Clinical trial results:
A Phase 2b Randomised, Double-Blind, Placebo-Controlled, Parallel Arm, Multi-Centre Study to Assess Efficacy and Safety of Multiple Dose Levels of AZD7594 DPI Given Once Daily for Twelve Weeks, Compared to Placebo, in Asthmatics Symptomatic on Low Dose ICS

Summary

EudraCT number	2017-002483-40
Trial protocol	DE HU BG PL
Global end of trial date	30 September 2019

Results information

Result version number	v1 (current)
This version publication date	20 September 2020
First version publication date	20 September 2020

Trial information

Trial identification

Sponsor protocol code	D3741C00007

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT03622112
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	AstraZeneca AB
Sponsor organisation address	Södertälje, Södertälje, Sweden, 151 85
Public contact	Global Clinical Lead, AstraZeneca AB, 301 3985799, ClinicalTrialTransparency@astrazeneca.com
Scientific contact	Global Clinical Lead, AstraZeneca AB, 301 3985799, 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	21 November 2019
Is this the analysis of the primary completion data?	No
Global end of trial reached?	Yes
Global end of trial date	30 September 2019
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To investigate the clinical efficacy of AZD7594 at different dose levels in asthmatics symptomatic on low dose Inhaled Corticosteroid (ICS)

Protection of trial subjects:

The global study protocol, the country-specific protocols and all protocol amendments, including all versions of informed consent forms (ICFs) and any other written information and/or materials provided to the subjects were approved by an Independent Ethics Committee/Institutional Review Board (IEC/ IRB) in writing. This study was performed in accordance with the ethical principles that have their origin in the Declaration of Helsinki and that are consistent with International Council for Harmonisation/Good Clinical Practice (ICH/ GCP), applicable regulatory requirements and the AstraZeneca policy on Bioethics.The applicable regulatory requirements in Japan were GCP for Trials on Drugs ((Ministry of Health, Labour and Welfare [MHLW] Ordinance No.28, 27 March 1997, partially revised by MHLW Ordinance and their related notifications). Before signing the ICF, each subject was given full and adequate oral and written information about the nature, purpose, possible risk and benefit of the study. Every subject was given the opportunity to ask questions and allowed time to consider the information provided and was notified that he/she was free to discontinue from the study at any time.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	02 January 2019
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	United States: 135
Country: Number of subjects enrolled	Japan: 82
Country: Number of subjects enrolled	Poland: 142
Country: Number of subjects enrolled	Ukraine: 125
Country: Number of subjects enrolled	Germany: 120
Country: Number of subjects enrolled	Hungary: 99
Country: Number of subjects enrolled	Bulgaria: 85
Country: Number of subjects enrolled	South Africa: 18
Worldwide total number of subjects	806
EEA total number of subjects	446

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)	630
From 65 to 84 years	176
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

The study was conducted in 92 sites in 8 countries; Bulgaria, Germany, Hungary, Poland, and Ukraine, United States (US), South Africa, and Japan. In this study, 806 subjects (including 82 Japanese subjects) were randomised. For sites in the US, no subjects were randomised to the AZD7594 792 µg/720 µg once daily (QD) treatment arm.

Pre-assignment

Screening details:

Subjects attended a Screening Visit within 28 days before receiving their first dose. All subjects underwent inclusion exclusion criteria assessment and all eligible subjects signed the informed consent before undergoing any study related procedures.

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	AZD7594 50 µg

Arm description:

Oral inhalation of AZD5794 55 µg/ 50 µg (nominal dose/delivered dose) once daily (QD).

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

Dosage and administration details:

55 µg/50 µg (nominal dose/delivered dose), Oral inhalation (by SD3FL inhaler, dry powder inhaler (DPI)) QD

Arm title	AZD7594 90 µg

Arm description:

Oral inhalation of AZD5794 99 µg/ 90 µg (nominal dose/delivered dose) once daily.

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

Dosage and administration details:

99 µg/90 µg (nominal dose/delivered dose), Oral inhalation (by SD3FL inhaler, DPI) QD

Arm title	AZD7594 180 µg

Arm description:

Oral inhalation of AZD5794 198 µg/ 180 µg (nominal dose/delivered dose) once daily.

Arm type	Experimental

Investigational medicinal product name	AZD7594
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Inhalation powder
Routes of administration	Oral use

Dosage and administration details:

198 µg/180 µg (nominal dose/delivered dose), Oral inhalation (by SD3FL inhaler, DPI) QD

Arm title	AZD7594 360 µg

Arm description:

Oral inhalation of AZD5794 396 µg/ 360 µg (nominal dose/delivered dose) once daily.

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

Dosage and administration details:

396 µg/360 µg (nominal dose/delivered dose), Oral inhalation (by SD3FL inhaler, DPI) QD

Arm title	AZD7594 720 µg

Arm description:

Oral inhalation of AZD5794 792 µg/ 720 µg (nominal dose/delivered dose) once daily.

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

Dosage and administration details:

792 µg/720 µg (nominal dose/delivered dose), Oral inhalation (by SD3FL inhaler, DPI) QD (US excluded)

Arm title	Placebo to AZD7594

Arm description:

Oral inhalation of placebo to AZD7594 once daily.

Arm type	Placebo
Investigational medicinal product name	Placebo to AZD7594
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Inhalation powder
Routes of administration	Oral use

Dosage and administration details:

Matching Placebo to AZD7594, Oral inhalation (by SD3FL inhaler, DPI) QD

Arm title	Fluticasone furoate

Arm description:

Oral inhalation of fluticasone furoate 100 µg once daily.

Arm type	Experimental
Investigational medicinal product name	Fluticasone furoate
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Inhalation powder
Routes of administration	Oral use

Dosage and administration details:

100 µg per nominal dose, Oral inhalation (by ELLIPTA inhaler, DPI) QD

Number of subjects in period 1[1]	AZD7594 50 µg	AZD7594 90 µg	AZD7594 180 µg
Started	110	112	111
Completed	85	92	95
Not completed	25	20	16
Study-specific withdrawal criteria	10	8	7
Protocol deviation	2	-	1
Adverse event, serious fatal	-	-	-
Adverse event, non-fatal	6	8	4
Consent withdrawn by subject	6	2	4
Reason not specified	-	1	-
Lost to follow-up	1	1	-

Number of subjects in period 1[1]	AZD7594 360 µg	AZD7594 720 µg	Placebo to AZD7594
Started	113	134	113
Completed	91	124	71
Not completed	22	10	42
Study-specific withdrawal criteria	6	4	18
Protocol deviation	1	-	-
Adverse event, serious fatal	1	-	-
Adverse event, non-fatal	11	4	20
Consent withdrawn by subject	2	1	2
Reason not specified	1	1	2
Lost to follow-up	-	-	-

Number of subjects in period 1[1]	Fluticasone furoate
Started	112
Completed	103
Not completed	9
Study-specific withdrawal criteria	4
Protocol deviation	-
Adverse event, serious fatal	-

Adverse event, non-fatal	2
Consent withdrawn by subject	2
Reason not specified	1
Lost to follow-up	-

Notes:

[1] - The number of subjects reported to be in the baseline period are not the same as the worldwide number enrolled in the trial. It is expected that these numbers will be the same.

Justification: One randomized subject did not receive treatment as the subject deviated from the protocol and was randomized in error.

Baseline characteristics

Reporting groups	
Reporting group title	AZD7594 50 µg
Reporting group description:	
Oral inhalation of AZD5794 55 µg/ 50 µg (nominal dose/delivered dose) once daily (QD).	
Reporting group title	AZD7594 90 µg
Reporting group description:	
Oral inhalation of AZD5794 99 µg/ 90 µg (nominal dose/delivered dose) once daily.	
Reporting group title	AZD7594 180 µg
Reporting group description:	
Oral inhalation of AZD5794 198 µg/ 180 µg (nominal dose/delivered dose) once daily.	
Reporting group title	AZD7594 360 µg
Reporting group description:	
Oral inhalation of AZD5794 396 µg/ 360 µg (nominal dose/delivered dose) once daily.	
Reporting group title	AZD7594 720 µg
Reporting group description:	
Oral inhalation of AZD5794 792 µg/ 720 µg (nominal dose/delivered dose) once daily.	
Reporting group title	Placebo to AZD7594
Reporting group description:	
Oral inhalation of placebo to AZD7594 once daily.	
Reporting group title	Fluticasone furoate
Reporting group description:	
Oral inhalation of fluticasone furoate 100 µg once daily.	

Reporting group values	AZD7594 50 µg	AZD7594 90 µg	AZD7594 180 µg
Number of subjects	110	112	111
Age Categorical Units: Subjects			
<=18 years	0	0	0
Between 18 and 65 years	90	92	79
>=65 years	20	20	32
Age Continuous Units: Years			
arithmetic mean	52.2	53.2	54.6
standard deviation	± 12.8	± 13.3	± 14.5
Sex: Female, Male Units: Subjects			
Female	59	66	72
Male	51	46	39
Race (NIH/OMB) Units: Subjects			
American Indian or Alaska Native	0	1	0
Asian	9	11	10
Native Hawaiian or Other Pacific Islander	0	0	0
Black or African American	5	5	5
White	95	93	94
More than one race	1	2	2

Unknown or Not Reported	0	0	0

Reporting group values	AZD7594 360 µg	AZD7594 720 µg	Placebo to AZD7594
Number of subjects	113	134	113
Age Categorical Units: Subjects			
<=18 years	0	0	0
Between 18 and 65 years	92	107	87
>=65 years	21	27	26
Age Continuous Units: Years			
arithmetic mean	52.8	52.2	53.4
standard deviation	± 13.2	± 13.0	± 13.7
Sex: Female, Male Units: Subjects			
Female	64	79	68
Male	49	55	45
Race (NIH/OMB) Units: Subjects			
American Indian or Alaska Native	0	0	0
Asian	13	16	13
Native Hawaiian or Other Pacific Islander	0	0	0
Black or African American	2	1	5
White	97	115	92
More than one race	1	2	3
Unknown or Not Reported	0	0	0

Reporting group values	Fluticasone furoate	Total	
Number of subjects	112	805	
Age Categorical Units: Subjects			
<=18 years	0	0	
Between 18 and 65 years	82	629	
>=65 years	30	176	
Age Continuous Units: Years			
arithmetic mean	53.7		
standard deviation	± 13.4	-	
Sex: Female, Male Units: Subjects			
Female	59	467	
Male	53	338	
Race (NIH/OMB) Units: Subjects			
American Indian or Alaska Native	0	1	
Asian	12	84	
Native Hawaiian or Other Pacific Islander	0	0	
Black or African American	7	30	

White	93	679	
More than one race	0	11	
Unknown or Not Reported	0	0	

End points

End points reporting groups

Reporting group title	AZD7594 50 µg
Reporting group description:	
Oral inhalation of AZD5794 55 µg/ 50 µg (nominal dose/delivered dose) once daily (QD).	
Reporting group title	AZD7594 90 µg
Reporting group description:	
Oral inhalation of AZD5794 99 µg/ 90 µg (nominal dose/delivered dose) once daily.	
Reporting group title	AZD7594 180 µg
Reporting group description:	
Oral inhalation of AZD5794 198 µg/ 180 µg (nominal dose/delivered dose) once daily.	
Reporting group title	AZD7594 360 µg
Reporting group description:	
Oral inhalation of AZD5794 396 µg/ 360 µg (nominal dose/delivered dose) once daily.	
Reporting group title	AZD7594 720 µg
Reporting group description:	
Oral inhalation of AZD5794 792 µg/ 720 µg (nominal dose/delivered dose) once daily.	
Reporting group title	Placebo to AZD7594
Reporting group description:	
Oral inhalation of placebo to AZD7594 once daily.	
Reporting group title	Fluticasone furoate
Reporting group description:	
Oral inhalation of fluticasone furoate 100 µg once daily.	

Primary: Change from baseline in trough Forced expiratory volume in 1 second (FEV1) at Week 12

End point title	Change from baseline in trough Forced expiratory volume in 1 second (FEV1) at Week 12

End point description:

To investigate the clinical efficacy of AZD7594 at different dose levels in asthmatics symptomatic on low dose ICS (Full Analysis Set). Trough value was defined as the mean of the 2 measurements 30 minutes apart (23 hours after last dose) pre-dose for every visit throughout the Treatment Period (Visit 4/Week 2 to Visit 7/Week 12). Baseline was defined as the mean of the 2 measured values before first investigational product (IP) administration (30 minutes apart, at −45 minutes and −15 minutes, before IP administration) on Day 1 (Visit 3). Analyses were based on a Mixed-effects model for repeated measures (MMRM) with treatment, visit, treatment by visit interaction and region as fixed effects, and baseline value and baseline by visit interaction as covariates.

End point type	Primary

End point timeframe:

At Baseline and Week 12

End point values	AZD7594 50 µg	AZD7594 90 µg	AZD7594 180 µg	AZD7594 360 µg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	83	90	92	90
Units: Liters				
least squares mean (confidence interval 95%)	-0.013 (-0.077 to 0.050)	-0.031 (-0.094 to 0.031)	0.062 (-0.001 to 0.124)	0.099 (0.036 to 0.161)

End point values	AZD7594 720 µg	Placebo to AZD7594	Fluticasone furoate	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	123	70	103	
Units: Liters				
least squares mean (confidence interval 95%)	0.104 (0.046 to 0.162)	0.022 (-0.046 to 0.091)	0.133 (0.073 to 0.193)	

Statistical analyses

Statistical analysis title	Statistical Analysis 1
Comparison groups	AZD7594 50 µg v Placebo to AZD7594
Number of subjects included in analysis	153
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.437
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)
Point estimate	-0.036
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.126
upper limit	0.054

Statistical analysis title	Statistical Analysis 2
Comparison groups	AZD7594 90 µg v Placebo to AZD7594
Number of subjects included in analysis	160
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.236
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)
Point estimate	-0.054
Confidence interval	
level	95 %
sides	2-sided

lower limit	-0.143
upper limit	0.035

Statistical analysis title	Statistical Analysis 3
Comparison groups	AZD7594 180 µg v Placebo to AZD7594
Number of subjects included in analysis	162
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.389
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)
Point estimate	0.039
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.05
upper limit	0.128

Statistical analysis title	Statistical Analysis 4
Comparison groups	AZD7594 360 µg v Placebo to AZD7594
Number of subjects included in analysis	160
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.094
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)
Point estimate	0.076
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.013
upper limit	0.165

Statistical analysis title	Statistical Analysis 5
Comparison groups	AZD7594 720 µg v Placebo to AZD7594
Number of subjects included in analysis	193
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.06
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)
Point estimate	0.082
Confidence interval	
level	95 %

sides	2-sided
lower limit	-0.003
upper limit	0.167

Statistical analysis title	Statistical Analysis 6
Comparison groups	Placebo to AZD7594 v Fluticasone furoate
Number of subjects included in analysis	173
Analysis specification	Pre-specified
Analysis type	superiority[1]
P-value	= 0.014
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)
Point estimate	0.111
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.023
upper limit	0.199

Notes:

[1] - The Statistical analysis is done to show the superiority of Fluticasone furoate over Placebo

Secondary: Change from baseline in trough FEV1 at Weeks 2, 4, 8 and average over the Treatment Period

End point title	Change from baseline in trough FEV1 at Weeks 2, 4, 8 and average over the Treatment Period

End point description:

To investigate the clinical efficacy of AZD7594 at different dose levels in asthmatics symptomatic on low dose ICS (Full Analysis Set). Trough value was defined as the mean of the 2 measurements 30 minutes apart (23 hours after last dose) pre-dose for every visit throughout the Treatment Period. Baseline was defined as the mean of the 2 measured values before first IP administration on Day 1. Analyses were based on a MMRM with treatment, visit, treatment by visit interaction and region as fixed effects, and baseline value and baseline by visit interaction as covariates. Analysis of covariance (ANCOVA) with treatment and region (ie, US, Japan, and Rest of the World [RoW]) as fixed effects, and baseline as covariate was used for the analysis of average over the Treatment Period. The reported number of subjects analysed corresponds to Week 2 and for Weeks 4, 8, 12 and average over the Treatment Period, the number of subjects analysed are provided as comment in the row titles.

End point type	Secondary

End point timeframe:

At Baseline and Weeks 2, 4 and 8

End point values	AZD7594 50 µg	AZD7594 90 µg	AZD7594 180 µg	AZD7594 360 µg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	108	107	108	104
Units: Liters				
least squares mean (confidence interval 95%)				
Week 2	0.018 (-0.038 to 0.073)	0.011 (-0.044 to 0.066)	0.067 (0.011 to 0.122)	0.091 (0.036 to 0.147)

Week 4 (n=98, 103, 103, 104, 127, 84, 110)	-0.002 (-0.063 to 0.059)	0.039 (-0.021 to 0.099)	0.078 (0.018 to 0.138)	0.086 (0.027 to 0.146)
Week 8 (n=90, 96, 100, 96, 125, 76, 105)	0.019 (-0.044 to 0.082)	0.007 (-0.055 to 0.069)	0.071 (0.010 to 0.133)	0.102 (0.040 to 0.163)
Treatment Period Avg(n=108,109,108,109,132,95,110)	0.005 (-0.049 to 0.059)	0.006 (-0.047 to 0.059)	0.069 (0.016 to 0.123)	0.094 (0.041 to 0.148)

End point values	AZD7594 720 µg	Placebo to AZD7594	Fluticasone furoate	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	132	95	109	
Units: Liters				
least squares mean (confidence interval 95%)				
Week 2	0.093 (0.041 to 0.146)	-0.011 (-0.070 to 0.048)	0.107 (0.052 to 0.161)	
Week 4 (n=98, 103, 103, 104, 127, 84, 110)	0.094 (0.037 to 0.151)	-0.020 (-0.085 to 0.045)	0.145 (0.086 to 0.204)	
Week 8 (n=90, 96, 100, 96, 125, 76, 105)	0.141 (0.083 to 0.199)	0.002 (-0.066 to 0.069)	0.124 (0.064 to 0.184)	
Treatment Period Avg(n=108,109,108,109,132,95,110)	0.108 (0.057 to 0.159)	-0.002 (-0.059 to 0.056)	0.127 (0.075 to 0.180)	

Statistical analyses

Statistical analysis title	Statistical Analysis at Week 2
Comparison groups	AZD7594 50 µg v Placebo to AZD7594
Number of subjects included in analysis	203
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.463
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)
Point estimate	0.029
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.048
upper limit	0.105

Statistical analysis title	Statistical Analysis at Week 2
Comparison groups	AZD7594 90 µg v Placebo to AZD7594
Number of subjects included in analysis	202
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.576
Method	Mixed models analysis

Parameter estimate	Mean difference (final values)
Point estimate	0.022
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.055
upper limit	0.098

Statistical analysis title	Statistical Analysis at Week 2
Comparison groups	AZD7594 180 µg v Placebo to AZD7594
Number of subjects included in analysis	203
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.047
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)
Point estimate	0.078
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.001
upper limit	0.154

Statistical analysis title	Statistical Analysis at Week 2
Comparison groups	AZD7594 360 µg v Placebo to AZD7594
Number of subjects included in analysis	199
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.009
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)
Point estimate	0.102
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.025
upper limit	0.179

Statistical analysis title	Statistical Analysis at Week 2
Comparison groups	AZD7594 720 µg v Placebo to AZD7594
Number of subjects included in analysis	227
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.006

Method	Mixed models analysis
Parameter estimate	Mean difference (final values)
Point estimate	0.104
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.031
upper limit	0.178

Statistical analysis title	Statistical Analysis at Week 2
Comparison groups	Placebo to AZD7594 v Fluticasone furoate
Number of subjects included in analysis	204
Analysis specification	Pre-specified
Analysis type	superiority[2]
P-value	= 0.003
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)
Point estimate	0.118
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.041
upper limit	0.194

Notes:

[2] - The Statistical analysis is done to show the superiority of Fluticasone furoate over Placebo

Statistical analysis title	Statistical Analysis at Week 4
Comparison groups	AZD7594 50 µg v Placebo to AZD7594
Number of subjects included in analysis	203
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.685
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)
Point estimate	0.018
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.068
upper limit	0.103

Statistical analysis title	Statistical Analysis at Week 4
Comparison groups	AZD7594 90 µg v Placebo to AZD7594
Number of subjects included in analysis	202
Analysis specification	Pre-specified
Analysis type	superiority

P-value	= 0.176
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)
Point estimate	0.059
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.026
upper limit	0.144

Statistical analysis title	Statistical Analysis at Week 4
Comparison groups	AZD7594 180 µg v Placebo to AZD7594
Number of subjects included in analysis	203
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.024
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)
Point estimate	0.098
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.013
upper limit	0.183

Statistical analysis title	Statistical Analysis at Week 4
Comparison groups	AZD7594 360 µg v Placebo to AZD7594
Number of subjects included in analysis	199
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.014
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)
Point estimate	0.106
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.021
upper limit	0.191

Statistical analysis title	Statistical Analysis at Week 4
Comparison groups	AZD7594 720 µg v Placebo to AZD7594
Number of subjects included in analysis	227
Analysis specification	Pre-specified

Analysis type	superiority
P-value	= 0.006
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)
Point estimate	0.114
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.032
upper limit	0.196

Statistical analysis title	Statistical Analysis at Week 4
Comparison groups	Placebo to AZD7594 v Fluticasone furoate
Number of subjects included in analysis	204
Analysis specification	Pre-specified
Analysis type	superiority[3]
P-value	< 0.001
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)
Point estimate	0.165
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.081
upper limit	0.249

Notes:

[3] - The Statistical analysis is done to show the superiority of Fluticasone furoate over Placebo

Statistical analysis title	Statistical Analysis at Week 8
Comparison groups	AZD7594 50 µg v Placebo to AZD7594
Number of subjects included in analysis	203
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.707
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)
Point estimate	0.017
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.072
upper limit	0.106

Statistical analysis title	Statistical Analysis at Week 8
Comparison groups	AZD7594 90 µg v Placebo to AZD7594
Number of subjects included in analysis	202

Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.904
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)
Point estimate	0.005
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.083
upper limit	0.094

Statistical analysis title	Statistical Analysis at Week 8
Comparison groups	AZD7594 180 µg v Placebo to AZD7594
Number of subjects included in analysis	203
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.121
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)
Point estimate	0.07
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.018
upper limit	0.157

Statistical analysis title	Statistical Analysis at Week 8
Comparison groups	AZD7594 360 µg v Placebo to AZD7594
Number of subjects included in analysis	199
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.026
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)
Point estimate	0.1
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.012
upper limit	0.188

Statistical analysis title	Statistical Analysis at Week 8
Comparison groups	AZD7594 720 µg v Placebo to AZD7594

Number of subjects included in analysis	227
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.001
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)
Point estimate	0.139
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.055
upper limit	0.224

Statistical analysis title	Statistical Analysis at Week 8
Comparison groups	Placebo to AZD7594 v Fluticasone furoate
Number of subjects included in analysis	204
Analysis specification	Pre-specified
Analysis type	superiority[4]
P-value	= 0.006
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)
Point estimate	0.122
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.035
upper limit	0.209

Notes:

[4] - The Statistical analysis is done to show the superiority of Fluticasone furoate over Placebo

Statistical analysis title	Statistical Analysis for Treatment period average
Comparison groups	AZD7594 50 µg v Placebo to AZD7594
Number of subjects included in analysis	203
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.856
Method	ANCOVA
Parameter estimate	Mean difference (final values)
Point estimate	0.007
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.068
upper limit	0.081

Statistical analysis title	Statistical Analysis for Treatment period average

Comparison groups	AZD7594 90 µg v Placebo to AZD7594
Number of subjects included in analysis	202
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.832
Method	ANCOVA
Parameter estimate	Mean difference (final values)
Point estimate	0.008
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.066
upper limit	0.082

Statistical analysis title	Statistical Analysis for Treatment period average
Comparison groups	AZD7594 180 µg v Placebo to AZD7594
Number of subjects included in analysis	203
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.06
Method	ANCOVA
Parameter estimate	Mean difference (final values)
Point estimate	0.071
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.003
upper limit	0.145

Statistical analysis title	Statistical Analysis for Treatment period average
Comparison groups	AZD7594 360 µg v Placebo to AZD7594
Number of subjects included in analysis	199
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.011
Method	ANCOVA
Parameter estimate	Mean difference (final values)
Point estimate	0.096
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.022
upper limit	0.17

Statistical analysis title	Statistical Analysis for Treatment period average
Comparison groups	AZD7594 720 µg v Placebo to AZD7594
Number of subjects included in analysis	227
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.003
Method	ANCOVA
Parameter estimate	Mean difference (final values)
Point estimate	0.11
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.039
upper limit	0.181

Statistical analysis title	Statistical Analysis for Treatment period average
Comparison groups	Placebo to AZD7594 v Fluticasone furoate
Number of subjects included in analysis	204
Analysis specification	Pre-specified
Analysis type	superiority[5]
P-value	< 0.001
Method	ANCOVA
Parameter estimate	Mean difference (final values)
Point estimate	0.129
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.055
upper limit	0.202

Notes:

[5] - The Statistical analysis is done to show the superiority of Fluticasone furoate over Placebo

Secondary: Change from baseline in Fractional exhaled nitic oxide (FENO) at Weeks 2, 4, 8, 12 and average over the Treatment Period

End point title	Change from baseline in Fractional exhaled nitic oxide (FENO) at Weeks 2, 4, 8, 12 and average over the Treatment Period

End point description:

To investigate the clinical efficacy of AZD7594 at different dose levels in asthmatics symptomatic on low dose ICS (Full Analysis Set). Baseline was defined as the last value obtained prior to the first dose of investigational product. Analyses were based on a MMRM with change from baseline on the log-scale as the response, treatment, visit, treatment by visit interaction and region as fixed effects, and log-transformed baseline value and baseline by visit interaction as covariates.
The reported number of subjects analysed corresponds to Week 2 and for Weeks 4, 8, 12 and average over the Treatment Period, the number of subjects analysed are provided as comment in the row titles.

End point type	Secondary

End point timeframe:

At Baseline and Weeks 2, 4, 8, and 12

End point values	AZD7594 50 µg	AZD7594 90 µg	AZD7594 180 µg	AZD7594 360 µg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	107	105	107	102
Units: ppb				
geometric mean (confidence interval 95%)				
Week 2	1.307 (1.190 to 1.436)	1.223 (1.113 to 1.343)	1.175 (1.070 to 1.290)	1.152 (1.048 to 1.267)
Week 4 (n=95,100,103,102,126,84,105)	1.229 (1.109 to 1.363)	1.203 (1.087 to 1.332)	1.220 (1.103 to 1.349)	1.118 (1.011 to 1.237)
Week 8 (n=87,90,97,93,122,76,101)	1.294 (1.157 to 1.447)	1.316 (1.179 to 1.470)	1.250 (1.122 to 1.392)	1.206 (1.082 to 1.345)
Week 12 (n=79,89,89,88,121,70,100)	1.367 (1.219 to 1.532)	1.405 (1.258 to 1.569)	1.281 (1.148 to 1.431)	1.198 (1.072 to 1.337)
Treatment Period Avg(n=109,107,108,109,132,95,110)	1.298 (1.188 to 1.419)	1.284 (1.176 to 1.402)	1.231 (1.128 to 1.343)	1.168 (1.070 to 1.275)

End point values	AZD7594 720 µg	Placebo to AZD7594	Fluticasone furoate	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	127	95	104	
Units: ppb				
geometric mean (confidence interval 95%)				
Week 2	0.959 (0.876 to 1.049)	1.396 (1.263 to 1.542)	0.880 (0.801 to 0.967)	
Week 4 (n=95,100,103,102,126,84,105)	0.980 (0.891 to 1.078)	1.321 (1.184 to 1.475)	0.928 (0.840 to 1.025)	
Week 8 (n=87,90,97,93,122,76,101)	1.021 (0.923 to 1.129)	1.411 (1.252 to 1.591)	0.906 (0.815 to 1.007)	
Week 12 (n=79,89,89,88,121,70,100)	0.958 (0.866 to 1.060)	1.474 (1.305 to 1.664)	0.918 (0.826 to 1.022)	
Treatment Period Avg(n=109,107,108,109,132,95,110)	0.979 (0.901 to 1.064)	1.399 (1.273 to 1.538)	0.908 (0.833 to 0.989)	

Statistical analyses

Statistical analysis title	Statistical Analysis at Week 2
Comparison groups	AZD7594 50 µg v Placebo to AZD7594
Number of subjects included in analysis	202
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.322
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)
Point estimate	0.936
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.822

upper limit	1.067

Statistical analysis title	Statistical Analysis at Week 2
Comparison groups	AZD7594 90 µg v Placebo to AZD7594
Number of subjects included in analysis	200
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.047
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)
Point estimate	0.876
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.768
upper limit	0.999

Statistical analysis title	Statistical Analysis at Week 2
Comparison groups	AZD7594 180 µg v Placebo to AZD7594
Number of subjects included in analysis	202
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.01
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)
Point estimate	0.842
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.739
upper limit	0.959

Statistical analysis title	Statistical Analysis at Week 2
Comparison groups	AZD7594 360 µg v Placebo to AZD7594
Number of subjects included in analysis	197
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.004
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)
Point estimate	0.825
Confidence interval	
level	95 %
sides	2-sided

lower limit	0.724
upper limit	0.941

Statistical analysis title	Statistical Analysis at Week 2
Comparison groups	AZD7594 720 µg v Placebo to AZD7594
Number of subjects included in analysis	222
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)
Point estimate	0.687
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.606
upper limit	0.779

Statistical analysis title	Statistical Analysis at Week 2
Comparison groups	Placebo to AZD7594 v Fluticasone furoate
Number of subjects included in analysis	199
Analysis specification	Pre-specified
Analysis type	superiority[6]
P-value	< 0.001
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)
Point estimate	0.63
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.553
upper limit	0.719

Notes:

[6] - The Statistical analysis is done to show the superiority of Fluticasone furoate over Placebo

Statistical analysis title	Statistical Analysis at Week 4
Comparison groups	AZD7594 50 µg v Placebo to AZD7594
Number of subjects included in analysis	202
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.329
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)
Point estimate	0.931
Confidence interval	
level	95 %

sides	2-sided
lower limit	0.805
upper limit	1.076

Statistical analysis title	Statistical Analysis at Week 4
Comparison groups	AZD7594 90 µg v Placebo to AZD7594
Number of subjects included in analysis	200
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.203
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)
Point estimate	0.911
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.789
upper limit	1.052

Statistical analysis title	Statistical Analysis at Week 4
Comparison groups	AZD7594 180 µg v Placebo to AZD7594
Number of subjects included in analysis	202
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.273
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)
Point estimate	0.923
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.8
upper limit	1.065

Statistical analysis title	Statistical Analysis at Week 4
Comparison groups	AZD7594 360 µg v Placebo to AZD7594
Number of subjects included in analysis	197
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.023
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)
Point estimate	0.846
Confidence interval	

level	95 %
sides	2-sided
lower limit	0.734
upper limit	0.977

Statistical analysis title	Statistical Analysis at Week 4
Comparison groups	AZD7594 720 µg v Placebo to AZD7594
Number of subjects included in analysis	222
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)
Point estimate	0.742
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.646
upper limit	0.852

Statistical analysis title	Statistical Analysis at Week 4
Comparison groups	Placebo to AZD7594 v Fluticasone furoate
Number of subjects included in analysis	199
Analysis specification	Pre-specified
Analysis type	superiority[7]
P-value	< 0.001
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)
Point estimate	0.703
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.609
upper limit	0.81

Notes:

[7] - The Statistical analysis is done to show the superiority of Fluticasone furoate over Placebo

Statistical analysis title	Statistical Analysis at Week 8
Comparison groups	AZD7594 50 µg v Placebo to AZD7594
Number of subjects included in analysis	202
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.283
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)
Point estimate	0.917

Confidence interval	
level	95 %
sides	2-sided
lower limit	0.783
upper limit	1.074

Statistical analysis title	Statistical Analysis at Week 8
Comparison groups	AZD7594 90 µg v Placebo to AZD7594
Number of subjects included in analysis	200
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.386
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)
Point estimate	0.933
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.797
upper limit	1.092

Statistical analysis title	Statistical Analysis at Week 8
Comparison groups	AZD7594 180 µg v Placebo to AZD7594
Number of subjects included in analysis	202
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.126
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)
Point estimate	0.886
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.758
upper limit	1.035

Statistical analysis title	Statistical Analysis at Week 8
Comparison groups	AZD7594 360 µg v Placebo to AZD7594
Number of subjects included in analysis	197
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.05
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)

Point estimate	0.855
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.731
upper limit	1

Statistical analysis title	Statistical Analysis at Week 8
Comparison groups	AZD7594 720 µg v Placebo to AZD7594
Number of subjects included in analysis	222
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)
Point estimate	0.723
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.623
upper limit	0.84

Statistical analysis title	Statistical Analysis at Week 8
Comparison groups	Placebo to AZD7594 v Fluticasone furoate
Number of subjects included in analysis	199
Analysis specification	Pre-specified
Analysis type	superiority[8]
P-value	< 0.001
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)
Point estimate	0.642
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.55
upper limit	0.749

Notes:

[8] - The Statistical analysis is done to show the superiority of Fluticasone furoate over Placebo

Statistical analysis title	Statistical Analysis at Week 12
Comparison groups	AZD7594 50 µg v Placebo to AZD7594
Number of subjects included in analysis	202
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.359
Method	Mixed models analysis

Parameter estimate	Mean difference (final values)
Point estimate	0.927
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.789
upper limit	1.09

Statistical analysis title	Statistical Analysis at Week 12
Comparison groups	Placebo to AZD7594 v AZD7594 90 µg
Number of subjects included in analysis	200
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.556
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)
Point estimate	0.953
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.813
upper limit	1.118

Statistical analysis title	Statistical Analysis at Week 12
Comparison groups	AZD7594 180 µg v Placebo to AZD7594
Number of subjects included in analysis	202
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.084
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)
Point estimate	0.869
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.742
upper limit	1.019

Statistical analysis title	Statistical Analysis at Week 12
Comparison groups	AZD7594 360 µg v Placebo to AZD7594
Number of subjects included in analysis	197
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.011

Method	Mixed models analysis
Parameter estimate	Mean difference (final values)
Point estimate	0.813
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.693
upper limit	0.953

Statistical analysis title	Statistical Analysis at Week 12
Comparison groups	AZD7594 720 µg v Placebo to AZD7594
Number of subjects included in analysis	222
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)
Point estimate	0.65
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.559
upper limit	0.757

Statistical analysis title	Statistical Analysis at Week 12
Comparison groups	Placebo to AZD7594 v Fluticasone furoate
Number of subjects included in analysis	199
Analysis specification	Pre-specified
Analysis type	superiority[9]
P-value	< 0.001
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)
Point estimate	0.623
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.533
upper limit	0.729

Notes:

[9] - The Statistical analysis is done to show the superiority of Fluticasone furoate over Placebo

Statistical analysis title	Statistical Analysis for Treatment period average
Comparison groups	AZD7594 50 µg v Placebo to AZD7594
Number of subjects included in analysis	202
Analysis specification	Pre-specified
Analysis type	superiority

P-value	= 0.231
Method	ANCOVA
Parameter estimate	Mean difference (final values)
Point estimate	0.928
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.821
upper limit	1.049

Statistical analysis title	Statistical Analysis for Treatment period average
Comparison groups	AZD7594 90 µg v Placebo to AZD7594
Number of subjects included in analysis	200
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.17
Method	ANCOVA
Parameter estimate	Mean difference (final values)
Point estimate	0.918
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.812
upper limit	1.037

Statistical analysis title	Statistical Analysis for Treatment period average
Comparison groups	AZD7594 180 µg v Placebo to AZD7594
Number of subjects included in analysis	202
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.039
Method	ANCOVA
Parameter estimate	Mean difference (final values)
Point estimate	0.879
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.778
upper limit	0.994

Statistical analysis title	Statistical Analysis for Treatment period average
Comparison groups	AZD7594 360 µg v Placebo to AZD7594
Number of subjects included in analysis	197
Analysis specification	Pre-specified

Analysis type	superiority
P-value	= 0.004
Method	ANCOVA
Parameter estimate	Mean difference (final values)
Point estimate	0.835
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.739
upper limit	0.943

Statistical analysis title	Statistical Analysis for Treatment period average
Comparison groups	AZD7594 720 µg v Placebo to AZD7594
Number of subjects included in analysis	222
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	ANCOVA
Parameter estimate	Mean difference (final values)
Point estimate	0.7
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.622
upper limit	0.787

Statistical analysis title	Statistical Analysis for Treatment period average
Comparison groups	Placebo to AZD7594 v Fluticasone furoate
Number of subjects included in analysis	199
Analysis specification	Pre-specified
Analysis type	superiority[10]
P-value	< 0.001
Method	ANCOVA
Parameter estimate	Mean difference (final values)
Point estimate	0.649
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.575
upper limit	0.732

Notes:

[10] - The Statistical analysis is done to show the superiority of Fluticasone furoate over Placebo

Secondary: Change from baseline in trough Forced vital capacity (FVC) at Week 12 and average over the Treatment Period	
End point title	Change from baseline in trough Forced vital capacity (FVC) at

	Week 12 and average over the Treatment Period

End point description:

To investigate the clinical efficacy of AZD7594 at different dose levels in asthmatics symptomatic on low dose ICS(Full Analysis Set).Trough value was defined as the mean of the 2 measurements 30 minutes apart(23 hours after last dose) pre-dose for every visit throughout the Treatment Period (Week 2 to Week 12).Baseline was defined as the mean of the 2 measured values before first IP administration(30 minutes apart, at −45 minutes and −15 minutes, before IP administration) on Day 1. Analyses were based on a MMRM with treatment, visit, treatment by visit interaction and region as fixed effects, and baseline value and baseline by visit interaction as covariates. Analysis of covariance with treatment and region as fixed effects, and baseline as covariate was used for the analysis of average over the Treatment Period. Reported number of subjects analysed corresponds to Week 12 and for average over the Treatment Period, the number of subjects analysed are provided as comment in row title.

End point type	Secondary

End point timeframe:

At Baseline and Week 12

End point values	AZD7594 50 µg	AZD7594 90 µg	AZD7594 180 µg	AZD7594 360 µg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	83	90	92	90
Units: Liters				
least squares mean (confidence interval 95%)				
Week 12	0.027 (-0.047 to 0.101)	-0.017 (-0.089 to 0.056)	0.076 (0.005 to 0.148)	0.119 (0.047 to 0.191)
Treatment Period Avg(n=108,109,108,109,132,95,110)	0.044 (-0.017 to 0.106)	0.019 (-0.041 to 0.080)	0.087 (0.026 to 0.148)	0.127 (0.066 to 0.188)

End point values	AZD7594 720 µg	Placebo to AZD7594	Fluticasone furoate	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	123	70	103	
Units: Liters				
least squares mean (confidence interval 95%)				
Week 12	0.088 (0.021 to 0.155)	0.061 (-0.018 to 0.141)	0.118 (0.048 to 0.188)	
Treatment Period Avg(n=108,109,108,109,132,95,110)	0.091 (0.033 to 0.149)	0.046 (-0.020 to 0.112)	0.121 (0.062 to 0.181)	

Statistical analyses

Statistical analysis title	Statistical Analysis at Week 12
Comparison groups	AZD7594 50 µg v Placebo to AZD7594
Number of subjects included in analysis	153
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.519
Method	Mixed models analysis

Parameter estimate	Mean difference (final values)
Point estimate	-0.034
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.139
upper limit	0.07

Statistical analysis title	Statistical Analysis at Week 12
Comparison groups	AZD7594 90 µg v Placebo to AZD7594
Number of subjects included in analysis	160
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.141
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)
Point estimate	-0.078
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.181
upper limit	0.026

Statistical analysis title	Statistical Analysis at Week 12
Comparison groups	AZD7594 180 µg v Placebo to AZD7594
Number of subjects included in analysis	162
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.772
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)
Point estimate	0.015
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.088
upper limit	0.119

Statistical analysis title	Statistical Analysis at Week 12
Comparison groups	AZD7594 360 µg v Placebo to AZD7594
Number of subjects included in analysis	160
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.27

Method	Mixed models analysis
Parameter estimate	Mean difference (final values)
Point estimate	0.058
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.045
upper limit	0.162

Statistical analysis title	Statistical Analysis at Week 12
Comparison groups	AZD7594 720 µg v Placebo to AZD7594
Number of subjects included in analysis	193
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.592
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)
Point estimate	0.027
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.072
upper limit	0.126

Statistical analysis title	Statistical Analysis at Week 12
Comparison groups	Placebo to AZD7594 v Fluticasone furoate
Number of subjects included in analysis	173
Analysis specification	Pre-specified
Analysis type	superiority[11]
P-value	= 0.275
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)
Point estimate	0.057
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.045
upper limit	0.158

Notes:

[11] - The Statistical analysis is done to show the superiority of Fluticasone furoate over Placebo

Statistical analysis title	Statistical Analysis for Treatment period average
Comparison groups	AZD7594 50 µg v Placebo to AZD7594
Number of subjects included in analysis	153
Analysis specification	Pre-specified
Analysis type	superiority

P-value	= 0.963
Method	ANCOVA
Parameter estimate	Mean difference (final values)
Point estimate	-0.002
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.087
upper limit	0.083

Statistical analysis title	Statistical Analysis for Treatment period average
Comparison groups	AZD7594 90 µg v Placebo to AZD7594
Number of subjects included in analysis	160
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.533
Method	ANCOVA
Parameter estimate	Mean difference (final values)
Point estimate	-0.027
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.112
upper limit	0.058

Statistical analysis title	Statistical Analysis for Treatment period average
Comparison groups	AZD7594 180 µg v Placebo to AZD7594
Number of subjects included in analysis	162
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.342
Method	ANCOVA
Parameter estimate	Mean difference (final values)
Point estimate	0.041
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.044
upper limit	0.126

Statistical analysis title	Statistical Analysis for Treatment period average
Comparison groups	AZD7594 360 µg v Placebo to AZD7594
Number of subjects included in analysis	160
Analysis specification	Pre-specified

Analysis type	superiority
P-value	= 0.061
Method	ANCOVA
Parameter estimate	Mean difference (final values)
Point estimate	0.081
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.004
upper limit	0.165

Statistical analysis title	Statistical Analysis for Treatment period average
Comparison groups	AZD7594 720 µg v Placebo to AZD7594
Number of subjects included in analysis	193
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.278
Method	ANCOVA
Parameter estimate	Mean difference (final values)
Point estimate	0.045
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.037
upper limit	0.127

Statistical analysis title	Statistical Analysis for Treatment period average
Comparison groups	Placebo to AZD7594 v Fluticasone furoate
Number of subjects included in analysis	173
Analysis specification	Pre-specified
Analysis type	superiority[12]
P-value	= 0.079
Method	ANCOVA
Parameter estimate	Mean difference (final values)
Point estimate	0.075
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.009
upper limit	0.159

Notes:

[12] - The Statistical analysis is done to show the superiority of Fluticasone furoate over Placebo

Secondary: Change from baseline in Asthma Control Questionnaire -5 (ACQ-5) at Week 12 and average over the Treatment Period

End point title	Change from baseline in Asthma Control Questionnaire -5

	(ACQ-5) at Week 12 and average over the Treatment Period

End point description:

To investigate the clinical efficacy of AZD7594 at different dose levels in asthmatics symptomatic on low dose ICS (Full Analysis Set). Baseline was defined as the ACQ-5 score at Visit 3. Analyses were based on a MMRM with treatment, visit, treatment by visit interaction and region as fixed effects, and baseline value and baseline by visit interaction as covariates. Analysis of covariance with treatment and region as fixed effects, and baseline as covariate was used for the analysis of average over the Treatment Period. The questionnaire has 5 items; each item is scored on a scale of 0 to 6, where higher scores represent more severe impairment/symptoms. The overall ACQ-5 score is the average of the scores for each of the questions included in the questionnaire. Reported number of subjects analysed corresponds to Week 12 and for average over the Treatment Period, the number of subjects analysed are provided as comment in row title.

End point type	Secondary

End point timeframe:

At Baseline and Week 12

End point values	AZD7594 50 µg	AZD7594 90 µg	AZD7594 180 µg	AZD7594 360 µg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	83	91	93	90
Units: units on a scale				
least squares mean (confidence interval 95%)				
Week 12	-0.289 (-0.412 to -0.166)	-0.394 (-0.513 to -0.274)	-0.357 (-0.476 to -0.239)	-0.330 (-0.449 to -0.210)
Treatment Period Avg(n=108,110,108,110,132,101,110	-0.215 (-0.307 to -0.122)	-0.230 (-0.322 to -0.139)	-0.220 (-0.311 to -0.128)	-0.291 (-0.382 to -0.199)

End point values	AZD7594 720 µg	Placebo to AZD7594	Fluticasone furoate	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	122	70	103	
Units: units on a scale				
least squares mean (confidence interval 95%)				
Week 12	-0.406 (-0.514 to -0.297)	-0.137 (-0.269 to -0.004)	-0.360 (-0.474 to -0.245)	
Treatment Period Avg(n=108,110,108,110,132,101,110	-0.306 (-0.394 to -0.219)	-0.090 (-0.187 to 0.008)	-0.269 (-0.359 to -0.179)	

Statistical analyses

Statistical analysis title	Statistical Analysis at Week 12
Comparison groups	AZD7594 50 µg v Placebo to AZD7594
Number of subjects included in analysis	153
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.088
Method	Mixed models analysis

Parameter estimate	Mean difference (final values)
Point estimate	-0.153
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.328
upper limit	0.023

Statistical analysis title	Statistical Analysis at Week 12
Comparison groups	AZD7594 90 µg v Placebo to AZD7594
Number of subjects included in analysis	161
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.004
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)
Point estimate	-0.257
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.43
upper limit	-0.084

Statistical analysis title	Statistical Analysis at Week 12
Comparison groups	AZD7594 180 µg v Placebo to AZD7594
Number of subjects included in analysis	163
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.012
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)
Point estimate	-0.221
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.393
upper limit	-0.049

Statistical analysis title	Statistical Analysis at Week 12
Comparison groups	AZD7594 360 µg v Placebo to AZD7594
Number of subjects included in analysis	160
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.029

Method	Mixed models analysis
Parameter estimate	Mean difference (final values)
Point estimate	-0.193
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.366
upper limit	-0.02

Statistical analysis title	Statistical Analysis at Week 12
Comparison groups	AZD7594 720 µg v Placebo to AZD7594
Number of subjects included in analysis	192
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.001
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)
Point estimate	-0.269
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.434
upper limit	-0.104

Statistical analysis title	Statistical Analysis at Week 12
Comparison groups	Placebo to AZD7594 v Fluticasone furoate
Number of subjects included in analysis	173
Analysis specification	Pre-specified
Analysis type	superiority[13]
P-value	= 0.01
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)
Point estimate	-0.223
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.393
upper limit	-0.054

Notes:

[13] - The Statistical analysis is done to show the superiority of Fluticasone furoate over Placebo

Statistical analysis title	Statistical Analysis for Treatment period average
Comparison groups	AZD7594 50 µg v Placebo to AZD7594
Number of subjects included in analysis	153
Analysis specification	Pre-specified
Analysis type	superiority

P-value	= 0.055
Method	ANCOVA
Parameter estimate	Mean difference (final values)
Point estimate	-0.125
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.253
upper limit	0.003

Statistical analysis title	Statistical Analysis for Treatment period average
Comparison groups	AZD7594 90 µg v Placebo to AZD7594
Number of subjects included in analysis	161
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.029
Method	ANCOVA
Parameter estimate	Mean difference (final values)
Point estimate	-0.141
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.268
upper limit	-0.014

Statistical analysis title	Statistical Analysis for Treatment period average
Comparison groups	AZD7594 180 µg v Placebo to AZD7594
Number of subjects included in analysis	163
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.044
Method	ANCOVA
Parameter estimate	Mean difference (final values)
Point estimate	-0.13
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.257
upper limit	-0.003

Statistical analysis title	Statistical Analysis for Treatment period average
Comparison groups	AZD7594 360 µg v Placebo to AZD7594
Number of subjects included in analysis	160
Analysis specification	Pre-specified

Analysis type	superiority
P-value	= 0.002
Method	ANCOVA
Parameter estimate	Mean difference (final values)
Point estimate	-0.201
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.328
upper limit	-0.074

Statistical analysis title	Statistical Analysis for Treatment period average
Comparison groups	AZD7594 720 µg v Placebo to AZD7594
Number of subjects included in analysis	192
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	ANCOVA
Parameter estimate	Mean difference (final values)
Point estimate	-0.217
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.339
upper limit	-0.094

Statistical analysis title	Statistical Analysis for Treatment period average
Comparison groups	Placebo to AZD7594 v Fluticasone furoate
Number of subjects included in analysis	173
Analysis specification	Pre-specified
Analysis type	superiority[14]
P-value	= 0.005
Method	ANCOVA
Parameter estimate	Mean difference (final values)
Point estimate	-0.179
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.305
upper limit	-0.053

Notes:

[14] - The Statistical analysis is done to show the superiority of Fluticasone furoate over Placebo

Secondary: Change from baseline in average morning Peak Expiratory Flow (PEF) over the Treatment Period

End point title	Change from baseline in average morning Peak Expiratory Flow

	(PEF) over the Treatment Period

End point description:

To investigate the clinical efficacy of AZD7594 at different dose levels in asthmatics symptomatic on low dose ICS (Full Analysis Set). Baseline was defined as the average over the 7 days prior to randomisation. Analyses were based on an ANCOVA model with treatment and region as fixed effects, and baseline value as a covariate.

End point type	Secondary

End point timeframe:

Week 0 (7 days prior to randomisation) to Week 12

End point values	AZD7594 50 µg	AZD7594 90 µg	AZD7594 180 µg	AZD7594 360 µg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	89	94	97	92
Units: Liters/minute				
least squares mean (confidence interval 95%)	-4.036 (-10.518 to 2.447)	-5.718 (-11.994 to 0.557)	-2.576 (-8.768 to 3.617)	3.745 (-2.558 to 10.048)

End point values	AZD7594 720 µg	Placebo to AZD7594	Fluticasone furoate	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	122	73	104	
Units: Liters/minute				
least squares mean (confidence interval 95%)	4.900 (-1.010 to 10.810)	-11.699 (-18.749 to -4.649)	-1.208 (-7.209 to 4.793)	

Statistical analyses

Statistical analysis title	Statistical Analysis 1
Comparison groups	AZD7594 50 µg v Placebo to AZD7594
Number of subjects included in analysis	162
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.097
Method	ANCOVA
Parameter estimate	Mean difference (final values)
Point estimate	7.664
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.403
upper limit	16.73

Statistical analysis title	Statistical Analysis 2
Comparison groups	AZD7594 90 µg v Placebo to AZD7594
Number of subjects included in analysis	167
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.19
Method	ANCOVA
Parameter estimate	Mean difference (final values)
Point estimate	5.981
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.98
upper limit	14.941

Statistical analysis title	Statistical Analysis 3
Comparison groups	AZD7594 180 µg v Placebo to AZD7594
Number of subjects included in analysis	170
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.045
Method	ANCOVA
Parameter estimate	Mean difference (final values)
Point estimate	9.123
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.195
upper limit	18.052

Statistical analysis title	Statistical Analysis 4
Comparison groups	AZD7594 360 µg v Placebo to AZD7594
Number of subjects included in analysis	165
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	ANCOVA
Parameter estimate	Mean difference (final values)
Point estimate	15.444
Confidence interval	
level	95 %
sides	2-sided
lower limit	6.443
upper limit	24.445

Statistical analysis title	Statistical Analysis 5
Comparison groups	AZD7594 720 µg v Placebo to AZD7594
Number of subjects included in analysis	195
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	ANCOVA
Parameter estimate	Mean difference (final values)
Point estimate	16.599
Confidence interval	
level	95 %
sides	2-sided
lower limit	8.031
upper limit	25.167

Statistical analysis title	Statistical Analysis 6
Comparison groups	Placebo to AZD7594 v Fluticasone furoate
Number of subjects included in analysis	177
Analysis specification	Pre-specified
Analysis type	superiority[15]
P-value	= 0.019
Method	ANCOVA
Parameter estimate	Mean difference (final values)
Point estimate	10.491
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.726
upper limit	19.256

Notes:

[15] - The Statistical analysis is done to show the superiority of Fluticasone furoate over Placebo

Secondary: Change from baseline in average evening PEF over the Treatment Period	
End point title	Change from baseline in average evening PEF over the Treatment Period

End point description:

To investigate the clinical efficacy of AZD7594 at different dose levels in asthmatics symptomatic on low dose ICS (Full Analysis Set). Baseline was defined as the average over the 7 days prior to randomisation. Analyses were based on an ANCOVA model with treatment and region as fixed effects, and baseline value as a covariate.

End point type	Secondary

End point timeframe:

Week 0 (7 days prior to randomisation) to Week 12

End point values	AZD7594 50 µg	AZD7594 90 µg	AZD7594 180 µg	AZD7594 360 µg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	88	93	96	92
Units: Liters/minute				
least squares mean (confidence interval 95%)	-5.418 (-11.792 to 0.955)	-5.654 (-11.843 to 0.534)	-3.983 (-10.081 to 2.114)	2.441 (-3.738 to 8.620)

End point values	AZD7594 720 µg	Placebo to AZD7594	Fluticasone furoate	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	119	73	102	
Units: Liters/minute				
least squares mean (confidence interval 95%)	4.178 (-1.642 to 9.997)	-7.816 (-14.712 to -0.921)	-1.687 (-7.602 to 4.227)	

Statistical analyses

Statistical analysis title	Statistical Analysis 1
Comparison groups	AZD7594 50 µg v Placebo to AZD7594
Number of subjects included in analysis	161
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.597
Method	ANCOVA
Parameter estimate	Mean difference (final values)
Point estimate	2.398
Confidence interval	
level	95 %
sides	2-sided
lower limit	-6.494
upper limit	11.29

Statistical analysis title	Statistical Analysis 2
Comparison groups	AZD7594 90 µg v Placebo to AZD7594
Number of subjects included in analysis	166
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.629
Method	ANCOVA
Parameter estimate	Mean difference (final values)
Point estimate	2.162
Confidence interval	
level	95 %

sides	2-sided
lower limit	-6.623
upper limit	10.948

Statistical analysis title	Statistical Analysis 3
Comparison groups	AZD7594 180 µg v Placebo to AZD7594
Number of subjects included in analysis	169
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.389
Method	ANCOVA
Parameter estimate	Mean difference (final values)
Point estimate	3.833
Confidence interval	
level	95 %
sides	2-sided
lower limit	-4.907
upper limit	12.573

Statistical analysis title	Statistical Analysis 4
Comparison groups	AZD7594 360 µg v Placebo to AZD7594
Number of subjects included in analysis	165
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.022
Method	ANCOVA
Parameter estimate	Mean difference (final values)
Point estimate	10.258
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.456
upper limit	19.059

Statistical analysis title	Statistical Analysis 5
Comparison groups	AZD7594 720 µg v Placebo to AZD7594
Number of subjects included in analysis	192
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.005
Method	ANCOVA
Parameter estimate	Mean difference (final values)
Point estimate	11.994
Confidence interval	

level	95 %
sides	2-sided
lower limit	3.571
upper limit	20.417

Statistical analysis title	Statistical Analysis 6
Comparison groups	Placebo to AZD7594 v Fluticasone furoate
Number of subjects included in analysis	175
Analysis specification	Pre-specified
Analysis type	superiority[16]
P-value	= 0.163
Method	ANCOVA
Parameter estimate	Mean difference (final values)
Point estimate	6.129
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.479
upper limit	14.737

Notes:

[16] - The Statistical analysis is done to show the superiority of Fluticasone furoate over Placebo

Secondary: Change from baseline in average daily use of rescue medication over the Treatment Period

End point title	Change from baseline in average daily use of rescue medication over the Treatment Period

End point description:

To investigate the clinical efficacy of AZD7594 at different dose levels in asthmatics symptomatic on low dose ICS (Full Analysis Set). Baseline was defined as the average over the 7 days prior to randomisation. Analyses were based on an ANCOVA model with treatment and region as fixed effects, and baseline value as a covariate.

End point type	Secondary

End point timeframe:

Week 0 (7 days prior to randomisation) to Week 12

End point values	AZD7594 50 µg	AZD7594 90 µg	AZD7594 180 µg	AZD7594 360 µg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	86	86	91	79
Units: number of puffs				
least squares mean (confidence interval 95%)	-0.370 (-0.502 to -0.237)	-0.282 (-0.415 to -0.149)	-0.226 (-0.356 to -0.096)	-0.435 (-0.572 to -0.297)

End point values	AZD7594 720 µg	Placebo to AZD7594	Fluticasone furoate	

Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	109	66	93	
Units: number of puffs				
least squares mean (confidence interval 95%)	-0.435 (-0.560 to -0.310)	-0.127 (-0.276 to 0.023)	-0.304 (-0.432 to -0.175)	

Statistical analyses

Statistical analysis title	Statistical Analysis 1
Comparison groups	AZD7594 50 µg v Placebo to AZD7594
Number of subjects included in analysis	152
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.012
Method	ANCOVA
Parameter estimate	Mean difference (final values)
Point estimate	-0.243
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.431
upper limit	-0.054

Statistical analysis title	Statistical Analysis 2
Comparison groups	AZD7594 90 µg v Placebo to AZD7594
Number of subjects included in analysis	152
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.108
Method	ANCOVA
Parameter estimate	Mean difference (final values)
Point estimate	-0.155
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.344
upper limit	0.034

Statistical analysis title	Statistical Analysis 3
Comparison groups	AZD7594 180 µg v Placebo to AZD7594
Number of subjects included in analysis	157
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.295

Method	ANCOVA
Parameter estimate	Mean difference (final values)
Point estimate	-0.099
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.286
upper limit	0.087

Statistical analysis title	Statistical Analysis 4
Comparison groups	AZD7594 360 µg v Placebo to AZD7594
Number of subjects included in analysis	145
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.002
Method	ANCOVA
Parameter estimate	Mean difference (final values)
Point estimate	-0.308
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.5
upper limit	-0.116

Statistical analysis title	Statistical Analysis 5
Comparison groups	AZD7594 720 µg v Placebo to AZD7594
Number of subjects included in analysis	175
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	ANCOVA
Parameter estimate	Mean difference (final values)
Point estimate	-0.308
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.489
upper limit	-0.126

Statistical analysis title	Statistical Analysis 6
Comparison groups	Placebo to AZD7594 v Fluticasone furoate
Number of subjects included in analysis	159
Analysis specification	Pre-specified
Analysis type	superiority[17]

P-value	= 0.062
Method	ANCOVA
Parameter estimate	Mean difference (final values)
Point estimate	-0.177
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.362
upper limit	0.009

Notes:

[17] - The Statistical analysis is done to show the superiority of Fluticasone furoate over Placebo

Secondary: Change from baseline in percent night-time awakening days over the Treatment Period

End point title	Change from baseline in percent night-time awakening days over the Treatment Period

End point description:

To investigate the clinical efficacy of AZD7594 at different dose levels in asthmatics symptomatic on low dose ICS (Full Analysis Set). Baseline was defined as the average over the 7 days prior to randomisation. Analyses were based on an ANCOVA model with treatment and region as fixed effects, and baseline value as a covariate.

End point type	Secondary

End point timeframe:

Week 0 (7 days prior to randomisation) to Week 12

End point values	AZD7594 50 µg	AZD7594 90 µg	AZD7594 180 µg	AZD7594 360 µg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	89	94	97	92
Units: percentage				
least squares mean (confidence interval 95%)	-14.281 (-18.408 to -10.154)	-12.260 (-16.263 to -8.257)	-8.649 (-12.579 to -4.718)	-12.085 (-16.102 to -8.068)

End point values	AZD7594 720 µg	Placebo to AZD7594	Fluticasone furoate	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	122	73	104	
Units: percentage				
least squares mean (confidence interval 95%)	-13.017 (-16.790 to -9.244)	-4.288 (-8.814 to 0.238)	-15.910 (-19.753 to -12.067)	

Statistical analyses

Statistical analysis title	Statistical Analysis 1
Comparison groups	AZD7594 50 µg v Placebo to AZD7594
Number of subjects included in analysis	162
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	ANCOVA
Parameter estimate	Mean difference (final values)
Point estimate	-9.993
Confidence interval	
level	95 %
sides	2-sided
lower limit	-15.795
upper limit	-4.191

Statistical analysis title	Statistical Analysis 2
Comparison groups	AZD7594 90 µg v Placebo to AZD7594
Number of subjects included in analysis	167
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.006
Method	ANCOVA
Parameter estimate	Mean difference (final values)
Point estimate	-7.972
Confidence interval	
level	95 %
sides	2-sided
lower limit	-13.694
upper limit	-2.251

Statistical analysis title	Statistical Analysis 3
Comparison groups	AZD7594 180 µg v Placebo to AZD7594
Number of subjects included in analysis	170
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.133
Method	ANCOVA
Parameter estimate	Mean difference (final values)
Point estimate	-4.361
Confidence interval	
level	95 %
sides	2-sided
lower limit	-10.051
upper limit	1.329

Statistical analysis title	Statistical Analysis 4
Comparison groups	AZD7594 360 µg v Placebo to AZD7594
Number of subjects included in analysis	165
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.008
Method	ANCOVA
Parameter estimate	Mean difference (final values)
Point estimate	-7.797
Confidence interval	
level	95 %
sides	2-sided
lower limit	-13.555
upper limit	-2.04

Statistical analysis title	Statistical Analysis 5
Comparison groups	AZD7594 720 µg v Placebo to AZD7594
Number of subjects included in analysis	195
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.002
Method	ANCOVA
Parameter estimate	Mean difference (final values)
Point estimate	-8.729
Confidence interval	
level	95 %
sides	2-sided
lower limit	-14.195
upper limit	-3.264

Statistical analysis title	Statistical Analysis 6
Comparison groups	Placebo to AZD7594 v Fluticasone furoate
Number of subjects included in analysis	177
Analysis specification	Pre-specified
Analysis type	superiority[18]
P-value	< 0.001
Method	ANCOVA
Parameter estimate	Mean difference (final values)
Point estimate	-11.622
Confidence interval	
level	95 %
sides	2-sided
lower limit	-17.211

upper limit	-6.034

Notes:

[18] - The Statistical analysis is done to show the superiority of Fluticasone furoate over Placebo

Secondary: Change from baseline in average daily asthma symptom score over the Treatment Period

End point title	Change from baseline in average daily asthma symptom score over the Treatment Period

End point description:

To investigate the clinical efficacy of AZD7594 at different dose levels in asthmatics symptomatic on low dose ICS (Full Analysis Set). Baseline was defined as the average over the 7 days prior to randomisation. Analyses were based on an ANCOVA model with treatment and region as fixed effects, and baseline value as a covariate. During the Run-in and Treatment Periods, subjects recorded the severity of their asthma symptoms during night-time and day-time each morning and evening, using the eDiary. Asthma symptom scores during night-time/day-time were assessed by the subject each morning/evening according to the following scoring system and recorded on the eDiary: 0: No asthma symptoms, 1: The subjects were aware of their asthma symptoms but they can easily tolerate the symptoms, 2: asthma was causing enough discomfort to cause problems with sleep, 3: Subjects were unable to sleep/do normal activities because of their asthma.

End point type	Secondary

End point timeframe:

Week 0 (7 days prior to randomisation) to Week 12

End point values	AZD7594 50 µg	AZD7594 90 µg	AZD7594 180 µg	AZD7594 360 µg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	86	86	91	79
Units: Unit on a scale				
least squares mean (confidence interval 95%)	-0.303 (-0.385 to -0.220)	-0.201 (-0.283 to -0.118)	-0.229 (-0.310 to -0.149)	-0.321 (-0.407 to -0.235)

End point values	AZD7594 720 µg	Placebo to AZD7594	Fluticasone furoate	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	109	66	93	
Units: Unit on a scale				
least squares mean (confidence interval 95%)	-0.275 (-0.353 to -0.198)	-0.091 (-0.184 to 0.003)	-0.296 (-0.376 to -0.216)	

Statistical analyses

Statistical analysis title	Statistical Analysis 1
Comparison groups	AZD7594 50 µg v Placebo to AZD7594
Number of subjects included in analysis	152
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	ANCOVA

Parameter estimate	Mean difference (final values)
Point estimate	-0.212
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.329
upper limit	-0.094

Statistical analysis title	Statistical Analysis 2
Comparison groups	AZD7594 90 µg v Placebo to AZD7594
Number of subjects included in analysis	152
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.066
Method	ANCOVA
Parameter estimate	Mean difference (final values)
Point estimate	-0.11
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.228
upper limit	0.007

Statistical analysis title	Statistical Analysis 3
Comparison groups	AZD7594 180 µg v Placebo to AZD7594
Number of subjects included in analysis	157
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.02
Method	ANCOVA
Parameter estimate	Mean difference (final values)
Point estimate	-0.139
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.255
upper limit	-0.022

Statistical analysis title	Statistical Analysis 4
Comparison groups	AZD7594 360 µg v Placebo to AZD7594
Number of subjects included in analysis	145
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001

Method	ANCOVA
Parameter estimate	Mean difference (final values)
Point estimate	-0.23
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.35
upper limit	-0.11

Statistical analysis title	Statistical Analysis 5
Comparison groups	AZD7594 720 µg v Placebo to AZD7594
Number of subjects included in analysis	175
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.001
Method	ANCOVA
Parameter estimate	Mean difference (final values)
Point estimate	-0.185
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.298
upper limit	-0.071

Statistical analysis title	Statistical Analysis 6
Comparison groups	Placebo to AZD7594 v Fluticasone furoate
Number of subjects included in analysis	159
Analysis specification	Pre-specified
Analysis type	superiority[19]
P-value	< 0.001
Method	ANCOVA
Parameter estimate	Mean difference (final values)
Point estimate	-0.206
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.321
upper limit	-0.09

Notes:

[19] - The Statistical analysis is done to show the superiority of Fluticasone furoate over Placebo

Secondary: Change from baseline in percent asthma control days over the Treatment Period

End point title	Change from baseline in percent asthma control days over the Treatment Period

End point description:

To investigate the clinical efficacy of AZD7594 at different dose levels in asthmatics symptomatic on low dose ICS (Full Analysis Set). Asthma-control days was defined as days with no symptoms, no night-waking, no use of rescue medication. Baseline was defined as the average over the 7 days prior to randomisation. Analyses were based on an ANCOVA model with treatment and region as fixed effects, and baseline value as a covariate.

End point type	Secondary

End point timeframe:

Week 0 (7 days prior to randomisation) to Week 12

End point values	AZD7594 50 µg	AZD7594 90 µg	AZD7594 180 µg	AZD7594 360 µg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	86	86	91	79
Units: percent				
least squares mean (confidence interval 95%)	15.470 (9.547 to 21.394)	11.362 (5.435 to 17.290)	12.646 (6.865 to 18.427)	15.925 (9.775 to 22.076)

End point values	AZD7594 720 µg	Placebo to AZD7594	Fluticasone furoate	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	109	66	93	
Units: percent				
least squares mean (confidence interval 95%)	14.479 (8.896 to 20.062)	5.859 (-0.813 to 12.532)	13.037 (7.301 to 18.772)	

Statistical analyses

Statistical analysis title	Statistical Analysis 1
Comparison groups	AZD7594 50 µg v Placebo to AZD7594
Number of subjects included in analysis	152
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.026
Method	ANCOVA
Parameter estimate	Mean difference (final values)
Point estimate	9.611
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.18
upper limit	18.042

Statistical analysis title	Statistical Analysis 2
Comparison groups	AZD7594 90 µg v Placebo to AZD7594

Number of subjects included in analysis	152
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.2
Method	ANCOVA
Parameter estimate	Mean difference (final values)
Point estimate	5.503
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.927
upper limit	13.933

Statistical analysis title	Statistical Analysis 3
Comparison groups	AZD7594 180 µg v Placebo to AZD7594
Number of subjects included in analysis	157
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.11
Method	ANCOVA
Parameter estimate	Mean difference (final values)
Point estimate	6.787
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.546
upper limit	15.119

Statistical analysis title	Statistical Analysis 4
Comparison groups	AZD7594 360 µg v Placebo to AZD7594
Number of subjects included in analysis	145
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.022
Method	ANCOVA
Parameter estimate	Mean difference (final values)
Point estimate	10.066
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.461
upper limit	18.672

Statistical analysis title	Statistical Analysis 5

Comparison groups	AZD7594 720 µg v Placebo to AZD7594
Number of subjects included in analysis	175
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.038
Method	ANCOVA
Parameter estimate	Mean difference (final values)
Point estimate	8.62
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.489
upper limit	16.75

Statistical analysis title	Statistical Analysis 6
Comparison groups	Placebo to AZD7594 v Fluticasone furoate
Number of subjects included in analysis	159
Analysis specification	Pre-specified
Analysis type	superiority[20]
P-value	= 0.09
Method	ANCOVA
Parameter estimate	Mean difference (final values)
Point estimate	7.178
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.112
upper limit	15.467

Notes:

[20] - The Statistical analysis is done to show the superiority of Fluticasone furoate over Placebo

Secondary: Change from baseline in percent rescue-free days over the Treatment Period

End point title	Change from baseline in percent rescue-free days over the Treatment Period

End point description:

To investigate the clinical efficacy of AZD7594 at different dose levels in asthmatics symptomatic on low dose ICS (Full Analysis Set). A rescue-free day (RFD) was defined as a day with no use of rescue medication. Baseline was defined as the average over the 7 days prior to randomisation. Analyses were based on an ANCOVA model with treatment and region as fixed effects, and baseline value as a covariate.

End point type	Secondary

End point timeframe:

Week 0 (7 days prior to randomisation) to Week 12

End point values	AZD7594 50 µg	AZD7594 90 µg	AZD7594 180 µg	AZD7594 360 µg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	86	86	91	79
Units: percent				
least squares mean (confidence interval 95%)	31.138 (24.019 to 38.257)	24.178 (17.045 to 31.312)	21.960 (14.940 to 28.980)	34.991 (27.549 to 42.433)

End point values	AZD7594 720 µg	Placebo to AZD7594	Fluticasone furoate	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	109	66	93	
Units: percent				
least squares mean (confidence interval 95%)	30.775 (24.025 to 37.526)	23.202 (15.188 to 31.215)	28.260 (21.308 to 35.211)	

Statistical analyses

Statistical analysis title	Statistical Analysis 1
Comparison groups	AZD7594 50 µg v Placebo to AZD7594
Number of subjects included in analysis	152
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.123
Method	ANCOVA
Parameter estimate	Mean difference (final values)
Point estimate	7.936
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.16
upper limit	18.031

Statistical analysis title	Statistical Analysis 2
Comparison groups	AZD7594 90 µg v Placebo to AZD7594
Number of subjects included in analysis	152
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.849
Method	ANCOVA
Parameter estimate	Mean difference (final values)
Point estimate	0.977
Confidence interval	
level	95 %

sides	2-sided
lower limit	-9.112
upper limit	11.065

Statistical analysis title	Statistical Analysis 3
Comparison groups	AZD7594 180 µg v Placebo to AZD7594
Number of subjects included in analysis	157
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.807
Method	ANCOVA
Parameter estimate	Mean difference (final values)
Point estimate	-1.242
Confidence interval	
level	95 %
sides	2-sided
lower limit	-11.233
upper limit	8.748

Statistical analysis title	Statistical Analysis 4
Comparison groups	AZD7594 360 µg v Placebo to AZD7594
Number of subjects included in analysis	145
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.025
Method	ANCOVA
Parameter estimate	Mean difference (final values)
Point estimate	11.789
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.488
upper limit	22.09

Statistical analysis title	Statistical Analysis 5
Comparison groups	AZD7594 720 µg v Placebo to AZD7594
Number of subjects included in analysis	175
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.127
Method	ANCOVA
Parameter estimate	Mean difference (final values)
Point estimate	7.574
Confidence interval	

level	95 %
sides	2-sided
lower limit	-2.16
upper limit	17.307

Statistical analysis title	Statistical Analysis 6
Comparison groups	Placebo to AZD7594 v Fluticasone furoate
Number of subjects included in analysis	159
Analysis specification	Pre-specified
Analysis type	superiority[21]
P-value	= 0.318
Method	ANCOVA
Parameter estimate	Mean difference (final values)
Point estimate	5.058
Confidence interval	
level	95 %
sides	2-sided
lower limit	-4.874
upper limit	14.99

Notes:

[21] - The Statistical analysis is done to show the superiority of Fluticasone furoate over Placebo

Secondary: Change from baseline in percent symptom-free days over the Treatment Period

End point title	Change from baseline in percent symptom-free days over the Treatment Period

End point description:

To investigate the clinical efficacy of AZD7594 at different dose levels in asthmatics symptomatic on low dose ICS (Full Analysis Set). Days without asthma symptoms, or symptom-free days, were defined as days without asthma symptoms, short-acting β-agonist (SABA) use, systemic corticosteroid use, or need for urgent asthma care.

End point type	Secondary

End point timeframe:

Week 0 (7 days prior to randomisation) to Week 12

End point values	AZD7594 50 µg	AZD7594 90 µg	AZD7594 180 µg	AZD7594 360 µg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	86	86	91	79
Units: percent				
least squares mean (confidence interval 95%)	13.780 (7.873 to 19.686)	10.521 (4.608 to 16.435)	11.935 (6.169 to 17.701)	14.673 (8.539 to 20.806)

End point values	AZD7594 720 µg	Placebo to AZD7594	Fluticasone furoate	

Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	109	66	93	
Units: percent				
least squares mean (confidence interval 95%)	13.451 (7.883 to 19.018)	3.329 (-3.319 to 9.977)	14.018 (8.293 to 19.743)	

Statistical analyses

Statistical analysis title	Statistical Analysis 1
Comparison groups	AZD7594 50 µg v Placebo to AZD7594
Number of subjects included in analysis	152
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.015
Method	ANCOVA
Parameter estimate	Mean difference (final values)
Point estimate	10.45
Confidence interval	
level	95 %
sides	2-sided
lower limit	2.046
upper limit	18.855

Statistical analysis title	Statistical Analysis 2
Comparison groups	AZD7594 90 µg v Placebo to AZD7594
Number of subjects included in analysis	152
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.093
Method	ANCOVA
Parameter estimate	Mean difference (final values)
Point estimate	7.192
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.208
upper limit	15.592

Statistical analysis title	Statistical Analysis 3
Comparison groups	AZD7594 180 µg v Placebo to AZD7594
Number of subjects included in analysis	157
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.042

Method	ANCOVA
Parameter estimate	Mean difference (final values)
Point estimate	8.606
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.298
upper limit	16.913

Statistical analysis title	Statistical Analysis 4
Comparison groups	AZD7594 360 µg v Placebo to AZD7594
Number of subjects included in analysis	145
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.01
Method	ANCOVA
Parameter estimate	Mean difference (final values)
Point estimate	11.344
Confidence interval	
level	95 %
sides	2-sided
lower limit	2.773
upper limit	19.914

Statistical analysis title	Statistical Analysis 5
Comparison groups	AZD7594 720 µg v Placebo to AZD7594
Number of subjects included in analysis	175
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.014
Method	ANCOVA
Parameter estimate	Mean difference (final values)
Point estimate	10.122
Confidence interval	
level	95 %
sides	2-sided
lower limit	2.021
upper limit	18.222

Statistical analysis title	Statistical Analysis 6
Comparison groups	Placebo to AZD7594 v Fluticasone furoate
Number of subjects included in analysis	159
Analysis specification	Pre-specified
Analysis type	superiority[22]

P-value	= 0.011
Method	ANCOVA
Parameter estimate	Mean difference (final values)
Point estimate	10.689
Confidence interval	
level	95 %
sides	2-sided
lower limit	2.424
upper limit	18.953

Notes:

[22] - The Statistical analysis is done to show the superiority of Fluticasone furoate over Placebo

Secondary: Time to recurrent Composite endpoint for severe exacerbations of asthma (CompEx) event

End point title	Time to recurrent Composite endpoint for severe exacerbations of asthma (CompEx) event

End point description:

To investigate the clinical efficacy of AZD7594 at different dose levels in asthmatics symptomatic on low dose ICS (Full Analysis Set).
CompEx is a composite endpoint combining severe exacerbations of asthma and diary events. CompEx is a composite surrogate endpoint for severe exacerbations of asthma, recently developed by AstraZeneca (it is not yet a regulatory-approved clinical endpoint). Severe exacerbations are defined as those episodes that lead to hospitalisation, emergency room visit and/or treatment with oral corticosteroids. Time at risk was calculated as [(date of last treatment – date of randomisation)+1 – recovery time. Recovery time was the sum (from i=1 to k) of (min with event end date +7, date of last treatment] – with event start date +1). No statistical analysis is done for this endpoint.

End point type	Secondary

End point timeframe:

From Screening (Within 21-28 days before randomisation) to Week 12/End of treatment or Early Termination Visit

End point values	AZD7594 50 µg	AZD7594 90 µg	AZD7594 180 µg	AZD7594 360 µg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	110	112	111	113
Units: Years				
number (not applicable)	21.3	22.2	22.6	23.1

End point values	AZD7594 720 µg	Placebo to AZD7594	Fluticasone furoate	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	134	113	112	
Units: Years				
number (not applicable)	29.0	18.6	24.4	

Statistical analyses

No statistical analyses for this end point

Secondary: Annualized CompEx event rate

End point title	Annualized CompEx event rate

End point description:

To investigate the clinical efficacy of AZD7594 at different dose levels in asthmatics symptomatic on low dose ICS (Full Analysis Set).
CompEx is a composite endpoint combining severe exacerbations of asthma and diary events. CompEx is a composite surrogate endpoint for severe exacerbations of asthma, recently developed by AstraZeneca (it is not yet a regulatory-approved clinical endpoint). Severe exacerbations are defined as those episodes that lead to hospitalisation, emergency room visit and/or treatment with oral corticosteroids. CompEx Model: Rates, rate ratios, and p-values were from a negative binomial model analysis, with event count as the dependent variable, with treatment and
region as covariates and log-transformed time at risk (days) as an offset variable to account for overdispersion.

End point type	Secondary

End point timeframe:

From Screening (Within 21-28 days before randomisation) to Week 12/End of treatment or Early Termination Visit

End point values	AZD7594 50 µg	AZD7594 90 µg	AZD7594 180 µg	AZD7594 360 µg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	110	112	111	113
Units: Annual rate				
number (not applicable)	2.06	2.20	2.04	0.67

End point values	AZD7594 720 µg	Placebo to AZD7594	Fluticasone furoate	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	134	113	112	
Units: Annual rate				
number (not applicable)	0.50	4.71	0.75	

Statistical analyses

Statistical analysis title	Statistical Analysis 1
Comparison groups	AZD7594 50 µg v Placebo to AZD7594
Number of subjects included in analysis	223
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.035
Method	Negative Binominal Model
Parameter estimate	Estimate
Point estimate	0.44
Confidence interval	
level	95 %

sides	2-sided
lower limit	0.2
upper limit	0.94

Statistical analysis title	Statistical Analysis 2
Comparison groups	AZD7594 90 µg v Placebo to AZD7594
Number of subjects included in analysis	225
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.05
Method	Negative Binominal Model
Parameter estimate	Estimate
Point estimate	0.47
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.22
upper limit	1

Statistical analysis title	Statistical Analysis 3
Comparison groups	AZD7594 180 µg v Placebo to AZD7594
Number of subjects included in analysis	224
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.032
Method	Negative Binominal Model
Parameter estimate	Estimate
Point estimate	0.43
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.2
upper limit	0.93

Statistical analysis title	Statistical Analysis 4
Comparison groups	AZD7594 360 µg v Placebo to AZD7594
Number of subjects included in analysis	226
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	Negative Binominal Model
Parameter estimate	Estimate
Point estimate	0.14
Confidence interval	

level	95 %
sides	2-sided
lower limit	0.06
upper limit	0.34

Statistical analysis title	Statistical Analysis 5
Comparison groups	AZD7594 720 µg v Placebo to AZD7594
Number of subjects included in analysis	247
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	Negative Binominal Model
Parameter estimate	Estimate
Point estimate	0.11
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.04
upper limit	0.25

Statistical analysis title	Statistical Analysis 6
Comparison groups	Placebo to AZD7594 v Fluticasone furoate
Number of subjects included in analysis	225
Analysis specification	Pre-specified
Analysis type	superiority[23]
P-value	< 0.001
Method	Negative Binominal Model
Parameter estimate	Estimate
Point estimate	0.16
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.07
upper limit	0.37

Notes:

[23] - The Statistical analysis is done to show the superiority of Fluticasone furoate over Placebo

Secondary: Observed maximum concentration at steady state (Css,max) of AZD7594 at Day 84

End point title	Observed maximum concentration at steady state (Css,max) of AZD7594 at Day 84

End point description:

To describe the (steady state) pharmacokinetic (PK) of AZD7594 in a subset of asthmatics symptomatic on low dose ICS (subset of subjects at EU sites) (PK Analysis Set). The presented results are summary statistics of the PK parameter.

End point type	Secondary

End point timeframe:

End point values	AZD7594 50 µg	AZD7594 90 µg	AZD7594 180 µg	AZD7594 360 µg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	17	14	15	16
Units: pmol/L				
geometric mean (geometric coefficient of variation)	48.45 (± 68.65)	114.90 (± 99.12)	69.71 (± 105.94)	154.50 (± 144.67)

End point values	AZD7594 720 µg	Placebo to AZD7594	Fluticasone furoate	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	27	0[24]	0[25]	
Units: pmol/L				
geometric mean (geometric coefficient of variation)	200.00 (± 113.05)	()	()	

Notes:

[24] - Subjects from this arm were excluded from the PK analysis set.

[25] - Subjects from this arm were excluded from the PK analysis set.

Statistical analyses

Statistical analysis title	Statistical Analysis 1

Statistical analysis description:

Assessment of Dose Proportionality of AZD7594 PK Parameter at Visit 7 (Day 84) (PK Analysis Set)

Comparison groups	AZD7594 50 µg v AZD7594 90 µg v AZD7594 180 µg v AZD7594 360 µg v AZD7594 720 µg
Number of subjects included in analysis	89
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Slope
Point estimate	0.476
Confidence interval	
level	90 %
sides	2-sided
lower limit	0.321
upper limit	0.632
Variability estimate	Standard error of the mean
Dispersion value	0.094

Secondary: Observed minimum concentration at the end of the dosing interval (Css,min) of AZD7594 at Day 84

End point title	Observed minimum concentration at the end of the dosing interval (Css,min) of AZD7594 at Day 84

End point description:

To describe the (steady state) PK of AZD7594 in a subset of asthmatics symptomatic on low dose ICS (subset of subjects at EU sites) (PK Analysis Set). The presented results are summary statistics of the PK parameter. No statistical analysis is done for this endpoint.

End point type	Secondary

End point timeframe:

Day 84 (pre-dose and 0.25, 0.5, 1.0, 2.0, 4.0, 8.0, 12.0, 16.0 and 24 h post-dose)

End point values	AZD7594 50 µg	AZD7594 90 µg	AZD7594 180 µg	AZD7594 360 µg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	3	10	11	13
Units: pmol/L				
geometric mean (geometric coefficient of variation)	14.41 (± 37.59)	21.45 (± 43.12)	30.22 (± 43.28)	70.58 (± 46.22)

End point values	AZD7594 720 µg	Placebo to AZD7594	Fluticasone furoate	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	26	0[26]	0[27]	
Units: pmol/L				
geometric mean (geometric coefficient of variation)	85.13 (± 108.41)	()	()	

Notes:

[26] - Subjects from this arm were excluded from the PK analysis set.

[27] - Subjects from this arm were excluded from the PK analysis set.

Statistical analyses

No statistical analyses for this end point

Secondary: Time to maximum concentration at steady state, taken directly from the individual concentration-time curve (tss, max) of AZD7594 at Day 84

End point title	Time to maximum concentration at steady state, taken directly from the individual concentration-time curve (tss, max) of AZD7594 at Day 84

End point description:

To describe the (steady state) PK of AZD7594 in a subset of asthmatics symptomatic on low dose ICS (subset of subjects at EU sites) (PK Analysis Set). The presented results are summary statistics of the PK parameter. No statistical analysis is done for this endpoint.

End point type	Secondary

End point timeframe:

Day 84 (pre-dose and 0.25, 0.5, 1.0, 2.0, 4.0, 8.0, 12.0, 16.0 and 24 h post-dose)

End point values	AZD7594 50 µg	AZD7594 90 µg	AZD7594 180 µg	AZD7594 360 µg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	17	14	15	16
Units: hours				
median (full range (min-max))	0.25 (0.23 to 2.17)	0.25 (0.00 to 0.98)	0.25 (0.20 to 2.00)	0.25 (0.00 to 2.00)

End point values	AZD7594 720 µg	Placebo to AZD7594	Fluticasone furoate	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	27	0[28]	0[29]	
Units: hours				
median (full range (min-max))	0.25 (0.00 to 23.98)	(to)	(to)	

Notes:

[28] - Subjects from this arm were excluded from the PK analysis set.

[29] - Subjects from this arm were excluded from the PK analysis set.

Statistical analyses

No statistical analyses for this end point

Secondary: Area under the plasma concentration-curve from time zero to the time of last quantifiable analyte concentration (AUClast) of AZD7594 at Day 84

End point title	Area under the plasma concentration-curve from time zero to the time of last quantifiable analyte concentration (AUClast) of AZD7594 at Day 84

End point description:

To describe the (steady state) PK of AZD7594 in a subset of asthmatics symptomatic on low dose ICS (subset of subjects at EU sites) (PK Analysis Set). The presented results are summary statistics of the PK parameter. No statistical analysis is done for this endpoint.

End point type	Secondary

End point timeframe:

Day 84 (pre-dose and 0.25, 0.5, 1.0, 2.0, 4.0, 8.0, 12.0, 16.0 and 24 h post-dose)

End point values	AZD7594 50 µg	AZD7594 90 µg	AZD7594 180 µg	AZD7594 360 µg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	15	14	14	16
Units: h*pmol/L				
geometric mean (geometric coefficient of variation)	167.50 (± 123.50)	573.00 (± 116.00)	719.10 (± 134.58)	1435.00 (± 140.28)

End point values	AZD7594 720 µg	Placebo to AZD7594	Fluticasone furoate	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	26	0[30]	0[31]	

Units: h*pmol/L				
geometric mean (geometric coefficient of variation)	2622.00 (± 98.88)	()	()	

Notes:

[30] - Subjects from this arm were excluded from the PK analysis set.

[31] - Subjects from this arm were excluded from the PK analysis set.

Statistical analyses

No statistical analyses for this end point

Secondary: Area under the plasma concentration-curve within a dosing interval (AUCτ) of AZD7594 at Day 84

End point title	Area under the plasma concentration-curve within a dosing interval (AUCτ) of AZD7594 at Day 84

End point description:

To describe the (steady state) PK of AZD7594 in a subset of asthmatics symptomatic on low dose ICS (subset of subjects at EU sites) (PK Analysis Set). The presented results are summary statistics of the PK parameter.

End point type	Secondary

End point timeframe:

Day 84 (pre-dose and 0.25, 0.5, 1.0, 2.0, 4.0, 8.0, 12.0, 16.0 and 24 h post-dose)

End point values	AZD7594 50 µg	AZD7594 90 µg	AZD7594 180 µg	AZD7594 360 µg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	3	10	11	13
Units: h*pmol/L				
geometric mean (geometric coefficient of variation)	530.50 (± 32.57)	928.60 (± 37.52)	1137.00 (± 52.06)	2205.00 (± 52.32)

End point values	AZD7594 720 µg	Placebo to AZD7594	Fluticasone furoate	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	26	0[32]	0[33]	
Units: h*pmol/L				
geometric mean (geometric coefficient of variation)	2622.00 (± 98.88)	()	()	

Notes:

[32] - Subjects from this arm were excluded from the PK analysis set.

[33] - Subjects from this arm were excluded from the PK analysis set.

Statistical analyses

Statistical analysis title	Statistical Analysis 1

Statistical analysis description:

Assessment of Dose Proportionality of AZD7594 PK Parameter at Visit 7 (Day 84) (PK Analysis Set)

Comparison groups	AZD7594 50 µg v AZD7594 90 µg v AZD7594 180 µg v AZD7594 360 µg v AZD7594 720 µg
Number of subjects included in analysis	63

Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Slope
Point estimate	0.555
Confidence interval	
level	90 %
sides	2-sided
lower limit	0.402
upper limit	0.709
Variability estimate	Standard error of the mean
Dispersion value	0.092

Secondary: Average plasma concentration during a dosing interval at steady state (Css,avg) of AZD7594 at Day 84

End point title	Average plasma concentration during a dosing interval at steady state (Css,avg) of AZD7594 at Day 84

End point description:

To describe the (steady state) PK of AZD7594 in a subset of asthmatics symptomatic on low dose ICS (subset of subjects at EU sites) (PK Analysis Set). The presented results are summary statistics of the PK parameter. No statistical analysis is done for this endpoint.

End point type	Secondary

End point timeframe:

Day 84 (pre-dose and 0.25, 0.5, 1.0, 2.0, 4.0, 8.0, 12.0, 16.0 and 24 h post-dose)

End point values	AZD7594 50 µg	AZD7594 90 µg	AZD7594 180 µg	AZD7594 360 µg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	3	10	11	13
Units: pmol/L				
geometric mean (geometric coefficient of variation)	22.10 (± 32.57)	38.69 (± 37.52)	47.37 (± 52.06)	91.86 (± 52.32)

End point values	AZD7594 720 µg	Placebo to AZD7594	Fluticasone furoate	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	26	0[34]	0[35]	
Units: pmol/L				
geometric mean (geometric coefficient of variation)	109.30 (± 98.88)	()	()	

Notes:

[34] - Subjects from this arm were excluded from the PK analysis set.

[35] - Subjects from this arm were excluded from the PK analysis set.

Statistical analyses

No statistical analyses for this end point

Secondary: Dose normalised Css,max (Css,max/D) of AZD7594 at Day 84

End point title	Dose normalised Css,max (Css,max/D) of AZD7594 at Day 84

End point description:

To describe the (steady state) PK of AZD7594 in a subset of asthmatics symptomatic on low dose ICS (subset of subjects at EU sites) (PK Analysis Set). The presented results are summary statistics of the PK parameter. No statistical analysis is done for this endpoint.

End point type	Secondary

End point timeframe:

Day 84 (pre-dose and 0.25, 0.5, 1.0, 2.0, 4.0, 8.0, 12.0, 16.0 and 24 h post-dose)

End point values	AZD7594 50 µg	AZD7594 90 µg	AZD7594 180 µg	AZD7594 360 µg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	17	14	15	16
Units: pmol/L/umol				
geometric mean (geometric coefficient of variation)	587.80 (± 68.65)	774.40 (± 99.12)	234.90 (± 105.94)	260.40 (± 144.67)

End point values	AZD7594 720 µg	Placebo to AZD7594	Fluticasone furoate	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	27	0[36]	0[37]	
Units: pmol/L/umol				
geometric mean (geometric coefficient of variation)	168.50 (± 113.05)	()	()	

Notes:

[36] - Subjects from this arm were excluded from the PK analysis set.

[37] - Subjects from this arm were excluded from the PK analysis set.

Statistical analyses

No statistical analyses for this end point

Secondary: Dose normalised AUCτ (AUCτ/D) of AZD7594 at Day 84

End point title	Dose normalised AUCτ (AUCτ/D) of AZD7594 at Day 84

End point description:

To describe the (steady state) PK of AZD7594 in a subset of asthmatics symptomatic on low dose ICS (subset of subjects at EU sites) (PK Analysis Set). The presented results are summary statistics of the PK parameter. No statistical analysis is done for this endpoint.

End point type	Secondary

End point timeframe:

Day 84 (pre-dose and 0.25, 0.5, 1.0, 2.0, 4.0, 8.0, 12.0, 16.0 and 24 h post-dose)

End point values	AZD7594 50 µg	AZD7594 90 µg	AZD7594 180 µg	AZD7594 360 µg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	3	10	11	13
Units: h*pmol/µmol				
geometric mean (geometric coefficient of variation)	6436.00 (± 32.57)	6259.00 (± 37.52)	3831.00 (± 52.06)	3715.00 (± 52.32)

End point values	AZD7594 720 µg	Placebo to AZD7594	Fluticasone furoate	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	26	0[38]	0[39]	
Units: h*pmol/µmol				
geometric mean (geometric coefficient of variation)	2209.00 (± 98.88)	()	()	

Notes:

[38] - Subjects from this arm were excluded from the PK analysis set.

[39] - Subjects from this arm were excluded from the PK analysis set.

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage Fluctuation index within a dosing interval of AZD7594 at Day 84

End point title	Percentage Fluctuation index within a dosing interval of AZD7594 at Day 84

End point description:

To describe the (steady state) PK of AZD7594 in a subset of asthmatics symptomatic on low dose ICS (subset of subjects at EU sites) (PK Analysis Set). The presented results are summary statistics of the PK parameter. No statistical analysis is done for this endpoint.

End point type	Secondary

End point timeframe:

Day 84 (pre-dose and 0.25, 0.5, 1.0, 2.0, 4.0, 8.0, 12.0, 16.0 and 24 h post-dose)

End point values	AZD7594 50 µg	AZD7594 90 µg	AZD7594 180 µg	AZD7594 360 µg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	3	10	11	13
Units: percentage				
geometric mean (geometric coefficient of variation)	387.80 (± 21.97)	326.60 (± 37.40)	148.90 (± 38.27)	172.10 (± 44.32)

End point values	AZD7594 720 µg	Placebo to AZD7594	Fluticasone furoate	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	26	0[40]	0[41]	

Units: percentage				
geometric mean (geometric coefficient of variation)	98.22 (± 61.36)	()	()	

Notes:

[40] - Subjects from this arm were excluded from the PK analysis set.

[41] - Subjects from this arm were excluded from the PK analysis set.

Statistical analyses

No statistical analyses for this end point

Secondary: Change from baseline of area under the plasma cortisol concentration-time curve from zero to 24 hours after dosing (AUEC0-24), compared to Placebo of AZD7594 at Day 84

End point title	Change from baseline of area under the plasma cortisol concentration-time curve from zero to 24 hours after dosing (AUEC0-24), compared to Placebo of AZD7594 at Day 84

End point description:

To describe the pharmacodynamics of AZD7594 by measuring cortisol suppression in a subset of asthmatics symptomatic on low dose ICS (subset of subjects at EU sites) (Pharmacodynamic Analysis Set). Baseline was defined as the Day -1 value. Analyses were based on an ANCOVA model with change from baseline on the log-scale as the response, treatment as a fixed effect, and log-transformed baseline value as a covariate.

End point type	Secondary

End point timeframe:

Day 84 (at 0 [pre-dose], 2, 4, 6, 8, 10, 12, 16, 20, 22 and 24 hours relative to IP administration)

End point values	AZD7594 50 µg	AZD7594 90 µg	AZD7594 180 µg	AZD7594 360 µg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	19	16	16	17
Units: ng/mL				
geometric mean (confidence interval 95%)	1.029 (0.920 to 1.152)	1.140 (1.009 to 1.287)	1.151 (1.018 to 1.300)	1.003 (0.891 to 1.129)

End point values	AZD7594 720 µg	Placebo to AZD7594	Fluticasone furoate	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	27	14	17	
Units: ng/mL				
geometric mean (confidence interval 95%)	0.934 (0.850 to 1.026)	1.019 (0.895 to 1.161)	1.011 (0.898 to 1.137)	

Statistical analyses

Statistical analysis title	Statistical Analysis 1
Comparison groups	AZD7594 50 µg v Placebo to AZD7594
Number of subjects included in analysis	33

Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.909
Method	ANCOVA
Parameter estimate	geometric LSMean ratio
Point estimate	1.01
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.851
upper limit	1.199

Statistical analysis title	Statistical Analysis 2
Comparison groups	AZD7594 90 µg v Placebo to AZD7594
Number of subjects included in analysis	30
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.218
Method	ANCOVA
Parameter estimate	geometric LSMean ratio
Point estimate	1.118
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.935
upper limit	1.336

Statistical analysis title	Statistical Analysis 3
Comparison groups	AZD7594 180 µg v Placebo to AZD7594
Number of subjects included in analysis	30
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.181
Method	ANCOVA
Parameter estimate	geometric LSMean ratio
Point estimate	1.129
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.944
upper limit	1.349

Statistical analysis title	Statistical Analysis 4
Comparison groups	AZD7594 360 µg v Placebo to AZD7594

Number of subjects included in analysis	31
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.859
Method	ANCOVA
Parameter estimate	geometric LSMean ratio
Point estimate	0.984
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.825
upper limit	1.174

Statistical analysis title	Statistical Analysis 5
Comparison groups	AZD7594 720 µg v Placebo to AZD7594
Number of subjects included in analysis	41
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.285
Method	ANCOVA
Parameter estimate	geometric LSMean ratio
Point estimate	0.916
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.78
upper limit	1.077

Statistical analysis title	Statistical Analysis 6
Comparison groups	Placebo to AZD7594 v Fluticasone furoate
Number of subjects included in analysis	31
Analysis specification	Pre-specified
Analysis type	superiority[42]
P-value	= 0.923
Method	ANCOVA
Parameter estimate	geometric LSMean ratio
Point estimate	0.991
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.831
upper limit	1.182

Notes:

[42] - The Statistical analysis is done to show the superiority of Fluticasone furoate over Placebo

Secondary: Number of subjects with adverse events

End point title	Number of subjects with adverse events

End point description:

To evaluate the safety and tolerability of AZD7594 in relation to Placebo in asthmatics symptomatic on low dose ICS (Safety Analysis Set). No statistical analysis is done for this endpoint.

End point type	Secondary

End point timeframe:

From screening to follow-up period (7 to 10 days after visit 7)

End point values	AZD7594 50 µg	AZD7594 90 µg	AZD7594 180 µg	AZD7594 360 µg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	110	112	111	113
Units: Subjects				
Any AE	35	45	39	54
death	0	0	0	1
Any SAE	0	3	1	3
Any AE leading to discontinuation of IP	6	8	4	11

End point values	AZD7594 720 µg	Placebo to AZD7594	Fluticasone furoate	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	134	113	112	
Units: Subjects				
Any AE	46	47	34	
death	0	0	0	
Any SAE	3	0	1	
Any AE leading to discontinuation of IP	4	20	2	

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information	
Timeframe for reporting adverse events: From Screening to follow-up period (7to 10 days after visit 7)	
Assessment type	Non-systematic
Dictionary used	
Dictionary name	MedDRA
Dictionary version	22.0
Reporting groups	
Reporting group title	AZD7594 50 µg
Reporting group description: Oral inhalation of AZD5794 55 microgram/ 50 microgram (nominal dose/delivered dose) once daily.	
Reporting group title	AZD7594 180 µg
Reporting group description: Oral inhalation of AZD5794 198 microgram/ 180 microgram (nominal dose/delivered dose) once daily.	
Reporting group title	AZD7594 90 µg
Reporting group description: Oral inhalation of AZD5794 99 microgram/ 90 microgram (nominal dose/delivered dose) once daily.	
Reporting group title	AZD7594 360 µg
Reporting group description: Oral inhalation of AZD5794 396 microgram/ 360 microgram (nominal dose/delivered dose) once daily.	
Reporting group title	AZD7594 720 µg
Reporting group description: Oral inhalation of AZD5794 792 microgram/ 720 microgram (nominal dose/delivered dose) once daily.	
Reporting group title	Placebo to AZD7594
Reporting group description: Oral inhalation of placebo to AZD7594 once daily.	
Reporting group title	Fluticasone furoate
Reporting group description: Oral inhalation of fluticasone furoate 100 microgram once daily.	

Serious adverse events	AZD7594 50 µg	AZD7594 180 µg	AZD7594 90 µg
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 110 (0.00%)	1 / 111 (0.90%)	3 / 112 (2.68%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Injury, poisoning and procedural complications			
Femur fracture			
subjects affected / exposed	0 / 110 (0.00%)	0 / 111 (0.00%)	0 / 112 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Spinal compression fracture			

subjects affected / exposed	0 / 110 (0.00%)	0 / 111 (0.00%)	0 / 112 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac disorders			
Angina pectoris			
subjects affected / exposed	0 / 110 (0.00%)	0 / 111 (0.00%)	0 / 112 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Atrial flutter			
subjects affected / exposed	0 / 110 (0.00%)	0 / 111 (0.00%)	0 / 112 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			
Asthma			
subjects affected / exposed	0 / 110 (0.00%)	1 / 111 (0.90%)	1 / 112 (0.89%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General disorders and administration site conditions			
Death			
subjects affected / exposed	0 / 110 (0.00%)	0 / 111 (0.00%)	0 / 112 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Colitis			
subjects affected / exposed	0 / 110 (0.00%)	0 / 111 (0.00%)	0 / 112 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatobiliary disorders			
Cholecystitis acute			
subjects affected / exposed	0 / 110 (0.00%)	0 / 111 (0.00%)	1 / 112 (0.89%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Musculoskeletal and connective tissue disorders			

Back pain			
subjects affected / exposed	0 / 110 (0.00%)	0 / 111 (0.00%)	1 / 112 (0.89%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Neck pain			
subjects affected / exposed	0 / 110 (0.00%)	0 / 111 (0.00%)	1 / 112 (0.89%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Sepsis			
subjects affected / exposed	0 / 110 (0.00%)	0 / 111 (0.00%)	1 / 112 (0.89%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	AZD7594 360 µg	AZD7594 720 µg	Placebo to AZD7594
Total subjects affected by serious adverse events			
subjects affected / exposed	3 / 113 (2.65%)	3 / 134 (2.24%)	0 / 113 (0.00%)
number of deaths (all causes)	1	0	0
number of deaths resulting from adverse events	0	0	0
Injury, poisoning and procedural complications			
Femur fracture			
subjects affected / exposed	0 / 113 (0.00%)	1 / 134 (0.75%)	0 / 113 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Spinal compression fracture			
subjects affected / exposed	0 / 113 (0.00%)	1 / 134 (0.75%)	0 / 113 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac disorders			
Angina pectoris			
subjects affected / exposed	0 / 113 (0.00%)	1 / 134 (0.75%)	0 / 113 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Atrial flutter			
subjects affected / exposed	0 / 113 (0.00%)	0 / 134 (0.00%)	0 / 113 (0.00%)

occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			
Asthma			
subjects affected / exposed	1 / 113 (0.88%)	0 / 134 (0.00%)	0 / 113 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General disorders and administration site conditions			
Death			
subjects affected / exposed	1 / 113 (0.88%)	0 / 134 (0.00%)	0 / 113 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Gastrointestinal disorders			
Colitis			
subjects affected / exposed	1 / 113 (0.88%)	0 / 134 (0.00%)	0 / 113 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatobiliary disorders			
Cholecystitis acute			
subjects affected / exposed	0 / 113 (0.00%)	0 / 134 (0.00%)	0 / 113 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	0 / 113 (0.00%)	0 / 134 (0.00%)	0 / 113 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Neck pain			
subjects affected / exposed	0 / 113 (0.00%)	0 / 134 (0.00%)	0 / 113 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Sepsis			
subjects affected / exposed	0 / 113 (0.00%)	0 / 134 (0.00%)	0 / 113 (0.00%)

occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	Fluticasone furoate		
Total subjects affected by serious adverse events			
subjects affected / exposed	1 / 112 (0.89%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events	0		
Injury, poisoning and procedural complications			
Femur fracture			
subjects affected / exposed	0 / 112 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Spinal compression fracture			
subjects affected / exposed	0 / 112 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Cardiac disorders			
Angina pectoris			
subjects affected / exposed	0 / 112 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Atrial flutter			
subjects affected / exposed	1 / 112 (0.89%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Respiratory, thoracic and mediastinal disorders			
Asthma			
subjects affected / exposed	0 / 112 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
General disorders and administration site conditions			
Death			
subjects affected / exposed	0 / 112 (0.00%)		

occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Gastrointestinal disorders			
Colitis			
subjects affected / exposed	0 / 112 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Hepatobiliary disorders			
Cholecystitis acute			
subjects affected / exposed	0 / 112 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	0 / 112 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Neck pain			
subjects affected / exposed	0 / 112 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Infections and infestations			
Sepsis			
subjects affected / exposed	0 / 112 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		

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

Non-serious adverse events	AZD7594 50 µg	AZD7594 180 µg	AZD7594 90 µg
Total subjects affected by non-serious adverse events			
subjects affected / exposed	14 / 110 (12.73%)	8 / 111 (7.21%)	15 / 112 (13.39%)
Respiratory, thoracic and mediastinal disorders			

Asthma			
subjects affected / exposed	7 / 110 (6.36%)	2 / 111 (1.80%)	6 / 112 (5.36%)
occurrences (all)	7	2	6
Infections and infestations			
Nasopharyngitis			
subjects affected / exposed	7 / 110 (6.36%)	6 / 111 (5.41%)	9 / 112 (8.04%)
occurrences (all)	7	6	9

Non-serious adverse events	AZD7594 360 µg	AZD7594 720 µg	Placebo to AZD7594
Total subjects affected by non-serious adverse events			
subjects affected / exposed	14 / 113 (12.39%)	8 / 134 (5.97%)	24 / 113 (21.24%)
Respiratory, thoracic and mediastinal disorders			
Asthma			
subjects affected / exposed	10 / 113 (8.85%)	3 / 134 (2.24%)	19 / 113 (16.81%)
occurrences (all)	10	3	20
Infections and infestations			
Nasopharyngitis			
subjects affected / exposed	4 / 113 (3.54%)	5 / 134 (3.73%)	6 / 113 (5.31%)
occurrences (all)	4	6	6

Non-serious adverse events	Fluticasone furoate		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	11 / 112 (9.82%)		
Respiratory, thoracic and mediastinal disorders			
Asthma			
subjects affected / exposed	3 / 112 (2.68%)		
occurrences (all)	3		
Infections and infestations			
Nasopharyngitis			
subjects affected / exposed	9 / 112 (8.04%)		
occurrences (all)	9		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
26 April 2019	Deletion of peak FEV1 from the secondary efficacy endpoints. Update of the inclusion criteria to include only subjects with BMI ≤ 35. Deletion of the expected number of subjects in the US vs. non-US sites. Removal of interim futility analysis. Specification of inclusion criterion #7 (pre-bronchodilator FEV1 at Visit 3 between 40% and 90% predicted). Deletion of QT interval corrected using Bazett's formula; addition of appropriate electrocardiogram parameters. Clarification of exclusion criterion #3 and exclusion criterion #21 for alcohol and drug abuse. Clarified the required treatments for postmenopausal subjects. Clarified that the subjects were discontinued when specified criteria are met. Deletion of measure peak expiratory flow at Screening. Clarification of the number of measurement and timing of spirometry. Clarification of the compliance rate in the Run-in Period and the expected compliance rate in the Treatment Period. Clarification that peak expiratory flow was measured at home after completing the morning and evening diary. Clarification that Forced oscillation technique evaluation and training took place at Visit 1, instead of Visit 2. Deletion of the description that rescue medication should be recorded as concomitant medication. Clarification that the analysis set used for demographic and baseline characteristics was Full analysis set. Clarification that baseline asthma severity was assessed using the pre-SABA value at Visit 2, instead of pre-bronchodilator value at Visit 1. The number of subjects who met the reversibility criteria was deleted. "Individual plasma concentrations vs. time on Week 12 (Day 84) plotted on linear and semi-logarithmic scale with all treatments overlaid on the same plot and separate plots for each subject" was no longer provided as part of PK analysis. Geometric SD was no longer presented on figures of geometric mean for concentration-time data as part of the PK analysis. Clarification of the definition of

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported