Clinical trial results:
An open, phase I study in male adolescents with asthma, aged 12 to 17 years, to assess pharmacokinetics of orally administered AZD1981 tablets
100 mg twice daily for 6½ days

Summary

EudraCT number	2010-021520-10
Trial protocol	SE
Global end of trial date	02 February 2011

Results information

Result version number	v1 (current)
This version publication date	01 February 2017
First version publication date	06 August 2015

Trial information

Trial identification

Sponsor protocol code	AZD1981

Additional study identifiers

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

Notes:

Sponsors

Sponsor organisation name	AstraZeneca
Sponsor organisation address	Christopher D. O'Brien, 1800 Concord Pike, C4B-125, Wilmington, United States, DE 19850
Public contact	Christopher D. O'Brien, MD, PhD, FCCP, Medical Science Director, AstraZeneca, +1 302 886 3577,
Scientific contact	Professor Lennart Nordvall, MD, PhD, Barnmedicin, Akademiska sjukhuset, SE-751 85 Uppsala, Sweden, +46 70 312 44 20,

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?	Yes

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	02 February 2011
Is this the analysis of the primary completion data?	Yes
Primary completion date	02 February 2011
Global end of trial reached?	Yes
Global end of trial date	02 February 2011
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To investigate the pharmacokinetics (PK) of orally administered AZD1981 in male adolescents with asthma.

Protection of trial subjects:

AstraZeneca's quality assurance and quality control procedures provide reassurance that the clinical study programme was carried out in accordance with GCP guidelines. AstraZeneca undertakes a GCP audit programme to ensure compliance with its procedures and to assess the adequacy of its quality control measures. Audits, by a Global Quality Assurance group operating independently of the study monitors and in accordance with documented policies and procedures, are directed towards all aspects of the clinical study process and its associated documentation.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	14 October 2010
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	Sweden: 23
Worldwide total number of subjects	23
EEA total number of subjects	23

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)	23

Adults (18-64 years)	0
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

Of the 23 enrolled patients, 22 started treatment with AZD1981. All 22 patients completed the study.

Pre-assignment period milestones

Number of subjects started	23
Number of subjects completed	22

Pre-assignment subject non-completion reasons

Reason: Number of subjects	Protocol deviation: 1

Period 1

Period 1 title	Overall trial (overall period)
Is this the baseline period?	Yes
Allocation method	Not applicable
Blinding used	Not blinded

Arms

Arm title	AZD1981 100 mg twice daily

Arm description: -

Arm type	Experimental
Investigational medicinal product name	AZD1981
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

100 mg twice daily

Number of subjects in period 1[1]	AZD1981 100 mg twice daily
Started	22
Completed	22

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: Patient has been excluded from the study due to not meeting one of the inclusion criteria.

Baseline characteristics

Reporting groups	
Reporting group title	AZD1981 100 mg twice daily

Reporting group description: -

Reporting group values	AZD1981 100 mg twice daily	Total	
Number of subjects	22	22	
Age categorical Units: Subjects			
Adolescents (12-17 years)	22	22	
Age continuous Units: years			
arithmetic mean	14.3		
full range (min-max)	12 to 17	-	
Gender categorical Units: Subjects			
Female	0	0	
Male	22	22	

End points

End points reporting groups

Reporting group title	AZD1981 100 mg twice daily

Reporting group description: -

Primary: AUC at steady state

End point title	AUC at steady state [1]

End point description:

Day 7, 30min, 1h, 3h, 4h, 6h, 8h and 12h efter last dose

End point type	Primary

End point timeframe:

Day 7

Notes:

[1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: There is no analysis for this trial, just summary statistics. This is observational study.

End point values	AZD1981 100 mg twice daily			
Subject group type	Reporting group			
Number of subjects analysed	22			
Units: nmol*h/L				
geometric mean (geometric coefficient of variation)	16248.4 (± 28.9)			

Statistical analyses

No statistical analyses for this end point

Primary: C-max at steady state

End point title	C-max at steady state[2]

End point description:

Day 7, 30min, 1h, 3h, 4h, 6h, 8h and 12h efter last dose

End point type	Primary

End point timeframe:

Day 7

Notes:

[2] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: There is no analysis for this trial, just summary statistics. This is observational study.

End point values	AZD1981 100 mg twice daily			
Subject group type	Reporting group			
Number of subjects analysed	22			
Units: nmol/L				
geometric mean (geometric coefficient of variation)	4157.2 (± 38.3)			

Statistical analyses

No statistical analyses for this end point

Primary: C-trough at steady state

End point title	C-trough at steady state[3]

End point description:

Day 7, 30min, 1h, 3h, 4h, 6h, 8h and 12h efter last dose

End point type	Primary

End point timeframe:

Day

Notes:

[3] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: There is no analysis for this trial, just summary statistics. This is observational study.

End point values	AZD1981 100 mg twice daily			
Subject group type	Reporting group			
Number of subjects analysed	22			
Units: nmol/L				
geometric mean (geometric coefficient of variation)	205.5 (± 56.9)			

Statistical analyses

No statistical analyses for this end point

Primary: CL/F

End point title	CL/F[4]

End point description:

Day 7, 30min, 1h, 3h, 4h, 6h, 8h and 12h efter last dose

End point type	Primary

End point timeframe:

Day 7

Notes:

[4] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: There is no analysis for this trial, just summary statistics. This is observational study.

End point values	AZD1981 100 mg twice daily			
Subject group type	Reporting group			
Number of subjects analysed	22			
Units: L/h				
geometric mean (geometric coefficient of variation)	15.83 (± 28.9)			

Statistical analyses

No statistical analyses for this end point

Secondary: Ae at steady state

End point title	Ae at steady state
End point description:	
Day 7, 30min, 1h, 3h, 4h, 6h, 8h and 12h efter last dose	
End point type	Secondary
End point timeframe:	
Day 7	

End point values	AZD1981 100 mg twice daily			
Subject group type	Reporting group			
Number of subjects analysed	22			
Units: nmol				
geometric mean (geometric coefficient of variation)	76645.3 (± 39.7)			

Statistical analyses

No statistical analyses for this end point

Secondary: Fe at steady state

End point title	Fe at steady state
End point description:	
Day 7, 30min, 1h, 3h, 4h, 6h, 8h and 12h efter last dose	
End point type	Secondary
End point timeframe:	
Day 7	

End point values	AZD1981 100 mg twice daily			
Subject group type	Reporting group			
Number of subjects analysed	22			
Units: NA				
geometric mean (geometric coefficient of variation)	0.298 (± 39.7)			

Statistical analyses

No statistical analyses for this end point

Secondary: CLR

End point title	CLR

End point description:

Day 7, 30min, 1h, 3h, 4h, 6h, 8h and 12h efter last dose

End point type	Secondary

End point timeframe:

Day 7

End point values	AZD1981 100 mg twice daily			
Subject group type	Reporting group			
Number of subjects analysed	22			
Units: L/h				
geometric mean (geometric coefficient of variation)	4.72 (± 45.1)			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information	
Timeframe for reporting adverse events: one month	
Assessment type	Systematic
Dictionary used	
Dictionary name	MedDRA
Dictionary version	13.0
Reporting groups	
Reporting group title	AZD1981
Reporting group description: 100 mg, 1x 100 mg bid;oral administration	

Serious adverse events	AZD1981		
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 22 (0.00%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events	0		

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

Non-serious adverse events	AZD1981		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	8 / 22 (36.36%)		
Investigations			
Thyroid function test abnormal			
subjects affected / exposed	1 / 22 (4.55%)		
occurrences (all)	1		
Thyroid function test	Additional description: Elevated TSH, Blood Thyroid stimulating hormone increased		
subjects affected / exposed	1 / 22 (4.55%)		
occurrences (all)	1		
Nervous system disorders			
Syncope			
subjects affected / exposed	2 / 22 (9.09%)		
occurrences (all)	2		
General disorders and administration site conditions			

Fatigue			
subjects affected / exposed	1 / 22 (4.55%)		
occurrences (all)	1		
Respiratory, thoracic and mediastinal disorders			
Asthmatic attack induced	Additional description: Exercise induced		
subjects affected / exposed	1 / 22 (4.55%)		
occurrences (all)	1		
Throat pain			
subjects affected / exposed	1 / 22 (4.55%)		
occurrences (all)	1		
Asthma NOS			
subjects affected / exposed	2 / 22 (9.09%)		
occurrences (all)	2		
Infections and infestations			
Upper resp tract infection			
subjects affected / exposed	1 / 22 (4.55%)		
occurrences (all)	1		
Nasopharyngeal disorder	Additional description: Nasopharyngitis		
subjects affected / exposed	2 / 22 (9.09%)		
occurrences (all)	2		
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	1 / 22 (4.55%)		
occurrences (all)	1		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
27 October 2010	According to the CSP, 1 centre was to be used for the investigation; by the amendment this was changed to at least 1 centre.
27 October 2010	Instead of having the treatment period of AZD1981 restricted to exactly 6½ days, a time window of –1 day and +2 days was allowed. Still steady state
27 October 2010	Visit 2 (the later of 2 screening occasions) was to take place within 21 days of Visit 3 (start of treatment). In previous text (CSP), it was not clear to which screening visit that the 21-day frame was related. Visit 1 and Visit 2 can occur at the same occasion.
27 October 2010	Instead of having a fix limit (4 weeks) ahead of Visit 3 with regards to nonallowed medication during treatment, the amendment states 2 weeks or 5 times the half-life, whichever was the longest.
27 October 2010	Allowed medication during treatment was changed from solely inhaled asthma medication to include medications for treatment of e.g. rhinitis and eczema. The pharmacokinetic evaluation of AZD1981 was considered to be unaffected by this change.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported