



Clinical trial results:

A double-blind (sponsor unblind), placebo controlled, randomised, parallel group study to evaluate the safety, tolerability and pharmacokinetics of multiple doses of GSK2269557 administered as a dry powder to COPD patients and assessment of dose response using sputum biomarkers.

Summary

EudraCT number	2014-000313-31
Trial protocol	DE
Global end of trial date	18 August 2015

Results information

Result version number	v1 (current)
This version publication date	21 April 2016
First version publication date	21 April 2016

Trial information

Trial identification

Sponsor protocol code	PII115119
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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 Clinical Support Helpdesk, GlaxoSmithKline, +44 02089904466, GSKClinicalSupportHD@gsk.com
Scientific contact	GSK Clinical Support Helpdesk, GlaxoSmithKline, +44 02089904466, 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	04 February 2016
Is this the analysis of the primary completion data?	No
Global end of trial reached?	Yes
Global end of trial date	18 August 2015
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

Part A

To assess the safety and tolerability of repeat doses of GSK2269557 administered as a dry powder to COPD patients.

Part B

To characterise the dose-response relationship of repeat doses of GSK2269557 administered as a dry powder to COPD patients using inflammatory cytokine biomarker.

Protection of trial subjects:

A subject may withdraw from study treatment at any time at his/her own request, or may be withdrawn at any time at the discretion of the investigator for safety, behavioral or administrative reasons.

There are subject specific dose adaptation/stopping criteria including Liver Chemistry and QTc

Liver chemistry threshold stopping criteria have been designed to assure subject safety and to evaluate liver event aetiology (in alignment with the FDA premarketing clinical liver safety guidance).

Subjects suffering from an exacerbation of COPD following screening or during the treatment phase of the study will be withdrawn.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	31 July 2014
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Germany: 64
Worldwide total number of subjects	64
EEA total number of subjects	64

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)	38
From 65 to 84 years	26
85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

This study was comprised of two parts. In Part A, participants were randomized to active or placebo treatment in a 3:1 ratio and in Part B, to placebo or one of the six doses of active treatment in an equal ratio. Each part comprised a separate sample of participants.

Period 1

Period 1 title	Part A and Part B (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	Part A: Placebo

Arm description:

Participants received 2 inhalations of matching placebo once daily for 14 consecutive days.

Arm type	Placebo
Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Inhalation powder
Routes of administration	Inhalation use

Dosage and administration details:

Lactose was contained in an inhalation device. Participants received multiple inhalation devices, each containing one of the 3 investigational medicinal products. Once daily for 14 consecutive days, participants took one inhalation from each device such that they received the total dose for the arm they were randomized to. Total dose for Part A: Placebo/GSK2269577 1000 mcg. Total dose for Part B: placebo/GSK2269577 100/200/500/700/1000/2000 mcg.

Arm title	Part A: GSK2269557 1000 µg
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Arm description:

Participants received repeat doses of GSK2269557 1000 micrograms (µg) (2 inhalations of 500 µg each from a single device) administered as a dry powder inhalation, once daily for 14 consecutive days.

Arm type	Experimental
Investigational medicinal product name	GSK2269557 500 micrograms
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Inhalation powder
Routes of administration	Inhalation use

Dosage and administration details:

GSK2269557 500 mcg blended in lactose was contained in an inhalation device.

Participants received multiple inhalation devices, each containing one of the 3 investigational medicinal products. Once daily for 14 consecutive days, participants took one inhalation from each device such that they received the total dose for the arm they were randomized to. Total dose for Part A: Placebo/GSK2269557 1000 mcg. Total dose for Part B: Placebo/GSK2269557 100/200/500/700/1000/2000 mcg.

Arm title	Part B: Placebo
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Arm description:

Participants received four inhalations of matching placebo (from four inhalation devices) once daily for 14 consecutive days.

Arm type	Placebo
Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Inhalation powder
Routes of administration	Inhalation use

Dosage and administration details:

Lactose was contained in an inhalation device.

Participants received multiple inhalation devices, each containing one of the 3 investigational medicinal products. Once daily for 14 consecutive days, participants took one inhalation from each device such that they received the total dose for the arm they were randomized to. Total dose for Part A: Placebo/GSK2269577 1000 mcg. Total dose for Part B: Placebo/GSK2269577 100/200/500/700/1000/2000 mcg.

Arm title	Part B: GSK2269557 100 µg
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Arm description:

Participants received repeat doses of GSK2269557 100 µg administered as a dry powder inhalation, once daily for 14 consecutive days. To maintain blinding, the total dose was delivered through four inhalation devices, each device containing either GSK2269557 100 µg or placebo.

Arm type	Experimental
Investigational medicinal product name	GSK2269557 100 micrograms
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Inhalation powder
Routes of administration	Inhalation use

Dosage and administration details:

GSK2269557 100 micrograms (mcg) blended in lactose was contained in an inhalation device.

Participants received multiple inhalation devices, each containing one of the 3 investigational medicinal products. Once daily for 14 consecutive days, participants took one inhalation from each device such that they received the total dose for the arm they were randomized to. Total dose for Part A: Placebo/GSK2269557 1000 mcg. Total dose for Part B: Placebo/GSK2269557 100/200/500/700/1000/2000 mcg.

Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Inhalation powder
Routes of administration	Inhalation use

Dosage and administration details:

Lactose was contained in an inhalation device.

Participants received multiple inhalation devices, each containing one of the 3 investigational medicinal products. Once daily for 14 consecutive days, participants took one inhalation from each device such that they received the total dose for the arm they were randomized to. Total dose for Part A: Placebo/GSK2269577 1000 mcg. Total dose for Part B: Placebo/GSK2269577 100/200/500/700/1000/2000 mcg.

Arm title	Part B: GSK2269557 200 µg
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Arm description:

Participants received repeat doses of GSK2269557 200 µg administered as a dry powder inhalation, once daily for 14 consecutive days. To maintain blinding, the total dose was delivered through four inhalation devices, each device containing either GSK2269557 100 µg or placebo.

Arm type	Experimental
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Investigational medicinal product name	GSK2269557 100 micrograms
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Inhalation powder
Routes of administration	Inhalation use

Dosage and administration details:

GSK2269557 100 micrograms (mcg) blended in lactose was contained in an inhalation device. Participants received multiple inhalation devices, each containing one of the 3 investigational medicinal products. Once daily for 14 consecutive days, participants took one inhalation from each device such that they received the total dose for the arm they were randomized to. Total dose for Part A: Placebo/GSK2269557 1000 mcg. Total dose for Part B: Placebo/GSK2269557 100/200/500/700/1000/2000 mcg.

Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Inhalation powder
Routes of administration	Inhalation use

Dosage and administration details:

Lactose was contained in an inhalation device. Participants received multiple inhalation devices, each containing one of the 3 investigational medicinal products. Once daily for 14 consecutive days, participants took one inhalation from each device such that they received the total dose for the arm they were randomized to. Total dose for Part A: Placebo/GSK2269577 1000 mcg. Total dose for Part B: Placebo/GSK2269577 100/200/500/700/1000/2000 mcg.

Arm title	Part B: GSK2269557 500 µg
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Arm description:

Participants received repeat doses of GSK2269557 500 µg administered as a dry powder inhalation, once daily for 14 consecutive days. To maintain blinding, the total dose was delivered through four inhalation devices, each device containing either GSK2269557 500 µg or placebo.

Arm type	Experimental
Investigational medicinal product name	GSK2269557 500 micrograms
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Inhalation powder
Routes of administration	Inhalation use

Dosage and administration details:

GSK2269557 500 mcg blended in lactose was contained in an inhalation device. Participants received multiple inhalation devices, each containing one of the 3 investigational medicinal products. Once daily for 14 consecutive days, participants took one inhalation from each device such that they received the total dose for the arm they were randomized to. Total dose for Part A: Placebo/GSK2269557 1000 mcg. Total dose for Part B: Placebo/GSK2269557 100/200/500/700/1000/2000 mcg.

Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Inhalation powder
Routes of administration	Inhalation use

Dosage and administration details:

Lactose was contained in an inhalation device. Participants received multiple inhalation devices, each containing one of the 3 investigational medicinal products. Once daily for 14 consecutive days, participants took one inhalation from each device such that they received the total dose for the arm they were randomized to. Total dose for Part A: Placebo/GSK2269577 1000 mcg. Total dose for Part B: Placebo/GSK2269577 100/200/500/700/1000/2000 mcg.

Arm title	Part B: GSK2269557 700 µg
Arm description: Participants received repeat doses of GSK2269557 700 µg administered as a dry powder inhalation, once daily for 14 consecutive days. To maintain blinding, the total dose was delivered through four inhalation devices, each device containing GSK2269557 100 µg, 500 µg, or placebo.	
Arm type	Experimental
Investigational medicinal product name	GSK2269557 500 micrograms
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Inhalation powder
Routes of administration	Inhalation use

Dosage and administration details:

GSK2269557 500 mcg blended in lactose was contained in an inhalation device. Participants received multiple inhalation devices, each containing one of the 3 investigational medicinal products. Once daily for 14 consecutive days, participants took one inhalation from each device such that they received the total dose for the arm they were randomized to. Total dose for Part A: Placebo/GSK2269557 1000 mcg. Total dose for Part B: Placebo/GSK2269557 100/200/500/700/1000/2000 mcg.

Investigational medicinal product name	GSK2269557 100 micrograms
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Inhalation powder
Routes of administration	Inhalation use

Dosage and administration details:

GSK2269557 100 micrograms (mcg) blended in lactose was contained in an inhalation device. Participants received multiple inhalation devices, each containing one of the 3 investigational medicinal products. Once daily for 14 consecutive days, participants took one inhalation from each device such that they received the total dose for the arm they were randomized to. Total dose for Part A: Placebo/GSK2269557 1000 mcg. Total dose for Part B: Placebo/GSK2269557 100/200/500/700/1000/2000 mcg.

Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Inhalation powder
Routes of administration	Inhalation use

Dosage and administration details:

Lactose was contained in an inhalation device. Participants received multiple inhalation devices, each containing one of the 3 investigational medicinal products. Once daily for 14 consecutive days, participants took one inhalation from each device such that they received the total dose for the arm they were randomized to. Total dose for Part A: Placebo/GSK2269577 1000 mcg. Total dose for Part B: Placebo/GSK2269577 100/200/500/700/1000/2000 mcg.

Arm title	Part B: GSK2269557 1000 µg
Arm description: Participants received repeat doses of GSK2269557 1000 µg administered as a dry powder inhalation, once daily for 14 consecutive days. To maintain blinding, the total dose was delivered through four inhalation devices, each device containing either GSK2269557 500 µg or placebo.	
Arm type	Experimental
Investigational medicinal product name	GSK2269557 500 micrograms
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Inhalation powder
Routes of administration	Inhalation use

Dosage and administration details:

GSK2269557 500 mcg blended in lactose was contained in an inhalation device. Participants received multiple inhalation devices, each containing one of the 3 investigational medicinal products. Once daily for 14 consecutive days, participants took one inhalation from each device such that they received the total dose for the arm they were randomized to. Total dose for Part A: Placebo/GSK2269557 1000 mcg. Total dose for Part B: Placebo/GSK2269557 100/200/500/700/1000/2000 mcg.

Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Inhalation powder
Routes of administration	Inhalation use

Dosage and administration details:

Lactose was contained in an inhalation device. Participants received multiple inhalation devices, each containing one of the 3 investigational medicinal products. Once daily for 14 consecutive days, participants took one inhalation from each device such that they received the total dose for the arm they were randomized to. Total dose for Part A: Placebo/GSK2269577 1000 mcg. Total dose for Part B: Placebo/GSK2269577 100/200/500/700/1000/2000 mcg.

Arm title	Part B: GSK2269557 2000 µg
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Arm description:

Participants received repeat doses of GSK2269557 2000 µg administered as a dry powder inhalation, once daily for 14 consecutive days. To maintain blinding, the total dose was delivered through four inhalation devices, each device containing GSK2269557 500 µg.

Arm type	Experimental
Investigational medicinal product name	GSK2269557 500 micrograms
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Inhalation powder
Routes of administration	Inhalation use

Dosage and administration details:

GSK2269557 500 mcg blended in lactose was contained in an inhalation device. Participants received multiple inhalation devices, each containing one of the 3 investigational medicinal products. Once daily for 14 consecutive days, participants took one inhalation from each device such that they received the total dose for the arm they were randomized to. Total dose for Part A: Placebo/GSK2269557 1000 mcg. Total dose for Part B: Placebo/GSK2269557 100/200/500/700/1000/2000 mcg.

Number of subjects in period 1	Part A: Placebo	Part A: GSK2269557 1000 µg	Part B: Placebo
Started	7	21	5
Completed	7	21	5

Number of subjects in period 1	Part B: GSK2269557 100 µg	Part B: GSK2269557 200 µg	Part B: GSK2269557 500 µg
Started	5	5	5
Completed	5	5	5

Number of subjects in period 1	Part B: GSK2269557 700 µg	Part B: GSK2269557 1000 µg	Part B: GSK2269557 2000 µg
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Started	6	5	5
Completed	6	5	5

Baseline characteristics

Reporting groups

Reporting group title	Part A: Placebo
Reporting group description: Participants received 2 inhalations of matching placebo once daily for 14 consecutive days.	
Reporting group title	Part A: GSK2269557 1000 µg
Reporting group description: Participants received repeat doses of GSK2269557 1000 micrograms (µg) (2 inhalations of 500 µg each from a single device) administered as a dry powder inhalation, once daily for 14 consecutive days.	
Reporting group title	Part B: Placebo
Reporting group description: Participants received four inhalations of matching placebo (from four inhalation devices) once daily for 14 consecutive days.	
Reporting group title	Part B: GSK2269557 100 µg
Reporting group description: Participants received repeat doses of GSK2269557 100 µg administered as a dry powder inhalation, once daily for 14 consecutive days. To maintain blinding, the total dose was delivered through four inhalation devices, each device containing either GSK2269557 100 µg or placebo.	
Reporting group title	Part B: GSK2269557 200 µg
Reporting group description: Participants received repeat doses of GSK2269557 200 µg administered as a dry powder inhalation, once daily for 14 consecutive days. To maintain blinding, the total dose was delivered through four inhalation devices, each device containing either GSK2269557 100 µg or placebo.	
Reporting group title	Part B: GSK2269557 500 µg
Reporting group description: Participants received repeat doses of GSK2269557 500 µg administered as a dry powder inhalation, once daily for 14 consecutive days. To maintain blinding, the total dose was delivered through four inhalation devices, each device containing either GSK2269557 500 µg or placebo.	
Reporting group title	Part B: GSK2269557 700 µg
Reporting group description: Participants received repeat doses of GSK2269557 700 µg administered as a dry powder inhalation, once daily for 14 consecutive days. To maintain blinding, the total dose was delivered through four inhalation devices, each device containing GSK2269557 100 µg, 500 µg, or placebo.	
Reporting group title	Part B: GSK2269557 1000 µg
Reporting group description: Participants received repeat doses of GSK2269557 1000 µg administered as a dry powder inhalation, once daily for 14 consecutive days. To maintain blinding, the total dose was delivered through four inhalation devices, each device containing either GSK2269557 500 µg or placebo.	
Reporting group title	Part B: GSK2269557 2000 µg
Reporting group description: Participants received repeat doses of GSK2269557 2000 µg administered as a dry powder inhalation, once daily for 14 consecutive days. To maintain blinding, the total dose was delivered through four inhalation devices, each device containing GSK2269557 500 µg.	

Reporting group values	Part A: Placebo	Part A: GSK2269557 1000 µg	Part B: Placebo
Number of subjects	7	21	5
Age categorical			
Units: Subjects			

Age continuous Units: years arithmetic mean standard deviation	65.1 ± 5.81	60.5 ± 6.68	64.4 ± 4.45
Gender categorical Units: Subjects			
Female	1	7	2
Male	6	14	3
Race, Customized Units: Subjects			
White-White/Caucasian/European Heritage	7	21	5

Reporting group values	Part B: GSK2269557 100 µg	Part B: GSK2269557 200 µg	Part B: GSK2269557 500 µg
Number of subjects	5	5	5
Age categorical Units: Subjects			

Age continuous Units: years arithmetic mean standard deviation	61.6 ± 4.56	62.2 ± 8.23	65.4 ± 5.81
Gender categorical Units: Subjects			
Female	4	1	0
Male	1	4	5
Race, Customized Units: Subjects			
White-White/Caucasian/European Heritage	5	5	5

Reporting group values	Part B: GSK2269557 700 µg	Part B: GSK2269557 1000 µg	Part B: GSK2269557 2000 µg
Number of subjects	6	5	5
Age categorical Units: Subjects			

Age continuous Units: years arithmetic mean standard deviation	64.7 ± 7.26	62.4 ± 9.24	62.4 ± 6.43
Gender categorical Units: Subjects			
Female	3	3	3
Male	3	2	2
Race, Customized Units: Subjects			
White-White/Caucasian/European Heritage	6	5	5

Reporting group values	Total		
Number of subjects	64		

Age categorical Units: Subjects			
Age continuous Units: years arithmetic mean standard deviation	-		
Gender categorical Units: Subjects			
Female	24		
Male	40		
Race, Customized Units: Subjects			
White-White/Caucasian/European Heritage	64		

End points

End points reporting groups

Reporting group title	Part A: Placebo
Reporting group description: Participants received 2 inhalations of matching placebo once daily for 14 consecutive days.	
Reporting group title	Part A: GSK2269557 1000 µg
Reporting group description: Participants received repeat doses of GSK2269557 1000 micrograms (µg) (2 inhalations of 500 µg each from a single device) administered as a dry powder inhalation, once daily for 14 consecutive days.	
Reporting group title	Part B: Placebo
Reporting group description: Participants received four inhalations of matching placebo (from four inhalation devices) once daily for 14 consecutive days.	
Reporting group title	Part B: GSK2269557 100 µg
Reporting group description: Participants received repeat doses of GSK2269557 100 µg administered as a dry powder inhalation, once daily for 14 consecutive days. To maintain blinding, the total dose was delivered through four inhalation devices, each device containing either GSK2269557 100 µg or placebo.	
Reporting group title	Part B: GSK2269557 200 µg
Reporting group description: Participants received repeat doses of GSK2269557 200 µg administered as a dry powder inhalation, once daily for 14 consecutive days. To maintain blinding, the total dose was delivered through four inhalation devices, each device containing either GSK2269557 100 µg or placebo.	
Reporting group title	Part B: GSK2269557 500 µg
Reporting group description: Participants received repeat doses of GSK2269557 500 µg administered as a dry powder inhalation, once daily for 14 consecutive days. To maintain blinding, the total dose was delivered through four inhalation devices, each device containing either GSK2269557 500 µg or placebo.	
Reporting group title	Part B: GSK2269557 700 µg
Reporting group description: Participants received repeat doses of GSK2269557 700 µg administered as a dry powder inhalation, once daily for 14 consecutive days. To maintain blinding, the total dose was delivered through four inhalation devices, each device containing GSK2269557 100 µg, 500 µg, or placebo.	
Reporting group title	Part B: GSK2269557 1000 µg
Reporting group description: Participants received repeat doses of GSK2269557 1000 µg administered as a dry powder inhalation, once daily for 14 consecutive days. To maintain blinding, the total dose was delivered through four inhalation devices, each device containing either GSK2269557 500 µg or placebo.	
Reporting group title	Part B: GSK2269557 2000 µg
Reporting group description: Participants received repeat doses of GSK2269557 2000 µg administered as a dry powder inhalation, once daily for 14 consecutive days. To maintain blinding, the total dose was delivered through four inhalation devices, each device containing GSK2269557 500 µg.	

Primary: Part A: Number of participants with at least one non-serious adverse event (AE), serious adverse event (SAE), or drug-related adverse event

End point title	Part A: Number of participants with at least one non-serious adverse event (AE), serious adverse event (SAE), or drug-related adverse event ^{[1][2]}
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End point description:

An AE is defined as any untoward medical occurrence in a participant, temporally associated with the use of a medicinal product, whether or not considered related to the medicinal product. An SAE is defined as any untoward medical occurrence that, at any dose, results in death, is life-threatening,

requires hospitalization or prolongation of existing hospitalization, results in disability/incapacity, or is a congenital anomaly/birth defect, may jeopardize the participant or may require medical or surgical intervention to prevent one of the other outcomes listed in this definition, associated with liver injury and impaired liver function defined as alanine aminotransferase $\geq 3 \times$ upper limit of normal (ULN), and total bilirubin $\geq 2 \times$ ULN or international normalised ratio > 1.5 . AEs were classified as potentially drug-related, based on the investigator's judgement. Refer to the general AE/SAE module for a list of AEs and SAEs.

End point type	Primary
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End point timeframe:

From the start of study treatment until follow-up (assessed for approximately 19 days)

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 for this primary endpoint; thus, no data are available

[2] - 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: No statistical analysis was performed for this primary endpoint; thus, no data are available

End point values	Part A: Placebo	Part A: GSK2269557 1000 µg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	7 ^[3]	21 ^[4]		
Units: Participants				
At least one AE	2	9		
At least one SAE	0	1		
At least one drug-related AE	2	6		

Notes:

[3] - Safety Population: all participants who received at least one dose of study treatment.

[4] - Safety Population: all participants who received at least one dose of study treatment.

Statistical analyses

No statistical analyses for this end point

Primary: Part A: Change from Baseline in counts of white blood cells (WBC), total neutrophils (total absolute neutrophil count [ANC]), lymphocytes, monocytes, eosinophils, basophils, and platelets at the indicated time points

End point title	Part A: Change from Baseline in counts of white blood cells (WBC), total neutrophils (total absolute neutrophil count [ANC]), lymphocytes, monocytes, eosinophils, basophils, and platelets at the indicated time points ^[5] ^[6]
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End point description:

Blood samples were collected for measurement for the indicated tests. Baseline is Day 1 pre-dose. Change from Baseline at any post-dose visit was calculated as the post-dose visit value minus the Baseline value. Day 7 assessments could be conducted on Day 7 or Day 8.

End point type	Primary
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End point timeframe:

Baseline (Day 1 [pre-dose]), Day 7 (pre-dose), and Day 14 (24 hours [h] post-dose)

Notes:

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

Justification: No statistical analysis was performed for this primary endpoint; thus, no data are available

[6] - 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: No statistical analysis was performed for this primary endpoint; thus, no data are available

End point values	Part A: Placebo	Part A: GSK2269557 1000 µg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	7 ^[7]	21 ^[8]		
Units: 10 ⁹ cells per liter (GI/L)				
arithmetic mean (standard deviation)				
WBC; Day 7/Day 8, pre-dose	-0.736 (± 0.937)	-0.08 (± 1.387)		
WBC; Day 14, 24 h post dose	-0.14 (± 1.22)	-0.51 (± 0.947)		
Total ANC; Day 7/Day 8, pre-dose	-0.664 (± 0.624)	-0.363 (± 1.342)		
Total ANC; Day 14, 24 h post dose	-0.153 (± 0.887)	-0.547 (± 0.977)		
Lymphocytes; Day 7/Day 8, pre-dose	-0.033 (± 0.321)	0.172 (± 0.597)		
Lymphocytes; Day 14, 24 h post dose	-0.049 (± 0.197)	0.03 (± 0.245)		
Monocytes; Day 7/Day 8, pre-dose	-0.036 (± 0.074)	0.046 (± 0.149)		
Monocytes; Day 14, 24 h post dose	0.039 (± 0.178)	-0.022 (± 0.116)		
Eosinophils; Day 7/Day 8, pre-dose	-0.006 (± 0.051)	0.032 (± 0.074)		
Eosinophils; Day 14, 24 h post dose	0.001 (± 0.085)	0.01 (± 0.075)		
Basophils; Day 7/Day 8, pre-dose	-0.001 (± 0.006)	0.006 (± 0.015)		
Basophils; Day 14, 24 h post dose	-0.003 (± 0.013)	0.002 (± 0.018)		
Platelets; Day 7/Day 8, pre-dose	1.6 (± 20.58)	17.9 (± 36.44)		
Platelets; Day 14, 24 h post dose	14.7 (± 21.8)	23.5 (± 37.43)		

Notes:

[7] - Safety Population

[8] - Safety Population

Statistical analyses

No statistical analyses for this end point

Primary: Part A: Change from Baseline in hemoglobin and mean corpuscle hemoglobin concentration (MCHC) at the indicated time points

End point title	Part A: Change from Baseline in hemoglobin and mean corpuscle hemoglobin concentration (MCHC) at the indicated time points ^{[9][10]}
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End point description:

Blood samples were collected for measurement for the indicated tests. Baseline is Day 1 pre-dose. MCHC is one of the red blood cell (RBC) indices. Change from Baseline at any post-dose visit was calculated as the post-dose visit value minus the Baseline value. Day 7 assessments could be conducted on Day 7 or Day 8.

End point type	Primary
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End point timeframe:

Baseline (Day 1 [pre-dose]), Day 7 (pre-dose), and Day 14 (24 h post-dose)

Notes:

[9] - 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 for this primary endpoint; thus, no data are available

[10] - 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: No statistical analysis was performed for this primary endpoint; thus, no data are available

End point values	Part A: Placebo	Part A: GSK2269557 1000 µg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	7 ^[11]	21 ^[12]		
Units: Grams/Liter (g/L)				
arithmetic mean (standard deviation)				
Hemoglobin; Day 7/Day 8, pre-dose	-1.3 (± 6.63)	1.6 (± 4.17)		
Hemoglobin; Day 14, 24 h post dose	0.3 (± 6.97)	1 (± 4.12)		
MCHC; Day 7/Day 8, pre-dose	-5.3 (± 7.32)	-2.2 (± 4.54)		
MCHC; Day 14, 24 h post dose	-8.4 (± 4.39)	-2.4 (± 6.45)		

Notes:

[11] - Safety Population

[12] - Safety Population

Statistical analyses

No statistical analyses for this end point

Primary: Part A: Change from Baseline in hematocrit at the indicated time points

End point title	Part A: Change from Baseline in hematocrit at the indicated time points ^{[13][14]}
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End point description:

Blood samples were collected for measurement for the indicated tests. Baseline is Day 1 pre-dose. Change from Baseline at any post-dose visit was calculated as the post-dose visit value minus the Baseline value. Day 7 assessments could be conducted on Day 7 or Day 8.

End point type	Primary
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End point timeframe:

Baseline (Day 1 [pre-dose]), Day 7 (pre-dose), and Day 14 (24 hours [h] post-dose)

Notes:

[13] - 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 for this primary endpoint; thus, no data are available

[14] - 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: No statistical analysis was performed for this primary endpoint; thus, no data are available

End point values	Part A: Placebo	Part A: GSK2269557 1000 µg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	7 ^[15]	21 ^[16]		
Units: Fraction of 1				
arithmetic mean (standard deviation)				
Hematocrit; Day 7/Day 8, pre-dose	0.003 (± 0.023)	0.007 (± 0.013)		
Hematocrit; Day 14, 24 h post dose	0.011 (± 0.019)	0.006 (± 0.016)		

Notes:

[15] - Safety Population

[16] - Safety Population

Statistical analyses

No statistical analyses for this end point

Primary: Part A: Change from Baseline in counts of RBCs and reticulocytes at the indicated time points

End point title	Part A: Change from Baseline in counts of RBCs and reticulocytes at the indicated time points ^{[17][18]}
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End point description:

Blood samples were collected for measurement for the indicated tests. Baseline is Day 1 pre-dose. Change from Baseline at any post-dose visit was calculated as the post-dose visit value minus the Baseline value. Day 7 assessments could be conducted on Day 7 or Day 8.

End point type	Primary
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End point timeframe:

Baseline (Day 1 [pre-dose]), Day 7 (pre-dose), and Day 14 (24 hours [h] post-dose)

Notes:

[17] - 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 for this primary endpoint; thus, no data are available

[18] - 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: No statistical analysis was performed for this primary endpoint; thus, no data are available

End point values	Part A: Placebo	Part A: GSK2269557 1000 µg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	7 ^[19]	21 ^[20]		
Units: 10 ¹² cells/Liter (TI/L)				
arithmetic mean (standard deviation)				
RBCs; Day 7/Day 8, pre-dose	0.023 (± 0.23)	0.06 (± 0.141)		
RBCs; Day 14, 24 h post dose	0.119 (± 0.201)	0.063 (± 0.16)		
Reticulocytes; Day 7/Day 8, pre-dose	0.005 (± 0.014)	0.003 (± 0.009)		
Reticulocytes; Day 14, 24 h post dose	0.009 (± 0.014)	0.003 (± 0.01)		

Notes:

[19] - Safety Population

[20] - Safety Population

Statistical analyses

No statistical analyses for this end point

Primary: Part A: Change from Baseline in mean corpuscle hemoglobin (MCH) at the indicated time points

End point title	Part A: Change from Baseline in mean corpuscle hemoglobin (MCH) at the indicated time points ^{[21][22]}
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End point description:

Blood samples were collected for measurement for the indicated tests. Baseline is Day 1 pre-dose. MCH is one of the red blood cell indices. Change from Baseline at any post-dose visit was calculated as the post-dose visit value minus the Baseline value. Day 7 assessments could be conducted on Day 7 or Day 8.

End point type	Primary
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End point timeframe:

Baseline (Day 1 [pre-dose]), Day 7 (pre-dose), and Day 14 (24 hours [h] post-dose)

Notes:

[21] - 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 for this primary endpoint; thus, no data are available

[22] - 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: No statistical analysis was performed for this primary endpoint; thus, no data are available

End point values	Part A: Placebo	Part A: GSK2269557 1000 µg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	7 ^[23]	21 ^[24]		
Units: Picograms (pg)				
arithmetic mean (standard deviation)				
MCH; Day 7/Day 8, pre-dose	-0.46 (± 0.602)	-0.06 (± 0.44)		
MCH; Day 14, 24 h post dose	-0.76 (± 0.586)	-0.23 (± 0.593)		

Notes:

[23] - Safety Population

[24] - Safety Population

Statistical analyses

No statistical analyses for this end point

Primary: Part A: Change from Baseline in mean corpuscle volume (MCV) at the indicated time points

End point title	Part A: Change from Baseline in mean corpuscle volume (MCV) at the indicated time points ^[25] ^[26]
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End point description:

Blood samples were collected for measurement for the indicated tests. Baseline is Day 1 pre-dose. MCV is one of the RBC indices. Change from Baseline at any post-dose visit was calculated as the post-dose visit value minus the Baseline value. Day 7 assessments could be conducted on Day 7 or Day 8.

End point type	Primary
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End point timeframe:

Baseline (Day 1 [pre-dose]), Day 7 (pre-dose), and Day 14 (24 hours [h] post-dose)

Notes:

[25] - 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 for this primary endpoint; thus, no data are available

[26] - 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: No statistical analysis was performed for this primary endpoint; thus, no data are available

End point values	Part A: Placebo	Part A: GSK2269557 1000 µg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	7 ^[27]	21 ^[28]		
Units: Femtoliters (fL)				
arithmetic mean (standard deviation)				
MCV; Day 7/Day 8, pre-dose	0.11 (± 0.687)	0.43 (± 0.697)		
MCV; Day 14, 24 h post dose	0.07 (± 0.848)	-0.03 (± 1.193)		

Notes:

[27] - Safety Population

[28] - Safety Population

Statistical analyses

No statistical analyses for this end point

Primary: Part A: Change from Baseline in albumin and total protein at the indicated time points

End point title	Part A: Change from Baseline in albumin and total protein at the indicated time points ^[29] ^[30]
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End point description:

Blood samples were collected for measurement for the indicated tests. Baseline is Day 1 pre-dose. Change from Baseline at any post-dose visit was calculated as the post-dose visit value minus the Baseline value. Day 7 assessments could be conducted on Day 7 or Day 8.

End point type	Primary
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End point timeframe:

Baseline (Day 1 [pre-dose]), Day 7 (pre-dose), and Day 14 (24 hours [h] post-dose)

Notes:

[29] - 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 for this primary endpoint; thus, no data are available

[30] - 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: No statistical analysis was performed for this primary endpoint; thus, no data are available

End point values	Part A: Placebo	Part A: GSK2269557 1000 µg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	7 ^[31]	21 ^[32]		
Units: g/L				
arithmetic mean (standard deviation)				
Albumin; Day 7/Day 8, pre-dose	0.56 (± 2.23)	0.8 (± 1.576)		
Albumin; Day 14, 24 h post dose	0.53 (± 2.379)	0.52 (± 2.004)		
Total protein; Day 7/Day 8, pre-dose	0.56 (± 3.619)	1.28 (± 2.599)		
Total protein; Day 14, 24 h post dose	0.84 (± 3.887)	1.15 (± 2.606)		

Notes:

[31] - Safety Population

[32] - Safety Population

Statistical analyses

Primary: Part A: Change from Baseline in alanine aminotransferase (ALT), alkaline phosphatase (ALP), aspartate aminotransferase (AST), and gamma glutamyl transferase (GGT) at the indicated time points

End point title	Part A: Change from Baseline in alanine aminotransferase (ALT), alkaline phosphatase (ALP), aspartate aminotransferase (AST), and gamma glutamyl transferase (GGT) at the indicated time points ^{[33][34]}
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End point description:

Blood samples were collected for measurement for the indicated tests. Baseline is Day 1 pre-dose. Change from Baseline at any post-dose visit was calculated as the post-dose visit value minus the Baseline value. Day 7 assessments could be conducted on Day 7 or Day 8.

End point type	Primary
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End point timeframe:

Baseline (Day 1 [pre-dose]), Day 7 (pre-dose), and Day 14 (24 hours [h] post-dose)

Notes:

[33] - 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 for this primary endpoint; thus, no data are available

[34] - 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: No statistical analysis was performed for this primary endpoint; thus, no data are available.

End point values	Part A: Placebo	Part A: GSK2269557 1000 µg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	7 ^[35]	21 ^[36]		
Units: International Units (IU/L)				
arithmetic mean (standard deviation)				
ALT; Day 7/Day 8, pre-dose	2.46 (± 2.585)	-0.61 (± 2.208)		
ALT; Day 14, 24 h post dose	1.51 (± 2.667)	-0.4 (± 4.117)		
ALP; Day 7/Day 8, pre-dose	-0.64 (± 6.937)	1.14 (± 8.586)		
ALP; Day 14, 24 h post dose	-2.23 (± 6.522)	-0.21 (± 9.785)		
AST; Day 7/Day 8, pre-dose	3.14 (± 7.674)	-1.03 (± 3.081)		
AST; Day 14, 24 h post dose	1.83 (± 4.75)	-0.71 (± 2.592)		
GGT; Day 7/Day 8, pre-dose	-0.91 (± 2.203)	0.11 (± 2.55)		
GGT; Day 14, 24 h post dose	-1.96 (± 2.873)	-0.46 (± 4.187)		

Notes:

[35] - Safety Population

[36] - Safety Population

Statistical analyses

No statistical analyses for this end point

Primary: Part A: Change from Baseline in creatinine, bilirubin, and total bilirubin at the indicated time points

End point title	Part A: Change from Baseline in creatinine, bilirubin, and total bilirubin at the indicated time points ^{[37][38]}
End point description: Blood samples were collected for measurement for the indicated tests. Baseline is Day 1 pre-dose. Change from Baseline at any post-dose visit was calculated as the post-dose visit value minus the Baseline value. Day 7 assessments could be conducted on Day 7 or Day 8.	
End point type	Primary
End point timeframe: Baseline (Day 1 [pre-dose]), Day 7 (pre-dose), and Day 14 (24 hours [h] post-dose)	

Notes:

[37] - 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 for this primary endpoint; thus, no data are available

[38] - 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: No statistical analysis was performed for this primary endpoint; thus, no data are available

End point values	Part A: Placebo	Part A: GSK2269557 1000 µg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	7 ^[39]	21 ^[40]		
Units: Micromoles/Liter (micromol/L)				
arithmetic mean (standard deviation)				
Creatinine; Day 7/Day 8, pre-dose	2.31 (± 4.385)	-0.62 (± 5.104)		
Creatinine; Day 14, 24 h post dose	3.64 (± 6.035)	0.07 (± 3.259)		
Direct bilirubin; Day 7/Day 8, pre-dose	0.33 (± 0.419)	0.04 (± 0.398)		
Direct bilirubin; Day 14, 24 h post dose	0.27 (± 0.496)	0.1 (± 0.329)		
Total bilirubin; Day 7/Day 8, pre-dose	1.23 (± 2.447)	0.02 (± 2.59)		
Total bilirubin; Day 14, 24 h post dose	0.9 (± 2.805)	0.78 (± 1.72)		

Notes:

[39] - Safety Population

[40] - Safety Population

Statistical analyses

No statistical analyses for this end point

Primary: Part A: Change from Baseline in calcium, potassium, sodium, glucose, and blood urea nitrogen (BUN) at the indicated time points

End point title	Part A: Change from Baseline in calcium, potassium, sodium, glucose, and blood urea nitrogen (BUN) at the indicated time points ^{[41][42]}
End point description: Blood samples were collected for measurement for the indicated tests. Baseline is Day 1 pre-dose. Change from Baseline at any post-dose visit was calculated as the post-dose visit value minus the Baseline value. Day 7 assessments could be conducted on Day 7 or Day 8.	
End point type	Primary
End point timeframe: Baseline (Day 1 [pre-dose]), Day 7 (pre-dose), and Day 14 (24 hours [h] post-dose)	

Notes:

[41] - 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 for this primary endpoint; thus, no data are available

[42] - 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: No statistical analysis was performed for this primary endpoint; thus, no data are available

End point values	Part A: Placebo	Part A: GSK2269557 1000 µg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	7 ^[43]	21 ^[44]		
Units: Millimoles per Liter (mmol/L)				
arithmetic mean (standard deviation)				
Calcium; Day 7/Day 8, pre-dose	0.033 (± 0.0535)	0.033 (± 0.0617)		
Calcium; Day 14, 24 h post dose	0.033 (± 0.085)	0.029 (± 0.0588)		
Glucose; Day 7/Day 8, pre-dose	-0.053 (± 0.3333)	0.012 (± 0.2888)		
Glucose; Day 14, 24 h post dose	0.161 (± 0.2659)	0.024 (± 0.4914)		
Potassium; Day 7/Day 8, pre-dose	0.103 (± 0.2279)	0.011 (± 0.3539)		
Potassium; Day 14, 24 h post dose	0.161 (± 0.2562)	0.065 (± 0.3347)		
Sodium; Day 7/Day 8, pre-dose	1.21 (± 2.8)	0.88 (± 1.56)		
Sodium; Day 14, 24 h post dose	0.81 (± 1.297)	0.83 (± 1.39)		
BUN; Day 7/Day 8, pre-dose	-0.53 (± 1.083)	-0.192 (± 0.8124)		
BUN; Day 14, 24 h post dose	-0.464 (± 1.1979)	0.111 (± 1.2147)		

Notes:

[43] - Safety Population

[44] - Safety Population

Statistical analyses

No statistical analyses for this end point

Primary: Part A: Number of participants meeting criteria of potential clinical importance for systolic blood pressure (SBP), diastolic blood pressure (DBP), and heart rate (HR) at any visit post-Baseline

End point title	Part A: Number of participants meeting criteria of potential clinical importance for systolic blood pressure (SBP), diastolic blood pressure (DBP), and heart rate (HR) at any visit post-Baseline ^[45] ^[46]
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End point description:

Baseline was the Day 1 pre-dose measurement. Vital signs (SBP, DBP, and HR) were measured at Day 1 (30 minutes [min] and 6 h post-dose), Day 7 (pre-dose), and Day 14 (24 h post-dose). Potential clinical concern range for SBP was <85 millimeters of mercury (mmHg) (low) and >160 mmHg (high), for DBP <45 mmHg (low) and >100 mmHg (high) and for HR <40 bpm and >110 bpm. All measurements were obtained in supine position, after a 5-minute rest. Day 7 assessments could be conducted on Day 7 or Day 8.

End point type	Primary
End point timeframe:	
Day 1, Day 7, and Day 14	

Notes:

[45] - 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 for this primary endpoint; thus, no data are available

[46] - 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: No statistical analysis was performed for this primary endpoint; thus, no data are available

End point values	Part A: Placebo	Part A: GSK2269557 1000 µg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	7 ^[47]	21 ^[48]		
Units: Participants				
SBP high	1	1		
SBP low	0	0		
DBP high	0	0		
DBP low	1	0		
HR high	0	1		
HR low	0	0		

Notes:

[47] - Safety Population

[48] - Safety Population

Statistical analyses

No statistical analyses for this end point

Primary: Part A: Number of participants with normal and abnormal (clinically significant or not clinically significant) findings in 12-lead electrocardiogram (ECG) at any visit post-Baseline

End point title	Part A: Number of participants with normal and abnormal (clinically significant or not clinically significant) findings in 12-lead electrocardiogram (ECG) at any visit post-Baseline ^[49] ^[50]
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End point description:

Baseline was the Day 1 (pre-dose) measurement. Single 12-lead ECGs were obtained using an ECG machine that automatically calculates the HR and measures PR, QRS, QT, and corrected QT intervals. Clinical significance was judged by the investigator. Day 7 assessments could be conducted on Day 7 or Day 8.

End point type	Primary
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End point timeframe:

Day 1, Day 7, and Day 14

Notes:

[49] - 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 for this primary endpoint; thus, no data are available

[50] - 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: No statistical analysis was performed for this primary endpoint; thus, no data are available

End point values	Part A: Placebo	Part A: GSK2269557 1000 µg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	7 ^[51]	21 ^[52]		
Units: Participants				
Normal	2	13		
Abnormal - not clinically significant	5	8		
Abnormal - clinically significant	0	0		

Notes:

[51] - Safety Population

[52] - Safety Population

Statistical analyses

No statistical analyses for this end point

Primary: Part A: Change from Baseline in forced expiratory volume in one second (FEV1) and forced vital capacity (FVC) at the indicated time points

End point title	Part A: Change from Baseline in forced expiratory volume in one second (FEV1) and forced vital capacity (FVC) at the indicated time points ^[53] ^[54]
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End point description:

Baseline is Day 1 pre-dose. FEV1 and FVC are measures of lung function. FEV1 is defined as the maximal amount of air that can be forcefully exhaled in one second. FVC is defined as the maximum amount of air that can be forcibly blown out after a maximum inspiration. FEV1 and FVC measurements were repeated until three technically acceptable measurements (within 150 milliliters of each other) had been made. Only the best of three measurements were recorded. Baseline was the maximum of the planned pre-dose measurements on Day 1. Change from Baseline at any post-dose time point was calculated as the post-dose value minus the Baseline value. Day 7 assessments could be conducted on Day 7 or Day 8.

End point type	Primary
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End point timeframe:

Baseline (Day 1 [pre-dose]), Day 1 (1 h post-dose), Day 7 (pre-dose and 1 h post-dose), and Day 14 (24 h post-dose)

Notes:

[53] - 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 for this primary endpoint; thus, no data are available

[54] - 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: No statistical analysis was performed for this primary endpoint; thus, no data are available

End point values	Part A: Placebo	Part A: GSK2269557 1000 µg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	7 ^[55]	21 ^[56]		
Units: Liters				
arithmetic mean (confidence interval 95%)				
FEV1, Day 1, 1 h post dose	0.15 (-0.01 to 0.3)	0.1 (0.02 to 0.18)		
FEV1, Day 7/8, Pre-dose	0.03 (-0.09 to 0.15)	-0.04 (-0.13 to 0.05)		
FEV1, Day 7/8, 1 h post dose	0.27 (0.15 to 0.39)	0.18 (0.1 to 0.26)		
FEV1, Day 14, 24 h post dose	-0.01 (-0.09 to 0.06)	0.01 (-0.07 to 0.09)		
FVC, Day 1, 1 h post dose	0.17 (-0.13 to 0.47)	0.16 (0.01 to 0.32)		
FVC, Day 7/8, Predose	0.02 (-0.23 to 0.26)	0 (-0.12 to 0.13)		

FVC, Day 7/8, 1 h post dose	0.33 (0.09 to 0.58)	0.22 (0.09 to 0.36)		
FVC, Day 14, 24 h post dose	-0.04 (-0.3 to 0.22)	0.1 (-0.07 to 0.27)		

Notes:

[55] - Safety Population

[56] - Safety Population

Statistical analyses

No statistical analyses for this end point

Primary: Part B: Adjusted median response of cytokine (Interleukin 6 [IL6], Interleukin 8 [IL8], Tumor Necrosis Factor alpha [TNFalpha]) concentrations in induced sputum, on Day 7 and Day 14

End point title	Part B: Adjusted median response of cytokine (Interleukin 6 [IL6], Interleukin 8 [IL8], Tumor Necrosis Factor alpha [TNFalpha]) concentrations in induced sputum, on Day 7 and Day 14 ^[57]
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End point description:

This outcome measure was used to estimate the inhibition levels of various doses of GSK2269557 by analyzing inflammatory cytokines IL6, IL8, and TNF alpha using Bayesian methods of statistical analysis, using non-informative prior distributions for all modeling parameters. Posterior medians (adjusted median response) and 95% credible intervals are reported here as medians and 95% confidence intervals respectively. 95% credible interval is reported as 2-sided 95% confidence in the statistical analyses. Day 7 assessments could be conducted on Day 7 or Day 8.

End point type	Primary
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End point timeframe:

Day 7 (pre-dose) and Day 14 (24 h post-dose)

Notes:

[57] - 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: No statistical analysis was performed for this primary endpoint; thus, no data are available

End point values	Part B: Placebo	Part B: GSK2269557 100 µg	Part B: GSK2269557 200 µg	Part B: GSK2269557 500 µg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	5 ^[58]	5 ^[59]	5 ^[60]	5 ^[61]
Units: Picograms/milliliter (pg/mL)				
median (confidence interval 95%)				
IL6, Day 7/Day 8	41.3 (22.07 to 78.24)	37.4 (19.64 to 70.65)	28.23 (14.8 to 53.18)	30.82 (16.23 to 58)
IL6, Day 14	35.15 (17.72 to 70.01)	37.6 (18.71 to 74.49)	28.27 (14.1 to 56.22)	22.68 (11.32 to 45.13)
IL8, Day 7/Day 8	2633.21 (1401.19 to 4879.27)	2118.15 (1157.33 to 3866.74)	1860.78 (995.35 to 3499.61)	1523.63 (834.99 to 2745.9)
IL8, Day 14	2942.28 (1375.08 to 6216.67)	2664.75 (1269.52 to 5544.49)	1879.92 (876.5 to 4056.53)	1619.12 (778.39 to 3309.81)
TNFalpha, Day 7/Day 8	3.35 (1.22 to 8.98)	1.55 (0.57 to 4.33)	1.16 (0.42 to 3.25)	1.54 (0.57 to 4.19)
TNFalpha, Day 14	2.91 (1.26 to 6.54)	3.02 (1.33 to 7)	1.25 (0.55 to 2.9)	1.26 (0.55 to 2.87)

Notes:

[58] - Safety Population

[59] - Safety Population

[60] - Safety Population

[61] - Safety Population

End point values	Part B: GSK2269557 700 µg	Part B: GSK2269557 1000 µg	Part B: GSK2269557 2000 µg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	6 ^[62]	5 ^[63]	5 ^[64]	
Units: Picograms/milliliter (pg/mL)				
median (confidence interval 95%)				
IL6, Day 7/Day 8	52.23 (28.73 to 94.94)	31.25 (16.01 to 63.01)	33.4 (17.52 to 63.23)	
IL6, Day 14	35.19 (18.32 to 66.93)	42.56 (20.57 to 90.25)	41.52 (20.62 to 82.81)	
IL8, Day 7/Day 8	2650.13 (1535.07 to 4634.07)	2636.08 (1412.65 to 4978.59)	2279.48 (1205.35 to 4210.75)	
IL8, Day 14	1356.35 (696.37 to 2645.82)	2394.65 (1125.17 to 5196.2)	2170.41 (1010.85 to 4582.03)	
TNFalpha, Day 7/Day 8	7.32 (3.02 to 17.85)	3.68 (1.26 to 10.51)	2.62 (0.94 to 7.15)	
TNFalpha, Day 14	3.99 (1.86 to 8.5)	3 (1.34 to 6.75)	1.53 (0.66 to 3.47)	

Notes:

[62] - Safety Population

[63] - Safety Population

[64] - Safety Population

Statistical analyses

Statistical analysis title	Statistical analysis 1
Statistical analysis description:	
Comparison of IL6 concentrations at Day 7	
Comparison groups	Part B: Placebo v Part B: GSK2269557 100 µg
Number of subjects included in analysis	10
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.599 ^[65]
Method	Posterior Probability
Parameter estimate	Adjusted Median Ratio
Point estimate	0.9
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.39
upper limit	2.07

Notes:

[65] - Posterior Probability the True Treatment Ratio <1 for Day 7.

Statistical analysis title	Statistical analysis 2
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Statistical analysis description:

Comparison of IL6 concentrations at Day 14

Comparison groups	Part B: Placebo v Part B: GSK2269557 100 µg
Number of subjects included in analysis	10
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.442 ^[66]
Method	Posterior Probability
Parameter estimate	Adjusted Median Ratio
Point estimate	1.07
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.43
upper limit	2.59

Notes:

[66] - Posterior Probability the True Treatment Ratio <1 for Day 14

Statistical analysis title	Statistical analysis 3
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Statistical analysis description:

Comparison of IL6 concentrations at Day 7

Comparison groups	Part B: Placebo v Part B: GSK2269557 200 µg
Number of subjects included in analysis	10
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.823 ^[67]
Method	Posterior Probability
Parameter estimate	Adjusted Median Ratio
Point estimate	0.68
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.3
upper limit	1.57

Notes:

[67] - Posterior Probability the True Treatment Ratio <1 for Day 7

Statistical analysis title	Statistical analysis 4
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Statistical analysis description:

Comparison of IL6 concentrations at Day 14

Comparison groups	Part B: Placebo v Part B: GSK2269557 200 µg
Number of subjects included in analysis	10
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.69 ^[68]
Method	Posterior Probability
Parameter estimate	Adjusted Median Ratio
Point estimate	0.81

Confidence interval	
level	95 %
sides	2-sided
lower limit	0.33
upper limit	1.97

Notes:

[68] - Posterior Probability the True Treatment Ratio <1 for Day 14

Statistical analysis title	Statistical analysis 5
Statistical analysis description:	
Comparison of IL6 concentrations at Day 7	
Comparison groups	Part B: Placebo v Part B: GSK2269557 500 µg
Number of subjects included in analysis	10
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.764 ^[69]
Method	Posterior Probability
Parameter estimate	Adjusted Median Ratio
Point estimate	0.75
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.33
upper limit	1.71

Notes:

[69] - Posterior Probability the True Treatment Ratio <1 for Day 7

Statistical analysis title	Statistical analysis 6
Statistical analysis description:	
Comparison of IL6 concentrations at Day 14	
Comparison groups	Part B: Placebo v Part B: GSK2269557 500 µg
Number of subjects included in analysis	10
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.841 ^[70]
Method	Posterior Probability
Parameter estimate	Adjusted Median Ratio
Point estimate	0.64
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.27
upper limit	1.56

Notes:

[70] - Posterior Probability the True Treatment Ratio <1 for Day 14

Statistical analysis title	Statistical analysis 7
Statistical analysis description:	
Comparison of IL8 concentrations at Day 7	
Comparison groups	Part B: Placebo v Part B: GSK2269557 100 µg

Number of subjects included in analysis	10
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.702 ^[71]
Method	Posterior Probability
Parameter estimate	Adjusted Median Ratio
Point estimate	0.81
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.35
upper limit	1.81

Notes:

[71] - Posterior Probability the True Treatment Ratio <1 for Day 7

Statistical analysis title	Statistical analysis 8
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Statistical analysis description:

Comparison of IL8 concentrations at Day 14

Comparison groups	Part B: Placebo v Part B: GSK2269557 100 µg
Number of subjects included in analysis	10
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.578 ^[72]
Method	Posterior Probability
Parameter estimate	Adjusted Median Ratio
Point estimate	0.91
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.33
upper limit	2.47

Notes:

[72] - Posterior Probability the True Treatment Ratio <1 for Day 14

Statistical analysis title	Statistical analysis 9
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Statistical analysis description:

Comparison of IL8 concentrations at Day 7

Comparison groups	Part B: Placebo v Part B: GSK2269557 200 µg
Number of subjects included in analysis	10
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.783 ^[73]
Method	Posterior Probability
Parameter estimate	Adjusted Median Ratio
Point estimate	0.71
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.29
upper limit	1.7

Notes:

[73] - Posterior Probability the True Treatment Ratio <1 for Day 7

Statistical analysis title	Statistical analysis 10
Statistical analysis description:	
Comparison of IL8 concentrations at Day 14	
Comparison groups	Part B: Placebo v Part B: GSK2269557 200 µg
Number of subjects included in analysis	10
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.797 ^[74]
Method	Posterior Probability
Parameter estimate	Adjusted Median Ratio
Point estimate	0.64
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.22
upper limit	1.87

Notes:

[74] - Posterior Probability the True Treatment Ratio <1 for Day 14

Statistical analysis title	Statistical analysis 11
Statistical analysis description:	
Comparison of IL8 concentrations at Day 7	
Comparison groups	Part B: Placebo v Part B: GSK2269557 500 µg
Number of subjects included in analysis	10
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.919 ^[75]
Method	Posterior Probability
Parameter estimate	Adjusted Median Ratio
Point estimate	0.58
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.27
upper limit	1.26

Notes:

[75] - Posterior Probability the True Treatment Ratio <1 for Day 7

Statistical analysis title	Statistical analysis 12
Statistical analysis description:	
Comparison of IL8 concentrations at Day 14	
Comparison groups	Part B: Placebo v Part B: GSK2269557 500 µg

Number of subjects included in analysis	10
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.892 ^[76]
Method	Posterior Probability
Parameter estimate	Adjusted Median Ratio
Point estimate	0.55
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.21
upper limit	1.43

Notes:

[76] - Posterior Probability the True Treatment Ratio <1 for Day 14

Statistical analysis title	Statistical analysis 13
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Statistical analysis description:

Comparison of TNFalpha concentrations at Day 7

Comparison groups	Part B: Placebo v Part B: GSK2269557 100 µg
Number of subjects included in analysis	10
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.86 ^[77]
Method	Posterior Probability
Parameter estimate	Adjusted Median Ratio
Point estimate	0.47
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.11
upper limit	1.93

Notes:

[77] - Posterior Probability the True Treatment Ratio <1 for Day 7

Statistical analysis title	Statistical analysis 14
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Statistical analysis description:

Comparison of TNFalpha concentrations at Day 14

Comparison groups	Part B: Placebo v Part B: GSK2269557 100 µg
Number of subjects included in analysis	10
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.463 ^[78]
Method	Posterior Probability
Parameter estimate	Adjusted Median Ratio
Point estimate	1.05
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.38
upper limit	2.86

Notes:

[78] - Posterior Probability the True Treatment Ratio <1 for Day 14

Statistical analysis title	Statistical analysis 15
Statistical analysis description:	
Comparison of TNFalpha concentrations at Day 7	
Comparison groups	Part B: Placebo v Part B: GSK2269557 200 µg
Number of subjects included in analysis	10
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.932 ^[79]
Method	Posterior Probability
Parameter estimate	Adjusted Median Ratio
Point estimate	0.35
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.09
upper limit	1.42

Notes:

[79] - Posterior Probability the True Treatment Ratio <1 for Day 7

Statistical analysis title	Statistical analysis 16
Statistical analysis description:	
Comparison of TNFalpha concentrations at Day 14	
Comparison groups	Part B: Placebo v Part B: GSK2269557 200 µg
Number of subjects included in analysis	10
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.952 ^[80]
Method	Posterior Probability
Parameter estimate	Adjusted Median Ratio
Point estimate	0.43
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.16
upper limit	1.17

Notes:

[80] - Posterior Probability the True Treatment Ratio <1 for Day 14

Statistical analysis title	Statistical analysis 17
Statistical analysis description:	
Comparison of TNFalpha concentrations at Day 7	
Comparison groups	Part B: Placebo v Part B: GSK2269557 500 µg

Number of subjects included in analysis	10
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.873 ^[81]
Method	Posterior Probability
Parameter estimate	Adjusted Median Ratio
Point estimate	0.46
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.12
upper limit	1.81

Notes:

[81] - Posterior Probability the True Treatment Ratio <1 for Day 7

Statistical analysis title	Statistical analysis 18
Statistical analysis description: Comparison of TNFalpha concentrations at Day 14	
Comparison groups	Part B: Placebo v Part B: GSK2269557 500 µg
Number of subjects included in analysis	10
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.953 ^[82]
Method	Posterior Probability
Parameter estimate	Adjusted Median Ratio
Point estimate	0.43
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.16
upper limit	1.16

Notes:

[82] - Posterior Probability the True Treatment Ratio <1 for Day 14

Statistical analysis title	Statistical analysis 19
Statistical analysis description: Comparison of IL6 concentrations at Day 7	
Comparison groups	Part B: Placebo v Part B: GSK2269557 700 µg
Number of subjects included in analysis	11
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.281 ^[83]
Method	Posterior Probability
Parameter estimate	Adjusted Median Ratio
Point estimate	1.26
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.56
upper limit	2.82

Notes:

[83] - Posterior Probability the True Treatment Ratio <1 for Day 7

Statistical analysis title	Statistical analysis 20
Statistical analysis description:	
Comparison of IL6 concentrations at Day 14	
Comparison groups	Part B: Placebo v Part B: GSK2269557 700 µg
Number of subjects included in analysis	11
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.5 ^[84]
Method	Posterior Probability
Parameter estimate	Adjusted Median Ratio
Point estimate	1
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.42
upper limit	2.35

Notes:

[84] - Posterior Probability the True Treatment Ratio <1 for Day 14

Statistical analysis title	Statistical analysis 21
Statistical analysis description:	
Comparison of IL6 concentrations at Day 7	
Comparison groups	Part B: Placebo v Part B: GSK2269557 1000 µg
Number of subjects included in analysis	10
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.744 ^[85]
Method	Posterior Probability
Parameter estimate	Adjusted Median Ratio
Point estimate	0.76
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.32
upper limit	1.77

Notes:

[85] - Posterior Probability the True Treatment Ratio <1 for Day 7

Statistical analysis title	Statistical analysis 22
Statistical analysis description:	
Comparison of IL6 concentrations at Day 14	
Comparison groups	Part B: Placebo v Part B: GSK2269557 1000 µg

Number of subjects included in analysis	10
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.334 ^[86]
Method	Posterior Probability
Parameter estimate	Adjusted Median Ratio
Point estimate	1.21
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.49
upper limit	3.04

Notes:

[86] - Posterior Probability the True Treatment Ratio <1 for Day 14

Statistical analysis title	Statistical analysis 23
Statistical analysis description:	
Comparison of IL6 concentrations at Day 7	
Comparison groups	Part B: Placebo v Part B: GSK2269557 2000 µg
Number of subjects included in analysis	10
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.698 ^[87]
Method	Posterior Probability
Parameter estimate	Adjusted Median Ratio
Point estimate	0.81
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.35
upper limit	1.85

Notes:

[87] - Posterior Probability the True Treatment Ratio <1 for Day 7

Statistical analysis title	Statistical analysis 24
Statistical analysis description:	
Comparison of IL6 concentrations at Day 14	
Comparison groups	Part B: Placebo v Part B: GSK2269557 2000 µg
Number of subjects included in analysis	10
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.353 ^[88]
Method	Posterior Probability
Parameter estimate	Adjusted Median Ratio
Point estimate	1.18
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.48
upper limit	2.88

Notes:

[88] - Posterior Probability the True Treatment Ratio <1 for Day 14

Statistical analysis title	Statistical analysis 25
Statistical analysis description:	
Comparison of IL8 concentrations at Day 7	
Comparison groups	Part B: Placebo v Part B: GSK2269557 700 µg
Number of subjects included in analysis	11
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.489 ^[89]
Method	Posterior Probability
Parameter estimate	Adjusted Median Ratio
Point estimate	1.01
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.45
upper limit	2.26

Notes:

[89] - Posterior Probability the True Treatment Ratio <1 for Day 7

Statistical analysis title	Statistical analysis 26
Statistical analysis description:	
Comparison of IL8 concentrations at Day 14	
Comparison groups	Part B: Placebo v Part B: GSK2269557 700 µg
Number of subjects included in analysis	11
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.94 ^[90]
Method	Posterior Probability
Parameter estimate	Adjusted Median Ratio
Point estimate	0.46
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.17
upper limit	1.23

Notes:

[90] - Posterior Probability the True Treatment Ratio <1 for Day 14

Statistical analysis title	Statistical analysis 27
Statistical analysis description:	
Comparison of IL8 concentrations at Day 7	
Comparison groups	Part B: Placebo v Part B: GSK2269557 1000 µg

Number of subjects included in analysis	10
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.495 ^[91]
Method	Posterior Probability
Parameter estimate	Adjusted Median Ratio
Point estimate	1.01
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.42
upper limit	2.4

Notes:

[91] - Posterior Probability the True Treatment Ratio <1 for Day 7

Statistical analysis title	Statistical analysis 28
Statistical analysis description:	
Comparison of IL8 concentrations at Day 14	
Comparison groups	Part B: Placebo v Part B: GSK2269557 1000 µg
Number of subjects included in analysis	10
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.647 ^[92]
Method	Posterior Probability
Parameter estimate	Adjusted Median Ratio
Point estimate	0.82
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.28
upper limit	2.37

Notes:

[92] - Posterior Probability the True Treatment Ratio <1 for Day 14

Statistical analysis title	Statistical analysis 29
Statistical analysis description:	
Comparison of IL8 concentrations at Day 7	
Comparison groups	Part B: Placebo v Part B: GSK2269557 2000 µg
Number of subjects included in analysis	10
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.646 ^[93]
Method	Posterior Probability
Parameter estimate	Adjusted Median Ratio
Point estimate	0.87
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.4
upper limit	1.86

Notes:

[93] - Posterior Probability the True Treatment Ratio <1 for Day 7

Statistical analysis title	Statistical analysis 30
Statistical analysis description:	
Comparison of IL8 concentrations at Day 14	
Comparison groups	Part B: Placebo v Part B: GSK2269557 2000 µg
Number of subjects included in analysis	10
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.741 ^[94]
Method	Posterior Probability
Parameter estimate	Adjusted Median Ratio
Point estimate	0.74
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.29
upper limit	1.9

Notes:

[94] - Posterior Probability the True Treatment Ratio <1 for Day 14

Statistical analysis title	Statistical analysis 31
Statistical analysis description:	
Comparison of TNFalpha concentrations at Day 7	
Comparison groups	Part B: Placebo v Part B: GSK2269557 700 µg
Number of subjects included in analysis	11
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.109 ^[95]
Method	Posterior Probability
Parameter estimate	Adjusted Median Ratio
Point estimate	2.18
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.62
upper limit	7.95

Notes:

[95] - Posterior Probability the True Treatment Ratio <1 for Day 7

Statistical analysis title	Statistical analysis 32
Statistical analysis description:	
Comparison of TNFalpha concentrations at Day 14	
Comparison groups	Part B: Placebo v Part B: GSK2269557 700 µg

Number of subjects included in analysis	11
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.24 ^[96]
Method	Posterior Probability
Parameter estimate	Adjusted Median Ratio
Point estimate	1.37
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.55
upper limit	3.45

Notes:

[96] - Posterior Probability the True Treatment Ratio <1 for Day 14

Statistical analysis title	Statistical analysis 33
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Statistical analysis description:

Comparison of TNFalpha concentrations at Day 7

Comparison groups	Part B: Placebo v Part B: GSK2269557 1000 µg
Number of subjects included in analysis	10
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.447 ^[97]
Method	Posterior Probability
Parameter estimate	Adjusted Median Ratio
Point estimate	1.1
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.27
upper limit	4.44

Notes:

[97] - Posterior Probability the True Treatment Ratio <1 for Day 7

Statistical analysis title	Statistical analysis 34
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Statistical analysis description:

Comparison of TNFalpha concentrations at Day 14

Comparison groups	Part B: Placebo v Part B: GSK2269557 1000 µg
Number of subjects included in analysis	10
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.472 ^[98]
Method	Posterior Probability
Parameter estimate	Adjusted Median Ratio
Point estimate	1.03
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.39
upper limit	2.74

Notes:

[98] - Posterior Probability the True Treatment Ratio <1 for Day 14

Statistical analysis title	Statistical analysis 35
Statistical analysis description: Comparison of TNFalpha concentrations at Day 7	
Comparison groups	Part B: Placebo v Part B: GSK2269557 2000 µg
Number of subjects included in analysis	10
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.698 ^[99]
Method	Posterior Probability
Parameter estimate	Adjusted Median Ratio
Point estimate	0.78
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.21
upper limit	2.9

Notes:

[99] - Posterior Probability the True Treatment Ratio <1 for Day 7

Statistical analysis title	Statistical analysis 36
Statistical analysis description: Comparison of TNFalpha concentrations at Day 14	
Comparison groups	Part B: Placebo v Part B: GSK2269557 2000 µg
Number of subjects included in analysis	10
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.911 ^[100]
Method	Posterior Probability
Parameter estimate	Adjusted Median Ratio
Point estimate	0.53
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.21
upper limit	1.37

Notes:

[100] - Posterior Probability the True Treatment Ratio <1 for Day 14

Secondary: Part A: Day 1 plasma concentration of GSK2269557 up to 6 hours post dose

End point title	Part A: Day 1 plasma concentration of GSK2269557 up to 6 hours post dose ^[101]
End point description: A 2 mL blood sample for pharmacokinetic (PK) analysis was collected at each of the indicated time point. Only those participants who were available at the indicated time points were analyzed (represented by n=X in the category titles). A value of 99999 indicates that the geometric mean or 95% confidence interval is not available.	
End point type	Secondary

End point timeframe:

Pre-dose, and 5 min, 30 min, 1 h, 2 h, 4 h, and 6 h post-dose on Day 1

Notes:

[101] - 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: No statistical analysis was performed for this primary endpoint; thus, no data are available

End point values	Part A: GSK2269557 1000 µg			
Subject group type	Reporting group			
Number of subjects analysed	21 ^[102]			
Units: pg/mL				
geometric mean (confidence interval 95%)				
Pre-dose; n=0	99999 (99999 to 99999)			
5 min; n=21	386.2 (287.5 to 518.7)			
30 min; n=21	337.2 (274.6 to 414)			
1 h; n=21	379.1 (320.2 to 448.9)			
2 h; n=21	531.1 (448.2 to 629.4)			
4 h; n=21	419.5 (357.6 to 492.1)			
6 h; n=21	334.4 (287 to 389.6)			

Notes:

[102] - PK Population: participants in the Safety Population for whom a PK sample was obtained and analyzed.

Statistical analyses

No statistical analyses for this end point

Secondary: Part B: Day 1 plasma concentration of GSK2269557 up to 6 hours post dose

End point title	Part B: Day 1 plasma concentration of GSK2269557 up to 6 hours post dose ^[103]
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End point description:

A 2 mL blood sample for pharmacokinetic (PK) analysis was collected at each of the indicated time point. Concentration measurements were log-transformed. Only those participants who were available at the indicated time points were analyzed (represented by n=X,X in the category titles). A value of 99999 indicates that the geometric mean or 95% confidence interval is not available.

End point type	Secondary
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End point timeframe:

Pre-dose, and 5 min, 30 min, 1 h, 2 h, 4 h, and 6 h post-dose on Day 1

Notes:

[103] - 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: No statistical analysis was performed for this primary endpoint; thus, no data are available

End point values	Part B: GSK2269557 100 µg	Part B: GSK2269557 200 µg	Part B: GSK2269557 500 µg	Part B: GSK2269557 700 µg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	5 ^[104]	5 ^[105]	5 ^[106]	6 ^[107]
Units: pg/mL				
geometric mean (confidence interval 95%)				
Pre-dose; n=0,0,0,0,0,0	99999 (99999 to 99999)	99999 (99999 to 99999)	99999 (99999 to 99999)	99999 (99999 to 99999)
5 min; n=5,5,5,6,5,5,5	55.3 (33.7 to 90.7)	80.4 (38.4 to 168.2)	173.1 (88.4 to 339)	466.6 (147.3 to 1478)
30 min; n=5,5,5,6,5,5,5	51.7 (36.2 to 74.1)	73.8 (41.6 to 130.8)	203 (111.2 to 370.5)	402.3 (218 to 742.5)
1 h; n=5,5,5,6,5,5,5	61.3 (45.7 to 82.3)	77.2 (44.1 to 135.2)	253.2 (155 to 413.8)	429.1 (294.2 to 626)
2 h; n=5,5,5,6,5,5,5	60.6 (44.8 to 81.9)	88.8 (60.2 to 130.9)	300.9 (173.7 to 521.1)	556.7 (372.4 to 832.3)
4 h; n=5,5,5,6,5,5,5	45 (33.1 to 61.2)	73.4 (60.5 to 89.1)	251 (146 to 431.6)	391.6 (303.3 to 505.5)
6 h; n=5,5,5,6,5,5,5	38.3 (29.7 to 49.5)	63.8 (50.7 to 80.3)	201.5 (128.3 to 316.6)	294.6 (222.3 to 390.4)

Notes:

[104] - PK Population

[105] - PK Population

[106] - PK Population

[107] - PK Population

End point values	Part B: GSK2269557 1000 µg	Part B: GSK2269557 2000 µg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	5 ^[108]	5 ^[109]		
Units: pg/mL				
geometric mean (confidence interval 95%)				
Pre-dose; n=0,0,0,0,0,0,0	99999 (99999 to 99999)	99999 (99999 to 99999)		
5 min; n=5,5,5,6,5,5,5	853.4 (380.2 to 1915.6)	982.9 (311.1 to 3105.3)		
30 min; n=5,5,5,6,5,5,5	556.9 (384.8 to 806)	1011.6 (757.1 to 1351.6)		
1 h; n=5,5,5,6,5,5,5	599.7 (370.5 to 970.7)	1203.3 (799.1 to 1812)		
2 h; n=5,5,5,6,5,5,5	672.3 (434 to 1041.5)	1402 (892.8 to 2201.4)		
4 h; n=5,5,5,6,5,5,5	468.7 (305.5 to 719.2)	1098.5 (781.9 to 1543.2)		
6 h; n=5,5,5,6,5,5,5	466.5 (273.1 to 796.6)	900.8 (723.8 to 1121)		

Notes:

[108] - PK Population

[109] - PK Population

Statistical analyses

No statistical analyses for this end point

Secondary: Part A: Maximum observed plasma concentration (Cmax) of GSK2269557 on Day 7

End point title	Part A: Maximum observed plasma concentration (Cmax) of GSK2269557 on Day 7 ^[110]
End point description: Blood samples were collected to determine the plasma concentrations of GSK2269557 immediately after dosing on Day 7. Day 7 sampling could be done on Day 7 or Day 8.	
End point type	Secondary
End point timeframe: Day 7 immediately after dosing	

Notes:

[110] - 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: No statistical analysis was performed for this primary endpoint; thus, no data are available

End point values	Part A: GSK2269557 1000 µg			
Subject group type	Reporting group			
Number of subjects analysed	21 ^[111]			
Units: pg/mL				
geometric mean (confidence interval 95%)	1109.1 (901.5 to 1364.5)			

Notes:

[111] - PK Population

Statistical analyses

No statistical analyses for this end point

Secondary: Part B: Maximum observed plasma concentration (Cmax) of GSK2269557 on Day 7

End point title	Part B: Maximum observed plasma concentration (Cmax) of GSK2269557 on Day 7 ^[112]
End point description: Blood samples were collected to determine the plasma concentrations of GSK2269557 immediately after dosing on Day 7. Concentration values were log-transformed. Day 7 sampling could be done on Day 7 or Day 8.	
End point type	Secondary
End point timeframe: Day 7 immediately after dosing	

Notes:

[112] - 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: No statistical analysis was performed for this primary endpoint; thus, no data are available

End point values	Part B: GSK2269557 100 µg	Part B: GSK2269557 200 µg	Part B: GSK2269557 500 µg	Part B: GSK2269557 700 µg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	5 ^[113]	5 ^[114]	5 ^[115]	6 ^[116]
Units: pg/mL				
geometric mean (confidence interval 95%)	109.6 (62.6 to 191.8)	203.4 (140.3 to 294.8)	511.8 (233.2 to 1123.3)	1022.2 (623.7 to 1675.2)

Notes:

[113] - PK Population

[114] - PK Population

[115] - PK Population

[116] - PK Population

End point values	Part B: GSK2269557 1000 µg	Part B: GSK2269557 2000 µg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	5 ^[117]	5 ^[118]		
Units: pg/mL				
geometric mean (confidence interval 95%)	1655.1 (803.2 to 3410.4)	2923.4 (1769.4 to 4830)		

Notes:

[117] - PK Population

[118] - PK Population

Statistical analyses

No statistical analyses for this end point

Secondary: Part A: Trough concentration (Ctau) of GSK2269557 on Day 7 and Day 15

End point title	Part A: Trough concentration (Ctau) of GSK2269557 on Day 7 and Day 15 ^[119]
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End point description:

Blood samples were collected to determine the (trough) plasma concentration of GSK2269557 on Day 7 (pre-dose) and Day 15 (24 hours after dosing on Day 14). Day 7 assessments could be done either on Day 7 or on Day 8.

End point type	Secondary
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End point timeframe:

Day 7 and Day 15

Notes:

[119] - 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: No statistical analysis was performed for this primary endpoint; thus, no data are available

End point values	Part A: GSK2269557 1000 µg			
Subject group type	Reporting group			
Number of subjects analysed	21 ^[120]			
Units: pg/mL				
geometric mean (confidence interval 95%)				
Day 7/Day 8	604.1 (496.6 to 735)			
Day 15	711.2 (561.8 to 900.3)			

Notes:

[120] - PK Population

Statistical analyses

No statistical analyses for this end point

Secondary: Part B: Trough concentration (Ctau) of GSK2269557 on Day 7 and Day 15

End point title	Part B: Trough concentration (Ctau) of GSK2269557 on Day 7 and Day 15 ^[121]
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End point description:

Blood samples were collected to determine the (trough) plasma concentration of GSK2269557 on Day 7 (pre-dose) and Day 15 (24 hours after dosing on Day 14). Day 7 assessments could be done either on Day 7 or on Day 8.

End point type	Secondary
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End point timeframe:

Day 7 and Day 15

Notes:

[121] - 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: No statistical analysis was performed for this primary endpoint; thus, no data are available

End point values	Part B: GSK2269557 100 µg	Part B: GSK2269557 200 µg	Part B: GSK2269557 500 µg	Part B: GSK2269557 700 µg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	5 ^[122]	5 ^[123]	5 ^[124]	6 ^[125]
Units: pg/mL				
geometric mean (confidence interval 95%)				
Day 7/Day 8	55.3 (41.22 to 74.21)	119.17 (78.47 to 180.97)	314.38 (182.64 to 541.16)	588.09 (486.63 to 710.69)
Day 15	74.93 (48.26 to 116.33)	128.71 (92.02 to 180.03)	237.36 (66.38 to 848.74)	665.9 (497.61 to 891.1)

Notes:

[122] - PK Population

[123] - PK Population

[124] - PK Population

[125] - PK Population

End point values	Part B: GSK2269557 1000 µg	Part B: GSK2269557 2000 µg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	5 ^[126]	5 ^[127]		
Units: pg/mL				
geometric mean (confidence interval 95%)				
Day 7/Day 8	724.33 (581.37 to 902.45)	1468.94 (1000.5 to 2156.7)		
Day 15	1218.5 (985.88 to 1506.01)	1767.34 (1079.72 to 2892.86)		

Notes:

[126] - PK Population

[127] - PK Population

Statistical analyses

No statistical analyses for this end point

Secondary: Part B: Number of times rescue medication was used by participants daily, during the treatment period

End point title	Part B: Number of times rescue medication was used by participants daily, during the treatment period ^[128]
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End point description:

Rescue medication was identified from concomitant medication records and the patient diaries which were provided to the participants to record data throughout the treatment period. Only participants who used rescue medication were analyzed. The value 99999 indicates that the standard deviation could not be calculated as only one participant was analyzed.

End point type	Secondary
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End point timeframe:

Day 1 to Day 15

Notes:

[128] - 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: No statistical analysis was performed for this primary endpoint; thus, no data are available

End point values	Part B: Placebo	Part B: GSK2269557 100 µg	Part B: GSK2269557 200 µg	Part B: GSK2269557 500 µg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	3 ^[129]	1 ^[130]	1 ^[131]	0 ^[132]
Units: Number of times				
arithmetic mean (standard deviation)	2 (± 0)	2.3 (± 99999)	2.2 (± 99999)	()

Notes:

[129] - Safety Population

[130] - Safety Population

[131] - Safety Population

[132] - Safety Population

End point values	Part B: GSK2269557 700 µg	Part B: GSK2269557 1000 µg	Part B: GSK2269557 2000 µg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	1 ^[133]	3 ^[134]	1 ^[135]	
Units: Number of times				
arithmetic mean (standard deviation)	1 (± 99999)	1.4 (± 0.63)	1.9 (± 99999)	

Notes:

[133] - Safety Population

[134] - Safety Population

[135] - Safety Population

Statistical analyses

No statistical analyses for this end point

Secondary: Part B: Number of participants with at least one non-serious adverse event (AE), serious adverse event (SAE), or drug-related adverse event

End point title	Part B: Number of participants with at least one non-serious adverse event (AE), serious adverse event (SAE), or drug-related adverse event ^[136]
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End point description:

An AE is defined as any untoward medical occurrence in a participant, temporally associated with the use of a medicinal product, whether or not considered related to the medicinal product. An SAE is defined as any untoward medical occurrence that, at any dose, results in death, is life-threatening, requires hospitalization or prolongation of existing hospitalization, results in disability/incapacity, or is a congenital anomaly/birth defect, may jeopardize the participant or may require medical or surgical intervention to prevent one of the other outcomes listed in this definition, associated with liver injury and impaired liver function defined as alanine aminotransferase $\geq 3 \times$ upper limit of normal (ULN), and total bilirubin $\geq 2 \times$ ULN or international normalised ratio > 1.5 . AEs were classified as potentially drug-related, based on the investigator's judgement. Refer to the general AE/SAE module for a list of AEs and SAEs.

End point type	Secondary
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End point timeframe:

From the start of study treatment until follow-up (assessed for approximately 19 days)

Notes:

[136] - 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: No statistical analysis was performed for this primary endpoint; thus, no data are available

End point values	Part B: Placebo	Part B: GSK2269557 100 µg	Part B: GSK2269557 200 µg	Part B: GSK2269557 500 µg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	5 ^[137]	5 ^[138]	5 ^[139]	5 ^[140]
Units: Participants				
At least one AE	3	3	2	1
At least one SAE	0	0	0	0
At least one drug-related AE	0	0	1	0

Notes:

[137] - Safety Population

[138] - Safety Population

[139] - Safety Population

[140] - Safety Population

End point values	Part B: GSK2269557 700 µg	Part B: GSK2269557 1000 µg	Part B: GSK2269557 2000 µg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	6 ^[141]	5 ^[142]	5 ^[143]	
Units: Participants				
At least one AE	3	4	2	
At least one SAE	0	0	0	
At least one drug-related AE	3	4	2	

Notes:

[141] - Safety Population

[142] - Safety Population

[143] - Safety Population

Statistical analyses

No statistical analyses for this end point

Secondary: Part B: Change from Baseline in counts of basophils, eosinophils, lymphocytes, monocytes, platelets, white blood cells (WBC), total neutrophils (total ANC) at the indicated time points

End point title	Part B: Change from Baseline in counts of basophils,
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eosinophils, lymphocytes, monocytes, platelets, white blood cells (WBC), total neutrophils (total ANC) at the indicated time points^[144]

End point description:

Blood samples were collected for measurement for the indicated tests. Change from Baseline at any post-dose visit was calculated as the post-dose visit value minus the Baseline value. Day 7 assessments could be conducted on Day 7 or Day 8.

End point type	Secondary
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End point timeframe:

Baseline (Day 1 [pre-dose]), Day 7 (pre-dose), and Day 14 (24 hours [h] post-dose)

Notes:

[144] - 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: No statistical analysis was performed for this primary endpoint; thus, no data are available

End point values	Part B: Placebo	Part B: GSK2269557 100 µg	Part B: GSK2269557 200 µg	Part B: GSK2269557 500 µg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	5 ^[145]	5 ^[146]	5 ^[147]	5 ^[148]
Units: 10 ⁹ cells per liter (GI/L)				
arithmetic mean (standard deviation)				
Basophils; Day 7/Day 8, pre-dose	0.014 (± 0.0241)	-0.002 (± 0.0228)	0.01 (± 0.0187)	0.004 (± 0.0182)
Basophils; Day 14, 24 h post dose	0.004 (± 0.0167)	-0.006 (± 0.0261)	0.01 (± 0.0122)	-0.002 (± 0.0192)
Eosinophils; Day 7/Day 8, pre-dose	-0.002 (± 0.0576)	0.01 (± 0.0485)	-0.034 (± 0.0702)	-0.026 (± 0.0498)
Eosinophils; Day 14, 24 h post dose	0.046 (± 0.0472)	-0.01 (± 0.0292)	-0.046 (± 0.0378)	-0.054 (± 0.1498)
Lymphocytes; Day 7/Day 8, pre-dose	0.242 (± 0.4797)	-0.178 (± 0.5657)	-0.022 (± 0.1326)	-0.094 (± 0.3092)
Lymphocytes; Day 14, 24 h post dose	-0.09 (± 0.4499)	-0.264 (± 0.3134)	-0.216 (± 0.208)	0.092 (± 0.9722)
Monocytes; Day 7/Day 8, pre-dose	-0.062 (± 0.0867)	0.05 (± 0.0941)	-0.02 (± 0.0806)	0.05 (± 0.2108)
Monocytes; Day 14, 24 h post dose	-0.022 (± 0.0676)	-0.012 (± 0.0926)	-0.036 (± 0.0829)	-0.004 (± 0.1313)
Platelets; Day 7/Day 8, pre-dose	-13.8 (± 14.22)	-0.8 (± 18.07)	10 (± 24.52)	15.6 (± 17.78)
Platelets; Day 14, 24 h post dose	-3.3 (± 22.25)	-13 (± 26.52)	-7.2 (± 20.41)	-1.4 (± 44.86)
WBC; Day 7/Day 8, pre-dose	0.372 (± 1.5852)	-0.024 (± 1.1519)	0.102 (± 1.1107)	0.926 (± 3.1314)
WBC; Day 14, 24 h post dose	-0.49 (± 0.5204)	-0.864 (± 1.4151)	-0.164 (± 0.7907)	-0.178 (± 2.2899)
Total ANC; Day 7/Day 8, pre-dose	0.164 (± 0.9782)	0.09 (± 0.6553)	0.17 (± 1.0481)	1.018 (± 2.6669)
Total ANC; Day 14, 24 h post dose	-0.44 (± 0.4288)	-0.538 (± 1.1027)	0.134 (± 0.801)	-0.18 (± 1.469)

Notes:

[145] - Safety Population

[146] - Safety Population

[147] - Safety Population

[148] - Safety Population

End point values	Part B: GSK2269557 700 µg	Part B: GSK2269557 1000 µg	Part B: GSK2269557 2000 µg	
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Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	6 ^[149]	4 ^[150]	5 ^[151]	
Units: 10 ⁹ cells per liter (GI/L)				
arithmetic mean (standard deviation)				
Basophils; Day 7/Day 8, pre-dose	0.007 (± 0.0052)	-0.005 (± 0.01)	0 (± 0.01)	
Basophils; Day 14, 24 h post dose	0.007 (± 0.0175)	-0.008 (± 0.0189)	0.01 (± 0.0122)	
Eosinophils; Day 7/Day 8, pre-dose	0.022 (± 0.1289)	-0.002 (± 0.0287)	0.012 (± 0.0438)	
Eosinophils; Day 14, 24 h post dose	0.025 (± 0.1078)	0.023 (± 0.0222)	0.022 (± 0.0396)	
Lymphocytes; Day 7/Day 8, pre-dose	0.093 (± 0.2813)	-0.118 (± 0.3223)	-0.218 (± 0.6236)	
Lymphocytes; Day 14, 24 h post dose	0.21 (± 0.3855)	-0.243 (± 0.3054)	-0.398 (± 0.736)	
Monocytes; Day 7/Day 8, pre-dose	0.018 (± 0.1209)	0.165 (± 0.5166)	-0.08 (± 0.1398)	
Monocytes; Day 14, 24 h post dose	0.03 (± 0.0699)	0.108 (± 0.3437)	-0.11 (± 0.0834)	
Platelets; Day 7/Day 8, pre-dose	11.7 (± 15.41)	26.5 (± 32.77)	-0.6 (± 14.4)	
Platelets; Day 14, 24 h post dose	7 (± 19.81)	-8.3 (± 51.57)	-11.4 (± 29.39)	
WBC; Day 7/Day 8, pre-dose	0.497 (± 0.8673)	0.5 (± 2.676)	-0.802 (± 0.7889)	
WBC; Day 14, 24 h post dose	0.648 (± 1.143)	0.825 (± 1.6016)	-1.012 (± 1.3388)	
Total ANC; Day 7/Day 8, pre-dose	0.335 (± 0.5921)	0.448 (± 2.153)	-0.51 (± 0.285)	
Total ANC; Day 14, 24 h post dose	0.385 (± 1.2151)	0.958 (± 1.8925)	-0.51 (± 0.7931)	

Notes:

[149] - Safety Population

[150] - Safety Population

[151] - Safety Population

Statistical analyses

No statistical analyses for this end point

Secondary: Part B: Change from Baseline in hemoglobin and mean corpuscle hemoglobin concentration (MCHC) at the indicated time points

End point title	Part B: Change from Baseline in hemoglobin and mean corpuscle hemoglobin concentration (MCHC) at the indicated time points ^[152]
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End point description:

Blood samples were collected for measurement for the indicated tests. MCHC is one of the red blood cell (RBC) indices. Change from Baseline at any post-dose visit was calculated as the post-dose visit value minus the Baseline value. Day 7 assessments could be conducted on Day 7 or Day 8.

End point type	Secondary
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End point timeframe:

Baseline (Day 1 [pre-dose]), Day 7 (pre-dose), and Day 14 (24 hours [h] post-dose)

Notes:

[152] - 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: No statistical analysis was performed for this primary endpoint; thus, no data are available

End point values	Part B: Placebo	Part B: GSK2269557 100 µg	Part B: GSK2269557 200 µg	Part B: GSK2269557 500 µg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	5 ^[153]	5 ^[154]	5 ^[155]	5 ^[156]
Units: g/L				
arithmetic mean (standard deviation)				
Hemoglobin; Day 7/Day 8, pre-dose	3 (± 2.55)	0.8 (± 5.76)	3.8 (± 6.76)	1 (± 4.74)
Hemoglobin; Day 14, 24 h post dose	4.2 (± 6.14)	-1.2 (± 6.14)	-0.6 (± 8.02)	-2 (± 6.86)
MCHC; Day 7/Day 8, pre-dose	-2.4 (± 2.07)	-0.6 (± 8.17)	-4 (± 7.31)	-4.4 (± 9.61)
MCHC; Day 14, 24 h post dose	3.8 (± 5.07)	-2.6 (± 3.51)	-4.4 (± 8.73)	3 (± 4)

Notes:

[153] - Safety Population

[154] - Safety Population

[155] - Safety Population

[156] - Safety Population

End point values	Part B: GSK2269557 700 µg	Part B: GSK2269557 1000 µg	Part B: GSK2269557 2000 µg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	6 ^[157]	4 ^[158]	5 ^[159]	
Units: g/L				
arithmetic mean (standard deviation)				
Hemoglobin; Day 7/Day 8, pre-dose	0.3 (± 5.65)	6 (± 5.89)	1 (± 3.39)	
Hemoglobin; Day 14, 24 h post dose	-2.2 (± 2.14)	-0.3 (± 4.65)	-0.2 (± 4.44)	
MCHC; Day 7/Day 8, pre-dose	0.5 (± 5.17)	3.3 (± 8.18)	7.8 (± 10.85)	
MCHC; Day 14, 24 h post dose	2.5 (± 3.83)	-8.5 (± 7.59)	1.6 (± 11.76)	

Notes:

[157] - Safety Population

[158] - Safety Population

[159] - Safety Population

Statistical analyses

No statistical analyses for this end point

Secondary: Part B: Change from Baseline in counts of RBCs and reticulocytes at the indicated time points

End point title	Part B: Change from Baseline in counts of RBCs and reticulocytes at the indicated time points ^[160]
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End point description:

Blood samples were collected for measurement for the indicated tests. Change from Baseline at any post-dose visit was calculated as the post-dose visit value minus the Baseline value. Day 7 assessments could be conducted on Day 7 or Day 8.

End point type	Secondary
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End point timeframe:

Baseline (Day 1 [pre-dose]), Day 7 (pre-dose), and Day 14 (24 hours [h] post-dose)

Notes:

[160] - 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: No statistical analysis was performed for this primary endpoint; thus, no data are available

End point values	Part B: Placebo	Part B: GSK2269557 100 µg	Part B: GSK2269557 200 µg	Part B: GSK2269557 500 µg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	5 ^[161]	5 ^[162]	5 ^[163]	5 ^[164]
Units: 10 ¹² cells/Liter (TI/L)				
arithmetic mean (standard deviation)				
RBC; Day 7/Day 8, pre-dose	0.076 (± 0.1148)	0.036 (± 0.1549)	0.18 (± 0.2703)	0.058 (± 0.1314)
RBC; Day 14, 24 h post dose	0.11 (± 0.1891)	-0.038 (± 0.1663)	0.034 (± 0.1785)	-0.07 (± 0.1815)
Reticulocytes; Day 7/Day 8, pre-dose	-0.00064 (± 0.01328)	0.00714 (± 0.020838)	0.01298 (± 0.011129)	0.01258 (± 0.014565)
Reticulocytes; Day 14, 24 h post dose	0.0034 (± 0.014934)	0.0006 (± 0.010183)	0.01032 (± 0.015404)	0.0156 (± 0.013092)

Notes:

[161] - Safety Population

[162] - Safety Population

[163] - Safety Population

[164] - Safety Population

End point values	Part B: GSK2269557 700 µg	Part B: GSK2269557 1000 µg	Part B: GSK2269557 2000 µg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	6 ^[165]	4 ^[166]	5 ^[167]	
Units: 10 ¹² cells/Liter (TI/L)				
arithmetic mean (standard deviation)				
RBC; Day 7/Day 8, pre-dose	-0.023 (± 0.1508)	0.14 (± 0.0879)	-0.058 (± 0.1252)	
RBC; Day 14, 24 h post dose	-0.083 (± 0.0958)	0.042 (± 0.1031)	-0.084 (± 0.1496)	
Reticulocytes; Day 7/Day 8, pre-dose	0.00397 (± 0.008856)	0.00882 (± 0.018576)	0.01792 (± 0.012824)	
Reticulocytes; Day 14, 24 h post dose	-0.00172 (± 0.005382)	-0.01063 (± 0.018329)	0.00884 (± 0.015546)	

Notes:

[165] - Safety Population

[166] - Safety Population

[167] - Safety Population

Statistical analyses

No statistical analyses for this end point

Secondary: Part B: Change from Baseline in hematocrit at the indicated time points

End point title	Part B: Change from Baseline in hematocrit at the indicated time points ^[168]
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End point description:

Blood samples were collected for measurement for the indicated tests. Change from Baseline at any post-dose visit was calculated as the post-dose visit value minus the Baseline value. Day 7 assessments could be conducted on Day 7 or Day 8.

End point type	Secondary
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End point timeframe:

Baseline (Day 1 [pre-dose]), Day 7 (pre-dose), and Day 14 (24 hours [h] post-dose)

Notes:

[168] - 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: No statistical analysis was performed for this primary endpoint; thus, no data are available

End point values	Part B: Placebo	Part B: GSK2269557 100 µg	Part B: GSK2269557 200 µg	Part B: GSK2269557 500 µg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	5 ^[169]	5 ^[170]	5 ^[171]	5 ^[172]
Units: Fraction of 1				
arithmetic mean (standard deviation)				
Day 7/Day 8, pre-dose	0.012 (± 0.0084)	0.004 (± 0.0182)	0.018 (± 0.0259)	0.01 (± 0.01)
Day 14, 24 h post dose	0.008 (± 0.0217)	0 (± 0.0212)	0.006 (± 0.0152)	-0.012 (± 0.0217)

Notes:

[169] - Safety Population

[170] - Safety Population

[171] - Safety Population

[172] - Safety Population

End point values	Part B: GSK2269557 700 µg	Part B: GSK2269557 1000 µg	Part B: GSK2269557 2000 µg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	6 ^[173]	4 ^[174]	5 ^[175]	
Units: Fraction of 1				
arithmetic mean (standard deviation)				
Day 7/Day 8, pre-dose	0 (± 0.0141)	0.015 (± 0.0058)	-0.01 (± 0.0235)	
Day 14, 24 h post dose	-0.01 (± 0.0063)	0.01 (± 0.0082)	-0.004 (± 0.0207)	

Notes:

[173] - Safety Population

[174] - Safety Population

[175] - Safety Population

Statistical analyses

No statistical analyses for this end point

Secondary: Part B: Change from Baseline in mean corpuscle hemoglobin (MCH) at the indicated time points

End point title	Part B: Change from Baseline in mean corpuscle hemoglobin (MCH) at the indicated time points ^[176]
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End point description:

Blood samples were collected for measurement for the indicated tests. MCH is one of the red blood cell indices. Change from Baseline at any post-dose visit was calculated as the post-dose visit value minus the Baseline value. Day 7 assessments could be conducted on Day 7 or Day 8.

End point type	Secondary
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End point timeframe:

Baseline (Day 1 [pre-dose]), Day 7 (pre-dose), and Day 14 (24 hours [h] post-dose)

Notes:

[176] - 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: No statistical analysis was performed for this primary endpoint; thus, no data are available

End point values	Part B: Placebo	Part B: GSK2269557 100 µg	Part B: GSK2269557 200 µg	Part B: GSK2269557 500 µg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	5 ^[177]	5 ^[178]	5 ^[179]	5 ^[180]
Units: pg				
arithmetic mean (standard deviation)				
Day 7/Day 8, pre-dose	0.18 (± 0.415)	-0.06 (± 0.397)	-0.36 (± 0.351)	-0.08 (± 0.669)
Day 14, 24 h post dose	0.18 (± 0.626)	0.02 (± 0.259)	-0.34 (± 0.74)	0.12 (± 0.396)

Notes:

[177] - Safety Population

[178] - Safety Population

[179] - Safety Population

[180] - Safety Population

End point values	Part B: GSK2269557 700 µg	Part B: GSK2269557 1000 µg	Part B: GSK2269557 2000 µg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	6 ^[181]	4 ^[182]	5 ^[183]	
Units: pg				
arithmetic mean (standard deviation)				
Day 7/Day 8, pre-dose	0.2 (± 0.529)	0.35 (± 0.961)	0.58 (± 0.46)	
Day 14, 24 h post dose	0.1 (± 0.363)	-0.33 (± 0.754)	0.52 (± 0.268)	

Notes:

[181] - Safety Population

[182] - Safety Population

[183] - Safety Population

Statistical analyses

No statistical analyses for this end point

Secondary: Part B: Change from Baseline in mean corpuscle volume (MCV) at the indicated time points

End point title	Part B: Change from Baseline in mean corpuscle volume (MCV) at the indicated time points ^[184]
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End point description:

Blood samples were collected for measurement for the indicated tests. MCV is one of the RBC indices. Change from Baseline at any post-dose visit was calculated as the post-dose visit value minus the Baseline value. Day 7 assessments could be conducted on Day 7 or Day 8.

End point type	Secondary
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End point timeframe:

Baseline (Day 1 [pre-dose]), Day 7 (pre-dose), and Day 14 (24 hours [h] post-dose)

Notes:

[184] - 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: No statistical analysis was performed for this primary endpoint; thus, no data are available

End point values	Part B: Placebo	Part B: GSK2269557 100 µg	Part B: GSK2269557 200 µg	Part B: GSK2269557 500 µg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	5 ^[185]	5 ^[186]	5 ^[187]	5 ^[188]
Units: fL				
arithmetic mean (standard deviation)				
MCV; Day 7/Day 8, pre-dose	1.24 (± 0.706)	-0.14 (± 1.794)	-0.12 (± 1.708)	0.88 (± 1.085)
MCV; Day 14, 24 h post dose	-0.66 (± 1.537)	0.8 (± 1.257)	0.26 (± 1.935)	-0.62 (± 1.281)

Notes:

[185] - Safety Population

[186] - Safety Population

[187] - Safety Population

[188] - Safety Population

End point values	Part B: GSK2269557 700 µg	Part B: GSK2269557 1000 µg	Part B: GSK2269557 2000 µg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	6 ^[189]	4 ^[190]	5 ^[191]	
Units: fL				
arithmetic mean (standard deviation)				
MCV; Day 7/Day 8, pre-dose	0.42 (± 2.302)	0.2 (± 0.583)	-0.7 (± 2.719)	
MCV; Day 14, 24 h post dose	-0.53 (± 1.601)	1.53 (± 0.699)	0.98 (± 3.155)	

Notes:

[189] - Safety Population

[190] - Safety Population

[191] - Safety Population

Statistical analyses

No statistical analyses for this end point

Secondary: Part B: Change from Baseline in albumin and total protein at the indicated time points

End point title	Part B: Change from Baseline in albumin and total protein at the indicated time points ^[192]
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End point description:

Blood samples were collected for measurement for the indicated tests. Change from Baseline at any post-dose visit was calculated as the post-dose visit value minus the Baseline value. Day 7 assessments could be conducted on Day 7 or Day 8.

End point type	Secondary
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End point timeframe:

Baseline (Day 1 [pre-dose]), Day 7 (pre-dose), and Day 14 (24 hours [h] post-dose)

Notes:

[192] - 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: No statistical analysis was performed for this primary endpoint; thus, no data are available

End point values	Part B: Placebo	Part B: GSK2269557 100 µg	Part B: GSK2269557 200 µg	Part B: GSK2269557 500 µg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	5 ^[193]	5 ^[194]	5 ^[195]	5 ^[196]
Units: g/L				
arithmetic mean (standard deviation)				
Albumin; Day 7/Day 8, pre-dose	0.96 (± 1.773)	1.22 (± 1.571)	0.96 (± 3.012)	0.88 (± 0.887)
Albumin; Day 14, 24 h post dose	0.9 (± 2.965)	0.7 (± 2.134)	-0.12 (± 2.538)	-1.16 (± 2.157)
Total protein; Day 7/Day 8, pre-dose	1.34 (± 2.46)	0.72 (± 1.203)	2.22 (± 4.953)	0.98 (± 2.039)
Total protein; Day 14, 24 h post dose	0.96 (± 3.392)	0.96 (± 2.393)	-0.16 (± 3.737)	-1.96 (± 3.635)

Notes:

[193] - Safety Population

[194] - Safety Population

[195] - Safety Population

[196] - Safety Population

End point values	Part B: GSK2269557 700 µg	Part B: GSK2269557 1000 µg	Part B: GSK2269557 2000 µg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	6 ^[197]	5 ^[198]	5 ^[199]	
Units: g/L				
arithmetic mean (standard deviation)				
Albumin; Day 7/Day 8, pre-dose	-0.6 (± 1.814)	1.18 (± 1.069)	0.3 (± 1.49)	
Albumin; Day 14, 24 h post dose	-1.13 (± 1.365)	0.44 (± 1.001)	0.26 (± 1.187)	
Total protein; Day 7/Day 8, pre-dose	-1.4 (± 2.662)	1.78 (± 2.338)	1.12 (± 1.571)	
Total protein; Day 14, 24 h post dose	-2.13 (± 2.156)	0.72 (± 1.154)	0.7 (± 2.277)	

Notes:

[197] - Safety Population

[198] - Safety Population

[199] - Safety Population

Statistical analyses

No statistical analyses for this end point

Secondary: Part B: Change from Baseline in alanine aminotransferase (ALT), alkaline phosphatase (ALP), aspartate aminotransferase (AST), and gamma glutamyl transferase (GGT) at the indicated time points

End point title	Part B: Change from Baseline in alanine aminotransferase (ALT), alkaline phosphatase (ALP), aspartate aminotransferase (AST), and gamma glutamyl transferase (GGT) at the indicated time points ^[200]
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End point description:

Blood samples were collected for measurement for the indicated tests. Change from Baseline at any post-dose visit was calculated as the post-dose visit value minus the Baseline value. Day 7 assessments could be conducted on Day 7 or Day 8.

End point type	Secondary
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End point timeframe:

Baseline (Day 1 [pre-dose]), Day 7 (pre-dose), and Day 14 (24 hours [h] post-dose)

Notes:

[200] - 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: No statistical analysis was performed for this primary endpoint; thus, no data are available

End point values	Part B: Placebo	Part B: GSK2269557 100 µg	Part B: GSK2269557 200 µg	Part B: GSK2269557 500 µg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	5 ^[201]	5 ^[202]	5 ^[203]	5 ^[204]
Units: International Units (IU/L)				
arithmetic mean (standard deviation)				
ALP; Day 7/Day 8, pre-dose	1.88 (± 5.45)	1.62 (± 5.756)	1.64 (± 7.946)	5.7 (± 9.986)
ALP; Day 14, 24 h post dose	1.54 (± 4.503)	4.78 (± 7.294)	-0.2 (± 6.109)	0.26 (± 9.829)
ALT; Day 7/Day 8, pre-dose	1.58 (± 2.24)	3.66 (± 6.057)	-2.44 (± 7.23)	2.6 (± 4.994)
ALT; Day 14, 24 h post dose	0.36 (± 2.268)	2.18 (± 3.17)	-2.76 (± 6.176)	0.84 (± 5.223)
AST; Day 7/Day 8, pre-dose	1.38 (± 2.464)	3.76 (± 11.142)	-0.42 (± 3.13)	0.26 (± 5.185)
AST; Day 14, 24 h post dose	0.44 (± 1.691)	0.16 (± 1.673)	-2.44 (± 3.443)	-1.64 (± 6.027)
GGT; Day 7/Day 8, pre-dose	-0.6 (± 2.119)	-0.3 (± 1.856)	-0.96 (± 4.556)	-0.3 (± 4.471)
GGT; Day 14, 24 h post dose	-0.64 (± 0.934)	0.1 (± 2.625)	-2.64 (± 6.532)	-0.72 (± 5.485)

Notes:

[201] - Safety Population

[202] - Safety Population

[203] - Safety Population

[204] - Safety Population

End point values	Part B: GSK2269557 700 µg	Part B: GSK2269557 1000 µg	Part B: GSK2269557 2000 µg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	6 ^[205]	5 ^[206]	5 ^[207]	
Units: International Units (IU/L)				
arithmetic mean (standard deviation)				
ALP; Day 7/Day 8, pre-dose	-0.95 (± 7.807)	-0.92 (± 22.572)	1.66 (± 5.465)	
ALP; Day 14, 24 h post dose	-1.1 (± 8.535)	-5.34 (± 19.016)	5.2 (± 4.038)	
ALT; Day 7/Day 8, pre-dose	-0.1 (± 2.994)	-2.4 (± 5.036)	1.42 (± 2.791)	
ALT; Day 14, 24 h post dose	-0.72 (± 4.63)	-2.86 (± 5.478)	1.58 (± 3.754)	
AST; Day 7/Day 8, pre-dose	-0.22 (± 3.672)	-2.56 (± 5.607)	3.04 (± 2.048)	
AST; Day 14, 24 h post dose	0.02 (± 3.129)	-1.66 (± 4.536)	2.66 (± 1.25)	
GGT; Day 7/Day 8, pre-dose	1.88 (± 4.747)	-3.18 (± 9.7)	0.74 (± 1.141)	
GGT; Day 14, 24 h post dose	1.52 (± 5.783)	-6.16 (± 17.113)	0.54 (± 1.923)	

Notes:

[205] - Safety Population

[206] - Safety Population

Statistical analyses

No statistical analyses for this end point

Secondary: Part B: Change from Baseline in creatinine, bilirubin, and total bilirubin at the indicated time points

End point title	Part B: Change from Baseline in creatinine, bilirubin, and total bilirubin at the indicated time points ^[208]
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End point description:

Blood samples were collected for measurement for the indicated tests. Change from Baseline at any post-dose visit was calculated as the post-dose visit value minus the Baseline value. Day 7 assessments could be conducted on Day 7 or Day 8.

End point type	Secondary
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End point timeframe:

Baseline (Day 1 [pre-dose]), Day 7 (pre-dose), and Day 14 (24 hours [h] post-dose)

Notes:

[208] - 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: No statistical analysis was performed for this primary endpoint; thus, no data are available

End point values	Part B: Placebo	Part B: GSK2269557 100 µg	Part B: GSK2269557 200 µg	Part B: GSK2269557 500 µg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	5 ^[209]	5 ^[210]	5 ^[211]	5 ^[212]
Units: Micromoles/Liter (micromol/L)				
arithmetic mean (standard deviation)				
Direct bilirubin; Day 7/Day 8, pre-dose	-0.02 (± 0.327)	0.24 (± 0.493)	-0.28 (± 0.881)	0.16 (± 0.261)
Direct bilirubin; Day 14, 24 h post dose	-0.1 (± 0.453)	-0.02 (± 0.192)	-0.58 (± 0.581)	0.22 (± 0.409)
Total bilirubin; Day 7/Day 8, pre-dose	0.28 (± 2.255)	0.56 (± 2.151)	-0.7 (± 4.049)	0.72 (± 2.196)
Total bilirubin; Day 14, 24 h post dose	-0.5 (± 3.389)	0.08 (± 0.87)	-2.08 (± 2.387)	0.52 (± 2.7)
Creatinine; Day 7/Day 8, pre-dose	4.52 (± 4.533)	1.6 (± 3.77)	4.38 (± 2.217)	-0.3 (± 4.567)
Creatinine; Day 14, 24 h post dose	1.58 (± 7.276)	0.76 (± 3.319)	4.84 (± 4.636)	-0.46 (± 6.98)

Notes:

[209] - Safety Population

[210] - Safety Population

[211] - Safety Population

[212] - Safety Population

End point values	Part B: GSK2269557 700 µg	Part B: GSK2269557 1000 µg	Part B: GSK2269557 2000 µg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	6 ^[213]	5 ^[214]	5 ^[215]	
Units: Micromoles/Liter (micromol/L)				

arithmetic mean (standard deviation)				
Direct bilirubin; Day 7/Day 8, pre-dose	0.23 (± 0.65)	-0.18 (± 0.349)	-0.32 (± 0.37)	
Direct bilirubin; Day 14, 24 h post dose	0.2 (± 0.429)	0.02 (± 0.554)	-0.14 (± 0.456)	
Total bilirubin; Day 7/Day 8, pre-dose	1.08 (± 2.775)	-0.86 (± 1.75)	-1.5 (± 1.739)	
Total bilirubin; Day 14, 24 h post dose	1.22 (± 3.008)	0.5 (± 2.804)	-1.06 (± 1.479)	
Creatinine; Day 7/Day 8, pre-dose	0.52 (± 4.397)	3.48 (± 3.084)	0.76 (± 5.421)	
Creatinine; Day 14, 24 h post dose	2.05 (± 3.17)	1.36 (± 2.545)	1.42 (± 5.058)	

Notes:

[213] - Safety Population

[214] - Safety Population

[215] - Safety Population

Statistical analyses

No statistical analyses for this end point

Secondary: Part B: Change from Baseline in calcium, potassium, sodium, glucose, and blood urea nitrogen (BUN) at the indicated time points

End point title	Part B: Change from Baseline in calcium, potassium, sodium, glucose, and blood urea nitrogen (BUN) at the indicated time points ^[216]
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End point description:

Blood samples were collected for measurement for the indicated tests. Change from Baseline at any post-dose visit was calculated as the post-dose visit value minus the Baseline value. Day 7 assessments could be conducted on Day 7 or Day 8.

End point type	Secondary
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End point timeframe:

Baseline (Day 1 [pre-dose]), Day 7 (pre-dose), and Day 14 (24 hours [h] post-dose)

Notes:

[216] - 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: No statistical analysis was performed for this primary endpoint; thus, no data are available

End point values	Part B: Placebo	Part B: GSK2269557 100 µg	Part B: GSK2269557 200 µg	Part B: GSK2269557 500 µg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	5 ^[217]	5 ^[218]	5 ^[219]	5 ^[220]
Units: Millimoles per Liter (mmol/L)				
arithmetic mean (standard deviation)				
Calcium; Day 7/Day 8, pre-dose	0.048 (± 0.0444)	0.044 (± 0.0397)	0.06 (± 0.0579)	0.01 (± 0.0648)
Calcium; Day 14, 24 h post dose	0.024 (± 0.0865)	-0.012 (± 0.0482)	0.05 (± 0.0696)	-0.01 (± 0.0758)
Glucose; Day 7/Day 8, pre-dose	-0.06 (± 0.2939)	0.054 (± 0.4057)	0.164 (± 0.1937)	-0.43 (± 1.4084)
Glucose; Day 14, 24 h post dose	-0.086 (± 0.3743)	-0.142 (± 0.3746)	0.26 (± 0.5456)	0.054 (± 0.2294)
Potassium; Day 7/Day 8, pre-dose	0.246 (± 0.3088)	0.09 (± 0.2793)	0.434 (± 0.5451)	-0.204 (± 0.2563)
Potassium; Day 14, 24 h post dose	0.19 (± 0.1944)	0.12 (± 0.4282)	0.336 (± 0.5268)	-0.128 (± 0.3241)
Sodium; Day 7/Day 8, pre-dose	0 (± 1.206)	0.6 (± 1.626)	-0.12 (± 1.714)	1.18 (± 1.139)

Sodium; Day 14, 24 h post dose	-0.16 (± 1.301)	-0.04 (± 3.233)	0.58 (± 1.399)	0.46 (± 1.447)
Urea/BUN; Day 7/Day 8, pre-dose	0.314 (± 0.7077)	-0.504 (± 0.6955)	0.342 (± 0.8193)	-0.91 (± 1.0653)
Urea/BUN; Day 14, 24 h post dose	-0.232 (± 0.3592)	-0.124 (± 0.7502)	0.142 (± 1.0269)	-0.906 (± 1.6431)

Notes:

[217] - Safety Population

[218] - Safety Population

[219] - Safety Population

[220] - Safety Population

End point values	Part B: GSK2269557 700 µg	Part B: GSK2269557 1000 µg	Part B: GSK2269557 2000 µg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	6 ^[221]	5 ^[222]	5 ^[223]	
Units: Millimoles per Liter (mmol/L)				
arithmetic mean (standard deviation)				
Calcium; Day 7/Day 8, pre-dose	-0.008 (± 0.0655)	0.066 (± 0.0811)	0.044 (± 0.0365)	
Calcium; Day 14, 24 h post dose	-0.042 (± 0.0422)	0.03 (± 0.0292)	0.036 (± 0.0568)	
Glucose; Day 7/Day 8, pre-dose	-0.11 (± 0.5658)	0.11 (± 0.4369)	-0.246 (± 0.273)	
Glucose; Day 14, 24 h post dose	-0.34 (± 0.7332)	-0.076 (± 0.3518)	-0.314 (± 0.3871)	
Potassium; Day 7/Day 8, pre-dose	0.135 (± 0.3172)	0.276 (± 0.3566)	0.192 (± 0.4587)	
Potassium; Day 14, 24 h post dose	0.013 (± 0.203)	0.14 (± 0.1259)	0.072 (± 0.5946)	
Sodium; Day 7/Day 8, pre-dose	-0.33 (± 2.072)	0.7 (± 1.815)	-0.84 (± 2.137)	
Sodium; Day 14, 24 h post dose	-0.18 (± 2.515)	1.06 (± 1.074)	-0.4 (± 2.72)	
Urea/BUN; Day 7/Day 8, pre-dose	-0.29 (± 0.4396)	-0.244 (± 1.2909)	0.162 (± 1.2285)	
Urea/BUN; Day 14, 24 h post dose	-0.335 (± 0.2793)	-0.364 (± 0.8554)	0.186 (± 2.0478)	

Notes:

[221] - Safety Population

[222] - Safety Population

[223] - Safety Population

Statistical analyses

No statistical analyses for this end point

Secondary: Part B: Number of participants meeting criteria of potential clinical importance for systolic blood pressure (SBP), diastolic blood pressure (DBP), and heart rate (HR) at any visit post-Baseline

End point title	Part B: Number of participants meeting criteria of potential clinical importance for systolic blood pressure (SBP), diastolic blood pressure (DBP), and heart rate (HR) at any visit post-Baseline ^[224]
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End point description:

Baseline was the Day 1 pre-dose measurement. Vital signs (SBP, DBP, and HR) were measured at Day 1 (30 minutes [min] and 6 h post-dose), Day 7 (pre-dose), and Day 14 (24 h post-dose). All measurements were obtained in supine position, after a 5-minute rest. Day 7 assessments could be

conducted on Day 7 or Day 8.

End point type	Secondary
End point timeframe:	
Day 1, Day 7, and Day 14	

Notes:

[224] - 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: No statistical analysis was performed for this primary endpoint; thus, no data are available

End point values	Part B: Placebo	Part B: GSK2269557 100 µg	Part B: GSK2269557 200 µg	Part B: GSK2269557 500 µg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	5 ^[225]	5 ^[226]	5 ^[227]	5 ^[228]
Units: Participants				
SBP high	0	0	1	1
SBP low	0	0	0	0
DBP high	0	0	0	0
DBP low	0	0	0	0
HR high	0	0	0	0
HR low	0	0	0	0

Notes:

[225] - Safety Population

[226] - Safety Population

[227] - Safety Population

[228] - Safety Population

End point values	Part B: GSK2269557 700 µg	Part B: GSK2269557 1000 µg	Part B: GSK2269557 2000 µg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	6 ^[229]	5 ^[230]	5 ^[231]	
Units: Participants				
SBP high	1	0	0	
SBP low	0	0	0	
DBP high	0	0	0	
DBP low	0	0	0	
HR high	0	0	0	
HR low	0	0	0	

Notes:

[229] - Safety Population

[230] - Safety Population

[231] - Safety Population

Statistical analyses

No statistical analyses for this end point

Secondary: Part B: Number of participants with normal and abnormal (clinically significant or not clinically significant) findings in 12-lead electrocardiogram (ECG) at any visit post-Baseline

End point title	Part B: Number of participants with normal and abnormal (clinically significant or not clinically significant) findings in 12-lead electrocardiogram (ECG) at any visit post-Baseline ^[232]
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End point description:

Baseline was the Day 1 (pre-dose) measurement. Single 12-lead ECGs were obtained using an ECG machine that automatically calculates the HR and measures PR, QRS, QT, and corrected QT intervals. Day 7 assessments could be conducted on Day 7 or Day 8.

End point type Secondary

End point timeframe:

Day 1, Day 7, and Day 14

Notes:

[232] - 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: No statistical analysis was performed for this primary endpoint; thus, no data are available

End point values	Part B: Placebo	Part B: GSK2269557 100 µg	Part B: GSK2269557 200 µg	Part B: GSK2269557 500 µg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	5 ^[233]	5 ^[234]	5 ^[235]	5 ^[236]
Units: Participants				
Normal	4	5	3	2
Abnormal - not clinically significant	1	0	2	3
Abnormal - clinically significant	0	0	0	0

Notes:

[233] - Safety Population

[234] - Safety Population

[235] - Safety Population

[236] - Safety Population

End point values	Part B: GSK2269557 700 µg	Part B: GSK2269557 1000 µg	Part B: GSK2269557 2000 µg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	6 ^[237]	5 ^[238]	5 ^[239]	
Units: Participants				
Normal	5	5	4	
Abnormal - not clinically significant	1	0	1	
Abnormal - clinically significant	0	0	0	

Notes:

[237] - Safety Population

[238] - Safety Population

[239] - Safety Population

Statistical analyses

No statistical analyses for this end point

Secondary: Part B: Forced expiratory volume in one second (FEV1) and forced vital capacity (FVC) at Screening and Follow-up

End point title Part B: Forced expiratory volume in one second (FEV1) and forced vital capacity (FVC) at Screening and Follow-up^[240]

End point description:

FEV1 and FVC are measures of lung function. FEV1 is defined as the maximal amount of air that can be forcefully exhaled in one second. FVC is defined as the maximum amount of air that can be forcibly blown out after a maximum inspiration. FEV1 and FVC measurements were repeated until three technically acceptable measurements (within 150 milliliters of each other) had been made. Only the best of three measurements were recorded.

End point type	Secondary
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End point timeframe:

Screening (up to 30 days prior to Day 1) and Follow-up (approximately Day 19)

Notes:

[240] - 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: No statistical analysis was performed for this primary endpoint; thus, no data are available

End point values	Part B: Placebo	Part B: GSK2269557 100 µg	Part B: GSK2269557 200 µg	Part B: GSK2269557 500 µg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	5 ^[241]	5 ^[242]	5 ^[243]	5 ^[244]
Units: Liters				
arithmetic mean (confidence interval 95%)				
FEV1, Screening	1.586 (1.093 to 2.079)	1.387 (0.783 to 1.99)	1.533 (0.784 to 2.282)	1.558 (0.916 to 2.199)
FEV1, Follow-up	1.494 (1.174 to 1.813)	1.272 (0.69 to 1.855)	1.523 (0.775 to 2.271)	1.34 (1.092 to 1.589)
FVC, Screening	3.05 (2.476 to 3.624)	3.08 (1.901 to 4.259)	3.632 (2.585 to 4.679)	4.348 (3.565 to 5.131)
FVC, Follow-up	2.96 (2.432 to 3.488)	3.042 (1.809 to 4.275)	3.764 (2.533 to 4.995)	4.192 (3.527 to 4.857)

Notes:

[241] - Safety Population

[242] - Safety Population

[243] - Safety Population

[244] - Safety Population

End point values	Part B: GSK2269557 700 µg	Part B: GSK2269557 1000 µg	Part B: GSK2269557 2000 µg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	6 ^[245]	5 ^[246]	5 ^[247]	
Units: Liters				
arithmetic mean (confidence interval 95%)				
FEV1, Screening	1.573 (1.092 to 2.055)	1.36 (1.126 to 1.594)	1.407 (0.768 to 2.046)	
FEV1, Follow-up	1.501 (0.989 to 2.013)	1.405 (0.948 to 1.861)	1.431 (0.834 to 2.028)	
FVC, Screening	3.277 (2.389 to 4.164)	2.958 (1.6 to 4.316)	3.156 (2.099 to 4.213)	
FVC, Follow-up	3.137 (2.057 to 4.217)	3.03 (1.691 to 4.369)	3.192 (1.968 to 4.416)	

Notes:

[245] - Safety Population

[246] - Safety Population

[247] - Safety Population

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

On-treatment serious adverse events (SAEs) and non-serious adverse events (AEs), defined as those events occurring from the start of treatment until follow-up (up to approximately 19 days), are reported.

Adverse event reporting additional description:

SAEs and non-serious AEs are reported for members of the Safety Population, comprised of all participants who received at least one dose of study treatment.

Assessment type	Systematic
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Dictionary used

Dictionary name	MedDRA
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Dictionary version	18.1
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Reporting groups

Reporting group title	Part A: Placebo
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Reporting group description:

Participants received 2 inhalations of matching placebo once daily for 14 consecutive days.

Reporting group title	Part A: GSK2269557 1000 µg
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Reporting group description:

Participants received repeat doses of GSK2269557 1000 micrograms (µg) (2 inhalations of 500 µg each from a single device) administered as a dry powder inhalation, once daily for 14 consecutive days.

Reporting group title	Part B: Placebo
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Reporting group description:

Participants received four inhalations of matching placebo (from four inhalation devices) once daily for 14 consecutive days.

Reporting group title	Part B: GSK2269557 100 µg
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Reporting group description:

Participants received repeat doses of GSK2269557 100 µg administered as a dry powder inhalation, once daily for 14 consecutive days. To maintain blinding, the total dose was delivered through four inhalation devices, each device containing either GSK2269557 100 µg or placebo.

Reporting group title	Part B: GSK2269557 200 µg
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Reporting group description:

Participants received repeat doses of GSK2269557 200 µg administered as a dry powder inhalation, once daily for 14 consecutive days. To maintain blinding, the total dose was delivered through four inhalation devices, each device containing either GSK2269557 100 µg or placebo.

Reporting group title	Part B: GSK2269557 500 µg
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Reporting group description:

Participants received repeat doses of GSK2269557 500 µg administered as a dry powder inhalation, once daily for 14 consecutive days. To maintain blinding, the total dose was delivered through four inhalation devices, each device containing either GSK2269557 500 µg or placebo.

Reporting group title	Part B: GSK2269557 700 µg
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Reporting group description:

Participants received repeat doses of GSK2269557 700 µg administered as a dry powder inhalation, once daily for 14 consecutive days. To maintain blinding, the total dose was delivered through four inhalation devices, each device containing GSK2269557 100 µg, 500 µg, or placebo.

Reporting group title	Part B: GSK2269557 1000 µg
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Reporting group description:

Participants received repeat doses of GSK2269557 1000 µg administered as a dry powder inhalation, once daily for 14 consecutive days. To maintain blinding, the total dose was delivered through four inhalation devices, each device containing either GSK2269557 500 µg or placebo.

Reporting group title	Part B: GSK2269557 2000 µg
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Reporting group description:

Participants received repeat doses of GSK2269557 2000 µg administered as a dry powder inhalation, once daily for 14 consecutive days. To maintain blinding, the total dose was delivered through four inhalation devices, each device containing GSK2269557 500 µg.

Serious adverse events	Part A: Placebo	Part A: GSK2269557 1000 µg	Part B: Placebo
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 7 (0.00%)	1 / 21 (4.76%)	0 / 5 (0.00%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Cardiac disorders			
Atrial fibrillation			
subjects affected / exposed	0 / 7 (0.00%)	1 / 21 (4.76%)	0 / 5 (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

Serious adverse events	Part B: GSK2269557 100 µg	Part B: GSK2269557 200 µg	Part B: GSK2269557 500 µg
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 5 (0.00%)	0 / 5 (0.00%)	0 / 5 (0.00%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Cardiac disorders			
Atrial fibrillation			
subjects affected / exposed	0 / 5 (0.00%)	0 / 5 (0.00%)	0 / 5 (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

Serious adverse events	Part B: GSK2269557 700 µg	Part B: GSK2269557 1000 µg	Part B: GSK2269557 2000 µg
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 6 (0.00%)	0 / 5 (0.00%)	0 / 5 (0.00%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Cardiac disorders			
Atrial fibrillation			
subjects affected / exposed	0 / 6 (0.00%)	0 / 5 (0.00%)	0 / 5 (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

Non-serious adverse events	Part A: Placebo	Part A: GSK2269557 1000 µg	Part B: Placebo
Total subjects affected by non-serious adverse events subjects affected / exposed	2 / 7 (28.57%)	7 / 21 (33.33%)	3 / 5 (60.00%)
Nervous system disorders			
Headache			
subjects affected / exposed	1 / 7 (14.29%)	3 / 21 (14.29%)	1 / 5 (20.00%)
occurrences (all)	2	4	1
Dizziness			
subjects affected / exposed	0 / 7 (0.00%)	0 / 21 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
General disorders and administration site conditions			
Catheter site haematoma			
subjects affected / exposed	0 / 7 (0.00%)	0 / 21 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Vessel puncture site inflammation			
subjects affected / exposed	0 / 7 (0.00%)	0 / 21 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Eye disorders			
Lacrimation increased			
subjects affected / exposed	0 / 7 (0.00%)	0 / 21 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	1 / 7 (14.29%)	0 / 21 (0.00%)	0 / 5 (0.00%)
occurrences (all)	1	0	0
Dry mouth			
subjects affected / exposed	0 / 7 (0.00%)	0 / 21 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Toothache			
subjects affected / exposed	0 / 7 (0.00%)	0 / 21 (0.00%)	1 / 5 (20.00%)
occurrences (all)	0	0	2
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	1 / 7 (14.29%)	4 / 21 (19.05%)	0 / 5 (0.00%)
occurrences (all)	1	17	0
Oropharyngeal pain			

subjects affected / exposed occurrences (all)	0 / 7 (0.00%) 0	0 / 21 (0.00%) 0	1 / 5 (20.00%) 1
Skin and subcutaneous tissue disorders			
Eczema			
subjects affected / exposed	0 / 7 (0.00%)	0 / 21 (0.00%)	1 / 5 (20.00%)
occurrences (all)	0	0	1
Hyperhidrosis			
subjects affected / exposed	0 / 7 (0.00%)	0 / 21 (0.00%)	1 / 5 (20.00%)
occurrences (all)	0	0	1
Psychiatric disorders			
Sleep disorder			
subjects affected / exposed	0 / 7 (0.00%)	0 / 21 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	0 / 7 (0.00%)	2 / 21 (9.52%)	0 / 5 (0.00%)
occurrences (all)	0	2	0
Neck pain			
subjects affected / exposed	0 / 7 (0.00%)	0 / 21 (0.00%)	1 / 5 (20.00%)
occurrences (all)	0	0	1
Pain in extremity			
subjects affected / exposed	0 / 7 (0.00%)	0 / 21 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Spinal pain			
subjects affected / exposed	0 / 7 (0.00%)	0 / 21 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Infections and infestations			
Gastroenteritis			
subjects affected / exposed	1 / 7 (14.29%)	0 / 21 (0.00%)	0 / 5 (0.00%)
occurrences (all)	1	0	0
Nasopharyngitis			
subjects affected / exposed	1 / 7 (14.29%)	1 / 21 (4.76%)	0 / 5 (0.00%)
occurrences (all)	1	1	0
Oral herpes			
subjects affected / exposed	1 / 7 (14.29%)	0 / 21 (0.00%)	0 / 5 (0.00%)
occurrences (all)	1	0	0

Rhinitis			
subjects affected / exposed	0 / 7 (0.00%)	0 / 21 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Sinusitis			
subjects affected / exposed	0 / 7 (0.00%)	0 / 21 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0

Non-serious adverse events	Part B: GSK2269557 100 µg	Part B: GSK2269557 200 µg	Part B: GSK2269557 500 µg
Total subjects affected by non-serious adverse events			
subjects affected / exposed	3 / 5 (60.00%)	2 / 5 (40.00%)	1 / 5 (20.00%)
Nervous system disorders			
Headache			
subjects affected / exposed	1 / 5 (20.00%)	0 / 5 (0.00%)	0 / 5 (0.00%)
occurrences (all)	1	0	0
Dizziness			
subjects affected / exposed	0 / 5 (0.00%)	0 / 5 (0.00%)	1 / 5 (20.00%)
occurrences (all)	0	0	1
General disorders and administration site conditions			
Catheter site haematoma			
subjects affected / exposed	0 / 5 (0.00%)	0 / 5 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Vessel puncture site inflammation			
subjects affected / exposed	0 / 5 (0.00%)	0 / 5 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Eye disorders			
Lacrimation increased			
subjects affected / exposed	0 / 5 (0.00%)	0 / 5 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	1 / 5 (20.00%)	0 / 5 (0.00%)	0 / 5 (0.00%)
occurrences (all)	1	0	0
Dry mouth			
subjects affected / exposed	1 / 5 (20.00%)	0 / 5 (0.00%)	0 / 5 (0.00%)
occurrences (all)	1	0	0
Toothache			

subjects affected / exposed occurrences (all)	0 / 5 (0.00%) 0	0 / 5 (0.00%) 0	0 / 5 (0.00%) 0
Respiratory, thoracic and mediastinal disorders Cough subjects affected / exposed occurrences (all)	0 / 5 (0.00%) 0	1 / 5 (20.00%) 1	0 / 5 (0.00%) 0
Oropharyngeal pain subjects affected / exposed occurrences (all)	0 / 5 (0.00%) 0	0 / 5 (0.00%) 0	0 / 5 (0.00%) 0
Skin and subcutaneous tissue disorders Eczema subjects affected / exposed occurrences (all)	0 / 5 (0.00%) 0	0 / 5 (0.00%) 0	0 / 5 (0.00%) 0
Hyperhidrosis subjects affected / exposed occurrences (all)	0 / 5 (0.00%) 0	0 / 5 (0.00%) 0	0 / 5 (0.00%) 0
Psychiatric disorders Sleep disorder subjects affected / exposed occurrences (all)	1 / 5 (20.00%) 1	0 / 5 (0.00%) 0	0 / 5 (0.00%) 0
Musculoskeletal and connective tissue disorders Arthralgia subjects affected / exposed occurrences (all)	1 / 5 (20.00%) 1	0 / 5 (0.00%) 0	0 / 5 (0.00%) 0
Neck pain subjects affected / exposed occurrences (all)	0 / 5 (0.00%) 0	0 / 5 (0.00%) 0	0 / 5 (0.00%) 0
Pain in extremity subjects affected / exposed occurrences (all)	1 / 5 (20.00%) 1	0 / 5 (0.00%) 0	0 / 5 (0.00%) 0
Spinal pain subjects affected / exposed occurrences (all)	0 / 5 (0.00%) 0	0 / 5 (0.00%) 0	0 / 5 (0.00%) 0
Infections and infestations Gastroenteritis			

subjects affected / exposed	0 / 5 (0.00%)	0 / 5 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Nasopharyngitis			
subjects affected / exposed	0 / 5 (0.00%)	1 / 5 (20.00%)	0 / 5 (0.00%)
occurrences (all)	0	1	0
Oral herpes			
subjects affected / exposed	0 / 5 (0.00%)	0 / 5 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Rhinitis			
subjects affected / exposed	1 / 5 (20.00%)	0 / 5 (0.00%)	0 / 5 (0.00%)
occurrences (all)	1	0	0
Sinusitis			
subjects affected / exposed	0 / 5 (0.00%)	0 / 5 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0

Non-serious adverse events	Part B: GSK2269557 700 µg	Part B: GSK2269557 1000 µg	Part B: GSK2269557 2000 µg
Total subjects affected by non-serious adverse events			
subjects affected / exposed	3 / 6 (50.00%)	4 / 5 (80.00%)	2 / 5 (40.00%)
Nervous system disorders			
Headache			
subjects affected / exposed	1 / 6 (16.67%)	1 / 5 (20.00%)	1 / 5 (20.00%)
occurrences (all)	2	1	1
Dizziness			
subjects affected / exposed	0 / 6 (0.00%)	0 / 5 (0.00%)	1 / 5 (20.00%)
occurrences (all)	0	0	1
General disorders and administration site conditions			
Catheter site haematoma			
subjects affected / exposed	0 / 6 (0.00%)	0 / 5 (0.00%)	1 / 5 (20.00%)
occurrences (all)	0	0	1
Vessel puncture site inflammation			
subjects affected / exposed	0 / 6 (0.00%)	0 / 5 (0.00%)	1 / 5 (20.00%)
occurrences (all)	0	0	1
Eye disorders			
Lacrimation increased			
subjects affected / exposed	0 / 6 (0.00%)	0 / 5 (0.00%)	1 / 5 (20.00%)
occurrences (all)	0	0	1

Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	0 / 6 (0.00%)	0 / 5 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Dry mouth			
subjects affected / exposed	0 / 6 (0.00%)	0 / 5 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Toothache			
subjects affected / exposed	0 / 6 (0.00%)	0 / 5 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	3 / 6 (50.00%)	4 / 5 (80.00%)	2 / 5 (40.00%)
occurrences (all)	5	5	3
Oropharyngeal pain			
subjects affected / exposed	0 / 6 (0.00%)	0 / 5 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Skin and subcutaneous tissue disorders			
Eczema			
subjects affected / exposed	0 / 6 (0.00%)	0 / 5 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Hyperhidrosis			
subjects affected / exposed	0 / 6 (0.00%)	0 / 5 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Psychiatric disorders			
Sleep disorder			
subjects affected / exposed	0 / 6 (0.00%)	0 / 5 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	0 / 6 (0.00%)	0 / 5 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Neck pain			
subjects affected / exposed	0 / 6 (0.00%)	0 / 5 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Pain in extremity			

subjects affected / exposed	0 / 6 (0.00%)	0 / 5 (0.00%)	1 / 5 (20.00%)
occurrences (all)	0	0	1
Spinal pain			
subjects affected / exposed	0 / 6 (0.00%)	0 / 5 (0.00%)	1 / 5 (20.00%)
occurrences (all)	0	0	1
Infections and infestations			
Gastroenteritis			
subjects affected / exposed	0 / 6 (0.00%)	0 / 5 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Nasopharyngitis			
subjects affected / exposed	0 / 6 (0.00%)	0 / 5 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Oral herpes			
subjects affected / exposed	0 / 6 (0.00%)	0 / 5 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Rhinitis			
subjects affected / exposed	0 / 6 (0.00%)	1 / 5 (20.00%)	1 / 5 (20.00%)
occurrences (all)	0	1	1
Sinusitis			
subjects affected / exposed	1 / 6 (16.67%)	0 / 5 (0.00%)	0 / 5 (0.00%)
occurrences (all)	1	0	0

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
03 July 2014	Amendment created to incorporate the comments received from the Ethics Committee and the Regulatory Authorities in Germany (BfArM).
09 September 2014	Amendment 2 was created to incorporate an early assessment of the exploratory data in sputum to help internal decision making
16 February 2015	Amendment 3 was created to incorporate Part B of the study (assessment of dose response using sputum biomarkers).
04 March 2015	Amendment 4 was created to include additional photosensitivity protection wording for consistency with other protocols for GSK2269557

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported