Clinical trial results:
Randomized, double-blind, parallel group, Phase 2b dose-finding, efficacy and safety study of 12-week twice daily oral administration of BAY 1817080 compared to placebo in the treatment of refractory and/or unexplained chronic cough (RUCC)

Summary

EudraCT number	2019-004169-42
Trial protocol	DE GB IT NL CZ HU SK BE PL FR
Global end of trial date	23 July 2021

Results information

Result version number	v1 (current)
This version publication date	04 July 2022
First version publication date	04 July 2022

Trial information

Trial identification

Sponsor protocol code	BAY1817080/20393

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT04562155
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Bayer AG
Sponsor organisation address	Kaiser Wilhelm Allee, Leverkusen, Germany, D-51368
Public contact	Therapeutic Area Head, Bayer AG, +49 30 300139003, clinical-trials-contact@bayer.com
Scientific contact	Therapeutic Area Head, Bayer AG, +49 30 300139003, clinical-trials-contact@bayer.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	23 July 2021
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	23 July 2021
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The objective of this study was to identify the optimal dose of P2X3 receptor antagonist eliapixant in patients with RUCC and further assess efficacy and characterize safety and tolerability profile of eliapixant.
The primary objective was to assess the efficacy of P2X3 receptor antagonist eliapixant as compared with placebo in terms of change in 24-hour cough count from baseline to week 12.

Protection of trial subjects:

The conduct of this clinical study met all local legal and regulatory requirements. The study was conducted in accordance with ethical principles that have their origin in the Declaration of Helsinki and the International Council for Harmonization guideline E6: Good Clinical Practice. Before entering the study, the informed consent was read by and explained to all the subjects. Participating subjects signed informed consent form and could withdraw from the study at any time without any disadvantage and without having to provide a reason for this decision. Only investigators qualified by training and experience were selected as appropriate experts to investigate the study drug.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	02 October 2020
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	Argentina: 12
Country: Number of subjects enrolled	Australia: 26
Country: Number of subjects enrolled	Belgium: 20
Country: Number of subjects enrolled	Canada: 8
Country: Number of subjects enrolled	Czechia: 12
Country: Number of subjects enrolled	Germany: 28
Country: Number of subjects enrolled	Spain: 9
Country: Number of subjects enrolled	France: 11
Country: Number of subjects enrolled	United Kingdom: 26
Country: Number of subjects enrolled	Hungary: 12
Country: Number of subjects enrolled	Italy: 10
Country: Number of subjects enrolled	Japan: 23
Country: Number of subjects enrolled	Netherlands: 12
Country: Number of subjects enrolled	Poland: 20
Country: Number of subjects enrolled	Russian Federation: 16

Country: Number of subjects enrolled	Slovakia: 9
Country: Number of subjects enrolled	Turkey: 17
Country: Number of subjects enrolled	Taiwan: 6
Country: Number of subjects enrolled	United States: 33
Worldwide total number of subjects	310
EEA total number of subjects	143

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)	193
From 65 to 84 years	117
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

The study was conducted at 99 centers in 19 countries/regions with first subject first visit on 02-Oct-2020 and last subject last visit on 23-Jul-2021.

Pre-assignment

Screening details:

Overall, 399 subjects were screened, 89 of whom were screening failures. The remaining 310 subjects were randomized to 4 treatment groups (75 to eliapixant 25 mg BID, 78 to eliapixant 75 mg BID, 80 to eliapixant 150 mg BID, and 77 to placebo).

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	Investigator, Monitor, Data analyst, Assessor, Subject

Blinding implementation details:

After randomization, subject, investigator and sponsor were blinded for the intervention subject received

Arms

Are arms mutually exclusive?	Yes
Arm title	Eliapixant 25 mg BID

Arm description:

Subjects were randomized to receive 25 mg oral doses of eliapixant, administered twice daily over the course of 12 weeks.

Arm type	Experimental
Investigational medicinal product name	Eliapixant
Investigational medicinal product code	BAY1817080
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Eliapixant 25 mg tablets were administered twice daily. Subjects were instructed to take the morning dose at approximately the same time of day, every day over the course of 12 weeks. The interval between the morning and the evening dose should have been approximately 12 hours. Tablets were not to be broken, halved or crushed; they were to be swallowed as a complete unit with water. Tablets could be taken with or without food. There were no dose modifications; subjects stayed on the dose which they were randomized to.

Arm title	Eliapixant 75 mg BID

Arm description:

Subjects were randomized to receive 75 mg oral doses of eliapixant, administered twice daily over the course of 12 weeks.

Arm type	Experimental
Investigational medicinal product name	Eliapixant
Investigational medicinal product code	BAY1817080
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Eliapixant tablets totaling 75 mg were administered twice daily. Subjects were instructed to take the morning dose at approximately the same time of day, every day over the course of 12 weeks. The interval between the morning and the evening dose should have been approximately 12 hours. Tablets

were not to be broken, halved or crushed; they were to be swallowed as a complete unit with water. Tablets could be taken with or without food. There were no dose modifications; subjects stayed on the dose which they were randomized to.

Arm title	Eliapixant 150 mg BID

Arm description:

Subjects were randomized to receive 150 mg oral doses of eliapixant, administered twice daily over the course of 12 weeks.

Arm type	Experimental
Investigational medicinal product name	Eliapixant
Investigational medicinal product code	BAY1817080
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Eliapixant tablets totaling 150 mg were administered twice daily. Subjects were instructed to take the morning dose at approximately the same time of day, every day over the course of 12 weeks. The interval between the morning and the evening dose should have been approximately 12 hours. Tablets were not to be broken, halved or crushed; they were to be swallowed as a complete unit with water. Tablets could be taken with or without food. There were no dose modifications; subjects stayed on the dose which they were randomized to.

Arm title	Placebo

Arm description:

Subjects were randomized to receive placebo for eliapixant, administered twice daily over the course of 12 weeks.

Arm type	Placebo
Investigational medicinal product name	Placebo for eliapixant
Investigational medicinal product code	Not applicable
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Placebo for eliapixant tablets were administered twice daily. Subjects were instructed to take the morning dose at approximately the same time of day, every day over the course of 12 weeks. The interval between the morning and the evening dose should have been approximately 12 hours. Tablets were not to be broken, halved or crushed; they were to be swallowed as a complete unit with water. Tablets could be taken with or without food.

Number of subjects in period 1	Eliapixant 25 mg BID	Eliapixant 75 mg BID	Eliapixant 150 mg BID
Started	75	78	80
Completed	64	69	67
Not completed	11	9	13
COVID-19 pandemic	-	-	-
Consent withdrawn by subject	3	6	3
Adverse event, non-fatal	7	3	8
Other	1	-	2

Number of subjects in period 1	Placebo
Started	77
Completed	71
Not completed	6
COVID-19 pandemic	1
Consent withdrawn by subject	3
Adverse event, non-fatal	1
Other	1

Baseline characteristics

Reporting groups	
Reporting group title	Eliapixant 25 mg BID
Reporting group description:	
Subjects were randomized to receive 25 mg oral doses of eliapixant, administered twice daily over the course of 12 weeks.	
Reporting group title	Eliapixant 75 mg BID
Reporting group description:	
Subjects were randomized to receive 75 mg oral doses of eliapixant, administered twice daily over the course of 12 weeks.	
Reporting group title	Eliapixant 150 mg BID
Reporting group description:	
Subjects were randomized to receive 150 mg oral doses of eliapixant, administered twice daily over the course of 12 weeks.	
Reporting group title	Placebo
Reporting group description:	
Subjects were randomized to receive placebo for eliapixant, administered twice daily over the course of 12 weeks.	

Reporting group values	Eliapixant 25 mg BID	Eliapixant 75 mg BID	Eliapixant 150 mg BID
Number of subjects	75	78	80
Age categorical			
Used full analysis set			
Units: Subjects			
Adults (18-64 years)	45	50	49
From 65-84 years	30	28	31
Age continuous			
Used full analysis set			
Units: years			
arithmetic mean	61.81	58.62	58.98
standard deviation	± 9.64	± 12.7	± 11.8
Gender categorical			
Used full analysis set			
Units: Subjects			
Female	56	63	61
Male	19	15	19
Baseline 24-hour coughs per hour			
Used per protocol set (PPS) Eliapixant 25 mg BID (N=67), Eliapixant 75 mg BID (N=69), Eliapixant 150 mg BID (N=73), Placebo (N=74)			
Units: 24-hour cough count per hour			
geometric mean	17.49	19.23	15.61
standard deviation	± 2.94	± 2.94	± 2.34
Baseline Leicester Cough Questionnaire (LCQ) Total Score			
Used per protocol set (PPS) Eliapixant 25 mg BID (N=67), Eliapixant 75 mg BID (N=69), Eliapixant 150 mg BID (N=73), Placebo (N=74)			
Units: Score of LCQ			
arithmetic mean	12.00	11.76	11.15

standard deviation	± 2.54	± 2.77	± 2.56
Baseline awake cough count per hour			
Used per protocol set (PPS) Eliapixant 25 mg BID (N=67), Eliapixant 75 mg BID (N=69), Eliapixant 150 mg BID (N=73), Placebo (N=74)			
Units: Cough count per hour			
geometric mean	23.62	26.41	21.19
standard deviation	± 3.02	± 2.97	± 2.39
Baseline Cough Severity Visual Analogue Scale [VAS] Value			
Used per protocol set (PPS) - Included the subjects in PPS with valid VAS value. Eliapixant 25 mg BID (N=62), Eliapixant 75 mg BID (N=68), Eliapixant 150 mg BID (N=67), Placebo (N=69)			
Units: Score of VAS			
arithmetic mean	65.51	67.08	66.79
standard deviation	± 14.64	± 14.89	± 15.86

Reporting group values	Placebo	Total	
Number of subjects	77	310	
Age categorical			
Used full analysis set			
Units: Subjects			
Adults (18-64 years)	49	193	
From 65-84 years	28	117	
Age continuous			
Used full analysis set			
Units: years			
arithmetic mean	56.91		
standard deviation	± 12.4	-	
Gender categorical			
Used full analysis set			
Units: Subjects			
Female	61	241	
Male	16	69	
Baseline 24-hour coughs per hour			
Used per protocol set (PPS) Eliapixant 25 mg BID (N=67), Eliapixant 75 mg BID (N=69), Eliapixant 150 mg BID (N=73), Placebo (N=74)			
Units: 24-hour cough count per hour			
geometric mean	17.63		
standard deviation	± 3.07	-	
Baseline Leicester Cough Questionnaire (LCQ) Total Score			
Used per protocol set (PPS) Eliapixant 25 mg BID (N=67), Eliapixant 75 mg BID (N=69), Eliapixant 150 mg BID (N=73), Placebo (N=74)			
Units: Score of LCQ			
arithmetic mean	11.53		
standard deviation	± 3.27	-	
Baseline awake cough count per hour			
Used per protocol set (PPS) Eliapixant 25 mg BID (N=67), Eliapixant 75 mg BID (N=69), Eliapixant 150 mg BID (N=73), Placebo (N=74)			
Units: Cough count per hour			
geometric mean	24.01		

standard deviation	± 3.18	-	
Baseline Cough Severity Visual Analogue Scale [VAS] Value			
Used per protocol set (PPS) - Included the subjects in PPS with valid VAS value. Eliapixant 25 mg BID (N=62), Eliapixant 75 mg BID (N=68), Eliapixant 150 mg BID (N=67), Placebo (N=69)			
Units: Score of VAS			
arithmetic mean	61.52		
standard deviation	± 18.51	-	

End points

End points reporting groups

Reporting group title	Eliapixant 25 mg BID
Reporting group description:	
Subjects were randomized to receive 25 mg oral doses of eliapixant, administered twice daily over the course of 12 weeks.	
Reporting group title	Eliapixant 75 mg BID
Reporting group description:	
Subjects were randomized to receive 75 mg oral doses of eliapixant, administered twice daily over the course of 12 weeks.	
Reporting group title	Eliapixant 150 mg BID
Reporting group description:	
Subjects were randomized to receive 150 mg oral doses of eliapixant, administered twice daily over the course of 12 weeks.	
Reporting group title	Placebo
Reporting group description:	
Subjects were randomized to receive placebo for eliapixant, administered twice daily over the course of 12 weeks.	
Subject analysis set title	Full analysis set (FAS)
Subject analysis set type	Full analysis
Subject analysis set description:	
All subjects randomly assigned to study intervention. Subjects were analyzed according to the intervention they were randomized to.	
Subject analysis set title	Safety analysis set (SAF)
Subject analysis set type	Safety analysis
Subject analysis set description:	
All subjects randomly assigned to study intervention and who took at least one tablet of study intervention. Subjects were analyzed according to the intervention they actually received.	
Subject analysis set title	Per protocol set (PPS)
Subject analysis set type	Per protocol
Subject analysis set description:	
All subjects randomly assigned to study intervention who did not have validity findings affecting efficacy. subjects were analyzed according to the intervention they actually received. If a subject received different interventions during the study, he/she was excluded from the PPS. The main reasons for excluding the subjects from the PPS were that there was no valid post-baseline measurement available due to an intercurrent event (15 subjects, 4.8%) or that the subject had used prohibited concomitant medication (9 subjects, 2.9%).	

Primary: Change from baseline in 24-hour cough count after 12 weeks of intervention

End point title	Change from baseline in 24-hour cough count after 12 weeks of intervention
End point description:	
Measured by cough recording digital wearable monitoring device. btw = between geo = geometric	
End point type	Primary
End point timeframe:	
From baseline up to 12 weeks	

End point values	Eliapixant 25 mg BID	Eliapixant 75 mg BID	Eliapixant 150 mg BID	Placebo
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	64[1]	68[2]	72[3]	73[4]
Units: Ratio btw geoMeans of 24h cough count				
geometric mean (standard deviation)	0.56 (± 0.9191)	0.47 (± 0.9019)	0.52 (± 0.8608)	0.64 (± 0.7855)

Notes:

[1] - PPS

[2] - PPS

[3] - PPS

[4] - PPS

Statistical analyses

Statistical analysis title	Detection of dose-response: Emax model (ED50=30)

Statistical analysis description:

Dose response relationship was assessed using the MCP-Mod method combining multiple comparison procedures (MCP) principles with modeling techniques. A generalized MCP approach (with adjustment for baseline cough count and geographic region) was applied to calculate the adjusted one-sided p-values of the contrast test. Pre-specified overall Type one error at alpha level of 0.1 (one-sided).

Comparison groups	Placebo v Eliapixant 25 mg BID v Eliapixant 75 mg BID v Eliapixant 150 mg BID
Number of subjects included in analysis	277
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0345 [5]
Method	MCP-Mod method

Notes:

[5] - Adjusted p-value

Statistical analysis title	DoD: sigm. Emax model (ED50=30, h=3)

Statistical analysis description:

DoD = Detection of dose-response
sigm = sigmoidal
h = hill parameter

Dose response relationship was assessed using the MCP-Mod method combining multiple comparison procedures (MCP) principles with modeling techniques. A generalized MCP approach (with adjustment for baseline cough count and geographic region) was applied to calculate the adjusted one-sided p-values of the contrast test. Pre-specified overall Type one error at alpha level of 0.1 (one-sided).

Comparison groups	Placebo v Eliapixant 25 mg BID v Eliapixant 75 mg BID v Eliapixant 150 mg BID
Number of subjects included in analysis	277
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0319 [6]
Method	MCP-Mod method

Notes:

[6] - Adjusted p-value

Statistical analysis title	DoD: sigm. Emax model (ED50=60, h=5)

Statistical analysis description:

DoD = Detection of dose-response
sigm = sigmoidal
h = hill parameter

Dose response relationship was assessed using the MCP-Mod method combining multiple comparison procedures (MCP) principles with modeling techniques. A generalized MCP approach (with adjustment for baseline cough count and geographic region) was applied to calculate the adjusted one-sided p-values of the contrast test. Pre-specified overall Type one error at alpha level of 0.1 (one-sided).

Comparison groups	Placebo v Eliapixant 25 mg BID v Eliapixant 75 mg BID v Eliapixant 150 mg BID
Number of subjects included in analysis	277
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0603 [7]
Method	MCP-Mod method

Notes:

[7] - Adjusted p-value

Statistical analysis title	Detection of dose-response: Emax model (ED50=50)

Statistical analysis description:

Dose response relationship was assessed using the MCP-Mod method combining multiple comparison procedures (MCP) principles with modeling techniques. A generalized MCP approach (with adjustment for baseline cough count and geographic region) was applied to calculate the adjusted one-sided p-values of the contrast test. Pre-specified overall Type one error at alpha level of 0.1 (one-sided).

Comparison groups	Placebo v Eliapixant 25 mg BID v Eliapixant 75 mg BID v Eliapixant 150 mg BID
Number of subjects included in analysis	277
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0376 [8]
Method	MCP-Mod method

Notes:

[8] - Adjusted p-value

Secondary: Percentage of subjects with a ≥30% reduction from baseline in 24-hour cough count after 12 weeks of intervention

End point title	Percentage of subjects with a ≥30% reduction from baseline in 24-hour cough count after 12 weeks of intervention

End point description:

Measured by cough recording digital wearable monitoring device

End point type	Secondary

End point timeframe:

From baseline up to 12 weeks

End point values	Eliapixant 25 mg BID	Eliapixant 75 mg BID	Eliapixant 150 mg BID	Placebo
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	67[9]	69[10]	73[11]	74[12]
Units: Percentage				
number (confidence interval 95%)	52.24 (39.67 to 64.60)	63.77 (51.31 to 75.01)	53.42 (41.37 to 65.20)	45.95 (34.29 to 57.93)

Notes:

[9] - PPS

[10] - PPS

[11] - PPS

[12] - PPS

Statistical analyses

No statistical analyses for this end point

Secondary: Change from baseline in 24-hour cough count after 2, 4, and 8 weeks of intervention

End point title	Change from baseline in 24-hour cough count after 2, 4, and 8 weeks of intervention

End point description:

Measured by cough recording digital wearable monitoring device

btw = between
geo = geometric

Number of subjects analysed at Week 2: Eliapixant 25 mg BID (N=66), Eliapixant 75 mg BID (N=67), Eliapixant 150 mg BID (N=72), Placebo (N=73)
Number of subjects analysed at Week 4: Eliapixant 25 mg BID (N=66), Eliapixant 75 mg BID (N=66), Eliapixant 150 mg BID (N=68), Placebo (N=71)
Number of subjects analysed at Week 8: Eliapixant 25 mg BID (N=64), Eliapixant 75 mg BID (N=65), Eliapixant 150 mg BID (N=69), Placebo (N=72)

End point type	Secondary

End point timeframe:

From baseline up to 2 weeks, 4 weeks and 8 weeks

End point values	Eliapixant 25 mg BID	Eliapixant 75 mg BID	Eliapixant 150 mg BID	Placebo
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	67[13]	69[14]	73[15]	74[16]
Units: Ratio btw geoMeans of 24h cough count				
geometric mean (standard deviation)				
Week 2	0.75 (± 0.6134)	0.58 (± 0.8209)	0.61 (± 0.6636)	0.75 (± 0.4762)
Week 4	0.64 (± 0.7237)	0.51 (± 0.8192)	0.58 (± 0.8589)	0.69 (± 0.6657)
Week 8	0.55 (± 0.8737)	0.46 (± 0.9484)	0.51 (± 0.8827)	0.70 (± 0.6451)

Notes:

[13] - PPS

[14] - PPS

[15] - PPS

[16] - PPS

Statistical analyses

No statistical analyses for this end point

Secondary: Change from baseline in awake cough frequency per hour after 2, 4, 8 and 12 weeks of intervention

End point title	Change from baseline in awake cough frequency per hour after 2, 4, 8 and 12 weeks of intervention

End point description:

Measured by cough recording digital wearable monitoring device

btw = between
geo = geometric

Number of subjects analysed at Week 2: Eliapixant 25 mg BID (N=65), Eliapixant 75 mg BID (N=67), Eliapixant 150 mg BID (N=72), Placebo (N=73)
Number of subjects analysed at Week 4: Eliapixant 25 mg BID (N=66), Eliapixant 75 mg BID (N=66), Eliapixant 150 mg BID (N=68), Placebo (N=71)
Number of subjects analysed at Week 8: Eliapixant 25 mg BID (N=64), Eliapixant 75 mg BID (N=65), Eliapixant 150 mg BID (N=69), Placebo (N=72)
Number of subjects analysed at Week 12: Eliapixant 25 mg BID (N=64), Eliapixant 75 mg BID (N=68), Eliapixant 150 mg BID (N=72), Placebo (N=73)

End point type	Secondary

End point timeframe:

From baseline up to 2 weeks, 4 weeks, 8 weeks and 12 weeks

End point values	Eliapixant 25 mg BID	Eliapixant 75 mg BID	Eliapixant 150 mg BID	Placebo
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	67[17]	69[18]	73[19]	74[20]
Units: Ratio btw geoMeans of 24h cough count				
geometric mean (standard deviation)				
Week 2	0.78 (± 0.6324)	0.60 (± 0.8295)	0.60 (± 0.6695)	0.77 (± 0.4660)
Week 4	0.67 (± 0.7390)	0.53 (± 0.8128)	0.57 (± 0.8983)	0.72 (± 0.6637)
Week 8	0.55 (± 0.9274)	0.47 (± 0.9576)	0.50 (± 0.9154)	0.72 (± 0.6698)
Week 12	0.56 (± 0.9582)	0.47 (± 0.9051)	0.47 (± 1.1338)	0.65 (± 0.7926)

Notes:

[17] - PPS

[18] - PPS

[19] - PPS

[20] - PPS

Statistical analyses

No statistical analyses for this end point

Secondary: Change from baseline in cough related quality of life after 12 weeks of intervention

End point title	Change from baseline in cough related quality of life after 12 weeks of intervention

End point description:

Measured by Leicester Cough Questionnaire [LCQ]

End point type	Secondary

End point timeframe:
From baseline up to 12 weeks

End point values	Eliapixant 25 mg BID	Eliapixant 75 mg BID	Eliapixant 150 mg BID	Placebo
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	67[21]	69[22]	73[23]	74[24]
Units: Score of the Questionnaire				
arithmetic mean (standard deviation)	2.18 (± 3.44)	2.50 (± 3.29)	2.73 (± 3.53)	2.16 (± 3.12)

Notes:
[21] - PPS
[22] - PPS
[23] - PPS
[24] - PPS

Statistical analyses

No statistical analyses for this end point

Secondary: Change from baseline in cough severity after 12 weeks of intervention

End point title	Change from baseline in cough severity after 12 weeks of intervention

End point description:
Measured by Cough Severity Visual Analogue Scale [VAS]

End point type	Secondary

End point timeframe:
From baseline up to 12 weeks

End point values	Eliapixant 25 mg BID	Eliapixant 75 mg BID	Eliapixant 150 mg BID	Placebo
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	61[25]	68[26]	67[27]	68[28]
Units: Score of VAS				
arithmetic mean (standard deviation)	-17.69 (± 23.87)	-22.66 (± 22.98)	-22.87 (± 24.54)	-17.02 (± 21.88)

Notes:
[25] - PPS
[26] - PPS
[27] - PPS
[28] - PPS

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of subjects with a ≥30 scale units reduction from baseline after 12 weeks of intervention

End point title	Percentage of subjects with a ≥30 scale units reduction from

	baseline after 12 weeks of intervention
End point description:	
Measured by cough Severity VAS	
End point type	Secondary
End point timeframe:	
From baseline up to 12 weeks	

End point values	Eliapixant 25 mg BID	Eliapixant 75 mg BID	Eliapixant 150 mg BID	Placebo
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	67[29]	69[30]	73[31]	74[32]
Units: Percentage				
number (confidence interval 95%)	26.87 (16.76 to 39.10)	36.23 (24.99 to 48.69)	27.40 (17.61 to 39.09)	20.27 (11.81 to 31.22)

Notes:

[29] - PPS

[30] - PPS

[31] - PPS

[32] - PPS

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of subjects with a ≥1.3-point increase from baseline after 12 weeks of intervention

End point title	Percentage of subjects with a ≥1.3-point increase from baseline after 12 weeks of intervention
End point description:	
Measured with LCQ Total Score	
End point type	Secondary
End point timeframe:	
From baseline up to 12 weeks	

End point values	Eliapixant 25 mg BID	Eliapixant 75 mg BID	Eliapixant 150 mg BID	Placebo
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	67[33]	69[34]	73[35]	74[36]
Units: Percentage				
number (confidence interval 95%)	47.76 (35.40 to 60.33)	60.87 (48.37 to 72.40)	64.38 (52.31 to 75.25)	51.35 (39.44 to 63.15)

Notes:

[33] - PPS

[34] - PPS

[35] - PPS

[36] - PPS

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with treatment-emergent adverse events (TEAEs) and associated severity

End point title	Number of subjects with treatment-emergent adverse events (TEAEs) and associated severity

End point description:

End point type	Secondary

End point timeframe:

From the start of study intervention administration until 14 days after the last study medication intake

End point values	Eliapixant 25 mg BID	Eliapixant 75 mg BID	Eliapixant 150 mg BID	Placebo
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	75[37]	78[38]	80[39]	77[40]
Units: Subjects				
Any TEAE	43	51	51	39
Maximum intensity for any TEAE - mild	21	32	23	18
Maximum intensity for any TEAE - moderate	22	16	25	20
Maximum intensity for any TEAE - severe	0	3	3	1
Any serious TEAE	0	1	2	1

Notes:

[37] - SAF

[38] - SAF

[39] - SAF

[40] - SAF

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information	
Timeframe for reporting adverse events: From the start of study intervention administration until 14 days after the last study medication intake	
Assessment type	Non-systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	24.0

Reporting groups	
Reporting group title	Eliapixant 25 mg BID
Reporting group description: Subjects were randomized to receive 25 mg oral doses of eliapixant, administered twice daily over the course of 12 weeks.	
Reporting group title	Eliapixant 75 mg BID
Reporting group description: Subjects were randomized to receive 75 mg oral doses of eliapixant, administered twice daily over the course of 12 weeks.	
Reporting group title	Eliapixant 150 mg BID
Reporting group description: Subjects were randomized to receive 150 mg oral doses of eliapixant, administered twice daily over the course of 12 weeks.	
Reporting group title	Placebo
Reporting group description: Subjects were randomized to receive placebo for eliapixant, administered twice daily over the course of 12 weeks.	

Serious adverse events	Eliapixant 25 mg BID	Eliapixant 75 mg BID	Eliapixant 150 mg BID
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 75 (0.00%)	1 / 78 (1.28%)	2 / 80 (2.50%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Investigations			
Liver function test abnormal			
subjects affected / exposed	0 / 75 (0.00%)	0 / 78 (0.00%)	1 / 80 (1.25%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Injury, poisoning and procedural complications			
Lumbar vertebral fracture			
subjects affected / exposed	0 / 75 (0.00%)	0 / 78 (0.00%)	1 / 80 (1.25%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Cardiac disorders			
Angina unstable			
subjects affected / exposed	0 / 75 (0.00%)	0 / 78 (0.00%)	0 / 80 (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			
Pneumonia			
subjects affected / exposed	0 / 75 (0.00%)	1 / 78 (1.28%)	0 / 80 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	Placebo		
Total subjects affected by serious adverse events			
subjects affected / exposed	1 / 77 (1.30%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events	0		
Investigations			
Liver function test abnormal			
subjects affected / exposed	0 / 77 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Injury, poisoning and procedural complications			
Lumbar vertebral fracture			
subjects affected / exposed	0 / 77 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Cardiac disorders			
Angina unstable			
subjects affected / exposed	1 / 77 (1.30%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Infections and infestations			
Pneumonia			
subjects affected / exposed	0 / 77 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		

Frequency threshold for reporting non-serious adverse events: 2 %

Non-serious adverse events	Eliapixant 25 mg BID	Eliapixant 75 mg BID	Eliapixant 150 mg BID
Total subjects affected by non-serious adverse events			
subjects affected / exposed	32 / 75 (42.67%)	37 / 78 (47.44%)	45 / 80 (56.25%)
Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	0 / 75 (0.00%)	1 / 78 (1.28%)	2 / 80 (2.50%)
occurrences (all)	0	1	2
Aspartate aminotransferase increased			
subjects affected / exposed	0 / 75 (0.00%)	0 / 78 (0.00%)	2 / 80 (2.50%)
occurrences (all)	0	0	2
Blood fibrinogen increased			
subjects affected / exposed	1 / 75 (1.33%)	1 / 78 (1.28%)	2 / 80 (2.50%)
occurrences (all)	1	1	2
Weight increased			
subjects affected / exposed	1 / 75 (1.33%)	1 / 78 (1.28%)	2 / 80 (2.50%)
occurrences (all)	1	1	2
Injury, poisoning and procedural complications			
Ligament sprain			
subjects affected / exposed	0 / 75 (0.00%)	2 / 78 (2.56%)	0 / 80 (0.00%)
occurrences (all)	0	2	0
Nervous system disorders			
Ageusia			
subjects affected / exposed	0 / 75 (0.00%)	0 / 78 (0.00%)	2 / 80 (2.50%)
occurrences (all)	0	0	2
Dizziness			
subjects affected / exposed	2 / 75 (2.67%)	2 / 78 (2.56%)	1 / 80 (1.25%)
occurrences (all)	2	2	1
Dysgeusia			
subjects affected / exposed	1 / 75 (1.33%)	9 / 78 (11.54%)	13 / 80 (16.25%)
occurrences (all)	1	9	14

Headache			
subjects affected / exposed	6 / 75 (8.00%)	5 / 78 (6.41%)	6 / 80 (7.50%)
occurrences (all)	6	10	7
Hypogeusia			
subjects affected / exposed	2 / 75 (2.67%)	1 / 78 (1.28%)	4 / 80 (5.00%)
occurrences (all)	2	1	4
Balance disorder			
subjects affected / exposed	0 / 75 (0.00%)	1 / 78 (1.28%)	2 / 80 (2.50%)
occurrences (all)	0	1	2
Taste disorder			
subjects affected / exposed	0 / 75 (0.00%)	2 / 78 (2.56%)	1 / 80 (1.25%)
occurrences (all)	0	2	1
General disorders and administration site conditions			
Chest discomfort			
subjects affected / exposed	2 / 75 (2.67%)	1 / 78 (1.28%)	0 / 80 (0.00%)
occurrences (all)	2	1	0
Fatigue			
subjects affected / exposed	2 / 75 (2.67%)	6 / 78 (7.69%)	5 / 80 (6.25%)
occurrences (all)	2	6	6
Oedema peripheral			
subjects affected / exposed	0 / 75 (0.00%)	2 / 78 (2.56%)	1 / 80 (1.25%)
occurrences (all)	0	2	1
Pyrexia			
subjects affected / exposed	3 / 75 (4.00%)	0 / 78 (0.00%)	0 / 80 (0.00%)
occurrences (all)	3	0	0
Swelling face			
subjects affected / exposed	2 / 75 (2.67%)	0 / 78 (0.00%)	0 / 80 (0.00%)
occurrences (all)	2	0	0
Gastrointestinal disorders			
Abdominal discomfort			
subjects affected / exposed	0 / 75 (0.00%)	0 / 78 (0.00%)	2 / 80 (2.50%)
occurrences (all)	0	0	2
Abdominal pain upper			
subjects affected / exposed	3 / 75 (4.00%)	3 / 78 (3.85%)	2 / 80 (2.50%)
occurrences (all)	3	3	2
Diarrhoea			

subjects affected / exposed	3 / 75 (4.00%)	2 / 78 (2.56%)	1 / 80 (1.25%)
occurrences (all)	3	2	1
Dry mouth			
subjects affected / exposed	1 / 75 (1.33%)	3 / 78 (3.85%)	2 / 80 (2.50%)
occurrences (all)	1	3	2
Flatulence			
subjects affected / exposed	2 / 75 (2.67%)	1 / 78 (1.28%)	0 / 80 (0.00%)
occurrences (all)	2	1	0
Gastrooesophageal reflux disease			
subjects affected / exposed	1 / 75 (1.33%)	2 / 78 (2.56%)	2 / 80 (2.50%)
occurrences (all)	1	2	2
Nausea			
subjects affected / exposed	2 / 75 (2.67%)	2 / 78 (2.56%)	5 / 80 (6.25%)
occurrences (all)	2	3	5
Vomiting			
subjects affected / exposed	0 / 75 (0.00%)	0 / 78 (0.00%)	3 / 80 (3.75%)
occurrences (all)	0	0	3
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	4 / 75 (5.33%)	7 / 78 (8.97%)	7 / 80 (8.75%)
occurrences (all)	4	7	7
Nasal dryness			
subjects affected / exposed	0 / 75 (0.00%)	0 / 78 (0.00%)	0 / 80 (0.00%)
occurrences (all)	0	0	0
Throat irritation			
subjects affected / exposed	0 / 75 (0.00%)	1 / 78 (1.28%)	2 / 80 (2.50%)
occurrences (all)	0	1	2
Oropharyngeal pain			
subjects affected / exposed	2 / 75 (2.67%)	0 / 78 (0.00%)	1 / 80 (1.25%)
occurrences (all)	2	0	1
Skin and subcutaneous tissue disorders			
Pruritus			
subjects affected / exposed	3 / 75 (4.00%)	0 / 78 (0.00%)	1 / 80 (1.25%)
occurrences (all)	3	0	1
Rash			

subjects affected / exposed	2 / 75 (2.67%)	0 / 78 (0.00%)	2 / 80 (2.50%)
occurrences (all)	2	0	4
Psychiatric disorders			
Anxiety			
subjects affected / exposed	1 / 75 (1.33%)	2 / 78 (2.56%)	0 / 80 (0.00%)
occurrences (all)	1	2	0
Insomnia			
subjects affected / exposed	4 / 75 (5.33%)	0 / 78 (0.00%)	1 / 80 (1.25%)
occurrences (all)	4	0	1
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	1 / 75 (1.33%)	2 / 78 (2.56%)	2 / 80 (2.50%)
occurrences (all)	2	2	2
Back pain			
subjects affected / exposed	0 / 75 (0.00%)	0 / 78 (0.00%)	1 / 80 (1.25%)
occurrences (all)	0	0	1
Myalgia			
subjects affected / exposed	2 / 75 (2.67%)	0 / 78 (0.00%)	0 / 80 (0.00%)
occurrences (all)	2	0	0
Pain in extremity			
subjects affected / exposed	2 / 75 (2.67%)	0 / 78 (0.00%)	2 / 80 (2.50%)
occurrences (all)	2	0	2
Infections and infestations			
Gastroenteritis			
subjects affected / exposed	2 / 75 (2.67%)	0 / 78 (0.00%)	0 / 80 (0.00%)
occurrences (all)	3	0	0
Nasopharyngitis			
subjects affected / exposed	2 / 75 (2.67%)	3 / 78 (3.85%)	2 / 80 (2.50%)
occurrences (all)	2	3	3
Sinusitis			
subjects affected / exposed	1 / 75 (1.33%)	0 / 78 (0.00%)	2 / 80 (2.50%)
occurrences (all)	1	0	2
Urinary tract infection			
subjects affected / exposed	1 / 75 (1.33%)	2 / 78 (2.56%)	3 / 80 (3.75%)
occurrences (all)	1	2	3
COVID-19			

subjects affected / exposed	2 / 75 (2.67%)	2 / 78 (2.56%)	0 / 80 (0.00%)
occurrences (all)	2	2	0

Non-serious adverse events	Placebo		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	25 / 77 (32.47%)		
Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	0 / 77 (0.00%)		
occurrences (all)	0		
Aspartate aminotransferase increased			
subjects affected / exposed	0 / 77 (0.00%)		
occurrences (all)	0		
Blood fibrinogen increased			
subjects affected / exposed	0 / 77 (0.00%)		
occurrences (all)	0		
Weight increased			
subjects affected / exposed	0 / 77 (0.00%)		
occurrences (all)	0		
Injury, poisoning and procedural complications			
Ligament sprain			
subjects affected / exposed	1 / 77 (1.30%)		
occurrences (all)	1		
Nervous system disorders			
Ageusia			
subjects affected / exposed	1 / 77 (1.30%)		
occurrences (all)	1		
Dizziness			
subjects affected / exposed	5 / 77 (6.49%)		
occurrences (all)	5		
Dysgeusia			
subjects affected / exposed	1 / 77 (1.30%)		
occurrences (all)	1		
Headache			
subjects affected / exposed	4 / 77 (5.19%)		
occurrences (all)	4		

Hypogeusia			
subjects affected / exposed	2 / 77 (2.60%)		
occurrences (all)	2		
Balance disorder			
subjects affected / exposed	0 / 77 (0.00%)		
occurrences (all)	0		
Taste disorder			
subjects affected / exposed	1 / 77 (1.30%)		
occurrences (all)	1		
General disorders and administration site conditions			
Chest discomfort			
subjects affected / exposed	0 / 77 (0.00%)		
occurrences (all)	0		
Fatigue			
subjects affected / exposed	2 / 77 (2.60%)		
occurrences (all)	2		
Oedema peripheral			
subjects affected / exposed	0 / 77 (0.00%)		
occurrences (all)	0		
Pyrexia			
subjects affected / exposed	1 / 77 (1.30%)		
occurrences (all)	1		
Swelling face			
subjects affected / exposed	0 / 77 (0.00%)		
occurrences (all)	0		
Gastrointestinal disorders			
Abdominal discomfort			
subjects affected / exposed	1 / 77 (1.30%)		
occurrences (all)	1		
Abdominal pain upper			
subjects affected / exposed	1 / 77 (1.30%)		
occurrences (all)	1		
Diarrhoea			
subjects affected / exposed	1 / 77 (1.30%)		
occurrences (all)	1		
Dry mouth			

subjects affected / exposed occurrences (all) Flatulence subjects affected / exposed occurrences (all) Gastrooesophageal reflux disease subjects affected / exposed occurrences (all) Nausea subjects affected / exposed occurrences (all) Vomiting subjects affected / exposed occurrences (all)	4 / 77 (5.19%) 5 0 / 77 (0.00%) 0 0 / 77 (0.00%) 0 1 / 77 (1.30%) 2 0 / 77 (0.00%) 0		
Respiratory, thoracic and mediastinal disorders Cough subjects affected / exposed occurrences (all) Nasal dryness subjects affected / exposed occurrences (all) Throat irritation subjects affected / exposed occurrences (all) Oropharyngeal pain subjects affected / exposed occurrences (all)	 3 / 77 (3.90%) 3 2 / 77 (2.60%) 3 0 / 77 (0.00%) 0 0 / 77 (0.00%) 0		
Skin and subcutaneous tissue disorders Pruritus subjects affected / exposed occurrences (all) Rash subjects affected / exposed occurrences (all)	 2 / 77 (2.60%) 2 0 / 77 (0.00%) 0		
Psychiatric disorders			

Anxiety			
subjects affected / exposed	0 / 77 (0.00%)		
occurrences (all)	0		
Insomnia			
subjects affected / exposed	0 / 77 (0.00%)		
occurrences (all)	0		
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	1 / 77 (1.30%)		
occurrences (all)	1		
Back pain			
subjects affected / exposed	2 / 77 (2.60%)		
occurrences (all)	2		
Myalgia			
subjects affected / exposed	1 / 77 (1.30%)		
occurrences (all)	1		
Pain in extremity			
subjects affected / exposed	2 / 77 (2.60%)		
occurrences (all)	2		
Infections and infestations			
Gastroenteritis			
subjects affected / exposed	0 / 77 (0.00%)		
occurrences (all)	0		
Nasopharyngitis			
subjects affected / exposed	1 / 77 (1.30%)		
occurrences (all)	1		
Sinusitis			
subjects affected / exposed	1 / 77 (1.30%)		
occurrences (all)	1		
Urinary tract infection			
subjects affected / exposed	0 / 77 (0.00%)		
occurrences (all)	0		
COVID-19			
subjects affected / exposed	3 / 77 (3.90%)		
occurrences (all)	3		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? No

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported