Clinical trial results:
A Double-Blind, Randomised, Placebo-Controlled, Multi-Centre Field Study to Assess the Efficacy and Safety of HDM-SPIRE in Subjects with a History of House Dust Mite-Induced Rhinoconjunctivitis

Summary

EudraCT number	2014-001662-94
Trial protocol	IT DE NL LT LV
Global end of trial date	13 April 2017

Results information

Result version number	v1 (current)
This version publication date	03 March 2018
First version publication date	03 March 2018

Trial information

Trial identification

Sponsor protocol code	TH005

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02150343
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Circassia Limited
Sponsor organisation address	Rober Robinson Avenue, Oxford, United Kingdom,
Public contact	TH005-ClinicalTrialInformation-Desk, Circassia Ltd., +44 01865 598078 , TH005ClinicalTrialInformationDesk@circassia.co.uk
Scientific contact	TH005-ClinicalTrialInformation-Desk, Circassia Ltd., +44 01865 598078 , TH005ClinicalTrialInformationDesk@circassia.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	28 June 2017
Is this the analysis of the primary completion data?	Yes
Primary completion date	13 April 2017
Global end of trial reached?	Yes
Global end of trial date	13 April 2017
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To evaluate the efficacy of HDM-SPIRE in the reduction of symptoms and the use of allergy rescue medication associated with HDM allergy in subjects with clinically relevant symptoms.

Protection of trial subjects:

None

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	24 September 2014
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Netherlands: 8
Country: Number of subjects enrolled	Spain: 49
Country: Number of subjects enrolled	France: 1
Country: Number of subjects enrolled	Germany: 64
Country: Number of subjects enrolled	Italy: 9
Country: Number of subjects enrolled	Latvia: 22
Country: Number of subjects enrolled	Lithuania: 45
Country: Number of subjects enrolled	United States: 372
Country: Number of subjects enrolled	Canada: 96
Country: Number of subjects enrolled	South Africa: 49
Worldwide total number of subjects	715
EEA total number of subjects	198

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	0

months)	
Children (2-11 years)	0
Adolescents (12-17 years)	0
Adults (18-64 years)	713
From 65 to 84 years	2
85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

3625 subjects were screened of which 2910 (80.3%) were not randomised. Most common reasons for screen failure were related to Der p/Der f specific IgE, TRSS, evidence of partly or uncontrolled asthma and history of another disease or disorder.

Period 1

Period 1 title	Randomisation
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator, Monitor, Data analyst, Assessor

Arms

Arm title	All Randomised

Arm description: -

Arm type	Experimental
Investigational medicinal product name	HDM-SPIRE 12 nmol
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Powder for solution for injection
Routes of administration	Intradermal use

Dosage and administration details:

12 nmol nanomole(s) per day intradermal injection given at 4 weekly intervals (4 administrations)

Investigational medicinal product name	HDM-SPIRE 20 nmol
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Powder for solution for injection
Routes of administration	Intradermal use

Dosage and administration details:

20 nmol nanomole(s) per day intradermal injection given at 4 weekly intervals (4 administrations)

Investigational medicinal product name	HDM-SPIRE 12 nmol
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Powder for solution for injection
Routes of administration	Intradermal use

Dosage and administration details:

12 nmol nanomole(s) per day intradermal injection given at 4 weekly intervals (8 administrations)

Investigational medicinal product name	HDM-SPIRE Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Powder for solution for injection
Routes of administration	Intradermal use

Dosage and administration details:

8 intradermal administrations at 4 weekly intervals

Number of subjects in period 1	All Randomised
Started	715
Completed	715

Period 2	
Period 2 title	Treatment and Assessment
Is this the baseline period?	No
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator, Monitor, Data analyst, Assessor

Arms	
Are arms mutually exclusive?	Yes
Arm title	4 x 12 nmol HDM-SPIRE

Arm description:

4 x 12 nmol HDM-SPIRE followed by 4 x placebo

Arm type	Experimental
Investigational medicinal product name	HDM-SPIRE 12 nmol
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Powder for solution for injection
Routes of administration	Intradermal use

Dosage and administration details:

12 nmol nanomole(s) per day intradermal injection given at 4 weekly intervals (4 administrations)

Investigational medicinal product name	HDM-SPIRE Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Powder for solution for injection
Routes of administration	Intradermal use

Dosage and administration details:

4 intradermal administrations at 4 weekly intervals

Arm title	4 x 20 nmol HDM-SPIRE

Arm description:

4 x 20 nmol HDM-SPIRE followed by 4 x placebo

Arm type	Experimental
Investigational medicinal product name	HDM-SPIRE 20 nmol
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Powder for solution for injection
Routes of administration	Intradermal use

Dosage and administration details:

20 nmol nanomole(s) per day intradermal injection given at 4 weekly intervals (4 administrations)

Investigational medicinal product name	HDM-SPIRE Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Powder for solution for injection
Routes of administration	Intradermal use

Dosage and administration details:

4 intradermal administrations at 4 weekly intervals

Arm title	8 x 12 nmol HDM-SPIRE

Arm description:

8 x 12 nmol HDM-SPIRE

Arm type	Experimental
Investigational medicinal product name	HDM-SPIRE 12 nmol
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Powder for solution for injection
Routes of administration	Intradermal use

Dosage and administration details:

12 nmol nanomole(s) per day intradermal injection given at 4 weekly intervals (8 administrations)

Arm title	Placebo

Arm description:

8 x placebo

Arm type	Placebo
Investigational medicinal product name	HDM-SPIRE Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Powder for solution for injection
Routes of administration	Intradermal use

Dosage and administration details:

8 intradermal administrations at 4 weekly intervals

Number of subjects in period 2	4 x 12 nmol HDM-SPIRE	4 x 20 nmol HDM-SPIRE	8 x 12 nmol HDM-SPIRE
Started	180	178	179
Completed	159	158	166
Not completed	21	20	13
Consent withdrawn by subject	13	10	9
Non-specified	2	6	1
Adverse event, non-fatal	2	-	1
Lost to follow-up	4	4	2

Number of subjects in period 2	Placebo
Started	178
Completed	168
Not completed	10
Consent withdrawn by subject	4
Non-specified	2

Adverse event, non-fatal	1
Lost to follow-up	3

Baseline characteristics

Reporting groups	
Reporting group title	Randomisation

Reporting group description: -

Reporting group values	Randomisation	Total	
Number of subjects	715	715	
Age categorical Units: Subjects			
Adults (18-64 years)	713	713	
From 65-84 years	2	2	
Gender categorical Units: Subjects			
Female	454	454	
Male	261	261	

End points

End points reporting groups

Reporting group title	All Randomised
Reporting group description: -	
Reporting group title	4 x 12 nmol HDM-SPIRE
Reporting group description:	
4 x 12 nmol HDM-SPIRE followed by 4 x placebo	
Reporting group title	4 x 20 nmol HDM-SPIRE
Reporting group description:	
4 x 20 nmol HDM-SPIRE followed by 4 x placebo	
Reporting group title	8 x 12 nmol HDM-SPIRE
Reporting group description:	
8 x 12 nmol HDM-SPIRE	
Reporting group title	Placebo
Reporting group description:	
8 x placebo	

Primary: Mean Combined Score (CS) during the PAC3 period in the HDM-SPIRE treatment groups compared with the mean CS in the placebo group.

End point title	Mean Combined Score (CS) during the PAC3 period in the HDM-SPIRE treatment groups compared with the mean CS in the placebo group.[1]
End point description:	
End point type	Primary
End point timeframe:	
Weeks 50 to 52 after randomisation	

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: The primary reporting value was least squares mean.

End point values	4 x 12 nmol HDM-SPIRE	4 x 20 nmol HDM-SPIRE	8 x 12 nmol HDM-SPIRE	Placebo
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	160	159	165	168
Units: Combined Score				
least squares mean (standard error)	1.69 (± 0.089)	1.51 (± 0.089)	1.40 (± 0.086)	1.56 (± 0.087)

Statistical analyses

No statistical analyses for this end point

Secondary: Clinical Global Impression of Change in Rhinoconjunctivitis Symptoms for the HDM-SPIRE treatment groups compared with placebo at the end of study.

End point title	Clinical Global Impression of Change in Rhinoconjunctivitis Symptoms for the HDM-SPIRE treatment groups compared with

	placebo at the end of study.

End point description:

End point type	Secondary

End point timeframe:

Weeks 50 to 52 after randomisation

End point values	4 x 12 nmol HDM-SPIRE	4 x 20 nmol HDM-SPIRE	8 x 12 nmol HDM-SPIRE	Placebo
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	159	156	158	160
Units: p-value				
Moderately or very much better	55	70	61	64
Any improvement	101	109	103	109
No change	45	41	48	43
Any worsening	13	6	7	8

Statistical analyses

No statistical analyses for this end point

Secondary: Mean TRSS in the HDM-SPIRE treatment groups compared with placebo during the PAC3 period

End point title	Mean TRSS in the HDM-SPIRE treatment groups compared with placebo during the PAC3 period

End point description:

End point type	Secondary

End point timeframe:

Weeks 50 to 52 after randomisation

End point values	4 x 12 nmol HDM-SPIRE	4 x 20 nmol HDM-SPIRE	8 x 12 nmol HDM-SPIRE	Placebo
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	160	159	165	168
Units: TRSS				
least squares mean (standard error)	8.96 (± 0.468)	8.03 (± 0.467)	7.97 (± 0.451)	8.16 (± 0.455)

Statistical analyses

No statistical analyses for this end point

Secondary: Mean component scores of the TRSS (nasal) in the HDM-SPIRE treatment groups compared with placebo during the PAC3 period.

End point title	Mean component scores of the TRSS (nasal) in the HDM-SPIRE treatment groups compared with placebo during the PAC3 period.

End point description:

End point type	Secondary

End point timeframe:

Weeks 50 to 52 after randomisation

End point values	4 x 12 nmol HDM-SPIRE	4 x 20 nmol HDM-SPIRE	8 x 12 nmol HDM-SPIRE	Placebo
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	160	159	165	168
Units: TNSS				
least squares mean (standard error)	4.99 (± 0.244)	4.40 (± 0.243)	4.45 (± 0.235)	4.44 (± 0.237)

Statistical analyses

No statistical analyses for this end point

Secondary: Mean component scores of the TRSS (non-nasal) in the HDM-SPIRE treatment groups compared with placebo during the PAC3 period.

End point title	Mean component scores of the TRSS (non-nasal) in the HDM-SPIRE treatment groups compared with placebo during the PAC3 period.

End point description:

End point type	Secondary

End point timeframe:

Weeks 50 to 52 after randomisation

End point values	4 x 12 nmol HDM-SPIRE	4 x 20 nmol HDM-SPIRE	8 x 12 nmol HDM-SPIRE	Placebo
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	160	159	165	168
Units: TNNSS				
least squares mean (standard error)	3.99 (± 0.242)	3.64 (± 0.242)	3.53 (± 0.233)	3.73 (± 0.235)

Statistical analyses

No statistical analyses for this end point

Secondary: Mean RMS in the HDM-SPIRE treatment groups compared with placebo during the PAC3 period

End point title	Mean RMS in the HDM-SPIRE treatment groups compared with placebo during the PAC3 period

End point description:

End point type	Secondary

End point timeframe:

Weeks 50 to 52 after randomisation

End point values	4 x 12 nmol HDM-SPIRE	4 x 20 nmol HDM-SPIRE	8 x 12 nmol HDM-SPIRE	Placebo
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	160	159	165	168
Units: RMS				
least squares mean (standard error)	0.57 (± 0.048)	0.51 (± 0.048)	0.41 (± 0.047)	0.55 (± 0.047)

Statistical analyses

No statistical analyses for this end point

Secondary: Mean Rhinoconjunctivitis Quality of Life Questionnaire (RQLQ) score in the HDM-SPIRE treatment groups compared with placebo at the end of the PAC3 period

End point title	Mean Rhinoconjunctivitis Quality of Life Questionnaire (RQLQ) score in the HDM-SPIRE treatment groups compared with placebo at the end of the PAC3 period

End point description:

End point type	Secondary

End point timeframe:

Weeks 50 to 52 after randomisation

End point values	4 x 12 nmol HDM-SPIRE	4 x 20 nmol HDM-SPIRE	8 x 12 nmol HDM-SPIRE	Placebo
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	160	158	166	167
Units: RQLQ Score				
least squares mean (standard error)	2.02 (± 0.098)	1.76 (± 0.098)	1.72 (± 0.095)	1.89 (± 0.095)

Statistical analyses

No statistical analyses for this end point

Secondary: Number of days subjects in the HDM-SPIRE treatment groups have no moderate or severe RSS symptoms without rescue medication usage compared with placebo during the PAC3 period.

End point title	Number of days subjects in the HDM-SPIRE treatment groups have no moderate or severe RSS symptoms without rescue medication usage compared with placebo during the PAC3 period.

End point description:

End point type	Secondary

End point timeframe:

Weeks 50 to 52 after randomisation

End point values	4 x 12 nmol HDM-SPIRE	4 x 20 nmol HDM-SPIRE	8 x 12 nmol HDM-SPIRE	Placebo
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	160	159	165	168
Units: Number of Days				
least squares mean (standard error)	25.9 (± 2.90)	33.5 (± 2.89)	33.9 (± 2.80)	31.1 (± 2.812)

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information	
Timeframe for reporting adverse events: Randomisation to end of study	
Assessment type	Systematic
Dictionary used	
Dictionary name	MedDRA
Dictionary version	17.1
Reporting groups	
Reporting group title	4 x 12 nmol HDM-SPIRE
Reporting group description: -	
Reporting group title	4 x 20 nmol HDM-SPIRE
Reporting group description: -	
Reporting group title	8 x 12 nmol HDM-SPIRE
Reporting group description: -	
Reporting group title	HDM-SPIRE Placebo
Reporting group description: -	

Serious adverse events	4 x 12 nmol HDM-SPIRE	4 x 20 nmol HDM-SPIRE	8 x 12 nmol HDM-SPIRE
Total subjects affected by serious adverse events			
subjects affected / exposed	6 / 180 (3.33%)	4 / 178 (2.25%)	4 / 178 (2.25%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Injury, poisoning and procedural complications			
Urinary retention postoperative			
subjects affected / exposed	0 / 180 (0.00%)	0 / 178 (0.00%)	0 / 178 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Postoperative wound complication			
subjects affected / exposed	1 / 180 (0.56%)	0 / 178 (0.00%)	0 / 178 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Jaw fracture			
subjects affected / exposed	1 / 180 (0.56%)	0 / 178 (0.00%)	0 / 178 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lower limb fracture			

subjects affected / exposed	0 / 180 (0.00%)	1 / 178 (0.56%)	0 / 178 (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
Post procedural haemorrhage			
subjects affected / exposed	0 / 180 (0.00%)	0 / 178 (0.00%)	1 / 178 (0.56%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac disorders			
Angina pectoris			
subjects affected / exposed	1 / 180 (0.56%)	0 / 178 (0.00%)	0 / 178 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	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 / 180 (0.00%)	1 / 178 (0.56%)	0 / 178 (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
Blood and lymphatic system disorders			
Leukocytosis			
subjects affected / exposed	0 / 180 (0.00%)	1 / 178 (0.56%)	0 / 178 (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
Gastrointestinal disorders			
Colitis			
subjects affected / exposed	0 / 180 (0.00%)	1 / 178 (0.56%)	0 / 178 (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
Large intestine perforation			
subjects affected / exposed	0 / 180 (0.00%)	1 / 178 (0.56%)	0 / 178 (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
Hepatobiliary disorders			
Cholecystitis			

subjects affected / exposed	1 / 180 (0.56%)	0 / 178 (0.00%)	0 / 178 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Skin and subcutaneous tissue disorders			
Dermatitis atopic			
subjects affected / exposed	0 / 180 (0.00%)	0 / 178 (0.00%)	1 / 178 (0.56%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Skin reaction			
subjects affected / exposed	0 / 180 (0.00%)	0 / 178 (0.00%)	1 / 178 (0.56%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Psychiatric disorders			
Psychotic disorder			
subjects affected / exposed	1 / 180 (0.56%)	0 / 178 (0.00%)	0 / 178 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal and urinary disorders			
Nephrolithiasis			
subjects affected / exposed	1 / 180 (0.56%)	0 / 178 (0.00%)	0 / 178 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Campylobacter gastroenteritis			
subjects affected / exposed	0 / 180 (0.00%)	0 / 178 (0.00%)	0 / 178 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Diverticulitis			
subjects affected / exposed	0 / 180 (0.00%)	1 / 178 (0.56%)	0 / 178 (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
Sinusitis			

subjects affected / exposed	0 / 180 (0.00%)	1 / 178 (0.56%)	0 / 178 (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
Cellulitis			
subjects affected / exposed	0 / 180 (0.00%)	0 / 178 (0.00%)	1 / 178 (0.56%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Wound infection			
subjects affected / exposed	0 / 180 (0.00%)	0 / 178 (0.00%)	1 / 178 (0.56%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	HDM-SPIRE Placebo		
Total subjects affected by serious adverse events			
subjects affected / exposed	3 / 178 (1.69%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events	0		
Injury, poisoning and procedural complications			
Urinary retention postoperative			
subjects affected / exposed	1 / 178 (0.56%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Postoperative wound complication			
subjects affected / exposed	0 / 178 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Jaw fracture			
subjects affected / exposed	0 / 178 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Lower limb fracture			
subjects affected / exposed	0 / 178 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		

Post procedural haemorrhage			
subjects affected / exposed	0 / 178 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Cardiac disorders			
Angina pectoris			
subjects affected / exposed	0 / 178 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
General disorders and administration site conditions			
Non-cardiac chest pain			
subjects affected / exposed	1 / 178 (0.56%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Blood and lymphatic system disorders			
Leukocytosis			
subjects affected / exposed	0 / 178 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Gastrointestinal disorders			
Colitis			
subjects affected / exposed	0 / 178 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Large intestine perforation			
subjects affected / exposed	0 / 178 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Hepatobiliary disorders			
Cholecystitis			
subjects affected / exposed	0 / 178 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Skin and subcutaneous tissue disorders			
Dermatitis atopic			

subjects affected / exposed	0 / 178 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Skin reaction			
subjects affected / exposed	0 / 178 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Psychiatric disorders			
Psychotic disorder			
subjects affected / exposed	0 / 178 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Renal and urinary disorders			
Nephrolithiasis			
subjects affected / exposed	0 / 178 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Infections and infestations			
Campylobacter gastroenteritis			
subjects affected / exposed	1 / 178 (0.56%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Diverticulitis			
subjects affected / exposed	0 / 178 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Sinusitis			
subjects affected / exposed	0 / 178 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Cellulitis			
subjects affected / exposed	0 / 178 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		

Wound infection			
subjects affected / exposed	0 / 178 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		

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

Non-serious adverse events	4 x 12 nmol HDM-SPIRE	4 x 20 nmol HDM-SPIRE	8 x 12 nmol HDM-SPIRE
Total subjects affected by non-serious adverse events			
subjects affected / exposed	137 / 180 (76.11%)	132 / 178 (74.16%)	132 / 178 (74.16%)
Nervous system disorders			
Headache			
subjects affected / exposed	10 / 180 (5.56%)	11 / 178 (6.18%)	13 / 178 (7.30%)
occurrences (all)	26	30	28
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	11 / 180 (6.11%)	4 / 178 (2.25%)	8 / 178 (4.49%)
occurrences (all)	11	4	9
Oropharyngeal pain			
subjects affected / exposed	6 / 180 (3.33%)	2 / 178 (1.12%)	14 / 178 (7.87%)
occurrences (all)	7	2	14
Infections and infestations			
Nasopharyngitis			
subjects affected / exposed	37 / 180 (20.56%)	32 / 178 (17.98%)	38 / 178 (21.35%)
occurrences (all)	59	54	54
Upper respiratory tract infection			
subjects affected / exposed	22 / 180 (12.22%)	24 / 178 (13.48%)	21 / 178 (11.80%)
occurrences (all)	27	32	32
Sinusitis			
subjects affected / exposed	13 / 180 (7.22%)	14 / 178 (7.87%)	15 / 178 (8.43%)
occurrences (all)	16	15	15
Influenza			
subjects affected / exposed	7 / 180 (3.89%)	12 / 178 (6.74%)	15 / 178 (8.43%)
occurrences (all)	7	15	15
Urinary tract infection			

subjects affected / exposed	5 / 180 (2.78%)	7 / 178 (3.93%)	10 / 178 (5.62%)
occurrences (all)	6	7	14
Bronchitis			
subjects affected / exposed	9 / 180 (5.00%)	4 / 178 (2.25%)	6 / 178 (3.37%)
occurrences (all)	9	4	8

Non-serious adverse events	HDM-SPIRE Placebo		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	129 / 178 (72.47%)		
Nervous system disorders			
Headache			
subjects affected / exposed	12 / 178 (6.74%)		
occurrences (all)	16		
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	9 / 178 (5.06%)		
occurrences (all)	11		
Oropharyngeal pain			
subjects affected / exposed	6 / 178 (3.37%)		
occurrences (all)	9		
Infections and infestations			
Nasopharyngitis			
subjects affected / exposed	41 / 178 (23.03%)		
occurrences (all)	58		
Upper respiratory tract infection			
subjects affected / exposed	20 / 178 (11.24%)		
occurrences (all)	26		
Sinusitis			
subjects affected / exposed	12 / 178 (6.74%)		
occurrences (all)	16		
Influenza			
subjects affected / exposed	11 / 178 (6.18%)		
occurrences (all)	12		
Urinary tract infection			
subjects affected / exposed	6 / 178 (3.37%)		
occurrences (all)	9		
Bronchitis			

subjects affected / exposed occurrences (all)	7 / 178 (3.93%) 7		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
09 September 2015	Protocol version 3.0 from 2.1. Changes to statistical analysis.
02 June 2016	Protocol version 4.0 from 3.0. Changes to eligibility criteria. Clarification on rescreening. Increase of age limit to 70.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported