



Clinical trial results:

A double blind (sponsor open) placebo-controlled, stratified, parallel group study to evaluate the efficacy and safety of repeat doses of GSK3772847 in participants with moderate to severe asthma with allergic fungal airway disease (AFAD)

Summary

EudraCT number	2017-003544-20
Trial protocol	GB FR NL
Global end of trial date	06 January 2020

Results information

Result version number	v1 (current)
This version publication date	15 October 2020
First version publication date	15 October 2020

Trial information

Trial identification

Sponsor protocol code	207972
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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	28 April 2020
Is this the analysis of the primary completion data?	No
Global end of trial reached?	Yes
Global end of trial date	06 January 2020
Was the trial ended prematurely?	Yes

Notes:

General information about the trial

Main objective of the trial:

To evaluate the efficacy of 3 doses of GSK3772847 (administered every 4 weeks) compared with placebo in moderate to severe asthma participants with allergic fungal airway disease (AFAD) who are currently on Standard of Care (SoC)

Protection of trial subjects:

Not applicable

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	18 April 2018
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	Netherlands: 3
Country: Number of subjects enrolled	France: 10
Country: Number of subjects enrolled	Russian Federation: 64
Country: Number of subjects enrolled	United Kingdom: 38
Worldwide total number of subjects	115
EEA total number of subjects	51

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)	89
From 65 to 84 years	26

Subject disposition

Recruitment

Recruitment details:

This was a double-blind, placebo-controlled, parallel group study conducted in participants with moderate to severe asthma with allergic fungal airway disease (AFAD). The study was conducted across 4 countries-France, Netherlands, Russian Federation and the United Kingdom.

Pre-assignment

Screening details:

A total of 17 participants were randomized in a ratio of 1:1 to receive either GSK3772847 10 milligrams per kilogram (mg/kg) or placebo. Recruitment in the study was terminated early due to the feasibility of completing the study in a timely manner.

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	Investigator, Subject, Monitor, Carer, Data analyst, Assessor

Arms

Are arms mutually exclusive?	Yes
Arm title	Placebo

Arm description:

Participants received three doses of placebo administered intravenously every 4 weeks (Weeks 0, 4 and 8) along with their standard of care treatment.

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

Dosage and administration details:

Placebo was sterile normal saline. Participants were administered three doses of placebo via the intravenous route every 4 weeks (Weeks 0, 4 and 8)

Arm title	GSK3772847
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Arm description:

Participants received three doses of GSK3772847 10 mg/kg administered intravenously every 4 weeks (Weeks 0, 4 and 8) along with their standard of care treatment.

Arm type	Experimental
Investigational medicinal product name	GSK3772847
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Powder for solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

GSK3772847 was available as white to yellow, uniform lyophilized cake in a 5 milliliter (mL) clear glass vial to be reconstituted and diluted with sterile normal saline. Participants were administered three doses of GSK3772847 10 mg/kg via the intravenous route every 4 weeks (Weeks 0, 4 and 8)

Number of subjects in period 1^[1]	Placebo	GSK3772847
Started	9	8
Completed	8	8
Not completed	1	0
Physician decision	1	-

Notes:

[1] - The number of subjects reported to be in the baseline period are not the same as the worldwide number enrolled in the trial. It is expected that these numbers will be the same.

Justification: A total of 115 participants were screened of which 17 participants were randomized in the study.

Baseline characteristics

Reporting groups

Reporting group title	Placebo
Reporting group description: Participants received three doses of placebo administered intravenously every 4 weeks (Weeks 0, 4 and 8) along with their standard of care treatment.	
Reporting group title	GSK3772847
Reporting group description: Participants received three doses of GSK3772847 10 mg/kg administered intravenously every 4 weeks (Weeks 0, 4 and 8) along with their standard of care treatment.	

Reporting group values	Placebo	GSK3772847	Total
Number of subjects	9	8	17
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)	6	6	12
From 65-84 years	3	2	5
85 years and over	0	0	0
Age Continuous			
Units: Years			
arithmetic mean	59.9	53.6	
standard deviation	± 9.57	± 12.59	-
Sex: Female, Male			
Units: Participants			
Female	3	2	5
Male	6	6	12
Race/Ethnicity, Customized			
Units: Subjects			
Asian-Japanese/East Asian (EA) /South EA Heritage	0	2	2
White	9	6	15

End points

End points reporting groups

Reporting group title	Placebo
Reporting group description: Participants received three doses of placebo administered intravenously every 4 weeks (Weeks 0, 4 and 8) along with their standard of care treatment.	
Reporting group title	GSK3772847
Reporting group description: Participants received three doses of GSK3772847 10 mg/kg administered intravenously every 4 weeks (Weeks 0, 4 and 8) along with their standard of care treatment.	

Primary: Percent change from Baseline in blood eosinophils over time

End point title	Percent change from Baseline in blood eosinophils over time ^[1]
End point description: Blood samples were collected at the indicated time points for assessment of blood eosinophil cell count. Baseline is the most recent recorded value before dosing on Day 1. Percent change from Baseline is calculated as (Ratio to Baseline minus 1)*100, where ratio to Baseline is the value at specified time point divided by Baseline value. Modified Intent-to-Treat (mITT) Population comprised of all randomized participants who took at least 1 dose of study treatment. Only those participants with data available at the specified time points were analyzed (represented by n=X in category titles).	
End point type	Primary
End point timeframe: Baseline (Day 1, pre-dose), Weeks 2, 4, 8 and 12	

Notes:

[1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.

Justification: No statistical analysis was performed

End point values	Placebo	GSK3772847		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	9 ^[2]	8 ^[3]		
Units: Percent change				
median (full range (min-max))				
Week 2; n=9, 8	30.8 (4 to 61)	28.1 (-46 to 550)		
Week 4; n=8, 8	16.0 (-17 to 77)	2.1 (-71 to 469)		
Week 8; n=8, 8	14.4 (-98 to 262)	-31.4 (-59 to 10)		
Week 12; n=5, 7	9.7 (-88 to 67)	-10.9 (-76 to 469)		

Notes:

[2] - mITT Population

[3] - mITT Population

Statistical analyses

No statistical analyses for this end point

Primary: Percent change from Baseline in fractional exhaled nitric oxide (FeNO) over time

End point title	Percent change from Baseline in fractional exhaled nitric oxide (FeNO) over time ^[4]
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End point description:

FeNO was assessed using a handheld electronic device. The measurements were obtained in accordance with the American Thoracic Society and the European Respiratory Society Recommendations for Standardized Procedures for the Online and Offline Measurement of Exhaled Lower Respiratory Nitric Oxide and Nasal Nitric Oxide. Participants did not use their rescue medication for at least 6 hours before each FeNO assessment, unless essential for clinical need. Baseline is the most recent recorded value before dosing on Day 1. Percent change from Baseline is calculated as (Ratio to Baseline minus 1)*100, where ratio to Baseline is the value at specified time point divided by Baseline value. Only those participants with data available at the specified time points were analyzed (represented by n=X in category titles).

End point type	Primary
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End point timeframe:

Baseline (Day 1, pre-dose), Weeks 2, 4, 8 and 12

Notes:

[4] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.

Justification: No statistical analysis was performed

End point values	Placebo	GSK3772847		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	9 ^[5]	8 ^[6]		
Units: Percent change				
median (full range (min-max))				
Week 2; n=9, 6	33.4 (-39 to 51)	-18.6 (-37 to 12)		
Week 4; n=8, 8	13.7 (-29 to 205)	-12.5 (-48 to 36)		
Week 8; n=8, 7	11.7 (-80 to 75)	-42.8 (-67 to 5)		
Week 12; n=5, 6	-37.2 (-65 to -16)	-45.6 (-68 to -34)		

Notes:

[5] - mITT Population

[6] - mITT Population

Statistical analyses

No statistical analyses for this end point

Secondary: Serum concentrations of GSK3772847

End point title	Serum concentrations of GSK3772847 ^[7]
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End point description:

Whole blood samples were collected at indicated time points for measurement of serum concentrations of GSK3772847. Pharmacokinetic (PK) Population comprised of all randomized participants who received at least one dose of study medication, and for whom at least one pharmacokinetic sample was obtained, analyzed and was measurable.

End point type	Secondary
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End point timeframe:

Week 0 (post-dose), Week 2, Week 4 (pre-dose), Week 8 (pre-dose and post-dose), Week 12 and Week 24

Notes:

[7] - 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: The end point is specific to GSK3772847 arm.

End point values	GSK3772847			
Subject group type	Reporting group			
Number of subjects analysed	8 ^[8]			
Units: Micrograms per milliliter				
arithmetic mean (standard deviation)				
Week 0, post-dose	156.50 (± 74.102)			
Week 2	65.35 (± 10.900)			
Week 4, pre-dose	39.13 (± 10.777)			
Week 8, pre-dose	56.24 (± 9.658)			
Week 8, post-dose	209.61 (± 93.217)			
Week 12	68.59 (± 15.570)			
Week 24	1.67 (± 1.276)			

Notes:

[8] - PK Population

Statistical analyses

No statistical analyses for this end point

Secondary: Serum levels of free suppressor of tumorigenicity 2 (ST2)

End point title	Serum levels of free suppressor of tumorigenicity 2 (ST2)		
End point description:	Serum samples were collected at indicated time points for assessment of free ST2 levels. Baseline is the most recent recorded value before dosing on Day 1 (Week 0). Only those participants with data available at the specified time points were analyzed (represented by n=X in category titles).		
End point type	Secondary		
End point timeframe:	Baseline, Week 0 (post-dose), Week 2, Week 4 (pre-dose), Week 8 (pre-dose and post-dose) and Week 12		

End point values	Placebo	GSK3772847		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	9 ^[9]	8 ^[10]		
Units: Micrograms per liter				
geometric mean (geometric coefficient of variation)				
Baseline; n=9, 8	2.365 (± 54.3)	2.418 (± 50.0)		
Week 0 (post-dose); n=9, 8	2.301 (± 46.9)	0.025 (± 668.2)		
Week 2; n=9, 8	2.286 (± 50.2)	0.156 (± 43.4)		
Week 4 (pre-dose); n=8, 8	2.382 (± 32.1)	0.197 (± 44.0)		
Week 8 (pre-dose); n=8, 8	2.563 (± 30.8)	0.181 (± 25.8)		
Week 8 (post-dose); n=8, 8	2.568 (± 33.7)	0.126 (± 38.2)		
Week 12; n=5, 6	2.194 (± 46.5)	0.144 (± 67.3)		

Notes:

[9] - mITT Population

[10] - mITT Population

Statistical analyses

No statistical analyses for this end point

Secondary: Serum levels of total soluble ST2

End point title	Serum levels of total soluble ST2
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End point description:

Serum samples were collected at indicated time points for assessment of total soluble ST2 levels. Baseline is the most recent recorded value before dosing on Day 1 (Week 0). Only those participants with data available at the specified time points were analyzed (represented by n=X in category titles).

End point type	Secondary
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End point timeframe:

Baseline, Week 0 (post-dose), Week 2, Week 4 (pre-dose), Week 8 (pre-dose and post-dose) and Week 12

End point values	Placebo	GSK3772847		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	9 ^[11]	8 ^[12]		
Units: Micrograms per liter				
geometric mean (geometric coefficient of variation)				
Baseline; n=9, 8	1.905 (± 71.4)	2.382 (± 51.1)		
Week 0 (post-dose); n=9, 8	1.884 (± 60.4)	3.258 (± 39.6)		
Week 2; n=9, 8	1.777 (± 65.5)	63.353 (± 44.7)		
Week 4 (pre-dose); n=8, 8	1.950 (± 35.6)	65.833 (± 47.3)		
Week 8 (pre-dose); n=8, 8	2.141 (± 39.9)	79.286 (± 31.6)		
Week 8 (post-dose); n=8, 8	2.201 (± 40.7)	74.046 (± 44.7)		
Week 12; n=5, 6	1.900 (± 61.3)	75.703 (± 54.1)		

Notes:

[11] - mITT Population

[12] - mITT Population

Statistical analyses

No statistical analyses for this end point

Secondary: Number of participants with positive anti-GSK3772847 antibodies post-dosing

End point title	Number of participants with positive anti-GSK3772847 antibodies post-dosing
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End point description:

Serum samples were collected at indicated time points and tested for the presence of antibodies that bind to GSK3772847. The presence of anti-GSK3772847 antibodies was assessed using a tiered approach including a screening assay, a confirmation assay and calculation of titre. Data for participants who showed positive results for confirmation assay has been presented. Safety Population consisted of all randomized participants who took at least 1 dose of study treatment. Only those participants with data available at the specified time points were analyzed (represented by n=X in category titles).

End point type	Secondary
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End point timeframe:

Weeks 0, 2, 4, 8, 12 and 24

End point values	Placebo	GSK3772847		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	9 ^[13]	8 ^[14]		
Units: Participants				
Week 0; n=9, 8	0	0		
Week 2; n=9, 8	0	0		
Week 4; n=8, 8	0	0		
Week 8; n=8, 8	0	0		
Week 12; n=8, 8	0	0		
Week 24; n=9, 8	0	0		

Notes:

[13] - Safety Population

[14] - Safety Population

Statistical analyses

No statistical analyses for this end point

Secondary: Number of participants for whom titers of anti-GSK3772847 antibodies was performed

End point title	Number of participants for whom titers of anti-GSK3772847 antibodies was performed
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End point description:

Serum samples were collected at indicated time points and tested for the presence of antibodies that bind to GSK3772847. The presence of anti-GSK3772847 antibodies was assessed using a tiered approach including a screening assay, a confirmation assay and calculation of titer. Data for number of participants for whom titers of anti-GSK3772847 antibodies was performed is presented. Only those participants with data available at the specified time points were analyzed (represented by n=X in category titles).

End point type	Secondary
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End point timeframe:

Weeks 0, 2, 4, 8, 12 and 24

End point values	Placebo	GSK3772847		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	9 ^[15]	8 ^[16]		
Units: Participants				
Week 0; n=9, 8	0	0		
Week 2; n=9, 8	0	0		
Week 4; n=8, 8	0	0		
Week 8; n=8, 8	0	0		
Week 12; n=8, 8	0	0		
Week 24; n=9, 8	0	0		

Notes:

[15] - Safety Population

[16] - Safety Population

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in Asthma Control Questionnaire-5 (ACQ-5) absolute score at Weeks 2, 4, 8 and 12

End point title	Change from Baseline in Asthma Control Questionnaire-5 (ACQ-5) absolute score at Weeks 2, 4, 8 and 12
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End point description:

The ACQ-5 is a five-item, self-completed questionnaire, which measures a participant's asthma control. The questions enquire about the frequency and/or severity of symptoms (nocturnal awakening, activity limitation, shortness of breath and wheeze) over the previous week. The response options for all these questions range from zero (no impairment/limitation) to six (total impairment/limitation) scale. ACQ-5 score is the mean of the five questions and ranges from 0 (totally controlled) to 6 (severely uncontrolled). Baseline value is defined as the ACQ-5 assessment on Day 1. Change from Baseline is calculated as the post-dose value minus Baseline value. Only those participants with data available at the specified time points were analyzed (represented by n=X in category titles).

End point type	Secondary
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End point timeframe:

Baseline (Day 1), Weeks 2, 4, 8 and 12

End point values	Placebo	GSK3772847		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	9 ^[17]	8 ^[18]		
Units: Scores on a scale				
arithmetic mean (standard deviation)				
Week 2; n=9, 8	-0.47 (± 0.616)	-0.65 (± 0.739)		
Week 4; n=8, 8	-0.23 (± 1.087)	-1.03 (± 0.897)		
Week 8; n=8, 8	-0.60 (± 0.986)	-1.23 (± 1.383)		
Week 12; n=5, 7	-0.12 (± 1.262)	-1.20 (± 1.095)		

Notes:

[17] - mITT Population

[18] - mITT Population

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in Asthma Quality of Life Questionnaire (AQLQ) total and domain scores at Weeks 2, 4, 8 and 12

End point title	Change from Baseline in Asthma Quality of Life Questionnaire (AQLQ) total and domain scores at Weeks 2, 4, 8 and 12
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End point description:

AQLQ is a disease-specific, self-administered quality of life questionnaire to evaluate the impact of asthma treatments on quality of life of asthma sufferers. AQLQ contains 32 items in four domains: activity limitation (11 items), symptoms (12 items), emotional function (five items), and environmental stimuli (four items). Participants recalled their experience over previous 14 days and responded to each question on a seven-point scale where, 1 indicated 'total impairment' and 7 indicated 'no impairment'. Total score is the mean of responses to all 32 questions and each individual domain score is the mean of items within that domain. Total and domain scores were each defined on a range from 1 to 7 with higher scores indicating a higher quality of life. Baseline value is the AQLQ assessment on Day 1. Change from Baseline=post-dose value minus Baseline value. Only participants with data available at specified time points were analyzed (represented by n=X in category titles).

End point type	Secondary
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End point timeframe:

Baseline (Day 1), Weeks 2, 4, 8 and 12

End point values	Placebo	GSK3772847		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	9 ^[19]	8 ^[20]		
Units: Scores on a scale				
arithmetic mean (standard deviation)				
Total score; Week 2; n=9, 8	0.31 (± 0.660)	0.45 (± 0.623)		
Total score; Week 4; n=8, 8	-0.22 (± 0.477)	0.56 (± 0.514)		
Total score; Week 8; n=8, 8	0.27 (± 0.846)	1.09 (± 0.940)		
Total score; Week 12; n=5, 7	0.10 (± 1.394)	1.13 (± 0.953)		
Activity limitation; Week 2; n=9, 8	0.20 (± 0.504)	0.31 (± 0.750)		
Activity limitation; Week 4; n=8, 8	-0.26 (± 0.499)	0.30 (± 0.570)		
Activity limitation; Week 8; n=8, 8	0.12 (± 0.603)	0.88 (± 0.900)		
Activity limitation; Week 12; n=5, 7	-0.07 (± 1.127)	0.91 (± 0.993)		
Symptoms; Week 2; n=9, 8	0.52 (± 0.924)	0.54 (± 0.641)		
Symptoms; Week 4; n=8, 8	-0.05 (± 0.774)	0.74 (± 0.627)		
Symptoms; Week 8; n=8, 8	0.57 (± 1.213)	1.24 (± 0.936)		
Symptoms; Week 12; n=5, 7	0.52 (± 1.740)	1.31 (± 0.810)		
Environmental stimuli; Week 2; n=9, 8	-0.14 (± 0.811)	0.22 (± 0.891)		
Environmental stimuli; Week 4; n=8, 8	-0.44 (± 0.884)	0.63 (± 0.886)		
Environmental stimuli; Week 8; n=8, 8	-0.44 (± 1.208)	1.06 (± 1.132)		
Environmental stimuli; Week 12; n=5, 7	-0.65 (± 1.025)	0.89 (± 1.257)		
Emotional function; Week 2; n=9, 8	0.40 (± 0.860)	0.75 (± 0.955)		
Emotional function; Week 4; n=8, 8	-0.35 (± 0.833)	0.65 (± 0.847)		

Emotional function; Week 8; n=8, 8	0.45 (± 1.165)	1.22 (± 1.289)		
Emotional function; Week 12; n=5, 7	0.08 (± 1.712)	1.37 (± 1.246)		

Notes:

[19] - mITT Population

[20] - mITT Population

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of responders to ACQ-5 at Weeks 2, 4, 8 and 12

End point title	Percentage of responders to ACQ-5 at Weeks 2, 4, 8 and 12
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End point description:

The ACQ-5 is a five-item, self-completed questionnaire, which measures a participant's asthma control. The questions enquire about the frequency and/or severity of symptoms (nocturnal awakening, activity limitation, shortness of breath and wheeze) over the previous week. The response options for all these questions range from zero (no impairment/limitation) to six (total impairment/limitation) scale. ACQ-5 score is the mean of the five questions and ranges from 0 (totally controlled) to 6 (severely uncontrolled). A responder to ACQ-5 is defined as a participant who has a decrease from Baseline in ACQ-5 score of 0.5 or more at Weeks 2, 4, 8 and 12. Only those participants with data available at the specified time points were analyzed (represented by n=X in category titles).

End point type	Secondary
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End point timeframe:

Weeks 2, 4, 8 and 12

End point values	Placebo	GSK3772847		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	9 ^[21]	8 ^[22]		
Units: Percentage of responders				
Week 2; n=9, 8	44	50		
Week 4; n=8, 8	63	50		
Week 8; n=8, 8	50	50		
Week 12; n=5, 7	20	71		

Notes:

[21] - mITT Population

[22] - mITT Population

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of responders to AQLQ at Weeks 2, 4, 8 and 12

End point title	Percentage of responders to AQLQ at Weeks 2, 4, 8 and 12
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End point description:

AQLQ is a disease-specific, self-administered quality of life questionnaire that was developed to evaluate the impact of asthma treatments on the quality of life of asthma sufferers. The AQLQ contains 32 items in four domains: activity limitation (11 items), symptoms (12 items), emotional function (five items), and environmental stimuli (four items). Participants were asked to recall their experience over the previous 14 days and respond to each question on a seven-point scale where a value of 1 indicates 'total impairment' and 7 indicates 'no impairment'. The total score is the mean of responses to all 32 questions. The total score was defined on a range from 1 to 7 with higher scores indicating a higher quality of life. A responder to AQLQ is defined as a participant who has an increase from Baseline in

AQLQ score of 0.5 or more at Weeks 2, 4, 8 and 12. Only those participants with data available at the specified time points were analyzed (represented by n=X in category titles).

End point type	Secondary
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End point timeframe:

Weeks 2, 4, 8 and 12

End point values	Placebo	GSK3772847		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	9 ^[23]	8 ^[24]		
Units: Percentage of responders				
Week 2; n=9, 8	44	50		
Week 4; n=8, 8	0	38		
Week 8; n=8, 8	25	63		
Week 12; n=5, 7	40	86		

Notes:

[23] - mITT Population

[24] - mITT Population

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in forced expiratory volume in 1 second (FEV1)

End point title	Change from Baseline in forced expiratory volume in 1 second (FEV1)
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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. FEV1 is measured using spirometry. Baseline is the most recent recorded value before dosing on Day 1. Change from Baseline is calculated as the post-dose value minus the Baseline value. Only those participants with data available at the specified time points were analyzed (represented by n=X in category titles).

End point type	Secondary
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End point timeframe:

Baseline (Day 1, pre-dose), Weeks 2, 4, 8 and 12

End point values	Placebo	GSK3772847		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	9 ^[25]	8 ^[26]		
Units: Liters				
arithmetic mean (standard deviation)				
Week 2; n=9, 8	0.076 (± 0.3383)	-0.137 (± 0.2640)		
Week 4; n=7, 8	-0.049 (± 0.2304)	-0.022 (± 0.2703)		
Week 8; n=7, 7	0.060 (± 0.4210)	0.040 (± 0.2381)		
Week 12; n=5, 7	0.102 (± 0.4879)	-0.013 (± 0.1923)		

Notes:

[25] - mITT Population

[26] - mITT Population

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in forced vital capacity (FVC)

End point title	Change from Baseline in forced vital capacity (FVC)
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End point description:

FVC is the maximal amount of air that can be forcibly exhaled from lungs after taking the deepest breath possible. FVC is measured by spirometry. Baseline is the most recent recorded value before dosing on Day 1. Change from Baseline is calculated as the post-dose value minus the Baseline value. Only those participants with data available at the specified time points were analyzed (represented by n=X in category titles).

End point type	Secondary
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End point timeframe:

Baseline (Day 1, pre-dose), Weeks 2, 4, 8 and 12

End point values	Placebo	GSK3772847		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	9 ^[27]	8 ^[28]		
Units: Liters				
arithmetic mean (standard deviation)				
Week 2; n=9, 8	0.078 (± 0.4201)	-0.074 (± 0.3761)		
Week 4; n=7, 8	0.091 (± 0.3163)	0.090 (± 0.3049)		
Week 8; n=7, 7	0.179 (± 0.5145)	0.030 (± 0.2291)		
Week 12; n=5, 7	0.136 (± 0.5351)	0.050 (± 0.2408)		

Notes:

[27] - mITT Population

[28] - mITT 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)
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End point description:

An AE is any untoward medical occurrence in a clinical study participant, temporally associated with the use of a study treatment, whether or not considered related to the study treatment. An SAE is defined as any untoward medical occurrence that, at any dose: results in death; is life-threatening; requires inpatient hospitalization or prolongation of existing hospitalization; results in persistent

disability/incapacity; is a congenital anomaly/birth defect; other important medical events that may jeopardize the participant or may require medical or surgical intervention to prevent one of the other outcomes listed before.

End point type	Secondary
End point timeframe:	
Up to Week 24	

End point values	Placebo	GSK3772847		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	9 ^[29]	8 ^[30]		
Units: Participants				
AEs	7	3		
SAEs	1	0		

Notes:

[29] - Safety Population

[30] - Safety Population

Statistical analyses

No statistical analyses for this end point

Secondary: Number of participants with worst case post-Baseline chemistry results relative to normal range at Baseline

End point title	Number of participants with worst case post-Baseline chemistry results relative to normal range at Baseline
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End point description:

Blood samples were collected for the assessment of following clinical chemistry parameters: alanine aminotransferase, albumin, alkaline phosphatase, aspartate aminotransferase, bilirubin, calcium, carbon dioxide, chloride, creatine kinase, creatinine, direct bilirubin, gamma glutamyl transferase, glucose, phosphate, potassium, protein, sodium and urea. Participants were counted in the worst case category that their value changed to (low, normal or high), unless there was no change in their category. Participants whose value category was unchanged (e.g., High to High), or whose value became normal, are recorded in the "To Normal or No Change" category. Participants were counted twice if the participant had values that changed 'To Low' and 'To High', so the percentages may not add to 100 percent (%). 'To Low' rows are not presented for tests that have lower limit of normal = 0.

End point type	Secondary
End point timeframe:	
Up to Week 24	

End point values	Placebo	GSK3772847		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	9 ^[31]	8 ^[32]		
Units: Participants				
Alanine aminotransferase; To normal or no change	9	8		
Alanine aminotransferase; To high	0	0		
Albumin; To low	0	0		
Albumin; To normal or no change	9	8		
Albumin; To high	0	0		

Alkaline Phosphatase; To low	0	0		
Alkaline Phosphatase; To normal or no change	9	8		
Alkaline Phosphatase; To high	0	0		
Aspartate Aminotransferase; To normal or no change	9	8		
Aspartate Aminotransferase; To high	0	0		
Bilirubin; To normal or no change	9	8		
Bilirubin; To high	0	0		
Calcium; To low	0	1		
Calcium; To normal or no change	9	7		
Calcium; To high	0	0		
Carbon Dioxide; To low	2	1		
Carbon Dioxide; To normal or no change	7	7		
Carbon Dioxide; To high	0	0		
Chloride; To low	0	0		
Chloride; To normal or no change	9	7		
Chloride; To high	0	1		
Creatine Kinase; To normal or no change	7	7		
Creatine Kinase; To high	2	1		
Creatinine; To low	0	1		
Creatinine; To normal or no change	9	7		
Creatinine; To high	0	0		
Direct Bilirubin; To normal or no change	9	8		
Direct Bilirubin; To high	0	0		
Gamma Glutamyl Transferase; To normal or no change	9	8		
Gamma Glutamyl Transferase; To high	0	0		
Glucose; To low	0	0		
Glucose; To normal or no change	7	7		
Glucose; To high	2	1		
Phosphate; To low	2	0		
Phosphate; To normal or no change	5	8		
Phosphate; To high	2	0		
Potassium; To low	0	0		
Potassium; To normal or no change	9	7		
Potassium; To high	0	1		
Protein; To low	0	1		
Protein; To normal or no change	9	7		
Protein; To high	0	0		
Sodium; To low	0	0		
Sodium; To normal or no change	8	7		
Sodium; To high	1	1		
Urea; To low	0	1		
Urea; To normal or no change	9	7		
Urea; To high	0	0		

Notes:

[31] - Safety Population

[32] - Safety Population

Statistical analyses

Secondary: Number of participants with worst case post-Baseline hematology results relative to normal range at Baseline

End point title	Number of participants with worst case post-Baseline hematology results relative to normal range at Baseline
End point description:	
Blood samples were collected for the assessment of following hematology parameters: basophils, eosinophils, erythrocyte (Ery.) mean hemoglobin concentration (MCHC), Ery. mean corpuscular hemoglobin (MCH), Ery mean corpuscular volume (MCV), erythrocytes, erythrocytes distribution width, hematocrit, hemoglobin, leukocytes, lymphocytes, monocytes, neutrophils and platelets. Participants were counted in the worst case category that their value changed to (low, normal or high), unless there was no change in their category. Participants whose value category was unchanged (e.g., High to High), or whose value became normal, are recorded in the "To Normal or No Change" category. Participants were counted twice if the participant had values that changed 'To Low' and 'To High', so the percentages may not add to 100%. 'To Low' rows are not presented for tests that have lower limit of normal = 0.	
End point type	Secondary
End point timeframe:	
Up to Week 24	

End point values	Placebo	GSK3772847		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	9 ^[33]	8 ^[34]		
Units: Participants				
Basophils; To normal or no change	9	8		
Basophils; To high	0	0		
Eosinophils; To low	1	0		
Eosinophils; To normal or no change	5	6		
Eosinophils; To high	3	2		
Ery. MCHC; To normal or no change	5	8		
Ery. MCHC; To high	0	0		
Ery. MCH; To low	0	0		
Ery. MCH; To normal or no change	9	8		
Ery. MCH; To high	0	0		
Ery. MCV; To low	0	0		
Ery. MCV; To normal or no change	9	8		
Ery. MCV; To high	0	0		
Erythrocytes; To low	0	1		
Erythrocytes; To normal or no change	9	7		
Erythrocytes; To high	0	0		
EDW; To low	0	0		
EDW; To normal or no change	7	7		
EDW; To high	2	1		
Hematocrit; To low	1	1		
Hematocrit; To normal or no change	8	6		
Hematocrit; To high	0	1		
Hemoglobin; To low	1	0		
Hemoglobin; To normal or no change	8	8		
Hemoglobin; To high	0	0		
Leukocytes; To low	0	1		
Leukocytes; To normal or no change	9	7		

Leukocytes; To high	0	0		
Lymphocytes; To low	0	0		
Lymphocytes To normal or no change	9	8		
Lymphocytes; To high	0	0		
Monocytes; To low	1	2		
Monocytes; To normal or no change	8	6		
Monocytes; To high	0	0		
Neutrophils; To low	1	1		
Neutrophils; To normal or no change	7	7		
Neutrophils; To high	1	0		
Platelets; To low	0	0		
Platelets; To normal or no change	9	8		
Platelets; To high	0	0		
Ery. MCHC; To low	4	0		

Notes:

[33] - Safety Population

[34] - Safety Population

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in systolic blood pressure (SBP) and diastolic blood pressure (DBP)

End point title	Change from Baseline in systolic blood pressure (SBP) and diastolic blood pressure (DBP)
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End point description:

SBP and DBP were measured in the supine position after five minutes of rest for the participant. Baseline is the most recent recorded value before dosing on Day 1 (Week 0). Change from Baseline is calculated as post-dose visit value minus Baseline value. Only those participants with data available at the specified time points were analyzed (represented by n=X in category titles).

End point type	Secondary
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End point timeframe:

Baseline (Day 1, pre-dose), Week 0 (post-dose), Weeks 4 and 8 (pre-dose and post-dose) Weeks 12 and 24

End point values	Placebo	GSK3772847		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	9 ^[35]	8 ^[36]		
Units: Millimeters of mercury				
arithmetic mean (standard deviation)				
SBP; Week 0 (post-dose); n=9, 8	3.7 (± 8.77)	1.4 (± 9.38)		
SBP; Week 4 (pre-dose); n=8, 8	0.1 (± 14.40)	-2.5 (± 18.05)		
SBP; Week 4 (post-dose); n=8, 8	4.5 (± 14.16)	4.5 (± 19.18)		
SBP; Week 8 (pre-dose); n=8, 8	0.5 (± 14.42)	7.3 (± 17.81)		
SBP; Week 8 (post-dose); n=8, 8	0.6 (± 15.27)	6.0 (± 18.97)		
SBP; Week 12; n=8, 8	4.1 (± 13.17)	7.1 (± 18.74)		
SBP; Week 24; n=9, 8	2.7 (± 17.00)	6.1 (± 14.97)		
DBP; Week 0 (post-dose); n=9, 8	0.1 (± 5.40)	0.6 (± 7.15)		
DBP; Week 4 (pre-dose); n=8, 8	-3.1 (± 3.72)	1.0 (± 14.11)		

DBP; Week 4 (post-dose); n=8, 8	-4.8 (± 4.92)	1.3 (± 12.90)		
DBP; Week 8 (pre-dose); n=8, 8	-7.8 (± 8.31)	0.6 (± 14.23)		
DBP; Week 8 (post-dose); n=8, 8	-11.3 (± 9.92)	-1.0 (± 13.63)		
DBP; Week 12; n=8, 8	-2.9 (± 4.49)	2.6 (± 12.34)		
DBP; Week 24; n=9, 8	-5.2 (± 6.98)	3.0 (± 14.93)		

Notes:

[35] - Safety Population

[36] - Safety Population

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in pulse rate

End point title	Change from Baseline in pulse rate
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End point description:

Pulse rate was measured in the supine position after five minutes of rest for the participant. Baseline is the most recent recorded value before dosing on Day 1 (Week 0). Change from Baseline is calculated as post-dose visit value minus Baseline value. Only those participants with data available at the specified time points were analyzed (represented by n=X in category titles).

End point type	Secondary
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End point timeframe:

Baseline (Day 1, pre-dose), Week 0 (post-dose), Weeks 4 and 8 (pre-dose and post-dose) Weeks 12 and 24

End point values	Placebo	GSK3772847		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	9 ^[37]	8 ^[38]		
Units: Beats per minute				
arithmetic mean (standard deviation)				
Week 0 (post-dose); n=9, 8	-0.8 (± 7.63)	-2.5 (± 5.37)		
Week 4 (pre-dose); n=8, 8	0.8 (± 9.60)	-1.8 (± 8.17)		
Week 4 (post-dose); n=8, 8	-6.8 (± 9.04)	-1.0 (± 9.80)		
Week 8 (pre-dose); n=8, 8	0.0 (± 8.26)	-1.5 (± 6.55)		
Week 8 (post-dose); n=8, 8	-6.3 (± 6.39)	-2.1 (± 6.22)		
Week 12; n=8, 8	1.6 (± 3.66)	-4.1 (± 6.64)		
Week 24; n=9, 8	2.2 (± 6.69)	-0.4 (± 6.99)		

Notes:

[37] - Safety Population

[38] - Safety Population

Statistical analyses

No statistical analyses for this end point

Secondary: Number of participants with abnormal Electrocardiogram (ECG) findings

End point title	Number of participants with abnormal Electrocardiogram (ECG) findings
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End point description:

Twelve lead ECGs were obtained using a standardized ECG machine that measured heart rate, PR, QRS, QT and corrected QT interval (QTc). ECG measurements were done with the participant in a supine

position having rested in this position for approximately 5 minutes before each reading. Clinically significant (CS) and not clinically significant (NCS) abnormal ECG findings at worst-case post-Baseline are presented. CS abnormal findings are those which are not associated with the underlying disease, unless judged by the investigator to be more severe than expected for the participant's condition. Data for worst-case post-Baseline is presented.

End point type	Secondary
End point timeframe:	
Up to Week 12	

End point values	Placebo	GSK3772847		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	9 ^[39]	8 ^[40]		
Units: Participants				
NCS	6	6		
CS	1	0		

Notes:

[39] - Safety Population

[40] - Safety Population

Statistical analyses

No statistical analyses for this end point

Secondary: Number of participants with abnormal 24-hour Holter findings

End point title	Number of participants with abnormal 24-hour Holter findings
End point description:	
A Holter monitor is a type of continuous ambulatory ECG device used for quantitative assessment of abnormal rhythm events. Number of participants with abnormal 24-hour Holter findings is presented. Data was summarized for participants with at least 16 hours of data.	
End point type	Secondary
End point timeframe:	
Week 0	

End point values	Placebo	GSK3772847		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	9 ^[41]	8 ^[42]		
Units: Participants	4	7		

Notes:

[41] - Safety Population

[42] - Safety Population

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

AEs and SAEs were collected from the start of study treatment up to Week 24

Adverse event reporting additional description:

AEs and SAEs were collected in the Safety Population which comprised of all randomized participants who took at least 1 dose of study treatment.

Assessment type	Systematic
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Dictionary used

Dictionary name	MedDRA
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Dictionary version	22.1
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Reporting groups

Reporting group title	GSK3772847
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Reporting group description:

Participants received three doses of GSK3772847 10 mg/kg administered intravenously every 4 weeks (Weeks 0, 4 and 8) along with their standard of care treatment.

Reporting group title	Placebo
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Reporting group description:

Participants received three doses of placebo administered intravenously every 4 weeks (Weeks 0, 4 and 8) along with their standard of care treatment.

Serious adverse events	GSK3772847	Placebo	
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 8 (0.00%)	1 / 9 (11.11%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events			
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Prostate cancer			
subjects affected / exposed	0 / 8 (0.00%)	1 / 9 (11.11%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

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

Non-serious adverse events	GSK3772847	Placebo	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	3 / 8 (37.50%)	7 / 9 (77.78%)	
Investigations			

Blood creatine phosphokinase increased subjects affected / exposed occurrences (all)	0 / 8 (0.00%) 0	1 / 9 (11.11%) 1	
Cardiac disorders Tachycardia subjects affected / exposed occurrences (all)	0 / 8 (0.00%) 0	1 / 9 (11.11%) 1	
Nervous system disorders Headache subjects affected / exposed occurrences (all) Lethargy subjects affected / exposed occurrences (all) Sciatica subjects affected / exposed occurrences (all)	1 / 8 (12.50%) 1 0 / 8 (0.00%) 0 0 / 8 (0.00%) 0	2 / 9 (22.22%) 2 1 / 9 (11.11%) 1 1 / 9 (11.11%) 1	
Blood and lymphatic system disorders Anaemia subjects affected / exposed occurrences (all)	0 / 8 (0.00%) 0	1 / 9 (11.11%) 1	
Eye disorders Conjunctivitis allergic subjects affected / exposed occurrences (all)	0 / 8 (0.00%) 0	1 / 9 (11.11%) 1	
Psychiatric disorders Alcoholism subjects affected / exposed occurrences (all)	0 / 8 (0.00%) 0	1 / 9 (11.11%) 1	
Musculoskeletal and connective tissue disorders Arthralgia subjects affected / exposed occurrences (all) Muscle spasms subjects affected / exposed occurrences (all)	0 / 8 (0.00%) 0 0 / 8 (0.00%) 0	1 / 9 (11.11%) 1 1 / 9 (11.11%) 1	
Infections and infestations			

Nasopharyngitis			
subjects affected / exposed	1 / 8 (12.50%)	2 / 9 (22.22%)	
occurrences (all)	1	2	
Bronchitis			
subjects affected / exposed	0 / 8 (0.00%)	1 / 9 (11.11%)	
occurrences (all)	0	1	
Upper respiratory tract infection			
subjects affected / exposed	1 / 8 (12.50%)	0 / 9 (0.00%)	
occurrences (all)	1	0	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
05 February 2018	Amendment 01-To address clarifications regarding the eligibility criteria, the study population, the schedule of activities and the clinical assessments. Also, a few typographical errors were corrected.
10 October 2018	Amendment 02- To include participants with severe asthma with AFAD treated with low dose oral corticosteroid who still demonstrate a lack of complete control as demonstrated by Asthma Control Questionnaire (ACQ)-5, Fractional exhaled Nitric Oxide (FeNO) and blood eosinophil levels. Also, a few clarifications were included.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported