Clinical trial results:
A Double-Blind, Randomised, Placebo-controlled, Cross-over, Phase 2 Mannitol Challenge Study, Investigating the Efficacy of CRD007 in Adult Subjects with Asthma

Summary

EudraCT number	2015-000120-28
Trial protocol	DK
Global end of trial date	02 July 2015

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-007

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02609334
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	RSPR Pharma AB
Sponsor organisation address	Kornhamnstorg 53, Stockholm, Sweden, SE-111
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	03 September 2015
Is this the analysis of the primary completion data?	Yes
Primary completion date	02 July 2015
Global end of trial reached?	Yes
Global end of trial date	02 July 2015
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To investigate the efficacy of single doses of 40 mg and 400 mg CRD007 in subjects with asthma

Protection of trial subjects:

AEs were reported in the period from the subject signed the informed consent form until the end of trial participation (Visit 5).
At each visit, the subject was asked about AEs in an objective manner, e.g.: "Have you experienced any problems since the last visit?" and was followed by safety laboratory sampling.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	02 March 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	Denmark: 24
Worldwide total number of subjects	24
EEA total number of subjects	24

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)	24
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

The patients were recruited at two trial sites in Denmark. First patient first visit (FPFV) took place on 26-Mar-2015 and Last patient last visit (LPLV) took place on 02-Jul-2015

Pre-assignment

Screening details:

A total of 83 subjects were screened in order to randomise 24 subjects. 57 subjects were screening failures and 2 subjects did not wish to continue to randomisation. At the screening visit, the subject was assigned a screening number and evaluated for eligibility according to the eligibility criteria (in- and exclusion criteria)

Pre-assignment period milestones

Number of subjects started	24
Number of subjects completed	24

Period 1

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

Arms

Arm title	Mannitol test crossover trial
Arm description: -	
Arm type	Experimental
Investigational medicinal product name	CRD007
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Low dose CRD007, High dose CRD007 and placebo

Number of subjects in period 1	Mannitol test crossover trial
Started	24
Low dose	24
High dose	24
Placebo	24
Completed	24

Baseline characteristics

Reporting groups	
Reporting group title	Mannitol testing
Reporting group description: -	

Reporting group values	Mannitol testing	Total	
Number of subjects	24	24	
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)	24	24	
From 65-84 years	0	0	
85 years and over	0	0	
Gender categorical Units: Subjects			
Female	11	11	
Male	13	13	

Subject analysis sets	
Subject analysis set title	Low dose
Subject analysis set type	Full analysis
Subject analysis set description: Low dose CRD007	
Subject analysis set title	High dose
Subject analysis set type	Full analysis
Subject analysis set description: High dose CRD007	
Subject analysis set title	Placebo
Subject analysis set type	Full analysis
Subject analysis set description: Placebo	

Reporting group values	Low dose	High dose	Placebo
Number of subjects	24	24	23
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)	24	24	23
From 65-84 years	0	0	0
85 years and over	0	0	0
Gender categorical Units: Subjects			
Female Male			

End points

End points reporting groups	
Reporting group title	Mannitol test crossover trial
Reporting group description: -	
Subject analysis set title	Low dose
Subject analysis set type	Full analysis
Subject analysis set description: Low dose CRD007	
Subject analysis set title	High dose
Subject analysis set type	Full analysis
Subject analysis set description: High dose CRD007	
Subject analysis set title	Placebo
Subject analysis set type	Full analysis
Subject analysis set description: Placebo	

Primary: PD15 for mannitol after treatment with CRD007 and placebo

End point title	PD15 for mannitol after treatment with CRD007 and placebo
End point description:	
End point type	Primary
End point timeframe: At least 2 repeatable FEV1 manoeuvers were performed 60 seconds after each dose and the highest FEV1 was used in the calculation.	

End point values	Mannitol test crossover trial	Low dose	High dose	Placebo
Subject group type	Reporting group	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	24	24	24	23
Units: mg				
median (full range (min-max))	158.4 (27.4 to 309)	305.4 (45.9 to 795)	256.7 (11.5 to 795)	234.6 (12.7 to 795)

Statistical analyses

Statistical analysis title	Analysis of variance
Statistical analysis description: With a two-sided test at a 5% significance level, 24 evaluable subjects provide an 80% chance to detect a true PD15 ratio between any two treatments of 1.5. PD15 mannitol was determined by linear interpolation on the log dose scale. PD15 mannitol was compared between the 3 treatments (placebo, CRD007 40 mg and CRD007 400 mg) using an analysis of variance model with fixed factors treatment, period and patient. The analysis was conducted on logged values and the result subsequently transformed ba	
Comparison groups	Mannitol test crossover trial v High dose v Low dose v Placebo

Number of subjects included in analysis	95
Analysis specification	Pre-specified
Analysis type	other
P-value	= 5
Method	t-test, 2-sided

Adverse events

Adverse events information

Timeframe for reporting adverse events:

All events meeting the definition of an AE were to be reported in the period from the subject has signed the informed consent form until the end of trial participation (Visit 5).

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	18

Reporting groups

Reporting group title	High dose
Reporting group description: -	
Reporting group title	Low dose
Reporting group description: -	
Reporting group title	Placebo
Reporting group description: -	

Serious adverse events	High dose	Low dose	Placebo
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 24 (0.00%)	0 / 24 (0.00%)	0 / 23 (0.00%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0

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

Non-serious adverse events	High dose	Low dose	Placebo
Total subjects affected by non-serious adverse events			
subjects affected / exposed	1 / 24 (4.17%)	0 / 24 (0.00%)	1 / 23 (4.35%)
Investigations			
Blood bilirubin abnormal			
subjects affected / exposed	0 / 24 (0.00%)	0 / 24 (0.00%)	1 / 23 (4.35%)
occurrences (all)	0	0	1
Nervous system disorders			
Headache			
subjects affected / exposed	1 / 24 (4.17%)	0 / 24 (0.00%)	0 / 23 (0.00%)
occurrences (all)	1	0	0

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