Clinical trial results:
A randomized, double-blind (sponsor unblind), placebo-controlled, multi-centered phase IIa study to evaluate the safety and efficacy of 13 weeks of once daily oral dosing of the selective androgen receptor modulator (SARM) GSK2881078 in older men and post menopausal women with COPD and muscle weakness, participating in home exercise

Summary

EudraCT number	2017-001148-37
Trial protocol	GB
Global end of trial date	19 November 2019

Results information

Result version number	v1 (current)
This version publication date	28 June 2020
First version publication date	28 June 2020

Trial information

Trial identification

Sponsor protocol code	200182

Additional study identifiers

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

Notes:

Sponsors

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

Notes:

Paediatric regulatory details

Is trial part of an agreed paediatric investigation plan (PIP)	No
Does article 45 of REGULATION (EC) No 1901/2006 apply to this trial?	No
Does article 46 of REGULATION (EC) No 1901/2006 apply to this trial?	No

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	17 March 2020
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	19 November 2019
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

1. Assess the safety and tolerability of approximately 13 weeks of dosing of GSK2881078.
2. Assess the effect of approximately 13 weeks of dosing of GSK2281078 on leg strength in older men and postmenopausal women with chronic obstructive pulmonary disease (COPD) and muscle weakness, participating in home exercise.

Protection of trial subjects:

Not Applicable

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	28 February 2018
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Germany: 33
Country: Number of subjects enrolled	United Kingdom: 13
Country: Number of subjects enrolled	United States: 50
Worldwide total number of subjects	96
EEA total number of subjects	46

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)	46
From 65 to 84 years	50

85 years and over	0

Subject disposition

Recruitment

Recruitment details:

This was a Phase II, double-blind, randomized, multicenter study to evaluate the safety and efficacy of GSK2881078 over 13 weeks of once daily oral dosing, first time administered in older men and post-menopausal female participants with chronic obstructive pulmonary disease (COPD) and muscle weakness, participating in home exercise.

Pre-assignment

Screening details:

A total of 200 participants were screened and 97 participants were enrolled in this study. Of which, 96 participants were randomized and received the study treatment. The remaining 1 participant was randomized without fulfilling the inclusion and exclusion criteria and therefore did not receive study medication.

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	Placebo- Female Participants

Arm description:

Post-menopausal female participants, 50 to 75 years of age, were administered orally two capsules of GSK2881078 matching placebo once daily over 13 weeks.

Arm type	Placebo
Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

Placebo was available as capsules. Post-menopausal female participants, 50 to 75 years of age, were administered orally two capsules of GSK2881078 matching placebo once daily.

Arm title	GSK2881078 1.0 mg- Female Participants

Arm description:

Post-menopausal female participants, 50 to 75 years of age, were administered orally two capsules of GSK2881078 of a unit dose strength 0.5 milligram (mg) once daily over 13 weeks.

Arm type	Experimental
Investigational medicinal product name	GSK2881078
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

GSK2881078 was available as capsules with unit dose strength of 0.5 milligram (mg). Post-menopausal female participants, 50 to 75 years of age, were administered 1.0 mg of GSK2881078 (2*0.5 mg capsules) once daily.

Arm title	Placebo- Male Participants

Arm description:

Male participants, 50 to 75 years of age, were administered orally two capsules of GSK2881078 matching placebo once daily over 13 weeks.

Arm type	Placebo
Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

Placebo was available as capsules. Male participants, 50 to 75 years of age, were administered orally two capsules of GSK2881078 matching placebo once daily.

Arm title	GSK2881078 2.0 mg- Male Participants

Arm description:

Male participants, 50 to 75 years of age, were administered orally two capsules of GSK2881078 of a unit dose strength 1.0 mg once daily over 13 weeks.

Arm type	Experimental
Investigational medicinal product name	GSK2881078
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

GSK2881078 was available as capsules with unit dose strength of 1.0 mg. Male participants, 50 to 75 years of age, were administered 2.0 mg of GSK2881078 (2*1.0 mg capsules) once daily.

Number of subjects in period 1	Placebo- Female Participants	GSK2881078 1.0 mg- Female Participants	Placebo- Male Participants
Started	23	24	24
Completed	21	18	18
Not completed	2	6	6
Consent withdrawn by subject	1	2	1
Physician decision	-	1	-
Protocol-defined stopping criteria	1	-	-
Adverse event, non-fatal	-	2	5
Lost to follow-up	-	1	-

Number of subjects in period 1	GSK2881078 2.0 mg- Male Participants
Started	25
Completed	20
Not completed	5
Consent withdrawn by subject	-
Physician decision	1
Protocol-defined stopping criteria	1
Adverse event, non-fatal	3

Lost to follow-up	-

Baseline characteristics

Reporting groups	
Reporting group title	Placebo- Female Participants
Reporting group description:	
Post-menopausal female participants, 50 to 75 years of age, were administered orally two capsules of GSK2881078 matching placebo once daily over 13 weeks.	
Reporting group title	GSK2881078 1.0 mg- Female Participants
Reporting group description:	
Post-menopausal female participants, 50 to 75 years of age, were administered orally two capsules of GSK2881078 of a unit dose strength 0.5 milligram (mg) once daily over 13 weeks.	
Reporting group title	Placebo- Male Participants
Reporting group description:	
Male participants, 50 to 75 years of age, were administered orally two capsules of GSK2881078 matching placebo once daily over 13 weeks.	
Reporting group title	GSK2881078 2.0 mg- Male Participants
Reporting group description:	
Male participants, 50 to 75 years of age, were administered orally two capsules of GSK2881078 of a unit dose strength 1.0 mg once daily over 13 weeks.	

Reporting group values	Placebo- Female Participants	GSK2881078 1.0 mg- Female Participants	Placebo- Male Participants
Number of subjects	23	24	24
Age categorical Units: Subjects			
Total Participants	23	24	24
Age Continuous Units: Years			
arithmetic mean	64.7	64.2	64.0
standard deviation	± 7.16	± 7.93	± 7.27
Sex: Female, Male Units: Participants			
Female	23	24	0
Male	0	0	24
Race/Ethnicity, Customized Units: Subjects			
Black or African American	0	1	2
White-White/Caucasian/European Heritage	23	23	22

Reporting group values	GSK2881078 2.0 mg- Male Participants	Total	
Number of subjects	25	96	
Age categorical Units: Subjects			
Total Participants	25	96	
Age Continuous Units: Years			
arithmetic mean	67.2		
standard deviation	± 6.08	-	

Sex: Female, Male Units: Participants			
Female	0	47	
Male	25	49	
Race/Ethnicity, Customized Units: Subjects			
Black or African American	2	5	
White-White/Caucasian/European Heritage	23	91	

End points

End points reporting groups

Reporting group title	Placebo- Female Participants
Reporting group description:	
Post-menopausal female participants, 50 to 75 years of age, were administered orally two capsules of GSK2881078 matching placebo once daily over 13 weeks.	
Reporting group title	GSK2881078 1.0 mg- Female Participants
Reporting group description:	
Post-menopausal female participants, 50 to 75 years of age, were administered orally two capsules of GSK2881078 of a unit dose strength 0.5 milligram (mg) once daily over 13 weeks.	
Reporting group title	Placebo- Male Participants
Reporting group description:	
Male participants, 50 to 75 years of age, were administered orally two capsules of GSK2881078 matching placebo once daily over 13 weeks.	
Reporting group title	GSK2881078 2.0 mg- Male Participants
Reporting group description:	
Male participants, 50 to 75 years of age, were administered orally two capsules of GSK2881078 of a unit dose strength 1.0 mg once daily over 13 weeks.	

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

End point title	Change from Baseline in systolic blood pressure (SBP) and diastolic blood pressure (DBP)[1]
End point description:	
SBP and DBP were measured in a seated position with a completely automated device. Baseline was defined as the latest pre-dose assessment with a non-missing value, including those from unscheduled visits. Change from Baseline was calculated as post-dose visit value minus the Baseline value. Safety Population comprised of all randomized participants who received at least one dose of study medication. This population was based on the treatment the participant received. Only those participants with data available at the specified data points were analyzed (represented by n=X in the category titles).	
End point type	Primary
End point timeframe:	
Baseline (Day 1, Pre-dose), Days 14, 28, 56 and 90	

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- Female Participants	GSK2881078 1.0 mg- Female Participants	Placebo- Male Participants	GSK2881078 2.0 mg- Male Participants
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	22[2]	23[3]	23[4]	24[5]
Units: Millimeters of mercury				
arithmetic mean (standard deviation)				
SBP,Day 14,n=22,23,23,24	3.0 (± 19.63)	2.1 (± 11.03)	-2.1 (± 9.33)	3.1 (± 11.65)
SBP,Day 28,n=22,20,23,24	3.7 (± 12.76)	-0.1 (± 12.82)	2.6 (± 14.39)	5.8 (± 9.49)
SBP,Day 56,n=21,19,20,21	3.3 (± 14.96)	7.8 (± 16.38)	-2.4 (± 17.68)	1.3 (± 9.12)
SBP,Day 90,n=21,18,18,20	1.0 (± 14.23)	7.6 (± 15.56)	-4.2 (± 18.52)	5.8 (± 18.61)
DBP,Day 14,n=22,23,23,24	1.9 (± 6.88)	1.1 (± 6.93)	-3.4 (± 6.20)	-0.4 (± 7.47)
DBP,Day 28,n=22,20,23,24	3.6 (± 7.08)	1.4 (± 7.58)	0.7 (± 7.90)	1.0 (± 5.36)

DBP,Day 56,n=21,19,20,21	2.1 (± 7.00)	2.9 (± 6.07)	-2.5 (± 10.38)	-1.6 (± 8.16)
DBP,Day 90,n=21,18,18,20	-1.0 (± 6.47)	2.9 (± 8.37)	-0.1 (± 12.98)	0.6 (± 6.95)

Notes:

[2] - Safety Population

[3] - Safety Population

[4] - Safety Population

[5] - Safety Population

Statistical analyses

No statistical analyses for this end point

Primary: Change from Baseline in heart rate

End point title	Change from Baseline in heart rate[6]

End point description:

Heart rate was measured in a seated position with a completely automated device. Baseline was defined as the latest pre-dose assessment with a non-missing value, including those from unscheduled visits. Change from Baseline was calculated as post-dose visit value minus the Baseline value. Only those participants with data available at the specified data points were analyzed (represented by n=X in the category titles).

End point type	Primary

End point timeframe:

Baseline (Day 1, Pre-dose), Days 14, 28, 56 and 90

Notes:

[6] - 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-Female Participants	GSK2881078 1.0 mg-Female Participants	Placebo- Male Participants	GSK2881078 2.0 mg- Male Participants
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	22[7]	23[8]	23[9]	24[10]
Units: Beats per minute				
arithmetic mean (standard deviation)				
Day 14,n=22,23,23,24	-0.7 (± 9.79)	3.3 (± 9.16)	1.7 (± 10.61)	-0.4 (± 6.60)
Day 28,n=22,20,23,24	2.2 (± 8.11)	2.1 (± 9.64)	4.6 (± 10.71)	-1.7 (± 10.71)
Day 56,n=21,19,20,21	0.2 (± 8.87)	-1.0 (± 8.81)	2.8 (± 7.17)	0.2 (± 6.36)
Day 90,n=21,18,18,20	1.1 (± 7.99)	2.3 (± 10.34)	7.4 (± 10.23)	-0.6 (± 8.17)

Notes:

[7] - Safety Population

[8] - Safety Population

[9] - Safety Population

[10] - Safety Population

Statistical analyses

No statistical analyses for this end point

Primary: Change from Baseline in PR Interval, QRS Duration, QT Interval, QT interval corrected for heart rate by Fridericia's formula (QTcF) and QT interval corrected for heart rate by Bazett's formula (QTcB)

End point title	Change from Baseline in PR Interval, QRS Duration, QT Interval, QT interval corrected for heart rate by Fridericia's

	formula (QTcF) and QT interval corrected for heart rate by Bazett's formula (QTcB)[11]

End point description:

Twelve-lead electrocardiograms (ECG) were obtained using an automated ECG machine to measure PR Interval, QRS Duration, QT Interval, QTcF Interval and QTcB Interval. Baseline was defined as the latest pre-dose assessment with a non-missing value, including those from unscheduled visits. Change from Baseline was calculated as post-dose visit value minus the Baseline value. Only those participants with data available at the specified data points were analyzed (represented by n=X in the category titles).

End point type	Primary

End point timeframe:

Baseline (Day 1, Pre-dose), Days 14, 28, 56 and 90

Notes:

[11] - 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- Female Participants	GSK2881078 1.0 mg- Female Participants	Placebo- Male Participants	GSK2881078 2.0 mg- Male Participants
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	22[12]	23[13]	23[14]	24[15]
Units: Milliseconds				
arithmetic mean (standard deviation)				
PR interval,Day 14,n=22,23,22,24	-1.303 (± 9.9261)	-0.377 (± 7.2588)	-2.455 (± 12.6556)	-2.875 (± 24.3370)
PR interval,,Day 28,n=22,20,22,24	-0.061 (± 7.9340)	-4.717 (± 19.3177)	-2.333 (± 17.5966)	4.139 (± 15.5796)
PR interval,,Day 56,n=21,19,20,21	1.302 (± 12.1220)	0.596 (± 6.5250)	0.483 (± 7.5436)	10.444 (± 27.5133)
PR interval,,Day 90,n=21,18,17,20	-0.270 (± 9.3111)	-6.167 (± 28.9117)	-3.373 (± 9.6845)	3.033 (± 20.7947)
QRS Duration,Day 14,n=22,23,23,24	4.364 (± 22.8107)	1.362 (± 10.4736)	-0.464 (± 7.4791)	1.167 (± 4.1772)
QRS Duration,Day 28,n=22,20,23,24	1.000 (± 7.7014)	6.200 (± 28.2707)	-1.478 (± 5.5047)	-0.542 (± 3.3547)
QRS Duration,Day 56,n=21,19,20,21	-0.095 (± 5.9639)	1.842 (± 5.4096)	-1.100 (± 4.9631)	-0.413 (± 4.6271)
QRS Duration,Day 90,n=21,18,18,20	-2.397 (± 14.1494)	-2.444 (± 4.5360)	1.333 (± 25.4163)	1.333 (± 6.3005)
QT Interval,Day 14,n=22,23,23,24	0.576 (± 19.8239)	-14.290 (± 17.7216)	-0.638 (± 22.5431)	-0.597 (± 15.5697)
QT Interval,Day 28,n=22,20,23,24	-1.333 (± 23.5300)	-16.133 (± 26.2775)	-4.203 (± 23.3733)	-1.750 (± 22.6539)
QT Interval,Day 56,n=21,19,20,21	-0.127 (± 13.5567)	-13.947 (± 18.3657)	-1.533 (± 20.5897)	-1.857 (± 14.6881)
QT Interval,Day 90,n=21,18,18,20	4.063 (± 16.9160)	-16.352 (± 20.7511)	-4.574 (± 17.1825)	-5.167 (± 17.7759)
QTcF Interval,Day 14,n=21,21,21,21	1.749 (± 11.7762)	-7.143 (± 9.2710)	-1.235 (± 11.3507)	-2.698 (± 9.7085)
QTcF Interval,Day 28,n=21,19,21,21	0.362 (± 15.7742)	-12.930 (± 11.7707)	-0.489 (± 10.5492)	-4.340 (± 12.8445)
QTcF Interval,Day 56,n=20,18,18,18	1.333 (± 8.5039)	-12.222 (± 10.2975)	1.093 (± 10.0462)	-3.357 (± 10.5127)
QTcF Interval,Day 90,n=20,17,18,17	3.600 (± 10.3526)	-12.627 (± 11.5776)	2.657 (± 12.2002)	-11.804 (± 11.7207)
QTcB Interval,Day 14,n=4,5,4,7	-4.333 (± 26.2100)	2.193 (± 12.5624)	12.917 (± 13.6582)	0.571 (± 11.0180)
QTcB Interval,Day 28,n=4,3,4,7	-1.167 (± 12.1549)	13.667 (± 24.7678)	-7.667 (± 8.8192)	-10.238 (± 11.6678)

QTcB Interval,Day 56,n=3,3,4,6	-13.556 (± 11.3741)	-7.667 (± 9.7125)	13.417 (± 8.0017)	-9.500 (± 7.2411)
QTcB Interval,Day 90,n=3,3,2,6	1.333 (± 15.9199)	-13.111 (± 3.0972)	32.000 (± 1.4142)	-10.278 (± 9.6088)

Notes:

[12] - Safety Population

[13] - Safety Population

[14] - Safety Population

[15] - Safety Population

Statistical analyses

No statistical analyses for this end point

Primary: Number of participants with grade increase post-Baseline relative to Baseline in hematology parameters

End point title	Number of participants with grade increase post-Baseline relative to Baseline in hematology parameters[16]

End point description:

Blood samples were collected for the analysis of following hematology parameters: hemoglobin (Hb), lymphocyte count (Lympho), neutrophil count (Neutro) and platelet count (PC). The laboratory parameters were graded according to National Cancer Institute – Common Terminology Criteria for Adverse Events (NCI-CTCAE) version 4.03. Grade 1: mild; Grade 2: moderate; Grade 3: severe or medically significant; Grade 4: life–threatening consequences. Baseline was defined as the latest pre-dose assessment with a non-missing value, including those from unscheduled visits. An increase is defined as an increase in CTCAE grade relative to Baseline grade. Only those participants with increase to grade 3 and increase to grade 4 are presented. Only those participants with data available at the specified data points were analyzed.

End point type	Primary

End point timeframe:

Baseline (Day 1, Pre-dose) and up to Day 132

Notes:

[16] - 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-Female Participants	GSK2881078 1.0 mg-Female Participants	Placebo- Male Participants	GSK2881078 2.0 mg- Male Participants
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	23[17]	22[18]	24[19]	25[20]
Units: Participants				
Hb, Anemia, increase to Grade 3	0	0	0	0
Hb, Anemia, increase to Grade 4	0	0	0	0
Hb, Hb increased, increase to Grade 3	0	0	0	0
Hb, Hb increased, increase to Grade 4	0	0	0	0
Lympho, Lymph count decreased, increase to Grade 3	0	0	0	0
Lympho, Lymph count decreased, increase to Grade 4	0	0	0	0
Lympho, Lymph count increased, increase to Grade 3	0	0	0	0
Lympho, Lymph count increased, increase to Grade 4	0	0	0	0
Neutro,Neutro count decreased,increase to Grade 3	0	0	0	0

Neutro,Neutro count decreased,increase to Grade 4	0	0	0	0
PC, PC decreased,increase to Grade 3	0	0	0	0
PC, PC decreased,increase to Grade 4	0	0	0	0
PC, PC increased,increase to Grade 3	0	0	0	0
PC, PC increased,increase to Grade 4	0	0	0	0

Notes:

[17] - Safety Population

[18] - Safety Population

[19] - Safety Population

[20] - Safety Population

Statistical analyses

No statistical analyses for this end point

Primary: Number of participants with grade increase post-Baseline relative to Baseline in clinical chemistry parameters

End point title	Number of participants with grade increase post-Baseline relative to Baseline in clinical chemistry parameters[21]

End point description:

Blood samples were collected for the analysis of following clinical chemistry parameters: alanine aminotransferase (ALT), alkaline phosphatase (ALP), aspartate aminotransferase (AST), bilirubin (Bil),calcium (Ca), cholesterol (Chol), creatinine (Creat), glucose(Gl), phosphate (Phos), potassium (Pot) and sodium (Sod). The laboratory parameters were graded according to NCI-CTCAE version 4.03. Grade 1: mild; Grade 2: moderate; Grade 3: severe or medically significant; Grade 4: life–threatening consequences. Baseline was defined as the latest pre-dose assessment with a non-missing value, including those from unscheduled visits. An increase is defined as an increase in CTCAE grade relative to Baseline grade. Values (Hyper and hypo) for Ca, Gl, Pot, Phos and Sod is presented. Only those participants with increase to grade 3 and increase to grade 4 are presented. Only those participants with data available at the specified data points were analyzed.

End point type	Primary

End point timeframe:

Baseline (Day 1, Pre-dose) and up to Day 132

Notes:

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

End point values	Placebo-Female Participants	GSK2881078 1.0 mg-Female Participants	Placebo- Male Participants	GSK2881078 2.0 mg- Male Participants
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	23[22]	22[23]	24[24]	25[25]
Units: Participants				
ALT, ALT increased, increase to Grade 3	0	1	0	1
ALT, ALT increased, increase to Grade 4	0	0	0	0
ALP, ALP increased, increase to Grade 3	0	0	0	0
ALP, ALP increased, increase to Grade 4	0	0	0	0
AST, AST increased, increase to Grade 3	0	0	0	0
AST, AST increased, increase to Grade 4	0	0	0	0
Bil, Blood Bil increased, increase to Grade 3	0	0	0	0
Bil, Blood Bil increased, increase to Grade 4	0	0	0	0
Ca, Hyper,increase to Grade 3	0	0	0	0

Ca, Hyper,increase to Grade 4	0	0	0	0
Ca, Hypo,increase to Grade 3	0	0	0	0
Ca, Hypo,increase to Grade 4	0	0	0	0
Chol, Chol high,increase to Grade 3	0	0	0	0
Chol, Chol high,increase to Grade 4	0	0	0	0
Creat, Creat increased,increase to Grade 3	0	0	0	0
Creat, Creat increased,increase to Grade 4	0	0	0	0
Gl, Hyper,increase to Grade 3	0	0	0	1
Gl, Hyper,increase to Grade 4	0	0	0	0
Gl, Hypo,increase to Grade 3	0	0	0	0
Gl, Hypo,increase to Grade 4	0	0	0	0
Phos, Hyper,increase to Grade 3	0	0	0	0
Phos, Hyper,increase to Grade 4	0	0	0	0
Phos, Hypo,increase to Grade 3	0	0	0	0
Phos, Hypo,increase to Grade 4	0	0	0	0
Pot, Hyper,increase to Grade 3	0	0	0	0
Pot, Hyper,increase to Grade 4	0	0	0	0
Pot, Hypo,increase to Grade 3	0	0	1	0
Pot, Hypo,increase to Grade 4	0	0	0	0
Sod, Hyper,increase to Grade 3	0	0	0	0
Sod, Hyper,increase to Grade 4	0	0	0	0
Sod, Hypo,increase to Grade 3	2	0	0	0
Sod, Hypo,increase to Grade 4	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

Primary: Change from Baseline in urinalysis parameter; Specific Gravity: Placebo-Female Participants

End point title	Change from Baseline in urinalysis parameter; Specific Gravity: Placebo-Female Participants[26][27]

End point description:

Urine samples were collected to analyze the urinalysis parameter: specific gravity. Urine specific gravity is a measure of the concentration of solutes in the urine and provides information on the kidney's ability to concentrate urine, indicated as ratio of urine density to water density. Baseline was defined as the latest pre-dose assessment with a non-missing value, including those from unscheduled visits. Change from Baseline was calculated as post-dose visit value minus the Baseline value. Only those participants with data available at the specified data points were analyzed (represented by n=X in the category titles). 99999 indicates that standard deviation could not be calculated as a single participant was analyzed.

End point type	Primary

End point timeframe:

Baseline (Day 1, Pre-dose), Days 28, 56 and 90

Notes:

[26] - 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.

[27] - 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	Placebo-Female Participants			
Subject group type	Reporting group			
Number of subjects analysed	21[28]			
Units: Ratio				
arithmetic mean (standard deviation)				
Day 28,n=1	0.0030 (± 99999)			
Day 56,n=1	0.0020 (± 99999)			
Day 90,n=21	-0.0006 (± 0.00612)			

Notes:

[28] - Safety Population

Statistical analyses

No statistical analyses for this end point

Primary: Change from Baseline in urinalysis parameter; Specific Gravity: GSK2881078 1.0 mg- Female Participants

End point title	Change from Baseline in urinalysis parameter; Specific Gravity: GSK2881078 1.0 mg- Female Participants[29][30]

End point description:

Urine samples were collected to analyze the urinalysis parameter: specific gravity. Urine specific gravity is a measure of the concentration of solutes in the urine and provides information on the kidney's ability to concentrate urine, indicated as ratio of urine density to water density. Baseline was defined as the latest pre-dose assessment with a non-missing value, including those from unscheduled visits. Change from Baseline was calculated as post-dose visit value minus the Baseline value. Only those participants with data available at the specified data points were analyzed (represented by n=X in the category titles). 99999 indicates that standard deviation could not be calculated as a single participant was analyzed.

End point type	Primary

End point timeframe:

Baseline (Day 1, Pre-dose), Days 14 and 90

Notes:

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

[30] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: This endpoint is only reporting on a subset of the arms that are contained in the baseline period.

End point values	GSK2881078 1.0 mg- Female Participants			
Subject group type	Reporting group			
Number of subjects analysed	18[31]			
Units: Ratio				
arithmetic mean (standard deviation)				
Day 14,n=1	0.000 (± 99999)			
Day 90,n=18	0.0049 (± 0.00711)			

Notes:

[31] - Safety Population

Statistical analyses

No statistical analyses for this end point

Primary: Change from Baseline in urinalysis parameter; Specific Gravity: Male Participants

End point title	Change from Baseline in urinalysis parameter; Specific Gravity: Male Participants[32][33]

End point description:

Urine samples were collected to analyze the urinalysis parameter: specific gravity. Urine specific gravity is a measure of the concentration of solutes in the urine and provides information on the kidney's ability to concentrate urine, indicated as ratio of urine density to water density. Baseline was defined as the latest pre-dose assessment with a non-missing value, including those from unscheduled visits. Change from Baseline was calculated as post-dose visit value minus the Baseline value. Only those participants with data available at the specified data points were analyzed (represented by n=X in the category titles). 99999 indicates that standard deviation could not be calculated as a single participant was analyzed.

End point type	Primary

End point timeframe:

Baseline (Day 1, Pre-dose), Days 28 and 90

Notes:

[32] - 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.

[33] - 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	Placebo- Male Participants	GSK2881078 2.0 mg- Male Participants		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	19[34]	20[35]		
Units: Ratio				
arithmetic mean (standard deviation)				
Day 28,n=1,1	-0.0080 (± 99999)	0.0040 (± 99999)		
Day 90,n=19,20	0.0017 (± 0.00870)	0.0018 (± 0.00610)		

Notes:

[34] - Safety Population

[35] - Safety Population

Statistical analyses

No statistical analyses for this end point

Primary: Change from Baseline in urinalysis parameter; potential of hydrogen (pH): Placebo- Female Participants

End point title	Change from Baseline in urinalysis parameter; potential of hydrogen (pH): Placebo- Female Participants[36][37]

End point description:

Urine samples were collected to analyze the urinalysis parameter: pH. Urine pH is an acid-base measurement. pH is measured on a numeric scale ranging from 0 to 14; values on the scale refer to the degree of alkalinity or acidity. A pH of 7 is neutral. A pH less than 7 is acidic, and a pH greater than 7 is basic. Normal urine has a slightly acidic pH (5.0 - 6.0). Baseline was defined as the latest pre-dose assessment with a non-missing value, including those from unscheduled visits. Change from Baseline was calculated as post-dose visit value minus the Baseline value. Only those participants with data available at the specified data points were analyzed (represented by n=X in the category titles). 99999 indicates that standard deviation could not be calculated as a single participant was analyzed.

End point type	Primary

End point timeframe:

Baseline (Day 1, Pre-dose), Days 28, 56 and 90

Notes:

[36] - 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.

[37] - 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	Placebo-Female Participants			
Subject group type	Reporting group			
Number of subjects analysed	21[38]			
Units: pH				
arithmetic mean (standard deviation)				
Day 28,n=1	0.0000 (± 99999)			
Day 56,n=1	-0.5000 (± 99999)			
Day 90,n=21	0.0000 (± 0.80623)			

Notes:

[38] - Safety Population

Statistical analyses

No statistical analyses for this end point

Primary: Change from Baseline in urinalysis parameter; pH: GSK2881078 1.0 mg- Female Participants

End point title	Change from Baseline in urinalysis parameter; pH: GSK2881078 1.0 mg- Female Participants[39][40]

End point description:

Urine samples were collected to analyze the urinalysis parameter: pH. Urine pH is an acid-base measurement. pH is measured on a numeric scale ranging from 0 to 14; values on the scale refer to the degree of alkalinity or acidity. A pH of 7 is neutral. A pH less than 7 is acidic, and a pH greater than 7 is basic. Normal urine has a slightly acidic pH (5.0 - 6.0). Baseline was defined as the latest pre-dose assessment with a non-missing value, including those from unscheduled visits. Change from Baseline was calculated as post-dose visit value minus the Baseline value. Only those participants with data available at the specified data points were analyzed (represented by n=X in the category titles). 99999 indicates that standard deviation could not be calculated as a single participant was analyzed.

End point type	Primary

End point timeframe:

Baseline (Day 1, Pre-dose), Days 14 and 90

Notes:

[39] - 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.

[40] - 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	GSK2881078 1.0 mg- Female Participants			
Subject group type	Reporting group			
Number of subjects analysed	18[41]			
Units: pH				
arithmetic mean (standard deviation)				
Day 14,n=1	1.0000 (± 99999)			
Day 90,n=18	-0.1111 (± 0.60768)			

Notes:

[41] - Safety Population

Statistical analyses

No statistical analyses for this end point

Primary: Change from Baseline in urinalysis parameter; pH: Male Participants

End point title	Change from Baseline in urinalysis parameter; pH: Male Participants[42][43]

End point description:

Urine samples were collected to analyze the urinalysis parameter: pH. Urine pH is an acid-base measurement. pH is measured on a numeric scale ranging from 0 to 14; values on the scale refer to the degree of alkalinity or acidity. A pH of 7 is neutral. A pH less than 7 is acidic, and a pH greater than 7 is basic. Normal urine has a slightly acidic pH (5.0 - 6.0). Baseline was defined as the latest pre-dose assessment with a non-missing value, including those from unscheduled visits. Change from Baseline was calculated as post-dose visit value minus the Baseline value. Only those participants with data available at the specified data points were analyzed (represented by n=X in the category titles). 99999 indicates that standard deviation could not be calculated as a single participant was analyzed.

End point type	Primary

End point timeframe:

Baseline (Day 1, Pre-dose), Days 28 and 90

Notes:

[42] - 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.

[43] - 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	Placebo- Male Participants	GSK2881078 2.0 mg- Male Participants		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	19[44]	20[45]		
Units: pH				
arithmetic mean (standard deviation)				
Day 28,n=1,1	1.0000 (± 99999)	0.5000 (± 99999)		
Day 90,n=19,20	-0.1579 (± 0.72749)	0.3000 (± 0.71451)		

Notes:

[44] - Safety Population

[45] - Safety Population

Statistical analyses

No statistical analyses for this end point

Primary: Number of participants with urinalysis dipstick results post-Baseline relative to Baseline

End point title	Number of participants with urinalysis dipstick results post-Baseline relative to Baseline[46]

End point description:

Urine samples were collected to analyze parameters including glucose, occult blood (OB) and protein levels by dipstick. The dipstick test gives results in a semi-quantitative manner, and results for urinalysis parameters can be read as increase to trace, increase to 1+ (low concentrations present), increase to 2+ (moderate concentrations present) and increase to 3+ (high concentrations present) indicating proportional concentrations in the urine sample. Baseline was defined as the latest pre-dose assessment with a non-missing value, including those from unscheduled visits. Data for worst-case post-Baseline relative to Baseline is presented. Only those participants with data available at the specified data points were analyzed.

End point type	Primary

End point timeframe:

Baseline (Day 1, Pre-dose) and up to Day 132

Notes:

[46] - 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-Female Participants	GSK2881078 1.0 mg-Female Participants	Placebo- Male Participants	GSK2881078 2.0 mg- Male Participants
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	23[47]	21[48]	23[49]	24[50]
Units: Participants				
Glucose: increase to trace	0	0	1	0
Glucose: increase to 1+	0	0	0	0
Glucose: increase to 2+	0	0	0	0
Glucose: increase to 3+	0	0	0	1
OB: increase to trace	1	0	1	1
OB: increase to 1+	1	1	1	0
OB: increase to 2+	1	2	0	0
OB: increase to 3+	0	0	0	1
Protein: increase to trace	2	2	3	6
Protein: increase to 1+	0	3	1	3
Protein: increase to 2+	0	1	0	1
Protein: increase to 3+	0	0	0	0

Notes:

[47] - Safety Population

[48] - Safety Population

[49] - Safety Population

[50] - Safety Population

Statistical analyses

No statistical analyses for this end point

Primary: Number of Participants with serious adverse events (SAEs) and non-serious adverse events

End point title	Number of Participants with serious adverse events (SAEs) and non-serious adverse events[51]

End point description:

An adverse event (AE) is any untoward medical occurrence in a clinical study participant, temporally associated with the use of a medicinal product, whether or not considered related to the medicinal product. SAE is defined as any untoward medical occurrence that; results in death, is life-threatening, requires hospitalization or prolongation of existing hospitalization, results in disability/incapacity, is a congenital anomaly/birth defect, other situations judged by physician, is associated with liver injury and impaired liver function. Number of participants who had SAEs and non-SAEs are presented.

End point type	Primary

End point timeframe:

Up to Day 132

Notes:

[51] - 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-Female Participants	GSK2881078 1.0 mg-Female Participants	Placebo- Male Participants	GSK2881078 2.0 mg- Male Participants
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	23[52]	24[53]	24[54]	25[55]
Units: Participants				
Non-SAEs	15	18	13	17

SAEs	1	2	2	0

Notes:

[52] - Safety Population

[53] - Safety Population

[54] - Safety Population

[55] - Safety Population

Statistical analyses

No statistical analyses for this end point

Primary: Percentage change from Baseline in maximum leg press strength following 1 repetition maximum (1-RM) at Day 28

End point title	Percentage change from Baseline in maximum leg press strength following 1 repetition maximum (1-RM) at Day 28

End point description:

Participants continued with a one set of 5 to 10 repetitions of lifting weights using 40 to 60% of estimated maximum, after warm up. Participants, then lifted progressively heavier weights in steps, with each step separated by rest period, until participant could not complete the lift. The last successfully completed lift is 1-RM. Baseline was defined as the latest pre-dose assessment with a non-missing value, including those from unscheduled visits. Percentage change from Baseline was calculated by 100*[(post-dose value minus Baseline value)/ Baseline value]. Adjusted means and standard error (SE) are presented. Analysis Population comprised of the participants in the 'All Participants (all randomized participants who received at least one dose of study medication)' Population having Baseline and at least one post-Baseline assessment of the treatment the participant was randomized to. Only those participants with data available at the specified data points were analyzed.

End point type	Primary

End point timeframe:

Baseline (Day 1, Pre-dose), Day 28

End point values	Placebo- Female Participants	GSK2881078 1.0 mg- Female Participants	Placebo- Male Participants	GSK2881078 2.0 mg- Male Participants
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	21[56]	20[57]	22[58]	23[59]
Units: Percentage change				
arithmetic mean (standard error)	4.82 (± 2.406)	9.34 (± 2.459)	1.55 (± 2.940)	9.35 (± 2.848)

Notes:

[56] - Analysis Population

[57] - Analysis Population

[58] - Analysis Population

[59] - Analysis Population

Statistical analyses

Statistical analysis title	Statistical Analysis 1

Statistical analysis description:

Analysis was performed by mixed model repeated measures including the covariates: treatment, Day, treatment* Day and Baseline leg press strength, with Day as the repeated factor.

Comparison groups	Placebo- Female Participants v GSK2881078 1.0 mg- Female Participants

Number of subjects included in analysis	41
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Mean difference (net)
Point estimate	4.53
Confidence interval	
level	90 %
sides	2-sided
lower limit	-1.3
upper limit	10.36

Statistical analysis title	Statistical Analysis 1

Statistical analysis description:

Analysis was performed by mixed model repeated measures including the covariates: treatment, Day, treatment* Day and Baseline leg press strength, with Day as the repeated factor.

Comparison groups	Placebo- Male Participants v GSK2881078 2.0 mg- Male Participants
Number of subjects included in analysis	45
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Mean difference (net)
Point estimate	7.8
Confidence interval	
level	90 %
sides	2-sided
lower limit	0.83
upper limit	14.76

Primary: Percentage change from Baseline in maximum leg press strength following 1 repetition maximum (1-RM) at Day 56

End point title	Percentage change from Baseline in maximum leg press strength following 1 repetition maximum (1-RM) at Day 56

End point description:

Lower extremity strength was measured as 1-RM on a leg press device. Participants continued with a one set of 5 to 10 repetitions of lifting weights using 40 to 60% of estimated maximum, after warm up. Participants, then lifted progressively heavier weights in steps, with each step separated by an appropriate rest period, until participant could not complete the lift. The last successfully completed lift was recorded as the 1-RM. Baseline was defined as the latest pre-dose assessment with a non-missing value, including those from unscheduled visits. Percentage change from Baseline was calculated by 100*[(post-dose value minus Baseline value)/ Baseline value]. Adjusted means and SE are presented. Only those participants with data available at the specified data points were analyzed.

End point type	Primary

End point timeframe:

Baseline (Day 1, Pre-dose), Day 56

End point values	Placebo- Female Participants	GSK2881078 1.0 mg- Female Participants	Placebo- Male Participants	GSK2881078 2.0 mg- Male Participants
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	20[60]	18[61]	21[62]	21[63]
Units: Percentage change				
arithmetic mean (standard error)	0.08 (± 2.787)	16.78 (± 2.925)	5.73 (± 3.921)	11.07 (± 3.922)

Notes:

[60] - Analysis Population

[61] - Analysis Population

[62] - Analysis Population

[63] - Analysis Population

Statistical analyses

Statistical analysis title	Statistical Analysis 1

Statistical analysis description:

Analysis was performed by mixed model repeated measures including the covariates: treatment, Day, treatment* Day and Baseline leg press strength, with Day as the repeated factor.

Comparison groups	Placebo- Female Participants v GSK2881078 1.0 mg- Female Participants
Number of subjects included in analysis	38
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Mean difference (net)
Point estimate	16.71
Confidence interval	
level	90 %
sides	2-sided
lower limit	9.86
upper limit	23.56

Statistical analysis title	Statistical Analysis 1

Statistical analysis description:

Analysis was performed by mixed model repeated measures including the covariates: treatment, Day, treatment* Day and Baseline leg press strength, with Day as the repeated factor.

Comparison groups	Placebo- Male Participants v GSK2881078 2.0 mg- Male Participants
Number of subjects included in analysis	42
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Mean difference (net)
Point estimate	5.35
Confidence interval	
level	90 %
sides	2-sided
lower limit	-4.09
upper limit	14.78

Primary: Percentage change from Baseline in maximum leg press strength following 1 repetition maximum (1-RM) at Day 90

End point title	Percentage change from Baseline in maximum leg press strength following 1 repetition maximum (1-RM) at Day 90

End point description:

Lower extremity strength was measured as 1-RM on a leg press device. Participants continued with a one set of 5 to 10 repetitions of lifting weights using 40 to 60% of estimated maximum, after warm up. Participants, then lifted progressively heavier weights in steps, with each step separated by an appropriate rest period, until participant could not complete the lift. The last successfully completed lift was recorded as the 1-RM. Baseline was defined as the latest pre-dose assessment with a non-missing value, including those from unscheduled visits. Percentage change from Baseline was calculated by 100*[(post-dose value minus Baseline value)/ Baseline value]. Adjusted means and SE are presented. Only those participants with data available at the specified data points were analyzed.

End point type	Primary

End point timeframe:

Baseline (Day 1, Pre-dose), Day 90

End point values	Placebo- Female Participants	GSK2881078 1.0 mg- Female Participants	Placebo- Male Participants	GSK2881078 2.0 mg- Male Participants
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	19[64]	18[65]	18[66]	20[67]
Units: Percentage change				
arithmetic mean (standard error)	12.76 (± 4.061)	17.93 (± 4.179)	7.15 (± 2.759)	14.17 (± 2.632)

Notes:

[64] - Analysis Population

[65] - Analysis Population

[66] - Analysis Population

[67] - Analysis Population

Statistical analyses

Statistical analysis title	Statistical Analysis 1

Statistical analysis description:

Analysis was performed by mixed model repeated measures including the covariates: treatment, Day, treatment* Day and Baseline leg press strength, with Day as the repeated factor.

Comparison groups	Placebo- Female Participants v GSK2881078 1.0 mg- Female Participants
Number of subjects included in analysis	37
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Mean difference (net)
Point estimate	5.17
Confidence interval	
level	90 %
sides	2-sided
lower limit	-4.67
upper limit	15.01

Statistical analysis title	Statistical Analysis 1

Statistical analysis description:

Analysis was performed by mixed model repeated measures including the covariates: treatment, Day, treatment* Day and Baseline leg press strength, with Day as the repeated factor.

Comparison groups	Placebo- Male Participants v GSK2881078 2.0 mg- Male Participants
Number of subjects included in analysis	38
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Mean difference (net)
Point estimate	7.02
Confidence interval	
level	90 %
sides	2-sided
lower limit	0.46
upper limit	13.58

Primary: Change from Baseline in maximum leg press strength following 1 repetition maximum (1-RM) at Day 28

End point title	Change from Baseline in maximum leg press strength following 1 repetition maximum (1-RM) at Day 28

End point description:

Lower extremity strength was measured as 1-RM on a leg press device. Participants continued with a one set of 5 to 10 repetitions of lifting weights using 40 to 60% of estimated maximum, after warm up. Participants, then lifted progressively heavier weights in steps, with each step separated by an appropriate rest period, until participant could not complete the lift. The last successfully completed lift was recorded as the 1-RM. Baseline was defined as the latest pre-dose assessment with a non-missing value, including those from unscheduled visits. Change from Baseline was calculated as post-dose visit value minus the Baseline value. Adjusted means and SE are presented. Only those participants with data available at the specified data points were analyzed.

End point type	Primary

End point timeframe:

Baseline (Day 1, Pre-dose), Day 28

End point values	Placebo-Female Participants	GSK2881078 1.0 mg-Female Participants	Placebo- Male Participants	GSK2881078 2.0 mg- Male Participants
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	21[68]	20[69]	22[70]	23[71]
Units: Kilograms				
arithmetic mean (standard error)	4.2 (± 3.01)	10.0 (± 3.08)	3.0 (± 5.06)	16.5 (± 4.90)

Notes:

[68] - Analysis Population

[69] - Analysis Population

[70] - Analysis Population

[71] - Analysis Population

Statistical analyses

Statistical analysis title	Statistical Analysis 1
Statistical analysis description:	
Analysis was performed by mixed model repeated measures including the covariates: treatment, Day, treatment* Day and Baseline leg press strength, with Day as the repeated factor.	
Comparison groups	Placebo- Female Participants v GSK2881078 1.0 mg- Female Participants
Number of subjects included in analysis	41
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Mean difference (net)
Point estimate	5.9
Confidence interval	
level	90 %
sides	2-sided
lower limit	-1.4
upper limit	13.2

Statistical analysis title	Statistical Analysis 1
Statistical analysis description:	
Analysis was performed by mixed model repeated measures including the covariates: treatment, Day, treatment* Day and Baseline leg press strength, with Day as the repeated factor.	
Comparison groups	Placebo- Male Participants v GSK2881078 2.0 mg- Male Participants
Number of subjects included in analysis	45
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Mean difference (net)
Point estimate	13.5
Confidence interval	
level	90 %
sides	2-sided
lower limit	1.6
upper limit	25.5

Primary: Change from Baseline in maximum leg press strength following 1 repetition maximum (1-RM) at Day 56

End point title	Change from Baseline in maximum leg press strength following 1 repetition maximum (1-RM) at Day 56

End point description:

Lower extremity strength was measured as 1-RM on a leg press device. Participants continued with a

one set of 5 to 10 repetitions of lifting weights using 40 to 60% of estimated maximum, after warm up. Participants, then lifted progressively heavier weights in steps, with each step separated by an appropriate rest period, until participant could not complete the lift. The last successfully completed lift was recorded as the 1-RM. Baseline was defined as the latest pre-dose assessment with a non-missing value, including those from unscheduled visits. Change from Baseline was calculated as post-dose visit value minus the Baseline value. Adjusted means and SE are presented. Only those participants with data available at the specified data points were analyzed.

End point type	Primary

End point timeframe:

Baseline (Day 1, Pre-dose), Day 56

End point values	Placebo- Female Participants	GSK2881078 1.0 mg- Female Participants	Placebo- Male Participants	GSK2881078 2.0 mg- Male Participants
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	20[72]	18[73]	21[74]	21[75]
Units: Kilograms				
arithmetic mean (standard error)	0.6 (± 4.29)	21.3 (± 4.50)	8.3 (± 7.69)	15.7 (± 7.69)

Notes:

[72] - Analysis Population

[73] - Analysis Population

[74] - Analysis Population

[75] - Analysis Population

Statistical analyses

Statistical analysis title	Statistical Analysis 1

Statistical analysis description:

Analysis was performed by mixed model repeated measures including the covariates: treatment, Day, treatment* Day and Baseline leg press strength, with Day as the repeated factor.

Comparison groups	Placebo- Female Participants v GSK2881078 1.0 mg- Female Participants
Number of subjects included in analysis	38
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Mean difference (net)
Point estimate	20.7
Confidence interval	
level	90 %
sides	2-sided
lower limit	10.1
upper limit	31.2

Statistical analysis title	Statistical Analysis 1

Statistical analysis description:

Analysis was performed by mixed model repeated measures including the covariates: treatment, Day, treatment* Day and Baseline leg press strength, with Day as the repeated factor.

Comparison groups	Placebo- Male Participants v GSK2881078 2.0 mg- Male Participants

Number of subjects included in analysis	42
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Mean difference (net)
Point estimate	7.3
Confidence interval	
level	90 %
sides	2-sided
lower limit	-11.1
upper limit	25.8

Primary: Change from Baseline in maximum leg press strength following 1 repetition maximum (1-RM) at Day 90

End point title	Change from Baseline in maximum leg press strength following 1 repetition maximum (1-RM) at Day 90

End point description:

Lower extremity strength was measured as 1-RM on a leg press device. Participants continued with a one set of 5 to 10 repetitions of lifting weights using 40 to 60% of estimated maximum, after warm up. Participants, then lifted progressively heavier weights in steps, with each step separated by an appropriate rest period, until participant could not complete the lift. The last successfully completed lift was recorded as the 1-RM. Baseline was defined as the latest pre-dose assessment with a non-missing value, including those from unscheduled visits. Change from Baseline was calculated as post-dose visit value minus the Baseline value. Adjusted means and SE are presented. Only those participants with data available at the specified data points were analyzed.

End point type	Primary

End point timeframe:

Baseline (Day 1, Pre-dose), Day 90

End point values	Placebo- Female Participants	GSK2881078 1.0 mg- Female Participants	Placebo- Male Participants	GSK2881078 2.0 mg- Male Participants
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	19[76]	18[77]	18[78]	20[79]
Units: Kilograms				
arithmetic mean (standard error)	12.3 (± 4.31)	20.3 (± 4.45)	14.2 (± 5.17)	26.0 (± 4.91)

Notes:

[76] - Analysis Population

[77] - Analysis Population

[78] - Analysis Population

[79] - Analysis Population

Statistical analyses

Statistical analysis title	Statistical Analysis 1

Statistical analysis description:

Analysis was performed by mixed model repeated measures including the covariates: treatment, Day, treatment* Day and Baseline leg press strength, with Day as the repeated factor.

Comparison groups	Placebo- Female Participants v GSK2881078 1.0 mg- Female Participants

Number of subjects included in analysis	37
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Mean difference (net)
Point estimate	8
Confidence interval	
level	90 %
sides	2-sided
lower limit	-2.5
upper limit	18.4

Statistical analysis title	Statistical Analysis 1

Statistical analysis description:

Analysis was performed by mixed model repeated measures including the covariates: treatment, Day, treatment* Day and Baseline leg press strength, with Day as the repeated factor.

Comparison groups	Placebo- Male Participants v GSK2881078 2.0 mg- Male Participants
Number of subjects included in analysis	38
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Mean difference (net)
Point estimate	11.8
Confidence interval	
level	90 %
sides	2-sided
lower limit	-0.5
upper limit	24

Secondary: Change from Baseline in appendicular lean mass as assessed by dual-energy X-ray absorptiometry (DXA) at Day 28

End point title	Change from Baseline in appendicular lean mass as assessed by dual-energy X-ray absorptiometry (DXA) at Day 28

End point description:

Participants were asked to lie on a padded platform while a mechanical arm passed over their body. Appendicular lean mass was calculated from the regional lean mass measurements of the arms and legs using DXA. Day 1 (Pre-dose) was considered as a Baseline. Analysis was performed using mixed model repeated measures. Change from Baseline was calculated as post-dose visit value minus the Baseline value. Adjusted means and SE are presented. Only those participants with data available at the specified data points were analyzed.

End point type	Secondary

End point timeframe:

Baseline (Day 1, Pre-dose), Day 28

End point values	Placebo- Female Participants	GSK2881078 1.0 mg- Female Participants	Placebo- Male Participants	GSK2881078 2.0 mg- Male Participants
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	21[80]	19[81]	20[82]	22[83]
Units: Kilograms				
arithmetic mean (standard error)	-0.240 (± 0.0974)	0.642 (± 0.1023)	0.055 (± 0.1920)	0.346 (± 0.1831)

Notes:

[80] - Analysis Population

[81] - Analysis Population

[82] - Analysis Population

[83] - Analysis Population

Statistical analyses

Statistical analysis title	Statistical Analysis 1

Statistical analysis description:

Analysis was performed by mixed model repeated measures including the covariates: treatment, Day, treatment* Day and Baseline appendicular lean mass, with Day as the repeated factor.

Comparison groups	Placebo- Female Participants v GSK2881078 1.0 mg- Female Participants
Number of subjects included in analysis	40
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Mean difference (net)
Point estimate	0.882
Confidence interval	
level	90 %
sides	2-sided
lower limit	0.643
upper limit	1.121

Statistical analysis title	Statistical Analysis 1

Statistical analysis description:

Analysis was performed by mixed model repeated measures including the covariates: treatment, Day, treatment* Day and Baseline appendicular lean mass, with Day as the repeated factor.

Comparison groups	Placebo- Male Participants v GSK2881078 2.0 mg- Male Participants
Number of subjects included in analysis	42
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Mean difference (net)
Point estimate	0.291
Confidence interval	
level	90 %
sides	2-sided
lower limit	-0.156
upper limit	0.738

Secondary: Change from Baseline in appendicular lean mass as assessed by dual-energy X-ray absorptiometry (DXA) at Day 56

End point title	Change from Baseline in appendicular lean mass as assessed by dual-energy X-ray absorptiometry (DXA) at Day 56

End point description:

Participants were asked to lie on a padded platform while a mechanical arm passed over their body. Appendicular lean mass was calculated from the regional lean mass measurements of the arms and legs using DXA. Day 1 (Pre-dose) was considered as a Baseline. Analysis was performed using mixed model repeated measures. Change from Baseline was calculated as post-dose visit value minus the Baseline value. Adjusted means and SE are presented. Only those participants with data available at the specified data points were analyzed.

End point type	Secondary

End point timeframe:

Baseline (Day 1, Pre-dose), Day 56

End point values	Placebo- Female Participants	GSK2881078 1.0 mg- Female Participants	Placebo- Male Participants	GSK2881078 2.0 mg- Male Participants
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	21[84]	17[85]	17[86]	18[87]
Units: Kilograms				
arithmetic mean (standard error)	-0.134 (± 0.1410)	0.848 (± 0.1540)	-0.464 (± 0.1887)	0.663 (± 0.1829)

Notes:

[84] - Analysis Population

[85] - Analysis Population

[86] - Analysis Population

[87] - Analysis Population

Statistical analyses

Statistical analysis title	Statistical Analysis 1

Statistical analysis description:

Analysis was performed by mixed model repeated measures including the covariates: treatment, Day, treatment* Day and Baseline appendicular lean mass, with Day as the repeated factor.

Comparison groups	Placebo- Female Participants v GSK2881078 1.0 mg- Female Participants
Number of subjects included in analysis	38
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Mean difference (net)
Point estimate	0.982
Confidence interval	
level	90 %
sides	2-sided
lower limit	0.629
upper limit	1.334

Statistical analysis title	Statistical Analysis 1
Statistical analysis description:	
Analysis was performed by mixed model repeated measures including the covariates: treatment, Day, treatment* Day and Baseline appendicular lean mass, with Day as the repeated factor.	
Comparison groups	Placebo- Male Participants v GSK2881078 2.0 mg- Male Participants
Number of subjects included in analysis	35
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Mean difference (net)
Point estimate	1.127
Confidence interval	
level	90 %
sides	2-sided
lower limit	0.682
upper limit	1.571

Secondary: Change from Baseline in appendicular lean mass as assessed by dual-energy X-ray absorptiometry (DXA) at Day 90

End point title	Change from Baseline in appendicular lean mass as assessed by dual-energy X-ray absorptiometry (DXA) at Day 90
End point description:	
Participants were asked to lie on a padded platform while a mechanical arm passed over their body. Appendicular lean mass was calculated from the regional lean mass measurements of the arms and legs using DXA. Day 1 (Pre-dose) was considered as a Baseline. Analysis was performed using mixed model repeated measures. Change from Baseline was calculated as post-dose visit value minus the Baseline value. Adjusted means and SE are presented. Only those participants with data available at the specified data points were analyzed.	
End point type	Secondary
End point timeframe:	
Baseline (Day 1, Pre-dose), Day 90	

End point values	Placebo-Female Participants	GSK2881078 1.0 mg-Female Participants	Placebo- Male Participants	GSK2881078 2.0 mg- Male Participants
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	21[88]	17[89]	15[90]	18[91]
Units: Kilograms				
arithmetic mean (standard error)	-0.434 (± 0.1657)	0.946 (± 0.1818)	-0.225 (± 0.2306)	0.899 (± 0.2117)

Notes:

[88] - Analysis Population

[89] - Analysis Population

[90] - Analysis Population

Statistical analyses

Statistical analysis title	Statistical Analysis 1
Statistical analysis description:	
Analysis was performed by mixed model repeated measures including the covariates: treatment, Day, treatment* Day and Baseline appendicular lean mass, with Day as the repeated factor.	
Comparison groups	Placebo- Male Participants v GSK2881078 2.0 mg- Male Participants
Number of subjects included in analysis	33
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Mean difference (net)
Point estimate	1.124
Confidence interval	
level	90 %
sides	2-sided
lower limit	0.594
upper limit	1.654

Statistical analysis title	Statistical Analysis 1
Statistical analysis description:	
Analysis was performed by mixed model repeated measures including the covariates: treatment, Day, treatment* Day and Baseline appendicular lean mass, with Day as the repeated factor.	
Comparison groups	Placebo- Female Participants v GSK2881078 1.0 mg- Female Participants
Number of subjects included in analysis	38
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Mean difference (net)
Point estimate	1.38
Confidence interval	
level	90 %
sides	2-sided
lower limit	0.964
upper limit	1.795

Secondary: Change from Baseline in total lean mass as assessed by dual-energy X-ray absorptiometry (DXA) at Day 28

End point title	Change from Baseline in total lean mass as assessed by dual-energy X-ray absorptiometry (DXA) at Day 28

End point description:

Participants were asked to lie on a padded platform while a mechanical arm passed over their body.

Total lean mass was measured using DXA. Day 1 (Pre-dose) was considered as a Baseline. Analysis was performed using mixed model repeated measures. Change from Baseline was calculated as post-dose visit value minus the Baseline value. Adjusted means and SE are presented. Only those participants with data available at the specified data points were analyzed.

End point type	Secondary

End point timeframe:

Baseline (Day 1, Pre-dose), Day 28

End point values	Placebo- Female Participants	GSK2881078 1.0 mg- Female Participants	Placebo- Male Participants	GSK2881078 2.0 mg- Male Participants
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	21[92]	19[93]	20[94]	22[95]
Units: Kilograms				
arithmetic mean (standard error)	-0.017 (± 0.2004)	1.150 (± 0.2106)	0.075 (± 0.3004)	0.998 (± 0.2869)

Notes:

[92] - Analysis Population

[93] - Analysis Population

[94] - Analysis Population

[95] - Analysis Population

Statistical analyses

Statistical analysis title	Statistical Analysis 1

Statistical analysis description:

Analysis was performed by mixed model repeated measures including the covariates: treatment, Day, treatment* Day and Baseline total lean mass, with Day as the repeated factor.

Comparison groups	Placebo- Male Participants v GSK2881078 2.0 mg- Male Participants
Number of subjects included in analysis	42
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Mean difference (net)
Point estimate	0.923
Confidence interval	
level	90 %
sides	2-sided
lower limit	0.222
upper limit	1.623

Statistical analysis title	Statistical Analysis 1

Statistical analysis description:

Analysis was performed by mixed model repeated measures including the covariates: treatment, Day, treatment* Day and Baseline total lean mass, with Day as the repeated factor.

Comparison groups	Placebo- Female Participants v GSK2881078 1.0 mg- Female Participants

Number of subjects included in analysis	40
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Mean difference (net)
Point estimate	1.167
Confidence interval	
level	90 %
sides	2-sided
lower limit	0.677
upper limit	1.658

Secondary: Change from Baseline in total lean mass as assessed by dual-energy X-ray absorptiometry (DXA) at Day 56

End point title	Change from Baseline in total lean mass as assessed by dual-energy X-ray absorptiometry (DXA) at Day 56

End point description:

Participants were asked to lie on a padded platform while a mechanical arm passed over their body. Total lean mass was measured using DXA. Day 1 (Pre-dose) was considered as a Baseline. Analysis was performed using mixed model repeated measures. Change from Baseline was calculated as post-dose visit value minus the Baseline value. Adjusted means and SE are presented. Only those participants with data available at the specified data points were analyzed.

End point type	Secondary

End point timeframe:

Baseline (Day 1, Pre-dose), Day 56

End point values	Placebo- Female Participants	GSK2881078 1.0 mg- Female Participants	Placebo- Male Participants	GSK2881078 2.0 mg- Male Participants
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	21[96]	17[97]	17[98]	18[99]
Units: Kilograms				
arithmetic mean (standard error)	-0.564 (± 0.2372)	1.522 (± 0.2587)	-0.373 (± 0.3820)	1.327 (± 0.3700)

Notes:

[96] - Analysis Population

[97] - Analysis Population

[98] - Analysis Population

[99] - Analysis Population

Statistical analyses

Statistical analysis title	Statistical Analysis 1

Statistical analysis description:

Analysis was performed by mixed model repeated measures including the covariates: treatment, Day, treatment* Day and Baseline total lean mass, with Day as the repeated factor.

Comparison groups	Placebo- Female Participants v GSK2881078 1.0 mg- Female Participants

Number of subjects included in analysis	38
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Mean difference (net)
Point estimate	2.085
Confidence interval	
level	90 %
sides	2-sided
lower limit	1.493
upper limit	2.678

Statistical analysis title	Statistical Analysis 1

Statistical analysis description:

Analysis was performed by mixed model repeated measures including the covariates: treatment, Day, treatment* Day and Baseline total lean mass, with Day as the repeated factor.

Comparison groups	Placebo- Male Participants v GSK2881078 2.0 mg- Male Participants
Number of subjects included in analysis	35
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Mean difference (net)
Point estimate	1.7
Confidence interval	
level	90 %
sides	2-sided
lower limit	0.801
upper limit	2.6

Secondary: Change from Baseline in total lean mass as assessed by dual-energy X-ray absorptiometry (DXA) at Day 90

End point title	Change from Baseline in total lean mass as assessed by dual-energy X-ray absorptiometry (DXA) at Day 90

End point description:

Participants were asked to lie on a padded platform while a mechanical arm passed over their body. Total lean mass was measured using DXA. Day 1 (Pre-dose) was considered as a Baseline. Analysis was performed using mixed model repeated measures. Change from Baseline was calculated as post-dose visit value minus the Baseline value. Adjusted means and SE are presented. Only those participants with data available at the specified data points were analyzed.

End point type	Secondary

End point timeframe:

Baseline (Day 1, Pre-dose), Day 90

End point values	Placebo- Female Participants	GSK2881078 1.0 mg- Female Participants	Placebo- Male Participants	GSK2881078 2.0 mg- Male Participants
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	21[100]	17[101]	15[102]	18[103]
Units: Kilograms				
arithmetic mean (standard error)	-0.531 (± 0.3349)	1.577 (± 0.3666)	-0.424 (± 0.5056)	1.689 (± 0.4666)

Notes:

[100] - Analysis Population

[101] - Analysis Population

[102] - Analysis Population

[103] - Analysis Population

Statistical analyses

Statistical analysis title	Statistical Analysis 1

Statistical analysis description:

Analysis was performed by mixed model repeated measures including the covariates: treatment, Day, treatment* Day and Baseline total lean mass, with Day as the repeated factor.

Comparison groups	Placebo- Male Participants v GSK2881078 2.0 mg- Male Participants
Number of subjects included in analysis	33
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Mean difference (net)
Point estimate	2.113
Confidence interval	
level	90 %
sides	2-sided
lower limit	0.949
upper limit	3.277

Statistical analysis title	Statistical Analysis 1

Statistical analysis description:

Analysis was performed by mixed model repeated measures including the covariates: treatment, Day, treatment* Day and Baseline total lean mass, with Day as the repeated factor.

Comparison groups	Placebo- Female Participants v GSK2881078 1.0 mg- Female Participants
Number of subjects included in analysis	38
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Mean difference (net)
Point estimate	2.108
Confidence interval	
level	90 %
sides	2-sided
lower limit	1.271
upper limit	2.945

Secondary: Change from Baseline in total Short Physical Performance Battery (SPPB) score at Day 28

End point title	Change from Baseline in total Short Physical Performance Battery (SPPB) score at Day 28

End point description:

Participants were assessed for balance, time for chair rise and gait speed. These are the three components of SPPB. Each component was scored from 0 to 4. The total SPPB score was calculated by taking sum of scores of all 3 components, which ranged from 0 (worst performance) to 12 (best performance). Higher scores indicated better performance. Scores 10 to 12 indicated 'fit/normal' and scores <=7 indicated frail participant. Baseline was defined as the latest pre-dose assessment with a non-missing value, including those from unscheduled visits. Change from Baseline was calculated as post-dose visit value minus the Baseline value. Adjusted means and SE are presented. Only those participants with data available at the specified data points were analyzed.

End point type	Secondary

End point timeframe:

Baseline (Day 1, Pre-dose), Day 28

End point values	Placebo- Female Participants	GSK2881078 1.0 mg- Female Participants	Placebo- Male Participants	GSK2881078 2.0 mg- Male Participants
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	21[104]	20[105]	22[106]	23[107]
Units: Scores on a scale				
arithmetic mean (standard error)	0.3 (± 0.25)	0.4 (± 0.26)	0.2 (± 0.19)	0.3 (± 0.18)

Notes:

[104] - Analysis Population

[105] - Analysis Population

[106] - Analysis Population

[107] - Analysis Population

Statistical analyses

Statistical analysis title	Statistical Analysis 1

Statistical analysis description:

Analysis was performed by mixed model repeated measures including the covariates: treatment, Day, treatment* Day and Baseline SPPB total score, with Day as the repeated factor.

Comparison groups	Placebo- Female Participants v GSK2881078 1.0 mg- Female Participants
Number of subjects included in analysis	41
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Mean difference (net)
Point estimate	0
Confidence interval	
level	90 %
sides	2-sided
lower limit	-0.6
upper limit	0.6

Statistical analysis title	Statistical Analysis 1
Statistical analysis description:	
Analysis was performed by mixed model repeated measures including the covariates: treatment, Day, treatment* Day and Baseline SPPB total score, with Day as the repeated factor.	
Comparison groups	Placebo- Male Participants v GSK2881078 2.0 mg- Male Participants
Number of subjects included in analysis	45
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Mean difference (net)
Point estimate	0
Confidence interval	
level	90 %
sides	2-sided
lower limit	-0.4
upper limit	0.5

Secondary: Change from Baseline in total Short Physical Performance Battery (SPPB) score at Day 56

End point title	Change from Baseline in total Short Physical Performance Battery (SPPB) score at Day 56
End point description:	
Participants were assessed for balance, time for chair rise and gait speed. These are the three components of SPPB. Each component was scored from 0 to 4. The total SPPB score was calculated by taking sum of scores of all 3 components, which ranged from 0 (worst performance) to 12 (best performance). Higher scores indicated better performance. Scores 10 to 12 indicated 'fit/normal' and scores <=7 indicated frail participant. Baseline was defined as the latest pre-dose assessment with a non-missing value, including those from unscheduled visits. Change from Baseline was calculated as post-dose visit value minus the Baseline value. Adjusted means and SE are presented. Only those participants with data available at the specified data points were analyzed.	
End point type	Secondary
End point timeframe:	
Baseline (Day 1, Pre-dose), Day 56	

End point values	Placebo-Female Participants	GSK2881078 1.0 mg-Female Participants	Placebo- Male Participants	GSK2881078 2.0 mg- Male Participants
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	21[108]	19[109]	21[110]	21[111]
Units: Scores on a scale				
arithmetic mean (standard error)	0.4 (± 0.24)	0.4 (± 0.25)	0.1 (± 0.24)	0.4 (± 0.24)

Notes:

[108] - Analysis Population

[109] - Analysis Population

[110] - Analysis Population

[111] - Analysis Population

Statistical analyses

Statistical analysis title	Statistical Analysis 1
Statistical analysis description:	
Analysis was performed by mixed model repeated measures including the covariates: treatment, Day, treatment* Day and Baseline SPPB total score, with Day as the repeated factor.	
Comparison groups	Placebo- Female Participants v GSK2881078 1.0 mg- Female Participants
Number of subjects included in analysis	40
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Mean difference (net)
Point estimate	0
Confidence interval	
level	90 %
sides	2-sided
lower limit	-0.6
upper limit	0.6

Statistical analysis title	Statistical Analysis 1
Statistical analysis description:	
Analysis was performed by mixed model repeated measures including the covariates: treatment, Day, treatment* Day and Baseline SPPB total score, with Day as the repeated factor.	
Comparison groups	Placebo- Male Participants v GSK2881078 2.0 mg- Male Participants
Number of subjects included in analysis	42
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Mean difference (net)
Point estimate	0.3
Confidence interval	
level	90 %
sides	2-sided
lower limit	-0.2
upper limit	0.9

Secondary: Change from Baseline in total Short Physical Performance Battery (SPPB) score at Day 90

End point title	Change from Baseline in total Short Physical Performance Battery (SPPB) score at Day 90

End point description:

Participants were assessed for balance, time for chair rise and gait speed. These are the three

components of SPPB. Each component was scored from 0 to 4. The total SPPB score was calculated by taking sum of scores of all 3 components, which ranged from 0 (worst performance) to 12 (best performance). Higher scores indicated better performance. Scores 10 to 12 indicated 'fit/normal' and scores <=7 indicated frail participant. Baseline was defined as the latest pre-dose assessment with a non-missing value, including those from unscheduled visits. Change from Baseline was calculated as post-dose visit value minus the Baseline value. Adjusted means and SE are presented. Only those participants with data available at the specified data points were analyzed.

End point type	Secondary

End point timeframe:

Baseline (Day 1, Pre-dose), Day 90

End point values	Placebo- Female Participants	GSK2881078 1.0 mg- Female Participants	Placebo- Male Participants	GSK2881078 2.0 mg- Male Participants
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	21[112]	18[113]	18[114]	20[115]
Units: Scores on a scale				
arithmetic mean (standard error)	0.3 (± 0.26)	0.5 (± 0.28)	0.4 (± 0.23)	0.5 (± 0.22)

Notes:

[112] - Analysis Population

[113] - Analysis Population

[114] - Analysis Population

[115] - Analysis Population

Statistical analyses

Statistical analysis title	Statistical Analysis 1

Statistical analysis description:

Analysis was performed by mixed model repeated measures including the covariates: treatment, Day, treatment* Day and Baseline SPPB total score, with Day as the repeated factor.

Comparison groups	Placebo- Female Participants v GSK2881078 1.0 mg- Female Participants
Number of subjects included in analysis	39
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Mean difference (net)
Point estimate	0.2
Confidence interval	
level	90 %
sides	2-sided
lower limit	-0.4
upper limit	0.9

Statistical analysis title	Statistical Analysis 1

Statistical analysis description:

Analysis was performed by mixed model repeated measures including the covariates: treatment, Day, treatment* Day and Baseline SPPB total score, with Day as the repeated factor.

Comparison groups	Placebo- Male Participants v GSK2881078 2.0 mg- Male Participants

Number of subjects included in analysis	38
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Mean difference (net)
Point estimate	0.1
Confidence interval	
level	90 %
sides	2-sided
lower limit	-0.5
upper limit	0.6

Secondary: Change from Baseline in 'time for chair rise' as assessed by SPPB at Day 28

End point title	Change from Baseline in 'time for chair rise' as assessed by SPPB at Day 28

End point description:

'Time for chair rise' is one of the 3 components of SPPB, which was assessed by repeated chair stand test and calculated as time for five successful chair stands measured in seconds. Baseline was defined as the latest pre-dose assessment with a non-missing value, including those from unscheduled visits. Analysis was performed using mixed model repeated measures. Change from Baseline was calculated as post-dose visit value minus the Baseline value. Adjusted means and SE are presented. Only those participants with data available at the specified data points were analyzed.

End point type	Secondary

End point timeframe:

Baseline (Day 1, Pre-dose), Day 28

End point values	Placebo- Female Participants	GSK2881078 1.0 mg- Female Participants	Placebo- Male Participants	GSK2881078 2.0 mg- Male Participants
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	21[116]	20[117]	22[118]	23[119]
Units: Seconds				
arithmetic mean (standard error)	-0.644 (± 0.6333)	-1.196 (± 0.6491)	-0.464 (± 0.3841)	-0.537 (± 0.3763)

Notes:

[116] - Analysis Population

[117] - Analysis Population

[118] - Analysis Population

[119] - Analysis Population

Statistical analyses

Statistical analysis title	Statistical Analysis 1

Statistical analysis description:

Analysis was performed by mixed model repeated measures including the covariates: treatment, Day, treatment* Day and corresponding Baseline time for chair rise, with Day as the repeated factor.

Comparison groups	Placebo- Female Participants v GSK2881078 1.0 mg- Female Participants

Number of subjects included in analysis	41
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Mean difference (net)
Point estimate	-0.553
Confidence interval	
level	90 %
sides	2-sided
lower limit	-2.082
upper limit	0.977

Statistical analysis title	Statistical Analysis 1
Statistical analysis description:	
Analysis was performed by mixed model repeated measures including the covariates: treatment, Day, treatment* Day and corresponding Baseline time for chair rise, with Day as the repeated factor.	
Comparison groups	Placebo- Male Participants v GSK2881078 2.0 mg- Male Participants
Number of subjects included in analysis	45
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Mean difference (net)
Point estimate	-0.073
Confidence interval	
level	90 %
sides	2-sided
lower limit	-0.977
upper limit	0.832

Secondary: Change from Baseline in 'time for chair rise' as assessed by SPPB at Day 56

End point title	Change from Baseline in 'time for chair rise' as assessed by SPPB at Day 56
End point description:	
'Time for chair rise' is one of the 3 components of SPPB, which was assessed by repeated chair stand test and calculated as time for five successful chair stands measured in seconds. Baseline was defined as the latest pre-dose assessment with a non-missing value, including those from unscheduled visits. Analysis was performed using mixed model repeated measures. Change from Baseline was calculated as post-dose visit value minus the Baseline value. Adjusted means and SE are presented. Only those participants with data available at the specified data points were analyzed.	
End point type	Secondary
End point timeframe:	
Baseline (Day 1, Pre-dose), Day 56	

End point values	Placebo- Female Participants	GSK2881078 1.0 mg- Female Participants	Placebo- Male Participants	GSK2881078 2.0 mg- Male Participants
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	21[120]	19[121]	21[122]	21[123]
Units: Seconds				
arithmetic mean (standard error)	-1.207 (± 0.5912)	-2.023 (± 0.6124)	-0.323 (± 0.5294)	-0.160 (± 0.5282)

Notes:

[120] - Analysis Population

[121] - Analysis Population

[122] - Analysis Population

[123] - Analysis Population

Statistical analyses

Statistical analysis title	Statistical Analysis 1

Statistical analysis description:

Analysis was performed by mixed model repeated measures including the covariates: treatment, Day, treatment* Day and corresponding Baseline time for chair rise, with Day as the repeated factor.

Comparison groups	Placebo- Female Participants v GSK2881078 1.0 mg- Female Participants
Number of subjects included in analysis	40
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Mean difference (net)
Point estimate	-0.816
Confidence interval	
level	90 %
sides	2-sided
lower limit	-2.252
upper limit	0.619

Statistical analysis title	Statistical Analysis 1

Statistical analysis description:

Analysis was performed by mixed model repeated measures including the covariates: treatment, Day, treatment* Day and corresponding Baseline time for chair rise, with Day as the repeated factor.

Comparison groups	Placebo- Male Participants v GSK2881078 2.0 mg- Male Participants
Number of subjects included in analysis	42
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Mean difference (net)
Point estimate	0.163
Confidence interval	
level	90 %
sides	2-sided
lower limit	-1.096
upper limit	1.422

Secondary: Change from Baseline in 'time for chair rise' as assessed by SPPB at Day 90

End point title	Change from Baseline in 'time for chair rise' as assessed by SPPB at Day 90

End point description:

'Time for chair rise' is one of the 3 components of SPPB, which was assessed by repeated chair stand test and calculated as time for five successful chair stands measured in seconds. Baseline was defined as the latest pre-dose assessment with a non-missing value, including those from unscheduled visits. Analysis was performed using mixed model repeated measures. Change from Baseline was calculated as post-dose visit value minus the Baseline value. Adjusted means and SE are presented. Only those participants with data available at the specified data points were analyzed.

End point type	Secondary

End point timeframe:

Baseline (Day 1, Pre-dose), Day 90

End point values	Placebo- Female Participants	GSK2881078 1.0 mg- Female Participants	Placebo- Male Participants	GSK2881078 2.0 mg- Male Participants
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	21[124]	18[125]	18[126]	20[127]
Units: Seconds				
arithmetic mean (standard error)	-1.070 (± 0.6956)	-2.030 (± 0.7362)	1.144 (± 1.4013)	-0.793 (± 1.3401)

Notes:

[124] - Analysis Population

[125] - Analysis Population

[126] - Analysis Population

[127] - Analysis Population

Statistical analyses

Statistical analysis title	Statistical Analysis 1

Statistical analysis description:

Analysis was performed by mixed model repeated measures including the covariates: treatment, Day, treatment* Day and corresponding Baseline time for chair rise, with Day as the repeated factor.

Comparison groups	Placebo- Female Participants v GSK2881078 1.0 mg- Female Participants
Number of subjects included in analysis	39
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Mean difference (net)
Point estimate	-0.96
Confidence interval	
level	90 %
sides	2-sided
lower limit	-2.668
upper limit	0.748

Statistical analysis title	Statistical Analysis 1
Statistical analysis description:	
Analysis was performed by mixed model repeated measures including the covariates: treatment, Day, treatment* Day and corresponding Baseline time for chair rise, with Day as the repeated factor.	
Comparison groups	Placebo- Male Participants v GSK2881078 2.0 mg- Male Participants
Number of subjects included in analysis	38
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Mean difference (net)
Point estimate	-1.937
Confidence interval	
level	90 %
sides	2-sided
lower limit	-5.208
upper limit	1.333

Secondary: Change from Baseline in 'time for fastest walk for 4 meter' as assessed by SPPB at Day 28

End point title	Change from Baseline in 'time for fastest walk for 4 meter' as assessed by SPPB at Day 28
End point description:	
''Time for fastest walk for 4 meter' was assessed by SPPB using 4 meter gait speed test. Baseline was defined as the latest pre-dose assessment with a non-missing value, including those from unscheduled visits. Analysis was performed using mixed model repeated measures. Change from Baseline was calculated as post-dose visit value minus the Baseline value. Adjusted means and SE are presented. Only those participants with data available at the specified data points were analyzed.	
End point type	Secondary
End point timeframe:	
Baseline (Day 1, Pre-dose), Day 28	

End point values	Placebo-Female Participants	GSK2881078 1.0 mg-Female Participants	Placebo- Male Participants	GSK2881078 2.0 mg- Male Participants
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	21[128]	20[129]	22[130]	23[131]
Units: Seconds				
arithmetic mean (standard error)	-0.236 (± 0.1132)	-0.277 (± 0.1161)	-0.167 (± 0.1133)	-0.110 (± 0.1108)

Notes:

[128] - Analysis Population

[129] - Analysis Population

[130] - Analysis Population

[131] - Analysis Population

Statistical analyses

Statistical analysis title	Statistical Analysis 1

Statistical analysis description:

Analysis was performed by mixed model repeated measures including the covariates: treatment, Day, treatment* Day and corresponding Baseline Time for fastest walk for 4 meter, with Day as the repeated factor.

Comparison groups	Placebo- Female Participants v GSK2881078 1.0 mg- Female Participants
Number of subjects included in analysis	41
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Mean difference (net)
Point estimate	-0.04
Confidence interval	
level	90 %
sides	2-sided
lower limit	-0.314
upper limit	0.233

Statistical analysis title	Statistical Analysis 1

Statistical analysis description:

Analysis was performed by mixed model repeated measures including the covariates: treatment, Day, treatment* Day and corresponding Baseline Time for fastest walk for 4 meter, with Day as the repeated factor.

Comparison groups	Placebo- Male Participants v GSK2881078 2.0 mg- Male Participants
Number of subjects included in analysis	45
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Mean difference (net)
Point estimate	0.058
Confidence interval	
level	90 %
sides	2-sided
lower limit	-0.209
upper limit	0.324

Secondary: Change from Baseline in 'time for fastest walk for 4 meter' as assessed by SPPB at Day 56

End point title	Change from Baseline in 'time for fastest walk for 4 meter' as assessed by SPPB at Day 56

End point description:

'Time for fastest walk for 4 meter' was assessed by SPPB using 4 meter gait speed test. Baseline was defined as the latest pre-dose assessment with a non-missing value, including those from unscheduled visits. Analysis was performed using mixed model repeated measures. Change from Baseline was calculated as post-dose visit value minus the Baseline value. Adjusted means and SE are presented. Only those participants with data available at the specified data points were analyzed.

End point type	Secondary

End point timeframe:

Baseline (Day 1, Pre-dose), Day 56

End point values	Placebo- Female Participants	GSK2881078 1.0 mg- Female Participants	Placebo- Male Participants	GSK2881078 2.0 mg- Male Participants
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	21[132]	19[133]	21[134]	21[135]
Units: Seconds				
arithmetic mean (standard error)	0.010 (± 0.1487)	-0.276 (± 0.1560)	-0.093 (± 0.1437)	-0.284 (± 0.1438)

Notes:

[132] - Analysis Population

[133] - Analysis Population

[134] - Analysis Population

[135] - Analysis Population

Statistical analyses

Statistical analysis title	Statistical Analysis 1

Statistical analysis description:

Analysis was performed by mixed model repeated measures including the covariates: treatment, Day, treatment* Day and corresponding Baseline Time for fastest walk for 4 meter, with Day as the repeated factor.

Comparison groups	Placebo- Female Participants v GSK2881078 1.0 mg- Female Participants
Number of subjects included in analysis	40
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Mean difference (net)
Point estimate	-0.287
Confidence interval	
level	90 %
sides	2-sided
lower limit	-0.65
upper limit	0.077

Statistical analysis title	Statistical Analysis 1

Statistical analysis description:

Analysis was performed by mixed model repeated measures including the covariates: treatment, Day, treatment* Day and corresponding Baseline Time for fastest walk for 4 meter, with Day as the repeated factor.

Comparison groups	Placebo- Male Participants v GSK2881078 2.0 mg- Male Participants

Number of subjects included in analysis	42
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Mean difference (net)
Point estimate	-0.191
Confidence interval	
level	90 %
sides	2-sided
lower limit	-0.534
upper limit	0.152

Secondary: Change from Baseline in 'time for fastest walk for 4 meter' as assessed by SPPB at Day 90

End point title	Change from Baseline in 'time for fastest walk for 4 meter' as assessed by SPPB at Day 90

End point description:

'Time for fastest walk for 4 meter' was assessed by SPPB using 4 meter gait speed test. Baseline was defined as the latest pre-dose assessment with a non-missing value, including those from unscheduled visits. Analysis was performed using mixed model repeated measures. Change from Baseline was calculated as post-dose visit value minus the Baseline value. Adjusted means and SE are presented. Only those participants with data available at the specified data points were analyzed.

End point type	Secondary

End point timeframe:

Baseline (Day 1, Pre-dose), Day 90

End point values	Placebo-Female Participants	GSK2881078 1.0 mg-Female Participants	Placebo- Male Participants	GSK2881078 2.0 mg- Male Participants
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	21[136]	18[137]	18[138]	20[139]
Units: Seconds				
arithmetic mean (standard error)	-0.043 (± 0.2194)	-0.055 (± 0.2361)	-0.130 (± 0.1331)	-0.360 (± 0.1275)

Notes:

[136] - Analysis Population

[137] - Analysis Population

[138] - Analysis Population

[139] - Analysis Population

Statistical analyses

Statistical analysis title	Statistical Analysis 1

Statistical analysis description:

Analysis was performed by mixed model repeated measures including the covariates: treatment, Day, treatment* Day and corresponding Baseline Time for fastest walk for 4 meter, with Day as the repeated factor.

Comparison groups	Placebo- Male Participants v GSK2881078 2.0 mg- Male Participants

Number of subjects included in analysis	38
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Mean difference (net)
Point estimate	-0.231
Confidence interval	
level	90 %
sides	2-sided
lower limit	-0.541
upper limit	0.08

Statistical analysis title	Statistical Analysis 1

Statistical analysis description:

Analysis was performed by mixed model repeated measures including the covariates: treatment, Day, treatment* Day and corresponding Baseline Time for fastest walk for 4 meter, with Day as the repeated factor.

Comparison groups	Placebo- Female Participants v GSK2881078 1.0 mg- Female Participants
Number of subjects included in analysis	39
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Mean difference (net)
Point estimate	-0.012
Confidence interval	
level	90 %
sides	2-sided
lower limit	-0.555
upper limit	0.532

Secondary: Change from Baseline in constant work rate (CWR) duration from endurance shuttle walking test

End point title	Change from Baseline in constant work rate (CWR) duration from endurance shuttle walking test

End point description:

The endurance shuttle walk test is a CWR test requiring the participant to walk around a flat 10 meter track at a constant individualized pace. The test was externally paced, set to elicit a maximal exercise response (pace was based on a fixed percentage of prior incremental shuttle walk test performance, which determined a participant’s peak exercise capacity). CWR duration is the time in seconds required by a participant to cover a flat 10 meter track during this test. Day 1 (Pre-dose) was considered as a Baseline. Analysis was performed using analysis of covariance (ANCOVA) model. Change from Baseline was calculated as post-dose visit value minus the Baseline value. Only those participants with data available at the specified data points were analyzed.

End point type	Secondary

End point timeframe:

Baseline (Day 1, Pre-dose), Day 90

End point values	Placebo- Female Participants	GSK2881078 1.0 mg- Female Participants	Placebo- Male Participants	GSK2881078 2.0 mg- Male Participants
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	19[140]	16[141]	18[142]	20[143]
Units: Seconds				
least squares mean (standard error)	-6.5 (± 26.78)	4.6 (± 29.25)	105.1 (± 54.94)	-44.2 (± 51.97)

Notes:

[140] - Analysis Population

[141] - Analysis Population

[142] - Analysis Population

[143] - Analysis Population

Statistical analyses

Statistical analysis title	Statistical Analysis 1

Statistical analysis description:

Analysis was performed by ANCOVA model with Baseline CWR duration as the covariate adjusting for the treatment.

Comparison groups	Placebo- Male Participants v GSK2881078 2.0 mg- Male Participants
Number of subjects included in analysis	38
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Difference in Least Square Means
Point estimate	-149.3
Confidence interval	
level	90 %
sides	2-sided
lower limit	-280.6
upper limit	-18.1

Statistical analysis title	Statistical Analysis 1

Statistical analysis description:

Analysis was performed by ANCOVA model with Baseline CWR duration as the covariate adjusting for the treatment.

Comparison groups	Placebo- Female Participants v GSK2881078 1.0 mg- Female Participants
Number of subjects included in analysis	35
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Difference in Least Square Means
Point estimate	11.1
Confidence interval	
level	90 %
sides	2-sided
lower limit	-57.1
upper limit	79.2

Secondary: Change from Baseline in peak performance from incremental shuttle walking test

End point title	Change from Baseline in peak performance from incremental shuttle walking test

End point description:

An incremental shuttle walk test is an externally paced maximal exercise test which determined a participant's peak exercise capacity. The maximum duration of the test is 20 minutes. Peak performance was measured in meters, which was defined as the maximum distance covered by a participant until the participant can no longer continue walking during this test. Baseline was defined as the highest non-missing pre-dose assessment from Day -9 and Day 1. Analysis was performed using ANCOVA model. Change from Baseline was calculated as post-dose visit value minus the Baseline value. Only those participants with data available at the specified data points were analyzed.

End point type	Secondary

End point timeframe:

Baseline (Highest non-missing pre-dose assessment from Day-9 and Day 1), Day 90

End point values	Placebo- Female Participants	GSK2881078 1.0 mg- Female Participants	Placebo- Male Participants	GSK2881078 2.0 mg- Male Participants
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	19[144]	18[145]	18[146]	20[147]
Units: Meters				
least squares mean (standard error)	-10.5 (± 14.76)	-17.2 (± 15.16)	-7.5 (± 15.84)	-42.3 (± 15.02)

Notes:

[144] - Analysis Population

[145] - Analysis Population

[146] - Analysis Population

[147] - Analysis Population

Statistical analyses

Statistical analysis title	Statistical Analysis 1

Statistical analysis description:

Analysis was performed by ANCOVA model with Baseline peak performance as the covariate adjusting for the treatment.

Comparison groups	Placebo- Female Participants v GSK2881078 1.0 mg- Female Participants
Number of subjects included in analysis	37
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Difference in Least Square Means
Point estimate	-6.7
Confidence interval	
level	90 %
sides	2-sided
lower limit	-42.7
upper limit	29.2

Statistical analysis title	Statistical Analysis 1
Statistical analysis description:	
Analysis was performed by ANCOVA model with Baseline peak performance as the covariate adjusting for the treatment.	
Comparison groups	Placebo- Male Participants v GSK2881078 2.0 mg- Male Participants
Number of subjects included in analysis	38
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Difference in Least Square Means
Point estimate	-34.8
Confidence interval	
level	90 %
sides	2-sided
lower limit	-72
upper limit	2.4

Secondary: Change from Baseline in chronic obstructive pulmonary disease (COPD) assessment test (CAT) score at Day 56

End point title	Change from Baseline in chronic obstructive pulmonary disease (COPD) assessment test (CAT) score at Day 56

End point description:

The CAT is a short and simple participant-completed questionnaire which was developed for use in routine clinical practice to measure the health status of participants with COPD. The CAT is an 8-item questionnaire suitable for completion by all participants diagnosed with COPD. Participants rated their experience on a 6-point scale, ranging from 0 (no impairment) to 5 (maximum impairment). A total CAT score was calculated by summing the non-missing scores of the eight items with a scoring range of 0-40. Higher scores indicated more severe disease impact. Day 1 (Pre-dose) was considered as a Baseline. Change from Baseline was calculated as post-dose visit value minus the Baseline value. Adjusted means and SE are presented. Only those participants with data available at the specified data points were analyzed.

End point type	Secondary

End point timeframe:

Baseline (Day 1, Pre-dose), Day 56

End point values	Placebo-Female Participants	GSK2881078 1.0 mg-Female Participants	Placebo- Male Participants	GSK2881078 2.0 mg- Male Participants
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	21[148]	19[149]	21[150]	21[151]
Units: Scores on a Scale				
arithmetic mean (standard error)	-0.8 (± 0.92)	-1.2 (± 0.97)	-0.4 (± 1.14)	-1.0 (± 1.14)

Notes:

[148] - Analysis Population

[149] - Analysis Population

[150] - Analysis Population

[151] - Analysis Population

Statistical analyses

Statistical analysis title	Statistical Analysis 1
Statistical analysis description:	
Analysis was performed by mixed model repeated measures including the covariates: treatment, Day, treatment* Day and Baseline CAT score, with Day as the repeated factor.	
Comparison groups	Placebo- Female Participants v GSK2881078 1.0 mg- Female Participants
Number of subjects included in analysis	40
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Mean difference (net)
Point estimate	-0.4
Confidence interval	
level	90 %
sides	2-sided
lower limit	-2.6
upper limit	1.9

Statistical analysis title	Statistical Analysis 1
Statistical analysis description:	
Analysis was performed by mixed model repeated measures including the covariates: treatment, Day, treatment* Day and Baseline CAT score, with Day as the repeated factor.	
Comparison groups	Placebo- Male Participants v GSK2881078 2.0 mg- Male Participants
Number of subjects included in analysis	42
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Mean difference (net)
Point estimate	-0.7
Confidence interval	
level	90 %
sides	2-sided
lower limit	-3.4
upper limit	2.1

Secondary: Change from Baseline in chronic obstructive pulmonary disease (COPD) assessment test (CAT) score at Day 90

End point title	Change from Baseline in chronic obstructive pulmonary disease (COPD) assessment test (CAT) score at Day 90

End point description:

The CAT is a short and simple participant-completed questionnaire which was developed for use in

routine clinical practice to measure the health status of participants with COPD. The CAT is an 8-item questionnaire suitable for completion by all participants diagnosed with COPD. Participants rated their experience on a 6-point scale, ranging from 0 (no impairment) to 5 (maximum impairment). A total CAT score was calculated by summing the non-missing scores of the eight items with a scoring range of 0-40. Higher scores indicated more severe disease impact. Day 1 (Pre-dose) was considered as a Baseline. Change from Baseline was calculated as post-dose visit value minus the Baseline value. Adjusted means and SE are presented. Only those participants with data available at the specified data points were analyzed.

End point type	Secondary

End point timeframe:

Baseline (Day 1, Pre-dose), Day 90

End point values	Placebo-Female Participants	GSK2881078 1.0 mg-Female Participants	Placebo- Male Participants	GSK2881078 2.0 mg- Male Participants
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	21[152]	18[153]	18[154]	20[155]
Units: Scores on a Scale				
arithmetic mean (standard error)	-1.3 (± 0.79)	-2.2 (± 0.85)	-1.4 (± 0.94)	0.8 (± 0.90)

Notes:

[152] - Analysis Population.

[153] - Analysis Population.

[154] - Analysis Population.

[155] - Analysis Population.

Statistical analyses

Statistical analysis title	Statistical Analysis 1

Statistical analysis description:

Analysis was performed by mixed model repeated measures including the covariates: treatment, Day, treatment* Day and Baseline CAT score, with Day as the repeated factor.

Comparison groups	Placebo- Male Participants v GSK2881078 2.0 mg- Male Participants
Number of subjects included in analysis	38
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Mean difference (net)
Point estimate	2.2
Confidence interval	
level	90 %
sides	2-sided
lower limit	0
upper limit	4.5

Statistical analysis title	Statistical Analysis 1

Statistical analysis description:

Analysis was performed by mixed model repeated measures including the covariates: treatment, Day, treatment* Day and Baseline CAT score, with Day as the repeated factor.

Comparison groups	Placebo- Female Participants v GSK2881078 1.0 mg- Female Participants

Number of subjects included in analysis	39
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Mean difference (net)
Point estimate	-0.9
Confidence interval	
level	90 %
sides	2-sided
lower limit	-2.9
upper limit	1.1

Secondary: Change from Baseline in participant reported outcome (PRO)active individual component: Difficulty score at Day 56

End point title	Change from Baseline in participant reported outcome (PRO)active individual component: Difficulty score at Day 56

End point description:

The daily PROactive instrument consisted of a PRO questionnaire and an activity monitor to measure participant experience of physical activity. It consisted of 9-item daily assessments covering 2 different domains (amount and difficulty). The 'amount' domain was covered by 2 questions combined with 2 activity monitor outputs. The 'difficulty' domain was covered by 5 questions. Individual domains were scored by simple adding items, gave raw score values 0 to 17 for 'amount' and 0 to 20 for 'difficulty'. The raw scores were then transformed to a 0 to 100 Rasch analysis based scale for each domain. Higher scores indicated worse experience with physical activity. Baseline was the average of the data collected from the 7-day period after dispensing of the device on Day -9. Change from Baseline was calculated as post-dose visit value minus the Baseline value. Adjusted means and SE are presented. Only those participants with data available at the specified data points were analyzed.

End point type	Secondary

End point timeframe:

Baseline (Day -9) and Day 56

End point values	Placebo- Female Participants	GSK2881078 1.0 mg- Female Participants	Placebo- Male Participants	GSK2881078 2.0 mg- Male Participants
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	17[156]	12[157]	12[158]	13[159]
Units: Scores on a Scale				
arithmetic mean (standard error)	3.7 (± 1.59)	-1.1 (± 1.80)	1.3 (± 2.16)	-0.8 (± 2.08)

Notes:

[156] - Analysis Population

[157] - Analysis Population

[158] - Analysis Population

[159] - Analysis Population

Statistical analyses

Statistical analysis title	Statistical Analysis 1

Statistical analysis description:

Analysis was performed by mixed model repeated measures including the covariates: treatment, Day, treatment* Day and corresponding Baseline difficulty scores, with Day as the repeated factor.

Comparison groups	Placebo- Female Participants v GSK2881078 1.0 mg- Female

	Participants
Number of subjects included in analysis	29
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Mean difference (net)
Point estimate	-4.7
Confidence interval	
level	90 %
sides	2-sided
lower limit	-8.9
upper limit	-0.6

Statistical analysis title	Statistical Analysis 1

Statistical analysis description:

Analysis was performed by mixed model repeated measures including the covariates: treatment, Day, treatment* Day and corresponding Baseline difficulty scores, with Day as the repeated factor.

Comparison groups	Placebo- Male Participants v GSK2881078 2.0 mg- Male Participants
Number of subjects included in analysis	25
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Mean difference (net)
Point estimate	-2.1
Confidence interval	
level	90 %
sides	2-sided
lower limit	-7.2
upper limit	3.1

Secondary: Change from Baseline in participant reported outcome (PRO)active individual component: Difficulty score at Day 90

End point title	Change from Baseline in participant reported outcome (PRO)active individual component: Difficulty score at Day 90

End point description:

The daily PROactive instrument consisted of a PRO questionnaire and an activity monitor to measure participant experience of physical activity. It consisted of 9-item daily assessments covering 2 different domains (amount and difficulty). The 'amount' domain was covered by 2 questions combined with 2 activity monitor outputs. The 'difficulty' domain was covered by 5 questions. Individual domains were scored by simple adding items, gave raw score values 0 to 17 for 'amount' and 0 to 20 for 'difficulty'. The raw scores were then transformed to a 0 to 100 Rasch analysis based scale for each domain. Higher scores indicated worse experience with physical activity. Baseline was the average of the data collected from the 7-day period after dispensing of the device on Day -9. Change from Baseline was calculated as post-dose visit value minus the Baseline value. Adjusted means and SE are presented. Only those participants with data available at the specified data points were analyzed.

End point type	Secondary

End point timeframe:

Baseline (Day -9) and Day 90

End point values	Placebo- Female Participants	GSK2881078 1.0 mg- Female Participants	Placebo- Male Participants	GSK2881078 2.0 mg- Male Participants
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	15[160]	17[161]	13[162]	11[163]
Units: Scores on a Scale				
arithmetic mean (standard error)	2.0 (± 1.90)	-2.9 (± 1.84)	2.8 (± 2.56)	-1.2 (± 2.65)

Notes:

[160] - Analysis Population

[161] - Analysis Population

[162] - Analysis Population

[163] - Analysis Population

Statistical analyses

Statistical analysis title	Statistical Analysis 1

Statistical analysis description:

Analysis was performed by mixed model repeated measures including the covariates: treatment, Day, treatment* Day and corresponding Baseline difficulty scores, with Day as the repeated factor.

Comparison groups	Placebo- Female Participants v GSK2881078 1.0 mg- Female Participants
Number of subjects included in analysis	32
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Mean difference (net)
Point estimate	-4.9
Confidence interval	
level	90 %
sides	2-sided
lower limit	-9.5
upper limit	-0.4

Statistical analysis title	Statistical Analysis 1

Statistical analysis description:

Analysis was performed by mixed model repeated measures including the covariates: treatment, Day, treatment* Day and corresponding Baseline difficulty scores, with Day as the repeated factor.

Comparison groups	Placebo- Male Participants v GSK2881078 2.0 mg- Male Participants
Number of subjects included in analysis	24
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Mean difference (net)
Point estimate	-4.1

Confidence interval	
level	90 %
sides	2-sided
lower limit	-10.3
upper limit	2.2

Secondary: Change from Baseline in participant reported outcome (PRO)active individual component: Amount score at Day 56

End point title	Change from Baseline in participant reported outcome (PRO)active individual component: Amount score at Day 56

End point description:

The daily PROactive instrument consisted of a PRO questionnaire and an activity monitor to measure participant experience of physical activity. It consisted of 9-item daily assessments covering 2 different domains (amount and difficulty). The 'amount' domain was covered by 2 questions combined with 2 activity monitor outputs. The 'difficulty' domain was covered by 5 questions. Individual domains were scored by simple adding items, gave raw score values 0 to 17 for 'amount' and 0 to 20 for 'difficulty'. The raw scores were then transformed to a 0 to 100 Rasch analysis based scale for each domain. Higher scores indicated worse experience with physical activity. Baseline was the average of the data collected from the 7-day period after dispensing of the device on Day -9. Change from Baseline was calculated as post-dose visit value minus the Baseline value. Adjusted means and SE are presented. Only those participants with data available at the specified data points were analyzed.

End point type	Secondary

End point timeframe:

Baseline (Day -9) and Day 56

End point values	Placebo- Female Participants	GSK2881078 1.0 mg- Female Participants	Placebo- Male Participants	GSK2881078 2.0 mg- Male Participants
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	17[164]	12[165]	12[166]	13[167]
Units: Scores on a Scale				
arithmetic mean (standard error)	3.3 (± 1.09)	0.2 (± 1.24)	2.5 (± 1.83)	2.3 (± 1.77)

Notes:

[164] - Analysis Population

[165] - Analysis Population

[166] - Analysis Population

[167] - Analysis Population

Statistical analyses

Statistical analysis title	Statistical Analysis 1

Statistical analysis description:

Analysis was performed by mixed model repeated measures including the covariates: treatment, Day, treatment* Day and corresponding Baseline amount scores, with Day as the repeated factor.

Comparison groups	Placebo- Female Participants v GSK2881078 1.0 mg- Female Participants

Number of subjects included in analysis	29
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Mean difference (net)
Point estimate	-3.1
Confidence interval	
level	90 %
sides	2-sided
lower limit	-5.9
upper limit	-0.3

Statistical analysis title	Statistical Analysis 1

Statistical analysis description:

Analysis was performed by mixed model repeated measures including the covariates: treatment, Day, treatment* Day and corresponding Baseline amount scores, with Day as the repeated factor.

Comparison groups	Placebo- Male Participants v GSK2881078 2.0 mg- Male Participants
Number of subjects included in analysis	25
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Mean difference (net)
Point estimate	-0.2
Confidence interval	
level	90 %
sides	2-sided
lower limit	-4.6
upper limit	4.2

Secondary: Change from Baseline in participant reported outcome (PRO)active individual component: Amount score at Day 90

End point title	Change from Baseline in participant reported outcome (PRO)active individual component: Amount score at Day 90

End point description:

The daily PROactive instrument consisted of a PRO questionnaire and an activity monitor to measure participant experience of physical activity. It consisted of 9-item daily assessments covering 2 different domains (amount and difficulty). The 'amount' domain was covered by 2 questions combined with 2 activity monitor outputs. The 'difficulty' domain was covered by 5 questions. Individual domains were scored by simple adding items, gave raw score values 0 to 17 for 'amount' and 0 to 20 for 'difficulty'. The raw scores were then transformed to a 0 to 100 Rasch analysis based scale for each domain. Higher scores indicated worse experience with physical activity. Baseline was the average of the data collected from the 7-day period after dispensing of the device on Day -9. Change from Baseline was calculated as post-dose visit value minus the Baseline value. Adjusted means and SE are presented. Only those participants with data available at the specified data points were analyzed.

End point type	Secondary

End point timeframe:

Baseline (Day -9) and Day 90

End point values	Placebo- Female Participants	GSK2881078 1.0 mg- Female Participants	Placebo- Male Participants	GSK2881078 2.0 mg- Male Participants
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	15[168]	17[169]	13[170]	11[171]
Units: Scores on a Scale				
arithmetic mean (standard error)	-0.2 (± 2.05)	3.8 (± 1.98)	-0.8 (± 2.33)	2.7 (± 2.47)

Notes:

[168] - Analysis Population

[169] - Analysis Population

[170] - Analysis Population

[171] - Analysis Population

Statistical analyses

Statistical analysis title	Statistical Analysis 1

Statistical analysis description:

Analysis was performed by repeated measures mixed model including the covariates; treatment, Day, treatment* Day and corresponding Baseline amount scores, with Day as the repeated factor.

Comparison groups	Placebo- Male Participants v GSK2881078 2.0 mg- Male Participants
Number of subjects included in analysis	24
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Mean difference (net)
Point estimate	3.5
Confidence interval	
level	90 %
sides	2-sided
lower limit	-2.3
upper limit	9.4

Statistical analysis title	Statistical Analysis 1

Statistical analysis description:

Analysis was performed by repeated measures mixed model including the covariates; treatment, Day, treatment* Day and corresponding Baseline amount scores, with Day as the repeated factor.

Comparison groups	Placebo- Female Participants v GSK2881078 1.0 mg- Female Participants
Number of subjects included in analysis	32
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Mean difference (net)
Point estimate	4
Confidence interval	
level	90 %
sides	2-sided
lower limit	-0.8
upper limit	8.8

Secondary: Change from Baseline in participant reported outcome (PRO)active total score at Day 56

End point title	Change from Baseline in participant reported outcome (PRO)active total score at Day 56

End point description:

The daily PROactive instrument consisted of a PRO questionnaire and an activity monitor to measure physical activity. It consisted of 9-item daily assessments covering 2 different domains(amount and difficulty). The‘amount’domain was covered by 2 questions combined with 2 activity monitor outputs. The ‘difficulty’domain was covered by 5 questions. Individual domains were scored by simple adding items, gave raw score values 0 to 17 for‘amount’and 0 to 20 for‘difficulty. The raw scores were then transformed to a 0 to 100 Rasch scale. The ‘total score’ was obtained by calculating the average between two domains (ranged from 0 to 100). Higher scores indicated worse experience with physical activity. Baseline was the average of the data collected from the 7-day period after dispensing of the device on Day -9. Change from Baseline was calculated as post-dose visit value minus the Baseline value. Only those participants with data available at the specified data points were analyzed.

End point type	Secondary

End point timeframe:

Baseline (Day -9) and Day 56

End point values	Placebo-Female Participants	GSK2881078 1.0 mg-Female Participants	Placebo- Male Participants	GSK2881078 2.0 mg- Male Participants
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	17[172]	12[173]	12[174]	13[175]
Units: Scores on a Scale				
arithmetic mean (standard error)	3.7 (± 0.89)	-0.5 (± 1.03)	2.1 (± 1.09)	0.5 (± 1.05)

Notes:

[172] - Analysis Population

[173] - Analysis Population

[174] - Analysis Population

[175] - Analysis Population

Statistical analyses

Statistical analysis title	Statistical Analysis 1

Statistical analysis description:

Analysis was performed by mixed model repeated measures including the covariates; treatment, Day, treatment* Day and corresponding Baseline total scores, with Day as the repeated factor.

Comparison groups	Placebo- Male Participants v GSK2881078 2.0 mg- Male Participants
Number of subjects included in analysis	25
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Mean difference (net)
Point estimate	-1.5

Confidence interval	
level	90 %
sides	2-sided
lower limit	-4.1
upper limit	1.1

Statistical analysis title	Statistical Analysis 1

Statistical analysis description:

Analysis was performed by mixed model repeated measures including the covariates; treatment, Day, treatment* Day and corresponding Baseline total scores, with Day as the repeated factor.

Comparison groups	Placebo- Female Participants v GSK2881078 1.0 mg- Female Participants
Number of subjects included in analysis	29
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Mean difference (net)
Point estimate	-4.2
Confidence interval	
level	90 %
sides	2-sided
lower limit	-6.5
upper limit	-1.9

Secondary: Change from Baseline in participant reported outcome (PRO)active total score at Day 90

End point title	Change from Baseline in participant reported outcome (PRO)active total score at Day 90

End point description:

The daily PROactive instrument consisted of a PRO questionnaire and an activity monitor to measure physical activity. It consisted of 9-item daily assessments covering 2 different domains(amount and difficulty). The‘amount’domain was covered by 2 questions combined with 2 activity monitor outputs. The ‘difficulty’domain was covered by 5 questions. Individual domains were scored by simple adding items, gave raw score values 0 to 17 for‘amount’and 0 to 20 for‘difficulty. The raw scores were then transformed to a 0 to 100 Rasch scale. The ‘total score’ was obtained by calculating the average between two domains (ranged from 0 to 100). Higher scores indicated worse experience with physical activity. Baseline was the average of the data collected from the 7-day period after dispensing of the device on Day -9. Change from Baseline was calculated as post-dose visit value minus the Baseline value. Only those participants with data available at the specified data points were analyzed.

End point type	Secondary

End point timeframe:

Baseline (Day -9) and Day 90

End point values	Placebo- Female Participants	GSK2881078 1.0 mg- Female Participants	Placebo- Male Participants	GSK2881078 2.0 mg- Male Participants
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	15[176]	17[177]	13[178]	11[179]
Units: Scores on a Scale				
arithmetic mean (standard error)	1.3 (± 1.20)	0.3 (± 1.14)	1.2 (± 1.57)	0.5 (± 1.66)

Notes:

[176] - Analysis Population

[177] - Analysis Population

[178] - Analysis Population

[179] - Analysis Population

Statistical analyses

Statistical analysis title	Statistical Analysis 1

Statistical analysis description:

Analysis was performed by mixed model repeated measures including the covariates; treatment, Day, treatment* Day and corresponding Baseline total scores, with Day as the repeated factor.

Comparison groups	Placebo- Male Participants v GSK2881078 2.0 mg- Male Participants
Number of subjects included in analysis	24
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Mean difference (net)
Point estimate	-0.7
Confidence interval	
level	90 %
sides	2-sided
lower limit	-4.6
upper limit	3.2

Statistical analysis title	Statistical Analysis 1

Statistical analysis description:

Analysis was performed by mixed model repeated measures including the covariates; treatment, Day, treatment* Day and corresponding Baseline total scores, with Day as the repeated factor.

Comparison groups	Placebo- Female Participants v GSK2881078 1.0 mg- Female Participants
Number of subjects included in analysis	32
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Mean difference (net)
Point estimate	-1
Confidence interval	
level	90 %
sides	2-sided
lower limit	-3.8
upper limit	1.8

Secondary: Change from Baseline in steps per day (physical activity measure) as assessed via an accelerometer

End point title	Change from Baseline in steps per day (physical activity measure) as assessed via an accelerometer

End point description:

Steps per day was assessed using an accelerometer, a clinically validated physical activity monitor which was used to measure the levels of physical activity. Participants wore an accelerometer for 7 days during individual timepoint. Values at Baseline, Day 56 and Day 90 were the average values collected from an accelerometer for 7 days after the Day -9, Day 56 and Day 90. Baseline was the average of the data collected from the 7-day period after dispensing of the device on Day -9. Change from Baseline was calculated as post-dose visit value minus the Baseline value. Only those participants with data available at the specified data points were analyzed (represented by n=X in the category titles).

End point type	Secondary

End point timeframe:

Baseline (Day -9), Days 56 and 90

End point values	Placebo-Female Participants	GSK2881078 1.0 mg-Female Participants	Placebo- Male Participants	GSK2881078 2.0 mg- Male Participants
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	17[180]	17[181]	14[182]	17[183]
Units: Steps per day				
arithmetic mean (standard deviation)				
Day 56,n=17,14,14,17	285.19 (± 1289.604)	389.58 (± 1322.701)	120.41 (± 1282.092)	-17.40 (± 1334.539)
Day 90,n=17,17,14,14	-246.45 (± 756.414)	786.21 (± 1439.988)	-527.07 (± 1077.747)	611.36 (± 1499.559)

Notes:

[180] - Analysis Population

[181] - Analysis Population

[182] - Analysis Population

[183] - Analysis Population

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in vector magnitude unit per wear time (physical activity measure) as assessed via an accelerometer

End point title	Change from Baseline in vector magnitude unit per wear time (physical activity measure) as assessed via an accelerometer

End point description:

Vector magnitude unit per wear time was assessed using an accelerometer, a clinically validated physical activity monitor which was used to measure the levels of physical activity. Participants wore an accelerometer for 7 days during individual timepoint. Values at Baseline, Day 56 and Day 90 were the average values collected from accelerometer for 7 days after the Day -9, Day 56 and Day 90. Data from an accelerator was uploaded to a central site. Baseline was the average of the data collected from the 7-day period after dispensing of the device on Day -9. Change from Baseline was calculated as post-dose visit value minus the Baseline value. Only those participants with data available at the specified data points were analyzed (represented by n=X in the category titles).

End point type	Secondary

End point timeframe:

Baseline (Day -9), Days 56 and 90

End point values	Placebo-Female Participants	GSK2881078 1.0 mg-Female Participants	Placebo- Male Participants	GSK2881078 2.0 mg- Male Participants
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	17[184]	17[185]	14[186]	17[187]
Units: Vector magnitude units per minute				
arithmetic mean (standard deviation)				
Day 56,n=17,14,14,17	9.19 (± 82.596)	-4.83 (± 66.400)	56.42 (± 86.284)	71.98 (± 175.403)
Day 90,n=17,17,14,14	-6.60 (± 65.648)	0.40 (± 64.670)	-3.73 (± 74.849)	42.36 (± 184.191)

Notes:

[184] - Analysis Population

[185] - Analysis Population

[186] - Analysis Population

[187] - Analysis Population

Statistical analyses

No statistical analyses for this end point

Secondary: Number of participants with participant global impression of change (PGIC) score over time

End point title	Number of participants with participant global impression of change (PGIC) score over time

End point description:

Participant-reported response to treatment was assessed using the PGIC measure, a single item completed by participant to assess the participant's impression of change in their disease severity since the beginning of the study. Responses to the PGIC question were on a 7 point Likert scale: Much Better, Better, Slightly Better, No Change, Slightly Worse, Worse, and Much Worse. Number of participants with PGIC score is presented by treatment group, visit and by 7 response categories. Only those participants with data available at the specified data points were analyzed (represented by n=X in the category titles).

End point type	Secondary

End point timeframe:

Days 14, 28, 56 and 90

End point values	Placebo-Female Participants	GSK2881078 1.0 mg-Female Participants	Placebo- Male Participants	GSK2881078 2.0 mg- Male Participants
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	21[188]	20[189]	23[190]	23[191]
Units: Participants				
Day 14, much worse,n=21,20,23,23	0	0	0	0

Day 14, worse,n=21,20,23,23	0	0	0	1
Day 14, slightly worse,n=21,20,23,23	0	1	0	0
Day 14, no change,n=21,20,23,23	6	5	9	9
Day 14, slightly better,n=21,20,23,23	7	7	4	4
Day 14, better,n=21,20,23,23	7	5	8	7
Day 14, much better,n=21,20,23,23	1	2	2	2
Day 28, much worse,n=21,20,21,22	0	0	0	0
Day 28, worse,n=21,20,21,22	0	0	0	0
Day 28, slightly worse,n=21,20,21,22	1	2	0	0
Day 28, no change,n=21,20,21,22	3	6	4	6
Day 28, slightly better,n=21,20,21,22	9	6	10	7
Day 28, better,n=21,20,21,22	5	6	5	7
Day 28, much better,n=21,20,21,22	3	0	2	2
Day 56, much worse,n=21,19,21,21	0	0	0	0
Day 56, worse,n=21,19,21,21	0	0	0	0
Day 56, slightly worse,n=21,19,21,21	1	3	1	4
Day 56, no change,n=21,19,21,21	2	5	4	5
Day 56, slightly better,n=21,19,21,21	6	4	7	5
Day 56, better,n=21,19,21,21	10	6	8	5
Day 56, much better,n=21,19,21,21	2	1	1	2
Day 90, much worse,n=21,18,18,20	0	0	0	0
Day 90, worse,n=21,18,18,20	0	1	0	0
Day 90, slightly worse,n=21,18,18,20	1	0	0	0
Day 90, no change,n=21,18,18,20	9	8	5	6
Day 90, slightly better,n=21,18,18,20	7	3	9	9
Day 90, better,n=21,18,18,20	3	4	4	4
Day 90, much better,n=21,18,18,20	1	2	0	1

Notes:

[188] - Analysis Population

[189] - Analysis Population

[190] - Analysis Population

[191] - Analysis Population

Statistical analyses

No statistical analyses for this end point

Secondary: Number of participants with participant global rating of severity (PGRS) score over time

End point title	Number of participants with participant global rating of severity (PGRS) score over time

End point description:

PGRS is a single global question and was asked to participants to rate their COPD severity on a four point scale ranging from 1 to 4 (1=mild, 2=moderate, 3=severe, 4=very severe). Number of participants with PGRS score ranging from mild to very severe are presented over time. Only those participants with data available at the specified data points were analyzed (represented by n=X in the category titles).

End point type	Secondary

End point timeframe:

Days 1 and 90

End point values	Placebo-Female Participants	GSK2881078 1.0 mg-Female Participants	Placebo- Male Participants	GSK2881078 2.0 mg- Male Participants
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	21[192]	20[193]	23[194]	23[195]
Units: Participants				
Day 1, mild,n=21,20,23,23	2	0	0	2
Day 1, moderate,n=21,20,23,23	9	13	11	12
Day 1, severe,n=21,20,23,23	8	7	12	8
Day 1, very severe,n=21,20,23,23	2	0	0	1
Day 90, mild,n=21,18,18,20	4	4	1	5
Day 90, moderate,n=21,18,18,20	9	7	9	2
Day 90, severe,n=21,18,18,20	6	6	8	12
Day 90, very severe,n=21,18,18,20	2	1	0	1

Notes:

[192] - Analysis Population

[193] - Analysis Population

[194] - Analysis Population

[195] - Analysis Population

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in St. George respiratory questionnaire (SGRQ) for COPD (SGRQ-c) total score

End point title	Change from Baseline in St. George respiratory questionnaire (SGRQ) for COPD (SGRQ-c) total score

End point description:

SGRQ-c is the COPD specific version of SGRQ. It consisted of 40 items in total, corresponding to 3 individual domains (components): symptoms, activity and impact, with different components carrying a different weighting. Component scores were calculated by summing the weights from all positive items in that component, dividing by the sum of maximum possible weights for all items in that component, and multiplying this number by 100. Total score was calculated by summing the weight to all the positive responses in each component. Total score has the range from 0 to 100. Higher scores indicated more severe disease impact. Day 1 (Pre-dose) was considered as a Baseline. Analysis was performed using ANCOVA model. Change from Baseline was calculated as post-dose visit value minus the Baseline value. Only those participants with data available at the specified data points were analyzed.

End point type	Secondary

End point timeframe:

Baseline (Day 1, Pre-dose), Day 90

End point values	Placebo-Female Participants	GSK2881078 1.0 mg-Female Participants	Placebo- Male Participants	GSK2881078 2.0 mg- Male Participants
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	21[196]	17[197]	18[198]	20[199]
Units: Scores on a scale				
least squares mean (standard error)	-3.9 (± 1.71)	-0.9 (± 1.90)	-1.7 (± 1.87)	0.4 (± 1.77)

Notes:
[196] - Analysis Population
[197] - Analysis Population
[198] - Analysis Population
[199] - Analysis Population

Statistical analyses

Statistical analysis title	Statistical Analysis 1
Statistical analysis description:	
Analysis was performed by ANCOVA model with Baseline total score as the covariate adjusting for the treatment.	
Comparison groups	Placebo- Female Participants v GSK2881078 1.0 mg- Female Participants
Number of subjects included in analysis	38
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Difference in Least Square Means
Point estimate	3
Confidence interval	
level	90 %
sides	2-sided
lower limit	-1.4
upper limit	7.4

Statistical analysis title	Statistical Analysis 1
Statistical analysis description:	
Analysis was performed by ANCOVA model with Baseline total score as the covariate adjusting for the treatment.	
Comparison groups	Placebo- Male Participants v GSK2881078 2.0 mg- Male Participants
Number of subjects included in analysis	38
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Difference in Least Square Means
Point estimate	2.1
Confidence interval	
level	90 %
sides	2-sided
lower limit	-2.3
upper limit	6.5

Secondary: Change from Baseline in SGRQ-c symptoms score

End point title	Change from Baseline in SGRQ-c symptoms score

End point description:

SGRQ-c is the COPD specific version of SGRQ. It consisted of 40 items in total, corresponding to 3 individual domains (components): symptoms, activity and impact, with different components carrying a different weighting. Component scores were calculated by summing the weights from all positive items

in that component, dividing by the sum of maximum possible weights for all items in that component, and multiplying this number by 100. Symptoms component consisted of questions 1 to 7 in Part 1. Symptoms score has the range from 0 to 100. Higher scores indicated more severe disease impact. Day 1 (Pre-dose) was considered as a Baseline. Analysis was performed using ANCOVA model. Change from Baseline was calculated as post-dose visit value minus the Baseline value. Only those participants with data available at the specified data points were analyzed.

End point type	Secondary

End point timeframe:

Baseline (Day 1, Pre-dose), Day 90

End point values	Placebo- Female Participants	GSK2881078 1.0 mg- Female Participants	Placebo- Male Participants	GSK2881078 2.0 mg- Male Participants
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	21[200]	17[201]	18[202]	20[203]
Units: Scores on a scale				
least squares mean (standard error)	-4.0 (± 2.95)	-1.4 (± 3.29)	-3.5 (± 3.38)	-4.0 (± 3.20)

Notes:

[200] - Analysis Population

[201] - Analysis Population

[202] - Analysis Population

[203] - Analysis Population

Statistical analyses

Statistical analysis title	Statistical Analysis 1

Statistical analysis description:

Analysis was performed by ANCOVA model with Baseline symptoms score as the covariate adjusting for the treatment.

Comparison groups	Placebo- Female Participants v GSK2881078 1.0 mg- Female Participants
Number of subjects included in analysis	38
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Difference in Least Square Means
Point estimate	2.6
Confidence interval	
level	90 %
sides	2-sided
lower limit	-5
upper limit	10.1

Statistical analysis title	Statistical Analysis 1

Statistical analysis description:

Analysis was performed by ANCOVA model with Baseline symptoms score as the covariate adjusting for the treatment.

Comparison groups	Placebo- Male Participants v GSK2881078 2.0 mg- Male Participants

Number of subjects included in analysis	38
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Difference in Least Square Means
Point estimate	-0.5
Confidence interval	
level	90 %
sides	2-sided
lower limit	-8.4
upper limit	7.5

Secondary: Change from Baseline in SGRQ-c activity score

End point title	Change from Baseline in SGRQ-c activity score

End point description:

SGRQ-c is the COPD specific version of SGRQ. It consisted of 40 items in total, corresponding to 3 individual domains (components): symptoms, activity and impact, with different components carrying a different weighting. Component scores were calculated by summing the weights from all positive items in that component, dividing by the sum of maximum possible weights for all items in that component, and multiplying this number by 100. Activity component consisted of questions 9 and 12 in Part 2 of the questionnaire. Activity score has the range from 0 to 100. Higher scores indicated more severe disease impact. Day 1 (Pre-dose) was considered as a Baseline. Analysis was performed using ANCOVA model. Change from Baseline was calculated as post-dose visit value minus the Baseline value. Only those participants with data available at the specified data points were analyzed.

End point type	Secondary

End point timeframe:

Baseline (Day 1, Pre-dose), Day 90

End point values	Placebo- Female Participants	GSK2881078 1.0 mg- Female Participants	Placebo- Male Participants	GSK2881078 2.0 mg- Male Participants
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	21[204]	17[205]	18[206]	20[207]
Units: Scores on a scale				
least squares mean (standard error)	-5.4 (± 2.00)	-3.4 (± 2.23)	1.2 (± 2.57)	1.6 (± 2.44)

Notes:

[204] - Analysis Population

[205] - Analysis Population

[206] - Analysis Population

[207] - Analysis Population

Statistical analyses

Statistical analysis title	Statistical Analysis 1

Statistical analysis description:

Analysis was performed by ANCOVA model with Baseline activity score as the covariate adjusting for the treatment.

Comparison groups	Placebo- Female Participants v GSK2881078 1.0 mg- Female Participants

Number of subjects included in analysis	38
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Difference in Least Square Means
Point estimate	2
Confidence interval	
level	90 %
sides	2-sided
lower limit	-3.2
upper limit	7.1

Statistical analysis title	Statistical Analysis 1

Statistical analysis description:

Analysis was performed by ANCOVA model with Baseline activity score as the covariate adjusting for the treatment.

Comparison groups	Placebo- Male Participants v GSK2881078 2.0 mg- Male Participants
Number of subjects included in analysis	38
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Difference in Least Square Means
Point estimate	0.5
Confidence interval	
level	90 %
sides	2-sided
lower limit	-5.6
upper limit	6.5

Secondary: Change from Baseline in SGRQ-c impact score

End point title	Change from Baseline in SGRQ-c impact score

End point description:

SGRQ-c is the COPD specific version of SGRQ. It consisted of 40 items in total, corresponding to 3 individual domains (components): symptoms, activity and impact, with different components carrying a different weighting. Component scores were calculated by summing the weights from all positive items in that component, dividing by the sum of maximum possible weights for all items in that component, and multiplying this number by 100. Impact component consisted of questions 8, 10, 11, 13, 14 in Part 2 of the questionnaire. Impact score has the range from 0 to 100. Higher scores indicated more severe disease impact. Day 1 (Pre-dose) was considered as a Baseline. Analysis was performed using ANCOVA model. Change from Baseline was calculated as post-dose visit value minus the Baseline value. Only those participants with data available at the specified data points were analyzed.

End point type	Secondary

End point timeframe:

Baseline (Day 1, Pre-dose), Day 90

End point values	Placebo- Female Participants	GSK2881078 1.0 mg- Female Participants	Placebo- Male Participants	GSK2881078 2.0 mg- Male Participants
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	21[208]	17[209]	18[210]	20[211]
Units: Scores on a scale				
least squares mean (standard error)	-2.8 (± 2.03)	0.6 (± 2.25)	-2.7 (± 1.76)	0.8 (± 1.67)

Notes:

[208] - Analysis Population

[209] - Analysis Population

[210] - Analysis Population

[211] - Analysis Population

Statistical analyses

Statistical analysis title	Statistical Analysis 1

Statistical analysis description:

Analysis was performed by ANCOVA model with Baseline impact score as the covariate adjusting for the treatment.

Comparison groups	Placebo- Female Participants v GSK2881078 1.0 mg- Female Participants
Number of subjects included in analysis	38
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Difference in Least Square Means
Point estimate	3.4
Confidence interval	
level	90 %
sides	2-sided
lower limit	-1.7
upper limit	8.6

Statistical analysis title	Statistical Analysis 1

Statistical analysis description:

Analysis was performed by ANCOVA model with Baseline impact score as the covariate adjusting for the treatment.

Comparison groups	Placebo- Male Participants v GSK2881078 2.0 mg- Male Participants
Number of subjects included in analysis	38
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Difference in Least Square Means
Point estimate	3.5
Confidence interval	
level	90 %
sides	2-sided
lower limit	-0.7
upper limit	7.7

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

End point title	Change from Baseline in forced expiratory volume in 1 second (FEV1)

End point description:

FEV1 is a measure of lung function and is defined as the maximal amount of air that can be forcefully exhaled in one second. FEV1 measurements were collected using a spirometer. Baseline was defined as the latest pre-dose assessment with a non-missing value, including those from unscheduled visits. Change from Baseline was calculated as post-dose visit value minus the Baseline value. Only those participants with data available at the specified data points were analyzed (represented by n=X in the category titles).

End point type	Secondary

End point timeframe:

Baseline (Day 1, Pre-dose), Days 56 and 90

End point values	Placebo-Female Participants	GSK2881078 1.0 mg-Female Participants	Placebo- Male Participants	GSK2881078 2.0 mg- Male Participants
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	21[212]	19[213]	21[214]	21[215]
Units: Liters				
arithmetic mean (standard deviation)				
Day 56,n=21,19,21,21	-0.000 (± 0.0918)	-0.028 (± 0.0747)	0.012 (± 0.1342)	-0.016 (± 0.2377)
Day 90,n=20,18,18,20	0.002 (± 0.0970)	-0.024 (± 0.0833)	0.050 (± 0.1130)	0.007 (± 0.2208)

Notes:

[212] - Analysis Population

[213] - Analysis Population

[214] - Analysis Population

[215] - Analysis Population

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in sniff nasal inspiratory pressure (SnIP)

End point title	Change from Baseline in sniff nasal inspiratory pressure (SnIP)

End point description:

A bung size-specific to the participant was placed in the nostril deemed to be most patent by the investigator. The participant was asked to make a maximum voluntary sniff effort via a peak flow meter and the greatest effort from 10 repeat measurements were recorded. SnIP was measured in centimeter of water (cm H2O). Baseline was defined as the latest pre-dose assessment with a non-missing value, including those from unscheduled visits. Change from Baseline was calculated as post-dose visit value minus the Baseline value. Only those participants with data available at the specified data points were analyzed (represented by n=X in the category titles).

End point type	Secondary

End point timeframe:

Baseline (Day 1, Pre-dose), Days 56 and 90

End point values	Placebo-Female Participants	GSK2881078 1.0 mg-Female Participants	Placebo- Male Participants	GSK2881078 2.0 mg- Male Participants
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	21[216]	19[217]	21[218]	21[219]
Units: centimeter of water				
arithmetic mean (standard deviation)				
Day 56,n=21,19,21,21	-6.0 (± 11.20)	3.4 (± 14.14)	0.7 (± 17.82)	-0.8 (± 15.51)
Day 90,n=20,18,18,20	-0.7 (± 8.55)	-0.4 (± 11.34)	-1.2 (± 15.21)	2.5 (± 21.39)

Notes:

[216] - Analysis Population

[217] - Analysis Population

[218] - Analysis Population

[219] - Analysis Population

Statistical analyses

No statistical analyses for this end point

Secondary: Clearance (CL) of GSK2881078 following oral dose in participants

End point title	Clearance (CL) of GSK2881078 following oral dose in participants[220]

End point description:

Blood samples were collected at designated timepoints. Pharmacokinetics (PK) parameters of GSK2881078 were calculated using non-compartmental methods. Pharmacokinetic Population comprised of participants in the 'All Participants (all randomized participants who received at least one dose of study medication)'' Population for whom a PK sample was obtained and analyzed for GSK2881078.

End point type	Secondary

End point timeframe:

Day 14 (Pre-dose), Day 28 (Pre-dose and at 1 to 4 hours Post-dose), Day 56 (at 5 to 8 hours Post-dose), Day 90 (Pre-dose)

Notes:

[220] - 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	GSK2881078 1.0 mg-Female Participants	GSK2881078 2.0 mg- Male Participants		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	21[221]	24[222]		
Units: Liters per hour				
geometric mean (geometric coefficient of variation)	0.393 (± 59.5)	0.476 (± 44.0)		

Notes:

[221] - Pharmacokinetic Population

[222] - Pharmacokinetic Population

Statistical analyses

No statistical analyses for this end point

Secondary: Volume of distribution at steady state (Vss) of GSK2881078 following oral dose in participants

End point title	Volume of distribution at steady state (Vss) of GSK2881078 following oral dose in participants[223]

End point description:

Blood samples were collected at designated timepoints. PK parameters of GSK2881078 were calculated using non-compartmental methods.

End point type	Secondary

End point timeframe:

Day 14 (Pre-dose), Day 28 (Pre-dose and at 1 to 4 hours Post-dose), Day 56 (at 5 to 8 hours Post-dose), Day 90 (Pre-dose)

Notes:

[223] - 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	GSK2881078 1.0 mg- Female Participants	GSK2881078 2.0 mg- Male Participants		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	21[224]	24[225]		
Units: Liters				
geometric mean (geometric coefficient of variation)	39.4 (± 16.3)	48.3 (± 29.8)		

Notes:

[224] - Pharmacokinetic Population

[225] - Pharmacokinetic Population

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Serious adverse events (SAEs) and non-serious AEs were collected from the start of study treatment until up to Day 132

Adverse event reporting additional description:

SAEs and non-serious AEs were reported for the Safety Population which comprised of all randomized participants who received at least one dose of study medication. This population was based on the treatment the participant received.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	22.0

Reporting groups

Reporting group title	Placebo- Female Participants

Reporting group description:

Post-menopausal female participants, 50 to 75 years of age, were administered orally two capsules of GSK2881078 matching placebo once daily over 13 weeks

Reporting group title	GSK2881078 1.0 mg- Female Participants

Reporting group description:

Post-menopausal female participants, 50 to 75 years of age, were administered orally two capsules of GSK2881078 of a unit dose strength 0.5 milligram (mg) once daily over 13 weeks

Reporting group title	Placebo- Male Participants

Reporting group description:

Male participants, 50 to 75 years of age, were administered orally two capsules of GSK2881078 matching placebo once daily over 13 weeks

Reporting group title	GSK2881078 2.0 mg- Male Participants

Reporting group description:

Male participants, 50 to 75 years of age, were administered orally two capsules of GSK2881078 of a unit dose strength 1.0 mg once daily over 13 weeks

Serious adverse events	Placebo- Female Participants	GSK2881078 1.0 mg- Female Participants	Placebo- Male Participants
Total subjects affected by serious adverse events			
subjects affected / exposed	1 / 23 (4.35%)	2 / 24 (8.33%)	2 / 24 (8.33%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events			
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Adenocarcinoma of colon			
subjects affected / exposed	0 / 23 (0.00%)	0 / 24 (0.00%)	1 / 24 (4.17%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac disorders			

Myocardial infarction			
subjects affected / exposed	0 / 23 (0.00%)	1 / 24 (4.17%)	0 / 24 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatobiliary disorders			
Cholecystitis acute			
subjects affected / exposed	0 / 23 (0.00%)	1 / 24 (4.17%)	0 / 24 (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
Infections and infestations			
Diverticulitis			
subjects affected / exposed	0 / 23 (0.00%)	0 / 24 (0.00%)	1 / 24 (4.17%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infective exacerbation of chronic obstructive airways disease			
subjects affected / exposed	1 / 23 (4.35%)	0 / 24 (0.00%)	0 / 24 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	GSK2881078 2.0 mg- Male Participants		
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 25 (0.00%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events			
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Adenocarcinoma of colon			
subjects affected / exposed	0 / 25 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Cardiac disorders			
Myocardial infarction			
subjects affected / exposed	0 / 25 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		

Hepatobiliary disorders			
Cholecystitis acute			
subjects affected / exposed	0 / 25 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Infections and infestations			
Diverticulitis			
subjects affected / exposed	0 / 25 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Infective exacerbation of chronic obstructive airways disease			
subjects affected / exposed	0 / 25 (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: 2 %

Non-serious adverse events	Placebo- Female Participants	GSK2881078 1.0 mg- Female Participants	Placebo- Male Participants
Total subjects affected by non-serious adverse events			
subjects affected / exposed	15 / 23 (65.22%)	18 / 24 (75.00%)	13 / 24 (54.17%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Adrenal adenoma			
subjects affected / exposed	0 / 23 (0.00%)	0 / 24 (0.00%)	1 / 24 (4.17%)
occurrences (all)	0	0	1
Vascular disorders			
Hypertension			
subjects affected / exposed	0 / 23 (0.00%)	1 / 24 (4.17%)	2 / 24 (8.33%)
occurrences (all)	0	1	2
Haematoma			
subjects affected / exposed	1 / 23 (4.35%)	1 / 24 (4.17%)	0 / 24 (0.00%)
occurrences (all)	1	1	0
Hypotension			
subjects affected / exposed	0 / 23 (0.00%)	0 / 24 (0.00%)	2 / 24 (8.33%)
occurrences (all)	0	0	2
General disorders and administration			

site conditions			
Chest pain			
subjects affected / exposed	0 / 23 (0.00%)	0 / 24 (0.00%)	1 / 24 (4.17%)
occurrences (all)	0	0	1
Fatigue			
subjects affected / exposed	1 / 23 (4.35%)	0 / 24 (0.00%)	0 / 24 (0.00%)
occurrences (all)	1	0	0
Non-cardiac chest pain			
subjects affected / exposed	1 / 23 (4.35%)	0 / 24 (0.00%)	1 / 24 (4.17%)
occurrences (all)	1	0	1
Respiratory, thoracic and mediastinal disorders			
Chronic obstructive pulmonary disease			
subjects affected / exposed	6 / 23 (26.09%)	7 / 24 (29.17%)	2 / 24 (8.33%)
occurrences (all)	6	8	2
Epistaxis			
subjects affected / exposed	0 / 23 (0.00%)	0 / 24 (0.00%)	2 / 24 (8.33%)
occurrences (all)	0	0	2
Dyspnoea			
subjects affected / exposed	1 / 23 (4.35%)	0 / 24 (0.00%)	1 / 24 (4.17%)
occurrences (all)	1	0	1
Pulmonary mass			
subjects affected / exposed	0 / 23 (0.00%)	0 / 24 (0.00%)	1 / 24 (4.17%)
occurrences (all)	0	0	1
Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	0 / 23 (0.00%)	1 / 24 (4.17%)	0 / 24 (0.00%)
occurrences (all)	0	1	0
Aspartate aminotransferase increased			
subjects affected / exposed	0 / 23 (0.00%)	1 / 24 (4.17%)	0 / 24 (0.00%)
occurrences (all)	0	1	0
Blood 25-hydroxycholecalciferol decreased			
subjects affected / exposed	0 / 23 (0.00%)	2 / 24 (8.33%)	0 / 24 (0.00%)
occurrences (all)	0	2	0
Low density lipoprotein increased			

subjects affected / exposed	0 / 23 (0.00%)	1 / 24 (4.17%)	0 / 24 (0.00%)
occurrences (all)	0	1	0
Injury, poisoning and procedural complications			
Contusion			
subjects affected / exposed	3 / 23 (13.04%)	1 / 24 (4.17%)	0 / 24 (0.00%)
occurrences (all)	3	1	0
Muscle strain			
subjects affected / exposed	0 / 23 (0.00%)	1 / 24 (4.17%)	1 / 24 (4.17%)
occurrences (all)	0	1	1
Nervous system disorders			
Headache			
subjects affected / exposed	0 / 23 (0.00%)	2 / 24 (8.33%)	0 / 24 (0.00%)
occurrences (all)	0	2	0
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	1 / 23 (4.35%)	0 / 24 (0.00%)	1 / 24 (4.17%)
occurrences (all)	1	0	1
Abdominal pain upper			
subjects affected / exposed	0 / 23 (0.00%)	1 / 24 (4.17%)	1 / 24 (4.17%)
occurrences (all)	0	1	1
Constipation			
subjects affected / exposed	0 / 23 (0.00%)	1 / 24 (4.17%)	0 / 24 (0.00%)
occurrences (all)	0	1	0
Nausea			
subjects affected / exposed	1 / 23 (4.35%)	1 / 24 (4.17%)	0 / 24 (0.00%)
occurrences (all)	1	1	0
Skin and subcutaneous tissue disorders			
Dry skin			
subjects affected / exposed	1 / 23 (4.35%)	1 / 24 (4.17%)	0 / 24 (0.00%)
occurrences (all)	1	1	0
Pruritus			
subjects affected / exposed	0 / 23 (0.00%)	1 / 24 (4.17%)	0 / 24 (0.00%)
occurrences (all)	0	1	0
Renal and urinary disorders			
Haematuria			

subjects affected / exposed	0 / 23 (0.00%)	1 / 24 (4.17%)	0 / 24 (0.00%)
occurrences (all)	0	1	0
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	0 / 23 (0.00%)	3 / 24 (12.50%)	2 / 24 (8.33%)
occurrences (all)	0	5	2
Muscle spasms			
subjects affected / exposed	1 / 23 (4.35%)	2 / 24 (8.33%)	0 / 24 (0.00%)
occurrences (all)	1	2	0
Back pain			
subjects affected / exposed	0 / 23 (0.00%)	3 / 24 (12.50%)	0 / 24 (0.00%)
occurrences (all)	0	3	0
Musculoskeletal chest pain			
subjects affected / exposed	0 / 23 (0.00%)	1 / 24 (4.17%)	0 / 24 (0.00%)
occurrences (all)	0	1	0
Musculoskeletal Pain			
subjects affected / exposed	1 / 23 (4.35%)	1 / 24 (4.17%)	0 / 24 (0.00%)
occurrences (all)	1	1	0
Neck pain			
subjects affected / exposed	1 / 23 (4.35%)	0 / 24 (0.00%)	1 / 24 (4.17%)
occurrences (all)	1	0	1
Infections and infestations			
Nasopharyngitis			
subjects affected / exposed	5 / 23 (21.74%)	2 / 24 (8.33%)	1 / 24 (4.17%)
occurrences (all)	5	3	1
Urinary tract infection			
subjects affected / exposed	1 / 23 (4.35%)	1 / 24 (4.17%)	0 / 24 (0.00%)
occurrences (all)	1	1	0
Sinusitis			
subjects affected / exposed	0 / 23 (0.00%)	0 / 24 (0.00%)	1 / 24 (4.17%)
occurrences (all)	0	0	1
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	0 / 23 (0.00%)	0 / 24 (0.00%)	1 / 24 (4.17%)
occurrences (all)	0	0	1

Non-serious adverse events	GSK2881078 2.0 mg- Male Participants		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	17 / 25 (68.00%)		
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Adrenal adenoma			
subjects affected / exposed	1 / 25 (4.00%)		
occurrences (all)	1		
Vascular disorders			
Hypertension			
subjects affected / exposed	0 / 25 (0.00%)		
occurrences (all)	0		
Haematoma			
subjects affected / exposed	0 / 25 (0.00%)		
occurrences (all)	0		
Hypotension			
subjects affected / exposed	0 / 25 (0.00%)		
occurrences (all)	0		
General disorders and administration site conditions			
Chest pain			
subjects affected / exposed	1 / 25 (4.00%)		
occurrences (all)	1		
Fatigue			
subjects affected / exposed	1 / 25 (4.00%)		
occurrences (all)	1		
Non-cardiac chest pain			
subjects affected / exposed	0 / 25 (0.00%)		
occurrences (all)	0		
Respiratory, thoracic and mediastinal disorders			
Chronic obstructive pulmonary disease			
subjects affected / exposed	3 / 25 (12.00%)		
occurrences (all)	4		
Epistaxis			
subjects affected / exposed	1 / 25 (4.00%)		
occurrences (all)	1		
Dyspnoea			

subjects affected / exposed	0 / 25 (0.00%)		
occurrences (all)	0		
Pulmonary mass			
subjects affected / exposed	1 / 25 (4.00%)		
occurrences (all)	1		
Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	2 / 25 (8.00%)		
occurrences (all)	2		
Aspartate aminotransferase increased			
subjects affected / exposed	1 / 25 (4.00%)		
occurrences (all)	1		
Blood 25-hydroxycholecalciferol decreased			
subjects affected / exposed	0 / 25 (0.00%)		
occurrences (all)	0		
Low density lipoprotein increased			
subjects affected / exposed	1 / 25 (4.00%)		
occurrences (all)	1		
Injury, poisoning and procedural complications			
Contusion			
subjects affected / exposed	0 / 25 (0.00%)		
occurrences (all)	0		
Muscle strain			
subjects affected / exposed	0 / 25 (0.00%)		
occurrences (all)	0		
Nervous system disorders			
Headache			
subjects affected / exposed	2 / 25 (8.00%)		
occurrences (all)	2		
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	1 / 25 (4.00%)		
occurrences (all)	1		
Abdominal pain upper			

subjects affected / exposed	0 / 25 (0.00%)		
occurrences (all)	0		
Constipation			
subjects affected / exposed	1 / 25 (4.00%)		
occurrences (all)	1		
Nausea			
subjects affected / exposed	0 / 25 (0.00%)		
occurrences (all)	0		
Skin and subcutaneous tissue disorders			
Dry skin			
subjects affected / exposed	1 / 25 (4.00%)		
occurrences (all)	1		
Pruritus			
subjects affected / exposed	1 / 25 (4.00%)		
occurrences (all)	1		
Renal and urinary disorders			
Haematuria			
subjects affected / exposed	1 / 25 (4.00%)		
occurrences (all)	1		
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	2 / 25 (8.00%)		
occurrences (all)	2		
Muscle spasms			
subjects affected / exposed	3 / 25 (12.00%)		
occurrences (all)	3		
Back pain			
subjects affected / exposed	2 / 25 (8.00%)		
occurrences (all)	3		
Musculoskeletal chest pain			
subjects affected / exposed	2 / 25 (8.00%)		
occurrences (all)	2		
Musculoskeletal Pain			
subjects affected / exposed	1 / 25 (4.00%)		
occurrences (all)	1		
Neck pain			

subjects affected / exposed occurrences (all)	0 / 25 (0.00%) 0		
Infections and infestations Nasopharyngitis subjects affected / exposed occurrences (all) Urinary tract infection subjects affected / exposed occurrences (all) Sinusitis subjects affected / exposed occurrences (all)	 1 / 25 (4.00%) 2 1 / 25 (4.00%) 2 1 / 25 (4.00%) 1		
Metabolism and nutrition disorders Decreased appetite subjects affected / exposed occurrences (all)	 1 / 25 (4.00%) 1		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
19 May 2017	Amendment 01: Removal of reference to measurement of lumbar bone density in the risk mitigation strategy for bone effects in section: risk assessment; removal of reference to measurement of lumbar bone density in section: dual-energy X-ray absorptiometry (DXA)
22 August 2017	Amendment 02: Removal of the stair climb test as a secondary endpoint in the study; removal of the requirements for vitamin D deficiency as an exclusion criteria; removal of reference to an independent monitoring committee; deletion of erroneous text describing supply of study drug to the participant at Day 90; reference to whole body multiple resonance imaging (MRI) removed and replaced with 'cardiac and liver MRI (additionally prostate MRI in males) for clarity; edits to clarify that only the safety assessments at the follow-up visit would be conducted in case of withdrawal from the study; wording to clarify that any chronic obstructive pulmonary disease exacerbation that requires steroid use requires participants to withdraw from the study; clarification in the duration of necessary contraception use following participation in the study.
11 October 2017	Amendment 03: Removal of inspiratory capacity as an endpoint, as well as peak oxygen uptake measurements during the shuttle walk tests; previous guidance prohibiting concomitant use of cytochrome P-450 isoenzyme 3A4 (CYP3A4) inhibitors was removed.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported