ClinicalTrials.gov Protocol and Results Registration System (PRS) Receipt
Release Date: 09/25/2012

ClinicalTrials.gov ID: NCT01048333

Study Identification

Unique Protocol ID:	D5127C00001
Brief Title:	Evaluate Onset of Effect in Patients With Chronic Obstructive Pulmonary Disease (COPD) Treated With Formoterol Turbuhaler®
Official Title:	A Randomised, Placebo-controlled, Double-blind (Double-dummy Technique),Crossover, Multi-centre Study, to Evaluate Onset of Effect in Patients With Chronic Obstructive Pulmonary Disease (COPD) Treated With Formoterol Turbuhaler® 9 µg, Compared With Serevent® Diskus® 50 µg.
Secondary IDs:	

Study Status

Record Verification:	September 2012
Overall Status:	Completed
Study Start:	January 2010
Primary Completion:	May 2010 [Actual]
Study Completion:	May 2010 [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?:	No
Review Board:	Approval Status: Approved Approval Number: 7/15/09 Board Name: Regionala Etikprövningsnämnden i Lund Board Affiliation: Regionala Etikprövningsnämnden i Lund Phone: +46 46 2224 180 Email: cecilia.mildner@epn.lu.se
Data Monitoring?:	No
Plan to Share Data?:	
Oversight Authorities:	Italy: The Italian Medicines Agency Spain: Spanish Agency of Medicines Sweden: Medical Products Agency

Study Description

Brief Summary:

- Primary objective is to evaluate time to onset of effect of formoterol, 9 µg single dose,compared with salmeterol, 50 µg single dose, in patients with moderate COPD.Forced Expiratory Volume in 1 second (FEV1) measured by spirometry 5 minutes postdose.
- Secondary efficacy variables: Average FEV1 during the first 15 minutes (area under the FEV1 curve from 0 to 15 minutes), Average FEV1 during 120 minutes (area under the FEV1 curve from 0 to 120 minutes)

Detailed Description:

Conditions

Conditions:	Chronic Obstructive Pulmonary Disease
Keywords:	Chronic Obstructive Pulmonary Disease Onset of effect COPD Oxis Turbuhaler

Study Design

Study Type:	Interventional
Primary Purpose:	Treatment
Study Phase:	Phase 2

Intervention Model:	Crossover Assignment
Number of Arms:	6
Masking:	Double Blind (Subject, Investigator)
Allocation:	Randomized
Endpoint Classification:	Safety/Efficacy Study
Enrollment:	109 [Actual]

Arms and Interventions

Arms	Assigned Interventions
Experimental: Formoterol, then Salmeterol, then Placebo Formoterol Turbuhaler 9 µg and Placebo Diskus first, then Salmeterol Diskus 50 µg and Placebo Turbuhaler, then Placebo Diskus and Placebo Turbuhaler	Drug: Formoterol Formoterol Turbuhaler 9 µg and Placebo Diskus Drug: Salmeterol Salmeterol Diskus 50 µg and Placebo Turbuhaler Drug: Placebo Placebo Diskus and Placebo Turbuhaler
Experimental: Salmeterol, then Palcebo, then Formoterol Salmeterol Diskus 50 µg and Placebo Turbuhaler first, then Placebo Diskus and Placebo Turbuhaler, then Formoterol Turbuhaler 9 µg and Placebo Diskus	Drug: Formoterol Formoterol Turbuhaler 9 µg and Placebo Diskus Drug: Salmeterol Salmeterol Diskus 50 µg and Placebo Turbuhaler Drug: Placebo Placebo Diskus and Placebo Turbuhaler
Experimental: Placebo, then Formoterol, then Salmeterol Placebo Diskus and Placebo Turbuhaler first,then Formoterol Turbuhaler 9 µg and Placebo Diskus, then Salmeterol Diskus 50 µg and Placebo Turbuhaler	Drug: Formoterol Formoterol Turbuhaler 9 µg and Placebo Diskus Drug: Salmeterol Salmeterol Diskus 50 µg and Placebo Turbuhaler Drug: Placebo Placebo Diskus and Placebo Turbuhaler
Experimental: Formoterol, then Placebo, then Salmeterol Formoterol Turbuhaler 9 µg and Placebo Diskus first, then Placebo Diskus and Placebo Turbuhaler, then Salmeterol Diskus 50 µg and Placebo Turbuhaler	Drug: Formoterol Formoterol Turbuhaler 9 µg and Placebo Diskus Drug: Salmeterol Salmeterol Diskus 50 µg and Placebo Turbuhaler Drug: Placebo Placebo Diskus and Placebo Turbuhaler
Experimental: Salmeterol, then Formoterol, then Placebo Salmeterol Diskus 50 µg and Placebo Turbuhaler first, then Formoterol Turbuhaler 9 µg and Placebo Diskus, then Placebo Diskus and Placebo Turbuhaler	Drug: Formoterol Formoterol Turbuhaler 9 µg and Placebo Diskus Drug: Salmeterol Salmeterol Diskus 50 µg and Placebo Turbuhaler Drug: Placebo Placebo Diskus and Placebo Turbuhaler
Experimental: Placebo, then Salmeterol, then Formoterol	Drug: Formoterol

Arms	Assigned Interventions
Placebo Diskus and Placebo Turbuhaler first, then Salmeterol Diskus 50 µg and Placebo Turbuhaler, then Formoterol Turbuhaler 9 µg and Placebo Diskus	Formoterol Turbuhaler 9 µg and Placebo Diskus Drug: Salmeterol Salmeterol Diskus 50 µg and Placebo Turbuhaler Drug: Placebo Placebo Diskus and Placebo Turbuhaler

Outcome Measures

[See Results Section.]

Eligibility

Minimum Age: 40 Years

Maximum Age:

Gender: Both

Accepts Healthy Volunteers?: No

Criteria: Inclusion Criteria:

- A clinical diagnosis of COPD according to GOLD guidelines, and current COPD symptoms
- A current or previous smoking history equivalent to 10 or more packs per year (1 pack year = 20 cigarettes smoked per day for one year).
- Documented use of a short-acting inhaled bronchodilator (β2-agonist or anticholinergics) as reliever medication.

Exclusion Criteria:

- A history and/or current diagnosis of asthma.
- Patients who have experienced COPD exacerbation requiring hospitalisation and/or a course of antibiotics and/or a course of systemic steroid within 30 days (from end of exacerbation treatment) prior to Visit 1 and/or during the run-in period.
- A history and/or current diagnosis of atopic diseases such as allergic rhinitis or eczema before the age of 40.

Contacts/Locations

Study Officials: Mario Cazzola, professor
Study Principal Investigator
Italy

Georgios Stratelis
Study Director
AstraZeneca MC Sweden

Locations: Sweden
Research Site
Goteborg, Sweden

Research Site
Linkoping, Sweden

Research Site
Lund, Sweden

Research Site
Lulea, Sweden

Italy
Research Site
Roma, Italy

Research Site
Pisa, Italy

Research Site
Prato, Italy

Research Site
Cava dei Tirreni, Italy

Research Site
Bussolengo, Italy

Research Site
Parma, Italy

Research Site
Napoli, Italy

Research Site
Catanzaro, Italy

Research Site
Cassano Delle Murge, Italy

Research Site
Palermo, Italy

Spain
Research Site

Barcelona, Spain

Research Site
Malaga, Spain

Research Site
Madrid, Spain

References

Citations:

Links:

Study Data/Documents:

Study Results

Participant Flow

Recruitment Details	Patients recruited at 14 clinics in 3 countries: Sweden (4 clinics); Italy (6 clinics); Spain (6 clinics)between January and May 2010
Pre-Assignment Details	141 patients enrolled; 32 excluded: 28 due to eligibility criteria not fulfilled and 4 for subject decision

Reporting Groups

	Description
Formoterol, Then Salmeterol, Then Placebo	Formoterol Turbuhaler 9 µg and Placebo Diskus first, then Salmeterol Diskus 50 µg and Placebo Turbuhaler, then Placebo Diskus and Placebo Turbuhaler
Salmeterol, Then Palcebo, Then Formoterol	Salmeterol Diskus 50 µg and Placebo Turbuhaler first, then Placebo Diskus and Placebo Turbuhaler, then Formoterol Turbuhaler 9 µg and Placebo Diskus
Placebo, Then Formoterol, Then Salmeterol	Placebo Diskus and Placebo Turbuhaler first,then Formoterol Turbuhaler 9 µg and Placebo Diskus, then Salmeterol Diskus 50 µg and Placebo Turbuhaler
Formoterol, Then Placebo, Then Salmeterol	Formoterol Turbuhaler 9 µg and Placebo Diskus first, then Placebo Diskus and Placebo Turbuhaler, then Salmeterol Diskus 50 µg and Placebo Turbuhaler
Salmeterol, Then Formoterol, Then Placebo	Salmeterol Diskus 50 µg and Placebo Turbuhaler first, then Formoterol Turbuhaler 9 µg and Placebo Diskus, then Placebo Diskus and Placebo Turbuhaler

	Description
Placebo, Then Salmeterol, Then Formoterol	Placebo Diskus and Placebo Turbuhaler first, then Salmeterol Diskus 50 µg and Placebo Turbuhaler, then Formoterol Turbuhaler 9 µg and Placebo Diskus

Treatment Period 1

	Formoterol, Then Salmeterol, Then Placebo	Salmeterol, Then Palcebo, Then Formoterol	Placebo, Then Formoterol, Then Salmeterol	Formoterol, Then Placebo, Then Salmeterol	Salmeterol, Then Formoterol, Then Placebo	Placebo, Then Salmeterol, Then Formoterol
Started	21	19	16	18	17	18
Completed	21	19	16	18	17	18
Not Completed	0	0	0	0	0	0

Wash-Out Period 1 of 2 - 7 Days

	Formoterol, Then Salmeterol, Then Placebo	Salmeterol, Then Palcebo, Then Formoterol	Placebo, Then Formoterol, Then Salmeterol	Formoterol, Then Placebo, Then Salmeterol	Salmeterol, Then Formoterol, Then Placebo	Placebo, Then Salmeterol, Then Formoterol
Started	21	19	16	18	17	18
Completed	21	19	16	18	17	18
Not Completed	0	0	0	0	0	0

Treatment Period 2

	Formoterol, Then Salmeterol, Then Placebo	Salmeterol, Then Palcebo, Then Formoterol	Placebo, Then Formoterol, Then Salmeterol	Formoterol, Then Placebo, Then Salmeterol	Salmeterol, Then Formoterol, Then Placebo	Placebo, Then Salmeterol, Then Formoterol
Started	21	19	16	18	17	18
Completed	21	19	16	18	17	18
Not Completed	0	0	0	0	0	0

Wash-Out Period 2 of 2 - 7 Days

	Formoterol, Then Salmeterol, Then Placebo	Salmeterol, Then Palcebo, Then Formoterol	Placebo, Then Formoterol, Then Salmeterol	Formoterol, Then Placebo, Then Salmeterol	Salmeterol, Then Formoterol, Then Placebo	Placebo, Then Salmeterol, Then Formoterol
Started	21	19	16	18	17	18
Completed	21	18	16	18	17	18
Not Completed	0	1	0	0	0	0
Adverse Event	0	1	0	0	0	0

Treatment Period 3

	Formoterol, Then Salmeterol, Then Placebo	Salmeterol, Then Palcebo, Then Formoterol	Placebo, Then Formoterol, Then Salmeterol	Formoterol, Then Placebo, Then Salmeterol	Salmeterol, Then Formoterol, Then Placebo	Placebo, Then Salmeterol, Then Formoterol
Started	21	18	16	18	17	18
Completed	21	18	16	18	17	18
Not Completed	0	0	0	0	0	0

Baseline Characteristics

Reporting Groups

	Description
Entire Study Population	Includes all 3 arms : Formoterol, Salmeterol and Placebo.

Baseline Measures

	Entire Study Population
Number of Participants	109
Age, Continuous [units: years] Mean (Full Range)	66.5 (41.0 to 84.0)
Gender, Male/Female [units: participants]	
Female	28

	Entire Study Population
Male	81

Outcome Measures

1. Primary Outcome Measure:

Measure Title	FEV1(Forced Expiratory Volume in 1 Second) Measured by Spirometry 5 Minutes Post Dose
Measure Description	FEV1(Forced Expiratory Volume in 1 second) measured by spirometry 5 minutes post dose, percentage change versus pre dose FEV1
Time Frame	Pre-dose and 5 minutes post-dose
Safety Issue?	No

Analysis Population Description

[Not Specified]

Reporting Groups

	Description
Formoterol	Formoterol Turbuhaler 9 mcg
Salmeterol	Serevent Diskus (salmeterol) 50 mcg
Placebo	Placebo salmeterol Diskus and Placebo Turbuhaler

Measured Values

	Formoterol	Salmeterol	Placebo
Number of Participants Analyzed	108	109	109
FEV1(Forced Expiratory Volume in 1 Second) Measured by Spirometry 5 Minutes Post Dose [units: percentage change] Geometric Mean (95% Confidence Interval)	1.072 (1.055 to 1.088)	1.041 (1.025 to 1.057)	1.007 (0.992 to 1.023)

2. Secondary Outcome Measure:

Measure Title	Average FEV1 During the First 15 Minutes Post Dose
Measure Description	Average FEV1 during the first 15 minutes post dose, change versus pre dose FEV1
Time Frame	Pre dose and 15 minutes post dose

Safety Issue?	No

Analysis Population Description
[Not Specified]

Reporting Groups

	Description
Formoterol	Formoterol Turbuhaler 9 mcg
Salmeterol	Serevent Diskus (salmeterol) 50 mcg
Placebo	Placebo salmeterol Diskus and Placebo Turbuhaler

Measured Values

	Formoterol	Salmeterol	Placebo
Number of Participants Analyzed	108	109	109
Average FEV1 During the First 15 Minutes Post Dose [units: percentage change] Geometric Mean (95% Confidence Interval)	1.064 (1.052 to 1.077)	1.041 (1.030 to 1.053)	1.012 (1.001 to 1.024)

3. Secondary Outcome Measure:

Measure Title	Average FEV1 During 120 Minutes Post Dose
Measure Description	Average FEV1 during 120 minutes post dose, change versus pre dose FEV1
Time Frame	Pre dose and 120 minutes post dose
Safety Issue?	No

Analysis Population Description
[Not Specified]

Reporting Groups

	Description
Formoterol	Formoterol Turbuhaler 9 mcg
Salmeterol	Serevent Diskus (salmeterol) 50 mcg
Placebo	Placebo salmeterol Diskus and Placebo Turbuhaler

Measured Values

	Formoterol	Salmeterol	Placebo
Number of Participants Analyzed	108	109	109
Average FEV1 During 120 Minutes Post Dose [units: percentage change] Geometric Mean (95% Confidence Interval)	1.096 (1.079 to 1.112)	1.082 (1.066 to 1.098)	1.014 (0.999 to 1.029)

4. Secondary Outcome Measure:

Measure Title	Percentage of Patients Who Has Achieved at Least 12 % Increase in FEV1
Measure Description	Percentage of patients who has achieved at least 12 % increase in FEV1 at each time point between 5 to 120 minutes post dose, change versus pre dose FEV1
Time Frame	Pre dose, 5, 10, 15, 20, 30, 40, 50, 60 and 120 minutes post dose
Safety Issue?	No

Analysis Population Description
[Not Specified]

Reporting Groups

	Description
Formoterol	Formoterol Turbuhaler 9 mcg
Salmeterol	Serevent Diskus (salmeterol) 50 mcg
Placebo	Placebo salmeterol Diskus and Placebo Turbuhaler

Measured Values

	Formoterol	Salmeterol	Placebo
Number of Participants Analyzed	108	109	109
Percentage of Patients Who Has Achieved at Least 12 % Increase in FEV1 [units: Percentage of Participants]			
5 min	23.1	9.2	6.4
10 min	38.0	17.6	7.3
15 min	39.8	23.9	9.2
20 min	44.4	27.5	10.1

	Formoterol	Salmeterol	Placebo
30 min	45.4	32.1	13.8
40 min	49.1	36.7	15.6
50 min	53.7	40.4	16.5
60 min	54.6	43.1	18.3
120 min	55.6	48.6	20.2

Statistical Analysis 1 for Percentage of Patients Who Has Achieved at Least 12 % Increase in FEV1

Statistical Analysis Overview	Comparison Groups	Formoterol, Salmeterol
	Comments	[Not specified]
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]

Statistical Test of Hypothesis	P-Value	0.002
	Comments	[Not specified]
	Method	Regression, Cox
	Comments	[Not specified]

Method of Estimation	Estimation Parameter	Hazard Ratio (HR)
	Estimated Value	2.090
	Confidence Interval	(2-Sided) 95% 1.31 to 3.35
	Estimation Comments	[Not specified]

Statistical Analysis 2 for Percentage of Patients Who Has Achieved at Least 12 % Increase in FEV1

Statistical Analysis Overview	Comparison Groups	Formoterol, Placebo
	Comments	[Not specified]
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]

Statistical Test of Hypothesis	P-Value	0.001
	Comments	[Not specified]
	Method	Regression, Cox
	Comments	[Not specified]

Method of Estimation	Estimation Parameter	Hazard Ratio (HR)
	Estimated Value	6.534
	Confidence Interval	(2-Sided) 95% 3.55 to 12.02
	Estimation Comments	[Not specified]

Statistical Analysis 3 for Percentage of Patients Who Has Achieved at Least 12 % Increase in FEV1

Statistical Analysis Overview	Comparison Groups	Salmeterol, Placebo
	Comments	[Not specified]
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]

Statistical Test of Hypothesis	P-Value	0.001
	Comments	[Not specified]
	Method	Regression, Cox
	Comments	[Not specified]

Method of Estimation	Estimation Parameter	Hazard Ratio (HR)
	Estimated Value	3.127
	Confidence Interval	(2-Sided) 95% 1.77 to 5.52
	Estimation Comments	[Not specified]

5. Secondary Outcome Measure:

Measure Title	Adverse Events
Measure Description	Number of participants with at least 1 AE.

Time Frame	At baseline and at each day of treatment
Safety Issue?	No

Analysis Population Description
[Not Specified]

Reporting Groups

	Description
Formoterol	Formoterol Turbuhaler 9 mcg
Salmeterol	Serevent Diskus (salmeterol) 50 mcg
Placebo	Placebo salmeterol Diskus and Placebo Turbuhaler

Measured Values

	Formoterol	Salmeterol	Placebo
Number of Participants Analyzed	108	109	109
Adverse Events [units: Participants]	6	6	2

Reported Adverse Events

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

Reporting Groups

	Description
Formoterol	Formoterol Turbuhaler 9 mcg
Salmeterol	Serevent Diskus (salmeterol) 50 mcg
Placebo	Placebo salmeterol Diskus and Placebo Turbuhaler

Serious Adverse Events

	Formoterol	Salmeterol	Placebo
	Affected/At Risk (%)	Affected/At Risk (%)	Affected/At Risk (%)
Total	0/108 (0%)	0/109 (0%)	0/109 (0%)

Other Adverse Events

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

	Formoterol	Salmeterol	Placebo
	Affected/At Risk (%)	Affected/At Risk (%)	Affected/At Risk (%)
Total	0/108 (0%)	0/109 (0%)	0/109 (0%)

Limitations and Caveats

[Not specified]

More Information

Certain Agreements:

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

The only disclosure restriction on the PI is that the sponsor can review results communications prior to public release and can embargo communications regarding trial results for a period that is less than or equal to 60 days from the time submitted to the sponsor for review. The sponsor cannot require changes to the communication and cannot extend the embargo.

Results Point of Contact:

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