Clinical trial results:
An Open Label Oxygen Enhanced Imaging Biomarker Study to Assess the Role of Fluticasone/Formoterol upon Airway Function in Moderate to Severe Persistent Asthma.

Summary

EudraCT number	2015-000172-98
Trial protocol	GB
Global end of trial date	31 January 2018

Results information

Result version number	v1 (current)
This version publication date	03 January 2020
First version publication date	03 January 2020
Summary attachment (see zip file)	study summary data tables (final study summary data tables.pdf) patient level data (OE-MRI_DATA_patient level_eudraCT.xlsx)

Trial information

Trial identification

Sponsor protocol code	2015-000172-98

Additional study identifiers

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

Notes:

Sponsors

Sponsor organisation name	University of Leicester
Sponsor organisation address	Gwendolen Road, Leicester, United Kingdom, LE5 4PW
Public contact	Salman Siddiqui, University Hospitals of Leicester NHS Trust, 0044 01162586841, ss338@le.ac.uk
Scientific contact	Salman Siddiqui, University Hospitals of Leicester NHS Trust, 0044 01162586841, ss338@le.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	07 October 2019
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	31 January 2018
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

Inhaled Fluticasone/Formoterol improves both large and small airway function in moderate to severe persistent asthma.

The primary objective of this study is to demonstrate a statistically significant change in both OE-MRI imaging biomarkers [oxygen exponential washout time (Tdown) and major airway ventilation (Tvent) time] using dynamic OE-MRI in moderate-to-severe asthmatics, within 30 minutes of administration of two observed inhalations via spacer of Fluticasone/Formoterol [250/10].

Protection of trial subjects:

All patients were given detailed information on Oe-MRI, had pre MRI safety questionnaires and were in regular communication with the MRI radiographers during the MRI scans.

Background therapy:

Controller medications used for moderate to severe persistent asthma.

Evidence for comparator:

Single MRI analyst blind and open label study

Actual start date of recruitment	01 January 2015
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: 16
Worldwide total number of subjects	16
EEA total number of subjects	16

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)	12
From 65 to 84 years	4
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Single centre recruitment, Glenfield Hospital, Leicester, UK.
All patients were identified and recruited from secondary care asthma clinics.

Pre-assignment

Screening details:

The study population includes male and female symptomatic patients with moderate-to-severe adult asthma (GINA 3-4).In addition patients selected had evidence of fixed spirometric airflow obstruction based upon post bronchodilator spirometry, to maximise the probability of small airways disease.

Pre-assignment period milestones

Number of subjects started	16
Number of subjects completed	16

Period 1

Period 1 title	pre FP/FORM
Is this the baseline period?	Yes
Allocation method	Not applicable
Blinding used	Not blinded

Blinding implementation details:

Oe-MRI analysts were blinded to MRI scan sequence (pre vs post FP/FORM)

Arms

Arm title	pre FP/FORM

Arm description:

pre inhalation of FP/FORM

Arm type	pre FP/FORM inhalation
Investigational medicinal product name	fluticasone prioprionate/formoterol fumarate [FP/FORM, 250/10 µg]
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Suspension and solution for spray
Routes of administration	Inhalation use

Dosage and administration details:

250/10 µg , two inhalations, via an aerochamber

Number of subjects in period 1	pre FP/FORM
Started	16
Completed	16

Period 2

Period 2 title	30 minutes Post FP/FORM
Is this the baseline period?	No
Allocation method	Not applicable
Blinding used	Not blinded

Blinding implementation details:

Oe-MRI analysts were blinded to MRI scan sequence (pre vs post FP/FORM)

Arms

Arm title	Post FP/FORM

Arm description:

30 minutes post inhalation of FP/FORM

Arm type	Experimental
Investigational medicinal product name	fluticasone prioprionate/formoterol fumarate [FP/FORM, 250/10 µg]
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Suspension and solution for spray
Routes of administration	Inhalation use

Dosage and administration details:

250/10 µg , two inhalations, via an aerochamber

Number of subjects in period 2	Post FP/FORM
Started	16
Completed	16

Baseline characteristics

Reporting groups	
Reporting group title	pre FP/FORM

Reporting group description: -

Reporting group values	pre FP/FORM	Total	
Number of subjects	16	16	
Age categorical Units: Subjects			
In utero	0	0	
Preterm newborn infants (gestational age < 37 wks)	0	0	
Newborns (0-27 days)	0	0	
Infants and toddlers (28 days-23 months)	0	0	
Children (2-11 years)	0	0	
Adolescents (12-17 years)	0	0	
Adults (18-64 years)	12	12	
From 65-84 years	4	4	
85 years and over	0	0	
Gender categorical Units: Subjects			
Female	8	8	
Male	8	8	

End points

End points reporting groups	
Reporting group title	pre FP/FORM
Reporting group description: pre inhalation of FP/FORM	
Reporting group title	Post FP/FORM
Reporting group description: 30 minutes post inhalation of FP/FORM	

Primary: Tvent - whole lung	
End point title	Tvent - whole lung
End point description: whole lung median Tvent	
End point type	Primary
End point timeframe: pre and 30 minutes post FP/FORM inhalation	

End point values	pre FP/FORM	Post FP/FORM		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	16	16		
Units: seconds				
median (inter-quartile range (Q1-Q3))	53.3 (47.6 to 60.2)	50.0 (37.2 to 55.9)		

Attachments (see zip file)	Tvent data/Tvent.xlsx

Statistical analyses

Statistical analysis title	Tvent analysis
Statistical analysis description: pre vs post FP/FORM analysis	
Comparison groups	pre FP/FORM v Post FP/FORM
Number of subjects included in analysis	32
Analysis specification	Pre-specified
Analysis type	equivalence[1]
P-value	= 0.05
Method	Wilcoxon signed-rank test

Notes:
[1] - paired analysis

Primary: Tdown

End point title	Tdown
End point description: whole lung median Tdown	
End point type	Primary
End point timeframe: pre and 30 minutes post FP/FORM inhalation	

End point values	pre FP/FORM	Post FP/FORM		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	16	16		
Units: minutes				
median (inter-quartile range (Q1-Q3))	1.29 (1.17 to 1.69)	1.27 (1.08 to 1.43)		

Attachments (see zip file)	Tdown data/Tdown.xlsx

Statistical analyses

Statistical analysis title	Tvent
Statistical analysis description: analysis of the change in Tvent 30 minutes following FP/FORM inhalation	
Comparison groups	pre FP/FORM v Post FP/FORM
Number of subjects included in analysis	32
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	= 0.17
Method	Wilcoxon signed-rank test

Adverse events

Adverse events information

Timeframe for reporting adverse events:

All SAEs, except those expected (as defined in the trial protocol) that do not require immediate reporting were required to be reported to the Sponsor within one working day of discovery or notification of the event

Assessment type	Systematic

Dictionary used

Dictionary name	Mannual
Dictionary version	0

Reporting groups

Reporting group title	Trial partipants that competed study screening

Reporting group description:

Participant that were screened for the study and an entered the study specific assessments

Serious adverse events	Trial partipants that competed study screening		
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 16 (0.00%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events	0		

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

Non-serious adverse events	Trial partipants that competed study screening		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	1 / 16 (6.25%)		
Respiratory, thoracic and mediastinal disorders			
chest infection	Additional description: Mild to Moderate chest infection in a single participant, deemed unlikely to be causality related to the IMP. start date: 20-05-2015 end date: 15-06-2016		
subjects affected / exposed	1 / 16 (6.25%)		
occurrences (all)	1		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
17 March 2017	Sample size was increased from 12 to a minimum of 15 participants to enable meaningful analysis and reporting of additional Oe-MRI secondary endpoints (EoxFb and Kox). Ethical approval was gained to screen an additional 6 participants to allow for screen failures.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported