



## Clinical trial results:

**GR activity in induced sputum macrophages, and a change in inflammatory biomarkers 2-hours after a single dose of either Symbicort®/Budesonide/Formoterol or placebo in Chronic Obstructive Pulmonary Disease (COPD).**

### Summary

EudraCT number	2010-020440-35
Trial protocol	GB
Global end of trial date	30 April 2015

### Results information

Result version number	v1 (current)
This version publication date	19 June 2020
First version publication date	19 June 2020

### Trial information

#### Trial identification

Sponsor protocol code	D589BC00004
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#### Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01787097
WHO universal trial number (UTN)	-

Notes:

### Sponsors

Sponsor organisation name	Imperial College London
Sponsor organisation address	South Kensington, London, United Kingdom, SW7 2AZ
Public contact	Omar Usmani, Imperial College London, o.usmani@imperial.ac.uk
Scientific contact	Omar Usmani, Imperial College London, o.usmani@imperial.ac.uk

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	30 April 2016
Is this the analysis of the primary completion data?	Yes
Primary completion date	30 April 2015
Global end of trial reached?	Yes
Global end of trial date	30 April 2015
Was the trial ended prematurely?	No

Notes:

## General information about the trial

Main objective of the trial:

The research question is whether inhaled drug treatments in combination (long-acting beta-2-agonists (LABA) together with inhaled corticosteroid (ICS)), that are routinely used for chronic obstructive pulmonary disease (COPD) patients can improve inflammation in the cells of the sputum/mucus from these patients compared to either drug component alone.

Protection of trial subjects:

N/A

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	01 January 2013
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 Kingdom: 31
Worldwide total number of subjects	31
EEA total number of subjects	31

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)	31
From 65 to 84 years	0
85 years and over	0

## Subject disposition

### Recruitment

Recruitment details:

Patients were recruited between January 2013 and April 2015. 1 participant withdrew before randomisation.

### Pre-assignment

Screening details:

Patients with chronic obstructive pulmonary disease (COPD).

### Period 1

Period 1 title	Overall (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?	No
<b>Arm title</b>	Formoterol 24ug

Arm description:

Formoterol (FORM) total dose 24ug

Arm type	Active comparator
Investigational medicinal product name	Formoterol (FORM) total dose 24ug
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Inhalation powder
Routes of administration	Inhalation use

Dosage and administration details:

Formoterol (FORM) total dose 24ug

<b>Arm title</b>	Symbicort® Total Dose 400ug/12ug
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Arm description:

Symbicort® Total Dose 400ug/12ug

Arm type	Active comparator
Investigational medicinal product name	Symbicort® Total Dose 400ug/12ug
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Inhalation powder
Routes of administration	Inhalation use

Dosage and administration details:

Symbicort® Total Dose 400ug/12ug

<b>Arm title</b>	Symbicort® Total Dose 800ug/24ug
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Arm description:

Symbicort® Total Dose 800ug/24ug

Arm type	Experimental
Investigational medicinal product name	Symbicort® Total Dose 800ug/24ug
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Inhalation powder
Routes of administration	Inhalation use

Dosage and administration details:  
Symbicort® Total Dose 800ug/24ug

<b>Arm title</b>	BUD Total Dose 800ug
Arm description: BUD Total Dose 800ug	
Arm type	Active comparator
Investigational medicinal product name	BUD Total Dose 800ug
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Inhalation powder
Routes of administration	Inhalation use
Dosage and administration details: BUD Total Dose 800ug	

<b>Number of subjects in period 1</b>	Formoterol 24ug	Symbicort® Total Dose 400ug/12ug	Symbicort® Total Dose 800ug/24ug
Started	8	7	7
Completed	7	7	7
Not completed	1	0	0
Consent withdrawn by subject	1	-	-

<b>Number of subjects in period 1</b>	BUD Total Dose 800ug
Started	9
Completed	9
Not completed	0
Consent withdrawn by subject	-

## Baseline characteristics

### Reporting groups<sup>[1]</sup>

Reporting group title	Overall
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Reporting group description: -

Notes:

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

Justification: subject withdrew before randomization.

Reporting group values	Overall	Total	
Number of subjects	30	30	
Age categorical			
Units: Subjects			
Adults (18-64 years)	30	30	
Age continuous			
Units: years			
arithmetic mean	66		
standard deviation	± 6.4	-	
Gender categorical			
Units: Subjects			
Female	20	20	
Male	10	10	
Pre-bronchodilator FEV1 (% pred.)			
Units: % predicted			
median	62		
inter-quartile range (Q1-Q3)	55 to 70	-	
Pre-bronchodilator FVC (% pred.)			
Units: % predicted			
median	93		
inter-quartile range (Q1-Q3)	83 to 103	-	
GR activity			
Units: Relative to baseline (%)			
arithmetic mean	1		
standard deviation	± 0	-	
Sputum CXCL8			
Units: ng/mL			
median	2.3		
inter-quartile range (Q1-Q3)	1.4 to 4	-	

## End points

### End points reporting groups

Reporting group title	Formoterol 24ug
Reporting group description: Formoterol (FORM) total dose 24ug	
Reporting group title	Symbicort® Total Dose 400ug/12ug
Reporting group description: Symbicort® Total Dose 400ug/12ug	
Reporting group title	Symbicort® Total Dose 800ug/24ug
Reporting group description: Symbicort® Total Dose 800ug/24ug	
Reporting group title	BUD Total Dose 800ug
Reporting group description: BUD Total Dose 800ug	

### Primary: GR-GRE Binding (Relative to Baseline)

End point title	GR-GRE Binding (Relative to Baseline)
End point description: Enzyme immunosorbent assay system	
End point type	Primary
End point timeframe: Screening visit and 2 hours post inhalation of treatment	

End point values	Formoterol 24ug	Symbicort® Total Dose 400ug/12ug	Symbicort® Total Dose 800ug/24ug	BUD Total Dose 800ug
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	5	6	6	7
Units: Fold activation				
arithmetic mean (standard error)	1.1 (± .1)	1.8 (± .1)	2.3 (± .4)	2.1 (± .2)

### Statistical analyses

Statistical analysis title	GR-GRE Binding (Relative to Baseline)
Statistical analysis description: Statistical Analysis 1 for GR-GRE Binding (Relative to Baseline)	
Comparison groups	Symbicort® Total Dose 400ug/12ug v Symbicort® Total Dose 800ug/24ug

Number of subjects included in analysis	12
Analysis specification	Pre-specified
Analysis type	superiority
P-value	$\leq 0.003$
Method	Wilcoxon (Mann-Whitney)

## Adverse events

### Adverse events information<sup>[1]</sup>

Timeframe for reporting adverse events:

4 months

Adverse event reporting additional description:

All Adverse Events during the clinical investigation will be recorded and documented in the relevant section of the Case Report Form

Assessment type	Systematic
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### Dictionary used

Dictionary name	MedDRA
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Dictionary version	1.0
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### Reporting groups

Reporting group title	Formoterol 24ug
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Reporting group description:

Formoterol (FORM) total dose 24ug

Reporting group title	Symbicort® Total Dose 400ug/12ug
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Reporting group description:

Symbicort® Total Dose 400ug/12ug

Reporting group title	Symbicort® Total Dose 800ug/24ug
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Reporting group description:

Symbicort® Total Dose 800ug/24ug

Reporting group title	BUD Total Dose 800ug
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Reporting group description:

BUD Total Dose 800ug

Serious adverse events	Formoterol 24ug	Symbicort® Total Dose 400ug/12ug	Symbicort® Total Dose 800ug/24ug
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 30 (0.00%)	0 / 30 (0.00%)	0 / 30 (0.00%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events			

Serious adverse events	BUD Total Dose 800ug		
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 30 (0.00%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events			

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



<b>Non-serious adverse events</b>	Formoterol 24ug	Symbicort® Total Dose 400ug/12ug	Symbicort® Total Dose 800ug/24ug
Total subjects affected by non-serious adverse events subjects affected / exposed	0 / 30 (0.00%)	0 / 30 (0.00%)	0 / 30 (0.00%)

<b>Non-serious adverse events</b>	BUD Total Dose 800ug		
Total subjects affected by non-serious adverse events subjects affected / exposed	0 / 30 (0.00%)		

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Notes:

[1] - There are no non-serious adverse events recorded for these results. It is expected that there will be at least one non-serious adverse event reported.

Justification: There were no adverse events.

## More information

### Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? No

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### Interruptions (globally)

Were there any global interruptions to the trial? No

### Limitations and caveats

Limitations of the trial such as small numbers of subjects analysed or technical problems leading to unreliable data.

Quality and quantity of sputum production varied between patients and between patient visits. Four patients withdrew consent prior to starting intervention. One patient discontinued- did not attend visit 2.
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Notes: