Clinical trial results:
A randomized, double-blind, placebo-controlled, parallel group, dose ranging study to assess the effect of repeat doses of GSK962040 on the pharmacokinetics of levodopa in subjects with Parkinson's disease exhibiting delayed gastric emptying

Summary

EudraCT number	2011-004438-32
Trial protocol	GB SE DE
Global end of trial date	01 May 2014

Results information

Result version number	v1 (current)
This version publication date	29 February 2016
First version publication date	27 December 2014

Trial information

Trial identification

Sponsor protocol code	MOT115816

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, 1 866-435-7343,
Scientific contact	GSK Response Center, GlaxoSmithKline, 1 866-435-7343,

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	01 May 2014
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	01 May 2014
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To measure the effect of co-administration of GSK962040 on levodopa pharmacokinetic exposure in subjects with Parkinson’s disease with delayed gastric emptying

Protection of trial subjects:

Not applicable.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	06 July 2012
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	Sweden: 10
Country: Number of subjects enrolled	United Kingdom: 25
Country: Number of subjects enrolled	Germany: 23
Country: Number of subjects enrolled	Australia: 1
Worldwide total number of subjects	59
EEA total number of subjects	58

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)	16
From 65 to 84 years	43
85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

The study consisted of a Screening/Baseline Period, a Treatment Period, and a 14-day post-treatment safety Follow-up Visit. Participants were randomized to receive GSK962040 50 milligrams or placebo in a 2:1 ratio; one participant was randomized to receive GSK962040 125 mg.

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	Placebo

Arm description:

Participants received placebo administered orally once daily for 7 to 9 days.

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

Dosage and administration details:

2x25 mg placebo tablets, once daily, 8 days; 1x125 mg placebo tablet, once daily, 8 days (2 subjects only)

Arm title	GSK962040 Total

Arm description:

Participants received GSK962040 50 milligrams (mg) (except for one participant who received GSK962040 125 mg) administered orally once daily for 7 to 9 days.

Arm type	Experimental
Investigational medicinal product name	GSK962040 (camicinal) 50 mg
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

2x25 mg tablets, once daily, 8 days; 1x125 mg tablet, once daily, 8 days (1 subject only)

Number of subjects in period 1[1]	Placebo	GSK962040 Total
Started	19	38
Completed	18	37
Not completed	1	1
Consent withdrawn by subject	1	-
Protocol deviation	-	1

Notes:

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

Justification: Baseline characteristic data are reported for members of the All Subjects Population, which is defined as all participants who received at least one dose of study medication. Not all enrolled participants were members of the All Subjects Population.

Baseline characteristics

Reporting groups	
Reporting group title	Placebo
Reporting group description:	
Participants received placebo administered orally once daily for 7 to 9 days.	
Reporting group title	GSK962040 Total
Reporting group description:	
Participants received GSK962040 50 milligrams (mg) (except for one participant who received GSK962040 125 mg) administered orally once daily for 7 to 9 days.	

Reporting group values	Placebo	GSK962040 Total	Total
Number of subjects	19	38	57
Age categorical			
Units: Subjects			
In utero			0
Preterm newborn infants (gestational age < 37 wks)			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)			0
From 65-84 years			0
85 years and over			0
Age continuous			
Units: years			
arithmetic mean	66.7	67.4	
standard deviation	± 8.04	± 7.97	-
Gender categorical			
Units: Subjects			
Female	11	9	20
Male	8	29	37
Race, customized			
Units: Subjects			
White - White/Caucasian/European Heritage	19	38	57

End points

End points reporting groups

Reporting group title	Placebo
Reporting group description:	
Participants received placebo administered orally once daily for 7 to 9 days.	
Reporting group title	GSK962040 Total
Reporting group description:	
Participants received GSK962040 50 milligrams (mg) (except for one participant who received GSK962040 125 mg) administered orally once daily for 7 to 9 days.	
Subject analysis set title	Placebo
Subject analysis set type	Sub-group analysis
Subject analysis set description:	
Participants received placebo administered orally once daily for 7 to 9 days.	
Subject analysis set title	GSK962040 50 mg
Subject analysis set type	Sub-group analysis
Subject analysis set description:	
Participants received GSK962040 50 milligrams (mg) administered orally once daily for 7 to 9 days.	
Subject analysis set title	GSK962040 Total
Subject analysis set type	Sub-group analysis
Subject analysis set description:	
Participants received GSK962040 50 milligrams (mg) (except for one participant who received GSK962040 125 mg) administered orally once daily for 7 to 9 days.	

Primary: Dose-normalized levodopa (L-DOPA) area under the plasma concentration-time curve from zero to 4 hours AUC(0-4) at Baseline

End point title	Dose-normalized levodopa (L-DOPA) area under the plasma concentration-time curve from zero to 4 hours AUC(0-4) at Baseline[1]
End point description:	
Dose-normalized L-DOPA AUC(0-4) was derived from L-DOPA plasma concentration-time data. AUC is a measure of levodopa exposure.	
End point type	Primary
End point timeframe:	
Baseline	

Notes:

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

End point values	Placebo	GSK962040 50 mg		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	17[2]	33[3]		
Units: Nanograms*hour/milliliter/milligram				
geometric mean (geometric coefficient of variation)	24.13 (± 37.5)	24.81 (± 36.1)		

Notes:

[2] - Pharmacodynamic (PD)/Efficacy Population: participants receiving >=1 dose placebo/GSK962040 50 mg
[3] - Pharmacodynamic (PD)/Efficacy Population: participants receiving >=1 dose placebo/GSK962040 50 mg

Statistical analyses

No statistical analyses for this end point

Primary: Dose-normalized L-DOPA AUC(0-4) at Day 1 and Day 8

End point title	Dose-normalized L-DOPA AUC(0-4) at Day 1 and Day 8

End point description:

Dose-normalized L-DOPA AUC(0-4) was derived from L-DOPA plasma concentration-time data. The adjusted means and ratios (GSK962040 50 mg: Placebo) were estimated using a mixed model fitting treatment, visit, treatment*visit, Baseline L-dopa pharmacokinetic (PK) parameter, and Baseline gastric emptying half-time as fixed effects, and participant as a random effect. AUC is a measure of levodopa exposure.

End point type	Primary

End point timeframe:

Day 1 and Day 8

End point values	Placebo	GSK962040 50 mg		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	19[4]	37[5]		
Units: Nanograms*hour/milliliter/milligram				
least squares mean (standard error)				
Day 1, n=17, 31	26.6 (± 0.058)	25.7 (± 0.047)		
Day 8, n=17, 32	27.1 (± 0.058)	24.1 (± 0.047)		

Notes:

[4] - PD/Efficacy Population. Participants with available data (n=X, X in category titles) were analyzed.

[5] - PD/Efficacy Population. Participants with available data (n=X, X in category titles) were analyzed.

Statistical analyses

Statistical analysis title	Day 1

Statistical analysis description:

Day 1: The adjusted means (AMs) and ratios were estimated using a mixed model (MM) fitting treatment, visit, treatment*visit, Baseline L-dopa PK parameter and Baseline gastric emptying half time as fixed effects, and participant as a random effect.

Comparison groups	Placebo v GSK962040 50 mg
Number of subjects included in analysis	56
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	Ratio of adjusted geometric means
Point estimate	0.965
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.831
upper limit	1.12

Statistical analysis title	Day 8

Statistical analysis description:

Day 8: The AMs and ratios were estimated using a mixed model fitting treatment, visit, treatment*visit, Baseline L-dopa PK parameter and Baseline gastric emptying half time as fixed effects, and participant as a random effect.

Comparison groups	Placebo v GSK962040 50 mg
Number of subjects included in analysis	56
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	Ratio of adjusted geometric means
Point estimate	0.886
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.763
upper limit	1.029

Primary: Dose-normalized L-DOPA maximum observed concentration (Cmax) at Baseline

End point title	Dose-normalized L-DOPA maximum observed concentration (Cmax) at Baseline[6]

End point description:

Dose-normalized L-DOPA Cmax was derived from L-DOPA plasma concentration-time data.

End point type	Primary

End point timeframe:

Baseline

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: No statistical analysis was performed for this endpoint at Baseline.

End point values	Placebo	GSK962040 50 mg		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	17[7]	35[8]		
Units: Nanograms/milliliter/milligram				
geometric mean (geometric coefficient of variation)	12.77 (± 28)	12.89 (± 42.6)		

Notes:

[7] - PD/Efficacy Population. Only those participants available at the specified time point were analyzed.

[8] - PD/Efficacy Population. Only those participants available at the specified time point were analyzed.

Statistical analyses

No statistical analyses for this end point

Primary: Dose-normalized L-DOPA Cmax at Day 1 and Day 8

End point title	Dose-normalized L-DOPA Cmax at Day 1 and Day 8

End point description:

Dose-normalized L-DOPA Cmax was derived from L-DOPA plasma concentration-time data. The adjusted means and ratios were estimated using a mixed model fitting treatment, visit, treatment*visit, Baseline L-dopa PK parameter, and Baseline gastric emptying half-time as fixed effects, and participant as a random effect.

End point type	Primary

End point timeframe:

Day 1 and Day 8

End point values	Placebo	GSK962040 50 mg		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	19[9]	37[10]		
Units: Nanograms/milliliter/milligram				
least squares mean (standard error)				
Day 1, n=18, 35	13.4 (± 0.081)	11.6 (± 0.065)		
Day 8, n=17, 35	11.6 (± 0.083)	11.8 (± 0.065)		

Notes:

[9] - PD/Efficacy Population. Participants with available data (n=X, X in category titles) were analyzed.

[10] - PD/Efficacy Population. Participants with available data (n=X, X in category titles) were analyzed.

Statistical analyses

Statistical analysis title	Day 1

Statistical analysis description:

Day 1: The AMs and ratios were estimated using a mixed model fitting treatment, visit, treatment*visit, Baseline L-dopa PK parameter and Baseline gastric emptying half time as fixed effects, and participant as a random effect.

Comparison groups	Placebo v GSK962040 50 mg
Number of subjects included in analysis	56
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	Ratio of adjusted geometric means
Point estimate	0.864
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.702
upper limit	1.064

Statistical analysis title	Day 8

Statistical analysis description:

Day 8: The AMs and ratios were estimated using a mixed model fitting treatment, visit, treatment*visit, Baseline L-dopa PK parameter and Baseline gastric emptying half time as fixed effects, and participant as a random effect.

Comparison groups	Placebo v GSK962040 50 mg
Number of subjects included in analysis	56
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	Ratio of adjusted geometric means
Point estimate	1.018

Confidence interval	
level	95 %
sides	2-sided
lower limit	0.824
upper limit	1.257

Primary: L-DOPA time of occurrence of Cmax (Tmax) at Baseline, Day 1,and Day 8

End point title	L-DOPA time of occurrence of Cmax (Tmax) at Baseline, Day 1,and Day 8

End point description:

L-DOPA Tmax was derived from L-DOPA plasma concentration-time data.

End point type	Primary

End point timeframe:

Baseline, Day 1, and Day 8

End point values	Placebo	GSK962040 50 mg		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	19[11]	37[12]		
Units: Hours				
median (full range (min-max))				
Baseline, n=17, 35	1.5 (0.3 to 3.6)	2 (0.3 to 4)		
Day 1, n=18, 35	1.61 (0.5 to 3.4)	1.5 (0.3 to 3.5)		
Day 8, n=17, 35	2 (0.5 to 3.5)	1.55 (0.3 to 4)		

Notes:

[11] - PD/Efficacy Population. Participants with available data (n=X, X in category titles) were analyzed.

[12] - PD/Efficacy Population. Participants with available data (n=X, X in category titles) were analyzed.

Statistical analyses

Statistical analysis title	Day 1
Comparison groups	Placebo v GSK962040 50 mg
Number of subjects included in analysis	56
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.157
Method	Wilcoxon rank-sum test

Statistical analysis title	Day 8
Comparison groups	Placebo v GSK962040 50 mg

Number of subjects included in analysis	56
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.186
Method	Wilcoxon rank-sum test

Primary: L-DOPA terminal phase half-life (t1/2) at Baseline, Day 1, and Day 8

End point title	L-DOPA terminal phase half-life (t1/2) at Baseline, Day 1, and Day 8[13]

End point description:

L-DOPA t1/2 was derived from L-DOPA plasma concentration-time data. This endpoint was not assessed because there were insufficient L-DOPA data/profiles to calculate this parameter.

End point type	Primary

End point timeframe:

Baseline, Day 1, and Day 8

Notes:

[13] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: No statistical analysis was performed for this endpoint.

End point values	Placebo	GSK962040 50 mg		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	0[14]	0[15]		
Units: Hours				
median (full range (min-max))	(to)	(to)		

Notes:

[14] - PD/Efficacy Population

[15] - PD/Efficacy Population

Statistical analyses

No statistical analyses for this end point

Secondary: Gastric half emptying time (GE t1/2) at Baseline (BL), Day 1, and Day 8

End point title	Gastric half emptying time (GE t1/2) at Baseline (BL), Day 1, and Day 8

End point description:

Gastric half emptying time is the time taken for half the contents of the stomach to empty. Gastric emptying was measured using the 13C-oral breath test, which is a tracer method that utilizes 13C, a non-radioactive isotope. Basal breath samples were obtained after an overnight fast or otherwise after 4 hours of fasting following a light meal. On Day 1 and Day 8, participants were then dosed with GSK962040 and additional breath test samples were taken prior to administration of a 13C-labelled test meal. The test meal was consumed approximately 80 minutes later. After consumption of the test meal, breath samples were collected at pre-specified time points over an approximately 4 hour period following the test meal. For the duration of the breath test, no food or drink were allowed. The 13C breath content was determined by isotope ratio mass spectrometry. GE t1/2 was determined by using the cumulative percentage of the administered dose of 13C excreted in breath over 4 hours.

End point type	Secondary

End point timeframe:

Baseline, Day 1, and Day 8

End point values	Placebo	GSK962040 50 mg		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	19[16]	37[17]		
Units: Minutes				
arithmetic mean (standard deviation)				
Baseline, n=19, 37	99.6 (± 21.26)	96.9 (± 21.67)		
Day 1, n=19, 37	97.5 (± 15.81)	91.9 (± 21.47)		
Day 8, n=17, 36	98.7 (± 25.03)	90.6 (± 26.75)		

Notes:

[16] - PD/Efficacy Population. Participants with available data (n=X, X in category titles) were analyzed.

[17] - PD/Efficacy Population. Participants with available data (n=X, X in category titles) were analyzed.

Statistical analyses

Statistical analysis title	Day 1

Statistical analysis description:

Day 1: The AMs and differences (GSK962040 minus Placebo) were estimated using a mixed model fitting treatment, visit, treatment*visit, and Baseline gastric half emptying time as fixed effects, and participant as a random effect.

Comparison groups	GSK962040 50 mg v Placebo
Number of subjects included in analysis	56
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	Difference in AMs of change from BL
Point estimate	-4.239
Confidence interval	
level	95 %
sides	2-sided
lower limit	-16.015
upper limit	7.537

Statistical analysis title	Day 8

Statistical analysis description:

Day 8: The AMs and differences (GSK962040 minus Placebo) were estimated using a mixed model fitting treatment, visit, treatment*visit, and Baseline gastric half emptying time as fixed effects, and participant as a random effect.

Comparison groups	Placebo v GSK962040 50 mg
Number of subjects included in analysis	56
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	Difference in AMs of change from BL
Point estimate	-5.327

Confidence interval	
level	95 %
sides	2-sided
lower limit	-17.567
upper limit	6.914

Secondary: Movement Disorder Society-Unified Parkinson's Disease Rating Scale (MDS-UPDRS) scores at Baseline, Day 1, and Day 8 (pre-levodopa dose)

End point title	Movement Disorder Society-Unified Parkinson's Disease Rating Scale (MDS-UPDRS) scores at Baseline, Day 1, and Day 8 (pre-levodopa dose)

End point description:

The MDS-UPDRS is used to assess the status of Parkinson's Disease. It has four parts: Part I (non-motor experiences of daily living), Part II (motor experiences of daily living), Part III (motor examination), and Part IV (motor complications). Each part is made up of several questions, with each question given a score ranging from 0 (normal) to 4 (severe). Part I and Part II consist of 13 items each, and have a score ranging between 0 (normal) and 52 (severe). Part III consists of 33 items, and has a score ranging between 0 (normal) and 132 (severe). Part IV consists of 6 items, and has a score ranging between 0 (normal) and 24 (severe). The total score is the summed score of all four parts and ranges between 0 (normal) and 260 (severe). A higher score indicates more severe symptoms.

End point type	Secondary

End point timeframe:

Baseline, Day 1, and Day 8 at pre-levodopa dose

End point values	Placebo	GSK962040 50 mg		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	19[18]	37[19]		
Units: Scores on a scale				
arithmetic mean (standard deviation)				
Part I: Baseline, n=19, 37	9.1 (± 4.56)	10.1 (± 6.17)		
Part I: Day 1, n=19, 37	10.1 (± 4.98)	8.6 (± 5.12)		
Part I: Day 8, n=18, 36	10 (± 5.25)	7.1 (± 4.67)		
Part II: Baseline, n=19, 37	14.9 (± 7.09)	12.5 (± 6.33)		
Part II: Day 1, n=19, 37	16.1 (± 9.09)	11.5 (± 6.54)		
Part II: Day 8, n=18, 36	15.3 (± 9.29)	10.3 (± 6.37)		
Part III: Baseline, n=19, 37	42.2 (± 14.63)	38 (± 18.95)		
Part III: Day 1, n=19, 37	40.4 (± 17.56)	34.9 (± 17.97)		
Part III: Day 8, n=18, 36	44.2 (± 19.25)	34 (± 17.46)		
Part IV: Baseline, n=19, 37	5.5 (± 2.7)	5.3 (± 3.63)		
Part IV: Day 1, n=19, 37	5.9 (± 3.07)	5.2 (± 3.61)		
Part IV: Day 8, n=18, 36	5.7 (± 3.79)	4.5 (± 3.41)		
Total: Baseline, n=19, 37	71.7 (± 23.53)	65.8 (± 27.02)		
Total: Day 1, n=19, 37	72.5 (± 29.01)	60.2 (± 25.9)		
Total: Day 8, n=18, 36	75.2 (± 34.27)	55.9 (± 25.34)		

Notes:

[18] - PD/Efficacy Population. Participants with available data (n=X, X in category titles) were analyzed.

[19] - PD/Efficacy Population. Participants with available data (n=X, X in category titles) were analyzed.

Statistical analyses

Statistical analysis title	Day 1; Part I

Statistical analysis description:

Day 1; Part I: The AMs and differences (GSK 962040 minus Placebo) were estimated using a mixed model fitting treatment, visit, treatment*visit interaction, and Baseline MDS-UPDR score as fixed effects, and participant as a random effect.

Comparison groups	Placebo v GSK962040 50 mg
Number of subjects included in analysis	56
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	Difference in AMs of change from BL
Point estimate	-2.16
Confidence interval	
level	95 %
sides	2-sided
lower limit	-3.9
upper limit	-0.41

Statistical analysis title	Day 8; Part I

Statistical analysis description:

Day 8; Part I: The AMs and differences (GSK 962040 minus Placebo) were estimated using a mixed model fitting treatment, visit, treatment*visit interaction, and Baseline MDS-UPDR score as fixed effects, and participant as a random effect.

Comparison groups	Placebo v GSK962040 50 mg
Number of subjects included in analysis	56
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	Difference in AMs of change from BL
Point estimate	-3.63
Confidence interval	
level	95 %
sides	2-sided
lower limit	-5.41
upper limit	-1.85

Statistical analysis title	Day 1; Part II

Statistical analysis description:

Day 1; Part II: The AMs and differences (GSK 962040 minus Placebo) were estimated using a mixed model fitting treatment, visit, treatment*visit interaction, and Baseline MDS-UPDR score as fixed effects, and participant as a random effect.

Comparison groups	Placebo v GSK962040 50 mg

Number of subjects included in analysis	56
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	Difference in AMs of change from BL
Point estimate	-2.29
Confidence interval	
level	95 %
sides	2-sided
lower limit	-4.65
upper limit	0.07

Statistical analysis title	Day 8; Part II

Statistical analysis description:

Day 8; Part II: The AMs and differences (GSK 962040 minus Placebo) were estimated using a mixed model fitting treatment, visit, treatment*visit interaction, and Baseline MDS-UPDR score as fixed effects, and participant as a random effect.

Comparison groups	Placebo v GSK962040 50 mg
Number of subjects included in analysis	56
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	Difference in AMs of change from BL
Point estimate	-2.46
Confidence interval	
level	95 %
sides	2-sided
lower limit	-4.85
upper limit	-0.07

Statistical analysis title	Day 1; Part III

Statistical analysis description:

Day 1; Part III: The AMs and differences (GSK 962040 minus Placebo) were estimated using a mixed model fitting treatment, visit, treatment*visit interaction, and Baseline MDS-UPDR score as fixed effects, and participant as a random effect.

Comparison groups	Placebo v GSK962040 50 mg
Number of subjects included in analysis	56
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	Difference in AMs of change from BL
Point estimate	-1.7
Confidence interval	
level	95 %
sides	2-sided
lower limit	-6.53
upper limit	3.13

Statistical analysis title	Day 8; Part III
Statistical analysis description:	
Day 8; Part III: The AMs and differences (GSK 962040 minus Placebo) were estimated using a mixed model fitting treatment, visit, treatment*visit interaction, and Baseline MDS-UPDR score as fixed effects, and participant as a random effect.	
Comparison groups	Placebo v GSK962040 50 mg
Number of subjects included in analysis	56
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	Difference in AMs of change from BL
Point estimate	-5.38
Confidence interval	
level	95 %
sides	2-sided
lower limit	-10.28
upper limit	-0.49

Statistical analysis title	Day 1; Part IV
Statistical analysis description:	
Day 1; Part IV: The AMs and differences (GSK 962040 minus Placebo) were estimated using a mixed model fitting treatment, visit, treatment*visit interaction, and Baseline MDS-UPDR score as fixed effects, and participant as a random effect.	
Comparison groups	Placebo v GSK962040 50 mg
Number of subjects included in analysis	56
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	Difference in AMs of change from BL
Point estimate	-0.56
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.65
upper limit	0.54

Statistical analysis title	Day 8; Part IV
Statistical analysis description:	
Day 8; Part IV: The AMs and differences (GSK 962040 minus Placebo) were estimated using a mixed model fitting treatment, visit, treatment*visit interaction, and Baseline MDS-UPDR score as fixed effects, and participant as a random effect.	
Comparison groups	Placebo v GSK962040 50 mg
Number of subjects included in analysis	56
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	Difference in AMs of change from BL
Point estimate	-0.9

Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.02
upper limit	0.22

Statistical analysis title	Day 1; Total

Statistical analysis description:

Day 1; Total: The AMs and differences (GSK 962040 minus Placebo) were estimated using a mixed model fitting treatment, visit, treatment*visit interaction, and Baseline MDS-UPDR score as fixed effects, and participant as a random effect.

Comparison groups	Placebo v GSK962040 50 mg
Number of subjects included in analysis	56
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	Difference in AMs of change from BL
Point estimate	-6.69
Confidence interval	
level	95 %
sides	2-sided
lower limit	-13.77
upper limit	0.39

Statistical analysis title	Day 8; Total

Statistical analysis description:

Day 8; Total: The AMs and differences (GSK 962040 minus Placebo) were estimated using a mixed model fitting treatment, visit, treatment*visit interaction, and Baseline MDS-UPDR score as fixed effects, and participant as a random effect.

Comparison groups	Placebo v GSK962040 50 mg
Number of subjects included in analysis	56
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	Difference in AMs of change from BL
Point estimate	-12.5
Confidence interval	
level	95 %
sides	2-sided
lower limit	-19.67
upper limit	-5.29

Secondary: Movement Disorder Society-Unified Parkinson's Disease Rating Scale (MDS-UPDRS) Part III scores at Baseline, Day 1, and Day 8 (pre-dose; 120, 180, and 240 minutes post-dose)

End point title	Movement Disorder Society-Unified Parkinson's Disease Rating Scale (MDS-UPDRS) Part III scores at Baseline, Day 1, and Day 8 (pre-dose; 120, 180, and 240 minutes post-dose)

End point description:

The MDS-UPDRS is used to assess the status of Parkinson's Disease. It has four parts: Part I (non-motor experiences of daily living), Part II (motor experiences of daily living), Part III (motor examination), and Part IV (motor complications). Each part is made up of several questions, with each question given a score ranging from 0 (normal) to 4 (severe). Part I and Part II consist of 13 items each, and have a score ranging between 0 (normal) and 52 (severe). Part III consists of 33 items, and has a score ranging between 0 (normal) and 132 (severe). Part IV consists of 6 items, and has a score ranging between 0 (normal) and 24 (severe). The total score is the summed score of all four parts and ranges between 0 (normal) and 260 (severe). A higher score indicates more severe symptoms.

End point type	Secondary

End point timeframe:

Baseline, Day 1, and Day 8 at pre-dose and 120, 180, and 240 minutes (min) post-dose (PD); Follow-up visit (up to Day 25)

End point values	Placebo	GSK962040 50 mg		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	19[20]	37[21]		
Units: Scores on a scale				
arithmetic mean (standard deviation)				
Baseline, pre-dose, n=19, 37	42.2 (± 14.63)	38 (± 18.95)		
Baseline, 120 minutes post-dose, n=19, 37	33.1 (± 16.61)	27.7 (± 16.04)		
Baseline, 180 minutes post-dose, n=19, 36	30.3 (± 14.55)	27.5 (± 14.21)		
Baseline, 240 minutes post-dose, n=19, 37	31.6 (± 16.27)	29.2 (± 16.62)		
Day 1, pre-dose, n=19, 37	40.4 (± 17.56)	34.9 (± 17.97)		
Day 1,120 minutes post-dose, n=19, 37	32.3 (± 15.01)	26.2 (± 16.25)		
Day 1, 180 minutes post-dose, n=19, 37	31 (± 17.1)	25.5 (± 18.04)		
Day 1, 240 minutes post-dose, n=19, 37	32.7 (± 20.5)	27.2 (± 17.68)		
Day 8, pre-dose n=18, 36	44.2 (± 19.25)	34 (± 17.46)		
Day 8, 120 minutes post-dose, n=18, 36	32.3 (± 14.9)	24.2 (± 14.24)		
Day 8, 180 minutes post-dose, n=18, 36	33.3 (± 16.17)	25.1 (± 14.27)		
Day 8, 240 minutes post-dose, n=18, 36	37.1 (± 20.19)	25.4 (± 15.27)		
Follow-up, n=19, 37	30.3 (± 13.45)	24.9 (± 11.79)		

Notes:

[20] - PD/Efficacy Population. Participants with available data (n=X, X in category titles) were analyzed.

[21] - PD/Efficacy Population. Participants with available data (n=X, X in category titles) were analyzed.

Statistical analyses

Statistical analysis title	Day 1; Pre-dose

Statistical analysis description:

Day 1; Pre-dose: The AMs and differences (GSK962040 minus Placebo) were estimated using a mixed model fitting treatment, visit, treatment*visit*time point interaction, and Baseline UPDRS-3 score as fixed effects, and participant as a random effect.

Comparison groups	Placebo v GSK962040 50 mg

Number of subjects included in analysis	56
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	Difference in AMs of change from BL
Point estimate	-3.14
Confidence interval	
level	95 %
sides	2-sided
lower limit	-9.07
upper limit	2.78

Statistical analysis title	Day 1; 120 min PD

Statistical analysis description:

Day 1; 120 min PD: The AMs and differences (GSK962040 minus Placebo) were estimated using a mixed model fitting treatment, visit, treatment*visit*time point interaction, and Baseline UPDRS-3 score as fixed effects, and participant as a random effect.

Comparison groups	Placebo v GSK962040 50 mg
Number of subjects included in analysis	56
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	Difference in AMs of change from BL
Point estimate	-3.18
Confidence interval	
level	95 %
sides	2-sided
lower limit	-9.11
upper limit	2.75

Statistical analysis title	Day 1; 180 min PD

Statistical analysis description:

Day 1; 180 min PD: The AMs and differences (GSK962040 minus Placebo) were estimated using a mixed model fitting treatment, visit, treatment*visit*time point interaction, and Baseline UPDRS-3 score as fixed effects, and participant as a random effect.

Comparison groups	Placebo v GSK962040 50 mg
Number of subjects included in analysis	56
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	Difference in AMs of change from BL
Point estimate	-3.66
Confidence interval	
level	95 %
sides	2-sided
lower limit	-9.59
upper limit	2.27

Statistical analysis title	Day 1; 240 min PD

Statistical analysis description:

Day 1; 240 min PD: The AMs and differences (GSK962040 minus Placebo) were estimated using a mixed model fitting treatment, visit, treatment*visit*time point interaction, and Baseline UPDRS-3 score as fixed effects, and participant as a random effect.

Comparison groups	Placebo v GSK962040 50 mg
Number of subjects included in analysis	56
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	Difference in AMs of change from BL
Point estimate	-4.15
Confidence interval	
level	95 %
sides	2-sided
lower limit	-10.07
upper limit	1.76

Statistical analysis title	Day 8; Pre-dose

Statistical analysis description:

Day 8; Pre-dose: The AMs and differences (GSK962040 minus Placebo) were estimated using a mixed model fitting treatment, visit, treatment*visit*time point interaction, and Baseline UPDRS-3 score as fixed effects, and participant as a random effect.

Comparison groups	Placebo v GSK962040 50 mg
Number of subjects included in analysis	56
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	Difference in AMs of change from BL
Point estimate	-6.8
Confidence interval	
level	95 %
sides	2-sided
lower limit	-12.79
upper limit	-0.81

Statistical analysis title	Day 8; 120 min PD

Statistical analysis description:

Day 8; 120 min PD: The AMs and differences (GSK962040 minus Placebo) were estimated using a mixed model fitting treatment, visit, treatment*visit*time point interaction, and Baseline UPDRS-3 score as fixed effects, and participant as a random effect.

Comparison groups	Placebo v GSK962040 50 mg
Number of subjects included in analysis	56
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	Difference in AMs of change from BL
Point estimate	-3.97

Confidence interval	
level	95 %
sides	2-sided
lower limit	-9.96
upper limit	2.03

Statistical analysis title	Day 8; 180 min PD

Statistical analysis description:

Day 8; 180 min PD: The AMs and differences (GSK962040 minus Placebo) were estimated using a mixed model fitting treatment, visit, treatment*visit*time point interaction, and Baseline UPDRS-3 score as fixed effects, and participant as a random effect.

Comparison groups	Placebo v GSK962040 50 mg
Number of subjects included in analysis	56
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	Difference in AMs of change from BL
Point estimate	-5.29
Confidence interval	
level	95 %
sides	2-sided
lower limit	-11.29
upper limit	0.71

Statistical analysis title	Day 8; 240 min PD

Statistical analysis description:

Day 8; 240 min PD: The AMs and differences (GSK962040 minus Placebo) were estimated using a mixed model fitting treatment, visit, treatment*visit*time point interaction, and Baseline UPDRS-3 score as fixed effects, and participant as a random effect.

Comparison groups	Placebo v GSK962040 50 mg
Number of subjects included in analysis	56
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	Difference in AMs of change from BL
Point estimate	-8.9
Confidence interval	
level	95 %
sides	2-sided
lower limit	-14.88
upper limit	-2.91

Secondary: Period mean amount of hours spent “ON,” “ON” without dyskinesia, "ON" with non-troublesome dyskinesia, "ON" with troublesome dyskinesia, and “OFF” at Baseline and during the treatment period (Days 1-8), Week 1 of Follow-up, and Week 2 of Follow-up

End point title	Period mean amount of hours spent “ON,” “ON” without dyskinesia, "ON" with non-troublesome dyskinesia, "ON" with

	troublesome dyskinesia, and "OFF" at Baseline and during the treatment period (Days 1-8), Week 1 of Follow-up, and Week 2 of Follow-up

End point description:

Participants were provided with the "ON/OFF" diary to capture details of the amount of awake time spent on/off of PD symptoms, and were asked to complete the diary daily. Participants checked the box most appropriate for their dominant motor state in the preceding 30-minute period. The catergories included: "ON" (including "ON without dyskinesia" and "ON with non-troublesome dyskinesia"), "ON" with troublesome dyskinesia (TD), and "OFF." For Baseline, data were collected for 2 days prior to Day 1, and the mean value of the 2 days was used.

End point type	Secondary

End point timeframe:

Baseline, Days 1-8, Week 1 of Follow-up (Days 6 and 7 of Follow-up; up to Day 16), and Week 2 of Follow-up (Days 13 and 14 of Follow-up; up to Day 23)

End point values	Placebo	GSK962040 50 mg		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	19[22]	37[23]		
Units: hours				
arithmetic mean (standard deviation)				
Baseline: "ON," n=18, 37	11.21 (± 3.602)	11.31 (± 3.021)		
Baseline: "ON" without dyskinesia, n=18, 37	10.11 (± 4.069)	9.65 (± 3.787)		
Baseline: "ON" with non-TD, n=18, 37	1.1 (± 1.787)	1.66 (± 2.956)		
Baseline: "ON" with TD, n=18, 37	0.54 (± 1.24)	0.4 (± 1.292)		
Baseline: "OFF," n=18, 37	4.92 (± 3.417)	4.23 (± 2.484)		
Treatment period: "ON," n=18, 36	10.61 (± 3.927)	12.44 (± 3.375)		
Treatment period: "ON" without dyskinesia, n=18, 3	9.82 (± 4.042)	10.47 (± 4.479)		
Treatment period: "ON" with non-TD, n=18, 36	0.79 (± 1.875)	1.98 (± 2.987)		
Treatment period: "ON" with TD, n=18, 36	0.47 (± 1.548)	0.59 (± 1.985)		
Treatment period: "OFF," n=18, 36	5.57 (± 4.364)	2.94 (± 2.954)		
Week 1 of FU: "ON," n=18, 36	11 (± 3.309)	12.13 (± 3.134)		
Week 1 of FU: "ON" without dyskinesia, n=18, 36	10.17 (± 4.232)	10.63 (± 3.948)		
Week 1 of FU: "ON" with non-TD, n=18, 36	0.83 (± 1.933)	1.5 (± 2.369)		
Week 1 of FU: "ON" with TD, n=18, 36	0.71 (± 2.083)	0.52 (± 1.986)		
Week 1 of FU: "OFF," n=18, 36	4.83 (± 3.7)	3.31 (± 2.642)		
Week 2 of FU: "ON," n=16, 32	11.34 (± 3.58)	11.69 (± 3.562)		
Week 2 of FU: "ON" without dyskinesia, n=16, 32	11.13 (± 4.138)	9.98 (± 4.872)		
Week 2 of FU: "ON" with non-TD, n=16, 32	0.22 (± 0.875)	1.7 (± 2.838)		
Week 2 of FU: "ON" with TD, n=16, 32	0.38 (± 1.5)	0.8 (± 2.362)		
Week 2 of FU: "OFF," n=16, 32	4.47 (± 3.601)	3.36 (± 2.857)		

Notes:

[22] - PD/Efficacy Population. Participants with available data (n=X, X in category titles) were analyzed.

[23] - PD/Efficacy Population. Participants with available data (n=X, X in category titles) were analyzed.

Statistical analyses

Statistical analysis title	OFF

Statistical analysis description:

OFF: Treatment Period: The AMs and differences (GSK962040 minus Placebo) were estimated using an analysis of covariance (ANCOVA) model fitting treatment and Baseline amount of hours spent ON/OFF as main effects.

Comparison groups	Placebo v GSK962040 50 mg
Number of subjects included in analysis	56
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	Difference in AMs of change from BL
Point estimate	-2.31
Confidence interval	
level	95 %
sides	2-sided
lower limit	-3.71
upper limit	-0.9

Statistical analysis title	ON

Statistical analysis description:

ON: Treatment Period: The AMs and differences (GSK962040 minus Placebo) were estimated using an analysis of covariance (ANCOVA) model fitting treatment and Baseline amount of hours spent ON/OFF as main effects.

Comparison groups	Placebo v GSK962040 50 mg
Number of subjects included in analysis	56
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	Difference in AMs of change from BL
Point estimate	1.88
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.28
upper limit	3.48

Secondary: Number of times a participant could alternatively tap two counter keys 30 centimeters apart in 1 minute (min) at Baseline, Day1, Day 8, and Follow-up

End point title	Number of times a participant could alternatively tap two counter keys 30 centimeters apart in 1 minute (min) at Baseline, Day1, Day 8, and Follow-up

End point description:

Participants were asked to alternatively tap two keys 30 centimeters apart in 1 minute in two trials with the most affected hand or the dominant hand in symmetric disease. The finger tapping was scored manually by the study staff. The finger-tapping assessment was repeated at eight separate time points (pre-dose, 0 min, 30 min, 60 min, 90 min, 120 min, 180 min, and 240 min post-dose) at each visit (Baseline, Day 1, and Day 8). At each time point, the mean of the two assessments was calculated.

End point type	Secondary

End point timeframe:

Baseline, Day 1, and Day 8 at pre-dose and 0, 30, 60, 90, 120, 180, and 240 minutes post-dose; Follow-up visit (up to Day 25)

End point values	Placebo	GSK962040 50 mg		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	19[24]	37[25]		
Units: Finger taps per minute				
arithmetic mean (standard deviation)				
Baseline: pre-dose, n=19, 37	92.4 (± 47.53)	77.8 (± 38)		
Baseline: 0 min, n=19, 35	91.2 (± 49.84)	80.1 (± 35.28)		
Baseline: 30 min, n=19, 34	89.3 (± 42.91)	85.2 (± 41.45)		
Baseline: 60 min, n=19, 36	88.6 (± 42.32)	89.3 (± 45.32)		
Baseline: 90 min, n=19, 36	91.2 (± 44.14)	90.8 (± 45.18)		
Baseline: 120 min, n=19, 37	92.6 (± 40.99)	92 (± 43.37)		
Baseline: 180 min, n=19, 37	94.1 (± 47.19)	92.8 (± 44.86)		
Baseline: 240 min, n=19, 37	95.2 (± 44.6)	93.2 (± 46.17)		
Day 1: pre-dose, n=19, 36	92.3 (± 43.44)	85.1 (± 40.05)		
Day 1: 0 min, n=19, 364	90.7 (± 40.78)	86.8 (± 44.65)		
Day 1: 30 min, n=18, 35	93.4 (± 43.95)	92.4 (± 49.92)		
Day 1: 60 min, n=18, 35	93.8 (± 44.8)	94.6 (± 44.06)		
Day 1: 90 min, n=19, 34	97.7 (± 50.46)	91.4 (± 42.09)		
Day 1: 120 min, n=19, 35	99.9 (± 50.51)	96.4 (± 42.06)		
Day 1: 180 min, n=18, 36	99 (± 49.44)	92.3 (± 41.01)		
Day 1: 240 min, n=18, 36	98.2 (± 51.97)	97.6 (± 48.4)		
Day 8: pre-dose, n=18, 35	95.7 (± 40.9)	92.8 (± 43.92)		
Day 8: 0 min, n=18, 35	92 (± 44.3)	91.1 (± 42.9)		
Day 8: 30 min, n=18, 34	95.8 (± 45.07)	92.2 (± 41.14)		
Day 8: 60 min, n=18, 35	94.6 (± 46.8)	93.2 (± 39.01)		
Day 8: 90 min, n=18, 34	95 (± 48.82)	95.5 (± 42.6)		
Day 8: 120 min, n=18, 35	97.2 (± 47.67)	97.4 (± 42.34)		
Day 8: 180 min, n=18, 34	96.8 (± 52.5)	101.2 (± 49.86)		
Day 8: 240 min, n=18, 35	98.3 (± 53.3)	102.8 (± 51.84)		
Follow-up: n=18, 35	104.4 (± 48.13)	105.7 (± 56.59)		

Notes:

[24] - PD/Efficacy Population. Participants with available data (n=X, X in category titles) were analyzed.

[25] - PD/Efficacy Population. Participants with available data (n=X, X in category titles) were analyzed.

Statistical analyses

Statistical analysis title	Day 1, pre-dose

Statistical analysis description:

Day 1, pre-dose: The AMs/differences (GSK962040 minus Placebo) were estimated using a MM fitting treatment, visit, time point (TP), treatment*visit*TP interaction, and BL score as fixed effects, TP as a repeated effect, and par. as a random effect.

Comparison groups	Placebo v GSK962040 50 mg
Number of subjects included in analysis	56
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	Difference in AMs of change from BL
Point estimate	-2.83
Confidence interval	
level	95 %
sides	2-sided
lower limit	-21.79
upper limit	16.13

Statistical analysis title	Day 1, 0 min PD

Statistical analysis description:

Day 1, 0 min PD: The AMs/differences (GSK962040 minus Placebo) were estimated using a MM fitting treatment, visit, time point (TP), treatment*visit*TP interaction, and BL score as fixed effects, TP as a repeated effect, and par. as a random effect.

Comparison groups	Placebo v GSK962040 50 mg
Number of subjects included in analysis	56
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	Difference in AMs of change from BL
Point estimate	0.58
Confidence interval	
level	95 %
sides	2-sided
lower limit	-18.39
upper limit	19.56

Statistical analysis title	Day 1, 30 min PD

Statistical analysis description:

Day 1, 30 min PD: The AMs/differences (GSK962040 minus Placebo) were estimated using a MM fitting treatment, visit, time point (TP), treatment*visit*TP interaction, and BL score as fixed effects, TP as a repeated effect, and par. as a random effect.

Comparison groups	Placebo v GSK962040 50 mg
Number of subjects included in analysis	56
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	Difference in AMs of change from BL
Point estimate	1.84

Confidence interval	
level	95 %
sides	2-sided
lower limit	-17.18
upper limit	20.86

Statistical analysis title	Day 1, 60 min PD

Statistical analysis description:

Day 1, 60 min PD: The AMs/differences (GSK962040 minus Placebo) were estimated using a MM fitting treatment, visit, time point (TP), treatment*visit*TP interaction, and BL score as fixed effects, TP as a repeated effect, and par. as a random effect.

Comparison groups	Placebo v GSK962040 50 mg
Number of subjects included in analysis	56
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	Difference in AMs of change from BL
Point estimate	0.28
Confidence interval	
level	95 %
sides	2-sided
lower limit	-18.72
upper limit	19.28

Statistical analysis title	Day 1, 90 min

Statistical analysis description:

Day 1, 90 min PD: The AMs/differences (GSK962040 minus Placebo) were estimated using a MM fitting treatment, visit, time point (TP), treatment*visit*TP interaction, and BL score as fixed effects, TP as a repeated effect, and par. as a random effect.

Comparison groups	Placebo v GSK962040 50 mg
Number of subjects included in analysis	56
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	Difference in AMs of change from BL
Point estimate	-3.38
Confidence interval	
level	95 %
sides	2-sided
lower limit	-22.35
upper limit	15.58

Statistical analysis title	Day 1, 120 min PD

Statistical analysis description:

Day 1, 120 min PD: The AMs/differences (GSK962040 minus Placebo) were estimated using a MM fitting treatment, visit, time point (TP), treatment*visit*TP interaction, and BL score as fixed effects, TP as a repeated effect, and par. as a random effect.

Comparison groups	Placebo v GSK962040 50 mg
Number of subjects included in analysis	56
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	Difference in AMs of change from BL
Point estimate	-4.18
Confidence interval	
level	95 %
sides	2-sided
lower limit	-23.13
upper limit	14.76

Statistical analysis title	Day 1, 180 min PD

Statistical analysis description:

Day 1, 180 min PD: The AMs/differences (GSK962040 minus Placebo) were estimated using a MM fitting treatment, visit, time point (TP), treatment*visit*TP interaction, and BL score as fixed effects, TP as a repeated effect, and par. as a random effect.

Comparison groups	Placebo v GSK962040 50 mg
Number of subjects included in analysis	56
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	Difference in AMs of change from BL
Point estimate	-6.39
Confidence interval	
level	95 %
sides	2-sided
lower limit	-25.36
upper limit	12.58

Statistical analysis title	Day 1, 240 min PD

Statistical analysis description:

Day 1, 240 min PD: The AMs/differences (GSK962040 minus Placebo) were estimated using a MM fitting treatment, visit, time point (TP), treatment*visit*TP interaction, and BL score as fixed effects, TP as a repeated effect, and par. as a random effect.

Comparison groups	Placebo v GSK962040 50 mg
Number of subjects included in analysis	56
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	Difference in AMs of change from BL
Point estimate	0.77
Confidence interval	
level	95 %
sides	2-sided
lower limit	-18.2
upper limit	19.75

Statistical analysis title	Day 8, pre-dose

Statistical analysis description:

Day 8, pre-dose: The AMs/differences (GSK962040 minus Placebo) were estimated using a MM fitting treatment, visit, time point (TP), treatment*visit*TP interaction, and BL score as fixed effects, TP as a repeated effect, and par. as a random effect.

Comparison groups	Placebo v GSK962040 50 mg
Number of subjects included in analysis	56
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	Difference in AMs of change from BL
Point estimate	0.51
Confidence interval	
level	95 %
sides	2-sided
lower limit	-18.51
upper limit	19.52

Statistical analysis title	Day 8, 0 min PD

Statistical analysis description:

Day 8, 0 min PD: The AMs/differences (GSK962040 minus Placebo) were estimated using a MM fitting treatment, visit, time point (TP), treatment*visit*TP interaction, and BL score as fixed effects, TP as a repeated effect, and par. as a random effect.

Comparison groups	Placebo v GSK962040 50 mg
Number of subjects included in analysis	56
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	Difference in AMs of change from BL
Point estimate	3.32
Confidence interval	
level	95 %
sides	2-sided
lower limit	-15.7
upper limit	22.33

Statistical analysis title	Day 8, 30 min PD

Statistical analysis description:

Day 8, 30 min PD: The AMs/differences (GSK962040 minus Placebo) were estimated using a MM fitting treatment, visit, time point (TP), treatment*visit*TP interaction, and BL score as fixed effects, TP as a repeated effect, and par. as a random effect.

Comparison groups	Placebo v GSK962040 50 mg

Number of subjects included in analysis	56
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	Difference in AMs of change from BL
Point estimate	-2.94
Confidence interval	
level	95 %
sides	2-sided
lower limit	-21.97
upper limit	16.08

Statistical analysis title	Day 8, 60 min PD

Statistical analysis description:

Day 8, 60 min PD: The AMs/differences (GSK962040 minus Placebo) were estimated using a MM fitting treatment, visit, time point (TP), treatment*visit*TP interaction, and BL score as fixed effects, TP as a repeated effect, and par. as a random effect.

Comparison groups	Placebo v GSK962040 50 mg
Number of subjects included in analysis	56
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	Difference in AMs of change from BL
Point estimate	-3.12
Confidence interval	
level	95 %
sides	2-sided
lower limit	-22.13
upper limit	15.88

Statistical analysis title	Day 8, 90 min PD

Statistical analysis description:

Day 8, 90 min PD: The AMs/differences (GSK962040 minus Placebo) were estimated using a MM fitting treatment, visit, time point (TP), treatment*visit*TP interaction, and BL score as fixed effects, TP as a repeated effect, and par. as a random effect.

Comparison groups	Placebo v GSK962040 50 mg
Number of subjects included in analysis	56
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	Difference in AMs of change from BL
Point estimate	-1.38
Confidence interval	
level	95 %
sides	2-sided
lower limit	-20.4
upper limit	17.63

Statistical analysis title	Day 8, 120 min PD
Statistical analysis description:	
Day 8, 120 min PD: The AMs/differences (GSK962040 minus Placebo) were estimated using a MM fitting treatment, visit, time point (TP), treatment*visit*TP interaction, and BL score as fixed effects, TP as a repeated effect, and par. as a random effect.	
Comparison groups	Placebo v GSK962040 50 mg
Number of subjects included in analysis	56
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	Difference in AMs of change from BL
Point estimate	-0.71
Confidence interval	
level	95 %
sides	2-sided
lower limit	-19.7
upper limit	18.28

Statistical analysis title	Day 8, 180 min PD
Statistical analysis description:	
Day 8, 180 min PD: The AMs/differences (GSK962040 minus Placebo) were estimated using a MM fitting treatment, visit, time point (TP), treatment*visit*TP interaction, and BL score as fixed effects, TP as a repeated effect, and par. as a random effect.	
Comparison groups	Placebo v GSK962040 50 mg
Number of subjects included in analysis	56
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	Difference in AMs of change from BL
Point estimate	3.02
Confidence interval	
level	95 %
sides	2-sided
lower limit	-15.98
upper limit	22.02

Statistical analysis title	Day 8, 240 min PD
Statistical analysis description:	
Day 8, 240 min PD: The AMs/differences (GSK962040 minus Placebo) were estimated using a MM fitting treatment, visit, time point (TP), treatment*visit*TP interaction, and BL score as fixed effects, TP as a repeated effect, and par. as a random effect.	
Comparison groups	Placebo v GSK962040 50 mg
Number of subjects included in analysis	56
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	Difference in AMs of change from BL
Point estimate	4.08

Confidence interval	
level	95 %
sides	2-sided
lower limit	-14.91
upper limit	23.07

Secondary: Total daily L-DOPA equivalent dose at Baseline and on Days 1, 2, 3, 4, 5, 6, 7, 8, and 9

End point title	Total daily L-DOPA equivalent dose at Baseline and on Days 1, 2, 3, 4, 5, 6, 7, 8, and 9

End point description:

Various formulations of L-DOPA were utilized by participants for the treatment of Parkinson's Disease. The total daily L-DOPA equivalent dose was calculated as the sum of all L-DOPA equivalent doses for each L-DOPA-containing drug taken on the same day.

End point type	Secondary

End point timeframe:

Baseline and Days 1, 2, 3, 4, 5, 6, 7, 8, and 9

End point values	Placebo	GSK962040 50 mg		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	19[26]	37[27]		
Units: Milligrams				
arithmetic mean (standard deviation)				
Baseline, n=19, 37	113.2 (± 41.14)	164.5 (± 119.66)		
Day 1, n=19, 37	353.9 (± 174.85)	368.6 (± 216.54)		
Day 2, n=19, 36	465.8 (± 229.61)	514.5 (± 300.44)		
Day 3, n=19, 36	481.6 (± 243.79)	516.9 (± 299.98)		
Day 4, n=19, 36	481.6 (± 241.5)	518.3 (± 313.07)		
Day 5, n=19, 36	484.2 (± 243.13)	503 (± 293.48)		
Day 6, n=17, 36	516.2 (± 249.21)	511.3 (± 307.31)		
Day 7, n=17, 35	486.8 (± 247.51)	499.6 (± 310.57)		
Day 8, n=17, 34	191.2 (± 175.43)	281.3 (± 234)		
Day 9, n=0, 5	0 (± 0)	235 (± 121.96)		

Notes:

[26] - PD/Efficacy Population. Participants with available data (n=X, X in category titles) were analyzed.

[27] - PD/Efficacy Population. Participants with available data (n=X, X in category titles) were analyzed.

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in systolic blood pressure (SBP) and diastolic blood pressure (DBP) at Day 1 and Day 8

End point title	Change from Baseline in systolic blood pressure (SBP) and diastolic blood pressure (DBP) at Day 1 and Day 8

End point description:

Blood pressure measurements were taken at pre-dose and at 0 min (completion of meal) on Day 1 and Day 8. The Baseline value was the Day 1 pre-dose value. Change from Baseline was calculated by subtracting the Baseline value from the individual post-Baseline value.

End point type	Secondary

End point timeframe:

Baseline, Day 1, and Day 8

End point values	Placebo	GSK962040 50 mg	GSK962040 Total	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	19[28]	37[29]	38[30]	
Units: Millimeters of mercury				
arithmetic mean (standard deviation)				
SBP, Day 1: 0 min, n=19, 37, 38	-4 (± 12.05)	-2.5 (± 18.66)	-2.1 (± 18.58)	
SBP, Day 8: pre-dose, n=18, 36, 37	-2.8 (± 13.24)	-3.9 (± 13.19)	-3.7 (± 13.06)	
SBP, Day 8: 0 min, n=18, 36, 37	-3.4 (± 11.55)	-1 (± 15.04)	-1.1 (± 14.84)	
DBP, Day 1: 0 min, n=19, 37, 38	-5.4 (± 7.67)	-0.9 (± 7.51)	-0.7 (± 7.55)	
DBP, Day 8: pre-dose, n=18, 36, 37	-4.2 (± 6.88)	-0.9 (± 8.54)	-0.8 (± 8.48)	
DBP, Day 8: 0 min, n=18, 36, 37	-3.7 (± 5.81)	0.9 (± 8.32)	0.9 (± 8.21)	

Notes:

[28] - All Subjects Population (ASP): all participants who received >=1 dose of study medication

[29] - All Subjects Population (ASP): all participants who received >=1 dose of study medication

[30] - All Subjects Population (ASP): all participants who received >=1 dose of study medication

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in heart rate at Day 1 and Day 8

End point title	Change from Baseline in heart rate at Day 1 and Day 8

End point description:

Heart rate measurements were taken at pre-dose and 0 min (completion of meal) on Day 1 and Day 8. The Baseline value was the Day 1 pre-dose value. Change from Baseline was calculated by subtracting the Baseline value from the individual post-Baseline value.

End point type	Secondary

End point timeframe:

Baseline, Day 1, and Day 8

End point values	Placebo	GSK962040 50 mg	GSK962040 Total	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	19[31]	37[32]	38[33]	
Units: Beats per minute				
arithmetic mean (standard deviation)				
Day 1: 0 min, n=19, 37, 38	-2.2 (± 7.3)	0.8 (± 9.19)	0.5 (± 9.26)	
Day 8: pre-dose, n=18, 36, 37	-2.9 (± 7.67)	0.6 (± 6.12)	0 (± 6.84)	
Day 8: 0 min, n=18, 36, 37	-2.5 (± 7.64)	-0.5 (± 6.8)	-0.5 (± 6.71)	

Notes:

[31] - ASP. Participants with available data (n=X, X in category titles) were analyzed.

[32] - ASP. Participants with available data (n=X, X in category titles) were analyzed.

[33] - ASP. Participants with available data (n=X, X in category titles) were analyzed.

Statistical analyses

No statistical analyses for this end point

Secondary: Number of participants with the indicated electrocardiogram (ECG) findings at Day 1 and Day 8

End point title	Number of participants with the indicated electrocardiogram (ECG) findings at Day 1 and Day 8

End point description:

ECG measurements were taken at pre-dose and 0 min (completion of meal) on Day 1 and Day 8. The Baseline value was the Day 1 pre-dose value. ECG findings were categorized as normal, abnormal - not clinically significant, and abnormal - clinically significant (CS), based on interpretation by the site.

End point type	Secondary

End point timeframe:

Day 1 and Day 8

End point values	Placebo	GSK962040 50 mg	GSK962040 Total	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	19[34]	37[35]	38[36]	
Units: participants				
Day 1: pre-dose, Normal, n=19, 37, 38	14	17	18	
Day 1: pre-dose, Abnormal - Not CS, n=19, 37, 38	5	19	19	
Day 1: pre-dose, Abnormal - CS, n=19, 37, 38	0	1	1	
Day 1: 0 min, Normal, n=19, 37, 38	12	16	16	
Day 1: 0 min, Abnormal - Not CS, n=19, 37, 38	7	20	21	
Day 1: 0 min, Abnormal - CS, n=19, 37, 38	0	1	1	
Day 8: pre-dose, Normal, n=18, 36, 37	14	18	19	
Day 8: pre-dose, Abnormal - Not CS, n=18, 36, 37	4	17	17	
Day 8: pre-dose, Abnormal - CS, n=18, 36, 37	0	1	1	
Day 8: 0 min, Normal, n=18, 36, 37	12	19	20	
Day 8: 0 min, Abnormal - Not CS, n=18, 36, 37	6	16	16	

Day 8: 0 min, Abnormal - CS, n=18, 36, 37	0	1	1	

Notes:

[34] - ASP. Participants with available data (n=X, X in category titles) were analyzed.

[35] - ASP. Participants with available data (n=X, X in category titles) were analyzed.

[36] - ASP. Participants with available data (n=X, X in category titles) were analyzed.

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in albumin (ALB) and total protein (TP) at Day 4 and Day 8

End point title	Change from Baseline in albumin (ALB) and total protein (TP) at Day 4 and Day 8

End point description:

ALB and TP measurements were taken at pre-dose on Day 1 (Baseline), Day 4, and Day 8. Baseline value was the Day 1 pre-dose value. Change from Baseline was calculated by subtracting the Baseline value from the individual post-Baseline value.

End point type	Secondary

End point timeframe:

Baseline, Day 4, and Day 8

End point values	Placebo	GSK962040 50 mg	GSK962040 Total	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	19[37]	37[38]	38[39]	
Units: Grams per liter				
arithmetic mean (standard deviation)				
ALB, Day 4, n=18, 34, 35	0.06 (± 2.313)	-0.38 (± 2.155)	-0.37 (± 2.124)	
ALB, Day 8, n=18, 34, 35	0.11 (± 2.22)	-0.33 (± 2.084)	-0.29 (± 2.065)	
TP, Day 4, n=18, 30, 31	-0.3 (± 3.28)	-0.9 (± 3.93)	-1 (± 3.97)	
TP, Day 8, n=15, 31, 32	0 (± 3.24)	-0.3 (± 3.72)	-0.3 (± 3.66)	

Notes:

[37] - ASP. Participants with available data (n=X, X in category titles) were analyzed.

[38] - ASP. Participants with available data (n=X, X in category titles) were analyzed.

[39] - ASP. Participants with available data (n=X, X in category titles) were analyzed.

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in alkaline phosphatase (ALP), alanine amino transferase (ALT), aspartate amino transferase (AST), and gamma glutamyl transferase (GGT) at Day 4 and Day 8

End point title	Change from Baseline in alkaline phosphatase (ALP), alanine amino transferase (ALT), aspartate amino transferase (AST), and gamma glutamyl transferase (GGT) at Day 4 and Day 8

End point description:

ALP, ALT, AST, and GGT measurements were taken at pre-dose on Day 1 (Baseline), Day 4, and Day 8. The Baseline value was the Day 1 pre-dose value. Change from Baseline was calculated by subtracting

the Baseline value from the individual post-Baseline value.

End point type	Secondary

End point timeframe:

Baseline, Day 4, and Day 8

End point values	Placebo	GSK962040 50 mg	GSK962040 Total	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	19[40]	37[41]	38[42]	
Units: International units per liter				
arithmetic mean (standard deviation)				
ALP, Day 4, n=19, 33, 34	-0.8 (± 5.26)	2.4 (± 14.14)	2.2 (± 13.98)	
ALP, Day 8, n=18, 34, 35	-0.1 (± 7.66)	1.4 (± 13.35)	1.2 (± 13.21)	
ALT, Day 4, n=19, 33, 34	-6.4 (± 10.45)	-5.9 (± 9.77)	-7.1 (± 11.72)	
ALT, Day 8, n=18, 34, 35	-1.6 (± 6.88)	-0.4 (± 5.46)	-0.6 (± 5.57)	
AST, Day 4, n=19, 32, 33	0.2 (± 3.16)	-1.2 (± 2.89)	-1.3 (± 2.96)	
AST, Day 8, n=16, 31, 32	0.6 (± 4.55)	1 (± 3.65)	0.9 (± 3.63)	
GGT, Day 4, n=19, 33, 34	-0.8 (± 3.2)	-0.8 (± 3.06)	-0.9 (± 3.04)	
GGT, Day 4, n=18, 33, 34	-0.1 (± 5.22)	-1 (± 5.02)	-1 (± 4.95)	

Notes:

[40] - ASP. Participants with available data (n=X, X in category titles) were analyzed.

[41] - ASP. Participants with available data (n=X, X in category titles) were analyzed.

[42] - ASP. Participants with available data (n=X, X in category titles) were analyzed.

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in direct bilirubin (D-Bil), total bilirubin (T-Bil), and creatinine (CRT) at Day 4 and Day 8

End point title	Change from Baseline in direct bilirubin (D-Bil), total bilirubin (T-Bil), and creatinine (CRT) at Day 4 and Day 8

End point description:

D-Bil, T-Bil, and CRT measurements were taken at pre-dose on Day 1 (Baseline), Day 4, and Day 8. The Baseline value was the Day 1 pre-dose value. Change from Baseline was calculated by subtracting the Baseline value from the individual post-Baseline value.

End point type	Secondary

End point timeframe:

Baseline, Day 4, and Day 8

End point values	Placebo	GSK962040 50 mg	GSK962040 Total	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	19[43]	37[44]	38[45]	
Units: Micromoles per liter				
arithmetic mean (standard deviation)				
D-Bil, Day 4, n=9, 14, 14	-0.5 (± 1.98)	-0.6 (± 0.76)	-0.6 (± 0.76)	
D-Bil, Day 8, n=9, 16, 16	0.2 (± 0.97)	-0.1 (± 0.61)	-0.1 (± 0.61)	

T-Bil, Day 4, n=19, 34, 35	0.1 (± 5.45)	-1.5 (± 2.53)	-1.5 (± 2.53)	
T-Bil, Day 8, n=18, 34, 35	0.1 (± 3.38)	-0.6 (± 3.82)	-0.6 (± 3.76)	
CRT, Day 4, n=19, 34, 35	1.29 (± 8.628)	3.85 (± 7.126)	4.22 (± 7.364)	
CRT, Day 8, n=18, 34, 35	2.84 (± 7.679)	7.31 (± 9.219)	7.04 (± 9.217)	

Notes:

[43] - ASP. Participants with available data (n=X, X in category titles) were analyzed.

[44] - ASP. Participants with available data (n=X, X in category titles) were analyzed.

[45] - ASP. Participants with available data (n=X, X in category titles) were analyzed.

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in calcium, chloride, carbon dioxide content (CO2)/bicarbonate (BC), glucose, potassium, sodium, urea/blood urea nitrogen (BUN), and uric acid (UA) at Day 4 and Day 8

End point title	Change from Baseline in calcium, chloride, carbon dioxide content (CO2)/bicarbonate (BC), glucose, potassium, sodium, urea/blood urea nitrogen (BUN), and uric acid (UA) at Day 4 and Day 8

End point description:

Calcium, chloride, CO2/BC, glucose, potassium, sodium, urea/BUN, and UA measurements were taken at pre-dose on Day 1 (Baseline), Day 4, and Day 8. The Baseline value was the Day 1 pre-dose value. Change from Baseline was calculated by subtracting the Baseline value from the individual post-Baseline value.

End point type	Secondary

End point timeframe:

Baseline, Day 4, and Day 8

End point values	Placebo	GSK962040 50 mg	GSK962040 Total	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	19[46]	37[47]	38[48]	
Units: Millimoles per liter				
arithmetic mean (standard deviation)				
Calcium, Day 4, n=19, 34, 35	0.01 (± 0.0746)	-0.009 (± 0.0659)	-0.011 (± 0.0667)	
Calcium, Day 8, n=18, 35, 36	0.026 (± 0.0756)	-0.018 (± 0.0662)	-0.017 (± 0.0652)	
Chloride, Day 4, n=19, 33, 34	-1.37 (± 1.832)	-0.42 (± 2.346)	-0.41 (± 2.311)	
Chloride, Day 8, n=18, 33, 34	0.39 (± 2.57)	0.52 (± 1.734)	0.53 (± 1.71)	
CO2/BC, Day 4, n=9, 21, 22	-0.06 (± 2.833)	0.16 (± 2.602)	0.2 (± 2.546)	
CO2/BC, Day 8, n=8, 22, 23	0.51 (± 2.053)	0.23 (± 2.139)	0.13 (± 2.141)	
Glucose, Day 4, n=19, 35, 36	1.14 (± 2.944)	0.14 (± 1.198)	0.15 (± 1.185)	
Glucose, Day 8, n=18, 36, 36	-0.03 (± 0.865)	0.09 (± 0.594)	-0.09 (± 0.594)	
Potassium, Day 4, n=19, 32, 33	0.008 (± 0.3393)	0.168 (± 0.3408)	0.151 (± 0.3497)	
Potassium, Day 8, n=16, 31, 32	0.055 (± 0.3405)	0.048 (± 0.2897)	0.043 (± 0.2862)	
Sodium, Day 4, n=19, 34, 35	-0.89 (± 2.787)	-0.56 (± 1.779)	-0.51 (± 1.772)	

Sodium, Day 8, n=18, 34, 35	1.39 (± 3.202)	0.21 (± 1.647)	0.29 (± 1.69)	
Urea/BUN, Day 4, n=17, 32, 33	-0.27 (± 1.757)	0 (± 1.496)	-0.02 (± 1.477)	
Urea/BUN, Day 8, n=17, 34, 35	-0.63 (± 1.318)	0.13 (± 1.308)	0.14 (± 1.289)	
UA, Day 4, n=16, 30, 31	-14.22 (± 23.416)	0.53 (± 29.735)	-0.78 (± 30.127)	
UA, Day 8, n=14, 29, 30	-1.56 (± 22.601)	6.39 (± 30.819)	6.17 (± 30.306)	

Notes:

[46] - ASP. Participants with available data (n=X, X in category titles) were analyzed.

[47] - ASP. Participants with available data (n=X, X in category titles) were analyzed.

[48] - ASP. Participants with available data (n=X, X in category titles) were analyzed.

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in basophils, eosinophils, lymphocytes, monocytes, total absolute neutrophil count (ANC), and platelet count (PC) at Day 4 and Day 8

End point title	Change from Baseline in basophils, eosinophils, lymphocytes, monocytes, total absolute neutrophil count (ANC), and platelet count (PC) at Day 4 and Day 8

End point description:

Basophils, eosinophils, lymphocytes, monocytes, total ANC, and PC measurements were taken at pre-dose on Day 1 (Baseline), Day 4, and Day 8. The Baseline value was the Day 1 pre-dose value. Change from Baseline was calculated by subtracting the Baseline value from the individual post-Baseline value.

End point type	Secondary

End point timeframe:

Baseline, Day 4, and Day 8

End point values	Placebo	GSK962040 50 mg	GSK962040 Total	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	19[49]	37[50]	38[51]	
Units: Giga (10^9) cells per liter				
arithmetic mean (standard deviation)				
Basophils, Day 4, n=19, 34, 35	-0.003 (± 0.02)	-0.006 (± 0.0247)	-0.006 (± 0.0244)	
Basophils, Day 8, n=17, 35, 36	-0.006 (± 0.0153)	-0.001 (± 0.0195)	-0.001 (± 0.0192)	
Eosinophils, Day 4, n=19, 34, 35	0.003 (± 0.1219)	-0.031 (± 0.0584)	-0.034 (± 0.0599)	
Eosinophils, Day 8, n=17, 35, 36	-0.016 (± 0.0519)	-0.001 (± 0.0466)	0 (± 0.0467)	
Lymphocytes, Day 4, n=19, 34, 35	0.093 (± 0.4326)	0.044 (± 0.3592)	0.033 (± 0.3592)	
Lymphocytes, Day 8, n=17, 35, 36	-0.049 (± 0.3258)	0.076 (± 0.5874)	0.073 (± 0.5793)	
Monocytes, Day 4, n=19, 34, 35	0.006 (± 0.1313)	0.002 (± 0.0923)	0.004 (± 0.0913)	
Monocytes, Day 8, n=17, 35, 36	-0.004 (± 0.086)	-0.013 (± 0.0928)	-0.013 (± 0.0916)	

Total ANC , Day 4, n=19, 34, 35	0.021 (± 0.8866)	0.392 (± 0.948)	0.406 (± 0.9377)	
Total ANC , Day 8, n=17, 35, 36	0.007 (± 0.8586)	-0.114 (± 0.85)	-0.122 (± 0.8392)	
PC, Day 4, n=19, 34, 35	4.5 (± 18.45)	3.6 (± 18.76)	3.3 (± 18.53)	
PC, Day 8, n=17, 35, 36	1.8 (± 24.42)	1.4 (± 22.97)	0.7 (± 22.97)	

Notes:

[49] - ASP. Participants with available data (n=X, X in category titles) were analyzed.

[50] - ASP. Participants with available data (n=X, X in category titles) were analyzed.

[51] - ASP. Participants with available data (n=X, X in category titles) were analyzed.

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in hemoglobin and mean corpuscle hemoglobin concentration (MCHC) at Day 4 and Day 8

End point title	Change from Baseline in hemoglobin and mean corpuscle hemoglobin concentration (MCHC) at Day 4 and Day 8

End point description:

Hemoglobin and MCHC measurements were taken at pre-dose on Day 1 (Baseline), Day 4, and Day 8. The Baseline value was the Day 1 pre-dose value. Change from Baseline was calculated by subtracting the Baseline value from the individual post-Baseline value.

End point type	Secondary

End point timeframe:

Baseline, Day 4, and Day 8

End point values	Placebo	GSK962040 50 mg	GSK962040 Total	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	19[52]	37[53]	38[54]	
Units: Grams per liter				
arithmetic mean (standard deviation)				
Hemoglobin, Day 4, n=19, 34, 35	-2.3 (± 6.53)	-2 (± 6.35)	-2.3 (± 6.44)	
Hemoglobin, Day 8, n=17, 35, 36	-2.4 (± 4.27)	-2.3 (± 4.71)	-2.2 (± 4.64)	
MCHC, Day 4, n=13, 24, 24	0 (± 8.85)	0.6 (± 8.83)	0.6 (± 8.83)	
MCHC, Day 8, n=12, 25, 25	0.4 (± 8.3)	-2.3 (± 8.47)	-2.3 (± 8.47)	

Notes:

[52] - ASP. Participants with available data (n=X, X in category titles) were analyzed.

[53] - ASP. Participants with available data (n=X, X in category titles) were analyzed.

[54] - ASP. Participants with available data (n=X, X in category titles) were analyzed.

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in hematocrit at Day 4 and Day 8

End point title	Change from Baseline in hematocrit at Day 4 and Day 8

End point description:

Hematocrit measurements were taken at pre-dose on Day 1 (Baseline), Day 4, and Day 8. The Baseline value was the Day 1 pre-dose value. Change from Baseline was calculated by subtracting the Baseline value from the individual post-Baseline value.

End point type	Secondary

End point timeframe:

Baseline, Day 4, and Day 8

End point values	Placebo	GSK962040 50 mg	GSK962040 Total	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	19[55]	37[56]	38[57]	
Units: proportion of 1				
arithmetic mean (standard deviation)				
Day 4, n=19, 34, 35	-0.0059 (± 0.02331)	-0.0059 (± 0.02029)	-0.0067 (± 0.02051)	
Day 8, n=17, 35, 36	-0.0044 (± 0.01383)	-0.0037 (± 0.01702)	-0.0039 (± 0.01682)	

Notes:

[55] - ASP. Participants with available data (n=X, X in category titles) were analyzed.

[56] - ASP. Participants with available data (n=X, X in category titles) were analyzed.

[57] - ASP. Participants with available data (n=X, X in category titles) were analyzed.

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in mean corpuscle hemoglobin (MCH) at Day 4 and Day 8

End point title	Change from Baseline in mean corpuscle hemoglobin (MCH) at Day 4 and Day 8

End point description:

MCH measurements were taken at pre-dose on Day 1 (Baseline), Day 4, and Day 8. The Baseline value was the Day 1 pre-dose value. Change from Baseline was calculated by subtracting the Baseline value from the individual post-Baseline value.

End point type	Secondary

End point timeframe:

Baseline, Day 4, and Day 8

End point values	Placebo	GSK962040 50 mg	GSK962040 Total	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	19[58]	37[59]	38[60]	
Units: Picograms				
arithmetic mean (standard deviation)				
Day 4, n=19, 34, 35	-0.12 (± 0.464)	-0.06 (± 0.744)	0.07 (± 0.737)	
Day 8, n=17, 35, 36	0.03 (± 0.718)	-0.2 (± 0.832)	0.19 (± 0.826)	

Notes:

[58] - ASP. Participants with available data (n=X, X in category titles) were analyzed.

[59] - ASP. Participants with available data (n=X, X in category titles) were analyzed.

[60] - ASP. Participants with available data (n=X, X in category titles) were analyzed.

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in mean corpuscle volume (MCV) at Day 4 and Day 8

End point title	Change from Baseline in mean corpuscle volume (MCV) at Day 4 and Day 8

End point description:

MCV measurements were taken at pre-dose on Day 1 (Baseline), Day 4, and Day 8. The Baseline value was the Day 1 pre-dose value. Change from Baseline was calculated by subtracting the Baseline value from the individual post-Baseline value.

End point type	Secondary

End point timeframe:

Baseline, Day 4, and Day 8

End point values	Placebo	GSK962040 50 mg	GSK962040 Total	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	19[61]	37[62]	38[63]	
Units: Femtoliters				
arithmetic mean (standard deviation)				
Day 4, n=19, 34, 35	-0.13 (± 1.945)	-0.14 (± 1.339)	-0.17 (± 1.334)	
Day 8, n=17, 35, 36	0.72 (± 1.322)	-0.05 (± 1.401)	-0.06 (± 1.381)	

Notes:

[61] - ASP. Participants with available data (n=X, X in category titles) were analyzed.

[62] - ASP. Participants with available data (n=X, X in category titles) were analyzed.

[63] - ASP. Participants with available data (n=X, X in category titles) were analyzed.

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in red blood cell count (RBC), reticulocytes (RET), and white blood cell count (WBC) at Day 4 and Day 8

End point title	Change from Baseline in red blood cell count (RBC), reticulocytes (RET), and white blood cell count (WBC) at Day 4 and Day 8

End point description:

RBC, RET, and WBC measurements were taken at pre-dose on Day 1 (Baseline), Day 4, and Day 8. The Baseline value was the Day 1 pre-dose value. Change from Baseline was calculated by subtracting the Baseline value from the individual post-Baseline value.

End point type	Secondary

End point timeframe:

Baseline, Day 4, and Day 8

End point values	Placebo	GSK962040 50 mg	GSK962040 Total	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	19[64]	37[65]	38[66]	
Units: Tera (10^12) cells per liter				
arithmetic mean (standard deviation)				
RBC, Day 4, n=19, 34, 35	-0.055 (± 0.2345)	0.068 (± 0.2138)	-0.074 (± 0.214)	
RBC, Day 8, n=17, 35, 36	-0.073 (± 0.127)	0.041 (± 0.1752)	-0.043 (± 0.173)	
RET, Day 4, n=16, 28, 29	0 (± 0.0075)	0.002 (± 0.0093)	0.001 (± 0.0098)	
RET, Day 8, n=13, 28, 29	0.004 (± 0.008)	0.001 (± 0.0093)	0.001 (± 0.0095)	
WBC, Day 4, n=19, 34, 35	0.14 (± 0.9284)	0.39 (± 1.0592)	0.392 (± 1.0437)	
WBC, Day 8, n=17, 35, 36	-0.036 (± 0.8961)	-0.154 (± 0.9006)	-0.161 (± 0.8886)	

Notes:

[64] - ASP. Participants with available data (n=X, X in category titles) were analyzed.

[65] - ASP. Participants with available data (n=X, X in category titles) were analyzed.

[66] - ASP. Participants with available data (n=X, X in category titles) were analyzed.

Statistical analyses

No statistical analyses for this end point

Secondary: Number of participants with any adverse event (AE) or serious adverse event (SAE)

End point title	Number of participants with any adverse event (AE) or serious adverse event (SAE)

End point description:

An AE is defined as any unfavorable and unintended sign (including an abnormal laboratory finding), symptom, or disease (new or exacerbated) temporally associated with the use of a medicinal product, whether or not considered related to the medicinal product. An SAE is defined as any untoward medical occurrence that, at any dose, results in death, is life threatening, requires hospitalization or prolongation of existing hospitalization, results in disability or incapacity, is a congenital anomaly or birth defect, is associated with liver injury and impaired liver function, or are serious events as per the medical or scientific judgment.

End point type	Secondary

End point timeframe:

From the start of study medication until Follow-up (up to Day 25)

End point values	Placebo	GSK962040 50 mg	GSK962040 Total	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	19[67]	37[68]	38[69]	
Units: participants				
Any AE	17	23	24	
Any SAE	2	2	2	

Notes:

[67] - All Subjects Population

[68] - All Subjects Population

[69] - All Subjects Population

Statistical analyses

No statistical analyses for this end point

Secondary: GSK962040 area under the plasma concentration-time curve from zero to 5.5 hours (AUC[0-5.5] and area under the plasma concentration-time curve from zero to infinity (AUC[0-inf]) at Days 1 and 8

End point title	GSK962040 area under the plasma concentration-time curve from zero to 5.5 hours (AUC[0-5.5] and area under the plasma concentration-time curve from zero to infinity (AUC[0-inf]) at Days 1 and 8

End point description:

GSK AUC(0-5.5) and AUC(0-inf) were derived from GSK962040 plasma concentration-time data. Only participants who received GSK962040 50 mg were analyzed. AUC is a measure of levodopa exposure.

End point type	Secondary

End point timeframe:

Day 1 and Day 8

End point values	GSK962040 50 mg			
Subject group type	Subject analysis set			
Number of subjects analysed	36[70]			
Units: Nanograms.hour/milliliter				
geometric mean (geometric coefficient of variation)				
AUC(0-5.5): Day 1	1632.5 (± 38.1)			
AUC(0-5.5): Day 8	3036.9 (± 45.8)			
AUC(0-inf): Day 1	2972.8 (± 49.2)			

Notes:

[70] - PD/Efficacy Population. Participants with available data (n=X, X in category titles) were analyzed.

Statistical analyses

No statistical analyses for this end point

Secondary: GSK962040 percentage of AUC(0-inf) obtained by extrapolation (%AUCex) at Day 1

End point title	GSK962040 percentage of AUC(0-inf) obtained by extrapolation (%AUCex) at Day 1

End point description:

GSK962040 %AUCex was derived from GSK962040 plasma concentration-time data. %AUCex is the percentage of the AUC(0-inf) extrapolated from the last PK sample drawn to infinity. This parameter is only reported in conjunction with single-dose AUC(0-inf). Only participants who received GSK962040 50

mg were analyzed. AUC is a measure of levodopa exposure.

End point type	Secondary

End point timeframe:

Day 1

End point values	GSK962040 50 mg			
Subject group type	Subject analysis set			
Number of subjects analysed	36[71]			
Units: Percentage				
geometric mean (geometric coefficient of variation)	41.64 (± 28.9)			

Notes:

[71] - PD/Efficacy Population. Participants with available data (n=X, X in category titles) were analyzed.

Statistical analyses

No statistical analyses for this end point

Secondary: GSK962040 Cmax at Day1 and Day 8

End point title	GSK962040 Cmax at Day1 and Day 8

End point description:

GSK962040 Cmax was derived from GSK962040 plasma concentration-time data. Only participants who received GSK962040 50 mg were analyzed.

End point type	Secondary

End point timeframe:

Day 1 and Day 8

End point values	GSK962040 50 mg			
Subject group type	Subject analysis set			
Number of subjects analysed	36[72]			
Units: Nanograms/milliliter				
geometric mean (geometric coefficient of variation)				
Day 1	501 (± 45.4)			
Day 8	788.3 (± 46)			

Notes:

[72] - PD/Efficacy Population. Participants with available data (n=X, X in category titles) were analyzed.

Statistical analyses

No statistical analyses for this end point

Secondary: GSK962040 tmax at Day1 and Day 8

End point title	GSK962040 tmax at Day1 and Day 8

End point description:

GSK962040 tmax was derived from GSK962040 plasma concentration-time data. Only participants who received GSK962040 50 mg were analyzed.

End point type	Secondary

End point timeframe:

Day 1 and Day 8

End point values	GSK962040 50 mg			
Subject group type	Subject analysis set			
Number of subjects analysed	36[73]			
Units: Hours				
median (full range (min-max))				
Day 1	0.75 (0.25 to 3.5)			
Day 8	1 (0.25 to 3.72)			

Notes:

[73] - PD/Efficacy Population. Participants with available data (n=X, X in category titles) were analyzed.

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information	
Timeframe for reporting adverse events:	
Post-randomization adverse events include those that occured on or after the randomization date.	
Assessment type	Systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	17.0

Reporting groups	
Reporting group title	Placebo
Reporting group description:	
Participants received placebo administered orally once daily for 7 to 9 days.	
Reporting group title	GSK962040 50 mg
Reporting group description:	
Participants received GSK962040 50 milligrams (mg) administered orally once daily for 7 to 9 days.	
Reporting group title	GSK962040 125 mg
Reporting group description:	
Participants received GSK962040 125 milligrams (mg) administered orally once daily for 7 to 9 days.	

Serious adverse events	Placebo	GSK962040 50 mg	GSK962040 125 mg
Total subjects affected by serious adverse events			
subjects affected / exposed	2 / 19 (10.53%)	2 / 37 (5.41%)	0 / 1 (0.00%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Injury, poisoning and procedural complications			
Ankle fracture			
subjects affected / exposed	1 / 19 (5.26%)	0 / 37 (0.00%)	0 / 1 (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
Rib fracture			
subjects affected / exposed	1 / 19 (5.26%)	0 / 37 (0.00%)	0 / 1 (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
Vascular disorders			
Circulatory collapse			
subjects affected / exposed	0 / 19 (0.00%)	1 / 37 (2.70%)	0 / 1 (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

Nervous system disorders			
Parkinson’s disease			
subjects affected / exposed	1 / 19 (5.26%)	0 / 37 (0.00%)	0 / 1 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Skin and subcutaneous tissue disorders			
Pruritus			
subjects affected / exposed	0 / 19 (0.00%)	1 / 37 (2.70%)	0 / 1 (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

Frequency threshold for reporting non-serious adverse events: 2 %

Non-serious adverse events	Placebo	GSK962040 50 mg	GSK962040 125 mg
Total subjects affected by non-serious adverse events			
subjects affected / exposed	17 / 19 (89.47%)	21 / 37 (56.76%)	1 / 1 (100.00%)
Vascular disorders			
Flushing			
subjects affected / exposed	1 / 19 (5.26%)	0 / 37 (0.00%)	0 / 1 (0.00%)
occurrences (all)	1	0	0
Hypertensive crisis			
subjects affected / exposed	0 / 19 (0.00%)	1 / 37 (2.70%)	0 / 1 (0.00%)
occurrences (all)	0	1	0
General disorders and administration site conditions			
Fatigue			
subjects affected / exposed	2 / 19 (10.53%)	5 / 37 (13.51%)	0 / 1 (0.00%)
occurrences (all)	2	12	0
Chills			
subjects affected / exposed	0 / 19 (0.00%)	1 / 37 (2.70%)	0 / 1 (0.00%)
occurrences (all)	0	1	0
Malaise			
subjects affected / exposed	0 / 19 (0.00%)	1 / 37 (2.70%)	0 / 1 (0.00%)
occurrences (all)	0	1	0
Medical device complication			
subjects affected / exposed	0 / 19 (0.00%)	1 / 37 (2.70%)	0 / 1 (0.00%)
occurrences (all)	0	1	0

Mucosal inflammation			
subjects affected / exposed	0 / 19 (0.00%)	1 / 37 (2.70%)	0 / 1 (0.00%)
occurrences (all)	0	1	0
Non-cardiac chest pain			
subjects affected / exposed	0 / 19 (0.00%)	1 / 37 (2.70%)	0 / 1 (0.00%)
occurrences (all)	0	3	0
Pain			
subjects affected / exposed	1 / 19 (5.26%)	0 / 37 (0.00%)	0 / 1 (0.00%)
occurrences (all)	1	0	0
Reproductive system and breast disorders			
Vaginal haemorrhage			
subjects affected / exposed	0 / 19 (0.00%)	1 / 37 (2.70%)	0 / 1 (0.00%)
occurrences (all)	0	1	0
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	1 / 19 (5.26%)	0 / 37 (0.00%)	0 / 1 (0.00%)
occurrences (all)	1	0	0
Psychiatric disorders			
Agitation			
subjects affected / exposed	1 / 19 (5.26%)	0 / 37 (0.00%)	0 / 1 (0.00%)
occurrences (all)	1	0	0
Nervousness			
subjects affected / exposed	0 / 19 (0.00%)	1 / 37 (2.70%)	0 / 1 (0.00%)
occurrences (all)	0	1	0
Nightmare			
subjects affected / exposed	0 / 19 (0.00%)	1 / 37 (2.70%)	0 / 1 (0.00%)
occurrences (all)	0	1	0
Sleep disorder			
subjects affected / exposed	1 / 19 (5.26%)	0 / 37 (0.00%)	0 / 1 (0.00%)
occurrences (all)	1	0	0
Investigations			
Blood alkaline phosphatase increased			
subjects affected / exposed	1 / 19 (5.26%)	0 / 37 (0.00%)	0 / 1 (0.00%)
occurrences (all)	1	0	0
Blood creatine phosphokinase increased			

subjects affected / exposed	0 / 19 (0.00%)	1 / 37 (2.70%)	0 / 1 (0.00%)
occurrences (all)	0	1	0
Blood creatinine increased			
subjects affected / exposed	0 / 19 (0.00%)	1 / 37 (2.70%)	0 / 1 (0.00%)
occurrences (all)	0	1	0
Gamma-glutamyltransferase increased			
subjects affected / exposed	1 / 19 (5.26%)	0 / 37 (0.00%)	0 / 1 (0.00%)
occurrences (all)	1	0	0
Injury, poisoning and procedural complications			
Contusion			
subjects affected / exposed	1 / 19 (5.26%)	1 / 37 (2.70%)	0 / 1 (0.00%)
occurrences (all)	1	1	0
Excoriation			
subjects affected / exposed	0 / 19 (0.00%)	1 / 37 (2.70%)	0 / 1 (0.00%)
occurrences (all)	0	1	0
Fall			
subjects affected / exposed	0 / 19 (0.00%)	1 / 37 (2.70%)	0 / 1 (0.00%)
occurrences (all)	0	1	0
Procedural pain			
subjects affected / exposed	0 / 19 (0.00%)	1 / 37 (2.70%)	0 / 1 (0.00%)
occurrences (all)	0	1	0
Nervous system disorders			
Headache			
subjects affected / exposed	7 / 19 (36.84%)	9 / 37 (24.32%)	0 / 1 (0.00%)
occurrences (all)	9	16	0
Dizziness			
subjects affected / exposed	4 / 19 (21.05%)	1 / 37 (2.70%)	0 / 1 (0.00%)
occurrences (all)	6	1	0
Dyskinesia			
subjects affected / exposed	0 / 19 (0.00%)	1 / 37 (2.70%)	1 / 1 (100.00%)
occurrences (all)	0	1	1
Somnolence			
subjects affected / exposed	0 / 19 (0.00%)	2 / 37 (5.41%)	0 / 1 (0.00%)
occurrences (all)	0	5	0
Clumsiness			

subjects affected / exposed	0 / 19 (0.00%)	1 / 37 (2.70%)	0 / 1 (0.00%)
occurrences (all)	0	1	0
Dysgeusia			
subjects affected / exposed	1 / 19 (5.26%)	0 / 37 (0.00%)	0 / 1 (0.00%)
occurrences (all)	1	0	0
Hypoaesthesia			
subjects affected / exposed	0 / 19 (0.00%)	1 / 37 (2.70%)	0 / 1 (0.00%)
occurrences (all)	0	1	0
Migraine			
subjects affected / exposed	0 / 19 (0.00%)	1 / 37 (2.70%)	0 / 1 (0.00%)
occurrences (all)	0	1	0
Paraesthesia			
subjects affected / exposed	1 / 19 (5.26%)	0 / 37 (0.00%)	0 / 1 (0.00%)
occurrences (all)	1	0	0
Parkinson's disease			
subjects affected / exposed	1 / 19 (5.26%)	0 / 37 (0.00%)	0 / 1 (0.00%)
occurrences (all)	2	0	0
Sensory disturbance			
subjects affected / exposed	0 / 19 (0.00%)	0 / 37 (0.00%)	1 / 1 (100.00%)
occurrences (all)	0	0	1
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	2 / 19 (10.53%)	0 / 37 (0.00%)	0 / 1 (0.00%)
occurrences (all)	2	0	0
Microcytic anaemia			
subjects affected / exposed	0 / 19 (0.00%)	1 / 37 (2.70%)	0 / 1 (0.00%)
occurrences (all)	0	1	0
Ear and labyrinth disorders			
Vertigo			
subjects affected / exposed	1 / 19 (5.26%)	0 / 37 (0.00%)	0 / 1 (0.00%)
occurrences (all)	1	0	0
Eye disorders			
Eye pain			
subjects affected / exposed	1 / 19 (5.26%)	0 / 37 (0.00%)	0 / 1 (0.00%)
occurrences (all)	1	0	0
Metamorphopsia			

subjects affected / exposed	1 / 19 (5.26%)	0 / 37 (0.00%)	0 / 1 (0.00%)
occurrences (all)	1	0	0
Gastrointestinal disorders			
Nausea			
subjects affected / exposed	4 / 19 (21.05%)	3 / 37 (8.11%)	0 / 1 (0.00%)
occurrences (all)	8	4	0
Constipation			
subjects affected / exposed	3 / 19 (15.79%)	1 / 37 (2.70%)	1 / 1 (100.00%)
occurrences (all)	3	1	1
Abdominal pain upper			
subjects affected / exposed	2 / 19 (10.53%)	2 / 37 (5.41%)	0 / 1 (0.00%)
occurrences (all)	2	2	0
Diarrhoea			
subjects affected / exposed	2 / 19 (10.53%)	1 / 37 (2.70%)	0 / 1 (0.00%)
occurrences (all)	2	1	0
Toothache			
subjects affected / exposed	2 / 19 (10.53%)	1 / 37 (2.70%)	0 / 1 (0.00%)
occurrences (all)	2	1	0
Dyspepsia			
subjects affected / exposed	1 / 19 (5.26%)	1 / 37 (2.70%)	0 / 1 (0.00%)
occurrences (all)	2	2	0
Abdominal pain			
subjects affected / exposed	0 / 19 (0.00%)	1 / 37 (2.70%)	0 / 1 (0.00%)
occurrences (all)	0	3	0
Abdominal pain lower			
subjects affected / exposed	0 / 19 (0.00%)	1 / 37 (2.70%)	0 / 1 (0.00%)
occurrences (all)	0	1	0
Flatulence			
subjects affected / exposed	1 / 19 (5.26%)	0 / 37 (0.00%)	0 / 1 (0.00%)
occurrences (all)	1	0	0
Frequent bowel movements			
subjects affected / exposed	0 / 19 (0.00%)	1 / 37 (2.70%)	0 / 1 (0.00%)
occurrences (all)	0	1	0
Gastritis			
subjects affected / exposed	1 / 19 (5.26%)	0 / 37 (0.00%)	0 / 1 (0.00%)
occurrences (all)	1	0	0

Gingival pain			
subjects affected / exposed	1 / 19 (5.26%)	0 / 37 (0.00%)	0 / 1 (0.00%)
occurrences (all)	1	0	0
Skin and subcutaneous tissue disorders			
Hyperhidrosis			
subjects affected / exposed	1 / 19 (5.26%)	0 / 37 (0.00%)	0 / 1 (0.00%)
occurrences (all)	1	0	0
Pruritus			
subjects affected / exposed	0 / 19 (0.00%)	1 / 37 (2.70%)	0 / 1 (0.00%)
occurrences (all)	0	1	0
Renal and urinary disorders			
Haematuria			
subjects affected / exposed	1 / 19 (5.26%)	0 / 37 (0.00%)	0 / 1 (0.00%)
occurrences (all)	1	0	0
Micturition disorder			
subjects affected / exposed	0 / 19 (0.00%)	1 / 37 (2.70%)	0 / 1 (0.00%)
occurrences (all)	0	1	0
Pollakiuria			
subjects affected / exposed	1 / 19 (5.26%)	0 / 37 (0.00%)	0 / 1 (0.00%)
occurrences (all)	1	0	0
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	1 / 19 (5.26%)	3 / 37 (8.11%)	0 / 1 (0.00%)
occurrences (all)	1	3	0
Muscle spasms			
subjects affected / exposed	3 / 19 (15.79%)	0 / 37 (0.00%)	0 / 1 (0.00%)
occurrences (all)	3	0	0
Arthralgia			
subjects affected / exposed	2 / 19 (10.53%)	0 / 37 (0.00%)	0 / 1 (0.00%)
occurrences (all)	4	0	0
Muscle twitching			
subjects affected / exposed	0 / 19 (0.00%)	1 / 37 (2.70%)	0 / 1 (0.00%)
occurrences (all)	0	1	0
Musculoskeletal pain			
subjects affected / exposed	1 / 19 (5.26%)	0 / 37 (0.00%)	0 / 1 (0.00%)
occurrences (all)	1	0	0

Pain in extremity			
subjects affected / exposed	0 / 19 (0.00%)	1 / 37 (2.70%)	0 / 1 (0.00%)
occurrences (all)	0	4	0
Spinal pain			
subjects affected / exposed	0 / 19 (0.00%)	1 / 37 (2.70%)	0 / 1 (0.00%)
occurrences (all)	0	1	0
Infections and infestations			
Cystitis			
subjects affected / exposed	1 / 19 (5.26%)	0 / 37 (0.00%)	0 / 1 (0.00%)
occurrences (all)	1	0	0
Escherichia urinary tract infection			
subjects affected / exposed	1 / 19 (5.26%)	0 / 37 (0.00%)	0 / 1 (0.00%)
occurrences (all)	1	0	0
Influenza			
subjects affected / exposed	0 / 19 (0.00%)	1 / 37 (2.70%)	0 / 1 (0.00%)
occurrences (all)	0	1	0
Nasopharyngitis			
subjects affected / exposed	0 / 19 (0.00%)	1 / 37 (2.70%)	0 / 1 (0.00%)
occurrences (all)	0	1	0
Rhinitis			
subjects affected / exposed	1 / 19 (5.26%)	0 / 37 (0.00%)	0 / 1 (0.00%)
occurrences (all)	1	0	0
Staphylococcal infection			
subjects affected / exposed	1 / 19 (5.26%)	0 / 37 (0.00%)	0 / 1 (0.00%)
occurrences (all)	1	0	0
Urinary tract infection			
subjects affected / exposed	0 / 19 (0.00%)	1 / 37 (2.70%)	0 / 1 (0.00%)
occurrences (all)	0	1	0
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	0 / 19 (0.00%)	1 / 37 (2.70%)	0 / 1 (0.00%)
occurrences (all)	0	1	0
Hyperkalaemia			
subjects affected / exposed	0 / 19 (0.00%)	1 / 37 (2.70%)	0 / 1 (0.00%)
occurrences (all)	0	1	0
Hypoglycaemia			

subjects affected / exposed occurrences (all)	0 / 19 (0.00%) 0	1 / 37 (2.70%) 1	0 / 1 (0.00%) 0

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
15 March 2012	MHRA requested addition of GFR limits as exclusion criteria and change to dose stopping criteria.
28 August 2012	Screening experience indicates that finger tapping trials must be reduced in number. Permitted medications have been updated to aid in recruitment.
05 November 2012	Protocol has been changed from a single-center to a multi-center study to allow for additional sites to aid in recruitment.
06 February 2013	Based on the available screening data, the current study design is believed to be not feasible in practice. Therefore, inclusion criteria have been adjusted to allow a greater proportion of screened subjects into the study, without diminishing the scientific validity of the study. The study design has been adjusted from 2 to 1 cohort, and the study will evaluate placebo and a single dose level of 50 milligrams of GSK962040 initially with the option of adding dose levels after an interim analysis. The randomization ratio has been updated to 2:1 for drug:placebo, respectively.
26 November 2013	The subject-completed "ON"/"OFF" symptoms diary has been added to the screening visit to allow for baseline comparisons. Additional MDS-UPDRS 3 assessments have been added to allow for evaluation of motor symptoms at the subject defined "ON" time. The overdose definition has been expanded for clarity.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? Yes

Date	Interruption	Restart date
21 November 2012	Interim analysis suggested that 125 milligrams camicinal may be higher in PD patients than anticipated. As a precaution, a substantial amendment was prepared to change the dose levels in study MOT115816. Study recruitment was paused during the amendment preparation. The pause was temporary and not safety related.	06 February 2013

Notes:

Limitations and caveats

None reported