Clinical trial results:
A Double-Blind, Randomised, Placebo-controlled, Parallel Group, International, Multi-centre Phase 2 Trial Investigating the Safety and Efficacy of CRD007 in Adult Subjects with Asthma

Summary

EudraCT number	2015-002656-26
Trial protocol	DK GB BG
Global end of trial date	17 February 2017

Results information

Result version number	v1 (current)
This version publication date	08 July 2017
First version publication date	08 July 2017

Trial information

Trial identification

Sponsor protocol code	RSPR-008

Additional study identifiers

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

Notes:

Sponsors

Sponsor organisation name	RSPR Pharma AB
Sponsor organisation address	Kornhamnstorg 53, Stockholm, Sweden, SE-111 27
Public contact	Carl-Johan Dalsgaard, Chief Executive Officer, RSPR Pharma AB, 46 709759863, carl-johan.dalsgaard@ofco.se
Scientific contact	Carl-Johan Dalsgaard, Chief Executive Officer, RSPR Pharma AB, 46 709759863, carl-johan.dalsgaard@ofco.se

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	11 May 2017
Is this the analysis of the primary completion data?	Yes
Primary completion date	17 February 2017
Global end of trial reached?	Yes
Global end of trial date	17 February 2017
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To investigate the efficacy of 200 mg CRD007 administered orally b.i.d. on asthma control during tapering of a background therapy of standard asthma controller medication (ICS and LABA).

Protection of trial subjects:

Before this trial was implemented, the protocol, the subject information and subject consent form, and other documents as required, were reviewed by properly constituted Independent Ethics Committees (IECs) and by the national regulatory authorities

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	02 November 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	Poland: 36
Country: Number of subjects enrolled	United Kingdom: 29
Country: Number of subjects enrolled	Bulgaria: 78
Country: Number of subjects enrolled	Denmark: 25
Worldwide total number of subjects	168
EEA total number of subjects	168

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)	168
From 65 to 84 years	0

85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Following a run-in period (screening) and initiation of background therapy, patients were randomised to either active treatment or placebo.

Pre-assignment

Screening details:

Patients were screened over a period of 4 weeks

Period 1

Period 1 title	Treatment (overall period)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Investigator, Subject

Arms

Are arms mutually exclusive?	Yes
Arm title	CRD007

Arm description:

Active

Arm type	Active comparator
Investigational medicinal product name	CRD007
Investigational medicinal product code	
Other name	Pemirolast
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

200mg CRD007 bid

Arm title	Placebo

Arm description: -

Arm type	Placebo
Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Two tablets bid

Number of subjects in period 1	CRD007	Placebo
Started	90	78
Completed	90	78

Baseline characteristics

Reporting groups	
Reporting group title	CRD007
Reporting group description: Active	
Reporting group title	Placebo
Reporting group description: -	

Reporting group values	CRD007	Placebo	Total
Number of subjects	90	78	168
Age categorical Units: Subjects			
In utero	0	0	0
Preterm newborn infants (gestational age < 37 wks)	0	0	0
Newborns (0-27 days)	0	0	0
Infants and toddlers (28 days-23 months)	0	0	0
Children (2-11 years)	0	0	0
Adolescents (12-17 years)	0	0	0
Adults (18-64 years)	90	78	168
From 65-84 years	0	0	0
85 years and over	0	0	0
Gender categorical Units: Subjects			
Female	61	48	109
Male	29	30	59

End points

End points reporting groups	
Reporting group title	CRD007
Reporting group description: Active	
Reporting group title	Placebo
Reporting group description: -	

Primary: ICS dose	
End point title	ICS dose
End point description:	
End point type	Primary
End point timeframe: Week 4 to 14	

End point values	CRD007	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	90	78		
Units: mg daily dose	735	731		

Statistical analyses

Statistical analysis title	Primary analysis
Comparison groups	Placebo v CRD007
Number of subjects included in analysis	168
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	< 0.05
Method	ANCOVA
Parameter estimate	Mean difference (final values)
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.05
upper limit	0.95
Variability estimate	Standard deviation

Adverse events

Adverse events information	
Timeframe for reporting adverse events:	
AEs were reported date of informed consent until end of trial	
Adverse event reporting additional description:	
NA	
Assessment type	Systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	18.1

Reporting groups	
Reporting group title	CRD007
Reporting group description:	
Active treatment	
Reporting group title	Placebo
Reporting group description:	
Placebo	

Serious adverse events	CRD007	Placebo	
Total subjects affected by serious adverse events			
subjects affected / exposed	2 / 90 (2.22%)	3 / 78 (3.85%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events	0	0	
Cardiac disorders			
Stroke			
subjects affected / exposed	0 / 90 (0.00%)	1 / 78 (1.28%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Angina pectoris			
subjects affected / exposed	0 / 90 (0.00%)	1 / 78 (1.28%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nervous system disorders			
Loss of consciousness			
subjects affected / exposed	1 / 90 (1.11%)	0 / 78 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cerebral ischaemia			

subjects affected / exposed	1 / 90 (1.11%)	0 / 78 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
Exacerbation of diverticular disease			
subjects affected / exposed	0 / 90 (0.00%)	1 / 78 (1.28%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Musculoskeletal and connective tissue disorders			
Arthritis			
subjects affected / exposed	0 / 90 (0.00%)	1 / 78 (1.28%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

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

Non-serious adverse events	CRD007	Placebo	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	52 / 90 (57.78%)	42 / 78 (53.85%)	
Investigations			
Blood creatine increased			
subjects affected / exposed	2 / 90 (2.22%)	0 / 78 (0.00%)	
occurrences (all)	2	0	
Injury, poisoning and procedural complications			
Arthropod bite			
subjects affected / exposed	0 / 90 (0.00%)	2 / 78 (2.56%)	
occurrences (all)	0	2	
Vascular disorders			
Hypertension			
subjects affected / exposed	3 / 90 (3.33%)	1 / 78 (1.28%)	
occurrences (all)	3	1	
Nervous system disorders			
Headache			
subjects affected / exposed	3 / 90 (3.33%)	6 / 78 (7.69%)	
occurrences (all)	4	6	
Dizziness			

subjects affected / exposed	3 / 90 (3.33%)	1 / 78 (1.28%)	
occurrences (all)	3	1	
Sciatica			
subjects affected / exposed	2 / 90 (2.22%)	0 / 78 (0.00%)	
occurrences (all)	2	0	
General disorders and administration site conditions			
Fatigue			
subjects affected / exposed	2 / 90 (2.22%)	0 / 78 (0.00%)	
occurrences (all)	2	0	
Influenza like illness			
subjects affected / exposed	2 / 90 (2.22%)	0 / 78 (0.00%)	
occurrences (all)	3	0	
Immune system disorders			
Seasonal allergy			
subjects affected / exposed	0 / 90 (0.00%)	2 / 78 (2.56%)	
occurrences (all)	0	2	
Gastrointestinal disorders			
Nausea			
subjects affected / exposed	3 / 90 (3.33%)	1 / 78 (1.28%)	
occurrences (all)	3	1	
Diarrhoea			
subjects affected / exposed	2 / 90 (2.22%)	1 / 78 (1.28%)	
occurrences (all)	2	1	
Respiratory, thoracic and mediastinal disorders			
Asthma			
subjects affected / exposed	4 / 90 (4.44%)	7 / 78 (8.97%)	
occurrences (all)	4	7	
Cough			
subjects affected / exposed	4 / 90 (4.44%)	1 / 78 (1.28%)	
occurrences (all)	4	2	
Dysphonia			
subjects affected / exposed	3 / 90 (3.33%)	0 / 78 (0.00%)	
occurrences (all)	5	0	
Rhinitis allergic			
subjects affected / exposed	1 / 90 (1.11%)	2 / 78 (2.56%)	
occurrences (all)	1	2	

Dyspnoea			
subjects affected / exposed	2 / 90 (2.22%)	0 / 78 (0.00%)	
occurrences (all)	2	0	
Musculoskeletal and connective tissue disorders			
Muscle spasms			
subjects affected / exposed	0 / 90 (0.00%)	2 / 78 (2.56%)	
occurrences (all)	0	3	
Infections and infestations			
Nasopharyngitis			
subjects affected / exposed	7 / 90 (7.78%)	9 / 78 (11.54%)	
occurrences (all)	10	11	
Rhinitis			
subjects affected / exposed	3 / 90 (3.33%)	4 / 78 (5.13%)	
occurrences (all)	3	4	
Upper respiratory tract infection			
subjects affected / exposed	5 / 90 (5.56%)	1 / 78 (1.28%)	
occurrences (all)	5	1	
Lower respiratory tract infection			
subjects affected / exposed	1 / 90 (1.11%)	3 / 78 (3.85%)	
occurrences (all)	2	3	
Cystitis			
subjects affected / exposed	1 / 90 (1.11%)	2 / 78 (2.56%)	
occurrences (all)	1	2	
Influenza			
subjects affected / exposed	2 / 90 (2.22%)	1 / 78 (1.28%)	
occurrences (all)	2	1	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
26 October 2015	To broaden the targeted patient population the requirement for patients having been on a specific LABA dose of ≥9 µg and ≤18 µg formoterol or 100 µg salmeterol prior to Visit 1 is removed. Instead, it is specified that patients must be treated with a daily stable LABA dose 12 weeks prior to Visit 1 in order to be eligible. In addition, the calculations for FEV1, FVC and reversibility in FEV1 are clarified
24 February 2016	To better reflect the target population, the following criteria are changed: Inclusion Criterion 6 Inclusion Criterion 8 and Randomisation Criterion 2 xclusion Criterion 5 To facilitate trial logistics, Visit 1 assessments are allowed to be conducted over a window of 3 days. To be aligned with standard practice at some of the participating sites, reversibility testing at Visit 1, Visit 2 and Visit 3 may be performed using Salbutamol Dry Powder Inhaler 200-800 µg (changed from 200-400 µg) or 400 µg Salbutamol via pressurised metered dose inhaler with or without spacer. To allow adequate time for trial completion, time-lines for last subject randomised and last subject Last Visit have been extended with 1 quarter. The number of trial subjects will be reduced from the present 200 (100 in each arm) to 160 (80 in each arm). The effect of the change in the sample size will be an increase in the detectable difference between treatment arms from 80 µg to 89 µg for the average daily budesonide dose, and from 20% to 22% for treatment failures. These effects on the detectable difference in the study are considered acceptable. Lastly, minor typographical errors are corrected

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported