



## 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     |
| <b>Arm title</b>             | 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)

|                  |                 |
|------------------|-----------------|
| <b>Arm title</b> | 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)

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| Consent withdrawn by subject                        | 1       | -               |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

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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<br>(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:<br>Participants received placebo administered orally once daily for 7 to 9 days.                                                                                      |                    |
| Reporting group title                                                                                                                                                                              | GSK962040 Total    |
| Reporting group description:<br>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:<br>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:<br>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:<br>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 <sup>[1]</sup> |
| End point description:<br>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:<br>Baseline                                                                                                                                                                                                                                     |                                                                                                                                           |
| Notes:<br>[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.<br>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 <sup>[2]</sup>    | 33 <sup>[3]</sup>    |  |  |
| Units:<br>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  $\geq 1$  dose placebo/GSK962040 50 mg

[3] - Pharmacodynamic (PD)/Efficacy Population: participants receiving  $\geq 1$  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 <sup>[4]</sup>    | 37 <sup>[5]</sup>    |  |  |
| Units:<br>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 <sup>[6]</sup> |
|-----------------|-----------------------------------------------------------------------------------------|

**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 <sup>[7]</sup>    | 35 <sup>[8]</sup>    |  |  |
| 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 <sup>[9]</sup>    | 37 <sup>[10]</sup>   |  |  |
| 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:<br>L-DOPA Tmax was derived from L-DOPA plasma concentration-time data. |                                                                        |
| End point type                                                                                | Primary                                                                |
| End point timeframe:<br>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 <sup>[11]</sup>   | 37 <sup>[12]</sup>   |  |  |
| 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 (t<sub>1/2</sub>) at Baseline, Day 1, and Day 8

|                 |                                                                                                   |
|-----------------|---------------------------------------------------------------------------------------------------|
| End point title | L-DOPA terminal phase half-life (t <sub>1/2</sub> ) at Baseline, Day 1, and Day 8 <sup>[13]</sup> |
|-----------------|---------------------------------------------------------------------------------------------------|

End point description:

L-DOPA t<sub>1/2</sub> 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 <sup>[14]</sup>    | 0 <sup>[15]</sup>    |  |  |
| 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 t<sub>1/2</sub>) at Baseline (BL), Day 1, and Day 8

|                 |                                                                                      |
|-----------------|--------------------------------------------------------------------------------------|
| End point title | Gastric half emptying time (GE t <sub>1/2</sub> ) 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 <sup>13</sup>C-oral breath test, which is a tracer method that utilizes <sup>13</sup>C, 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 <sup>13</sup>C-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 <sup>13</sup>C breath content was determined by isotope ratio mass spectrometry. GE t<sub>1/2</sub> was determined by using the cumulative percentage of the administered dose of <sup>13</sup>C 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 <sup>[16]</sup>   | 37 <sup>[17]</sup>   |  |  |
| 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 <sup>[18]</sup>   | 37 <sup>[19]</sup>   |  |  |
| 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:<br>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:<br>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:<br>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                                |

|                                   |                |
|-----------------------------------|----------------|
| <b>Statistical analysis title</b> | 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                               |

|                                   |                 |
|-----------------------------------|-----------------|
| <b>Statistical analysis title</b> | 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                                |

|                                                                                                                                                                                                                                                 |                                     |
|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-------------------------------------|
| <b>Statistical analysis title</b>                                                                                                                                                                                                               | 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                               |

|                                                                                                                                                                                                                                                |                                     |
|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-------------------------------------|
| <b>Statistical analysis title</b>                                                                                                                                                                                                              | 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                                |

|                                                                                                                                                                                                                                                |                                     |
|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-------------------------------------|
| <b>Statistical analysis title</b>                                                                                                                                                                                                              | 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    |

|                                   |              |
|-----------------------------------|--------------|
| <b>Statistical analysis title</b> | 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                                |

|                                   |              |
|-----------------------------------|--------------|
| <b>Statistical analysis title</b> | 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 <sup>[20]</sup>   | 37 <sup>[21]</sup>   |  |  |
| 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**

|                                                                                                                                                                                                                                                          |                           |
|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|---------------------------|
| <b>Statistical analysis title</b>                                                                                                                                                                                                                        | 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                                |

|                                   |                   |
|-----------------------------------|-------------------|
| <b>Statistical analysis title</b> | 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                                |

|                                   |                   |
|-----------------------------------|-------------------|
| <b>Statistical analysis title</b> | 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                                |

|                                                                                                                                                                                                                                                            |                                     |
|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-------------------------------------|
| <b>Statistical analysis title</b>                                                                                                                                                                                                                          | 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                                |

|                                                                                                                                                                                                                                                          |                                     |
|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-------------------------------------|
| <b>Statistical analysis title</b>                                                                                                                                                                                                                        | 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                               |

|                                                                                                                                                                                                                                                            |                                     |
|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-------------------------------------|
| <b>Statistical analysis title</b>                                                                                                                                                                                                                          | 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    |

|                                   |                   |
|-----------------------------------|-------------------|
| <b>Statistical analysis title</b> | 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                                |

|                                   |                   |
|-----------------------------------|-------------------|
| <b>Statistical analysis title</b> | 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 categories 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 <sup>[22]</sup>   | 37 <sup>[23]</sup>   |  |  |
| 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

|                                                                                                                                                                                                                     |                                     |
|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-------------------------------------|
| <b>Statistical analysis title</b>                                                                                                                                                                                   | 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                                |

|                                                                                                                                                                                                                    |                                     |
|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-------------------------------------|
| <b>Statistical analysis title</b>                                                                                                                                                                                  | 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 <sup>[24]</sup>   | 37 <sup>[25]</sup>   |  |  |
| 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**



|                                                                                                                                                                                                                                                          |                                     |
|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-------------------------------------|
| <b>Statistical analysis title</b>                                                                                                                                                                                                                        | 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                               |

|                                                                                                                                                                                                                                                          |                                     |
|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-------------------------------------|
| <b>Statistical analysis title</b>                                                                                                                                                                                                                        | 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                               |

|                                                                                                                                                                                                                                                           |                                     |
|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-------------------------------------|
| <b>Statistical analysis title</b>                                                                                                                                                                                                                         | 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   |

|                                   |                  |
|-----------------------------------|------------------|
| <b>Statistical analysis title</b> | 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   |

|                                   |               |
|-----------------------------------|---------------|
| <b>Statistical analysis title</b> | 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   |

|                                   |                   |
|-----------------------------------|-------------------|
| <b>Statistical analysis title</b> | 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                               |

|                                   |                   |
|-----------------------------------|-------------------|
| <b>Statistical analysis title</b> | 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                               |

|                                   |                   |
|-----------------------------------|-------------------|
| <b>Statistical analysis title</b> | 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                               |

|                                                                                                                                                                                                                                                          |                                     |
|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-------------------------------------|
| <b>Statistical analysis title</b>                                                                                                                                                                                                                        | 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                               |

|                                                                                                                                                                                                                                                          |                                     |
|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-------------------------------------|
| <b>Statistical analysis title</b>                                                                                                                                                                                                                        | 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                               |

|                                                                                                                                                                                                                                                           |                           |
|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|---------------------------|
| <b>Statistical analysis title</b>                                                                                                                                                                                                                         | 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                               |

|                                   |                  |
|-----------------------------------|------------------|
| <b>Statistical analysis title</b> | 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                               |

|                                   |                  |
|-----------------------------------|------------------|
| <b>Statistical analysis title</b> | 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                               |

|                                                                                                                                                                                                                                                            |                                     |
|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-------------------------------------|
| <b>Statistical analysis title</b>                                                                                                                                                                                                                          | 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                               |

|                                                                                                                                                                                                                                                            |                                     |
|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-------------------------------------|
| <b>Statistical analysis title</b>                                                                                                                                                                                                                          | 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                               |

|                                                                                                                                                                                                                                                            |                                     |
|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-------------------------------------|
| <b>Statistical analysis title</b>                                                                                                                                                                                                                          | 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:<br>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:<br>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 <sup>[26]</sup>   | 37 <sup>[27]</sup>   |  |  |
| 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 <sup>[28]</sup>   | 37 <sup>[29]</sup>   | 38 <sup>[30]</sup>   |  |
| 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  $\geq 1$  dose of study medication

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

[30] - All Subjects Population (ASP): all participants who received  $\geq 1$  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 <sup>[31]</sup>   | 37 <sup>[32]</sup>   | 38 <sup>[33]</sup>   |  |
| 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 <sup>[34]</sup>   | 37 <sup>[35]</sup>   | 38 <sup>[36]</sup>   |  |
| 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 <sup>[37]</sup>   | 37 <sup>[38]</sup>   | 38 <sup>[39]</sup>   |  |
| 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 <sup>[40]</sup>   | 37 <sup>[41]</sup>   | 38 <sup>[42]</sup>   |  |
| 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 8, 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 <sup>[43]</sup>   | 37 <sup>[44]</sup>   | 38 <sup>[45]</sup>   |  |
| 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 (CO<sub>2</sub>)/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 (CO <sub>2</sub> )/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, CO<sub>2</sub>/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 <sup>[46]</sup>   | 37 <sup>[47]</sup>   | 38 <sup>[48]</sup>   |  |
| 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)        |  |
| CO <sub>2</sub> /BC, Day 4, n=9, 21, 22 | -0.06 (± 2.833)      | 0.16 (± 2.602)       | 0.2 (± 2.546)        |  |
| CO <sub>2</sub> /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 <sup>[49]</sup>   | 37 <sup>[50]</sup>   | 38 <sup>[51]</sup>   |  |
| Units: Giga (10 <sup>9</sup> ) 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 <sup>[52]</sup>   | 37 <sup>[53]</sup>   | 38 <sup>[54]</sup>   |  |
| 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 <sup>[55]</sup>   | 37 <sup>[56]</sup>   | 38 <sup>[57]</sup>   |  |
| 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 <sup>[58]</sup>   | 37 <sup>[59]</sup>   | 38 <sup>[60]</sup>   |  |
| 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 <sup>[61]</sup>   | 37 <sup>[62]</sup>   | 38 <sup>[63]</sup>   |  |
| 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 <sup>[64]</sup>   | 37 <sup>[65]</sup>   | 38 <sup>[66]</sup>   |  |
| Units: Tera (10 <sup>12</sup> ) 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 <sup>[67]</sup>   | 37 <sup>[68]</sup>   | 38 <sup>[69]</sup>   |  |
| Units: participants         |                      |                      |                      |  |
| Any AE                      | 17                   | 23                   | 24                   |  |
| Any SAE                     | 2                    | 2                    | 2                    |  |

Notes:

[67] - All Subjects Population

[68] - 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 <sup>[70]</sup>   |  |  |  |
| 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                |           |

|                                                     |                      |  |  |  |
|-----------------------------------------------------|----------------------|--|--|--|
| <b>End point values</b>                             | GSK962040 50 mg      |  |  |  |
| Subject group type                                  | Subject analysis set |  |  |  |
| Number of subjects analysed                         | 36 <sup>[71]</sup>   |  |  |  |
| 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                                                                                                                         |                                  |

|                                                     |                      |  |  |  |
|-----------------------------------------------------|----------------------|--|--|--|
| <b>End point values</b>                             | GSK962040 50 mg      |  |  |  |
| Subject group type                                  | Subject analysis set |  |  |  |
| Number of subjects analysed                         | 36 <sup>[72]</sup>   |  |  |  |
| 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

---

|                               |                      |  |  |  |
|-------------------------------|----------------------|--|--|--|
| <b>End point values</b>       | GSK962040 50 mg      |  |  |  |
| Subject group type            | Subject analysis set |  |  |  |
| Number of subjects analysed   | 36 <sup>[73]</sup>   |  |  |  |
| 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 occurred 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 %

| <b>Non-serious adverse events</b>                     | 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<br>subjects affected / exposed<br>occurrences (all)                                            | 0 / 19 (0.00%)<br>0 | 1 / 37 (2.70%)<br>1 | 0 / 1 (0.00%)<br>0 |
| Non-cardiac chest pain<br>subjects affected / exposed<br>occurrences (all)                                          | 0 / 19 (0.00%)<br>0 | 1 / 37 (2.70%)<br>3 | 0 / 1 (0.00%)<br>0 |
| Pain<br>subjects affected / exposed<br>occurrences (all)                                                            | 1 / 19 (5.26%)<br>1 | 0 / 37 (0.00%)<br>0 | 0 / 1 (0.00%)<br>0 |
| Reproductive system and breast disorders<br>Vaginal haemorrhage<br>subjects affected / exposed<br>occurrences (all) | 0 / 19 (0.00%)<br>0 | 1 / 37 (2.70%)<br>1 | 0 / 1 (0.00%)<br>0 |
| Respiratory, thoracic and mediastinal disorders<br>Cough<br>subjects affected / exposed<br>occurrences (all)        | 1 / 19 (5.26%)<br>1 | 0 / 37 (0.00%)<br>0 | 0 / 1 (0.00%)<br>0 |
| Psychiatric disorders<br>Agitation<br>subjects affected / exposed<br>occurrences (all)                              | 1 / 19 (5.26%)<br>1 | 0 / 37 (0.00%)<br>0 | 0 / 1 (0.00%)<br>0 |
| Nervousness<br>subjects affected / exposed<br>occurrences (all)                                                     | 0 / 19 (0.00%)<br>0 | 1 / 37 (2.70%)<br>1 | 0 / 1 (0.00%)<br>0 |
| Nightmare<br>subjects affected / exposed<br>occurrences (all)                                                       | 0 / 19 (0.00%)<br>0 | 1 / 37 (2.70%)<br>1 | 0 / 1 (0.00%)<br>0 |
| Sleep disorder<br>subjects affected / exposed<br>occurrences (all)                                                  | 1 / 19 (5.26%)<br>1 | 0 / 37 (0.00%)<br>0 | 0 / 1 (0.00%)<br>0 |
| Investigations<br>Blood alkaline phosphatase increased<br>subjects affected / exposed<br>occurrences (all)          | 1 / 19 (5.26%)<br>1 | 0 / 37 (0.00%)<br>0 | 0 / 1 (0.00%)<br>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<br>occurrences (all) | 1 / 19 (5.26%)<br>1 | 0 / 37 (0.00%)<br>0 | 0 / 1 (0.00%)<br>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<br>subjects affected / exposed<br>occurrences (all)        | 1 / 19 (5.26%)<br>1  | 0 / 37 (0.00%)<br>0 | 0 / 1 (0.00%)<br>0 |
| Skin and subcutaneous tissue disorders                                   |                      |                     |                    |
| Hyperhidrosis<br>subjects affected / exposed<br>occurrences (all)        | 1 / 19 (5.26%)<br>1  | 0 / 37 (0.00%)<br>0 | 0 / 1 (0.00%)<br>0 |
| Pruritus<br>subjects affected / exposed<br>occurrences (all)             | 0 / 19 (0.00%)<br>0  | 1 / 37 (2.70%)<br>1 | 0 / 1 (0.00%)<br>0 |
| Renal and urinary disorders                                              |                      |                     |                    |
| Haematuria<br>subjects affected / exposed<br>occurrences (all)           | 1 / 19 (5.26%)<br>1  | 0 / 37 (0.00%)<br>0 | 0 / 1 (0.00%)<br>0 |
| Micturition disorder<br>subjects affected / exposed<br>occurrences (all) | 0 / 19 (0.00%)<br>0  | 1 / 37 (2.70%)<br>1 | 0 / 1 (0.00%)<br>0 |
| Pollakiuria<br>subjects affected / exposed<br>occurrences (all)          | 1 / 19 (5.26%)<br>1  | 0 / 37 (0.00%)<br>0 | 0 / 1 (0.00%)<br>0 |
| Musculoskeletal and connective tissue disorders                          |                      |                     |                    |
| Back pain<br>subjects affected / exposed<br>occurrences (all)            | 1 / 19 (5.26%)<br>1  | 3 / 37 (8.11%)<br>3 | 0 / 1 (0.00%)<br>0 |
| Muscle spasms<br>subjects affected / exposed<br>occurrences (all)        | 3 / 19 (15.79%)<br>3 | 0 / 37 (0.00%)<br>0 | 0 / 1 (0.00%)<br>0 |
| Arthralgia<br>subjects affected / exposed<br>occurrences (all)           | 2 / 19 (10.53%)<br>4 | 0 / 37 (0.00%)<br>0 | 0 / 1 (0.00%)<br>0 |
| Muscle twitching<br>subjects affected / exposed<br>occurrences (all)     | 0 / 19 (0.00%)<br>0  | 1 / 37 (2.70%)<br>1 | 0 / 1 (0.00%)<br>0 |
| Musculoskeletal pain<br>subjects affected / exposed<br>occurrences (all) | 1 / 19 (5.26%)<br>1  | 0 / 37 (0.00%)<br>0 | 0 / 1 (0.00%)<br>0 |

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

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