ClinicalTrials.gov Protocol and Results Registration System (PRS) Receipt
Release Date: 04/12/2012

ClinicalTrials.gov ID: NCT00703391

Study Identification

Unique Protocol ID:	D0520C00002
Brief Title:	A Two Week Study to Assess the Tolerability of AZD9668 in Chronic Obstructive Pulmonary Disease (COPD) Patients
Official Title:	A 2-week, Randomized, Double-blind, Placebo-controlled, Parallel Group Study to Assess the Tolerability and Pharmacokinetics of Orally Administered AZD9668 in Patients With COPD
Secondary IDs:	

Study Status

Record Verification:	April 2012
Overall Status:	Completed
Study Start:	June 2008
Primary Completion:	September 2008 [Actual]
Study Completion:	September 2008 [Actual]

Sponsor/Collaborators

Sponsor:	AstraZeneca
Responsible Party:	Sponsor
Collaborators:	

Oversight

FDA Regulated?:	Yes
Applicable Trial?:	Section 801 Clinical Trial? Yes

	Delayed Posting? No
IND/IDE Protocol?:	Yes
IND/IDE Information:	Grantor: CDER IND/IDE Number: 101,534 Serial Number: 000 Has Expanded Access? No
Review Board:	Approval Status: Approved Approval Number: ZS EK 11 160/09 Board Name: Ethics Committee of the Land Berlin Board Affiliation: Phone: 49-030-9012-0 Email: ethik-kommission@lageso.verwalt-berlin.de
Data Monitoring?:	No
Plan to Share Data?:	
Oversight Authorities:	United States: Food and Drug Administration Germany: Federal Institute for Drugs and Medical Devices

Study Description

Brief Summary:	The purpose of this study is to assess the tolerability (effect of drug on body) and pharmacokinetics (effect of body on drug) of AZD9668 in patients with mild to moderate COPD
Detailed Description:	

Conditions

Conditions:	Chronic Obstructive Pulmonary Disease (COPD)
Keywords:	Chronic obstructive pulmonary lung respiratory disease tolerability placebo-controlled pharmacokinetics COPD

Study Design

Study Type:	Interventional
Primary Purpose:	Basic Science
Study Phase:	Phase 2
Intervention Model:	Parallel Assignment
Number of Arms:	2
Masking:	Double Blind (Subject, Caregiver, Investigator, Outcomes Assessor)
Allocation:	Randomized
Endpoint Classification:	Safety Study
Enrollment:	18 [Actual]

Arms and Interventions

Arms	Assigned Interventions
Experimental: 1 Active Treatment	Drug: AZD9668 30mg oral tablets twice daily (bid) for 14 days
Placebo Comparator: 2 Placebo Treatment	Drug: Placebo Matched placebo to 30mg oral tablet twice daily (bid) for 14 days

Outcome Measures

[See Results Section.]

Eligibility

Minimum Age:	40 Years
Maximum Age:	80 Years
Gender:	Both
Accepts Healthy Volunteers?:	No
Criteria:	Inclusion Criteria:

- Mild to moderate COPD
- Smokers or ex-smokers
- post-menopausal females

Exclusion Criteria:

- Past history or current evidence of clinically significant heart disease
- Lung disease other than COPD
- Treatment with systemic steroids within 8 weeks of study visit 2
- Treatment with antibiotics within 4 weeks of study visit 1 or study visit 2

Contacts/Locations

Study Officials: Kristina Panke
Study Principal Investigator
Parexel International GmbhH (CRO)

Locations: Germany
Research Site
Berlin, Germany

References

Citations:

Links:

Study Data/Documents:

Study Results

Participant Flow

Recruitment Details	First patient enrolled: 11 June 2008. Last patient completed: 09 October 2008. Single-centre study performed at a Clinical Pharmacology Unit
Pre-Assignment Details	None

Reporting Groups

	Description
AZD9668	AZD9668 2x30mg oral tablets twice daily (bid) for 14 days
Placebo	Matched placebo tablets twice daily (bid) for 14 days

Overall Study

	AZD9668	Placebo
Started	12	6
Completed	12	6
Not Completed	0	0

Baseline Characteristics

Reporting Groups

	Description
AZD9668	AZD9668 2x30mg oral tablets twice daily (bid) for 14 days
Placebo	Matched placebo tablets twice daily (bid) for 14 days

Baseline Measures

	AZD9668	Placebo	Total
Number of Participants	12	6	18
Age, Continuous [units: Years] Mean (Full Range)	57.6 (42 to 70)	52.8 (44 to 65)	56 (42 to 70)
Gender, Male/Female [units: Participants]			
Female	3	2	5
Male	9	4	13

Outcome Measures

1. Primary Outcome Measure:

Measure Title	Alanine Aminotransferase (ALT)
Measure Description	ALT level greater than 3 times the upper limit of normal
Time Frame	Throughout the duration of the study (pre-dose, cmax, steady state, end of dosing and post dose)
Safety Issue?	Yes

Analysis Population Description

[Not Specified]

Reporting Groups

	Description
AZD9668	AZD9668 2x30mg oral tablets twice daily (bid) for 14 days
Placebo	Matched placebo tablets twice daily (bid) for 14 days

Measured Values

	AZD9668	Placebo
Number of Participants Analyzed	12	6
Alanine Aminotransferase (ALT) [units: Participants]	0	0

2. Primary Outcome Measure:

Measure Title	Aspartate Aminotransferase (AST)
Measure Description	AST level greater than 3 times the upper limit of normal
Time Frame	Throughout the duration of the study (pre-dose, cmax, steady state, end of dosing and post dose)
Safety Issue?	Yes

Analysis Population Description

[Not Specified]

Reporting Groups

	Description
AZD9668	AZD9668 2x30mg oral tablets twice daily (bid) for 14 days
Placebo	Matched placebo tablets twice daily (bid) for 14 days

Measured Values

	AZD9668	Placebo
Number of Participants Analyzed	12	6
Aspartate Aminotransferase (AST) [units: Participants]	0	0

3. Primary Outcome Measure:

Measure Title	Creatine Kinase (CK)
Measure Description	Change from baseline to Day 14
Time Frame	Throughout the duration of the study (pre-dose, cmax, steady state, end of dosing and post dose)
Safety Issue?	Yes

Analysis Population Description
[Not Specified]

Reporting Groups

	Description
AZD9668	AZD9668 2x30mg oral tablets twice daily (bid) for 14 days
Placebo	Matched placebo tablets twice daily (bid) for 14 days

Measured Values

	AZD9668	Placebo
Number of Participants Analyzed	12	6
Creatine Kinase (CK) [units: IU/L] Mean (Standard Deviation)	2.57 (19.260)	-69.57 (141.383)

4. Primary Outcome Measure:

Measure Title	Total Bilirubin
Measure Description	Change from baseline to Day 14
Time Frame	Throughout the duration of the study (pre-dose, cmax, steady state, end of dosing and post dose)
Safety Issue?	Yes

Analysis Population Description
[Not Specified]

Reporting Groups

	Description
AZD9668	AZD9668 2x30mg oral tablets twice daily (bid) for 14 days

	Description
Placebo	Matched placebo tablets twice daily (bid) for 14 days

Measured Values

	AZD9668	Placebo
Number of Participants Analyzed	12	6
Total Bilirubin [units: micromol/L] Mean (Standard Deviation)	0.11 (2.124)	-0.28 (2.563)

5. Primary Outcome Measure:

Measure Title	Creatinine
Measure Description	Creatinine level greater than the upper limit of normal
Time Frame	Throughout the duration of the study (pre-dose, cmax, steady state, end of dosing and post dose)
Safety Issue?	Yes

Analysis Population Description

[Not Specified]

Reporting Groups

	Description
AZD9668	AZD9668 2x30mg oral tablets twice daily (bid) for 14 days
Placebo	Matched placebo tablets twice daily (bid) for 14 days

Measured Values

	AZD9668	Placebo
Number of Participants Analyzed	12	6
Creatinine [units: Participants]	1	1

6. Primary Outcome Measure:

Measure Title	Haemoglobin (Hb)
Measure Description	Change from baseline to Day 14
Time Frame	Throughout the duration of the study (pre-dose, cmax, steady state, end of dosing and post dose)
Safety Issue?	Yes

Analysis Population Description
[Not Specified]

Reporting Groups

	Description
AZD9668	AZD9668 2x30mg oral tablets twice daily (bid) for 14 days
Placebo	Matched placebo tablets twice daily (bid) for 14 days

Measured Values

	AZD9668	Placebo
Number of Participants Analyzed	12	6
Haemoglobin (Hb) [units: g/L] Mean (Standard Deviation)	-2.0 (4.73)	-0.2 (6.18)

7. Primary Outcome Measure:

Measure Title	Reticulocytes
Measure Description	Change from baseline to Day 14
Time Frame	Throughout the duration of the study (pre-dose, cmax, steady state, end of dosing and post dose)
Safety Issue?	Yes

Analysis Population Description
[Not Specified]

Reporting Groups

	Description
AZD9668	AZD9668 2x30mg oral tablets twice daily (bid) for 14 days

	Description
Placebo	Matched placebo tablets twice daily (bid) for 14 days

Measured Values

	AZD9668	Placebo
Number of Participants Analyzed	12	6
Reticulocytes [units: relative particle count (%)] Mean (Standard Deviation)	-0.15 (2.851)	1.73 (1.605)

8. Primary Outcome Measure:

Measure Title	Leucocytes
Measure Description	Change from baseline to Day 14
Time Frame	Throughout the duration of the study (pre-dose, cmax, steady state, end of dosing and post dose)
Safety Issue?	Yes

Analysis Population Description

[Not Specified]

Reporting Groups

	Description
AZD9668	AZD9668 2x30mg oral tablets twice daily (bid) for 14 days
Placebo	Matched placebo tablets twice daily (bid) for 14 days

Measured Values

	AZD9668	Placebo
Number of Participants Analyzed	12	6
Leucocytes [units: 10**9/L] Mean (Standard Deviation)	-0.001 (0.8816)	0.265 (0.4657)

9. Primary Outcome Measure:

Measure Title	QTcF (QT Interval Corrected for Heart Rate by Fridericia's Method)
Measure Description	QTcF interval greater than 450 ms
Time Frame	Throughout the duration of the study (pre-dose, cmax, steady state, end of dosing and post dose)
Safety Issue?	Yes

Analysis Population Description
[Not Specified]

Reporting Groups

	Description
AZD9668	AZD9668 2x30mg oral tablets twice daily (bid) for 14 days
Placebo	Matched placebo tablets twice daily (bid) for 14 days

Measured Values

	AZD9668	Placebo
Number of Participants Analyzed	12	6
QTcF (QT Interval Corrected for Heart Rate by Fridericia's Method) [units: Participants]	0	0

10. Primary Outcome Measure:

Measure Title	QTcF
Measure Description	QTcF change from baseline greater than 60 ms
Time Frame	Throughout the duration of the study (pre-dose, cmax, steady state, end of dosing and post dose)
Safety Issue?	Yes

Analysis Population Description
[Not Specified]

Reporting Groups

	Description
AZD9668	AZD9668 2x30mg oral tablets twice daily (bid) for 14 days

	Description
Placebo	Matched placebo tablets twice daily (bid) for 14 days

Measured Values

	AZD9668	Placebo
Number of Participants Analyzed	12	6
QTcF [units: Participants]	0	0

11. Primary Outcome Measure:

Measure Title	FEV1 (Forced Expiratory Volume in the First Second)
Measure Description	Change from baseline to Day 14
Time Frame	Throughout the duration of the study (pre-dose, cmax, steady state, end of dosing and post dose)
Safety Issue?	Yes

Analysis Population Description

[Not Specified]

Reporting Groups

	Description
AZD9668	AZD9668 2x30mg oral tablets twice daily (bid) for 14 days
Placebo	Matched placebo tablets twice daily (bid) for 14 days

Measured Values

	AZD9668	Placebo
Number of Participants Analyzed	12	6
FEV1 (Forced Expiratory Volume in the First Second) [units: L] Mean (Standard Deviation)	0.039 (0.2173)	-0.110 (0.3043)

12. Primary Outcome Measure:

Measure Title	Area Under the Plasma Concentration-time Curve From Time Zero to 12 Hours Post-dose (AUC(0-12))
Measure Description	AUC(0-12) following 14 days' dosing
Time Frame	Pre-dose on day -1 to day 15 (end of dosing)
Safety Issue?	No

Analysis Population Description
[Not Specified]

Reporting Groups

	Description
AZD9668	AZD9668 2x30mg oral tablets twice daily (bid) for 14 days
Placebo	Matched placebo tablets twice daily (bid) for 14 days

Measured Values

	AZD9668	Placebo
Number of Participants Analyzed	12	0
Area Under the Plasma Concentration-time Curve From Time Zero to 12 Hours Post-dose (AUC(0-12)) [units: nM.h] Geometric Mean (Full Range)	7560 (5820 to 9570)	

13. Primary Outcome Measure:

Measure Title	Observed Peak or Maximum Plasma Concentration Following Drug Administration (Cmax)
Measure Description	Cmax following 14 days' dosing
Time Frame	Pre-dose on day -1 to day 15 (end of dosing)
Safety Issue?	No

Analysis Population Description
[Not Specified]

Reporting Groups

	Description
AZD9668	AZD9668 2x30mg oral tablets twice daily (bid) for 14 days

	Description
Placebo	Matched placebo tablets twice daily (bid) for 14 days

Measured Values

	AZD9668	Placebo
Number of Participants Analyzed	12	0
Observed Peak or Maximum Plasma Concentration Following Drug Administration (Cmax) [units: nM] Geometric Mean (Full Range)	1420 (1030 to 1930)	

14. Primary Outcome Measure:

Measure Title	Time to Reach Observed Peak or Maximum Concentration Following Oral Drug Administration (Tmax)
Measure Description	tmax following 14 days' dosing
Time Frame	Pre-dose on day -1 to day 15 (end of dosing)
Safety Issue?	No

Analysis Population Description

[Not Specified]

Reporting Groups

	Description
AZD9668	AZD9668 2x30mg oral tablets twice daily (bid) for 14 days
Placebo	Matched placebo tablets twice daily (bid) for 14 days

Measured Values

	AZD9668	Placebo
Number of Participants Analyzed	12	0
Time to Reach Observed Peak or Maximum Concentration Following Oral Drug Administration (Tmax) [units: hours] Median (Full Range)	1.01 (0.490 to 2.01)	

15. Primary Outcome Measure:

Measure Title	Terminal Half-life of Drug in Plasma (t1/2)
Measure Description	t1/2 following 14 days' dosing
Time Frame	Pre-dose on day -1 to day 15 (end of dosing)
Safety Issue?	No

Analysis Population Description
[Not Specified]

Reporting Groups

	Description
AZD9668	AZD9668 2x30mg oral tablets twice daily (bid) for 14 days
Placebo	Matched placebo tablets twice daily (bid) for 14 days

Measured Values

	AZD9668	Placebo
Number of Participants Analyzed	12	0
Terminal Half-life of Drug in Plasma (t1/2) [units: hours] Median (Full Range)	5.89 (5.00 to 6.46)	

16. Primary Outcome Measure:

Measure Title	Renal Clearance of Drug From Plasma (CLR)
Measure Description	CLR following 14 days' dosing
Time Frame	Pre-dose on day -1 to day 15 (end of dosing)
Safety Issue?	No

Analysis Population Description
[Not Specified]

Reporting Groups

	Description
AZD9668	AZD9668 2x30mg oral tablets twice daily (bid) for 14 days
Placebo	Matched placebo tablets twice daily (bid) for 14 days

Measured Values

	AZD9668	Placebo
Number of Participants Analyzed	12	0
Renal Clearance of Drug From Plasma (CLR) [units: L/h] Geometric Mean (Full Range)	6.13 (3.49 to 8.22)	

17. Secondary Outcome Measure:

Measure Title	Sputum Absolute Neutrophil Count
Measure Description	Change from baseline to Day 14 in absolute neutrophil count
Time Frame	Pre-dose day -1 to post-dose on day 14
Safety Issue?	Yes

Analysis Population Description

[Not Specified]

Reporting Groups

	Description
AZD9668	AZD9668 2x30mg oral tablets twice daily (bid) for 14 days
Placebo	Matched placebo tablets twice daily (bid) for 14 days

Measured Values

	AZD9668	Placebo
Number of Participants Analyzed	7	4
Sputum Absolute Neutrophil Count [units: 10**9/L] Median (Full Range)	-0.4890 (-1.439 to 0.439)	-2.5645 (-9.198 to -0.283)

18. Secondary Outcome Measure:

Measure Title	Sputum Differential Neutrophil Count
Measure Description	Change from baseline to Day 14 in percentage neutrophil count
Time Frame	Pre-dose day -1 to post-dose on day 14
Safety Issue?	Yes

Analysis Population Description
[Not Specified]

Reporting Groups

	Description
AZD9668	AZD9668 2x30mg oral tablets twice daily (bid) for 14 days
Placebo	Matched placebo tablets twice daily (bid) for 14 days

Measured Values

	AZD9668	Placebo
Number of Participants Analyzed	12	6
Sputum Differential Neutrophil Count [units: Percentage] Median (Full Range)	1.8 (-11.0 to 10.0)	-4.25 (-9.0 to 8.7)

19. Secondary Outcome Measure:

Measure Title	AZD9668 Sputum Concentrations
Measure Description	
Time Frame	Pre-dose day -1 to post-dose on day 14
Safety Issue?	No

Analysis Population Description
[Not Specified]

Reporting Groups

	Description
AZD9668	AZD9668 2x30mg oral tablets twice daily (bid) for 14 days
Placebo	Matched placebo tablets twice daily (bid) for 14 days

Measured Values

	AZD9668	Placebo
Number of Participants Analyzed	11	0
AZD9668 Sputum Concentrations [units: nM] Geometric Mean (Full Range)	41.7 (26.5 to 64.3)	

20. Secondary Outcome Measure:

Measure Title	Quantitative Sputum Bacteriology
Measure Description	Number of patients with an increase in bacteriological count from Day -1 to Day 15
Time Frame	Pre-dose day -1 to post-dose on day 15
Safety Issue?	Yes

Analysis Population Description
[Not Specified]

Reporting Groups

	Description
AZD9668	AZD9668 2x30mg oral tablets twice daily (bid) for 14 days
Placebo	Matched placebo tablets twice daily (bid) for 14 days

Measured Values

	AZD9668	Placebo
Number of Participants Analyzed	12	6
Quantitative Sputum Bacteriology [units: Participants]	3	2

Reported Adverse Events

Time Frame	[Not specified]
Additional Description	[Not specified]

Reporting Groups

	Description
AZD9668	AZD9668 2x30mg oral tablets twice daily (bid) for 14 days
Placebo	Matched placebo tablets twice daily (bid) for 14 days

Serious Adverse Events

	AZD9668	Placebo
	Affected/At Risk (%)	Affected/At Risk (%)
Total	0/12 (0%)	0/6 (0%)

Other Adverse Events

Frequency Threshold Above Which Other Adverse Events are Reported: 5%

	AZD9668	Placebo
	Affected/At Risk (%)	Affected/At Risk (%)
Total	5/12 (41.67%)	4/6 (66.67%)
Cardiac disorders		
Palpitations [A] †	1/12 (8.33%)	0/6 (0%)
Ear and labyrinth disorders		
Back pain [A] †	2/12 (16.67%)	0/6 (0%)
Gastrointestinal disorders		
Diarrhoea [A] †	1/12 (8.33%)	0/6 (0%)
Dyspepsia [A] †	0/12 (0%)	1/6 (16.67%)
Nausea [A] †	1/12 (8.33%)	0/6 (0%)

	AZD9668	Placebo
	Affected/At Risk (%)	Affected/At Risk (%)
Vomiting [A] †	1/12 (8.33%)	0/6 (0%)
General disorders		
Chest discomfort [A]	1/12 (8.33%)	0/6 (0%)
Fatigue [A] †	0/12 (0%)	1/6 (16.67%)
Infections and infestations		
Respiratory tract infection [A] †	1/12 (8.33%)	0/6 (0%)
Musculoskeletal and connective tissue disorders		
Musculoskeletal pain [A] †	1/12 (8.33%)	0/6 (0%)
Nervous system disorders		
Headache [A] †	1/12 (8.33%)	4/6 (66.67%)
Skin and subcutaneous tissue disorders		
Hyperhidrosis [A] †	1/12 (8.33%)	0/6 (0%)

† Indicates events were collected by systematic assessment.
A Term from vocabulary, MedDRA 10.0

Limitations and Caveats

[Not specified]

More Information

Certain Agreements:

Principal Investigators are NOT employed by the organization sponsoring the study.

There is NOT an agreement between the Principal Investigator and the Sponsor (or its agents) that restricts the PI's rights to discuss or publish trial results after the trial is completed.

Results Point of Contact:

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