Clinical trial results:
A randomised, double-blind, placebo-controlled study to investigate the safety and tolerability of EP395 in patients with chronic obstructive pulmonary disease (COPD)

Summary

EudraCT number	2021-005787-22
Trial protocol	DE
Global end of trial date	24 November 2023

Results information

Result version number	v1 (current)
This version publication date	24 October 2024
First version publication date	24 October 2024

Trial information

Trial identification

Sponsor protocol code	EP395-003

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT05572333
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	EpiEndo Pharmaceuticals
Sponsor organisation address	Bjargargata 1, 102 Reykjavik, Iceland,
Public contact	Project Manager Kate Hanrott , EpiEndo Pharmaceuticals, +354 4540095, info@epiendo.com
Scientific contact	Project Manager Kate Hanrott , EpiEndo Pharmaceuticals, +354 4540095, info@epiendo.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 February 2024
Is this the analysis of the primary completion data?	Yes
Primary completion date	24 November 2023
Global end of trial reached?	Yes
Global end of trial date	24 November 2023
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To assess the safety and tolerability of repeat doses of EP395 in patients with COPD

Protection of trial subjects:

This trial was performed in accordance with the ethical principles that have their origin in the Declaration of Helsinki and that are consistent with International Council for Harmonisation Good Clinical Practice, and applicable regulatory requirements. The trial was conducted by investigators experienced in the treatment of patients with COPD.

Background therapy:

Patients continued their COPD background therapy throughout the trial.

Evidence for comparator: -

Actual start date of recruitment	01 October 2022
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	Germany: 47
Country: Number of subjects enrolled	United Kingdom: 14
Worldwide total number of subjects	61
EEA total number of subjects	47

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)	25
From 65 to 84 years	36

85 years and over	0

Subject disposition

Recruitment

Recruitment details:

123 patients were screened. 59 patients were screening failures and 3 dropped out before randomisation. 61 patients were randomised, 42 to receive EP395 and 19 to receive placebo.

Pre-assignment

Screening details:

Patients who met all inclusion criteria and none of the exclusion criteria were eligible to participate in the trial.

Period 1

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

Blinding implementation details:

EP395 capsules and placebo capsules were identical in appearance, packaging and labelling.

Arms

Are arms mutually exclusive?	Yes
Arm title	EP395 375mg

Arm description:

3 capsules of 125 mg EP395 each, administered once daily for 12 weeks.

Arm type	Experimental
Investigational medicinal product name	EP395
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

Participants took 3 capsules once daily for 12 weeks (in the morning with a glass of water after an overnight fast).

Arm title	Placebo

Arm description:

3 capsules of placebo, administered once daily for 12 weeks.

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

Dosage and administration details:

Participants took 3 capsules once daily for 12 weeks (in the morning with a glass of water after an overnight fast).

Number of subjects in period 1	EP395 375mg	Placebo
Started	42	19
Completed	39	18
Not completed	3	1
Adverse event, non-fatal	3	1

Baseline characteristics

Reporting groups	
Reporting group title	EP395 375mg
Reporting group description:	
3 capsules of 125 mg EP395 each, administered once daily for 12 weeks.	
Reporting group title	Placebo
Reporting group description:	
3 capsules of placebo, administered once daily for 12 weeks.	

Reporting group values	EP395 375mg	Placebo	Total
Number of subjects	42	19	61
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)	17	8	25
From 65-84 years	25	11	36
85 years and over	0	0	0
Age continuous Units: years			
median	66	66	
full range (min-max)	46 to 82	50 to 76	-
Gender categorical Units: Subjects			
Female	15	9	24
Male	27	10	37
Body mass index Units: kg/m²			
arithmetic mean	27.20	26.60	
standard deviation	± 4.57	± 4.27	-

End points

End points reporting groups

Reporting group title	EP395 375mg
Reporting group description:	
3 capsules of 125 mg EP395 each, administered once daily for 12 weeks.	
Reporting group title	Placebo
Reporting group description:	
3 capsules of placebo, administered once daily for 12 weeks.	

Primary: Safety and tolerability

End point title	Safety and tolerability[1]
End point description:	
The safety and tolerability of repeat doses of EP395 in patients with COPD were evaluated by the assessment of adverse events, laboratory safety parameters, vital signs, 12-lead electrocardiograms, and physical examinations during the treatment period and follow-up.	
End point type	Primary
End point timeframe:	
From first intake of investigational product (IP) until trial completion.	

Notes:

[1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: The primary endpoint was safety and tolerability and not associated with a hypothesis; therefore, no statistical analysis was performed.

End point values	EP395 375mg	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	42	19		
Units: Subject(s)				
Any treatment-emergent adverse event (TEAE)	27	12		
Any TEAE related to IP	9	5		
Any TEAE related to any trial procedure	2	2		
Any TEAE leading to IP withdrawal	3	1		
Clinical laboratory abnormalities reported as TEAE	2	0		
Clinically significant (CS) changes in vital signs	2	0		
CS abnormalities in electrocardiogram	0	0		
CS findings in physical examination	4	0		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information	
Timeframe for reporting adverse events: TEAEs from first intake of IP until trial completion.	
Assessment type	Systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	25.0

Reporting groups	
Reporting group title	EP395 375mg
Reporting group description: 3 capsules of 125 mg EP395 each, administered once daily for 12 weeks.	
Reporting group title	Placebo
Reporting group description: 3 capsules of placebo, administered once daily for 12 weeks.	

Serious adverse events	EP395 375mg	Placebo	
Total subjects affected by serious adverse events			
subjects affected / exposed	2 / 42 (4.76%)	0 / 19 (0.00%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events	0	0	
Injury, poisoning and procedural complications			
Radius fracture			
subjects affected / exposed	1 / 42 (2.38%)	0 / 19 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Pneumonia			
subjects affected / exposed	1 / 42 (2.38%)	0 / 19 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Frequency threshold for reporting non-serious adverse events: 0 %

Non-serious adverse events	EP395 375mg	Placebo	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	25 / 42 (59.52%)	12 / 19 (63.16%)	
Investigations			
Hepatic enzyme increased			
subjects affected / exposed	2 / 42 (4.76%)	0 / 19 (0.00%)	
occurrences (all)	2	0	
Pulmonary function test decreased			
subjects affected / exposed	1 / 42 (2.38%)	0 / 19 (0.00%)	
occurrences (all)	1	0	
Injury, poisoning and procedural complications			
Contusion			
subjects affected / exposed	0 / 42 (0.00%)	1 / 19 (5.26%)	
occurrences (all)	0	1	
Skin abrasion			
subjects affected / exposed	0 / 42 (0.00%)	1 / 19 (5.26%)	
occurrences (all)	0	1	
Vascular disorders			
Hypertension			
subjects affected / exposed	2 / 42 (4.76%)	0 / 19 (0.00%)	
occurrences (all)	2	0	
Cardiac disorders			
Ventricular extrasystoles			
subjects affected / exposed	1 / 42 (2.38%)	0 / 19 (0.00%)	
occurrences (all)	1	0	
Nervous system disorders			
Dizziness			
subjects affected / exposed	0 / 42 (0.00%)	1 / 19 (5.26%)	
occurrences (all)	0	1	
Dizziness postural			
subjects affected / exposed	1 / 42 (2.38%)	0 / 19 (0.00%)	
occurrences (all)	2	0	
Headache			
subjects affected / exposed	3 / 42 (7.14%)	0 / 19 (0.00%)	
occurrences (all)	3	0	
General disorders and administration site conditions			

Catheter site haematoma			
subjects affected / exposed	0 / 42 (0.00%)	1 / 19 (5.26%)	
occurrences (all)	0	1	
Chest discomfort			
subjects affected / exposed	2 / 42 (4.76%)	0 / 19 (0.00%)	
occurrences (all)	2	0	
Chest pain			
subjects affected / exposed	1 / 42 (2.38%)	0 / 19 (0.00%)	
occurrences (all)	1	0	
Fatigue			
subjects affected / exposed	1 / 42 (2.38%)	1 / 19 (5.26%)	
occurrences (all)	1	1	
Pyrexia			
subjects affected / exposed	1 / 42 (2.38%)	0 / 19 (0.00%)	
occurrences (all)	1	0	
Eye disorders			
Vision blurred			
subjects affected / exposed	0 / 42 (0.00%)	1 / 19 (5.26%)	
occurrences (all)	0	1	
Gastrointestinal disorders			
Abdominal pain upper			
subjects affected / exposed	1 / 42 (2.38%)	1 / 19 (5.26%)	
occurrences (all)	1	1	
Barrett's oesophagus			
subjects affected / exposed	1 / 42 (2.38%)	0 / 19 (0.00%)	
occurrences (all)	1	0	
Diarrhoea			
subjects affected / exposed	2 / 42 (4.76%)	1 / 19 (5.26%)	
occurrences (all)	2	1	
Dry mouth			
subjects affected / exposed	1 / 42 (2.38%)	0 / 19 (0.00%)	
occurrences (all)	1	0	
Duodenitis			
subjects affected / exposed	1 / 42 (2.38%)	0 / 19 (0.00%)	
occurrences (all)	1	0	
Dyspepsia			

subjects affected / exposed	1 / 42 (2.38%)	0 / 19 (0.00%)	
occurrences (all)	1	0	
Gastrooesophageal reflux disease			
subjects affected / exposed	1 / 42 (2.38%)	1 / 19 (5.26%)	
occurrences (all)	1	1	
Nausea			
subjects affected / exposed	3 / 42 (7.14%)	1 / 19 (5.26%)	
occurrences (all)	3	1	
Toothache			
subjects affected / exposed	0 / 42 (0.00%)	1 / 19 (5.26%)	
occurrences (all)	0	1	
Respiratory, thoracic and mediastinal disorders			
Aspiration			
subjects affected / exposed	1 / 42 (2.38%)	0 / 19 (0.00%)	
occurrences (all)	1	0	
Chronic obstructive pulmonary disease			
subjects affected / exposed	6 / 42 (14.29%)	2 / 19 (10.53%)	
occurrences (all)	6	2	
Cough			
subjects affected / exposed	1 / 42 (2.38%)	1 / 19 (5.26%)	
occurrences (all)	1	1	
Dyspnoea			
subjects affected / exposed	1 / 42 (2.38%)	0 / 19 (0.00%)	
occurrences (all)	1	0	
Nasal congestion			
subjects affected / exposed	0 / 42 (0.00%)	1 / 19 (5.26%)	
occurrences (all)	0	1	
Oropharyngeal pain			
subjects affected / exposed	2 / 42 (4.76%)	0 / 19 (0.00%)	
occurrences (all)	2	0	
Respiratory tract congestion			
subjects affected / exposed	1 / 42 (2.38%)	0 / 19 (0.00%)	
occurrences (all)	1	0	
Rhinitis allergic			

subjects affected / exposed	1 / 42 (2.38%)	0 / 19 (0.00%)	
occurrences (all)	1	0	
Sputum increased			
subjects affected / exposed	1 / 42 (2.38%)	0 / 19 (0.00%)	
occurrences (all)	2	0	
Wheezing			
subjects affected / exposed	2 / 42 (4.76%)	0 / 19 (0.00%)	
occurrences (all)	2	0	
Skin and subcutaneous tissue disorders			
Hyperhidrosis			
subjects affected / exposed	1 / 42 (2.38%)	0 / 19 (0.00%)	
occurrences (all)	1	0	
Pruritus			
subjects affected / exposed	2 / 42 (4.76%)	0 / 19 (0.00%)	
occurrences (all)	2	0	
Rash			
subjects affected / exposed	1 / 42 (2.38%)	0 / 19 (0.00%)	
occurrences (all)	1	0	
Rash erythematous			
subjects affected / exposed	1 / 42 (2.38%)	0 / 19 (0.00%)	
occurrences (all)	1	0	
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	1 / 42 (2.38%)	1 / 19 (5.26%)	
occurrences (all)	1	1	
Musculoskeletal stiffness			
subjects affected / exposed	1 / 42 (2.38%)	0 / 19 (0.00%)	
occurrences (all)	1	0	
Myalgia			
subjects affected / exposed	1 / 42 (2.38%)	1 / 19 (5.26%)	
occurrences (all)	1	1	
Osteoarthritis			
subjects affected / exposed	0 / 42 (0.00%)	1 / 19 (5.26%)	
occurrences (all)	0	1	
Infections and infestations			

Bacteriuria			
subjects affected / exposed	0 / 42 (0.00%)	1 / 19 (5.26%)	
occurrences (all)	0	1	
COVID-19			
subjects affected / exposed	1 / 42 (2.38%)	0 / 19 (0.00%)	
occurrences (all)	1	0	
Gastrointestinal infection			
subjects affected / exposed	0 / 42 (0.00%)	1 / 19 (5.26%)	
occurrences (all)	0	1	
Lower respiratory tract infection			
subjects affected / exposed	1 / 42 (2.38%)	0 / 19 (0.00%)	
occurrences (all)	1	0	
Nasopharyngitis			
subjects affected / exposed	6 / 42 (14.29%)	4 / 19 (21.05%)	
occurrences (all)	7	4	
Pulpitis dental			
subjects affected / exposed	0 / 42 (0.00%)	1 / 19 (5.26%)	
occurrences (all)	0	1	
Sinusitis			
subjects affected / exposed	1 / 42 (2.38%)	1 / 19 (5.26%)	
occurrences (all)	1	1	
Upper respiratory tract infection			
subjects affected / exposed	1 / 42 (2.38%)	0 / 19 (0.00%)	
occurrences (all)	1	0	
Urinary tract infection			
subjects affected / exposed	1 / 42 (2.38%)	1 / 19 (5.26%)	
occurrences (all)	1	1	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
06 September 2022	Changes to v1.0: - Clarification regarding the contraception requirements for male participants - Clarification that participants lacking the capacity to understand the study would be excluded - Clarification that participants required a history of sputum production for at least 3 months (not consecutive) within the last year - Additional information confirming that flu vaccination was allowed during the trial - Additional information that participants who tested positive for Covid-19 would be allowed to remain in the trial and to continue treatment, with adjustment for remote visits, if required - New exploratory endpoints were added

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported