



## Clinical trial results:

### A Phase IIa, Double-Blind, Mechanistic Study of GSK3196165 in Combination with Methotrexate Therapy in Subjects with Active Rheumatoid Arthritis Despite Treatment with DMARDs

#### Summary

|                          |                 |
|--------------------------|-----------------|
| EudraCT number           | 2015-004386-91  |
| Trial protocol           | DE PL           |
| Global end of trial date | 30 October 2017 |

#### Results information

|                                |                  |
|--------------------------------|------------------|
| Result version number          | v1 (current)     |
| This version publication date  | 13 November 2018 |
| First version publication date | 13 November 2018 |

#### Trial information

##### Trial identification

|                       |        |
|-----------------------|--------|
| Sponsor protocol code | 205180 |
|-----------------------|--------|

##### Additional study identifiers

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

Notes:

#### Sponsors

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

Notes:

#### Paediatric regulatory details

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

Notes:

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**Results analysis stage**

|                                                      |                 |
|------------------------------------------------------|-----------------|
| Analysis stage                                       | Final           |
| Date of interim/final analysis                       | 31 January 2018 |
| Is this the analysis of the primary completion data? | No              |

|                                  |                 |
|----------------------------------|-----------------|
| Global end of trial reached?     | Yes             |
| Global end of trial date         | 30 October 2017 |
| Was the trial ended prematurely? | No              |

Notes:

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**General information about the trial**

Main objective of the trial:

The main objectives of this study are to explore the activity of Granulocyte-macrophage colony-stimulating factor (GM-CSF) signaling pathway characterized by exploratory biomarkers in participants with rheumatoid arthritis, the impact of GSK3196165 therapy, and whether there are any differences in this GM-CSF signaling pathway between participants with early RA or established RA.

Protection of trial subjects:

Not Applicable

Background therapy: -

Evidence for comparator: -

|                                                           |              |
|-----------------------------------------------------------|--------------|
| Actual start date of recruitment                          | 15 June 2016 |
| Long term follow-up planned                               | No           |
| Independent data monitoring committee (IDMC) involvement? | No           |

Notes:

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**Population of trial subjects**

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**Subjects enrolled per country**

|                                      |                   |
|--------------------------------------|-------------------|
| Country: Number of subjects enrolled | United States: 32 |
| Country: Number of subjects enrolled | Poland: 6         |
| Country: Number of subjects enrolled | Germany: 1        |
| Worldwide total number of subjects   | 39                |
| EEA total number of subjects         | 7                 |

Notes:

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**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)                      | 30 |
| From 65 to 84 years                       | 9  |

|                   |   |
|-------------------|---|
| 85 years and over | 0 |
|-------------------|---|

## Subject disposition

### Recruitment

Recruitment details:

A total of 39 participants with active early/established Rheumatoid arthritis were randomized across 9 centers in 3 countries from 15 June 2016 to 30 October 2017.

### Pre-assignment

Screening details:

Out of the 88 participants screened for this study, 49 participants were screen failures and 39 participants were randomized and received treatment in the study.

### Period 1

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

### Arms

|                              |         |
|------------------------------|---------|
| Are arms mutually exclusive? | Yes     |
| <b>Arm title</b>             | Placebo |

Arm description:

Eligible participants received matching placebo subcutaneously (SC) into thigh or abdomen once weekly for 5 weeks, and then every other week until Week 10. In addition to placebo, participants also received methotrexate (MTX) 7.5–25 mg/week and folic (or folinic) acid  $\geq 5$  mg/week during the combination treatment period.

|                                        |                  |
|----------------------------------------|------------------|
| Arm type                               | Placebo          |
| Investigational medicinal product name | Placebo          |
| Investigational medicinal product code |                  |
| Other name                             |                  |
| Pharmaceutical forms                   | Injection        |
| Routes of administration               | Subcutaneous use |

Dosage and administration details:

Sterile 0.9% weight by volume (w/v) sodium chloride solution to be administered as subcutaneous injection into thigh or abdomen once weekly for 5 weeks

|                                        |                            |
|----------------------------------------|----------------------------|
| Investigational medicinal product name | Methotrexate               |
| Investigational medicinal product code |                            |
| Other name                             |                            |
| Pharmaceutical forms                   | Injection, Tablet          |
| Routes of administration               | Subcutaneous use, Oral use |

Dosage and administration details:

Tablet or liquid administered orally or subcutaneously

|                                        |                              |
|----------------------------------------|------------------------------|
| Investigational medicinal product name | Folic acid or folinic acid   |
| Investigational medicinal product code |                              |
| Other name                             |                              |
| Pharmaceutical forms                   | Capsule, Tablet, Oral liquid |
| Routes of administration               | Oral use                     |

Dosage and administration details:

Capsule, tablet or liquid taken orally

|                  |                   |
|------------------|-------------------|
| <b>Arm title</b> | GSK3196165 180 mg |
|------------------|-------------------|

Arm description:

Eligible participants received GSK3196165 180 milligrams (mg) SC into thigh or abdomen once weekly for 5 weeks, and then every other week until Week 10. In addition to GSK3196165, participants also

received MTX 7.5–5 mg/week and folic (or folinic) acid  $\geq 5$  mg/week during the combination treatment period.

|                                        |                  |
|----------------------------------------|------------------|
| Arm type                               | Experimental     |
| Investigational medicinal product name | GSK3196165       |
| Investigational medicinal product code |                  |
| Other name                             |                  |
| Pharmaceutical forms                   | Injection        |
| Routes of administration               | Subcutaneous use |

Dosage and administration details:

GSK3196165 is available as sterile solution to be administered as subcutaneous injection into thigh or abdomen once weekly for 5 weeks.

|                                        |                            |
|----------------------------------------|----------------------------|
| Investigational medicinal product name | Methotrexate               |
| Investigational medicinal product code |                            |
| Other name                             |                            |
| Pharmaceutical forms                   | Injection, Tablet          |
| Routes of administration               | Subcutaneous use, Oral use |

Dosage and administration details:

Tablet or liquid administered orally or subcutaneously.

|                                        |                              |
|----------------------------------------|------------------------------|
| Investigational medicinal product name | Folic acid or folinic acid   |
| Investigational medicinal product code |                              |
| Other name                             |                              |
| Pharmaceutical forms                   | Tablet, Capsule, Oral liquid |
| Routes of administration               | Oral use                     |

Dosage and administration details:

Capsule, table or liquid taken orally

| <b>Number of subjects in period 1</b> | Placebo | GSK3196165 180 mg |
|---------------------------------------|---------|-------------------|
| Started                               | 11      | 28                |
| Completed                             | 7       | 23                |
| Not completed                         | 4       | 5                 |
| Consent withdrawn by subject          | 2       | 4                 |
| Lost to follow-up                     | -       | 1                 |
| Lack of efficacy                      | 2       | -                 |

## Baseline characteristics

### Reporting groups

|                                                                                                                                                                                                                                                                                                                                        |                   |
|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-------------------|
| Reporting group title                                                                                                                                                                                                                                                                                                                  | Placebo           |
| Reporting group description:                                                                                                                                                                                                                                                                                                           |                   |
| Eligible participants received matching placebo subcutaneously (SC) into thigh or abdomen once weekly for 5 weeks, and then every other week until Week 10. In addition to placebo, participants also received methotrexate (MTX) 7.5–25 mg/week and folic (or folinic) acid $\geq 5$ mg/week during the combination treatment period. |                   |
| Reporting group title                                                                                                                                                                                                                                                                                                                  | GSK3196165 180 mg |
| Reporting group description:                                                                                                                                                                                                                                                                                                           |                   |
| Eligible participants received GSK3196165 180 milligrams (mg) SC into thigh or abdomen once weekly for 5 weeks, and then every other week until Week 10. In addition to GSK3196165, participants also received MTX 7.5–5 mg/week and folic (or folinic) acid $\geq 5$ mg/week during the combination treatment period.                 |                   |

| Reporting group values              | Placebo     | GSK3196165 180 mg | Total |
|-------------------------------------|-------------|-------------------|-------|
| Number of subjects                  | 11          | 28                | 39    |
| Age categorical                     |             |                   |       |
| Units: Subjects                     |             |                   |       |
| Overall number of baseline subjects | 11          | 28                | 39    |
| Age Continuous                      |             |                   |       |
| Units: years                        |             |                   |       |
| arithmetic mean                     | 50.3        | 59.1              |       |
| standard deviation                  | $\pm 11.57$ | $\pm 9.47$        | -     |
| Sex: Female, Male                   |             |                   |       |
| Units: Subjects                     |             |                   |       |
| Female                              | 10          | 24                | 34    |
| Male                                | 1           | 4                 | 5     |
| Race/Ethnicity, Customized          |             |                   |       |
| Units: Subjects                     |             |                   |       |
| Black or African American           | 2           | 4                 | 6     |
| White                               | 9           | 24                | 33    |

## End points

### End points reporting groups

|                                                                                                                                                                                                                                                                                                                                        |                   |
|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-------------------|
| Reporting group title                                                                                                                                                                                                                                                                                                                  | Placebo           |
| Reporting group description:                                                                                                                                                                                                                                                                                                           |                   |
| Eligible participants received matching placebo subcutaneously (SC) into thigh or abdomen once weekly for 5 weeks, and then every other week until Week 10. In addition to placebo, participants also received methotrexate (MTX) 7.5–25 mg/week and folic (or folinic) acid $\geq 5$ mg/week during the combination treatment period. |                   |
| Reporting group title                                                                                                                                                                                                                                                                                                                  | GSK3196165 180 mg |
| Reporting group description:                                                                                                                                                                                                                                                                                                           |                   |
| Eligible participants received GSK3196165 180 milligrams (mg) SC into thigh or abdomen once weekly for 5 weeks, and then every other week until Week 10. In addition to GSK3196165, participants also received MTX 7.5–5 mg/week and folic (or folinic) acid $\geq 5$ mg/week during the combination treatment period.                 |                   |

### Primary: Change from Baseline in Target Engagement biomarkers- soluble Granulocyte-macrophage colony-stimulating factor (GM-CSF) complexed to GSK3196165

|                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                         |                                                                                                                                                 |
|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-------------------------------------------------------------------------------------------------------------------------------------------------|
| End point title                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                         | Change from Baseline in Target Engagement biomarkers- soluble Granulocyte-macrophage colony-stimulating factor (GM-CSF) complexed to GSK3196165 |
| End point description:                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                  |                                                                                                                                                 |
| Blood samples were collected for markers which may influence rheumatoid arthritis. Target engagement biomarkers included soluble GM-CSF complexed to GSK3196165. Baseline was defined at Day 1. Change from Baseline was calculated as ratio of Baseline value to post-dose value. Analysis was performed using repeated measures analysis adjusted for GM-CSF - Complex log(Baseline value), treatment group, disease duration ( $\leq 2$ or $> 2$ years), visit and treatment group by visit interaction. Analysis was performed on Intent-to-Treat (ITT) Population which consisted of all participants who were randomized to treatment and who received at least one dose of study treatment. Only those participants with data available at the specified data points were analyzed (represented by n= X in the category titles). |                                                                                                                                                 |
| End point type                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                          | Primary                                                                                                                                         |
| End point timeframe:                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                    |                                                                                                                                                 |
| Baseline and Weeks 1, 2, 4, 6, 8, 12, 12-Week follow-up (FU) (Week 22)                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                  |                                                                                                                                                 |

| End point values                                        | Placebo              | GSK3196165 180 mg     |  |  |
|---------------------------------------------------------|----------------------|-----------------------|--|--|
| Subject group type                                      | Reporting group      | Reporting group       |  |  |
| Number of subjects analysed                             | 11 <sup>[1]</sup>    | 28 <sup>[2]</sup>     |  |  |
| Units: Ratio of GM-CSF complex                          |                      |                       |  |  |
| least squares mean (geometric coefficient of variation) |                      |                       |  |  |
| GM-CSF - Complex, Week 1, n=9, 27                       | 0.972 ( $\pm$ 35.98) | 13.799 ( $\pm$ 20.65) |  |  |
| GM-CSF - Complex, Week 2, n=8, 26                       | 0.960 ( $\pm$ 31.23) | 31.056 ( $\pm$ 17.58) |  |  |
| GM-CSF - Complex, Week 4, n=8, 27                       | 0.959 ( $\pm$ 34.51) | 53.496 ( $\pm$ 18.55) |  |  |
| GM-CSF - Complex, Week 6, n=7, 26                       | 0.964 ( $\pm$ 40.96) | 46.620 ( $\pm$ 22.37) |  |  |
| GM-CSF - Complex, Week 8, n=7, 24                       | 0.964 ( $\pm$ 41.80) | 33.404 ( $\pm$ 22.47) |  |  |

|                                       |                 |                  |  |  |
|---------------------------------------|-----------------|------------------|--|--|
| GM-CSF - Complex, Week 12, n=7, 24    | 0.970 (± 44.95) | 22.556 (± 24.38) |  |  |
| GM-CSF - Complex, 12-Week FU, n=8, 21 | 0.954 (± 20.80) | 1.176 (± 12.88)  |  |  |

Notes:

[1] - ITT Population

[2] - ITT Population

## Statistical analyses

|                                         |                             |
|-----------------------------------------|-----------------------------|
| <b>Statistical analysis title</b>       | GM-CSF - Complex, Week 1    |
| Comparison groups                       | Placebo v GSK3196165 180 mg |
| Number of subjects included in analysis | 39                          |
| Analysis specification                  | Pre-specified               |
| Analysis type                           | other                       |
| P-value                                 | < 0.001                     |
| Method                                  | Repeated measures analysis  |
| Parameter estimate                      | Ratio                       |
| Point estimate                          | 14.201                      |
| Confidence interval                     |                             |
| level                                   | 95 %                        |
| sides                                   | 2-sided                     |
| lower limit                             | 6.251                       |
| upper limit                             | 32.262                      |

|                                         |                             |
|-----------------------------------------|-----------------------------|
| <b>Statistical analysis title</b>       | GM-CSF - Complex, Week 2    |
| Comparison groups                       | Placebo v GSK3196165 180 mg |
| Number of subjects included in analysis | 39                          |
| Analysis specification                  | Pre-specified               |
| Analysis type                           | other                       |
| P-value                                 | < 0.001                     |
| Method                                  | Repeated measures analysis  |
| Parameter estimate                      | Ratio                       |
| Point estimate                          | 32.36                       |
| Confidence interval                     |                             |
| level                                   | 95 %                        |
| sides                                   | 2-sided                     |
| lower limit                             | 15.828                      |
| upper limit                             | 66.156                      |

|                                   |                             |
|-----------------------------------|-----------------------------|
| <b>Statistical analysis title</b> | GM-CSF - Complex, Week 4    |
| Comparison groups                 | Placebo v GSK3196165 180 mg |

|                                         |                            |
|-----------------------------------------|----------------------------|
| Number of subjects included in analysis | 39                         |
| Analysis specification                  | Pre-specified              |
| Analysis type                           | other                      |
| P-value                                 | < 0.001                    |
| Method                                  | Repeated measures analysis |
| Parameter estimate                      | Ratio                      |
| Point estimate                          | 55.772                     |
| Confidence interval                     |                            |
| level                                   | 95 %                       |
| sides                                   | 2-sided                    |
| lower limit                             | 25.646                     |
| upper limit                             | 121.287                    |

|                                         |                             |
|-----------------------------------------|-----------------------------|
| <b>Statistical analysis title</b>       | GM-CSF - Complex, Week 6    |
| Comparison groups                       | Placebo v GSK3196165 180 mg |
| Number of subjects included in analysis | 39                          |
| Analysis specification                  | Pre-specified               |
| Analysis type                           | other                       |
| P-value                                 | < 0.001                     |
| Method                                  | Repeated measures analysis  |
| Parameter estimate                      | Ratio                       |
| Point estimate                          | 48.336                      |
| Confidence interval                     |                             |
| level                                   | 95 %                        |
| sides                                   | 2-sided                     |
| lower limit                             | 19.341                      |
| upper limit                             | 120.798                     |

|                                         |                             |
|-----------------------------------------|-----------------------------|
| <b>Statistical analysis title</b>       | GM-CSF - Complex, Week 8    |
| Comparison groups                       | Placebo v GSK3196165 180 mg |
| Number of subjects included in analysis | 39                          |
| Analysis specification                  | Pre-specified               |
| Analysis type                           | other                       |
| P-value                                 | < 0.001                     |
| Method                                  | Repeated measures analysis  |
| Parameter estimate                      | Ratio                       |
| Point estimate                          | 34.635                      |
| Confidence interval                     |                             |
| level                                   | 95 %                        |
| sides                                   | 2-sided                     |
| lower limit                             | 13.69                       |
| upper limit                             | 87.629                      |

|                                   |                           |
|-----------------------------------|---------------------------|
| <b>Statistical analysis title</b> | GM-CSF - Complex, Week 12 |
|-----------------------------------|---------------------------|

|                                         |                             |
|-----------------------------------------|-----------------------------|
| Comparison groups                       | Placebo v GSK3196165 180 mg |
| Number of subjects included in analysis | 39                          |
| Analysis specification                  | Pre-specified               |
| Analysis type                           | other                       |
| P-value                                 | < 0.001                     |
| Method                                  | Repeated measures analysis  |
| Parameter estimate                      | Ratio                       |
| Point estimate                          | 23.249                      |
| Confidence interval                     |                             |
| level                                   | 95 %                        |
| sides                                   | 2-sided                     |
| lower limit                             | 8.579                       |
| upper limit                             | 63.005                      |

|                                         |                              |
|-----------------------------------------|------------------------------|
| <b>Statistical analysis title</b>       | GM-CSF - Complex, 12-Week FU |
| Comparison groups                       | Placebo v GSK3196165 180 mg  |
| Number of subjects included in analysis | 39                           |
| Analysis specification                  | Pre-specified                |
| Analysis type                           | other                        |
| P-value                                 | = 0.401                      |
| Method                                  | Repeated measures analysis   |
| Parameter estimate                      | Ratio                        |
| Point estimate                          | 1.233                        |
| Confidence interval                     |                              |
| level                                   | 95 %                         |
| sides                                   | 2-sided                      |
| lower limit                             | 0.742                        |
| upper limit                             | 2.048                        |

### **Primary: Change from Baseline in Predictive Biomarkers: 14-3-3 ETA Protein, S100 Calcium Binding Protein (CBP) A8 and A9**

|                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                           |                                                                                                                 |
|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-----------------------------------------------------------------------------------------------------------------|
| End point title                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                           | Change from Baseline in Predictive Biomarkers: 14-3-3 ETA Protein, S100 Calcium Binding Protein (CBP) A8 and A9 |
| End point description:                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                    |                                                                                                                 |
| <p>Blood samples were collected and analyzed for markers which may be predictive of rheumatoid arthritis disease activity. Predictive biomarkers included analysis of 14-3-3 ETA Protein, S100 CBP A8 and A9. Baseline was defined at Day 1. Change from Baseline was calculated as ratio of Baseline value to post-dose value. Analysis was performed using repeated measures analysis adjusted for 14-3-3 ETA Protein (mg/L) and S100 CBP A8 and A9 log(Baseline value), treatment group, disease duration (<math>\leq 2</math> or <math>&gt; 2</math> years), visit and treatment group by visit interaction. Only those participants with data available at the specified data points were analyzed (represented by n= X in the category titles).</p> |                                                                                                                 |
| End point type                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            | Primary                                                                                                         |
| End point timeframe:                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      |                                                                                                                 |
| Baseline and Weeks 1, 2, 4, 6, 8, 12, 12-Week FU (Week 22)                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                |                                                                                                                 |

| End point values                                        | Placebo           | GSK3196165<br>180 mg |  |  |
|---------------------------------------------------------|-------------------|----------------------|--|--|
| Subject group type                                      | Reporting group   | Reporting group      |  |  |
| Number of subjects analysed                             | 11 <sup>[3]</sup> | 28 <sup>[4]</sup>    |  |  |
| Units: Ratio of predictive biomarker                    |                   |                      |  |  |
| least squares mean (geometric coefficient of variation) |                   |                      |  |  |
| 14-3-3 ETA Protein, Week 1, n=9, 27                     | 1.046 (± 3.88)    | 0.986 (± 2.16)       |  |  |
| 14-3-3 ETA Protein, Week 2, n=8, 26                     | 0.959 (± 12.14)   | 0.986 (± 6.70)       |  |  |
| 14-3-3 ETA Protein, Week 4, n=9, 26                     | 1.128 (± 16.59)   | 0.838 (± 9.55)       |  |  |
| 14-3-3 ETA Protein, Week 6, n=7, 26                     | 1.093 (± 15.55)   | 0.833 (± 8.88)       |  |  |
| 14-3-3 ETA Protein, Week 8, n=7, 23                     | 0.950 (± 15.19)   | 0.842 (± 8.48)       |  |  |
| 14-3-3 ETA Protein, Week 12, n=7, 24                    | 1.131 (± 20.90)   | 0.897 (± 11.89)      |  |  |
| 14-3-3 ETA Protein, 12-Week FU, n=7, 21                 | 1.040 (± 24.06)   | 0.893 (± 13.45)      |  |  |
| S100 CBP A8 and A9, Week 1, n=9, 27                     | 0.940 (± 15.20)   | 0.939 (± 8.92)       |  |  |
| S100 CBP A8 and A9, Week 2, n=8, 26                     | 0.871 (± 15.28)   | 0.823 (± 8.65)       |  |  |
| S100 CBP A8 and A9, Week 4, n=9, 27                     | 0.874 (± 19.20)   | 0.889 (± 11.26)      |  |  |
| S100 CBP A8 and A9, Week 6, n=7, 27                     | 0.828 (± 21.92)   | 0.812 (± 11.81)      |  |  |
| S100 CBP A8 and A9, Week 8, n=7, 25                     | 0.804 (± 21.04)   | 0.857 (± 11.46)      |  |  |
| S100 CBP A8 and A9, Week 12, n=7, 24                    | 0.694 (± 21.61)   | 0.879 (± 12.05)      |  |  |
| S100 CBP A8 and A9, 12-Week FU, n=7, 21                 | 0.582 (± 20.60)   | 1.018 (± 11.83)      |  |  |

Notes:

[3] - ITT Population

[4] - ITT Population

## Statistical analyses

|                                         |                             |
|-----------------------------------------|-----------------------------|
| Statistical analysis title              | 14-3-3 ETA Protein, Week 1  |
| Comparison groups                       | Placebo v GSK3196165 180 mg |
| Number of subjects included in analysis | 39                          |
| Analysis specification                  | Pre-specified               |
| Analysis type                           | other                       |
| P-value                                 | = 0.193                     |
| Method                                  | Repeated measures analysis  |
| Parameter estimate                      | Ratio                       |
| Point estimate                          | 0.943                       |
| Confidence interval                     |                             |
| level                                   | 95 %                        |
| sides                                   | 2-sided                     |
| lower limit                             | 0.861                       |
| upper limit                             | 1.032                       |

|                                         |                             |
|-----------------------------------------|-----------------------------|
| <b>Statistical analysis title</b>       | 14-3-3 ETA Protein, Week 2  |
| Comparison groups                       | Placebo v GSK3196165 180 mg |
| Number of subjects included in analysis | 39                          |
| Analysis specification                  | Pre-specified               |
| Analysis type                           | other                       |
| P-value                                 | = 0.842                     |
| Method                                  | Repeated measures analysis  |
| Parameter estimate                      | Ratio                       |
| Point estimate                          | 1.028                       |
| Confidence interval                     |                             |
| level                                   | 95 %                        |
| sides                                   | 2-sided                     |
| lower limit                             | 0.776                       |
| upper limit                             | 1.362                       |

|                                         |                             |
|-----------------------------------------|-----------------------------|
| <b>Statistical analysis title</b>       | 14-3-3 ETA Protein, Week 4  |
| Comparison groups                       | Placebo v GSK3196165 180 mg |
| Number of subjects included in analysis | 39                          |
| Analysis specification                  | Pre-specified               |
| Analysis type                           | other                       |
| P-value                                 | = 0.127                     |
| Method                                  | Repeated measures analysis  |
| Parameter estimate                      | Ratio                       |
| Point estimate                          | 0.743                       |
| Confidence interval                     |                             |
| level                                   | 95 %                        |
| sides                                   | 2-sided                     |
| lower limit                             | 0.505                       |
| upper limit                             | 1.093                       |

|                                         |                             |
|-----------------------------------------|-----------------------------|
| <b>Statistical analysis title</b>       | 14-3-3 ETA Protein, Week 6  |
| Comparison groups                       | Placebo v GSK3196165 180 mg |
| Number of subjects included in analysis | 39                          |
| Analysis specification                  | Pre-specified               |
| Analysis type                           | other                       |
| P-value                                 | = 0.137                     |
| Method                                  | Repeated measures analysis  |
| Parameter estimate                      | Ratio                       |
| Point estimate                          | 0.762                       |
| Confidence interval                     |                             |
| level                                   | 95 %                        |
| sides                                   | 2-sided                     |
| lower limit                             | 0.531                       |
| upper limit                             | 1.095                       |

|                                         |                             |
|-----------------------------------------|-----------------------------|
| <b>Statistical analysis title</b>       | 14-3-3 ETA Protein, Week 8  |
| Comparison groups                       | Placebo v GSK3196165 180 mg |
| Number of subjects included in analysis | 39                          |
| Analysis specification                  | Pre-specified               |
| Analysis type                           | other                       |
| P-value                                 | = 0.488                     |
| Method                                  | Repeated measures analysis  |
| Parameter estimate                      | Ratio                       |
| Point estimate                          | 0.886                       |
| Confidence interval                     |                             |
| level                                   | 95 %                        |
| sides                                   | 2-sided                     |
| lower limit                             | 0.623                       |
| upper limit                             | 1.259                       |

|                                         |                             |
|-----------------------------------------|-----------------------------|
| <b>Statistical analysis title</b>       | 14-3-3 ETA Protein, Week 12 |
| Comparison groups                       | Placebo v GSK3196165 180 mg |
| Number of subjects included in analysis | 39                          |
| Analysis specification                  | Pre-specified               |
| Analysis type                           | other                       |
| P-value                                 | = 0.338                     |
| Method                                  | Repeated measures analysis  |
| Parameter estimate                      | Ratio                       |
| Point estimate                          | 0.793                       |
| Confidence interval                     |                             |
| level                                   | 95 %                        |
| sides                                   | 2-sided                     |
| lower limit                             | 0.488                       |
| upper limit                             | 1.29                        |

|                                         |                                |
|-----------------------------------------|--------------------------------|
| <b>Statistical analysis title</b>       | 14-3-3 ETA Protein, 12-Week FU |
| Comparison groups                       | Placebo v GSK3196165 180 mg    |
| Number of subjects included in analysis | 39                             |
| Analysis specification                  | Pre-specified                  |
| Analysis type                           | other                          |
| P-value                                 | = 0.582                        |
| Method                                  | Repeated measures analysis     |
| Parameter estimate                      | Ratio                          |
| Point estimate                          | 0.859                          |

|                     |         |
|---------------------|---------|
| Confidence interval |         |
| level               | 95 %    |
| sides               | 2-sided |
| lower limit         | 0.491   |
| upper limit         | 1.502   |

|                                         |                             |
|-----------------------------------------|-----------------------------|
| <b>Statistical analysis title</b>       | S100 CBP A8 and A9, Week 1  |
| Comparison groups                       | Placebo v GSK3196165 180 mg |
| Number of subjects included in analysis | 39                          |
| Analysis specification                  | Pre-specified               |
| Analysis type                           | other                       |
| P-value                                 | = 0.996                     |
| Method                                  | Repeated measures analysis  |
| Parameter estimate                      | Ratio                       |
| Point estimate                          | 0.999                       |
| Confidence interval                     |                             |
| level                                   | 95 %                        |
| sides                                   | 2-sided                     |
| lower limit                             | 0.699                       |
| upper limit                             | 1.427                       |

|                                         |                             |
|-----------------------------------------|-----------------------------|
| <b>Statistical analysis title</b>       | S100 CBP A8 and A9, Week 2  |
| Comparison groups                       | Placebo v GSK3196165 180 mg |
| Number of subjects included in analysis | 39                          |
| Analysis specification                  | Pre-specified               |
| Analysis type                           | other                       |
| P-value                                 | = 0.745                     |
| Method                                  | Repeated measures analysis  |
| Parameter estimate                      | Ratio                       |
| Point estimate                          | 0.944                       |
| Confidence interval                     |                             |
| level                                   | 95 %                        |
| sides                                   | 2-sided                     |
| lower limit                             | 0.662                       |
| upper limit                             | 1.346                       |

|                                   |                             |
|-----------------------------------|-----------------------------|
| <b>Statistical analysis title</b> | S100 CBP A8 and A9, Week 4  |
| Comparison groups                 | Placebo v GSK3196165 180 mg |

|                                         |                            |
|-----------------------------------------|----------------------------|
| Number of subjects included in analysis | 39                         |
| Analysis specification                  | Pre-specified              |
| Analysis type                           | other                      |
| P-value                                 | = 0.939                    |
| Method                                  | Repeated measures analysis |
| Parameter estimate                      | Ratio                      |
| Point estimate                          | 1.017                      |
| Confidence interval                     |                            |
| level                                   | 95 %                       |
| sides                                   | 2-sided                    |
| lower limit                             | 0.649                      |
| upper limit                             | 1.593                      |

|                                         |                             |
|-----------------------------------------|-----------------------------|
| <b>Statistical analysis title</b>       | S100 CBP A8 and A9, Week 6  |
| Comparison groups                       | Placebo v GSK3196165 180 mg |
| Number of subjects included in analysis | 39                          |
| Analysis specification                  | Pre-specified               |
| Analysis type                           | other                       |
| P-value                                 | = 0.937                     |
| Method                                  | Repeated measures analysis  |
| Parameter estimate                      | Ratio                       |
| Point estimate                          | 0.981                       |
| Confidence interval                     |                             |
| level                                   | 95 %                        |
| sides                                   | 2-sided                     |
| lower limit                             | 0.595                       |
| upper limit                             | 1.617                       |

|                                         |                             |
|-----------------------------------------|-----------------------------|
| <b>Statistical analysis title</b>       | S100 CBP A8 and A9, Week 8  |
| Comparison groups                       | Placebo v GSK3196165 180 mg |
| Number of subjects included in analysis | 39                          |
| Analysis specification                  | Pre-specified               |
| Analysis type                           | other                       |
| P-value                                 | = 0.787                     |
| Method                                  | Repeated measures analysis  |
| Parameter estimate                      | Ratio                       |
| Point estimate                          | 1.067                       |
| Confidence interval                     |                             |
| level                                   | 95 %                        |
| sides                                   | 2-sided                     |
| lower limit                             | 0.659                       |
| upper limit                             | 1.727                       |

|                                   |                             |
|-----------------------------------|-----------------------------|
| <b>Statistical analysis title</b> | S100 CBP A8 and A9, Week 12 |
|-----------------------------------|-----------------------------|

|                                         |                             |
|-----------------------------------------|-----------------------------|
| Comparison groups                       | Placebo v GSK3196165 180 mg |
| Number of subjects included in analysis | 39                          |
| Analysis specification                  | Pre-specified               |
| Analysis type                           | other                       |
| P-value                                 | = 0.342                     |
| Method                                  | Repeated measures analysis  |
| Parameter estimate                      | Ratio                       |
| Point estimate                          | 1.267                       |
| Confidence interval                     |                             |
| level                                   | 95 %                        |
| sides                                   | 2-sided                     |
| lower limit                             | 0.769                       |
| upper limit                             | 2.086                       |

|                                         |                                |
|-----------------------------------------|--------------------------------|
| <b>Statistical analysis title</b>       | S100 CBP A8 and A9, 12-Week FU |
| Comparison groups                       | Placebo v GSK3196165 180 mg    |
| Number of subjects included in analysis | 39                             |
| Analysis specification                  | Pre-specified                  |
| Analysis type                           | other                          |
| P-value                                 | = 0.026                        |
| Method                                  | Repeated measures analysis     |
| Parameter estimate                      | Ratio                          |
| Point estimate                          | 1.748                          |
| Confidence interval                     |                                |
| level                                   | 95 %                           |
| sides                                   | 2-sided                        |
| lower limit                             | 1.076                          |
| upper limit                             | 2.838                          |

|                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               |                                                          |
|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|----------------------------------------------------------|
| <b>Primary: Change from Baseline in Predictive Biomarkers: Amyloid A</b>                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      |                                                          |
| End point title                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               | Change from Baseline in Predictive Biomarkers: Amyloid A |
| End point description:                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                        |                                                          |
| <p>Blood samples were collected and analyzed for markers which may be predictive of rheumatoid arthritis disease activity. Predictive biomarkers included analysis of Amyloid A. Baseline was defined at Day 1. Change from Baseline was calculated as ratio of Baseline value to post-dose value. Analysis was performed using repeated measures analysis adjusted for Amyloid A log(Baseline value), treatment group, disease duration (<math>\leq 2</math> or <math>&gt; 2</math> years), visit and treatment group by visit interaction. Only those participants with data available at the specified data points were analyzed (represented by n= X in the category titles). Data has been presented for only those time points at which the samples were collected.</p> |                                                          |
| End point type                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                | Primary                                                  |
| End point timeframe:                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                          |                                                          |
| Baseline and Week 12, 12-Week FU (Week 22)                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                    |                                                          |

|                                                            |                    |                      |  |  |
|------------------------------------------------------------|--------------------|----------------------|--|--|
| <b>End point values</b>                                    | Placebo            | GSK3196165<br>180 mg |  |  |
| Subject group type                                         | Reporting group    | Reporting group      |  |  |
| Number of subjects analysed                                | 11 <sup>[5]</sup>  | 28 <sup>[6]</sup>    |  |  |
| Units: Ratio of predictive biomarker                       |                    |                      |  |  |
| least squares mean (geometric<br>coefficient of variation) |                    |                      |  |  |
| Amyloid A, Week 12, n=7, 24                                | 0.845 (±<br>49.31) | 0.653 (±<br>25.45)   |  |  |
| Amyloid A, 12-Week FU, n=7, 21                             | 0.529 (±<br>35.12) | 0.623 (±<br>19.68)   |  |  |

Notes:

[5] - ITT Population

[6] - ITT Population

## Statistical analyses

|                                         |                             |
|-----------------------------------------|-----------------------------|
| <b>Statistical analysis title</b>       | Amyloid A, Week 12          |
| Comparison groups                       | Placebo v GSK3196165 180 mg |
| Number of subjects included in analysis | 39                          |
| Analysis specification                  | Pre-specified               |
| Analysis type                           | other                       |
| P-value                                 | = 0.632                     |
| Method                                  | Repeated measures analysis  |
| Parameter estimate                      | Ratio                       |
| Point estimate                          | 0.774                       |
| Confidence interval                     |                             |
| level                                   | 95 %                        |
| sides                                   | 2-sided                     |
| lower limit                             | 0.261                       |
| upper limit                             | 2.29                        |

|                                         |                             |
|-----------------------------------------|-----------------------------|
| <b>Statistical analysis title</b>       | Amyloid A, 12-Week FU       |
| Comparison groups                       | Placebo v GSK3196165 180 mg |
| Number of subjects included in analysis | 39                          |
| Analysis specification                  | Pre-specified               |
| Analysis type                           | other                       |
| P-value                                 | = 0.685                     |
| Method                                  | Repeated measures analysis  |
| Parameter estimate                      | Ratio                       |
| Point estimate                          | 1.176                       |
| Confidence interval                     |                             |
| level                                   | 95 %                        |
| sides                                   | 2-sided                     |
| lower limit                             | 0.519                       |
| upper limit                             | 2.663                       |

## Primary: Change from Baseline in Predictive Biomarkers: Amyloid A, Chemokine (C-

# C Motif) Ligand 17, Chemokine (C-X-C Motif) Ligand 13, Interleukin 6, Macrophage-Derived Chemokine

|                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      |                                                                                                                                                                           |
|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| End point title                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      | Change from Baseline in Predictive Biomarkers: Amyloid A, Chemokine (C-C Motif) Ligand 17, Chemokine (C-X-C Motif) Ligand 13, Interleukin 6, Macrophage-Derived Chemokine |
| End point description:                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               |                                                                                                                                                                           |
| Blood samples were collected and analyzed for markers which may be predictive of rheumatoid arthritis disease activity. Predictive biomarkers included analysis of Chemokine (C-C Motif) Ligand 17 (CL17), Chemokine (C-X-C Motif) Ligand 13 (CL13), Interleukin 6, Macrophage-Derived Chemokine (MDC). Baseline was defined at Day 1. Change from Baseline was calculated as ratio of Baseline value to post-dose value. Analysis was performed using repeated measures analysis adjusted for CL17, CL13, Interleukin 6, MDC log(Baseline value), treatment group, disease duration (<=2 or >2 years), visit and treatment group by visit interaction. Only those participants with data available at the specified data points were analyzed (represented by n= X in the category titles). Data has been presented for only those time points at which the samples were collected. |                                                                                                                                                                           |
| End point type                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       | Primary                                                                                                                                                                   |
| End point timeframe:                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                 |                                                                                                                                                                           |
| Baseline and Weeks 1, 2, 4, 6, 8, 12, 12-Week FU (Week 22)                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                           |                                                                                                                                                                           |

| End point values                                        | Placebo           | GSK3196165<br>180 mg |  |  |
|---------------------------------------------------------|-------------------|----------------------|--|--|
| Subject group type                                      | Reporting group   | Reporting group      |  |  |
| Number of subjects analysed                             | 11 <sup>[7]</sup> | 28 <sup>[8]</sup>    |  |  |
| Units: Ratio of predictive biomarker                    |                   |                      |  |  |
| least squares mean (geometric coefficient of variation) |                   |                      |  |  |
| CL17, Week 1, n=9, 27                                   | 1.117 (± 18.81)   | 0.773 (± 10.94)      |  |  |
| CL17, Week 2, n=8, 26                                   | 0.912 (± 24.37)   | 0.651 (± 13.60)      |  |  |
| CL17, Week 4, n=9, 27                                   | 1.117 (± 21.91)   | 0.679 (± 12.51)      |  |  |
| CL17, Week 6, n=7, 27                                   | 1.032 (± 24.38)   | 0.779 (± 12.48)      |  |  |
| CL17, Week 8, n=7, 25                                   | 1.211 (± 20.63)   | 0.675 (± 11.21)      |  |  |
| CL17, Week 12, n=7, 24                                  | 1.711 (± 24.96)   | 0.890 (± 13.90)      |  |  |
| CL17, 12-Week FU, n=7, 20                               | 1.434 (± 23.26)   | 1.357 (± 13.59)      |  |  |
| CL13, Week 1, n=9, 27                                   | 1.198 (± 15.63)   | 0.915 (± 8.87)       |  |  |
| CL13, Week 2, n=8, 26                                   | 1.090 (± 13.98)   | 1.095 (± 7.78)       |  |  |
| CL13, Week 4, n=9, 27                                   | 0.947 (± 15.58)   | 1.170 (± 8.90)       |  |  |
| CL13, Week 6, n=7, 27                                   | 0.839 (± 17.20)   | 1.038 (± 8.91)       |  |  |
| CL13, Week 8, n=7, 25                                   | 0.913 (± 23.70)   | 1.021 (± 12.38)      |  |  |
| CL13, Week 12, n=7,24                                   | 0.924 (± 31.17)   | 1.077 (± 16.31)      |  |  |
| CL13, 12-Week FU, n=7,21                                | 0.774 (± 27.82)   | 1.224 (± 15.04)      |  |  |
| Interleukin 6, Week 1, n=9, 26                          | 1.179 (± 27.92)   | 1.064 (± 16.38)      |  |  |

|                                    |                 |                 |  |  |
|------------------------------------|-----------------|-----------------|--|--|
| Interleukin 6, Week 2, n=8, 26     | 1.153 (± 29.33) | 0.830 (± 16.63) |  |  |
| Interleukin 6, Week 4, n=9, 27     | 0.986 (± 26.22) | 0.811 (± 15.10) |  |  |
| Interleukin 6, Week 6, n=7, 27     | 1.136 (± 24.95) | 0.748 (± 13.51) |  |  |
| Interleukin 6, Week 8, n=7, 25     | 1.275 (± 23.65) | 0.872 (± 13.35) |  |  |
| Interleukin 6, Week 12, n=7, 24    | 0.770 (± 21.89) | 0.939 (± 12.35) |  |  |
| Interleukin 6, 12-Week FU, n=7, 21 | 0.817 (± 33.13) | 1.308 (± 18.63) |  |  |
| MDC, Week 1, n=9, 27               | 0.987 (± 5.02)  | 0.914 (± 2.89)  |  |  |
| MDC, Week 2, n=8, 26               | 0.925 (± 7.33)  | 0.911 (± 4.15)  |  |  |
| MDC, Week 4, n=9, 27               | 0.936 (± 8.13)  | 0.895 (± 4.67)  |  |  |
| MDC, Week 6, n=7, 27               | 0.984 (± 8.38)  | 0.994 (± 4.48)  |  |  |
| MDC, Week 8, n=7, 25               | 1.049 (± 9.36)  | 0.899 (± 5.09)  |  |  |
| MDC, Week 12, n=7, 24              | 1.245 (± 9.51)  | 1.058 (± 5.23)  |  |  |
| MDC, 12-Week FU, n=7, 20           | 1.303 (± 12.66) | 1.321 (± 7.53)  |  |  |

Notes:

[7] - ITT Population

[8] - ITT Population

### Statistical analyses

|                                         |                             |
|-----------------------------------------|-----------------------------|
| <b>Statistical analysis title</b>       | CL17, Week 1                |
| Comparison groups                       | Placebo v GSK3196165 180 mg |
| Number of subjects included in analysis | 39                          |
| Analysis specification                  | Pre-specified               |
| Analysis type                           | other                       |
| P-value                                 | = 0.097                     |
| Method                                  | Repeated measures analysis  |
| Parameter estimate                      | Ratio                       |
| Point estimate                          | 0.692                       |
| Confidence interval                     |                             |
| level                                   | 95 %                        |
| sides                                   | 2-sided                     |
| lower limit                             | 0.445                       |
| upper limit                             | 1.074                       |

|                                         |                             |
|-----------------------------------------|-----------------------------|
| <b>Statistical analysis title</b>       | CL17, Week 2                |
| Comparison groups                       | Placebo v GSK3196165 180 mg |
| Number of subjects included in analysis | 39                          |
| Analysis specification                  | Pre-specified               |
| Analysis type                           | other                       |
| P-value                                 | = 0.229                     |
| Method                                  | Repeated measures analysis  |
| Parameter estimate                      | Ratio                       |
| Point estimate                          | 0.713                       |

|                     |         |
|---------------------|---------|
| Confidence interval |         |
| level               | 95 %    |
| sides               | 2-sided |
| lower limit         | 0.407   |
| upper limit         | 1.249   |

|                                         |                             |
|-----------------------------------------|-----------------------------|
| <b>Statistical analysis title</b>       | CL17, Week 4                |
| Comparison groups                       | Placebo v GSK3196165 180 mg |
| Number of subjects included in analysis | 39                          |
| Analysis specification                  | Pre-specified               |
| Analysis type                           | other                       |
| P-value                                 | = 0.055                     |
| Method                                  | Repeated measures analysis  |
| Parameter estimate                      | Ratio                       |
| Point estimate                          | 0.608                       |
| Confidence interval                     |                             |
| level                                   | 95 %                        |
| sides                                   | 2-sided                     |
| lower limit                             | 0.365                       |
| upper limit                             | 1.012                       |

|                                         |                             |
|-----------------------------------------|-----------------------------|
| <b>Statistical analysis title</b>       | CL17, Week 6                |
| Comparison groups                       | Placebo v GSK3196165 180 mg |
| Number of subjects included in analysis | 39                          |
| Analysis specification                  | Pre-specified               |
| Analysis type                           | other                       |
| P-value                                 | = 0.307                     |
| Method                                  | Repeated measures analysis  |
| Parameter estimate                      | Ratio                       |
| Point estimate                          | 0.755                       |
| Confidence interval                     |                             |
| level                                   | 95 %                        |
| sides                                   | 2-sided                     |
| lower limit                             | 0.435                       |
| upper limit                             | 1.309                       |

|                                   |                             |
|-----------------------------------|-----------------------------|
| <b>Statistical analysis title</b> | CL17, Week 8                |
| Comparison groups                 | Placebo v GSK3196165 180 mg |

|                                         |                            |
|-----------------------------------------|----------------------------|
| Number of subjects included in analysis | 39                         |
| Analysis specification                  | Pre-specified              |
| Analysis type                           | other                      |
| P-value                                 | = 0.017                    |
| Method                                  | Repeated measures analysis |
| Parameter estimate                      | Ratio                      |
| Point estimate                          | 0.557                      |
| Confidence interval                     |                            |
| level                                   | 95 %                       |
| sides                                   | 2-sided                    |
| lower limit                             | 0.348                      |
| upper limit                             | 0.894                      |

|                                         |                             |
|-----------------------------------------|-----------------------------|
| <b>Statistical analysis title</b>       | CL17, Week 12               |
| Comparison groups                       | Placebo v GSK3196165 180 mg |
| Number of subjects included in analysis | 39                          |
| Analysis specification                  | Pre-specified               |
| Analysis type                           | other                       |
| P-value                                 | = 0.026                     |
| Method                                  | Repeated measures analysis  |
| Parameter estimate                      | Ratio                       |
| Point estimate                          | 0.52                        |
| Confidence interval                     |                             |
| level                                   | 95 %                        |
| sides                                   | 2-sided                     |
| lower limit                             | 0.294                       |
| upper limit                             | 0.922                       |

|                                         |                             |
|-----------------------------------------|-----------------------------|
| <b>Statistical analysis title</b>       | CL17, 12-Week FU            |
| Comparison groups                       | Placebo v GSK3196165 180 mg |
| Number of subjects included in analysis | 39                          |
| Analysis specification                  | Pre-specified               |
| Analysis type                           | other                       |
| P-value                                 | = 0.839                     |
| Method                                  | Repeated measures analysis  |
| Parameter estimate                      | Ratio                       |
| Point estimate                          | 0.947                       |
| Confidence interval                     |                             |
| level                                   | 95 %                        |
| sides                                   | 2-sided                     |
| lower limit                             | 0.548                       |
| upper limit                             | 1.636                       |

|                                   |              |
|-----------------------------------|--------------|
| <b>Statistical analysis title</b> | CL13, Week 1 |
|-----------------------------------|--------------|

|                                         |                             |
|-----------------------------------------|-----------------------------|
| Comparison groups                       | Placebo v GSK3196165 180 mg |
| Number of subjects included in analysis | 39                          |
| Analysis specification                  | Pre-specified               |
| Analysis type                           | other                       |
| P-value                                 | = 0.142                     |
| Method                                  | Repeated measures analysis  |
| Parameter estimate                      | Ratio                       |
| Point estimate                          | 0.764                       |
| Confidence interval                     |                             |
| level                                   | 95 %                        |
| sides                                   | 2-sided                     |
| lower limit                             | 0.53                        |
| upper limit                             | 1.1                         |

|                                         |                             |
|-----------------------------------------|-----------------------------|
| <b>Statistical analysis title</b>       | CL13, Week 2                |
| Comparison groups                       | Placebo v GSK3196165 180 mg |
| Number of subjects included in analysis | 39                          |
| Analysis specification                  | Pre-specified               |
| Analysis type                           | other                       |
| P-value                                 | = 0.976                     |
| Method                                  | Repeated measures analysis  |
| Parameter estimate                      | Ratio                       |
| Point estimate                          | 1.005                       |
| Confidence interval                     |                             |
| level                                   | 95 %                        |
| sides                                   | 2-sided                     |
| lower limit                             | 0.726                       |
| upper limit                             | 1.39                        |

|                                         |                             |
|-----------------------------------------|-----------------------------|
| <b>Statistical analysis title</b>       | CL13, Week 4                |
| Comparison groups                       | Placebo v GSK3196165 180 mg |
| Number of subjects included in analysis | 39                          |
| Analysis specification                  | Pre-specified               |
| Analysis type                           | other                       |
| P-value                                 | = 0.244                     |
| Method                                  | Repeated measures analysis  |
| Parameter estimate                      | Ratio                       |
| Point estimate                          | 1.236                       |
| Confidence interval                     |                             |
| level                                   | 95 %                        |
| sides                                   | 2-sided                     |
| lower limit                             | 0.859                       |
| upper limit                             | 1.778                       |

|                                         |                             |
|-----------------------------------------|-----------------------------|
| <b>Statistical analysis title</b>       | CL13, Week 6                |
| Comparison groups                       | Placebo v GSK3196165 180 mg |
| Number of subjects included in analysis | 39                          |
| Analysis specification                  | Pre-specified               |
| Analysis type                           | other                       |
| P-value                                 | = 0.278                     |
| Method                                  | Repeated measures analysis  |
| Parameter estimate                      | Ratio                       |
| Point estimate                          | 1.237                       |
| Confidence interval                     |                             |
| level                                   | 95 %                        |
| sides                                   | 2-sided                     |
| lower limit                             | 0.836                       |
| upper limit                             | 1.83                        |

|                                         |                             |
|-----------------------------------------|-----------------------------|
| <b>Statistical analysis title</b>       | CL13, Week 8                |
| Comparison groups                       | Placebo v GSK3196165 180 mg |
| Number of subjects included in analysis | 39                          |
| Analysis specification                  | Pre-specified               |
| Analysis type                           | other                       |
| P-value                                 | = 0.677                     |
| Method                                  | Repeated measures analysis  |
| Parameter estimate                      | Ratio                       |
| Point estimate                          | 1.118                       |
| Confidence interval                     |                             |
| level                                   | 95 %                        |
| sides                                   | 2-sided                     |
| lower limit                             | 0.651                       |
| upper limit                             | 1.92                        |

|                                         |                             |
|-----------------------------------------|-----------------------------|
| <b>Statistical analysis title</b>       | CL13, Week 12               |
| Comparison groups                       | Placebo v GSK3196165 180 mg |
| Number of subjects included in analysis | 39                          |
| Analysis specification                  | Pre-specified               |
| Analysis type                           | other                       |
| P-value                                 | = 0.661                     |
| Method                                  | Repeated measures analysis  |
| Parameter estimate                      | Ratio                       |
| Point estimate                          | 1.165                       |
| Confidence interval                     |                             |
| level                                   | 95 %                        |
| sides                                   | 2-sided                     |
| lower limit                             | 0.573                       |
| upper limit                             | 2.369                       |

|                                         |                             |
|-----------------------------------------|-----------------------------|
| <b>Statistical analysis title</b>       | CL13, 12-Week FU            |
| Comparison groups                       | Placebo v GSK3196165 180 mg |
| Number of subjects included in analysis | 39                          |
| Analysis specification                  | Pre-specified               |
| Analysis type                           | other                       |
| P-value                                 | = 0.154                     |
| Method                                  | Repeated measures analysis  |
| Parameter estimate                      | Ratio                       |
| Point estimate                          | 1.581                       |
| Confidence interval                     |                             |
| level                                   | 95 %                        |
| sides                                   | 2-sided                     |
| lower limit                             | 0.832                       |
| upper limit                             | 3.007                       |

|                                         |                             |
|-----------------------------------------|-----------------------------|
| <b>Statistical analysis title</b>       | Interleukin 6, Week 1       |
| Comparison groups                       | Placebo v GSK3196165 180 mg |
| Number of subjects included in analysis | 39                          |
| Analysis specification                  | Pre-specified               |
| Analysis type                           | other                       |
| P-value                                 | = 0.751                     |
| Method                                  | Repeated measures analysis  |
| Parameter estimate                      | Ratio                       |
| Point estimate                          | 0.903                       |
| Confidence interval                     |                             |
| level                                   | 95 %                        |
| sides                                   | 2-sided                     |
| lower limit                             | 0.471                       |
| upper limit                             | 1.729                       |

|                                         |                             |
|-----------------------------------------|-----------------------------|
| <b>Statistical analysis title</b>       | Interleukin 6, Week 2       |
| Comparison groups                       | Placebo v GSK3196165 180 mg |
| Number of subjects included in analysis | 39                          |
| Analysis specification                  | Pre-specified               |
| Analysis type                           | other                       |
| P-value                                 | = 0.33                      |
| Method                                  | Repeated measures analysis  |
| Parameter estimate                      | Ratio                       |
| Point estimate                          | 0.72                        |

|                     |         |
|---------------------|---------|
| Confidence interval |         |
| level               | 95 %    |
| sides               | 2-sided |
| lower limit         | 0.367   |
| upper limit         | 1.413   |

|                                         |                             |
|-----------------------------------------|-----------------------------|
| <b>Statistical analysis title</b>       | Interleukin 6, Week 4       |
| Comparison groups                       | Placebo v GSK3196165 180 mg |
| Number of subjects included in analysis | 39                          |
| Analysis specification                  | Pre-specified               |
| Analysis type                           | other                       |
| P-value                                 | = 0.519                     |
| Method                                  | Repeated measures analysis  |
| Parameter estimate                      | Ratio                       |
| Point estimate                          | 0.822                       |
| Confidence interval                     |                             |
| level                                   | 95 %                        |
| sides                                   | 2-sided                     |
| lower limit                             | 0.447                       |
| upper limit                             | 1.512                       |

|                                         |                             |
|-----------------------------------------|-----------------------------|
| <b>Statistical analysis title</b>       | Interleukin 6, Week 6       |
| Comparison groups                       | Placebo v GSK3196165 180 mg |
| Number of subjects included in analysis | 39                          |
| Analysis specification                  | Pre-specified               |
| Analysis type                           | other                       |
| P-value                                 | = 0.147                     |
| Method                                  | Repeated measures analysis  |
| Parameter estimate                      | Ratio                       |
| Point estimate                          | 0.659                       |
| Confidence interval                     |                             |
| level                                   | 95 %                        |
| sides                                   | 2-sided                     |
| lower limit                             | 0.372                       |
| upper limit                             | 1.167                       |

|                                   |                             |
|-----------------------------------|-----------------------------|
| <b>Statistical analysis title</b> | Interleukin 6, Week 8       |
| Comparison groups                 | Placebo v GSK3196165 180 mg |

|                                         |                            |
|-----------------------------------------|----------------------------|
| Number of subjects included in analysis | 39                         |
| Analysis specification                  | Pre-specified              |
| Analysis type                           | other                      |
| P-value                                 | = 0.166                    |
| Method                                  | Repeated measures analysis |
| Parameter estimate                      | Ratio                      |
| Point estimate                          | 0.684                      |
| Confidence interval                     |                            |
| level                                   | 95 %                       |
| sides                                   | 2-sided                    |
| lower limit                             | 0.396                      |
| upper limit                             | 1.18                       |

|                                         |                             |
|-----------------------------------------|-----------------------------|
| <b>Statistical analysis title</b>       | Interleukin 6, Week 12      |
| Comparison groups                       | Placebo v GSK3196165 180 mg |
| Number of subjects included in analysis | 39                          |
| Analysis specification                  | Pre-specified               |
| Analysis type                           | other                       |
| P-value                                 | = 0.432                     |
| Method                                  | Repeated measures analysis  |
| Parameter estimate                      | Ratio                       |
| Point estimate                          | 1.221                       |
| Confidence interval                     |                             |
| level                                   | 95 %                        |
| sides                                   | 2-sided                     |
| lower limit                             | 0.734                       |
| upper limit                             | 2.031                       |

|                                         |                             |
|-----------------------------------------|-----------------------------|
| <b>Statistical analysis title</b>       | Interleukin 6, 12-Week FU   |
| Comparison groups                       | Placebo v GSK3196165 180 mg |
| Number of subjects included in analysis | 39                          |
| Analysis specification                  | Pre-specified               |
| Analysis type                           | other                       |
| P-value                                 | = 0.216                     |
| Method                                  | Repeated measures analysis  |
| Parameter estimate                      | Ratio                       |
| Point estimate                          | 1.602                       |
| Confidence interval                     |                             |
| level                                   | 95 %                        |
| sides                                   | 2-sided                     |
| lower limit                             | 0.75                        |
| upper limit                             | 3.423                       |

|                                   |             |
|-----------------------------------|-------------|
| <b>Statistical analysis title</b> | MDC, Week 1 |
|-----------------------------------|-------------|

|                                         |                             |
|-----------------------------------------|-----------------------------|
| Comparison groups                       | Placebo v GSK3196165 180 mg |
| Number of subjects included in analysis | 39                          |
| Analysis specification                  | Pre-specified               |
| Analysis type                           | other                       |
| P-value                                 | = 0.195                     |
| Method                                  | Repeated measures analysis  |
| Parameter estimate                      | Ratio                       |
| Point estimate                          | 0.926                       |
| Confidence interval                     |                             |
| level                                   | 95 %                        |
| sides                                   | 2-sided                     |
| lower limit                             | 0.823                       |
| upper limit                             | 1.042                       |

|                                         |                             |
|-----------------------------------------|-----------------------------|
| <b>Statistical analysis title</b>       | MDC, Week 2                 |
| Comparison groups                       | Placebo v GSK3196165 180 mg |
| Number of subjects included in analysis | 39                          |
| Analysis specification                  | Pre-specified               |
| Analysis type                           | other                       |
| P-value                                 | = 0.851                     |
| Method                                  | Repeated measures analysis  |
| Parameter estimate                      | Ratio                       |
| Point estimate                          | 0.984                       |
| Confidence interval                     |                             |
| level                                   | 95 %                        |
| sides                                   | 2-sided                     |
| lower limit                             | 0.829                       |
| upper limit                             | 1.168                       |

|                                         |                             |
|-----------------------------------------|-----------------------------|
| <b>Statistical analysis title</b>       | MDC, Week 4                 |
| Comparison groups                       | Placebo v GSK3196165 180 mg |
| Number of subjects included in analysis | 39                          |
| Analysis specification                  | Pre-specified               |
| Analysis type                           | other                       |
| P-value                                 | = 0.637                     |
| Method                                  | Repeated measures analysis  |
| Parameter estimate                      | Ratio                       |
| Point estimate                          | 0.956                       |
| Confidence interval                     |                             |
| level                                   | 95 %                        |
| sides                                   | 2-sided                     |
| lower limit                             | 0.79                        |
| upper limit                             | 1.158                       |

|                                         |                             |
|-----------------------------------------|-----------------------------|
| <b>Statistical analysis title</b>       | MDC, Week 6                 |
| Comparison groups                       | Placebo v GSK3196165 180 mg |
| Number of subjects included in analysis | 39                          |
| Analysis specification                  | Pre-specified               |
| Analysis type                           | other                       |
| P-value                                 | = 0.915                     |
| Method                                  | Repeated measures analysis  |
| Parameter estimate                      | Ratio                       |
| Point estimate                          | 1.01                        |
| Confidence interval                     |                             |
| level                                   | 95 %                        |
| sides                                   | 2-sided                     |
| lower limit                             | 0.833                       |
| upper limit                             | 1.225                       |

|                                         |                             |
|-----------------------------------------|-----------------------------|
| <b>Statistical analysis title</b>       | MDC, Week 8                 |
| Comparison groups                       | Placebo v GSK3196165 180 mg |
| Number of subjects included in analysis | 39                          |
| Analysis specification                  | Pre-specified               |
| Analysis type                           | other                       |
| P-value                                 | = 0.157                     |
| Method                                  | Repeated measures analysis  |
| Parameter estimate                      | Ratio                       |
| Point estimate                          | 0.857                       |
| Confidence interval                     |                             |
| level                                   | 95 %                        |
| sides                                   | 2-sided                     |
| lower limit                             | 0.69                        |
| upper limit                             | 1.064                       |

|                                         |                             |
|-----------------------------------------|-----------------------------|
| <b>Statistical analysis title</b>       | MDC, Week 12                |
| Comparison groups                       | Placebo v GSK3196165 180 mg |
| Number of subjects included in analysis | 39                          |
| Analysis specification                  | Pre-specified               |
| Analysis type                           | other                       |
| P-value                                 | = 0.142                     |
| Method                                  | Repeated measures analysis  |
| Parameter estimate                      | Ratio                       |
| Point estimate                          | 0.849                       |
| Confidence interval                     |                             |
| level                                   | 95 %                        |
| sides                                   | 2-sided                     |
| lower limit                             | 0.681                       |
| upper limit                             | 1.059                       |

|                                         |                             |
|-----------------------------------------|-----------------------------|
| <b>Statistical analysis title</b>       | MDC, 12-Week FU             |
| Comparison groups                       | Placebo v GSK3196165 180 mg |
| Number of subjects included in analysis | 39                          |
| Analysis specification                  | Pre-specified               |
| Analysis type                           | other                       |
| P-value                                 | = 0.929                     |
| Method                                  | Repeated measures analysis  |
| Parameter estimate                      | Ratio                       |
| Point estimate                          | 1.013                       |
| Confidence interval                     |                             |
| level                                   | 95 %                        |
| sides                                   | 2-sided                     |
| lower limit                             | 0.745                       |
| upper limit                             | 1.378                       |

**Primary: Change from Baseline in Predictive Biomarkers: Chitinase 3 Like 1, Matrix Metalloproteinase 3 (MMP-3)**

|                 |                                                                                                       |
|-----------------|-------------------------------------------------------------------------------------------------------|
| End point title | Change from Baseline in Predictive Biomarkers: Chitinase 3 Like 1, Matrix Metalloproteinase 3 (MMP-3) |
|-----------------|-------------------------------------------------------------------------------------------------------|

End point description:

Blood samples were collected and analyzed for markers which may be predictive of rheumatoid arthritis disease activity. Predictive biomarkers included analysis of Chitinase 3 Like 1 and MMP-3. Baseline was defined at Day 1. Change from Baseline was calculated as ratio of Baseline value to post-dose value. Analysis was performed using repeated measures analysis adjusted for Chitinase 3 Like 1 and MMP-3 log(Baseline value), treatment group, disease duration ( $\leq 2$  or  $> 2$  years), visit and treatment group by visit interaction. Only those participants with data available at the specified data points were analyzed (represented by n= X in the category titles).

|                |         |
|----------------|---------|
| End point type | Primary |
|----------------|---------|

End point timeframe:

Baseline and Weeks 1, 2, 4, 6, 8, 12, 12-Week FU (Week 22)

| <b>End point values</b>                                 | Placebo           | GSK3196165<br>180 mg |  |  |
|---------------------------------------------------------|-------------------|----------------------|--|--|
| Subject group type                                      | Reporting group   | Reporting group      |  |  |
| Number of subjects analysed                             | 11 <sup>[9]</sup> | 28 <sup>[10]</sup>   |  |  |
| Units: Ratio of predictive biomarker                    |                   |                      |  |  |
| least squares mean (geometric coefficient of variation) |                   |                      |  |  |
| Chitinase 3 Like 1, Week 1, n=9, 27                     | 1.033 (± 13.97)   | 0.917 (± 8.13)       |  |  |
| Chitinase 3 Like 1, Week 2, n=8, 26                     | 1.013 (± 15.05)   | 0.966 (± 8.55)       |  |  |
| Chitinase 3 Like 1, Week 4, n=9, 27                     | 0.961 (± 17.14)   | 1.088 (± 9.96)       |  |  |
| Chitinase 3 Like 1, Week 6, n=7, 27                     | 0.897 (± 17.08)   | 1.031 (± 8.80)       |  |  |

|                                         |                 |                 |  |  |
|-----------------------------------------|-----------------|-----------------|--|--|
| Chitinase 3 Like 1, Week 8, n=7, 25     | 0.851 (± 18.24) | 0.947 (± 9.70)  |  |  |
| Chitinase 3 Like 1, Week 12, n=7, 24    | 1.066 (± 21.53) | 1.071 (± 11.64) |  |  |
| Chitinase 3 Like 1, 12-Week FU, n=7, 21 | 0.735 (± 16.87) | 1.019 (± 9.75)  |  |  |
| MMP 3, Week 1, n=9, 27                  | 1.076 (± 6.72)  | 0.984 (± 3.88)  |  |  |
| MMP-3, Week 2, n=8, 26                  | 1.067 (± 7.26)  | 1.024 (± 4.09)  |  |  |
| MMP-3, Week 4, n=9, 27                  | 1.112 (± 8.30)  | 1.016 (± 4.73)  |  |  |
| MMP-3, Week 6, n=7, 27                  | 1.005 (± 26.26) | 0.804 (± 13.44) |  |  |
| MMP-3, Week 8, n=7, 25                  | 0.939 (± 15.43) | 1.088 (± 8.21)  |  |  |
| MMP-3, Week 12, n=7, 24                 | 1.000 (± 13.57) | 0.951 (± 7.35)  |  |  |
| MMP-3, 12-Week FU, n=7, 21              | 0.803 (± 16.05) | 0.984 (± 9.00)  |  |  |

Notes:

[9] - ITT Population

[10] - ITT Population

### Statistical analyses

|                                         |                             |
|-----------------------------------------|-----------------------------|
| <b>Statistical analysis title</b>       | Chitinase 3 Like 1, Week 1  |
| Comparison groups                       | Placebo v GSK3196165 180 mg |
| Number of subjects included in analysis | 39                          |
| Analysis specification                  | Pre-specified               |
| Analysis type                           | other                       |
| P-value                                 | = 0.463                     |
| Method                                  | Repeated measures analysis  |
| Parameter estimate                      | Ratio                       |
| Point estimate                          | 0.887                       |
| Confidence interval                     |                             |
| level                                   | 95 %                        |
| sides                                   | 2-sided                     |
| lower limit                             | 0.64                        |
| upper limit                             | 1.231                       |

|                                         |                             |
|-----------------------------------------|-----------------------------|
| <b>Statistical analysis title</b>       | Chitinase 3 Like 1, Week 2  |
| Comparison groups                       | Placebo v GSK3196165 180 mg |
| Number of subjects included in analysis | 39                          |
| Analysis specification                  | Pre-specified               |
| Analysis type                           | other                       |
| P-value                                 | = 0.782                     |
| Method                                  | Repeated measures analysis  |
| Parameter estimate                      | Ratio                       |
| Point estimate                          | 0.953                       |
| Confidence interval                     |                             |
| level                                   | 95 %                        |
| sides                                   | 2-sided                     |
| lower limit                             | 0.672                       |
| upper limit                             | 1.352                       |

|                                         |                             |
|-----------------------------------------|-----------------------------|
| <b>Statistical analysis title</b>       | Chitinase 3 Like 1, Week 4  |
| Comparison groups                       | Placebo v GSK3196165 180 mg |
| Number of subjects included in analysis | 39                          |
| Analysis specification                  | Pre-specified               |
| Analysis type                           | other                       |
| P-value                                 | = 0.533                     |
| Method                                  | Repeated measures analysis  |
| Parameter estimate                      | Ratio                       |
| Point estimate                          | 1.132                       |
| Confidence interval                     |                             |
| level                                   | 95 %                        |
| sides                                   | 2-sided                     |
| lower limit                             | 0.759                       |
| upper limit                             | 1.69                        |

|                                         |                             |
|-----------------------------------------|-----------------------------|
| <b>Statistical analysis title</b>       | Chitinase 3 Like 1, Week 6  |
| Comparison groups                       | Placebo v GSK3196165 180 mg |
| Number of subjects included in analysis | 39                          |
| Analysis specification                  | Pre-specified               |
| Analysis type                           | other                       |
| P-value                                 | = 0.473                     |
| Method                                  | Repeated measures analysis  |
| Parameter estimate                      | Ratio                       |
| Point estimate                          | 1.149                       |
| Confidence interval                     |                             |
| level                                   | 95 %                        |
| sides                                   | 2-sided                     |
| lower limit                             | 0.779                       |
| upper limit                             | 1.694                       |

|                                         |                             |
|-----------------------------------------|-----------------------------|
| <b>Statistical analysis title</b>       | Chitinase 3 Like 1, Week 8  |
| Comparison groups                       | Placebo v GSK3196165 180 mg |
| Number of subjects included in analysis | 39                          |
| Analysis specification                  | Pre-specified               |
| Analysis type                           | other                       |
| P-value                                 | = 0.608                     |
| Method                                  | Repeated measures analysis  |
| Parameter estimate                      | Ratio                       |
| Point estimate                          | 1.112                       |

|                     |         |
|---------------------|---------|
| Confidence interval |         |
| level               | 95 %    |
| sides               | 2-sided |
| lower limit         | 0.733   |
| upper limit         | 1.687   |

|                                         |                             |
|-----------------------------------------|-----------------------------|
| <b>Statistical analysis title</b>       | Chitinase 3 Like 1, Week 12 |
| Comparison groups                       | Placebo v GSK3196165 180 mg |
| Number of subjects included in analysis | 39                          |
| Analysis specification                  | Pre-specified               |
| Analysis type                           | other                       |
| P-value                                 | = 0.985                     |
| Method                                  | Repeated measures analysis  |
| Parameter estimate                      | Ratio                       |
| Point estimate                          | 1.005                       |
| Confidence interval                     |                             |
| level                                   | 95 %                        |
| sides                                   | 2-sided                     |
| lower limit                             | 0.613                       |
| upper limit                             | 1.645                       |

|                                         |                                |
|-----------------------------------------|--------------------------------|
| <b>Statistical analysis title</b>       | Chitinase 3 Like 1, 12-Week FU |
| Comparison groups                       | Placebo v GSK3196165 180 mg    |
| Number of subjects included in analysis | 39                             |
| Analysis specification                  | Pre-specified                  |
| Analysis type                           | other                          |
| P-value                                 | = 0.102                        |
| Method                                  | Repeated measures analysis     |
| Parameter estimate                      | Ratio                          |
| Point estimate                          | 1.386                          |
| Confidence interval                     |                                |
| level                                   | 95 %                           |
| sides                                   | 2-sided                        |
| lower limit                             | 0.934                          |
| upper limit                             | 2.057                          |

|                                   |                             |
|-----------------------------------|-----------------------------|
| <b>Statistical analysis title</b> | MMP-3, Week 1               |
| Comparison groups                 | Placebo v GSK3196165 180 mg |

|                                         |                            |
|-----------------------------------------|----------------------------|
| Number of subjects included in analysis | 39                         |
| Analysis specification                  | Pre-specified              |
| Analysis type                           | other                      |
| P-value                                 | = 0.259                    |
| Method                                  | Repeated measures analysis |
| Parameter estimate                      | Ratio                      |
| Point estimate                          | 0.915                      |
| Confidence interval                     |                            |
| level                                   | 95 %                       |
| sides                                   | 2-sided                    |
| lower limit                             | 0.781                      |
| upper limit                             | 1.071                      |

|                                         |                             |
|-----------------------------------------|-----------------------------|
| <b>Statistical analysis title</b>       | MMP-3, Week 2               |
| Comparison groups                       | Placebo v GSK3196165 180 mg |
| Number of subjects included in analysis | 39                          |
| Analysis specification                  | Pre-specified               |
| Analysis type                           | other                       |
| P-value                                 | = 0.621                     |
| Method                                  | Repeated measures analysis  |
| Parameter estimate                      | Ratio                       |
| Point estimate                          | 0.959                       |
| Confidence interval                     |                             |
| level                                   | 95 %                        |
| sides                                   | 2-sided                     |
| lower limit                             | 0.809                       |
| upper limit                             | 1.137                       |

|                                         |                             |
|-----------------------------------------|-----------------------------|
| <b>Statistical analysis title</b>       | MMP-3, Week 4               |
| Comparison groups                       | Placebo v GSK3196165 180 mg |
| Number of subjects included in analysis | 39                          |
| Analysis specification                  | Pre-specified               |
| Analysis type                           | other                       |
| P-value                                 | = 0.354                     |
| Method                                  | Repeated measures analysis  |
| Parameter estimate                      | Ratio                       |
| Point estimate                          | 0.914                       |
| Confidence interval                     |                             |
| level                                   | 95 %                        |
| sides                                   | 2-sided                     |
| lower limit                             | 0.752                       |
| upper limit                             | 1.11                        |

|                                   |               |
|-----------------------------------|---------------|
| <b>Statistical analysis title</b> | MMP-3, Week 6 |
|-----------------------------------|---------------|

|                                         |                             |
|-----------------------------------------|-----------------------------|
| Comparison groups                       | Placebo v GSK3196165 180 mg |
| Number of subjects included in analysis | 39                          |
| Analysis specification                  | Pre-specified               |
| Analysis type                           | other                       |
| P-value                                 | = 0.448                     |
| Method                                  | Repeated measures analysis  |
| Parameter estimate                      | Ratio                       |
| Point estimate                          | 0.8                         |
| Confidence interval                     |                             |
| level                                   | 95 %                        |
| sides                                   | 2-sided                     |
| lower limit                             | 0.443                       |
| upper limit                             | 1.444                       |

|                                         |                             |
|-----------------------------------------|-----------------------------|
| <b>Statistical analysis title</b>       | MMP-3, Week 8               |
| Comparison groups                       | Placebo v GSK3196165 180 mg |
| Number of subjects included in analysis | 39                          |
| Analysis specification                  | Pre-specified               |
| Analysis type                           | other                       |
| P-value                                 | = 0.402                     |
| Method                                  | Repeated measures analysis  |
| Parameter estimate                      | Ratio                       |
| Point estimate                          | 1.16                        |
| Confidence interval                     |                             |
| level                                   | 95 %                        |
| sides                                   | 2-sided                     |
| lower limit                             | 0.813                       |
| upper limit                             | 1.653                       |

|                                         |                             |
|-----------------------------------------|-----------------------------|
| <b>Statistical analysis title</b>       | MMP-3, Week 12              |
| Comparison groups                       | Placebo v GSK3196165 180 mg |
| Number of subjects included in analysis | 39                          |
| Analysis specification                  | Pre-specified               |
| Analysis type                           | other                       |
| P-value                                 | = 0.745                     |
| Method                                  | Repeated measures analysis  |
| Parameter estimate                      | Ratio                       |
| Point estimate                          | 0.951                       |
| Confidence interval                     |                             |
| level                                   | 95 %                        |
| sides                                   | 2-sided                     |
| lower limit                             | 0.695                       |
| upper limit                             | 1.301                       |

|                                         |                             |
|-----------------------------------------|-----------------------------|
| <b>Statistical analysis title</b>       | MMP-3, 12-Week FU           |
| Comparison groups                       | Placebo v GSK3196165 180 mg |
| Number of subjects included in analysis | 39                          |
| Analysis specification                  | Pre-specified               |
| Analysis type                           | other                       |
| P-value                                 | = 0.279                     |
| Method                                  | Repeated measures analysis  |
| Parameter estimate                      | Ratio                       |
| Point estimate                          | 1.226                       |
| Confidence interval                     |                             |
| level                                   | 95 %                        |
| sides                                   | 2-sided                     |
| lower limit                             | 0.837                       |
| upper limit                             | 1.796                       |

### Primary: Change from Baseline in Cartilage Biomarkers

|                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                    |                                              |
|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|----------------------------------------------|
| End point title                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                    | Change from Baseline in Cartilage Biomarkers |
| End point description:                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                             |                                              |
| <p>Blood samples were collected and analyzed for markers that may be predictive of rheumatoid arthritis disease activity. Cartilage biomarkers included analysis of ARGS Neo-Epitope, Citrullinated MMP-Degraded Vimentin (CMDV), MMP-Degraded C Reactive Protein (CRP), MMP-Degraded Type I Collagen (MD1C), MMP-Degraded Type II Collagen (MD2C), MMP-Degraded Type III Collagen (MD3C). Baseline was defined at Day 1. Change from Baseline was calculated as ratio of Baseline value to post-dose value. Analysis was performed using repeated measures analysis adjusted for ARGS Neo-Epitope, Citrullinated MMP-Degraded Vimentin, MMP-Degraded CRP, MMP-Degraded Type I Collagen, MMP-Degraded Type II Collagen and MMP-Degraded Type III Collagen log(Baseline value), treatment group, disease duration (&lt;=2 or &gt;2 years), visit and treatment group by visit interaction. Only those participants with data available at the specified data points were analyzed (represented by n= X in the category titles).</p> |                                              |
| End point type                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     | Primary                                      |
| End point timeframe:                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               |                                              |
| Baseline and Weeks 1, 2, 4, 6, 8, 12, 12-Week FU (Week 22)                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                         |                                              |

| End point values                                        | Placebo            | GSK3196165 180 mg  |  |  |
|---------------------------------------------------------|--------------------|--------------------|--|--|
| Subject group type                                      | Reporting group    | Reporting group    |  |  |
| Number of subjects analysed                             | 11 <sup>[11]</sup> | 28 <sup>[12]</sup> |  |  |
| Units: Ratio of cartilage biomarker                     |                    |                    |  |  |
| least squares mean (geometric coefficient of variation) |                    |                    |  |  |
| ARGS Neo-Epitope, Week 1, n=9, 27                       | 0.979 (± 16.10)    | 1.075 (± 9.67)     |  |  |
| ARGS Neo-Epitope, Week 2, n=8, 25                       | 0.790 (± 17.38)    | 1.249 (± 9.87)     |  |  |
| ARGS Neo-Epitope, Week 4, n=8, 26                       | 0.904 (± 17.02)    | 1.104 (± 10.05)    |  |  |
| ARGS Neo-Epitope, Week 6, n=6, 26                       | 0.894 (± 14.28)    | 1.164 (± 7.82)     |  |  |
| ARGS Neo-Epitope, Week 8, n=7, 24                       | 0.854 (± 26.42)    | 1.238 (± 14.20)    |  |  |

|                                       |                 |                 |  |  |
|---------------------------------------|-----------------|-----------------|--|--|
| ARGS Neo-Epitope, Week 12, n=7, 24    | 0.913 (± 13.97) | 1.156 (± 7.78)  |  |  |
| ARGS Neo-Epitope, 12-Week FU, n=8, 21 | 1.129 (± 17.44) | 1.124 (± 9.86)  |  |  |
| CMDV, Week 1, n=9, 27                 | 0.981 (± 24.12) | 0.876 (± 13.80) |  |  |
| CMDV, Week 2, n=8, 26                 | 0.820 (± 28.46) | 0.714 (± 15.89) |  |  |
| CMDV, Week 4, n=9, 27                 | 0.715 (± 27.30) | 0.801 (± 15.52) |  |  |
| CMDV, Week 6, n=7, 27                 | 1.099 (± 30.47) | 0.726 (± 15.94) |  |  |
| CMDV, Week 8, n=7, 25                 | 0.929 (± 24.72) | 0.759 (± 13.39) |  |  |
| CMDV, Week 12, n=7, 24                | 1.123 (± 29.34) | 0.917 (± 16.00) |  |  |
| CMDV, 12-Week FU, n=7, 21             | 0.936 (± 28.05) | 0.769 (± 15.81) |  |  |
| MMP-Degraded CRP, Week 1, n=9, 27     | 0.971 (± 6.83)  | 1.021 (± 3.99)  |  |  |
| MMP-Degraded CRP, Week 2, n=8, 26     | 0.970 (± 5.55)  | 1.000 (± 3.07)  |  |  |
| MMP-Degraded CRP, Week 4, n=9, 27     | 0.992 (± 6.01)  | 1.004 (± 3.49)  |  |  |
| MMP-Degraded CRP, Week 6, n=7, 27     | 1.122 (± 6.55)  | 1.099 (± 3.50)  |  |  |
| MMP-Degraded CRP, Week 8, n=7, 25     | 0.977 (± 7.37)  | 1.087 (± 4.05)  |  |  |
| MMP-Degraded CRP, Week 12, n=7, 24    | 1.006 (± 7.13)  | 1.108 (± 3.95)  |  |  |
| MMP-Degraded CRP, 12-Week FU, n=7, 21 | 1.075 (± 8.01)  | 1.129 (± 4.48)  |  |  |
| MD1C, Week 1, n=9, 27                 | 1.079 (± 9.60)  | 0.858 (± 5.63)  |  |  |
| MD1C, Week 2, n=8, 26                 | 1.028 (± 11.98) | 0.907 (± 6.63)  |  |  |
| MD1C, Week 4, n=9, 27                 | 1.142 (± 14.57) | 0.896 (± 8.35)  |  |  |
| MD1C, Week 6, n=7, 27                 | 1.392 (± 12.64) | 0.889 (± 6.98)  |  |  |
| MD1C, Week 8, n=7, 25                 | 1.131 (± 13.05) | 0.904 (± 7.23)  |  |  |
| MD1C, Week 12, n=7, 24                | 1.148 (± 13.74) | 1.023 (± 7.81)  |  |  |
| MD1C, 12-Week FU, n=7, 21             | 1.095 (± 14.21) | 0.952 (± 8.31)  |  |  |
| MD2C, Week 1, n=9, 27                 | 1.059 (± 11.83) | 1.038 (± 6.88)  |  |  |
| MD2C, Week 2, n=8, 26                 | 1.046 (± 11.27) | 1.015 (± 6.28)  |  |  |
| MD2C, Week 4, n=9, 27                 | 1.035 (± 10.18) | 1.003 (± 5.86)  |  |  |
| MD2C, Week 6, n=7, 27                 | 1.158 (± 12.07) | 1.064 (± 6.30)  |  |  |
| MD2C, Week 8, n=7, 25                 | 1.091 (± 11.42) | 1.023 (± 6.12)  |  |  |
| MD2C, Week 12, n=7, 24                | 1.174 (± 10.73) | 1.072 (± 5.87)  |  |  |
| MD2C, 12-Week FU, n=7, 21             | 1.338 (± 13.10) | 1.041 (± 7.50)  |  |  |
| MD3C, Week 1, n=9, 27                 | 0.950 (± 6.44)  | 0.959 (± 3.74)  |  |  |
| MD3C, Week 2, n=8, 26                 | 0.920 (± 6.82)  | 0.954 (± 3.91)  |  |  |
| MD3C, Week 4, n=9, 27                 | 0.940 (± 8.06)  | 0.886 (± 4.68)  |  |  |
| MD3C, Week 6, n=7, 27                 | 1.013 (± 8.09)  | 0.894 (± 4.34)  |  |  |
| MD3C, Week 8, n=7, 25                 | 0.918 (± 9.04)  | 0.881 (± 4.84)  |  |  |
| MD3C, Week 12, n=7, 24                | 0.929 (± 9.28)  | 0.910 (± 5.08)  |  |  |

|                           |                     |                     |  |  |
|---------------------------|---------------------|---------------------|--|--|
| MD3C, 12-Week FU, n=7, 21 | 0.847 ( $\pm$ 9.75) | 0.910 ( $\pm$ 5.46) |  |  |
|---------------------------|---------------------|---------------------|--|--|

Notes:

[11] - ITT Population

[12] - ITT Population

## Statistical analyses

|                                         |                             |
|-----------------------------------------|-----------------------------|
| <b>Statistical analysis title</b>       | ARGS Neo-Epitope, Week 1    |
| Comparison groups                       | Placebo v GSK3196165 180 mg |
| Number of subjects included in analysis | 39                          |
| Analysis specification                  | Pre-specified               |
| Analysis type                           | other                       |
| P-value                                 | = 0.621                     |
| Method                                  | Repeated measures analysis  |
| Parameter estimate                      | Ratio                       |
| Point estimate                          | 1.098                       |
| Confidence interval                     |                             |
| level                                   | 95 %                        |
| sides                                   | 2-sided                     |
| lower limit                             | 0.75                        |
| upper limit                             | 1.606                       |

|                                         |                             |
|-----------------------------------------|-----------------------------|
| <b>Statistical analysis title</b>       | ARGS Neo-Epitope, Week 2    |
| Comparison groups                       | Placebo v GSK3196165 180 mg |
| Number of subjects included in analysis | 39                          |
| Analysis specification                  | Pre-specified               |
| Analysis type                           | other                       |
| P-value                                 | = 0.031                     |
| Method                                  | Repeated measures analysis  |
| Parameter estimate                      | Ratio                       |
| Point estimate                          | 1.581                       |
| Confidence interval                     |                             |
| level                                   | 95 %                        |
| sides                                   | 2-sided                     |
| lower limit                             | 1.046                       |
| upper limit                             | 2.388                       |

|                                   |                             |
|-----------------------------------|-----------------------------|
| <b>Statistical analysis title</b> | ARGS Neo-Epitope, Week 4    |
| Comparison groups                 | Placebo v GSK3196165 180 mg |

|                                         |                            |
|-----------------------------------------|----------------------------|
| Number of subjects included in analysis | 39                         |
| Analysis specification                  | Pre-specified              |
| Analysis type                           | other                      |
| P-value                                 | = 0.317                    |
| Method                                  | Repeated measures analysis |
| Parameter estimate                      | Ratio                      |
| Point estimate                          | 1.222                      |
| Confidence interval                     |                            |
| level                                   | 95 %                       |
| sides                                   | 2-sided                    |
| lower limit                             | 0.817                      |
| upper limit                             | 1.827                      |

|                                         |                             |
|-----------------------------------------|-----------------------------|
| <b>Statistical analysis title</b>       | ARGS Neo-Epitope, Week 6    |
| Comparison groups                       | Placebo v GSK3196165 180 mg |
| Number of subjects included in analysis | 39                          |
| Analysis specification                  | Pre-specified               |
| Analysis type                           | other                       |
| P-value                                 | = 0.113                     |
| Method                                  | Repeated measures analysis  |
| Parameter estimate                      | Ratio                       |
| Point estimate                          | 1.302                       |
| Confidence interval                     |                             |
| level                                   | 95 %                        |
| sides                                   | 2-sided                     |
| lower limit                             | 0.936                       |
| upper limit                             | 1.81                        |

|                                         |                             |
|-----------------------------------------|-----------------------------|
| <b>Statistical analysis title</b>       | ARGS Neo-Epitope, Week 8    |
| Comparison groups                       | Placebo v GSK3196165 180 mg |
| Number of subjects included in analysis | 39                          |
| Analysis specification                  | Pre-specified               |
| Analysis type                           | other                       |
| P-value                                 | = 0.217                     |
| Method                                  | Repeated measures analysis  |
| Parameter estimate                      | Ratio                       |
| Point estimate                          | 1.45                        |
| Confidence interval                     |                             |
| level                                   | 95 %                        |
| sides                                   | 2-sided                     |
| lower limit                             | 0.795                       |
| upper limit                             | 2.645                       |

|                                   |                           |
|-----------------------------------|---------------------------|
| <b>Statistical analysis title</b> | ARGS Neo-Epitope, Week 12 |
|-----------------------------------|---------------------------|

|                                         |                             |
|-----------------------------------------|-----------------------------|
| Comparison groups                       | Placebo v GSK3196165 180 mg |
| Number of subjects included in analysis | 39                          |
| Analysis specification                  | Pre-specified               |
| Analysis type                           | other                       |
| P-value                                 | = 0.147                     |
| Method                                  | Repeated measures analysis  |
| Parameter estimate                      | Ratio                       |
| Point estimate                          | 1.266                       |
| Confidence interval                     |                             |
| level                                   | 95 %                        |
| sides                                   | 2-sided                     |
| lower limit                             | 0.916                       |
| upper limit                             | 1.75                        |

|                                         |                              |
|-----------------------------------------|------------------------------|
| <b>Statistical analysis title</b>       | ARGS Neo-Epitope, 12-Week FU |
| Comparison groups                       | Placebo v GSK3196165 180 mg  |
| Number of subjects included in analysis | 39                           |
| Analysis specification                  | Pre-specified                |
| Analysis type                           | other                        |
| P-value                                 | = 0.985                      |
| Method                                  | Repeated measures analysis   |
| Parameter estimate                      | Ratio                        |
| Point estimate                          | 0.996                        |
| Confidence interval                     |                              |
| level                                   | 95 %                         |
| sides                                   | 2-sided                      |
| lower limit                             | 0.662                        |
| upper limit                             | 1.499                        |

|                                         |                             |
|-----------------------------------------|-----------------------------|
| <b>Statistical analysis title</b>       | CMDV, Week 1                |
| Comparison groups                       | Placebo v GSK3196165 180 mg |
| Number of subjects included in analysis | 39                          |
| Analysis specification                  | Pre-specified               |
| Analysis type                           | other                       |
| P-value                                 | = 0.681                     |
| Method                                  | Repeated measures analysis  |
| Parameter estimate                      | Ratio                       |
| Point estimate                          | 0.892                       |
| Confidence interval                     |                             |
| level                                   | 95 %                        |
| sides                                   | 2-sided                     |
| lower limit                             | 0.511                       |
| upper limit                             | 1.56                        |

|                                         |                             |
|-----------------------------------------|-----------------------------|
| <b>Statistical analysis title</b>       | CMDV, Week 2                |
| Comparison groups                       | Placebo v GSK3196165 180 mg |
| Number of subjects included in analysis | 39                          |
| Analysis specification                  | Pre-specified               |
| Analysis type                           | other                       |
| P-value                                 | = 0.668                     |
| Method                                  | Repeated measures analysis  |
| Parameter estimate                      | Ratio                       |
| Point estimate                          | 0.87                        |
| Confidence interval                     |                             |
| level                                   | 95 %                        |
| sides                                   | 2-sided                     |
| lower limit                             | 0.454                       |
| upper limit                             | 1.669                       |

|                                         |                             |
|-----------------------------------------|-----------------------------|
| <b>Statistical analysis title</b>       | CMDV, Week 4                |
| Comparison groups                       | Placebo v GSK3196165 180 mg |
| Number of subjects included in analysis | 39                          |
| Analysis specification                  | Pre-specified               |
| Analysis type                           | other                       |
| P-value                                 | = 0.717                     |
| Method                                  | Repeated measures analysis  |
| Parameter estimate                      | Ratio                       |
| Point estimate                          | 1.12                        |
| Confidence interval                     |                             |
| level                                   | 95 %                        |
| sides                                   | 2-sided                     |
| lower limit                             | 0.597                       |
| upper limit                             | 2.101                       |

|                                         |                             |
|-----------------------------------------|-----------------------------|
| <b>Statistical analysis title</b>       | CMDV, Week 6                |
| Comparison groups                       | Placebo v GSK3196165 180 mg |
| Number of subjects included in analysis | 39                          |
| Analysis specification                  | Pre-specified               |
| Analysis type                           | other                       |
| P-value                                 | = 0.227                     |
| Method                                  | Repeated measures analysis  |
| Parameter estimate                      | Ratio                       |
| Point estimate                          | 0.661                       |
| Confidence interval                     |                             |
| level                                   | 95 %                        |
| sides                                   | 2-sided                     |
| lower limit                             | 0.333                       |
| upper limit                             | 1.31                        |

|                                         |                             |
|-----------------------------------------|-----------------------------|
| <b>Statistical analysis title</b>       | CMDV, Week 8                |
| Comparison groups                       | Placebo v GSK3196165 180 mg |
| Number of subjects included in analysis | 39                          |
| Analysis specification                  | Pre-specified               |
| Analysis type                           | other                       |
| P-value                                 | = 0.471                     |
| Method                                  | Repeated measures analysis  |
| Parameter estimate                      | Ratio                       |
| Point estimate                          | 0.817                       |
| Confidence interval                     |                             |
| level                                   | 95 %                        |
| sides                                   | 2-sided                     |
| lower limit                             | 0.464                       |
| upper limit                             | 1.437                       |

|                                         |                             |
|-----------------------------------------|-----------------------------|
| <b>Statistical analysis title</b>       | CMDV, Week 12               |
| Comparison groups                       | Placebo v GSK3196165 180 mg |
| Number of subjects included in analysis | 39                          |
| Analysis specification                  | Pre-specified               |
| Analysis type                           | other                       |
| P-value                                 | = 0.541                     |
| Method                                  | Repeated measures analysis  |
| Parameter estimate                      | Ratio                       |
| Point estimate                          | 0.816                       |
| Confidence interval                     |                             |
| level                                   | 95 %                        |
| sides                                   | 2-sided                     |
| lower limit                             | 0.417                       |
| upper limit                             | 1.597                       |

|                                         |                             |
|-----------------------------------------|-----------------------------|
| <b>Statistical analysis title</b>       | CMDV, 12-Week FU            |
| Comparison groups                       | Placebo v GSK3196165 180 mg |
| Number of subjects included in analysis | 39                          |
| Analysis specification                  | Pre-specified               |
| Analysis type                           | other                       |
| P-value                                 | = 0.544                     |
| Method                                  | Repeated measures analysis  |
| Parameter estimate                      | Ratio                       |
| Point estimate                          | 0.822                       |

|                     |         |
|---------------------|---------|
| Confidence interval |         |
| level               | 95 %    |
| sides               | 2-sided |
| lower limit         | 0.422   |
| upper limit         | 1.602   |

|                                         |                             |
|-----------------------------------------|-----------------------------|
| <b>Statistical analysis title</b>       | MMP-Degraded CRP, Week 1    |
| Comparison groups                       | Placebo v GSK3196165 180 mg |
| Number of subjects included in analysis | 39                          |
| Analysis specification                  | Pre-specified               |
| Analysis type                           | other                       |
| P-value                                 | = 0.537                     |
| Method                                  | Repeated measures analysis  |
| Parameter estimate                      | Ratio                       |
| Point estimate                          | 1.051                       |
| Confidence interval                     |                             |
| level                                   | 95 %                        |
| sides                                   | 2-sided                     |
| lower limit                             | 0.895                       |
| upper limit                             | 1.233                       |

|                                         |                             |
|-----------------------------------------|-----------------------------|
| <b>Statistical analysis title</b>       | MMP-Degraded CRP, Week 2    |
| Comparison groups                       | Placebo v GSK3196165 180 mg |
| Number of subjects included in analysis | 39                          |
| Analysis specification                  | Pre-specified               |
| Analysis type                           | other                       |
| P-value                                 | = 0.635                     |
| Method                                  | Repeated measures analysis  |
| Parameter estimate                      | Ratio                       |
| Point estimate                          | 1.031                       |
| Confidence interval                     |                             |
| level                                   | 95 %                        |
| sides                                   | 2-sided                     |
| lower limit                             | 0.906                       |
| upper limit                             | 1.173                       |

|                                   |                             |
|-----------------------------------|-----------------------------|
| <b>Statistical analysis title</b> | MMP-Degraded CRP, Week 4    |
| Comparison groups                 | Placebo v GSK3196165 180 mg |

|                                         |                            |
|-----------------------------------------|----------------------------|
| Number of subjects included in analysis | 39                         |
| Analysis specification                  | Pre-specified              |
| Analysis type                           | other                      |
| P-value                                 | = 0.866                    |
| Method                                  | Repeated measures analysis |
| Parameter estimate                      | Ratio                      |
| Point estimate                          | 1.012                      |
| Confidence interval                     |                            |
| level                                   | 95 %                       |
| sides                                   | 2-sided                    |
| lower limit                             | 0.879                      |
| upper limit                             | 1.165                      |

|                                         |                             |
|-----------------------------------------|-----------------------------|
| <b>Statistical analysis title</b>       | MMP-Degraded CRP, Week 6    |
| Comparison groups                       | Placebo v GSK3196165 180 mg |
| Number of subjects included in analysis | 39                          |
| Analysis specification                  | Pre-specified               |
| Analysis type                           | other                       |
| P-value                                 | = 0.78                      |
| Method                                  | Repeated measures analysis  |
| Parameter estimate                      | Ratio                       |
| Point estimate                          | 0.979                       |
| Confidence interval                     |                             |
| level                                   | 95 %                        |
| sides                                   | 2-sided                     |
| lower limit                             | 0.842                       |
| upper limit                             | 1.139                       |

|                                         |                             |
|-----------------------------------------|-----------------------------|
| <b>Statistical analysis title</b>       | MMP-Degraded CRP, Week 8    |
| Comparison groups                       | Placebo v GSK3196165 180 mg |
| Number of subjects included in analysis | 39                          |
| Analysis specification                  | Pre-specified               |
| Analysis type                           | other                       |
| P-value                                 | = 0.212                     |
| Method                                  | Repeated measures analysis  |
| Parameter estimate                      | Ratio                       |
| Point estimate                          | 1.113                       |
| Confidence interval                     |                             |
| level                                   | 95 %                        |
| sides                                   | 2-sided                     |
| lower limit                             | 0.938                       |
| upper limit                             | 1.32                        |

|                                   |                           |
|-----------------------------------|---------------------------|
| <b>Statistical analysis title</b> | MMP-Degraded CRP, Week 12 |
|-----------------------------------|---------------------------|

|                                         |                             |
|-----------------------------------------|-----------------------------|
| Comparison groups                       | Placebo v GSK3196165 180 mg |
| Number of subjects included in analysis | 39                          |
| Analysis specification                  | Pre-specified               |
| Analysis type                           | other                       |
| P-value                                 | = 0.242                     |
| Method                                  | Repeated measures analysis  |
| Parameter estimate                      | Ratio                       |
| Point estimate                          | 1.102                       |
| Confidence interval                     |                             |
| level                                   | 95 %                        |
| sides                                   | 2-sided                     |
| lower limit                             | 0.934                       |
| upper limit                             | 1.3                         |

|                                         |                              |
|-----------------------------------------|------------------------------|
| <b>Statistical analysis title</b>       | MMP-Degraded CRP, 12-Week FU |
| Comparison groups                       | Placebo v GSK3196165 180 mg  |
| Number of subjects included in analysis | 39                           |
| Analysis specification                  | Pre-specified                |
| Analysis type                           | other                        |
| P-value                                 | = 0.597                      |
| Method                                  | Repeated measures analysis   |
| Parameter estimate                      | Ratio                        |
| Point estimate                          | 1.05                         |
| Confidence interval                     |                              |
| level                                   | 95 %                         |
| sides                                   | 2-sided                      |
| lower limit                             | 0.87                         |
| upper limit                             | 1.267                        |

|                                         |                             |
|-----------------------------------------|-----------------------------|
| <b>Statistical analysis title</b>       | MD1C, Week 1                |
| Comparison groups                       | Placebo v GSK3196165 180 mg |
| Number of subjects included in analysis | 39                          |
| Analysis specification                  | Pre-specified               |
| Analysis type                           | other                       |
| P-value                                 | = 0.047                     |
| Method                                  | Repeated measures analysis  |
| Parameter estimate                      | Ratio                       |
| Point estimate                          | 0.795                       |
| Confidence interval                     |                             |
| level                                   | 95 %                        |
| sides                                   | 2-sided                     |
| lower limit                             | 0.634                       |
| upper limit                             | 0.997                       |

|                                         |                             |
|-----------------------------------------|-----------------------------|
| <b>Statistical analysis title</b>       | MD1C, Week 2                |
| Comparison groups                       | Placebo v GSK3196165 180 mg |
| Number of subjects included in analysis | 39                          |
| Analysis specification                  | Pre-specified               |
| Analysis type                           | other                       |
| P-value                                 | = 0.367                     |
| Method                                  | Repeated measures analysis  |
| Parameter estimate                      | Ratio                       |
| Point estimate                          | 0.883                       |
| Confidence interval                     |                             |
| level                                   | 95 %                        |
| sides                                   | 2-sided                     |
| lower limit                             | 0.668                       |
| upper limit                             | 1.165                       |

|                                         |                             |
|-----------------------------------------|-----------------------------|
| <b>Statistical analysis title</b>       | MD1C, Week 4                |
| Comparison groups                       | Placebo v GSK3196165 180 mg |
| Number of subjects included in analysis | 39                          |
| Analysis specification                  | Pre-specified               |
| Analysis type                           | other                       |
| P-value                                 | = 0.155                     |
| Method                                  | Repeated measures analysis  |
| Parameter estimate                      | Ratio                       |
| Point estimate                          | 0.784                       |
| Confidence interval                     |                             |
| level                                   | 95 %                        |
| sides                                   | 2-sided                     |
| lower limit                             | 0.558                       |
| upper limit                             | 1.102                       |

|                                         |                             |
|-----------------------------------------|-----------------------------|
| <b>Statistical analysis title</b>       | MD1C, Week 6                |
| Comparison groups                       | Placebo v GSK3196165 180 mg |
| Number of subjects included in analysis | 39                          |
| Analysis specification                  | Pre-specified               |
| Analysis type                           | other                       |
| P-value                                 | = 0.004                     |
| Method                                  | Repeated measures analysis  |
| Parameter estimate                      | Ratio                       |
| Point estimate                          | 0.638                       |
| Confidence interval                     |                             |
| level                                   | 95 %                        |
| sides                                   | 2-sided                     |
| lower limit                             | 0.477                       |
| upper limit                             | 0.855                       |

|                                         |                             |
|-----------------------------------------|-----------------------------|
| <b>Statistical analysis title</b>       | MD1C, Week 8                |
| Comparison groups                       | Placebo v GSK3196165 180 mg |
| Number of subjects included in analysis | 39                          |
| Analysis specification                  | Pre-specified               |
| Analysis type                           | other                       |
| P-value                                 | = 0.14                      |
| Method                                  | Repeated measures analysis  |
| Parameter estimate                      | Ratio                       |
| Point estimate                          | 0.799                       |
| Confidence interval                     |                             |
| level                                   | 95 %                        |
| sides                                   | 2-sided                     |
| lower limit                             | 0.591                       |
| upper limit                             | 1.08                        |

|                                         |                             |
|-----------------------------------------|-----------------------------|
| <b>Statistical analysis title</b>       | MD1C, Week 12               |
| Comparison groups                       | Placebo v GSK3196165 180 mg |
| Number of subjects included in analysis | 39                          |
| Analysis specification                  | Pre-specified               |
| Analysis type                           | other                       |
| P-value                                 | = 0.47                      |
| Method                                  | Repeated measures analysis  |
| Parameter estimate                      | Ratio                       |
| Point estimate                          | 0.891                       |
| Confidence interval                     |                             |
| level                                   | 95 %                        |
| sides                                   | 2-sided                     |
| lower limit                             | 0.647                       |
| upper limit                             | 1.228                       |

|                                         |                             |
|-----------------------------------------|-----------------------------|
| <b>Statistical analysis title</b>       | MD1C, 12-Week FU            |
| Comparison groups                       | Placebo v GSK3196165 180 mg |
| Number of subjects included in analysis | 39                          |
| Analysis specification                  | Pre-specified               |
| Analysis type                           | other                       |
| P-value                                 | = 0.401                     |
| Method                                  | Repeated measures analysis  |
| Parameter estimate                      | Ratio                       |
| Point estimate                          | 0.869                       |

|                     |         |
|---------------------|---------|
| Confidence interval |         |
| level               | 95 %    |
| sides               | 2-sided |
| lower limit         | 0.621   |
| upper limit         | 1.217   |

|                                         |                             |
|-----------------------------------------|-----------------------------|
| <b>Statistical analysis title</b>       | MD2C, Week 1                |
| Comparison groups                       | Placebo v GSK3196165 180 mg |
| Number of subjects included in analysis | 39                          |
| Analysis specification                  | Pre-specified               |
| Analysis type                           | other                       |
| P-value                                 | = 0.887                     |
| Method                                  | Repeated measures analysis  |
| Parameter estimate                      | Ratio                       |
| Point estimate                          | 0.981                       |
| Confidence interval                     |                             |
| level                                   | 95 %                        |
| sides                                   | 2-sided                     |
| lower limit                             | 0.742                       |
| upper limit                             | 1.296                       |

|                                         |                             |
|-----------------------------------------|-----------------------------|
| <b>Statistical analysis title</b>       | MD2C, Week 2                |
| Comparison groups                       | Placebo v GSK3196165 180 mg |
| Number of subjects included in analysis | 39                          |
| Analysis specification                  | Pre-specified               |
| Analysis type                           | other                       |
| P-value                                 | = 0.814                     |
| Method                                  | Repeated measures analysis  |
| Parameter estimate                      | Ratio                       |
| Point estimate                          | 0.97                        |
| Confidence interval                     |                             |
| level                                   | 95 %                        |
| sides                                   | 2-sided                     |
| lower limit                             | 0.744                       |
| upper limit                             | 1.263                       |

|                                   |                             |
|-----------------------------------|-----------------------------|
| <b>Statistical analysis title</b> | MD2C, Week 4                |
| Comparison groups                 | Placebo v GSK3196165 180 mg |

|                                         |                            |
|-----------------------------------------|----------------------------|
| Number of subjects included in analysis | 39                         |
| Analysis specification                  | Pre-specified              |
| Analysis type                           | other                      |
| P-value                                 | = 0.794                    |
| Method                                  | Repeated measures analysis |
| Parameter estimate                      | Ratio                      |
| Point estimate                          | 0.969                      |
| Confidence interval                     |                            |
| level                                   | 95 %                       |
| sides                                   | 2-sided                    |
| lower limit                             | 0.762                      |
| upper limit                             | 1.233                      |

|                                         |                             |
|-----------------------------------------|-----------------------------|
| <b>Statistical analysis title</b>       | MD2C, Week 6                |
| Comparison groups                       | Placebo v GSK3196165 180 mg |
| Number of subjects included in analysis | 39                          |
| Analysis specification                  | Pre-specified               |
| Analysis type                           | other                       |
| P-value                                 | = 0.539                     |
| Method                                  | Repeated measures analysis  |
| Parameter estimate                      | Ratio                       |
| Point estimate                          | 0.919                       |
| Confidence interval                     |                             |
| level                                   | 95 %                        |
| sides                                   | 2-sided                     |
| lower limit                             | 0.696                       |
| upper limit                             | 1.213                       |

|                                         |                             |
|-----------------------------------------|-----------------------------|
| <b>Statistical analysis title</b>       | MD2C, Week 8                |
| Comparison groups                       | Placebo v GSK3196165 180 mg |
| Number of subjects included in analysis | 39                          |
| Analysis specification                  | Pre-specified               |
| Analysis type                           | other                       |
| P-value                                 | = 0.623                     |
| Method                                  | Repeated measures analysis  |
| Parameter estimate                      | Ratio                       |
| Point estimate                          | 0.937                       |
| Confidence interval                     |                             |
| level                                   | 95 %                        |
| sides                                   | 2-sided                     |
| lower limit                             | 0.719                       |
| upper limit                             | 1.221                       |

|                                   |               |
|-----------------------------------|---------------|
| <b>Statistical analysis title</b> | MD2C, Week 12 |
|-----------------------------------|---------------|

|                                         |                             |
|-----------------------------------------|-----------------------------|
| Comparison groups                       | Placebo v GSK3196165 180 mg |
| Number of subjects included in analysis | 39                          |
| Analysis specification                  | Pre-specified               |
| Analysis type                           | other                       |
| P-value                                 | = 0.467                     |
| Method                                  | Repeated measures analysis  |
| Parameter estimate                      | Ratio                       |
| Point estimate                          | 0.913                       |
| Confidence interval                     |                             |
| level                                   | 95 %                        |
| sides                                   | 2-sided                     |
| lower limit                             | 0.711                       |
| upper limit                             | 1.173                       |

|                                         |                             |
|-----------------------------------------|-----------------------------|
| <b>Statistical analysis title</b>       | MD2C, 12-Week FU            |
| Comparison groups                       | Placebo v GSK3196165 180 mg |
| Number of subjects included in analysis | 39                          |
| Analysis specification                  | Pre-specified               |
| Analysis type                           | other                       |
| P-value                                 | = 0.108                     |
| Method                                  | Repeated measures analysis  |
| Parameter estimate                      | Ratio                       |
| Point estimate                          | 0.778                       |
| Confidence interval                     |                             |
| level                                   | 95 %                        |
| sides                                   | 2-sided                     |
| lower limit                             | 0.57                        |
| upper limit                             | 1.061                       |

|                                         |                             |
|-----------------------------------------|-----------------------------|
| <b>Statistical analysis title</b>       | MD3C, Week 1                |
| Comparison groups                       | Placebo v GSK3196165 180 mg |
| Number of subjects included in analysis | 39                          |
| Analysis specification                  | Pre-specified               |
| Analysis type                           | other                       |
| P-value                                 | = 0.897                     |
| Method                                  | Repeated measures analysis  |
| Parameter estimate                      | Ratio                       |
| Point estimate                          | 1.01                        |
| Confidence interval                     |                             |
| level                                   | 95 %                        |
| sides                                   | 2-sided                     |
| lower limit                             | 0.868                       |
| upper limit                             | 1.175                       |

|                                         |                             |
|-----------------------------------------|-----------------------------|
| <b>Statistical analysis title</b>       | MD3C, Week 2                |
| Comparison groups                       | Placebo v GSK3196165 180 mg |
| Number of subjects included in analysis | 39                          |
| Analysis specification                  | Pre-specified               |
| Analysis type                           | other                       |
| P-value                                 | = 0.644                     |
| Method                                  | Repeated measures analysis  |
| Parameter estimate                      | Ratio                       |
| Point estimate                          | 1.037                       |
| Confidence interval                     |                             |
| level                                   | 95 %                        |
| sides                                   | 2-sided                     |
| lower limit                             | 0.884                       |
| upper limit                             | 1.218                       |

|                                         |                             |
|-----------------------------------------|-----------------------------|
| <b>Statistical analysis title</b>       | MD3C, Week 4                |
| Comparison groups                       | Placebo v GSK3196165 180 mg |
| Number of subjects included in analysis | 39                          |
| Analysis specification                  | Pre-specified               |
| Analysis type                           | other                       |
| P-value                                 | = 0.53                      |
| Method                                  | Repeated measures analysis  |
| Parameter estimate                      | Ratio                       |
| Point estimate                          | 0.943                       |
| Confidence interval                     |                             |
| level                                   | 95 %                        |
| sides                                   | 2-sided                     |
| lower limit                             | 0.78                        |
| upper limit                             | 1.139                       |

|                                         |                             |
|-----------------------------------------|-----------------------------|
| <b>Statistical analysis title</b>       | MD3C, Week 6                |
| Comparison groups                       | Placebo v GSK3196165 180 mg |
| Number of subjects included in analysis | 39                          |
| Analysis specification                  | Pre-specified               |
| Analysis type                           | other                       |
| P-value                                 | = 0.182                     |
| Method                                  | Repeated measures analysis  |
| Parameter estimate                      | Ratio                       |
| Point estimate                          | 0.882                       |
| Confidence interval                     |                             |
| level                                   | 95 %                        |
| sides                                   | 2-sided                     |
| lower limit                             | 0.733                       |
| upper limit                             | 1.063                       |

|                                         |                             |
|-----------------------------------------|-----------------------------|
| <b>Statistical analysis title</b>       | MD3C, Week 8                |
| Comparison groups                       | Placebo v GSK3196165 180 mg |
| Number of subjects included in analysis | 39                          |
| Analysis specification                  | Pre-specified               |
| Analysis type                           | other                       |
| P-value                                 | = 0.691                     |
| Method                                  | Repeated measures analysis  |
| Parameter estimate                      | Ratio                       |
| Point estimate                          | 0.96                        |
| Confidence interval                     |                             |
| level                                   | 95 %                        |
| sides                                   | 2-sided                     |
| lower limit                             | 0.779                       |
| upper limit                             | 1.182                       |

|                                         |                             |
|-----------------------------------------|-----------------------------|
| <b>Statistical analysis title</b>       | MD3C, Week 12               |
| Comparison groups                       | Placebo v GSK3196165 180 mg |
| Number of subjects included in analysis | 39                          |
| Analysis specification                  | Pre-specified               |
| Analysis type                           | other                       |
| P-value                                 | = 0.843                     |
| Method                                  | Repeated measures analysis  |
| Parameter estimate                      | Ratio                       |
| Point estimate                          | 0.979                       |
| Confidence interval                     |                             |
| level                                   | 95 %                        |
| sides                                   | 2-sided                     |
| lower limit                             | 0.79                        |
| upper limit                             | 1.214                       |

|                                         |                             |
|-----------------------------------------|-----------------------------|
| <b>Statistical analysis title</b>       | MD3C, 12-Week FU            |
| Comparison groups                       | Placebo v GSK3196165 180 mg |
| Number of subjects included in analysis | 39                          |
| Analysis specification                  | Pre-specified               |
| Analysis type                           | other                       |
| P-value                                 | = 0.524                     |
| Method                                  | Repeated measures analysis  |
| Parameter estimate                      | Ratio                       |
| Point estimate                          | 1.075                       |

|                     |         |
|---------------------|---------|
| Confidence interval |         |
| level               | 95 %    |
| sides               | 2-sided |
| lower limit         | 0.855   |
| upper limit         | 1.351   |

### Primary: Change from Baseline in Flow Cytometry: Helper/Suppressor cells

|                 |                                                                 |
|-----------------|-----------------------------------------------------------------|
| End point title | Change from Baseline in Flow Cytometry: Helper/Suppressor cells |
|-----------------|-----------------------------------------------------------------|

End point description:

Whole blood samples were collected and analyzed for markers which may be predictive of rheumatoid arthritis disease activity. Flow cytometry assessment included assessment of Helper/Suppressor. Baseline was defined at Day 1. Change from Baseline was calculated as ratio of Baseline value to post-dose value. Analysis was performed using repeated measures analysis adjusted for Helper/Suppressor log(Baseline value), treatment group, disease duration ( $\leq 2$  or  $> 2$  years), visit and treatment group by visit interaction. Only those participants with data available at the specified data points were analyzed (represented by n= X in the category titles).

|                |         |
|----------------|---------|
| End point type | Primary |
|----------------|---------|

End point timeframe:

Baseline and Weeks 1, 4, 12, 12-Week FU (Week 22)

| End point values                                        | Placebo             | GSK3196165 180 mg   |  |  |
|---------------------------------------------------------|---------------------|---------------------|--|--|
| Subject group type                                      | Reporting group     | Reporting group     |  |  |
| Number of subjects analysed                             | 11 <sup>[13]</sup>  | 28 <sup>[14]</sup>  |  |  |
| Units: Ratio of Helper/Suppressor cells                 |                     |                     |  |  |
| least squares mean (geometric coefficient of variation) |                     |                     |  |  |
| Helper/Suppressor, Week 1, n=8, 25                      | 1.024 ( $\pm$ 6.98) | 0.976 ( $\pm$ 4.00) |  |  |
| Helper/Suppressor, Week 4, n=8, 25                      | 1.053 ( $\pm$ 7.18) | 0.998 ( $\pm$ 4.11) |  |  |
| Helper/Suppressor, Week 12, n=6, 25                     | 1.040 ( $\pm$ 6.83) | 1.088 ( $\pm$ 3.49) |  |  |
| Helper/Suppressor, 12-Week FU, n=6, 21                  | 1.051 ( $\pm$ 8.99) | 1.065 ( $\pm$ 4.88) |  |  |

Notes:

[13] - ITT Population

[14] - ITT Population

### Statistical analyses

|                                         |                             |
|-----------------------------------------|-----------------------------|
| Statistical analysis title              | Helper/Suppressor, Week 1   |
| Comparison groups                       | Placebo v GSK3196165 180 mg |
| Number of subjects included in analysis | 39                          |
| Analysis specification                  | Pre-specified               |
| Analysis type                           | other                       |
| P-value                                 | = 0.558                     |
| Method                                  | Repeated measures analysis  |
| Parameter estimate                      | Ratio                       |
| Point estimate                          | 0.953                       |

|                     |         |
|---------------------|---------|
| Confidence interval |         |
| level               | 95 %    |
| sides               | 2-sided |
| lower limit         | 0.809   |
| upper limit         | 1.123   |

|                                         |                             |
|-----------------------------------------|-----------------------------|
| <b>Statistical analysis title</b>       | Helper/Suppressor, Week 4   |
| Comparison groups                       | Placebo v GSK3196165 180 mg |
| Number of subjects included in analysis | 39                          |
| Analysis specification                  | Pre-specified               |
| Analysis type                           | other                       |
| P-value                                 | = 0.515                     |
| Method                                  | Repeated measures analysis  |
| Parameter estimate                      | Ratio                       |
| Point estimate                          | 0.947                       |
| Confidence interval                     |                             |
| level                                   | 95 %                        |
| sides                                   | 2-sided                     |
| lower limit                             | 0.801                       |
| upper limit                             | 1.12                        |

|                                         |                             |
|-----------------------------------------|-----------------------------|
| <b>Statistical analysis title</b>       | Helper/Suppressor, Week 12  |
| Comparison groups                       | Placebo v GSK3196165 180 mg |
| Number of subjects included in analysis | 39                          |
| Analysis specification                  | Pre-specified               |
| Analysis type                           | other                       |
| P-value                                 | = 0.565                     |
| Method                                  | Repeated measures analysis  |
| Parameter estimate                      | Ratio                       |
| Point estimate                          | 1.046                       |
| Confidence interval                     |                             |
| level                                   | 95 %                        |
| sides                                   | 2-sided                     |
| lower limit                             | 0.895                       |
| upper limit                             | 1.222                       |

|                                   |                               |
|-----------------------------------|-------------------------------|
| <b>Statistical analysis title</b> | Helper/Suppressor, 12-Week FU |
| Comparison groups                 | Placebo v GSK3196165 180 mg   |

|                                         |                            |
|-----------------------------------------|----------------------------|
| Number of subjects included in analysis | 39                         |
| Analysis specification                  | Pre-specified              |
| Analysis type                           | other                      |
| P-value                                 | = 0.897                    |
| Method                                  | Repeated measures analysis |
| Parameter estimate                      | Ratio                      |
| Point estimate                          | 1.013                      |
| Confidence interval                     |                            |
| level                                   | 95 %                       |
| sides                                   | 2-sided                    |
| lower limit                             | 0.822                      |
| upper limit                             | 1.249                      |

**Primary: Change from Baseline in Flow Cytometry: 6 Colour TB natural killer (NK) Panel- CD16+CD56+, CD19, CD3, CD3+CD4+**

|                 |                                                                                                                |
|-----------------|----------------------------------------------------------------------------------------------------------------|
| End point title | Change from Baseline in Flow Cytometry: 6 Colour TB natural killer (NK) Panel- CD16+CD56+, CD19, CD3, CD3+CD4+ |
|-----------------|----------------------------------------------------------------------------------------------------------------|

End point description:

Whole blood samples were collected and analyzed for markers which may be predictive of rheumatoid arthritis disease activity. Flow cytometry assessment included assessment of cluster of differentiation (CD)16+CD56+, CD19, CD3, CD3+CD4+. Baseline was defined at Day 1. Change from Baseline was calculated as ratio of Baseline value to post-dose value. Repeated measures analysis adjusted for CD16+CD56+, CD19, CD3, CD3+CD4+, CD3+CD8+ and T Cell B Cell NK log(Baseline value), treatment group, disease duration ( $\leq 2$  or  $> 2$  years), visit and treatment group by visit interaction. Only those participants with data available at the specified data points were analyzed (represented by n= X in the category titles).

|                |         |
|----------------|---------|
| End point type | Primary |
|----------------|---------|

End point timeframe:

Baseline and Weeks 1, 4, 12, 12-Week FU (Week 22)

| End point values                                        | Placebo              | GSK3196165<br>180 mg |  |  |
|---------------------------------------------------------|----------------------|----------------------|--|--|
| Subject group type                                      | Reporting group      | Reporting group      |  |  |
| Number of subjects analysed                             | 11 <sup>[15]</sup>   | 28 <sup>[16]</sup>   |  |  |
| Units: Ratio of biomarker                               |                      |                      |  |  |
| least squares mean (geometric coefficient of variation) |                      |                      |  |  |
| CD16+CD56+, Week 1, n=8, 25                             | 0.989 ( $\pm$ 11.39) | 1.025 ( $\pm$ 6.30)  |  |  |
| CD16+CD56+, Week 4, n=8, 25                             | 1.163 ( $\pm$ 12.97) | 0.951 ( $\pm$ 7.25)  |  |  |
| CD16+CD56+, Week 12, n=6, 25                            | 1.193 ( $\pm$ 15.49) | 0.911 ( $\pm$ 7.81)  |  |  |
| CD16+CD56+, 12-Week FU, n=6, 21                         | 1.298 ( $\pm$ 15.10) | 0.920 ( $\pm$ 7.98)  |  |  |
| CD19, Week 1, n=8, 25                                   | 0.880 ( $\pm$ 11.05) | 0.984 ( $\pm$ 6.23)  |  |  |
| CD19, Week 4, n=8, 25                                   | 1.090 ( $\pm$ 15.31) | 0.971 ( $\pm$ 8.60)  |  |  |
| CD19, Week 12, n=6, 25                                  | 1.054 ( $\pm$ 12.26) | 1.003 ( $\pm$ 6.51)  |  |  |

|                               |                 |                |  |  |
|-------------------------------|-----------------|----------------|--|--|
| CD19, Week 22, n=6, 21        | 0.980 (± 17.75) | 0.938 (± 9.75) |  |  |
| CD3, Week 1, n=8, 25          | 0.918 (± 8.73)  | 0.994 (± 4.95) |  |  |
| CD3, Week 4, n=8, 25          | 0.997 (± 11.79) | 0.934 (± 6.66) |  |  |
| CD3, Week 12, n=6, 25         | 0.912 (± 9.01)  | 0.992 (± 4.60) |  |  |
| CD3, 12-Week FU, n=6, 21      | 0.931 (± 9.17)  | 0.989 (± 4.98) |  |  |
| CD3+CD4+, Week 1, n=8, 25     | 0.926 (± 9.56)  | 0.991 (± 5.42) |  |  |
| CD3+CD4+, Week 4, n=8, 25     | 1.028 (± 12.80) | 0.933 (± 7.23) |  |  |
| CD3+CD4+, Week 12, n=6, 25    | 0.952 (± 9.69)  | 1.013 (± 4.94) |  |  |
| CD3+CD4+, 12-Week FU, n=6, 21 | 0.970 (± 9.92)  | 1.000 (± 5.37) |  |  |

Notes:

[15] - ITT Population

[16] - ITT Population

## Statistical analyses

|                                         |                             |
|-----------------------------------------|-----------------------------|
| <b>Statistical analysis title</b>       | CD16+CD56+, Week 1          |
| Comparison groups                       | Placebo v GSK3196165 180 mg |
| Number of subjects included in analysis | 39                          |
| Analysis specification                  | Pre-specified               |
| Analysis type                           | other                       |
| P-value                                 | = 0.786                     |
| Method                                  | Repeated measures analysis  |
| Parameter estimate                      | Ratio                       |
| Point estimate                          | 1.037                       |
| Confidence interval                     |                             |
| level                                   | 95 %                        |
| sides                                   | 2-sided                     |
| lower limit                             | 0.794                       |
| upper limit                             | 1.354                       |

|                                         |                             |
|-----------------------------------------|-----------------------------|
| <b>Statistical analysis title</b>       | CD16+CD56+, Week 4          |
| Comparison groups                       | Placebo v GSK3196165 180 mg |
| Number of subjects included in analysis | 39                          |
| Analysis specification                  | Pre-specified               |
| Analysis type                           | other                       |
| P-value                                 | = 0.188                     |
| Method                                  | Repeated measures analysis  |
| Parameter estimate                      | Ratio                       |
| Point estimate                          | 0.818                       |
| Confidence interval                     |                             |
| level                                   | 95 %                        |
| sides                                   | 2-sided                     |
| lower limit                             | 0.603                       |
| upper limit                             | 1.109                       |

|                                         |                             |
|-----------------------------------------|-----------------------------|
| <b>Statistical analysis title</b>       | CD16+CD56+, Week 12         |
| Comparison groups                       | Placebo v GSK3196165 180 mg |
| Number of subjects included in analysis | 39                          |
| Analysis specification                  | Pre-specified               |
| Analysis type                           | other                       |
| P-value                                 | = 0.129                     |
| Method                                  | Repeated measures analysis  |
| Parameter estimate                      | Ratio                       |
| Point estimate                          | 0.763                       |
| Confidence interval                     |                             |
| level                                   | 95 %                        |
| sides                                   | 2-sided                     |
| lower limit                             | 0.536                       |
| upper limit                             | 1.087                       |

|                                         |                             |
|-----------------------------------------|-----------------------------|
| <b>Statistical analysis title</b>       | CD16+CD56+, 12-Week FU      |
| Comparison groups                       | Placebo v GSK3196165 180 mg |
| Number of subjects included in analysis | 39                          |
| Analysis specification                  | Pre-specified               |
| Analysis type                           | other                       |
| P-value                                 | = 0.054                     |
| Method                                  | Repeated measures analysis  |
| Parameter estimate                      | Ratio                       |
| Point estimate                          | 0.709                       |
| Confidence interval                     |                             |
| level                                   | 95 %                        |
| sides                                   | 2-sided                     |
| lower limit                             | 0.499                       |
| upper limit                             | 1.006                       |

|                                         |                             |
|-----------------------------------------|-----------------------------|
| <b>Statistical analysis title</b>       | CD19, Week 1                |
| Comparison groups                       | Placebo v GSK3196165 180 mg |
| Number of subjects included in analysis | 39                          |
| Analysis specification                  | Pre-specified               |
| Analysis type                           | other                       |
| P-value                                 | = 0.383                     |
| Method                                  | Repeated measures analysis  |
| Parameter estimate                      | Ratio                       |
| Point estimate                          | 1.119                       |
| Confidence interval                     |                             |
| level                                   | 95 %                        |
| sides                                   | 2-sided                     |
| lower limit                             | 0.863                       |
| upper limit                             | 1.45                        |

|                                         |                             |
|-----------------------------------------|-----------------------------|
| <b>Statistical analysis title</b>       | CD19, Week 4                |
| Comparison groups                       | Placebo v GSK3196165 180 mg |
| Number of subjects included in analysis | 39                          |
| Analysis specification                  | Pre-specified               |
| Analysis type                           | other                       |
| P-value                                 | = 0.51                      |
| Method                                  | Repeated measures analysis  |
| Parameter estimate                      | Ratio                       |
| Point estimate                          | 0.89                        |
| Confidence interval                     |                             |
| level                                   | 95 %                        |
| sides                                   | 2-sided                     |
| lower limit                             | 0.623                       |
| upper limit                             | 1.271                       |

|                                         |                             |
|-----------------------------------------|-----------------------------|
| <b>Statistical analysis title</b>       | CD19, Week 12               |
| Comparison groups                       | Placebo v GSK3196165 180 mg |
| Number of subjects included in analysis | 39                          |
| Analysis specification                  | Pre-specified               |
| Analysis type                           | other                       |
| P-value                                 | = 0.724                     |
| Method                                  | Repeated measures analysis  |
| Parameter estimate                      | Ratio                       |
| Point estimate                          | 0.952                       |
| Confidence interval                     |                             |
| level                                   | 95 %                        |
| sides                                   | 2-sided                     |
| lower limit                             | 0.718                       |
| upper limit                             | 1.262                       |

|                                         |                             |
|-----------------------------------------|-----------------------------|
| <b>Statistical analysis title</b>       | CD19, 12-Week FU            |
| Comparison groups                       | Placebo v GSK3196165 180 mg |
| Number of subjects included in analysis | 39                          |
| Analysis specification                  | Pre-specified               |
| Analysis type                           | other                       |
| P-value                                 | = 0.831                     |
| Method                                  | Repeated measures analysis  |
| Parameter estimate                      | Ratio                       |
| Point estimate                          | 0.958                       |

|                     |         |
|---------------------|---------|
| Confidence interval |         |
| level               | 95 %    |
| sides               | 2-sided |
| lower limit         | 0.635   |
| upper limit         | 1.443   |

|                                         |                             |
|-----------------------------------------|-----------------------------|
| <b>Statistical analysis title</b>       | CD3, Week 1                 |
| Comparison groups                       | Placebo v GSK3196165 180 mg |
| Number of subjects included in analysis | 39                          |
| Analysis specification                  | Pre-specified               |
| Analysis type                           | other                       |
| P-value                                 | = 0.437                     |
| Method                                  | Repeated measures analysis  |
| Parameter estimate                      | Ratio                       |
| Point estimate                          | 1.082                       |
| Confidence interval                     |                             |
| level                                   | 95 %                        |
| sides                                   | 2-sided                     |
| lower limit                             | 0.882                       |
| upper limit                             | 1.328                       |

|                                         |                             |
|-----------------------------------------|-----------------------------|
| <b>Statistical analysis title</b>       | CD3, Week 4                 |
| Comparison groups                       | Placebo v GSK3196165 180 mg |
| Number of subjects included in analysis | 39                          |
| Analysis specification                  | Pre-specified               |
| Analysis type                           | other                       |
| P-value                                 | = 0.632                     |
| Method                                  | Repeated measures analysis  |
| Parameter estimate                      | Ratio                       |
| Point estimate                          | 0.937                       |
| Confidence interval                     |                             |
| level                                   | 95 %                        |
| sides                                   | 2-sided                     |
| lower limit                             | 0.711                       |
| upper limit                             | 1.234                       |

|                                   |                             |
|-----------------------------------|-----------------------------|
| <b>Statistical analysis title</b> | CD3, Week 12                |
| Comparison groups                 | Placebo v GSK3196165 180 mg |

|                                         |                            |
|-----------------------------------------|----------------------------|
| Number of subjects included in analysis | 39                         |
| Analysis specification                  | Pre-specified              |
| Analysis type                           | other                      |
| P-value                                 | = 0.413                    |
| Method                                  | Repeated measures analysis |
| Parameter estimate                      | Ratio                      |
| Point estimate                          | 1.088                      |
| Confidence interval                     |                            |
| level                                   | 95 %                       |
| sides                                   | 2-sided                    |
| lower limit                             | 0.885                      |
| upper limit                             | 1.336                      |

|                                         |                             |
|-----------------------------------------|-----------------------------|
| <b>Statistical analysis title</b>       | CD3, 12-Week FU             |
| Comparison groups                       | Placebo v GSK3196165 180 mg |
| Number of subjects included in analysis | 39                          |
| Analysis specification                  | Pre-specified               |
| Analysis type                           | other                       |
| P-value                                 | = 0.567                     |
| Method                                  | Repeated measures analysis  |
| Parameter estimate                      | Ratio                       |
| Point estimate                          | 1.062                       |
| Confidence interval                     |                             |
| level                                   | 95 %                        |
| sides                                   | 2-sided                     |
| lower limit                             | 0.858                       |
| upper limit                             | 1.316                       |

|                                         |                             |
|-----------------------------------------|-----------------------------|
| <b>Statistical analysis title</b>       | CD3+CD4+, Week 1            |
| Comparison groups                       | Placebo v GSK3196165 180 mg |
| Number of subjects included in analysis | 39                          |
| Analysis specification                  | Pre-specified               |
| Analysis type                           | other                       |
| P-value                                 | = 0.547                     |
| Method                                  | Repeated measures analysis  |
| Parameter estimate                      | Ratio                       |
| Point estimate                          | 1.069                       |
| Confidence interval                     |                             |
| level                                   | 95 %                        |
| sides                                   | 2-sided                     |
| lower limit                             | 0.855                       |
| upper limit                             | 1.338                       |

|                                   |                  |
|-----------------------------------|------------------|
| <b>Statistical analysis title</b> | CD3+CD4+, Week 4 |
|-----------------------------------|------------------|

|                                         |                             |
|-----------------------------------------|-----------------------------|
| Comparison groups                       | Placebo v GSK3196165 180 mg |
| Number of subjects included in analysis | 39                          |
| Analysis specification                  | Pre-specified               |
| Analysis type                           | other                       |
| P-value                                 | = 0.512                     |
| Method                                  | Repeated measures analysis  |
| Parameter estimate                      | Ratio                       |
| Point estimate                          | 0.907                       |
| Confidence interval                     |                             |
| level                                   | 95 %                        |
| sides                                   | 2-sided                     |
| lower limit                             | 0.673                       |
| upper limit                             | 1.223                       |

|                                         |                             |
|-----------------------------------------|-----------------------------|
| <b>Statistical analysis title</b>       | CD3+CD4+, Week 12           |
| Comparison groups                       | Placebo v GSK3196165 180 mg |
| Number of subjects included in analysis | 39                          |
| Analysis specification                  | Pre-specified               |
| Analysis type                           | other                       |
| P-value                                 | = 0.573                     |
| Method                                  | Repeated measures analysis  |
| Parameter estimate                      | Ratio                       |
| Point estimate                          | 1.064                       |
| Confidence interval                     |                             |
| level                                   | 95 %                        |
| sides                                   | 2-sided                     |
| lower limit                             | 0.853                       |
| upper limit                             | 1.328                       |

|                                         |                             |
|-----------------------------------------|-----------------------------|
| <b>Statistical analysis title</b>       | CD3+CD4+, 12-Week FU        |
| Comparison groups                       | Placebo v GSK3196165 180 mg |
| Number of subjects included in analysis | 39                          |
| Analysis specification                  | Pre-specified               |
| Analysis type                           | other                       |
| P-value                                 | = 0.789                     |
| Method                                  | Repeated measures analysis  |
| Parameter estimate                      | Ratio                       |
| Point estimate                          | 1.031                       |
| Confidence interval                     |                             |
| level                                   | 95 %                        |
| sides                                   | 2-sided                     |
| lower limit                             | 0.818                       |
| upper limit                             | 1.3                         |

**Primary: Change from Baseline in Flow Cytometry: 6 Colour TBNK Panel- CD3+CD8+ and T Cell B Cell Natural Killer Lymphocytes (NKL)**

|                 |                                                                                                                          |
|-----------------|--------------------------------------------------------------------------------------------------------------------------|
| End point title | Change from Baseline in Flow Cytometry: 6 Colour TBNK Panel- CD3+CD8+ and T Cell B Cell Natural Killer Lymphocytes (NKL) |
|-----------------|--------------------------------------------------------------------------------------------------------------------------|

End point description:

Whole blood samples were collected and analyzed for markers which may be predictive of rheumatoid arthritis disease activity. Flow cytometry assessment included assessment of CD3+CD8+ and T Cell B Cell NKL. Baseline was defined at Day 1. Change from Baseline was calculated by subtracting the post-dose value from the Baseline value. Analysis was performed using repeated measures analysis adjusted for CD3+CD8+ and T Cell B Cell NKL log(Baseline value), treatment group, disease duration ( $\leq 2$  or  $> 2$  years), visit and treatment group by visit interaction. Only those participants with data available at the specified data points were analyzed (represented by n= X in the category titles).

|                |         |
|----------------|---------|
| End point type | Primary |
|----------------|---------|

End point timeframe:

Baseline and Weeks 1, 4, 12, 12-Week FU (Week 22)

| End point values                       | Placebo                | GSK3196165 180 mg      |  |  |
|----------------------------------------|------------------------|------------------------|--|--|
| Subject group type                     | Reporting group        | Reporting group        |  |  |
| Number of subjects analysed            | 11 <sup>[17]</sup>     | 28 <sup>[18]</sup>     |  |  |
| Units: 10 <sup>9</sup> cells/Liter     |                        |                        |  |  |
| least squares mean (standard error)    |                        |                        |  |  |
| CD3+CD8+, Week 1, n=8, 25              | -0.041 ( $\pm$ 0.0390) | -0.005 ( $\pm$ 0.0222) |  |  |
| CD3+CD8+, Week 4, n=8, 25              | 0.000 ( $\pm$ 0.0580)  | -0.023 ( $\pm$ 0.0327) |  |  |
| CD3+CD8+, Week 12, n=6, 25             | -0.056 ( $\pm$ 0.0418) | -0.037 ( $\pm$ 0.0215) |  |  |
| CD3+CD8+, 12-Week FU, n=6, 21          | -0.060 ( $\pm$ 0.0506) | -0.027 ( $\pm$ 0.0279) |  |  |
| T Cell B Cell NKL, Week 1, n=8, 25     | -0.123 ( $\pm$ 0.1557) | -0.020 ( $\pm$ 0.0881) |  |  |
| T Cell B Cell NKL, Week 4, n=8, 25     | 0.108 ( $\pm$ 0.2174)  | -0.050 ( $\pm$ 0.1229) |  |  |
| T Cell B Cell NKL, Week 12, n=6, 25    | -0.093 ( $\pm$ 0.1792) | -0.006 ( $\pm$ 0.0925) |  |  |
| T Cell B Cell NKL, 12-Week FU, n=6, 21 | -0.029 ( $\pm$ 0.2168) | -0.050 ( $\pm$ 0.1183) |  |  |

Notes:

[17] - ITT Population

[18] - ITT Population

**Statistical analyses**

|                                         |                             |
|-----------------------------------------|-----------------------------|
| Statistical analysis title              | CD3+CD8+, Week 1            |
| Comparison groups                       | Placebo v GSK3196165 180 mg |
| Number of subjects included in analysis | 39                          |
| Analysis specification                  | Pre-specified               |
| Analysis type                           | other                       |
| P-value                                 | = 0.428                     |
| Method                                  | Repeated measures analysis  |
| Parameter estimate                      | Mean difference (net)       |
| Point estimate                          | 0.036                       |

|                     |         |
|---------------------|---------|
| Confidence interval |         |
| level               | 95 %    |
| sides               | 2-sided |
| lower limit         | -0.056  |
| upper limit         | 0.128   |

|                                         |                             |
|-----------------------------------------|-----------------------------|
| <b>Statistical analysis title</b>       | CD3+CD8+, Week 4            |
| Comparison groups                       | Placebo v GSK3196165 180 mg |
| Number of subjects included in analysis | 39                          |
| Analysis specification                  | Pre-specified               |
| Analysis type                           | other                       |
| P-value                                 | = 0.733                     |
| Method                                  | Repeated measures analysis  |
| Parameter estimate                      | Mean difference (net)       |
| Point estimate                          | -0.023                      |
| Confidence interval                     |                             |
| level                                   | 95 %                        |
| sides                                   | 2-sided                     |
| lower limit                             | -0.159                      |
| upper limit                             | 0.113                       |

|                                         |                             |
|-----------------------------------------|-----------------------------|
| <b>Statistical analysis title</b>       | CD3+CD8+, Week 12           |
| Comparison groups                       | Placebo v GSK3196165 180 mg |
| Number of subjects included in analysis | 39                          |
| Analysis specification                  | Pre-specified               |
| Analysis type                           | other                       |
| P-value                                 | = 0.677                     |
| Method                                  | Repeated measures analysis  |
| Parameter estimate                      | Mean difference (net)       |
| Point estimate                          | 0.02                        |
| Confidence interval                     |                             |
| level                                   | 95 %                        |
| sides                                   | 2-sided                     |
| lower limit                             | -0.076                      |
| upper limit                             | 0.115                       |

|                                   |                             |
|-----------------------------------|-----------------------------|
| <b>Statistical analysis title</b> | CD3+CD8+, 12-Week FU        |
| Comparison groups                 | Placebo v GSK3196165 180 mg |

|                                         |                            |
|-----------------------------------------|----------------------------|
| Number of subjects included in analysis | 39                         |
| Analysis specification                  | Pre-specified              |
| Analysis type                           | other                      |
| P-value                                 | = 0.569                    |
| Method                                  | Repeated measures analysis |
| Parameter estimate                      | Mean difference (net)      |
| Point estimate                          | 0.033                      |
| Confidence interval                     |                            |
| level                                   | 95 %                       |
| sides                                   | 2-sided                    |
| lower limit                             | -0.084                     |
| upper limit                             | 0.151                      |

|                                         |                             |
|-----------------------------------------|-----------------------------|
| <b>Statistical analysis title</b>       | T Cell B Cell NKL, Week 1   |
| Comparison groups                       | Placebo v GSK3196165 180 mg |
| Number of subjects included in analysis | 39                          |
| Analysis specification                  | Pre-specified               |
| Analysis type                           | other                       |
| P-value                                 | = 0.569                     |
| Method                                  | Repeated measures analysis  |
| Parameter estimate                      | Mean difference (net)       |
| Point estimate                          | 0.103                       |
| Confidence interval                     |                             |
| level                                   | 95 %                        |
| sides                                   | 2-sided                     |
| lower limit                             | -0.263                      |
| upper limit                             | 0.469                       |

|                                         |                             |
|-----------------------------------------|-----------------------------|
| <b>Statistical analysis title</b>       | T Cell B Cell NKL, Week 4   |
| Comparison groups                       | Placebo v GSK3196165 180 mg |
| Number of subjects included in analysis | 39                          |
| Analysis specification                  | Pre-specified               |
| Analysis type                           | other                       |
| P-value                                 | = 0.534                     |
| Method                                  | Repeated measures analysis  |
| Parameter estimate                      | Mean difference (net)       |
| Point estimate                          | -0.157                      |
| Confidence interval                     |                             |
| level                                   | 95 %                        |
| sides                                   | 2-sided                     |
| lower limit                             | -0.668                      |
| upper limit                             | 0.354                       |

|                                   |                            |
|-----------------------------------|----------------------------|
| <b>Statistical analysis title</b> | T Cell B Cell NKL, Week 12 |
|-----------------------------------|----------------------------|

|                                         |                             |
|-----------------------------------------|-----------------------------|
| Comparison groups                       | Placebo v GSK3196165 180 mg |
| Number of subjects included in analysis | 39                          |
| Analysis specification                  | Pre-specified               |
| Analysis type                           | other                       |
| P-value                                 | = 0.668                     |
| Method                                  | Repeated measures analysis  |
| Parameter estimate                      | Mean difference (net)       |
| Point estimate                          | 0.087                       |
| Confidence interval                     |                             |
| level                                   | 95 %                        |
| sides                                   | 2-sided                     |
| lower limit                             | -0.323                      |
| upper limit                             | 0.498                       |

|                                         |                               |
|-----------------------------------------|-------------------------------|
| <b>Statistical analysis title</b>       | T Cell B Cell NKL, 12-Week FU |
| Comparison groups                       | Placebo v GSK3196165 180 mg   |
| Number of subjects included in analysis | 39                            |
| Analysis specification                  | Pre-specified                 |
| Analysis type                           | other                         |
| P-value                                 | = 0.934                       |
| Method                                  | Repeated measures analysis    |
| Parameter estimate                      | Mean difference (net)         |
| Point estimate                          | -0.021                        |
| Confidence interval                     |                               |
| level                                   | 95 %                          |
| sides                                   | 2-sided                       |
| lower limit                             | -0.526                        |
| upper limit                             | 0.484                         |

### **Primary: Change from Baseline in Flow Cytometry: T Regulatory (Reg) Cell Foxp3- CD3+ CD4+, CD3+ CD8+ and CD3+**

|                                                   |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                         |
|---------------------------------------------------|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| End point title                                   | Change from Baseline in Flow Cytometry: T Regulatory (Reg) Cell Foxp3- CD3+ CD4+, CD3+ CD8+ and CD3+                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                    |
| End point description:                            | Whole blood samples were collected and analyzed for markers which may be predictive of rheumatoid arthritis disease activity. Flow cytometry assessment included assessment of CD3+ CD4+, CD3+ CD8+ and CD3+. Baseline was defined at Day 1. Change from Baseline was calculated as ratio of Baseline value to post-dose value. Analysis was performed using repeated measures analysis adjusted for CD3+ CD4+, CD3+ CD8+ and CD3+ Number of Cells ( $10^6/L$ ) log(Baseline value), treatment group, disease duration ( $\leq 2$ or $> 2$ years), visit and treatment group by visit interaction. Only those participants with data available at the specified data points were analyzed (represented by n= X in the category titles). |
| End point type                                    | Primary                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                 |
| End point timeframe:                              |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                         |
| Baseline and Weeks 1, 4, 12, 12-Week FU (Week 22) |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                         |

| <b>End point values</b>                                 | Placebo            | GSK3196165<br>180 mg |  |  |
|---------------------------------------------------------|--------------------|----------------------|--|--|
| Subject group type                                      | Reporting group    | Reporting group      |  |  |
| Number of subjects analysed                             | 11 <sup>[19]</sup> | 28 <sup>[20]</sup>   |  |  |
| Units: Ratio of T Reg cell                              |                    |                      |  |  |
| least squares mean (geometric coefficient of variation) |                    |                      |  |  |
| CD3+ CD4+, Week 1, n=7, 23                              | 0.905 (± 10.21)    | 1.007 (± 5.65)       |  |  |
| CD3+ CD4+, Week 4, n=7, 22                              | 1.038 (± 11.31)    | 0.976 (± 6.38)       |  |  |
| CD3+ CD4+, Week 12, n=5, 21                             | 0.981 (± 10.55)    | 1.004 (± 5.31)       |  |  |
| CD3+ CD4+, 12-Week FU, n=5, 17                          | 0.926 (± 11.70)    | 1.003 (± 6.39)       |  |  |
| CD3+ CD8+, Week 1, n=7, 23                              | 0.885 (± 9.97)     | 0.983 (± 5.50)       |  |  |
| CD3+ CD8+, Week 4, n=7, 22                              | 0.981 (± 11.89)    | 0.939 (± 6.66)       |  |  |
| CD3+ CD8+, Week 12, n=5, 21                             | 0.878 (± 10.50)    | 0.945 (± 5.40)       |  |  |
| CD3+ CD8+, 12-Week FU, n=5, 17                          | 0.936 (± 10.99)    | 0.965 (± 6.05)       |  |  |
| CD3+, Week 1, n=7, 23                                   | 0.901 (± 9.98)     | 0.992 (± 5.54)       |  |  |
| CD3+, Week 4, n=7, 22                                   | 1.034 (± 12.99)    | 0.938 (± 7.33)       |  |  |
| CD3+, Week 12, n=5, 21                                  | 0.959 (± 9.62)     | 0.993 (± 4.90)       |  |  |
| CD3+, 12-Week FU, n=5, 17                               | 0.944 (± 10.88)    | 0.991 (± 6.00)       |  |  |

Notes:

[19] - ITT Population

[20] - ITT Population

## Statistical analyses

| <b>Statistical analysis title</b>       | CD3+ CD4+, Week 1           |
|-----------------------------------------|-----------------------------|
| Comparison groups                       | Placebo v GSK3196165 180 mg |
| Number of subjects included in analysis | 39                          |
| Analysis specification                  | Pre-specified               |
| Analysis type                           | other                       |
| P-value                                 | = 0.369                     |
| Method                                  | Repeated measures analysis  |
| Parameter estimate                      | Ratio                       |
| Point estimate                          | 1.112                       |
| Confidence interval                     |                             |
| level                                   | 95 %                        |
| sides                                   | 2-sided                     |
| lower limit                             | 0.876                       |
| upper limit                             | 1.412                       |

| <b>Statistical analysis title</b> | CD3+ CD4+, Week 4           |
|-----------------------------------|-----------------------------|
| Comparison groups                 | Placebo v GSK3196165 180 mg |

|                                         |                            |
|-----------------------------------------|----------------------------|
| Number of subjects included in analysis | 39                         |
| Analysis specification                  | Pre-specified              |
| Analysis type                           | other                      |
| P-value                                 | = 0.641                    |
| Method                                  | Repeated measures analysis |
| Parameter estimate                      | Ratio                      |
| Point estimate                          | 0.941                      |
| Confidence interval                     |                            |
| level                                   | 95 %                       |
| sides                                   | 2-sided                    |
| lower limit                             | 0.721                      |
| upper limit                             | 1.228                      |

|                                         |                             |
|-----------------------------------------|-----------------------------|
| <b>Statistical analysis title</b>       | CD3+ CD4+, Week 12          |
| Comparison groups                       | Placebo v GSK3196165 180 mg |
| Number of subjects included in analysis | 39                          |
| Analysis specification                  | Pre-specified               |
| Analysis type                           | other                       |
| P-value                                 | = 0.844                     |
| Method                                  | Repeated measures analysis  |
| Parameter estimate                      | Ratio                       |
| Point estimate                          | 1.024                       |
| Confidence interval                     |                             |
| level                                   | 95 %                        |
| sides                                   | 2-sided                     |
| lower limit                             | 0.804                       |
| upper limit                             | 1.303                       |

|                                         |                             |
|-----------------------------------------|-----------------------------|
| <b>Statistical analysis title</b>       | CD3+ CD4+, 12-Week FU       |
| Comparison groups                       | Placebo v GSK3196165 180 mg |
| Number of subjects included in analysis | 39                          |
| Analysis specification                  | Pre-specified               |
| Analysis type                           | other                       |
| P-value                                 | = 0.558                     |
| Method                                  | Repeated measures analysis  |
| Parameter estimate                      | Ratio                       |
| Point estimate                          | 1.082                       |
| Confidence interval                     |                             |
| level                                   | 95 %                        |
| sides                                   | 2-sided                     |
| lower limit                             | 0.821                       |
| upper limit                             | 1.427                       |

|                                   |                   |
|-----------------------------------|-------------------|
| <b>Statistical analysis title</b> | CD3+ CD8+, Week 1 |
|-----------------------------------|-------------------|

|                                         |                             |
|-----------------------------------------|-----------------------------|
| Comparison groups                       | Placebo v GSK3196165 180 mg |
| Number of subjects included in analysis | 39                          |
| Analysis specification                  | Pre-specified               |
| Analysis type                           | other                       |
| P-value                                 | = 0.363                     |
| Method                                  | Repeated measures analysis  |
| Parameter estimate                      | Ratio                       |
| Point estimate                          | 1.111                       |
| Confidence interval                     |                             |
| level                                   | 95 %                        |
| sides                                   | 2-sided                     |
| lower limit                             | 0.88                        |
| upper limit                             | 1.402                       |

|                                         |                             |
|-----------------------------------------|-----------------------------|
| <b>Statistical analysis title</b>       | CD3+ CD8+, Week 4           |
| Comparison groups                       | Placebo v GSK3196165 180 mg |
| Number of subjects included in analysis | 39                          |
| Analysis specification                  | Pre-specified               |
| Analysis type                           | other                       |
| P-value                                 | = 0.751                     |
| Method                                  | Repeated measures analysis  |
| Parameter estimate                      | Ratio                       |
| Point estimate                          | 0.957                       |
| Confidence interval                     |                             |
| level                                   | 95 %                        |
| sides                                   | 2-sided                     |
| lower limit                             | 0.724                       |
| upper limit                             | 1.265                       |

|                                         |                             |
|-----------------------------------------|-----------------------------|
| <b>Statistical analysis title</b>       | CD3+ CD8+, Week 12          |
| Comparison groups                       | Placebo v GSK3196165 180 mg |
| Number of subjects included in analysis | 39                          |
| Analysis specification                  | Pre-specified               |
| Analysis type                           | other                       |
| P-value                                 | = 0.537                     |
| Method                                  | Repeated measures analysis  |
| Parameter estimate                      | Ratio                       |
| Point estimate                          | 1.076                       |
| Confidence interval                     |                             |
| level                                   | 95 %                        |
| sides                                   | 2-sided                     |
| lower limit                             | 0.846                       |
| upper limit                             | 1.37                        |

|                                         |                             |
|-----------------------------------------|-----------------------------|
| <b>Statistical analysis title</b>       | CD3+ CD8+, 12-Week FU       |
| Comparison groups                       | Placebo v GSK3196165 180 mg |
| Number of subjects included in analysis | 39                          |
| Analysis specification                  | Pre-specified               |
| Analysis type                           | other                       |
| P-value                                 | = 0.806                     |
| Method                                  | Repeated measures analysis  |
| Parameter estimate                      | Ratio                       |
| Point estimate                          | 1.032                       |
| Confidence interval                     |                             |
| level                                   | 95 %                        |
| sides                                   | 2-sided                     |
| lower limit                             | 0.797                       |
| upper limit                             | 1.335                       |

|                                         |                             |
|-----------------------------------------|-----------------------------|
| <b>Statistical analysis title</b>       | CD3+, Week 1                |
| Comparison groups                       | Placebo v GSK3196165 180 mg |
| Number of subjects included in analysis | 39                          |
| Analysis specification                  | Pre-specified               |
| Analysis type                           | other                       |
| P-value                                 | = 0.405                     |
| Method                                  | Repeated measures analysis  |
| Parameter estimate                      | Ratio                       |
| Point estimate                          | 1.101                       |
| Confidence interval                     |                             |
| level                                   | 95 %                        |
| sides                                   | 2-sided                     |
| lower limit                             | 0.872                       |
| upper limit                             | 1.391                       |

|                                         |                             |
|-----------------------------------------|-----------------------------|
| <b>Statistical analysis title</b>       | CD3+, Week 4                |
| Comparison groups                       | Placebo v GSK3196165 180 mg |
| Number of subjects included in analysis | 39                          |
| Analysis specification                  | Pre-specified               |
| Analysis type                           | other                       |
| P-value                                 | = 0.519                     |
| Method                                  | Repeated measures analysis  |
| Parameter estimate                      | Ratio                       |
| Point estimate                          | 0.907                       |
| Confidence interval                     |                             |
| level                                   | 95 %                        |
| sides                                   | 2-sided                     |
| lower limit                             | 0.668                       |
| upper limit                             | 1.232                       |

|                                         |                             |
|-----------------------------------------|-----------------------------|
| <b>Statistical analysis title</b>       | CD3+, Week 12               |
| Comparison groups                       | Placebo v GSK3196165 180 mg |
| Number of subjects included in analysis | 39                          |
| Analysis specification                  | Pre-specified               |
| Analysis type                           | other                       |
| P-value                                 | = 0.748                     |
| Method                                  | Repeated measures analysis  |
| Parameter estimate                      | Ratio                       |
| Point estimate                          | 1.036                       |
| Confidence interval                     |                             |
| level                                   | 95 %                        |
| sides                                   | 2-sided                     |
| lower limit                             | 0.831                       |
| upper limit                             | 1.291                       |

|                                         |                             |
|-----------------------------------------|-----------------------------|
| <b>Statistical analysis title</b>       | CD3+, 12-Week FU            |
| Comparison groups                       | Placebo v GSK3196165 180 mg |
| Number of subjects included in analysis | 39                          |
| Analysis specification                  | Pre-specified               |
| Analysis type                           | other                       |
| P-value                                 | = 0.704                     |
| Method                                  | Repeated measures analysis  |
| Parameter estimate                      | Ratio                       |
| Point estimate                          | 1.049                       |
| Confidence interval                     |                             |
| level                                   | 95 %                        |
| sides                                   | 2-sided                     |
| lower limit                             | 0.811                       |
| upper limit                             | 1.356                       |

**Primary: Change from Baseline in Flow Cytometry: T Reg Cell Foxp3: CD3+CD4+CD25+CD127-, CD3+CD4+foxP3+CD25+CD127-**

|                 |                                                                                                          |
|-----------------|----------------------------------------------------------------------------------------------------------|
| End point title | Change from Baseline in Flow Cytometry: T Reg Cell Foxp3: CD3+CD4+CD25+CD127-, CD3+CD4+foxP3+CD25+CD127- |
|-----------------|----------------------------------------------------------------------------------------------------------|

**End point description:**

Whole blood samples were collected and analyzed for markers which may be predictive of rheumatoid arthritis disease activity. Flow cytometry assessment included assessment of CD3+CD4+CD25+CD127- and CD3+CD4+foxP3+CD25+CD127-. Baseline was defined at Day 1. Change from Baseline was calculated by subtracting the post-dose value from the Baseline value. Analysis was performed using repeated measures analysis adjusted for CD3+CD4+CD25+CD127- and CD3+CD4+foxP3+CD25+CD127-Number of Cells ( $10^6$  cells/L) log(Baseline value), treatment group, disease duration ( $\leq 2$  or  $> 2$  years), visit and treatment group by visit interaction. Only those participants with data available at the specified data points were analyzed (represented by n= X in the category titles).

|                |         |
|----------------|---------|
| End point type | Primary |
|----------------|---------|

End point timeframe:

Baseline and Weeks 1, 4, 12, 12-Week FU (Week 22)

| End point values                            | Placebo            | GSK3196165<br>180 mg |  |  |
|---------------------------------------------|--------------------|----------------------|--|--|
| Subject group type                          | Reporting group    | Reporting group      |  |  |
| Number of subjects analysed                 | 11 <sup>[21]</sup> | 28 <sup>[22]</sup>   |  |  |
| Units: 10 <sup>6</sup> cells/Liter          |                    |                      |  |  |
| least squares mean (standard error)         |                    |                      |  |  |
| CD3+CD4+CD25+CD127-, Week 1, n=7, 23        | -3.6 (± 8.35)      | 2.9 (± 4.67)         |  |  |
| CD3+CD4+CD25+CD127-, Week 4, n=7, 22        | 1.4 (± 8.34)       | -0.4 (± 4.70)        |  |  |
| CD3+CD4+CD25+CD127-, Week 12, n=5, 21       | -9.4 (± 9.87)      | -3.1 (± 4.94)        |  |  |
| CD3+CD4+CD25+CD127-, 12-Week FU, n=5, 17    | -12.9 (± 9.92)     | -2.3 (± 5.43)        |  |  |
| CD3+CD4+foxP3+CD25+CD127, Week 1, n=7, 23   | 0.8 (± 6.39)       | 2.8 (± 3.58)         |  |  |
| CD3+CD4+foxP3+CD25+CD127, Week 4, n=7, 22   | 4.3 (± 7.05)       | 2.0 (± 3.98)         |  |  |
| CD3+CD4+foxP3+CD25+CD127, Week 12, n=5, 21  | 2.7 (± 7.99)       | -4.4 (± 3.91)        |  |  |
| CD3+CD4+foxP3+CD25+CD127,12-Week FU, n=5,17 | -8.7 (± 5.94)      | -4.6 (± 3.15)        |  |  |

Notes:

[21] - ITT Population

[22] - ITT Population

## Statistical analyses

|                                         |                             |
|-----------------------------------------|-----------------------------|
| <b>Statistical analysis title</b>       | CD3+CD4+CD25+CD127-, Week 1 |
| Comparison groups                       | Placebo v GSK3196165 180 mg |
| Number of subjects included in analysis | 39                          |
| Analysis specification                  | Pre-specified               |
| Analysis type                           | other                       |
| P-value                                 | = 0.501                     |
| Method                                  | Repeated measures analysis  |
| Parameter estimate                      | Mean difference (net)       |
| Point estimate                          | 6.5                         |
| Confidence interval                     |                             |
| level                                   | 95 %                        |
| sides                                   | 2-sided                     |
| lower limit                             | -13.1                       |
| upper limit                             | 26.1                        |

|                                   |                             |
|-----------------------------------|-----------------------------|
| <b>Statistical analysis title</b> | CD3+CD4+CD25+CD127-, Week 4 |
| Comparison groups                 | Placebo v GSK3196165 180 mg |

|                                         |                            |
|-----------------------------------------|----------------------------|
| Number of subjects included in analysis | 39                         |
| Analysis specification                  | Pre-specified              |
| Analysis type                           | other                      |
| P-value                                 | = 0.852                    |
| Method                                  | Repeated measures analysis |
| Parameter estimate                      | Mean difference (net)      |
| Point estimate                          | -1.8                       |
| Confidence interval                     |                            |
| level                                   | 95 %                       |
| sides                                   | 2-sided                    |
| lower limit                             | -21.6                      |
| upper limit                             | 18                         |

|                                         |                              |
|-----------------------------------------|------------------------------|
| <b>Statistical analysis title</b>       | CD3+CD4+CD25+CD127-, Week 12 |
| Comparison groups                       | Placebo v GSK3196165 180 mg  |
| Number of subjects included in analysis | 39                           |
| Analysis specification                  | Pre-specified                |
| Analysis type                           | other                        |
| P-value                                 | = 0.572                      |
| Method                                  | Repeated measures analysis   |
| Parameter estimate                      | Mean difference (net)        |
| Point estimate                          | 6.3                          |
| Confidence interval                     |                              |
| level                                   | 95 %                         |
| sides                                   | 2-sided                      |
| lower limit                             | -16.4                        |
| upper limit                             | 29                           |

|                                         |                                 |
|-----------------------------------------|---------------------------------|
| <b>Statistical analysis title</b>       | CD3+CD4+CD25+CD127-, 12-Week FU |
| Comparison groups                       | Placebo v GSK3196165 180 mg     |
| Number of subjects included in analysis | 39                              |
| Analysis specification                  | Pre-specified                   |
| Analysis type                           | other                           |
| P-value                                 | = 0.363                         |
| Method                                  | Repeated measures analysis      |
| Parameter estimate                      | Mean difference (net)           |
| Point estimate                          | 10.5                            |
| Confidence interval                     |                                 |
| level                                   | 95 %                            |
| sides                                   | 2-sided                         |
| lower limit                             | -13                             |
| upper limit                             | 34.1                            |

|                                   |                                   |
|-----------------------------------|-----------------------------------|
| <b>Statistical analysis title</b> | CD3+CD4+foxP3+CD25+CD127-, Week 1 |
|-----------------------------------|-----------------------------------|

|                                         |                             |
|-----------------------------------------|-----------------------------|
| Comparison groups                       | Placebo v GSK3196165 180 mg |
| Number of subjects included in analysis | 39                          |
| Analysis specification                  | Pre-specified               |
| Analysis type                           | other                       |
| P-value                                 | = 0.788                     |
| Method                                  | Repeated measures analysis  |
| Parameter estimate                      | Mean difference (net)       |
| Point estimate                          | 2                           |
| Confidence interval                     |                             |
| level                                   | 95 %                        |
| sides                                   | 2-sided                     |
| lower limit                             | -13                         |
| upper limit                             | 17                          |

|                                         |                                   |
|-----------------------------------------|-----------------------------------|
| <b>Statistical analysis title</b>       | CD3+CD4+foxP3+CD25+CD127-, Week 4 |
| Comparison groups                       | Placebo v GSK3196165 180 mg       |
| Number of subjects included in analysis | 39                                |
| Analysis specification                  | Pre-specified                     |
| Analysis type                           | other                             |
| P-value                                 | = 0.786                           |
| Method                                  | Repeated measures analysis        |
| Parameter estimate                      | Mean difference (net)             |
| Point estimate                          | -2.2                              |
| Confidence interval                     |                                   |
| level                                   | 95 %                              |
| sides                                   | 2-sided                           |
| lower limit                             | -18.8                             |
| upper limit                             | 14.4                              |

|                                         |                                    |
|-----------------------------------------|------------------------------------|
| <b>Statistical analysis title</b>       | CD3+CD4+foxP3+CD25+CD127-, Week 12 |
| Comparison groups                       | Placebo v GSK3196165 180 mg        |
| Number of subjects included in analysis | 39                                 |
| Analysis specification                  | Pre-specified                      |
| Analysis type                           | other                              |
| P-value                                 | = 0.433                            |
| Method                                  | Repeated measures analysis         |
| Parameter estimate                      | Mean difference (net)              |
| Point estimate                          | -7.1                               |
| Confidence interval                     |                                    |
| level                                   | 95 %                               |
| sides                                   | 2-sided                            |
| lower limit                             | -25.4                              |
| upper limit                             | 11.2                               |

|                                         |                                       |
|-----------------------------------------|---------------------------------------|
| <b>Statistical analysis title</b>       | CD3+CD4+foxP3+CD25+CD127-, 12-Week FU |
| Comparison groups                       | Placebo v GSK3196165 180 mg           |
| Number of subjects included in analysis | 39                                    |
| Analysis specification                  | Pre-specified                         |
| Analysis type                           | other                                 |
| P-value                                 | = 0.55                                |
| Method                                  | Repeated measures analysis            |
| Parameter estimate                      | Mean difference (net)                 |
| Point estimate                          | 4.1                                   |
| Confidence interval                     |                                       |
| level                                   | 95 %                                  |
| sides                                   | 2-sided                               |
| lower limit                             | -9.8                                  |
| upper limit                             | 18                                    |

### Primary: Change from Baseline in T Helper Cell Panel events

|                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       |                                                    |
|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|----------------------------------------------------|
| End point title                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       | Change from Baseline in T Helper Cell Panel events |
| End point description:                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                |                                                    |
| <p>Blood samples were collected and analyzed for markers which may be predictive of rheumatoid arthritis disease activity. T Helper Cell Panel included analysis of CD45+3+8-4+CCR6+CXCR3+38+DR+, CD45+3+8-4+CCR6+CXCR3-38+DR+, CD45+3+8-4+CCR6-CXCR3+38+DR+, CD45+3+8-4+CCR6-CXCR3-38+DR+, CD45+CD3+CD8-CD4+, CD45+CD3+CD8-CD4+CCR6+CXCR3+, CD45+CD3+CD8-CD4+CCR6+CXCR3-, CD45+CD3+CD8-CD4+CCR6-CXCR3+ and CD45+CD3+CD8-CD4+CCR6-CXCR3-. Baseline was defined at Day 1. Change from Baseline was calculated by subtracting the post-dose value from the Baseline value. Analysis was performed using repeated measures analysis adjusted for T Helper Cell Panel Events (EVENTS) Baseline value, treatment group, disease duration (&lt;=2 or &gt;2 years), visit and treatment group by visit interaction. Only those participants with data available at the specified data points were analyzed (represented by n= X in the category titles).</p> |                                                    |
| End point type                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                        | Primary                                            |
| End point timeframe:                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                  |                                                    |
| Baseline and Weeks 1, 4, 12, 12-Week FU (Week 22)                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     |                                                    |

| End point values                               | Placebo            | GSK3196165 180 mg  |  |  |
|------------------------------------------------|--------------------|--------------------|--|--|
| Subject group type                             | Reporting group    | Reporting group    |  |  |
| Number of subjects analysed                    | 11 <sup>[23]</sup> | 28 <sup>[24]</sup> |  |  |
| Units: Events                                  |                    |                    |  |  |
| least squares mean (standard error)            |                    |                    |  |  |
| CD45+3+8-4+CCR6+CXCR3+38+DR+, Week 1, n=7, 23  | -48.6 (± 13.50)    | -34.0 (± 7.35)     |  |  |
| CD45+3+8-4+CCR6+CXCR3+38+DR+, Week 4, n=7, 21  | -14.5 (± 18.36)    | -6.1 (± 10.63)     |  |  |
| CD45+3+8-4+CCR6+CXCR3+38+DR+, Week 12, n=5, 22 | 42.3 (± 37.80)     | -6.9 (± 17.69)     |  |  |
| CD45+3+8-4+CCR6+CXCR3+38+DR+, 12-Week          | 11.5 (± 16.47)     | -18.7 (± 8.66)     |  |  |
| CD45+3+8-4+CCR6+CXCR3-38+DR+, Week 1, n=7, 23  | -17.0 (± 6.80)     | -10.5 (± 3.62)     |  |  |
| CD45+3+8-4+CCR6+CXCR3-38+DR+, Week 4, n=7, 21  | 14.2 (± 15.65)     | 12.2 (± 9.10)      |  |  |

|                                                      |                        |                        |  |  |
|------------------------------------------------------|------------------------|------------------------|--|--|
| CD45+3+8-4+CCR6+CXCR3-38+DR+,<br>Week 12, n=5, 22    | 3.4 (± 16.09)          | -3.0 (± 7.55)          |  |  |
| CD45+3+8-4+CCR6+CXCR3-38+DR+,<br>12-Week FU, n=5, 18 | 8.9 (± 12.29)          | 3.3 (± 6.36)           |  |  |
| CD45+3+8-4+CCR6-CXCR3+38+DR+,<br>Week 1, n=7, 23     | -73.2 (±<br>82.46)     | -129.2 (±<br>46.04)    |  |  |
| CD45+3+8-4+CCR6-CXCR3+38+DR+,<br>Week 4, n=7, 21     | -159.6 (±<br>60.51)    | -108.0 (±<br>35.05)    |  |  |
| CD45+3+8-4+CCR6-CXCR3+38+DR+,<br>Week 12, n=5, 22    | 219.2 (±<br>299.65)    | 77.7 (±<br>146.73)     |  |  |
| CD45+3+8-4+CCR6-CXCR3+38+DR+,<br>12-Week FU, n=5, 18 | 33.9 (± 66.09)         | -104.0 (±<br>34.73)    |  |  |
| CD45+3+8-4+CCR6-CXCR3-38+DR+,<br>Week 1, n=7, 23     | -70.9 (±<br>25.90)     | -70.5 (±<br>14.03)     |  |  |
| CD45+3+8-4+CCR6-CXCR3-38+DR+,<br>Week 4, n=7, 21     | -38.9 (±<br>30.69)     | -56.3 (±<br>17.93)     |  |  |
| CD45+3+8-4+CCR6-CXCR3-38+DR+,<br>Week 12, n=5, 22    | -16.4 (±<br>198.13)    | 43.0 (± 92.38)         |  |  |
| CD45+3+8-4+CCR6-CXCR3-38+DR+,<br>12-Week FU, n=5, 18 | -12.7 (±<br>33.50)     | -59.9 (±<br>17.32)     |  |  |
| CD45+CD3+CD8-CD4+, Week 1, n=7,<br>23                | -3845.3 (±<br>2648.60) | -163.0 (±<br>1444.61)  |  |  |
| CD45+CD3+CD8-CD4+, Week 4, n=7,<br>21                | 1622.8 (±<br>2973.60)  | 1075.1 (±<br>1723.09)  |  |  |
| vCD45+CD3+CD8-CD4+, Week 12,<br>n=5, 22              | 2112.9 (±<br>4211.63)  | 1006.9 (±<br>2026.47)  |  |  |
| CD45+CD3+CD8-CD4+, 12-Week FU,<br>n=5, 18            | 1799.0 (±<br>2589.05)  | -1832.0 (±<br>1366.65) |  |  |
| CD45+CD3+CD8-CD4+CCR6+CXCR3+,<br>Week 1, n=7, 23     | -514.6 (±<br>647.85)   | -1030.2 (±<br>345.07)  |  |  |
| CD45+CD3+CD8-CD4+CCR6+CXCR3+,<br>Week 4, n=7, 21     | -116.6 (±<br>757.58)   | -316.5 (±<br>438.76)   |  |  |
| CD45+CD3+CD8-CD4+CCR6+CXCR3+,<br>Week 12, n=5, 22    | -252.9 (±<br>827.53)   | -506.4 (±<br>389.97)   |  |  |
| CD45+CD3+CD8-CD4+CCR6+CXCR3+,<br>12-Week FU, n=5, 18 | -688.1 (±<br>792.26)   | -463.0 (±<br>412.22)   |  |  |
| CD45+CD3+CD8-CD4+CCR6+CXCR3-<br>Week 1, n=7, 23      | -817.1 (±<br>393.10)   | -654.5 (±<br>212.18)   |  |  |
| CD45+CD3+CD8-CD4+CCR6+CXCR3-<br>Week 4, n=7, 21      | 197.7 (±<br>475.88)    | 14.2 (±<br>277.06)     |  |  |
| CD45+CD3+CD8-CD4+CCR6+CXCR3-<br>Week 12, n=5, 22     | 48.8 (±<br>541.14)     | -219.7 (±<br>253.92)   |  |  |
| CD45+CD3+CD8-CD4+CCR6+CXCR3-<br>12-Week FU, n=5, 18  | -311.6 (±<br>553.32)   | -509.2 (±<br>291.09)   |  |  |
| CD45+CD3+CD8-CD4+CCR6-CXCR3+<br>Week 1, n=7, 23      | 371.8 (±<br>1026.17)   | 1521.8 (±<br>547.18)   |  |  |
| CD45+CD3+CD8-CD4+CCR6-CXCR3+<br>Week 4, n=7, 21      | -24.5 (±<br>1678.23)   | -292.5 (±<br>967.00)   |  |  |
| CD45+CD3+CD8-CD4+CCR6-CXCR3+<br>Week 12, n=5, 22     | 2790.5 (±<br>2510.67)  | 1443.1 (±<br>1209.66)  |  |  |
| CD45+CD3+CD8-CD4+CCR6-CXCR3+<br>12-Week FU, n=5, 18  | 2295.9 (±<br>1787.02)  | 607.0 (±<br>927.11)    |  |  |
| CD45+CD3+CD8-CD4+CCR6-CXCR3-<br>Week 1, n=7, 23      | -3231.4 (±<br>2162.58) | 45.4 (±<br>1187.37)    |  |  |
| CD45+CD3+CD8-CD4+CCR6-CXCR3-<br>Week 4, n=7, 21      | 2084.9 (±<br>2873.95)  | 1637.6 (±<br>1665.46)  |  |  |
| CD45+CD3+CD8-CD4+CCR6-CXCR3-<br>Week 12, n=5, 22     | -1273.9 (±<br>2413.90) | 161.4 (±<br>1209.82)   |  |  |
| CD45+CD3+CD8-CD4+CCR6-CXCR3-<br>12-Week FU, n=5, 18  | -106.6 (±<br>1690.64)  | -1316.7 (±<br>892.55)  |  |  |

Notes:

[23] - ITT Population

[24] - ITT Population

### Statistical analyses

|                                         |                                      |
|-----------------------------------------|--------------------------------------|
| <b>Statistical analysis title</b>       | CD45+3+8-4+CCR6+CXCR3+38+DR+, Week 1 |
| Comparison groups                       | Placebo v GSK3196165 180 mg          |
| Number of subjects included in analysis | 39                                   |
| Analysis specification                  | Pre-specified                        |
| Analysis type                           | other                                |
| P-value                                 | = 0.35                               |
| Method                                  | Repeated measures analysis           |
| Parameter estimate                      | Mean difference (net)                |
| Point estimate                          | 14.6                                 |
| Confidence interval                     |                                      |
| level                                   | 95 %                                 |
| sides                                   | 2-sided                              |
| lower limit                             | -16.9                                |
| upper limit                             | 46.1                                 |

|                                         |                                      |
|-----------------------------------------|--------------------------------------|
| <b>Statistical analysis title</b>       | CD45+3+8-4+CCR6+CXCR3+38+DR+, Week 4 |
| Comparison groups                       | Placebo v GSK3196165 180 mg          |
| Number of subjects included in analysis | 39                                   |
| Analysis specification                  | Pre-specified                        |
| Analysis type                           | other                                |
| P-value                                 | = 0.697                              |
| Method                                  | Repeated measures analysis           |
| Parameter estimate                      | Mean difference (net)                |
| Point estimate                          | 8.4                                  |
| Confidence interval                     |                                      |
| level                                   | 95 %                                 |
| sides                                   | 2-sided                              |
| lower limit                             | -35.3                                |
| upper limit                             | 52                                   |

|                                   |                                       |
|-----------------------------------|---------------------------------------|
| <b>Statistical analysis title</b> | CD45+3+8-4+CCR6+CXCR3+38+DR+, Week 12 |
| Comparison groups                 | Placebo v GSK3196165 180 mg           |

|                                         |                            |
|-----------------------------------------|----------------------------|
| Number of subjects included in analysis | 39                         |
| Analysis specification                  | Pre-specified              |
| Analysis type                           | other                      |
| P-value                                 | = 0.249                    |
| Method                                  | Repeated measures analysis |
| Parameter estimate                      | Mean difference (net)      |
| Point estimate                          | -49.2                      |
| Confidence interval                     |                            |
| level                                   | 95 %                       |
| sides                                   | 2-sided                    |
| lower limit                             | -135.2                     |
| upper limit                             | 36.8                       |

|                                         |                                          |
|-----------------------------------------|------------------------------------------|
| <b>Statistical analysis title</b>       | CD45+3+8-4+CCR6+CXCR3+38+DR+, 12-Week FU |
| Comparison groups                       | Placebo v GSK3196165 180 mg              |
| Number of subjects included in analysis | 39                                       |
| Analysis specification                  | Pre-specified                            |
| Analysis type                           | other                                    |
| P-value                                 | = 0.119                                  |
| Method                                  | Repeated measures analysis               |
| Parameter estimate                      | Mean difference (net)                    |
| Point estimate                          | -30.1                                    |
| Confidence interval                     |                                          |
| level                                   | 95 %                                     |
| sides                                   | 2-sided                                  |
| lower limit                             | -68.6                                    |
| upper limit                             | 8.3                                      |

|                                         |                                      |
|-----------------------------------------|--------------------------------------|
| <b>Statistical analysis title</b>       | CD45+3+8-4+CCR6+CXCR3-38+DR+, Week 1 |
| Comparison groups                       | Placebo v GSK3196165 180 mg          |
| Number of subjects included in analysis | 39                                   |
| Analysis specification                  | Pre-specified                        |
| Analysis type                           | other                                |
| P-value                                 | = 0.403                              |
| Method                                  | Repeated measures analysis           |
| Parameter estimate                      | Mean difference (net)                |
| Point estimate                          | 6.5                                  |
| Confidence interval                     |                                      |
| level                                   | 95 %                                 |
| sides                                   | 2-sided                              |
| lower limit                             | -9.3                                 |
| upper limit                             | 22.4                                 |

|                                   |                                      |
|-----------------------------------|--------------------------------------|
| <b>Statistical analysis title</b> | CD45+3+8-4+CCR6+CXCR3-38+DR+, Week 4 |
|-----------------------------------|--------------------------------------|

|                                         |                             |
|-----------------------------------------|-----------------------------|
| Comparison groups                       | Placebo v GSK3196165 180 mg |
| Number of subjects included in analysis | 39                          |
| Analysis specification                  | Pre-specified               |
| Analysis type                           | other                       |
| P-value                                 | = 0.91                      |
| Method                                  | Repeated measures analysis  |
| Parameter estimate                      | Mean difference (net)       |
| Point estimate                          | -2.1                        |
| Confidence interval                     |                             |
| level                                   | 95 %                        |
| sides                                   | 2-sided                     |
| lower limit                             | -39.4                       |
| upper limit                             | 35.2                        |

|                                         |                                       |
|-----------------------------------------|---------------------------------------|
| <b>Statistical analysis title</b>       | CD45+3+8-4+CCR6+CXCR3-38+DR+, Week 12 |
| Comparison groups                       | Placebo v GSK3196165 180 mg           |
| Number of subjects included in analysis | 39                                    |
| Analysis specification                  | Pre-specified                         |
| Analysis type                           | other                                 |
| P-value                                 | = 0.718                               |
| Method                                  | Repeated measures analysis            |
| Parameter estimate                      | Mean difference (net)                 |
| Point estimate                          | -6.5                                  |
| Confidence interval                     |                                       |
| level                                   | 95 %                                  |
| sides                                   | 2-sided                               |
| lower limit                             | -43.1                                 |
| upper limit                             | 30.1                                  |

|                                         |                                          |
|-----------------------------------------|------------------------------------------|
| <b>Statistical analysis title</b>       | CD45+3+8-4+CCR6+CXCR3-38+DR+, 12-Week FU |
| Comparison groups                       | Placebo v GSK3196165 180 mg              |
| Number of subjects included in analysis | 39                                       |
| Analysis specification                  | Pre-specified                            |
| Analysis type                           | other                                    |
| P-value                                 | = 0.687                                  |
| Method                                  | Repeated measures analysis               |
| Parameter estimate                      | Mean difference (net)                    |
| Point estimate                          | -5.7                                     |
| Confidence interval                     |                                          |
| level                                   | 95 %                                     |
| sides                                   | 2-sided                                  |
| lower limit                             | -34.4                                    |
| upper limit                             | 23                                       |

|                                         |                                      |
|-----------------------------------------|--------------------------------------|
| <b>Statistical analysis title</b>       | CD45+3+8-4+CCR6-CXCR3+38+DR+, Week 1 |
| Comparison groups                       | Placebo v GSK3196165 180 mg          |
| Number of subjects included in analysis | 39                                   |
| Analysis specification                  | Pre-specified                        |
| Analysis type                           | other                                |
| P-value                                 | = 0.559                              |
| Method                                  | Repeated measures analysis           |
| Parameter estimate                      | Mean difference (net)                |
| Point estimate                          | -56                                  |
| Confidence interval                     |                                      |
| level                                   | 95 %                                 |
| sides                                   | 2-sided                              |
| lower limit                             | -249.8                               |
| upper limit                             | 137.7                                |

|                                         |                                      |
|-----------------------------------------|--------------------------------------|
| <b>Statistical analysis title</b>       | CD45+3+8-4+CCR6-CXCR3+38+DR+, Week 4 |
| Comparison groups                       | Placebo v GSK3196165 180 mg          |
| Number of subjects included in analysis | 39                                   |
| Analysis specification                  | Pre-specified                        |
| Analysis type                           | other                                |
| P-value                                 | = 0.47                               |
| Method                                  | Repeated measures analysis           |
| Parameter estimate                      | Mean difference (net)                |
| Point estimate                          | 51.6                                 |
| Confidence interval                     |                                      |
| level                                   | 95 %                                 |
| sides                                   | 2-sided                              |
| lower limit                             | -93.9                                |
| upper limit                             | 197                                  |

|                                         |                                       |
|-----------------------------------------|---------------------------------------|
| <b>Statistical analysis title</b>       | CD45+3+8-4+CCR6-CXCR3+38+DR+, Week 12 |
| Comparison groups                       | Placebo v GSK3196165 180 mg           |
| Number of subjects included in analysis | 39                                    |
| Analysis specification                  | Pre-specified                         |
| Analysis type                           | other                                 |
| P-value                                 | = 0.675                               |
| Method                                  | Repeated measures analysis            |
| Parameter estimate                      | Mean difference (net)                 |
| Point estimate                          | -141.5                                |
| Confidence interval                     |                                       |
| level                                   | 95 %                                  |
| sides                                   | 2-sided                               |
| lower limit                             | -829.2                                |
| upper limit                             | 546.3                                 |

|                                         |                                          |
|-----------------------------------------|------------------------------------------|
| <b>Statistical analysis title</b>       | CD45+3+8-4+CCR6-CXCR3+38+DR+, 12-Week FU |
| Comparison groups                       | Placebo v GSK3196165 180 mg              |
| Number of subjects included in analysis | 39                                       |
| Analysis specification                  | Pre-specified                            |
| Analysis type                           | other                                    |
| P-value                                 | = 0.08                                   |
| Method                                  | Repeated measures analysis               |
| Parameter estimate                      | Mean difference (net)                    |
| Point estimate                          | -137.9                                   |
| Confidence interval                     |                                          |
| level                                   | 95 %                                     |
| sides                                   | 2-sided                                  |
| lower limit                             | -294                                     |
| upper limit                             | 18.2                                     |

|                                         |                                      |
|-----------------------------------------|--------------------------------------|
| <b>Statistical analysis title</b>       | CD45+3+8-4+CCR6-CXCR3-38+DR+, Week 1 |
| Comparison groups                       | Placebo v GSK3196165 180 mg          |
| Number of subjects included in analysis | 39                                   |
| Analysis specification                  | Pre-specified                        |
| Analysis type                           | other                                |
| P-value                                 | = 0.989                              |
| Method                                  | Repeated measures analysis           |
| Parameter estimate                      | Mean difference (net)                |
| Point estimate                          | 0.4                                  |
| Confidence interval                     |                                      |
| level                                   | 95 %                                 |
| sides                                   | 2-sided                              |
| lower limit                             | -60.5                                |
| upper limit                             | 61.3                                 |

|                                         |                                      |
|-----------------------------------------|--------------------------------------|
| <b>Statistical analysis title</b>       | CD45+3+8-4+CCR6-CXCR3-38+DR+, Week 4 |
| Comparison groups                       | Placebo v GSK3196165 180 mg          |
| Number of subjects included in analysis | 39                                   |
| Analysis specification                  | Pre-specified                        |
| Analysis type                           | other                                |
| P-value                                 | = 0.634                              |
| Method                                  | Repeated measures analysis           |
| Parameter estimate                      | Mean difference (net)                |
| Point estimate                          | -17.4                                |

|                     |         |
|---------------------|---------|
| Confidence interval |         |
| level               | 95 %    |
| sides               | 2-sided |
| lower limit         | -94.3   |
| upper limit         | 59.6    |

|                                         |                                       |
|-----------------------------------------|---------------------------------------|
| <b>Statistical analysis title</b>       | CD45+3+8-4+CCR6-CXCR3-38+DR+, Week 12 |
| Comparison groups                       | Placebo v GSK3196165 180 mg           |
| Number of subjects included in analysis | 39                                    |
| Analysis specification                  | Pre-specified                         |
| Analysis type                           | other                                 |
| P-value                                 | = 0.789                               |
| Method                                  | Repeated measures analysis            |
| Parameter estimate                      | Mean difference (net)                 |
| Point estimate                          | 59.4                                  |
| Confidence interval                     |                                       |
| level                                   | 95 %                                  |
| sides                                   | 2-sided                               |
| lower limit                             | -395.2                                |
| upper limit                             | 513.9                                 |

|                                         |                                          |
|-----------------------------------------|------------------------------------------|
| <b>Statistical analysis title</b>       | CD45+3+8-4+CCR6-CXCR3-38+DR+, 12-Week FU |
| Comparison groups                       | Placebo v GSK3196165 180 mg              |
| Number of subjects included in analysis | 39                                       |
| Analysis specification                  | Pre-specified                            |
| Analysis type                           | other                                    |
| P-value                                 | = 0.249                                  |
| Method                                  | Repeated measures analysis               |
| Parameter estimate                      | Mean difference (net)                    |
| Point estimate                          | -47.2                                    |
| Confidence interval                     |                                          |
| level                                   | 95 %                                     |
| sides                                   | 2-sided                                  |
| lower limit                             | -135.5                                   |
| upper limit                             | 41                                       |

|                                   |                             |
|-----------------------------------|-----------------------------|
| <b>Statistical analysis title</b> | CD45+CD3+CD8-CD4+, Week 1   |
| Comparison groups                 | Placebo v GSK3196165 180 mg |

|                                         |                            |
|-----------------------------------------|----------------------------|
| Number of subjects included in analysis | 39                         |
| Analysis specification                  | Pre-specified              |
| Analysis type                           | other                      |
| P-value                                 | = 0.234                    |
| Method                                  | Repeated measures analysis |
| Parameter estimate                      | Mean difference (net)      |
| Point estimate                          | 3682.3                     |
| Confidence interval                     |                            |
| level                                   | 95 %                       |
| sides                                   | 2-sided                    |
| lower limit                             | -2511.9                    |
| upper limit                             | 9876.5                     |

|                                         |                             |
|-----------------------------------------|-----------------------------|
| <b>Statistical analysis title</b>       | CD45+CD3+CD8-CD4+, Week 4   |
| Comparison groups                       | Placebo v GSK3196165 180 mg |
| Number of subjects included in analysis | 39                          |
| Analysis specification                  | Pre-specified               |
| Analysis type                           | other                       |
| P-value                                 | = 0.875                     |
| Method                                  | Repeated measures analysis  |
| Parameter estimate                      | Mean difference (net)       |
| Point estimate                          | -547.6                      |
| Confidence interval                     |                             |
| level                                   | 95 %                        |
| sides                                   | 2-sided                     |
| lower limit                             | -7612.6                     |
| upper limit                             | 6517.3                      |

|                                         |                             |
|-----------------------------------------|-----------------------------|
| <b>Statistical analysis title</b>       | CD45+CD3+CD8-CD4+, Week 12  |
| Comparison groups                       | Placebo v GSK3196165 180 mg |
| Number of subjects included in analysis | 39                          |
| Analysis specification                  | Pre-specified               |
| Analysis type                           | other                       |
| P-value                                 | = 0.815                     |
| Method                                  | Repeated measures analysis  |
| Parameter estimate                      | Mean difference (net)       |
| Point estimate                          | -1106                       |
| Confidence interval                     |                             |
| level                                   | 95 %                        |
| sides                                   | 2-sided                     |
| lower limit                             | -10706                      |
| upper limit                             | 8494.1                      |

|                                   |                               |
|-----------------------------------|-------------------------------|
| <b>Statistical analysis title</b> | CD45+CD3+CD8-CD4+, 12-Week FU |
|-----------------------------------|-------------------------------|

|                                         |                             |
|-----------------------------------------|-----------------------------|
| Comparison groups                       | Placebo v GSK3196165 180 mg |
| Number of subjects included in analysis | 39                          |
| Analysis specification                  | Pre-specified               |
| Analysis type                           | other                       |
| P-value                                 | = 0.23                      |
| Method                                  | Repeated measures analysis  |
| Parameter estimate                      | Mean difference (net)       |
| Point estimate                          | -3631                       |
| Confidence interval                     |                             |
| level                                   | 95 %                        |
| sides                                   | 2-sided                     |
| lower limit                             | -9738.9                     |
| upper limit                             | 2476.8                      |

|                                         |                                      |
|-----------------------------------------|--------------------------------------|
| <b>Statistical analysis title</b>       | CD45+CD3+CD8-CD4+CCR6+CXCR3+, Week 1 |
| Comparison groups                       | Placebo v GSK3196165 180 mg          |
| Number of subjects included in analysis | 39                                   |
| Analysis specification                  | Pre-specified                        |
| Analysis type                           | other                                |
| P-value                                 | = 0.489                              |
| Method                                  | Repeated measures analysis           |
| Parameter estimate                      | Mean difference (net)                |
| Point estimate                          | -515.6                               |
| Confidence interval                     |                                      |
| level                                   | 95 %                                 |
| sides                                   | 2-sided                              |
| lower limit                             | -2021.4                              |
| upper limit                             | 990.1                                |

|                                         |                                      |
|-----------------------------------------|--------------------------------------|
| <b>Statistical analysis title</b>       | CD45+CD3+CD8-CD4+CCR6+CXCR3+, Week 4 |
| Comparison groups                       | Placebo v GSK3196165 180 mg          |
| Number of subjects included in analysis | 39                                   |
| Analysis specification                  | Pre-specified                        |
| Analysis type                           | other                                |
| P-value                                 | = 0.822                              |
| Method                                  | Repeated measures analysis           |
| Parameter estimate                      | Mean difference (net)                |
| Point estimate                          | -199.8                               |
| Confidence interval                     |                                      |
| level                                   | 95 %                                 |
| sides                                   | 2-sided                              |
| lower limit                             | -2001.7                              |
| upper limit                             | 1602                                 |

|                                         |                                       |
|-----------------------------------------|---------------------------------------|
| <b>Statistical analysis title</b>       | CD45+CD3+CD8-CD4+CCR6+CXCR3+, Week 12 |
| Comparison groups                       | Placebo v GSK3196165 180 mg           |
| Number of subjects included in analysis | 39                                    |
| Analysis specification                  | Pre-specified                         |
| Analysis type                           | other                                 |
| P-value                                 | = 0.784                               |
| Method                                  | Repeated measures analysis            |
| Parameter estimate                      | Mean difference (net)                 |
| Point estimate                          | -253.5                                |
| Confidence interval                     |                                       |
| level                                   | 95 %                                  |
| sides                                   | 2-sided                               |
| lower limit                             | -2136.7                               |
| upper limit                             | 1629.7                                |

|                                         |                                          |
|-----------------------------------------|------------------------------------------|
| <b>Statistical analysis title</b>       | CD45+CD3+CD8-CD4+CCR6+CXCR3+, 12-Week FU |
| Comparison groups                       | Placebo v GSK3196165 180 mg              |
| Number of subjects included in analysis | 39                                       |
| Analysis specification                  | Pre-specified                            |
| Analysis type                           | other                                    |
| P-value                                 | = 0.804                                  |
| Method                                  | Repeated measures analysis               |
| Parameter estimate                      | Mean difference (net)                    |
| Point estimate                          | 225.1                                    |
| Confidence interval                     |                                          |
| level                                   | 95 %                                     |
| sides                                   | 2-sided                                  |
| lower limit                             | -1633.1                                  |
| upper limit                             | 2083.2                                   |

|                                         |                                      |
|-----------------------------------------|--------------------------------------|
| <b>Statistical analysis title</b>       | CD45+CD3+CD8-CD4+CCR6+CXCR3-, Week 1 |
| Comparison groups                       | Placebo v GSK3196165 180 mg          |
| Number of subjects included in analysis | 39                                   |
| Analysis specification                  | Pre-specified                        |
| Analysis type                           | other                                |
| P-value                                 | = 0.719                              |
| Method                                  | Repeated measures analysis           |
| Parameter estimate                      | Mean difference (net)                |
| Point estimate                          | 162.7                                |
| Confidence interval                     |                                      |
| level                                   | 95 %                                 |
| sides                                   | 2-sided                              |
| lower limit                             | -754.5                               |
| upper limit                             | 1079.9                               |

|                                         |                                      |
|-----------------------------------------|--------------------------------------|
| <b>Statistical analysis title</b>       | CD45+CD3+CD8-CD4+CCR6+CXCR3-, Week 4 |
| Comparison groups                       | Placebo v GSK3196165 180 mg          |
| Number of subjects included in analysis | 39                                   |
| Analysis specification                  | Pre-specified                        |
| Analysis type                           | other                                |
| P-value                                 | = 0.742                              |
| Method                                  | Repeated measures analysis           |
| Parameter estimate                      | Mean difference (net)                |
| Point estimate                          | -183.5                               |
| Confidence interval                     |                                      |
| level                                   | 95 %                                 |
| sides                                   | 2-sided                              |
| lower limit                             | -1317.4                              |
| upper limit                             | 950.3                                |

|                                         |                                       |
|-----------------------------------------|---------------------------------------|
| <b>Statistical analysis title</b>       | CD45+CD3+CD8-CD4+CCR6+CXCR3-, Week 12 |
| Comparison groups                       | Placebo v GSK3196165 180 mg           |
| Number of subjects included in analysis | 39                                    |
| Analysis specification                  | Pre-specified                         |
| Analysis type                           | other                                 |
| P-value                                 | = 0.658                               |
| Method                                  | Repeated measures analysis            |
| Parameter estimate                      | Mean difference (net)                 |
| Point estimate                          | -268.5                                |
| Confidence interval                     |                                       |
| level                                   | 95 %                                  |
| sides                                   | 2-sided                               |
| lower limit                             | -1507.5                               |
| upper limit                             | 970.5                                 |

|                                         |                                          |
|-----------------------------------------|------------------------------------------|
| <b>Statistical analysis title</b>       | CD45+CD3+CD8-CD4+CCR6+CXCR3-, 12-Week FU |
| Comparison groups                       | Placebo v GSK3196165 180 mg              |
| Number of subjects included in analysis | 39                                       |
| Analysis specification                  | Pre-specified                            |
| Analysis type                           | other                                    |
| P-value                                 | = 0.755                                  |
| Method                                  | Repeated measures analysis               |
| Parameter estimate                      | Mean difference (net)                    |
| Point estimate                          | -197.6                                   |

|                     |         |
|---------------------|---------|
| Confidence interval |         |
| level               | 95 %    |
| sides               | 2-sided |
| lower limit         | -1499.3 |
| upper limit         | 1104.2  |

|                                         |                                      |
|-----------------------------------------|--------------------------------------|
| <b>Statistical analysis title</b>       | CD45+CD3+CD8-CD4+CCR6-CXCR3+, Week 1 |
| Comparison groups                       | Placebo v GSK3196165 180 mg          |
| Number of subjects included in analysis | 39                                   |
| Analysis specification                  | Pre-specified                        |
| Analysis type                           | other                                |
| P-value                                 | = 0.333                              |
| Method                                  | Repeated measures analysis           |
| Parameter estimate                      | Mean difference (net)                |
| Point estimate                          | 1150                                 |
| Confidence interval                     |                                      |
| level                                   | 95 %                                 |
| sides                                   | 2-sided                              |
| lower limit                             | -1250                                |
| upper limit                             | 3550                                 |

|                                         |                                      |
|-----------------------------------------|--------------------------------------|
| <b>Statistical analysis title</b>       | CD45+CD3+CD8-CD4+CCR6-CXCR3+, Week 4 |
| Comparison groups                       | Placebo v GSK3196165 180 mg          |
| Number of subjects included in analysis | 39                                   |
| Analysis specification                  | Pre-specified                        |
| Analysis type                           | other                                |
| P-value                                 | = 0.891                              |
| Method                                  | Repeated measures analysis           |
| Parameter estimate                      | Mean difference (net)                |
| Point estimate                          | -268                                 |
| Confidence interval                     |                                      |
| level                                   | 95 %                                 |
| sides                                   | 2-sided                              |
| lower limit                             | -4269.2                              |
| upper limit                             | 3733.3                               |

|                                   |                                       |
|-----------------------------------|---------------------------------------|
| <b>Statistical analysis title</b> | CD45+CD3+CD8-CD4+CCR6-CXCR3+, Week 12 |
| Comparison groups                 | Placebo v GSK3196165 180 mg           |

|                                         |                            |
|-----------------------------------------|----------------------------|
| Number of subjects included in analysis | 39                         |
| Analysis specification                  | Pre-specified              |
| Analysis type                           | other                      |
| P-value                                 | = 0.633                    |
| Method                                  | Repeated measures analysis |
| Parameter estimate                      | Mean difference (net)      |
| Point estimate                          | -1347.4                    |
| Confidence interval                     |                            |
| level                                   | 95 %                       |
| sides                                   | 2-sided                    |
| lower limit                             | -7073.1                    |
| upper limit                             | 4378.3                     |

|                                         |                                          |
|-----------------------------------------|------------------------------------------|
| <b>Statistical analysis title</b>       | CD45+CD3+CD8-CD4+CCR6-CXCR3+, 12-Week FU |
| Comparison groups                       | Placebo v GSK3196165 180 mg              |
| Number of subjects included in analysis | 39                                       |
| Analysis specification                  | Pre-specified                            |
| Analysis type                           | other                                    |
| P-value                                 | = 0.41                                   |
| Method                                  | Repeated measures analysis               |
| Parameter estimate                      | Mean difference (net)                    |
| Point estimate                          | -1688.9                                  |
| Confidence interval                     |                                          |
| level                                   | 95 %                                     |
| sides                                   | 2-sided                                  |
| lower limit                             | -5864.1                                  |
| upper limit                             | 2486.2                                   |

|                                         |                                      |
|-----------------------------------------|--------------------------------------|
| <b>Statistical analysis title</b>       | CD45+CD3+CD8-CD4+CCR6-CXCR3-, Week 1 |
| Comparison groups                       | Placebo v GSK3196165 180 mg          |
| Number of subjects included in analysis | 39                                   |
| Analysis specification                  | Pre-specified                        |
| Analysis type                           | other                                |
| P-value                                 | = 0.196                              |
| Method                                  | Repeated measures analysis           |
| Parameter estimate                      | Mean difference (net)                |
| Point estimate                          | 3276.8                               |
| Confidence interval                     |                                      |
| level                                   | 95 %                                 |
| sides                                   | 2-sided                              |
| lower limit                             | -1786                                |
| upper limit                             | 8339.6                               |

|                                   |                                      |
|-----------------------------------|--------------------------------------|
| <b>Statistical analysis title</b> | CD45+CD3+CD8-CD4+CCR6-CXCR3-, Week 4 |
|-----------------------------------|--------------------------------------|

|                                         |                             |
|-----------------------------------------|-----------------------------|
| Comparison groups                       | Placebo v GSK3196165 180 mg |
| Number of subjects included in analysis | 39                          |
| Analysis specification                  | Pre-specified               |
| Analysis type                           | other                       |
| P-value                                 | = 0.894                     |
| Method                                  | Repeated measures analysis  |
| Parameter estimate                      | Mean difference (net)       |
| Point estimate                          | -447.3                      |
| Confidence interval                     |                             |
| level                                   | 95 %                        |
| sides                                   | 2-sided                     |
| lower limit                             | -7285.5                     |
| upper limit                             | 6390.8                      |

|                                         |                                       |
|-----------------------------------------|---------------------------------------|
| <b>Statistical analysis title</b>       | CD45+CD3+CD8-CD4+CCR6-CXCR3-, Week 12 |
| Comparison groups                       | Placebo v GSK3196165 180 mg           |
| Number of subjects included in analysis | 39                                    |
| Analysis specification                  | Pre-specified                         |
| Analysis type                           | other                                 |
| P-value                                 | = 0.6                                 |
| Method                                  | Repeated measures analysis            |
| Parameter estimate                      | Mean difference (net)                 |
| Point estimate                          | 1435.3                                |
| Confidence interval                     |                                       |
| level                                   | 95 %                                  |
| sides                                   | 2-sided                               |
| lower limit                             | -4101.4                               |
| upper limit                             | 6972                                  |

|                                         |                                          |
|-----------------------------------------|------------------------------------------|
| <b>Statistical analysis title</b>       | CD45+CD3+CD8-CD4+CCR6-CXCR3-, 12-Week FU |
| Comparison groups                       | Placebo v GSK3196165 180 mg              |
| Number of subjects included in analysis | 39                                       |
| Analysis specification                  | Pre-specified                            |
| Analysis type                           | other                                    |
| P-value                                 | = 0.534                                  |
| Method                                  | Repeated measures analysis               |
| Parameter estimate                      | Mean difference (net)                    |
| Point estimate                          | -1210.2                                  |
| Confidence interval                     |                                          |
| level                                   | 95 %                                     |
| sides                                   | 2-sided                                  |
| lower limit                             | -5213.1                                  |
| upper limit                             | 2792.7                                   |

**Primary: Change from Baseline in Flow Cytometry: CD16+ Monocyte Panel: CD14-HLA-DR+CD11cbr+CD123-, CD14br+CD16+, CD14br+CD16-, CD14lo+CD16br+**

|                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            |                                                                                                                                      |
|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|--------------------------------------------------------------------------------------------------------------------------------------|
| End point title                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            | Change from Baseline in Flow Cytometry: CD16+ Monocyte Panel: CD14-HLA-DR+CD11cbr+CD123-, CD14br+CD16+, CD14br+CD16-, CD14lo+CD16br+ |
| End point description:                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     |                                                                                                                                      |
| Whole blood samples were collected and analyzed for markers which may be predictive of rheumatoid arthritis disease activity. Flow cytometry assessment included assessment of CD14-HLA-DR+CD11cbr+CD123-, CD14br+CD16+, CD14br+CD16- and CD14lo+CD16br+. Baseline was defined at Day 1. Change from Baseline was calculated by subtracting the post-dose value from the Baseline value. Analysis was performed using repeated measures analysis adjusted for CD14-HLA-DR+CD11cbr+CD123-, CD14br+CD16+, CD14br+CD16- and CD14lo+CD16br+ (10 <sup>3</sup> /Liter) baseline value, treatment group, disease duration (<=2 or >2 years), visit and treatment group by visit interaction. Only those participants with data available at the specified data points were analyzed (represented by n= X in the category titles). |                                                                                                                                      |
| End point type                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                             | Primary                                                                                                                              |
| End point timeframe:                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       |                                                                                                                                      |
| Baseline and Weeks 1, 4, 12, 12-Week FU (Week 22)                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                          |                                                                                                                                      |

| End point values                                | Placebo               | GSK3196165<br>180 mg  |  |  |
|-------------------------------------------------|-----------------------|-----------------------|--|--|
| Subject group type                              | Reporting group       | Reporting group       |  |  |
| Number of subjects analysed                     | 11 <sup>[25]</sup>    | 28 <sup>[26]</sup>    |  |  |
| Units: 10 <sup>3</sup> cells/Liter              |                       |                       |  |  |
| least squares mean (standard error)             |                       |                       |  |  |
| CD14-HLA-DR+CD11cbr+CD123-, Week 1, n=5, 18     | -2017.6 (± 2452.91)   | 738.7 (± 1266.25)     |  |  |
| CD14-HLA-DR+CD11cbr+CD123-, Week 4, n=6, 22     | 2766.3 (± 3220.54)    | 2278.8 (± 1696.12)    |  |  |
| CD14-HLA-DR+CD11cbr+CD123-, Week 12, n=5, 21    | 5730.4 (± 5085.86)    | 5453.0 (± 2399.11)    |  |  |
| CD14-HLA-DR+CD11cbr+CD123-, 12-Week FU, n=5, 18 | 5785.6 (± 5081.59)    | 5474.0 (± 2439.59)    |  |  |
| CD14br+CD16+, Week 1, n=5, 18                   | -5376.0 (± 4748.95)   | 1491.0 (± 2452.69)    |  |  |
| CD14br+CD16+, Week 4, n=6, 22                   | -5635.3 (± 5971.99)   | 2724.3 (± 3117.17)    |  |  |
| CD14br+CD16+, Week 12, n=5, 21                  | 25351.6 (± 9433.73)   | 2668.0 (± 4589.28)    |  |  |
| CD14br+CD16+, 12-Week FU, n=5, 18               | 8557.2 (± 9914.93)    | 4800.0 (± 5266.23)    |  |  |
| CD14br+CD16-, Week 1, n=5, 18                   | 40079.7 (± 40456.86)  | 17662.7 (± 21211.91)  |  |  |
| CD14br+CD16-, Week 4, n=6, 22                   | -17173.8 (± 24181.15) | 10485.9 (± 12635.98)  |  |  |
| CD14br+CD16-, Week 12, n=5, 21                  | -2981.8 (± 37788.70)  | 13201.2 (± 18684.22)  |  |  |
| CD14br+CD16-, 12-Week FU, n=5, 18               | 31906.6 (± 45766.70)  | -31512.8 (± 24027.16) |  |  |
| CD14lo+CD16br+, Week 1, n=5, 18                 | 11248.2 (± 6598.36)   | 4334.6 (± 3466.71)    |  |  |
| CD14lo+CD16br+, Week 4, n=6, 22                 | 2522.9 (± 3757.96)    | 291.3 (± 1959.54)     |  |  |
| CD14lo+CD16br+, Week 12, n=5, 21                | 10938.4 (± 5088.36)   | 759.2 (± 2534.27)     |  |  |
| CD14lo+CD16br+, 12-Week FU, n=5, 18             | 24737.0 (± 7758.65)   | 3992.8 (± 4134.52)    |  |  |

Notes:

[25] - ITT Population

[26] - ITT Population

### Statistical analyses

|                                         |                                    |
|-----------------------------------------|------------------------------------|
| <b>Statistical analysis title</b>       | CD14-HLA-DR+CD11cbr+CD123-, Week 1 |
| Comparison groups                       | Placebo v GSK3196165 180 mg        |
| Number of subjects included in analysis | 39                                 |
| Analysis specification                  | Pre-specified                      |
| Analysis type                           | other                              |
| P-value                                 | = 0.328                            |
| Method                                  | Repeated measures analysis         |
| Parameter estimate                      | Mean difference (net)              |
| Point estimate                          | 2756.3                             |
| Confidence interval                     |                                    |
| level                                   | 95 %                               |
| sides                                   | 2-sided                            |
| lower limit                             | -2953.7                            |
| upper limit                             | 8466.3                             |

|                                         |                                    |
|-----------------------------------------|------------------------------------|
| <b>Statistical analysis title</b>       | CD14-HLA-DR+CD11cbr+CD123-, Week 4 |
| Comparison groups                       | Placebo v GSK3196165 180 mg        |
| Number of subjects included in analysis | 39                                 |
| Analysis specification                  | Pre-specified                      |
| Analysis type                           | other                              |
| P-value                                 | = 0.895                            |
| Method                                  | Repeated measures analysis         |
| Parameter estimate                      | Mean difference (net)              |
| Point estimate                          | -487.5                             |
| Confidence interval                     |                                    |
| level                                   | 95 %                               |
| sides                                   | 2-sided                            |
| lower limit                             | -8003.7                            |
| upper limit                             | 7028.6                             |

|                                   |                                     |
|-----------------------------------|-------------------------------------|
| <b>Statistical analysis title</b> | CD14-HLA-DR+CD11cbr+CD123-, Week 12 |
| Comparison groups                 | Placebo v GSK3196165 180 mg         |

|                                         |                            |
|-----------------------------------------|----------------------------|
| Number of subjects included in analysis | 39                         |
| Analysis specification                  | Pre-specified              |
| Analysis type                           | other                      |
| P-value                                 | = 0.961                    |
| Method                                  | Repeated measures analysis |
| Parameter estimate                      | Mean difference (net)      |
| Point estimate                          | -277.4                     |
| Confidence interval                     |                            |
| level                                   | 95 %                       |
| sides                                   | 2-sided                    |
| lower limit                             | -12001                     |
| upper limit                             | 11446.2                    |

|                                         |                                        |
|-----------------------------------------|----------------------------------------|
| <b>Statistical analysis title</b>       | CD14-HLA-DR+CD11cbr+CD123-, 12-Week FU |
| Comparison groups                       | Placebo v GSK3196165 180 mg            |
| Number of subjects included in analysis | 39                                     |
| Analysis specification                  | Pre-specified                          |
| Analysis type                           | other                                  |
| P-value                                 | = 0.956                                |
| Method                                  | Repeated measures analysis             |
| Parameter estimate                      | Mean difference (net)                  |
| Point estimate                          | -311.6                                 |
| Confidence interval                     |                                        |
| level                                   | 95 %                                   |
| sides                                   | 2-sided                                |
| lower limit                             | -11960.5                               |
| upper limit                             | 11337.4                                |

|                                         |                             |
|-----------------------------------------|-----------------------------|
| <b>Statistical analysis title</b>       | CD14br+CD16+, Week 1        |
| Comparison groups                       | Placebo v GSK3196165 180 mg |
| Number of subjects included in analysis | 39                          |
| Analysis specification                  | Pre-specified               |
| Analysis type                           | other                       |
| P-value                                 | = 0.212                     |
| Method                                  | Repeated measures analysis  |
| Parameter estimate                      | Mean difference (net)       |
| Point estimate                          | 6866.9                      |
| Confidence interval                     |                             |
| level                                   | 95 %                        |
| sides                                   | 2-sided                     |
| lower limit                             | -4230.7                     |
| upper limit                             | 17964.6                     |

|                                   |                      |
|-----------------------------------|----------------------|
| <b>Statistical analysis title</b> | CD14br+CD16+, Week 4 |
|-----------------------------------|----------------------|

|                                         |                             |
|-----------------------------------------|-----------------------------|
| Comparison groups                       | Placebo v GSK3196165 180 mg |
| Number of subjects included in analysis | 39                          |
| Analysis specification                  | Pre-specified               |
| Analysis type                           | other                       |
| P-value                                 | = 0.227                     |
| Method                                  | Repeated measures analysis  |
| Parameter estimate                      | Mean difference (net)       |
| Point estimate                          | 8359.6                      |
| Confidence interval                     |                             |
| level                                   | 95 %                        |
| sides                                   | 2-sided                     |
| lower limit                             | -5533.3                     |
| upper limit                             | 22252.5                     |

|                                         |                             |
|-----------------------------------------|-----------------------------|
| <b>Statistical analysis title</b>       | CD14br+CD16+, Week 12       |
| Comparison groups                       | Placebo v GSK3196165 180 mg |
| Number of subjects included in analysis | 39                          |
| Analysis specification                  | Pre-specified               |
| Analysis type                           | other                       |
| P-value                                 | = 0.04                      |
| Method                                  | Repeated measures analysis  |
| Parameter estimate                      | Mean difference (net)       |
| Point estimate                          | -22683.6                    |
| Confidence interval                     |                             |
| level                                   | 95 %                        |
| sides                                   | 2-sided                     |
| lower limit                             | -44298.5                    |
| upper limit                             | -1068.8                     |

|                                         |                             |
|-----------------------------------------|-----------------------------|
| <b>Statistical analysis title</b>       | CD14br+CD16+, 12-Week FU    |
| Comparison groups                       | Placebo v GSK3196165 180 mg |
| Number of subjects included in analysis | 39                          |
| Analysis specification                  | Pre-specified               |
| Analysis type                           | other                       |
| P-value                                 | = 0.741                     |
| Method                                  | Repeated measures analysis  |
| Parameter estimate                      | Mean difference (net)       |
| Point estimate                          | -3757.2                     |
| Confidence interval                     |                             |
| level                                   | 95 %                        |
| sides                                   | 2-sided                     |
| lower limit                             | -27146                      |
| upper limit                             | 19631.6                     |

|                                         |                             |
|-----------------------------------------|-----------------------------|
| <b>Statistical analysis title</b>       | CD14br+CD16-, Week 1        |
| Comparison groups                       | Placebo v GSK3196165 180 mg |
| Number of subjects included in analysis | 39                          |
| Analysis specification                  | Pre-specified               |
| Analysis type                           | other                       |
| P-value                                 | = 0.628                     |
| Method                                  | Repeated measures analysis  |
| Parameter estimate                      | Mean difference (net)       |
| Point estimate                          | -22417                      |
| Confidence interval                     |                             |
| level                                   | 95 %                        |
| sides                                   | 2-sided                     |
| lower limit                             | -116678                     |
| upper limit                             | 71843.8                     |

|                                         |                             |
|-----------------------------------------|-----------------------------|
| <b>Statistical analysis title</b>       | CD14br+CD16-, Week 4        |
| Comparison groups                       | Placebo v GSK3196165 180 mg |
| Number of subjects included in analysis | 39                          |
| Analysis specification                  | Pre-specified               |
| Analysis type                           | other                       |
| P-value                                 | = 0.321                     |
| Method                                  | Repeated measures analysis  |
| Parameter estimate                      | Mean difference (net)       |
| Point estimate                          | 27659.7                     |
| Confidence interval                     |                             |
| level                                   | 95 %                        |
| sides                                   | 2-sided                     |
| lower limit                             | -28567.8                    |
| upper limit                             | 83887.1                     |

|                                         |                             |
|-----------------------------------------|-----------------------------|
| <b>Statistical analysis title</b>       | CD14br+CD16-, Week 12       |
| Comparison groups                       | Placebo v GSK3196165 180 mg |
| Number of subjects included in analysis | 39                          |
| Analysis specification                  | Pre-specified               |
| Analysis type                           | other                       |
| P-value                                 | = 0.704                     |
| Method                                  | Repeated measures analysis  |
| Parameter estimate                      | Mean difference (net)       |
| Point estimate                          | 16182.9                     |
| Confidence interval                     |                             |
| level                                   | 95 %                        |
| sides                                   | 2-sided                     |
| lower limit                             | -70377                      |
| upper limit                             | 102742.9                    |

|                                         |                             |
|-----------------------------------------|-----------------------------|
| <b>Statistical analysis title</b>       | CD14br+CD16-, 12-Week FU    |
| Comparison groups                       | Placebo v GSK3196165 180 mg |
| Number of subjects included in analysis | 39                          |
| Analysis specification                  | Pre-specified               |
| Analysis type                           | other                       |
| P-value                                 | = 0.232                     |
| Method                                  | Repeated measures analysis  |
| Parameter estimate                      | Mean difference (net)       |
| Point estimate                          | -63419                      |
| Confidence interval                     |                             |
| level                                   | 95 %                        |
| sides                                   | 2-sided                     |
| lower limit                             | -170365                     |
| upper limit                             | 43526.1                     |

|                                         |                             |
|-----------------------------------------|-----------------------------|
| <b>Statistical analysis title</b>       | CD14lo+CD16br+, Week 1      |
| Comparison groups                       | Placebo v GSK3196165 180 mg |
| Number of subjects included in analysis | 39                          |
| Analysis specification                  | Pre-specified               |
| Analysis type                           | other                       |
| P-value                                 | = 0.366                     |
| Method                                  | Repeated measures analysis  |
| Parameter estimate                      | Mean difference (net)       |
| Point estimate                          | -6913.6                     |
| Confidence interval                     |                             |
| level                                   | 95 %                        |
| sides                                   | 2-sided                     |
| lower limit                             | -22588.4                    |
| upper limit                             | 8761.1                      |

|                                         |                             |
|-----------------------------------------|-----------------------------|
| <b>Statistical analysis title</b>       | CD14lo+CD16br+, Week 4      |
| Comparison groups                       | Placebo v GSK3196165 180 mg |
| Number of subjects included in analysis | 39                          |
| Analysis specification                  | Pre-specified               |
| Analysis type                           | other                       |
| P-value                                 | = 0.603                     |
| Method                                  | Repeated measures analysis  |
| Parameter estimate                      | Mean difference (net)       |
| Point estimate                          | -2231.6                     |

|                     |          |
|---------------------|----------|
| Confidence interval |          |
| level               | 95 %     |
| sides               | 2-sided  |
| lower limit         | -10976.8 |
| upper limit         | 6513.6   |

|                                         |                             |
|-----------------------------------------|-----------------------------|
| <b>Statistical analysis title</b>       | CD14lo+CD16br+, Week 12     |
| Comparison groups                       | Placebo v GSK3196165 180 mg |
| Number of subjects included in analysis | 39                          |
| Analysis specification                  | Pre-specified               |
| Analysis type                           | other                       |
| P-value                                 | = 0.084                     |
| Method                                  | Repeated measures analysis  |
| Parameter estimate                      | Mean difference (net)       |
| Point estimate                          | -10179.1                    |
| Confidence interval                     |                             |
| level                                   | 95 %                        |
| sides                                   | 2-sided                     |
| lower limit                             | -21827.4                    |
| upper limit                             | 1469.2                      |

|                                         |                             |
|-----------------------------------------|-----------------------------|
| <b>Statistical analysis title</b>       | CD14lo+CD16br+, 12-Week FU  |
| Comparison groups                       | Placebo v GSK3196165 180 mg |
| Number of subjects included in analysis | 39                          |
| Analysis specification                  | Pre-specified               |
| Analysis type                           | other                       |
| P-value                                 | = 0.026                     |
| Method                                  | Repeated measures analysis  |
| Parameter estimate                      | Mean difference (net)       |
| Point estimate                          | -20744.2                    |
| Confidence interval                     |                             |
| level                                   | 95 %                        |
| sides                                   | 2-sided                     |
| lower limit                             | -38771.8                    |
| upper limit                             | -2716.5                     |

**Primary: Change from Baseline in Flow Cytometry: CD16+ Monocyte Panel: CD14-CD16+CD66b+**

|                 |                                                                                |
|-----------------|--------------------------------------------------------------------------------|
| End point title | Change from Baseline in Flow Cytometry: CD16+ Monocyte Panel: CD14-CD16+CD66b+ |
|-----------------|--------------------------------------------------------------------------------|

**End point description:**

Whole blood samples were collected and analyzed for markers which may be predictive of rheumatoid arthritis disease activity. Flow cytometry assessment included assessment of CD14-CD16+CD66b+ cell. Baseline was defined at Day 1. Change from Baseline was calculated by subtracting the post-dose value from the Baseline value. Analysis was performed using repeated measures analysis adjusted for CD14-

CD16+CD66b+ ( $10^6$ /Liter) baseline value, treatment group, disease duration ( $\leq 2$  or  $> 2$  years), visit and treatment group by visit interaction. Only those participants with data available at the specified data points were analyzed (represented by n= X in the category titles).

|                                                   |         |
|---------------------------------------------------|---------|
| End point type                                    | Primary |
| End point timeframe:                              |         |
| Baseline and Weeks 1, 4, 12, 12-Week FU (Week 22) |         |

| End point values                    | Placebo                   | GSK3196165<br>180 mg      |  |  |
|-------------------------------------|---------------------------|---------------------------|--|--|
| Subject group type                  | Reporting group           | Reporting group           |  |  |
| Number of subjects analysed         | 11 <sup>[27]</sup>        | 28 <sup>[28]</sup>        |  |  |
| Units: $10^6$ cells/Liter           |                           |                           |  |  |
| least squares mean (standard error) |                           |                           |  |  |
| Week 1, n=5, 19                     | -559.0 ( $\pm$<br>269.84) | -380.9 ( $\pm$<br>137.31) |  |  |
| Week 4, n=6, 22                     | -581.9 ( $\pm$<br>377.03) | -41.5 ( $\pm$<br>196.72)  |  |  |
| Week 12, n=5, 21                    | -125.9 ( $\pm$<br>460.53) | -378.6 ( $\pm$<br>229.47) |  |  |
| 12-Week FU, n=5, 18                 | -240.9 ( $\pm$<br>430.65) | -199.3 ( $\pm$<br>219.73) |  |  |

Notes:

[27] - ITT Population

[28] - ITT Population

## Statistical analyses

| Statistical analysis title              | Week 1                      |
|-----------------------------------------|-----------------------------|
| Comparison groups                       | Placebo v GSK3196165 180 mg |
| Number of subjects included in analysis | 39                          |
| Analysis specification                  | Pre-specified               |
| Analysis type                           | other                       |
| P-value                                 | = 0.564                     |
| Method                                  | Repeated measures analysis  |
| Parameter estimate                      | Mean difference (net)       |
| Point estimate                          | 178.2                       |
| Confidence interval                     |                             |
| level                                   | 95 %                        |
| sides                                   | 2-sided                     |
| lower limit                             | -448.3                      |
| upper limit                             | 804.6                       |

| Statistical analysis title | Week 4                      |
|----------------------------|-----------------------------|
| Comparison groups          | Placebo v GSK3196165 180 mg |

|                                         |                            |
|-----------------------------------------|----------------------------|
| Number of subjects included in analysis | 39                         |
| Analysis specification                  | Pre-specified              |
| Analysis type                           | other                      |
| P-value                                 | = 0.216                    |
| Method                                  | Repeated measures analysis |
| Parameter estimate                      | Mean difference (net)      |
| Point estimate                          | 540.4                      |
| Confidence interval                     |                            |
| level                                   | 95 %                       |
| sides                                   | 2-sided                    |
| lower limit                             | -335.7                     |
| upper limit                             | 1416.5                     |

|                                         |                             |
|-----------------------------------------|-----------------------------|
| <b>Statistical analysis title</b>       | Week 12                     |
| Comparison groups                       | Placebo v GSK3196165 180 mg |
| Number of subjects included in analysis | 39                          |
| Analysis specification                  | Pre-specified               |
| Analysis type                           | other                       |
| P-value                                 | = 0.629                     |
| Method                                  | Repeated measures analysis  |
| Parameter estimate                      | Mean difference (net)       |
| Point estimate                          | -252.6                      |
| Confidence interval                     |                             |
| level                                   | 95 %                        |
| sides                                   | 2-sided                     |
| lower limit                             | -1326                       |
| upper limit                             | 820.8                       |

|                                         |                             |
|-----------------------------------------|-----------------------------|
| <b>Statistical analysis title</b>       | 12-Week FU                  |
| Comparison groups                       | Placebo v GSK3196165 180 mg |
| Number of subjects included in analysis | 39                          |
| Analysis specification                  | Pre-specified               |
| Analysis type                           | other                       |
| P-value                                 | = 0.932                     |
| Method                                  | Repeated measures analysis  |
| Parameter estimate                      | Mean difference (net)       |
| Point estimate                          | 41.6                        |
| Confidence interval                     |                             |
| level                                   | 95 %                        |
| sides                                   | 2-sided                     |
| lower limit                             | -962.2                      |
| upper limit                             | 1045.5                      |

---

## Primary: Change from Baseline in Complement Biomarkers: Complement component

---

### 3 (C3), Complement component 4 (C4)

|                 |                                                                                                                         |
|-----------------|-------------------------------------------------------------------------------------------------------------------------|
| End point title | Change from Baseline in Complement Biomarkers: Complement component 3 (C3), Complement component 4 (C4) <sup>[29]</sup> |
|-----------------|-------------------------------------------------------------------------------------------------------------------------|

End point description:

Blood samples were collected and analyzed for markers which may be predictive of rheumatoid arthritis disease activity. Complement biomarkers included analysis of Complement C3 and Complement C4. Baseline was defined at Day 1. Change from Baseline was calculated as ratio of Baseline value to post-dose value. Only those participants with data available at the specified data points were analyzed (represented by n= X in the category titles).

|                |         |
|----------------|---------|
| End point type | Primary |
|----------------|---------|

End point timeframe:

Baseline and Weeks 1, 2, 4, 6, 8, 12, 12-Week FU (Week 22)

Notes:

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

Justification: There are no statistical data to report

| End point values                                                                               | Placebo            | GSK3196165<br>180 mg |  |  |
|------------------------------------------------------------------------------------------------|--------------------|----------------------|--|--|
| Subject group type                                                                             | Reporting group    | Reporting group      |  |  |
| Number of subjects analysed                                                                    | 11 <sup>[30]</sup> | 28 <sup>[31]</sup>   |  |  |
| Units: Ratio of complement biomarker<br>geometric mean (geometric coefficient<br>of variation) |                    |                      |  |  |
| Complement C3, Week 1, n=9, 25                                                                 | 0.967 (± 7.43)     | 0.982 (± 11.76)      |  |  |
| Complement C3, Week 2, n=8, 26                                                                 | 0.957 (± 11.72)    | 0.963 (± 14.15)      |  |  |
| Complement C3, Week 4, n=9, 27                                                                 | 1.045 (± 18.42)    | 0.959 (± 12.62)      |  |  |
| Complement C3, Week 6, n=7, 27                                                                 | 1.060 (± 12.00)    | 0.991 (± 11.71)      |  |  |
| Complement C3, Week 8, n=7, 25                                                                 | 1.021 (± 12.54)    | 1.009 (± 10.85)      |  |  |
| Complement C3, Week 12, n=7, 24                                                                | 0.988 (± 9.37)     | 1.003 (± 11.34)      |  |  |
| Complement C3, 12-Week FU, n=7, 22                                                             | 1.005 (± 19.15)    | 0.995 (± 10.65)      |  |  |
| Complement C4, Week 1, n=9, 25                                                                 | 1.005 (± 11.40)    | 0.969 (± 13.13)      |  |  |
| Complement C4, Week 2, n=8, 26                                                                 | 0.949 (± 9.64)     | 0.984 (± 16.45)      |  |  |
| Complement C4, Week 4, n=9, 27                                                                 | 0.999 (± 12.06)    | 0.945 (± 14.63)      |  |  |
| Complement C4, Week 6, n=7, 27                                                                 | 0.990 (± 10.31)    | 0.985 (± 17.32)      |  |  |
| Complement C4, Week 8, n=7, 25                                                                 | 0.979 (± 7.66)     | 1.006 (± 13.53)      |  |  |
| Complement C4, Week 12, n=7, 24                                                                | 0.942 (± 15.57)    | 0.994 (± 12.75)      |  |  |
| Complement C4, 12-Week FU, n=7, 22                                                             | 0.982 (± 12.88)    | 0.986 (± 14.72)      |  |  |

Notes:

[30] - ITT Population

[31] - ITT Population

### Statistical analyses

**Primary: Change from Baseline in Complement Biomarkers: Complement component 4a (C4a), Complement component 5a (C5a), Complement Split Factor SC5b-9, Soluble cluster of differentiation 163 (sCD163)**

|                 |                                                                                                                                                                                                              |
|-----------------|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| End point title | Change from Baseline in Complement Biomarkers: Complement component 4a (C4a), Complement component 5a (C5a), Complement Split Factor SC5b-9, Soluble cluster of differentiation 163 (sCD163) <sup>[32]</sup> |
|-----------------|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|

## End point description:

Blood samples were collected and analyzed for markers which may be predictive of rheumatoid arthritis disease activity. Complement biomarkers included analysis of Complement C4a, Complement C5a, Complement Split Factor SC5b-9 and Soluble CD163. Baseline was defined at Day 1. Change from Baseline was calculated as ratio of Baseline value to post-dose value. Only those participants with data available at the specified data points were analyzed (represented by n= X in the category titles).

|                |         |
|----------------|---------|
| End point type | Primary |
|----------------|---------|

## End point timeframe:

Baseline and Weeks 1, 2, 4, 6, 8, 12, 12-Week FU (Week 22)

## Notes:

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

Justification: There are no statistical data to report

| End point values                                    | Placebo            | GSK3196165<br>180 mg |  |  |
|-----------------------------------------------------|--------------------|----------------------|--|--|
| Subject group type                                  | Reporting group    | Reporting group      |  |  |
| Number of subjects analysed                         | 11 <sup>[33]</sup> | 28 <sup>[34]</sup>   |  |  |
| Units: Ratio of complement biomarker                |                    |                      |  |  |
| geometric mean (geometric coefficient of variation) |                    |                      |  |  |
| Complement C4a, Week 1, n=9, 27                     | 1.159 (± 115.81)   | 0.990 (± 67.63)      |  |  |
| Complement C4a, Week 2, n=8, 26                     | 0.881 (± 55.58)    | 1.156 (± 75.77)      |  |  |
| Complement C4a, Week 4, n=9, 27                     | 0.840 (± 40.85)    | 1.100 (± 46.87)      |  |  |
| Complement C4a, Week 6, n=7, 27                     | 0.914 (± 66.71)    | 0.860 (± 53.87)      |  |  |
| Complement C4a, Week 8, n=7, 25                     | 1.017 (± 44.16)    | 0.998 (± 60.41)      |  |  |
| Complement C4a, Week 12, n=7, 24                    | 0.927 (± 58.05)    | 0.901 (± 93.48)      |  |  |
| Complement C4a, 12-Week FU, n=7, 21                 | 1.104 (± 40.27)    | 1.221 (± 56.53)      |  |  |
| Complement C5a, Week 1, n=9, 27                     | 0.927 (± 19.42)    | 0.991 (± 29.67)      |  |  |
| Complement C5a, Week 2, n=8, 26                     | 1.154 (± 36.82)    | 1.015 (± 55.60)      |  |  |
| Complement C5a, Week 4, n=9, 27                     | 0.943 (± 16.76)    | 1.010 (± 35.63)      |  |  |
| Complement C5a, Week 6, n=7, 27                     | 1.139 (± 61.77)    | 1.044 (± 33.94)      |  |  |
| Complement C5a, Week 8, n=7, 25                     | 0.980 (± 13.71)    | 0.957 (± 26.95)      |  |  |
| Complement C5a, Week 12, n=7, 24                    | 1.012 (± 8.41)     | 0.995 (± 29.49)      |  |  |
| Complement C5a, 12-Week FU, n=7, 22                 | 1.152 (± 42.75)    | 1.130 (± 32.16)      |  |  |

|                                                     |                 |                 |  |  |
|-----------------------------------------------------|-----------------|-----------------|--|--|
| Complement Split Factor SC5b-9, Week 1, n=9, 27     | 0.971 (± 37.46) | 1.020 (± 43.70) |  |  |
| Complement Split Factor SC5b-9, Week 2, n=8, 26     | 1.078 (± 28.80) | 1.040 (± 60.64) |  |  |
| Complement Split Factor SC5b-9, Week 4, n=9, 27     | 0.930 (± 43.01) | 1.126 (± 41.04) |  |  |
| Complement Split Factor SC5b-9, Week 6, n=7, 27     | 0.989 (± 23.18) | 1.084 (± 53.90) |  |  |
| Complement Split Factor SC5b-9, Week 8, n=7, 25     | 0.889 (± 35.48) | 1.055 (± 67.53) |  |  |
| Complement Split Factor SC5b-9, Week 12, n=7, 24    | 0.883 (± 30.26) | 0.843 (± 72.14) |  |  |
| Complement Split Factor SC5b-9, 12-Week FU, n=7, 22 | 1.039 (± 69.05) | 1.041 (± 38.60) |  |  |
| sCD163, Week 1, n=9, 27                             | 0.993 (± 24.28) | 0.963 (± 16.38) |  |  |
| sCD163, Week 2, n=8, 26                             | 1.101 (± 17.80) | 0.954 (± 17.14) |  |  |
| sCD163, Week 4, n=9, 27                             | 0.986 (± 15.89) | 0.947 (± 27.10) |  |  |
| sCD163, Week 6, n=7, 27                             | 0.938 (± 20.83) | 0.959 (± 30.14) |  |  |
| sCD163, Week 8, n=7, 25                             | 0.938 (± 30.03) | 0.950 (± 28.73) |  |  |
| sCD163, Week 12, n=7, 24                            | 0.937 (± 24.86) | 0.915 (± 35.29) |  |  |
| sCD163, 12-Week FU, n=7, 21                         | 1.200 (± 32.94) | 0.994 (± 28.84) |  |  |

Notes:

[33] - ITT Population

[34] - ITT Population

## Statistical analyses

No statistical analyses for this end point

## Primary: Change from Baseline in Mechanistic Biomarkers

|                 |                                                                |
|-----------------|----------------------------------------------------------------|
| End point title | Change from Baseline in Mechanistic Biomarkers <sup>[35]</sup> |
|-----------------|----------------------------------------------------------------|

End point description:

Blood samples were collected and analyzed for markers which may be predictive of rheumatoid arthritis disease activity. Mechanistic biomarkers included analysis of Interleukin 1 Beta, Interleukin 10, Interleukin 15, Interleukin 17 Alpha, Interleukin 17F, Interleukin 8 and Tumor Necrosis Factor. Baseline was defined at Day 1. Change from Baseline was calculated as ratio of Baseline value to post-dose value. 99999 indicates that data is not available since 100% of the data was below limit of quantification at all time points. Only those participants with data available at the specified data points were analyzed (represented by n= X in the category titles).

|                |         |
|----------------|---------|
| End point type | Primary |
|----------------|---------|

End point timeframe:

Baseline and Weeks 1, 2, 4, 6, 8, 12, 12-Week FU (Week 22)

Notes:

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

Justification: There are no statistical data to report

| End point values                                    | Placebo            | GSK3196165<br>180 mg |  |  |
|-----------------------------------------------------|--------------------|----------------------|--|--|
| Subject group type                                  | Reporting group    | Reporting group      |  |  |
| Number of subjects analysed                         | 11 <sup>[36]</sup> | 28 <sup>[37]</sup>   |  |  |
| Units: Ratio of mechanistic biomarker               |                    |                      |  |  |
| geometric mean (geometric coefficient of variation) |                    |                      |  |  |
| Interleukin 1 Beta, Week 1, n=9, 26                 | 1.000 (± 99999)    | 1.000 (± 99999)      |  |  |
| Interleukin 1 Beta, Week 2, n=8, 26                 | 1.000 (± 99999)    | 1.000 (± 99999)      |  |  |
| Interleukin 1 Beta, Week 4, n=9, 27                 | 1.000 (± 99999)    | 1.000 (± 99999)      |  |  |
| Interleukin 1 Beta, Week 6, n=7, 27                 | 1.000 (± 99999)    | 1.000 (± 99999)      |  |  |
| Interleukin 1 Beta, Week 8, n=7, 25                 | 1.000 (± 99999)    | 1.000 (± 99999)      |  |  |
| Interleukin 1 Beta, Week 12, n=7, 24                | 1.000 (± 99999)    | 1.000 (± 99999)      |  |  |
| Interleukin 1 Beta, 12-Week FU, n=7, 21             | 1.000 (± 99999)    | 1.000 (± 99999)      |  |  |
| Interleukin 10, Week 1, n=9, 26                     | 0.962 (± 11.55)    | 0.994 (± 28.47)      |  |  |
| Interleukin 10, Week 2, n=8, 26                     | 1.206 (± 45.35)    | 1.048 (± 37.27)      |  |  |
| Interleukin 10, Week 4, n=9, 27                     | 0.875 (± 41.69)    | 0.985 (± 32.52)      |  |  |
| Interleukin 10, Week 6, n=7, 27                     | 0.842 (± 47.84)    | 0.960 (± 17.66)      |  |  |
| Interleukin 10, Week 8, n=7, 25                     | 1.197 (± 50.41)    | 0.969 (± 30.23)      |  |  |
| Interleukin 10, Week 12, n=7, 24                    | 0.842 (± 47.84)    | 0.989 (± 21.36)      |  |  |
| Interleukin 10, 12-Week FU, n=7, 21                 | 0.842 (± 47.84)    | 1.230 (± 62.91)      |  |  |
| Interleukin 15, Week 1, n=9, 27                     | 1.001 (± 12.70)    | 0.950 (± 59.23)      |  |  |
| Interleukin 15, Week 2, n=8, 26                     | 0.882 (± 41.99)    | 0.849 (± 102.76)     |  |  |
| Interleukin 15, Week 4, n=9, 27                     | 1.206 (± 47.87)    | 0.831 (± 84.07)      |  |  |
| Interleukin 15, Week 6, n=7, 27                     | 1.297 (± 48.81)    | 0.904 (± 90.53)      |  |  |
| Interleukin 15, Week 8, n=7, 25                     | 0.871 (± 37.95)    | 0.865 (± 90.30)      |  |  |
| Interleukin 15, Week 12, n=7, 24                    | 0.871 (± 37.95)    | 0.771 (± 82.21)      |  |  |
| Interleukin 15, 12-Week FU, n=7, 21                 | 0.871 (± 37.95)    | 0.636 (± 111.86)     |  |  |
| Interleukin 17 Alpha, Week 1, n=9, 25               | 0.806 (± 53.03)    | 1.054 (± 93.04)      |  |  |
| Interleukin 17 Alpha, Week 2, n=8, 25               | 0.935 (± 75.58)    | 0.942 (± 72.24)      |  |  |
| Interleukin 17 Alpha, Week 4, n=9, 26               | 0.995 (± 91.45)    | 0.911 (± 102.66)     |  |  |
| Interleukin 17 Alpha, Week 6, n=7, 26               | 1.015 (± 76.60)    | 0.867 (± 90.15)      |  |  |
| Interleukin 17 Alpha, Week 8, n=7, 23               | 0.905 (± 77.24)    | 1.005 (± 135.76)     |  |  |
| Interleukin 17 Alpha, Week 12, n=7, 23              | 1.007 (± 87.84)    | 0.857 (± 101.45)     |  |  |

|                                            |                  |                  |  |  |
|--------------------------------------------|------------------|------------------|--|--|
| Interleukin 17 Alpha, 12-Week FU, n=7, 20  | 0.969 (± 155.67) | 0.999 (± 150.12) |  |  |
| Interleukin 17F, Week 1, n=9, 25           | 1.153 (± 36.21)  | 0.797 (± 78.96)  |  |  |
| Interleukin 17F, Week 2, n=8, 26           | 1.062 (± 74.38)  | 0.911 (± 72.36)  |  |  |
| Interleukin 17F, Week 4, n=9, 26           | 0.966 (± 21.09)  | 0.948 (± 89.47)  |  |  |
| Interleukin 17F, Week 6, n=7, 25           | 0.787 (± 32.55)  | 1.013 (± 107.49) |  |  |
| Interleukin 17F, Week 8, n=7, 25           | 0.947 (± 19.20)  | 0.815 (± 91.93)  |  |  |
| Interleukin 17F, Week 12, n=7, 23          | 1.002 (± 74.09)  | 0.884 (± 100.03) |  |  |
| Interleukin 17F, 12-Week FU, n=7, 21       | 1.130 (± 101.51) | 0.741 (± 90.62)  |  |  |
| Interleukin 8, Week 1, n=9, 26             | 1.104 (± 40.98)  | 1.081 (± 74.78)  |  |  |
| Interleukin 8, Week 2, n=8, 26             | 1.505 (± 43.78)  | 0.861 (± 78.64)  |  |  |
| Interleukin 8, Week 4, n=9, 27             | 1.102 (± 38.30)  | 0.773 (± 82.48)  |  |  |
| Interleukin 8, Week 6, n=7, 27             | 1.229 (± 61.82)  | 0.720 (± 72.70)  |  |  |
| Interleukin 8, Week 8, n=7, 25             | 1.547 (± 53.88)  | 0.761 (± 80.51)  |  |  |
| Interleukin 8, Week 12, n=7, 24            | 1.240 (± 49.03)  | 0.850 (± 80.98)  |  |  |
| Interleukin 8, 12-Week FU, n=7, 21         | 1.191 (± 42.58)  | 0.841 (± 96.92)  |  |  |
| Tumor Necrosis Factor, Week 1, n=9, 26     | 0.976 (± 15.20)  | 0.994 (± 18.45)  |  |  |
| Tumor Necrosis Factor, Week 2, n=8, 26     | 0.951 (± 19.84)  | 0.977 (± 16.81)  |  |  |
| Tumor Necrosis Factor, Week 4, n=9, 27     | 0.933 (± 17.70)  | 0.871 (± 48.19)  |  |  |
| Tumor Necrosis Factor, Week 6, n=7, 27     | 1.087 (± 36.81)  | 0.929 (± 21.48)  |  |  |
| Tumor Necrosis Factor, Week 8, n=7, 25     | 1.110 (± 25.33)  | 0.930 (± 20.85)  |  |  |
| Tumor Necrosis Factor, Week 12, n=7, 24    | 1.021 (± 38.53)  | 0.969 (± 29.74)  |  |  |
| Tumor Necrosis Factor, 12-Week FU, n=7, 21 | 1.619 (± 180.16) | 1.057 (± 34.72)  |  |  |

Notes:

[36] - ITT Population

[37] - ITT Population

## Statistical analyses

No statistical analyses for this end point

## Primary: Change from Baseline in Safety Biomarkers: 3B-Cholestenoic Acid, Surfactant Protein D

|                 |                                                                                                       |
|-----------------|-------------------------------------------------------------------------------------------------------|
| End point title | Change from Baseline in Safety Biomarkers: 3B-Cholestenoic Acid, Surfactant Protein D <sup>[38]</sup> |
|-----------------|-------------------------------------------------------------------------------------------------------|

End point description:

Blood samples were collected and analyzed for markers which may be predictive of rheumatoid arthritis disease activity. Safety biomarkers included analysis of 3B-Cholestenoic Acid and Surfactant Protein D. Baseline was defined at Day 1. Change from Baseline was calculated as ratio of Baseline value to post-dose value. Only those participants with data available at the specified data points were analyzed

(represented by n= X in the category titles).

|                                            |         |
|--------------------------------------------|---------|
| End point type                             | Primary |
| End point timeframe:                       |         |
| Baseline and Week 12, 12-Week FU (Week 22) |         |

Notes:

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

Justification: There are no statistical data to report

| End point values                                    | Placebo            | GSK3196165<br>180 mg |  |  |
|-----------------------------------------------------|--------------------|----------------------|--|--|
| Subject group type                                  | Reporting group    | Reporting group      |  |  |
| Number of subjects analysed                         | 11 <sup>[39]</sup> | 28 <sup>[40]</sup>   |  |  |
| Units: Ratio of safety biomarker                    |                    |                      |  |  |
| geometric mean (geometric coefficient of variation) |                    |                      |  |  |
| 3B-Cholestenoic Acid, Week 12, n=7, 24              | 1.012 (± 16.52)    | 1.094 (± 19.45)      |  |  |
| 3B-Cholestenoic Acid, Week 22, n=7, 22              | 1.020 (± 20.25)    | 1.009 (± 22.67)      |  |  |
| Surfactant Protein D, Week 12, n=7, 24              | 1.003 (± 23.10)    | 1.134 (± 27.96)      |  |  |
| Surfactant Protein D, 12-Week FU, n=7, 21           | 1.140 (± 45.71)    | 0.985 (± 31.32)      |  |  |

Notes:

[39] - ITT Population

[40] - ITT Population

## Statistical analyses

No statistical analyses for this end point

## Primary: Change from Baseline in Safety Biomarkers: KL-6 Antigen

|                                                                                                                                                                                                                                                                                                                                                                                                                                    |                                                                         |
|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-------------------------------------------------------------------------|
| End point title                                                                                                                                                                                                                                                                                                                                                                                                                    | Change from Baseline in Safety Biomarkers: KL-6 Antigen <sup>[41]</sup> |
| End point description:                                                                                                                                                                                                                                                                                                                                                                                                             |                                                                         |
| Blood samples were collected and analyzed for markers which may be predictive of rheumatoid arthritis disease activity. Safety biomarker included analysis of KL-6 Antigen. Baseline was defined at Day 1. Change from Baseline was calculated as ratio of Baseline value to post-dose value. Only those participants with data available at the specified data points were analyzed (represented by n= X in the category titles). |                                                                         |
| End point type                                                                                                                                                                                                                                                                                                                                                                                                                     | Primary                                                                 |
| End point timeframe:                                                                                                                                                                                                                                                                                                                                                                                                               |                                                                         |
| Baseline and Week 12, 12-Week FU (Week 22)                                                                                                                                                                                                                                                                                                                                                                                         |                                                                         |

Notes:

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

Justification: There are no statistical data to report

| End point values                                    | Placebo            | GSK3196165<br>180 mg |  |  |
|-----------------------------------------------------|--------------------|----------------------|--|--|
| Subject group type                                  | Reporting group    | Reporting group      |  |  |
| Number of subjects analysed                         | 11 <sup>[42]</sup> | 28 <sup>[43]</sup>   |  |  |
| Units: Ratio of safety biomarker                    |                    |                      |  |  |
| geometric mean (geometric coefficient of variation) |                    |                      |  |  |
| Week 12, n=6, 24                                    | 1.416 (± 220.58)   | 1.099 (± 66.17)      |  |  |

|                     |                 |                 |  |  |
|---------------------|-----------------|-----------------|--|--|
| 12-Week FU, n=6, 21 | 0.937 (± 62.43) | 1.024 (± 93.56) |  |  |
|---------------------|-----------------|-----------------|--|--|

Notes:

[42] - ITT Population

[43] - ITT Population

## Statistical analyses

No statistical analyses for this end point

## Secondary: Number of participants with adverse events (AEs), serious adverse events (SAEs) and adverse events of special interest (AESI)

|                 |                                                                                                                               |
|-----------------|-------------------------------------------------------------------------------------------------------------------------------|
| End point title | Number of participants with adverse events (AEs), serious adverse events (SAEs) and adverse events of special interest (AESI) |
|-----------------|-------------------------------------------------------------------------------------------------------------------------------|

End point description:

An AE is any untoward medical occurrence in a participant, temporally associated with the use of a medicinal product, whether or not considered related to the medicinal product. An SAE is defined as any untoward medical occurrence that, at any dose results in death, is life-threatening, requires hospitalization or prolongation of existing hospitalization, results in disability/incapacity, is a congenital anomaly/birth defect and associated with liver injury and impaired liver function. An AESI include serious infections, opportunistic infections, neutropenia, respiratory events, pulmonary alveolar proteinosis, hypersensitivity reactions, injection site reactions, persistent cough or dyspnea.

|                |           |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

Up to 12-Week FU (Week 22)

| End point values            | Placebo            | GSK3196165 180 mg  |  |  |
|-----------------------------|--------------------|--------------------|--|--|
| Subject group type          | Reporting group    | Reporting group    |  |  |
| Number of subjects analysed | 11 <sup>[44]</sup> | 28 <sup>[45]</sup> |  |  |
| Units: Participants         |                    |                    |  |  |
| Any AEs                     | 4                  | 11                 |  |  |
| Any SAEs                    | 0                  | 0                  |  |  |
| AESI                        | 0                  | 1                  |  |  |

Notes:

[44] - ITT Population

[45] - ITT Population

## Statistical analyses

No statistical analyses for this end point

## Secondary: Number of participants who tested positive for Anti-GSK3196165 Binding Antibody Detection at any time post-Baseline

|                 |                                                                                                                     |
|-----------------|---------------------------------------------------------------------------------------------------------------------|
| End point title | Number of participants who tested positive for Anti-GSK3196165 Binding Antibody Detection at any time post-Baseline |
|-----------------|---------------------------------------------------------------------------------------------------------------------|

End point description:

Immunogenicity samples for determination of anti-drug-antibody (ADA) were collected. The presence of treatment emergent ADA was determined using a GSK3196165 bridging style ADA assay with a bio-analytically determined cut point determined during assay validation. Samples taken after dosing with GSK3196165 that had a value at or above the cut-point was considered potentially treatment-emergent

ADA-positive. The immunogenicity population consisted of all participants in the ITT population, who had at least one valid immunogenicity assessment.

|                            |           |
|----------------------------|-----------|
| End point type             | Secondary |
| End point timeframe:       |           |
| Up to 12-Week FU (Week 22) |           |

| End point values            | Placebo            | GSK3196165<br>180 mg |  |  |
|-----------------------------|--------------------|----------------------|--|--|
| Subject group type          | Reporting group    | Reporting group      |  |  |
| Number of subjects analysed | 11 <sup>[46]</sup> | 28 <sup>[47]</sup>   |  |  |
| Units: Participants         | 0                  | 0                    |  |  |

Notes:

[46] - Immunogenicity Population

[47] - Immunogenicity Population

## Statistical analyses

No statistical analyses for this end point

## Secondary: Change from Baseline in synovitis as assessed by Outcome Measures in Rheumatology (OMERACT) rheumatoid arthritis magnetic resonance imaging scoring system (RAMRIS) in the most affected hand/wrist

|                 |                                                                                                                                                                                                     |
|-----------------|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| End point title | Change from Baseline in synovitis as assessed by Outcome Measures in Rheumatology (OMERACT) rheumatoid arthritis magnetic resonance imaging scoring system (RAMRIS) in the most affected hand/wrist |
|-----------------|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|

End point description:

For synovitis a total of 8 joints were evaluated. Individual joint scores range from 0-3, where 0= normal, 1=mild, 2=moderate and 3=severe. The final synovitis score is the sum of the individual joint scores. Total score range from 0 (best) to 24 (worst). If an individual location is scored either 'Not Visible' or 'Surgically Modified' then the score for that location was set to missing. Missing joint scores was imputed as the mean of the non-missing joint scores. Baseline was defined at Day 1. Change from Baseline was calculated by subtracting the post-dose value from the Baseline value. Repeated measures analysis adjusted for synovitis score baseline value, treatment group, disease duration ( $\leq 2$  or  $> 2$  years), visit and treatment group by visit interaction. Data has been presented for Median and 95% credible interval. Only those participants with data available at the specified data points were analyzed (represented by n= X in the category titles).

|                                                |           |
|------------------------------------------------|-----------|
| End point type                                 | Secondary |
| End point timeframe:                           |           |
| Baseline and Weeks 4, 12, 12-Week FU (Week 22) |           |

| End point values                 | Placebo              | GSK3196165<br>180 mg   |  |  |
|----------------------------------|----------------------|------------------------|--|--|
| Subject group type               | Reporting group      | Reporting group        |  |  |
| Number of subjects analysed      | 11 <sup>[48]</sup>   | 28 <sup>[49]</sup>     |  |  |
| Units: Scores on a scale         |                      |                        |  |  |
| median (confidence interval 95%) |                      |                        |  |  |
| Week 4, n=6, 12                  | 0.05 (-1.92 to 1.95) | -0.07 (-1.19 to 1.12)  |  |  |
| Week 12, n=5, 21                 | 0.84 (-1.57 to 3.12) | -1.33 (-2.54 to -0.13) |  |  |

|                     |                      |                       |  |  |
|---------------------|----------------------|-----------------------|--|--|
| 12-Week FU, n=7, 19 | 1.13 (-1.32 to 3.55) | -1.13 (-2.47 to 0.20) |  |  |
|---------------------|----------------------|-----------------------|--|--|

Notes:

[48] - ITT Population

[49] - ITT Population

## Statistical analyses

| Statistical analysis title                                                   | Week 4                           |
|------------------------------------------------------------------------------|----------------------------------|
| Statistical analysis description:<br>For Posterior Probability Difference <0 |                                  |
| Comparison groups                                                            | Placebo v GSK3196165 180 mg      |
| Number of subjects included in analysis                                      | 39                               |
| Analysis specification                                                       | Pre-specified                    |
| Analysis type                                                                | other                            |
| P-value                                                                      | = 0.547                          |
| Method                                                                       | Repeated Measures Bayesian Model |
| Parameter estimate                                                           | Median difference (net)          |
| Point estimate                                                               | -0.13                            |
| Confidence interval                                                          |                                  |
| level                                                                        | 95 %                             |
| sides                                                                        | 2-sided                          |
| lower limit                                                                  | -2.32                            |
| upper limit                                                                  | 2.23                             |

| Statistical analysis title              | Week 12, For Posterior Probability Difference <0 |
|-----------------------------------------|--------------------------------------------------|
| Comparison groups                       | Placebo v GSK3196165 180 mg                      |
| Number of subjects included in analysis | 39                                               |
| Analysis specification                  | Pre-specified                                    |
| Analysis type                           | other                                            |
| P-value                                 | = 0.948                                          |
| Method                                  | Repeated Measures Bayesian Model                 |
| Parameter estimate                      | Median difference (net)                          |
| Point estimate                          | -2.18                                            |
| Confidence interval                     |                                                  |
| level                                   | 95 %                                             |
| sides                                   | 2-sided                                          |
| lower limit                             | -4.77                                            |
| upper limit                             | 0.51                                             |

| Statistical analysis title                                                   | 12-Week FU                  |
|------------------------------------------------------------------------------|-----------------------------|
| Statistical analysis description:<br>For Posterior Probability Difference <0 |                             |
| Comparison groups                                                            | Placebo v GSK3196165 180 mg |

|                                         |                                  |
|-----------------------------------------|----------------------------------|
| Number of subjects included in analysis | 39                               |
| Analysis specification                  | Pre-specified                    |
| Analysis type                           | other                            |
| P-value                                 | = 0.949                          |
| Method                                  | Repeated Measures Bayesian Model |
| Parameter estimate                      | Median difference (net)          |
| Point estimate                          | -2.28                            |
| Confidence interval                     |                                  |
| level                                   | 95 %                             |
| sides                                   | 2-sided                          |
| lower limit                             | -5.02                            |
| upper limit                             | 0.45                             |

|                                         |                                                 |
|-----------------------------------------|-------------------------------------------------|
| <b>Statistical analysis title</b>       | Week 4, For Posterior Probability Difference >0 |
| Comparison groups                       | Placebo v GSK3196165 180 mg                     |
| Number of subjects included in analysis | 39                                              |
| Analysis specification                  | Pre-specified                                   |
| Analysis type                           | other                                           |
| P-value                                 | = 0.453                                         |
| Method                                  | Repeated Measures Bayesian Model                |
| Parameter estimate                      | Median difference (net)                         |
| Point estimate                          | -0.13                                           |
| Confidence interval                     |                                                 |
| level                                   | 95 %                                            |
| sides                                   | 2-sided                                         |
| lower limit                             | -2.32                                           |
| upper limit                             | 2.23                                            |

|                                         |                                                  |
|-----------------------------------------|--------------------------------------------------|
| <b>Statistical analysis title</b>       | Week 12, For Posterior Probability Difference >0 |
| Comparison groups                       | Placebo v GSK3196165 180 mg                      |
| Number of subjects included in analysis | 39                                               |
| Analysis specification                  | Pre-specified                                    |
| Analysis type                           | other                                            |
| P-value                                 | = 0.052                                          |
| Method                                  | Repeated Measures Bayesian Model                 |
| Parameter estimate                      | Median difference (net)                          |
| Point estimate                          | -2.18                                            |
| Confidence interval                     |                                                  |
| level                                   | 95 %                                             |
| sides                                   | 2-sided                                          |
| lower limit                             | -4.77                                            |
| upper limit                             | 0.51                                             |

|                                   |            |
|-----------------------------------|------------|
| <b>Statistical analysis title</b> | 12-Week FU |
|-----------------------------------|------------|

# Statistical analysis description:

For Posterior Probability Difference >0

|                                         |                                  |
|-----------------------------------------|----------------------------------|
| Comparison groups                       | Placebo v GSK3196165 180 mg      |
| Number of subjects included in analysis | 39                               |
| Analysis specification                  | Pre-specified                    |
| Analysis type                           | other                            |
| P-value                                 | = 0.051                          |
| Method                                  | Repeated Measures Bayesian Model |
| Parameter estimate                      | Median difference (net)          |
| Point estimate                          | -2.28                            |
| Confidence interval                     |                                  |
| level                                   | 95 %                             |
| sides                                   | 2-sided                          |
| lower limit                             | -5.02                            |
| upper limit                             | 0.45                             |

## Secondary: Change from Baseline in osteitis as assessed by OMERACT RAMRI scoring system in the most affected hand/wrist

|                 |                                                                                                              |
|-----------------|--------------------------------------------------------------------------------------------------------------|
| End point title | Change from Baseline in osteitis as assessed by OMERACT RAMRI scoring system in the most affected hand/wrist |
|-----------------|--------------------------------------------------------------------------------------------------------------|

### End point description:

For bone edema/osteitis a total of 25 locations was evaluated. Individual location scores ranged from 0-3, where, 0: no edema; 1: 1-33% of bone edematous; 2: 34-66% of bone edematous; 3: 67-100% of bone edematous. Final bone edema/osteitis score is sum of individual location scores. Total score ranged from 0 (best) to 75 (worst). Baseline was defined at Day 1. Change from Baseline was calculated by subtracting post-dose value from Baseline value. If an individual location was scored either 'Not Visible' or 'Surgically Modified' or 'Not Assessable' then the score for that location was set to be missing. Missing joint scores was imputed as mean of non-missing location scores. Repeated measures analysis adjusted for Bone Edema/Osteitis Score baseline value, treatment group, disease duration ( $\leq 2$  or  $> 2$  years), visit and treatment group by visit interaction. Only those participants with data available at the specified data points were analyzed (represented by n= X in the category titles).

|                |           |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

### End point timeframe:

Baseline and Weeks 4, 12, 12-Week FU (Week 22)

| End point values                    | Placebo            | GSK3196165 180 mg  |  |  |
|-------------------------------------|--------------------|--------------------|--|--|
| Subject group type                  | Reporting group    | Reporting group    |  |  |
| Number of subjects analysed         | 11 <sup>[50]</sup> | 28 <sup>[51]</sup> |  |  |
| Units: Scores on a scale            |                    |                    |  |  |
| least squares mean (standard error) |                    |                    |  |  |
| Week 4, n=6, 12                     | -0.1 ( $\pm$ 0.11) | -0.1 ( $\pm$ 0.06) |  |  |
| Week 12, n=5, 21                    | 0.0 ( $\pm$ 1.04)  | -0.8 ( $\pm$ 0.56) |  |  |
| 12-Week FU, n=7,19                  | 0.5 ( $\pm$ 1.33)  | -0.9 ( $\pm$ 0.74) |  |  |

### Notes:

[50] - ITT Population

[51] - ITT Population

## Statistical analyses

|                                         |                             |
|-----------------------------------------|-----------------------------|
| <b>Statistical analysis title</b>       | Week 4                      |
| Comparison groups                       | Placebo v GSK3196165 180 mg |
| Number of subjects included in analysis | 39                          |
| Analysis specification                  | Pre-specified               |
| Analysis type                           | other                       |
| P-value                                 | = 0.94                      |
| Method                                  | Repeated measures analysis  |
| Parameter estimate                      | Mean difference (net)       |
| Point estimate                          | 0                           |
| Confidence interval                     |                             |
| level                                   | 95 %                        |
| sides                                   | 2-sided                     |
| lower limit                             | -0.2                        |
| upper limit                             | 0.3                         |

|                                         |                             |
|-----------------------------------------|-----------------------------|
| <b>Statistical analysis title</b>       | Week 12                     |
| Comparison groups                       | Placebo v GSK3196165 180 mg |
| Number of subjects included in analysis | 39                          |
| Analysis specification                  | Pre-specified               |
| Analysis type                           | other                       |
| P-value                                 | = 0.521                     |
| Method                                  | Repeated measures analysis  |
| Parameter estimate                      | Mean difference (net)       |
| Point estimate                          | -0.8                        |
| Confidence interval                     |                             |
| level                                   | 95 %                        |
| sides                                   | 2-sided                     |
| lower limit                             | -3.2                        |
| upper limit                             | 1.6                         |

|                                         |                             |
|-----------------------------------------|-----------------------------|
| <b>Statistical analysis title</b>       | 12-Week FU                  |
| Comparison groups                       | Placebo v GSK3196165 180 mg |
| Number of subjects included in analysis | 39                          |
| Analysis specification                  | Pre-specified               |
| Analysis type                           | other                       |
| P-value                                 | = 0.396                     |
| Method                                  | Repeated measures analysis  |
| Parameter estimate                      | Mean difference (net)       |
| Point estimate                          | -1.3                        |
| Confidence interval                     |                             |
| level                                   | 95 %                        |
| sides                                   | 2-sided                     |
| lower limit                             | -4.4                        |
| upper limit                             | 1.8                         |

## Secondary: Change from Baseline in erosion as assessed by OMERACT RAMRI scoring system in the most affected hand/wrist

|                 |                                                                                                             |
|-----------------|-------------------------------------------------------------------------------------------------------------|
| End point title | Change from Baseline in erosion as assessed by OMERACT RAMRI scoring system in the most affected hand/wrist |
|-----------------|-------------------------------------------------------------------------------------------------------------|

### End point description:

For bone erosion a total of 25 locations were evaluated. Individual location scores range from 0-10, where, 0: no erosion; 1: 1-10% of bone eroded and 10: 91-100% of bone eroded. The final bone erosion score is the sum of the individual location scores. The total score ranged from 0 (best) to 250 (worst). If an individual location was scored either 'Not Visible' or 'Surgically Modified' or 'Not Assessable' then the score for that location was set to be missing. Missing joint scores was imputed as the mean of the non-missing location scores. Baseline was defined at Day 1. Change from Baseline was calculated by subtracting the post-dose value from the Baseline value. Analysis was performed using repeated measures analysis adjusted for Bone Erosion Score baseline value, treatment group, disease duration ( $\leq 2$  or  $> 2$  years), visit and treatment group. Only those participants with data available at the specified data points were analyzed (represented by n= X in the category titles).

|                |           |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

### End point timeframe:

Baseline and Weeks 4, 12, 12-Week FU (Week 22)

| End point values                    | Placebo            | GSK3196165<br>180 mg |  |  |
|-------------------------------------|--------------------|----------------------|--|--|
| Subject group type                  | Reporting group    | Reporting group      |  |  |
| Number of subjects analysed         | 11 <sup>[52]</sup> | 28 <sup>[53]</sup>   |  |  |
| Units: Scores on a scale            |                    |                      |  |  |
| least squares mean (standard error) |                    |                      |  |  |
| Week 4, n=6, 12                     | 0.2 ( $\pm$ 0.49)  | 0.3 ( $\pm$ 0.30)    |  |  |
| Week 12, n=5, 21                    | 0.8 ( $\pm$ 0.50)  | 0.4 ( $\pm$ 0.26)    |  |  |
| 12-Week FU, n=7, 19                 | 1.5 ( $\pm$ 0.47)  | 0.5 ( $\pm$ 0.27)    |  |  |

Notes:

[52] - ITT Population

[53] - ITT Population

## Statistical analyses

|                                         |                             |
|-----------------------------------------|-----------------------------|
| Statistical analysis title              | Week 4                      |
| Comparison groups                       | Placebo v GSK3196165 180 mg |
| Number of subjects included in analysis | 39                          |
| Analysis specification                  | Pre-specified               |
| Analysis type                           | other                       |
| P-value                                 | = 0.945                     |
| Method                                  | Repeated measures analysis  |
| Parameter estimate                      | Mean difference (net)       |
| Point estimate                          | 0                           |
| Confidence interval                     |                             |
| level                                   | 95 %                        |
| sides                                   | 2-sided                     |
| lower limit                             | -1.1                        |
| upper limit                             | 1.2                         |

|                                         |                             |
|-----------------------------------------|-----------------------------|
| <b>Statistical analysis title</b>       | Week 12                     |
| Comparison groups                       | Placebo v GSK3196165 180 mg |
| Number of subjects included in analysis | 39                          |
| Analysis specification                  | Pre-specified               |
| Analysis type                           | other                       |
| P-value                                 | = 0.475                     |
| Method                                  | Repeated measures analysis  |
| Parameter estimate                      | Mean difference (net)       |
| Point estimate                          | -0.4                        |
| Confidence interval                     |                             |
| level                                   | 95 %                        |
| sides                                   | 2-sided                     |
| lower limit                             | -1.5                        |
| upper limit                             | 0.7                         |

|                                         |                             |
|-----------------------------------------|-----------------------------|
| <b>Statistical analysis title</b>       | 12-Week FU                  |
| Comparison groups                       | Placebo v GSK3196165 180 mg |
| Number of subjects included in analysis | 39                          |
| Analysis specification                  | Pre-specified               |
| Analysis type                           | other                       |
| P-value                                 | = 0.086                     |
| Method                                  | Repeated measures analysis  |
| Parameter estimate                      | Mean difference (net)       |
| Point estimate                          | -0.9                        |
| Confidence interval                     |                             |
| level                                   | 95 %                        |
| sides                                   | 2-sided                     |
| lower limit                             | -2                          |
| upper limit                             | 0.1                         |

## **Secondary: Change from Baseline in synovitis as assessed by rheumatoid arthritis MRI quantitative (RAMRIQ) assessment in the most affected hand/wrist**

|                 |                                                                                                                                            |
|-----------------|--------------------------------------------------------------------------------------------------------------------------------------------|
| End point title | Change from Baseline in synovitis as assessed by rheumatoid arthritis MRI quantitative (RAMRIQ) assessment in the most affected hand/wrist |
|-----------------|--------------------------------------------------------------------------------------------------------------------------------------------|

### **End point description:**

RAMRIQ is an automated volume quantification assessment. RAMRIQ assessed same pathologies and joints (except metacarpophalangeal joint [MCP1]) as RAMRIS allowing for direct comparison of results obtained using the two methods. Bones were automatically identified in pre-contrast, coronal T1 images using active appearance modelling (AAMs). Joint capsules and soft tissues were also segmented with AAMs, providing consistent 3D regions of interest (ROI) for synovial enhancement across all time points. Synovial volume was calculated as voxels that enhance within each ROI. Baseline was defined at Day 1. Change from Baseline was calculated by subtracting the post-dose value from the Baseline value. Repeated measures analysis adjusted for Synovitis baseline value, treatment group, disease duration ( $\leq 2$  or  $> 2$  years), visit and treatment group by visit interaction. Only those participants with data available at the specified data points were analyzed (represented by  $n = X$  in the category titles).

|                                                   |           |
|---------------------------------------------------|-----------|
| End point type                                    | Secondary |
| End point timeframe:                              |           |
| Baseline and Weeks 4, 12 and 12-Week FU (Week 22) |           |

| End point values                    | Placebo               | GSK3196165<br>180 mg  |  |  |
|-------------------------------------|-----------------------|-----------------------|--|--|
| Subject group type                  | Reporting group       | Reporting group       |  |  |
| Number of subjects analysed         | 11 <sup>[54]</sup>    | 28 <sup>[55]</sup>    |  |  |
| Units: Milliliters                  |                       |                       |  |  |
| least squares mean (standard error) |                       |                       |  |  |
| Week 4, n=6, 12                     | 34.1 (±<br>1052.52)   | 245.5 (±<br>776.24)   |  |  |
| Week 12, n=5, 21                    | -912.3 (±<br>1405.77) | -1417.0 (±<br>671.54) |  |  |
| 12-Week FU, n=7, 19                 | 364.0 (±<br>1372.20)  | -1172.1 (±<br>844.13) |  |  |

Notes:

[54] - ITT Population

[55] - ITT Population

### Statistical analyses

| Statistical analysis title              | Week 4                      |
|-----------------------------------------|-----------------------------|
| Comparison groups                       | Placebo v GSK3196165 180 mg |
| Number of subjects included in analysis | 39                          |
| Analysis specification                  | Pre-specified               |
| Analysis type                           | other                       |
| P-value                                 | = 0.874                     |
| Method                                  | Repeated measures analysis  |
| Parameter estimate                      | Mean difference (net)       |
| Point estimate                          | 211.4                       |
| Confidence interval                     |                             |
| level                                   | 95 %                        |
| sides                                   | 2-sided                     |
| lower limit                             | -2589.2                     |
| upper limit                             | 3012                        |

| Statistical analysis title              | Week 12                     |
|-----------------------------------------|-----------------------------|
| Comparison groups                       | Placebo v GSK3196165 180 mg |
| Number of subjects included in analysis | 39                          |
| Analysis specification                  | Pre-specified               |
| Analysis type                           | other                       |
| P-value                                 | = 0.749                     |
| Method                                  | Repeated measures analysis  |
| Parameter estimate                      | Mean difference (net)       |
| Point estimate                          | -504.8                      |

|                     |         |
|---------------------|---------|
| Confidence interval |         |
| level               | 95 %    |
| sides               | 2-sided |
| lower limit         | -3730.4 |
| upper limit         | 2720.9  |

|                                         |                             |
|-----------------------------------------|-----------------------------|
| <b>Statistical analysis title</b>       | 12-Week FU                  |
| Comparison groups                       | Placebo v GSK3196165 180 mg |
| Number of subjects included in analysis | 39                          |
| Analysis specification                  | Pre-specified               |
| Analysis type                           | other                       |
| P-value                                 | = 0.352                     |
| Method                                  | Repeated measures analysis  |
| Parameter estimate                      | Mean difference (net)       |
| Point estimate                          | -1536                       |
| Confidence interval                     |                             |
| level                                   | 95 %                        |
| sides                                   | 2-sided                     |
| lower limit                             | -4884.2                     |
| upper limit                             | 1812.1                      |

### Secondary: Change from Baseline in osteitis as assessed by RAMRIQ assessment in the most affected hand/wrist

|                 |                                                                                                   |
|-----------------|---------------------------------------------------------------------------------------------------|
| End point title | Change from Baseline in osteitis as assessed by RAMRIQ assessment in the most affected hand/wrist |
|-----------------|---------------------------------------------------------------------------------------------------|

End point description:

RAMRIQ is an automated volume quantification assessment for edema volume. RAMRIQ assessed the same pathologies and joints (except MCP1) as RAMRIS, allowing for direct comparison of results obtained using the two methods. Bones were automatically identified in pre-contrast, coronal T1 images using AAMs. Joint capsules and soft tissues were also segmented with AAMs, providing consistent 3D ROI for synovial enhancement across all time points. Edema volume was defined as non-erosion contrast-enhancing voxels inside the bone. Baseline was defined at Day 1. Change from Baseline was calculated by subtracting the post-dose value from the Baseline value. Only those participants with data available at the specified data points were analyzed (represented by n= X in the category titles).

|                |           |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

Baseline and Weeks 4, 12 and 12-Week FU (Week 22)

|                                     |                    |                    |  |  |
|-------------------------------------|--------------------|--------------------|--|--|
| <b>End point values</b>             | Placebo            | GSK3196165 180 mg  |  |  |
| Subject group type                  | Reporting group    | Reporting group    |  |  |
| Number of subjects analysed         | 11 <sup>[56]</sup> | 28 <sup>[57]</sup> |  |  |
| Units: Milliliters                  |                    |                    |  |  |
| least squares mean (standard error) |                    |                    |  |  |
| Week 4, n=6, 12                     | -0.0045 (± 0.0102) | 0.0084 (± 0.0057)  |  |  |

|                     |                    |                    |  |  |
|---------------------|--------------------|--------------------|--|--|
| Week 12, n=5, 21    | -0.0045 (± 0.0035) | -0.0009 (± 0.0019) |  |  |
| 12-Week FU, n=7, 19 | -0.0038 (± 0.0016) | -0.0027 (± 0.0009) |  |  |

Notes:

[56] - ITT Population

[57] - ITT Population

## Statistical analyses

|                                         |                             |
|-----------------------------------------|-----------------------------|
| <b>Statistical analysis title</b>       | Week 4                      |
| Comparison groups                       | Placebo v GSK3196165 180 mg |
| Number of subjects included in analysis | 39                          |
| Analysis specification                  | Pre-specified               |
| Analysis type                           | other                       |
| P-value                                 | = 0.291                     |
| Method                                  | Repeated measures analysis  |
| Parameter estimate                      | Mean difference (net)       |
| Point estimate                          | 0.0128                      |
| Confidence interval                     |                             |
| level                                   | 95 %                        |
| sides                                   | 2-sided                     |
| lower limit                             | -0.0123                     |
| upper limit                             | 0.038                       |

|                                         |                             |
|-----------------------------------------|-----------------------------|
| <b>Statistical analysis title</b>       | Week 12                     |
| Comparison groups                       | Placebo v GSK3196165 180 mg |
| Number of subjects included in analysis | 39                          |
| Analysis specification                  | Pre-specified               |
| Analysis type                           | other                       |
| P-value                                 | = 0.375                     |
| Method                                  | Repeated measures analysis  |
| Parameter estimate                      | Mean difference (net)       |
| Point estimate                          | 0.0036                      |
| Confidence interval                     |                             |
| level                                   | 95 %                        |
| sides                                   | 2-sided                     |
| lower limit                             | -0.0046                     |
| upper limit                             | 0.0118                      |

|                                   |                             |
|-----------------------------------|-----------------------------|
| <b>Statistical analysis title</b> | 12-Week FU                  |
| Comparison groups                 | Placebo v GSK3196165 180 mg |

|                                         |                            |
|-----------------------------------------|----------------------------|
| Number of subjects included in analysis | 39                         |
| Analysis specification                  | Pre-specified              |
| Analysis type                           | other                      |
| P-value                                 | = 0.588                    |
| Method                                  | Repeated measures analysis |
| Parameter estimate                      | Mean difference (net)      |
| Point estimate                          | 0.001                      |
| Confidence interval                     |                            |
| level                                   | 95 %                       |
| sides                                   | 2-sided                    |
| lower limit                             | -0.0028                    |
| upper limit                             | 0.0049                     |

## Secondary: Change from Baseline in erosion as assessed by RAMRIQ assessment in the most affected hand/wrist

|                 |                                                                                                  |
|-----------------|--------------------------------------------------------------------------------------------------|
| End point title | Change from Baseline in erosion as assessed by RAMRIQ assessment in the most affected hand/wrist |
|-----------------|--------------------------------------------------------------------------------------------------|

### End point description:

RAMRIQ is an automated volume quantification assessment for erosion volume. RAMRIQ assessed the same pathologies and joints (except MCP1) as RAMRIS, allowing for direct comparison of results obtained using the two methods. Bones were automatically identified in pre-contrast, coronal T1 images using AAMs. Joint capsules and soft tissues were also segmented with AAMs, providing consistent 3D ROI for synovial enhancement across all time points. Erosion volume was identified inside the bone surfaces using voxel-based classification. The volume of BME and erosions was normalised to total bone volume for statistical analysis. Baseline was defined at Day 1. Change from Baseline was calculated by subtracting the post-dose value from the Baseline value. Only those participants with data available at the specified data points were analyzed (represented by n= X in the category titles).

|                |           |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

### End point timeframe:

Baseline and Weeks 4, 12 and 12-Week FU (Week 22)

| End point values                    | Placebo               | GSK3196165<br>180 mg  |  |  |
|-------------------------------------|-----------------------|-----------------------|--|--|
| Subject group type                  | Reporting group       | Reporting group       |  |  |
| Number of subjects analysed         | 11 <sup>[58]</sup>    | 28 <sup>[59]</sup>    |  |  |
| Units: Milliliters                  |                       |                       |  |  |
| least squares mean (standard error) |                       |                       |  |  |
| Week 4, n=6, 12                     | 0.0007 (±<br>0.0012)  | 0.0006 (±<br>0.0008)  |  |  |
| Week 12, n=5, 21                    | 0.0003 (±<br>0.0011)  | -0.0000 (±<br>0.0006) |  |  |
| 12-Week FU, n=7, 19                 | -0.0002 (±<br>0.0023) | 0.0003 (±<br>0.0013)  |  |  |

Notes:

[58] - ITT Population

[59] - ITT Population

## Statistical analyses

|                                         |                             |
|-----------------------------------------|-----------------------------|
| <b>Statistical analysis title</b>       | Week 4                      |
| Comparison groups                       | Placebo v GSK3196165 180 mg |
| Number of subjects included in analysis | 39                          |
| Analysis specification                  | Pre-specified               |
| Analysis type                           | other                       |
| P-value                                 | = 0.915                     |
| Method                                  | Repeated measures analysis  |
| Parameter estimate                      | Mean difference (net)       |
| Point estimate                          | -0.0002                     |
| Confidence interval                     |                             |
| level                                   | 95 %                        |
| sides                                   | 2-sided                     |
| lower limit                             | -0.0033                     |
| upper limit                             | 0.0029                      |

|                                         |                             |
|-----------------------------------------|-----------------------------|
| <b>Statistical analysis title</b>       | Week 12                     |
| Comparison groups                       | Placebo v GSK3196165 180 mg |
| Number of subjects included in analysis | 39                          |
| Analysis specification                  | Pre-specified               |
| Analysis type                           | other                       |
| P-value                                 | = 0.771                     |
| Method                                  | Repeated measures analysis  |
| Parameter estimate                      | Mean difference (net)       |
| Point estimate                          | -0.0004                     |
| Confidence interval                     |                             |
| level                                   | 95 %                        |
| sides                                   | 2-sided                     |
| lower limit                             | -0.0028                     |
| upper limit                             | 0.0021                      |

|                                         |                             |
|-----------------------------------------|-----------------------------|
| <b>Statistical analysis title</b>       | 12-Week FU                  |
| Comparison groups                       | Placebo v GSK3196165 180 mg |
| Number of subjects included in analysis | 39                          |
| Analysis specification                  | Pre-specified               |
| Analysis type                           | other                       |
| P-value                                 | = 0.85                      |
| Method                                  | Repeated measures analysis  |
| Parameter estimate                      | Mean difference (net)       |
| Point estimate                          | 0.0005                      |
| Confidence interval                     |                             |
| level                                   | 95 %                        |
| sides                                   | 2-sided                     |
| lower limit                             | -0.0048                     |
| upper limit                             | 0.0058                      |



## Adverse events

### Adverse events information

Timeframe for reporting adverse events:

AEs and SAEs were collected from start of study treatment up to 12-Week FU (Week 22)

Adverse event reporting additional description:

ITT Population was used for the analysis of safety data.

|                 |            |
|-----------------|------------|
| Assessment type | Systematic |
|-----------------|------------|

### Dictionary used

|                 |        |
|-----------------|--------|
| Dictionary name | MedDRA |
|-----------------|--------|

|                    |      |
|--------------------|------|
| Dictionary version | 20.1 |
|--------------------|------|

### Reporting groups

|                       |                   |
|-----------------------|-------------------|
| Reporting group title | GSK3196165 180 mg |
|-----------------------|-------------------|

Reporting group description:

Eligible participants received GSK3196165 180 mg SC into thigh or abdomen once weekly for 5 weeks, and then every other week until Week 10. In addition to GSK3196165, participants also received MTX 7.5–5 mg/week and folic (or folinic) acid  $\geq 5$  mg/week during the combination treatment period.

|                       |         |
|-----------------------|---------|
| Reporting group title | Placebo |
|-----------------------|---------|

Reporting group description:

Eligible participants received matching placebo SC into thigh or abdomen once weekly for 5 weeks, and then every other week until Week 10. In addition to placebo, participants also received MTX 7.5–25 mg/week and folic (or folinic) acid  $\geq 5$  mg/week during the combination treatment period.

| Serious adverse events                            | GSK3196165 180 mg | Placebo        |  |
|---------------------------------------------------|-------------------|----------------|--|
| Total subjects affected by serious adverse events |                   |                |  |
| subjects affected / exposed                       | 0 / 28 (0.00%)    | 0 / 11 (0.00%) |  |
| number of deaths (all causes)                     | 0                 | 0              |  |
| number of deaths resulting from adverse events    |                   |                |  |

Frequency threshold for reporting non-serious adverse events: 0 %

| Non-serious adverse events                            | GSK3196165 180 mg | Placebo         |  |
|-------------------------------------------------------|-------------------|-----------------|--|
| Total subjects affected by non-serious adverse events |                   |                 |  |
| subjects affected / exposed                           | 11 / 28 (39.29%)  | 4 / 11 (36.36%) |  |
| Investigations                                        |                   |                 |  |
| Weight increased                                      |                   |                 |  |
| subjects affected / exposed                           | 1 / 28 (3.57%)    | 0 / 11 (0.00%)  |  |
| occurrences (all)                                     | 1                 | 0               |  |
| Cardiac disorders                                     |                   |                 |  |

|                                                                                                                                                                                           |                                                |                                                |  |
|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|------------------------------------------------|------------------------------------------------|--|
| Coronary artery disease<br>subjects affected / exposed<br>occurrences (all)                                                                                                               | 0 / 28 (0.00%)<br>0                            | 1 / 11 (9.09%)<br>1                            |  |
| Tachycardia<br>subjects affected / exposed<br>occurrences (all)                                                                                                                           | 1 / 28 (3.57%)<br>1                            | 0 / 11 (0.00%)<br>0                            |  |
| Nervous system disorders<br>Headache<br>subjects affected / exposed<br>occurrences (all)                                                                                                  | 1 / 28 (3.57%)<br>1                            | 0 / 11 (0.00%)<br>0                            |  |
| Blood and lymphatic system disorders<br>Neutropenia<br>subjects affected / exposed<br>occurrences (all)                                                                                   | 1 / 28 (3.57%)<br>1                            | 0 / 11 (0.00%)<br>0                            |  |
| General disorders and administration<br>site conditions<br>Fatigue<br>subjects affected / exposed<br>occurrences (all)                                                                    | 0 / 28 (0.00%)<br>0                            | 1 / 11 (9.09%)<br>1                            |  |
| Gastrointestinal disorders<br>Nausea<br>subjects affected / exposed<br>occurrences (all)                                                                                                  | 1 / 28 (3.57%)<br>1                            | 0 / 11 (0.00%)<br>0                            |  |
| Respiratory, thoracic and mediastinal<br>disorders<br>Cough<br>subjects affected / exposed<br>occurrences (all)<br><br>Asthma<br>subjects affected / exposed<br>occurrences (all)         | 2 / 28 (7.14%)<br>3<br><br>1 / 28 (3.57%)<br>1 | 0 / 11 (0.00%)<br>0<br><br>0 / 11 (0.00%)<br>0 |  |
| Skin and subcutaneous tissue disorders<br>Alopecia<br>subjects affected / exposed<br>occurrences (all)<br><br>Erythema<br>subjects affected / exposed<br>occurrences (all)<br><br>Rosacea | 0 / 28 (0.00%)<br>0<br><br>1 / 28 (3.57%)<br>1 | 1 / 11 (9.09%)<br>1<br><br>0 / 11 (0.00%)<br>0 |  |

|                                                                                                                          |                     |                      |  |
|--------------------------------------------------------------------------------------------------------------------------|---------------------|----------------------|--|
| subjects affected / exposed<br>occurrences (all)                                                                         | 1 / 28 (3.57%)<br>1 | 0 / 11 (0.00%)<br>0  |  |
| Seborrhoeic dermatitis<br>subjects affected / exposed<br>occurrences (all)                                               | 1 / 28 (3.57%)<br>1 | 0 / 11 (0.00%)<br>0  |  |
| Psychiatric disorders<br>Initial insomnia<br>subjects affected / exposed<br>occurrences (all)                            | 1 / 28 (3.57%)<br>1 | 0 / 11 (0.00%)<br>0  |  |
| Musculoskeletal and connective tissue disorders<br>Pain in extremity<br>subjects affected / exposed<br>occurrences (all) | 0 / 28 (0.00%)<br>0 | 2 / 11 (18.18%)<br>2 |  |
| Rheumatoid arthritis<br>subjects affected / exposed<br>occurrences (all)                                                 | 0 / 28 (0.00%)<br>0 | 2 / 11 (18.18%)<br>2 |  |
| Musculoskeletal pain<br>subjects affected / exposed<br>occurrences (all)                                                 | 1 / 28 (3.57%)<br>1 | 0 / 11 (0.00%)<br>0  |  |
| Infections and infestations<br>Upper respiratory tract infection<br>subjects affected / exposed<br>occurrences (all)     | 1 / 28 (3.57%)<br>1 | 1 / 11 (9.09%)<br>1  |  |
| Laryngitis<br>subjects affected / exposed<br>occurrences (all)                                                           | 1 / 28 (3.57%)<br>1 | 0 / 11 (0.00%)<br>0  |  |
| Nasopharyngitis<br>subjects affected / exposed<br>occurrences (all)                                                      | 1 / 28 (3.57%)<br>1 | 0 / 11 (0.00%)<br>0  |  |

## More information

### Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

| Date          | Amendment                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                 |
|---------------|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| 01 March 2016 | This amendment includes classification of primary and secondary objectives and endpoints in Section 1 and Section 3; extension of the screening window to six weeks in Section 1, Section 4.1, Section 5.3.1, Section 7.1, and Section 7.2; correction of several typographical errors; clarification of likely numbers of participants screened in Section 4.3; correction of >15% relative decrease in DLCO as a trigger point in Section 4.6.1; clarification of DLCO testing in Section 5.1, Section 5.3.2.2, Section 7.1, Section 7.2, and Section 7.6.12; addition of Day 1 joint count and correction of mandatory chest HRCT if DLCO $\geq 60\%$ - <70% predicted in Section 5.1; revision that participants must have passed all screening assessments (including laboratory tests) prior to undertaking MRI scanning, and that whole blood flow cytometry is scheduled on Day 1 in Section 7.1; an additional Exclusion Criterion for MRI in Section 5.2; correction that re-screening is permitted in Section 5.3.1; correction that RNA analysis is not part of the pharmacogenetics substudy in Section 7.1 and Section 7.2; clarification of the RA Symptom and Impact Diary in Section 7.5.2; clarification of PK sample in Section 7.2; clarification of MRI image processing in Section 7.9; clarification of abbreviations in Appendix 12.1; revision of contraception guidance in Appendix 12.2; and clarification of data recording in Appendix 12.7. |

Notes:

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### Interruptions (globally)

Were there any global interruptions to the trial? No

### Limitations and caveats

None reported