Clinical trial results:
A pilot double-blind, placebo-controlled, 2 period crossover clinical study to assess the effect of aclidinium bromide 400 g BID on COPD symptoms and sleep quality after 3 weeks of treatment in patients with stable moderate to severe chronic obstructive pulmonary disease (COPD)

Summary

EudraCT number	2013-003373-10
Trial protocol	DE
Global end of trial date	02 June 2015

Results information

Result version number	v1 (current)
This version publication date	17 June 2016
First version publication date	17 June 2016

Trial information

Trial identification

Sponsor protocol code	M/34273/47

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02153489
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	AstraZeneca
Sponsor organisation address	2 Kingdom St, London, United Kingdom, W2 6BD
Public contact	Study Director, AstraZeneca, ClinicalTrialTransparency@astrazeneca.com
Scientific contact	Study Director, AstraZeneca, ClinicalTrialTransparency@astrazeneca.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	02 June 2015
Is this the analysis of the primary completion data?	Yes
Primary completion date	02 June 2015
Global end of trial reached?	Yes
Global end of trial date	02 June 2015
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The objectives of this study were to assess the effect of aclidinium bromide versus placebo in improving bronchodilation, chronic obstructive pulmonary disease (COPD) symptoms, sleep quality and physical activity after 3 weeks of treatment in patients with stable moderate and severe COPD and to assess the safety and tolerability of aclidinium bromide 400 µg administered twice daily (BID) in the same target population

Protection of trial subjects:

This study was conducted in accordance with the recommendations guiding physicians in biomedical research involving human subjects adopted by the 18th World Medical Assembly of Helsinki (1964), revised at Tokyo (1975), Venice (1983), Hong-Kong (1989) and Somerset West (1996) as well as in compliance with International Conference on Harmonisation (ICH) Good Clinical Practice (GCP) guidelines. Patients were provided with relief medication, salbutamol pressurised metered dose inhaler (pMDI), 100 µg/puff, which could be used on from the time of signing of the informed consent until the end of treatment period

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	22 April 2015
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Germany: 30
Worldwide total number of subjects	30
EEA total number of subjects	30

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)	15
From 65 to 84 years	15
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

This study was conducted by 3 investigators at 3 sites in Germany. The first patient was screened in April 2015 and the last patient visit was in June 2015

Pre-assignment

Screening details:

All patients who met the study entry criteria and completed the screening assessments and the 7-day run-in period were randomised. Nine (9/39) subjects were not randomized due to screening failure (primarily for non-fulfillment of inclusion/exclusion criteria)

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	Sequence A

Arm description:

Aclidinium 400 µg - Placebo

Arm type	Experimental
Investigational medicinal product name	Aclidinium bromide
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Inhalation powder
Routes of administration	Inhalation use

Dosage and administration details:

400 µg twice-daily (BID)

Arm title	Sequence B

Arm description:

Placebo - Aclidinium 400 µg

Arm type	Experimental
Investigational medicinal product name	Aclidinium bromide
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Inhalation powder
Routes of administration	Inhalation use

Dosage and administration details:

400 µg twice-daily (BID)

Number of subjects in period 1	Sequence A	Sequence B
Started	15	15
Started Period 1	15	15
Completed Period 1	15	15
Started Period 2	15	15
Completed Period 2	15	15
Completed	15	15

Baseline characteristics

Reporting groups	
Reporting group title	Overall Study

Reporting group description: -

Reporting group values	Overall Study	Total	
Number of subjects	30	30	
Age categorical Units: Subjects			
Adults (18-64 years)	15	15	
Elderly (From 65-84 years)	15	15	
Age continuous Units: years			
arithmetic mean	64.4		
standard deviation	± 7	-	
Gender categorical Units: Subjects			
Female	15	15	
Male	15	15	

End points

End points reporting groups	
Reporting group title	Sequence A
Reporting group description: Aclidinium 400 µg - Placebo	
Reporting group title	Sequence B
Reporting group description: Placebo - Aclidinium 400 µg	
Subject analysis set title	Aclidinium
Subject analysis set type	Per protocol
Subject analysis set description: Aclidinium bromide 400 ug BID	
Subject analysis set title	Placebo
Subject analysis set type	Per protocol
Subject analysis set description: Placebo BID	

Primary: Change from baseline in normalised forced expiratory volume in one second (FEV1) AUC0-24hr

End point title	Change from baseline in normalised forced expiratory volume in one second (FEV1) AUC0-24hr
End point description:	
End point type	Primary
End point timeframe: Week 3 of treatment	

End point values	Aclidinium	Placebo		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	30	30		
Units: L/sec.hr				
least squares mean (standard error)	0.0953 (± 0.0381)	-0.0429 (± 0.0381)		

Statistical analyses

Statistical analysis title	Aclidinium v Placebo
Comparison groups	Aclidinium v Placebo
Number of subjects included in analysis	60
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0035
Method	ANCOVA
Parameter estimate	Least squares mean difference
Point estimate	0.1382

Confidence interval	
level	95 %
sides	2-sided
lower limit	0.0515
upper limit	0.225
Variability estimate	Standard error of the mean
Dispersion value	0.0415

Other pre-specified: Change from baseline in morning trough FEV1

End point title	Change from baseline in morning trough FEV1

End point description:

End point type	Other pre-specified

End point timeframe:

Week 3 of treatment

End point values	Aclidinium	Placebo		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	30	30		
Units: Litres/sec				
least squares mean (standard error)	0.1128 (± 0.0395)	-0.0106 (± 0.0395)		

Statistical analyses

No statistical analyses for this end point

Other pre-specified: Change from baseline in peak FEV1

End point title	Change from baseline in peak FEV1

End point description:

End point type	Other pre-specified

End point timeframe:

Week 3 of treatment

End point values	Aclidinium	Placebo		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	30	30		
Units: Litres/sec				
least squares mean (standard error)	0.1605 (± 0.0391)	-0.0149 (± 0.0391)		

Statistical analyses

No statistical analyses for this end point

Other pre-specified: Change from baseline in normalised FEV1 AUC0-12hr

End point title	Change from baseline in normalised FEV1 AUC0-12hr

End point description:

End point type	Other pre-specified

End point timeframe:

Week 3 of treatment

End point values	Aclidinium	Placebo		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	30	30		
Units: L/sec.hr				
least squares mean (standard error)	0.1394 (± 0.0406)	-0.01 (± 0.0406)		

Statistical analyses

No statistical analyses for this end point

Other pre-specified: Change from baseline in normalised FEV1 AUC12-24hr

End point title	Change from baseline in normalised FEV1 AUC12-24hr

End point description:

End point type	Other pre-specified

End point timeframe:

Week 3 of treatment

End point values	Aclidinium	Placebo		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	30	30		
Units: L/sec.hr				
least squares mean (standard error)	0.0513 (± 0.0369)	-0.0758 (± 0.0369)		

Statistical analyses

No statistical analyses for this end point

Other pre-specified: Change from baseline in the average rating of COPD symptoms limiting early morning activities

End point title	Change from baseline in the average rating of COPD symptoms limiting early morning activities

End point description:

End point type	Other pre-specified

End point timeframe:

Week 3 of treatment

End point values	Aclidinium	Placebo		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	30	30		
Units: Score				
arithmetic mean (standard deviation)	-0.02 (± 0.457)	0.16 (± 0.43)		

Statistical analyses

No statistical analyses for this end point

Other pre-specified: Change from baseline in the average rating of overall early morning COPD symptom severity

End point title	Change from baseline in the average rating of overall early morning COPD symptom severity

End point description:

End point type	Other pre-specified

End point timeframe:

Week 3 of treatment

End point values	Aclidinium	Placebo		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	30	30		
Units: Score				
arithmetic mean (standard deviation)	-0.07 (± 0.575)	0.09 (± 0.476)		

Statistical analyses

No statistical analyses for this end point

Other pre-specified: Change from baseline in the average rating of COPD symptoms limiting evening activities

End point title	Change from baseline in the average rating of COPD symptoms limiting evening activities

End point description:

End point type	Other pre-specified

End point timeframe:

Week 3 of treatment

End point values	Aclidinium	Placebo		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	30	30		
Units: Score				
arithmetic mean (standard deviation)	-0.18 (± 0.488)	0.03 (± 0.45)		

Statistical analyses

No statistical analyses for this end point

Other pre-specified: Change from baseline in the average rating of overall evening COPD symptom severity

End point title	Change from baseline in the average rating of overall evening COPD symptom severity

End point description:

End point type	Other pre-specified

End point timeframe:

Week 3 of treatment

End point values	Aclidinium	Placebo		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	30	30		
Units: Score				
arithmetic mean (standard deviation)	-0.15 (± 0.661)	0.11 (± 0.559)		

Statistical analyses

No statistical analyses for this end point

Other pre-specified: Change from baseline in the average rating of overall night-time COPD symptom severity

End point title	Change from baseline in the average rating of overall night-time COPD symptom severity

End point description:

End point type	Other pre-specified

End point timeframe:

Week 3 of treatment

End point values	Aclidinium	Placebo		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	30	30		
Units: Score				
arithmetic mean (standard deviation)	-0.14 (± 0.612)	-0.03 (± 0.526)		

Statistical analyses

No statistical analyses for this end point

Other pre-specified: Change from baseline in duration of at least moderate activity

End point title	Change from baseline in duration of at least moderate activity

End point description:

Moderate activity was defined as any physical activity >3 metabolic equivalents

End point type	Other pre-specified

End point timeframe:

Week 3 of treatment

End point values	Aclidinium	Placebo		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	30	30		
Units: Minutes				
least squares mean (standard error)	9.446 (± 6.7081)	-8.5943 (± 6.5879)		

Statistical analyses

No statistical analyses for this end point

Other pre-specified: Change from baseline in number of steps

End point title	Change from baseline in number of steps

End point description:

End point type	Other pre-specified

End point timeframe:

Week 3 of treatment

End point values	Aclidinium	Placebo		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	30	30		
Units: Steps				
least squares mean (standard error)	268.5891 (± 326.3649)	22.2652 (± 320.6754)		

Statistical analyses

No statistical analyses for this end point

Other pre-specified: Change from baseline in oxygen desaturation index (ODI) per hour of total sleep time

End point title	Change from baseline in oxygen desaturation index (ODI) per hour of total sleep time

End point description:

End point type	Other pre-specified

End point timeframe:

Week 3 of treatment

End point values	Aclidinium	Placebo		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	30	30		
Units: /hr				
least squares mean (standard error)	-0.3033 (± 0.9754)	2.24 (± 0.9754)		

Statistical analyses

No statistical analyses for this end point

Other pre-specified: Change from baseline in sleep efficiency

End point title	Change from baseline in sleep efficiency

End point description:

End point type	Other pre-specified

End point timeframe:

Week 3 of treatment

End point values	Aclidinium	Placebo		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	30	30		
Units: Percentage				
least squares mean (standard error)	1 (± 2.4046)	-2.55 (± 2.4046)		

Statistical analyses

No statistical analyses for this end point

Other pre-specified: Change from baseline in sleep stage REM

End point title	Change from baseline in sleep stage REM

End point description:

End point type	Other pre-specified

End point timeframe:

Week 3 of treatment

End point values	Aclidinium	Placebo		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	30	30		
Units: Percentage				
arithmetic mean (standard error)	1.41 (± 0.9851)	-1.1167 (± 0.9851)		

Statistical analyses

No statistical analyses for this end point

Other pre-specified: Change from baseline in total sleep time

End point title	Change from baseline in total sleep time

End point description:

End point type	Other pre-specified

End point timeframe:

Week 3 of treatment

End point values	Aclidinium	Placebo		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	30	30		
Units: Minutes				
least squares mean (standard error)	6.92 (± 11.5802)	-11.85 (± 11.5802)		

Statistical analyses

No statistical analyses for this end point

Other pre-specified: Change from baseline in apnea-hypopnea index (AHI) per hour of total sleep time

End point title	Change from baseline in apnea-hypopnea index (AHI) per hour of total sleep time

End point description:

End point type	Other pre-specified

End point timeframe:

Week 3 of treatment

End point values	Aclidinium	Placebo		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	30	30		
Units: /hr				
least squares mean (standard error)	0.4767 (± 0.4478)	0.77 (± 0.4478)		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information	
Timeframe for reporting adverse events: Up to 30 days after last study drug administration	
Assessment type	Systematic
Dictionary used	
Dictionary name	MedDRA
Dictionary version	17.1
Reporting groups	
Reporting group title	Placebo
Reporting group description: Placebo BID	
Reporting group title	Aclidinium
Reporting group description: Aclidinium bromide 400 µg BID	

Serious adverse events	Placebo	Aclidinium	
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 30 (0.00%)	0 / 30 (0.00%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events	0	0	

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

Non-serious adverse events	Placebo	Aclidinium	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	0 / 30 (0.00%)	3 / 30 (10.00%)	
Skin and subcutaneous tissue disorders			
Erythema			
subjects affected / exposed	0 / 30 (0.00%)	3 / 30 (10.00%)	
occurrences (all)	0	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