in Weekly Mean DCS at Week 12

End point description:

The DCS has a score ranging from 0 (best) to 10 (worst). Weekly mean daily score was defined as the average of the daily scores for each week. Baseline was defined as the average DCS score collected during the week prior to Day 1 (Day -7 to Day -1). Participants rated the severity of their cough using the DCS each day. LS mean change from baseline with associated SE reported for each treatment group.

All randomized participants who had taken at least 1 dose of study medication and provided at least 1 baseline and at least one post baseline endpoint observation during the treatment period were analysed.

End point type	Secondary

End point timeframe:

Baseline, Week 12

End point values	Placebo	Gefapixant 7.5 mg	Gefapixant 20 mg	Gefapixant 50 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	61	59	59	57
Units: score on a scale				
least squares mean (standard error)	-1.5 (± 0.26)	-1.8 (± 0.26)	-2.2 (± 0.26)	-2.2 (± 0.27)

Statistical analyses

Statistical analysis title	Week 12 DCS Total Score: 7.5 mg gefapixant v PBO
Statistical analysis description:	
Week 12 estimated treatment differences (gefapixant vs. placebo) and corresponding 95% CIs were estimated using a MMRM model, which included fixed effects for treatment group, visit, country, treatment-by-visit interaction, and Baseline value as a covariate.	
Comparison groups	Placebo v Gefapixant 7.5 mg
Number of subjects included in analysis	120
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.4163
Method	Mixed Effect Repeated Measures model
Parameter estimate	LS Mean Difference
Point estimate	-0.3
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1
upper limit	0.4

Statistical analysis title	Week 12 DCS Total Score: 20 mg gefapixant v PBO
Statistical analysis description:	
Week 12 estimated treatment differences (gefapixant vs. placebo) and corresponding 95% CIs were estimated using a MMRM model, which included fixed effects for treatment group, visit, country, treatment-by-visit interaction, and Baseline value as a covariate.	
Comparison groups	Placebo v Gefapixant 20 mg
Number of subjects included in analysis	120
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.0882
Method	Mixed Effect Repeated Measures model
Parameter estimate	LS Mean Difference
Point estimate	-0.6
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.3
upper limit	0.1

Statistical analysis title	Week 12 DCS Total Score: 50 mg gefapixant v PBO

Statistical analysis description:

Week 12 estimated treatment differences (gefapixant vs. placebo) and corresponding 95% CIs were estimated using a MMRM model, which included fixed effects for treatment group, visit, country, treatment-by-visit interaction, and Baseline value as a covariate.

Comparison groups	Placebo v Gefapixant 50 mg
Number of subjects included in analysis	118
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.0961
Method	Mixed Effect Repeated Measures model
Parameter estimate	LS Mean Difference
Point estimate	-0.6
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.4
upper limit	0.1

Secondary: Change from Baseline in Leicester Cough Questionnaire (LCQ) Total Score after 4 Weeks of Treatment (Day 28)

End point title	Change from Baseline in Leicester Cough Questionnaire (LCQ) Total Score after 4 Weeks of Treatment (Day 28)

End point description:

The LCQ instrument is designed to assess the impact of cough on various aspects of a participant's life over the preceding 2 weeks. It consists of 19 items which are divided over 3 domains: Physical (items 1, 2, 3, 9, 10, 11, 14 and 15), Psychological (4, 5, 6, 12, 13, 16, and 17), and Social (7, 8, 18, 19). A 7-point Likert scale is used to rate each item. For each domain, the domain score (range 1-7) is the sum of the individual item scores within the domain divided by the number of items in the domain. The total score is the sum of the three domain scores and ranges from 3-21; a higher score corresponds to a better health status. Baseline LCQ was defined as the LCQ collected at Baseline (Study Day -1). LS mean change from baseline with associated SE reported for each treatment group.

All randomized participants who had taken ≥1 dose of study medication and provided ≥1 baseline and at least one post baseline endpoint observation during the treatment period were analysed.

End point type	Secondary

End point timeframe:

Baseline, Day 28

End point values	Placebo	Gefapixant 7.5 mg	Gefapixant 20 mg	Gefapixant 50 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	61	59	59	57
Units: score on a scale				
least squares mean (standard error)	2.1 (± 0.40)	2.9 (± 0.40)	2.3 (± 0.40)	4.2 (± 0.4)

Statistical analyses

Statistical analysis title	Day 28 LCQ Total Score: 7.5 mg gefapixant v PBO

Statistical analysis description:

Day 28 estimated treatment differences (gefapixant vs. placebo) and corresponding 95% CIs were estimated using a MMRM model, which included fixed effects for treatment group, visit, country, treatment-by-visit interaction, and Baseline value as a covariate.

Comparison groups	Placebo v Gefapixant 7.5 mg
Number of subjects included in analysis	120
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.163
Method	Mixed Effect Repeated Measures model
Parameter estimate	LS Mean Difference
Point estimate	0.8
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.3
upper limit	1.9

Statistical analysis title	Day 28 LCQ Total Score: 20 mg gefapixant v PBO

Statistical analysis description:

Day 28 estimated treatment differences (gefapixant vs. placebo) and corresponding 95% CIs were estimated using a MMRM model, which included fixed effects for treatment group, visit, country, treatment-by-visit interaction, and Baseline value as a covariate.

Comparison groups	Placebo v Gefapixant 20 mg
Number of subjects included in analysis	120
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.7601
Method	Mixed Effect Repeated Measures model
Parameter estimate	LS Mean Difference
Point estimate	0.2
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1
upper limit	1.3

Statistical analysis title	Day 28 LCQ Total Score: 50 mg gefapixant v PBO

Statistical analysis description:

Day 28 estimated treatment differences (gefapixant vs. placebo) and corresponding 95% CIs were estimated using a MMRM model, which included fixed effects for treatment group, visit, country, treatment-by-visit interaction, and Baseline value as a covariate.

Comparison groups	Placebo v Gefapixant 50 mg
Number of subjects included in analysis	118
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.0004
Method	Mixed Effect Repeated Measures model
Parameter estimate	LS Mean Difference
Point estimate	2.1
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.9
upper limit	3.2

Secondary: Change from Baseline in Leicester Cough Questionnaire (LCQ) Total Score after 8 Weeks of Treatment (Day 56)

End point title	Change from Baseline in Leicester Cough Questionnaire (LCQ) Total Score after 8 Weeks of Treatment (Day 56)

End point description:

The LCQ instrument is designed to assess the impact of cough on various aspects of a participant's life over the preceding 2 weeks. It consists of 19 items which are divided over 3 domains: Physical (items 1, 2, 3, 9, 10, 11, 14 and 15), Psychological (4, 5, 6, 12, 13, 16, and 17), and Social (7, 8, 18, 19). A 7-point Likert scale is used to rate each item. For each domain, the domain score (range 1-7) is the sum of the individual item scores within the domain divided by the number of items in the domain. The total score is the sum of the three domain scores and ranges from 3-21; a higher score corresponds to a better health status. Baseline LCQ was defined as the LCQ collected at Baseline (Study Day -1). LS mean change from baseline with associated SE reported for each treatment group.

All randomized participants who had taken ≥1 dose of study medication and provided ≥1 baseline and at least one post baseline endpoint observation during the treatment period were analysed.

End point type	Secondary

End point timeframe:

Baseline, Day 56

End point values	Placebo	Gefapixant 7.5 mg	Gefapixant 20 mg	Gefapixant 50 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	61	59	59	57
Units: score on a scale				
least squares mean (standard error)	2.0 (± 0.4)	3.1 (± 0.4)	3.0 (± 0.4)	3.5 (± 0.5)

Statistical analyses

Statistical analysis title	Day 56 LCQ Total Score: 7.5 mg gefapixant v PBO
Statistical analysis description:	
Day 56 estimated treatment differences (gefapixant vs. placebo) and corresponding 95% CIs were estimated using a MMRM model, which included fixed effects for treatment group, visit, country, treatment-by-visit interaction, and Baseline value as a covariate.	
Comparison groups	Placebo v Gefapixant 7.5 mg
Number of subjects included in analysis	120
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.0941
Method	Mixed Effect Repeated Measures model
Parameter estimate	LS Mean Difference
Point estimate	1
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.2
upper limit	2.3

Statistical analysis title	Day 56 LCQ Total Score: 20 mg gefapixant v PBO
Statistical analysis description:	
Day 56 estimated treatment differences (gefapixant vs. placebo) and corresponding 95% CIs were estimated using a MMRM model, which included fixed effects for treatment group, visit, country, treatment-by-visit interaction, and Baseline value as a covariate.	
Comparison groups	Placebo v Gefapixant 20 mg
Number of subjects included in analysis	120
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.1321
Method	Mixed Effect Repeated Measures model
Parameter estimate	LS Mean Difference
Point estimate	0.9
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.3
upper limit	2.2

Statistical analysis title	Day 56 LCQ Total Score: 50 mg gefapixant v PBO
Statistical analysis description:	
Day 56 estimated treatment differences (gefapixant vs. placebo) and corresponding 95% CIs were estimated using a MMRM model, which included fixed effects for treatment group, visit, country, treatment-by-visit interaction, and Baseline value as a covariate.	
Comparison groups	Placebo v Gefapixant 50 mg

Number of subjects included in analysis	118
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.0192
Method	Mixed Effect Repeated Measures model
Parameter estimate	LS Mean Difference
Point estimate	1.5
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.2
upper limit	2.7

Secondary: Change from Baseline in Leicester Cough Questionnaire (LCQ) Total Score At Day 85/Early Termination

End point title	Change from Baseline in Leicester Cough Questionnaire (LCQ) Total Score At Day 85/Early Termination

End point description:

The LCQ instrument is designed to assess the impact of cough on various aspects of a participant's life over the preceding 2 weeks. It consists of 19 items which are divided over 3 domains: Physical (items 1, 2, 3, 9, 10, 11, 14 and 15), Psychological (4, 5, 6, 12, 13, 16, and 17), and Social (7, 8, 18, 19). A 7-point Likert scale is used to rate each item. For each domain, the domain score (range 1-7) is the sum of the individual item scores within the domain divided by the number of items in the domain. The total score is the sum of the three domain scores and ranges from 3-21; a higher score corresponds to a better health status. Baseline LCQ was defined as the LCQ collected at Baseline (Study Day -1). LS mean change from baseline with associated SE reported for each treatment group.

All randomized participants who had taken ≥1 dose of study medication and provided ≥1 baseline and at least one post baseline endpoint observation during the treatment period were analysed.

End point type	Secondary

End point timeframe:

Baseline, Day 85/Early Termination

End point values	Placebo	Gefapixant 7.5 mg	Gefapixant 20 mg	Gefapixant 50 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	61	59	59	57
Units: score on a scale				
least squares mean (standard error)	2.1 (± 0.4)	3.3 (± 0.4)	3.2 (± 0.4)	4.0 (± 0.5)

Statistical analyses

Statistical analysis title	Day 85 LCQ Total Score: 7.5 mg gefapixant v PBO

Statistical analysis description:

Day 85/Early Termination estimated treatment differences (gefapixant vs. placebo) and corresponding 95% CIs were estimated using a MMRM model, which included fixed effects for treatment group, visit, country, treatment-by-visit interaction, and Baseline value as a covariate.

Comparison groups	Placebo v Gefapixant 7.5 mg

Number of subjects included in analysis	120
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.0626
Method	Mixed Effect Repeated Measures model
Parameter estimate	LS Mean Difference
Point estimate	1.2
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.1
upper limit	2.4

Statistical analysis title	Day 85 LCQ Total Score: 20 mg gefapixant v PBO

Statistical analysis description:

Day 85/Early Termination estimated treatment differences (gefapixant vs. placebo) and corresponding 95% CIs were estimated using a MMRM model, which included fixed effects for treatment group, visit, country, treatment-by-visit interaction, and Baseline value as a covariate.

Comparison groups	Placebo v Gefapixant 20 mg
Number of subjects included in analysis	120
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.0967
Method	Mixed Effect Repeated Measures model
Parameter estimate	LS Mean Difference
Point estimate	1
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.2
upper limit	2.3

Statistical analysis title	Day 85 LCQ Total Score: 50 mg gefapixant v PBO

Statistical analysis description:

Day 85/Early Termination estimated treatment differences (gefapixant vs. placebo) and corresponding 95% CIs were estimated using a MMRM model, which included fixed effects for treatment group, visit, country, treatment-by-visit interaction, and Baseline value as a covariate.

Comparison groups	Placebo v Gefapixant 50 mg
Number of subjects included in analysis	118
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.0028
Method	Mixed Effect Repeated Measures model
Parameter estimate	LS Mean Difference
Point estimate	1.9

Confidence interval	
level	95 %
sides	2-sided
lower limit	0.7
upper limit	3.1

Secondary: Percentage of Participants Reporting "Very Much Improved" or "Much Improved" According to the Patient's Global Impression of Change (PGIC) after 4 Weeks of Treatment (Day 28)

End point title	Percentage of Participants Reporting "Very Much Improved" or "Much Improved" According to the Patient's Global Impression of Change (PGIC) after 4 Weeks of Treatment (Day 28)

End point description:

The self-reported measure Patient's Global Impression of Change (PGIC) reflects a participant's belief about the efficacy of treatment. PGIC is a 7-point scale depicting a patient's rating of overall improvement. Participants rate their change as "very much improved," "much improved," "minimally improved," "no change," "minimally worse," "much worse," or "very much worse." The counts and percentages of ordered responses to the participant's global perception of change were computed for each treatment group on Day 28 and the percentage of participants with improvements (either "very much improved" or "much improved" on the PGIC scale) was reported for each treatment group.

All randomised participants who had taken at least 1 dose of study medication and provided at least 1 baseline and 1 Day 28 PGIC observation during the treatment period were analysed.

End point type	Secondary

End point timeframe:

Day 28

End point values	Placebo	Gefapixant 7.5 mg	Gefapixant 20 mg	Gefapixant 50 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	60	58	59	56
Units: percentage of participants				
number (not applicable)	30.0	37.9	35.6	46.4

Statistical analyses

Statistical analysis title	Day 28 PGIC: 7.5 mg gefapixant v PBO

Statistical analysis description:

The distribution of responses were compared between each of the gefapixant treatment groups and placebo using the stratified CMH test (stratified by country). P-values calculated using CMH test.

Comparison groups	Placebo v Gefapixant 7.5 mg
Number of subjects included in analysis	118
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.3182
Method	Cochran-Mantel-Haenszel

Statistical analysis title	Day 28 PGIC: 20 mg gefapixant v PBO

Statistical analysis description:

The distribution of responses were compared between each of the gefapixant treatment groups and placebo using the stratified CMH test (stratified by country). P-values calculated using CMH test.

Comparison groups	Placebo v Gefapixant 20 mg
Number of subjects included in analysis	119
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.5021
Method	Cochran-Mantel-Haenszel

Statistical analysis title	Day 28 PGIC: 50 mg gefapixant v PBO

Statistical analysis description:

The distribution of responses were compared between each of the gefapixant treatment groups and placebo using the stratified CMH test (stratified by country). P-values calculated using CMH test.

Comparison groups	Placebo v Gefapixant 50 mg
Number of subjects included in analysis	116
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.0665
Method	Cochran-Mantel-Haenszel

Secondary: Percentage of Participants Reporting “Very Much Improved” or “Much Improved” According to the PGIC after 8 Weeks of Treatment (Day 56)

End point title	Percentage of Participants Reporting “Very Much Improved” or “Much Improved” According to the PGIC after 8 Weeks of Treatment (Day 56)

End point description:

The self-reported measure Patient’s Global Impression of Change (PGIC) reflects a participant’s belief about the efficacy of treatment. PGIC is a 7-point scale depicting a patient's rating of overall improvement. Participants rate their change as “very much improved,” “much improved,” “minimally improved,” “no change,” “minimally worse,” “much worse,” or “very much worse.” The counts and percentages of ordered responses to the participant’s global perception of change were computed for each treatment group on Day 28 and the percentage of participants with improvements (either "very much improved" or "much improved" on the PGIC scale) was reported for each treatment group.

All randomised participants who had taken at least 1 dose of study medication and provided at least 1 baseline and 1 Day 56 PGIC observation during the treatment period were analysed.

End point type	Secondary

End point timeframe:

Day 56

End point values	Placebo	Gefapixant 7.5 mg	Gefapixant 20 mg	Gefapixant 50 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	58	58	59	51
Units: percentage of participants				
number (not applicable)	29.3	44.8	44.1	60.8

Statistical analyses

Statistical analysis title	Day 56 PGIC: 7.5 mg gefapixant v PBO
Statistical analysis description:	
The distribution of responses were compared between each of the gefapixant treatment groups and placebo using the stratified CMH test (stratified by country). P-values calculated using CMH test.	
Comparison groups	Placebo v Gefapixant 7.5 mg
Number of subjects included in analysis	116
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.0872
Method	Cochran-Mantel-Haenszel

Statistical analysis title	Day 56 PGIC: 20 mg gefapixant v PBO
Statistical analysis description:	
The distribution of responses were compared between each of the gefapixant treatment groups and placebo using the stratified CMH test (stratified by country). P-values calculated using CMH test.	
Comparison groups	Placebo v Gefapixant 20 mg
Number of subjects included in analysis	117
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.0994
Method	Cochran-Mantel-Haenszel

Statistical analysis title	Day 56 PGIC: 50 mg gefapixant v PBO
Statistical analysis description:	
The distribution of responses were compared between each of the gefapixant treatment groups and placebo using the stratified CMH test (stratified by country). P-values calculated using CMH test.	
Comparison groups	Placebo v Gefapixant 50 mg
Number of subjects included in analysis	109
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.0009
Method	Cochran-Mantel-Haenszel

Secondary: Percentage of Participants Reporting "Very Much Improved" or "Much

Improved" According to the PGIC at Day 85/Early Termination	
End point title	Percentage of Participants Reporting "Very Much Improved" or "Much Improved" According to the PGIC at Day 85/Early Termination

End point description:

The self-reported measure Patient's Global Impression of Change (PGIC) reflects a participant's belief about the efficacy of treatment. PGIC is a 7-point scale depicting a patient's rating of overall improvement. Participants rate their change as "very much improved," "much improved," "minimally improved," "no change," "minimally worse," "much worse," or "very much worse." The counts and percentages of ordered responses to the participant's global perception of change were computed for each treatment group on Day 28 and the percentage of participants with improvements (either "very much improved" or "much improved" on the PGIC scale) was reported for each treatment group.

All randomised participants who had taken at least 1 dose of study medication and provided at least 1 baseline and 1 Day 85 PGIC observation during the treatment period were analysed.

End point type	Secondary

End point timeframe:

Day 85/Early Termination

End point values	Placebo	Gefapixant 7.5 mg	Gefapixant 20 mg	Gefapixant 50 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	60	58	59	57
Units: percentage of participants				
number (not applicable)	28.3	53.4	49.2	64.9

Statistical analyses

Statistical analysis title	Day 85 PGIC: 7.5 mg gefapixant v PBO

Statistical analysis description:

The distribution of responses were compared between each of the gefapixant treatment groups and placebo using the stratified CMH test (stratified by country). P-values calculated using CMH test.

Comparison groups	Placebo v Gefapixant 7.5 mg
Number of subjects included in analysis	118
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.0037
Method	Cochran-Mantel-Haenszel

Statistical analysis title	Day 85 PGIC: 20 mg gefapixant v PBO

Statistical analysis description:

The distribution of responses were compared between each of the gefapixant treatment groups and placebo using the stratified CMH test (stratified by country). P-values calculated using CMH test.

Comparison groups	Placebo v Gefapixant 20 mg

Number of subjects included in analysis	119
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.0166
Method	Cochran-Mantel-Haenszel

Statistical analysis title	Day 85: 50 mg gefapixant v PBO

Statistical analysis description:

The distribution of responses were compared between each of the gefapixant treatment groups and placebo using the stratified CMH test (stratified by country). P-values calculated using CMH test.

Comparison groups	Placebo v Gefapixant 50 mg
Number of subjects included in analysis	117
Analysis specification	Pre-specified
Analysis type	
P-value	< 0.0001
Method	Cochran-Mantel-Haenszel

Secondary: Percentage of Participants Rated as "Very Much Improved" or "Much Improved" by Clinicians according to the Clinician's Global Impression of Change (CGIC) at Day 85/Early Termination

End point title	Percentage of Participants Rated as "Very Much Improved" or "Much Improved" by Clinicians according to the Clinician's Global Impression of Change (CGIC) at Day 85/Early Termination

End point description:

The Clinician's Global Impression of Change (CGIC) reflects a clinician's belief about the efficacy of treatment. CGIC is a 7-point scale depicting a clinician's rating of a participant's overall improvement. Clinicians rated the participant's change at Week 12 (Day 85) as "very much improved," "much improved," "minimally improved," "no change," "minimally worse," "much worse," or "very much worse." The counts and percentages of ordered responses to the clinician's global perception of change were computed for each treatment group, and the percentage of participants rated by clinicians as having improvement (either "very much improved" or "much improved" on the CGIC scale) was reported for each treatment group.

All randomised participants who had taken at least 1 dose of study medication and provided at least 1 baseline and 1 Day 85 CGIC observation during the treatment period were analysed.

End point type	Secondary

End point timeframe:

Day 85/Early Termination

End point values	Placebo	Gefapixant 7.5 mg	Gefapixant 20 mg	Gefapixant 50 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	60	58	59	57
Units: percentage of participants				
number (not applicable)	35.0	53.4	50.8	64.9

Statistical analyses

Statistical analysis title	Day 85 CGIC: 7.5 mg gefapixant v PBO
Statistical analysis description:	
The distribution of responses were compared between each of the gefapixant treatment groups and placebo using the stratified CMH test (stratified by country). P-values calculated using CMH test.	
Comparison groups	Placebo v Gefapixant 7.5 mg
Number of subjects included in analysis	118
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.0396
Method	Cochran-Mantel-Haenszel

Statistical analysis title	Day 85 CGIC: 20 mg gefapixant v PBO
Statistical analysis description:	
The distribution of responses were compared between each of the gefapixant treatment groups and placebo using the stratified CMH test (stratified by country). P-values calculated using CMH test.	
Comparison groups	Placebo v Gefapixant 20 mg
Number of subjects included in analysis	119
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.0751
Method	Cochran-Mantel-Haenszel

Statistical analysis title	Day 85 CGIC: 50 mg gefapixant v PBO
Statistical analysis description:	
The distribution of responses were compared between each of the gefapixant treatment groups and placebo using the stratified CMH test (stratified by country). P-values calculated using CMH test.	
Comparison groups	Placebo v Gefapixant 50 mg
Number of subjects included in analysis	117
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.001
Method	Cochran-Mantel-Haenszel

Secondary: Acceptability Questionnaire: Percentage of Participants That Were Likely to Take Study Medication For At Least One Year

End point title	Acceptability Questionnaire: Percentage of Participants That Were Likely to Take Study Medication For At Least One Year

End point description:

At the end of the treatment period (Day 85), participants were asked "How likely would you be to take this medication?" This question was asked in reference to the time frame of "At least one year". The counts and percentages of ordered categorical responses to this question were computed for each treatment group.

All randomised participants who had taken at least 1 dose of study medication and had available Acceptability Questionnaire data at Day 85 were analysed.

End point type	Secondary

End point timeframe:

Day 85/Early Termination

End point values	Placebo	Gefapixant 7.5 mg	Gefapixant 20 mg	Gefapixant 50 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	60	58	58	57
Units: percentage of participants				
number (not applicable)				
Extremely unlikely	3.3	6.9	5.2	1.8
Unlikely	3.3	1.7	3.4	12.3
Neither likely or unlikely	5.0	5.2	12.1	1.8
Likely	30.0	15.5	13.8	29.8
Extremely likely	58.3	70.7	65.5	54.4

Statistical analyses

Statistical analysis title	1 Year Acceptability: 7.5 mg gefapixant v PBO

Statistical analysis description:

The distribution of "Extremely likely" responses was compared between each of the gefapixant treatment groups and placebo using the stratified CMH test (stratified by country). P-values calculated for the gefapixant vs. placebo using CMH test.

Comparison groups	Placebo v Gefapixant 7.5 mg
Number of subjects included in analysis	118
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.8464
Method	Cochran-Mantel-Haenszel

Statistical analysis title	1 Year Acceptability: 50 mg gefapixant v PBO

Statistical analysis description:

The distribution of "Extremely likely" responses was compared between each of the gefapixant treatment groups and placebo using the stratified CMH test (stratified by country). P-values calculated for gefapixant vs. placebo using CMH test.

Comparison groups	Placebo v Gefapixant 50 mg

Number of subjects included in analysis	117
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.4364
Method	Cochran-Mantel-Haenszel

Statistical analysis title	1 Year Acceptability: 20 mg gefapixant v PBO

Statistical analysis description:

The distribution of "Extremely likely" responses was compared between each of the gefapixant treatment groups and placebo using the stratified CMH test (stratified by country). P-values calculated for gefapixant vs. placebo using CMH test.

Comparison groups	Placebo v Gefapixant 20 mg
Number of subjects included in analysis	118
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.7687
Method	Cochran-Mantel-Haenszel

Secondary: Acceptability Questionnaire: Percentage of Participants That Were Likely to Take Study Medication For At Least Six Months

End point title	Acceptability Questionnaire: Percentage of Participants That Were Likely to Take Study Medication For At Least Six Months

End point description:

At the end of the treatment period (Day 85), participants were asked "How likely would you be to take this medication?" This question was asked in reference to the time frame of "At least six months". The counts and percentages of ordered categorical responses to this question were computed for each treatment group.

All randomised participants who had taken at least 1 dose of study medication and had available Acceptability Questionnaire data at Day 85 were analysed.

End point type	Secondary

End point timeframe:

Day 85/Early Termination

End point values	Placebo	Gefapixant 7.5 mg	Gefapixant 20 mg	Gefapixant 50 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	60	57	58	57
Units: percentage of participants				
number (not applicable)				
Extremely unlikely	3.3	5.3	5.2	1.8
Unlikely	1.7	3.5	3.4	10.5
Neither likely or unlikely	6.7	3.5	6.9	3.5
Likely	21.7	14.0	17.2	29.8
Extremely likely	66.7	73.7	67.2	54.4

Statistical analyses

Statistical analysis title	6 Month Acceptability: 7.5 mg gefapixant v PBO

Statistical analysis description:

The distribution of "Extremely likely" responses were compared between each of the gefapixant treatment groups and placebo using the stratified CMH test (stratified by country). P-values calculated for gefapixant vs. placebo using CMH test.

Comparison groups	Placebo v Gefapixant 7.5 mg
Number of subjects included in analysis	117
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.9966
Method	Cochran-Mantel-Haenszel

Statistical analysis title	6 Month Acceptability: 50 mg gefapixant v PBO

Statistical analysis description:

The distribution of "Extremely likely" responses were compared between each of the gefapixant treatment groups and placebo using the stratified CMH test (stratified by country). P-values calculated for gefapixant vs. placebo using CMH test.

Comparison groups	Placebo v Gefapixant 50 mg
Number of subjects included in analysis	117
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.2155
Method	Cochran-Mantel-Haenszel

Statistical analysis title	6 Month Acceptability: 20 mg gefapixant v PBO

Statistical analysis description:

The distribution of "Extremely likely" responses were compared between each of the gefapixant treatment groups and placebo using the stratified CMH test (stratified by country). P-values calculated for gefapixant vs. placebo using CMH test.

Comparison groups	Placebo v Gefapixant 20 mg
Number of subjects included in analysis	118
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.6372
Method	Cochran-Mantel-Haenszel

Secondary: Acceptability Questionnaire: Percentage of Participants That Were Likely

to Take Study Medication For At Least Four Weeks	
End point title	Acceptability Questionnaire: Percentage of Participants That Were Likely to Take Study Medication For At Least Four Weeks

End point description:

At the end of the treatment period (Day 85), participants were asked "How likely would you be to take this medication?" This question was asked in reference to the time frame of "At least four weeks". The counts and percentages of ordered categorical responses to this question were computed for each treatment group.

All randomised participants who had taken at least 1 dose of study medication and had available Acceptability Questionnaire data at Day 85 were analysed.

End point type	Secondary

End point timeframe:

Day 85/Early Termination

End point values	Placebo	Gefapixant 7.5 mg	Gefapixant 20 mg	Gefapixant 50 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	60	58	58	57
Units: percentage of participants				
number (not applicable)				
Extremely unlikely	3.3	5.2	5.2	0.0
Unlikely	1.7	1.7	1.7	5.3
Neither likely or unlikely	3.3	1.7	6.9	8.8
Likely	18.3	19.0	15.5	26.3
Extremely likely	73.3	72.4	70.7	59.6

Statistical analyses

Statistical analysis title	4 Week Acceptability: 7.5 mg gefapixant v PBO

Statistical analysis description:

The distribution of "Extremely likely" responses were compared between each of the gefapixant treatment groups and placebo using the stratified CMH test (stratified by country). P-values calculated for gefapixant vs. placebo using CMH test.

Comparison groups	Placebo v Gefapixant 7.5 mg
Number of subjects included in analysis	118
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.7559
Method	Cochran-Mantel-Haenszel

Statistical analysis title	4 Week Acceptability: 50 mg gefapixant v PBO

Statistical analysis description:

The distribution of "Extremely likely" responses were compared between each of the gefapixant treatment groups and placebo using the stratified CMH test (stratified by country). P-values calculated for gefapixant vs. placebo using CMH test.

Comparison groups	Placebo v Gefapixant 50 mg

Number of subjects included in analysis	117
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.279
Method	Cochran-Mantel-Haenszel

Statistical analysis title	4 Week Acceptability: 20 mg gefapixant v PBO

Statistical analysis description:

The distribution of "Extremely likely" responses were compared between each of the gefapixant treatment groups and placebo using the stratified CMH test (stratified by country). P-values calculated for gefapixant vs. placebo using CMH test.

Comparison groups	Placebo v Gefapixant 20 mg
Number of subjects included in analysis	118
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.5091
Method	Cochran-Mantel-Haenszel

Secondary: Acceptability Questionnaire: Percentage of Participants That Were Likely to Take Study Medication Twice Daily

End point title	Acceptability Questionnaire: Percentage of Participants That Were Likely to Take Study Medication Twice Daily

End point description:

At the end of the treatment period (Day 85), participants were asked "How likely would you be to take this medication?" This question was asked in reference to the time frame of "Twice daily". The counts and percentages of ordered categorical responses to this question were computed for each treatment group.

All randomised participants who had taken at least 1 dose of study medication and had available Acceptability Questionnaire data at Day 85 were analysed.

End point type	Secondary

End point timeframe:

Day 85/Early Termination

End point values	Placebo	Gefapixant 7.5 mg	Gefapixant 20 mg	Gefapixant 50 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	60	57	57	56
Units: percentage of participants				
number (not applicable)				
Extremely unlikely	3.3	7.0	5.3	1.8
Unlikely	0.0	0.0	3.5	5.4
Neither likely or unlikely	3.3	5.3	3.5	8.9
Likely	20.0	15.8	22.8	30.4
Extremely likely	73.3	71.9	64.9	53.6

Statistical analyses

Statistical analysis title	Twice Daily Acceptability: 7.5 mg gefapixant v PBO

Statistical analysis description:

The distribution of "Extremely likely" responses were compared between each of the gefapixant treatment groups and placebo using the stratified CMH test (stratified by country). P-values calculated for gefapixant vs. placebo using CMH test.

Comparison groups	Placebo v Gefapixant 7.5 mg
Number of subjects included in analysis	117
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.3887
Method	Cochran-Mantel-Haenszel

Statistical analysis title	Twice Daily Acceptability: 20 mg gefapixant v PBO

Statistical analysis description:

The distribution of "Extremely likely" responses were compared between each of the gefapixant treatment groups and placebo using the stratified CMH test (stratified by country). P-values calculated for gefapixant vs. placebo using CMH test.

Comparison groups	Placebo v Gefapixant 20 mg
Number of subjects included in analysis	117
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.2333
Method	Cochran-Mantel-Haenszel

Statistical analysis title	Twice Daily Acceptability: 50 mg gefapixant v PBO

Statistical analysis description:

The distribution of "Extremely likely" responses were compared between each of the gefapixant treatment groups and placebo using the stratified CMH test (stratified by country). P-values calculated for gefapixant vs. placebo using CMH test.

Comparison groups	Placebo v Gefapixant 50 mg
Number of subjects included in analysis	116
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.0534
Method	Cochran-Mantel-Haenszel

Secondary: Taste Questionnaire: Percentage of Participants That Experienced Taste

Effect After Taking Medication by Frequency after 12 Weeks of Treatment (Day 84)

End point title	Taste Questionnaire: Percentage of Participants That Experienced Taste Effect After Taking Medication by Frequency after 12 Weeks of Treatment (Day 84)

End point description:

The tolerance to taste-related adverse events (AEs) was evaluated at the end of the study (Day 84) and a structured taste questionnaire was administered to participants experiencing a taste-related AE. Participants were asked to indicate the frequency that they experienced the taste effect by answering the question "How frequently do you experience the taste effect after taking each dose of medication?" The counts and percentages of categorical frequency responses to the individual items were computed for each treatment group.

All randomised participants who had taken at least 1 dose of study medication, who had experienced a taste-related AE, and who had Day 84 taste questionnaire data available were analysed.

End point type	Secondary

End point timeframe:

Day 84

End point values	Placebo	Gefapixant 7.5 mg	Gefapixant 20 mg	Gefapixant 50 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	57	56	57	51
Units: percentage of participants				
number (not applicable)				
No Taste Effect Noted	96.5	96.4	61.4	35.3
Never	1.8	0.0	0.0	0.0
Occasionally	1.8	1.8	8.8	0.0
Often	0.0	1.8	7.0	3.9
Almost Always	0.0	0.0	7.0	9.8
Always	0.0	0.0	15.8	51.0
No Taste Effect Noted + Never	98.2	96.4	61.4	35.3

Statistical analyses

Statistical analysis title	Taste Effect Frequency: 7.5 mg gefapixant v PBO

Statistical analysis description:

The distribution of "No Taste Effect Noted" or "Never" responses were compared between each of the gefapixant treatment groups and placebo using the stratified CMH test (stratified by country). P-values calculated for gefapixant vs. placebo using CMH test.

Comparison groups	Placebo v Gefapixant 7.5 mg
Number of subjects included in analysis	113
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.6115
Method	Cochran-Mantel-Haenszel

Statistical analysis title	Taste Effect Frequency: 20 mg gefapixant v PBO

Statistical analysis description:

The distribution of "No Taste Effect Noted" or "Never" responses were compared between each of the gefapixant treatment groups and placebo using the stratified CMH test (stratified by country). P-values calculated for gefapixant vs. placebo using CMH test.

Comparison groups	Placebo v Gefapixant 20 mg
Number of subjects included in analysis	114
Analysis specification	Pre-specified
Analysis type	
P-value	< 0.0001
Method	Cochran-Mantel-Haenszel

Statistical analysis title	Taste Effect Frequency: 50 mg gefapixant v PBO

Statistical analysis description:

The distribution of "No Taste Effect Noted" or "Never" responses were compared between each of the gefapixant treatment groups and placebo using the stratified CMH test (stratified by country). P-values calculated for gefapixant vs. placebo using CMH test.

Comparison groups	Placebo v Gefapixant 50 mg
Number of subjects included in analysis	108
Analysis specification	Pre-specified
Analysis type	
P-value	< 0.0001
Method	Cochran-Mantel-Haenszel

Secondary: Taste Questionnaire: Percentage of Participants That Found Taste Effect of Study Medication Bothersome after 12 Weeks of Treatment (Day 84)

End point title	Taste Questionnaire: Percentage of Participants That Found Taste Effect of Study Medication Bothersome after 12 Weeks of Treatment (Day 84)

End point description:

The tolerance to taste-related adverse events (AEs) was evaluated at the end of the study (Day 84) and a structured taste questionnaire was administered to participants experiencing a taste-related AE to determine what degree the participant found the taste effect bothersome by answering the question "How bothersome is the taste effect of the medication? The counts and percentages of categorical responses to the individual items were computed for each treatment group.

All randomised participants who had taken at least 1 dose of study medication, who had experienced a taste-related AE, and who had Day 84 taste questionnaire data available were analysed.

End point type	Secondary

End point timeframe:

Day 84

End point values	Placebo	Gefapixant 7.5 mg	Gefapixant 20 mg	Gefapixant 50 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	57	56	57	51
Units: percentage of participants				
number (not applicable)				
No Taste Effect Noted	96.5	96.4	61.4	35.3

Not At All	3.5	3.6	7.0	5.9
A Little	0.0	0.0	8.8	3.9
Somewhat	0.0	0.0	17.5	13.7
Very	0.0	0.0	5.3	29.4
Extremely	0.0	0.0	0.0	11.8
No Taste Effect Noted + Not At All	100.0	100.0	68.4	41.2

Statistical analyses

Statistical analysis title	Taste Effect Frequency: 7.5 mg gefapixant v PBO

Statistical analysis description:

The distribution of "No Taste Effect Noted" or "Not at All" responses were compared between each of the gefapixant treatment groups and placebo using the stratified CMH test (stratified by country). P-values calculated for gefapixant vs. placebo using CMH test.

Comparison groups	Placebo v Gefapixant 7.5 mg
Number of subjects included in analysis	113
Analysis specification	Pre-specified
Analysis type	
P-value	= 0 [1]
Method	Cochran-Mantel-Haenszel

Notes:

[1] - A p-value of zero was calculated if all participants (100%) had "No Taste Effect Noted" or "Not at All" responses in both comparison groups.

Statistical analysis title	Taste Effect Frequency: 20 mg gefapixant v PBO

Statistical analysis description:

The distribution of "No Taste Effect Noted" or "Not at All" responses were compared between each of the gefapixant treatment groups and placebo using the stratified CMH test (stratified by country). P-values calculated for gefapixant vs. placebo using CMH test.

Comparison groups	Placebo v Gefapixant 20 mg
Number of subjects included in analysis	114
Analysis specification	Pre-specified
Analysis type	
P-value	< 0.0001
Method	Cochran-Mantel-Haenszel

Statistical analysis title	Taste Effect Frequency: 50 mg gefapixant v PBO

Statistical analysis description:

The distribution of "No Taste Effect Noted" or "Not at All" responses were compared between each of the gefapixant treatment groups and placebo using the stratified CMH test (stratified by country). P-values calculated for gefapixant vs. placebo using CMH test.

Comparison groups	Placebo v Gefapixant 50 mg
Number of subjects included in analysis	108
Analysis specification	Pre-specified
Analysis type	
P-value	< 0.0001
Method	Cochran-Mantel-Haenszel

Adverse events

Adverse events information	
Timeframe for reporting adverse events:	
Up to ~14 weeks (Day 99)	
Adverse event reporting additional description:	
All randomised participants who received at least 1 dose of study drug. One participant randomised to receive 7.5 mg gefapixant was discontinued before receiving treatment.	
Assessment type	Systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	17.0

Reporting groups	
Reporting group title	Placebo
Reporting group description:	
Participants received one matching placebo tablet administered by mouth twice daily for 12 weeks.	
Reporting group title	Gefapixant 20 mg
Reporting group description:	
Participants received one 20 mg gefapixant tablet administered by mouth twice daily for 12 weeks.	
Reporting group title	Gefapixant 7.5 mg
Reporting group description:	
Participants received one 7.5 mg gefapixant tablet administered by mouth twice daily for 12 weeks.	
Reporting group title	Gefapixant 50 mg
Reporting group description:	
Participants received one 50 mg gefapixant tablet administered by mouth twice daily for 12 weeks.	

Serious adverse events	Placebo	Gefapixant 20 mg	Gefapixant 7.5 mg
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 63 (0.00%)	0 / 63 (0.00%)	0 / 63 (0.00%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Injury, poisoning and procedural complications			
Frostbite			
subjects affected / exposed	0 / 63 (0.00%)	0 / 63 (0.00%)	0 / 63 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	Gefapixant 50 mg		
Total subjects affected by serious adverse events			
subjects affected / exposed	1 / 63 (1.59%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events	0		

Injury, poisoning and procedural complications			
Frostbite			
subjects affected / exposed	1 / 63 (1.59%)		
occurrences causally related to treatment / all	2 / 2		
deaths causally related to treatment / all	0 / 0		

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

Non-serious adverse events	Placebo	Gefapixant 20 mg	Gefapixant 7.5 mg
Total subjects affected by non-serious adverse events			
subjects affected / exposed	21 / 63 (33.33%)	45 / 63 (71.43%)	26 / 63 (41.27%)
Investigations			
Blood creatine phosphokinase increased			
subjects affected / exposed	0 / 63 (0.00%)	2 / 63 (3.17%)	5 / 63 (7.94%)
occurrences (all)	0	2	5
Nervous system disorders			
Ageusia			
subjects affected / exposed	1 / 63 (1.59%)	3 / 63 (4.76%)	0 / 63 (0.00%)
occurrences (all)	1	3	0
Dysgeusia			
subjects affected / exposed	3 / 63 (4.76%)	21 / 63 (33.33%)	6 / 63 (9.52%)
occurrences (all)	4	26	7
Headache			
subjects affected / exposed	3 / 63 (4.76%)	12 / 63 (19.05%)	4 / 63 (6.35%)
occurrences (all)	4	16	4
Hypogeusia			
subjects affected / exposed	1 / 63 (1.59%)	11 / 63 (17.46%)	0 / 63 (0.00%)
occurrences (all)	1	12	0
Gastrointestinal disorders			
Dry mouth			
subjects affected / exposed	6 / 63 (9.52%)	3 / 63 (4.76%)	2 / 63 (3.17%)
occurrences (all)	7	3	2
Hypoaesthesia oral			
subjects affected / exposed	3 / 63 (4.76%)	4 / 63 (6.35%)	2 / 63 (3.17%)
occurrences (all)	4	4	2
Nausea			

subjects affected / exposed	0 / 63 (0.00%)	4 / 63 (6.35%)	0 / 63 (0.00%)
occurrences (all)	0	4	0
Paraesthesia oral			
subjects affected / exposed	5 / 63 (7.94%)	5 / 63 (7.94%)	4 / 63 (6.35%)
occurrences (all)	8	5	6
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	2 / 63 (3.17%)	5 / 63 (7.94%)	2 / 63 (3.17%)
occurrences (all)	2	5	3
Oropharyngeal pain			
subjects affected / exposed	2 / 63 (3.17%)	0 / 63 (0.00%)	1 / 63 (1.59%)
occurrences (all)	2	0	1
Infections and infestations			
Nasopharyngitis			
subjects affected / exposed	2 / 63 (3.17%)	4 / 63 (6.35%)	0 / 63 (0.00%)
occurrences (all)	3	4	0
Upper respiratory tract infection			
subjects affected / exposed	2 / 63 (3.17%)	9 / 63 (14.29%)	5 / 63 (7.94%)
occurrences (all)	2	9	5
Urinary tract infection			
subjects affected / exposed	2 / 63 (3.17%)	5 / 63 (7.94%)	3 / 63 (4.76%)
occurrences (all)	2	6	3

Non-serious adverse events	Gefapixant 50 mg		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	52 / 63 (82.54%)		
Investigations			
Blood creatine phosphokinase increased			
subjects affected / exposed	0 / 63 (0.00%)		
occurrences (all)	0		
Nervous system disorders			
Ageusia			
subjects affected / exposed	13 / 63 (20.63%)		
occurrences (all)	14		
Dysgeusia			

subjects affected / exposed	30 / 63 (47.62%)		
occurrences (all)	39		
Headache			
subjects affected / exposed	4 / 63 (6.35%)		
occurrences (all)	4		
Hypogeusia			
subjects affected / exposed	15 / 63 (23.81%)		
occurrences (all)	18		
Gastrointestinal disorders			
Dry mouth			
subjects affected / exposed	3 / 63 (4.76%)		
occurrences (all)	3		
Hypoaesthesia oral			
subjects affected / exposed	5 / 63 (7.94%)		
occurrences (all)	5		
Nausea			
subjects affected / exposed	6 / 63 (9.52%)		
occurrences (all)	6		
Paraesthesia oral			
subjects affected / exposed	4 / 63 (6.35%)		
occurrences (all)	4		
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	5 / 63 (7.94%)		
occurrences (all)	5		
Oropharyngeal pain			
subjects affected / exposed	4 / 63 (6.35%)		
occurrences (all)	4		
Infections and infestations			
Nasopharyngitis			
subjects affected / exposed	0 / 63 (0.00%)		
occurrences (all)	0		
Upper respiratory tract infection			
subjects affected / exposed	6 / 63 (9.52%)		
occurrences (all)	6		
Urinary tract infection			

subjects affected / exposed occurrences (all)	2 / 63 (3.17%) 3		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
22 December 2015	Amendment 1 (AM1) included revisions to inclusion and exclusion criteria, revisions to Subject Discontinuation criteria, and addition of Interactive Web Response System (IWRS) as a randomization method. AM1 also revised the selection and timing of dose for each subject, revised the primary endpoint to specify "after 4 weeks (Day 28)", and removed the safety assessment for renal/urological AEs.
11 March 2016	AM2 included revisions to inclusion and exclusion criteria and to the Prohibited Concomitant Therapy section, and updated the Independent Data Monitoring Committee section of the protocol.
04 November 2016	AM3 removed the Week 4 timepoint from the primary objective and primary endpoint, and moved this timepoint to the Secondary Objectives/Endpoints. AM3 also revised the Secondary Objectives and divided the Secondary Endpoints into "key" and "other" categories. The statistical sections were also updated to reflect the changes made to the primary endpoint and primary analysis. This protocol amendment aligned key aspects of the statistical section of the study protocol with the statistical analysis plan. These revisions to the protocol, which provided additional detail and specificity of the planned analyses in order to facilitate the validity of the conclusions from the trial, were finalized after Last Subject Last Visit (LSLV) but prior to database lock, as was the statistical analysis plan. These changes did not result in any changes to the conduct of the trial. AM3 was approved on 15 December 2016, but due to system limitations, the Global End of Trial Date (LSLV) was imputed as the Amendment Date.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported