EU Clinical Trials Register

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:

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:

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:

Population of trial subjects

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:

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
Arm title	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 >=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

Arm title	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 >=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

Number of subjects in period 1	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 >=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 >=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	± 11.57	± 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 >=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 >=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 (<=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[1]	28[2]		
Units: Ratio of GM-CSF complex				
least squares mean (geometric coefficient of variation)				
GM-CSF - Complex, Week 1, n=9, 27|	0.972 (± 35.98)	13.799 (± 20.65)		
GM-CSF - Complex, Week 2, n=8, 26|	0.960 (± 31.23)	31.056 (± 17.58)		
GM-CSF - Complex, Week 4, n=8, 27|	0.959 (± 34.51)	53.496 (± 18.55)		
GM-CSF - Complex, Week 6, n=7, 26|	0.964 (± 40.96)	46.620 (± 22.37)		
GM-CSF - Complex, Week 8, n=7, 24|	0.964 (± 41.80)	33.404 (± 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

Statistical analysis title	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

Statistical analysis title	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

Statistical analysis title	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

Statistical analysis title	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

Statistical analysis title	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

Statistical analysis title	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

Statistical analysis title	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:

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 (<=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)

End point values	Placebo	GSK3196165 180 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	11[3]	28[4]		
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

Statistical analysis title	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

Statistical analysis title	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

Statistical analysis title	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

Statistical analysis title	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

Statistical analysis title	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

Statistical analysis title	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

Statistical analysis title	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

Statistical analysis title	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

Statistical analysis title	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

Statistical analysis title	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

Statistical analysis title	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

Statistical analysis title	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

Statistical analysis title	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

Primary: Change from Baseline in Predictive Biomarkers: Amyloid A

End point title	Change from Baseline in Predictive Biomarkers: Amyloid A

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 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 (<=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 Week 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[5]	28[6]		
Units: Ratio of predictive biomarker				
least squares mean (geometric coefficient of variation)				
Amyloid A, Week 12, n=7, 24|	0.845 (± 49.31)	0.653 (± 25.45)		
Amyloid A, 12-Week FU, n=7, 21|	0.529 (± 35.12)	0.623 (± 19.68)		

Notes:

[5] - ITT Population

[6] - ITT Population

Statistical analyses

Statistical analysis title	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

Statistical analysis title	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 180 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	11[7]	28[8]		
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

Statistical analysis title	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

Statistical analysis title	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

Statistical analysis title	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

Statistical analysis title	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

Statistical analysis title	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

Statistical analysis title	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

Statistical analysis title	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

Statistical analysis title	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

Statistical analysis title	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

Statistical analysis title	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

Statistical analysis title	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

Statistical analysis title	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

Statistical analysis title	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

Statistical analysis title	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

Statistical analysis title	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

Statistical analysis title	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

Statistical analysis title	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

Statistical analysis title	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

Statistical analysis title	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

Statistical analysis title	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

Statistical analysis title	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

Statistical analysis title	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

Statistical analysis title	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

Statistical analysis title	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

Statistical analysis title	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

Statistical analysis title	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

Statistical analysis title	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

Statistical analysis title	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 (<=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)

End point values	Placebo	GSK3196165 180 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	11[9]	28[10]		
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

Statistical analysis title	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

Statistical analysis title	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

Statistical analysis title	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

Statistical analysis title	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

Statistical analysis title	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

Statistical analysis title	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

Statistical analysis title	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

Statistical analysis title	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

Statistical analysis title	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

Statistical analysis title	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

Statistical analysis title	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

Statistical analysis title	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

Statistical analysis title	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

Statistical analysis title	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:

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 (<=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)

End point values	Placebo	GSK3196165 180 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	11[11]	28[12]		
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, Week12,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 (± 9.75)	0.910 (± 5.46)			

Notes:

[11] - ITT Population

[12] - ITT Population

Statistical analyses

Statistical analysis title	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

Statistical analysis title	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

Statistical analysis title	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

Statistical analysis title	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

Statistical analysis title	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

Statistical analysis title	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

Statistical analysis title	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

Statistical analysis title	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

Statistical analysis title	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

Statistical analysis title	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

Statistical analysis title	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

Statistical analysis title	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

Statistical analysis title	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

Statistical analysis title	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

Statistical analysis title	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

Statistical analysis title	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

Statistical analysis title	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

Statistical analysis title	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

Statistical analysis title	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

Statistical analysis title	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

Statistical analysis title	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

Statistical analysis title	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

Statistical analysis title	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

Statistical analysis title	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

Statistical analysis title	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

Statistical analysis title	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

Statistical analysis title	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

Statistical analysis title	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

Statistical analysis title	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

Statistical analysis title	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

Statistical analysis title	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

Statistical analysis title	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

Statistical analysis title	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

Statistical analysis title	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

Statistical analysis title	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

Statistical analysis title	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

Statistical analysis title	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

Statistical analysis title	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

Statistical analysis title	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

Statistical analysis title	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

Statistical analysis title	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

Statistical analysis title	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 (<=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[13]	28[14]		
Units: Ratio of Helper/Suppressor cells				
least squares mean (geometric coefficient of variation)				
Helper/Suppressor, Week 1, n=8, 25|	1.024 (± 6.98)	0.976 (± 4.00)		
Helper/Suppressor, Week 4, n=8, 25|	1.053 (± 7.18)	0.998 (± 4.11)		
Helper/Suppressor, Week 12, n=6, 25|	1.040 (± 6.83)	1.088 (± 3.49)		
Helper/Suppressor, 12-Week FU, n=6, 21|	1.051 (± 8.99)	1.065 (± 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

Statistical analysis title	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

Statistical analysis title	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

Statistical analysis title	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 NKL 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).

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[15]	28[16]		
Units: Ratio of biomarker				
least squares mean (geometric coefficient of variation)				
CD16+CD56+, Week 1, n=8, 25|	0.989 (± 11.39)	1.025 (± 6.30)		
CD16+CD56+, Week 4, n=8, 25|	1.163 (± 12.97)	0.951 (± 7.25)		
CD16+CD56+, Week 12, n=6, 25|	1.193 (± 15.49)	0.911 (± 7.81)		
CD16+CD56+, 12-Week FU, n=6, 21|	1.298 (± 15.10)	0.920 (± 7.98)		
CD19, Week 1, n=8, 25|	0.880 (± 11.05)	0.984 (± 6.23)		
CD19, Week 4, n=8, 25|	1.090 (± 15.31)	0.971 (± 8.60)		
CD19, Week 12, n=6, 25|	1.054 (± 12.26)	1.003 (± 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

Statistical analysis title	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

Statistical analysis title	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

Statistical analysis title	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

Statistical analysis title	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

Statistical analysis title	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

Statistical analysis title	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

Statistical analysis title	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

Statistical analysis title	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

Statistical analysis title	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

Statistical analysis title	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

Statistical analysis title	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

Statistical analysis title	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

Statistical analysis title	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

Statistical analysis title	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

Statistical analysis title	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

Statistical analysis title	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 (<=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[17]	28[18]		
Units: 10^9 cells/Liter				
least squares mean (standard error)				
CD3+CD8+, Week 1, n=8, 25|	-0.041 (± 0.0390)	-0.005 (± 0.0222)		
CD3+CD8+, Week 4, n=8, 25|	0.000 (± 0.0580)	-0.023 (± 0.0327)		
CD3+CD8+, Week 12, n=6, 25|	-0.056 (± 0.0418)	-0.037 (± 0.0215)		
CD3+CD8+, 12-Week FU, n=6, 21|	-0.060 (± 0.0506)	-0.027 (± 0.0279)		
T Cell B Cell NKL, Week 1, n=8, 25|	-0.123 (± 0.1557)	-0.020 (± 0.0881)		
T Cell B Cell NKL, Week 4, n=8, 25|	0.108 (± 0.2174)	-0.050 (± 0.1229)		
T Cell B Cell NKL, Week 12, n=6, 25|	-0.093 (± 0.1792)	-0.006 (± 0.0925)		
T Cell B Cell NKL, 12-Week FU, n=6, 21|	-0.029 (± 0.2168)	-0.050 (± 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

Statistical analysis title	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

Statistical analysis title	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

Statistical analysis title	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

Statistical analysis title	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

Statistical analysis title	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

Statistical analysis title	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

Statistical analysis title	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 (<=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[19]	28[20]		
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

Statistical analysis title	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

Statistical analysis title	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

Statistical analysis title	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

Statistical analysis title	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

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	= 0.363
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

Statistical analysis title	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

Statistical analysis title	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

Statistical analysis title	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

Statistical analysis title	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

Statistical analysis title	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

Statistical analysis title	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

Statistical analysis title	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 (<=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[21]	28[22]		
Units: 10^6 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

Statistical analysis title	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

Statistical analysis title	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

Statistical analysis title	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

Statistical analysis title	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

Statistical analysis title	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

Statistical analysis title	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

Statistical analysis title	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

Statistical analysis title	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:

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 (<=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[23]	28[24]		
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+, Week 12, n=5, 22|	3.4 (± 16.09)	-3.0 (± 7.55)	
CD45+3+8-4+CCR6+CXCR3-38+DR+, 12-Week FU, n=5, 18|	8.9 (± 12.29)	3.3 (± 6.36)	
CD45+3+8-4+CCR6-CXCR3+38+DR+, Week 1, n=7, 23|	-73.2 (± 82.46)	-129.2 (± 46.04)	
CD45+3+8-4+CCR6-CXCR3+38+DR+, Week 4, n=7, 21|	-159.6 (± 60.51)	-108.0 (± 35.05)	
CD45+3+8-4+CCR6-CXCR3+38+DR+, Week 12, n=5, 22|	219.2 (± 299.65)	77.7 (± 146.73)	
CD45+3+8-4+CCR6-CXCR3+38+DR+, 12-Week FU, n=5, 18|	33.9 (± 66.09)	-104.0 (± 34.73)	
CD45+3+8-4+CCR6-CXCR3-38+DR+, Week 1, n=7, 23|	-70.9 (± 25.90)	-70.5 (± 14.03)	
CD45+3+8-4+CCR6-CXCR3-38+DR+, Week 4, n=7, 21|	-38.9 (± 30.69)	-56.3 (± 17.93)	
CD45+3+8-4+CCR6-CXCR3-38+DR+, Week 12, n=5, 22|	-16.4 (± 198.13)	43.0 (± 92.38)	
CD45+3+8-4+CCR6-CXCR3-38+DR+, 12-Week FU, n=5, 18|	-12.7 (± 33.50)	-59.9 (± 17.32)	
CD45+CD3+CD8-CD4+, Week 1, n=7, 23|	-3845.3 (± 2648.60)	-163.0 (± 1444.61)	
CD45+CD3+CD8-CD4+, Week 4, n=7, 21|	1622.8 (± 2973.60)	1075.1 (± 1723.09)	
vCD45+CD3+CD8-CD4+, Week 12, n=5, 22|	2112.9 (± 4211.63)	1006.9 (± 2026.47)	
CD45+CD3+CD8-CD4+, 12-Week FU, n=5, 18|	1799.0 (± 2589.05)	-1832.0 (± 1366.65)	
CD45+CD3+CD8-CD4+CCR6+CXCR3+, Week 1, n=7, 23|	-514.6 (± 647.85)	-1030.2 (± 345.07)	
CD45+CD3+CD8-CD4+CCR6+CXCR3+, Week 4, n=7, 21|	-116.6 (± 757.58)	-316.5 (± 438.76)	
CD45+CD3+CD8-CD4+CCR6+CXCR3+, Week 12, n=5, 22|	-252.9 (± 827.53)	-506.4 (± 389.97)	
CD45+CD3+CD8-CD4+CCR6+CXCR3+, 12-Week FU, n=5, 18|	-688.1 (± 792.26)	-463.0 (± 412.22)	
CD45+CD3+CD8-CD4+CCR6+CXCR3-, Week 1, n=7, 23|	-817.1 (± 393.10)	-654.5 (± 212.18)	
CD45+CD3+CD8-CD4+CCR6+CXCR3-, Week 4, n=7, 21|	197.7 (± 475.88)	14.2 (± 277.06)	
CD45+CD3+CD8-CD4+CCR6+CXCR3-, Week 12, n=5, 22|	48.8 (± 541.14)	-219.7 (± 253.92)	
CD45+CD3+CD8-CD4+CCR6+CXCR3-, 12-Week FU, n=5, 18|	-311.6 (± 553.32)	-509.2 (± 291.09)	
CD45+CD3+CD8-CD4+CCR6-CXCR3+, Week 1, n=7, 23|	371.8 (± 1026.17)	1521.8 (± 547.18)	
CD45+CD3+CD8-CD4+CCR6-CXCR3+, Week 4, n=7, 21|	-24.5 (± 1678.23)	-292.5 (± 967.00)	
CD45+CD3+CD8-CD4+CCR6-CXCR3+, Week 12, n=5, 22|	2790.5 (± 2510.67)	1443.1 (± 1209.66)	
CD45+CD3+CD8-CD4+CCR6-CXCR3+, 12-Week FU, n=5, 18|	2295.9 (± 1787.02)	607.0 (± 927.11)	
CD45+CD3+CD8-CD4+CCR6-CXCR3-, Week 1, n=7, 23|	-3231.4 (± 2162.58)	45.4 (± 1187.37)	
CD45+CD3+CD8-CD4+CCR6-CXCR3-, Week 4, n=7, 21|	2084.9 (± 2873.95)	1637.6 (± 1665.46)	
CD45+CD3+CD8-CD4+CCR6-CXCR3-, Week 12, n=5, 22|	-1273.9 (± 2413.90)	161.4 (± 1209.82)	
CD45+CD3+CD8-CD4+CCR6-CXCR3-, 12-Week FU, n=5, 18|	-106.6 (± 1690.64)	-1316.7 (± 892.55)	

Notes:

[23] - ITT Population

[24] - ITT Population

Statistical analyses

Statistical analysis title	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

Statistical analysis title	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

Statistical analysis title	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

Statistical analysis title	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

Statistical analysis title	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

Statistical analysis title	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

Statistical analysis title	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

Statistical analysis title	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

Statistical analysis title	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

Statistical analysis title	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

Statistical analysis title	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

Statistical analysis title	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

Statistical analysis title	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

Statistical analysis title	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

Statistical analysis title	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

Statistical analysis title	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

Statistical analysis title	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

Statistical analysis title	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

Statistical analysis title	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

Statistical analysis title	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

Statistical analysis title	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

Statistical analysis title	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

Statistical analysis title	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

Statistical analysis title	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

Statistical analysis title	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

Statistical analysis title	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

Statistical analysis title	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

Statistical analysis title	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

Statistical analysis title	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

Statistical analysis title	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

Statistical analysis title	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

Statistical analysis title	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

Statistical analysis title	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

Statistical analysis title	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

Statistical analysis title	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

Statistical analysis title	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+ (10^3/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 180 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	11[25]	28[26]		
Units: 10^3 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

Statistical analysis title	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

Statistical analysis title	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

Statistical analysis title	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

Statistical analysis title	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

Statistical analysis title	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

Statistical analysis title	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

Statistical analysis title	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

Statistical analysis title	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

Statistical analysis title	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

Statistical analysis title	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

Statistical analysis title	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

Statistical analysis title	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

Statistical analysis title	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

Statistical analysis title	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

Statistical analysis title	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

Statistical analysis title	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 (<=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[27]	28[28]		
Units: 10^6 cells/Liter				
least squares mean (standard error)				
Week 1, n=5, 19|	-559.0 (± 269.84)	-380.9 (± 137.31)		
Week 4, n=6, 22|	-581.9 (± 377.03)	-41.5 (± 196.72)		
Week 12, n=5, 21|	-125.9 (± 460.53)	-378.6 (± 229.47)		
12-Week FU, n=5, 18|	-240.9 (± 430.65)	-199.3 (± 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

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	= 0.629
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

Statistical analysis title	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)[29]

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 180 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	11[30]	28[31]		
Units: Ratio of complement biomarker				
geometric mean (geometric coefficient 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

No statistical analyses for this end point

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)[32]

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 180 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	11[33]	28[34]		
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[35]

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 180 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	11[36]	28[37]		
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[38]

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 180 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	11[39]	28[40]		
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[41]

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 180 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	11[42]	28[43]		
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[44]	28[45]		
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 180 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	11[46]	28[47]		
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 (<=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 180 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	11[48]	28[49]		
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:	
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:	
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

Statistical analysis title	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

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	= 0.052
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

Statistical analysis title	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 (<=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[50]	28[51]		
Units: Scores on a scale				
least squares mean (standard error)				
Week 4, n=6, 12|	-0.1 (± 0.11)	-0.1 (± 0.06)		
Week 12, n=5, 21|	0.0 (± 1.04)	-0.8 (± 0.56)		
12-Week FU, n=7,19|	0.5 (± 1.33)	-0.9 (± 0.74)		

Notes:

[50] - ITT Population

[51] - 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	= 0.94
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

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	= 0.521
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

Statistical analysis title	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 (<=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 180 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	11[52]	28[53]		
Units: Scores on a scale				
least squares mean (standard error)				
Week 4, n=6, 12|	0.2 (± 0.49)	0.3 (± 0.30)		
Week 12, n=5, 21|	0.8 (± 0.50)	0.4 (± 0.26)		
12-Week FU, n=7, 19|	1.5 (± 0.47)	0.5 (± 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

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	= 0.475
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

Statistical analysis title	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 (<=2 or >2years), 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 180 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	11[54]	28[55]		
Units: Milliliters				
least squares mean (standard error)				
Week 4, n=6, 12|	34.1 (± 1052.52)	245.5 (± 776.24)		
Week 12, n=5, 21|	-912.3 (± 1405.77)	-1417.0 (± 671.54)		
12-Week FU, n=7, 19|	364.0 (± 1372.20)	-1172.1 (± 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

Statistical analysis title	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)

End point values	Placebo	GSK3196165 180 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	11[56]	28[57]		
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

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	= 0.291
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

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	= 0.375
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

Statistical analysis title	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 180 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	11[58]	28[59]		
Units: Milliliters				
least squares mean (standard error)				
Week 4, n=6, 12|	0.0007 (± 0.0012)	0.0006 (± 0.0008)		
Week 12, n=5, 21|	0.0003 (± 0.0011)	-0.0000 (± 0.0006)		
12-Week FU, n=7, 19|	-0.0002 (± 0.0023)	0.0003 (± 0.0013)		

Notes:

[58] - ITT Population

[59] - 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	= 0.915
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

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	= 0.771
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

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

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

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

 None reported