Clinical trial results:
A Placebo Controlled, Double-blind, Multi-centre, Single Dose, Parallel Group, Randomised Clinical Trial of GSK2862277 in Patients undergoing Oesophagectomy Surgery

Summary

EudraCT number	2014-000643-33
Trial protocol	GB
Global end of trial date	28 June 2017

Results information

Result version number	v1 (current)
This version publication date	13 July 2018
First version publication date	13 July 2018

Trial information

Trial identification

Sponsor protocol code	116341

Additional study identifiers

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

Notes:

Sponsors

Sponsor organisation name	GlaxoSmithKline
Sponsor organisation address	980 Great West Road, Brentford, Middlesex, United Kingdom,
Public contact	GSK Response Center, GlaxoSmithKline, 1 8664357343,
Scientific contact	GSK Response Center, GlaxoSmithKline, 1 8664357343,

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	15 November 2017
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	28 June 2017
Was the trial ended prematurely?	Yes

Notes:

General information about the trial

Main objective of the trial:

To evaluate whether a single nebulized dose of GSK2862277 prevents peri-operative lung injury compared to placebo, as assessed by measurement of pulmonary vascular permeability.

Protection of trial subjects:

Not Applicable

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	28 April 2015
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	United Kingdom: 33
Worldwide total number of subjects	33
EEA total number of subjects	33

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)	20
From 65 to 84 years	13
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

The study was conducted at 8 centers in the United Kingdom from 28-Apr-2015 to 28-Jun-2017.

Pre-assignment

Screening details:

A total of 54 participants (included 2 participants who were screen-failures and were re-screened) were screened, of which 21 participants (2 re-entered study) were screen-failures (SF). Reasons for SF: study procedure could not be performed (4), inclusion/exclusion criteria not met (14), study closed/terminated (1) and investigator discretion (2).

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	Placebo (BAL collapsed lung)

Arm description:

Eligible participants received a single dose of matching placebo on Day 1 via oral inhalation route over approximately 3 to 5 minutes; approximately 1 to 3 hours prior to scheduled surgery. After surgery, participants in this arm underwent collapsed lung broncho-alveolar lavage (BAL) procedure on Day 1.

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

Dosage and administration details:

It was a clear, colorless to pale yellow liquid, which was administered in volume to match active dose as solution for inhalation with duration of nebulization as approximately 3 to 5 minutes and was administered using "Pari eFlow with s30 mesh" device.

Arm title	Placebo (BAL ventilated lung)

Arm description:

Eligible participants received a single dose of matching placebo on Day 1 via oral inhalation route over approximately 3 to 5 minutes; approximately 1 to 3 hours prior to scheduled surgery. After surgery, participants in this arm underwent ventilated lung BAL procedure on Day 1.

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

Dosage and administration details:

It was a clear, colorless to pale yellow liquid, which was administered in volume to match active dose as solution for inhalation with duration of nebulization as approximately 3 to 5 minutes and was administered using "Pari eFlow with s30 mesh" device.

Arm title	GSK2862277 26 mg (BAL collapsed lung)

Arm description:

Eligible participants received a single dose of GSK2862277 26 milligrams (mg) on Day 1 via oral inhalation route over approximately 3 to 5 minutes; approximately 1 to 3 hours prior to scheduled surgery. After surgery, participants in this arm underwent collapsed lung BAL procedure on Day 1.

Arm type	Experimental
Investigational medicinal product name	GSK2862277
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Inhalation vapour, solution
Routes of administration	Inhalation use

Dosage and administration details:

It was available as 26 mg white to off-white, uniform lyophilized cake that will be reconstituted (using reconstitution fluid formulated with polysorbate 80 in Water for Injection) to 40 mg/vial of Lyophile for reconstitution for inhalation with duration of nebulization as approximately 3 to 5 minutes and was administered using "Pari eFlow with s30 mesh" device.

Arm title	GSK2862277 26 mg (BAL ventilated lung)

Arm description:

Eligible participants received a single dose of GSK2862277 26 mg on Day 1 via oral inhalation route over approximately 3 to 5 minutes; approximately 1 to 3 hours prior to scheduled surgery. After surgery, participants in this arm underwent ventilated lung BAL procedure on Day 1.

Arm type	Experimental
Investigational medicinal product name	GSK2862277
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Inhalation vapour, solution
Routes of administration	Inhalation use

Dosage and administration details:

It was available as 26 mg white to off-white, uniform lyophilized cake that will be reconstituted (using reconstitution fluid formulated with polysorbate 80 in Water for Injection) to 40 mg/vial of Lyophile for reconstitution for inhalation with duration of nebulization as approximately 3 to 5 minutes and was administered using "Pari eFlow with s30 mesh" device.

Number of subjects in period 1	Placebo (BAL collapsed lung)	Placebo (BAL ventilated lung)	GSK2862277 26 mg (BAL collapsed lung)
Started	5	11	8
Completed	5	11	7
Not completed	0	0	1
Physician decision	-	-	1

Number of subjects in period 1	GSK2862277 26 mg (BAL ventilated lung)
Started	9
Completed	9
Not completed	0
Physician decision	-

Baseline characteristics

Reporting groups	
Reporting group title	Placebo (BAL collapsed lung)
Reporting group description:	
Eligible participants received a single dose of matching placebo on Day 1 via oral inhalation route over approximately 3 to 5 minutes; approximately 1 to 3 hours prior to scheduled surgery. After surgery, participants in this arm underwent collapsed lung broncho-alveolar lavage (BAL) procedure on Day 1.	
Reporting group title	Placebo (BAL ventilated lung)
Reporting group description:	
Eligible participants received a single dose of matching placebo on Day 1 via oral inhalation route over approximately 3 to 5 minutes; approximately 1 to 3 hours prior to scheduled surgery. After surgery, participants in this arm underwent ventilated lung BAL procedure on Day 1.	
Reporting group title	GSK2862277 26 mg (BAL collapsed lung)
Reporting group description:	
Eligible participants received a single dose of GSK2862277 26 milligrams (mg) on Day 1 via oral inhalation route over approximately 3 to 5 minutes; approximately 1 to 3 hours prior to scheduled surgery. After surgery, participants in this arm underwent collapsed lung BAL procedure on Day 1.	
Reporting group title	GSK2862277 26 mg (BAL ventilated lung)
Reporting group description:	
Eligible participants received a single dose of GSK2862277 26 mg on Day 1 via oral inhalation route over approximately 3 to 5 minutes; approximately 1 to 3 hours prior to scheduled surgery. After surgery, participants in this arm underwent ventilated lung BAL procedure on Day 1.	

Reporting group values	Placebo (BAL collapsed lung)	Placebo (BAL ventilated lung)	GSK2862277 26 mg (BAL collapsed lung)
Number of subjects	5	11	8
Age categorical			
Units: Subjects			
Age continuous			
Safety Population which comprised of all participants who received at least one complete dose of study treatment.			
Units: years			
arithmetic mean	63.0	63.5	62.0
standard deviation	± 9.70	± 10.47	± 4.69
Gender categorical			
Safety Population which comprised of all participants who received at least one complete dose of study treatment.			
Units: Subjects			
Female	0	4	0
Male	5	7	8
Race/Ethnicity, Customized			
Safety Population which comprised of all participants who received at least one complete dose of study treatment.			
Units: Subjects			
White	5	11	8

Reporting group values	GSK2862277 26 mg (BAL ventilated lung)	Total	
Number of subjects	9	33	

Age categorical Units: Subjects			

Age continuous			
Safety Population which comprised of all participants who received at least one complete dose of study treatment.			
Units: years			
arithmetic mean	59.3		
standard deviation	± 10.76	-	
Gender categorical			
Safety Population which comprised of all participants who received at least one complete dose of study treatment.			
Units: Subjects			
Female	2	6	
Male	7	27	
Race/Ethnicity, Customized			
Safety Population which comprised of all participants who received at least one complete dose of study treatment.			
Units: Subjects			
White	9	33	

End points

End points reporting groups

Reporting group title	Placebo (BAL collapsed lung)

Reporting group description:

Eligible participants received a single dose of matching placebo on Day 1 via oral inhalation route over approximately 3 to 5 minutes; approximately 1 to 3 hours prior to scheduled surgery. After surgery, participants in this arm underwent collapsed lung broncho-alveolar lavage (BAL) procedure on Day 1.

Reporting group title	Placebo (BAL ventilated lung)

Reporting group description:

Eligible participants received a single dose of matching placebo on Day 1 via oral inhalation route over approximately 3 to 5 minutes; approximately 1 to 3 hours prior to scheduled surgery. After surgery, participants in this arm underwent ventilated lung BAL procedure on Day 1.

Reporting group title	GSK2862277 26 mg (BAL collapsed lung)

Reporting group description:

Eligible participants received a single dose of GSK2862277 26 milligrams (mg) on Day 1 via oral inhalation route over approximately 3 to 5 minutes; approximately 1 to 3 hours prior to scheduled surgery. After surgery, participants in this arm underwent collapsed lung BAL procedure on Day 1.

Reporting group title	GSK2862277 26 mg (BAL ventilated lung)

Reporting group description:

Eligible participants received a single dose of GSK2862277 26 mg on Day 1 via oral inhalation route over approximately 3 to 5 minutes; approximately 1 to 3 hours prior to scheduled surgery. After surgery, participants in this arm underwent ventilated lung BAL procedure on Day 1.

Subject analysis set title	Placebo (pooling BAL collapsed and ventilated lungs)
Subject analysis set type	Per protocol

Subject analysis set description:

Eligible participants received a single dose of matching placebo on Day 1 via oral inhalation route over approximately 3 to 5 minutes; approximately 1 to 3 hours prior to scheduled surgery. After surgery, participants in this arm underwent either collapsed lung BAL procedure or ventilated lung BAL procedure on Day 1.

Subject analysis set title	GSK2862277 26 mg (pooling BAL collapsed and ventilated lungs)
Subject analysis set type	Per protocol

Subject analysis set description:

Eligible participants received a single dose of GSK2862277 26 mg on Day 1 via oral inhalation route over approximately 3 to 5 minutes; approximately 1 to 3 hours prior to scheduled surgery. After surgery, participants in this arm underwent either collapsed lung BAL procedure or ventilated lung BAL procedure on Day 1.

Primary: Baseline adjusted change in Pulmonary vascular permeability index (PVPI) on completion of surgery

End point title	Baseline adjusted change in Pulmonary vascular permeability index (PVPI) on completion of surgery[1]

End point description:

PVPI is a derived value from extra vascular lung water (EVLW), and is considered to be less variable than extra vascular lung water Index (EVLWI). PVPI was measured via single-indicator transpulmonary thermodilution with a patent indwelling Pulse Contour Cardiac Output (PiCCO) catheter. Baseline was Day 1 (immediately prior to start of surgery). Change from Baseline value was the post-Baseline value (on completion of surgery on Day 1) minus Baseline value. Per-Protocol 1 (PP1) Population comprised of all the participants in the Safety population for whom the treatment actually received was the same one when they were randomized to (both study drug and BAL sampling location).

End point type	Primary

End point timeframe:

Baseline (Day 1 [immediately prior to start of surgery]) and Day 1 (on completion of surgery)

Notes:

[1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: There are no statistical data to report.

End point values	Placebo (BAL collapsed lung)	Placebo (BAL ventilated lung)	GSK2862277 26 mg (BAL collapsed lung)	GSK2862277 26 mg (BAL ventilated lung)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	5[2]	10[3]	5[4]	8[5]
Units: Ratio				
arithmetic mean (standard deviation)				
Ratio	0.00 (± 0.367)	0.11 (± 0.664)	-0.18 (± 0.536)	0.21 (± 0.449)

Notes:

[2] - PP1 Population.

[3] - PP1 Population.

[4] - PP1 Population.

[5] - PP1 Population.

Statistical analyses

No statistical analyses for this end point

Secondary: Baseline adjusted change in EVLWI on completion of surgery

End point title	Baseline adjusted change in EVLWI on completion of surgery

End point description:

EVLW refers to the fluid within the lung but outside the vascular compartment. It includes extravasated plasma, intracellular water, lymphatic fluid, and surfactant. EVLWI was measured by trans-pulmonary thermodilution via a PiCCO hemodynamic monitor. Baseline was Day 1 (immediately prior to start of surgery). Change from Baseline value was the post-Baseline value (on completion of surgery on Day 1) minus Baseline value. Only those participants with data available at the specified time points were analyzed.

End point type	Secondary

End point timeframe:

Baseline (Day 1 [immediately prior to start of surgery]) and Day 1 (on completion of surgery)

End point values	Placebo (BAL collapsed lung)	Placebo (BAL ventilated lung)	GSK2862277 26 mg (BAL collapsed lung)	GSK2862277 26 mg (BAL ventilated lung)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	5[6]	8[7]	5[8]	8[9]
Units: Milliliters per kilograms				
arithmetic mean (standard deviation)				
Milliliters per kilograms	0.462 (± 1.4731)	-0.317 (± 1.3436)	0.008 (± 1.2527)	-0.300 (± 3.8403)

Notes:

[6] - PP1 Population.

[7] - PP1 Population.

[8] - PP1 Population.

[9] - PP1 Population.

Statistical analyses

No statistical analyses for this end point

Secondary: Number of participants with adverse events (AE) and serious adverse events (SAE)

End point title	Number of participants with adverse events (AE) and serious adverse events (SAE)

End point description:

AE is any untoward medical occurrence in a participant or clinical investigation participant, temporally associated with use of a medicinal product (MP), whether or not considered related to MP. AE can therefore be any unfavorable and unintended sign (including an abnormal laboratory finding), symptom, or disease (new or exacerbated) temporally associated with use of MP. SAE is 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 or is medically significant or all events of possible drug induced liver injury with hyperbilirubinemia. Safety Population comprised of all participants who received at least one complete dose of study treatment.

End point type	Secondary

End point timeframe:

Up to Day 31

End point values	Placebo (BAL collapsed lung)	Placebo (BAL ventilated lung)	GSK2862277 26 mg (BAL collapsed lung)	GSK2862277 26 mg (BAL ventilated lung)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	5[10]	11[11]	8[12]	9[13]
Units: Participants				
AE	5	10	6	9
SAE	3	5	5	4

Notes:

[10] - Safety Population.

[11] - Safety Population.

[12] - Safety Population.

[13] - Safety Population.

Statistical analyses

No statistical analyses for this end point

Secondary: Number of participants with hematology abnormalities of potential clinical importance

End point title	Number of participants with hematology abnormalities of potential clinical importance

End point description:

Hematology parameters included basophils, eosinophils, hematocrit, hemoglobin, lymphocytes, monocytes, neutrophils, neutrophil bands, platelets, red blood cell (RBC) count, segmented neutrophils

and white blood cell (WBC) count. The potential clinical concern values were: hematocrit (low: <0.3 fraction and high: >0.54 fraction), Hemoglobin (low: <90 gram per Liter and high: >180 gram per Liter), lymphocytes (low: <0.6 x 10^9 cells/Liter and high: >3.0 x 10^9 cells/Liter), neutrophils: (low: <1.5 x 10^9 cells/Liter and high: >20 x 10^9 cells/Liter), platelets: (low: <100 x 10^9 cells/Liter and high: >600 x 10^9 cells/Liter) and WBC: (low: <3 x 10^9 cells/Liter and high: >20 x 10^9 cells/Liter). Only those participants for which at least one value of potential clinical concern was reported are summarized.

End point type	Secondary

End point timeframe:

Up to Day 8

End point values	Placebo (BAL collapsed lung)	Placebo (BAL ventilated lung)	GSK2862277 26 mg (BAL collapsed lung)	GSK2862277 26 mg (BAL ventilated lung)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	5[14]	11[15]	8[16]	9[17]
Units: Participants				
Participants	5	10	5	8

Notes:

[14] - Safety Population.

[15] - Safety Population.

[16] - Safety Population.

[17] - Safety Population.

Statistical analyses

No statistical analyses for this end point

Secondary: Number of participants with clinical chemistry abnormalities of potential clinical importance

End point title	Number of participants with clinical chemistry abnormalities of potential clinical importance

End point description:

Clinical chemistry parameters and their potential clinical concern values were: albumin (low: <25 millimole [mmol]/L and high: >60 mmol/L), calcium (low: <1.8 mmoL/L and high: >2.75 mmol/L), creatinine (low: <30 mmol/L and high: >160 mmol/L), glucose (low: <3 mmol/L and high: >9 mmol/L), potassium (low: <2.5 mmol/L and high: >5.5 mmol/L), sodium (low: <120 mmol/L and high: >160 mmol/L), total carbon dioxide content (low: <16 mmol/L and high: >35 mmol/L) and blood urea nitrogen (low: <3 mmol/L and high: >15 mmol/L). Number of participants with clinical chemistry abnormalities of potential clinical importance are presented.

End point type	Secondary

End point timeframe:

Up to Day 8

End point values	Placebo (BAL collapsed lung)	Placebo (BAL ventilated lung)	GSK2862277 26 mg (BAL collapsed lung)	GSK2862277 26 mg (BAL ventilated lung)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	5[18]	11[19]	8[20]	9[21]
Units: Participants				
Participants	4	5	4	4

Notes:

[18] - Safety Population.

[19] - Safety Population.

[20] - Safety Population.

[21] - Safety Population.

Statistical analyses

No statistical analyses for this end point

Secondary: Number of participants with abnormal urinalysis parameters

End point title	Number of participants with abnormal urinalysis parameters

End point description:

Urinalysis included dipstick urine test which was used to screen for glucose, ketones, occult blood and protein on Day 1 (pre-dose) and Day 8. The dipstick test gives results in a semi-quantitative manner, and results for urinalysis parameters of urine glucose, ketones, occult blood and protein can be read as Trace, 1+, 2+ and 3+, indicating proportional concentrations in the urine sample.

End point type	Secondary

End point timeframe:

Day 1 (pre-dose) and Day 8

End point values	Placebo (BAL collapsed lung)	Placebo (BAL ventilated lung)	GSK2862277 26 mg (BAL collapsed lung)	GSK2862277 26 mg (BAL ventilated lung)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	5[22]	11[23]	8[24]	9[25]
Units: Participants				
Urine glucose: Day 1 (pre-dose): Trace	0	0	0	0
Urine glucose: Day 1 (pre-dose): 1+	0	0	0	0
Urine glucose: Day 1 (pre-dose): 2+	1	0	0	0
Urine glucose: Day 1 (pre-dose): 3+	0	0	1	0
Urine glucose: Day 8: Trace	0	1	0	2
Urine glucose: Day 8: 1+	0	0	0	0
Urine glucose: Day 8: 2+	1	0	0	0
Urine glucose: Day 8: 3+	0	0	0	0
Urine ketones: Day 1 (pre-dose): Trace	1	0	1	0
Urine ketones: Day 1 (pre-dose): 1+	0	0	0	0
Urine ketones: Day 1 (pre-dose): 2+	0	0	0	0
Urine ketones: Day 1 (pre-dose): 3+	0	0	0	0
Urine ketones: Day 8: Trace	0	0	0	2
Urine ketones: Day 8: 1+	0	0	1	0
Urine ketones: Day 8: 2+	0	0	0	0
Urine ketones: Day 8: 3+	0	0	0	0

Urine occult blood: Day 1 (pre-dose): Trace	0	0	1	0
Urine occult blood: Day 1 (pre-dose): 1+	0	2	1	0
Urine occult blood: Day 1 (pre-dose): 2+	0	0	0	0
Urine occult blood: Day 1 (pre-dose): 3+	0	0	0	0
Urine occult blood: Day 8: Trace	0	0	0	0
Urine occult blood: Day 8: 1+	1	1	0	0
Urine occult blood: Day 8: 2+	0	0	0	2
Urine occult blood: Day 8: 3+	0	1	0	0
Urine protein: Day 1 (pre-dose): Trace	0	0	0	2
Urine protein: Day 1 (pre-dose): 1+	1	0	1	0
Urine protein: Day 1 (pre-dose): 2+	0	1	0	1
Urine protein: Day 1 (pre-dose): 3+	0	0	0	0
Urine protein: Day 8: Trace	1	5	0	3
Urine protein: Day 8: 1+	2	4	2	2
Urine protein: Day 8: 2+	0	0	1	2
Urine protein: Day 8: 3+	0	0	0	0

Notes:

[22] - Safety Population.

[23] - Safety Population.

[24] - Safety Population.

[25] - Safety Population.

Statistical analyses

No statistical analyses for this end point

Secondary: Number of participants with electrocardiogram (ECG) values of potential clinical importance

End point title	Number of participants with electrocardiogram (ECG) values of potential clinical importance

End point description:

Single 12-lead ECGs were obtained thereafter during the study, using an ECG machine that automatically calculated the heart rate and measured PR, QRS, QT, RR and corrected QT (QTc) intervals. Number of participants with ECG values of potential clinical importance are presented.

End point type	Secondary

End point timeframe:

Days 1, 2, 4 and 8

End point values	Placebo (BAL collapsed lung)	Placebo (BAL ventilated lung)	GSK2862277 26 mg (BAL collapsed lung)	GSK2862277 26 mg (BAL ventilated lung)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	5[26]	11[27]	8[28]	9[29]
Units: Participants				
Participants	5	7	4	8

Notes:

[26] - Safety Population.

[27] - Safety Population.

[28] - Safety Population.

[29] - Safety Population.

Statistical analyses

No statistical analyses for this end point

Secondary: Number of participants with vital signs of potential clinical importance

End point title	Number of participants with vital signs of potential clinical importance

End point description:

Vital sign measurements included systolic and diastolic blood pressure, pulse rate, temperature and respiratory rate. Vital sign measurements were measured in a semi-recumbent or supine position after 5 minutes rest. The potential clinical concern range for systolic blood pressure: <85 and >160 millimeters of mercury, for diastolic: <45 and >100 millimeters of mercury and heart rate: <40 and >110 beats per minute. Number of participants with vital signs of potential clinical importance are presented.

End point type	Secondary

End point timeframe:

Up to Day 31

End point values	Placebo (BAL collapsed lung)	Placebo (BAL ventilated lung)	GSK2862277 26 mg (BAL collapsed lung)	GSK2862277 26 mg (BAL ventilated lung)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	5[30]	11[31]	8[32]	9[33]
Units: Participants				
Participants	2	3	3	3

Notes:

[30] - Safety Population.

[31] - Safety Population.

[32] - Safety Population.

[33] - Safety Population.

Statistical analyses

No statistical analyses for this end point

Secondary: Baseline adjusted change in PaO2/FiO2 on completion of surgery

End point title	Baseline adjusted change in PaO2/FiO2 on completion of surgery

End point description:

Oxygenation and function of gas exchange was assessed by the comparison of partial pressure of oxygen arterially (PaO2) divided by the fraction of oxygen that is being inspired (FiO2), sometimes referred to simply as the 'P to F ratio'. The P to F ratio was assessed at time points during the period of intubation and mechanical ventilation. An arterial blood sample was required for determination of the partial pressure of oxygen and the percentage of O2 which is being inspired was recorded at the corresponding time point. Baseline was Day 1 (immediately prior to start of surgery). Change from Baseline value was the post-Baseline value (on completion of surgery on Day 1) minus Baseline value.

End point type	Secondary

End point timeframe:

Baseline (Day 1 [immediately prior to start of surgery]) and Day 1 (on completion of surgery)

End point values	Placebo (BAL collapsed lung)	Placebo (BAL ventilated lung)	GSK2862277 26 mg (BAL collapsed lung)	GSK2862277 26 mg (BAL ventilated lung)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	5[34]	10[35]	5[36]	8[37]
Units: Millimiters of Mercury				
arithmetic mean (standard deviation)				
Millimiters of Mercury	8.9 (± 141.10)	18.5 (± 160.82)	-47.5 (± 252.16)	11.2 (± 98.12)

Notes:

[34] - PP1 Population.

[35] - PP1 Population.

[36] - PP1 Population.

[37] - PP1 Population.

Statistical analyses

No statistical analyses for this end point

Secondary: Levels of BAL biomarkers on completion of surgery

End point title	Levels of BAL biomarkers on completion of surgery

End point description:

Samples were collected to determine concentrations of biomarkers in BAL using an appropriately validated assay on Day 1 after completion of surgery. BAL biomarkers included soluble tumor necrosis factor receptor (STNFR) type I, free, STNFR type I, total, tumor necrosis factor alpha, interleukin 6, interleukin 8, interleukin 1 beta, monocyte chemotactic protein-1, macrophage inflammatory protein 1 alpha, macrophage inflammatory protein 1 beta, interleukin 10 and soluble receptor for advanced glycation end (sRAGE) products. Any value below limit of quantification was replaced with half the lower limit of quantification (LLQ) prior to deriving the summary measures. Mean levels of BAL biomarkers on completion of surgery are presented. Only those participants available at the specified time points were analyzed represented by n=X,X,X,X in the category titles.

End point type	Secondary

End point timeframe:

Day 1 (on completion of surgery)

End point values	Placebo (BAL collapsed lung)	Placebo (BAL ventilated lung)	GSK2862277 26 mg (BAL collapsed lung)	GSK2862277 26 mg (BAL ventilated lung)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	5[38]	10[39]	5[40]	8[41]
Units: Picograms per milliliter				
arithmetic mean (standard deviation)				
STNFR type I, Free, n=5,9,5,8	645.5400 (± 398.14834)	278.2529 (± 201.58668)	106.1600 (± 168.39828)	67.7713 (± 69.69634)
STNFR I, Total, n=5,9,5,8	299.4000 (± 168.92556)	310.8136 (± 307.29751)	175.5660 (± 167.67312)	183.9000 (± 229.72939)

Tumor necrosis factor alpha, n=5,9,5,7	3.5110 (± 2.68376)	24.3850 (± 33.67945)	6.1040 (± 12.51974)	3.7814 (± 5.33211)
Interleukin 6, n=5,9,5,8	63.580 (± 66.8285)	138.917 (± 217.3948)	15.844 (± 30.5243)	43.828 (± 64.0092)
Interleukin 8, n=5,9,5,8	8041.600 (± 16369.4998)	3822.170 (± 6270.8199)	126.340 (± 145.1019)	432.513 (± 731.0601)
Interleukin 1 beta, n=5,9,5,8	70.2376 (± 123.55622)	66.3749 (± 99.46797)	1.1674 (± 0.78732)	18.6054 (± 38.61022)
Monocyte chemotactic protein-1, n=5,9,5,8	118.1600 (± 124.52553)	122.2649 (± 170.65326)	53.4260 (± 75.21106)	51.5713 (± 59.72512)
Macrophage inflammatory protein 1 alpha, n=5,9,5,8	63.348 (± 54.8461)	165.300 (± 203.2446)	9.140 (± 0.0000)	23.942 (± 32.7837)
Macrophage inflammatory protein 1 beta, n=5,9,5,8	142.040 (± 132.7086)	219.891 (± 264.1694)	28.292 (± 41.4424)	48.413 (± 82.2684)
Interleukin 10, n=5,9,5,8	1.7098 (± 1.93498)	5.2672 (± 8.39023)	0.5130 (± 0.00000)	1.8123 (± 3.23279)
sRAGE products, n=5,9,5,8	1440.2 (± 1144.89)	2121.7 (± 2078.47)	1966.0 (± 2734.60)	1044.6 (± 1560.45)

Notes:

[38] - PP1 Population.

[39] - PP1 Population.

[40] - PP1 Population.

[41] - PP1 Population.

Statistical analyses

No statistical analyses for this end point

Secondary: Levels of BAL biomarkers (C-reactive protein and total proteins) on completion of surgery

End point title	Levels of BAL biomarkers (C-reactive protein and total proteins) on completion of surgery

End point description:

Samples were collected to determine concentrations of biomarkers in BAL using an appropriately validated assay. BAL biomarkers included C-reactive protein and total proteins. Any value below limit of quantification was replaced with half the LLQ prior to deriving the summary measures. All BAL C-reactive protein samples were below limit of quantification and all were assigned to half the LLQ prior to deriving the summary measures. Mean levels of BAL biomarkers on completion of surgery are presented. Only those participants available at the specified time points were analyzed represented by n=X,X,X,X in the category titles.

End point type	Secondary

End point timeframe:

Day 1 (on completion of surgery)

End point values	Placebo (BAL collapsed lung)	Placebo (BAL ventilated lung)	GSK2862277 26 mg (BAL collapsed lung)	GSK2862277 26 mg (BAL ventilated lung)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	5[42]	10[43]	5[44]	8[45]
Units: Milligrams per Liters				
arithmetic mean (standard deviation)				
C-reactive protein, n=5,9,5,8	0.04650 (± 0.000000)	0.04650 (± 0.000000)	0.04650 (± 0.000000)	0.04650 (± 0.000000)
Total proteins, n=5,10,5,8	423.6 (± 182.80)	605.1 (± 670.60)	136.8 (± 108.33)	303.0 (± 274.85)

Notes:

[42] - PP1 Population.

[43] - PP1 Population.

[44] - PP1 Population.

[45] - PP1 Population.

Statistical analyses

No statistical analyses for this end point

Secondary: Levels of BAL biomarkers (surfactant protein and clara cell secretory protein) on completion of surgery

End point title	Levels of BAL biomarkers (surfactant protein and clara cell secretory protein) on completion of surgery

End point description:

Samples were collected to determine concentrations of biomarkers in BAL using an appropriately validated assay. BAL biomarkers included surfactant protein D and clara cell secretory protein. Any value below limit of quantification was replaced with half the LLQ prior to deriving the summary measures. Mean levels of BAL biomarkers on completion of surgery are presented. Only those participants available at the specified time points were analyzed represented by n=X,X,X,X in the category titles.

End point type	Secondary

End point timeframe:

Day 1 (on completion of surgery)

End point values	Placebo (BAL collapsed lung)	Placebo (BAL ventilated lung)	GSK2862277 26 mg (BAL collapsed lung)	GSK2862277 26 mg (BAL ventilated lung)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	5[46]	10[47]	5[48]	8[49]
Units: Nanograms per milliliter				
arithmetic mean (standard deviation)				
Surfactant Protein D, n=5,9,5,8	411.92 (± 472.487)	760.04 (± 898.224)	872.88 (± 848.358)	551.31 (± 943.640)
Clara cell secretory protein, n=5,7,5,7	3635.40 (± 2575.875)	2131.66 (± 3217.852)	1000.40 (± 1167.704)	1409.21 (± 2358.501)

Notes:

[46] - PP1 Population.

[47] - PP1 Population.

[48] - PP1 Population.

[49] - PP1 Population.

Statistical analyses

No statistical analyses for this end point

Secondary: Change over time in PaO2/FiO2 post-operatively on Day 2 through to Day 4

End point title	Change over time in PaO2/FiO2 post-operatively on Day 2 through to Day 4

End point description:

Oxygenation and function of gas exchange was assessed by the comparison of PaO2 divided by the

FiO2, sometimes referred to simply as the 'P to F ratio'. The P to F ratio was assessed at time points during the period of intubation and mechanical ventilation. An arterial blood sample was required for determination of the partial pressure of oxygen and the percentage of O2 which is being inspired was recorded at the corresponding time point. Baseline was Day 1 (immediately prior to start of surgery). Change from Baseline value was the post-Baseline value (on completion of surgery on Day 1) minus Baseline value. PP1 Population was analyzed. Only those participants available at the specified time points were analyzed represented by n=X,X in the category titles.

End point type	Secondary

End point timeframe:

Baseline (Day 1 [immediately prior to start of surgery]) to Days 2, 3 and 4

End point values	Placebo (BAL collapsed lung)	Placebo (BAL ventilated lung)	GSK2862277 26 mg (BAL collapsed lung)	GSK2862277 26 mg (BAL ventilated lung)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	5[50]	10[51]	5[52]	8[53]
Units: Millimeters of Mercury				
arithmetic mean (standard deviation)				
Day 2, n=5,8,5,6	-15.1 (± 171.84)	-103.3 (± 87.24)	38.9 (± 312.28)	-79.3 (± 199.85)
Day 3, n=5,8,5,5	-53.7 (± 120.35)	-43.0 (± 179.64)	-9.5 (± 325.46)	-119.0 (± 148.67)
Day 4, n=5,8,5,5	-36.3 (± 139.18)	-123.6 (± 68.14)	-22.3 (± 342.46)	-56.5 (± 123.31)

Notes:

[50] - PP1 Population.

[51] - PP1 Population.

[52] - PP1 Population.

[53] - PP1 Population.

Statistical analyses

No statistical analyses for this end point

Secondary: Change over time in PVPI post-operatively on Day 2 through to Day 4

End point title	Change over time in PVPI post-operatively on Day 2 through to Day 4

End point description:

PVPI is a derived value from EVLW, and is considered to be less variable than EVLWI. PVPI was measured via single-indicator transpulmonary thermodilution as long as the participant remained in the ICU with a patent indwelling PiCCO catheter. Baseline was Day 1 (immediately prior to start of surgery). Change from Baseline value was the post-Baseline value minus Baseline value. PP1 Population was analyzed. Only those participants available at the specified time points were analyzed represented by n=X,X,X,X in the category titles.

End point type	Secondary

End point timeframe:

Baseline (Day 1 [immediately prior to start of surgery]) to Days 2, 3 and 4

End point values	Placebo (BAL collapsed lung)	Placebo (BAL ventilated lung)	GSK2862277 26 mg (BAL collapsed lung)	GSK2862277 26 mg (BAL ventilated lung)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	5[54]	10[55]	5[56]	8[57]
Units: Ratio				
arithmetic mean (standard deviation)				
Day 2, n=5,6,3,5	-0.22 (± 0.259)	-0.27 (± 0.427)	-0.50 (± 0.346)	-0.42 (± 0.630)
Day 3, n=4,6,3,5	-0.20 (± 0.648)	-0.23 (± 0.516)	-0.30 (± 0.529)	-0.32 (± 0.756)
Day 4, n=3,5,2,4	-0.40 (± 0.200)	-0.24 (± 0.666)	-0.20 (± 0.000)	-0.08 (± 0.850)

Notes:

[54] - PP1 Population.

[55] - PP1 Population.

[56] - PP1 Population.

[57] - PP1 Population.

Statistical analyses

No statistical analyses for this end point

Secondary: Change over time in EVLWI post-operatively on Day 2 through to Day 4

End point title	Change over time in EVLWI post-operatively on Day 2 through to Day 4

End point description:

EVLW refers to the fluid within the lung but outside the vascular compartment. It includes extravasated plasma, intracellular water, lymphatic fluid, and surfactant. EVLWI was measured by trans-pulmonary thermodilution via a PiCCO hemodynamic monitor. Change from Baseline value was the post-Baseline value minus Baseline value. PP1 Population was analyzed. Only those participants available at the specified time points were analyzed represented by n=X,X,X,X in the category titles.

End point type	Secondary

End point timeframe:

Baseline (Day 1 [immediately prior to start of surgery]) to Days 2, 3 and 4

End point values	Placebo (BAL collapsed lung)	Placebo (BAL ventilated lung)	GSK2862277 26 mg (BAL collapsed lung)	GSK2862277 26 mg (BAL ventilated lung)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	5[58]	10[59]	5[60]	8[61]
Units: Millimeters per kilogram				
arithmetic mean (standard deviation)				
Day 2, n=5,6,3,5	-0.033 (± 1.1203)	-1.120 (± 2.4825)	-0.694 (± 0.8710)	0.604 (± 1.3370)
Day 3, n=4,5,3,5	0.062 (± 1.2468)	-0.190 (± 1.4762)	-0.203 (± 2.3349)	0.755 (± 1.4801)
Day 4, n=3,5,2,4	-0.621 (± 0.2646)	0.828 (± 4.1772)	0.311 (± 1.9297)	1.981 (± 2.8449)

Notes:

[58] - PP1 Population.

[59] - PP1 Population.

[60] - PP1 Population.

[61] - PP1 Population.

Statistical analyses

No statistical analyses for this end point

Secondary: Daily Sequential Organ Failure Assessment (SOFA) scores on Day 2 through to Day 4

End point title	Daily Sequential Organ Failure Assessment (SOFA) scores on Day 2 through to Day 4

End point description:

The SOFA score defines the presence and severity of dysfunction within 6 organ systems (cardiovascular, respiratory, coagulation, liver, renal, and nervous system) with a value of "0" for assigned to normal function to a maximum value of "4" for severe dysfunction in each of the organ systems. Each component of the SOFA score was added together, ranging from "0" indicating no organ dysfunction in any of the 6 organ systems, to "24" indicating maximal organ dysfunction across all 6 organ systems. Per-Protocol (PP) 2 Population comprised of all the participants in the Safety population for whom the study drug actually received was the same one they were randomized to (study drug).

End point type	Secondary

End point timeframe:

Day 2 to Day 4

End point values	Placebo (BAL collapsed lung)	Placebo (BAL ventilated lung)	GSK2862277 26 mg (BAL collapsed lung)	GSK2862277 26 mg (BAL ventilated lung)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	5[62]	11[63]	6[64]	8[65]
Units: Scores on a Scale				
arithmetic mean (standard deviation)				
Day 2	1.0 (± 2.24)	1.6 (± 1.39)	1.5 (± 2.54)	2.1 (± 1.92)
Day 3	3.4 (± 4.72)	1.5 (± 1.80)	1.8 (± 2.86)	1.6 (± 1.43)
Day 4	2.2 (± 3.96)	1.3 (± 0.90)	1.3 (± 3.56)	1.6 (± 1.69)

Notes:

[62] - PP 2 Population.

[63] - PP 2 Population.

[64] - PP 2 Population.

[65] - PP 2 Population.

Statistical analyses

No statistical analyses for this end point

Secondary: Area under the concentration-time curve from time zero (pre-dose) to last time of quantifiable concentration (AUC [0 to t])

End point title	Area under the concentration-time curve from time zero (pre-dose) to last time of quantifiable concentration (AUC [0 to t])[66]

End point description:

Blood samples for pharmacokinetic analysis of GSK2862277 were collected at the indicated time points. Pharmacokinetic (PK) Population comprised of all participants in the Safety population for whom a pharmacokinetic sample (plasma and/or BAL) was obtained and analyzed. Only those participants available at the specified time points were analyzed.

End point type	Secondary

End point timeframe:

Day 1 (pre-dose, 1 hour post-dose and on completion of surgery), Day 2 (24 to 26 hours post-dose) and Day 3 (46 to 50 hours post-dose)

Notes:

[66] - 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: This endpoint is only reporting on a subset of the arms that are contained in the baseline period.

End point values	GSK2862277 26 mg (BAL collapsed lung)	GSK2862277 26 mg (BAL ventilated lung)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	3[67]	6[68]		
Units: Hours*picograms/milliliter				
geometric mean (geometric coefficient of variation)				
Hours*picograms/milliliter	340505.15 (± 45.284)	290102.64 (± 76.450)		

Notes:

[67] - PK Population.

[68] - PK Population.

Statistical analyses

No statistical analyses for this end point

Secondary: Maximum observed concentration (Cmax)

End point title	Maximum observed concentration (Cmax)[69]

End point description:

Blood samples for pharmacokinetic analysis of GSK2862277 were collected at the indicated time points. Only those participants available at the specified time points were analyzed.

End point type	Secondary

End point timeframe:

Day 1 (pre-dose, 1 hour post-dose and on completion of surgery), Day 2 (24 to 26 hours post-dose) and Day 3 (46 to 50 hours post-dose)

Notes:

[69] - 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: This endpoint is only reporting on a subset of the arms that are contained in the baseline period.

End point values	GSK2862277 26 mg (BAL collapsed lung)	GSK2862277 26 mg (BAL ventilated lung)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	3[70]	6[71]		
Units: Picograms per milliliter				

geometric mean (geometric coefficient of variation)				
Picograms per milliliters	31123.58 (± 64.452)	25469.14 (± 93.307)		

Notes:

[70] - PK Population.

[71] - PK Population.

Statistical analyses

No statistical analyses for this end point

Secondary: Derived pharmacokinetic parameter- Half-life (t1/2) and time of occurrence of Cmax (Tmax)

End point title	Derived pharmacokinetic parameter- Half-life (t1/2) and time of occurrence of Cmax (Tmax)[72]

End point description:

Half-life (t1/2) is the time required for a quantity to reduce to half its initial value. t1/2 was not determined in all cases due to insufficient data in the terminal phase. Blood samples for pharmacokinetic analysis of GSK2862277 were collected at the indicated time points. Only those participants available at the specified time points were analyzed represented by n=X,X in the category titles.

End point type	Secondary

End point timeframe:

Day 1 (pre-dose, 1 hour post-dose and on completion of surgery), Day 2 (24 to 26 hours post-dose) and Day 3 (46 to 50 hours post-dose)

Notes:

[72] - 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: This endpoint is only reporting on a subset of the arms that are contained in the baseline period.

End point values	GSK2862277 26 mg (BAL collapsed lung)	GSK2862277 26 mg (BAL ventilated lung)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	8[73]	9[74]		
Units: Hours				
geometric mean (geometric coefficient of variation)				
t1/2, n=0,0	99999 (± 99999)	99999 (± 99999)		
Tmax, n=3,6	7.584 (± 11.4958)	7.583 (± 11.4119)		

Notes:

[73] - PK Population.

[74] - PK Population.

Statistical analyses

No statistical analyses for this end point

Secondary: Ratio of total protein derived from BAL and plasma values

End point title	Ratio of total protein derived from BAL and plasma values

End point description:

BAL sampling and plasma sampling was done on Day 1 (on completion of surgery). Raw summary statistics for the derived ratio were not produced. Only statistical modeling was performed that produced

a posterior distribution for each treatment. Summary measure for the posterior distribution was the median. The quantity being modeled was the mean treatment effect (pooling data from BAL Collapsed and Ventilated Lungs). The standard deviation is capturing the dispersion of the estimate for the mean effect. Ratio of total protein (Ratio was derived from BAL and Plasma values) is presented.

End point type	Secondary

End point timeframe:

Day 1 (on completion of surgery)

End point values	Placebo (pooling BAL collapsed and ventilated lungs)	GSK2862277 26 mg (pooling BAL collapsed and ventilated lungs)		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	15[75]	13[76]		
Units: Ratio				
median (standard deviation)				
Ratio	0.005 (± 0.0020)	0.002 (± 0.0009)		

Notes:

[75] - PP1 Population.

[76] - PP1 Population.

Statistical analyses

No statistical analyses for this end point

Secondary: Number of participants with positive immunogenicity results post-dosing

End point title	Number of participants with positive immunogenicity results post-dosing

End point description:

Serum samples were obtained to determine incidence and titers of serum anti-GSK2862277 antibodies at the specified time points. The binding antibody detection assay was performed at the specified time points. Number of participants with positive immunogenicity results post-dosing is presented.

End point type	Secondary

End point timeframe:

Day 8 and Day 31

End point values	Placebo (BAL collapsed lung)	Placebo (BAL ventilated lung)	GSK2862277 26 mg (BAL collapsed lung)	GSK2862277 26 mg (BAL ventilated lung)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	5[77]	11[78]	8[79]	9[80]
Units: Participants				
Participants	0	0	0	0

Notes:

[77] - Safety Population.

[78] - Safety Population.

[79] - Safety Population.

[80] - Safety Population.

Statistical analyses

No statistical analyses for this end point

Secondary: BAL concentrations of GSK2862277

End point title	BAL concentrations of GSK2862277[81]

End point description:

BAL samples were collected on Day 1 (on completion of surgery) and BAL concentrations of GSK2862277 and derived PK parameters were determined. Only those participants available at the specified time points were analyzed. 99999 indicates that standard deviation could not be calculated because a single participant was analyzed.

End point type	Secondary

End point timeframe:

Day 1 (on completion of surgery)

Notes:

[81] - 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: This endpoint is only reporting on a subset of the arms that are contained in the baseline period.

End point values	GSK2862277 26 mg (BAL collapsed lung)	GSK2862277 26 mg (BAL ventilated lung)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	1[82]	5[83]		
Units: Nanograms per milliliter				
geometric mean (geometric coefficient of variation)				
Nanograms per milliliter	11220.00 (± 99999)	74155.37 (± 377)		

Notes:

[82] - PK Population.

[83] - PK Population.

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Serious adverse events and non-serious adverse events were collected from start of the study medication (Day 1) to Follow-up (Day 31)

Adverse event reporting additional description:

Serious adverse events and non-serious adverse events were collected for the Safety Population which comprised of all participants who received at least one complete dose of study treatment.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	20.1

Reporting groups

Reporting group title	Placebo (BAL collapsed lung)

Reporting group description:

Eligible participants received a single dose of matching placebo on Day 1 via oral inhalation route over approximately 3 to 5 minutes; approximately 1 to 3 hours prior to scheduled surgery. After surgery, participants in this arm underwent collapsed lung BAL procedure on Day 1.

Reporting group title	Placebo (BAL ventilated lung)

Reporting group description:

Eligible participants received a single dose of matching placebo on Day 1 via oral inhalation route over approximately 3 to 5 minutes; approximately 1 to 3 hours prior to scheduled surgery. After surgery, participants in this arm underwent ventilated lung BAL procedure on Day 1.

Reporting group title	GSK2862277 26 mg (BAL collapsed lung)

Reporting group description:

Eligible participants received a single dose of GSK2862277 26 mg on Day 1 via oral inhalation route over approximately 3 to 5 minutes; approximately 1 to 3 hours prior to scheduled surgery. After surgery, participants in this arm underwent collapsed lung BAL procedure on Day 1.

Reporting group title	GSK2862277 26 mg (BAL ventilated lung)

Reporting group description:

Eligible participants received a single dose of GSK2862277 26 mg on Day 1 via oral inhalation route over approximately 3 to 5 minutes; approximately 1 to 3 hours prior to scheduled surgery. After surgery, participants in this arm underwent ventilated lung BAL procedure on Day 1.

Serious adverse events	Placebo (BAL collapsed lung)	Placebo (BAL ventilated lung)	GSK2862277 26 mg (BAL collapsed lung)
Total subjects affected by serious adverse events			
subjects affected / exposed	3 / 5 (60.00%)	5 / 11 (45.45%)	5 / 8 (62.50%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events			
Injury, poisoning and procedural complications			
Failure to anastomose			
subjects affected / exposed	1 / 5 (20.00%)	0 / 11 (0.00%)	0 / 8 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Anastomotic leak			

subjects affected / exposed	0 / 5 (0.00%)	1 / 11 (9.09%)	0 / 8 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Iatrogenic injury			
subjects affected / exposed	1 / 5 (20.00%)	0 / 11 (0.00%)	0 / 8 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Procedural pneumothorax			
subjects affected / exposed	0 / 5 (0.00%)	0 / 11 (0.00%)	1 / 8 (12.50%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vascular disorders			
Femoral artery embolism			
subjects affected / exposed	0 / 5 (0.00%)	0 / 11 (0.00%)	0 / 8 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac disorders			
Atrial fibrillation			
subjects affected / exposed	1 / 5 (20.00%)	0 / 11 (0.00%)	0 / 8 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood and lymphatic system disorders			
Neutropenia			
subjects affected / exposed	0 / 5 (0.00%)	0 / 11 (0.00%)	1 / 8 (12.50%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pancytopenia			
subjects affected / exposed	0 / 5 (0.00%)	0 / 11 (0.00%)	1 / 8 (12.50%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Splenic infarction			
subjects affected / exposed	0 / 5 (0.00%)	0 / 11 (0.00%)	1 / 8 (12.50%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

General disorders and administration site conditions			
Complication associated with device			
subjects affected / exposed	0 / 5 (0.00%)	0 / 11 (0.00%)	1 / 8 (12.50%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Diaphragmatic hernia			
subjects affected / exposed	1 / 5 (20.00%)	0 / 11 (0.00%)	0 / 8 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Small intestinal obstruction			
subjects affected / exposed	1 / 5 (20.00%)	0 / 11 (0.00%)	0 / 8 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal ischaemia			
subjects affected / exposed	0 / 5 (0.00%)	0 / 11 (0.00%)	1 / 8 (12.50%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			
Aspiration			
subjects affected / exposed	0 / 5 (0.00%)	0 / 11 (0.00%)	0 / 8 (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
Pleural effusion			
subjects affected / exposed	0 / 5 (0.00%)	1 / 11 (9.09%)	0 / 8 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumothorax spontaneous			
subjects affected / exposed	0 / 5 (0.00%)	0 / 11 (0.00%)	0 / 8 (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
Pulmonary embolism			

subjects affected / exposed	2 / 5 (40.00%)	0 / 11 (0.00%)	1 / 8 (12.50%)
occurrences causally related to treatment / all	1 / 2	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Chylothorax			
subjects affected / exposed	0 / 5 (0.00%)	0 / 11 (0.00%)	1 / 8 (12.50%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Diaphragmatic rupture			
subjects affected / exposed	0 / 5 (0.00%)	1 / 11 (9.09%)	0 / 8 (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
Skin and subcutaneous tissue disorders			
Subcutaneous emphysema			
subjects affected / exposed	0 / 5 (0.00%)	0 / 11 (0.00%)	0 / 8 (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
Psychiatric disorders			
Delirium			
subjects affected / exposed	0 / 5 (0.00%)	0 / 11 (0.00%)	1 / 8 (12.50%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Empyema			
subjects affected / exposed	1 / 5 (20.00%)	0 / 11 (0.00%)	0 / 8 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lower respiratory tract infection			
subjects affected / exposed	0 / 5 (0.00%)	0 / 11 (0.00%)	1 / 8 (12.50%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia			
subjects affected / exposed	0 / 5 (0.00%)	2 / 11 (18.18%)	2 / 8 (25.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	1 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Staphylococcal infection			
subjects affected / exposed	0 / 5 (0.00%)	0 / 11 (0.00%)	1 / 8 (12.50%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	GSK2862277 26 mg (BAL ventilated lung)		
Total subjects affected by serious adverse events			
subjects affected / exposed	4 / 9 (44.44%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events			
Injury, poisoning and procedural complications			
Failure to anastomose			
subjects affected / exposed	0 / 9 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Anastomotic leak			
subjects affected / exposed	2 / 9 (22.22%)		
occurrences causally related to treatment / all	1 / 2		
deaths causally related to treatment / all	0 / 0		
Iatrogenic injury			
subjects affected / exposed	0 / 9 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Procedural pneumothorax			
subjects affected / exposed	0 / 9 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Vascular disorders			
Femoral artery embolism			
subjects affected / exposed	1 / 9 (11.11%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Cardiac disorders			
Atrial fibrillation			

subjects affected / exposed	0 / 9 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Blood and lymphatic system disorders			
Neutropenia			
subjects affected / exposed	0 / 9 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Pancytopenia			
subjects affected / exposed	0 / 9 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Splenic infarction			
subjects affected / exposed	0 / 9 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
General disorders and administration site conditions			
Complication associated with device			
subjects affected / exposed	0 / 9 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Gastrointestinal disorders			
Diaphragmatic hernia			
subjects affected / exposed	0 / 9 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Small intestinal obstruction			
subjects affected / exposed	0 / 9 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Gastrointestinal ischaemia			
subjects affected / exposed	0 / 9 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		

Respiratory, thoracic and mediastinal disorders			
Aspiration			
subjects affected / exposed	1 / 9 (11.11%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Pleural effusion			
subjects affected / exposed	0 / 9 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Pneumothorax spontaneous			
subjects affected / exposed	1 / 9 (11.11%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Pulmonary embolism			
subjects affected / exposed	0 / 9 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Chylothorax			
subjects affected / exposed	1 / 9 (11.11%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Diaphragmatic rupture			
subjects affected / exposed	0 / 9 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Skin and subcutaneous tissue disorders			
Subcutaneous emphysema			
subjects affected / exposed	1 / 9 (11.11%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Psychiatric disorders			
Delirium			

subjects affected / exposed	0 / 9 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Infections and infestations			
Empyema			
subjects affected / exposed	0 / 9 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Lower respiratory tract infection			
subjects affected / exposed	0 / 9 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Pneumonia			
subjects affected / exposed	1 / 9 (11.11%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Staphylococcal infection			
subjects affected / exposed	0 / 9 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		

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

Non-serious adverse events	Placebo (BAL collapsed lung)	Placebo (BAL ventilated lung)	GSK2862277 26 mg (BAL collapsed lung)
Total subjects affected by non-serious adverse events			
subjects affected / exposed	5 / 5 (100.00%)	10 / 11 (90.91%)	5 / 8 (62.50%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Metastases to lymph nodes			
subjects affected / exposed	0 / 5 (0.00%)	0 / 11 (0.00%)	1 / 8 (12.50%)
occurrences (all)	0	0	1
Vascular disorders			
Hypertension			
subjects affected / exposed	1 / 5 (20.00%)	1 / 11 (9.09%)	1 / 8 (12.50%)
occurrences (all)	1	1	1

Hypotension			
subjects affected / exposed	2 / 5 (40.00%)	0 / 11 (0.00%)	1 / 8 (12.50%)
occurrences (all)	2	0	1
General disorders and administration site conditions			
Chest pain			
subjects affected / exposed	0 / 5 (0.00%)	0 / 11 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Fatigue			
subjects affected / exposed	0 / 5 (0.00%)	0 / 11 (0.00%)	1 / 8 (12.50%)
occurrences (all)	0	0	1
Hypothermia			
subjects affected / exposed	0 / 5 (0.00%)	1 / 11 (9.09%)	0 / 8 (0.00%)
occurrences (all)	0	1	0
Pyrexia			
subjects affected / exposed	1 / 5 (20.00%)	3 / 11 (27.27%)	2 / 8 (25.00%)
occurrences (all)	1	3	3
Catheter site haemorrhage			
subjects affected / exposed	0 / 5 (0.00%)	0 / 11 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Catheter site pain			
subjects affected / exposed	0 / 5 (0.00%)	0 / 11 (0.00%)	1 / 8 (12.50%)
occurrences (all)	0	0	1
Catheter site haematoma			
subjects affected / exposed	0 / 5 (0.00%)	1 / 11 (9.09%)	0 / 8 (0.00%)
occurrences (all)	0	1	0
Catheter site discharge			
subjects affected / exposed	0 / 5 (0.00%)	1 / 11 (9.09%)	0 / 8 (0.00%)
occurrences (all)	0	1	0
Complication associated with device			
subjects affected / exposed	0 / 5 (0.00%)	0 / 11 (0.00%)	1 / 8 (12.50%)
occurrences (all)	0	0	1
Respiratory, thoracic and mediastinal disorders			
Acute respiratory distress syndrome			
subjects affected / exposed	0 / 5 (0.00%)	0 / 11 (0.00%)	1 / 8 (12.50%)
occurrences (all)	0	0	1
Atelectasis			

subjects affected / exposed	0 / 5 (0.00%)	0 / 11 (0.00%)	1 / 8 (12.50%)
occurrences (all)	0	0	1
Cough			
subjects affected / exposed	1 / 5 (20.00%)	1 / 11 (9.09%)	0 / 8 (0.00%)
occurrences (all)	1	1	0
Hypoxia			
subjects affected / exposed	0 / 5 (0.00%)	0 / 11 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Lung consolidation			
subjects affected / exposed	0 / 5 (0.00%)	1 / 11 (9.09%)	0 / 8 (0.00%)
occurrences (all)	0	1	0
Pleural effusion			
subjects affected / exposed	0 / 5 (0.00%)	0 / 11 (0.00%)	2 / 8 (25.00%)
occurrences (all)	0	0	2
Pleuritic pain			
subjects affected / exposed	0 / 5 (0.00%)	0 / 11 (0.00%)	1 / 8 (12.50%)
occurrences (all)	0	0	1
Pneumothorax			
subjects affected / exposed	0 / 5 (0.00%)	0 / 11 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Respiratory failure			
subjects affected / exposed	0 / 5 (0.00%)	0 / 11 (0.00%)	1 / 8 (12.50%)
occurrences (all)	0	0	1
Respiratory tract irritation			
subjects affected / exposed	0 / 5 (0.00%)	0 / 11 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Tachypnoea			
subjects affected / exposed	0 / 5 (0.00%)	0 / 11 (0.00%)	1 / 8 (12.50%)
occurrences (all)	0	0	1
Throat irritation			
subjects affected / exposed	1 / 5 (20.00%)	3 / 11 (27.27%)	0 / 8 (0.00%)
occurrences (all)	1	4	0
Wheezing			
subjects affected / exposed	0 / 5 (0.00%)	0 / 11 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Oropharyngeal discomfort			

subjects affected / exposed	0 / 5 (0.00%)	0 / 11 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Oropharyngeal pain			
subjects affected / exposed	0 / 5 (0.00%)	0 / 11 (0.00%)	1 / 8 (12.50%)
occurrences (all)	0	0	1
Psychiatric disorders			
Agitation			
subjects affected / exposed	0 / 5 (0.00%)	0 / 11 (0.00%)	1 / 8 (12.50%)
occurrences (all)	0	0	1
Confusional state			
subjects affected / exposed	0 / 5 (0.00%)	1 / 11 (9.09%)	1 / 8 (12.50%)
occurrences (all)	0	1	1
Delirium			
subjects affected / exposed	1 / 5 (20.00%)	0 / 11 (0.00%)	1 / 8 (12.50%)
occurrences (all)	1	0	1
Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	2 / 5 (40.00%)	2 / 11 (18.18%)	2 / 8 (25.00%)
occurrences (all)	2	2	2
Blood albumin decreased			
subjects affected / exposed	0 / 5 (0.00%)	1 / 11 (9.09%)	1 / 8 (12.50%)
occurrences (all)	0	1	1
Blood calcium decreased			
subjects affected / exposed	1 / 5 (20.00%)	0 / 11 (0.00%)	0 / 8 (0.00%)
occurrences (all)	1	0	0
Blood creatine phosphokinase increased			
subjects affected / exposed	0 / 5 (0.00%)	0 / 11 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Blood creatinine increased			
subjects affected / exposed	0 / 5 (0.00%)	0 / 11 (0.00%)	1 / 8 (12.50%)
occurrences (all)	0	0	1
Blood lactic acid increased			
subjects affected / exposed	0 / 5 (0.00%)	0 / 11 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Blood sodium decreased			

subjects affected / exposed	0 / 5 (0.00%)	0 / 11 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Blood urea increased			
subjects affected / exposed	0 / 5 (0.00%)	0 / 11 (0.00%)	1 / 8 (12.50%)
occurrences (all)	0	0	1
C-reactive protein increased			
subjects affected / exposed	0 / 5 (0.00%)	0 / 11 (0.00%)	1 / 8 (12.50%)
occurrences (all)	0	0	1
Electrocardiogram T wave inversion			
subjects affected / exposed	0 / 5 (0.00%)	1 / 11 (9.09%)	0 / 8 (0.00%)
occurrences (all)	0	1	0
Gamma-glutamyltransferase increased			
subjects affected / exposed	0 / 5 (0.00%)	3 / 11 (27.27%)	0 / 8 (0.00%)
occurrences (all)	0	3	0
Glomerular filtration rate decreased			
subjects affected / exposed	0 / 5 (0.00%)	0 / 11 (0.00%)	1 / 8 (12.50%)
occurrences (all)	0	0	1
Haematocrit decreased			
subjects affected / exposed	0 / 5 (0.00%)	0 / 11 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Haemoglobin decreased			
subjects affected / exposed	1 / 5 (20.00%)	0 / 11 (0.00%)	0 / 8 (0.00%)
occurrences (all)	1	0	0
Lymphocyte count decreased			
subjects affected / exposed	0 / 5 (0.00%)	0 / 11 (0.00%)	1 / 8 (12.50%)
occurrences (all)	0	0	2
Monocyte count decreased			
subjects affected / exposed	0 / 5 (0.00%)	0 / 11 (0.00%)	1 / 8 (12.50%)
occurrences (all)	0	0	1
Neutrophil count decreased			
subjects affected / exposed	0 / 5 (0.00%)	0 / 11 (0.00%)	1 / 8 (12.50%)
occurrences (all)	0	0	2
Oxygen saturation decreased			
subjects affected / exposed	0 / 5 (0.00%)	0 / 11 (0.00%)	1 / 8 (12.50%)
occurrences (all)	0	0	2

Platelet count decreased			
subjects affected / exposed	0 / 5 (0.00%)	0 / 11 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
PO2 decreased			
subjects affected / exposed	0 / 5 (0.00%)	0 / 11 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Red blood cell count decreased			
subjects affected / exposed	0 / 5 (0.00%)	0 / 11 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Reticulocyte count increased			
subjects affected / exposed	0 / 5 (0.00%)	0 / 11 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
White blood cell count decreased			
subjects affected / exposed	0 / 5 (0.00%)	0 / 11 (0.00%)	1 / 8 (12.50%)
occurrences (all)	0	0	1
White blood cell count increased			
subjects affected / exposed	0 / 5 (0.00%)	1 / 11 (9.09%)	1 / 8 (12.50%)
occurrences (all)	0	1	1
Blood phosphorus decreased			
subjects affected / exposed	0 / 5 (0.00%)	0 / 11 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Platelet count increased			
subjects affected / exposed	0 / 5 (0.00%)	0 / 11 (0.00%)	2 / 8 (25.00%)
occurrences (all)	0	0	2
Nasogastric output high			
subjects affected / exposed	0 / 5 (0.00%)	0 / 11 (0.00%)	1 / 8 (12.50%)
occurrences (all)	0	0	1
Fungal test positive			
subjects affected / exposed	0 / 5 (0.00%)	1 / 11 (9.09%)	0 / 8 (0.00%)
occurrences (all)	0	1	0
Blood alkaline phosphatase increased			
subjects affected / exposed	0 / 5 (0.00%)	4 / 11 (36.36%)	1 / 8 (12.50%)
occurrences (all)	0	4	1
Urine output decreased			
subjects affected / exposed	0 / 5 (0.00%)	1 / 11 (9.09%)	0 / 8 (0.00%)
occurrences (all)	0	1	0

Electrocardiogram change			
subjects affected / exposed	0 / 5 (0.00%)	1 / 11 (9.09%)	0 / 8 (0.00%)
occurrences (all)	0	1	0
Staphylococcus test positive			
subjects affected / exposed	0 / 5 (0.00%)	1 / 11 (9.09%)	0 / 8 (0.00%)
occurrences (all)	0	1	0
Streptococcus test positive			
subjects affected / exposed	0 / 5 (0.00%)	1 / 11 (9.09%)	0 / 8 (0.00%)
occurrences (all)	0	1	0
Escherichia test positive			
subjects affected / exposed	0 / 5 (0.00%)	0 / 11 (0.00%)	1 / 8 (12.50%)
occurrences (all)	0	0	1
Klebsiella test positive			
subjects affected / exposed	1 / 5 (20.00%)	0 / 11 (0.00%)	0 / 8 (0.00%)
occurrences (all)	2	0	0
Nuclear magnetic resonance imaging spinal abnormal			
subjects affected / exposed	0 / 5 (0.00%)	0 / 11 (0.00%)	1 / 8 (12.50%)
occurrences (all)	0	0	1
Injury, poisoning and procedural complications			
Anaemia postoperative			
subjects affected / exposed	0 / 5 (0.00%)	1 / 11 (9.09%)	0 / 8 (0.00%)
occurrences (all)	0	1	0
Postoperative hernia			
subjects affected / exposed	0 / 5 (0.00%)	0 / 11 (0.00%)	1 / 8 (12.50%)
occurrences (all)	0	0	1
Postoperative thoracic procedure complication			
subjects affected / exposed	0 / 5 (0.00%)	1 / 11 (9.09%)	0 / 8 (0.00%)
occurrences (all)	0	1	0
Procedural complication			
subjects affected / exposed	1 / 5 (20.00%)	0 / 11 (0.00%)	0 / 8 (0.00%)
occurrences (all)	1	0	0
Procedural hypotension			
subjects affected / exposed	1 / 5 (20.00%)	0 / 11 (0.00%)	1 / 8 (12.50%)
occurrences (all)	1	0	1
Endotracheal intubation complication			

subjects affected / exposed	0 / 5 (0.00%)	0 / 11 (0.00%)	1 / 8 (12.50%)
occurrences (all)	0	0	1
Procedural pain			
subjects affected / exposed	1 / 5 (20.00%)	1 / 11 (9.09%)	1 / 8 (12.50%)
occurrences (all)	1	1	1
Unintentional medical device removal			
subjects affected / exposed	0 / 5 (0.00%)	0 / 11 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Cardiac disorders			
Atrial fibrillation			
subjects affected / exposed	2 / 5 (40.00%)	2 / 11 (18.18%)	1 / 8 (12.50%)
occurrences (all)	2	2	1
Atrial flutter			
subjects affected / exposed	0 / 5 (0.00%)	0 / 11 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Bradycardia			
subjects affected / exposed	0 / 5 (0.00%)	0 / 11 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Tachycardia			
subjects affected / exposed	0 / 5 (0.00%)	1 / 11 (9.09%)	2 / 8 (25.00%)
occurrences (all)	0	1	2
Nervous system disorders			
Dizziness			
subjects affected / exposed	1 / 5 (20.00%)	0 / 11 (0.00%)	0 / 8 (0.00%)
occurrences (all)	1	0	0
Dizziness postural			
subjects affected / exposed	0 / 5 (0.00%)	0 / 11 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Hypoaesthesia			
subjects affected / exposed	0 / 5 (0.00%)	0 / 11 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Presyncope			
subjects affected / exposed	1 / 5 (20.00%)	0 / 11 (0.00%)	0 / 8 (0.00%)
occurrences (all)	1	0	0
Blood and lymphatic system disorders			

Anaemia			
subjects affected / exposed	1 / 5 (20.00%)	3 / 11 (27.27%)	0 / 8 (0.00%)
occurrences (all)	1	3	0
Anaemia folate deficiency			
subjects affected / exposed	0 / 5 (0.00%)	1 / 11 (9.09%)	0 / 8 (0.00%)
occurrences (all)	0	1	0
Eye disorders			
Diabetic retinopathy			
subjects affected / exposed	0 / 5 (0.00%)	0 / 11 (0.00%)	1 / 8 (12.50%)
occurrences (all)	0	0	1
Diplopia			
subjects affected / exposed	0 / 5 (0.00%)	0 / 11 (0.00%)	1 / 8 (12.50%)
occurrences (all)	0	0	1
Visual acuity reduced			
subjects affected / exposed	0 / 5 (0.00%)	0 / 11 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Gastrointestinal disorders			
Constipation			
subjects affected / exposed	2 / 5 (40.00%)	0 / 11 (0.00%)	2 / 8 (25.00%)
occurrences (all)	2	0	2
Diarrhoea			
subjects affected / exposed	0 / 5 (0.00%)	1 / 11 (9.09%)	0 / 8 (0.00%)
occurrences (all)	0	1	0
Dry mouth			
subjects affected / exposed	0 / 5 (0.00%)	1 / 11 (9.09%)	0 / 8 (0.00%)
occurrences (all)	0	1	0
Haematochezia			
subjects affected / exposed	0 / 5 (0.00%)	0 / 11 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Impaired gastric emptying			
subjects affected / exposed	0 / 5 (0.00%)	1 / 11 (9.09%)	0 / 8 (0.00%)
occurrences (all)	0	1	0
Nausea			
subjects affected / exposed	1 / 5 (20.00%)	1 / 11 (9.09%)	2 / 8 (25.00%)
occurrences (all)	1	1	2
Vomiting			

subjects affected / exposed	0 / 5 (0.00%)	0 / 11 (0.00%)	1 / 8 (12.50%)
occurrences (all)	0	0	2
Skin and subcutaneous tissue disorders			
Subcutaneous emphysema			
subjects affected / exposed	1 / 5 (20.00%)	0 / 11 (0.00%)	0 / 8 (0.00%)
occurrences (all)	1	0	0
Renal and urinary disorders			
Dysuria			
subjects affected / exposed	1 / 5 (20.00%)	0 / 11 (0.00%)	0 / 8 (0.00%)
occurrences (all)	1	0	0
Pollakiuria			
subjects affected / exposed	0 / 5 (0.00%)	0 / 11 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Urinary retention			
subjects affected / exposed	0 / 5 (0.00%)	0 / 11 (0.00%)	1 / 8 (12.50%)
occurrences (all)	0	0	1
Urine odour abnormal			
subjects affected / exposed	0 / 5 (0.00%)	0 / 11 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Acute kidney injury			
subjects affected / exposed	0 / 5 (0.00%)	2 / 11 (18.18%)	1 / 8 (12.50%)
occurrences (all)	0	2	1
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	0 / 5 (0.00%)	0 / 11 (0.00%)	1 / 8 (12.50%)
occurrences (all)	0	0	1
Joint swelling			
subjects affected / exposed	0 / 5 (0.00%)	1 / 11 (9.09%)	0 / 8 (0.00%)
occurrences (all)	0	1	0
Musculoskeletal pain			
subjects affected / exposed	2 / 5 (40.00%)	0 / 11 (0.00%)	1 / 8 (12.50%)
occurrences (all)	2	0	1
Joint range of motion decreased			
subjects affected / exposed	0 / 5 (0.00%)	1 / 11 (9.09%)	0 / 8 (0.00%)
occurrences (all)	0	1	0
Musculoskeletal chest pain			

subjects affected / exposed	1 / 5 (20.00%)	0 / 11 (0.00%)	0 / 8 (0.00%)
occurrences (all)	1	0	0
Infections and infestations			
Injection site abscess			
subjects affected / exposed	0 / 5 (0.00%)	0 / 11 (0.00%)	1 / 8 (12.50%)
occurrences (all)	0	0	1
Lower respiratory tract infection			
subjects affected / exposed	0 / 5 (0.00%)	0 / 11 (0.00%)	3 / 8 (37.50%)
occurrences (all)	0	0	3
Oral candidiasis			
subjects affected / exposed	0 / 5 (0.00%)	0 / 11 (0.00%)	1 / 8 (12.50%)
occurrences (all)	0	0	1
Pneumonia			
subjects affected / exposed	1 / 5 (20.00%)	1 / 11 (9.09%)	0 / 8 (0.00%)
occurrences (all)	1	1	0
Pneumonia klebsiella			
subjects affected / exposed	1 / 5 (20.00%)	0 / 11 (0.00%)	0 / 8 (0.00%)
occurrences (all)	1	0	0
Postoperative wound infection			
subjects affected / exposed	0 / 5 (0.00%)	1 / 11 (9.09%)	0 / 8 (0.00%)
occurrences (all)	0	1	0
Urinary tract infection			
subjects affected / exposed	0 / 5 (0.00%)	1 / 11 (9.09%)	0 / 8 (0.00%)
occurrences (all)	0	1	0
Staphylococcal bacteraemia			
subjects affected / exposed	1 / 5 (20.00%)	0 / 11 (0.00%)	0 / 8 (0.00%)
occurrences (all)	1	0	0
Febrile infection			
subjects affected / exposed	0 / 5 (0.00%)	0 / 11 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Enterobacter sepsis			
subjects affected / exposed	0 / 5 (0.00%)	0 / 11 (0.00%)	1 / 8 (12.50%)
occurrences (all)	0	0	1
Staphylococcal infection			
subjects affected / exposed	0 / 5 (0.00%)	0 / 11 (0.00%)	1 / 8 (12.50%)
occurrences (all)	0	0	1

Wound infection staphylococcal			
subjects affected / exposed	1 / 5 (20.00%)	1 / 11 (9.09%)	0 / 8 (0.00%)
occurrences (all)	1	1	0
Klebsiella infection			
subjects affected / exposed	0 / 5 (0.00%)	0 / 11 (0.00%)	1 / 8 (12.50%)
occurrences (all)	0	0	1
Device related infection			
subjects affected / exposed	0 / 5 (0.00%)	0 / 11 (0.00%)	1 / 8 (12.50%)
occurrences (all)	0	0	1
Infectious pleural effusion			
subjects affected / exposed	0 / 5 (0.00%)	1 / 11 (9.09%)	0 / 8 (0.00%)
occurrences (all)	0	1	0
Stoma site cellulitis			
subjects affected / exposed	0 / 5 (0.00%)	0 / 11 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Metabolism and nutrition disorders			
Hyperkalaemia			
subjects affected / exposed	0 / 5 (0.00%)	1 / 11 (9.09%)	1 / 8 (12.50%)
occurrences (all)	0	1	1
Hypoalbuminaemia			
subjects affected / exposed	0 / 5 (0.00%)	0 / 11 (0.00%)	1 / 8 (12.50%)
occurrences (all)	0	0	1
Hypocalcaemia			
subjects affected / exposed	0 / 5 (0.00%)	0 / 11 (0.00%)	1 / 8 (12.50%)
occurrences (all)	0	0	1
Hypoglycaemia			
subjects affected / exposed	0 / 5 (0.00%)	1 / 11 (9.09%)	0 / 8 (0.00%)
occurrences (all)	0	1	0
Hypokalaemia			
subjects affected / exposed	0 / 5 (0.00%)	0 / 11 (0.00%)	2 / 8 (25.00%)
occurrences (all)	0	0	2
Hypomagnesaemia			
subjects affected / exposed	0 / 5 (0.00%)	1 / 11 (9.09%)	1 / 8 (12.50%)
occurrences (all)	0	1	1
Hypophosphataemia			

subjects affected / exposed	1 / 5 (20.00%)	1 / 11 (9.09%)	0 / 8 (0.00%)
occurrences (all)	1	1	0
Hypoproteinaemia			
subjects affected / exposed	0 / 5 (0.00%)	0 / 11 (0.00%)	1 / 8 (12.50%)
occurrences (all)	0	0	1
Magnesium deficiency			
subjects affected / exposed	0 / 5 (0.00%)	0 / 11 (0.00%)	1 / 8 (12.50%)
occurrences (all)	0	0	1
Mineral deficiency			
subjects affected / exposed	0 / 5 (0.00%)	0 / 11 (0.00%)	1 / 8 (12.50%)
occurrences (all)	0	0	1

Non-serious adverse events	GSK2862277 26 mg (BAL ventilated lung)		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	8 / 9 (88.89%)		
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Metastases to lymph nodes			
subjects affected / exposed	0 / 9 (0.00%)		
occurrences (all)	0		
Vascular disorders			
Hypertension			
subjects affected / exposed	0 / 9 (0.00%)		
occurrences (all)	0		
Hypotension			
subjects affected / exposed	1 / 9 (11.11%)		
occurrences (all)	1		
General disorders and administration site conditions			
Chest pain			
subjects affected / exposed	2 / 9 (22.22%)		
occurrences (all)	2		
Fatigue			
subjects affected / exposed	0 / 9 (0.00%)		
occurrences (all)	0		
Hypothermia			

subjects affected / exposed	0 / 9 (0.00%)		
occurrences (all)	0		
Pyrexia			
subjects affected / exposed	1 / 9 (11.11%)		
occurrences (all)	1		
Catheter site haemorrhage			
subjects affected / exposed	1 / 9 (11.11%)		
occurrences (all)	1		
Catheter site pain			
subjects affected / exposed	0 / 9 (0.00%)		
occurrences (all)	0		
Catheter site haematoma			
subjects affected / exposed	0 / 9 (0.00%)		
occurrences (all)	0		
Catheter site discharge			
subjects affected / exposed	0 / 9 (0.00%)		
occurrences (all)	0		
Complication associated with device			
subjects affected / exposed	0 / 9 (0.00%)		
occurrences (all)	0		
Respiratory, thoracic and mediastinal disorders			
Acute respiratory distress syndrome			
subjects affected / exposed	0 / 9 (0.00%)		
occurrences (all)	0		
Atelectasis			
subjects affected / exposed	0 / 9 (0.00%)		
occurrences (all)	0		
Cough			
subjects affected / exposed	2 / 9 (22.22%)		
occurrences (all)	3		
Hypoxia			
subjects affected / exposed	1 / 9 (11.11%)		
occurrences (all)	1		
Lung consolidation			

subjects affected / exposed	0 / 9 (0.00%)		
occurrences (all)	0		
Pleural effusion			
subjects affected / exposed	0 / 9 (0.00%)		
occurrences (all)	0		
Pleuritic pain			
subjects affected / exposed	0 / 9 (0.00%)		
occurrences (all)	0		
Pneumothorax			
subjects affected / exposed	1 / 9 (11.11%)		
occurrences (all)	1		
Respiratory failure			
subjects affected / exposed	0 / 9 (0.00%)		
occurrences (all)	0		
Respiratory tract irritation			
subjects affected / exposed	2 / 9 (22.22%)		
occurrences (all)	2		
Tachypnoea			
subjects affected / exposed	0 / 9 (0.00%)		
occurrences (all)	0		
Throat irritation			
subjects affected / exposed	0 / 9 (0.00%)		
occurrences (all)	0		
Wheezing			
subjects affected / exposed	1 / 9 (11.11%)		
occurrences (all)	1		
Oropharyngeal discomfort			
subjects affected / exposed	1 / 9 (11.11%)		
occurrences (all)	1		
Oropharyngeal pain			
subjects affected / exposed	1 / 9 (11.11%)		
occurrences (all)	1		
Psychiatric disorders			
Agitation			
subjects affected / exposed	0 / 9 (0.00%)		
occurrences (all)	0		

Confusional state			
subjects affected / exposed	0 / 9 (0.00%)		
occurrences (all)	0		
Delirium			
subjects affected / exposed	1 / 9 (11.11%)		
occurrences (all)	1		
Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	2 / 9 (22.22%)		
occurrences (all)	2		
Blood albumin decreased			
subjects affected / exposed	0 / 9 (0.00%)		
occurrences (all)	0		
Blood calcium decreased			
subjects affected / exposed	0 / 9 (0.00%)		
occurrences (all)	0		
Blood creatine phosphokinase increased			
subjects affected / exposed	1 / 9 (11.11%)		
occurrences (all)	1		
Blood creatinine increased			
subjects affected / exposed	0 / 9 (0.00%)		
occurrences (all)	0		
Blood lactic acid increased			
subjects affected / exposed	1 / 9 (11.11%)		
occurrences (all)	1		
Blood sodium decreased			
subjects affected / exposed	1 / 9 (11.11%)		
occurrences (all)	1		
Blood urea increased			
subjects affected / exposed	0 / 9 (0.00%)		
occurrences (all)	0		
C-reactive protein increased			
subjects affected / exposed	1 / 9 (11.11%)		
occurrences (all)	1		
Electrocardiogram T wave inversion			

subjects affected / exposed	0 / 9 (0.00%)			
occurrences (all)	0			
Gamma-glutamyltransferase increased				
subjects affected / exposed	0 / 9 (0.00%)			
occurrences (all)	0			
Glomerular filtration rate decreased				
subjects affected / exposed	0 / 9 (0.00%)			
occurrences (all)	0			
Haematocrit decreased				
subjects affected / exposed	1 / 9 (11.11%)			
occurrences (all)	1			
Haemoglobin decreased				
subjects affected / exposed	1 / 9 (11.11%)			
occurrences (all)	1			
Lymphocyte count decreased				
subjects affected / exposed	0 / 9 (0.00%)			
occurrences (all)	0			
Monocyte count decreased				
subjects affected / exposed	0 / 9 (0.00%)			
occurrences (all)	0			
Neutrophil count decreased				
subjects affected / exposed	0 / 9 (0.00%)			
occurrences (all)	0			
Oxygen saturation decreased				
subjects affected / exposed	1 / 9 (11.11%)			
occurrences (all)	1			
Platelet count decreased				
subjects affected / exposed	1 / 9 (11.11%)			
occurrences (all)	1			
PO2 decreased				
subjects affected / exposed	1 / 9 (11.11%)			
occurrences (all)	1			
Red blood cell count decreased				
subjects affected / exposed	1 / 9 (11.11%)			
occurrences (all)	1			

Reticulocyte count increased				
subjects affected / exposed	1 / 9 (11.11%)			
occurrences (all)	1			
White blood cell count decreased				
subjects affected / exposed	0 / 9 (0.00%)			
occurrences (all)	0			
White blood cell count increased				
subjects affected / exposed	1 / 9 (11.11%)			
occurrences (all)	1			
Blood phosphorus decreased				
subjects affected / exposed	3 / 9 (33.33%)			
occurrences (all)	3			
Platelet count increased				
subjects affected / exposed	0 / 9 (0.00%)			
occurrences (all)	0			
Nasogastric output high				
subjects affected / exposed	0 / 9 (0.00%)			
occurrences (all)	0			
Fungal test positive				
subjects affected / exposed	0 / 9 (0.00%)			
occurrences (all)	0			
Blood alkaline phosphatase increased				
subjects affected / exposed	0 / 9 (0.00%)			
occurrences (all)	0			
Urine output decreased				
subjects affected / exposed	0 / 9 (0.00%)			
occurrences (all)	0			
Electrocardiogram change				
subjects affected / exposed	0 / 9 (0.00%)			
occurrences (all)	0			
Staphylococcus test positive				
subjects affected / exposed	1 / 9 (11.11%)			
occurrences (all)	1			
Streptococcus test positive				
subjects affected / exposed	0 / 9 (0.00%)			
occurrences (all)	0			

Escherichia test positive			
subjects affected / exposed	0 / 9 (0.00%)		
occurrences (all)	0		
Klebsiella test positive			
subjects affected / exposed	0 / 9 (0.00%)		
occurrences (all)	0		
Nuclear magnetic resonance imaging spinal abnormal			
subjects affected / exposed	0 / 9 (0.00%)		
occurrences (all)	0		
Injury, poisoning and procedural complications			
Anaemia postoperative			
subjects affected / exposed	0 / 9 (0.00%)		
occurrences (all)	0		
Postoperative hernia			
subjects affected / exposed	0 / 9 (0.00%)		
occurrences (all)	0		
Postoperative thoracic procedure complication			
subjects affected / exposed	0 / 9 (0.00%)		
occurrences (all)	0		
Procedural complication			
subjects affected / exposed	0 / 9 (0.00%)		
occurrences (all)	0		
Procedural hypotension			
subjects affected / exposed	0 / 9 (0.00%)		
occurrences (all)	0		
Endotracheal intubation complication			
subjects affected / exposed	0 / 9 (0.00%)		
occurrences (all)	0		
Procedural pain			
subjects affected / exposed	0 / 9 (0.00%)		
occurrences (all)	0		
Unintentional medical device removal			
subjects affected / exposed	1 / 9 (11.11%)		
occurrences (all)	1		
Cardiac disorders			

Atrial fibrillation subjects affected / exposed occurrences (all)	1 / 9 (11.11%) 2		
Atrial flutter subjects affected / exposed occurrences (all)	1 / 9 (11.11%) 1		
Bradycardia subjects affected / exposed occurrences (all)	1 / 9 (11.11%) 1		
Tachycardia subjects affected / exposed occurrences (all)	0 / 9 (0.00%) 0		
Nervous system disorders Dizziness subjects affected / exposed occurrences (all)	1 / 9 (11.11%) 1		
Dizziness postural subjects affected / exposed occurrences (all)	2 / 9 (22.22%) 2		
Hypoaesthesia subjects affected / exposed occurrences (all)	1 / 9 (11.11%) 1		
Presyncope subjects affected / exposed occurrences (all)	0 / 9 (0.00%) 0		
Blood and lymphatic system disorders Anaemia subjects affected / exposed occurrences (all)	0 / 9 (0.00%) 0		
Anaemia folate deficiency subjects affected / exposed occurrences (all)	0 / 9 (0.00%) 0		
Eye disorders Diabetic retinopathy subjects affected / exposed occurrences (all)	0 / 9 (0.00%) 0		
Diplopia			

subjects affected / exposed	0 / 9 (0.00%)		
occurrences (all)	0		
Visual acuity reduced			
subjects affected / exposed	1 / 9 (11.11%)		
occurrences (all)	1		
Gastrointestinal disorders			
Constipation			
subjects affected / exposed	1 / 9 (11.11%)		
occurrences (all)	1		
Diarrhoea			
subjects affected / exposed	1 / 9 (11.11%)		
occurrences (all)	1		
Dry mouth			
subjects affected / exposed	0 / 9 (0.00%)		
occurrences (all)	0		
Haematochezia			
subjects affected / exposed	1 / 9 (11.11%)		
occurrences (all)	1		
Impaired gastric emptying			
subjects affected / exposed	0 / 9 (0.00%)		
occurrences (all)	0		
Nausea			
subjects affected / exposed	1 / 9 (11.11%)		
occurrences (all)	1		
Vomiting			
subjects affected / exposed	1 / 9 (11.11%)		
occurrences (all)	1		
Skin and subcutaneous tissue disorders			
Subcutaneous emphysema			
subjects affected / exposed	0 / 9 (0.00%)		
occurrences (all)	0		
Renal and urinary disorders			
Dysuria			
subjects affected / exposed	0 / 9 (0.00%)		
occurrences (all)	0		
Pollakiuria			

subjects affected / exposed	1 / 9 (11.11%)		
occurrences (all)	1		
Urinary retention			
subjects affected / exposed	0 / 9 (0.00%)		
occurrences (all)	0		
Urine odour abnormal			
subjects affected / exposed	1 / 9 (11.11%)		
occurrences (all)	1		
Acute kidney injury			
subjects affected / exposed	0 / 9 (0.00%)		
occurrences (all)	0		
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	0 / 9 (0.00%)		
occurrences (all)	0		
Joint swelling			
subjects affected / exposed	0 / 9 (0.00%)		
occurrences (all)	0		
Musculoskeletal pain			
subjects affected / exposed	2 / 9 (22.22%)		
occurrences (all)	2		
Joint range of motion decreased			
subjects affected / exposed	0 / 9 (0.00%)		
occurrences (all)	0		
Musculoskeletal chest pain			
subjects affected / exposed	0 / 9 (0.00%)		
occurrences (all)	0		
Infections and infestations			
Injection site abscess			
subjects affected / exposed	0 / 9 (0.00%)		
occurrences (all)	0		
Lower respiratory tract infection			
subjects affected / exposed	1 / 9 (11.11%)		
occurrences (all)	1		
Oral candidiasis			

subjects affected / exposed	0 / 9 (0.00%)			
occurrences (all)	0			
Pneumonia				
subjects affected / exposed	0 / 9 (0.00%)			
occurrences (all)	0			
Pneumonia klebsiella				
subjects affected / exposed	0 / 9 (0.00%)			
occurrences (all)	0			
Postoperative wound infection				
subjects affected / exposed	0 / 9 (0.00%)			
occurrences (all)	0			
Urinary tract infection				
subjects affected / exposed	0 / 9 (0.00%)			
occurrences (all)	0			
Staphylococcal bacteraemia				
subjects affected / exposed	0 / 9 (0.00%)			
occurrences (all)	0			
Febrile infection				
subjects affected / exposed	1 / 9 (11.11%)			
occurrences (all)	1			
Enterobacter sepsis				
subjects affected / exposed	0 / 9 (0.00%)			
occurrences (all)	0			
Staphylococcal infection				
subjects affected / exposed	0 / 9 (0.00%)			
occurrences (all)	0			
Wound infection staphylococcal				
subjects affected / exposed	0 / 9 (0.00%)			
occurrences (all)	0			
Klebsiella infection				
subjects affected / exposed	0 / 9 (0.00%)			
occurrences (all)	0			
Device related infection				
subjects affected / exposed	0 / 9 (0.00%)			
occurrences (all)	0			
Infectious pleural effusion				

subjects affected / exposed	0 / 9 (0.00%)		
occurrences (all)	0		
Stoma site cellulitis			
subjects affected / exposed	1 / 9 (11.11%)		
occurrences (all)	1		
Metabolism and nutrition disorders			
Hyperkalaemia			
subjects affected / exposed	0 / 9 (0.00%)		
occurrences (all)	0		
Hypoalbuminaemia			
subjects affected / exposed	0 / 9 (0.00%)		
occurrences (all)	0		
Hypocalcaemia			
subjects affected / exposed	0 / 9 (0.00%)		
occurrences (all)	0		
Hypoglycaemia			
subjects affected / exposed	0 / 9 (0.00%)		
occurrences (all)	0		
Hypokalaemia			
subjects affected / exposed	1 / 9 (11.11%)		
occurrences (all)	1		
Hypomagnesaemia			
subjects affected / exposed	1 / 9 (11.11%)		
occurrences (all)	1		
Hypophosphataemia			
subjects affected / exposed	1 / 9 (11.11%)		
occurrences (all)	1		
Hypoproteinaemia			
subjects affected / exposed	0 / 9 (0.00%)		
occurrences (all)	0		
Magnesium deficiency			
subjects affected / exposed	0 / 9 (0.00%)		
occurrences (all)	0		
Mineral deficiency			
subjects affected / exposed	0 / 9 (0.00%)		
occurrences (all)	0		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
02 June 2014	The amendment was made to correct an error in the study title and to revise the limits on exclusion criteria for alcohol consumption.
23 July 2014	The amendment was made to reduce the upper threshold for Aspartate aminotransferase (AST) & Alanine aminotransferase (ALT) liver enzyme values for inclusion in the study, as per instruction from the United Kingdom (UK) competent authority (Medicines and Healthcare Regulatory Authority [MHRA]). A change to the corrected QT (QTc) inclusion criteria was also made to correct an error not previously identified.
16 November 2014	The amendment was made to account for the possibility of inoperable cases during the initial stages of oesophagectomy surgery, where participants would have to be withdrawn; additional time window for dosing; amending randomization window to up to 72 hours prior to day of surgery. Blood sample aliquots for a translational sub-study clarified, materials and methods of dose preparation added as an appendix. Additional minor/typographical updates and typographical changes have also been made.
16 February 2015	The amendment was made to remove the mandatory 1 hour post-dose electrocardiogram (ECG) due to concerns over logistics prior to surgery (on the condition that alternative cardiac monitoring is in place). Also, a 24 hour window has been added for the pre-dose assessments and a typographical error in exclusion criteria number 6 has been amended. A pharmacokinetic (PK) sample has also been included if a liver event occurs as this had been omitted in error. The opportunity has also been taken to make some other minor amendments.
23 August 2016	The amendment was made to detail the inclusion of an external expert to the safety review team. The opportunity has also been taken to make some other minor amendments.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? Yes

Date	Interruption	Restart date
17 December 2015	Placebo/diluent to match inhaled GSK2862277 (placebo) on stability test delivered an out of specification (OOS) result for the Visual Inspection Test requiring a recall and temporary halt.	18 January 2016

Notes:

Limitations and caveats

None reported