Clinical trial results:
AN OPEN STUDY TO ASSESS THE ROBUSTNESS OF THE CRC749 DEVICE BY PHARMACEUTICAL PERFORMANCE FOLLOWING TWICE DAILY DOSING OF MGR001 ADMINISTERED VIA ORAL INHALATION IN SUBJECTS WITH ASTHMA OR CHRONIC OBSTRUCTIVE PULMONARY DISEASE (COPD)

Summary

EudraCT number	2015-000463-13
Trial protocol	GB
Global end of trial date	12 June 2015

Results information

Result version number	v1 (current)
This version publication date	28 June 2020
First version publication date	28 June 2020

Trial information

Trial identification

Sponsor protocol code	MGR001-1010

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02474017
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Mylan Pharma UK Ltd
Sponsor organisation address	20 Station Close, Potters Bar, Hertfordshire, United Kingdom, EN6 1TL
Public contact	Richard Allan, Mylan Pharma UK Ltd, +44 1304 626255, richard.allan@mylan.co.uk
Scientific contact	Richard Allan, Mylan Pharma UK Ltd, +44 1304 626255, richard.allan@mylan.co.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	23 October 2015
Is this the analysis of the primary completion data?	Yes
Primary completion date	12 June 2015
Global end of trial reached?	Yes
Global end of trial date	12 June 2015
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To confirm the robustness of the CRC749 inhaler following 21 (±3) days BID (twice a day) dosing of MGR001 (250/50 µg).
- The MGR001 product will be considered robust if inhalers returned in a testable condition meet the proposed commercial specification upon in vitro testing of pharmaceutical performance

Protection of trial subjects:

Prior to the initiation of the study at each study center, the clinical study protocol, subject information sheet, informed consent form (ICF), and all other relevant study documentation were submitted to and approved by the responsible national Independent Ethics Committee (IEC) / Institutional Review Board (IRB).
The study was conducted in accordance with the guidelines set forth in 21 Code of Federal Regulations (CFR), parts 312, 50 and 56.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	09 May 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: 111
Worldwide total number of subjects	111
EEA total number of subjects	111

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)	11
Adults (18-64 years)	90

From 65 to 84 years	10
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

One hundred forty-three subjects were screened for the study; one hundred eleven subjects met inclusion criteria, received MGR001 250/50, and were included in Safety Analysis Set.

Pre-assignment

Screening details:

Subject eligibility were reviewed and documented by an appropriately qualified member of the Investigator’s study team before subjects were included in the study.

Period 1

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

Arms

Arm title	MGR001 250/50

Arm description:

Each subject was given MGR001 250/50, which contained 250 mcg FP and 50 mcg salmeterol [as xinafoate salt] inhalation powder, pre-dispensed for oral inhalation in the CRC749 inhaler.
The following treatment was administered during the study: MGR001 250/50 BID for 21.5 (±3) days with the final dose in the clinic at Visit 3 (Day 22 [±3]). Each inhaler contained 60 doses.

Arm type	Experimental
Investigational medicinal product name	MGR001 250/50
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Inhalation powder
Routes of administration	Inhalation use, Oral use

Dosage and administration details:

one 250/50 inhalation twice a day

Number of subjects in period 1	MGR001 250/50
Started	111
Completed	108
Not completed	3
Adverse event, non-fatal	1
Protocol deviation	2

Baseline characteristics

Reporting groups

Reporting group title	MGR001 250/50

Reporting group description:

Each subject was given MGR001 250/50, which contained 250 mcg FP and 50 mcg salmeterol [as xinafoate salt] inhalation powder, pre-dispensed for oral inhalation in the CRC749 inhaler.
The following treatment was administered during the study: MGR001 250/50 BID for 21.5 (±3) days with the final dose in the clinic at Visit 3 (Day 22 [±3]). Each inhaler contained 60 doses.

Reporting group values	MGR001 250/50	Total	
Number of subjects	111	111	
Age categorical Units: Subjects			
Children (2-11 years)	0	0	
Adolescents (12-17 years)	11	11	
Adults (18-64 years)	90	90	
From 65-84 years	10	10	
85 years and over	0	0	
Age continuous Units: years			
arithmetic mean	41.4		
standard deviation	± 16.33	-	
Gender categorical Units: Subjects			
Female	48	48	
Male	63	63	
Disorder Units: Subjects			
Asthma	94	94	
Chronic obstructive pulmonary disease (COPD)	17	17	

Subject analysis sets

Subject analysis set title	Subjects with COPD
Subject analysis set type	Per protocol

Subject analysis set description:

Number of subjects with COPD in safety analysis set

Subject analysis set title	Subjects with Asthma
Subject analysis set type	Per protocol

Subject analysis set description:

Number of subjects with asthma in safety analysis set

Reporting group values	Subjects with COPD	Subjects with Asthma	
Number of subjects	17	94	
Age categorical Units: Subjects			
Children (2-11 years)	0	0	

Adolescents (12-17 years)	0	11	
Adults (18-64 years)	7	83	
From 65-84 years	10	0	
85 years and over	0	0	
Age continuous Units: years arithmetic mean standard deviation	±	±	
Gender categorical Units: Subjects			
Female Male			
Disorder Units: Subjects			
Asthma Chronic obstructive pulmonary disease (COPD)			

End points

End points reporting groups

Reporting group title	MGR001 250/50

Reporting group description:

Each subject was given MGR001 250/50, which contained 250 mcg FP and 50 mcg salmeterol [as xinafoate salt] inhalation powder, pre-dispensed for oral inhalation in the CRC749 inhaler.
The following treatment was administered during the study: MGR001 250/50 BID for 21.5 (±3) days with the final dose in the clinic at Visit 3 (Day 22 [±3]). Each inhaler contained 60 doses.

Subject analysis set title	Subjects with COPD
Subject analysis set type	Per protocol

Subject analysis set description:

Number of subjects with COPD in safety analysis set

Subject analysis set title	Subjects with Asthma
Subject analysis set type	Per protocol

Subject analysis set description:

Number of subjects with asthma in safety analysis set

Primary: In Vitro Testing of FP and salmeterol pharmaceutical performance

End point title	In Vitro Testing of FP and salmeterol pharmaceutical performance[1]

End point description:

All results obtained during analytical testing (i.e., microbiology, water content, emitted dose content uniformity, aerodynamic particle size distribution (APSD), assay, and degradations products) demonstrate that the fluticasone propionate (FP) and salmeterol pharmaceutical performance was preserved.

The data were not analysed in a standard way, hence only the conclusions from in vitro testing have been disclosed.

End point type	Primary

End point timeframe:

At Visit 3 Day 22

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: A statistical analysis of the in vitro data was not required per the protocol, therefore no statistical analysis was performed.

End point values	MGR001 250/50			
Subject group type	Reporting group			
Number of subjects analysed	111[2]			
Units: Number	0			

Notes:

[2] - The data were not analysed in a standard way.

Statistical analyses

No statistical analyses for this end point

Secondary: Disposition of Inhalers Dispensed and Suitability for Testing

End point title	Disposition of Inhalers Dispensed and Suitability for Testing

End point description:

End point type	Secondary

End point timeframe:

From Screening to Day 22, Visit 3

End point values	MGR001 250/50			
Subject group type	Reporting group			
Number of subjects analysed	111			
Units: Number				
Inhalers Issued	111			
Inhalers Returned	111			
Inhalers Unsuitable or Unavailable for Testing	4			
Inhalers Available for Testing	107			
Inhalers Utilized for Testing	84			
Spare Inhalers	23			

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with treatment-emergent adverse event (TEAE)

End point title	Number of subjects with treatment-emergent adverse event (TEAE)

End point description:

End point type	Secondary

End point timeframe:

From screening to Day 22, Visit 3

End point values	MGR001 250/50			
Subject group type	Reporting group			
Number of subjects analysed	111			
Units: Number				
Number of Subjects With a TEAE	34			
Number of Subjects With a Serious TEAE	0			
Number of Subjects With a Treatment-Related TEAE	15			
Leading to Discontinuation of Study Medication	1			
Number of Subjects Who Had TEAE Leading to Death	0			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information	
Timeframe for reporting adverse events: From screening to Day 22, Visit 3 (End of Study)	
Assessment type	Non-systematic
Dictionary used	
Dictionary name	MedDRA
Dictionary version	18_E
Reporting groups	
Reporting group title	MGR001 250/50

Reporting group description: -

Serious adverse events	MGR001 250/50		
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 111 (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	MGR001 250/50		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	34 / 111 (30.63%)		
Injury, poisoning and procedural complications			
Muscle strain			
subjects affected / exposed	1 / 111 (0.90%)		
occurrences (all)	1		
Cardiac disorders			
Atrial fibrillation			
subjects affected / exposed	1 / 111 (0.90%)		
occurrences (all)	1		
Nervous system disorders			
Headache			
subjects affected / exposed	11 / 111 (9.91%)		
occurrences (all)	15		
General disorders and administration site conditions			

Malaise			
subjects affected / exposed	1 / 111 (0.90%)		
occurrences (all)	2		
Gastrointestinal disorders			
Diarrhea			
subjects affected / exposed	1 / 111 (0.90%)		
occurrences (all)	1		
Dyspepsia			
subjects affected / exposed	2 / 111 (1.80%)		
occurrences (all)	2		
Mouth Ulceration			
subjects affected / exposed	1 / 111 (0.90%)		
occurrences (all)	1		
Respiratory, thoracic and mediastinal disorders			
Dysphonia			
subjects affected / exposed	4 / 111 (3.60%)		
occurrences (all)	4		
Oropharyngeal Pain			
subjects affected / exposed	4 / 111 (3.60%)		
occurrences (all)	5		
Cough			
subjects affected / exposed	2 / 111 (1.80%)		
occurrences (all)	2		
Dry throat			
subjects affected / exposed	1 / 111 (0.90%)		
occurrences (all)	1		
Dyspnoea			
subjects affected / exposed	1 / 111 (0.90%)		
occurrences (all)	1		
Haemoptysis			
subjects affected / exposed	1 / 111 (0.90%)		
occurrences (all)	1		
Wheezing			
subjects affected / exposed	2 / 111 (1.80%)		
occurrences (all)	2		
Skin and subcutaneous tissue disorders			

Urticaria			
subjects affected / exposed	1 / 111 (0.90%)		
occurrences (all)	1		
Psychiatric disorders			
Conversion disorder			
subjects affected / exposed	1 / 111 (0.90%)		
occurrences (all)	1		
Sleep terror			
subjects affected / exposed	1 / 111 (0.90%)		
occurrences (all)	1		
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	1 / 111 (0.90%)		
occurrences (all)	1		
Muscle spasms			
subjects affected / exposed	1 / 111 (0.90%)		
occurrences (all)	1		
Myalgia			
subjects affected / exposed	1 / 111 (0.90%)		
occurrences (all)	1		
Infections and infestations			
Ear Infection			
subjects affected / exposed	1 / 111 (0.90%)		
occurrences (all)	1		
Gastroenteritis			
subjects affected / exposed	1 / 111 (0.90%)		
occurrences (all)	1		
Oral Candidiasis			
subjects affected / exposed	1 / 111 (0.90%)		
occurrences (all)	1		
Pharyngitis			
subjects affected / exposed	2 / 111 (1.80%)		
occurrences (all)	2		
Respiratory Tract Infection			
subjects affected / exposed	1 / 111 (0.90%)		
occurrences (all)	1		

Rhinitis subjects affected / exposed occurrences (all)	2 / 111 (1.80%) 2		
Upper Respiratory Tract Infection subjects affected / exposed occurrences (all)	2 / 111 (1.80%) 2		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? No

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported