Clinical trial results:
A Study to Measure Serum Periostin, Asthma-Related Biomarkers and Response to Prednisolone in Adult and Adolescent Patients With Severe Oral Corticosteroid-Dependent Asthma

Summary

EudraCT number	2013-000900-41
Trial protocol	GB
Global end of trial date	28 April 2014

Results information

Result version number	v1 (current)
This version publication date	21 April 2016
First version publication date	21 April 2016
Summary attachment (see zip file)	Supporting document for 1 participant with missing age (Supporting Document.docx)

Trial information

Trial identification

Sponsor protocol code	WB28850

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01948401
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	F. Hoffmann-La Roche, Ltd
Sponsor organisation address	Grenzacherstrasse 124, Basel, Switzerland, 4070
Public contact	Regulatory Affairs, Roche Trial Information Hotline, +41 61 6878333, global.trial_information@roche.com
Scientific contact	Regulatory Affairs, Roche Trial Information Hotline, +41 61 6878333, global.trial_information@roche.com

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	06 March 2015
Is this the analysis of the primary completion data?	Yes
Primary completion date	28 April 2014
Global end of trial reached?	Yes
Global end of trial date	28 April 2014
Was the trial ended prematurely?	Yes

Notes:

General information about the trial

Main objective of the trial:

To evaluate the levels of serum periostin in a population of patients with severe oral corticosteroid (OCS) dependent asthma at Baseline
To examine the stability of serum periostin levels and individual patient phenotypes in relation to sputum eosinophils (as defined by % eosinophils), blood eosinophil count, fractional exhaled nitric oxide (FeNO [parts-per-billion]), lung function (forced expiratory volume in 1 second [FEV1]), and Asthma Control Questionnaire (ACQ-7)
To examine the changes in serum periostin levels in a study population with uncontrolled asthma that receives 7 days of high-dose OCS treatment and relate these changes to blood eosinophils, FeNO, lung function, Asthma Quality of Life Questionnaire for adults and adolescents age 12 years and older [AQLQ12+], and ACQ-7

Protection of trial subjects:

The conduct of this clinical study met all local legal and regulatory requirements. The study was conducted in accordance with the ethical principles that have their origin in the Declaration of Helsinki and the International Conference on Harmonization guideline E6: Good Clinical Practice. Before entering the study, the informed consent form was read by and explained to all participants and/or their legally authorized representative. Participants signed informed consent form and could withdraw from the study at any time without any disadvantage and without having to provide a reason for this decision. Only investigators qualified by training and experience were selected as appropriate experts to investigate the study drug.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	01 July 2013
Long term follow-up planned	Yes
Long term follow-up rationale	Safety, Efficacy
Long term follow-up duration	3 Months
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	United Kingdom: 54
Worldwide total number of subjects	54
EEA total number of subjects	54

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)	47
From 65 to 84 years	7
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Overall 54 participants were randomized. Of these, 42 participated in the follow-up phase and 40 participants completed the study.

Pre-assignment

Screening details:

Approximately 130 participants were planned at study centers in the UK. However, the study was terminated early due to slow recruitment. Sites were planned to participate in Study WB28182 and participation in Study WB28850 ended when Study WB28182 was ready to begin enrolment. Therefore, the final number of participants enrolled was 54.

Period 1

Period 1 title	Overall (overall period)
Is this the baseline period?	Yes
Allocation method	Non-randomised - controlled
Blinding used	Not blinded

Arms

Are arms mutually exclusive?	Yes
Arm title	Controlled Asthma

Arm description:

Participants with controlled asthma were included in this arm. Participants not meeting the "uncontrolled" asthma criteria listed were defined as "controlled". "Uncontrolled" asthma criteria were: Asthma Control Questionnaire (ACQ)-7 >1.25 or persistent blood eosinophil count (>0.4 X 10^9/milliliter [mL]) or persistent sputum eosinophilia (>3%) or recurrent exacerbations requiring a boost in steroid dose.

Arm type	No intervention

No investigational medicinal product assigned in this arm

Arm title	Uncontrolled Asthma with OCS

Arm description:

Participants with uncontrolled asthma who consented to additional use of oral corticosteroid were included in this arm. "Uncontrolled" asthma criteria: ACQ-7 >1.25 or persistent blood eosinophil count (>0.4 X 10^9/mL) or persistent sputum eosinophilia (>3%) or recurrent exacerbations requiring a boost in steroid dose.

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

Dosage and administration details:

Participants with uncontrolled asthma were administered prednisolone tablets 0.5 mg/kg (to the nearest 5 mg) be taken daily for 7 days in addition to their maintenance OCS.

Arm title	Uncontrolled Asthma with No OCS

Arm description:

Participants with uncontrolled asthma who did not consent to additional use of oral corticosteroid were included in this arm. "Uncontrolled" asthma criteria: ACQ-7 >1.25 or persistent blood eosinophil count (>0.4 X 10^9/mL) or persistent sputum eosinophilia (>3%) or recurrent exacerbations requiring a boost in steroid dose.

Arm type	No intervention

No investigational medicinal product assigned in this arm

Number of subjects in period 1	Controlled Asthma	Uncontrolled Asthma with OCS	Uncontrolled Asthma with No OCS
Started	3	45	6
Completed	3	43	6
Not completed	0	2	0
Unavailable/do not wish to attend the last visit	-	2	-

Baseline characteristics

Reporting groups	
Reporting group title	Controlled Asthma
Reporting group description:	
Participants with controlled asthma were included in this arm. Participants not meeting the "uncontrolled" asthma criteria listed were defined as "controlled". "Uncontrolled" asthma criteria were: Asthma Control Questionnaire (ACQ)-7 >1.25 or persistent blood eosinophil count (>0.4 X 10^9/milliliter [mL]) or persistent sputum eosinophilia (>3%) or recurrent exacerbations requiring a boost in steroid dose.	
Reporting group title	Uncontrolled Asthma with OCS
Reporting group description:	
Participants with uncontrolled asthma who consented to additional use of oral corticosteroid were included in this arm. "Uncontrolled" asthma criteria: ACQ-7 >1.25 or persistent blood eosinophil count (>0.4 X 10^9/mL) or persistent sputum eosinophilia (>3%) or recurrent exacerbations requiring a boost in steroid dose.	
Reporting group title	Uncontrolled Asthma with No OCS
Reporting group description:	
Participants with uncontrolled asthma who did not consent to additional use of oral corticosteroid were included in this arm. "Uncontrolled" asthma criteria: ACQ-7 >1.25 or persistent blood eosinophil count (>0.4 X 10^9/mL) or persistent sputum eosinophilia (>3%) or recurrent exacerbations requiring a boost in steroid dose.	

Reporting group values	Controlled Asthma	Uncontrolled Asthma with OCS	Uncontrolled Asthma with No OCS
Number of subjects	3	45	6
Age categorical			
Units: Subjects			
Adults (18-64 years)	2	40	4
From 65-84 years	1	4	2
Missing	0	1	0
Age continuous			
Units: years			
arithmetic mean	57.3	52.9	56.3
standard deviation	± 7.5	± 10.4	± 13.9
Gender categorical			
Units: Subjects			
Male	3	21	2
Female	0	24	4

Reporting group values	Total		
Number of subjects	54		
Age categorical			
Units: Subjects			
Adults (18-64 years)	46		
From 65-84 years	7		
Missing	1		
Age continuous			
Units: years			
arithmetic mean			
standard deviation	-		

Gender categorical Units: Subjects			
Male	26		
Female	28		

End points

End points reporting groups

Reporting group title	Controlled Asthma

Reporting group description:

Participants with controlled asthma were included in this arm. Participants not meeting the "uncontrolled" asthma criteria listed were defined as "controlled". "Uncontrolled" asthma criteria were: Asthma Control Questionnaire (ACQ)-7 >1.25 or persistent blood eosinophil count (>0.4 X 10^9/milliliter [mL]) or persistent sputum eosinophilia (>3%) or recurrent exacerbations requiring a boost in steroid dose.

Reporting group title	Uncontrolled Asthma with OCS

Reporting group description:

Participants with uncontrolled asthma who consented to additional use of oral corticosteroid were included in this arm. "Uncontrolled" asthma criteria: ACQ-7 >1.25 or persistent blood eosinophil count (>0.4 X 10^9/mL) or persistent sputum eosinophilia (>3%) or recurrent exacerbations requiring a boost in steroid dose.

Reporting group title	Uncontrolled Asthma with No OCS

Reporting group description:

Participants with uncontrolled asthma who did not consent to additional use of oral corticosteroid were included in this arm. "Uncontrolled" asthma criteria: ACQ-7 >1.25 or persistent blood eosinophil count (>0.4 X 10^9/mL) or persistent sputum eosinophilia (>3%) or recurrent exacerbations requiring a boost in steroid dose.

Subject analysis set title	Full-analysis set
Subject analysis set type	Full analysis

Subject analysis set description:

The full-analysis set (FAS) was used in all analyses and consisted of all participants who met the criteria for entering the study.

Primary: Change from Baseline in serum periostin levels at Visits 2, 3, 4 and 5

End point title	Change from Baseline in serum periostin levels at Visits 2, 3, 4 and 5[1]

End point description:

Change from Baseline values were measured by participant group and by serum periostin level, where Baseline was Day 0 (Visit 1) or last non-missing measurement of screening. Baseline periostin <50 ng/mL was classed as low (PL) and Baseline serum periostin >=50 ng/mL was classed as high (PH). Change from Baseline: Post baseline value — Baseline value. The full-analysis set (FAS) was used for analysis and consisted of all participants who met the criteria for entering the study. Participants only with a value at Baseline and post-baseline are analysed and are represented by n=X, X, X. Parameters for which values are not calculated are presented as zero (0).

End point type	Primary

End point timeframe:

From Baseline (Day 0) to Visit 2 (Day 8), Visit 3 (Day 39), Visit 4 (Day 67) and Visit 5 (Day 95)

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: No statistical analyses was performed.

End point values	Controlled Asthma	Uncontrolled Asthma with OCS	Uncontrolled Asthma with No OCS	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	3	45	6	
Units: nanogram/milliliter				
arithmetic mean (standard deviation)				
PL Visit 2, n=2, 23, 3	1.39 (± 0.35)	-3.81 (± 5.05)	-0.68 (± 3.91)	
PL Visit 3, n=1, 21, 2	3.43 (± 0)	1.15 (± 7.09)	11.44 (± 9.02)	

PL Visit 4, n=1, 21, 2	3.12 (± 0)	0.4 (± 5.5)	1.02 (± 8.63)	
PL Visit 5, n=1, 20, 2	2.91 (± 0)	-0.88 (± 7.42)	3.23 (± 8.62)	
PH Visit 2, n=1, 20, 2	-0.46 (± 0)	-11.09 (± 5.35)	4.03 (± 12.39)	
PH Visit 3, n=0, 17, 0	0 (± 0)	-0.19 (± 9.6)	0 (± 0)	
PH Visit 4, n=0, 16, 0	0 (± 0)	-1.94 (± 8.48)	0 (± 0)	
PH Visit 5, n=0, 14, 0	0 (± 0)	1.56 (± 7.22)	0 (± 0)	

Statistical analyses

No statistical analyses for this end point

Primary: Change from Baseline in serum periostin in relation to blood eosinophil count at Visits 2, 3, 4 and 5

End point title	Change from Baseline in serum periostin in relation to blood eosinophil count at Visits 2, 3, 4 and 5[2]

End point description:

Change from baseline values were measured in serum periostin in relation to blood eosinophil count, where baseline was Day 0 (Visit 1) or last non-missing measurement of screening. Change from Baseline: Post baseline value — Baseline value. The FAS was used for analysis. Participants only with a value at Baseline and post-baseline are analysed and are represented by n=X, X, X. Parameters for which values are not calculated are presented as zero (0). A line plot of serum periostin versus blood eosinophil counts by low baseline serum periostin level and high baseline serum periostin level is provided in Figure 2 (as attachment). The figure illustrates that both blood eosinophil counts and serum periostin decrease in a response to additional OCS but then return to baseline levels, the effect being more pronounced in the group with high baseline serum periostin.

End point type	Primary

End point timeframe:

From Baseline (Day 0) to Visit 2 (Day 8), Visit 3 (Day 39), Visit 4 (Day 67) and Visit 5 (Day 95)

Notes:

[2] - 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: No statistical analyses was performed.

End point values	Controlled Asthma	Uncontrolled Asthma with OCS	Uncontrolled Asthma with No OCS	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	3	45	6	
Units: Giga Cells Per Liter				
arithmetic mean (standard deviation)				
Visit 2, n=3, 44, 5	0.03 (± 0.08)	-0.15 (± 0.21)	0.04 (± 0.16)	
Visit 3, n=1, 37, 2	-0.06 (± 0)	0.04 (± 0.25)	0.04 (± 0.12)	
Visit 4, n=1, 35, 2	0.15 (± 0)	-0.02 (± 0.2)	0.05 (± 0.1)	
Visit 5, n=1, 36, 2	-0.03 (± 0)	-0.01 (± 0.18)	-0.04 (± 0.05)	

Attachments (see zip file)	Serum Periostin in relation Blood Eosinophils/Eosinophil.JPG

Statistical analyses

No statistical analyses for this end point

Primary: Change from Baseline in serum periostin in relation to Fractional Exhaled Nitric Oxide at Visits 2, 3, 4 and 5

End point title	Change from Baseline in serum periostin in relation to Fractional Exhaled Nitric Oxide at Visits 2, 3, 4 and 5[3]

End point description:

Change from Baseline values were measured in serum periostin in relation to FeNO, where Baseline is Day 0 (Visit 1) or last non-missing measurement of screening. Change from Baseline: Post baseline value — Baseline value. FeNO is a quantitative, noninvasive, simple, and safe method of measuring airway inflammation that provides a complementary tool to other ways of assessing airways disease, including asthma. The FAS was used for analysis. Participants only with a value at Baseline and post-baseline are analysed and are represented by n=X, X, X. Parameters for which values are not calculated are presented as zero (0). A line plot of serum periostin versus FeNO by low baseline serum periostin level and high baseline serum periostin level is provided in Figure 4 (as attachment). The figure illustrates that both FeNO and serum periostin decrease in a response to additional OCS, the effect being more pronounced in the group with high baseline serum periostin.

End point type	Primary

End point timeframe:

From Baseline (Day 0) to Visit 2 (Day 8), Visit 3 (Day 39), Visit 4 (Day 67) and Visit 5 (Day 95)

Notes:

[3] - 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: No statistical analyses was performed.

End point values	Controlled Asthma	Uncontrolled Asthma with OCS	Uncontrolled Asthma with No OCS	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	3	45	6	
Units: Parts per billion				
arithmetic mean (standard deviation)				
Visit 2, n=3, 39, 4	-3.67 (± 7.57)	-19.61 (± 29.59)	-14.38 (± 29.85)	
Visit 3, n=1, 35, 2	2 (± 0)	-6.28 (± 37.04)	-18.25 (± 42.78)	
Visit 4, n=1, 35, 2	25 (± 0)	-0.39 (± 39.21)	-0.5 (± 12.02)	
Visit 5, n=1, 35, 2	8 (± 0)	-2.59 (± 30.98)	-3.5 (± 9.19)	

Attachments (see zip file)	Serum Periostin in Relation to FeNO/FeNO.JPG

Statistical analyses

No statistical analyses for this end point

Primary: Change from Baseline in serum periostin in relation to Asthma Control Questionnaire-7 score at Visits 2, 3, 4 and 5

End point title	Change from Baseline in serum periostin in relation to Asthma Control Questionnaire-7 score at Visits 2, 3, 4 and 5[4]

End point description:

Change from Baseline (BL) was measured in serum periostin (SP) in relation to ACQ-7 score. It describes questions related to frequency and severity of asthma. Participants recall about their asthma during the previous week and have to respond to questions about symptoms and bronchodilator use on

a 7-point scale (where 0=no impairment, 6=maximum impairment). The ACQ score is the mean of the 7 questions; scores lie between 0 (totally controlled) and 6 (severely uncontrolled). The FAS was used for analysis. Participants only with a value at BL and Post-BL are analysed (presented as n=X, X, X). Change from BL (BL: Day 0 or last non-missing value): Post BL value —BL value. Not calculated parameters are presented as 0. A line plot of SP in relation to ACQ-7 is presented in Figure 6, which illustrates that both ACQ-7 score and SP decrease in a response to additional OCS but then return to BL levels, the effect being more pronounced in the group with high baseline serum periostin levels.

End point type	Primary

End point timeframe:

From Baseline (Day 0) to Visit 2 (Day 8), Visit 3 (Day 39), Visit 4 (Day 67) and Visit 5 (Day 95)

Notes:

[4] - 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: No statistical analyses was performed.

End point values	Controlled Asthma	Uncontrolled Asthma with OCS	Uncontrolled Asthma with No OCS	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	3	45	6	
Units: Scores on a scale				
arithmetic mean (standard deviation)				
Visit 2, n=3, 45, 5	0.29 (± 0.14)	-0.45 (± 0.88)	0.23 (± 0.37)	
Visit 3, n=1, 39, 2	0.15 (± 0)	0.07 (± 0.65)	0.14 (± 0.01)	
Visit 4, n=1, 37, 2	0.86 (± 0)	0.26 (± 0.82)	0.28 (± 0.4)	
Visit 5, n=1, 37, 2	0.72 (± 0)	0.12 (± 0.92)	0.07 (± 0.5)	

Attachments (see zip file)	Serum Periostin in Relation to ACQ-7/ACQ7.JPG

Statistical analyses

No statistical analyses for this end point

Primary: Change from Baseline in serum periostin in relation to Asthma Quality of Life Questionnaire 12+ at Visits 2, 3, 4 and 5

End point title	Change from Baseline in serum periostin in relation to Asthma Quality of Life Questionnaire 12+ at Visits 2, 3, 4 and 5[5]

End point description:

Change from Baseline (BL) was measured in serum periostin (SP) in relation to AQLQ12+ score by participant group. The questionnaire contains 4 domains: activity limitations, symptoms, emotional function, and environmental stimuli. The AQLQ12+ is based on a 2-week recall period and consists of 32 questions, each scored from 1 (Worse) to 7 (Better). An increase in the AQLQ score indicates a better quality of life. The FAS was used for analysis. Participants only with a value at BL and Post-BL are analysed (presented as n=X, X, X). Change from BL (BL: Day 0 or last non-missing value): Post BL value —BL value. Not calculated parameters are presented as 0. A line plot of SP in relation to AQLQ12+ is presented in Figure 8. The figure illustrates a small increase between BL and subsequent visits for AQLQ12+ score. However, overall the AQLQ12+ scores remain stable and do not appear to be meaningfully impacted by the increase in OCS. A similar pattern was observed between the BL SP levels.

End point type	Primary

End point timeframe:

From Baseline (Day 0) to Visit 2 (Day 8), Visit 3 (Day 39), Visit 4 (Day 67) and Visit 5 (Day 95)

Notes:

[5] - 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: No statistical analyses was performed.

End point values	Controlled Asthma	Uncontrolled Asthma with OCS	Uncontrolled Asthma with No OCS	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	3	45	6	
Units: Scores on a scale				
arithmetic mean (standard deviation)				
Visit 2, n=2, 42, 5	0.1 (± 0.18)	0.25 (± 0.5)	0.06 (± 0.37)	
Visit 3, n=1, 34, 2	-0.15 (± 0)	0.13 (± 0.48)	0.14 (± 0.33)	
Visit 4, n=1, 34, 2	-0.25 (± 0)	-0.09 (± 0.64)	-0.31 (± 0.71)	
Visit 5, n=1, 33, 2	-0.25 (± 0)	-0.03 (± 0.81)	0.02 (± 0.16)	

Attachments (see zip file)	Serum Periostin in Relation to AQLQ12+/AQOL12+.JPG

Statistical analyses

No statistical analyses for this end point

Primary: Change from Baseline in serum periostin in relation to FEV1 at Visits 2, 3, 4 and 5

End point title	Change from Baseline in serum periostin in relation to FEV1 at Visits 2, 3, 4 and 5[6]

End point description:

Pulmonary function was measured by forced expiratory volume in one second (FEV1), defined as the maximal amount of air that can be forcefully exhaled from the lungs in one second. Change from baseline value in serum periostin in relation to pre-bronchodilator FEV1 was measured, where baseline was Day 0 (Visit 1) or last non-missing measurement prior to dosing. Change from Baseline: Post baseline value — Baseline value. The FAS was used for analysis. Participants only with a value at Baseline and post-baseline are analysed and are represented by n=X, X, X. Parameters for which values are not calculated are presented as zero (0). A line plot of serum periostin versus FEV1 by low baseline serum periostin level and high baseline serum periostin level is provided in Figure 10 (as attachment). The figure illustrates that FEV1 levels show an increase with an increase in OCS, the effect being more pronounced in the group with high baseline serum periostin levels.

End point type	Primary

End point timeframe:

From Baseline (Day 0) to Visit 2 (Day 8), Visit 3 (Day 39), Visit 4 (Day 67) and Visit 5 (Day 95)

Notes:

[6] - 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: No statistical analyses was performed.

End point values	Controlled Asthma	Uncontrolled Asthma with OCS	Uncontrolled Asthma with No OCS	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	3	45	6	
Units: Liter				
arithmetic mean (standard deviation)				
Visit 2, n=3, 43, 5	-0.06 (± 0.46)	0.19 (± 0.35)	-0.07 (± 0.23)	

Visit 3, n=1, 37, 2	-0.11 (± 0)	0.03 (± 0.31)	0.1 (± 0.47)	
Visit 4, n=1, 34, 2	-0.42 (± 0)	-0.03 (± 0.36)	0.12 (± 0.31)	
Visit 5, n=1, 34, 2	-0.32 (± 0)	0.04 (± 0.43)	0.58 (± 0.21)	

Attachments (see zip file)	Serum Periostin in Relation to FEV1/FEV1.JPG

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Approximately up to 95 days

Adverse event reporting additional description:

Serious adverse events and non-serious adverse events are reported in Full Analysis Set, which consists of all participants who met the criteria for entering the study.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	15.1

Reporting groups

Reporting group title	Controlled Asthma

Reporting group description:

Participants with controlled asthma were included in this arm. Participants not meeting the "uncontrolled" asthma criteria listed were defined as "controlled". "Uncontrolled" asthma criteria: Asthma Control Questionnaire (ACQ)-7 >1.25 or persistent blood eosinophil count (>0.4 X 10^9/mL) or persistent sputum eosinophilia (>3%) or recurrent exacerbations requiring a boost in steroid dose

Reporting group title	Uncontrolled Asthma with OCS

Reporting group description:

Participants with uncontrolled asthma who consented to additional use of oral corticosteroid were included in this arm. "Uncontrolled" asthma criteria: ACQ-7 >1.25 or persistent blood eosinophil count (>0.4 X 10^9/mL) or persistent sputum eosinophilia (>3%) or recurrent exacerbations requiring a boost in steroid dose.

Reporting group title	Uncontrolled Asthma with No OCS

Reporting group description:

Participants with uncontrolled asthma who did not consent to additional use of oral corticosteroid were included in this arm. "Uncontrolled" asthma criteria: ACQ-7 >1.25 or persistent blood eosinophil count (>0.4 X 10^9/mL) or persistent sputum eosinophilia (>3%) or recurrent exacerbations requiring a boost in steroid dose

Serious adverse events	Controlled Asthma	Uncontrolled Asthma with OCS	Uncontrolled Asthma with No OCS
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 3 (0.00%)	7 / 45 (15.56%)	1 / 6 (16.67%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Injury, poisoning and procedural complications			
Patella fracture			
subjects affected / exposed	0 / 3 (0.00%)	0 / 45 (0.00%)	1 / 6 (16.67%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac disorders			
Myocardial infarction			

subjects affected / exposed	0 / 3 (0.00%)	1 / 45 (2.22%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General disorders and administration site conditions			
Non-cardiac chest pain			
subjects affected / exposed	0 / 3 (0.00%)	2 / 45 (4.44%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			
Asthma			
subjects affected / exposed	0 / 3 (0.00%)	5 / 45 (11.11%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 5	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

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

Non-serious adverse events	Controlled Asthma	Uncontrolled Asthma with OCS	Uncontrolled Asthma with No OCS
Total subjects affected by non-serious adverse events			
subjects affected / exposed	1 / 3 (33.33%)	35 / 45 (77.78%)	3 / 6 (50.00%)
Nervous system disorders			
Headache			
subjects affected / exposed	0 / 3 (0.00%)	3 / 45 (6.67%)	0 / 6 (0.00%)
occurrences (all)	0	3	0
General disorders and administration site conditions			
Chest discomfort			
subjects affected / exposed	0 / 3 (0.00%)	5 / 45 (11.11%)	0 / 6 (0.00%)
occurrences (all)	0	7	0
Respiratory, thoracic and mediastinal disorders			
Asthma			
subjects affected / exposed	0 / 3 (0.00%)	17 / 45 (37.78%)	2 / 6 (33.33%)
occurrences (all)	0	18	2
Cough			
subjects affected / exposed	0 / 3 (0.00%)	3 / 45 (6.67%)	0 / 6 (0.00%)
occurrences (all)	0	3	0

Dyspnoea			
subjects affected / exposed	0 / 3 (0.00%)	4 / 45 (8.89%)	0 / 6 (0.00%)
occurrences (all)	0	6	0
Wheezing			
subjects affected / exposed	0 / 3 (0.00%)	3 / 45 (6.67%)	0 / 6 (0.00%)
occurrences (all)	0	5	0
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	1 / 3 (33.33%)	3 / 45 (6.67%)	0 / 6 (0.00%)
occurrences (all)	1	4	0
Infections and infestations			
Lower respiratory tract infection			
subjects affected / exposed	0 / 3 (0.00%)	4 / 45 (8.89%)	0 / 6 (0.00%)
occurrences (all)	0	4	0
Oral candidiasis			
subjects affected / exposed	0 / 3 (0.00%)	1 / 45 (2.22%)	1 / 6 (16.67%)
occurrences (all)	0	1	1

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
27 February 2013	After seeking advice from Medicines and Healthcare products Regulatory Agency (MHRA), the trial was classified as interventional due to the use of Prednisolone as an investigational product. The protocol was amended and the word 'non-investigational' was replaced by 'investigational'.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported