Clinical trial results:
A randomized, double-blind, multiple dosing (14 days), placebo-controlled, incomplete block crossover, multi-center study to assess efficacy and safety of three dose levels of AZD7594, given once daily by inhalation, in patients with mild to moderate asthma.

Summary

EudraCT number	2014-005306-37
Trial protocol	DE BG
Global end of trial date	08 February 2016

Results information

Result version number	v1 (current)
This version publication date	19 February 2017
First version publication date	19 February 2017

Trial information

Trial identification

Sponsor protocol code	D3741C00003

Additional study identifiers

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

Notes:

Sponsors

Sponsor organisation name	AstraZeneca AB
Sponsor organisation address	Forskargatan 18,, Södertälje, Sweden, 15185
Public contact	Information Centre, AstraZeneca AB, Information Centre, AstraZeneca AB, +1 800 2369933, information.centre@astrazeneca.com
Scientific contact	Global Clinical Leader, Information Centre, AstraZeneca AB, 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	08 February 2016
Is this the analysis of the primary completion data?	Yes
Primary completion date	08 February 2016
Global end of trial reached?	Yes
Global end of trial date	08 February 2016
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The primary objective was to investigate the efficacy of AZD7594 as measured by change in trough forced expiratory volume in 1 sec (FEV1) from baseline, as compared to placebo.

Protection of trial subjects:

This study was designed and monitored in accordance with with the ethical principles of Good Clinical Practice (GCP) guidelines of the International Conference on Harmonization (ICH) as required by the major regulatory authorities, and in accordance with the Declaration of Helsinki (1996). The study was carried out in keeping with local legal requirements as well. The patients were informed of the nature, significance, implications, and risks of the research study. Informed consent was recorded in writing, dated, and signed by the patients before the start of the study, as evidence to indicate that their informed consent was given freely. This consent form was dated and retained by the Investigator as part of the study records. No study-related procedure was performed prior to obtaining informed consent from the patient. The terms of the consent and when it was obtained was also documented in the electronic case report form (eCRF). Informed consent was obtained in line with the Declaration of Helsinki (1996), the current requirements of GCP (Committee for Proprietary Medicinal Products/ICH/135/95), and local regulation – whichever afforded the greatest patient protection. If a protocol amendment was required, the informed consent form (ICF) was revised to reflect the changes to the protocol. If the ICF was revised, it was reviewed and approved by the appropriate independent ethics committee (IEC), and signed by all patients subsequently enrolled in the study as well as those currently enrolled in the study.

Background therapy:

-

Evidence for comparator:

-

Actual start date of recruitment	25 June 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: 50
Country: Number of subjects enrolled	Bulgaria: 4
Worldwide total number of subjects	54
EEA total number of subjects	54

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)	54
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

The study was conducted in Germany (9 centers) & Bulgaria (1 center).110 participants were enrolled (signed informed consent). A total of 54 participants with mild to moderate asthma were randomized after screening, and received study treatment (AZD7594 or placebo) given over 3 Treatment Periods in an incomplete block crossover design.

Pre-assignment

Screening details:

The study consisted of a 2-part run-in period, 3 treatment periods separated by intervening wash-out periods, and a final period of safety follow-up .

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, Subject

Blinding implementation details:

The study blind was to be broken only in the case of a medical emergency, where knowledge of the IP received could affect the choice of treatment, and in case of a regulatory requirement (eg, for a serious adverse event [SAE] or death).

Arms

Are arms mutually exclusive?	Yes
Arm title	Sequence 1 (Placebo + AZD7594 58 µg + AZD7594 250 µg)

Arm description:

Placebo once daily for 14 days in Period 1, 58 µg AZD7594 once daily for 14 days in Period 2 and 250 µg AZD7594 once daily for 14 days in Period 3

Arm type	Experimental
Investigational medicinal product name	AZD7594
Investigational medicinal product code	AZD7594
Other name	
Pharmaceutical forms	Inhalation powder, hard capsule
Routes of administration	Inhalation use

Dosage and administration details:

Placebo once daily for 14 days in Period 1, AZD7594 58 µg once daily for 14 days in Period 2 and AZD7594 250 µg once daily for 14 days in Period 3

Arm title	Sequence 2 (Placebo + AZD7594 250 µg + AZD7594 800 µg)

Arm description:

Placebo once daily for 14 days in Period 1, 250 µg AZD7594 once daily for 14 days in Period 2 and 800 µg AZD7594 once daily for 14 days in Period 3

Arm type	Experimental
Investigational medicinal product name	AZD7594
Investigational medicinal product code	AZD7594
Other name	
Pharmaceutical forms	Inhalation powder, hard capsule
Routes of administration	Inhalation use

Dosage and administration details:

Placebo once daily for 14 days in Period 1, AZD7594 250 µg once daily for 14 days in Period 2 and AZD7594 800 µg once daily for 14 days in Period 3

Arm title	Sequence 3 (Placebo + AZD7594 800 µg + AZD7594 58 µg)

Arm description:

Placebo once daily for 14 days in Period 1, 800 µg AZD7594 once daily for 14 days in Period 2 and 58 µg AZD7594 once daily for 14 days in Period 3

Arm type	Experimental
Investigational medicinal product name	AZD7594
Investigational medicinal product code	AZD7594
Other name	
Pharmaceutical forms	Inhalation powder, hard capsule
Routes of administration	Inhalation use

Dosage and administration details:

Placebo once daily for 14 days in Period 1, AZD7594 800 µg once daily for 14 days in Period 2 and AZD7594 58 µg once daily for 14 days in Period 3

Arm title	Sequence 4 (AZD7594 58 µg + Placebo + AZD7594 800 µg)

Arm description:

58 µg AZD7594 once daily for 14 days in Period 1, Placebo once daily for 14 days in Period 2 and 800 µg AZD7594 once daily for 14 days in Period 3

Arm type	Experimental
Investigational medicinal product name	AZD7594
Investigational medicinal product code	AZD7594
Other name	
Pharmaceutical forms	Inhalation powder, hard capsule
Routes of administration	Inhalation use

Dosage and administration details:

AZD7594 58 µg once daily for 14 days in Period 1, Placebo once daily for 14 days in Period 2 and AZD7594 800 µg once daily for 14 days in Period 3

Arm title	Sequence 5 (AZD7594 58 µg + AZD7594 800 µg + Placebo)

Arm description:

58 µg AZD7594 once daily for 14 days in Period 1, 800 µg AZD7594 once daily for 14 days in Period 2 and Placebo once daily for 14 days in Period 3

Arm type	Experimental
Investigational medicinal product name	AZD7594
Investigational medicinal product code	AZD7594
Other name	
Pharmaceutical forms	Inhalation powder, hard capsule
Routes of administration	Inhalation use

Dosage and administration details:

AZD7594 58 µg once daily for 14 days in Period 1, AZD7594 800 µg once daily for 14 days in Period 2 and Placebo once daily for 14 days in Period 3

Arm title	Sequence 6 (AZD7594 250 µg + Placebo + AZD7594 58 µg)

Arm description:

250 µg AZD7594 once daily for 14 days in Period 1, Placebo once daily for 14 days in Period 2 and 58 µg AZD7594 once daily for 14 days in Period 3

Arm type	Experimental
Investigational medicinal product name	AZD7594
Investigational medicinal product code	AZD7594
Other name	
Pharmaceutical forms	Inhalation powder, hard capsule
Routes of administration	Inhalation use

Dosage and administration details:

AZD7594 250 µg once daily for 14 days in Period 1, Placebo once daily for 14 days in Period 2 and AZD7594 58 µg once daily for 14 days in Period 3

Arm title	Sequence 7 (AZD7594 250 µg + AZD7594 58 µg + Placebo)

Arm description:	
250 µg AZD7594 once daily for 14 days in Period 1, 58 µg AZD7594 once daily for 14 days in Period 2 and Placebo once daily for 14 days in Period 3	
Arm type	Experimental
Investigational medicinal product name	AZD7594
Investigational medicinal product code	AZD7594
Other name	
Pharmaceutical forms	Inhalation powder, hard capsule
Routes of administration	Inhalation use
Dosage and administration details:	
AZD7594 250 µg once daily for 14 days in Period 1, AZD7594 58 µg once daily for 14 days in Period 2 and Placebo once daily for 14 days in Period 3	
Arm title	Sequence 8 (AZD7594 800 µg + Placebo + AZD7594 250 µg)
Arm description:	
800 µg AZD7594 once daily for 14 days in Period 1, Placebo once daily for 14 days in Period 2 and 250 µg AZD7594 once daily for 14 days	
Arm type	Experimental
Investigational medicinal product name	AZD7594
Investigational medicinal product code	AZD7594
Other name	
Pharmaceutical forms	Inhalation powder, hard capsule
Routes of administration	Inhalation use
Dosage and administration details:	
AZD7594 800 µg once daily for 14 days in Period 1, Placebo once daily for 14 days in Period 2 and AZD7594 250 µg once daily for 14 days	
Arm title	Sequence 9 (AZD7594 800 µg + AZD7594 250 µg + Placebo)
Arm description:	
800 µg AZD7594 once daily for 14 days in Period 1, 250 µg AZD7594 once daily for 14 days in Period 2 and Placebo once daily for 14 days in Period 3	
Arm type	Experimental
Investigational medicinal product name	AZD7594
Investigational medicinal product code	AZD7594
Other name	
Pharmaceutical forms	Inhalation powder, hard capsule
Routes of administration	Inhalation use
Dosage and administration details:	
AZD7594 800 µg once daily for 14 days in Period 1, AZD7594 250 µg once daily for 14 days in Period 2 and Placebo once daily for 14 days in Period 3	

Number of subjects in period 1	Sequence 1 (Placebo + AZD7594 58 µg + AZD7594 250 µg)	Sequence 2 (Placebo + AZD7594 250 µg + AZD7594 800 µg)	Sequence 3 (Placebo + AZD7594 800 µg + AZD7594 58 µg)
Started	6	6	6
Completed	6	6	4
Not completed	0	0	2
Adverse event, non-fatal	-	-	1
Study-specific withdrawal criteria	-	-	1
Randomization to wrong PK sampling group	-	-	-

Number of subjects in period 1	Sequence 4 (AZD7594 58 µg + Placebo + AZD7594 800 µg)	Sequence 5 (AZD7594 58 µg + AZD7594 800 µg + Placebo)	Sequence 6 (AZD7594 250 µg + Placebo + AZD7594 58 µg)
Started	7	6	5
Completed	6	5	5
Not completed	1	1	0
Adverse event, non-fatal	-	-	-
Study-specific withdrawal criteria	1	-	-
Randomization to wrong PK sampling group	-	1	-

Number of subjects in period 1	Sequence 7 (AZD7594 250 µg + AZD7594 58 µg + Placebo)	Sequence 8 (AZD7594 800 µg + Placebo + AZD7594 250 µg)	Sequence 9 (AZD7594 800 µg + AZD7594 250 µg + Placebo)
Started	6	5	7
Completed	6	4	6
Not completed	0	1	1
Adverse event, non-fatal	-	-	-
Study-specific withdrawal criteria	-	1	1
Randomization to wrong PK sampling group	-	-	-

Baseline characteristics

Reporting groups	
Reporting group title	Sequence 1 (Placebo + AZD7594 58 µg + AZD7594 250 µg)
Reporting group description:	
Placebo once daily for 14 days in Period 1, 58 µg AZD7594 once daily for 14 days in Period 2 and 250 µg AZD7594 once daily for 14 days in Period 3	
Reporting group title	Sequence 2 (Placebo + AZD7594 250 µg + AZD7594 800 µg)
Reporting group description:	
Placebo once daily for 14 days in Period 1, 250 µg AZD7594 once daily for 14 days in Period 2 and 800 µg AZD7594 once daily for 14 days in Period 3	
Reporting group title	Sequence 3 (Placebo + AZD7594 800 µg + AZD7594 58 µg)
Reporting group description:	
Placebo once daily for 14 days in Period 1, 800 µg AZD7594 once daily for 14 days in Period 2 and 58 µg AZD7594 once daily for 14 days in Period 3	
Reporting group title	Sequence 4 (AZD7594 58 µg + Placebo + AZD7594 800 µg)
Reporting group description:	
58 µg AZD7594 once daily for 14 days in Period 1, Placebo once daily for 14 days in Period 2 and 800 µg AZD7594 once daily for 14 days in Period 3	
Reporting group title	Sequence 5 (AZD7594 58 µg + AZD7594 800 µg + Placebo)
Reporting group description:	
58 µg AZD7594 once daily for 14 days in Period 1, 800 µg AZD7594 once daily for 14 days in Period 2 and Placebo once daily for 14 days in Period 3	
Reporting group title	Sequence 6 (AZD7594 250 µg + Placebo + AZD7594 58 µg)
Reporting group description:	
250 µg AZD7594 once daily for 14 days in Period 1, Placebo once daily for 14 days in Period 2 and 58 µg AZD7594 once daily for 14 days in Period 3	
Reporting group title	Sequence 7 (AZD7594 250 µg + AZD7594 58 µg + Placebo)
Reporting group description:	
250 µg AZD7594 once daily for 14 days in Period 1, 58 µg AZD7594 once daily for 14 days in Period 2 and Placebo once daily for 14 days in Period 3	
Reporting group title	Sequence 8 (AZD7594 800 µg + Placebo + AZD7594 250 µg)
Reporting group description:	
800 µg AZD7594 once daily for 14 days in Period 1, Placebo once daily for 14 days in Period 2 and 250 µg AZD7594 once daily for 14 days	
Reporting group title	Sequence 9 (AZD7594 800 µg + AZD7594 250 µg + Placebo)
Reporting group description:	
800 µg AZD7594 once daily for 14 days in Period 1, 250 µg AZD7594 once daily for 14 days in Period 2 and Placebo once daily for 14 days in Period 3	

Reporting group values	Sequence 1 (Placebo + AZD7594 58 µg + AZD7594 250 µg)	Sequence 2 (Placebo + AZD7594 250 µg + AZD7594 800 µg)	Sequence 3 (Placebo + AZD7594 800 µg + AZD7594 58 µg)
Number of subjects	6	6	6
Age categorical Units: Subjects			
18 - 75 years	6	6	6
Age Continuous | Age (years) Units: years			
arithmetic mean	49	50	56
standard deviation	± 14	± 10	± 10

Gender, Male/Female Units: Participants			
Female	1	0	2
Male	5	6	4

Reporting group values	Sequence 4 (AZD7594 58 µg + Placebo + AZD7594 800 µg)	Sequence 5 (AZD7594 58 µg + AZD7594 800 µg + Placebo)	Sequence 6 (AZD7594 250 µg + Placebo + AZD7594 58 µg)
Number of subjects	7	6	5
Age categorical Units: Subjects			
18 - 75 years	7	6	5
Age Continuous | Age (years) Units: years			
arithmetic mean	50	49	55
standard deviation	± 17	± 7	± 9
Gender, Male/Female Units: Participants			
Female	0	3	2
Male	7	3	3

Reporting group values	Sequence 7 (AZD7594 250 µg + AZD7594 58 µg + Placebo)	Sequence 8 (AZD7594 800 µg + Placebo + AZD7594 250 µg)	Sequence 9 (AZD7594 800 µg + AZD7594 250 µg + Placebo)
Number of subjects	6	5	7
Age categorical Units: Subjects			
18 - 75 years	6	5	7
Age Continuous | Age (years) Units: years			
arithmetic mean	48	55	46
standard deviation	± 14	± 14	± 13
Gender, Male/Female Units: Participants			
Female	0	1	1
Male	6	4	6

Reporting group values	Total		
Number of subjects	54		
Age categorical Units: Subjects			
18 - 75 years	54		
Age Continuous | Age (years) Units: years			
arithmetic mean			
standard deviation	-		
Gender, Male/Female Units: Participants			
Female	10		
Male	44		

Subject analysis sets	
Subject analysis set title	AZD7594
Subject analysis set type	Full analysis
Subject analysis set description: AZD7594 DPI once daily	
Subject analysis set title	Placebo (PBO)
Subject analysis set type	Full analysis
Subject analysis set description: Placebo for AZD7594 DPI once daily	
Subject analysis set title	AZD7594 58 µg
Subject analysis set type	Full analysis
Subject analysis set description: AZD7594 DPI once daily - 2 capsules of 29 µg	
Subject analysis set title	AZD7594 250 µg
Subject analysis set type	Full analysis
Subject analysis set description: AZD7594 DPI once daily - 2 capsules of 125 µg	
Subject analysis set title	AZD7594 800 µg
Subject analysis set type	Full analysis
Subject analysis set description: AZD7594 DPI once daily - 2 capsules of 400 µg	

Reporting group values	AZD7594	Placebo (PBO)	AZD7594 58 µg
Number of subjects	34	52	34
Age categorical Units: Subjects			
18 - 75 years		52	34
Age Continuous | Age (years) Units: years			
arithmetic mean		51	51
standard deviation	±	± 12	± 12
Gender, Male/Female Units: Participants			
Female	0	8	8
Male	0	44	26

Reporting group values	AZD7594 250 µg	AZD7594 800 µg	
Number of subjects	34	34	
Age categorical Units: Subjects			
18 - 75 years	34	34	
Age Continuous | Age (years) Units: years			
arithmetic mean	50	51	
standard deviation	± 12	± 12	
Gender, Male/Female Units: Participants			
Female	4	6	
Male	30	28	

End points

End points reporting groups

Reporting group title	Sequence 1 (Placebo + AZD7594 58 µg + AZD7594 250 µg)
Reporting group description:	
Placebo once daily for 14 days in Period 1, 58 µg AZD7594 once daily for 14 days in Period 2 and 250 µg AZD7594 once daily for 14 days in Period 3	
Reporting group title	Sequence 2 (Placebo + AZD7594 250 µg + AZD7594 800 µg)
Reporting group description:	
Placebo once daily for 14 days in Period 1, 250 µg AZD7594 once daily for 14 days in Period 2 and 800 µg AZD7594 once daily for 14 days in Period 3	
Reporting group title	Sequence 3 (Placebo + AZD7594 800 µg + AZD7594 58 µg)
Reporting group description:	
Placebo once daily for 14 days in Period 1, 800 µg AZD7594 once daily for 14 days in Period 2 and 58 µg AZD7594 once daily for 14 days in Period 3	
Reporting group title	Sequence 4 (AZD7594 58 µg + Placebo + AZD7594 800 µg)
Reporting group description:	
58 µg AZD7594 once daily for 14 days in Period 1, Placebo once daily for 14 days in Period 2 and 800 µg AZD7594 once daily for 14 days in Period 3	
Reporting group title	Sequence 5 (AZD7594 58 µg + AZD7594 800 µg + Placebo)
Reporting group description:	
58 µg AZD7594 once daily for 14 days in Period 1, 800 µg AZD7594 once daily for 14 days in Period 2 and Placebo once daily for 14 days in Period 3	
Reporting group title	Sequence 6 (AZD7594 250 µg + Placebo + AZD7594 58 µg)
Reporting group description:	
250 µg AZD7594 once daily for 14 days in Period 1, Placebo once daily for 14 days in Period 2 and 58 µg AZD7594 once daily for 14 days in Period 3	
Reporting group title	Sequence 7 (AZD7594 250 µg + AZD7594 58 µg + Placebo)
Reporting group description:	
250 µg AZD7594 once daily for 14 days in Period 1, 58 µg AZD7594 once daily for 14 days in Period 2 and Placebo once daily for 14 days in Period 3	
Reporting group title	Sequence 8 (AZD7594 800 µg + Placebo + AZD7594 250 µg)
Reporting group description:	
800 µg AZD7594 once daily for 14 days in Period 1, Placebo once daily for 14 days in Period 2 and 250 µg AZD7594 once daily for 14 days	
Reporting group title	Sequence 9 (AZD7594 800 µg + AZD7594 250 µg + Placebo)
Reporting group description:	
800 µg AZD7594 once daily for 14 days in Period 1, 250 µg AZD7594 once daily for 14 days in Period 2 and Placebo once daily for 14 days in Period 3	
Subject analysis set title	AZD7594
Subject analysis set type	Full analysis
Subject analysis set description:	
AZD7594 DPI once daily	
Subject analysis set title	Placebo (PBO)
Subject analysis set type	Full analysis
Subject analysis set description:	
Placebo for AZD7594 DPI once daily	
Subject analysis set title	AZD7594 58 µg
Subject analysis set type	Full analysis
Subject analysis set description:	
AZD7594 DPI once daily - 2 capsules of 29 µg	
Subject analysis set title	AZD7594 250 µg
Subject analysis set type	Full analysis

Subject analysis set description:

AZD7594 DPI once daily - 2 capsules of 125 µg

Subject analysis set title	AZD7594 800 µg
Subject analysis set type	Full analysis

Subject analysis set description:

AZD7594 DPI once daily - 2 capsules of 400 µg

Primary: Efficacy of AZD7594 by assessment of the change from baseline in morning trough forced expiratory volume in 1 second (FEV1) on Day 15

End point title	Efficacy of AZD7594 by assessment of the change from baseline in morning trough forced expiratory volume in 1 second (FEV1) on Day 15

End point description:

Comparison of the efficacy of AZD7594 in terms of change from baseline in morning trough forced expiratory volume in 1 second (FEV1) on Day 15 (defined as the average of the values at 23:00 and 23:30 hours after last dose of investigational medicinal product [IMP] on Day 14) with placebo

End point type	Primary

End point timeframe:

On Day 1 (pre-dose) and on Day 15 in each period

End point values	AZD7594	Placebo (PBO)		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	33	51		
Units: Liters				
least squares mean (confidence interval 95%)				
AZD7594 58 µg vs. PBO	0.08639 (-0.0165 to 0.1893)	0.05948 (-0.02453 to 0.1435)		
AZD7594 250 µg vs. PBO	0.1355 (0.03283 to 0.2382)	0.05948 (-0.02453 to 0.1435)		
AZD7594 800 µg vs. PBO	0.2072 (0.1041 to 0.3104)	0.05948 (-0.02453 to 0.1435)		

Statistical analyses

Statistical analysis title	Statistical analysis 1

Statistical analysis description:

AZD7594 58 µg vs. Placebo

Comparison groups	AZD7594 v Placebo (PBO)
Number of subjects included in analysis	84
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.6379
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)
Point estimate	0.02691

Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.08626
upper limit	0.1401
Variability estimate	Standard error of the mean
Dispersion value	0.05697

Statistical analysis title	Statistical analysis 2
Statistical analysis description: AZD7594 250 µg vs.PBO	
Comparison groups	AZD7594 v Placebo (PBO)
Number of subjects included in analysis	84
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.1827
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)
Point estimate	0.07604
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.03645
upper limit	0.1885
Variability estimate	Standard error of the mean
Dispersion value	0.05663

Statistical analysis title	Statistical analysis 3
Statistical analysis description: AZD7594 800 µg vs. PBO	
Comparison groups	AZD7594 v Placebo (PBO)
Number of subjects included in analysis	84
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0108
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)
Point estimate	0.1478
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.03494
upper limit	0.2606
Variability estimate	Standard error of the mean
Dispersion value	0.05679

Secondary: Efficacy of AZD7594 by assessment of the change from baseline in fractional exhaled nitric oxide (FeNO) on Day 8

End point title	Efficacy of AZD7594 by assessment of the change from baseline in fractional exhaled nitric oxide (FeNO) on Day 8

End point description:

The efficacy of AZD7594 will be assessed in terms of change from baseline in fractional exhaled nitric oxide (FeNO) on Day 8

End point type	Secondary

End point timeframe:

On Day 1 (pre-dose) and on Day 8 in each period

End point values	AZD7594	Placebo (PBO)		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	34	52		
Units: Parts per billion (ppb)				
least squares mean (confidence interval 95%)				
AZD7594 58 µg vs. PBO (n=32 for AZD7594)	-9.153 (-15.08 to -3.23)	-4.296 (-9.046 to 0.4536)		
AZD7594 250 µg vs. PBO (n=33 for AZD7594)	-14.71 (-20.56 to -8.862)	-4.296 (-9.046 to 0.4536)		
AZD7594 800 µg vs. PBO (n=32 for AZD7594)	-19.04 (-24.99 to -13.1)	-4.296 (-9.046 to 0.4536)		

Statistical analyses

Statistical analysis title	Statistical analysis 1

Statistical analysis description:

AZD7594 58 µg vs. PBO

Comparison groups	AZD7594 v Placebo (PBO)
Number of subjects included in analysis	86
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.1342
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)
Point estimate	-4.857
Confidence interval	
level	95 %
sides	2-sided
lower limit	-11.24
upper limit	1.528
Variability estimate	Standard error of the mean
Dispersion value	3.214

Statistical analysis title	Statistical analysis 2
Statistical analysis description: AZD7594 250 µg vs. PBO	
Comparison groups	AZD7594 v Placebo (PBO)
Number of subjects included in analysis	86
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0016
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)
Point estimate	-10.41
Confidence interval	
level	95 %
sides	2-sided
lower limit	-16.75
upper limit	-4.075
Variability estimate	Standard error of the mean
Dispersion value	3.19

Statistical analysis title	Statistical analysis 3
Statistical analysis description: AZD7594 800 µg vs. PBO	
Comparison groups	AZD7594 v Placebo (PBO)
Number of subjects included in analysis	86
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)
Point estimate	-14.75
Confidence interval	
level	95 %
sides	2-sided
lower limit	-21.18
upper limit	-8.319
Variability estimate	Standard error of the mean
Dispersion value	3.236

Secondary: Efficacy of AZD7594 by assessment of the change from baseline in fractional exhaled nitric oxide (FeNO) on Day 15

End point title	Efficacy of AZD7594 by assessment of the change from baseline in fractional exhaled nitric oxide (FeNO) on Day 15

End point description:

The efficacy of AZD7594 will be assessed in terms of change from baseline in fractional exhaled nitric oxide (FeNO) on Day 15

End point type	Secondary

End point timeframe:

On Day 1 (pre-dose) and on Day 15 in each period

End point values	AZD7594	Placebo (PBO)		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	34	51		
Units: Parts per billion (ppb)				
least squares mean (confidence interval 95%)				
AZD7594 58 µg vs. PBO (n= 32 for AZD7594)	-14.4 (-22.67 to -6.129)	-0.5488 (-6.723 to 5.626)		
AZD7594 250 µg vs. PBO (n= 33 for AZD7594)	-14.81 (-22.96 to -6.657)	-0.5488 (-6.723 to 5.626)		
AZD7594 800 µg vs. PBO (n= 32 for AZD7594)	-20.44 (-28.72 to -12.17)	-0.5488 (-6.723 to 5.626)		

Statistical analyses

Statistical analysis title	Statistical analysis 1

Statistical analysis description:

AZD7594 58 µg vs. PBO

Comparison groups	AZD7594 v Placebo (PBO)
Number of subjects included in analysis	85
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0084
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)
Point estimate	-13.85
Confidence interval	
level	95 %
sides	2-sided
lower limit	-24.06
upper limit	-3.642
Variability estimate	Standard error of the mean
Dispersion value	5.139

Statistical analysis title	Statistical analysis 2

Statistical analysis description: AZD7594 250 µg vs. PBO	
Comparison groups	AZD7594 v Placebo (PBO)
Number of subjects included in analysis	85
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0062
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)
Point estimate	-14.26
Confidence interval	
level	95 %
sides	2-sided
lower limit	-24.37
upper limit	-4.149
Variability estimate	Standard error of the mean
Dispersion value	5.088

Statistical analysis title	Statistical analysis 3
Statistical analysis description: AZD7594 800 µg vs. PBO	
Comparison groups	AZD7594 v Placebo (PBO)
Number of subjects included in analysis	85
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0002
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)
Point estimate	-19.9
Confidence interval	
level	95 %
sides	2-sided
lower limit	-30.1
upper limit	-9.689
Variability estimate	Standard error of the mean
Dispersion value	5.137

Secondary: Efficacy of AZD7594 by assessment of the change from baseline in trough forced expiratory volume in 1 second (FEV1) on Day 8

End point title	Efficacy of AZD7594 by assessment of the change from baseline in trough forced expiratory volume in 1 second (FEV1) on Day 8

End point description:

The efficacy of AZD7594 will be assessed in terms of change from baseline in morning trough forced expiratory volume in 1 second (FEV1) on Day 8 (defined as the average of the values at 23:00 and 23:30 hours after last dose of investigational medicinal product [IMP] on Day 7)

End point type	Secondary

End point timeframe:

On Day 1 (pre-dose) and on Day 8 (pre-dose) in each period

End point values	AZD7594	Placebo (PBO)		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	33	52		
Units: Liters				
least squares mean (confidence interval 95%)				
AZD7594 58 µg vs. PBO	0.1016 (-0.00007 to 0.2033)	0.07112 (-0.00922 to 0.1515)		
AZD7594 250 µg vs. PBO	0.08856 (-0.01295 to 0.1901)	0.07112 (-0.00922 to 0.1515)		
AZD7594 800 µg vs. PBO	0.2272 (0.1252 to 0.3293)	0.07112 (-0.00922 to 0.1515)		

Statistical analyses

Statistical analysis title	Statistical analysis 1
Statistical analysis description: AZD7594 58 µg vs. PBO	
Comparison groups	AZD7594 v Placebo (PBO)
Number of subjects included in analysis	85
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.6036
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)
Point estimate	0.03051
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.08579
upper limit	0.1468
Variability estimate	Standard error of the mean
Dispersion value	0.05856

Statistical analysis title	Statistical analysis 2
Statistical analysis description: AZD7594 250 µg vs. PBO	
Comparison groups	AZD7594 v Placebo (PBO)

Number of subjects included in analysis	85
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.767
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)
Point estimate	0.01744
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.09912
upper limit	0.134
Variability estimate	Standard error of the mean
Dispersion value	0.05869

Statistical analysis title	Statistical analysis 3
Statistical analysis description:	
AZD7594 800 µg vs. PBO	
Comparison groups	AZD7594 v Placebo (PBO)
Number of subjects included in analysis	85
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0093
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)
Point estimate	0.1561
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.03943
upper limit	0.2728
Variability estimate	Standard error of the mean
Dispersion value	0.05874

Secondary: Efficacy of AZD7594 by assessment of the change from baseline in trough forced vital capacity (FVC) on Day 15

End point title	Efficacy of AZD7594 by assessment of the change from baseline in trough forced vital capacity (FVC) on Day 15

End point description:

The efficacy of AZD7594 will be assessed in terms of change from baseline in morning trough forced vital capacity (FVC) on Day 15 (defined as the average of the values at 23:00 and 23:30 hours after last dose of investigational medicinal product [IMP] on Day 14)

End point type	Secondary

End point timeframe:

On Day 1 (pre-dose) and on Day 15 (pre-dose) in each period

End point values	AZD7594	Placebo (PBO)		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	33	51		
Units: Liters				
least squares mean (confidence interval 95%)				
AZD7594 58 µg vs. PBO	0.04186 (-0.06673 to 0.1505)	0.07653 (-0.01626 to 0.1693)		
AZD7594 250 µg vs. PBO	0.1047 (-0.0036 to 0.2131)	0.07653 (-0.01626 to 0.1693)		
AZD7594 800 µg vs. PBO	0.1382 (0.02938 to 0.2471)	0.07653 (-0.01626 to 0.1693)		

Statistical analyses

Statistical analysis title	Statistical analysis 1
Statistical analysis description: AZD7594 58 µg vs. PBO	
Comparison groups	AZD7594 v Placebo (PBO)
Number of subjects included in analysis	84
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.5207
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)
Point estimate	-0.03467
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.1415
upper limit	0.07213
Variability estimate	Standard error of the mean
Dispersion value	0.05377

Statistical analysis title	Statistical analysis 2
Statistical analysis description: AZD7594 250 µg vs. PBO	
Comparison groups	AZD7594 v Placebo (PBO)

Number of subjects included in analysis	84
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.5983
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)
Point estimate	0.02821
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.07778
upper limit	0.1342
Variability estimate	Standard error of the mean
Dispersion value	0.05336

Statistical analysis title	Statistical analysis 3
Statistical analysis description:	
AZD7594 800 µg vs. PBO	
Comparison groups	AZD7594 v Placebo (PBO)
Number of subjects included in analysis	84
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.2538
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)
Point estimate	0.06169
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.04501
upper limit	0.1684
Variability estimate	Standard error of the mean
Dispersion value	0.05371

Secondary: Efficacy of AZD7594 by assessment of the change from baseline in trough forced vital capacity (FVC) on Day 8

End point title	Efficacy of AZD7594 by assessment of the change from baseline in trough forced vital capacity (FVC) on Day 8
End point description:	
The efficacy of AZD7594 will be assessed in terms of change from baseline in morning trough forced vital capacity (FVC) on Day 8 (defined as the average of the values at 23:00 and 23:30 hours after last dose of investigational medicinal product [IMP] on Day 7)	
End point type	Secondary
End point timeframe:	
On Day 1 (pre-dose) and on Day 8 (pre-dose) in each period	

End point values	AZD7594	Placebo (PBO)		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	33	52		
Units: Liters				
least squares mean (confidence interval 95%)				
AZD7594 58 µg vs. PBO	0.06179 (-0.04132 to 0.1649)	0.08441 (0.00163 to 0.1672)		
AZD7594 250 µg vs. PBO	0.0841 (-0.01877 to 0.187)	0.08441 (0.00163 to 0.1672)		
AZD7594 800 µg vs. PBO	0.1527 (0.04929 to 0.2562)	0.08441 (0.00163 to 0.1672)		

Statistical analyses

Statistical analysis title	Statistical analysis 1
Statistical analysis description: AZD7594 58 µg vs. PBO	
Comparison groups	AZD7594 v Placebo (PBO)
Number of subjects included in analysis	85
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.6945
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)
Point estimate	-0.02262
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.1367
upper limit	0.09144
Variability estimate	Standard error of the mean
Dispersion value	0.05743

Statistical analysis title	Statistical analysis 2
Statistical analysis description: AZD7594 250 µg vs. PBO	
Comparison groups	AZD7594 v Placebo (PBO)

Number of subjects included in analysis	85
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.9957
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)
Point estimate	-0.00031
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.1146
upper limit	0.114
Variability estimate	Standard error of the mean
Dispersion value	0.05755

Statistical analysis title	Statistical analysis 3
Statistical analysis description:	
AZD7594 800 µg vs. PBO	
Comparison groups	AZD7594 v Placebo (PBO)
Number of subjects included in analysis	85
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.2398
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)
Point estimate	0.06831
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.04637
upper limit	0.183
Variability estimate	Standard error of the mean
Dispersion value	0.05774

Secondary: Efficacy of AZD7594 by assessment of the change from baseline in morning peak expiratory flow (mPEF) before administration over the treatment period

End point title	Efficacy of AZD7594 by assessment of the change from baseline in morning peak expiratory flow (mPEF) before administration over the treatment period

End point description:

The efficacy of AZD7594 will be assessed in terms of change from baseline in morning peak expiratory flow (mPEF) before administration of the investigational medicinal product (IMP) in each treatment period. The first PEF measurement was on the evening of Visit 1. Every morning and every evening after Visit 1, patients were required to perform 3 maneuvers for PEF assessment. The highest value from among the 3 assessments was marked as mPEF with the date and time of the measurement. The final PEF assessment was done on the morning of Visit 11 (Day 15 of Treatment Period 3).

End point type	Secondary

End point timeframe:

Every morning at pre-dose from Day 1 to Day 15

End point values	AZD7594	Placebo (PBO)		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	33	52		
Units: L/min				
least squares mean (confidence interval 95%)				
AZD7594 58 µg vs. PBO	10.42 (-1.909 to 22.74)	0.08136 (-10.5 to 10.66)		
AZD7594 250 µg vs. PBO	5.334 (-6.975 to 17.64)	0.08136 (-10.5 to 10.66)		
AZD7594 800 µg vs. PBO	12.6 (0.2402 to 24.96)	0.08136 (-10.5 to 10.66)		

Statistical analyses

Statistical analysis title	Statistical analysis 1
Statistical analysis description: AZD7594 58 µg vs. PBO	
Comparison groups	AZD7594 v Placebo (PBO)
Number of subjects included in analysis	85
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0819
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)
Point estimate	10.34
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.335
upper limit	22.01
Variability estimate	Standard error of the mean
Dispersion value	5.877

Statistical analysis title	Statistical analysis 2
Statistical analysis description: AZD7594 250 µg vs. PBO	
Comparison groups	AZD7594 v Placebo (PBO)

Number of subjects included in analysis	85
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.3741
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)
Point estimate	5.253
Confidence interval	
level	95 %
sides	2-sided
lower limit	-6.427
upper limit	16.93
Variability estimate	Standard error of the mean
Dispersion value	5.881

Statistical analysis title	Statistical analysis 3
Statistical analysis description:	
AZD7594 800 µg vs. PBO	
Comparison groups	AZD7594 v Placebo (PBO)
Number of subjects included in analysis	85
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0374
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)
Point estimate	12.52
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.7481
upper limit	24.29
Variability estimate	Standard error of the mean
Dispersion value	5.926

Secondary: Efficacy of AZD7594 by assessment of the change from baseline in evening peak expiratory flow (ePEF) before administration over the treatment period

End point title	Efficacy of AZD7594 by assessment of the change from baseline in evening peak expiratory flow (ePEF) before administration over the treatment period

End point description:

The efficacy of AZD7594 was assessed in terms of change from baseline in evening peak expiratory flow (ePEF) in each treatment period. The first PEF measurement was on the evening of Visit 1. Every morning and every evening after Visit 1, patients were required to perform 3 maneuvers for PEF assessment. The highest value from among the 3 assessments was marked as ePEF together with the date and time of the measurement. The final PEF assessment was done on the morning of Visit 11 (Day 15 of Treatment Period 3).

End point type	Secondary

End point timeframe:

Every evening from Day 1 to Day 14 in each period

End point values	AZD7594	Placebo (PBO)		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	33	51		
Units: L/min				
least squares mean (confidence interval 95%)				
AZD7594 58 µg vs. PBO	7.475 (-4.426 to 19.38)	-8.257 (-18.71 to 2.193)		
AZD7594 250 µg vs. PBO	6.04 (-5.839 to 17.92)	-8.257 (-18.71 to 2.193)		
AZD7594 800 µg vs. PBO	11.65 (-0.2692 to 23.58)	-8.257 (-18.71 to 2.193)		

Statistical analyses

Statistical analysis title	Statistical analysis 1
Statistical analysis description: AZD7594 58 µg vs. PBO	
Comparison groups	AZD7594 v Placebo (PBO)
Number of subjects included in analysis	84
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0044
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)
Point estimate	15.73
Confidence interval	
level	95 %
sides	2-sided
lower limit	5.039
upper limit	26.43
Variability estimate	Standard error of the mean
Dispersion value	5.384

Statistical analysis title	Statistical analysis 2
Statistical analysis description: AZD7594 250 µg vs. PBO	
Comparison groups	AZD7594 v Placebo (PBO)

Number of subjects included in analysis	84
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0098
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)
Point estimate	14.3
Confidence interval	
level	95 %
sides	2-sided
lower limit	3.534
upper limit	25.06
Variability estimate	Standard error of the mean
Dispersion value	5.419

Statistical analysis title	Statistical analysis 3
Statistical analysis description:	
AZD7594 800 µg vs. PBO	
Comparison groups	AZD7594 v Placebo (PBO)
Number of subjects included in analysis	84
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0004
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)
Point estimate	19.91
Confidence interval	
level	95 %
sides	2-sided
lower limit	9.068
upper limit	30.75
Variability estimate	Standard error of the mean
Dispersion value	5.459

Secondary: Efficacy of AZD7594 by assessment of the change from baseline in average daily use of rescue salbutamol over the treatment period

End point title	Efficacy of AZD7594 by assessment of the change from baseline in average daily use of rescue salbutamol over the treatment period
End point description:	
The efficacy of AZD7594 will be assessed in terms of change from baseline in average daily use of salbutamol (each morning and evening) in each treatment period	
End point type	Secondary
End point timeframe:	
Every day from Day 1 to Day 15 (from evening of Day 1 to morning of Day 15)	

End point values	AZD7594	Placebo (PBO)		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	33	51		
Units: Number of inhalations				
least squares mean (confidence interval 95%)				
AZD7594 58 µg vs. PBO	-0.6776 (-1.071 to -0.2841)	-0.334 (-0.6733 to 0.00522)		
AZD7594 250 µg vs. PBO	-0.8193 (-1.212 to -0.4267)	-0.334 (-0.6733 to 0.00522)		
AZD7594 800 µg vs. PBO	-1.137 (-1.531 to -0.7422)	-0.334 (-0.6733 to 0.00522)		

Statistical analyses

Statistical analysis title	Statistical analysis 1
Statistical analysis description: AZD7594 58 µg vs. PBO	
Comparison groups	AZD7594 v Placebo (PBO)
Number of subjects included in analysis	84
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0723
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)
Point estimate	-0.3435
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.7189
upper limit	0.03179
Variability estimate	Standard error of the mean
Dispersion value	0.189

Statistical analysis title	Statistical analysis 2
Statistical analysis description: AZD7594 250 µg vs. PBO	
Comparison groups	AZD7594 v Placebo (PBO)

Number of subjects included in analysis	84
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0124
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)
Point estimate	-0.4852
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.8631
upper limit	-0.1073
Variability estimate	Standard error of the mean
Dispersion value	0.1903

Statistical analysis title	Statistical analysis 3
Statistical analysis description:	
AZD7594 800 µg vs. PBO	
Comparison groups	AZD7594 v Placebo (PBO)
Number of subjects included in analysis	84
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)
Point estimate	-0.8026
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.183
upper limit	-0.4224
Variability estimate	Standard error of the mean
Dispersion value	0.1914

Secondary: Efficacy of AZD7594 by assessment of the change from baseline to Day 15 in Asthma Control Questionnaire-5

End point title	Efficacy of AZD7594 by assessment of the change from baseline to Day 15 in Asthma Control Questionnaire-5

End point description:

The efficacy of AZD7594 was assessed in terms of change from baseline to Day 15 in Asthma Control Questionnaire-5 in each treatment period. Each question was scored on a scale of 0 to 6, where a lower score represents a more severe impairment/symptom. The ACQ-5 score at a given visit was defined as the average of the scores given for each of the questions (ACQ-5 score = Sum of 5 scores/5).

End point type	Secondary

End point timeframe:

At baseline and on Day 15 in each period

End point values	AZD7594	Placebo (PBO)		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	33	52		
Units: Unit on a scale				
least squares mean (confidence interval 95%)				
AZD7594 58 µg vs. PBO	-0.2929 (-0.4744 to -0.1113)	0.01428 (-0.1281 to 0.1567)		
AZD7594 250 µg vs. PBO	-0.1681 (-0.3496 to 0.01335)	0.01428 (-0.1281 to 0.1567)		
AZD7594 800 µg vs. PBO	-0.4158 (-0.5975 to -0.2342)	0.01428 (-0.1281 to 0.1567)		

Statistical analyses

Statistical analysis title	Statistical analysis 1
Statistical analysis description: AZD7594 58 µg vs. PBO	
Comparison groups	AZD7594 v Placebo (PBO)
Number of subjects included in analysis	85
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0044
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)
Point estimate	-0.3071
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.5159
upper limit	-0.09836
Variability estimate	Standard error of the mean
Dispersion value	0.1051

Statistical analysis title	Statistical analysis 2
Statistical analysis description: AZD7594 250 µg vs. PBO	
Comparison groups	AZD7594 v Placebo (PBO)

Number of subjects included in analysis	85
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0883
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)
Point estimate	-0.1824
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.3927
upper limit	0.02789
Variability estimate	Standard error of the mean
Dispersion value	0.1059

Statistical analysis title	Statistical analysis 3
Statistical analysis description:	
AZD7594 800 µg vs. PBO	
Comparison groups	AZD7594 v Placebo (PBO)
Number of subjects included in analysis	85
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)
Point estimate	-0.4301
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.6397
upper limit	-0.2205
Variability estimate	Standard error of the mean
Dispersion value	0.1055

Secondary: Efficacy of AZD7594 by assessment of the change from baseline to Day 8 in Asthma Control Questionnaire-5

End point title	Efficacy of AZD7594 by assessment of the change from baseline to Day 8 in Asthma Control Questionnaire-5

End point description:

The efficacy of AZD7594 was assessed in terms of change from baseline to Day 8 in Asthma Control Questionnaire-5 in each treatment period. Each question was scored on a scale of 0 to 6, where a lower score represents a more severe impairment/symptom. The ACQ-5 score at a given visit was defined as the average of the scores given for each of the questions (ACQ-5 score = Sum of 5 scores/5)

End point type	Secondary

End point timeframe:

At baseline and on Day 8 in each period

End point values	AZD7594	Placebo (PBO)		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	33	52		
Units: Unit on a scale				
least squares mean (confidence interval 95%)				
AZD7594 58 µg vs. PBO	-0.2724 (-0.4309 to -0.1138)	-0.1072 (-0.232 to 0.01748)		
AZD7594 250 µg vs. PBO	-0.198 (-0.3565 to -0.03952)	-0.1072 (-0.232 to 0.01748)		
AZD7594 800 µg vs. PBO	-0.3604 (-0.5191 to -0.2017)	-0.1072 (-0.232 to 0.01748)		

Statistical analyses

Statistical analysis title	Statistical analysis 1
Statistical analysis description: AZD7594 58 µg vs. PBO	
Comparison groups	AZD7594 v Placebo (PBO)
Number of subjects included in analysis	85
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0741
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)
Point estimate	-0.1651
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.3466
upper limit	0.01638
Variability estimate	Standard error of the mean
Dispersion value	0.09139

Statistical analysis title	Statistical analysis 2
Statistical analysis description: AZD7594 250 µg vs. PBO	
Comparison groups	AZD7594 v Placebo (PBO)

Number of subjects included in analysis	85
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.3265
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)
Point estimate	-0.09079
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.2736
upper limit	0.09201
Variability estimate	Standard error of the mean
Dispersion value	0.09204

Statistical analysis title	Statistical analysis 3
Statistical analysis description:	
AZD7594 800 µg vs. PBO	
Comparison groups	AZD7594 v Placebo (PBO)
Number of subjects included in analysis	85
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.007
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)
Point estimate	-0.2532
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.4354
upper limit	-0.07092
Variability estimate	Standard error of the mean
Dispersion value	0.09176

Secondary: Efficacy of AZD7594 by assessment of night-time awakenings

End point title	Efficacy of AZD7594 by assessment of night-time awakenings

End point description:

The efficacy of AZD7594 was assessed in terms of change in nighttime awakenings in each treatment period. The patients were asked to answer ‘Yes’ or ‘No’ to the question of "Did your asthma cause you to wake up last night?”. If yes, the number and percentage of days that had a night-time awakening were determined for each of the study periods.

End point type	Secondary

End point timeframe:

At baseline and from Day 1 to Day 14 in each period

End point values	AZD7594	Placebo (PBO)		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	33	52		
Units: Number of nighttime awakenings				
least squares mean (confidence interval 95%)				
AZD7594 58 µg vs. PBO	-0.412 (-0.7229 to -0.101)	0.006541 (-0.2509 to 0.264)		
AZD7594 250 µg vs. PBO	-0.1729 (-0.4833 to 0.1376)	0.006541 (-0.2509 to 0.264)		
AZD7594 800 µg vs. PBO	-0.7595 (-1.071 to -0.4479)	0.006541 (-0.2509 to 0.264)		

Statistical analyses

Statistical analysis title	Statistical analysis 1
Statistical analysis description: AZD7594 58 µg vs. PBO	
Comparison groups	AZD7594 v Placebo (PBO)
Number of subjects included in analysis	85
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0116
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)
Point estimate	-0.4185
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.7414
upper limit	-0.09563
Variability estimate	Standard error of the mean
Dispersion value	0.1626

Statistical analysis title	Statistical analysis 2
Statistical analysis description: AZD7594 250 µg vs. PBO	
Comparison groups	AZD7594 v Placebo (PBO)

Number of subjects included in analysis	85
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.2732
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)
Point estimate	-0.1794
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.5027
upper limit	0.1438
Variability estimate	Standard error of the mean
Dispersion value	0.1628

Statistical analysis title	Statistical analysis 3
Statistical analysis description:	
AZD7594 800 µg vs. PBO	
Comparison groups	AZD7594 v Placebo (PBO)
Number of subjects included in analysis	85
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)
Point estimate	-0.7661
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.091
upper limit	-0.4411
Variability estimate	Standard error of the mean
Dispersion value	0.1636

Secondary: Efficacy of AZD7594 by assessment of daily symptom score

End point title	Efficacy of AZD7594 by assessment of daily symptom score

End point description:

The efficacy of AZD7594 was assessed in terms of change in daily symptom score from baseline to average of treatment period post dose (Day 1-14) in each treatment period. Severity scores for asthma symptoms were recorded twice daily, once in the morning and once in the evening with the scoring system of 0-no asthma symptoms, 1-toleratable asthma symptoms, 2-discomfort asthma symptoms with normal activities (or with sleep) and 3-asthma symptoms with impaired normal activities (or to sleep).

End point type	Secondary

End point timeframe:

At baseline and from Day 1 to Day 15 in each period

End point values	AZD7594	Placebo (PBO)		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	33	51		
Units: Unit on a scale				
least squares mean (confidence interval 95%)				
AZD7594 58 µg vs. PBO	-0.119 (-0.219 to -0.01903)	-0.01229 (-0.09729 to 0.0727)		
AZD7594 250 µg vs. PBO	-0.09435 (-0.1941 to 0.00541)	-0.01229 (-0.09729 to 0.0727)		
AZD7594 800 µg vs. PBO	-0.215 (-0.3151 to -0.1149)	-0.01229 (-0.09729 to 0.0727)		

Statistical analyses

Statistical analysis title	Statistical analysis 1
Statistical analysis description: AZD7594 58 µg vs. PBO	
Comparison groups	AZD7594 v Placebo (PBO)
Number of subjects included in analysis	84
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0349
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)
Point estimate	-0.1067
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.2057
upper limit	-0.00775
Variability estimate	Standard error of the mean
Dispersion value	0.04982

Statistical analysis title	Statistical analysis 2
Statistical analysis description: AZD7594 250 µg vs. PBO	
Comparison groups	AZD7594 v Placebo (PBO)

Number of subjects included in analysis	84
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.1052
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)
Point estimate	-0.08205
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.1817
upper limit	0.01756
Variability estimate	Standard error of the mean
Dispersion value	0.05015

Statistical analysis title	Statistical analysis 3
Statistical analysis description:	
AZD7594 800 µg vs. PBO	
Comparison groups	AZD7594 v Placebo (PBO)
Number of subjects included in analysis	84
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0001
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)
Point estimate	-0.2027
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.3028
upper limit	-0.1025
Variability estimate	Standard error of the mean
Dispersion value	0.05044

Secondary: Efficacy of AZD7594 by assessment of asthma control days

End point title	Efficacy of AZD7594 by assessment of asthma control days

End point description:

The efficacy of AZD7594 was assessed in terms of amount of asthma control days in each treatment period. An asthma control day was defined as a day with asthma symptom score = 0, a night with no awakenings due to asthma symptoms and a day with no use of rescue medication. A given calendar day was defined as an asthma control day if it fulfills the criteria for a symptom-free day and for a rescue medication-free day.

End point type	Secondary

End point timeframe:

At baseline and from Day 1 to Day 14 post-dose in each period

End point values	AZD7594	Placebo (PBO)		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	33	51		
Units: Average number of asthma control days				
least squares mean (confidence interval 95%)				
AZD7594 58 µg vs. PBO	0.9502 (0.3166 to 1.584)	0.2773 (-0.2745 to 0.829)		
AZD7594 250 µg vs. PBO	0.7054 (0.07299 to 1.338)	0.2773 (-0.2745 to 0.829)		
AZD7594 800 µg vs. PBO	1.219 (0.5843 to 1.853)	0.2773 (-0.2745 to 0.829)		

Statistical analyses

Statistical analysis title	Statistical analysis 1
Statistical analysis description: AZD7594 58 µg vs. PBO	
Comparison groups	AZD7594 v Placebo (PBO)
Number of subjects included in analysis	84
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0247
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)
Point estimate	0.673
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.08779
upper limit	1.258
Variability estimate	Standard error of the mean
Dispersion value	0.2946

Statistical analysis title	Statistical analysis 2
Statistical analysis description: AZD7594 250 µg vs. PBO	
Comparison groups	AZD7594 v Placebo (PBO)

Number of subjects included in analysis	84
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.1521
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)
Point estimate	0.4281
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.1607
upper limit	1.017
Variability estimate	Standard error of the mean
Dispersion value	0.2965

Statistical analysis title	Statistical analysis 3
Statistical analysis description:	
AZD7594 800 µg vs. PBO	
Comparison groups	AZD7594 v Placebo (PBO)
Number of subjects included in analysis	84
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0022
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)
Point estimate	0.9415
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.3483
upper limit	1.535
Variability estimate	Standard error of the mean
Dispersion value	0.2987

Secondary: Safety of AZD7594 by assessment of adverse events

End point title	Safety of AZD7594 by assessment of adverse events
End point description:	
Assessment of safety and tolerability of three dose levels of AZD7594 in participants with mild to moderate asthma. IP referred to investigational product.	
End point type	Secondary
End point timeframe:	
From Screening to Follow-up (these two examinations are up to 165 days apart)	

End point values	Placebo (PBO)	AZD7594 58 µg	AZD7594 250 µg	AZD7594 800 µg
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	52	34	34	34
Units: Number				
Any AE	17	13	9	12
AE causally related to IMP	3	1	1	2
Any AE with an outcome of death	0	0	0	0
Any SAE (including events with outcome of death)	0	0	0	0
Any AE leading to discontinuation of IMP	1	0	0	0

Statistical analyses

No statistical analyses for this end point

Secondary: Rate and extent of absorption of three dose levels of AZD7594 by assessment of Cmax of AZD7594

End point title	Rate and extent of absorption of three dose levels of AZD7594 by assessment of Cmax of AZD7594

End point description:

Comparison of Cmax (maximum observed plasma concentration) of AZD7594 on Day 1 of each treatment period; up to 6 samples were collected in each period (i.e. in participants with intensive pharmacokinetic assessments, at pre-dose and 15 and 30 minutes, and 1, 2, and 4 h post-dose)

End point type	Secondary

End point timeframe:

On Day 1 in each period (in subjects with intensive pharmacokinetic assessments, at pre-dose and 15 and 30 minutes, and 1, 2, and 4 h post-dose)

End point values	AZD7594 58 µg	AZD7594 250 µg	AZD7594 800 µg	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	9	9	8	
Units: pmol/L				
geometric mean (geometric coefficient of variation)				
Cmax	36.4 (± 32.8)	92.02 (± 34.17)	169.7 (± 43.21)	

Statistical analyses

No statistical analyses for this end point

Secondary: Rate and extent of absorption of three dose levels of AZD7594 by assessment of AUC(0-4) of AZD7594

End point title	Rate and extent of absorption of three dose levels of AZD7594 by assessment of AUC(0-4) of AZD7594

End point description:

Comparison of AUC(0-4) (Area under the plasma concentration-time curve from time zero to 4 hours after administration) of AZD7594 on Day 1 of each treatment period; up to 6 samples were collected in each period (i.e. in subjects with intensive pharmacokinetic assessments, at pre-dose and 15 and 30 minutes, and 1, 2, and 4 h post-dose)

End point type	Secondary

End point timeframe:

On Day 1 in each period (in subjects with intensive pharmacokinetic assessments, at pre-dose and 15 and 30 minutes, and 1, 2, and 4 h post-dose)

End point values	AZD7594 58 µg	AZD7594 250 µg	AZD7594 800 µg	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	4	9	8	
Units: h×pmol/L				
geometric mean (geometric coefficient of variation)				
AUC(0-4)	85.02 (± 8.21)	188.4 (± 30.58)	371.1 (± 31.55)	

Statistical analyses

No statistical analyses for this end point

Secondary: Rate and extent of absorption of three dose levels of AZD7594 following multiple dose administration by assessment of Cmax,ss of AZD7594

End point title	Rate and extent of absorption of three dose levels of AZD7594 following multiple dose administration by assessment of Cmax,ss of AZD7594

End point description:

Comparison of Cmax,ss (observed maximum plasma concentration at steady state) of AZD7594 on Day 14 of each treatment period; up to 10 samples were collected in each period (i.e. in subjects with intensive pharmacokinetic assessments, at pre-dose and 15 and 30 minutes, and 1, 2, 4, 8, 12, 16 and 24 h post-dose)

End point type	Secondary

End point timeframe:

On Day 14 in each period (in subjects with intensive pharmacokinetic assessments, at pre-dose and 15 and 30 minutes, and 1, 2, 4, 8, 12, 16 and 24 h post-dose)

End point values	AZD7594 58 µg	AZD7594 250 µg	AZD7594 800 µg	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	9	9	8	
Units: pmol/L				
geometric mean (geometric coefficient of variation)				
Cmax,ss	54.97 (± 19.7)	158.7 (± 35.01)	421.6 (± 37.26)	

Statistical analyses

Statistical analysis title	Statistical analysis 1
Statistical analysis description: AZD7594 250 µg versus AZD7594 58 µg	
Comparison groups	AZD7594 58 µg v AZD7594 250 µg
Number of subjects included in analysis	18
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001
Method	ANOVA
Parameter estimate	Ratio Estimate (%)
Point estimate	272.2
Confidence interval	
level	90 %
sides	2-sided
lower limit	237.43
upper limit	312.05

Statistical analysis title	Statistical analysis 2
Statistical analysis description: AZD7594 800 µg versus AZD7594 58 µg	
Comparison groups	AZD7594 58 µg v AZD7594 800 µg
Number of subjects included in analysis	17
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001
Method	ANOVA
Parameter estimate	Ratio Estimate (%)
Point estimate	676.13
Confidence interval	
level	90 %
sides	2-sided
lower limit	580.91
upper limit	786.95

Secondary: Rate and extent of absorption of three dose levels of AZD7594 following multiple dose administration by assessment of AUC(0-24) of AZD7594

End point title	Rate and extent of absorption of three dose levels of AZD7594 following multiple dose administration by assessment of AUC(0-24) of AZD7594

End point description:

Comparison of AUC(0-24) (Area under the plasma concentration-time curve from time zero to 24 hours after administration) of AZD7594 on Day 14 of each treatment period; up to 10 samples were collected in each period (i.e. in subjects with intensive pharmacokinetic assessments, at pre-dose and 15 and 30 minutes, and 1, 2, 4, 8, 12, 16 and 24 h post-dose)

End point type	Secondary

End point timeframe:

On Day 14 in each period (in subjects with intensive pharmacokinetic assessments, at pre-dose and 15 and 30 minutes, and 1, 2, 4, 8, 12, 16 and 24 h post-dose)

End point values	AZD7594 58 µg	AZD7594 250 µg	AZD7594 800 µg	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	9	9	8	
Units: h×pmol/L				
geometric mean (geometric coefficient of variation)				
AUC(0-24)	467.1 (± 17.91)	1725 (± 44.33)	4894 (± 52.48)	

Statistical analyses

Statistical analysis title	Statistical analysis 1
Statistical analysis description: AZD7594 250 µg versus AZD7594 58 µg	
Comparison groups	AZD7594 58 µg v AZD7594 250 µg
Number of subjects included in analysis	18
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001
Method	ANOVA
Parameter estimate	Ratio Estimate (%)
Point estimate	337.82
Confidence interval	
level	90 %
sides	2-sided
lower limit	290.8
upper limit	392.43

Statistical analysis title	Statistical analysis 2
Statistical analysis description: AZD7594 800 µg versus AZD7594 58 µg	
Comparison groups	AZD7594 58 µg v AZD7594 800 µg

Number of subjects included in analysis	17
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001
Method	ANOVA
Parameter estimate	Ratio Estimate (%)
Point estimate	964.62
Confidence interval	
level	90 %
sides	2-sided
lower limit	816.13
upper limit	1140.13

Secondary: Rate and extent of absorption of three dose levels of AZD7594 following multiple dose administration by assessment of AUC(0-last) of AZD7594

End point title	Rate and extent of absorption of three dose levels of AZD7594 following multiple dose administration by assessment of AUC(0-last) of AZD7594

End point description:

Comparison of AUC(0-last) (Area under the plasma concentration-time curve from time zero to the time of the last quantifiable concentration) of AZD7594 (i.e. in subjects with intensive pharmacokinetic assessments)

End point type	Secondary

End point timeframe:

On Day 1 and Day 14 in each period (in subjects with intensive pharmacokinetic assessments, on Day 1 at pre-dose and 15 and 30 minutes, and 1, 2 and 4 h post-dose, on Day 14 at pre-dose and 15 and 30 minutes, and 1, 2, 4, 8, 12, 16 and 24 h post-dose)

End point values	AZD7594 58 µg	AZD7594 250 µg	AZD7594 800 µg	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	9	9	8	
Units: h*pmol/L				
geometric mean (geometric coefficient of variation)				
Day 1	56.85 (± 45.4)	188.5 (± 30.57)	371.8 (± 31.63)	
Day 14	467.3 (± 17.93)	1728 (± 44.36)	4897 (± 52.48)	

Statistical analyses

No statistical analyses for this end point

Secondary: Rate and extent of absorption of three dose levels of AZD7594 by assessment of tmax of AZD7594

End point title	Rate and extent of absorption of three dose levels of AZD7594

	by assessment of tmax of AZD7594

End point description:

Comparison of tmax (time to reach maximum plasma concentration) of AZD7594 on Day 1 of each treatment period; up to 6 samples were collected in each period (i.e. in subjects with intensive pharmacokinetic assessments, at pre-dose and 15 and 30 minutes, and 1, 2, and 4 hours post-dose)

End point type	Secondary

End point timeframe:

On Day 1 in each period (in subjects with intensive pharmacokinetic assessments, at pre-dose and 15 and 30 minutes, and 1, 2, and 4 h post-dose)

End point values	AZD7594 58 µg	AZD7594 250 µg	AZD7594 800 µg	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	9	9	8	
Units: Hour				
median (full range (min-max))				
tmax	0.25 (0.23 to 0.27)	0.25 (0.25 to 0.5)	0.25 (0.25 to 0.55)	

Statistical analyses

No statistical analyses for this end point

Secondary: Rate and extent of absorption of three dose levels of AZD7594 following multiple dose administration by assessment of tmax,ss of AZD7594

End point title	Rate and extent of absorption of three dose levels of AZD7594 following multiple dose administration by assessment of tmax,ss of AZD7594

End point description:

Comparison of tmax,ss (time to reach maximum plasma concentration at steady state) of AZD7594 on Day 14 of each treatment period; up to 10 samples were collected in each period (i.e. in subjects with intensive pharmacokinetic assessments, at pre-dose and 15 and 30 minutes, and 1, 2, 4, 8, 12, 16 and 24 hours post-dose)

End point type	Secondary

End point timeframe:

On Day 14 in each period (in subjects with intensive pharmacokinetic assessments, at pre-dose and 15 and 30 minutes, and 1, 2, 4, 8, 12, 16 and 24 h post-dose)

End point values	AZD7594 58 µg	AZD7594 250 µg	AZD7594 800 µg	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	9	9	8	
Units: Hour				
median (full range (min-max))				
tmax,ss	0.25 (0.25 to 0.5)	0.25 (0.23 to 0.27)	0.25 (0.25 to 0.98)	

Statistical analyses

No statistical analyses for this end point

Secondary: Rate and extent of absorption of three dose levels of AZD7594 following multiple dose administration by assessment of Cavg,ss of AZD7594

End point title	Rate and extent of absorption of three dose levels of AZD7594 following multiple dose administration by assessment of Cavg,ss of AZD7594

End point description:

Comparison of Cavg,ss (average plasma concentration during a dosing interval at steady state) of AZD7594 on Day 14 of each treatment period; up to 10 samples were collected in each period (i.e. in subjects with intensive pharmacokinetic assessments, at pre-dose and 15 and 30 minutes, and 1, 2, 4, 8, 12, 16 and 24 h post-dose)

End point type	Secondary

End point timeframe:

On Day 14 in each period (in subjects with intensive pharmacokinetic assessments, at pre-dose and 15 and 30 minutes, and 1, 2, 4, 8, 12, 16 and 24 h post-dose)

End point values	AZD7594 58 µg	AZD7594 250 µg	AZD7594 800 µg	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	9	9	8	
Units: pmol/L				
geometric mean (geometric coefficient of variation)				
AZD7594 58 µg (n=9)	19.48 (± 17.93)	71.89 (± 44.33)	203.9 (± 52.55)	

Statistical analyses

No statistical analyses for this end point

Secondary: Rate and extent of absorption of three dose levels of AZD7594 following multiple dose administration by assessment of Cmax/D of AZD7594

End point title	Rate and extent of absorption of three dose levels of AZD7594 following multiple dose administration by assessment of Cmax/D of AZD7594

End point description:

Comparison of Cmax/D (dose-normalized Cmax) of AZD7594

End point type	Secondary

End point timeframe:

On Day 1 in each period

End point values	AZD7594 58 µg	AZD7594 250 µg	AZD7594 800 µg	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	9	9	8	
Units: pmol/L/µmol				
geometric mean (geometric coefficient of variation)				
Cmax/D	380.8 (± 32.8)	223.4 (± 34.17)	128.5 (± 43.21)	

Statistical analyses

No statistical analyses for this end point

Secondary: Rate and extent of absorption of three dose levels of AZD7594 following multiple dose administration by assessment of AUC(0-24)/D of AZD7594

End point title	Rate and extent of absorption of three dose levels of AZD7594 following multiple dose administration by assessment of AUC(0-24)/D of AZD7594

End point description:

Comparison of AUC(0-24)/D (dose-normalized AUC(0-24)) of AZD7594

End point type	Secondary

End point timeframe:

On Day 14 in each period

End point values	AZD7594 58 µg	AZD7594 250 µg	AZD7594 800 µg	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	9	9	8	
Units: h×pmol/L/µmol				
geometric mean (geometric coefficient of variation)				
AUC (0-24)/D	4886 (± 17.91)	4188 (± 44.33)	3708 (± 52.48)	

Statistical analyses

No statistical analyses for this end point

Secondary: Rate and extent of absorption of three dose levels of AZD7594 following multiple dose administration by assessment of steady-state Cmin of AZD7594

End point title	Rate and extent of absorption of three dose levels of AZD7594 following multiple dose administration by assessment of steady-state Cmin of AZD7594

End point description:

Comparison of Cmin (predose concentration) of AZD7594 in each treatment period

End point type	Secondary

End point timeframe:

On Day 1 and on Day 14 at pre-dose in each period

End point values	AZD7594 250 µg	AZD7594 800 µg		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	9	8		
Units: pmol/L				
geometric mean (geometric coefficient of variation)				
Steady-state Cmin	55.95 (± 51.74)	191.6 (± 68.27)		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information	
Timeframe for reporting adverse events: From Screening to Follow-up (these two examinations are up to 165 days apart)	
Assessment type	Non-systematic
Dictionary used	
Dictionary name	MedDRA
Dictionary version	18.1.
Reporting groups	
Reporting group title	Placebo (PBO)
Reporting group description: Placebo for AZD7594 DPI once daily	
Reporting group title	AZD7594 58 µg
Reporting group description: AZD7594 DPI once daily - 2 capsules of 29 µg	
Reporting group title	AZD7594 250 µg
Reporting group description: AZD7594 DPI once daily - 2 capsules of 125 µg	
Reporting group title	AZD7594 800 µg
Reporting group description: AZD7594 DPI once daily - 2 capsules of 400 µg	

Serious adverse events	Placebo (PBO)	AZD7594 58 µg	AZD7594 250 µg
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 52 (0.00%)	0 / 34 (0.00%)	0 / 34 (0.00%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0

Serious adverse events	AZD7594 800 µg		
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 34 (0.00%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events	0		

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

Non-serious adverse events	Placebo (PBO)	AZD7594 58 µg	AZD7594 250 µg
Total subjects affected by non-serious adverse events			
subjects affected / exposed	17 / 52 (32.69%)	13 / 34 (38.24%)	9 / 34 (26.47%)
Investigations			
Blood lactate dehydrogenase increased			
subjects affected / exposed	0 / 52 (0.00%)	0 / 34 (0.00%)	0 / 34 (0.00%)
occurrences (all)	0	0	0
Hepatic enzyme increased			
subjects affected / exposed	1 / 52 (1.92%)	0 / 34 (0.00%)	1 / 34 (2.94%)
occurrences (all)	1	0	1
Injury, poisoning and procedural complications			
Contusion			
subjects affected / exposed	0 / 52 (0.00%)	0 / 34 (0.00%)	1 / 34 (2.94%)
occurrences (all)	0	0	1
Nervous system disorders			
Headache			
subjects affected / exposed	0 / 52 (0.00%)	0 / 34 (0.00%)	3 / 34 (8.82%)
occurrences (all)	0	0	3
Migraine			
subjects affected / exposed	0 / 52 (0.00%)	1 / 34 (2.94%)	0 / 34 (0.00%)
occurrences (all)	0	1	0
Blood and lymphatic system disorders			
Anaemia vitamin B12 deficiency			
subjects affected / exposed	1 / 52 (1.92%)	0 / 34 (0.00%)	0 / 34 (0.00%)
occurrences (all)	1	0	0
Eye disorders			
Eye irritation			
subjects affected / exposed	1 / 52 (1.92%)	0 / 34 (0.00%)	0 / 34 (0.00%)
occurrences (all)	1	0	0
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	0 / 52 (0.00%)	0 / 34 (0.00%)	0 / 34 (0.00%)
occurrences (all)	0	0	0
Abdominal discomfort			
subjects affected / exposed	0 / 52 (0.00%)	1 / 34 (2.94%)	0 / 34 (0.00%)
occurrences (all)	0	1	0
Dental caries			

subjects affected / exposed	0 / 52 (0.00%)	1 / 34 (2.94%)	0 / 34 (0.00%)
occurrences (all)	0	1	0
Abdominal pain upper			
subjects affected / exposed	1 / 52 (1.92%)	0 / 34 (0.00%)	0 / 34 (0.00%)
occurrences (all)	1	0	0
Gingival bleeding			
subjects affected / exposed	1 / 52 (1.92%)	0 / 34 (0.00%)	0 / 34 (0.00%)
occurrences (all)	1	0	0
Toothache			
subjects affected / exposed	1 / 52 (1.92%)	0 / 34 (0.00%)	0 / 34 (0.00%)
occurrences (all)	1	0	0
Vomiting			
subjects affected / exposed	1 / 52 (1.92%)	0 / 34 (0.00%)	0 / 34 (0.00%)
occurrences (all)	1	0	0
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	1 / 52 (1.92%)	2 / 34 (5.88%)	0 / 34 (0.00%)
occurrences (all)	1	2	0
Oropharyngeal pain			
subjects affected / exposed	0 / 52 (0.00%)	1 / 34 (2.94%)	1 / 34 (2.94%)
occurrences (all)	0	1	1
Asthma			
subjects affected / exposed	1 / 52 (1.92%)	0 / 34 (0.00%)	1 / 34 (2.94%)
occurrences (all)	1	0	1
Epistaxis			
subjects affected / exposed	0 / 52 (0.00%)	0 / 34 (0.00%)	0 / 34 (0.00%)
occurrences (all)	0	0	0
Respiratory distress			
subjects affected / exposed	0 / 52 (0.00%)	0 / 34 (0.00%)	0 / 34 (0.00%)
occurrences (all)	0	0	0
Sputum increased			
subjects affected / exposed	1 / 52 (1.92%)	1 / 34 (2.94%)	0 / 34 (0.00%)
occurrences (all)	1	1	0
Dyspnoea			

subjects affected / exposed	2 / 52 (3.85%)	0 / 34 (0.00%)	0 / 34 (0.00%)
occurrences (all)	2	0	0
Nasal inflammation			
subjects affected / exposed	1 / 52 (1.92%)	0 / 34 (0.00%)	0 / 34 (0.00%)
occurrences (all)	1	0	0
Productive cough			
subjects affected / exposed	1 / 52 (1.92%)	0 / 34 (0.00%)	0 / 34 (0.00%)
occurrences (all)	1	0	0
Hepatobiliary disorders			
Hepatosplenomegaly			
subjects affected / exposed	0 / 52 (0.00%)	0 / 34 (0.00%)	0 / 34 (0.00%)
occurrences (all)	0	0	0
Skin and subcutaneous tissue disorders			
Pruritus			
subjects affected / exposed	0 / 52 (0.00%)	1 / 34 (2.94%)	0 / 34 (0.00%)
occurrences (all)	0	1	0
Eczema			
subjects affected / exposed	1 / 52 (1.92%)	0 / 34 (0.00%)	0 / 34 (0.00%)
occurrences (all)	1	0	0
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	0 / 52 (0.00%)	1 / 34 (2.94%)	0 / 34 (0.00%)
occurrences (all)	0	1	0
Back pain			
subjects affected / exposed	0 / 52 (0.00%)	0 / 34 (0.00%)	0 / 34 (0.00%)
occurrences (all)	0	0	0
Musculoskeletal pain			
subjects affected / exposed	0 / 52 (0.00%)	1 / 34 (2.94%)	0 / 34 (0.00%)
occurrences (all)	0	1	0
Infections and infestations			
Nasopharyngitis			
subjects affected / exposed	8 / 52 (15.38%)	4 / 34 (11.76%)	2 / 34 (5.88%)
occurrences (all)	8	4	2
Gastroenteritis			
subjects affected / exposed	0 / 52 (0.00%)	3 / 34 (8.82%)	0 / 34 (0.00%)
occurrences (all)	0	3	0

Gastrointestinal infection			
subjects affected / exposed	0 / 52 (0.00%)	0 / 34 (0.00%)	1 / 34 (2.94%)
occurrences (all)	0	0	1
Hordeolum			
subjects affected / exposed	0 / 52 (0.00%)	0 / 34 (0.00%)	1 / 34 (2.94%)
occurrences (all)	0	0	1
Rhinitis			
subjects affected / exposed	0 / 52 (0.00%)	0 / 34 (0.00%)	1 / 34 (2.94%)
occurrences (all)	0	0	1
Sinusitis			
subjects affected / exposed	1 / 52 (1.92%)	0 / 34 (0.00%)	0 / 34 (0.00%)
occurrences (all)	1	0	0

Non-serious adverse events	AZD7594 800 µg		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	12 / 34 (35.29%)		
Investigations			
Blood lactate dehydrogenase increased			
subjects affected / exposed	1 / 34 (2.94%)		
occurrences (all)	1		
Hepatic enzyme increased			
subjects affected / exposed	0 / 34 (0.00%)		
occurrences (all)	0		
Injury, poisoning and procedural complications			
Contusion			
subjects affected / exposed	0 / 34 (0.00%)		
occurrences (all)	0		
Nervous system disorders			
Headache			
subjects affected / exposed	2 / 34 (5.88%)		
occurrences (all)	2		
Migraine			
subjects affected / exposed	1 / 34 (2.94%)		
occurrences (all)	1		
Blood and lymphatic system disorders			

Anaemia vitamin B12 deficiency subjects affected / exposed occurrences (all)	0 / 34 (0.00%) 0		
Eye disorders Eye irritation subjects affected / exposed occurrences (all)	0 / 34 (0.00%) 0		
Gastrointestinal disorders Diarrhoea subjects affected / exposed occurrences (all) Abdominal discomfort subjects affected / exposed occurrences (all) Dental caries subjects affected / exposed occurrences (all) Abdominal pain upper subjects affected / exposed occurrences (all) Gingival bleeding subjects affected / exposed occurrences (all) Toothache subjects affected / exposed occurrences (all) Vomiting subjects affected / exposed occurrences (all)	3 / 34 (8.82%) 3 0 / 34 (0.00%) 0 0 / 34 (0.00%) 0 0 / 34 (0.00%) 0 0 / 34 (0.00%) 0 0 / 34 (0.00%) 0 0 / 34 (0.00%) 0		
Respiratory, thoracic and mediastinal disorders Cough subjects affected / exposed occurrences (all) Oropharyngeal pain subjects affected / exposed occurrences (all)	0 / 34 (0.00%) 0 0 / 34 (0.00%) 0		

Asthma subjects affected / exposed occurrences (all)	0 / 34 (0.00%) 0		
Epistaxis subjects affected / exposed occurrences (all)	1 / 34 (2.94%) 1		
Respiratory distress subjects affected / exposed occurrences (all)	1 / 34 (2.94%) 1		
Sputum increased subjects affected / exposed occurrences (all)	0 / 34 (0.00%) 0		
Dyspnoea subjects affected / exposed occurrences (all)	0 / 34 (0.00%) 0		
Nasal inflammation subjects affected / exposed occurrences (all)	0 / 34 (0.00%) 0		
Productive cough subjects affected / exposed occurrences (all)	0 / 34 (0.00%) 0		
Hepatobiliary disorders Hepatosplenomegaly subjects affected / exposed occurrences (all)	1 / 34 (2.94%) 1		
Skin and subcutaneous tissue disorders Pruritus subjects affected / exposed occurrences (all)	0 / 34 (0.00%) 0		
Eczema subjects affected / exposed occurrences (all)	0 / 34 (0.00%) 0		
Musculoskeletal and connective tissue disorders Arthralgia subjects affected / exposed occurrences (all)	0 / 34 (0.00%) 0		

Back pain			
subjects affected / exposed	1 / 34 (2.94%)		
occurrences (all)	1		
Musculoskeletal pain			
subjects affected / exposed	0 / 34 (0.00%)		
occurrences (all)	0		
Infections and infestations			
Nasopharyngitis			
subjects affected / exposed	4 / 34 (11.76%)		
occurrences (all)	4		
Gastroenteritis			
subjects affected / exposed	0 / 34 (0.00%)		
occurrences (all)	0		
Gastrointestinal infection			
subjects affected / exposed	0 / 34 (0.00%)		
occurrences (all)	0		
Hordeolum			
subjects affected / exposed	0 / 34 (0.00%)		
occurrences (all)	0		
Rhinitis			
subjects affected / exposed	0 / 34 (0.00%)		
occurrences (all)	0		
Sinusitis			
subjects affected / exposed	0 / 34 (0.00%)		
occurrences (all)	0		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
26 June 2015	Changes are made in the following: Number of study centers, inclusion criteria included reversibility to salbutamol testing in spirometry and a repeat Visit 1 in case reversibility test was negative., exclusion criteria of hypersensitivity to the active substance or to any of the excipients of the Run-in medication, budesonide , thyroid function test (safety laboratory assessments schedule), run-in part 1 (length of budesonide treatment), duration of run-in period (parts 1 & 2) and total study duration for each individual patient

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported