Clinical trial results:
A Phase IIb, Randomized, Double-blind, Placebo-controlled, Multicenter, Dose-ranging
Study to Assess the Efficacy and Safety of MSTT1041A in Patients with Uncontrolled Severe Asthma

Summary

EudraCT number	2016-001549-13
Trial protocol	BE DE CZ PL
Global end of trial date	26 July 2019

Results information

Result version number	v1 (current)
This version publication date	02 August 2020
First version publication date	02 August 2020

Trial information

Trial identification

Sponsor protocol code	GB39242

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02918019
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Hoffmann-La Roche
Sponsor organisation address	Grenzacherstrasse 124, Basel, Switzerland, 4070
Public contact	F. Hoffmann-La Roche AG, Hoffmann-La Roche, +41 616878333, global.trial_information@roche.com
Scientific contact	F. Hoffmann-La Roche AG, Hoffmann-La Roche, +41 616878333, 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	26 July 2019
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	26 July 2019
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

This was a study to evaluate the efficacy, safety, and pharmacokinetics of astegolimab (MSTT1041A) compared to placebo as add-on therapy in participants with severe, uncontrolled asthma receiving medium- or high-dose inhaled corticosteroid (ICS) therapy and at least one of the following additional controller medications: long-acting beta-agonists (LABA), leukotriene modifier (LTM), long-acting muscarinic antagonist (LAMA), or long-acting theophylline preparation.

Protection of trial subjects:

All participants were required to sign an informed consent form.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	20 September 2016
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	Argentina: 33
Country: Number of subjects enrolled	Belgium: 5
Country: Number of subjects enrolled	Bulgaria: 52
Country: Number of subjects enrolled	Canada: 7
Country: Number of subjects enrolled	Czech Republic: 40
Country: Number of subjects enrolled	Germany: 13
Country: Number of subjects enrolled	Korea, Republic of: 5
Country: Number of subjects enrolled	New Zealand: 2
Country: Number of subjects enrolled	Peru: 26
Country: Number of subjects enrolled	Poland: 68
Country: Number of subjects enrolled	Romania: 13
Country: Number of subjects enrolled	Russian Federation: 38
Country: Number of subjects enrolled	Ukraine: 72
Country: Number of subjects enrolled	United States: 111
Country: Number of subjects enrolled	South Africa: 17
Worldwide total number of subjects	502
EEA total number of subjects	191

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)	427
From 65 to 84 years	75
85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

Adult participants with severe, uncontrolled asthma receiving medium- or high-dose inhaled corticosteroid (ICS) therapy and at least one additional controller medication

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 subcutaneous (SC) placebo matched to astegolimab (MSTT1041A) at randomization (Week 2), Week 6, and every 4 weeks (Q4W) thereafter through Week 50.

Arm type	Placebo
Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Participants received SC placebo matched to astegolimab (MSTT1041A) at randomization (Week 2), Week 6, and every 4 weeks (Q4W) thereafter through Week 50.

Arm title	Astegolimab (MSTT1041A) 70mg

Arm description:

Participants received 70mg of SC astegolimab (MSTT1041A) at randomization (Week 2), Week 6, and every 4 weeks (Q4W) thereafter through Week 50.

Arm type	Experimental
Investigational medicinal product name	Astegolimab
Investigational medicinal product code	
Other name	MSTT1041A
Pharmaceutical forms	Solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Participants received 70mg SC astegolimab (MSTT1041A) at randomization (Week 2), Week 6, and every 4 weeks (Q4W) thereafter through Week 50.

Arm title	Astegolimab (MSTT1041A) 210mg

Arm description:

Participants received 210mg of SC astegolimab (MSTT1041A) at randomization (Week 2), Week 6, and every 4 weeks (Q4W) thereafter through Week 50.

Arm type	Experimental

Investigational medicinal product name	Astegolimab
Investigational medicinal product code	
Other name	MSTT1041A
Pharmaceutical forms	Solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Participants received 210mg SC astegolimab (MSTT1041A) at randomization (Week 2), Week 6, and every 4 weeks (Q4W) thereafter through Week 50.

Arm title	Astegolimab (MSTT1041A) 490mg

Arm description:

Participants received 490mg of SC astegolimab (MSTT1041A) at randomization (Week 2), Week 6, and every 4 weeks (Q4W) thereafter through Week 50.

Arm type	Experimental
Investigational medicinal product name	Astegolimab
Investigational medicinal product code	
Other name	MSTT1041A
Pharmaceutical forms	Solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Participants received 490mg SC astegolimab (MSTT1041A) at randomization (Week 2), Week 6, and every 4 weeks (Q4W) thereafter through Week 50.

Number of subjects in period 1	Placebo	Astegolimab (MSTT1041A) 70mg	Astegolimab (MSTT1041A) 210mg
Started	127	127	126
Completed	121	117	117
Not completed	6	10	9
Physician decision	1	3	2
Consent withdrawn by subject	3	4	6
Adverse event, non-fatal	-	1	-
Death	-	-	1
Protocol deviation	1	1	-
Lost to follow-up	1	1	-
Principal investigator request	-	-	-

Number of subjects in period 1	Astegolimab (MSTT1041A) 490mg
Started	122
Completed	113
Not completed	9
Physician decision	-
Consent withdrawn by subject	4
Adverse event, non-fatal	1
Death	-
Protocol deviation	2

Lost to follow-up	1
Principal investigator request	1

Baseline characteristics

Reporting groups	
Reporting group title	Placebo
Reporting group description:	
Participants received subcutaneous (SC) placebo matched to astegolimab (MSTT1041A) at randomization (Week 2), Week 6, and every 4 weeks (Q4W) thereafter through Week 50.	
Reporting group title	Astegolimab (MSTT1041A) 70mg
Reporting group description:	
Participants received 70mg of SC astegolimab (MSTT1041A) at randomization (Week 2), Week 6, and every 4 weeks (Q4W) thereafter through Week 50.	
Reporting group title	Astegolimab (MSTT1041A) 210mg
Reporting group description:	
Participants received 210mg of SC astegolimab (MSTT1041A) at randomization (Week 2), Week 6, and every 4 weeks (Q4W) thereafter through Week 50.	
Reporting group title	Astegolimab (MSTT1041A) 490mg
Reporting group description:	
Participants received 490mg of SC astegolimab (MSTT1041A) at randomization (Week 2), Week 6, and every 4 weeks (Q4W) thereafter through Week 50.	

Reporting group values	Placebo	Astegolimab (MSTT1041A) 70mg	Astegolimab (MSTT1041A) 210mg
Number of subjects	127	127	126
Age Categorical Units: Subjects			
Adults (18-64 years)	111	106	107
From 65-84 years	16	21	19
Age Continuous Units: years			
arithmetic mean	51.4	52.4	52.5
standard deviation	± 12.2	± 11.9	± 12.0
Gender Categorical Units: Subjects			
Female	82	81	90
Male	45	46	36
Race (NIH/OMB) Units: Subjects			
American Indian or Alaska Native	5	5	8
Asian	6	4	4
Black	8	9	6
White	107	105	108
Multiple	1	4	0
Ethnicity (NIH/OMB) Units: Subjects			
Hispanic or Latino	18	19	15
Not Hispanic or Latino	109	108	110
Not Stated	0	0	1

Reporting group values	Astegolimab (MSTT1041A) 490mg	Total	

Number of subjects	122	502	
Age Categorical Units: Subjects			
Adults (18-64 years)	103	427	
From 65-84 years	19	75	
Age Continuous Units: years			
arithmetic mean	51.4		
standard deviation	± 12.0	-	
Gender Categorical Units: Subjects			
Female	79	332	
Male	43	170	
Race (NIH/OMB) Units: Subjects			
American Indian or Alaska Native	4	22	
Asian	9	23	
Black	6	29	
White	102	422	
Multiple	1	6	
Ethnicity (NIH/OMB) Units: Subjects			
Hispanic or Latino	14	66	
Not Hispanic or Latino	108	435	
Not Stated	0	1	

End points

End points reporting groups

Reporting group title	Placebo
Reporting group description:	
Participants received subcutaneous (SC) placebo matched to astegolimab (MSTT1041A) at randomization (Week 2), Week 6, and every 4 weeks (Q4W) thereafter through Week 50.	
Reporting group title	Astegolimab (MSTT1041A) 70mg
Reporting group description:	
Participants received 70mg of SC astegolimab (MSTT1041A) at randomization (Week 2), Week 6, and every 4 weeks (Q4W) thereafter through Week 50.	
Reporting group title	Astegolimab (MSTT1041A) 210mg
Reporting group description:	
Participants received 210mg of SC astegolimab (MSTT1041A) at randomization (Week 2), Week 6, and every 4 weeks (Q4W) thereafter through Week 50.	
Reporting group title	Astegolimab (MSTT1041A) 490mg
Reporting group description:	
Participants received 490mg of SC astegolimab (MSTT1041A) at randomization (Week 2), Week 6, and every 4 weeks (Q4W) thereafter through Week 50.	

Primary: Reduction in Rate of Asthma Exacerbations

End point title	Reduction in Rate of Asthma Exacerbations
End point description:	
Asthma exacerbation was defined as new or increased asthma symptoms (wheezing, coughing, dyspnea, chest tightness, and/or nighttime awakenings due to these symptoms) that result in one or both of the following: Hospitalization or emergency department visit with administration of systemic corticosteroid treatment; Treatment with systemic corticosteroids for at least 3 days, or a long-acting depot corticosteroid preparation with a therapeutic effectiveness of at least 3 days.	
End point type	Primary
End point timeframe:	
Baseline to Week 54	

End point values	Placebo	Astegolimab (MSTT1041A) 70mg	Astegolimab (MSTT1041A) 210mg	Astegolimab (MSTT1041A) 490mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	127[1]	127[2]	126[3]	122[4]
Units: Percentage				
number (not applicable)	9999	36.9	21.9	43

Notes:

[1] - 9999= value not reported

[2] - adjusted rate reported

[3] - adjusted rate reported

[4] - adjusted rate reported

Statistical analyses

Statistical analysis title	MSTT1041A 490mg/Placebo
Comparison groups	Placebo v Astegolimab (MSTT1041A) 490mg

Number of subjects included in analysis	249
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.0049
Method	Poisson regression
Parameter estimate	Rate Ratio
Point estimate	0.57
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.39
upper limit	0.84

Secondary: Absolute Change in Pre-Bronchodilator Forced Expiratory Volume in 1 Second (FEV1)

End point title	Absolute Change in Pre-Bronchodilator Forced Expiratory Volume in 1 Second (FEV1)

End point description:

FEV1 measures how much air a person can exhale during the first second of a forced breath.

End point type	Secondary

End point timeframe:

Baseline to Week 54

End point values	Placebo	Astegolimab (MSTT1041A) 70mg	Astegolimab (MSTT1041A) 210mg	Astegolimab (MSTT1041A) 490mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	120[5]	117[6]	115[7]	113[8]
Units: Milliliters (mL)				
arithmetic mean (confidence interval 95%)	107 (47 to 167)	130 (70 to 191)	154 (93 to 215)	172 (110 to 234)

Notes:

[5] - adjusted mean reported

[6] - adjusted mean reported

[7] - adjusted mean reported

[8] - adjusted mean reported

Statistical analyses

No statistical analyses for this end point

Secondary: Time to First Asthma Exacerbation

End point title	Time to First Asthma Exacerbation

End point description:

Asthma exacerbation was defined as new or increased asthma symptoms (wheezing, coughing, dyspnea, chest tightness, and/or nighttime awakenings due to these symptoms) that result in one or both of the following: Hospitalization or emergency department visit with administration of systemic corticosteroid treatment; Treatment with systemic corticosteroids for at least 3 days, or a long-acting depot corticosteroid preparation with a therapeutic effectiveness of at least 3 days.

End point type	Secondary

End point timeframe:

52 Weeks

End point values	Placebo	Astegolimab (MSTT1041A) 70mg	Astegolimab (MSTT1041A) 210mg	Astegolimab (MSTT1041A) 490mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	127[9]	127[10]	126[11]	122[12]
Units: Weeks				
median (confidence interval 95%)	9999 (46.6 to 9999)	9999 (9999 to 9999)	9999 (9999 to 9999)	9999 (9999 to 9999)

Notes:

[9] - 9999 = Value not estimable due to insufficient no. of participants with event

[10] - 9999 = Value not estimable due to insufficient no. of participants with event

[11] - 9999 = Value not estimable due to insufficient no. of participants with event

[12] - 9999 = Value not estimable due to insufficient no. of participants with event

Statistical analyses

No statistical analyses for this end point

Secondary: Achievement in Improvement in Standardized Asthma Quality-of-Life Questionnaire (AQLQ(S)) Score

End point title	Achievement in Improvement in Standardized Asthma Quality-of-Life Questionnaire (AQLQ(S)) Score

End point description:

The AQLQ measures the functional problems (physical, emotional, social, and occupational) most troublesome to adults (17-70 years) with asthma. There are 32 questions in 4 domains - symptoms, activity limitation, emotional function, and environmental stimuli - scored on a 7 point scale, with 7= no impairment and 1= severely impaired. For this study, improvement achievement was defined as an increase of at least 0.5 points from baseline to week 54.

End point type	Secondary

End point timeframe:

Week 54

End point values	Placebo	Astegolimab (MSTT1041A) 70mg	Astegolimab (MSTT1041A) 210mg	Astegolimab (MSTT1041A) 490mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	116[13]	116[14]	115[15]	112[16]
Units: Percentage				
number (not applicable)				
Week 54 - Responder	55.3	64.8	61.3	68.9
Week 54 - Non-responder	44.7	35.2	38.7	31.1

Notes:

[13] - adjusted rate reported

[14] - adjusted rate reported

[15] - adjusted rate reported

[16] - adjusted rate reported

Statistical analyses

No statistical analyses for this end point

Secondary: Absolute Change in Patient-Reported Use of Short-Acting Rescue Therapy

End point title	Absolute Change in Patient-Reported Use of Short-Acting Rescue Therapy

End point description:

9999 = adjusted mean value is equal to zero. 9999 is reported due to limitations in the EudraCT results reporting system.

End point type	Secondary

End point timeframe:

Baseline to Week 54

End point values	Placebo	Astegolimab (MSTT1041A) 70mg	Astegolimab (MSTT1041A) 210mg	Astegolimab (MSTT1041A) 490mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	107	106	102	99
Units: Usage				
number (not applicable)	9999	9999	9999	9999

Statistical analyses

No statistical analyses for this end point

Secondary: Proportion of Weeks Without Patient-Reported Asthma-Related Nighttime Awakenings

End point title	Proportion of Weeks Without Patient-Reported Asthma-Related Nighttime Awakenings

End point description:

End point type	Secondary

End point timeframe:

Baseline through Week 54

End point values	Placebo	Astegolimab (MSTT1041A) 70mg	Astegolimab (MSTT1041A) 210mg	Astegolimab (MSTT1041A) 490mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	127[17]	126[18]	126[19]	122[20]
Units: Percentage				
number (not applicable)	0.4	0.4	0.3	0.3

Notes:

[17] - adjusted mean reported

[18] - adjusted mean reported

[19] - adjusted mean reported

[20] - adjusted mean reported

Statistical analyses

No statistical analyses for this end point

Secondary: Absolute Change in Patient-Reported Daytime Asthma Symptom Severity as Measured by the Asthma Daily Symptom Diary (ADSD)

End point title	Absolute Change in Patient-Reported Daytime Asthma Symptom Severity as Measured by the Asthma Daily Symptom Diary (ADSD)

End point description:

End point type	Secondary

End point timeframe:

Baseline to Week 54

End point values	Placebo	Astegolimab (MSTT1041A) 70mg	Astegolimab (MSTT1041A) 210mg	Astegolimab (MSTT1041A) 490mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	126[21]	124[22]	125[23]	122[24]
Units: Units on a scale				
number (not applicable)	-1	-2	-1	-1

Notes:

[21] - adjusted mean reported

[22] - adjusted mean reported

[23] - adjusted mean reported

[24] - adjusted mean reported

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants with Adverse Events

End point title	Percentage of Participants with Adverse Events

End point description:

An adverse event is any untoward medical occurrence in a participant administered a pharmaceutical product and which does not necessarily have to have a causal relationship with the treatment. An adverse event can therefore be any unfavorable and unintended sign (including an abnormal laboratory finding, for example), symptom, or disease temporally associated with the use of a pharmaceutical

product, whether or not considered related to the pharmaceutical product. Preexisting conditions which worsen during a study are also considered as adverse events.

End point type	Secondary

End point timeframe:

Baseline to Week 54

End point values	Placebo	Astegolimab (MSTT1041A) 70mg	Astegolimab (MSTT1041A) 210mg	Astegolimab (MSTT1041A) 490mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	127	127	126	122
Units: Percentage				
number (not applicable)	77.2	70.9	72.2	72.1

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants with Anti-Drug Antibodies (ADAs)

End point title	Percentage of Participants with Anti-Drug Antibodies (ADAs)

End point description:

The prevalence of ADAs at baseline was defined as the proportion of the evaluable participant population in a study that is ADA positive at baseline.

End point type	Secondary

End point timeframe:

Baseline

End point values	Placebo	Astegolimab (MSTT1041A) 70mg	Astegolimab (MSTT1041A) 210mg	Astegolimab (MSTT1041A) 490mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	124	126	126	121
Units: Percentage				
number (not applicable)	5.6	0.8	1.6	1.7

Statistical analyses

No statistical analyses for this end point

Secondary: Serum Concentration of Astegolimab (MSTT1041A)

End point title	Serum Concentration of Astegolimab (MSTT1041A)[25]

End point description:

End point type	Secondary

End point timeframe:

Baseline to Week 54

Notes:

[25] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Values were only collected for arms receiving active treatment, which did not include the placebo arm.

End point values	Astegolimab (MSTT1041A) 70mg	Astegolimab (MSTT1041A) 210mg	Astegolimab (MSTT1041A) 490mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	125	126	117	
Units: ug/mL				
geometric mean (geometric coefficient of variation)				
Week 26 pre-dose	4.75 (± 123.3)	16.9 (± 167.3)	40.5 (± 161.2)	
Week 54	4.47 (± 144.1)	17.4 (± 155.4)	38.7 (± 226.4)	

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants with Treatment-Emergent ADAs

End point title	Percentage of Participants with Treatment-Emergent ADAs

End point description:

The incidence of ADAs at post-baseline timepoints was defined as the proportion of the study population found to have developed treatment-emergent ADAs.

End point type	Secondary

End point timeframe:

Post-baseline

End point values	Placebo	Astegolimab (MSTT1041A) 70mg	Astegolimab (MSTT1041A) 210mg	Astegolimab (MSTT1041A) 490mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	126	125	123	120
Units: Percentage				
number (not applicable)	7.1	9.6	8.9	3.3

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information	
Timeframe for reporting adverse events:	
Baseline to Week 54	
Assessment type	Non-systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	22.0

Reporting groups	
Reporting group title	Placebo
Reporting group description:	
Participants received subcutaneous (SC) placebo matched to astegolimab (MSTT1041A) at randomization (Week 2), Week 6, and every 4 weeks (Q4W) thereafter through Week 50.	
Reporting group title	Astegolimab (MSTT1041A) 210mg
Reporting group description:	
Participants received 210mg of SC astegolimab (MSTT1041A) at randomization (Week 2), Week 6, and every 4 weeks (Q4W) thereafter through Week 50.	
Reporting group title	Astegolimab (MSTT1041A) 490mg
Reporting group description:	
Participants received 490mg of SC astegolimab (MSTT1041A) at randomization (Week 2), Week 6, and every 4 weeks (Q4W) thereafter through Week 50.	
Reporting group title	Astegolimab (MSTT1041A) 70mg
Reporting group description:	
Participants received 70mg of SC astegolimab (MSTT1041A) at randomization (Week 2), Week 6, and every 4 weeks (Q4W) thereafter through Week 50.	

Serious adverse events	Placebo	Astegolimab (MSTT1041A) 210mg	Astegolimab (MSTT1041A) 490mg
Total subjects affected by serious adverse events			
subjects affected / exposed	8 / 127 (6.30%)	9 / 126 (7.14%)	6 / 122 (4.92%)
number of deaths (all causes)	0	1	1
number of deaths resulting from adverse events			
Vascular disorders			
Deep vein thrombosis			
subjects affected / exposed	0 / 127 (0.00%)	0 / 126 (0.00%)	0 / 122 (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
Hypertension			
subjects affected / exposed	1 / 127 (0.79%)	1 / 126 (0.79%)	0 / 122 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypertensive crisis			

subjects affected / exposed	0 / 127 (0.00%)	0 / 126 (0.00%)	1 / 122 (0.82%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General disorders and administration site conditions			
Chest pain			
subjects affected / exposed	0 / 127 (0.00%)	0 / 126 (0.00%)	0 / 122 (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
Death			
subjects affected / exposed	0 / 127 (0.00%)	1 / 126 (0.79%)	1 / 122 (0.82%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 1
Immune system disorders			
Anaphylactic reaction			
subjects affected / exposed	1 / 127 (0.79%)	0 / 126 (0.00%)	0 / 122 (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
Reproductive system and breast disorders			
Vaginal prolapse			
subjects affected / exposed	0 / 127 (0.00%)	0 / 126 (0.00%)	0 / 122 (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
Respiratory, thoracic and mediastinal disorders			
Asthma			
subjects affected / exposed	2 / 127 (1.57%)	4 / 126 (3.17%)	1 / 122 (0.82%)
occurrences causally related to treatment / all	0 / 2	0 / 4	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
Chronic rhinosinusitis with nasal polyps			
subjects affected / exposed	1 / 127 (0.79%)	0 / 126 (0.00%)	0 / 122 (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
Pulmonary embolism			

subjects affected / exposed	0 / 127 (0.00%)	0 / 126 (0.00%)	0 / 122 (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
Vocal cord disorder			
subjects affected / exposed	0 / 127 (0.00%)	0 / 126 (0.00%)	1 / 122 (0.82%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	0 / 127 (0.00%)	1 / 126 (0.79%)	0 / 122 (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
Aspartate aminotransferase increased			
subjects affected / exposed	0 / 127 (0.00%)	1 / 126 (0.79%)	0 / 122 (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
Injury, poisoning and procedural complications			
Ankle fracture			
subjects affected / exposed	1 / 127 (0.79%)	0 / 126 (0.00%)	0 / 122 (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
Concussion			
subjects affected / exposed	0 / 127 (0.00%)	0 / 126 (0.00%)	0 / 122 (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
Pubis fracture			
subjects affected / exposed	1 / 127 (0.79%)	0 / 126 (0.00%)	0 / 122 (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
Road traffic accident			
subjects affected / exposed	0 / 127 (0.00%)	0 / 126 (0.00%)	0 / 122 (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

Cardiac disorders			
Atrial fibrillation			
subjects affected / exposed	0 / 127 (0.00%)	2 / 126 (1.59%)	0 / 122 (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
Atrial tachycardia			
subjects affected / exposed	1 / 127 (0.79%)	0 / 126 (0.00%)	0 / 122 (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
Nervous system disorders			
Headache			
subjects affected / exposed	0 / 127 (0.00%)	1 / 126 (0.79%)	0 / 122 (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
Migraine			
subjects affected / exposed	0 / 127 (0.00%)	0 / 126 (0.00%)	0 / 122 (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
Syncope			
subjects affected / exposed	0 / 127 (0.00%)	0 / 126 (0.00%)	0 / 122 (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
Eye disorders			
Cataract			
subjects affected / exposed	0 / 127 (0.00%)	0 / 126 (0.00%)	1 / 122 (0.82%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Rectal haemorrhage			
subjects affected / exposed	0 / 127 (0.00%)	0 / 126 (0.00%)	0 / 122 (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
Hepatobiliary disorders			
Cholecystitis acute			

subjects affected / exposed	0 / 127 (0.00%)	1 / 126 (0.79%)	0 / 122 (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
Drug-induced liver injury			
subjects affected / exposed	0 / 127 (0.00%)	0 / 126 (0.00%)	0 / 122 (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
Hepatotoxicity			
subjects affected / exposed	0 / 127 (0.00%)	0 / 126 (0.00%)	0 / 122 (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
Skin and subcutaneous tissue disorders			
Livedo reticularis			
subjects affected / exposed	0 / 127 (0.00%)	0 / 126 (0.00%)	0 / 122 (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
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	0 / 127 (0.00%)	0 / 126 (0.00%)	0 / 122 (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
Osteoarthritis			
subjects affected / exposed	0 / 127 (0.00%)	0 / 126 (0.00%)	0 / 122 (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
Infections and infestations			
Bacteraemia			
subjects affected / exposed	0 / 127 (0.00%)	0 / 126 (0.00%)	0 / 122 (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
Cellulitis			
subjects affected / exposed	0 / 127 (0.00%)	0 / 126 (0.00%)	1 / 122 (0.82%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Chronic sinusitis			
subjects affected / exposed	1 / 127 (0.79%)	0 / 126 (0.00%)	0 / 122 (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
Pneumonia			
subjects affected / exposed	1 / 127 (0.79%)	0 / 126 (0.00%)	1 / 122 (0.82%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pyelonephritis			
subjects affected / exposed	1 / 127 (0.79%)	0 / 126 (0.00%)	0 / 122 (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

Serious adverse events	Astegolimab (MSTT1041A) 70mg		
Total subjects affected by serious adverse events			
subjects affected / exposed	14 / 127 (11.02%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events			
Vascular disorders			
Deep vein thrombosis			
subjects affected / exposed	1 / 127 (0.79%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Hypertension			
subjects affected / exposed	0 / 127 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Hypertensive crisis			
subjects affected / exposed	0 / 127 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
General disorders and administration site conditions			
Chest pain			

subjects affected / exposed	1 / 127 (0.79%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Death				
subjects affected / exposed	0 / 127 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Immune system disorders				
Anaphylactic reaction				
subjects affected / exposed	0 / 127 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Reproductive system and breast disorders				
Vaginal prolapse				
subjects affected / exposed	1 / 127 (0.79%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Respiratory, thoracic and mediastinal disorders				
Asthma				
subjects affected / exposed	2 / 127 (1.57%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
Chronic rhinosinusitis with nasal polyps				
subjects affected / exposed	0 / 127 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Pulmonary embolism				
subjects affected / exposed	2 / 127 (1.57%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
Vocal cord disorder				

subjects affected / exposed	0 / 127 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	0 / 127 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Aspartate aminotransferase increased			
subjects affected / exposed	0 / 127 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Injury, poisoning and procedural complications			
Ankle fracture			
subjects affected / exposed	0 / 127 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Concussion			
subjects affected / exposed	1 / 127 (0.79%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Pubis fracture			
subjects affected / exposed	0 / 127 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Road traffic accident			
subjects affected / exposed	1 / 127 (0.79%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Cardiac disorders			
Atrial fibrillation			

subjects affected / exposed	0 / 127 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Atrial tachycardia			
subjects affected / exposed	0 / 127 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Nervous system disorders			
Headache			
subjects affected / exposed	0 / 127 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Migraine			
subjects affected / exposed	1 / 127 (0.79%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Syncope			
subjects affected / exposed	1 / 127 (0.79%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Eye disorders			
Cataract			
subjects affected / exposed	0 / 127 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Gastrointestinal disorders			
Rectal haemorrhage			
subjects affected / exposed	1 / 127 (0.79%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Hepatobiliary disorders			
Cholecystitis acute			

subjects affected / exposed	0 / 127 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Drug-induced liver injury			
subjects affected / exposed	1 / 127 (0.79%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Hepatotoxicity			
subjects affected / exposed	1 / 127 (0.79%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Skin and subcutaneous tissue disorders			
Livedo reticularis			
subjects affected / exposed	1 / 127 (0.79%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	1 / 127 (0.79%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Osteoarthritis			
subjects affected / exposed	2 / 127 (1.57%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Infections and infestations			
Bacteraemia			
subjects affected / exposed	1 / 127 (0.79%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Cellulitis			
subjects affected / exposed	0 / 127 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		

Chronic sinusitis			
subjects affected / exposed	0 / 127 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Pneumonia			
subjects affected / exposed	1 / 127 (0.79%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Pyelonephritis			
subjects affected / exposed	1 / 127 (0.79%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		

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

Non-serious adverse events	Placebo	Astegolimab (MSTT1041A) 210mg	Astegolimab (MSTT1041A) 490mg
Total subjects affected by non-serious adverse events			
subjects affected / exposed	76 / 127 (59.84%)	75 / 126 (59.52%)	68 / 122 (55.74%)
Nervous system disorders			
Headache			
subjects affected / exposed	6 / 127 (4.72%)	6 / 126 (4.76%)	14 / 122 (11.48%)
occurrences (all)	6	7	20
General disorders and administration site conditions			
Injection site reaction			
subjects affected / exposed	1 / 127 (0.79%)	8 / 126 (6.35%)	6 / 122 (4.92%)
occurrences (all)	3	23	107
Respiratory, thoracic and mediastinal disorders			
Asthma			
subjects affected / exposed	58 / 127 (45.67%)	53 / 126 (42.06%)	39 / 122 (31.97%)
occurrences (all)	108	83	61
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	2 / 127 (1.57%)	4 / 126 (3.17%)	4 / 122 (3.28%)
occurrences (all)	3	5	4

Back pain			
subjects affected / exposed	7 / 127 (5.51%)	5 / 126 (3.97%)	4 / 122 (3.28%)
occurrences (all)	8	5	4
Infections and infestations			
Influenza			
subjects affected / exposed	5 / 127 (3.94%)	2 / 126 (1.59%)	7 / 122 (5.74%)
occurrences (all)	5	2	7
Nasopharyngitis			
subjects affected / exposed	13 / 127 (10.24%)	21 / 126 (16.67%)	16 / 122 (13.11%)
occurrences (all)	18	30	23
Rhinitis			
subjects affected / exposed	7 / 127 (5.51%)	3 / 126 (2.38%)	2 / 122 (1.64%)
occurrences (all)	8	3	3
Sinusitis			
subjects affected / exposed	3 / 127 (2.36%)	3 / 126 (2.38%)	5 / 122 (4.10%)
occurrences (all)	3	3	7
Upper respiratory tract infection			
subjects affected / exposed	12 / 127 (9.45%)	8 / 126 (6.35%)	6 / 122 (4.92%)
occurrences (all)	19	9	6

Non-serious adverse events	Astegolimab (MSTT1041A) 70mg		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	65 / 127 (51.18%)		
Nervous system disorders			
Headache			
subjects affected / exposed	8 / 127 (6.30%)		
occurrences (all)	10		
General disorders and administration site conditions			
Injection site reaction			
subjects affected / exposed	10 / 127 (7.87%)		
occurrences (all)	38		
Respiratory, thoracic and mediastinal disorders			
Asthma			
subjects affected / exposed	42 / 127 (33.07%)		
occurrences (all)	68		
Musculoskeletal and connective tissue disorders			

Arthralgia subjects affected / exposed occurrences (all) Back pain subjects affected / exposed occurrences (all)	 7 / 127 (5.51%) 7 5 / 127 (3.94%) 5		
Infections and infestations Influenza subjects affected / exposed occurrences (all) Nasopharyngitis subjects affected / exposed occurrences (all) Rhinitis subjects affected / exposed occurrences (all) Sinusitis subjects affected / exposed occurrences (all) Upper respiratory tract infection subjects affected / exposed occurrences (all)	 2 / 127 (1.57%) 2 12 / 127 (9.45%) 21 7 / 127 (5.51%) 11 7 / 127 (5.51%) 9 9 / 127 (7.09%) 10		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
10 October 2017	Addition/clarification of primary and secondary endpoints; eligibility criteria updates
23 January 2019	Updated timepoints for efficacy objectives

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

Limitations of the trial such as small numbers of subjects analysed or technical problems leading to unreliable data.

Further development of the investigational medical product (IMP) has been discontinued.

Notes: