Clinical trial results:
A Phase 3, Randomized, Double-Blind, Placebo-Controlled, 12-Month Study to Evaluate the Efficacy and Safety of MK-7264 in Adult Participants with Chronic Cough (PN030)

Summary

EudraCT number	2017-003559-49
Trial protocol	CZ DE DK PL GB HU IT
Global end of trial date	30 October 2020

Results information

Result version number	v1 (current)
This version publication date	08 October 2021
First version publication date	08 October 2021

Trial information

Trial identification

Sponsor protocol code	MK-7264-030

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT03449147
WHO universal trial number (UTN)	-

Notes:

Sponsors

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

Notes:

Paediatric regulatory details

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

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	30 October 2020
Is this the analysis of the primary completion data?	Yes
Primary completion date	20 August 2020
Global end of trial reached?	Yes
Global end of trial date	30 October 2020
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The primary objective of this study will be to evaluate the efficacy of gefapixant (MK-7264) in reducing cough frequency as measured over a 24-hour period. It is hypothesized that at least one dose of gefapixant is superior to placebo in reducing coughs per hour (over 24 hours) at Week 24. This study will have a main 24-week treatment period and a 28-week extension period of treatment. Participants at selected sites and countries who complete the main and extension study periods may consent to participate in an observational, 3-month, Off-treatment Durability Study Period.

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 March 2018
Long term follow-up planned	Yes
Long term follow-up rationale	Safety
Long term follow-up duration	3 Months
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Australia: 33
Country: Number of subjects enrolled	Canada: 76
Country: Number of subjects enrolled	China: 4
Country: Number of subjects enrolled	Colombia: 100
Country: Number of subjects enrolled	Czechia: 45
Country: Number of subjects enrolled	Denmark: 26
Country: Number of subjects enrolled	Germany: 65
Country: Number of subjects enrolled	Guatemala: 52
Country: Number of subjects enrolled	Hungary: 45
Country: Number of subjects enrolled	Israel: 14
Country: Number of subjects enrolled	Italy: 17
Country: Number of subjects enrolled	Malaysia: 6
Country: Number of subjects enrolled	New Zealand: 38
Country: Number of subjects enrolled	Peru: 72
Country: Number of subjects enrolled	Poland: 115

Country: Number of subjects enrolled	South Africa: 46
Country: Number of subjects enrolled	Turkey: 42
Country: Number of subjects enrolled	Ukraine: 118
Country: Number of subjects enrolled	United Kingdom: 184
Country: Number of subjects enrolled	United States: 219
Worldwide total number of subjects	1317
EEA total number of subjects	313

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)	883
From 65 to 84 years	432
85 years and over	2

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

1317 participants were randomized to the 52-week treatment period, and 1314 participants received at least 1 dose of study intervention. After the main study, 122 participants continued in an optional Off-Treatment observational study period (no treatment).

Period 1

Period 1 title	52-week Treatment Period
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator

Arms

Are arms mutually exclusive?	Yes
Arm title	Placebo

Arm description:

Participants received dose-matched placebo tablets twice daily (BID) during the 24-week main study period and 28-week extension period.

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

Dosage and administration details:

Placebo tablet administered orally BID

Arm title	Gefapixant 15 mg BID

Arm description:

Participants received a gefapixant 15 mg tablet and placebo tablet to match gefapixant 45 mg BID during the 24-week main study period and 28-week extension period.

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

Dosage and administration details:

Placebo tablet administered orally BID

Investigational medicinal product name	Gefapixant 15 mg BID
Investigational medicinal product code	
Other name	MK-7264
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Gefapixant 15 mg tablet administered orally BID

Arm title	Gefapixant 45 mg BID

Arm description:

Participants received a gefapixant 45 mg tablet and placebo tablet to match gefapixant 15 mg BID during the 24-week main study period and 28-week extension period.

Arm type	Experimental
Investigational medicinal product name	Gefapixant 45 mg BID
Investigational medicinal product code	
Other name	MK-7264
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Gefapixant 45 mg tablet administered orally BID

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

Dosage and administration details:

Placebo tablet administered orally BID

Number of subjects in period 1	Placebo	Gefapixant 15 mg BID	Gefapixant 45 mg BID
Started	436	442	439
Completed	382	368	355
Not completed	54	74	84
Physician decision	1	-	3
Consent withdrawn by subject	46	68	74
Screen Failure	1	2	-
Death	-	1	-
Unknown	-	1	2
Lost to follow-up	6	2	5

Period 2

Period 2 title	12-Week Off-Treatment Durability Period
Is this the baseline period?	No
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator

Arms

Are arms mutually exclusive?	Yes

Arm title	Placebo

Arm description:

Participants received dose-matched placebo tablets twice daily (BID) during the 24-week main study period and 28-week extension period.

Arm type	No intervention

No investigational medicinal product assigned in this arm

Arm title	Gefapixant 15 mg BID

Arm description:

Participants received a gefapixant 15 mg tablet and placebo tablet to match gefapixant 45 mg BID during the 24-week main study period and 28-week extension period.

Arm type	No intervention

No investigational medicinal product assigned in this arm

Arm title	Gefapixant 45 mg BID

Arm description:

Participants received a gefapixant 45 mg tablet and placebo tablet to match gefapixant 15 mg BID during the 24-week main study period and 28-week extension period.

Arm type	No intervention

No investigational medicinal product assigned in this arm

Number of subjects in period 2[1]	Placebo	Gefapixant 15 mg BID	Gefapixant 45 mg BID
Started	48	37	37
Completed	47	36	37
Not completed	1	1	0
Consent withdrawn by subject	1	-	-
Unknown	-	1	-

Notes:

[1] - The number of subjects starting the period is not consistent with the number completing the preceding period. It is expected the number of subjects starting the subsequent period will be the same as the number completing the preceding period.
Justification: Not all participants completing the preceding period continued in the optional Off-Treatment Period.

Baseline characteristics

Reporting groups	
Reporting group title	Placebo
Reporting group description:	
Participants received dose-matched placebo tablets twice daily (BID) during the 24-week main study period and 28-week extension period.	
Reporting group title	Gefapixant 15 mg BID
Reporting group description:	
Participants received a gefapixant 15 mg tablet and placebo tablet to match gefapixant 45 mg BID during the 24-week main study period and 28-week extension period.	
Reporting group title	Gefapixant 45 mg BID
Reporting group description:	
Participants received a gefapixant 45 mg tablet and placebo tablet to match gefapixant 15 mg BID during the 24-week main study period and 28-week extension period.	

Reporting group values	Placebo	Gefapixant 15 mg BID	Gefapixant 45 mg BID
Number of subjects	436	442	439
Age categorical Units: Subjects			
In utero	0	0	0
Preterm newborn infants (gestational age < 37 wks)	0	0	0
Newborns (0-27 days)	0	0	0
Infants and toddlers (28 days-23 months)	0	0	0
Children (2-11 years)	0	0	0
Adolescents (12-17 years)	0	0	0
Adults (18-64 years)	292	298	293
From 65-84 years	144	143	145
85 years and over	0	1	1
Age Continuous Units: Years			
arithmetic mean	58.4	58.4	57.8
standard deviation	± 12.5	± 11.3	± 12.4
Sex: Female, Male Units: Participants			
Female	326	331	329
Male	110	111	110
Race (NIH/OMB) Units: Subjects			
American Indian or Alaska Native	20	28	24
Asian	15	14	15
Native Hawaiian or Other Pacific Islander	4	2	3
Black or African American	5	9	14
White	356	358	346
More than one race	36	31	37
Unknown or Not Reported	0	0	0
Ethnicity (NIH/OMB)			

Units: Subjects			
Hispanic or Latino	85	93	89
Not Hispanic or Latino	348	347	344
Unknown or Not Reported	3	2	6
Baseline 24-Hour Coughs Per Hour			
24-hour coughs per hour is defined as the average hourly cough frequency based on 24-hour sound recordings using a digital recording device (cough monitor). The measure analysis population included all participants with 24-hour coughs per hour data available at baseline (n=1297).			
Units: Coughs/Hour			
arithmetic mean	27.45	26.82	26.84
standard deviation	± 24.44	± 21.25	± 27.04

Reporting group values	Total		
Number of subjects	1317		
Age categorical Units: Subjects			
In utero	0		
Preterm newborn infants (gestational age < 37 wks)	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)	883		
From 65-84 years	432		
85 years and over	2		
Age Continuous Units: Years			
arithmetic mean			
standard deviation	-		
Sex: Female, Male Units: Participants			
Female	986		
Male	331		
Race (NIH/OMB) Units: Subjects			
American Indian or Alaska Native	72		
Asian	44		
Native Hawaiian or Other Pacific Islander	9		
Black or African American	28		
White	1060		
More than one race	104		
Unknown or Not Reported	0		
Ethnicity (NIH/OMB) Units: Subjects			
Hispanic or Latino	267		
Not Hispanic or Latino	1039		
Unknown or Not Reported	11		
Baseline 24-Hour Coughs Per Hour			
24-hour coughs per hour is defined as the average hourly cough frequency based on 24-hour sound recordings using a digital recording device (cough monitor). The measure analysis population included			

all participants with 24-hour coughs per hour data available at baseline (n=1297).			
Units: Coughs/Hour arithmetic mean standard deviation	- -		

End points

End points reporting groups

Reporting group title	Placebo
Reporting group description:	
Participants received dose-matched placebo tablets twice daily (BID) during the 24-week main study period and 28-week extension period.	
Reporting group title	Gefapixant 15 mg BID
Reporting group description:	
Participants received a gefapixant 15 mg tablet and placebo tablet to match gefapixant 45 mg BID during the 24-week main study period and 28-week extension period.	
Reporting group title	Gefapixant 45 mg BID
Reporting group description:	
Participants received a gefapixant 45 mg tablet and placebo tablet to match gefapixant 15 mg BID during the 24-week main study period and 28-week extension period.	
Reporting group title	Placebo
Reporting group description:	
Participants received dose-matched placebo tablets twice daily (BID) during the 24-week main study period and 28-week extension period.	
Reporting group title	Gefapixant 15 mg BID
Reporting group description:	
Participants received a gefapixant 15 mg tablet and placebo tablet to match gefapixant 45 mg BID during the 24-week main study period and 28-week extension period.	
Reporting group title	Gefapixant 45 mg BID
Reporting group description:	
Participants received a gefapixant 45 mg tablet and placebo tablet to match gefapixant 15 mg BID during the 24-week main study period and 28-week extension period.	
Subject analysis set title	Placebo
Subject analysis set type	Safety analysis
Subject analysis set description:	
Participants received dose-matched placebo tablets twice daily (BID) during the 24-week main study period and 28-week extension period.	
Subject analysis set title	Gefapixant 15 mg BID
Subject analysis set type	Safety analysis
Subject analysis set description:	
Participants received a gefapixant 15 mg tablet and placebo tablet to match gefapixant 45 mg BID during the 24-week main study period and 28-week extension period.	
Subject analysis set title	Gefapixant 45 mg
Subject analysis set type	Safety analysis
Subject analysis set description:	
Participants received a gefapixant 45 mg tablet and placebo tablet to match gefapixant 15 mg BID during the 24-week main study period and 28-week extension period.	

Primary: Model-Based Geometric Mean Ratio (GMR) of 24-Hour Coughs per Hour at Week 24/Baseline

End point title	Model-Based Geometric Mean Ratio (GMR) of 24-Hour Coughs per Hour at Week 24/Baseline

End point description:

24-hour coughs per hour was defined as the average hourly cough frequency based on 24-hour sound recordings using a digital recording device (cough monitor). A longitudinal analysis of covariance (ANCOVA) model was applied to log-transformed cough data to determine geometric mean (GM) 24-hour coughs per hour at baseline and week 24. The GMR (Week 24 GM 24-hour coughs per hour divided by Baseline GM 24-hour coughs per hour) is reported. The population analyzed included all randomized participants who took at least 1 dose of study intervention, had available 24-hour cough data at baseline and at least one available post-baseline measurement during the treatment period.

End point type	Primary

End point timeframe:

Baseline, Week 24

End point values	Placebo	Gefapixant 15 mg BID	Gefapixant 45 mg BID	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	419	415	409	
Units: Ratio				
geometric mean (confidence interval 95%)	0.43 (0.39 to 0.48)	0.43 (0.38 to 0.47)	0.37 (0.33 to 0.41)	

Statistical analyses

Statistical analysis title	Difference in 24-Hour Coughs per Hour at Week 24

Statistical analysis description:

Estimated relative reduction (ERR) relative to Placebo (i.e. estimated percent change difference) was calculated by 100 (e**DIFF -1), where e = exponent of difference; and DIFF= treatment difference in change from baseline at Week 24 based on log transformed data.

Comparison groups	Placebo v Gefapixant 15 mg BID
Number of subjects included in analysis	834
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.875 [1]
Method	ANCOVA
Parameter estimate	Estimated Relative Reduction (%)
Point estimate	-1.14
Confidence interval	
level	95 %
sides	2-sided
lower limit	-14.27
upper limit	14.02

Notes:

[1] - Comparison based on a longitudinal ANCOVA model that included treatment, visit, treatment-by-visit interaction, gender, region, log-transformed baseline value, and log-transformed baseline value-by-visit as covariates.

Statistical analysis title	Difference in 24-Hour Coughs Per Hour at Week 24

Statistical analysis description:

ERR relative to Placebo (i.e. estimated percent change difference) was calculated by 100 (e**DIFF -1), where e = exponent of difference; and DIFF= treatment difference in change from baseline at Week 24 based on log transformed data.

Comparison groups	Placebo v Gefapixant 45 mg BID

Number of subjects included in analysis	828
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.031 [2]
Method	ANCOVA
Parameter estimate	Estimated Relative Reduction (%)
Point estimate	-14.64
Confidence interval	
level	95 %
sides	2-sided
lower limit	-26.07
upper limit	-1.43

Notes:

[2] - Comparison based on a longitudinal ANCOVA model that included treatment, visit, treatment-by-visit interaction, gender, region, log-transformed baseline value, and log-transformed baseline value-by-visit as covariates.

Primary: Number of Participants Who Experienced At Least One Adverse Event (AE) During Treatment and Follow-up

End point title	Number of Participants Who Experienced At Least One Adverse Event (AE) During Treatment and Follow-up[3]

End point description:

An AE is any untoward medical occurrence in a clinical study participant, temporally associated with the use of study intervention, whether or not considered related to the study intervention. An AE can therefore be any unfavorable and unintended sign (including an abnormal laboratory finding), symptom, or disease (new or exacerbated) temporally associated with the use of a study intervention. The population analyzed included all randomized participants who received at least one dose of study intervention during the 52-week treatment period. Per protocol, participants in the optional off-treatment observational period were not included. 3 participants randomized to placebo group who took 1 or more incorrect dose(s) of study drug were counted in the higher dose group of gefapixant received: 2 participants were analyzed in the gefapixant 15 mg group and 1 was analyzed in the gefapixant 45 mg group.

End point type	Primary

End point timeframe:

Up to 54 Weeks

Notes:

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

End point values	Placebo	Gefapixant 15 mg BID	Gefapixant 45 mg	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	432	442	440	
Units: Participants	349	373	399	

Statistical analyses

No statistical analyses for this end point

Primary: Number of Participants Who Discontinued a Study Drug Due to an AE

End point title	Number of Participants Who Discontinued a Study Drug Due to an AE[4]

End point description:

An AE is any untoward medical occurrence in a clinical study participant, temporally associated with the use of study intervention, whether or not considered related to the study intervention. An AE can therefore be any unfavorable and unintended sign (including an abnormal laboratory finding), symptom, or disease (new or exacerbated) temporally associated with the use of a study intervention. The population analyzed included all randomized participants who received at least one dose of study intervention during the 52-week treatment period. Per protocol, participants in the optional off-treatment observational period were not included. 3 participants randomized to placebo group who took 1 or more incorrect dose(s) of study drug were counted in the higher dose group of gefapixant received: 2 participants were analyzed in the gefapixant 15 mg group and 1 was analyzed in the gefapixant 45 mg group.

End point type	Primary

End point timeframe:

Up to 52 weeks

Notes:

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

End point values	Placebo	Gefapixant 15 mg BID	Gefapixant 45 mg	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	432	442	440	
Units: Participants	25	40	100	

Statistical analyses

No statistical analyses for this end point

Secondary: Model-Based GMR of Awake Coughs Per Hour at Week 24/Baseline

End point title	Model-Based GMR of Awake Coughs Per Hour at Week 24/Baseline

End point description:

Awake coughs per hour was defined as the average hourly cough frequency while the participant is awake, based on a 24-hour interval of sound recordings using a digital recording device (cough monitor). ANCOVA model was applied to log-transformed cough data to determine GM of awake coughs per hour at baseline and week 24. The GMR (Week 24 GM awake coughs per hour divided by Baseline GM awake coughs per hour) is reported. The population analyzed included all randomized participants who took at least 1 dose of study intervention, had available awake 24-hour cough data at baseline and at least one available post-baseline measurement during the treatment period.

End point type	Secondary

End point timeframe:

Baseline, Week 24

End point values	Placebo	Gefapixant 15 mg BID	Gefapixant 45 mg BID	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	419	415	409	
Units: Ratio				
geometric mean (confidence interval 95%)	0.42 (0.38 to 0.47)	0.41 (0.37 to 0.46)	0.36 (0.32 to 0.40)	

Statistical analyses

Statistical analysis title	Difference in Awake Coughs per Hour at Week 24

Statistical analysis description:

ERR relative to Placebo (i.e. estimated percent change difference) was calculated by 100 (e**DIFF -1), where e = exponent of difference; and DIFF= treatment difference in change from baseline at Week 24 based on log transformed data.

Comparison groups	Placebo v Gefapixant 45 mg BID
Number of subjects included in analysis	828
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.022 [5]
Method	ANCOVA
Parameter estimate	Estimated Relative Reduction (%)
Point estimate	-15.79
Confidence interval	
level	95 %
sides	2-sided
lower limit	-27.27
upper limit	-2.5

Notes:

[5] - Comparison based on a longitudinal ANCOVA model that included treatment, visit, treatment-by-visit interaction, gender, region, log-transformed baseline value, and log-transformed baseline value-by-visit as covariates.

Statistical analysis title	Difference in Awake Coughs per Hour at Week 24

Statistical analysis description:

Estimated relative reduction (ERR) relative to Placebo (i.e. estimated percent change difference) was calculated by 100 (e**DIFF -1), where e = exponent of difference; and DIFF= treatment difference in change from baseline at Week 24 based on log transformed data.

Comparison groups	Placebo v Gefapixant 15 mg BID
Number of subjects included in analysis	834
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.677 [6]
Method	ANCOVA
Parameter estimate	Estimated Relative Reduction (%)
Point estimate	-3.03
Confidence interval	
level	95 %
sides	2-sided
lower limit	-16.14
upper limit	12.12

Notes:

[6] - Comparison based on a longitudinal ANCOVA model that included treatment, visit, treatment-by-visit interaction, gender, region, log-transformed baseline value, and log-transformed baseline value-by-visit as covariates.

Secondary: Percentage of Participants With a ≥1.3 Point Change From Baseline in the Leicester Questionnaire (LCQ) Total Score at Week 24

End point title	Percentage of Participants With a ≥1.3 Point Change From Baseline in the Leicester Questionnaire (LCQ) Total Score at Week 24

End point description:

The 19-item LCQ assessed the impact of chronic cough in three health-related quality of life (HRQoL) domains (physical, social and psychological). The LCQ is calculated as a mean score for each domain ranging from 1 to 7, with a total score ranging from 3 to 21. Higher scores indicate better HRQoL. A clinically meaningful improvement from baseline in HRQoL was defined as ≥1.3-point increase in the LCQ total score at Week 24. The percentage of participants (logistic regression model-based) with a ≥1.3-point increase in the LCQ total score at Week 24 is presented. The population analyzed included all randomized participants who had taken at least 1 dose of study intervention, had available LCQ data at baseline, and at least one available post-baseline measurement in the treatment period.

End point type	Secondary

End point timeframe:

Baseline, Week 24

End point values	Placebo	Gefapixant 15 mg BID	Gefapixant 45 mg BID	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	406	404	399	
Units: Percentage of Participants				
number (not applicable)	70.1	75.9	76.8	

Statistical analyses

Statistical analysis title	Difference in Percentage of Participants
Comparison groups	Placebo v Gefapixant 15 mg BID
Number of subjects included in analysis	810
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.077 [7]
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	1.34
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.97
upper limit	1.85

Notes:

[7] - Comparison based on logistic regression model that included treatment, visit, treatment-by-visit interaction, gender, region, baseline LCQ total score, and the interaction of baseline LCQ total score by visit as covariates.

Statistical analysis title	Difference in Percentage of Participants
Comparison groups	Placebo v Gefapixant 45 mg BID

Number of subjects included in analysis	805
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.04 [8]
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	1.41
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.02
upper limit	1.96

Notes:

[8] - Comparison based on logistic regression model that included treatment, visit, treatment-by-visit interaction, gender, region, baseline LCQ total score, and the interaction of baseline LCQ total score by visit as covariates.

Secondary: Percentage of Participants With a ≤-30% Change From Baseline in 24-hour Coughs Per Hour at Week 24

End point title	Percentage of Participants With a ≤-30% Change From Baseline in 24-hour Coughs Per Hour at Week 24

End point description:

24-hour coughs per hour was defined as the average hourly cough frequency based on 24-hour sound recordings using a digital recording device (cough monitor). A clinically meaningful improvement from baseline is defined as a ≤-30% change (≥30% reduction) in 24-hour coughs per hour at week 24. The percentage of participants (logistic regression model-based) with a ≤ -30% change from baseline in 24-hour coughs per hour at Week 24 (≥30% reduction from baseline) is presented. The population analyzed included all randomized participants who took at least 1 dose of study intervention, had available 24-hour cough data at baseline and at least one available post-baseline measurement in the treatment period.

End point type	Secondary

End point timeframe:

Baseline, Week 24

End point values	Placebo	Gefapixant 15 mg BID	Gefapixant 45 mg BID	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	419	415	409	
Units: Percentage of Participants				
number (not applicable)	66.9	67.4	72.9	

Statistical analyses

Statistical analysis title	Difference in Percentage of Participants
Comparison groups	Placebo v Gefapixant 15 mg BID

Number of subjects included in analysis	834
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.872 [9]
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	1.03
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.75
upper limit	1.4

Notes:

[9] - Comparison based on a logistic regression model that included treatment, visit, treatment-by-visit interaction, gender, region, baseline 24-hour coughs per hour and the interaction of baseline 24-hour coughs per hour as covariates.

Statistical analysis title	Difference in Percentage of Participants
Comparison groups	Placebo v Gefapixant 45 mg BID
Number of subjects included in analysis	828
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.082 [10]
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	1.33
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.96
upper limit	1.83

Notes:

[10] - Comparison based on a logistic regression model that included treatment, visit, treatment-by-visit interaction, gender, region, baseline 24-hour coughs per hour and the interaction of baseline 24-hour coughs per hour as covariates.

Secondary: Percentage of Participants with ≤-1.3 Point Change From Baseline of Mean Weekly Cough Severity Diary (CSD) Total Score at Week 24

End point title	Percentage of Participants with ≤-1.3 Point Change From Baseline of Mean Weekly Cough Severity Diary (CSD) Total Score at Week 24

End point description:

The 7-item CSD was used to record participants' daily cough frequency, cough intensity, and disruption due to cough. Each item was rated on an 11-point scale ranging from 0 (best) to 10 (worst); the total daily CSD score was the sum of these seven item scores (Min=0, Max=70). Mean weekly CSD total score was defined as the average of the mean total daily scores collected during the week prior to each visit. The percentage of participants (logistic regression model-based) with a ≤-1.3 point change from baseline in CSD at Week 24 (or ≥1.3 point reduction from baseline) is reported. The population analyzed included all randomized participants who had taken at least 1 dose of study intervention, had available CSD data at baseline, and at least one available post-baseline measurement in the treatment period.

End point type	Secondary

End point timeframe:

Baseline, Week 24

End point values	Placebo	Gefapixant 15 mg BID	Gefapixant 45 mg BID	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	428	426	425	
Units: Percentage of Participants				
number (not applicable)	69.1	74.8	77.1	

Statistical analyses

Statistical analysis title	Difference in Percentage of Participants
Statistical analysis description:	
Comparison based on a logistic regression model that included treatment, visit, treatment-by-visit interaction, gender, region, baseline mean weekly CSD total score, and the interaction of baseline mean weekly CSD total score by visit as covariates.	
Comparison groups	Placebo v Gefapixant 45 mg BID
Number of subjects included in analysis	853
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Odds ratio (OR)
Point estimate	1.5
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.08
upper limit	2.09

Statistical analysis title	Difference in Percentage of Participants
Statistical analysis description:	
Comparison based on a logistic regression model that included treatment, visit, treatment-by-visit interaction, gender, region, baseline mean weekly CSD total score, and the interaction of baseline mean weekly CSD total score by visit as covariates.	
Comparison groups	Placebo v Gefapixant 15 mg BID
Number of subjects included in analysis	854
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Odds ratio (OR)
Point estimate	1.33
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.96
upper limit	1.83

Secondary: Percentage of Participants with ≤-2.7 Point Change From Baseline of Mean Weekly CSD Total Score at Week 24

End point title	Percentage of Participants with ≤-2.7 Point Change From Baseline of Mean Weekly CSD Total Score at Week 24

End point description:

The 7-item CSD was used to record participants' daily cough frequency, cough intensity, and disruption due to cough. Each item was rated on an 11-point scale ranging from 0 (best) to 10 (worst); the total daily CSD score was the sum of these seven item scores (Min=0, Max=70). Mean weekly CSD total score was defined as the average of the mean total daily scores collected during the week prior to each visit. The percentage of participants (logistic regression model-based) with a ≤-2.7 point change from baseline in CSD at Week 24 (or ≥2.7 point reduction from baseline) is reported. The population analyzed included all randomized participants who had taken at least 1 dose of study intervention, had available CSD data at baseline, and at least one available post-baseline measurement in the treatment period.

End point type	Secondary

End point timeframe:

Baseline, Week 24

End point values	Placebo	Gefapixant 15 mg BID	Gefapixant 45 mg BID	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	428	426	425	
Units: Percentage of Participants				
number (not applicable)	41.0	46.6	55.2	

Statistical analyses

Statistical analysis title	Difference in Percentage of Participants

Statistical analysis description:

Comparison based on a logistic regression model that included treatment, visit, treatment-by-visit interaction, gender, region, baseline mean weekly CSD total score, and the interaction of baseline mean weekly CSD total score by visit as covariates.

Comparison groups	Placebo v Gefapixant 45 mg BID
Number of subjects included in analysis	853
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Odds ratio (OR)
Point estimate	1.77
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.31
upper limit	2.39

	Difference in Percentage of Participants

Statistical analysis title	

Statistical analysis description:

Comparison based on a logistic regression model that included treatment, visit, treatment-by-visit interaction, gender, region, baseline mean weekly CSD total score, and the interaction of baseline mean weekly CSD total score by visit as covariates.

Comparison groups	Placebo v Gefapixant 15 mg BID
Number of subjects included in analysis	854
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Odds ratio (OR)
Point estimate	1.25
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.93
upper limit	1.69

Secondary: Percentage of Participants With a ≤-30 Millimeter (mm) Change From Baseline in Cough Severity Visual Analog Scale (VAS) Score at Week 24

End point title	Percentage of Participants With a ≤-30 Millimeter (mm) Change From Baseline in Cough Severity Visual Analog Scale (VAS) Score at Week 24

End point description:

The VAS is a single-item questionnaire with the response on a 100-point scale ranging from 0 ("No Cough") to 100 ("Extremely Severe Cough"). Mean weekly VAS score was defined as the average of the VAS scores collected during the week prior to each visit. The percentage of participants (logistic regression model-based) with a ≤-30 mm change from baseline in cough severity VAS score at Week 24 is reported. The population analyzed included all randomized participants who had taken at least 1 dose of study intervention, had available VAS data at baseline, and at least one available post-baseline measurement in the treatment period.

End point type	Secondary

End point timeframe:

Baseline, Week 24

End point values	Placebo	Gefapixant 15 mg BID	Gefapixant 45 mg BID	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	428	426	425	
Units: Percentage of participants				
number (not applicable)	40.9	51.4	53.3	

Statistical analyses

Statistical analysis title	Difference in Percentage of Partcipants

Statistical analysis description:

Comparison based on a logistic regression model that included treatment, visit, treatment-by-visit interaction, gender, region, baseline mean weekly VAS score, and the interaction of baseline mean

weekly VAS score by visit as covariates.

Comparison groups	Placebo v Gefapixant 45 mg BID
Number of subjects included in analysis	853
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Odds ratio (OR)
Point estimate	1.65
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.23
upper limit	2.22

Statistical analysis title	Difference in Percentage of Participants

Statistical analysis description:

Comparison based on a logistic regression model that included treatment, visit, treatment-by-visit interaction, gender, region, baseline mean weekly VAS score, and the interaction of baseline mean weekly VAS score by visit as covariates.

Comparison groups	Placebo v Gefapixant 15 mg BID
Number of subjects included in analysis	854
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Odds ratio (OR)
Point estimate	1.53
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.14
upper limit	2.05

Adverse events

Adverse events information

Timeframe for reporting adverse events:

On-Treatment Period: Up to Week 54; Off-Treatment (Off-Tx) Period: From Week 52 through Week 64 (approximately 12 weeks)

Adverse event reporting additional description:

AE reporting groups include all randomized participants who took ≥1 one dose of study drug. In the treatment period, 3 participants randomized to placebo who took ≥1 incorrect dose(s) of study drug were counted as follows: 2 participants were analyzed in the gefapixant 15 mg arm and 1 in the gefapixant 45 mg arm.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	23.0, 23.1

Reporting groups

Reporting group title	Placebo: On Tx

Reporting group description:

Participants received dose-matched placebo tablets twice daily (BID) during the 24-week main study period and 28-week extension period.

Reporting group title	Gefapixant 15 mg BID: On Tx

Reporting group description:

Participants received a gefapixant 15 mg tablet and placebo tablet to match gefapixant 45 mg BID during the 24-week main study period and 28-week extension period.

Reporting group title	Gefapixant 15 mg BID: Off Tx

Reporting group description:

Participants previously treated with gefapixant 15 mg BID for 52 weeks during the main study and extension study periods were observed for up to 3 months during an optional Off-Treatment Durability study period (participants received no treatment).

Reporting group title	Placebo: Off Tx

Reporting group description:

Participants previously treated with dose-matched placebo BID for 52 weeks during the main study and extension study periods were observed for up to 3 months during an optional Off-Treatment Durability study period (participants received no treatment).

Reporting group title	Gefapixant 45 mg BID: Off Tx

Reporting group description:

Participants previously treated with gefapixant BID for 52 weeks during the main study and extension study periods were observed for up to 3 months during an optional Off-Treatment Durability study period (participants received no treatment).

Reporting group title	Gefapixant 45 mg BID: On Tx

Reporting group description:

Participants received a gefapixant 45 mg tablet and placebo tablet to match gefapixant 15 mg BID during the 24-week main study period and 28-week extension period.

Serious adverse events	Placebo: On Tx	Gefapixant 15 mg BID: On Tx	Gefapixant 15 mg BID: Off Tx
Total subjects affected by serious adverse events			
subjects affected / exposed	25 / 432 (5.79%)	24 / 442 (5.43%)	0 / 37 (0.00%)
number of deaths (all causes)	0	1	0
number of deaths resulting from adverse events	0	0	0

Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Basal cell carcinoma			
subjects affected / exposed	0 / 432 (0.00%)	1 / 442 (0.23%)	0 / 37 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Colon cancer metastatic			
subjects affected / exposed	0 / 432 (0.00%)	1 / 442 (0.23%)	0 / 37 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Salivary gland neoplasm			
subjects affected / exposed	1 / 432 (0.23%)	0 / 442 (0.00%)	0 / 37 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Spinal meningioma benign			
subjects affected / exposed	0 / 432 (0.00%)	0 / 442 (0.00%)	0 / 37 (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
Uterine leiomyoma			
subjects affected / exposed	0 / 432 (0.00%)	1 / 442 (0.23%)	0 / 37 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vascular disorders			
Aortic dissection			
subjects affected / exposed	1 / 432 (0.23%)	0 / 442 (0.00%)	0 / 37 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypertensive crisis			
subjects affected / exposed	0 / 432 (0.00%)	1 / 442 (0.23%)	0 / 37 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Orthostatic hypotension			
subjects affected / exposed	0 / 432 (0.00%)	0 / 442 (0.00%)	0 / 37 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

General disorders and administration site conditions			
Pyrexia			
subjects affected / exposed	1 / 432 (0.23%)	0 / 442 (0.00%)	0 / 37 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			
Asthma			
subjects affected / exposed	1 / 432 (0.23%)	1 / 442 (0.23%)	0 / 37 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bronchial hyperreactivity			
subjects affected / exposed	1 / 432 (0.23%)	0 / 442 (0.00%)	0 / 37 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cough			
subjects affected / exposed	0 / 432 (0.00%)	0 / 442 (0.00%)	0 / 37 (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
Idiopathic pulmonary fibrosis			
subjects affected / exposed	1 / 432 (0.23%)	0 / 442 (0.00%)	0 / 37 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Laryngeal stenosis			
subjects affected / exposed	2 / 432 (0.46%)	0 / 442 (0.00%)	0 / 37 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pulmonary embolism			
subjects affected / exposed	0 / 432 (0.00%)	1 / 442 (0.23%)	0 / 37 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pulmonary fibrosis			

subjects affected / exposed	1 / 432 (0.23%)	0 / 442 (0.00%)	0 / 37 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Psychiatric disorders			
Confusional state			
subjects affected / exposed	1 / 432 (0.23%)	0 / 442 (0.00%)	0 / 37 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Stress			
subjects affected / exposed	0 / 432 (0.00%)	1 / 442 (0.23%)	0 / 37 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Suicide attempt			
subjects affected / exposed	1 / 432 (0.23%)	0 / 442 (0.00%)	0 / 37 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Injury, poisoning and procedural complications			
Ankle fracture			
subjects affected / exposed	0 / 432 (0.00%)	1 / 442 (0.23%)	0 / 37 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cervical vertebral fracture			
subjects affected / exposed	1 / 432 (0.23%)	0 / 442 (0.00%)	0 / 37 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Concussion			
subjects affected / exposed	0 / 432 (0.00%)	0 / 442 (0.00%)	0 / 37 (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
Disinfectant poisoning			
subjects affected / exposed	0 / 432 (0.00%)	0 / 442 (0.00%)	0 / 37 (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

Ligament injury			
subjects affected / exposed	0 / 432 (0.00%)	1 / 442 (0.23%)	0 / 37 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Procedural pain			
subjects affected / exposed	0 / 432 (0.00%)	0 / 442 (0.00%)	0 / 37 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Rib fracture			
subjects affected / exposed	1 / 432 (0.23%)	0 / 442 (0.00%)	0 / 37 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Sternal fracture			
subjects affected / exposed	1 / 432 (0.23%)	0 / 442 (0.00%)	0 / 37 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Stress fracture			
subjects affected / exposed	0 / 432 (0.00%)	0 / 442 (0.00%)	0 / 37 (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
Upper limb fracture			
subjects affected / exposed	0 / 432 (0.00%)	0 / 442 (0.00%)	0 / 37 (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
Wrist fracture			
subjects affected / exposed	1 / 432 (0.23%)	0 / 442 (0.00%)	0 / 37 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Congenital, familial and genetic disorders			
Congenital choroid plexus cyst			
subjects affected / exposed	0 / 432 (0.00%)	1 / 442 (0.23%)	0 / 37 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Cardiac disorders			
Arrhythmia			
subjects affected / exposed	0 / 432 (0.00%)	0 / 442 (0.00%)	0 / 37 (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
Atrial fibrillation			
subjects affected / exposed	0 / 432 (0.00%)	0 / 442 (0.00%)	0 / 37 (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
Cardiopulmonary failure			
subjects affected / exposed	0 / 432 (0.00%)	1 / 442 (0.23%)	0 / 37 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
Myocardial infarction			
subjects affected / exposed	1 / 432 (0.23%)	0 / 442 (0.00%)	0 / 37 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Myocardial ischaemia			
subjects affected / exposed	0 / 432 (0.00%)	0 / 442 (0.00%)	0 / 37 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nervous system disorders			
Cerebrospinal fluid leakage			
subjects affected / exposed	0 / 432 (0.00%)	1 / 442 (0.23%)	0 / 37 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cerebrovascular accident			
subjects affected / exposed	0 / 432 (0.00%)	1 / 442 (0.23%)	0 / 37 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypertensive encephalopathy			
subjects affected / exposed	1 / 432 (0.23%)	0 / 442 (0.00%)	0 / 37 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Migraine			
subjects affected / exposed	0 / 432 (0.00%)	1 / 442 (0.23%)	0 / 37 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Myasthenia gravis			
subjects affected / exposed	0 / 432 (0.00%)	0 / 442 (0.00%)	0 / 37 (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
Syncope			
subjects affected / exposed	1 / 432 (0.23%)	0 / 442 (0.00%)	0 / 37 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Transient ischaemic attack			
subjects affected / exposed	0 / 432 (0.00%)	1 / 442 (0.23%)	0 / 37 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood and lymphatic system disorders			
Leukopenia			
subjects affected / exposed	0 / 432 (0.00%)	0 / 442 (0.00%)	0 / 37 (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
Eye disorders			
Cataract			
subjects affected / exposed	0 / 432 (0.00%)	0 / 442 (0.00%)	0 / 37 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Constipation			
subjects affected / exposed	0 / 432 (0.00%)	1 / 442 (0.23%)	0 / 37 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastritis			

subjects affected / exposed	2 / 432 (0.46%)	0 / 442 (0.00%)	0 / 37 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Small intestinal obstruction			
subjects affected / exposed	0 / 432 (0.00%)	0 / 442 (0.00%)	0 / 37 (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
Umbilical hernia			
subjects affected / exposed	0 / 432 (0.00%)	1 / 442 (0.23%)	0 / 37 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatobiliary disorders			
Bile duct stone			
subjects affected / exposed	0 / 432 (0.00%)	1 / 442 (0.23%)	0 / 37 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal and urinary disorders			
Nephrolithiasis			
subjects affected / exposed	0 / 432 (0.00%)	0 / 442 (0.00%)	0 / 37 (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
Urinary retention			
subjects affected / exposed	0 / 432 (0.00%)	1 / 442 (0.23%)	0 / 37 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	0 / 432 (0.00%)	0 / 442 (0.00%)	0 / 37 (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
Groin pain			
subjects affected / exposed	0 / 432 (0.00%)	1 / 442 (0.23%)	0 / 37 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Intervertebral disc protrusion			
subjects affected / exposed	0 / 432 (0.00%)	1 / 442 (0.23%)	0 / 37 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Muscle twitching			
subjects affected / exposed	0 / 432 (0.00%)	1 / 442 (0.23%)	0 / 37 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Osteoarthritis			
subjects affected / exposed	1 / 432 (0.23%)	0 / 442 (0.00%)	0 / 37 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Rotator cuff syndrome			
subjects affected / exposed	0 / 432 (0.00%)	0 / 442 (0.00%)	0 / 37 (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
Spinal stenosis			
subjects affected / exposed	1 / 432 (0.23%)	1 / 442 (0.23%)	0 / 37 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Spondylolisthesis			
subjects affected / exposed	0 / 432 (0.00%)	0 / 442 (0.00%)	0 / 37 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Bronchitis			
subjects affected / exposed	1 / 432 (0.23%)	0 / 442 (0.00%)	0 / 37 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
COVID-19 pneumonia			
subjects affected / exposed	1 / 432 (0.23%)	0 / 442 (0.00%)	0 / 37 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Chronic tonsillitis			

subjects affected / exposed	0 / 432 (0.00%)	1 / 442 (0.23%)	0 / 37 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Diverticulitis			
subjects affected / exposed	1 / 432 (0.23%)	0 / 442 (0.00%)	0 / 37 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastroenteritis			
subjects affected / exposed	1 / 432 (0.23%)	0 / 442 (0.00%)	0 / 37 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Influenza			
subjects affected / exposed	0 / 432 (0.00%)	2 / 442 (0.45%)	0 / 37 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lung abscess			
subjects affected / exposed	1 / 432 (0.23%)	0 / 442 (0.00%)	0 / 37 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Osteomyelitis			
subjects affected / exposed	0 / 432 (0.00%)	0 / 442 (0.00%)	0 / 37 (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
Pneumonia			
subjects affected / exposed	0 / 432 (0.00%)	3 / 442 (0.68%)	0 / 37 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 3	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia bacterial			
subjects affected / exposed	0 / 432 (0.00%)	1 / 442 (0.23%)	0 / 37 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory tract infection			

subjects affected / exposed	1 / 432 (0.23%)	0 / 442 (0.00%)	0 / 37 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Tonsillitis bacterial			
subjects affected / exposed	0 / 432 (0.00%)	0 / 442 (0.00%)	0 / 37 (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
Upper respiratory tract infection			
subjects affected / exposed	1 / 432 (0.23%)	0 / 442 (0.00%)	0 / 37 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Urinary tract infection enterococcal			
subjects affected / exposed	0 / 432 (0.00%)	0 / 442 (0.00%)	0 / 37 (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
Urosepsis			
subjects affected / exposed	2 / 432 (0.46%)	0 / 442 (0.00%)	0 / 37 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vulval abscess			
subjects affected / exposed	0 / 432 (0.00%)	0 / 442 (0.00%)	0 / 37 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metabolism and nutrition disorders			
Hypoglycaemia			
subjects affected / exposed	0 / 432 (0.00%)	0 / 442 (0.00%)	0 / 37 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	Placebo: Off Tx	Gefapixant 45 mg BID: Off Tx	Gefapixant 45 mg BID: On Tx
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 48 (0.00%)	1 / 37 (2.70%)	25 / 440 (5.68%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0

Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Basal cell carcinoma			
subjects affected / exposed	0 / 48 (0.00%)	0 / 37 (0.00%)	0 / 440 (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
Colon cancer metastatic			
subjects affected / exposed	0 / 48 (0.00%)	0 / 37 (0.00%)	0 / 440 (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
Salivary gland neoplasm			
subjects affected / exposed	0 / 48 (0.00%)	0 / 37 (0.00%)	0 / 440 (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
Spinal meningioma benign			
subjects affected / exposed	0 / 48 (0.00%)	0 / 37 (0.00%)	1 / 440 (0.23%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Uterine leiomyoma			
subjects affected / exposed	0 / 48 (0.00%)	0 / 37 (0.00%)	0 / 440 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vascular disorders			
Aortic dissection			
subjects affected / exposed	0 / 48 (0.00%)	0 / 37 (0.00%)	0 / 440 (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
Hypertensive crisis			
subjects affected / exposed	0 / 48 (0.00%)	0 / 37 (0.00%)	0 / 440 (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
Orthostatic hypotension			
subjects affected / exposed	0 / 48 (0.00%)	0 / 37 (0.00%)	1 / 440 (0.23%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

General disorders and administration site conditions			
Pyrexia			
subjects affected / exposed	0 / 48 (0.00%)	0 / 37 (0.00%)	0 / 440 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			
Asthma			
subjects affected / exposed	0 / 48 (0.00%)	0 / 37 (0.00%)	1 / 440 (0.23%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bronchial hyperreactivity			
subjects affected / exposed	0 / 48 (0.00%)	0 / 37 (0.00%)	0 / 440 (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
Cough			
subjects affected / exposed	0 / 48 (0.00%)	0 / 37 (0.00%)	1 / 440 (0.23%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Idiopathic pulmonary fibrosis			
subjects affected / exposed	0 / 48 (0.00%)	0 / 37 (0.00%)	0 / 440 (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
Laryngeal stenosis			
subjects affected / exposed	0 / 48 (0.00%)	0 / 37 (0.00%)	0 / 440 (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
Pulmonary embolism			
subjects affected / exposed	0 / 48 (0.00%)	0 / 37 (0.00%)	1 / 440 (0.23%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pulmonary fibrosis			

subjects affected / exposed	0 / 48 (0.00%)	0 / 37 (0.00%)	0 / 440 (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
Psychiatric disorders			
Confusional state			
subjects affected / exposed	0 / 48 (0.00%)	0 / 37 (0.00%)	0 / 440 (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
Stress			
subjects affected / exposed	0 / 48 (0.00%)	0 / 37 (0.00%)	0 / 440 (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
Suicide attempt			
subjects affected / exposed	0 / 48 (0.00%)	0 / 37 (0.00%)	0 / 440 (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
Injury, poisoning and procedural complications			
Ankle fracture			
subjects affected / exposed	0 / 48 (0.00%)	0 / 37 (0.00%)	0 / 440 (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
Cervical vertebral fracture			
subjects affected / exposed	0 / 48 (0.00%)	0 / 37 (0.00%)	0 / 440 (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
Concussion			
subjects affected / exposed	0 / 48 (0.00%)	0 / 37 (0.00%)	1 / 440 (0.23%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Disinfectant poisoning			
subjects affected / exposed	0 / 48 (0.00%)	0 / 37 (0.00%)	1 / 440 (0.23%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Ligament injury			
subjects affected / exposed	0 / 48 (0.00%)	0 / 37 (0.00%)	0 / 440 (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
Procedural pain			
subjects affected / exposed	0 / 48 (0.00%)	0 / 37 (0.00%)	1 / 440 (0.23%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Rib fracture			
subjects affected / exposed	0 / 48 (0.00%)	0 / 37 (0.00%)	0 / 440 (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
Sternal fracture			
subjects affected / exposed	0 / 48 (0.00%)	0 / 37 (0.00%)	0 / 440 (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
Stress fracture			
subjects affected / exposed	0 / 48 (0.00%)	0 / 37 (0.00%)	1 / 440 (0.23%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Upper limb fracture			
subjects affected / exposed	0 / 48 (0.00%)	0 / 37 (0.00%)	1 / 440 (0.23%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Wrist fracture			
subjects affected / exposed	0 / 48 (0.00%)	0 / 37 (0.00%)	0 / 440 (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
Congenital, familial and genetic disorders			
Congenital choroid plexus cyst			
subjects affected / exposed	0 / 48 (0.00%)	0 / 37 (0.00%)	0 / 440 (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

Cardiac disorders			
Arrhythmia			
subjects affected / exposed	0 / 48 (0.00%)	1 / 37 (2.70%)	0 / 440 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Atrial fibrillation			
subjects affected / exposed	0 / 48 (0.00%)	0 / 37 (0.00%)	1 / 440 (0.23%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiopulmonary failure			
subjects affected / exposed	0 / 48 (0.00%)	0 / 37 (0.00%)	0 / 440 (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
Myocardial infarction			
subjects affected / exposed	0 / 48 (0.00%)	0 / 37 (0.00%)	0 / 440 (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
Myocardial ischaemia			
subjects affected / exposed	0 / 48 (0.00%)	0 / 37 (0.00%)	1 / 440 (0.23%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nervous system disorders			
Cerebrospinal fluid leakage			
subjects affected / exposed	0 / 48 (0.00%)	0 / 37 (0.00%)	0 / 440 (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
Cerebrovascular accident			
subjects affected / exposed	0 / 48 (0.00%)	0 / 37 (0.00%)	0 / 440 (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
Hypertensive encephalopathy			
subjects affected / exposed	0 / 48 (0.00%)	0 / 37 (0.00%)	0 / 440 (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

Migraine			
subjects affected / exposed	0 / 48 (0.00%)	0 / 37 (0.00%)	0 / 440 (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
Myasthenia gravis			
subjects affected / exposed	0 / 48 (0.00%)	0 / 37 (0.00%)	1 / 440 (0.23%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Syncope			
subjects affected / exposed	0 / 48 (0.00%)	0 / 37 (0.00%)	0 / 440 (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
Transient ischaemic attack			
subjects affected / exposed	0 / 48 (0.00%)	0 / 37 (0.00%)	0 / 440 (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
Blood and lymphatic system disorders			
Leukopenia			
subjects affected / exposed	0 / 48 (0.00%)	0 / 37 (0.00%)	1 / 440 (0.23%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Eye disorders			
Cataract			
subjects affected / exposed	0 / 48 (0.00%)	0 / 37 (0.00%)	1 / 440 (0.23%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Constipation			
subjects affected / exposed	0 / 48 (0.00%)	0 / 37 (0.00%)	0 / 440 (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
Gastritis			

subjects affected / exposed	0 / 48 (0.00%)	0 / 37 (0.00%)	0 / 440 (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
Small intestinal obstruction			
subjects affected / exposed	0 / 48 (0.00%)	0 / 37 (0.00%)	1 / 440 (0.23%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Umbilical hernia			
subjects affected / exposed	0 / 48 (0.00%)	0 / 37 (0.00%)	0 / 440 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatobiliary disorders			
Bile duct stone			
subjects affected / exposed	0 / 48 (0.00%)	0 / 37 (0.00%)	0 / 440 (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
Renal and urinary disorders			
Nephrolithiasis			
subjects affected / exposed	0 / 48 (0.00%)	0 / 37 (0.00%)	1 / 440 (0.23%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Urinary retention			
subjects affected / exposed	0 / 48 (0.00%)	0 / 37 (0.00%)	0 / 440 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	0 / 48 (0.00%)	0 / 37 (0.00%)	1 / 440 (0.23%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Groin pain			
subjects affected / exposed	0 / 48 (0.00%)	0 / 37 (0.00%)	0 / 440 (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

Intervertebral disc protrusion			
subjects affected / exposed	0 / 48 (0.00%)	0 / 37 (0.00%)	0 / 440 (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
Muscle twitching			
subjects affected / exposed	0 / 48 (0.00%)	0 / 37 (0.00%)	0 / 440 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Osteoarthritis			
subjects affected / exposed	0 / 48 (0.00%)	0 / 37 (0.00%)	1 / 440 (0.23%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Rotator cuff syndrome			
subjects affected / exposed	0 / 48 (0.00%)	0 / 37 (0.00%)	1 / 440 (0.23%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Spinal stenosis			
subjects affected / exposed	0 / 48 (0.00%)	0 / 37 (0.00%)	0 / 440 (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
Spondylolisthesis			
subjects affected / exposed	0 / 48 (0.00%)	0 / 37 (0.00%)	1 / 440 (0.23%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Bronchitis			
subjects affected / exposed	0 / 48 (0.00%)	0 / 37 (0.00%)	0 / 440 (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
COVID-19 pneumonia			
subjects affected / exposed	0 / 48 (0.00%)	0 / 37 (0.00%)	0 / 440 (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
Chronic tonsillitis			

subjects affected / exposed	0 / 48 (0.00%)	0 / 37 (0.00%)	0 / 440 (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
Diverticulitis			
subjects affected / exposed	0 / 48 (0.00%)	0 / 37 (0.00%)	0 / 440 (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
Gastroenteritis			
subjects affected / exposed	0 / 48 (0.00%)	0 / 37 (0.00%)	0 / 440 (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
Influenza			
subjects affected / exposed	0 / 48 (0.00%)	0 / 37 (0.00%)	0 / 440 (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
Lung abscess			
subjects affected / exposed	0 / 48 (0.00%)	0 / 37 (0.00%)	0 / 440 (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
Osteomyelitis			
subjects affected / exposed	0 / 48 (0.00%)	0 / 37 (0.00%)	1 / 440 (0.23%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia			
subjects affected / exposed	0 / 48 (0.00%)	0 / 37 (0.00%)	1 / 440 (0.23%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia bacterial			
subjects affected / exposed	0 / 48 (0.00%)	0 / 37 (0.00%)	0 / 440 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory tract infection			

subjects affected / exposed	0 / 48 (0.00%)	0 / 37 (0.00%)	0 / 440 (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
Tonsillitis bacterial			
subjects affected / exposed	0 / 48 (0.00%)	0 / 37 (0.00%)	1 / 440 (0.23%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Upper respiratory tract infection			
subjects affected / exposed	0 / 48 (0.00%)	0 / 37 (0.00%)	0 / 440 (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
Urinary tract infection enterococcal			
subjects affected / exposed	0 / 48 (0.00%)	0 / 37 (0.00%)	1 / 440 (0.23%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Urosepsis			
subjects affected / exposed	0 / 48 (0.00%)	0 / 37 (0.00%)	0 / 440 (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
Vulval abscess			
subjects affected / exposed	0 / 48 (0.00%)	0 / 37 (0.00%)	1 / 440 (0.23%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metabolism and nutrition disorders			
Hypoglycaemia			
subjects affected / exposed	0 / 48 (0.00%)	0 / 37 (0.00%)	1 / 440 (0.23%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

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

Non-serious adverse events	Placebo: On Tx	Gefapixant 15 mg BID: On Tx	Gefapixant 15 mg BID: Off Tx
Total subjects affected by non-serious adverse events			
subjects affected / exposed	248 / 432 (57.41%)	290 / 442 (65.61%)	3 / 37 (8.11%)
Nervous system disorders			
Ageusia			
subjects affected / exposed	6 / 432 (1.39%)	13 / 442 (2.94%)	0 / 37 (0.00%)
occurrences (all)	6	14	0
Dysgeusia			
subjects affected / exposed	28 / 432 (6.48%)	56 / 442 (12.67%)	0 / 37 (0.00%)
occurrences (all)	30	64	0
Headache			
subjects affected / exposed	67 / 432 (15.51%)	74 / 442 (16.74%)	0 / 37 (0.00%)
occurrences (all)	128	131	0
Hypogeusia			
subjects affected / exposed	3 / 432 (0.69%)	17 / 442 (3.85%)	0 / 37 (0.00%)
occurrences (all)	3	18	0
Taste disorder			
subjects affected / exposed	1 / 432 (0.23%)	8 / 442 (1.81%)	0 / 37 (0.00%)
occurrences (all)	1	8	0
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	18 / 432 (4.17%)	27 / 442 (6.11%)	0 / 37 (0.00%)
occurrences (all)	20	29	0
Dry mouth			
subjects affected / exposed	11 / 432 (2.55%)	15 / 442 (3.39%)	0 / 37 (0.00%)
occurrences (all)	12	15	0
Nausea			
subjects affected / exposed	32 / 432 (7.41%)	26 / 442 (5.88%)	0 / 37 (0.00%)
occurrences (all)	42	33	0
Respiratory, thoracic and mediastinal disorders			
Asthma			
subjects affected / exposed	11 / 432 (2.55%)	13 / 442 (2.94%)	3 / 37 (8.11%)
occurrences (all)	13	18	3
Cough			
subjects affected / exposed	18 / 432 (4.17%)	30 / 442 (6.79%)	0 / 37 (0.00%)
occurrences (all)	20	37	0

Oropharyngeal pain			
subjects affected / exposed	19 / 432 (4.40%)	13 / 442 (2.94%)	0 / 37 (0.00%)
occurrences (all)	21	13	0
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	30 / 432 (6.94%)	22 / 442 (4.98%)	0 / 37 (0.00%)
occurrences (all)	37	26	0
Back pain			
subjects affected / exposed	25 / 432 (5.79%)	30 / 442 (6.79%)	0 / 37 (0.00%)
occurrences (all)	33	34	0
Infections and infestations			
Bronchitis			
subjects affected / exposed	23 / 432 (5.32%)	20 / 442 (4.52%)	0 / 37 (0.00%)
occurrences (all)	27	24	0
Influenza			
subjects affected / exposed	35 / 432 (8.10%)	29 / 442 (6.56%)	0 / 37 (0.00%)
occurrences (all)	45	35	0
Nasopharyngitis			
subjects affected / exposed	70 / 432 (16.20%)	93 / 442 (21.04%)	0 / 37 (0.00%)
occurrences (all)	101	128	0
Sinusitis			
subjects affected / exposed	18 / 432 (4.17%)	23 / 442 (5.20%)	0 / 37 (0.00%)
occurrences (all)	20	25	0
Upper respiratory tract infection			
subjects affected / exposed	26 / 432 (6.02%)	38 / 442 (8.60%)	0 / 37 (0.00%)
occurrences (all)	32	47	0
Urinary tract infection			
subjects affected / exposed	23 / 432 (5.32%)	34 / 442 (7.69%)	0 / 37 (0.00%)
occurrences (all)	27	40	0

Non-serious adverse events	Placebo: Off Tx	Gefapixant 45 mg BID: Off Tx	Gefapixant 45 mg BID: On Tx
Total subjects affected by non-serious adverse events			
subjects affected / exposed	6 / 48 (12.50%)	1 / 37 (2.70%)	359 / 440 (81.59%)
Nervous system disorders			
Ageusia			

subjects affected / exposed	0 / 48 (0.00%)	0 / 37 (0.00%)	67 / 440 (15.23%)
occurrences (all)	0	0	75
Dysgeusia			
subjects affected / exposed	0 / 48 (0.00%)	0 / 37 (0.00%)	193 / 440 (43.86%)
occurrences (all)	0	0	220
Headache			
subjects affected / exposed	1 / 48 (2.08%)	0 / 37 (0.00%)	70 / 440 (15.91%)
occurrences (all)	1	0	131
Hypogeusia			
subjects affected / exposed	0 / 48 (0.00%)	0 / 37 (0.00%)	60 / 440 (13.64%)
occurrences (all)	0	0	60
Taste disorder			
subjects affected / exposed	0 / 48 (0.00%)	0 / 37 (0.00%)	37 / 440 (8.41%)
occurrences (all)	0	0	39
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	0 / 48 (0.00%)	0 / 37 (0.00%)	27 / 440 (6.14%)
occurrences (all)	0	0	34
Dry mouth			
subjects affected / exposed	0 / 48 (0.00%)	0 / 37 (0.00%)	32 / 440 (7.27%)
occurrences (all)	0	0	34
Nausea			
subjects affected / exposed	0 / 48 (0.00%)	0 / 37 (0.00%)	47 / 440 (10.68%)
occurrences (all)	0	0	57
Respiratory, thoracic and mediastinal disorders			
Asthma			
subjects affected / exposed	1 / 48 (2.08%)	1 / 37 (2.70%)	19 / 440 (4.32%)
occurrences (all)	1	1	29
Cough			
subjects affected / exposed	0 / 48 (0.00%)	0 / 37 (0.00%)	31 / 440 (7.05%)
occurrences (all)	0	0	38
Oropharyngeal pain			
subjects affected / exposed	0 / 48 (0.00%)	0 / 37 (0.00%)	23 / 440 (5.23%)
occurrences (all)	0	0	24
Musculoskeletal and connective tissue disorders			

Arthralgia			
subjects affected / exposed	0 / 48 (0.00%)	0 / 37 (0.00%)	21 / 440 (4.77%)
occurrences (all)	0	0	25
Back pain			
subjects affected / exposed	0 / 48 (0.00%)	0 / 37 (0.00%)	16 / 440 (3.64%)
occurrences (all)	0	0	17
Infections and infestations			
Bronchitis			
subjects affected / exposed	2 / 48 (4.17%)	0 / 37 (0.00%)	18 / 440 (4.09%)
occurrences (all)	2	0	19
Influenza			
subjects affected / exposed	0 / 48 (0.00%)	0 / 37 (0.00%)	24 / 440 (5.45%)
occurrences (all)	0	0	27
Nasopharyngitis			
subjects affected / exposed	2 / 48 (4.17%)	0 / 37 (0.00%)	70 / 440 (15.91%)
occurrences (all)	2	0	95
Sinusitis			
subjects affected / exposed	1 / 48 (2.08%)	0 / 37 (0.00%)	14 / 440 (3.18%)
occurrences (all)	1	0	16
Upper respiratory tract infection			
subjects affected / exposed	0 / 48 (0.00%)	0 / 37 (0.00%)	30 / 440 (6.82%)
occurrences (all)	0	0	39
Urinary tract infection			
subjects affected / exposed	1 / 48 (2.08%)	0 / 37 (0.00%)	19 / 440 (4.32%)
occurrences (all)	1	0	26

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
15 December 2017	Amendment 01: Clarifications of eligibility criteria, schedule of assessments, study population, and formatting.
27 September 2018	Amendment 02: Primary reason for amendment was to clarify that individuals with co-morbid conditions associated with cough should receive appropriate treatment(s) for at least 2 months with continuance of cough prior to being eligible for participation in the study.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported