Clinical trial results:
A randomised, double-blind (sponsor open) placebo-controlled, parallel group, 8-week treatment study to investigate the safety, pharmacodynamics and effect of the TLR7 agonist, GSK2245035, on the allergen-induced asthmatic response in subjects with mild allergic asthma.

Summary

EudraCT number	2015-005645-31
Trial protocol	GB DE
Global end of trial date	04 May 2018

Results information

Result version number	v1 (current)
This version publication date	27 February 2019
First version publication date	27 February 2019

Trial information

Trial identification

Sponsor protocol code	205540

Additional study identifiers

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

Notes:

Sponsors

Sponsor organisation name	GlaxoSmithKline
Sponsor organisation address	980 Great West Road, Brentford, Middlesex, United Kingdom,
Public contact	GSK Response Center, GlaxoSmithKline, 1 8664357343, GSKClinicalSupportHD@gsk.com
Scientific contact	GSK Response Center, GlaxoSmithKline, 1 8664357343, GSKClinicalSupportHD@gsk.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	11 September 2018
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	04 May 2018
Was the trial ended prematurely?	Yes

Notes:

General information about the trial

Main objective of the trial:

To evaluate the effect of treatment with i.n. GSK2245035 compared to placebo on the allergen-induced late asthmatic response (LAR) in subjects with allergic asthma.

Protection of trial subjects:

Not Applicable

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	05 December 2016
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	Germany: 14
Country: Number of subjects enrolled	United Kingdom: 22
Worldwide total number of subjects	36
EEA total number of subjects	36

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)	36
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

This study investigated the safety, pharmacodynamics, and effect of the Toll-like receptor 7 (TLR7) agonist, GSK2245035, on allergen-induced asthmatic response in participants with mild allergic asthma. Participants received either intranasal 20 nanogram (ng) GSK2245035 or placebo once weekly for 8 weeks.

Pre-assignment

Screening details:

A total of 36 participants were randomized at different centers in United Kingdom and Germany..

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	Placebo

Arm description:

Participants received placebo matching GSK2245035 intranasal spray solution once weekly for 8 weeks

Arm type	Placebo
Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Nasal spray
Routes of administration	Intranasal use

Dosage and administration details:

Participants were administered placebo matching GSK2245035 intranasal spray solution

Arm title	GSK2245035 20 ng

Arm description:

Participants received 20 ng GSK2245035 intranasal spray solution at the rate of 1 spray per nostril (10 ng per actuation) once weekly for 8 weeks.

Arm type	Experimental
Investigational medicinal product name	GSK2245035 20 ng
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Nasal spray
Routes of administration	Intranasal use

Dosage and administration details:

Participants were administered 20 ng GSK2245035 intranasal spray solution at the rate of 1 spray per nostril (10 ng per actuation)

Number of subjects in period 1	Placebo	GSK2245035 20 ng
Started	14	22
Completed	13	19
Not completed	1	3
Adverse event, non-fatal	-	3
Lost to follow-up	1	-

Baseline characteristics

Reporting groups	
Reporting group title	Placebo
Reporting group description:	
Participants received placebo matching GSK2245035 intranasal spray solution once weekly for 8 weeks	
Reporting group title	GSK2245035 20 ng
Reporting group description:	
Participants received 20 ng GSK2245035 intranasal spray solution at the rate of 1 spray per nostril (10 ng per actuation) once weekly for 8 weeks.	

Reporting group values	Placebo	GSK2245035 20 ng	Total
Number of subjects	14	22	36
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)	14	22	36
From 65-84 years	0	0	0
85 years and over	0	0	0
Age Continuous			
Units: Years			
arithmetic mean	36.6	36.0	
standard deviation	± 12.26	± 11.65	-
Sex: Female, Male			
Units: Subjects			
Female	2	1	3
Male	12	21	33
Race/Ethnicity, Customized			
Units: Subjects			
African American/African Heritage	0	2	2
Asian – Central/South Asian Heritage	0	1	1
White	14	19	33

End points

End points reporting groups

Reporting group title	Placebo
Reporting group description:	
Participants received placebo matching GSK2245035 intranasal spray solution once weekly for 8 weeks	
Reporting group title	GSK2245035 20 ng
Reporting group description:	
Participants received 20 ng GSK2245035 intranasal spray solution at the rate of 1 spray per nostril (10 ng per actuation) once weekly for 8 weeks.	

Primary: Late Asthmatic Response (LAR): absolute change from saline in minimum forced expiratory volume in 1 second (FEV1) between 4-10 hours following allergen challenge one week after treatment

End point title	Late Asthmatic Response (LAR): absolute change from saline in minimum forced expiratory volume in 1 second (FEV1) between 4-10 hours following allergen challenge one week after treatment[1]

End point description:

FEV1 is a measure of lung function and is defined as the maximal amount of air that can be forcefully exhaled in one second. Participants were exposed to bronchial allergen challenge (BAC) at the one-week follow-up visit (one week after the eighth dose of the study treatment). Minimum FEV1 over 4-10 hours post-allergen challenge (minimum LAR) is the minimum value of all of the post-saline time points between 4 and 10 hours post-allergen challenge, inclusive of the 4 and 10 hours timepoints. Absolute change from saline in minimum FEV1 was calculated as the minimum FEV1 minus the saline FEV1 value. Per-Protocol Population comprises of all randomized participants who received at least one dose of study treatment and commence a BAC at follow-up and comply with the protocol. Only those participants with data available at specified time points were analyzed

End point type	Primary

End point timeframe:

Week 9

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: There are no statistical analysis to report.

End point values	Placebo	GSK2245035 20 ng		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	10[2]	17[3]		
Units: Liters				
arithmetic mean (standard deviation)	-1.107 (± 0.7195)	-0.885 (± 0.5353)		

Notes:

[2] - Per-Protocol Population.

[3] - Per-Protocol Population.

Statistical analyses

No statistical analyses for this end point

Primary: LAR: absolute change from saline in weighted mean FEV1 between 4-10 hours following allergen challenge one week after treatment

End point title	LAR: absolute change from saline in weighted mean FEV1 between 4-10 hours following allergen challenge one week after treatment[4]

End point description:

FEV1 is a measure of lung function and is defined as the maximal amount of air that can be forcefully exhaled in one second. Participants were exposed to BAC at the one-week follow-up visit (one week after the eighth dose of the study treatment). Weighted mean FEV1 over 4-10 hours post-allergen challenge includes all post-saline time points between 4 and 10 hours post-allergen challenge, inclusive of the 4 and 10 hours timepoints. The weighted mean FEV1 was derived by calculating the area under the curve, and dividing the value by the relevant time interval. Absolute change from saline at each time point was calculated as the highest allergen challenge FEV1 value minus the highest saline FEV1 value. Only those participants with data available at specified time points were analyzed

End point type	Primary

End point timeframe:

Week 9

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: There are no statistical analysis to report.

End point values	Placebo	GSK2245035 20 ng		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	10[5]	17[6]		
Units: Liters				
arithmetic mean (standard deviation)	-0.546 (± 0.3932)	-0.576 (± 0.4018)		

Notes:

[5] - Per-Protocol Population.

[6] - Per-Protocol Population.

Statistical analyses

No statistical analyses for this end point

Secondary: Early Asthmatic Response (EAR): absolute change from saline in minimum FEV1 Between 0-2 hours following allergen challenge one week after treatment

End point title	Early Asthmatic Response (EAR): absolute change from saline in minimum FEV1 Between 0-2 hours following allergen challenge one week after treatment

End point description:

FEV1 is a measure of lung function and is defined as the maximal amount of air that can be forcefully exhaled in one second. Participants were exposed to BAC at the one-week follow-up visit (one week after the eighth dose of the study treatment). Minimum FEV1 over 0-2 hours post-allergen challenge (minimum LAR) is the minimum value of all of the post-saline time points between 0 and 2 hours post-allergen challenge, inclusive of the 0 and 2 hours timepoints. Absolute change from saline in minimum FEV1 was calculated as the minimum FEV1 minus the saline FEV1 value. Only those participants with data available at specified time points were analyzed

End point type	Secondary

End point timeframe:

Week 9

End point values	Placebo	GSK2245035 20 ng		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	10[7]	17[8]		
Units: Liters				
arithmetic mean (standard deviation)	-1.246 (± 0.6052)	-1.096 (± 0.4113)		

Notes:

[7] - Per-Protocol Population

[8] - Per-Protocol Population

Statistical analyses

No statistical analyses for this end point

Secondary: EAR: absolute change from saline in weighted mean FEV1 between 0-2 hours following allergen challenge one week after treatment.

End point title	EAR: absolute change from saline in weighted mean FEV1 between 0-2 hours following allergen challenge one week after treatment.

End point description:

FEV1 is a measure of lung function and is defined as the maximal amount of air that can be forcefully exhaled in one second. Participants were exposed to BAC at the one-week follow-up visit (one week after the eighth dose of the study treatment). Weighted mean FEV1 over 0-2 hours post-allergen challenge includes all post-saline time points between 0-2 hours post-allergen challenge, inclusive of 0 and 2 hours timepoints. The weighted mean FEV1 was derived by calculating the area under the curve, and dividing the value by the relevant time interval. Absolute change from saline at each time point was calculated as the highest allergen challenge FEV1 value minus the highest saline FEV1 value. Only those participants with data available at specified time points were analyzed

End point type	Secondary

End point timeframe:

Week 9

End point values	Placebo	GSK2245035 20 ng		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	10[9]	17[10]		
Units: Liters				
arithmetic mean (standard deviation)	-0.604 (± 0.2670)	-0.587 (± 0.2388)		

Notes:

[9] - Per-Protocol Population.

[10] - Per-Protocol Population.

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants with Adverse Events (AEs) and Serious Adverse Events (SAEs)

End point title	Number of Participants with Adverse Events (AEs) and Serious Adverse Events (SAEs)

End point description:

An AE is any untoward medical occurrence in a clinical investigation participant, temporally associated

with the use of a medicinal product, whether or not considered related to the medicinal product. Any untoward event resulting in death, life threatening, requires hospitalization or prolongation of existing hospitalization, results in disability/incapacity, congenital anomaly/birth defect, any other situation according to medical or scientific judgment or all events of possible drug-induced liver injury with hyperbilirubinemia were categorized as SAE. Number of participants with AEs and SAEs have been reported. All Subjects Population comprise of all participants who received at least one dose of study treatment.

End point type	Secondary

End point timeframe:

Up to Week 20

End point values	Placebo	GSK2245035 20 ng		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	14[11]	22[12]		
Units: Participants				
Any AE	10	21		
Any SAE	0	0		

Notes:

[11] - All Subjects Population

[12] - All Subjects Population

Statistical analyses

No statistical analyses for this end point

Secondary: Number of participants with abnormal peak expiratory flow (PEF)

End point title	Number of participants with abnormal peak expiratory flow (PEF)

End point description:

The PEF is defined as the greatest rate of airflow that can be achieved during forced exhalation beginning with the lungs fully inflated. Participants were instructed to record their PEF readings each morning and evening into the diary card that was provided by the investigator. The minimum and maximum range ranges for PEF were <=205 and >=980 liters per minute.

End point type	Secondary

End point timeframe:

Up to Week 12

End point values	Placebo	GSK2245035 20 ng		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	14[13]	22[14]		
Units: Participants	0	0		

Notes:

[13] - All Subjects Population

[14] - All Subjects Population

Statistical analyses

No statistical analyses for this end point

Secondary: Number of participants receiving rescue medication

End point title	Number of participants receiving rescue medication

End point description:

Salbutamol was administered as rescue medication only to participants who experienced serious discomfort. The data below exclude any Salbutamol administered as part of the planned study procedures (for example the Salbutamol administered after the Bronchial Allergen Challenge [BAC] is not counted as a rescue medication).

End point type	Secondary

End point timeframe:

Up to Week 20

End point values	Placebo	GSK2245035 20 ng		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	14[15]	22[16]		
Units: Participants	1	2		

Notes:

[15] - All Subjects Population

[16] - All Subjects Population

Statistical analyses

No statistical analyses for this end point

Secondary: Number of participants with hematology values of potential clinical concern

End point title	Number of participants with hematology values of potential clinical concern

End point description:

Blood samples were collected for analysis of hematology parameters. Hematology parameters included hematocrit, hemoglobin, platelet count, neutrophils, lymphocytes, monocytes, eosinophils, basophils, mean corpuscular volume, mean corpuscular hemoglobin, and red blood cells (RBC).

End point type	Secondary

End point timeframe:

Up to Week 20

End point values	Placebo	GSK2245035 20 ng		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	14[17]	22[18]		
Units: Participants	9	14		

Notes:

[17] - All Subjects Population

[18] - All Subjects Population

Statistical analyses

No statistical analyses for this end point

Secondary: Number of participants with clinical chemistry values of potential clinical concern

End point title	Number of participants with clinical chemistry values of potential clinical concern

End point description:

Blood samples were collected for analysis of clinical chemistry parameters. Clinical chemistry parameters included blood urea nitrogen, aspartate aminotransferase, alanine aminotransferase, alkaline phosphatase, total protein, total and direct bilirubin, albumin, calcium, creatinine, glucose, potassium and sodium.

End point type	Secondary

End point timeframe:

Up to Week 8

End point values	Placebo	GSK2245035 20 ng		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	14[19]	22[20]		
Units: Participants	1	2		

Notes:

[19] - All Subjects Population

[20] - All Subjects Population

Statistical analyses

No statistical analyses for this end point

Secondary: Number of participants with abnormal urine analysis findings

End point title	Number of participants with abnormal urine analysis findings

End point description:

Urine samples were collected for analysis of specific gravity, potential of hydrogen ions, glucose, protein, blood and ketones by dipstick method. Microscopic examination were performed if blood or protein values were abnormal.

End point type	Secondary

End point timeframe:

Up to Week 8

End point values	Placebo	GSK2245035 20 ng		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	14[21]	22[22]		
Units: Participants	0	0		

Notes:

[21] - All Subjects Population

[22] - All Subjects Population

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Serious adverse events and non serious adverse events were collected from the start of study treatment up to Week 20

Adverse event reporting additional description:

All Subjects Population comprised of all participants who received at least one dose of study treatment.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	21.0

Reporting groups

Reporting group title	GSK2245035 20 ng

Reporting group description:

Participants received 20 ng GSK2245035 intranasal spray solution at the rate of 1 spray per nostril (10 ng per actuation) once weekly for 8 weeks.

Reporting group title	Placebo

Reporting group description:

Participants received placebo matching GSK2245035 intranasal spray solution once weekly for 8 weeks

Serious adverse events	GSK2245035 20 ng	Placebo	
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 22 (0.00%)	0 / 14 (0.00%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events			

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

Non-serious adverse events	GSK2245035 20 ng	Placebo	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	21 / 22 (95.45%)	10 / 14 (71.43%)	
Vascular disorders			
Flushing			
subjects affected / exposed	1 / 22 (4.55%)	0 / 14 (0.00%)	
occurrences (all)	1	0	
Hypertension			
subjects affected / exposed	1 / 22 (4.55%)	0 / 14 (0.00%)	
occurrences (all)	4	0	
General disorders and administration			

site conditions			
Pyrexia			
subjects affected / exposed	1 / 22 (4.55%)	1 / 14 (7.14%)	
occurrences (all)	2	1	
Chest discomfort			
subjects affected / exposed	1 / 22 (4.55%)	0 / 14 (0.00%)	
occurrences (all)	1	0	
Influenza like illness			
subjects affected / exposed	0 / 22 (0.00%)	1 / 14 (7.14%)	
occurrences (all)	0	1	
Malaise			
subjects affected / exposed	1 / 22 (4.55%)	0 / 14 (0.00%)	
occurrences (all)	1	0	
Pain			
subjects affected / exposed	1 / 22 (4.55%)	0 / 14 (0.00%)	
occurrences (all)	2	0	
Vessel puncture site bruise			
subjects affected / exposed	1 / 22 (4.55%)	0 / 14 (0.00%)	
occurrences (all)	1	0	
Immune system disorders			
Seasonal allergy			
subjects affected / exposed	1 / 22 (4.55%)	1 / 14 (7.14%)	
occurrences (all)	2	1	
Hypersensitivity			
subjects affected / exposed	1 / 22 (4.55%)	0 / 14 (0.00%)	
occurrences (all)	1	0	
Respiratory, thoracic and mediastinal disorders			
Oropharyngeal pain			
subjects affected / exposed	7 / 22 (31.82%)	0 / 14 (0.00%)	
occurrences (all)	8	0	
Epistaxis			
subjects affected / exposed	2 / 22 (9.09%)	1 / 14 (7.14%)	
occurrences (all)	2	1	
Nasal congestion			
subjects affected / exposed	2 / 22 (9.09%)	0 / 14 (0.00%)	
occurrences (all)	2	0	

Nasal dryness			
subjects affected / exposed	2 / 22 (9.09%)	0 / 14 (0.00%)	
occurrences (all)	2	0	
Wheezing			
subjects affected / exposed	2 / 22 (9.09%)	0 / 14 (0.00%)	
occurrences (all)	2	0	
Cough			
subjects affected / exposed	1 / 22 (4.55%)	0 / 14 (0.00%)	
occurrences (all)	1	0	
Dry throat			
subjects affected / exposed	1 / 22 (4.55%)	0 / 14 (0.00%)	
occurrences (all)	1	0	
Dyspnoea exertional			
subjects affected / exposed	1 / 22 (4.55%)	0 / 14 (0.00%)	
occurrences (all)	1	0	
Nasal discomfort			
subjects affected / exposed	1 / 22 (4.55%)	0 / 14 (0.00%)	
occurrences (all)	1	0	
Nasal inflammation			
subjects affected / exposed	0 / 22 (0.00%)	1 / 14 (7.14%)	
occurrences (all)	0	1	
Nasal oedema			
subjects affected / exposed	1 / 22 (4.55%)	0 / 14 (0.00%)	
occurrences (all)	1	0	
Rhinorrhoea			
subjects affected / exposed	1 / 22 (4.55%)	0 / 14 (0.00%)	
occurrences (all)	2	0	
Sinonasal obstruction			
subjects affected / exposed	0 / 22 (0.00%)	1 / 14 (7.14%)	
occurrences (all)	0	1	
Psychiatric disorders			
Initial insomnia			
subjects affected / exposed	1 / 22 (4.55%)	0 / 14 (0.00%)	
occurrences (all)	1	0	
Investigations			

Peak expiratory flow rate decreased			
subjects affected / exposed	1 / 22 (4.55%)	0 / 14 (0.00%)	
occurrences (all)	1	0	
Injury, poisoning and procedural complications			
Bone contusion			
subjects affected / exposed	1 / 22 (4.55%)	0 / 14 (0.00%)	
occurrences (all)	1	0	
Fall			
subjects affected / exposed	1 / 22 (4.55%)	0 / 14 (0.00%)	
occurrences (all)	1	0	
Iliotibial band syndrome			
subjects affected / exposed	0 / 22 (0.00%)	1 / 14 (7.14%)	
occurrences (all)	0	1	
Joint injury			
subjects affected / exposed	1 / 22 (4.55%)	0 / 14 (0.00%)	
occurrences (all)	1	0	
Nervous system disorders			
Headache			
subjects affected / exposed	9 / 22 (40.91%)	8 / 14 (57.14%)	
occurrences (all)	16	18	
Dizziness			
subjects affected / exposed	0 / 22 (0.00%)	1 / 14 (7.14%)	
occurrences (all)	0	1	
Facial paralysis			
subjects affected / exposed	1 / 22 (4.55%)	0 / 14 (0.00%)	
occurrences (all)	1	0	
Parosmia			
subjects affected / exposed	0 / 22 (0.00%)	1 / 14 (7.14%)	
occurrences (all)	0	1	
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	0 / 22 (0.00%)	1 / 14 (7.14%)	
occurrences (all)	0	1	
Ear and labyrinth disorders			
Ear pruritus			

subjects affected / exposed	1 / 22 (4.55%)	0 / 14 (0.00%)	
occurrences (all)	1	0	
Vertigo			
subjects affected / exposed	0 / 22 (0.00%)	1 / 14 (7.14%)	
occurrences (all)	0	1	
Eye disorders			
Conjunctivitis allergic			
subjects affected / exposed	1 / 22 (4.55%)	0 / 14 (0.00%)	
occurrences (all)	1	0	
Gastrointestinal disorders			
Nausea			
subjects affected / exposed	1 / 22 (4.55%)	1 / 14 (7.14%)	
occurrences (all)	1	1	
Abdominal pain upper			
subjects affected / exposed	1 / 22 (4.55%)	0 / 14 (0.00%)	
occurrences (all)	2	0	
Odynophagia			
subjects affected / exposed	1 / 22 (4.55%)	0 / 14 (0.00%)	
occurrences (all)	1	0	
Toothache			
subjects affected / exposed	1 / 22 (4.55%)	0 / 14 (0.00%)	
occurrences (all)	1	0	
Skin and subcutaneous tissue disorders			
Ingrowing nail			
subjects affected / exposed	0 / 22 (0.00%)	1 / 14 (7.14%)	
occurrences (all)	0	1	
Rash			
subjects affected / exposed	1 / 22 (4.55%)	0 / 14 (0.00%)	
occurrences (all)	8	0	
Skin exfoliation			
subjects affected / exposed	1 / 22 (4.55%)	0 / 14 (0.00%)	
occurrences (all)	1	0	
Renal and urinary disorders			
Renal pain			
subjects affected / exposed	1 / 22 (4.55%)	0 / 14 (0.00%)	
occurrences (all)	1	0	
Musculoskeletal and connective tissue			

disorders			
Back pain			
subjects affected / exposed	4 / 22 (18.18%)	0 / 14 (0.00%)	
occurrences (all)	4	0	
Femoroacetabular impingement			
subjects affected / exposed	0 / 22 (0.00%)	1 / 14 (7.14%)	
occurrences (all)	0	1	
Musculoskeletal chest pain			
subjects affected / exposed	1 / 22 (4.55%)	0 / 14 (0.00%)	
occurrences (all)	1	0	
Musculoskeletal pain			
subjects affected / exposed	1 / 22 (4.55%)	0 / 14 (0.00%)	
occurrences (all)	1	0	
Myalgia			
subjects affected / exposed	1 / 22 (4.55%)	0 / 14 (0.00%)	
occurrences (all)	1	0	
Neck pain			
subjects affected / exposed	1 / 22 (4.55%)	0 / 14 (0.00%)	
occurrences (all)	2	0	
Osteoarthritis			
subjects affected / exposed	0 / 22 (0.00%)	1 / 14 (7.14%)	
occurrences (all)	0	1	
Myositis			
subjects affected / exposed	0 / 22 (0.00%)	1 / 14 (7.14%)	
occurrences (all)	0	1	
Infections and infestations			
Nasopharyngitis			
subjects affected / exposed	6 / 22 (27.27%)	3 / 14 (21.43%)	
occurrences (all)	6	5	
Upper respiratory tract infection			
subjects affected / exposed	3 / 22 (13.64%)	0 / 14 (0.00%)	
occurrences (all)	3	0	
Rhinitis			
subjects affected / exposed	1 / 22 (4.55%)	1 / 14 (7.14%)	
occurrences (all)	2	1	
Bacterial rhinitis			

subjects affected / exposed	0 / 22 (0.00%)	1 / 14 (7.14%)	
occurrences (all)	0	1	
Infection			
subjects affected / exposed	1 / 22 (4.55%)	0 / 14 (0.00%)	
occurrences (all)	1	0	
Bronchitis			
subjects affected / exposed	1 / 22 (4.55%)	0 / 14 (0.00%)	
occurrences (all)	1	0	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
15 June 2016	Amendment_01: Section 4.6.1 and Section 7.1.1 have been adjusted slightly to make it clearer that subjects will be provided with a thermometer to be able to record temperature as part of capturing adverse event information. In Section 5.2, exclusion criterion 13 has been updated to reflect the revised recommended alcohol consumption guidelines.
17 August 2016	Amendment_02: The protocol title and text have been amended to clarify that while the investigator and subjects are blinded the sponsor-is unblinded. Details of the procedures required at early withdrawal visits have been added to the Time and Events Table, Section 7.1. Details around the Safety Review Team have been added to include a consultant external to GSK to Section 6.3. The inclusion and exclusion criteria have been updated in Section 5.1 and Section 5.2. and clarification around prohibited medications has been provided in Section 6.11.2. to align with updated exclusion criteria (Section 5.2). Administrative changes have been made to the T&E table (Section 7.1) and text to ensure consistency throughout.
26 May 2017	Amendment_03: Changes in the Primary Medical Monitor and contact details. Alignment of contraception requirements in Section 5.1 and Section 12.5.1 for partners of male subjects that are female of reproductive potential. Section 5.1, Inclusion Criteria, has been updated to align with Section 12.5.1 contraception requirements for partners of male subjects that are female of reproductive potential. Changes made to these sections. Section 5.1 Inclusion Criteria, bullets have been replaced with numbers.
10 July 2017	Amendment_04: Section 4.4 Design Justification, has been updated to permit earlier interim analysis. Section 5.3, Screening Failures/Re-Screening, has been updated to allow re-screening. Section 7.1.1 Time and Events Table – Screening Visit(s), has been updated to clarify timing of screening visits. Section 10.2 Regulatory and Ethical Considerations, Including the Informed Consent Process, to clarify that a new ICF should be completed for each re-screened subject.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported