Clinical trial results:
A multi-centre Phase IIa double-blind, placebo-controlled study to investigate the efficacy and safety of GSK3196165 in subjects with inflammatory hand osteoarthritis.

Summary

EudraCT number	2015-003089-96
Trial protocol	GB DE NL PL
Global end of trial date	29 November 2017

Results information

Result version number	v1
This version publication date	12 December 2018
First version publication date	12 December 2018

Trial information

Trial identification

Sponsor protocol code	204851

Additional study identifiers

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

Notes:

Sponsors

Sponsor organisation name	GlaxoSmithKline
Sponsor organisation address	980 Great West Road, Brentford, Middlesex, United Kingdom,
Public contact	GSK Response Center, GlaxoSmithKline, 1 866-435-7343,
Scientific contact	GSK Response Center, GlaxoSmithKline, 1 866-435-7343,

Notes:

Paediatric regulatory details

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

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	13 April 2018
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	29 November 2017
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To assess the efficacy potential of GSK3196165 on pain in inflammatory hand osteoarthritis.

Protection of trial subjects:

Paracetamol (acetaminophen) was a permitted concomitant medication for hand pain, for the duration of this study and could be taken on an as needed basis up to 4gram per day or to the maximum permitted under local label.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	17 March 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	Germany: 11
Country: Number of subjects enrolled	Netherlands: 8
Country: Number of subjects enrolled	Poland: 8
Country: Number of subjects enrolled	United Kingdom: 10
Country: Number of subjects enrolled	United States: 7
Worldwide total number of subjects	44
EEA total number of subjects	37

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)	36

From 65 to 84 years	8
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

This was a multi-center, double-blind, placebo-controlled study to investigate the efficacy and safety of GSK3196165 in participants with inflammatory hand osteoarthritis. The study was conducted in five countries in Poland, United Kingdom, Netherlands, Germany and United States.

Pre-assignment

Screening details:

A total 121 participants were screened of which 77 were screen failures and 44 participants were enrolled 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	Subject, Investigator, Monitor, Carer, Data analyst, Assessor

Arms

Are arms mutually exclusive?	Yes
Arm title	Placebo

Arm description:

Participants randomized to Placebo group received total of 8 subcutaneous injections of placebo over a 12-week treatment period. Participants were administered loading doses on Days 1, 8, 15, 22 and 29 which was followed by 3 doses every other week (Days 43, 57, 71).

Arm type	Placebo
Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Participants were administered sterile 0.9 percentage (w/v) sodium chloride solution.

Arm title	GSK3196165 180mg

Arm description:

Participants randomized to GSK3196165 group received total of 8 doses of GSK3196165 over a 12-week treatment period. Participants were administered loading doses on Days 1, 8, 15, 22 and 29 which was followed by 3 doses every other week (Days 43, 57, 71).

Arm type	Experimental
Investigational medicinal product name	GSK3196165
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Participants were administered 180 milligram (1.2 milliliter) of GSK3196165 aqueous solution of purified monoclonal antibody.

Number of subjects in period 1	Placebo	GSK3196165 180mg
Started	22	22
Completed	21	18
Not completed	1	4
Consent withdrawn by subject	1	1
Adverse event, non-fatal	-	2
Lost to follow-up	-	1

Baseline characteristics

Reporting groups	
Reporting group title	Placebo
Reporting group description:	
Participants randomized to Placebo group received total of 8 subcutaneous injections of placebo over a 12-week treatment period. Participants were administered loading doses on Days 1, 8, 15, 22 and 29 which was followed by 3 doses every other week (Days 43, 57, 71).	
Reporting group title	GSK3196165 180mg
Reporting group description:	
Participants randomized to GSK3196165 group received total of 8 doses of GSK3196165 over a 12-week treatment period. Participants were administered loading doses on Days 1, 8, 15, 22 and 29 which was followed by 3 doses every other week (Days 43, 57, 71).	

Reporting group values	Placebo	GSK3196165 180mg	Total
Number of subjects	22	22	44
Age categorical Units: Subjects			
In utero	0	0	0
Preterm newborn infants (gestational age < 37 wks)	0	0	0
Newborns (0-27 days)	0	0	0
Infants and toddlers (28 days-23 months)	0	0	0
Children (2-11 years)	0	0	0
Adolescents (12-17 years)	0	0	0
Adults (18-64 years)	19	17	36
From 65-84 years	3	5	8
85 years and over	0	0	0
Age Continuous Units: Years			
arithmetic mean	56.7	60.9	
standard deviation	± 6.80	± 6.25	-
Sex: Female, Male Units: Subjects			
Female	20	20	40
Male	2	2	4
Race/Ethnicity, Customized Units: Subjects			

End points

End points reporting groups

Reporting group title	Placebo
Reporting group description:	
Participants randomized to Placebo group received total of 8 subcutaneous injections of placebo over a 12-week treatment period. Participants were administered loading doses on Days 1, 8, 15, 22 and 29 which was followed by 3 doses every other week (Days 43, 57, 71).	
Reporting group title	GSK3196165 180mg
Reporting group description:	
Participants randomized to GSK3196165 group received total of 8 doses of GSK3196165 over a 12-week treatment period. Participants were administered loading doses on Days 1, 8, 15, 22 and 29 which was followed by 3 doses every other week (Days 43, 57, 71).	

Primary: Change from Baseline in 24-hour average hand pain intensity, averaged over the 7 days prior to Week 6

End point title	Change from Baseline in 24-hour average hand pain intensity, averaged over the 7 days prior to Week 6
End point description:	
Participants were required to complete a daily pain NRS based on their 24-hour average hand pain intensity with the anchors "0" (no pain) and "10" (worst imaginable pain), which was averaged over the 7 days prior to assessment visit. The 7 day average score was calculated as sum of daily 24 hours average hand pain NRS scores in the 7 days prior to assessment visit, divided by number of entries recorded in those 7 days. Baseline visit was at Day 1 and Baseline value was defined as the average of the 7 days prior to baseline visit (Day 1 pre-dose). Change from Baseline is equal to post-dose visit value minus Baseline value. Intent-To-Treat Population comprised of all randomized participants who received at least one dose of study treatment (GSK3196165 or placebo). n=X in category titles represents the number of participants with non-missing data at the specified time-point. Only non-missing data is included in the MMRM model.	
End point type	Primary
End point timeframe:	
Baseline (Day 1 Pre-dose) and Week 6	

End point values	Placebo	GSK3196165 180mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	21[1]	20[2]		
Units: Scores on scale				
least squares mean (standard error)	-1.34 (± 0.325)	-1.70 (± 0.334)		

Notes:

[1] - Intent To Treat Population.

[2] - Intent To Treat Population.

Statistical analyses

Statistical analysis title	Difference from placebo for Week 6 is presented
Comparison groups	GSK3196165 180mg v Placebo

Number of subjects included in analysis	41
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.442 [3]
Method	Mixed Model Repeated Measures Analysis
Parameter estimate	Mean difference (net)
Point estimate	-0.36
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.31
upper limit	0.58

Notes:

[3] - MMRM model with fixed effects of Baseline Value,Treatment Group,Visit and Treatment Group by Visit Interaction was used. Unstructured covariance structure was used.p-value corresponds to the difference over placebo measure and confidence interval

Secondary: Change from Baseline in 24 hours average hand pain intensity averaged over the 7 days prior to each visit

End point title	Change from Baseline in 24 hours average hand pain intensity averaged over the 7 days prior to each visit

End point description:

Participants were required to complete a daily pain NRS based on their 24-hour average hand pain intensity with the anchors "0" (no pain) and "10" (worst imaginable pain), which was averaged over the 7 days prior to assessment visit. The 7 day average score is calculated by sum of daily 24 hours average hand pain NRS scores in the 7 days prior to assessment visit, divided by number of entries recorded in those 7 days. Baseline visit was at Day 1 and Baseline value was defined as the average of the 7 days prior to baseline visit (Day 1 pre-dose). Change from Baseline is equal to post-dose visit value minus Baseline value. n=X in category titles represents the number of participants with non-missing data at the specified time-point. Only non-missing data is included in the MMRM model.

End point type	Secondary

End point timeframe:

Baseline (Pre-dose Day 1), Weeks 1, 2, 3, 4, 6, 8, 10 and 12

End point values	Placebo	GSK3196165 180mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	22[4]	22[5]		
Units: Scores on scale				
least squares mean (standard error)				
Week 1, n=22, 20|	-0.13 (± 0.152)	-0.59 (± 0.160)		
Week 2, n=21, 20|	-0.48 (± 0.230)	-0.86 (± 0.239)		
Week 3, n=21, 20|	-0.74 (± 0.279)	-1.24 (± 0.289)		
Week 4, n=21, 20|	-0.91 (± 0.291)	-1.65 (± 0.301)		
Week 6, n=21, 20|	-1.34 (± 0.325)	-1.70 (± 0.334)		
Week 8, n=20, 19|	-1.27 (± 0.382)	-2.10 (± 0.393)		
Week 10, n=20, 19|	-1.18 (± 0.376)	-2.09 (± 0.389)		

Week 12, n=19, 18|	-1.35 (± 0.402)	-2.24 (± 0.416)		

Notes:

[4] - Intent-to-Treat Population.

[5] - Intent-to-Treat Population.

Statistical analyses

Statistical analysis title	Difference from placebo for Week 1 is presented
Comparison groups	Placebo v GSK3196165 180mg
Number of subjects included in analysis	44
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.046 [6]
Method	Mixed Model Repeated Measures Analysis
Parameter estimate	Mean difference (net)
Point estimate	-0.46
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.9
upper limit	-0.01

Notes:

[6] - MMRM model with fixed effects of Baseline Value, Treatment Group, Visit and Treatment Group by Visit Interaction was used. Unstructured covariance structure was used. p-value corresponds to the difference over placebo measure and confidence interval.

Statistical analysis title	Difference from placebo for Week 2 is presented
Comparison groups	Placebo v GSK3196165 180mg
Number of subjects included in analysis	44
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.257 [7]
Method	Mixed Model Repeated Measures Analysis
Parameter estimate	Mean difference (net)
Point estimate	-0.38
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.05
upper limit	0.29

Notes:

[7] - MMRM model with fixed effects of Baseline Value, Treatment Group, Visit and Treatment Group by Visit Interaction was used. Unstructured covariance structure was used. p-value corresponds to the difference over placebo measure and confidence interval.

Statistical analysis title	Difference from placebo for Week 3 is presented
Comparison groups	Placebo v GSK3196165 180mg

Number of subjects included in analysis	44
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.22 [8]
Method	Mixed Model Repeated Measures Analysis
Parameter estimate	Mean difference (net)
Point estimate	-0.5
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.31
upper limit	0.31

Notes:

[8] - MMRM model with fixed effects of Baseline Value, Treatment Group, Visit and Treatment Group by Visit Interaction was used. Unstructured covariance structure was used. p-value corresponds to the difference over placebo measure and confidence interval.

Statistical analysis title	Difference from placebo for Week 4 is presented
Comparison groups	Placebo v GSK3196165 180mg
Number of subjects included in analysis	44
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.085 [9]
Method	Mixed Model Repeated Measures Analysis
Parameter estimate	Mean difference (net)
Point estimate	-0.74
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.59
upper limit	0.11

Notes:

[9] - MMRM model with fixed effects of Baseline Value, Treatment Group, Visit and Treatment Group by Visit Interaction was used. Unstructured covariance structure was used. p-value corresponds to the difference over placebo measure and confidence interval.

Statistical analysis title	Difference from placebo for Week 6 is presented
Comparison groups	Placebo v GSK3196165 180mg
Number of subjects included in analysis	44
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.442 [10]
Method	Mixed Model Repeated Measures Analysis
Parameter estimate	Mean difference (net)
Point estimate	-0.36
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.31
upper limit	0.58

Notes:

[10] - MMRM model with fixed effects of Baseline Value, Treatment Group, Visit and Treatment Group by Visit Interaction was used. Unstructured covariance structure was used. p-value corresponds to the difference over placebo measure and confidence interval.

Statistical analysis title	Difference from placebo for Week 8 is presented
Comparison groups	Placebo v GSK3196165 180mg
Number of subjects included in analysis	44
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.139 [11]
Method	Mixed Model Repeated Measures Analysis
Parameter estimate	Mean difference (net)
Point estimate	-0.83
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.93
upper limit	0.28

Notes:

[11] - MMRM model with fixed effects of Baseline Value, Treatment Group, Visit and Treatment Group by Visit Interaction was used. Unstructured covariance structure was used. p-value corresponds to the difference over placebo measure and confidence interval.

Statistical analysis title	Difference from placebo for Week 10 is presented
Comparison groups	Placebo v GSK3196165 180mg
Number of subjects included in analysis	44
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.103 [12]
Method	Mixed Model Repeated Measures Analysis
Parameter estimate	Mean difference (net)
Point estimate	-0.9
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2
upper limit	0.19

Notes:

[12] - MMRM model with fixed effects of Baseline Value, Treatment Group, Visit and Treatment Group by Visit Interaction was used. Unstructured covariance structure was used. p-value corresponds to the difference over placebo measure and confidence interval.

Statistical analysis title	Difference from placebo for Week 12 is presented
Comparison groups	Placebo v GSK3196165 180mg
Number of subjects included in analysis	44
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.132 [13]
Method	Mixed Model Repeated Measures Analysis
Parameter estimate	Mean difference (net)
Point estimate	-0.89

Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.06
upper limit	0.28

Notes:

[13] - MMRM model with fixed effects of Baseline Value, Treatment Group, Visit and Treatment Group by Visit Interaction was used. Unstructured covariance structure was used. p-value corresponds to the difference over placebo measure and confidence interval.

Secondary: Change from Baseline of worst hand pain intensity over 24 hours averaged over the 7 days prior to each visit

End point title	Change from Baseline of worst hand pain intensity over 24 hours averaged over the 7 days prior to each visit

End point description:

Participants were required to complete a daily pain NRS based on their 24-hour worst hand pain intensity with the anchors "0" (no pain) and "10" (worst imaginable pain), which was averaged over the 7 days prior to assessment visit. The score is calculated as sum of daily 24 hours worst hand pain NRS scores in the 7 days prior to assessment visit, divided by number of entries recorded in those 7 days. Baseline visit was at Day 1 and Baseline value was defined as the average of the 7 days prior to baseline visit (Day 1 pre-dose). Change from Baseline is equal to post-dose visit value minus Baseline value. n=X in category titles represents the number of participants with non-missing data at the specified time-point. Only non-missing data is included in the MMRM model.

End point type	Secondary

End point timeframe:

Baseline (Pre-dose Day 1), Weeks 1, 2, 3, 4, 6, 8, 10 and 12

End point values	Placebo	GSK3196165 180mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	22[14]	22[15]		
Units: Scores on scale				
least squares mean (standard error)				
Week 1, n=22, 20|	0.01 (± 0.174)	-0.45 (± 0.183)		
Week 2, n=21, 20|	-0.42 (± 0.235)	-0.69 (± 0.245)		
Week 3, n=21, 20|	-0.63 (± 0.269)	-1.23 (± 0.278)		
Week 4, n= 21, 20|	-0.72 (± 0.289)	-1.51 (± 0.299)		
Week 6, n= 21, 20|	-1.30 (± 0.328)	-1.63 (± 0.337)		
Week 8, n= 20, 19|	-1.18 (± 0.394)	-2.11 (± 0.406)		
Week 10, n= 20, 19|	-1.15 (± 0.394)	-2.13 (± 0.407)		
Week 12, n= 19, 18|	-1.32 (± 0.415)	-2.34 (± 0.430)		

Notes:

[14] - Intent-to-Treat Population.

[15] - Intent-to-Treat Population.

Statistical analyses

Statistical analysis title	Difference from placebo for Week 1 is presented
Comparison groups	Placebo v GSK3196165 180mg
Number of subjects included in analysis	44
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.082 [16]
Method	Mixed Model Repeated Measures Analysis
Parameter estimate	Mean difference (net)
Point estimate	-0.45
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.97
upper limit	0.06

Notes:

[16] - MMRM model with fixed effects of Baseline Value, Treatment Group, Visit and Treatment Group by Visit Interaction was used. Unstructured covariance structure was used. p-value corresponds to the difference over placebo measure and confidence interval.

Statistical analysis title	Difference from placebo for Week 2 is presented
Comparison groups	Placebo v GSK3196165 180mg
Number of subjects included in analysis	44
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.426 [17]
Method	Mixed Model Repeated Measures Analysis
Parameter estimate	Mean difference (net)
Point estimate	-0.27
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.96
upper limit	0.41

Notes:

[17] - MMRM model with fixed effects of Baseline Value, Treatment Group, Visit and Treatment Group by Visit Interaction was used. Unstructured covariance structure was used. p-value corresponds to the difference over placebo measure and confidence interval.

Statistical analysis title	Difference from placebo for Week 3 is presented
Comparison groups	Placebo v GSK3196165 180mg
Number of subjects included in analysis	44
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.129 [18]
Method	Mixed Model Repeated Measures Analysis
Parameter estimate	Mean difference (net)
Point estimate	-0.6
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.38
upper limit	0.18

Notes:

[18] - MMRM model with fixed effects of Baseline Value, Treatment Group, Visit and Treatment Group by Visit Interaction was used. Unstructured covariance structure was used. p-value corresponds to the difference over placebo measure and confidence interval.

Statistical analysis title	Difference from placebo for Week 4 is presented
Comparison groups	Placebo v GSK3196165 180mg
Number of subjects included in analysis	44
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.067 [19]
Method	Mixed Model Repeated Measures Analysis
Parameter estimate	Mean difference (net)
Point estimate	-0.78
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.63
upper limit	0.06

Notes:

[19] - MMRM model with fixed effects of Baseline Value, Treatment Group, Visit and Treatment Group by Visit Interaction was used. Unstructured covariance structure was used. p-value corresponds to the difference over placebo measure and confidence interval.

Statistical analysis title	Difference from placebo for Week 6 is presented
Comparison groups	Placebo v GSK3196165 180mg
Number of subjects included in analysis	44
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.494 [20]
Method	Mixed Model Repeated Measures Analysis
Parameter estimate	Mean difference (net)
Point estimate	-0.33
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.28
upper limit	0.63

Notes:

[20] - MMRM model with fixed effects of Baseline Value, Treatment Group, Visit and Treatment Group by Visit Interaction was used. Unstructured covariance structure was used. p-value corresponds to the difference over placebo measure and confidence interval.

Statistical analysis title	Difference from placebo for Week 8 is presented
Comparison groups	Placebo v GSK3196165 180mg
Number of subjects included in analysis	44
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.107 [21]
Method	Mixed Model Repeated Measures Analysis
Parameter estimate	Mean difference (net)
Point estimate	-0.94

Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.08
upper limit	0.21

Notes:

[21] - MMRM model with fixed effects of Baseline Value, Treatment Group, Visit and Treatment Group by Visit Interaction was used. Unstructured covariance structure was used. p-value corresponds to the difference over placebo measure and confidence interval.

Statistical analysis title	Difference from placebo for Week 10 is presented
Comparison groups	Placebo v GSK3196165 180mg
Number of subjects included in analysis	44
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.092 [22]
Method	Mixed Model Repeated Measures Analysis
Parameter estimate	Mean difference (net)
Point estimate	-0.98
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.13
upper limit	0.17

Notes:

[22] - MMRM model with fixed effects of Baseline Value, Treatment Group, Visit and Treatment Group by Visit Interaction was used. Unstructured covariance structure was used. p-value corresponds to the difference over placebo measure and confidence interval.

Statistical analysis title	Difference from placebo for Week 12 is presented
Comparison groups	Placebo v GSK3196165 180mg
Number of subjects included in analysis	44
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.098 [23]
Method	Mixed Model Repeated Measures Analysis
Parameter estimate	Mean difference (net)
Point estimate	-1.01
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.22
upper limit	0.2

Notes:

[23] - MMRM model with fixed effects of Baseline Value, Treatment Group, Visit and Treatment Group by Visit Interaction was used. Unstructured covariance structure was used. p-value corresponds to the difference over placebo measure and confidence interval.

Secondary: Percentage of participants achieving a 30 percentage reduction from Baseline in 24 hours average hand pain intensity at each visit

End point title	Percentage of participants achieving a 30 percentage reduction from Baseline in 24 hours average hand pain intensity at each visit

End point description:

Participants were required to complete average pain NRS daily and rate the average hand pain over last

24 hours on a scale of 0 (no pain) to 10 (worst imaginable pain). The percentage of participants who achieved at least 30 percentage reduction from Baseline in the 24-hours average hand pain intensity as measured by daily NRS and averaged over 7 days prior to each visit is reported. Participants with missing data at a particular visit had been assumed to be non-responders.

End point type	Secondary

End point timeframe:

Baseline (Pre-dose, Day 1), Weeks 1, 2, 3, 4, 6, 8, 10, 12 and follow up (Week 22)

End point values	Placebo	GSK3196165 180mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	22[24]	22[25]		
Units: Percentage of participants				
Week 1|	0	9		
Week 2|	0	18		
Week 3|	5	23		
Week 4|	14	41		
Week 6|	23	45		
Week 8|	18	50		
Week 10|	18	50		
Week 12|	23	45		
Follow up (Week 22)|	23	27		

Notes:

[24] - Intent-to-Treat Population.

[25] - Intent-to-Treat Population.

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of participants achieving a 50 percentage reduction from Baseline in 24 hours average hand pain intensity at each visit

End point title	Percentage of participants achieving a 50 percentage reduction from Baseline in 24 hours average hand pain intensity at each visit

End point description:

Participants were required to complete average pain NRS daily and rate the average hand pain over last 24 hours on a scale of 0 (no pain) to 10 (worst imaginable pain). The percentage of participants who achieved at least 50 percentage reduction from Baseline in the 24-hours average hand pain intensity as measured by daily NRS and averaged over 7 days prior to each visit is presented. Participants with missing data at a particular visit had been assumed to be non-responders.

End point type	Secondary

End point timeframe:

Baseline (Pre-dose, Day 1), Weeks 1, 2, 3, 4, 6, 8, 10, 12 and follow up (Week 22)

End point values	Placebo	GSK3196165 180mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	22[26]	22[27]		
Units: Percentage of participants				
Week 1|	0	0		
Week 2|	0	9		
Week 3|	0	18		
Week 4|	0	23		
Week 6|	14	27		
Week 8|	14	41		
Week 10|	9	36		
Week 12|	14	41		
Follow up (Week 22)|	9	23		

Notes:

[26] - Intent-to-Treat Population.

[27] - Intent-to-Treat Population.

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of participants achieving a 30 percentage reduction from Baseline in 24 hours worst hand pain intensity at each visit

End point title	Percentage of participants achieving a 30 percentage reduction from Baseline in 24 hours worst hand pain intensity at each visit

End point description:

Participants were required to complete worst pain NRS daily and rate the hand pain at its worst over last 24 hours on a scale of 0 (no pain) to 10 (worst imaginable pain). The percentage of participants achieving at least 30 percentage reduction from Baseline in the 24-hours worst hand pain intensity as measured by daily NRS and averaged over 7 days prior to each visit is presented. Participants with missing data at a particular visit had been assumed to be non-responders.

End point type	Secondary

End point timeframe:

Baseline (Pre-dose, Day 1), Weeks 1, 2, 3, 4, 6, 8, 10, 12 and follow up (Week 22)

End point values	Placebo	GSK3196165 180mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	22[28]	22[29]		
Units: Percentage of participants				
Week 1|	0	9		
Week 2|	0	18		
Week 3|	0	23		
Week 4|	0	32		
Week 6|	9	36		
Week 8|	9	45		
Week 10|	14	45		
Week 12|	14	45		
Follow up (Week 22)|	14	32		

Notes:

[28] - Intent-to-Treat Population.

[29] - Intent-to-Treat Population.

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of participants achieving a 50 percentage reduction from Baseline in 24 hours worst hand pain intensity at each visit

End point title	Percentage of participants achieving a 50 percentage reduction from Baseline in 24 hours worst hand pain intensity at each visit

End point description:

Participants were required to complete worst pain NRS daily and rate the hand pain at its worst over last 24 hours on a scale of 0 (no pain) to 10 (worst imaginable pain). The percentage of participants achieving at least 50 percentage reduction from Baseline in the 24-hours worst hand pain intensity as measured by daily NRS and averaged over 7 days prior to each visit is presented. Participants with missing data at a particular visit had been assumed to be non-responders.

End point type	Secondary

End point timeframe:

Baseline (Pre-dose, Day 1), Weeks 1, 2, 3, 4, 6, 8, 10, 12 and follow up (Week 22)

End point values	Placebo	GSK3196165 180mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	22[30]	22[31]		
Units: Percentage of participants				
Week 1|	0	0		
Week 2|	0	5		
Week 3|	0	14		
Week 4|	0	18		
Week 6|	5	18		
Week 8|	5	32		
Week 10|	5	27		
Week 12|	9	36		
Follow up (Week 22)|	5	23		

Notes:

[30] - Intent-to-Treat Population.

[31] - Intent-to-Treat Population.

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in Australian Canadian Hand Osteoarthritis Index (AUSCAN) 3.1 NRS scores at each visit.

End point title	Change from Baseline in Australian Canadian Hand Osteoarthritis Index (AUSCAN) 3.1 NRS scores at each visit.

End point description:

The AUSCAN Index is a self-administered questionnaire consisting of a 15-item scale which measures pain (5 items), stiffness (1 item) and degree of disability/physical function (9 items) during the preceding 48 hours. All items are rated on NRS scale with anchors "0" (none) to "10" (extreme). The scores for the pain and physical function components were calculated as simple summation of the item scores relating to that domain, so the Pain component ranges from 0 (i.e. all pain item scores are scored 0 [none]) to 50 (i.e. all pain item scores are scored 10 [extreme]), and the Physical Function component ranges from 0 (i.e. all physical function item scores are scored 0 [none]) to 90 (i.e. all physical function item scores are scored 10 [extreme]). The total AUSCAN score was calculated as simple summation of the 15 item scores and therefore ranges from 0 to 150. Baseline is defined as Day 1 pre-dose value. Change from Baseline is equal to post-dose visit value minus Baseline value.

End point type	Secondary

End point timeframe:

Baseline (Day 1 Pre-dose), Weeks 1, 2, 4, 6, 8, 10, and 12

End point values	Placebo	GSK3196165 180mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	22[32]	22[33]		
Units: Scores on scale				
least squares mean (standard error)				
Pain, Week 1, n=22, 20|	0.8 (± 0.98)	-1.9 (± 1.03)		
Pain, Week 2, n=21, 21|	-1.8 (± 1.27)	-3.7 (± 1.28)		
Pain, Week 4, n=22, 21|	-3.5 (± 1.61)	-7.2 (± 1.64)		
Pain, Week 6, n=22, 21|	-6.6 (± 1.72)	-7.6 (± 1.76)		
Pain, Week 8, n=20, 20|	-4.9 (± 1.93)	-8.7 (± 1.97)		
Pain, Week 10, n=20, 20|	-5.3 (± 1.82)	-10.9 (± 1.87)		
Pain, Week 12, n=21, 19|	-4.6 (± 1.84)	-9.3 (± 1.91)		
Stiffness, Week 1, n= 22, 20|	-0.4 (± 0.29)	-0.6 (± 0.31)		
Stiffness, Week 2, n= 21, 21|	-0.8 (± 0.33)	-1.1 (± 0.33)		
Stiffness, Week 4, n= 22, 21|	-1.2 (± 0.41)	-1.8 (± 0.42)		
Stiffness, Week 6, n= 22, 21|	-1.4 (± 0.39)	-1.6 (± 0.40)		
Stiffness, Week 8, n= 20, 20|	-1.2 (± 0.41)	-1.9 (± 0.42)		
Stiffness, Week 10, n= 20, 20|	-1.6 (± 0.44)	-2.2 (± 0.45)		
Stiffness, Week 12, n= 21, 19|	-1.5 (± 0.45)	-2.2 (± 0.47)		
Physical function, Week 1, n=22, 20|	-0.7 (± 2.08)	-3.6 (± 2.16)		
Physical function, Week 2, n=21,21|	-2.8 (± 2.35)	-5.7 (± 2.37)		
Physical function, Week 4, n=22, 21|	-6.4 (± 3.01)	-11.3 (± 3.07)		
Physical function, Week 6, n=22, 21|	-9.1 (± 3.25)	-11.8 (± 3.32)		
Physical function, Week 8, n=20, 20|	-8.3 (± 3.57)	-13.2 (± 3.64)		
Physical function, Week 10, n=20, 20|	-9.0 (± 3.82)	-15.2 (± 3.92)		
Physical function, Week 12, n=21, 19|	-7.2 (± 3.74)	-15.4 (± 3.87)		
Total, Week 1, n= 22, 20|	-0.5 (± 3.07)	-6.0 (± 3.20)		
Total, Week 2, n= 21, 21|	-5.7 (± 3.66)	-10.4 (± 3.70)		
Total, Week 4, n= 22, 21|	-11.4 (± 4.72)	-20.1 (± 4.83)		
Total, Week 6, n= 22, 21|	-17.3 (± 5.17)	-20.7 (± 5.28)		
Total, Week 8, n= 20, 20|	-14.6 (± 5.70)	-23.6 (± 5.81)		
Total, Week 10, n= 20, 20|	-16.1 (± 5.88)	-28.2 (± 6.04)		
Total, Week 12, n= 21, 19|	-13.5 (± 5.92)	-26.7 (± 6.12)		

Notes:

[32] - Intent-to-Treat Population.

[33] - Intent-to-Treat Population.

Statistical analyses

Statistical analysis title	For Pain component, Week 1
Comparison groups	Placebo v GSK3196165 180mg
Number of subjects included in analysis	44
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.061 [34]
Method	Mixed Model Repeated Measures Analysis
Parameter estimate	Mean difference (net)
Point estimate	-2.8
Confidence interval	
level	95 %
sides	2-sided
lower limit	-5.6
upper limit	0.1

Notes:

[34] - MMRM model with fixed effects of Baseline Value, Treatment Group, Visit and Treatment Group by Visit Interaction was used. Unstructured covariance structure was used. p-value corresponds to the difference over placebo measure and confidence interval

Statistical analysis title	For Pain component, Week 2
Comparison groups	Placebo v GSK3196165 180mg
Number of subjects included in analysis	44
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.282 [35]
Method	Mixed Model Repeated Measures Analysis
Parameter estimate	Mean difference (net)
Point estimate	-2
Confidence interval	
level	95 %
sides	2-sided
lower limit	-5.6
upper limit	1.7

Notes:

[35] - MMRM model with fixed effects of Baseline Value, Treatment Group, Visit and Treatment Group by Visit Interaction was used. Unstructured covariance structure was used. p-value corresponds to the difference over placebo measure and confidence interval.

Statistical analysis title	For Pain componentWeek 4
Comparison groups	Placebo v GSK3196165 180mg

Number of subjects included in analysis	44
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.113 [36]
Method	Mixed Model Repeated Measures Analysis
Parameter estimate	Mean difference (net)
Point estimate	-3.7
Confidence interval	
level	95 %
sides	2-sided
lower limit	-8.4
upper limit	0.9

Notes:

[36] - MMRM model with fixed effects of Baseline Value, Treatment Group, Visit and Treatment Group by Visit Interaction was used. Unstructured covariance structure was used. p-value corresponds to the difference over placebo measure and confidence interval

Statistical analysis title	For Pain component, Week 6
Comparison groups	Placebo v GSK3196165 180mg
Number of subjects included in analysis	44
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.695 [37]
Method	Mixed Model Repeated Measures Analysis
Parameter estimate	Mean difference (net)
Point estimate	-1
Confidence interval	
level	95 %
sides	2-sided
lower limit	-5.9
upper limit	4

Notes:

[37] - MMRM model with fixed effects of Baseline Value, Treatment Group, Visit and Treatment Group by Visit Interaction was used. Unstructured covariance structure was used. p-value corresponds to the difference over placebo measure and confidence interval

Statistical analysis title	For Pain component, Week 8
Comparison groups	Placebo v GSK3196165 180mg
Number of subjects included in analysis	44
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.176 [38]
Method	Mixed Model Repeated Measures Analysis
Parameter estimate	Mean difference (net)
Point estimate	-3.8
Confidence interval	
level	95 %
sides	2-sided
lower limit	-9.4
upper limit	1.8

Notes:

[38] - MMRM model with fixed effects of Baseline Value, Treatment Group, Visit and Treatment Group by Visit Interaction was used. Unstructured covariance structure was used. p-value corresponds to the difference over placebo measure and confidence interval

Statistical analysis title	For Pain component, Week 10
Comparison groups	Placebo v GSK3196165 180mg
Number of subjects included in analysis	44
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.041 [39]
Method	Mixed Model Repeated Measures Analysis
Parameter estimate	Mean difference (net)
Point estimate	-5.5
Confidence interval	
level	95 %
sides	2-sided
lower limit	-10.8
upper limit	-0.2

Notes:

[39] - MMRM model with fixed effects of Baseline Value, Treatment Group, Visit and Treatment Group by Visit Interaction was used. Unstructured covariance structure was used. p-value corresponds to the difference over placebo measure and confidence interval

Statistical analysis title	For Pain component, Week 12
Comparison groups	Placebo v GSK3196165 180mg
Number of subjects included in analysis	44
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.082 [40]
Method	Mixed Model Repeated Measures Analysis
Parameter estimate	Mean difference (net)
Point estimate	-4.7
Confidence interval	
level	95 %
sides	2-sided
lower limit	-10.1
upper limit	0.6

Notes:

[40] - MMRM model with fixed effects of Baseline Value, Treatment Group, Visit and Treatment Group by Visit Interaction was used. Unstructured covariance structure was used. p-value corresponds to the difference over placebo measure and confidence interval

Statistical analysis title	For Stiffness component, Week 1
Comparison groups	Placebo v GSK3196165 180mg
Number of subjects included in analysis	44
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.587 [41]
Method	Mixed Model Repeated Measures Analysis
Parameter estimate	Mean difference (net)
Point estimate	-0.2

Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.1
upper limit	0.6

Notes:

[41] - MMRM model with fixed effects of Baseline Value, Treatment Group, Visit and Treatment Group by Visit Interaction was used. Unstructured covariance structure was used. p-value corresponds to the difference over placebo measure and confidence interval

Statistical analysis title	For Stiffness component, Week 2
Comparison groups	Placebo v GSK3196165 180mg
Number of subjects included in analysis	44
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.457 [42]
Method	Mixed Model Repeated Measures Analysis
Parameter estimate	Mean difference (net)
Point estimate	-0.4
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.3
upper limit	0.6

Notes:

[42] - MMRM model with fixed effects of Baseline Value, Treatment Group, Visit and Treatment Group by Visit Interaction was used. Unstructured covariance structure was used. p-value corresponds to the difference over placebo measure and confidence interval

Statistical analysis title	For Stiffness component, Week 4
Comparison groups	Placebo v GSK3196165 180mg
Number of subjects included in analysis	44
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.298 [43]
Method	Mixed Model Repeated Measures Analysis
Parameter estimate	Mean difference (net)
Point estimate	-0.6
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.8
upper limit	0.6

Notes:

[43] - MMRM model with fixed effects of Baseline Value, Treatment Group, Visit and Treatment Group by Visit Interaction was used. Unstructured covariance structure was used. p-value corresponds to the difference over placebo measure and confidence interval

Statistical analysis title	For Stiffness component, Week 6
Comparison groups	Placebo v GSK3196165 180mg

Number of subjects included in analysis	44
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.726 [44]
Method	Mixed Model Repeated Measures Analysis
Parameter estimate	Mean difference (net)
Point estimate	-0.2
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.3
upper limit	0.9

Notes:

[44] - MMRM model with fixed effects of Baseline Value, Treatment Group, Visit and Treatment Group by Visit Interaction was used. Unstructured covariance structure was used. p-value corresponds to the difference over placebo measure and confidence interval.

Statistical analysis title	For Stiffness component, Week 8
Comparison groups	Placebo v GSK3196165 180mg
Number of subjects included in analysis	44
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.213 [45]
Method	Mixed Model Repeated Measures Analysis
Parameter estimate	Mean difference (net)
Point estimate	-0.7
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.9
upper limit	0.4

Notes:

[45] - MMRM model with fixed effects of Baseline Value, Treatment Group, Visit and Treatment Group by Visit Interaction was used. Unstructured covariance structure was used. p-value corresponds to the difference over placebo measure and confidence interval.

Statistical analysis title	For Stiffness component, Week 10
Comparison groups	Placebo v GSK3196165 180mg
Number of subjects included in analysis	44
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.331 [46]
Method	Mixed Model Repeated Measures Analysis
Parameter estimate	Mean difference (net)
Point estimate	-0.6
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.9
upper limit	0.7

Notes:

[46] - MMRM model with fixed effects of Baseline Value, Treatment Group, Visit and Treatment Group by Visit Interaction was used. Unstructured covariance structure was used. p-value corresponds to the difference over placebo measure and confidence interval.

Statistical analysis title	For Stiffness component, Week 12
Comparison groups	Placebo v GSK3196165 180mg
Number of subjects included in analysis	44
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.248 [47]
Method	Mixed Model Repeated Measures Analysis
Parameter estimate	Mean difference (net)
Point estimate	-0.8
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.1
upper limit	0.6

Notes:

[47] - MMRM model with fixed effects of Baseline Value, Treatment Group, Visit and Treatment Group by Visit Interaction was used. Unstructured covariance structure was used. p-value corresponds to the difference over placebo measure and confidence interval.

Statistical analysis title	For Physical Function component, Week 1
Comparison groups	Placebo v GSK3196165 180mg
Number of subjects included in analysis	44
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.35 [48]
Method	Mixed Model Repeated Measures Analysis
Parameter estimate	Mean difference (net)
Point estimate	-2.9
Confidence interval	
level	95 %
sides	2-sided
lower limit	-9
upper limit	3.3

Notes:

[48] - MMRM model with fixed effects of Baseline Value, Treatment Group, Visit and Treatment Group by Visit Interaction was used. Unstructured covariance structure was used. p-value corresponds to the difference over placebo measure and confidence interval.

Statistical analysis title	For Physical Function component, Week 2
Comparison groups	Placebo v GSK3196165 180mg
Number of subjects included in analysis	44
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.383 [49]
Method	Mixed Model Repeated Measures Analysis
Parameter estimate	Mean difference (net)
Point estimate	-3

Confidence interval	
level	95 %
sides	2-sided
lower limit	-9.8
upper limit	3.8

Notes:

[49] - MMRM model with fixed effects of Baseline Value, Treatment Group, Visit and Treatment Group by Visit Interaction was used. Unstructured covariance structure was used. p-value corresponds to the difference over placebo measure and confidence interval.

Statistical analysis title	For Physical Function component, Week 4
Comparison groups	Placebo v GSK3196165 180mg
Number of subjects included in analysis	44
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.271 [50]
Method	Mixed Model Repeated Measures Analysis
Parameter estimate	Mean difference (net)
Point estimate	-4.8
Confidence interval	
level	95 %
sides	2-sided
lower limit	-13.5
upper limit	3.9

Notes:

[50] - MMRM model with fixed effects of Baseline Value, Treatment Group, Visit and Treatment Group by Visit Interaction was used. Unstructured covariance structure was used. p-value corresponds to the difference over placebo measure and confidence interval.

Statistical analysis title	For Physical Function component, Week 6
Comparison groups	Placebo v GSK3196165 180mg
Number of subjects included in analysis	44
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.565 [51]
Method	Mixed Model Repeated Measures Analysis
Parameter estimate	Mean difference (net)
Point estimate	-2.7
Confidence interval	
level	95 %
sides	2-sided
lower limit	-12.1
upper limit	6.7

Notes:

[51] - MMRM model with fixed effects of Baseline Value, Treatment Group, Visit and Treatment Group by Visit Interaction was used. Unstructured covariance structure was used. p-value corresponds to the difference over placebo measure and confidence interval

Statistical analysis title	For Physical Function component, Week 8
Comparison groups	Placebo v GSK3196165 180mg

Number of subjects included in analysis	44
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.343 [52]
Method	Mixed Model Repeated Measures Analysis
Parameter estimate	Mean difference (net)
Point estimate	-4.9
Confidence interval	
level	95 %
sides	2-sided
lower limit	-15.2
upper limit	5.4

Notes:

[52] - MMRM model with fixed effects of Baseline Value, Treatment Group, Visit and Treatment Group by Visit Interaction was used. Unstructured covariance structure was used. p-value corresponds to the difference over placebo measure and confidence interval.

Statistical analysis title	For Physical Function component, Week 10
Comparison groups	Placebo v GSK3196165 180mg
Number of subjects included in analysis	44
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.266 [53]
Method	Mixed Model Repeated Measures Analysis
Parameter estimate	Mean difference (net)
Point estimate	-6.2
Confidence interval	
level	95 %
sides	2-sided
lower limit	-17.3
upper limit	4.9

Notes:

[53] - MMRM model with fixed effects of Baseline Value, Treatment Group, Visit and Treatment Group by Visit Interaction was used. Unstructured covariance structure was used. p-value corresponds to the difference over placebo measure and confidence interval.

Statistical analysis title	For Physical Function component, Week 12
Comparison groups	Placebo v GSK3196165 180mg
Number of subjects included in analysis	44
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.136 [54]
Method	Mixed Model Repeated Measures Analysis
Parameter estimate	Mean difference (net)
Point estimate	-8.2
Confidence interval	
level	95 %
sides	2-sided
lower limit	-19.1
upper limit	2.7

Notes:

[54] - MMRM model with fixed effects of Baseline Value, Treatment Group, Visit and Treatment Group by Visit Interaction was used. Unstructured covariance structure was used. p-value corresponds to the difference over placebo measure and confidence interval.

Statistical analysis title	For Total of all component scores, Week 1
Comparison groups	Placebo v GSK3196165 180mg
Number of subjects included in analysis	44
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.23 [55]
Method	Mixed Model Repeated Measures Analysis
Parameter estimate	Mean difference (net)
Point estimate	-5.5
Confidence interval	
level	95 %
sides	2-sided
lower limit	-14.5
upper limit	3.6

Notes:

[55] - MMRM model with fixed effects of Baseline Value, Treatment Group, Visit and Treatment Group by Visit Interaction was used. Unstructured covariance structure was used. p-value corresponds to the difference over placebo measure and confidence interval.

Statistical analysis title	For Total of all component scores, Week 2
Comparison groups	Placebo v GSK3196165 180mg
Number of subjects included in analysis	44
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.381 [56]
Method	Mixed Model Repeated Measures Analysis
Parameter estimate	Mean difference (net)
Point estimate	-4.6
Confidence interval	
level	95 %
sides	2-sided
lower limit	-15.2
upper limit	5.9

Notes:

[56] - MMRM model with fixed effects of Baseline Value, Treatment Group, Visit and Treatment Group by Visit Interaction was used. Unstructured covariance structure was used. p-value corresponds to the difference over placebo measure and confidence interval.

Statistical analysis title	For Total of all component scores, Week 4
Comparison groups	Placebo v GSK3196165 180mg
Number of subjects included in analysis	44
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.207 [57]
Method	Mixed Model Repeated Measures Analysis
Parameter estimate	Mean difference (net)
Point estimate	-8.7

Confidence interval	
level	95 %
sides	2-sided
lower limit	-22.4
upper limit	5

Notes:

[57] - MMRM model with fixed effects of Baseline Value, Treatment Group, Visit and Treatment Group by Visit Interaction was used. Unstructured covariance structure was used. p-value corresponds to the difference over placebo measure and confidence interval.

Statistical analysis title	For Total of all component scores, Week 6
Comparison groups	Placebo v GSK3196165 180mg
Number of subjects included in analysis	44
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.648 [58]
Method	Mixed Model Repeated Measures Analysis
Parameter estimate	Mean difference (net)
Point estimate	-3.4
Confidence interval	
level	95 %
sides	2-sided
lower limit	-18.4
upper limit	11.6

Notes:

[58] - MMRM model with fixed effects of Baseline Value, Treatment Group, Visit and Treatment Group by Visit Interaction was used. Unstructured covariance structure was used. p-value corresponds to the difference over placebo measure and confidence interval.

Statistical analysis title	For Total of all component scores, Week 8
Comparison groups	Placebo v GSK3196165 180mg
Number of subjects included in analysis	44
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.278 [59]
Method	Mixed Model Repeated Measures Analysis
Parameter estimate	Mean difference (net)
Point estimate	-9
Confidence interval	
level	95 %
sides	2-sided
lower limit	-25.4
upper limit	7.5

Notes:

[59] - MMRM model with fixed effects of Baseline Value, Treatment Group, Visit and Treatment Group by Visit Interaction was used. Unstructured covariance structure was used. p-value corresponds to the difference over placebo measure and confidence interval.

Statistical analysis title	For Total of all component scores, Week 10
Comparison groups	Placebo v GSK3196165 180mg

Number of subjects included in analysis	44
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.16 [60]
Method	Mixed Model Repeated Measures Analysis
Parameter estimate	Mean difference (net)
Point estimate	-12.1
Confidence interval	
level	95 %
sides	2-sided
lower limit	-29.1
upper limit	5

Notes:

[60] - MMRM model with fixed effects of Baseline Value, Treatment Group, Visit and Treatment Group by Visit Interaction was used. Unstructured covariance structure was used. p-value corresponds to the difference over placebo measure and confidence interval.

Statistical analysis title	For Total of all component scores, Week 12
Comparison groups	Placebo v GSK3196165 180mg
Number of subjects included in analysis	44
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.127 [61]
Method	Mixed Model Repeated Measures Analysis
Parameter estimate	Mean difference (net)
Point estimate	-13.3
Confidence interval	
level	95 %
sides	2-sided
lower limit	-30.5
upper limit	3.9

Notes:

[61] - MMRM model with fixed effects of Baseline Value, Treatment Group, Visit and Treatment Group by Visit Interaction was used. Unstructured covariance structure was used. p-value corresponds to the difference over placebo measure and confidence interval.

Secondary: Change from Baseline in number of soft tissue swollen hand joints at each visit

End point title	Change from Baseline in number of soft tissue swollen hand joints at each visit

End point description:

Swollen Hand Joint Count was measured by the total number of soft tissue swollen hand joints out of a possible 30 joints: 8 distal interphalangeal, 8 proximal interphalangeal, 2 interphalangeal joints, 10 metacarpophalangeal joints, 2 carpometacarpal joint across both hands. In case of missing observations for soft tissue swollen hand joints then the remaining observations were assessed and weighted by dividing the number presented by the number of non-missing, and by multiplying by 30 for the joint count. Baseline is defined as Day 1 pre-dose value. Change from Baseline is equal to post-dose visit value minus Baseline value. n=X in category titles represents the number of participants with non-missing data at the specified time-point. Only non-missing data is included in the MMRM model.

End point type	Secondary

End point timeframe:

Baseline (Day 1 Pre-dose), Weeks 1, 2, 4, 6, 8, 10, and 12

End point values	Placebo	GSK3196165 180mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	22[62]	22[63]		
Units: Swollen joints				
least squares mean (standard error)				
Week 1, n = 22, 21|	-0.3 (± 0.64)	-0.3 (± 0.66)		
Week 2, n = 21, 21|	-1.6 (± 0.85)	-1.2 (± 0.86)		
Week 4, n = 22, 21|	-1.6 (± 0.76)	-2.1 (± 0.78)		
Week 6, n = 22, 21|	-3.7 (± 0.83)	-2.3 (± 0.85)		
Week 8, n = 20, 20|	-3.0 (± 0.92)	-2.8 (± 0.94)		
Week 10, n = 20, 20|	-2.6 (± 1.08)	-2.9 (± 1.10)		
Week 12, n = 21, 19|	-2.9 (± 0.91)	-3.1 (± 0.93)		

Notes:

[62] - Intent-to-Treat Population.

[63] - Intent-to-Treat Population.

Statistical analyses

Statistical analysis title	Difference from placebo for Week 1 is presented
Comparison groups	Placebo v GSK3196165 180mg
Number of subjects included in analysis	44
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.957 [64]
Method	Mixed Model Repeated Measures Analysis
Parameter estimate	Mean difference (net)
Point estimate	0
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.9
upper limit	1.8

Notes:

[64] - MMRM model with fixed effects of Baseline Value, Treatment Group, Visit and Treatment Group by Visit Interaction was used. Unstructured covariance structure was used. p-value corresponds to the difference over placebo measure and confidence interval.

Statistical analysis title	Difference from placebo for Week 2 is presented
Comparison groups	Placebo v GSK3196165 180mg
Number of subjects included in analysis	44
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.775 [65]
Method	Mixed Model Repeated Measures Analysis
Parameter estimate	Mean difference (net)
Point estimate	0.3
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.1
upper limit	2.8

Notes:

[65] - MMRM model with fixed effects of Baseline Value, Treatment Group, Visit and Treatment Group by Visit Interaction was used. Unstructured covariance structure was used. p-value corresponds to the difference over placebo measure and confidence interval.

Statistical analysis title	Difference from placebo for Week 4 is presented
Comparison groups	Placebo v GSK3196165 180mg
Number of subjects included in analysis	44
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.624 [66]
Method	Mixed Model Repeated Measures Analysis
Parameter estimate	Mean difference (net)
Point estimate	-0.5
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.7
upper limit	1.7

Notes:

[66] - MMRM model with fixed effects of Baseline Value, Treatment Group, Visit and Treatment Group by Visit Interaction was used. Unstructured covariance structure was used. p-value corresponds to the difference over placebo measure and confidence interval.

Statistical analysis title	Difference from placebo for Week 6 is presented
Comparison groups	Placebo v GSK3196165 180mg
Number of subjects included in analysis	44
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.243 [67]
Method	Mixed Model Repeated Measures Analysis
Parameter estimate	Mean difference (net)
Point estimate	1.4
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1
upper limit	3.8

Notes:

[67] - MMRM model with fixed effects of Baseline Value, Treatment Group, Visit and Treatment Group by Visit Interaction was used. Unstructured covariance structure was used. p-value corresponds to the difference over placebo measure and confidence interval.

Statistical analysis title	Difference from placebo for Week 8 is presented
Comparison groups	Placebo v GSK3196165 180mg
Number of subjects included in analysis	44
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.875 [68]
Method	Mixed Model Repeated Measures Analysis
Parameter estimate	Mean difference (net)
Point estimate	0.2

Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.5
upper limit	2.9

Notes:

[68] - MMRM model with fixed effects of Baseline Value, Treatment Group, Visit and Treatment Group by Visit Interaction was used. Unstructured covariance structure was used. p-value corresponds to the difference over placebo measure and confidence interval.

Statistical analysis title	Difference from placebo for Week 10 is presented
Comparison groups	Placebo v GSK3196165 180mg
Number of subjects included in analysis	44
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.848 [69]
Method	Mixed Model Repeated Measures Analysis
Parameter estimate	Mean difference (net)
Point estimate	-0.3
Confidence interval	
level	95 %
sides	2-sided
lower limit	-3.4
upper limit	2.8

Notes:

[69] - MMRM model with fixed effects of Baseline Value, Treatment Group, Visit and Treatment Group by Visit Interaction was used. Unstructured covariance structure was used. p-value corresponds to the difference over placebo measure and confidence interval.

Statistical analysis title	Difference from placebo for Week 12 is presented
Comparison groups	Placebo v GSK3196165 180mg
Number of subjects included in analysis	44
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.883 [70]
Method	Mixed Model Repeated Measures Analysis
Parameter estimate	Mean difference (net)
Point estimate	-0.2
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.8
upper limit	2.4

Notes:

[70] - MMRM model with fixed effects of Baseline Value, Treatment Group, Visit and Treatment Group by Visit Interaction was used. Unstructured covariance structure was used. p-value corresponds to the difference over placebo measure and confidence interval.

Secondary: Change from Baseline in number of tender hand joints at each visit

End point title	Change from Baseline in number of tender hand joints at each visit

End point description:

Tender Hand Joint Count was measured by the total number of tender joints out of a possible 30 joints: 8 distal interphalangeal, 8 proximal interphalangeal, 2 interphalangeal joints, 10 metacarpophalangeal joints, 2 carpometacarpal joints across both hands. A joint was considered tender if it was scored >0 on

the tender joint severity scale. Joints were rated 0=no pain/tenderness, 1=mild pain, 2=moderate pain and 3=severe pain. Baseline is defined as Day 1 pre-dose value. Change from Baseline is equal to post-dose visit value minus Baseline value. n=X in category titles represents the number of participants with non-missing data at the specified time-point. Only non-missing data is included in the MMRM model.

End point type	Secondary

End point timeframe:

Baseline, Weeks 1, 2, 4, 6, 8, 10, and 12

End point values	Placebo	GSK3196165 180mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	22[71]	22[72]		
Units: Scores on scale				
least squares mean (standard error)				
Week 1, n= 22, 21|	-0.6 (± 1.10)	-1.8 (± 1.13)		
Week 2, n= 21, 21|	-1.7 (± 1.15)	-2.1 (± 1.17)		
Week 4, n= 22, 21|	-1.1 (± 1.33)	-3.0 (± 1.36)		
Week 6, n= 22, 21|	-3.7 (± 1.27)	-4.2 (± 1.30)		
Week 8, n= 20, 20|	-2.4 (± 1.36)	-3.9 (± 1.39)		
Week 10, n= 20, 20|	-3.7 (± 1.45)	-4.4 (± 1.48)		
Week 12, n= 21, 19|	-3.5 (± 1.46)	-4.0 (± 1.51)		

Notes:

[71] - Intent-to-Treat Population.

[72] - Intent-to-Treat Population.

Statistical analyses

Statistical analysis title	Difference from placebo for Week 1 is presented
Comparison groups	Placebo v GSK3196165 180mg
Number of subjects included in analysis	44
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.463 [73]
Method	Mixed Model Repeated Measures Analysis
Parameter estimate	Mean difference (net)
Point estimate	-1.2
Confidence interval	
level	95 %
sides	2-sided
lower limit	-4.4
upper limit	2

Notes:

[73] - MMRM model with fixed effects of Baseline Value, Treatment Group, Visit and Treatment Group by Visit Interaction was used. Unstructured covariance structure was used. p-value corresponds to the difference over placebo measure and confidence interval.

Statistical analysis title	Difference from placebo for Week 2 is presented
Comparison groups	Placebo v GSK3196165 180mg

Number of subjects included in analysis	44
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.809 [74]
Method	Mixed Model Repeated Measures Analysis
Parameter estimate	Mean difference (net)
Point estimate	-0.4
Confidence interval	
level	95 %
sides	2-sided
lower limit	-3.7
upper limit	2.9

Notes:

[74] - MMRM model with fixed effects of Baseline Value, Treatment Group, Visit and Treatment Group by Visit Interaction was used. Unstructured covariance structure was used. p-value corresponds to the difference over placebo measure and confidence interval.

Statistical analysis title	Difference from placebo for Week 4 is presented
Comparison groups	Placebo v GSK3196165 180mg
Number of subjects included in analysis	44
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.324 [75]
Method	Mixed Model Repeated Measures Analysis
Parameter estimate	Mean difference (net)
Point estimate	-1.9
Confidence interval	
level	95 %
sides	2-sided
lower limit	-5.8
upper limit	2

Notes:

[75] - MMRM model with fixed effects of Baseline Value, Treatment Group, Visit and Treatment Group by Visit Interaction was used. Unstructured covariance structure was used. p-value corresponds to the difference over placebo measure and confidence interval.

Statistical analysis title	Difference from placebo for Week 6 is presented
Comparison groups	Placebo v GSK3196165 180mg
Number of subjects included in analysis	44
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.783 [76]
Method	Mixed Model Repeated Measures Analysis
Parameter estimate	Mean difference (net)
Point estimate	-0.5
Confidence interval	
level	95 %
sides	2-sided
lower limit	-4.2
upper limit	3.2

Notes:

[76] - MMRM model with fixed effects of Baseline Value, Treatment Group, Visit and Treatment Group by Visit Interaction was used. Unstructured covariance structure was used. p-value corresponds to the difference over placebo measure and confidence interval.

Statistical analysis title	Difference from placebo for Week 8 is presented
Comparison groups	Placebo v GSK3196165 180mg
Number of subjects included in analysis	44
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.464 [77]
Method	Mixed Model Repeated Measures Analysis
Parameter estimate	Mean difference (net)
Point estimate	-1.4
Confidence interval	
level	95 %
sides	2-sided
lower limit	-5.4
upper limit	2.5

Notes:

[77] - MMRM model with fixed effects of Baseline Value, Treatment Group, Visit and Treatment Group by Visit Interaction was used. Unstructured covariance structure was used. p-value corresponds to the difference over placebo measure and confidence interval.

Statistical analysis title	Difference from placebo for Week 10 is presented
Comparison groups	Placebo v GSK3196165 180mg
Number of subjects included in analysis	44
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.736 [78]
Method	Mixed Model Repeated Measures Analysis
Parameter estimate	Mean difference (net)
Point estimate	-0.7
Confidence interval	
level	95 %
sides	2-sided
lower limit	-4.9
upper limit	3.5

Notes:

[78] - MMRM model with fixed effects of Baseline Value, Treatment Group, Visit and Treatment Group by Visit Interaction was used. Unstructured covariance structure was used. p-value corresponds to the difference over placebo measure and confidence interval.

Statistical analysis title	Difference from placebo for Week 12 is presented
Comparison groups	Placebo v GSK3196165 180mg
Number of subjects included in analysis	44
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.806 [79]
Method	Mixed Model Repeated Measures Analysis
Parameter estimate	Mean difference (net)
Point estimate	-0.5

Confidence interval	
level	95 %
sides	2-sided
lower limit	-4.8
upper limit	3.7

Notes:

[79] - MMRM model with fixed effects of Baseline Value, Treatment Group, Visit and Treatment Group by Visit Interaction was used. Unstructured covariance structure was used. p-value corresponds to the difference over placebo measure and confidence interval.

Secondary: Change from Baseline in physician global assessment (PhGA) of disease activity

End point title	Change from Baseline in physician global assessment (PhGA) of disease activity

End point description:

Physicians were required to complete the global assessment of disease activity using single PhGA item with a NRS ranging from 0 (none) to 10 (extremely active). Baseline was defined as Day 1 pre-dose value. Change from Baseline is equal to post-dose visit value minus Baseline value. n=X in category titles represents the number of participants with non-missing data at the specified time-point. Only non-missing data is included in the MMRM model.

End point type	Secondary

End point timeframe:

Baseline (Day 1 Pre-dose), Weeks 2, 4, 8, and 12

End point values	Placebo	GSK3196165 180mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	22[80]	22[81]		
Units: Scores on scale				
least squares mean (standard error)				
Week 2, n= 19, 14|	-1.8 (± 0.39)	-1.5 (± 0.45)		
Week 4, n= 20, 15|	-2.1 (± 0.44)	-2.6 (± 0.50)		
Week 8, n= 17, 15|	-2.2 (± 0.52)	-3.4 (± 0.57)		
Week 12, n= 18, 14|	-2.7 (± 0.56)	-3.0 (± 0.63)		

Notes:

[80] - Intent-to-Treat Population.

[81] - Intent-to-Treat Population.

Statistical analyses

Statistical analysis title	Difference from placebo for Week 2 is presented
Comparison groups	Placebo v GSK3196165 180mg
Number of subjects included in analysis	44
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.586 [82]
Method	Mixed Model Repeated Measures Analysis
Parameter estimate	Mean difference (net)
Point estimate	0.3

Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.9
upper limit	1.6

Notes:

[82] - MMRM model with fixed effects of Baseline Value, Treatment Group, Visit and Treatment Group by Visit Interaction was used. Unstructured covariance structure was used. p-value corresponds to the difference over placebo measure and confidence interval.

Statistical analysis title	Difference from placebo for Week 4 is presented
Comparison groups	Placebo v GSK3196165 180mg
Number of subjects included in analysis	44
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.416 [83]
Method	Mixed Model Repeated Measures Analysis
Parameter estimate	Mean difference (net)
Point estimate	-0.5
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.9
upper limit	0.8

Notes:

[83] - MMRM model with fixed effects of Baseline Value, Treatment Group, Visit and Treatment Group by Visit Interaction was used. Unstructured covariance structure was used. p-value corresponds to the difference over placebo measure and confidence interval.

Statistical analysis title	Difference from placebo for Week 8 is presented
Comparison groups	Placebo v GSK3196165 180mg
Number of subjects included in analysis	44
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.12 [84]
Method	Mixed Model Repeated Measures Analysis
Parameter estimate	Mean difference (net)
Point estimate	-1.2
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.8
upper limit	0.3

Notes:

[84] - MMRM model with fixed effects of Baseline Value, Treatment Group, Visit and Treatment Group by Visit Interaction was used. Unstructured covariance structure was used. p-value corresponds to the difference over placebo measure and confidence interval.

Statistical analysis title	Difference from placebo for Week 12 is presented
Comparison groups	Placebo v GSK3196165 180mg

Number of subjects included in analysis	44
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.687 [85]
Method	Mixed Model Repeated Measures Analysis
Parameter estimate	Mean difference (net)
Point estimate	-0.3
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.1
upper limit	1.4

Notes:

[85] - MMRM model with fixed effects of Baseline Value, Treatment Group, Visit and Treatment Group by Visit Interaction was used. Unstructured covariance structure was used. p-value corresponds to the difference over placebo measure and confidence interval.

Secondary: Change from Baseline in patient global assessment (PtGA) of disease activity

End point title	Change from Baseline in patient global assessment (PtGA) of disease activity

End point description:

Participants were required to complete the global assessment of disease activity using single PtGA item with an NRS ranging from 0 (very well) to 10 (very poor). Baseline was defined as Day 1 pre-dose value. Change from Baseline is equal to post-dose visit value minus Baseline value. n=X in category titles represents the number of participants with non-missing data at the specified time-point. Only non-missing data is included in the MMRM model.

End point type	Secondary

End point timeframe:

Baseline, Weeks 2, 4, 8, and 12

End point values	Placebo	GSK3196165 180mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	22[86]	22[87]		
Units: Scores on scale				
least squares mean (standard error)				
Week 2, n= 20, 21|	-0.4 (± 0.36)	-0.6 (± 0.35)		
Week 4, n= 21, 21|	-0.6 (± 0.42)	-1.3 (± 0.42)		
Week 8, n= 19, 20|	-0.9 (± 0.47)	-1.8 (± 0.46)		
Week 12, n= 20, 19|	-0.7 (± 0.46)	-1.8 (± 0.46)		

Notes:

[86] - Intent-to-Treat Population.

[87] - Intent-to-Treat Population.

Statistical analyses

Statistical analysis title	Difference from placebo for Week 2 is presented
Comparison groups	Placebo v GSK3196165 180mg

Number of subjects included in analysis	44
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.651 [88]
Method	Mixed Model Repeated Measures Analysis
Parameter estimate	Mean difference (net)
Point estimate	-0.2
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.3
upper limit	0.8

Notes:

[88] - MMRM model with fixed effects of Baseline Value, Treatment Group, Visit and Treatment Group by Visit Interaction was used. Unstructured covariance structure was used. p-value corresponds to the difference over placebo measure and confidence interval.

Statistical analysis title	Difference from placebo for Week 4 is presented
Comparison groups	Placebo v GSK3196165 180mg
Number of subjects included in analysis	44
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.271 [89]
Method	Mixed Model Repeated Measures Analysis
Parameter estimate	Mean difference (net)
Point estimate	-0.7
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.9
upper limit	0.5

Notes:

[89] - MMRM model with fixed effects of Baseline Value, Treatment Group, Visit and Treatment Group by Visit Interaction was used. Unstructured covariance structure was used. p-value corresponds to the difference over placebo measure and confidence interval.

Statistical analysis title	Difference from placebo for Week 8 is presented
Comparison groups	Placebo v GSK3196165 180mg
Number of subjects included in analysis	44
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.186 [90]
Method	Mixed Model Repeated Measures Analysis
Parameter estimate	Mean difference (net)
Point estimate	-0.9
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.2
upper limit	0.4

Notes:

[90] - MMRM model with fixed effects of Baseline Value, Treatment Group, Visit and Treatment Group by Visit Interaction was used. Unstructured covariance structure was used. p-value corresponds to the difference over placebo measure and confidence interval.

Statistical analysis title	Difference from placebo for Week 12 is presented
Comparison groups	Placebo v GSK3196165 180mg
Number of subjects included in analysis	44
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.109 [91]
Method	Mixed Model Repeated Measures Analysis
Parameter estimate	Mean difference (net)
Point estimate	-1.1
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.4
upper limit	0.2

Notes:

[91] - MMRM model with fixed effects of Baseline Value, Treatment Group, Visit and Treatment Group by Visit Interaction was used. Unstructured covariance structure was used. p-value corresponds to the difference over placebo measure and confidence interval.

Secondary: Number of participants with adverse events (AE) and serious adverse events (SAE)

End point title	Number of participants with adverse events (AE) and serious adverse events (SAE)

End point description:

An AE is any untoward medical occurrence in a clinical investigation participant, temporally associated with the use of a medicinal product, whether or not considered related to the medicinal product. Any untoward event resulting in death, life threatening, requires hospitalization or prolongation of existing hospitalization, results in disability/incapacity, congenital anomaly/birth defect, any other situation according to medical or scientific judgment or events associated with liver injury and impaired liver function were categorized as SAE. All participants who received at least one dose of study treatment (GSK3196165 or placebo) were included in Safety Population.

End point type	Secondary

End point timeframe:

Up to Week 22

End point values	Placebo	GSK3196165 180mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	22	22		
Units: Participants				
Any AE|	11	13		
Any SAE|	1	2		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of participants with infections

End point title	Number of participants with infections

End point description:

Adverse events of special interest (AESI) included serious infections like serious respiratory infections and tuberculosis and other opportunistic infections. Number of participants with infections has been reported.

End point type	Secondary

End point timeframe:

Up to Week 22

End point values	Placebo	GSK3196165 180mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	22	22		
Units: Participants				
Serious Infections|	0	0		
Opportunistic Infections|	0	0		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of participants with pulmonary events

End point title	Number of participants with pulmonary events

End point description:

Pulmonary events like pulmonary alveolar proteinosis (PAP), persistent (for 3 consecutive weeks) reduction in diffusing capacity of the lungs for carbon monoxide (DLCO) > 15 percentage, persistent (for 3 consecutive weeks) cough and/or dyspnea and non- life threatening pulmonary changes related to surfactant accumulation is presented.

End point type	Secondary

End point timeframe:

Up to Week 22

End point values	Placebo	GSK3196165 180mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	22	22		
Units: Participants				
Persistent dyspnea|	0	0		
Persistent decrease in DLCO|	0	0		
Persistent Cough|	0	0		
Abnormal Lung Auscultation|	0	0		
PAP|	0	0		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of participants with anti-GSK3196165 binding antibodies

End point title	Number of participants with anti-GSK3196165 binding antibodies

End point description:

Serum samples were collected at indicated time points for anti-drug antibody (ADA) measurements. Anti-GSK3196165 binding antibody detection assay using tiered testing schema: screening, confirmation and titration steps was used for immunogenicity analysis. Samples taken after dosing with GSK3196165 that have a value at or above the cut-point were considered treatment-emergent ADA-positive. The number of participants with change from Baseline to any time post Baseline in the results of immunogenicity assessment as indicated by: negative to positive, positive to positive, positive to negative and negative to negative are presented.

End point type	Secondary

End point timeframe:

Up to Week 22

End point values	Placebo	GSK3196165 180mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	22	22		
Units: Participants				
Negative to positive|	0	1		
Positive to positive|	0	0		
Positive to negative|	0	0		
Negative to negative|	22	20		

Statistical analyses

No statistical analyses for this end point

Secondary: Total body clearance from plasma after subcutaneous administration (CL/F) of GSK3196165

End point title	Total body clearance from plasma after subcutaneous administration (CL/F) of GSK3196165

End point description:

Blood samples were collected at indicated time points to analyze CL/F. Participants in the 'Safety' population for whom a pharmacokinetic sample was obtained and analyzed were included Pharmacokinetic (PK) Population.

End point type	Secondary

End point timeframe:

Pre-dose on Day 4, Day 9, Day 30, Day 45, and Day 88

End point values	Placebo	GSK3196165 180mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	0[92]	0[93]		
Units: Milliliter per minute.				
arithmetic mean (standard deviation)	()	()		

Notes:

[92] - Results not posted

[93] - Results not posted

Statistical analyses

No statistical analyses for this end point

Secondary: Total volume of distribution after subcutaneous administration (Vss/F) of GSK3196165

End point title	Total volume of distribution after subcutaneous administration (Vss/F) of GSK3196165

End point description:

Blood samples were collected at indicated time points to analyze Vss/F.

End point type	Secondary

End point timeframe:

Pre-dose on Day 4, Day 9, Day 30, Day 45, and Day 88

End point values	Placebo	GSK3196165 180mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	0[94]	0[95]		
Units: Liters per kilogram				
arithmetic mean (standard deviation)	()	()		

Notes:

[94] - Results not posted

[95] - Results not posted

Statistical analyses

No statistical analyses for this end point

Secondary: Absoption rate constant (Ka) of GSK3196165

End point title	Absoption rate constant (Ka) of GSK3196165

End point description:

Blood samples were collected at indicated time points to analyze Ka.

End point type	Secondary

End point timeframe:

Pre-dose on Day 4, Day 9, Day 30, Day 45, and Day 88

End point values	Placebo	GSK3196165 180mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	0[96]	0[97]		
Units: Per hour				
arithmetic mean (standard deviation)	()	()		

Notes:

[96] - Results not posted

[97] - Results not posted

Statistical analyses

No statistical analyses for this end point

Secondary: Serum concentration of GSK3196165 by visit

End point title	Serum concentration of GSK3196165 by visit[98]

End point description:

Blood samples were collected at indicated time points for pharmacokinetic analysis. Only those participants with data available at the specified time points were analyzed (represented by n= X in the category titles).

End point type	Secondary

End point timeframe:

Pre-dose on Day 3, Weeks 1, 4, 6, 12, follow up (Week 22)

Notes:

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

End point values	GSK3196165 180mg			
Subject group type	Reporting group			
Number of subjects analysed	22[99]			
Units: Nanogram per milliliter				
geometric mean (geometric coefficient of variation)				
Day 3, n = 18|	2457.05 (± 94.74)			
Week 1, n = 21|	1767.55 (± 46.96)			
Week 4, n = 21|	2821.12 (± 61.00)			
Week 6, n = 20|	1802.09 (± 60.42)			
Week 12, n = 8|	800.96 (± 176.33)			
Follow up (Week 22), n = 12|	56.40 (± 346.41)			

Notes:

[99] - PK Population

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information	
Timeframe for reporting adverse events:	
Non-serious adverse events (AEs) and serious AEs were collected up to Week 22.	
Adverse event reporting additional description:	
Non-serious AEs and SAE for Safety Population was reported.	
Assessment type	Systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	20.1

Reporting groups	
Reporting group title	GSK3196165 180mg
Reporting group description:	
Participants randomized to GSK3196165 group received total of 8 doses of GSK3196165 over a 12-week treatment period. Participants were administered loading doses on Days 1, 8, 15, 22 and 29 which was followed by 3 doses every other week (Days 43, 57, 71).	
Reporting group title	Placebo
Reporting group description:	
Participants randomized to Placebo group received total of 8 subcutaneous injections of placebo over a 12-week treatment period. Participants were administered loading doses on Days 1, 8, 15, 22 and 29 which was followed by 3 doses every other week (Days 43, 57, 71).	

Serious adverse events	GSK3196165 180mg	Placebo	
Total subjects affected by serious adverse events			
subjects affected / exposed	2 / 22 (9.09%)	1 / 22 (4.55%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events			
Injury, poisoning and procedural complications			
HUMERUS FRACTURE			
subjects affected / exposed	1 / 22 (4.55%)	0 / 22 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vascular disorders			
HYPERTENSIVE CRISIS			
subjects affected / exposed	1 / 22 (4.55%)	0 / 22 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac disorders			
ATRIAL FIBRILLATION			

subjects affected / exposed	0 / 22 (0.00%)	1 / 22 (4.55%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

Frequency threshold for reporting non-serious adverse events: 5 %

Non-serious adverse events	GSK3196165 180mg	Placebo	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	10 / 22 (45.45%)	4 / 22 (18.18%)	
Cardiac disorders			
PALPITATIONS			
subjects affected / exposed	0 / 22 (0.00%)	2 / 22 (9.09%)	
occurrences (all)	0	2	
General disorders and administration site conditions			
INJECTION SITE ERYTHEMA			
subjects affected / exposed	2 / 22 (9.09%)	0 / 22 (0.00%)	
occurrences (all)	3	0	
INJECTION SITE RASH			
subjects affected / exposed	2 / 22 (9.09%)	0 / 22 (0.00%)	
occurrences (all)	6	0	
Respiratory, thoracic and mediastinal disorders			
COUGH			
subjects affected / exposed	2 / 22 (9.09%)	2 / 22 (9.09%)	
occurrences (all)	2	3	
Infections and infestations			
CONJUNCTIVITIS			
subjects affected / exposed	2 / 22 (9.09%)	0 / 22 (0.00%)	
occurrences (all)	2	0	
HERPES ZOSTER			
subjects affected / exposed	2 / 22 (9.09%)	0 / 22 (0.00%)	
occurrences (all)	2	0	
NASOPHARYNGITIS			
subjects affected / exposed	2 / 22 (9.09%)	1 / 22 (4.55%)	
occurrences (all)	3	1	
URINARY TRACT INFECTION			

subjects affected / exposed occurrences (all)	2 / 22 (9.09%) 2	0 / 22 (0.00%) 0	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
16 November 2015	Amendment No. 1: Correction of contraceptive requirements in Appendix 5, in response to regulatory review comments. Minor correction of question number in post-treatment interview guidance.
03 January 2017	Amendment No. 2: Amendment of inclusion criteria, #2, #3 and #5, clarification of exclusion criteria #9 and amendment of exclusion criteria #19(d). Addition of two planned interim analyses to Section Data Analysis Considerations and associated update to study blinding details. Addition of two PK sample time points (one on Day 85 and one on Day 155). Further minor corrections and clarifications to wording throughout the protocol.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported