Clinical trial results:
A 52-week, phase 3, multicentre, randomised, double blind, efficacy and safety study, comparing GSK3196165 with placebo and with tofacitinib in combination with conventional synthetic DMARDs, in participants with moderately to severely active rheumatoid arthritis who have an inadequate response to conventional synthetic DMARDs or biologic DMARDs.

Summary

EudraCT number	2019-000867-26
Trial protocol	GB DE ES PL BG EE HU
Global end of trial date	18 January 2023

Results information

Result version number	v1
This version publication date	08 October 2023
First version publication date	08 October 2023

Trial information

Trial identification

Sponsor protocol code	201791

Additional study identifiers

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

Notes:

Sponsors

Sponsor organisation name	GlaxoSmithKline
Sponsor organisation address	GreatWest Road, Brentford,Middlesex, United Kingdom, TW8 9GS
Public contact	GlaxoSmithKline, GSK Response Center, +1 8664357343, GSKClinicalSupportHD@gsk.com
Scientific contact	GlaxoSmithKline, GSK Response Center, +1 8664357343, GSKClinicalSupportHD@gsk.com

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	09 March 2023
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	18 January 2023
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To compare the efficacy of GSK3196165 at doses of 90 mg and 150 mg weekly versus placebo for the treatment of participants with moderately to severely active RA who are on a stable background of csDMARDs and who have had an inadequate response to csDMARDs or bDMARDs.

Protection of trial subjects:

Not Applicable

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	05 June 2019
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Argentina: 187
Country: Number of subjects enrolled	Australia: 6
Country: Number of subjects enrolled	Bulgaria: 80
Country: Number of subjects enrolled	China: 165
Country: Number of subjects enrolled	Colombia: 45
Country: Number of subjects enrolled	Estonia: 48
Country: Number of subjects enrolled	France: 2
Country: Number of subjects enrolled	Germany: 22
Country: Number of subjects enrolled	Hungary: 28
Country: Number of subjects enrolled	Japan: 224
Country: Number of subjects enrolled	Mexico: 124
Country: Number of subjects enrolled	Poland: 467
Country: Number of subjects enrolled	Russian Federation: 141
Country: Number of subjects enrolled	Korea, Democratic People's Republic of: 27
Country: Number of subjects enrolled	Spain: 11
Country: Number of subjects enrolled	Thailand: 9
Country: Number of subjects enrolled	United Kingdom: 11
Country: Number of subjects enrolled	United States: 167
Worldwide total number of subjects	1764
EEA total number of subjects	658

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)	1375
From 65 to 84 years	388
85 years and over	1

Subject disposition

Recruitment

Recruitment details:

For Global and Asia cohorts, participants were randomized in ratio of 6:6:3:1:1:1 to 3 experimental and 3 Placebo arms. At Week 12, participants from one of the three placebo arms switched to experimental arms, receiving intervention for 40 weeks. Participants who were randomized to experimental arms from day 1, received intervention for 52 weeks.

Pre-assignment

Screening details:

Total of 1764 participants were enrolled(1625 in Global and 139 in Asia cohorts which is supplementary to Global Cohort). One participant from GSK3196165 150mg (Asia cohort) arm was randomized but not treated. Study was terminated early only for Asia Cohort as limited efficacy did not support benefit risk profile of Otilimab as potential treatment.

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, Assessor

Arms

Are arms mutually exclusive?	Yes
Arm title	GSK3196165 90mg + csDMARD (Global Cohort)

Arm description:

Participants in Global Cohort received GSK3196165 90 mg subcutaneous (SC) injection once weekly for 52 weeks in combination with conventional synthetic disease-modifying antirheumatic drugs (csDMARD).

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:

Participants received GSK3196165 90 mg subcutaneous (SC) injection once weekly for 52 weeks in combination with csDMARD.

Arm title	GSK3196165 150mg + csDMARD (Global Cohort)

Arm description:

Participants in Global Cohort received GSK3196165 150 mg subcutaneous (SC) injection once weekly for 52 weeks in combination with csDMARD.

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:

Participants received GSK3196165 150 mg subcutaneous (SC) injection once weekly for 52 weeks in combination with csDMARD.

Arm title	Tofacitinib 5mg + csDMARD (Global Cohort)

Arm description:

Participants in Global Cohort received Tofacitinib 5mg capsule, orally, twice daily (BID) in combination

with csDMARD plus placebo injection weekly to maintain the blind for 52 weeks

Arm type	Active comparator
Investigational medicinal product name	Tofacitinib
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

Participants received Tofacitinib 5mg capsule, orally, twice daily (BID) in combination with csDMARD plus placebo injection weekly to maintain the blind for 52 weeks

Arm title	Placebo+csDMARD and GSK3196165 90mg+csDMARD (Global Cohort)

Arm description:

Participants in Global Cohort received Placebo weekly SC injection in combination with csDMARD for 12 weeks. At week 12, participants were switched from placebo to GSK3196165 90 mg, SC injection, once weekly in combination with csDMARD until 52 weeks

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

Dosage and administration details:

Participants received GSK3196165 90 mg, SC injection, once weekly in combination with csDMARD from week 12 to week 52.

Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Participants received Placebo weekly SC injection in combination with csDMARD until Week 12.

Arm title	Placebo +csDMARD and GSK3196165 150mg +csDMARD (Global Cohort)

Arm description:

Participants in Global Cohort received Placebo weekly SC injection in combination with csDMARD for 12 weeks. At week 12, participants were switched from placebo to GSK3196165 150 mg, SC injection, once weekly in combination with csDMARD until 52 weeks

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:

Participants received Placebo weekly SC injection in combination with csDMARD until Week 12.

Investigational medicinal product name	GSK3196165
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Participants received GSK3196165 150 mg, SC injection, once weekly in combination with csDMARD from week 12 to week 52.

Arm title	Placebo +csDMARD and Tofacitinib 5mg +csDMARD (Global Cohort)

Arm description:

Participants in Global Cohort received Placebo capsule BID in combination with csDMARD for 12 weeks. At week 12, participants were switched from placebo capsule to Tofacitinib 5mg, capsule, orally, BID in combination with csDMARD plus placebo injection to maintain the blind for 52 weeks.

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

Dosage and administration details:

Participants received Tofacitinib 5mg, capsule, orally, BID in combination with csDMARD plus placebo injection to maintain the blind from week 12 to week 52 weeks.

Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Participants received Placebo weekly SC injection in combination with csDMARD until Week 12.

Arm title	GSK3196165 90mg + csDMARD (Asia Cohort)

Arm description:

Participants in Asia Cohort received GSK3196165 90 mg subcutaneous (SC) injection once weekly for 52 weeks in combination with csDMARD.

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:

Participants received GSK3196165 90 mg subcutaneous (SC) injection once weekly for 52 weeks in combination with csDMARD.

Arm title	GSK3196165 150mg + csDMARD (Asia Cohort)

Arm description:

Participants in Asia Cohort received GSK3196165 150 mg subcutaneous (SC) injection once weekly for 52 weeks in combination with csDMARD.

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:

Participants received GSK3196165 150 mg subcutaneous (SC) injection once weekly for 52 weeks in combination with csDMARD.

Arm title	Tofacitinib 5mg + csDMARD (Asia Cohort)

Arm description:

Participants in Asia Cohort received Tofacitinib 5mg capsule, orally, twice daily (BID) in combination with csDMARD plus placebo injection weekly to maintain the blind for 52 weeks

Arm type	Active comparator

Investigational medicinal product name	Tofacitinib
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

Participants received Tofacitinib 5mg capsule, orally, twice daily (BID) in combination with csDMARD plus placebo injection weekly to maintain the blind for 52 weeks

Arm title	Placebo + csDMARD and GSK3196165 90mg + csDMARD (Asia Cohort)

Arm description:

Participants in Asia Cohort received Placebo weekly SC injection in combination with csDMARD for 12 weeks. At week 12, participants were switched from placebo to GSK3196165 90 mg, SC injection, once weekly in combination with csDMARD until 52 weeks

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

Dosage and administration details:

Participants received GSK3196165 90 mg, SC injection, once weekly in combination with csDMARD from week 12 to week 52.

Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Participants received Placebo weekly SC injection in combination with csDMARD until Week 12.

Arm title	Placebo + csDMARD and GSK3196165 150mg + csDMARD (Asia Cohort)

Arm description:

Participants in Asia Cohort received Placebo weekly SC injection in combination with csDMARD for 12 weeks. At week 12, participants were switched from placebo to GSK3196165 150 mg, SC injection, once weekly in combination with csDMARD until 52 weeks

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

Dosage and administration details:

Participants received GSK3196165 150 mg, SC injection, once weekly in combination with csDMARD from week 12 to week 52.

Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Participants received Placebo weekly SC injection in combination with csDMARD until Week 12.

Arm title	Placebo + csDMARD and Tofacitinib 5mg + csDMARD (Asia Cohort)

Arm description:

Participants in Asia Cohort received Placebo capsule BID in combination with csDMARD for 12 weeks. At week 12, participants were switched from placebo capsule to Tofacitinib 5mg, capsule, orally, BID in combination with csDMARD plus placebo injection to maintain the blind for 52 weeks.

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

Dosage and administration details:

Participants received Tofacitinib 5mg, capsule, orally, BID in combination with csDMARD plus placebo injection to maintain the blind from week 12 to week 52 weeks.

Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Participants received Placebo weekly SC injection in combination with csDMARD until Week 12.

Number of subjects in period 1[1]	GSK3196165 90mg + csDMARD (Global Cohort)	GSK3196165 150mg + csDMARD (Global Cohort)	Tofacitinib 5mg + csDMARD (Global Cohort)
Started	545	539	271
Completed	461	447	231
Not completed	84	92	40
Physician decision	5	8	4
Consent withdrawn by subject	32	35	12
Adverse event, non-fatal	23	20	16
STUDY TERMINATED BY SPONSOR	-	-	-
PROTOCOL-SPECIFIED WITHDRAWAL CRITERION MET	3	12	2
Lost to follow-up	6	5	5
Lack of efficacy	14	12	1
Protocol deviation	1	-	-

Number of subjects in period 1[1]	Placebo+csDMARD and GSK3196165 90mg+csDMARD (Global Cohort)	Placebo +csDMARD and GSK3196165 150mg +csDMARD (Global Cohort)	Placebo +csDMARD and Tofacitinib 5mg +csDMARD (Global Cohort)
Started	91	89	90
Completed	73	69	68
Not completed	18	20	22
Physician decision	1	5	2
Consent withdrawn by subject	8	6	8
Adverse event, non-fatal	6	4	5
STUDY TERMINATED BY SPONSOR	-	-	-

PROTOCOL-SPECIFIED WITHDRAWAL CRITERION MET	-	2	1
Lost to follow-up	1	-	2
Lack of efficacy	2	3	4
Protocol deviation	-	-	-

Number of subjects in period 1[1]	GSK3196165 90mg + csDMARD (Asia Cohort)	GSK3196165 150mg + csDMARD (Asia Cohort)	Tofacitinib 5mg + csDMARD (Asia Cohort)
Started	47	49	19
Completed	25	23	15
Not completed	22	26	4
Physician decision	4	5	-
Consent withdrawn by subject	2	3	-
Adverse event, non-fatal	1	5	-
STUDY TERMINATED BY SPONSOR	8	11	2
PROTOCOL-SPECIFIED WITHDRAWAL CRITERION MET	1	1	1
Lost to follow-up	-	-	-
Lack of efficacy	6	1	1
Protocol deviation	-	-	-

Number of subjects in period 1[1]	Placebo + csDMARD and GSK3196165 90mg + csDMARD (Asia Cohort)	Placebo + csDMARD and GSK3196165 150mg + csDMARD (Asia Cohort)	Placebo + csDMARD and Tofacitinib 5mg + csDMARD (Asia Cohort)
Started	6	8	9
Completed	4	5	4
Not completed	2	3	5
Physician decision	1	-	-
Consent withdrawn by subject	-	-	1
Adverse event, non-fatal	-	1	1
STUDY TERMINATED BY SPONSOR	1	2	3
PROTOCOL-SPECIFIED WITHDRAWAL CRITERION MET	-	-	-
Lost to follow-up	-	-	-
Lack of efficacy	-	-	-
Protocol deviation	-	-	-

Notes:

[1] - The number of subjects reported to be in the baseline period are not the same as the worldwide number enrolled in the trial. It is expected that these numbers will be the same.
Justification: Total 1764 participants were randomized; one participant withdrew from 150mg GSK3196165 (Asia Cohort) before receiving intervention due to Physician Decision. The participant was removed from intent-to-treat and safety population (N=1763).

Reporting groups

Reporting group title	GSK3196165 90mg + csDMARD (Global Cohort)
Reporting group description:	
Participants in Global Cohort received GSK3196165 90 mg subcutaneous (SC) injection once weekly for 52 weeks in combination with conventional synthetic disease-modifying antirheumatic drugs (csDMARD).	
Reporting group title	GSK3196165 150mg + csDMARD (Global Cohort)
Reporting group description:	
Participants in Global Cohort received GSK3196165 150 mg subcutaneous (SC) injection once weekly for 52 weeks in combination with csDMARD.	
Reporting group title	Tofacitinib 5mg + csDMARD (Global Cohort)
Reporting group description:	
Participants in Global Cohort received Tofacitinib 5mg capsule, orally, twice daily (BID) in combination with csDMARD plus placebo injection weekly to maintain the blind for 52 weeks	
Reporting group title	Placebo+csDMARD and GSK3196165 90mg+csDMARD (Global Cohort)
Reporting group description:	
Participants in Global Cohort received Placebo weekly SC injection in combination with csDMARD for 12 weeks. At week 12, participants were switched from placebo to GSK3196165 90 mg, SC injection, once weekly in combination with csDMARD until 52 weeks	
Reporting group title	Placebo +csDMARD and GSK3196165 150mg +csDMARD (Global Cohort)
Reporting group description:	
Participants in Global Cohort received Placebo weekly SC injection in combination with csDMARD for 12 weeks. At week 12, participants were switched from placebo to GSK3196165 150 mg, SC injection, once weekly in combination with csDMARD until 52 weeks	
Reporting group title	Placebo +csDMARD and Tofacitinib 5mg +csDMARD (Global Cohort)
Reporting group description:	
Participants in Global Cohort received Placebo capsule BID in combination with csDMARD for 12 weeks. At week 12, participants were switched from placebo capsule to Tofacitinib 5mg, capsule, orally, BID in combination with csDMARD plus placebo injection to maintain the blind for 52 weeks.	
Reporting group title	GSK3196165 90mg + csDMARD (Asia Cohort)
Reporting group description:	
Participants in Asia Cohort received GSK3196165 90 mg subcutaneous (SC) injection once weekly for 52 weeks in combination with csDMARD.	
Reporting group title	GSK3196165 150mg + csDMARD (Asia Cohort)
Reporting group description:	
Participants in Asia Cohort received GSK3196165 150 mg subcutaneous (SC) injection once weekly for 52 weeks in combination with csDMARD.	
Reporting group title	Tofacitinib 5mg + csDMARD (Asia Cohort)
Reporting group description:	
Participants in Asia Cohort received Tofacitinib 5mg capsule, orally, twice daily (BID) in combination with csDMARD plus placebo injection weekly to maintain the blind for 52 weeks	
Reporting group title	Placebo + csDMARD and GSK3196165 90mg + csDMARD (Asia Cohort)
Reporting group description:	
Participants in Asia Cohort received Placebo weekly SC injection in combination with csDMARD for 12 weeks. At week 12, participants were switched from placebo to GSK3196165 90 mg, SC injection, once weekly in combination with csDMARD until 52 weeks	
Reporting group title	Placebo + csDMARD and GSK3196165 150mg + csDMARD (Asia Cohort)
Reporting group description:	
Participants in Asia Cohort received Placebo weekly SC injection in combination with csDMARD for 12 weeks. At week 12, participants were switched from placebo to GSK3196165 150 mg, SC injection, once weekly in combination with csDMARD until 52 weeks	

Reporting group title	Placebo + csDMARD and Tofacitinib 5mg + csDMARD (Asia Cohort)

Reporting group description:

Participants in Asia Cohort received Placebo capsule BID in combination with csDMARD for 12 weeks. At week 12, participants were switched from placebo capsule to Tofacitinib 5mg, capsule, orally, BID in combination with csDMARD plus placebo injection to maintain the blind for 52 weeks.

Reporting group values	GSK3196165 90mg + csDMARD (Global Cohort)	GSK3196165 150mg + csDMARD (Global Cohort)	Tofacitinib 5mg + csDMARD (Global Cohort)
Number of subjects	545	539	271
Age Categorical Units: Participants			
18-49	172	150	79
50-64	254	264	125
>=65	119	125	67
Sex: Female, Male Units: Participants			
Female	431	430	229
Male	114	109	42
Race/Ethnicity, Customized Units: Subjects			
AMERICAN INDIAN OR ALASKA NATIVE	29	39	21
ASIAN	96	98	49
BLACK OR AFRICAN AMERICAN	10	8	3
WHITE	409	393	197
MULTIPLE	1	0	0
MISSING	0	1	1

Reporting group values	Placebo+csDMARD and GSK3196165 90mg+csDMARD (Global Cohort)	Placebo +csDMARD and GSK3196165 150mg +csDMARD (Global Cohort)	Placebo +csDMARD and Tofacitinib 5mg +csDMARD (Global Cohort)
Number of subjects	91	89	90
Age Categorical Units: Participants			
18-49	30	23	23
50-64	47	43	45
>=65	14	23	22
Sex: Female, Male Units: Participants			
Female	68	73	73
Male	23	16	17
Race/Ethnicity, Customized Units: Subjects			
AMERICAN INDIAN OR ALASKA NATIVE	6	4	6
ASIAN	16	16	16
BLACK OR AFRICAN AMERICAN	2	0	1
WHITE	67	69	67
MULTIPLE	0	0	0
MISSING	0	0	0

Reporting group values	GSK3196165 90mg + csDMARD (Asia Cohort)	GSK3196165 150mg + csDMARD (Asia Cohort)	Tofacitinib 5mg + csDMARD (Asia Cohort)
Number of subjects	47	49	19
Age Categorical Units: Participants			
18-49	19	21	3
50-64	23	22	11
>=65	5	6	5
Sex: Female, Male Units: Participants			
Female	34	37	12
Male	13	12	7
Race/Ethnicity, Customized Units: Subjects			
AMERICAN INDIAN OR ALASKA NATIVE	0	0	0
ASIAN	47	49	19
BLACK OR AFRICAN AMERICAN	0	0	0
WHITE	0	0	0
MULTIPLE	0	0	0
MISSING	0	0	0

Reporting group values	Placebo + csDMARD and GSK3196165 90mg + csDMARD (Asia Cohort)	Placebo + csDMARD and GSK3196165 150mg + csDMARD (Asia Cohort)	Placebo + csDMARD and Tofacitinib 5mg + csDMARD (Asia Cohort)
Number of subjects	6	8	9
Age Categorical Units: Participants			
18-49	2	3	3
50-64	3	5	5
>=65	1	0	1
Sex: Female, Male Units: Participants			
Female	4	5	7
Male	2	3	2
Race/Ethnicity, Customized Units: Subjects			
AMERICAN INDIAN OR ALASKA NATIVE	0	0	0
ASIAN	6	8	9
BLACK OR AFRICAN AMERICAN	0	0	0
WHITE	0	0	0
MULTIPLE	0	0	0
MISSING	0	0	0

Reporting group values	Total		
Number of subjects	1763		
Age Categorical Units: Participants			
18-49	528		
50-64	847		

>=65	388		

Sex: Female, Male Units: Participants			
Female	1403		
Male	360		
Race/Ethnicity, Customized Units: Subjects			
AMERICAN INDIAN OR ALASKA NATIVE	105		
ASIAN	429		
BLACK OR AFRICAN AMERICAN	24		
WHITE	1202		
MULTIPLE	1		
MISSING	2		

End points reporting groups

Reporting group title	GSK3196165 90mg + csDMARD (Global Cohort)
Reporting group description:	
Participants in Global Cohort received GSK3196165 90 mg subcutaneous (SC) injection once weekly for 52 weeks in combination with conventional synthetic disease-modifying antirheumatic drugs (csDMARD).	
Reporting group title	GSK3196165 150mg + csDMARD (Global Cohort)
Reporting group description:	
Participants in Global Cohort received GSK3196165 150 mg subcutaneous (SC) injection once weekly for 52 weeks in combination with csDMARD.	
Reporting group title	Tofacitinib 5mg + csDMARD (Global Cohort)
Reporting group description:	
Participants in Global Cohort received Tofacitinib 5mg capsule, orally, twice daily (BID) in combination with csDMARD plus placebo injection weekly to maintain the blind for 52 weeks	
Reporting group title	Placebo+csDMARD and GSK3196165 90mg+csDMARD (Global Cohort)
Reporting group description:	
Participants in Global Cohort received Placebo weekly SC injection in combination with csDMARD for 12 weeks. At week 12, participants were switched from placebo to GSK3196165 90 mg, SC injection, once weekly in combination with csDMARD until 52 weeks	
Reporting group title	Placebo +csDMARD and GSK3196165 150mg +csDMARD (Global Cohort)
Reporting group description:	
Participants in Global Cohort received Placebo weekly SC injection in combination with csDMARD for 12 weeks. At week 12, participants were switched from placebo to GSK3196165 150 mg, SC injection, once weekly in combination with csDMARD until 52 weeks	
Reporting group title	Placebo +csDMARD and Tofacitinib 5mg +csDMARD (Global Cohort)
Reporting group description:	
Participants in Global Cohort received Placebo capsule BID in combination with csDMARD for 12 weeks. At week 12, participants were switched from placebo capsule to Tofacitinib 5mg, capsule, orally, BID in combination with csDMARD plus placebo injection to maintain the blind for 52 weeks.	
Reporting group title	GSK3196165 90mg + csDMARD (Asia Cohort)
Reporting group description:	
Participants in Asia Cohort received GSK3196165 90 mg subcutaneous (SC) injection once weekly for 52 weeks in combination with csDMARD.	
Reporting group title	GSK3196165 150mg + csDMARD (Asia Cohort)
Reporting group description:	
Participants in Asia Cohort received GSK3196165 150 mg subcutaneous (SC) injection once weekly for 52 weeks in combination with csDMARD.	
Reporting group title	Tofacitinib 5mg + csDMARD (Asia Cohort)
Reporting group description:	
Participants in Asia Cohort received Tofacitinib 5mg capsule, orally, twice daily (BID) in combination with csDMARD plus placebo injection weekly to maintain the blind for 52 weeks	
Reporting group title	Placebo + csDMARD and GSK3196165 90mg + csDMARD (Asia Cohort)
Reporting group description:	
Participants in Asia Cohort received Placebo weekly SC injection in combination with csDMARD for 12 weeks. At week 12, participants were switched from placebo to GSK3196165 90 mg, SC injection, once weekly in combination with csDMARD until 52 weeks	
Reporting group title	Placebo + csDMARD and GSK3196165 150mg + csDMARD (Asia Cohort)
Reporting group description:	
Participants in Asia Cohort received Placebo weekly SC injection in combination with csDMARD for 12 weeks. At week 12, participants were switched from placebo to GSK3196165 150 mg, SC injection, once weekly in combination with csDMARD until 52 weeks	

Reporting group title	Placebo + csDMARD and Tofacitinib 5mg + csDMARD (Asia Cohort)

Reporting group description:

Participants in Asia Cohort received Placebo capsule BID in combination with csDMARD for 12 weeks. At week 12, participants were switched from placebo capsule to Tofacitinib 5mg, capsule, orally, BID in combination with csDMARD plus placebo injection to maintain the blind for 52 weeks.

Subject analysis set title	Pooled Placebo (Global Cohort)
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Participants received Placebo weekly SC injection in combination with csDMARD until Week 12. The placebo arms are pooled into a single placebo arm.

Subject analysis set title	Pooled Placebo (Asia Cohort)
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Participants in Asia Cohort received Placebo weekly SC injection in combination with csDMARD until Week 12. The placebo arms are pooled into a single placebo arm.

Subject analysis set title	Tofacitinib 5mg + csDMARD (Global Cohort)
Subject analysis set type	Safety analysis

Subject analysis set description:

Participants received Tofacitinib 5mg capsule, orally, twice daily (BID) in combination with csDMARD plus placebo injection weekly to maintain the blind for 52 weeks

Subject analysis set title	Pooled Placebo (Global Cohort)
Subject analysis set type	Safety analysis

Subject analysis set description:

Participants received Placebo weekly SC injection in combination with csDMARD until Week 12. The placebo arms are pooled into a single placebo arm.

Primary: Percentage (%) of participants with 20% improvement in American College of Rheumatology criteria (ACR20) at Week 12 superiority comparison with placebo (Global Cohort)

End point title	Percentage (%) of participants with 20% improvement in American College of Rheumatology criteria (ACR20) at Week 12 superiority comparison with placebo (Global Cohort)[1]

End point description:

ACR20 is calculated as 20% improvement from Baseline in Tender Joint Count 68 (TJC68), Swollen Joint Count 66 (SJC66) and 20% improvement in 3 of the following 5 measures:Patient's Global Assessment of Arthritis Disease Activity (PtGA), Physician Global Assessment of Arthritis Disease Activity (PhGA) (visual analogue scale [VAS] with values from 0=best to 100=worst), Patient Assessment of Arthritis Pain (VAS with values from 0=no pain and 100=most severe pain), Health Assessment Questionnaire-Disability Index (HAQ-DI) (ranges from 0=least difficulty to 3=extreme difficulty) and an acute-phase reactant [high sensitivity C-reactive Protein milligram per liter (mg/L) (hsCRP)]. For the purpose of all analyses up to week 12, the placebo arms were pooled into a single placebo arm to primarily serve as reference for the comparison of active treatment arms. The analysis was performed on Intent-to-Treat (ITT) set. Analysis was performed using multiple imputation method to handle missing data.

End point type	Primary

End point timeframe:

Week 12

Notes:

[1] - 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: The endpoints are different for the different parts of the study.

End point values	GSK3196165 90mg + csDMARD (Global Cohort)	GSK3196165 150mg + csDMARD (Global Cohort)	Tofacitinib 5mg + csDMARD (Global Cohort)	Pooled Placebo (Global Cohort)
Subject group type	Reporting group	Reporting group	Reporting group	Subject analysis set
Number of subjects analysed	545	539	271	270
Units: Percentage of participants				
number (not applicable)	54.9	54.5	71.1	32.5

Statistical analyses

Statistical analysis title	Statistical Analysis 1

Statistical analysis description:

The null hypothesis is defined as there is no difference between the 90mg dose of GSK3196165 and placebo in the proportion of participants achieving ACR20 response at Week 12, versus the alternative hypothesis that the 90mg dose of GSK3196165 differs from placebo in the proportion of participants achieving ACR20 response at Week 12.

Comparison groups	GSK3196165 90mg + csDMARD (Global Cohort) v Pooled Placebo (Global Cohort)
Number of subjects included in analysis	815
Analysis specification	Pre-specified
Analysis type	
P-value	< 0.0001
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	2.57
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.87
upper limit	3.53

Statistical analysis title	Statistical Analysis 2

Statistical analysis description:

The null hypothesis is defined as there is no difference between the 150mg dose of GSK3196165 and placebo in the proportion of participants achieving ACR20 response at Week 12, versus the alternative hypothesis that the 150mg dose of GSK3196165 differs from placebo in the proportion of participants achieving ACR20 response at Week 12.

Comparison groups	GSK3196165 150mg + csDMARD (Global Cohort) v Pooled Placebo (Global Cohort)
Number of subjects included in analysis	809
Analysis specification	Pre-specified
Analysis type	
P-value	< 0.0001
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	2.55

Confidence interval	
level	95 %
sides	2-sided
lower limit	1.85
upper limit	3.5

Statistical analysis title	Statistical Analysis 3

Statistical analysis description:

The null hypothesis is defined as there is no difference between the 05mg dose of Tofacitinib and placebo in the proportion of participants achieving ACR20 response at Week 12, versus the alternative hypothesis that the 05mg dose of Tofacitinib differs from placebo in the proportion of participants achieving ACR20 response at Week 12.

Comparison groups	Tofacitinib 5mg + csDMARD (Global Cohort) v Pooled Placebo (Global Cohort)
Number of subjects included in analysis	541
Analysis specification	Pre-specified
Analysis type	
P-value	< 0.0001
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	5.38
Confidence interval	
level	95 %
sides	2-sided
lower limit	3.66
upper limit	7.9

Statistical analysis title	Statistical Analysis 4

Statistical analysis description:

The null hypothesis is defined as there is no difference between the 90 mg dose of GSK3196165 and 05mg dose of Tofacitinib in the proportion of participants achieving ACR20 response at Week 12, versus the alternative hypothesis that the 90 mg dose of GSK3196165 differs from 05mg dose of Tofacitinib in the proportion of participants achieving ACR20 response at Week 12.

Comparison groups	GSK3196165 90mg + csDMARD (Global Cohort) v Tofacitinib 5mg + csDMARD (Global Cohort)
Number of subjects included in analysis	816
Analysis specification	Pre-specified
Analysis type	
P-value	< 0.0001
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	0.48
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.34
upper limit	0.66

Statistical analysis title	Statistical Analysis 5

Statistical analysis description:

The null hypothesis is defined as there is no difference between the 150mg dose of GSK3196165 and 05mg dose of Tofacitinib in the proportion of participants achieving ACR20 response at Week 12, versus the alternative hypothesis that the 150mg dose of GSK3196165 differs from 05mg dose of Tofacitinib in the proportion of participants achieving ACR20 response at Week 12.

Comparison groups	GSK3196165 150mg + csDMARD (Global Cohort) v Tofacitinib 5mg + csDMARD (Global Cohort)
Number of subjects included in analysis	810
Analysis specification	Pre-specified
Analysis type	
P-value	< 0.0001
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	0.47
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.34
upper limit	0.66

Primary: Percentage (%) of participants with 20% improvement in American College of Rheumatology criteria (ACR20) at Week 12 (Asia Cohort)

End point title	Percentage (%) of participants with 20% improvement in American College of Rheumatology criteria (ACR20) at Week 12 (Asia Cohort)[2][3]

End point description:

ACR20 is calculated as 20% improvement from Baseline in Tender Joint Count 68 (TJC68), Swollen Joint Count 66 (SJC66) and 20% improvement in 3 of the following 5 measures:Patient's Global Assessment of Arthritis Disease Activity (PtGA), Physician Global Assessment of Arthritis Disease Activity (PhGA) (visual analogue scale [VAS] with values from 0=best to 100=worst), Patient Assessment of Arthritis Pain (VAS with values from 0=no pain and 100=most severe pain), Health Assessment Questionnaire-Disability Index (HAQ-DI) (ranges from 0=least difficulty to 3=extreme difficulty) and an acute-phase reactant [high sensitivity C-reactive Protein milligram per liter (mg/L) (hsCRP)]. For the purpose of all analyses up to week 12, the placebo arms were pooled into a single placebo arm to primarily serve as reference for the comparison of active treatment arms. The analysis was performed on ITT - Supplementary Asia Cohort set. Participants with data available at indicated timepoints are analyzed.

End point type	Primary

End point timeframe:

Week 12

Notes:

[2] - 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: The scope of this primary end point was descriptive analysis. Therefore, no statistical data are reported.
[3] - 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: The endpoints are different for the different parts of the study.

End point values	GSK3196165 90mg + csDMARD (Asia Cohort)	GSK3196165 150mg + csDMARD (Asia Cohort)	Tofacitinib 5mg + csDMARD (Asia Cohort)	Pooled Placebo (Asia Cohort)
Subject group type	Reporting group	Reporting group	Reporting group	Subject analysis set
Number of subjects analysed	44	42	19	21
Units: Percentage of participants				
number (not applicable)	45.0	40.0	68.0	14.0

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of participants achieving Clinical disease activity index (CDAI) total score less than or equal to (<=)10 [CDAI Low disease activity (LDA)] at Week 12 (Global Cohort)

End point title	Percentage of participants achieving Clinical disease activity index (CDAI) total score less than or equal to (<=)10 [CDAI Low disease activity (LDA)] at Week 12 (Global Cohort)[4]

End point description:

Clinical Disease Activity Index (CDAI) total score is a composite score consisting of the sum of Swollen Joint Count 28 (SJC28), Tender Joint Count 28 (TJC28), Patient's Global Assessment of Arthritis Disease Activity (PtGA) (visual analogue scale [VAS] with values from 0=best to 100=worst) and Physician Global Assessment of Arthritis Disease Activity (PhGA) (VAS with values from 0=best to 100=worst). PtGA and PhGA are transformed to a 0-10 scale before computing the CDAI total score. CDAI total score ranges from 0 to 76 with higher values representing higher disease activity. Low disease activity (LDA) is achieved when CDAI total score <=10. For the purpose of all analyses up to week 12, the placebo arms were pooled into single placebo arm to primarily serve as reference for the comparison of active treatment arms. Analysis was performed on ITT set. Analysis was performed using multiple imputation method to handle missing data.

End point type	Secondary

End point timeframe:

Week 12

Notes:

[4] - 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: The endpoints are different for the different parts of the study.

End point values	GSK3196165 90mg + csDMARD (Global Cohort)	GSK3196165 150mg + csDMARD (Global Cohort)	Tofacitinib 5mg + csDMARD (Global Cohort)	Pooled Placebo (Global Cohort)
Subject group type	Reporting group	Reporting group	Reporting group	Subject analysis set
Number of subjects analysed	545	539	271	270
Units: Percentage of participants				
number (not applicable)	26.5	25.1	36.8	11.4

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of participants achieving 20% improvement in ACR20 at

Week 24: non-inferiority comparison with tofacitinib (Global Cohort)

End point title	Percentage of participants achieving 20% improvement in ACR20 at Week 24: non-inferiority comparison with tofacitinib (Global Cohort)[5]

End point description:

ACR20 is calculated as a 20% improvement from Baseline in Tender Joint Count 68 (TJC68) and Swollen Joint Count 66 (SJC66) and a 20% improvement in 3 of the following 5 measures: Patient's Global Assessment of Arthritis Disease Activity (PtGA) [visual analogue scale (VAS) with values from 0=best to 100=worst], Physician Global Assessment of Arthritis Disease Activity (PhGA) (VAS with values from 0=best to 100=worst), Patient Assessment of Arthritis Pain (VAS with values from 0=no pain and 100=most severe pain), Health Assessment Questionnaire-Disability Index (HAQ-DI) (ranges from 0 to 3 where 0 = least difficulty and 3 = extreme difficulty) and an acute-phase reactant [high sensitivity C-reactive Protein milligram per liter (mg/L) (hsCRP)]. The analysis was performed on the ITT set using multiple imputation method to handle missing data.

End point type	Secondary

End point timeframe:

Week 24

Notes:

[5] - 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: The endpoints are different for the different parts of the study.

End point values	GSK3196165 90mg + csDMARD (Global Cohort)	GSK3196165 150mg + csDMARD (Global Cohort)	Tofacitinib 5mg + csDMARD (Global Cohort)	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	545	539	271	
Units: Percentage of participants				
number (not applicable)	65.0	62.5	79.8	

Statistical analyses

Statistical analysis title	Statistical Analysis 2
Comparison groups	GSK3196165 150mg + csDMARD (Global Cohort) v Tofacitinib 5mg + csDMARD (Global Cohort)
Number of subjects included in analysis	810
Analysis specification	Pre-specified
Analysis type	
Method	Regression, Logistic
Parameter estimate	Mean difference (final values)
Point estimate	-17.2
Confidence interval	
level	95 %
sides	2-sided
lower limit	-23.9
upper limit	-10.6

Statistical analysis title	Statistical Analysis 1
Comparison groups	GSK3196165 90mg + csDMARD (Global Cohort) v Tofacitinib 5mg + csDMARD (Global Cohort)

Number of subjects included in analysis	816
Analysis specification	Pre-specified
Analysis type	
Method	Regression, Logistic
Parameter estimate	Mean difference (final values)
Point estimate	-14.7
Confidence interval	
level	95 %
sides	2-sided
lower limit	-21.3
upper limit	-8.1

Secondary: Change from Baseline in Health Assessment Questionnaire Disability Index (HAQ-DI) at Week 12 (Global Cohort)

End point title	Change from Baseline in Health Assessment Questionnaire Disability Index (HAQ-DI) at Week 12 (Global Cohort)[6]

End point description:

Health Assessment Questionnaire-Disability Index (HAQ-DI) is 20-question instrument that assesses degree of difficulty in accomplishing tasks in eight functional areas:dressing and grooming, arising, eating, walking, hygiene, reach, grip and common daily activities. Overall HAQ-DI score is sum of domain scores divided by number of domains answered. The score ranges from 0 to 3 where 0=least difficulty and 3=extreme difficulty. Higher overall score indicates greater disability. A negative change from baseline indicates an improvement. Baseline was defined as latest pre-dose assessment with a non-missing value, including from unscheduled visits. Change from Baseline was calculated by subtracting post dose value from Baseline. For the purpose of all analyses up to week 12, placebo arms were pooled into single placebo arm to primarily serve as reference for comparison of active treatment arms. The analysis was performed on ITT set using multiple imputation method to handle missing data.

End point type	Secondary

End point timeframe:

Baseline (Day 1) and Week 12

Notes:

[6] - 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: The endpoints are different for the different parts of the study.

End point values	GSK3196165 90mg + csDMARD (Global Cohort)	GSK3196165 150mg + csDMARD (Global Cohort)	Tofacitinib 5mg + csDMARD (Global Cohort)	Pooled Placebo (Global Cohort)
Subject group type	Reporting group	Reporting group	Reporting group	Subject analysis set
Number of subjects analysed	545	539	271	270
Units: Scores on a scale				
least squares mean (standard error)	-0.32 (± 0.029)	-0.31 (± 0.029)	-0.46 (± 0.037)	-0.14 (± 0.038)

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of participants achieving CDAI total score <=10 (CDAI LDA) at Week 24 and Week 52 for treatment arms who started study intervention from

Day 1 (Global Cohort)

End point title	Percentage of participants achieving CDAI total score <=10 (CDAI LDA) at Week 24 and Week 52 for treatment arms who started study intervention from Day 1 (Global Cohort)[7]

End point description:

Clinical Disease Activity Index (CDAI) total score is a composite score consisting of the sum of Swollen Joint Count 28 (SJC28), Tender Joint Count 28 (TJC28), Patient's Global Assessment of Arthritis Disease Activity (PtGA) (visual analogue scale with values from 0=best to 100=worst) and Physician Global Assessment of Arthritis Disease Activity (PhGA) (visual analogue scale with values from 0=best to 100=worst). PtGA and PhGA are transformed to a 0-10 scale before computing the CDAI total score. CDAI total score ranges from 0 to 76 with higher values representing higher disease activity. Low disease activity (LDA) is achieved when CDAI total score <=10. The analysis was performed on all randomized participants who received study intervention from Day 01 to Week 52. Analysis was performed using multiple imputation method to handle missing data.

End point type	Secondary

End point timeframe:

Week 24 and Week 52

Notes:

[7] - 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: The endpoints are different for the different parts of the study.

End point values	GSK3196165 90mg + csDMARD (Global Cohort)	GSK3196165 150mg + csDMARD (Global Cohort)	Tofacitinib 5mg + csDMARD (Global Cohort)	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	545	539	271	
Units: Percentage of participants				
number (not applicable)				
Week 24	32.8	34.3	49.6	
Week 52	38.3	38.0	56.8	

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of participants achieving CDAI total score <=2.8 (CDAI Remission) at Week 12 (Global Cohort)

End point title	Percentage of participants achieving CDAI total score <=2.8 (CDAI Remission) at Week 12 (Global Cohort)[8]

End point description:

Clinical Disease Activity Index (CDAI) total score is a composite score consisting of the sum of Swollen Joint Count 28 (SJC28), Tender Joint Count 28 (TJC28), Patient's Global Assessment of Arthritis Disease Activity (PtGA) (visual analogue scale with values from 0=best to 100=worst) and Physician Global Assessment of Arthritis Disease Activity (PhGA) (visual analogue scale with values from 0=best to 100=worst). PtGA and PhGA are transformed to a 0-10 scale before computing the CDAI total score. CDAI total score ranges from 0 to 76 with higher values representing higher disease activity. CDAI remission is achieved when CDAI total score <=2.8. For the purpose of all analyses up to week 12, the placebo arms were pooled into a single placebo arm to primarily serve as a reference for the comparison of active treatment arms. The analysis was performed on the ITT set. Analysis was performed using multiple imputation method to handle missing data.

End point type	Secondary

End point timeframe:

Week 12

Notes:

[8] - 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: The endpoints are different for the different parts of the study.

End point values	GSK3196165 90mg + csDMARD (Global Cohort)	GSK3196165 150mg + csDMARD (Global Cohort)	Tofacitinib 5mg + csDMARD (Global Cohort)	Pooled Placebo (Global Cohort)
Subject group type	Reporting group	Reporting group	Reporting group	Subject analysis set
Number of subjects analysed	545	539	271	270
Units: Percentage of participants				
number (not applicable)	4.7	4.5	9.7	3.8

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of participants achieving CDAI total score <=10 (CDAI LDA) at Week 24 and Week 52 for placebo switched arms (Global Cohort)

End point title	Percentage of participants achieving CDAI total score <=10 (CDAI LDA) at Week 24 and Week 52 for placebo switched arms (Global Cohort)[9]

End point description:

Clinical Disease Activity Index (CDAI) total score is a composite score consisting of the sum of Swollen Joint Count 28 (SJC28), Tender Joint Count 28 (TJC28), Patient's Global Assessment of Arthritis Disease Activity (PtGA) (visual analogue scale with values from 0=best to 100=worst) and Physician Global Assessment of Arthritis Disease Activity (PhGA) (visual analogue scale with values from 0=best to 100=worst). PtGA and PhGA are transformed to a 0-10 scale before computing the CDAI total score. CDAI total score ranges from 0 to 76 with higher values representing higher disease activity. Low disease activity (LDA) is achieved when CDAI total score <=10. The analysis was performed on all randomized participants who switched from placebo to study intervention at Week 12. Analysis was performed using multiple imputation method to handle missing data.

End point type	Secondary

End point timeframe:

Week 24 and Week 52

Notes:

[9] - 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: The endpoints are different for the different parts of the study.

End point values	Placebo+csDMARD and GSK3196165 90mg+csDMARD (Global Cohort)	Placebo +csDMARD and GSK3196165 150mg +csDMARD (Global Cohort)	Placebo +csDMARD and Tofacitinib 5mg +csDMARD (Global Cohort)	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	91	89	90	
Units: Percentage of participants				
number (not applicable)				
Week 24	37.5	15.9	46.4	
Week 52	40.2	38.2	41.3	

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of participants achieving CDAI total score <=2.8 (CDAI Remission) at Week 24 and Week 52 for treatment arms who started study intervention from Day 1 (Global Cohort)

End point title	Percentage of participants achieving CDAI total score <=2.8 (CDAI Remission) at Week 24 and Week 52 for treatment arms who started study intervention from Day 1 (Global Cohort)[10]

End point description:

Clinical Disease Activity Index (CDAI) total score is a composite score consisting of the sum of Swollen Joint Count 28 (SJC28), Tender Joint Count 28 (TJC28), Patient's Global Assessment of Arthritis Disease Activity (PtGA) (visual analogue scale with values from 0=best to 100=worst) and Physician Global Assessment of Arthritis Disease Activity (PhGA) (visual analogue scale with values from 0=best to 100=worst). PtGA and PhGA are transformed to a 0-10 scale before computing the CDAI total score. CDAI total score ranges from 0 to 76 with higher values representing higher disease activity. CDAI remission is achieved when CDAI total score <=2.8. The analysis was performed on all randomized participants who received study intervention from Day 01 to Week 52. Analysis was performed using multiple imputation method to handle missing data.

End point type	Secondary

End point timeframe:

Week 24 and Week 52

Notes:

[10] - 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: The endpoints are different for the different parts of the study.

End point values	GSK3196165 90mg + csDMARD (Global Cohort)	GSK3196165 150mg + csDMARD (Global Cohort)	Tofacitinib 5mg + csDMARD (Global Cohort)	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	545	539	271	
Units: Percentage of participants				
number (not applicable)				
Week 24	6.9	7.2	17.9	
Week 52	11.9	10.8	21.2	

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of participants achieving CDAI total score <=2.8 (CDAI Remission) at Week 24 and Week 52 for placebo switched arms (Global Cohort)

End point title	Percentage of participants achieving CDAI total score <=2.8 (CDAI Remission) at Week 24 and Week 52 for placebo

	switched arms (Global Cohort)[11]

End point description:

Clinical Disease Activity Index (CDAI) total score is a composite score consisting of the sum of Swollen Joint Count 28 (SJC28), Tender Joint Count 28 (TJC28), Patient's Global Assessment of Arthritis Disease Activity (PtGA) (visual analogue scale with values from 0=best to 100=worst) and Physician Global Assessment of Arthritis Disease Activity (PhGA) (visual analogue scale with values from 0=best to 100=worst). PtGA and PhGA are transformed to a 0-10 scale before computing the CDAI total score. CDAI total score ranges from 0 to 76 with higher values representing higher disease activity. CDAI remission is achieved when CDAI total score <=2.8. The analysis was performed on all randomized participants who switched from placebo to study intervention at Week 12. Analysis was performed using multiple imputation method to handle missing data.

End point type	Secondary

End point timeframe:

Week 24 and Week 52

Notes:

[11] - 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: The endpoints are different for the different parts of the study.

End point values	Placebo+csDMARD and GSK3196165 90mg+csDMARD (Global Cohort)	Placebo +csDMARD and GSK3196165 150mg +csDMARD (Global Cohort)	Placebo +csDMARD and Tofacitinib 5mg +csDMARD (Global Cohort)	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	91	89	90	
Units: Percentage of participants				
number (not applicable)				
Week 24	6.6	5.7	11.0	
Week 52	11.4	5.6	17.2	

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of participants achieving 50%/70% improvement in American College of Rheumatology Criteria(ACR50/70) at Week 12 (Global Cohort)

End point title	Percentage of participants achieving 50%/70% improvement in American College of Rheumatology Criteria(ACR50/70) at Week 12 (Global Cohort)[12]

End point description:

Clinical Disease Activity Index (CDAI) total score is a composite score consisting of the sum of Swollen Joint Count 28 (SJC28), Tender Joint Count 28 (TJC28), Patient's Global Assessment of Arthritis Disease Activity (PtGA) (visual analogue scale with values from 0=best to 100=worst) and Physician Global Assessment of Arthritis Disease Activity (PhGA) (visual analogue scale with values from 0=best to 100=worst). PtGA and PhGA are transformed to a 0-10 scale before computing the CDAI total score. CDAI total score ranges from 0 to 76 with higher values representing higher disease activity. CDAI remission is achieved when CDAI total score <=2.8. The analysis was performed on all randomized participants who switched from placebo to study intervention at Week 12. Analysis was performed using multiple imputation method to handle missing data.

End point type	Secondary

End point timeframe:

Week 12

Notes:

[12] - 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: The endpoints are different for the different parts of the study.

End point values	GSK3196165 90mg + csDMARD (Global Cohort)	GSK3196165 150mg + csDMARD (Global Cohort)	Tofacitinib 5mg + csDMARD (Global Cohort)	Pooled Placebo (Global Cohort)
Subject group type	Reporting group	Reporting group	Reporting group	Subject analysis set
Number of subjects analysed	545	539	271	270
Units: Percentage of participants				
number (not applicable)				
ACR50	21.6	25.1	39.4	9.5
ACR70	6.9	9.6	18.9	4.2

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of participants achieving ACR50/70 at Week 24 and ACR20/50/70 Week 52 for treatment arms who started study intervention from Day 1 (Global Cohort)

End point title	Percentage of participants achieving ACR50/70 at Week 24 and ACR20/50/70 Week 52 for treatment arms who started study intervention from Day 1 (Global Cohort)[13]

End point description:

Clinical Disease Activity Index (CDAI) total score is a composite score consisting of the sum of Swollen Joint Count 28 (SJC28), Tender Joint Count 28 (TJC28), Patient's Global Assessment of Arthritis Disease Activity (PtGA) (visual analogue scale with values from 0=best to 100=worst) and Physician Global Assessment of Arthritis Disease Activity (PhGA) (visual analogue scale with values from 0=best to 100=worst). PtGA and PhGA are transformed to a 0-10 scale before computing the CDAI total score. CDAI total score ranges from 0 to 76 with higher values representing higher disease activity. CDAI remission is achieved when CDAI total score <=2.8. The analysis was performed on all randomized participants who switched from placebo to study intervention at Week 12. Analysis was performed using multiple imputation method to handle missing data.

End point type	Secondary

End point timeframe:

Week 24 and Week 52

Notes:

[13] - 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: The endpoints are different for the different parts of the study.

End point values	GSK3196165 90mg + csDMARD (Global Cohort)	GSK3196165 150mg + csDMARD (Global Cohort)	Tofacitinib 5mg + csDMARD (Global Cohort)	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	545	539	271	
Units: Percentage of participants				
number (not applicable)				
ACR20, Week 52	64.3	65.3	75.6	

ACR50, Week 24	31.6	32.8	53.6	
ACR50, Week 52	36.5	36.9	52.9	
ACR70, Week 24	14.0	13.0	28.7	
ACR70, Week 52	19.1	17.5	35.7	

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of participants achieving ACR20/50/70 at Week 24 and Week 52 for placebo switched arms (Global Cohort)

End point title	Percentage of participants achieving ACR20/50/70 at Week 24 and Week 52 for placebo switched arms (Global Cohort)[14]

End point description:

Clinical Disease Activity Index (CDAI) total score is a composite score consisting of the sum of Swollen Joint Count 28 (SJC28), Tender Joint Count 28 (TJC28), Patient's Global Assessment of Arthritis Disease Activity (PtGA) (visual analogue scale with values from 0=best to 100=worst) and Physician Global Assessment of Arthritis Disease Activity (PhGA) (visual analogue scale with values from 0=best to 100=worst). PtGA and PhGA are transformed to a 0-10 scale before computing the CDAI total score. CDAI total score ranges from 0 to 76 with higher values representing higher disease activity. CDAI remission is achieved when CDAI total score <=2.8. The analysis was performed on all randomized participants who switched from placebo to study intervention at Week 12. Analysis was performed using multiple imputation method to handle missing data.

End point type	Secondary

End point timeframe:

Week 24 and Week 52

Notes:

[14] - 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: The endpoints are different for the different parts of the study.

End point values	Placebo+csDMARD and GSK3196165 90mg+csDMARD (Global Cohort)	Placebo +csDMARD and GSK3196165 150mg +csDMARD (Global Cohort)	Placebo +csDMARD and Tofacitinib 5mg +csDMARD (Global Cohort)	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	91	89	90	
Units: Percentage of participants				
number (not applicable)				
ACR20, Week 52	56.3	63.4	70.1	
ACR50, Week 24	35.6	27.6	41.8	
ACR50, Week 52	43.7	38.5	47.2	
ACR70, Week 24	18.7	10.5	21.8	
ACR70, Week 52	22.6	15.4	20.7	

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of participants achieving Disease Activity Score using 28 joint count and C-Reactive Protein (DAS28-CRP) <=3.2 (DAS28-CRP LDA) at Week 12 (Global Cohort)

End point title	Percentage of participants achieving Disease Activity Score using 28 joint count and C-Reactive Protein (DAS28-CRP) <=3.2 (DAS28-CRP LDA) at Week 12 (Global Cohort)[15]

End point description:

Clinical Disease Activity Index (CDAI) total score is a composite score consisting of the sum of Swollen Joint Count 28 (SJC28), Tender Joint Count 28 (TJC28), Patient's Global Assessment of Arthritis Disease Activity (PtGA) (visual analogue scale with values from 0=best to 100=worst) and Physician Global Assessment of Arthritis Disease Activity (PhGA) (visual analogue scale with values from 0=best to 100=worst). PtGA and PhGA are transformed to a 0-10 scale before computing the CDAI total score. CDAI total score ranges from 0 to 76 with higher values representing higher disease activity. CDAI remission is achieved when CDAI total score <=2.8. The analysis was performed on all randomized participants who switched from placebo to study intervention at Week 12. Analysis was performed using multiple imputation method to handle missing data.

End point type	Secondary

End point timeframe:

Week 12

Notes:

[15] - 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: The endpoints are different for the different parts of the study.

End point values	GSK3196165 90mg + csDMARD (Global Cohort)	GSK3196165 150mg + csDMARD (Global Cohort)	Tofacitinib 5mg + csDMARD (Global Cohort)	Pooled Placebo (Global Cohort)
Subject group type	Reporting group	Reporting group	Reporting group	Subject analysis set
Number of subjects analysed	545	539	271	270
Units: Percentage of participants				
number (not applicable)	23.2	23.6	40.7	10.4

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of participants achieving DAS28 Erythrocyte Sedimentation Rate (ESR) <=3.2 (DAS28-ESR LDA) at Week 12 (Global Cohort)

End point title	Percentage of participants achieving DAS28 Erythrocyte Sedimentation Rate (ESR) <=3.2 (DAS28-ESR LDA) at Week 12 (Global Cohort)[16]

End point description:

The DAS28-ESR is a measure of RA disease activity calculated using Tender Joint Count 28 (TJC28), Swollen Joint Count 28 (SJC28), Erythrocyte sedimentation rate (ESR) (in millimeter [mm]/hour[hr]), Patient's Global Assessment of Arthritis Disease Activity (PtGA) (visual analogue scale with values from 0=best to 100=worst). DAS28-ESR scores range from 1.0 to 9.4, where lower scores indicate less disease activity. Low disease activity (LDA) is achieved when DAS28-ESR<=3.2. A negative change from baseline in DAS28-ESR indicates an improvement. For the purpose of all analyses up to week 12, the placebo arms were pooled into a single placebo arm to primarily serve as a reference for the comparison of active treatment arms. The analysis was performed on the ITT set. Analysis was performed using multiple imputation method to handle missing data.

End point type	Secondary

End point timeframe:

Week 12

Notes:

[16] - 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: The endpoints are different for the different parts of the study.

End point values	GSK3196165 90mg + csDMARD (Global Cohort)	GSK3196165 150mg + csDMARD (Global Cohort)	Tofacitinib 5mg + csDMARD (Global Cohort)	Pooled Placebo (Global Cohort)
Subject group type	Reporting group	Reporting group	Reporting group	Subject analysis set
Number of subjects analysed	545	539	271	270
Units: Percentage of participants				
number (not applicable)	13.2	14.6	23.6	7.3

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of participants achieving DAS28-CRP <=3.2 (DAS28-CRP LDA) at Week 24 and Week 52 for treatment arms who started study intervention from Day 1 (Global Cohort)

End point title	Percentage of participants achieving DAS28-CRP <=3.2 (DAS28-CRP LDA) at Week 24 and Week 52 for treatment arms who started study intervention from Day 1 (Global Cohort)[17]

End point description:

The DAS28-CRP is a measure of RA disease activity calculated using Tender Joint Count 28 (TJC28), Swollen Joint Count 28 (SJC28), C-reactive protein (CRP) (in mg/L), Patient's Global Assessment of Arthritis Disease Activity (PtGA) (visual analogue scale with values from 0=best to 100=worst). DAS28-CRP scores range from 1.0 to 9.4, where lower scores indicate less disease activity. Low disease activity (LDA) is achieved when DAS28-CRP greater than or equal to (<=)3.2. A negative change from baseline in DAS28-CRP indicates an improvement. The analysis was performed on all randomized participants who received study intervention from Day 01 to Week 52. Analysis was performed using multiple imputation method to handle missing data.

End point type	Secondary

End point timeframe:

Week 24 and Week 52

Notes:

[17] - 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: The endpoints are different for the different parts of the study.

End point values	GSK3196165 90mg + csDMARD (Global Cohort)	GSK3196165 150mg + csDMARD (Global Cohort)	Tofacitinib 5mg + csDMARD (Global Cohort)	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	545	539	271	
Units: Percentage of participants				
number (not applicable)				
Week 24	31.3	33.0	55.3	
Week 52	35.4	36.4	53.9	

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of participants achieving DAS28-ESR <=3.2 (DAS28-ESR LDA) at Week 24 and Week 52 for treatment arms who started study intervention from Day 1 (Global Cohort)

End point title	Percentage of participants achieving DAS28-ESR <=3.2 (DAS28-ESR LDA) at Week 24 and Week 52 for treatment arms who started study intervention from Day 1 (Global Cohort)[18]

End point description:

The DAS28-ESR is a measure of RA disease activity calculated using Tender Joint Count 28 (TJC28), Swollen Joint Count 28 (SJC28), Erythrocyte sedimentation rate (ESR) (in millimeter [mm]/hour[hr]), Patient's Global Assessment of Arthritis Disease Activity (PtGA) (visual analogue scale with values from 0=best to 100=worst). DAS28-ESR scores range from 1.0 to 9.4, where lower scores indicate less disease activity. Low disease activity (LDA) is achieved when DAS28-ESR<=3.2. A negative change from baseline in DAS28-ESR indicates an improvement. The analysis was performed on all randomized participants who received study intervention from Day 01 to Week 52. Analysis was performed using multiple imputation method to handle missing data.

End point type	Secondary

End point timeframe:

Week 24 and Week 52

Notes:

[18] - 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: The endpoints are different for the different parts of the study.

End point values	GSK3196165 90mg + csDMARD (Global Cohort)	GSK3196165 150mg + csDMARD (Global Cohort)	Tofacitinib 5mg + csDMARD (Global Cohort)	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	545	539	271	
Units: Percentage of participants				
number (not applicable)				
Week 24	19.9	24.1	37.1	
Week 52	26.2	22.9	38.8	

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of participants achieving DAS28-ESR <=3.2 (DAS28-ESR LDA) at Week 24 and Week 52 for placebo switched arms (Global Cohort)

End point title	Percentage of participants achieving DAS28-ESR <=3.2 (DAS28-ESR LDA) at Week 24 and Week 52 for placebo switched arms (Global Cohort)[19]

End point description:

The DAS28-ESR is a measure of RA disease activity calculated using Tender Joint Count 28 (TJC28), Swollen Joint Count 28 (SJC28), Erythrocyte sedimentation rate (ESR) (in millimeter [mm]/hour[hr]), Patient's Global Assessment of Arthritis Disease Activity (PtGA) (visual analogue scale with values from 0=best to 100=worst). DAS28-ESR scores range from 1.0 to 9.4, where lower scores indicate less disease activity. Low disease activity (LDA) is achieved when DAS28-ESR<=3.2. A negative change from baseline in DAS28-ESR indicates an improvement. The analysis was performed on all randomized participants who switched from placebo to study intervention at Week 12. Analysis was performed using multiple imputation method to handle missing data.

End point type	Secondary

End point timeframe:

Week 24 and Week 52

Notes:

[19] - 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: The endpoints are different for the different parts of the study.

End point values	Placebo+csDMARD and GSK3196165 90mg+csDMARD (Global Cohort)	Placebo +csDMARD and GSK3196165 150mg +csDMARD (Global Cohort)	Placebo +csDMARD and Tofacitinib 5mg +csDMARD (Global Cohort)	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	91	89	90	
Units: Percentage of participants				
number (not applicable)				
Week 24	30.2	14.2	23.4	
Week 52	28.0	16.6	31.5	

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of participants achieving DAS28-CRP <=3.2 (DAS28-CRP LDA) at Week 24 and Week 52 for placebo switched arms (Global Cohort)

End point title	Percentage of participants achieving DAS28-CRP <=3.2 (DAS28-CRP LDA) at Week 24 and Week 52 for placebo switched arms (Global Cohort)[20]

End point description:

The DAS28-CRP is a measure of RA disease activity calculated using Tender Joint Count 28 (TJC28), Swollen Joint Count 28 (SJC28), C-reactive protein (CRP) (in mg/L), Patient's Global Assessment of Arthritis Disease Activity (PtGA) (visual analogue scale with values from 0=best to 100=worst). DAS28-CRP scores range from 1.0 to 9.4, where lower scores indicate less disease activity. Low disease activity (LDA) is achieved when DAS28-CRP greater than or equal to (<=)3.2. A negative change from baseline in DAS28-CRP indicates an improvement. The analysis was performed on all randomized participants who switched from placebo to study intervention at Week 12. Analysis was performed using multiple imputation method to handle missing data.

End point type	Secondary

End point timeframe:

Week 24 and Week 52

Notes:

[20] - 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: The endpoints are different for the different parts of the study.

End point values	Placebo+csDMARD and GSK3196165 90mg+csDMARD (Global Cohort)	Placebo +csDMARD and GSK3196165 150mg +csDMARD (Global Cohort)	Placebo +csDMARD and Tofacitinib 5mg +csDMARD (Global Cohort)	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	91	89	90	
Units: Percentage of participants				
number (not applicable)				
Week 24	37.5	19.3	42.7	
Week 52	41.4	31.4	39.6	

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of participants achieving DAS28-CRP <2.6 (DAS28-CRP Remission) at Week 12 (Global Cohort)

End point title	Percentage of participants achieving DAS28-CRP <2.6 (DAS28-CRP Remission) at Week 12 (Global Cohort)[21]

End point description:

The DAS28-ESR is a measure of RA disease activity calculated using Tender Joint Count 28 (TJC28), Swollen Joint Count 28 (SJC28), Erythrocyte sedimentation rate (ESR) (in millimeter [mm]/hour[hr]), Patient's Global Assessment of Arthritis Disease Activity (PtGA) (visual analogue scale with values from 0=best to 100=worst). DAS28-ESR scores range from 1.0 to 9.4, where lower scores indicate less disease activity. Low disease activity (LDA) is achieved when DAS28-ESR<=3.2. A negative change from baseline in DAS28-ESR indicates an improvement. The analysis was performed on all randomized participants who switched from placebo to study intervention at Week 12. Analysis was performed using multiple imputation method to handle missing data.

End point type	Secondary

End point timeframe:

Week 12

Notes:

[21] - 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: The endpoints are different for the different parts of the study.

End point values	GSK3196165 90mg + csDMARD (Global Cohort)	GSK3196165 150mg + csDMARD (Global Cohort)	Tofacitinib 5mg + csDMARD (Global Cohort)	Pooled Placebo (Global Cohort)
Subject group type	Reporting group	Reporting group	Reporting group	Subject analysis set
Number of subjects analysed	545	539	271	270
Units: Percentage of participants				
number (not applicable)	11.5	12.0	23.2	5.5

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of participants achieving DAS28 ESR <2.6 (DAS28-ESR Remission) at Week 12 (Global Cohort)

End point title	Percentage of participants achieving DAS28 ESR <2.6 (DAS28-ESR Remission) at Week 12 (Global Cohort)[22]

End point description:

The DAS28-ESR is a measure of RA disease activity calculated using Tender Joint Count 28 (TJC28), Swollen Joint Count 28 (SJC28), Erythrocyte sedimentation rate (ESR) (in mm/hr), Patient's Global Assessment of Arthritis Disease Activity (PtGA) (visual analogue scale with values from 0=best to 100=worst). DAS28-ESR scores range from 1.0 to 9.4, where lower scores indicate less disease activity. Remission is achieved when DAS28-ESR <2.6. A negative change from baseline in DAS28-ESR indicates an improvement. For the purpose of all analyses up to week 12, the placebo arms were pooled into a single placebo arm to primarily serve as a reference for the comparison of active treatment arms. The analysis was performed on the ITT set. Analysis was performed using multiple imputation method to handle missing data.

End point type	Secondary

End point timeframe:

Week 12

Notes:

[22] - 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: The endpoints are different for the different parts of the study.

End point values	GSK3196165 90mg + csDMARD (Global Cohort)	GSK3196165 150mg + csDMARD (Global Cohort)	Tofacitinib 5mg + csDMARD (Global Cohort)	Pooled Placebo (Global Cohort)
Subject group type	Reporting group	Reporting group	Reporting group	Subject analysis set
Number of subjects analysed	545	539	271	270
Units: Percentage of participants				
number (not applicable)	7.1	6.1	12.6	3.8

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of participants achieving DAS28-CRP <2.6 (DAS28-CRP Remission) at Week 24 and Week 52 for treatment arms who started study intervention from Day 1 (Global Cohort)

End point title	Percentage of participants achieving DAS28-CRP <2.6 (DAS28-CRP Remission) at Week 24 and Week 52 for treatment arms who started study intervention from Day 1 (Global Cohort)[23]

End point description:

The DAS28-CRP is a measure of RA disease activity calculated using Tender Joint Count 28 (TJC28), Swollen Joint Count 28 (SJC28), C-reactive protein (CRP) (in mg/L), Patient's Global Assessment of Arthritis Disease Activity (PtGA) (visual analogue scale with values from 0=best to 100=worst). DAS28-CRP scores range from 1.0 to 9.4, where lower scores indicate less disease activity. Remission is achieved when DAS28-CRP less than (<)2.6. A negative change from baseline in DAS28-CRP indicates an improvement. The analysis was performed on all randomized participants who received study intervention from Day 01 to Week 52. Analysis was performed using multiple imputation method to handle missing data.

End point type	Secondary

End point timeframe:

Week 24 and Week 52

Notes:

[23] - 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: The endpoints are different for the different parts of the study.

End point values	GSK3196165 90mg + csDMARD (Global Cohort)	GSK3196165 150mg + csDMARD (Global Cohort)	Tofacitinib 5mg + csDMARD (Global Cohort)	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	545	539	271	
Units: Percentage of participants				
number (not applicable)				
Week 24	16.7	19.6	38.0	
Week 52	23.6	21.2	41.2	

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of participants achieving DAS28 ESR <2.6 (DAS28-ESR Remission) at Week 24 and Week 52 for treatment arms who started study intervention from Day 1 (Global Cohort)

End point title	Percentage of participants achieving DAS28 ESR <2.6 (DAS28-ESR Remission) at Week 24 and Week 52 for treatment arms who started study intervention from Day 1 (Global Cohort)[24]

End point description:

The DAS28-ESR is a measure of RA disease activity calculated using Tender Joint Count 28 (TJC28), Swollen Joint Count 28 (SJC28), Erythrocyte sedimentation rate (ESR) (in mm/hr), Patient's Global Assessment of Arthritis Disease Activity (PtGA) (visual analogue scale with values from 0=best to 100=worst). DAS28-ESR scores range from 1.0 to 9.4, where lower scores indicate less disease activity. Remission is achieved when DAS28-ESR <2.6. A negative change from baseline in DAS28-ESR indicates an improvement. The analysis was performed on all randomized participants who received study intervention from Day 01 to Week 52. Analysis was performed using multiple imputation method to handle missing data.

End point type	Secondary

End point timeframe:

Week 24 and Week 52

Notes:

[24] - 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: The endpoints are different for the different parts of the study.

End point values	GSK3196165 90mg + csDMARD (Global Cohort)	GSK3196165 150mg + csDMARD (Global Cohort)	Tofacitinib 5mg + csDMARD (Global Cohort)	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	545	539	271	
Units: Percentage of participants				
number (not applicable)				

Week 24	8.7	11.7	23.4	
Week 52	14.3	11.7	19.9	

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of participants achieving DAS28-CRP <2.6 (DAS28-CRP Remission) at Week 24 and Week 52 for placebo switched arms (Global Cohort)

End point title	Percentage of participants achieving DAS28-CRP <2.6 (DAS28-CRP Remission) at Week 24 and Week 52 for placebo switched arms (Global Cohort)[25]

End point description:

The DAS28-CRP is a measure of RA disease activity calculated using Tender Joint Count 28 (TJC28), Swollen Joint Count 28 (SJC28), C-reactive protein (CRP) (in mg/L), Patient's Global Assessment of Arthritis Disease Activity (PtGA) (visual analogue scale with values from 0=best to 100=worst). DAS28-CRP scores range from 1.0 to 9.4, where lower scores indicate less disease activity. Remission is achieved when DAS28-CRP less than (<)2.6. A negative change from baseline in DAS28-CRP indicates an improvement. The analysis was performed on all randomized participants who switched from placebo to study intervention at Week 12. Analysis was performed using multiple imputation method to handle missing data.

End point type	Secondary

End point timeframe:

Week 24 and Week 52

Notes:

[25] - 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: The endpoints are different for the different parts of the study.

End point values	Placebo+csDMARD and GSK3196165 90mg+csDMARD (Global Cohort)	Placebo +csDMARD and GSK3196165 150mg +csDMARD (Global Cohort)	Placebo +csDMARD and Tofacitinib 5mg +csDMARD (Global Cohort)	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	91	89	90	
Units: Percentage of participants				
number (not applicable)				
Week 24	23.3	11.5	23.8	
Week 52	30.4	19.8	26.4	

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of participants achieving DAS28 ESR <2.6 (DAS28-ESR Remission) at Week 24 and Week 52 for placebo switched arms (Global Cohort)

End point title	Percentage of participants achieving DAS28 ESR <2.6 (DAS28-ESR Remission) at Week 24 and Week 52 for placebo switched

	arms (Global Cohort)[26]

End point description:

The DAS28-ESR is a measure of RA disease activity calculated using Tender Joint Count 28 (TJC28), Swollen Joint Count 28 (SJC28), Erythrocyte sedimentation rate (ESR) (in mm/hr), Patient's Global Assessment of Arthritis Disease Activity (PtGA) (visual analogue scale with values from 0=best to 100=worst). DAS28-ESR scores range from 1.0 to 9.4, where lower scores indicate less disease activity. Remission is achieved when DAS28-ESR <2.6. A negative change from baseline in DAS28-ESR indicates an improvement. The analysis was performed on all randomized participants who switched from placebo to study intervention at Week 12. Analysis was performed using multiple imputation method to handle missing data.

End point type	Secondary

End point timeframe:

Week 24 and Week 52

Notes:

[26] - 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: The endpoints are different for the different parts of the study.

End point values	Placebo+csDMARD and GSK3196165 90mg+csDMARD (Global Cohort)	Placebo +csDMARD and GSK3196165 150mg +csDMARD (Global Cohort)	Placebo +csDMARD and Tofacitinib 5mg +csDMARD (Global Cohort)	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	91	89	90	
Units: Percentage of participants				
number (not applicable)				
Week 24	13.4	6.2	13.4	
Week 52	16.1	11.5	13.4	

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of participants achieving a good/moderate EULAR response at Week 24 and Week 52 for treatment arms who started study intervention from Day 1 (Global Cohort)

End point title	Percentage of participants achieving a good/moderate EULAR response at Week 24 and Week 52 for treatment arms who started study intervention from Day 1 (Global Cohort)[27]

End point description:

DAS28-CRP and DAS28-ESR scores were categorized using EULAR response criteria. Response was defined based on combination of current DAS28 score and improvement in current score relative to Baseline. The definition of no response, moderate response and good response was as; DAS28 <=3.2 and DAS28 decrease from Baseline (>1.2:good response, >0.6 to <=1.2:moderate response, <=0.6:no response); DAS28 >3.2 to <=5.1 and DAS28 decrease from Baseline (>1.2:moderate response, >0.6 to <=1.2:moderate response, <=0.6:no response) and DAS28 >5.1 and DAS28 decrease from Baseline (>1.2:moderate response, >0.6 to <=1.2:no response, <=0.6:no response). If the post-Baseline DAS28-CRP score was missing, then the corresponding EULAR category was set to missing. The analysis was performed on all randomized participants who received study intervention from Day 01 to Week 52. Analysis was performed using multiple imputation method to handle missing data.

End point type	Secondary

End point timeframe:

Week 24 and Week 52

Notes:

[27] - 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: The endpoints are different for the different parts of the study.

End point values	GSK3196165 90mg + csDMARD (Global Cohort)	GSK3196165 150mg + csDMARD (Global Cohort)	Tofacitinib 5mg + csDMARD (Global Cohort)	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	545	539	271	
Units: Percentage of participants				
number (not applicable)				
Week 24	79.8	80.5	90.4	
Week 52	80.3	78.9	88.4	

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of participants achieving a good/moderate European league against rheumatism (EULAR) response at Week 12 (Global Cohort)

End point title	Percentage of participants achieving a good/moderate European league against rheumatism (EULAR) response at Week 12 (Global Cohort)[28]

End point description:

DAS28-CRP and DAS28-ESR scores were categorized using EULAR response criteria. Response was defined based on combination of current DAS28 score and improvement in current score relative to Baseline. The definition of no response, moderate response and good response was as; DAS28 <=3.2 and DAS28 decrease from Baseline (>1.2:good response, >0.6 to <=1.2:moderate response, <=0.6:no response); DAS28 >3.2 to <=5.1 and DAS28 decrease from Baseline (>1.2:moderate response, >0.6 to <=1.2:moderate response, <=0.6:no response) and DAS28 >5.1 and DAS28 decrease from Baseline (>1.2:moderate response, >0.6 to <=1.2:no response, <=0.6:no response). If the post-Baseline DAS28-CRP score was missing, then the corresponding EULAR category was set to missing. For purpose of all analyses up to week 12, placebo arms were pooled into single arm to primarily serve as reference for comparison of active treatment arms. Analysis was performed on ITT set using multiple imputation method to handle missing data.

End point type	Secondary

End point timeframe:

Week 12

Notes:

[28] - 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: The endpoints are different for the different parts of the study.

End point values	GSK3196165 90mg + csDMARD (Global Cohort)	GSK3196165 150mg + csDMARD (Global Cohort)	Tofacitinib 5mg + csDMARD (Global Cohort)	Pooled Placebo (Global Cohort)
Subject group type	Reporting group	Reporting group	Reporting group	Subject analysis set
Number of subjects analysed	545	539	271	270
Units: Percentage of participants				
number (not applicable)	70.0	71.3	83.8	46.3

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of participants achieving a good/moderate EULAR response at Week 24 and Week 52 for placebo switched arms (Global Cohort)

End point title	Percentage of participants achieving a good/moderate EULAR response at Week 24 and Week 52 for placebo switched arms (Global Cohort)[29]

End point description:

DAS28-CRP and DAS28-ESR scores were categorized using EULAR response criteria. Response was defined based on combination of current DAS28 score and improvement in current score relative to Baseline. The definition of no response, moderate response and good response was as; DAS28 <=3.2 and DAS28 decrease from Baseline (>1.2:good response, >0.6 to <=1.2:moderate response, <=0.6:no response); DAS28 >3.2 to <=5.1 and DAS28 decrease from Baseline (>1.2:moderate response, >0.6 to <=1.2:moderate response, <=0.6:no response) and DAS28 >5.1 and DAS28 decrease from Baseline (>1.2:moderate response, >0.6 to <=1.2:no response, <=0.6:no response). If the post-Baseline DAS28-CRP score was missing, then the corresponding EULAR category was set to missing. The analysis was performed on all randomized participants who switched from placebo to study intervention at Week 12. Analysis was performed using multiple imputation method to handle missing data.

End point type	Secondary

End point timeframe:

Week 24 and Week 52

Notes:

[29] - 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: The endpoints are different for the different parts of the study.

End point values	Placebo+csDMARD and GSK3196165 90mg+csDMARD (Global Cohort)	Placebo +csDMARD and GSK3196165 150mg +csDMARD (Global Cohort)	Placebo +csDMARD and Tofacitinib 5mg +csDMARD (Global Cohort)	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	91	89	90	
Units: Percentage of participants				
number (not applicable)				
Week 24	78.4	73.0	82.7	
Week 52	74.5	81.1	81.5	

Statistical analyses

No statistical analyses for this end point

Secondary: Number of participants achieving ACR/EULAR remission at Week 12 (Global Cohort)

End point title	Number of participants achieving ACR/EULAR remission at Week 12 (Global Cohort)[30]

End point description:

Boolean-based ACR/EULAR remission is achieved if all of the following requirements are met at the same timepoint: Tender Joint Count 68 (TJC68) <= 1, Swollen Joint Count 66 (SJC66) <= 1, high sensitivity C-reactive Protein (hsCRP) <= 1mg/dl and patient's global assessment of disease activity (PtGA) <= 10. For the purpose of all analyses up to week 12, the placebo arms were pooled into a single placebo arm to primarily serve as a reference for the comparison of active treatment arms. The analysis was performed on the ITT set that includes all randomized participants who received at least one dose of study treatment. This population was based on the treatment the participant was randomized to. Only those participants with data available at the specified time points were analyzed.

End point type	Secondary

End point timeframe:

Week 12

Notes:

[30] - 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: The endpoints are different for the different parts of the study.

End point values	GSK3196165 90mg + csDMARD (Global Cohort)	GSK3196165 150mg + csDMARD (Global Cohort)	Tofacitinib 5mg + csDMARD (Global Cohort)	Pooled Placebo (Global Cohort)
Subject group type	Reporting group	Reporting group	Reporting group	Subject analysis set
Number of subjects analysed	545	539	271	270
Units: Participants	13	12	15	3

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of participants achieving no radiographic progression Van der Heijde modified total sharp scores (mTSS) <= 0.5) at Week 12 (Global Cohort)

End point title	Percentage of participants achieving no radiographic progression Van der Heijde modified total sharp scores (mTSS) <= 0.5) at Week 12 (Global Cohort)[31]

End point description:

Van der Heijde mTSS is utilized for scoring radiographs of hands and feet in rheumatoid arthritis. This method includes 16 areas of erosions, and 15 areas for joint space narrowing (JSN) in each hand, and 6 areas for erosions and 6 areas JSN in each foot. The total mTSS score is the sum of erosion (maximum of 280) and JSN (maximum of 168) scores. The score ranges from 0 to 448 for mTSS with higher values representing higher disease activity. No radiographic progression is defined as a change from Baseline in van der Heijde mTSS score of <=0.5. For the purpose of all analyses up to week 12, the placebo arms were pooled into a single placebo arm to primarily serve as a reference for the comparison of active treatment arms. The analysis was performed on the ITT set. Analysis was performed using multiple imputation method to handle missing data.

End point type	Secondary

End point timeframe:

Week 12

Notes:

[31] - 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: The endpoints are different for the different parts of the study.

End point values	GSK3196165 90mg + csDMARD (Global Cohort)	GSK3196165 150mg + csDMARD (Global Cohort)	Tofacitinib 5mg + csDMARD (Global Cohort)	Pooled Placebo (Global Cohort)
Subject group type	Reporting group	Reporting group	Reporting group	Subject analysis set
Number of subjects analysed	545	539	271	270
Units: Percentage of participants				
number (not applicable)	88.2	92.7	94.1	85.8

Statistical analyses

No statistical analyses for this end point

Secondary: Number of participants achieving ACR/EULAR remission at Week 24 and Week 52 for treatment arms who started study intervention from Day 1 (Global Cohort)

End point title	Number of participants achieving ACR/EULAR remission at Week 24 and Week 52 for treatment arms who started study intervention from Day 1 (Global Cohort)[32]

End point description:

Boolean-based ACR/EULAR remission is achieved if all of the following requirements are met at the same timepoint: Tender Joint Count 68 (TJC68) <= 1, Swollen Joint Count 66 (SJC66) <= 1, high sensitivity C-reactive Protein (hsCRP) <= 1mg/dl and patient's global assessment of disease activity (PtGA) <= 10. The analysis was performed on all randomized participants who received study intervention from Day 01 to Week 52. Only those participants with data available at the specified time points were analyzed.

End point type	Secondary

End point timeframe:

Week 24 and Week 52

Notes:

[32] - 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: The endpoints are different for the different parts of the study.

End point values	GSK3196165 90mg + csDMARD (Global Cohort)	GSK3196165 150mg + csDMARD (Global Cohort)	Tofacitinib 5mg + csDMARD (Global Cohort)	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	497	477	247	
Units: Participants				
Week 24, n=497,477,247	21	18	28	
Week 52, n=461,448,227	37	26	27	

Statistical analyses

No statistical analyses for this end point

Secondary: Number of participants achieving ACR/EULAR remission at Week 24 and Week 52 for placebo switched arms (Global Cohort)

End point title	Number of participants achieving ACR/EULAR remission at Week 24 and Week 52 for placebo switched arms (Global

	Cohort)[33]

End point description:

Boolean-based ACR/EULAR remission is achieved if all of the following requirements are met at the same timepoint: Tender Joint Count 68 (TJC68) <= 1, Swollen Joint Count 66 (SJC66) <= 1, high sensitivity C-reactive Protein (hsCRP) <= 1mg/dl and patient's global assessment of disease activity (PtGA) <= 10. The analysis was performed on all randomized participants who switched from placebo to study intervention at Week 12. Only those participants with data available at the specified time points were analyzed.

End point type	Secondary

End point timeframe:

Week 24 and Week 52

Notes:

[33] - 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: The endpoints are different for the different parts of the study.

End point values	Placebo+csDMARD and GSK3196165 90mg+csDMARD (Global Cohort)	Placebo +csDMARD and GSK3196165 150mg +csDMARD (Global Cohort)	Placebo +csDMARD and Tofacitinib 5mg +csDMARD (Global Cohort)	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	83	75	76	
Units: Participants				
Week 24, n=83,75,76	4	2	3	
Week 52, n=74,68,67	8	4	7	

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of participants achieving no radiographic progression (mTSS <= 0.5) at Week 24 and Week 52 for treatment arms who started study intervention from Day 1 (Global Cohort)

End point title	Percentage of participants achieving no radiographic progression (mTSS <= 0.5) at Week 24 and Week 52 for treatment arms who started study intervention from Day 1 (Global Cohort)[34]

End point description:

Van der Heijde mTSS is utilized for scoring radiographs of hands and feet in rheumatoid arthritis. This method includes 16 areas of erosions, and 15 areas for joint space narrowing (JSN) in each hand, and 6 areas for erosions and 6 areas JSN in each foot. The total mTSS score is the sum of erosion (maximum of 280) and JSN (maximum of 168) scores. The score ranges from 0 to 448 for mTSS with higher values representing higher disease activity. No radiographic progression is defined as a change from Baseline in van der Heijde mTSS score of <=0.5. The analysis was performed on all randomized participants who received study intervention from Day 01 to Week 52. Analysis was performed using multiple imputation method to handle missing data.

End point type	Secondary

End point timeframe:

Week 24 and Week 52

Notes:

[34] - 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: The endpoints are different for the different parts of the study.

End point values	GSK3196165 90mg + csDMARD (Global Cohort)	GSK3196165 150mg + csDMARD (Global Cohort)	Tofacitinib 5mg + csDMARD (Global Cohort)	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	545	539	271	
Units: Percentage of participants				
number (not applicable)				
Week 24	84.6	89.9	92.7	
Week 52	78.2	83.8	87.7	

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of participants achieving no radiographic progression (mTSS <= 0.5) at Week 24 and Week 52 for placebo switched arms (Global Cohort)

End point title	Percentage of participants achieving no radiographic progression (mTSS <= 0.5) at Week 24 and Week 52 for placebo switched arms (Global Cohort)[35]

End point description:

Van der Heijde mTSS is utilized for scoring radiographs of hands and feet in rheumatoid arthritis. This method includes 16 areas of erosions, and 15 areas for joint space narrowing (JSN) in each hand, and 6 areas for erosions and 6 areas JSN in each foot. The total mTSS score is the sum of erosion (maximum of 280) and JSN (maximum of 168) scores. The score ranges from 0 to 448 for mTSS with higher values representing higher disease activity. No radiographic progression is defined as a change from Baseline in van der Heijde mTSS score of <=0.5. The analysis was performed on all randomized participants who switched from placebo to study intervention at Week 12. Analysis was performed using multiple imputation method to handle missing data.

End point type	Secondary

End point timeframe:

Week 24 and Week 52

Notes:

[35] - 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: The endpoints are different for the different parts of the study.

End point values	Placebo+csDMARD and GSK3196165 90mg+csDMARD (Global Cohort)	Placebo +csDMARD and GSK3196165 150mg +csDMARD (Global Cohort)	Placebo +csDMARD and Tofacitinib 5mg +csDMARD (Global Cohort)	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	91	89	90	
Units: Percentage of participants				
number (not applicable)				
Week 24	88.1	82.2	83.9	
Week 52	85.6	71.9	87.9	

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in CDAI total score at Week 12 (Global Cohort)

End point title	Change from Baseline in CDAI total score at Week 12 (Global Cohort)[36]

End point description:

Clinical Disease Activity Index (CDAI) total score is a composite score consisting of sum of Swollen Joint Count 28 (SJC28), Tender Joint Count 28 (TJC28), Patient's Global Assessment of Arthritis Disease Activity (PtGA) and Physician Global Assessment of Arthritis Disease Activity (PhGA) (VAS with values from 0=best to 100=worst). PtGA and PhGA are transformed to 0-10 scale. CDAI total score ranges from 0 to 76 with higher values representing higher disease activity. Low disease activity (LDA) is achieved when CDAI total score <=10. Baseline was defined as latest pre-dose assessment with a non-missing value, including from unscheduled visits. Change from Baseline was calculated by subtracting post dose value from Baseline. For the purpose of analyses up to week 12, the placebo arms were pooled into single placebo arm to primarily serve as reference for comparison of active treatment arms. Analysis was performed on ITT set. Multiple imputation method was used to handle missing data.

End point type	Secondary

End point timeframe:

Baseline (Day 1) and week 12

Notes:

[36] - 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: The endpoints are different for the different parts of the study.

End point values	GSK3196165 90mg + csDMARD (Global Cohort)	GSK3196165 150mg + csDMARD (Global Cohort)	Tofacitinib 5mg + csDMARD (Global Cohort)	Pooled Placebo (Global Cohort)
Subject group type	Reporting group	Reporting group	Reporting group	Subject analysis set
Number of subjects analysed	545	539	271	270
Units: Scores on a scale				
least squares mean (standard error)	-15.50 (± 0.680)	-16.31 (± 0.678)	-21.06 (± 0.878)	-9.56 (± 0.896)

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in CDAI total score at Week 24 and Week 52 for treatment arms who started study intervention from Day 1 (Global Cohort)

End point title	Change from Baseline in CDAI total score at Week 24 and Week 52 for treatment arms who started study intervention from Day 1 (Global Cohort)[37]

End point description:

Clinical Disease Activity Index (CDAI) total score is a composite score consisting of sum of Swollen Joint

Count 28 (SJC28), Tender Joint Count 28 (TJC28), Patient's Global Assessment of Arthritis Disease Activity (PtGA) and Physician Global Assessment of Arthritis Disease Activity (PhGA) (VAS with values from 0=best to 100=worst). PtGA and PhGA are transformed to a 0-10 scale . CDAI total score ranges from 0 to 76 with higher values representing higher disease activity. Low disease activity (LDA) is achieved when CDAI total score <=10. Baseline was defined as latest pre-dose assessment with a non-missing value, including from unscheduled visits. Change from Baseline was calculated by subtracting post dose value from Baseline. The analysis was performed on all randomized participants who received study intervention from Day 01 to Week 52. Analysis was performed using multiple imputation method to handle missing data.

End point type	Secondary

End point timeframe:

Baseline (Day 1), Week 24 and Week 52

Notes:

[37] - 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: The endpoints are different for the different parts of the study.

End point values	GSK3196165 90mg + csDMARD (Global Cohort)	GSK3196165 150mg + csDMARD (Global Cohort)	Tofacitinib 5mg + csDMARD (Global Cohort)	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	545	539	271	
Units: Scores on a scale				
least squares mean (standard error)				
Week 24	-20.14 (± 0.669)	-20.68 (± 0.677)	-24.93 (± 0.848)	
Week 52	-20.84 (± 0.750)	-21.14 (± 0.762)	-24.87 (± 0.936)	

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in CDAI total score at Week 24 and Week 52 for placebo switched arms (Global Cohort)

End point title	Change from Baseline in CDAI total score at Week 24 and Week 52 for placebo switched arms (Global Cohort)[38]

End point description:

Clinical Disease Activity Index (CDAI) total score is a composite score consisting of sum of Swollen Joint Count 28 (SJC28), Tender Joint Count 28 (TJC28), Patient's Global Assessment of Arthritis Disease Activity (PtGA) and Physician Global Assessment of Arthritis Disease Activity (PhGA) (VAS with values from 0=best to 100=worst). PtGA and PhGA are transformed to a 0-10 scale. CDAI total score ranges from 0 to 76 with higher values representing higher disease activity. Low disease activity (LDA) is achieved when CDAI total score <=10. Baseline was defined as latest pre-dose assessment with a non-missing value, including from unscheduled visits. Change from Baseline was calculated by subtracting post dose value from Baseline. The analysis was performed on all randomized participants who switched from placebo to study intervention at Week 12. Analysis was performed using multiple imputation method to handle missing data. For efficacy assessments baseline is interpreted as Day 1.

End point type	Secondary

End point timeframe:

Baseline (Day 1), Week 24 and Week 52

Notes:

[38] - 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: The endpoints are different for the different parts of the study.

End point values	Placebo+csDMARD and GSK3196165 90mg+csDMARD (Global Cohort)	Placebo +csDMARD and GSK3196165 150mg +csDMARD (Global Cohort)	Placebo +csDMARD and Tofacitinib 5mg +csDMARD (Global Cohort)	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	91	89	90	
Units: Scores on a scale				
least squares mean (standard error)				
Week 24	-20.26 (± 1.334)	-16.78 (± 1.396)	-20.60 (± 1.385)	
Week 52	-20.52 (± 1.472)	-20.95 (± 1.547)	-22.01 (± 1.545)	

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in DAS28-CRP/DAS28-ESR at Week 12 (Global Cohort)

End point title	Change from Baseline in DAS28-CRP/DAS28-ESR at Week 12 (Global Cohort)[39]

End point description:

DAS28-CRP and DAS28-ESR are measure of RA disease activity calculated using Swollen Joint Count 28 (SJC28), Tender Joint Count 28 (TJC28), high sensitivity C-reactive Protein (hsCRP in mg/L)/Erythrocyte sedimentation rate (ESR) [ESR in millimeter/hour (mm/hr)] and patient's global assessment of disease activity (PtGA) transformed to a 0-10 scale. Total score range from 0-9.4, with higher scores indicating more disease activity. Baseline was defined as the latest pre-dose assessment with a non-missing value, including those from unscheduled visits. Change from Baseline was calculated by subtracting the post dose visit value from the Baseline value. For the purpose of all analyses up to week 12, the placebo arms were pooled into a single placebo arm to primarily serve as a reference for the comparison of active treatment arms. The analysis was performed on the ITT set. Analysis was performed using multiple imputation method to handle missing data.

End point type	Secondary

End point timeframe:

Baseline (Day 1) and Week 12

Notes:

[39] - 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: The endpoints are different for the different parts of the study.

End point values	GSK3196165 90mg + csDMARD (Global Cohort)	GSK3196165 150mg + csDMARD (Global Cohort)	Tofacitinib 5mg + csDMARD (Global Cohort)	Pooled Placebo (Global Cohort)
Subject group type	Reporting group	Reporting group	Reporting group	Subject analysis set
Number of subjects analysed	545	539	271	270
Units: Scores on a scale				
least squares mean (standard error)				

DAS28-CRP	-1.28 (± 0.064)	-1.35 (± 0.064)	-2.02 (± 0.082)	-0.71 (± 0.085)
DAS28-ESR	-1.34 (± 0.066)	-1.40 (± 0.066)	-1.95 (± 0.084)	-0.73 (± 0.087)

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in DAS28-CRP/DAS28-ESR at Week 24 and Week 52 for treatment arms who started study intervention from Day 1 (Global Cohort)

End point title	Change from Baseline in DAS28-CRP/DAS28-ESR at Week 24 and Week 52 for treatment arms who started study intervention from Day 1 (Global Cohort)[40]

End point description:

DAS28-CRP and DAS28-ESR are measure of RA disease activity calculated using Swollen Joint Count 28 (SJC28), Tender Joint Count 28 (TJC28), high sensitivity C-reactive Protein (hsCRP in mg/L)/Erythrocyte sedimentation rate (ESR) [ESR in millimeter/hour (mm/hr)] and patient's global assessment of disease activity (PtGA) transformed to a 0-10 scale. Total score range from 0-9.4, with higher scores indicating more disease activity. Baseline was defined as the latest pre-dose assessment with a non-missing value, including those from unscheduled visits. Change from Baseline was calculated by subtracting the post dose visit value from the Baseline value. The analysis was performed on all randomized participants who received study intervention from Day 01 to Week 52. Analysis was performed using multiple imputation method to handle missing data.

End point type	Secondary

End point timeframe:

Baseline (Day 1), Week 24 and Week 52

Notes:

[40] - 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: The endpoints are different for the different parts of the study.

End point values	GSK3196165 90mg + csDMARD (Global Cohort)	GSK3196165 150mg + csDMARD (Global Cohort)	Tofacitinib 5mg + csDMARD (Global Cohort)	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	545	539	271	
Units: Scores on a scale				
least squares mean (standard error)				
DAS28-CRP, Week 24	-1.65 (± 0.070)	-1.71 (± 0.071)	-2.45 (± 0.089)	
DAS28-CRP, Week 52	-1.77 (± 0.079)	-1.76 (± 0.080)	-2.40 (± 0.098)	
DAS28-ESR, Week 24	-1.73 (± 0.073)	-1.79 (± 0.074)	-2.40 (± 0.092)	
DAS28-ESR, Week 52	-1.87 (± 0.084)	-1.82 (± 0.084)	-2.38 (± 0.102)	

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in DAS28-CRP/DAS28-ESR at Week 24 and Week 52 for placebo switched arms (Global Cohort)

End point title	Change from Baseline in DAS28-CRP/DAS28-ESR at Week 24 and Week 52 for placebo switched arms (Global Cohort)[41]

End point description:

DAS28-CRP and DAS28-ESR are measure of RA disease activity calculated using Swollen Joint Count 28 (SJC28), Tender Joint Count 28 (TJC28), high sensitivity C-reactive Protein (hsCRP in mg/L)/Erythrocyte sedimentation rate (ESR) [ESR in millimeter/hour (mm/hr)] and patient's global assessment of disease activity (PtGA) transformed to a 0-10 scale. Total score range from 0-9.4, with higher scores indicating more disease activity. Baseline was defined as the latest pre-dose assessment with a non-missing value, including those from unscheduled visits. Change from Baseline was calculated by subtracting the post dose visit value from the Baseline value. The analysis was performed on all randomized participants who switched from placebo to study intervention at Week 12. Analysis was performed using multiple imputation method to handle missing data. For efficacy assessments baseline is interpreted as Day 1.

End point type	Secondary

End point timeframe:

Baseline (Day 1), Week 24 and Week 52

Notes:

[41] - 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: The endpoints are different for the different parts of the study.

End point values	Placebo+csDMARD and GSK3196165 90mg+csDMARD (Global Cohort)	Placebo +csDMARD and GSK3196165 150mg +csDMARD (Global Cohort)	Placebo +csDMARD and Tofacitinib 5mg +csDMARD (Global Cohort)	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	91	89	90	
Units: Scores on a scale				
least squares mean (standard error)				
DAS28-CRP, Week 24	-1.76 (± 0.139)	-1.39 (± 0.146)	-1.88 (± 0.145)	
DAS28-CRP, Week 52	-1.81 (± 0.156)	-1.70 (± 0.164)	-1.97 (± 0.165)	
DAS28-ESR, Week 24	-1.88 (± 0.144)	-1.48 (± 0.149)	-1.93 (± 0.148)	
DAS28-ESR, Week 52	-1.88 (± 0.165)	-1.74 (± 0.172)	-1.96 (± 0.169)	

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in Van der Heijde mTSS at Week 12 (Global Cohort)

End point title	Change from Baseline in Van der Heijde mTSS at Week 12 (Global Cohort)[42]

End point description:

Van der Heijde mTSS is utilized for scoring radiographs of hands and feet in rheumatoid arthritis. This method includes 16 areas of erosions, and 15 areas for joint space narrowing (JSN) in each hand, and 6 areas for erosions and 6 areas JSN in each foot. The total mTSS score is the sum of erosion (maximum

of 280) and JSN (maximum of 168) scores. The score range from 0 to 448 for mTSS with higher values representing higher disease activity. Baseline was defined as the latest pre-dose assessment with a non-missing value, including those from unscheduled visits. Change from Baseline was calculated by subtracting the post dose visit value from the Baseline value. For the purpose of all analyses up to week 12, the placebo arms were pooled into a single placebo arm to primarily serve as a reference for the comparison of active treatment arms. The analysis was performed on the ITT set. Analysis was performed using multiple imputation method to handle missing data.

End point type	Secondary

End point timeframe:

Baseline (Day 1) and Week 12

Notes:

[42] - 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: The endpoints are different for the different parts of the study.

End point values	GSK3196165 90mg + csDMARD (Global Cohort)	GSK3196165 150mg + csDMARD (Global Cohort)	Tofacitinib 5mg + csDMARD (Global Cohort)	Pooled Placebo (Global Cohort)
Subject group type	Reporting group	Reporting group	Reporting group	Subject analysis set
Number of subjects analysed	545	539	271	270
Units: Scores on a scale				
least squares mean (standard error)	0.31 (± 0.072)	0.15 (± 0.073)	0.09 (± 0.092)	0.13 (± 0.095)

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in Van der Heijde mTSS at Week 24 and Week 52 for treatment arms who started study intervention from Day 1 (Global Cohort)

End point title	Change from Baseline in Van der Heijde mTSS at Week 24 and Week 52 for treatment arms who started study intervention from Day 1 (Global Cohort)[43]

End point description:

Van der Heijde mTSS is utilized for scoring radiographs of hands and feet in rheumatoid arthritis. This method includes 16 areas of erosions, and 15 areas for joint space narrowing (JSN) in each hand, and 6 areas for erosions and 6 areas JSN in each foot. The total mTSS score is the sum of erosion (maximum of 280) and JSN (maximum of 168) scores. The score range from 0 to 448 for mTSS with higher values representing higher disease activity. Baseline was defined as the latest pre-dose assessment with a non-missing value, including those from unscheduled visits. Change from Baseline was calculated by subtracting the post dose visit value from the Baseline value. The analysis was performed on all randomized participants who received study intervention from Day 01 to Week 52. Analysis was performed using multiple imputation method to handle missing data.

End point type	Secondary

End point timeframe:

Baseline (Day 1), Week 24 and Week 52

Notes:

[43] - 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: The endpoints are different for the different parts of the study.

End point values	GSK3196165 90mg + csDMARD (Global Cohort)	GSK3196165 150mg + csDMARD (Global Cohort)	Tofacitinib 5mg + csDMARD (Global Cohort)	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	545	539	271	
Units: Scores on a scale				
least squares mean (standard error)				
Week 24	0.42 (± 0.092)	0.32 (± 0.094)	0.15 (± 0.115)	
Week 52	0.84 (± 0.148)	0.46 (± 0.150)	0.30 (± 0.184)	

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in Van der Heijde mTSS at Week 24 and Week 52 for placebo switched arms (Global Cohort)

End point title	Change from Baseline in Van der Heijde mTSS at Week 24 and Week 52 for placebo switched arms (Global Cohort)[44]

End point description:

Van der Heijde mTSS is utilized for scoring radiographs of hands and feet in rheumatoid arthritis. This method includes 16 areas of erosions, and 15 areas for joint space narrowing (JSN) in each hand, and 6 areas for erosions and 6 areas JSN in each foot. The total mTSS score is the sum of erosion (maximum of 280) and JSN (maximum of 168) scores. The score range from 0 to 448 for mTSS with higher values representing higher disease activity. Baseline was defined as the latest pre-dose assessment with a non-missing value, including those from unscheduled visits. Change from Baseline was calculated by subtracting the post dose visit value from the Baseline value. The analysis was performed on all randomized participants who switched from placebo to study intervention at Week 12. Analysis was performed using multiple imputation method to handle missing data. For efficacy assessments baseline is interpreted as Day 1.

End point type	Secondary

End point timeframe:

Baseline (Day 1), Week 24 and Week 52

Notes:

[44] - 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: The endpoints are different for the different parts of the study.

End point values	Placebo+csDMARD and GSK3196165 90mg+csDMARD (Global Cohort)	Placebo +csDMARD and GSK3196165 150mg +csDMARD (Global Cohort)	Placebo +csDMARD and Tofacitinib 5mg +csDMARD (Global Cohort)	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	91	89	90	
Units: Scores on a scale				
least squares mean (standard error)				
Week 24	0.18 (± 0.185)	0.51 (± 0.196)	0.21 (± 0.196)	
Week 52	-0.05 (± 0.288)	0.76 (± 0.304)	0.09 (± 0.307)	

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in HAQ-DI at Week 24 and Week 52 for treatment arms who started study intervention from Day 1 (Global Cohort)

End point title	Change from Baseline in HAQ-DI at Week 24 and Week 52 for treatment arms who started study intervention from Day 1 (Global Cohort)[45]

End point description:

HAQ-DI is a 20-question instrument that assesses the degree of difficulty of a participant in accomplishing tasks in eight functional areas: dressing and grooming, arising, eating, walking, hygiene, reach, grip and common daily activities. Overall HAQ-DI score was computed as sum of the domain scores divided by the number of domains answered. The total possible score ranges from 0 to 3 where 0 = least difficulty and 3 = extreme difficulty. Higher overall score indicates greater disability. A negative change from baseline indicates an improvement. Baseline was defined as the latest pre-dose assessment with a non-missing value, including those from unscheduled visits. Change from Baseline was calculated by subtracting the post dose visit value from the Baseline value. The analysis was performed on all randomized participants who received study intervention from Day 01 to Week 52. Analysis was performed using multiple imputation method to handle missing data.

End point type	Secondary

End point timeframe:

Baseline (Day 1) and Week 24

Notes:

[45] - 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: The endpoints are different for the different parts of the study.

End point values	GSK3196165 90mg + csDMARD (Global Cohort)	GSK3196165 150mg + csDMARD (Global Cohort)	Tofacitinib 5mg + csDMARD (Global Cohort)	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	545	539	271	
Units: Scores on a scale				
least squares mean (standard error)				
Week 24	-0.38 (± 0.033)	-0.37 (± 0.033)	-0.53 (± 0.041)	
Week 52	-0.40 (± 0.035)	-0.37 (± 0.035)	-0.52 (± 0.043)	

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in HAQ-DI at Week 24 and Week 52 for placebo switched arms (Global Cohort)

End point title	Change from Baseline in HAQ-DI at Week 24 and Week 52 for placebo switched arms (Global Cohort)[46]

End point description:

HAQ-DI is a 20-question instrument that assesses degree of difficulty of participant in accomplishing tasks in 8 functional areas: dressing and grooming, arising, eating, walking, hygiene, reach, grip and common daily activities. Overall HAQ-DI score was computed as sum of domain scores divided by number of domains answered. Total possible score ranges from 0 to 3 where 0=least difficulty and 3=extreme difficulty. Higher overall score indicates greater disability. Negative change from baseline indicates an improvement. Baseline was defined as the latest pre-dose assessment with a non-missing

value, including those from unscheduled visits. Change from Baseline was calculated by subtracting post dose visit value from Baseline value. Analysis was performed on all randomized participants who switched from placebo to study intervention at Week 12. Analysis was performed using multiple imputation method to handle missing data. For efficacy assessments baseline is interpreted as Day 1.

End point type	Secondary

End point timeframe:

Baseline (Day 1) and Week 52

Notes:

[46] - 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: The endpoints are different for the different parts of the study.

End point values	Placebo+csDMARD and GSK3196165 90mg+csDMARD (Global Cohort)	Placebo +csDMARD and GSK3196165 150mg +csDMARD (Global Cohort)	Placebo +csDMARD and Tofacitinib 5mg +csDMARD (Global Cohort)	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	91	89	90	
Units: Scores on a scale				
least squares mean (standard error)				
Week 24	-0.36 (± 0.065)	-0.38 (± 0.067)	-0.33 (± 0.067)	
Week 52	-0.30 (± 0.069)	-0.37 (± 0.070)	-0.40 (± 0.071)	

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in Arthritis pain VAS at Week 12 (Global Cohort)

End point title	Change from Baseline in Arthritis pain VAS at Week 12 (Global Cohort)[47]

End point description:

For the Arthritis Pain VAS, participants assess the severity of their current arthritis pain using a continuous visual analogue scale (VAS) with anchors at "0" (no pain) and "100" (most severe pain). A negative change from baseline indicates an improvement. Baseline was defined as the latest pre-dose assessment with a non-missing value, including those from unscheduled visits. Change from Baseline was calculated by subtracting the post dose visit value from the Baseline value. For the purpose of all analyses up to week 12, the placebo arms were pooled into a single placebo arm to primarily serve as a reference for the comparison of active treatment arms. The analysis was performed on the ITT set. Analysis was performed using multiple imputation method to handle missing data.

End point type	Secondary

End point timeframe:

Baseline (Day 1) and Week 12

Notes:

[47] - 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: The endpoints are different for the different parts of the study.

End point values	GSK3196165 90mg + csDMARD (Global Cohort)	GSK3196165 150mg + csDMARD (Global Cohort)	Tofacitinib 5mg + csDMARD (Global Cohort)	Pooled Placebo (Global Cohort)
Subject group type	Reporting group	Reporting group	Reporting group	Subject analysis set
Number of subjects analysed	545	539	271	270
Units: Scores on a scale				
least squares mean (standard error)	-18.06 (± 1.266)	-17.13 (± 1.256)	-27.17 (± 1.610)	-10.28 (± 1.657)

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in Arthritis pain VAS at Week 24 and Week 52 for treatment arms who started study intervention from Day 1 (Global Cohort)

End point title	Change from Baseline in Arthritis pain VAS at Week 24 and Week 52 for treatment arms who started study intervention from Day 1 (Global Cohort)[48]

End point description:

For the Arthritis Pain VAS, participants assess the severity of their current arthritis pain using a continuous visual analogue scale (VAS) with anchors at "0" (no pain) and "100" (most severe pain). A negative change from baseline indicates an improvement. Baseline was defined as the latest pre-dose assessment with a non-missing value, including those from unscheduled visits. Change from Baseline was calculated by subtracting the post dose visit value from the Baseline value. The analysis was performed on all randomized participants who received study intervention from Day 01 to Week 52. Analysis was performed using multiple imputation method to handle missing data.

End point type	Secondary

End point timeframe:

Baseline (Day 1) and Week 24 and Week 52

Notes:

[48] - 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: The endpoints are different for the different parts of the study.

End point values	GSK3196165 90mg + csDMARD (Global Cohort)	GSK3196165 150mg + csDMARD (Global Cohort)	Tofacitinib 5mg + csDMARD (Global Cohort)	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	545	539	271	
Units: Scores on a scale				
least squares mean (standard error)				
Week 24	-23.32 (± 1.351)	-22.32 (± 1.371)	-31.27 (± 1.699)	
Week 52	-25.42 (± 1.506)	-25.14 (± 1.525)	-31.49 (± 1.846)	

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in Arthritis pain VAS at Week 24 and Week 52 for placebo switched arms (Global Cohort)

End point title	Change from Baseline in Arthritis pain VAS at Week 24 and Week 52 for placebo switched arms (Global Cohort)[49]

End point description:

For the Arthritis Pain VAS, participants assess the severity of their current arthritis pain using a continuous visual analogue scale (VAS) with anchors at "0" (no pain) and "100" (most severe pain). A negative change from baseline indicates an improvement. Baseline was defined as the latest pre-dose assessment with a non-missing value, including those from unscheduled visits. Change from Baseline was calculated by subtracting the post dose visit value from the Baseline value. The analysis was performed on all randomized participants who switched from placebo to study intervention at Week 12. Analysis was performed using multiple imputation method to handle missing data. For efficacy assessments baseline is interpreted as Day 1.

End point type	Secondary

End point timeframe:

Baseline (Day 1) and Week 24 and Week 52

Notes:

[49] - 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: The endpoints are different for the different parts of the study.

End point values	Placebo+csDMARD and GSK3196165 90mg+csDMARD (Global Cohort)	Placebo +csDMARD and GSK3196165 150mg +csDMARD (Global Cohort)	Placebo +csDMARD and Tofacitinib 5mg +csDMARD (Global Cohort)	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	91	89	90	
Units: Scores on a scale				
least squares mean (standard error)				
Week 24	-23.26 (± 2.710)	-18.45 (± 2.793)	-22.88 (± 2.791)	
Week 52	-23.71 (± 2.967)	-21.72 (± 3.071)	-21.62 (± 3.082)	

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in Short form (SF)-36 physical component scores at Week 12 (Global Cohort)

End point title	Change from Baseline in Short form (SF)-36 physical component scores at Week 12 (Global Cohort)[50]

End point description:

SF-36 survey evaluates health-related quality of life, covering physical functioning(PF),bodily pain(BP),role limitations due to physical/emotional issues,general health(GH),mental health,social functioning,vitality. Each of 8 domains is scored using average, 0-100; higher score represents better health.PCS was aggregated across the domains and scaled to T-score with mean of 50 and SD of 10; higher score represents better health.PCS is primarily derived from 4 domains(PF,role-physical,BP,GH) representing overall physical health.Positive change from baseline, reported using T-score change, indicates improvement in overall physical health.Quality Metric software was used for scoring.Baseline was defined as most recent pre-dose NMV, including unscheduled visits.CB=subtracting PD value from BV.For analysis up to week 12, placebo arms were pooled into single arm to serve as reference for active treatment arm comparison.ITT set was analyzed using multiple imputation to manage missing

End point type	Secondary

End point timeframe:

Baseline (Day 1) and Week 12

Notes:

[50] - 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: The endpoints are different for the different parts of the study.

End point values	GSK3196165 90mg + csDMARD (Global Cohort)	GSK3196165 150mg + csDMARD (Global Cohort)	Tofacitinib 5mg + csDMARD (Global Cohort)	Pooled Placebo (Global Cohort)
Subject group type	Reporting group	Reporting group	Reporting group	Subject analysis set
Number of subjects analysed	545	539	271	270
Units: T-Score				
least squares mean (standard error)	4.29 (± 0.363)	4.48 (± 0.361)	6.58 (± 0.464)	2.05 (± 0.478)

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in SF-36 domain scores at Week 12 (Global Cohort)

End point title	Change from Baseline in SF-36 domain scores at Week 12 (Global Cohort)[51]

End point description:

SF-36 is a health-related survey that assesses quality of life covering 8 domains: physical functioning (PF), bodily pain (BP), role limitations due to physical/emotional problems, general health (GH), mental health (MH), social functioning (SF), vitality. The MCS consists of 4 domains (SF, MH, vitality, role-emotional) and PCS consists of 4 domains (PF, role-physical, BP, GH). The individual question items are first summed for each item under the various sections. Then, those domain scores are weighted to a scale between 0 to 100, where higher score represents better health. Positive change from baseline indicates an improvement. Quality Metric software was used for scoring for SF-36. Baseline was defined as latest pre-dose assessment with a non-missing value, including those from unscheduled visits. Change from Baseline was calculated by subtracting post dose visit value from Baseline value. ITT set was analyzed for participants with data available at the indicated time points.

End point type	Secondary

End point timeframe:

Baseline (Day 1) and Week 12

Notes:

[51] - 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: The endpoints are different for the different parts of the study.

End point values	GSK3196165 90mg + csDMARD (Global Cohort)	GSK3196165 150mg + csDMARD (Global Cohort)	Tofacitinib 5mg + csDMARD (Global Cohort)	Pooled Placebo (Global Cohort)
Subject group type	Reporting group	Reporting group	Reporting group	Subject analysis set
Number of subjects analysed	506	514	252	244
Units: Scores on a scale				
least squares mean (standard error)				
Bodily Pain, n=506,514,252,244	14.82 (± 20.264)	16.13 (± 20.997)	23.75 (± 22.916)	9.21 (± 21.040)

General Health, n=506,514,252,244	7.48 (± 16.025)	6.74 (± 15.582)	10.48 (± 15.647)	5.16 (± 14.863)
Mental Health, n=506,514,252,244	6.21 (± 17.655)	6.96 (± 18.312)	9.13 (± 19.229)	4.88 (± 18.257)
Physical Function, n=506,514,252,244	12.78 (± 19.321)	14.47 (± 21.133)	18.63 (± 20.724)	8.42 (± 20.505)
Role Emotional, n=506,514,252,244	6.41 (± 24.390)	7.90 (± 25.675)	9.85 (± 24.815)	7.00 (± 23.912)
Role Physical, n=506,514,252,244	12.08 (± 21.650)	12.57 (± 22.044)	17.66 (± 21.724)	9.78 (± 20.593)
Social Function, n=506,514,252,244	8.10 (± 23.132)	9.75 (± 25.484)	14.78 (± 25.900)	6.76 (± 23.984)
Vitality, n=506,514,252,244	8.99 (± 18.971)	10.54 (± 19.349)	15.18 (± 21.491)	7.07 (± 18.624)

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in SF-36 mental component scores at Week 12 (Global Cohort)

End point title	Change from Baseline in SF-36 mental component scores at Week 12 (Global Cohort)[52]

End point description:

SF-36 survey evaluates health-related quality of life, covering physical functioning,bodily pain,role limitations due to physical/emotional issues,general health,mental health(MH),social functioning(SF),vitality. Each of 8 domains is scored using average, 0-100; higher score represents better health.MCS was aggregated across the domains and scaled to T-score with mean of 50 and SD of 10; higher score represents better health.MCS is primarily derived from 4 domains(SF,MH,vitality,role-emotional) representing overall mental health.Positive change from baseline, reported using T-score change, indicates improvement in overall mental health.Quality Metric software was used for scoring.Baseline was defined as most recent pre-dose NMV, including unscheduled visits.CB=subtracting PD value from BV.For analysis up to week 12, placebo arms were pooled into single arm to serve as reference for active treatment arm comparison.ITT set was analyzed using multiple imputation to manage missing data.

End point type	Secondary

End point timeframe:

Baseline (Day 1) and Week 12

Notes:

[52] - 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: The endpoints are different for the different parts of the study.

End point values	GSK3196165 90mg + csDMARD (Global Cohort)	GSK3196165 150mg + csDMARD (Global Cohort)	Tofacitinib 5mg + csDMARD (Global Cohort)	Pooled Placebo (Global Cohort)
Subject group type	Reporting group	Reporting group	Reporting group	Subject analysis set
Number of subjects analysed	545	539	271	270
Units: T-Score				
least squares mean (standard error)	2.24 (± 0.474)	2.68 (± 0.471)	3.56 (± 0.604)	2.21 (± 0.624)

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in SF-36 mental component scores at Week 24 and Week 52 for treatment arms who started study intervention from Day 1 (Global Cohort)

End point title	Change from Baseline in SF-36 mental component scores at Week 24 and Week 52 for treatment arms who started study intervention from Day 1 (Global Cohort)[53]

End point description:

SF-36 survey evaluates health-related quality of life, covering physical functioning, bodily pain, role limitations due to physical/emotional issues, general health, mental health(MH), social functioning(SF), vitality. Each of 8 domains is scored using average, 0-100; higher score represents better health. MCS was aggregated across the domains and scaled to T-score with mean of 50 and SD of 10; higher score represents better health. MCS is primarily derived from 4 domains(SF, MH, vitality, role-emotional) representing overall mental health. Positive change from baseline, reported using T-score change, indicates improvement in overall mental health. Quality Metric software was used for scoring. Baseline was defined as latest pre-dose assessment with a non-missing value, including those from unscheduled visits. Change from Baseline was calculated by subtracting post dose visit value from Baseline value. ITT set was analyzed using multiple imputation to manage missing data.

End point type	Secondary

End point timeframe:

Baseline (Day 1), Week 24 and Week 52

Notes:

[53] - 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: The endpoints are different for the different parts of the study.

End point values	GSK3196165 90mg + csDMARD (Global Cohort)	GSK3196165 150mg + csDMARD (Global Cohort)	Tofacitinib 5mg + csDMARD (Global Cohort)	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	545	539	271	
Units: T-Score				
least squares mean (standard error)				
Week 24	2.69 (± 0.522)	3.16 (± 0.528)	4.80 (± 0.652)	
Week 52	3.06 (± 0.527)	3.38 (± 0.530)	4.08 (± 0.650)	

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in SF-36 physical component scores at Week 24 and Week 52 for treatment arms who started study intervention from Day 1 (Global Cohort)

End point title	Change from Baseline in SF-36 physical component scores at Week 24 and Week 52 for treatment arms who started study intervention from Day 1 (Global Cohort)[54]

End point description:

SF-36 survey evaluates health-related quality of life, covering physical functioning(PF) ,bodily pain(BP) ,role limitations due to physical/emotional issues, general health(GH), mental health, social functioning, vitality. Each of 8 domains is scored using average, 0-100; higher score represents better health. PCS was aggregated across the domains and scaled to T-score with mean of 50 and SD of 10; higher score

represents better health. PCS is primarily derived from 4 domains(PF, role-physical, BP, GH) representing overall physical health. Positive change from baseline, reported using T-score change, indicates improvement in overall physical health. Quality Metric software was used for scoring. Baseline was defined as latest pre-dose assessment with a non-missing value, including those from unscheduled visits. Change from Baseline was calculated by subtracting post dose visit value from Baseline value. ITT set was analyzed using multiple imputation to manage missing data.

End point type	Secondary

End point timeframe:

Baseline (Day 1), Week 24 and Week 52

Notes:

[54] - 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: The endpoints are different for the different parts of the study.

End point values	GSK3196165 90mg + csDMARD (Global Cohort)	GSK3196165 150mg + csDMARD (Global Cohort)	Tofacitinib 5mg + csDMARD (Global Cohort)	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	545	539	271	
Units: T-Score				
least squares mean (standard error)				
Week 24	5.42 (± 0.416)	5.24 (± 0.421)	7.33 (± 0.520)	
Week 52	5.08 (± 0.460)	5.06 (± 0.464)	7.47 (± 0.569)	

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in SF-36 domain scores at Week 24 and Week 52 for treatment arms who started study intervention from Day 1 (Global Cohort)

End point title	Change from Baseline in SF-36 domain scores at Week 24 and Week 52 for treatment arms who started study intervention from Day 1 (Global Cohort)[55]

End point description:

SF-36 is a health-related survey that assesses quality of life covering 8 domains: physical functioning (PF), bodily pain (BP), role limitations due to physical/emotional problems, general health (GH), mental health (MH), social functioning (SF), vitality. The MCS consists of 4 domains (SF, MH, vitality, role-emotional) and PCS consists of 4 domains (PF, role-physical, BP, GH). The individual question items are first summed for each item under the various sections. Then, those domain scores are weighted to a scale between 0 to 100, where higher score represents better health. Positive change from baseline indicates an improvement. Quality Metric software was used for scoring for SF-36. Baseline was defined as latest pre-dose assessment with a non-missing value, including those from unscheduled visits. Change from Baseline was calculated by subtracting post dose visit value from Baseline value. ITT set was analyzed for participants with data available at the indicated time points.

End point type	Secondary

End point timeframe:

Baseline (Day 1), Week 24 and Week 52

Notes:

[55] - 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: The endpoints are different for the different parts of the study.

End point values	GSK3196165 90mg + csDMARD (Global Cohort)	GSK3196165 150mg + csDMARD (Global Cohort)	Tofacitinib 5mg + csDMARD (Global Cohort)	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	494	486	249	
Units: Scores on a scale				
least squares mean (standard error)				
Bodily Pain, Week 24, n=494,486,249	18.06 (± 21.568)	18.87 (± 23.164)	26.26 (± 24.870)	
Bodily Pain, Week 52, n=461,459,234	19.38 (± 22.807)	20.50 (± 23.781)	27.01 (± 24.068)	
General Health, Week 24, n=494,486,249	8.80 (± 17.357)	8.18 (± 16.569)	11.82 (± 18.258)	
General Health, Week 52, n=461,459,234	8.72 (± 17.635)	8.74 (± 17.157)	12.71 (± 18.374)	
Mental Health, Week 24, n=494,486,249	7.33 (± 18.871)	7.81 (± 19.930)	11.24 (± 19.875)	
Mental Health, Week 52, n=461,459,234	8.03 (± 18.819)	8.21 (± 19.132)	9.87 (± 19.417)	
Physical Function, Week 24, n=494,486,249	16.20 (± 21.646)	16.59 (± 22.660)	21.73 (± 23.769)	
Physical Function, Week 52, n=461,459,234	16.90 (± 21.458)	17.40 (± 23.162)	22.31 (± 26.462)	
Role Emotional, Week 24, n=494,486,249	8.33 (± 27.318)	10.01 (± 24.860)	13.45 (± 24.656)	
Role Emotional, Week 52, n=461,459,234	9.31 (± 24.987)	10.77 (± 25.914)	13.85 (± 25.643)	
Role Physical, Week 24, n=494,486,249	15.51 (± 22.052)	15.60 (± 22.507)	18.90 (± 22.618)	
Role Physical, Week 52, n=461,459,234	15.58 (± 23.558)	16.29 (± 24.110)	21.98 (± 24.671)	
Social Function, Week 24, n=494,486,249	10.25 (± 24.377)	11.34 (± 26.893)	15.91 (± 27.581)	
Social Function, Week 52, n=461,459,234	11.23 (± 24.368)	12.06 (± 26.941)	14.42 (± 27.313)	
Vitality, Week 24, n=494,486,249	11.21 (± 20.320)	12.71 (± 20.389)	18.02 (± 22.463)	
Vitality, Week 52, n=461,459,234	12.96 (± 20.197)	12.58 (± 19.150)	16.35 (± 22.327)	

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in SF-36 mental component scores at Week 24 and Week 52 for placebo switched arms (Global Cohort)

End point title	Change from Baseline in SF-36 mental component scores at Week 24 and Week 52 for placebo switched arms (Global Cohort)[56]

End point description:

SF-36 survey evaluates health-related quality of life, covering PF, BP, role limitations due to physical/emotional issues, GH, mental health(MH), social functioning(SF), vitality. Each domains is scored using average, 0-100; higher score represents better health. MCS was aggregated across domains and scaled to T-score with mean of 50 and SD of 10; higher score represents better health. MCS is primarily derived from 4 domains(SF, MH, vitality, role-emotional) representing overall mental health. Positive change from baseline, reported using T-score change, indicates improvement in overall mental health. Quality Metric software was used for scoring. Baseline was defined as latest pre-dose

assessment with a non-missing value, including those from unscheduled visits. Change from Baseline was calculated by subtracting post dose visit value from Baseline value. ITT set was analyzed using multiple imputation to manage missing data. For efficacy assessments baseline is interpreted as Day 1.

End point type	Secondary

End point timeframe:

Baseline (Day 1), Week 24 and Week 52

Notes:

[56] - 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: The endpoints are different for the different parts of the study.

End point values	Placebo+csDMARD and GSK3196165 90mg+csDMARD (Global Cohort)	Placebo +csDMARD and GSK3196165 150mg +csDMARD (Global Cohort)	Placebo +csDMARD and Tofacitinib 5mg +csDMARD (Global Cohort)	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	91	89	90	
Units: T-Score				
least squares mean (standard error)				
Week 24	3.59 (± 1.041)	4.37 (± 1.076)	3.76 (± 1.082)	
Week 52	2.87 (± 1.051)	4.53 (± 1.081)	2.74 (± 1.092)	

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in SF-36 physical component scores at Week 24 and Week 52 for placebo switched arms (Global Cohort)

End point title	Change from Baseline in SF-36 physical component scores at Week 24 and Week 52 for placebo switched arms (Global Cohort)[57]

End point description:

SF-36 survey evaluates health-related quality of life, covering physical functioning(PF), bodily pain(BP), role limitations due to physical/emotional issues, general health(GH), MH, SF, vitality. Each domains is scored using average, 0-100; higher score represents better health. PCS was aggregated across domains and scaled to T-score with mean of 50 and SD of 10; higher score represents better health. PCS is primarily derived from 4 domains(PF, role-physical, BP, GH) representing overall physical health. Positive change from baseline, reported using T-score change, indicates improvement in overall physical health. Quality Metric software was used for scoring. Baseline was defined as latest pre-dose assessment with a non-missing value, including from unscheduled visits. Change from Baseline was calculated by subtracting post dose value from Baseline value. ITT set was analyzed using multiple imputation to manage missing data. For efficacy assessments baseline is interpreted as Day 1.

End point type	Secondary

End point timeframe:

Baseline (Day 1), Week 24 and Week 52

Notes:

[57] - 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: The endpoints are different for the different parts of the study.

End point values	Placebo+csDMARD and GSK3196165 90mg+csDMARD (Global Cohort)	Placebo +csDMARD and GSK3196165 150mg +csDMARD (Global Cohort)	Placebo +csDMARD and Tofacitinib 5mg +csDMARD (Global Cohort)	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	91	89	90	
Units: T-Score				
least squares mean (standard error)				
Week 24	5.89 (± 0.821)	4.36 (± 0.851)	5.43 (± 0.857)	
Week 52	4.15 (± 0.902)	4.89 (± 0.929)	3.99 (± 0.941)	

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in SF-36 domain scores at Week 24 and Week 52 for placebo switched arms (Global Cohort)

End point title	Change from Baseline in SF-36 domain scores at Week 24 and Week 52 for placebo switched arms (Global Cohort)[58]

End point description:

SF-36 is a health-related survey that assesses quality of life covering 8 domains: physical functioning(PF),bodily pain(BP),role limitations due to physical/emotional problems,general health(GH),mental health(MH),social functioning(SF),vitality. The MCS consists of 4 domains (SF,MH,vitality,role-emotional) and PCS consists of 4 domains (PF,role-physical,BP,GH). The individual question items are first summed, then domain scores are weighted to a scale between 0 to 100, where higher score represents better health. Positive change from baseline indicates an improvement. Quality Metric software was used for scoring for SF-36. Baseline was defined as latest pre-dose assessment with a non-missing value, including those from unscheduled visits. Change from Baseline was calculated by subtracting post dose value from Baseline value. For efficacy assessments baseline is interpreted as Day 1. ITT set was analyzed for participants with data available at the indicated time points.

End point type	Secondary

End point timeframe:

Baseline (Day 1), Week 24 and Week 52

Notes:

[58] - 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: The endpoints are different for the different parts of the study.

End point values	Placebo+csDMARD and GSK3196165 90mg+csDMARD (Global Cohort)	Placebo +csDMARD and GSK3196165 150mg +csDMARD (Global Cohort)	Placebo +csDMARD and Tofacitinib 5mg +csDMARD (Global Cohort)	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	82	76	75	
Units: Scores on a scale				
least squares mean (standard error)				
Bodily Pain, Week 24, n=82,76,75	19.61 (± 22.430)	17.93 (± 17.710)	22.73 (± 21.012)	
Bodily Pain, Week 52, n=76,71,68	18.43 (± 23.444)	19.35 (± 19.873)	20.69 (± 23.501)	

General Health, Week 24, n=82,76,75	9.34 (± 13.259)	8.96 (± 16.231)	8.35 (± 17.087)	
General Health, Week 52, n=76,71,68	6.16 (± 15.885)	10.52 (± 17.755)	6.69 (± 16.707)	
Mental Health, Week 24, n=82,76,75	8.72 (± 19.623)	10.20 (± 15.842)	8.87 (± 19.270)	
Mental Health, Week 52, n=76,71,68	8.68 (± 19.585)	12.25 (± 19.907)	8.60 (± 19.256)	
Physical Function, Week 24, n=82,76,75	16.89 (± 20.407)	17.30 (± 20.744)	16.93 (± 21.433)	
Physical Function, Week 52, n=76,71,68	13.55 (± 24.025)	19.72 (± 20.769)	18.53 (± 20.608)	
Role Emotional, Week 24, n=82,76,75	9.35 (± 26.495)	15.57 (± 25.325)	11.44 (± 27.901)	
Role Emotional, Week 52, n=76,71,68	6.91 (± 27.467)	16.78 (± 28.189)	10.29 (± 28.907)	
Role Physical, Week 24, n=82,76,75	16.92 (± 22.168)	17.02 (± 19.568)	20.17 (± 21.197)	
Role Physical, Week 52, n=76,71,68	14.80 (± 23.581)	20.86 (± 20.727)	17.46 (± 24.087)	
Social Function, Week 24, n=82,76,75	12.80 (± 25.381)	12.17 (± 25.247)	14.33 (± 24.634)	
Social Function, Week 52, n=76,71,68	8.55 (± 29.312)	16.20 (± 25.477)	15.26 (± 24.131)	
Vitality, Week 24, n=82,76,75	14.25 (± 18.770)	13.40 (± 18.839)	13.67 (± 21.100)	
Vitality, Week 52, n=76,71,68	13.32 (± 19.826)	12.50 (± 21.417)	11.31 (± 20.581)	

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in FACIT-Fatigue at Week 24 and Week 52 for treatment arms who started study intervention from Day 1 (Global Cohort)

End point title	Change from Baseline in FACIT-Fatigue at Week 24 and Week 52 for treatment arms who started study intervention from Day 1 (Global Cohort)[59]

End point description:

The Functional Assessment of Chronic Illness Therapy (FACIT)-fatigue is a validated patient-reported measure of 13 statements regarding the feeling of fatigue. The total score ranges from 0 to 52 with higher values representing a lower fatigue and a better quality of life. A positive change from baseline in FACIT-fatigue indicates an improvement. Baseline was defined as the latest pre-dose assessment with a non-missing value, including those from unscheduled visits. Change from Baseline was calculated by subtracting the post dose visit value from the Baseline value. Participants who received study intervention from Day 1 to Week 52 were analyzed. Missing data was handled by multiple imputation method.

End point type	Secondary

End point timeframe:

Baseline (Day 1), Week 24 and Week 52

Notes:

[59] - 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: The endpoints are different for the different parts of the study.

End point values	GSK3196165 90mg + csDMARD (Global Cohort)	GSK3196165 150mg + csDMARD (Global Cohort)	Tofacitinib 5mg + csDMARD (Global Cohort)	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	545	539	271	
Units: Scores on a scale				
least squares mean (standard error)				
Week 24	6.10 (± 0.523)	6.12 (± 0.528)	8.37 (± 0.654)	
Week 52	6.97 (± 0.538)	6.41 (± 0.543)	8.38 (± 0.664)	

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in Functional assessment of chronic illness therapy (FACIT)-Fatigue at Week 12 (Global Cohort)

End point title	Change from Baseline in Functional assessment of chronic illness therapy (FACIT)-Fatigue at Week 12 (Global Cohort)[60]

End point description:

The Functional Assessment of Chronic Illness Therapy (FACIT)-fatigue is a validated patient-reported measure of 13 statements regarding the feeling of fatigue. The total score ranges from 0 to 52 with higher values representing a lower fatigue and a better quality of life. A positive change from baseline in FACIT-fatigue indicates an improvement. Baseline was defined as the latest pre-dose assessment with a non-missing value, including those from unscheduled visits. Change from Baseline was calculated by subtracting the post dose visit value from the Baseline value. For the purpose of all analyses up to week 12, the placebo arms were pooled into a single placebo arm to primarily serve as a reference for the comparison of active treatment arms. The analysis was performed on the ITT set. Analysis was performed using multiple imputation method to handle missing data.

End point type	Secondary

End point timeframe:

Baseline (Day 1) and Week 12

Notes:

[60] - 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: The endpoints are different for the different parts of the study.

End point values	GSK3196165 90mg + csDMARD (Global Cohort)	GSK3196165 150mg + csDMARD (Global Cohort)	Tofacitinib 5mg + csDMARD (Global Cohort)	Pooled Placebo (Global Cohort)
Subject group type	Reporting group	Reporting group	Reporting group	Subject analysis set
Number of subjects analysed	545	539	271	270
Units: Scores on a scale				
least squares mean (standard error)	4.76 (± 0.482)	4.91 (± 0.479)	7.92 (± 0.615)	3.68 (± 0.637)

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) (Global Cohort)

End point title	Number of participants with adverse events (AEs), serious adverse events (SAEs) and adverse events of special interest (AESI) (Global Cohort)[61]

End point description:

AE is defined as any untoward medical occurrence in a clinical study participant, temporally associated with use of a study intervention, whether or not considered related to study intervention. SAEs are defined as any untoward medical occurrence that, at any dose: results in death, cause life threatening events which requires inpatient hospitalization or prolongation of existing hospitalization, results in persistent disability or incapacity and birth defect or congenital anomaly. Protocol defined AESIs were included. Fifteen participants in Pooled placebo received active treatment of Tofacitinib from Week 4 instead of Week 12 as planned. They were pooled with the Tofacitinib arm. The analysis was performed on Safety Set that includes all randomized participants who received at least one dose of study treatment. Pooled Placebo collected data from Day 01 to Week 12. Placebo switched arms collected data from Week 12 to 59. Experimental arms collected data from Day 01 to Week 59.

End point type	Secondary

End point timeframe:

Up to Week 59

Notes:

[61] - 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: The endpoints are different for the different parts of the study.

End point values	GSK3196165 90mg + csDMARD (Global Cohort)	GSK3196165 150mg + csDMARD (Global Cohort)	Tofacitinib 5mg + csDMARD (Global Cohort)	Pooled Placebo (Global Cohort)
Subject group type	Reporting group	Reporting group	Subject analysis set	Subject analysis set
Number of subjects analysed	545	539	286	255
Units: Participants				
AE	420	408	127	127
SAE	44	43	6	6
AESI	72	75	5	5

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in FACIT-Fatigue at Week 24 and Week 52 for placebo switched arms (Global Cohort)

End point title	Change from Baseline in FACIT-Fatigue at Week 24 and Week 52 for placebo switched arms (Global Cohort)[62]

End point description:

The Functional Assessment of Chronic Illness Therapy (FACIT)-fatigue is a validated patient-reported measure of 13 statements regarding the feeling of fatigue. The total score ranges from 0 to 52 with higher values representing a lower fatigue and a better quality of life. A positive change from baseline in FACIT-fatigue indicates an improvement. Baseline was defined as the latest pre-dose assessment with a non-missing value, including those from unscheduled visits. Change from Baseline was calculated by subtracting the post dose visit value from the Baseline value. Participants who received study intervention from Week 12 to Week 52 were analyzed. For efficacy assessments baseline is interpreted as Day 1. Missing data was handled by multiple imputation method.

End point type	Secondary

End point timeframe:

Baseline (Day 1), Week 24 and Week 52

Notes:

[62] - 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: The endpoints are different for the different parts of the study.

End point values	Placebo+csDMARD and GSK3196165 90mg+csDMARD (Global Cohort)	Placebo +csDMARD and GSK3196165 150mg +csDMARD (Global Cohort)	Placebo +csDMARD and Tofacitinib 5mg +csDMARD (Global Cohort)	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	91	89	90	
Units: Scores on a scale				
least squares mean (standard error)				
Week 24	6.95 (± 1.034)	6.08 (± 1.072)	6.87 (± 1.070)	
Week 52	5.73 (± 1.061)	6.50 (± 1.096)	6.01 (± 1.105)	

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in hematology parameter of white blood cell (WBC) count, platelet count, neutrophils, lymphocytes at Week 12 (Giga cells per liter) (Global Cohort)

End point title	Change from Baseline in hematology parameter of white blood cell (WBC) count, platelet count, neutrophils, lymphocytes at Week 12 (Giga cells per liter) (Global Cohort)[63]

End point description:

Blood samples were collected for the assessment of change from baseline in hematology parameters including WBC count, platelet count, neutrophils, lymphocytes. Baseline was defined as the latest pre-dose assessment with a non-missing value, including those from unscheduled visits. Change from Baseline was calculated by subtracting the post dose visit value from the Baseline value. For the purpose of all analyses up to week 12, the placebo arms were pooled into a single placebo arm to primarily serve as a reference for the comparison of active treatment arms. The analysis was performed on the Safety Set. Fifteen participants in Placebo group received active treatment of Tofacitinib mistakenly from Week 4 instead of Week 12 as planned. They were added with the Tofacitinib arm in safety analysis. Only those participants with data available at the specified data points were analyzed.

End point type	Secondary

End point timeframe:

Baseline (Day 1) and Week 12

Notes:

[63] - 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: The endpoints are different for the different parts of the study.

End point values	GSK3196165 90mg + csDMARD (Global Cohort)	GSK3196165 150mg + csDMARD (Global Cohort)	Tofacitinib 5mg + csDMARD (Global Cohort)	Pooled Placebo (Global Cohort)
Subject group type	Reporting group	Reporting group	Subject analysis set	Subject analysis set
Number of subjects analysed	494	490	267	229
Units: Giga cells per liter (10^9/L)				
arithmetic mean (standard deviation)				

Lymphocytes	0.002 (± 0.5235)	-0.019 (± 0.5304)	0.045 (± 0.5477)	-0.011 (± 0.4783)
Neutrophils	-0.444 (± 1.8305)	-0.647 (± 1.9192)	-1.054 (± 2.1874)	0.053 (± 1.9956)
Platelets	-19.0 (± 50.74)	-19.9 (± 53.15)	-34.3 (± 64.33)	0.8 (± 54.75)
Leukocytes	-0.45 (± 1.919)	-0.70 (± 1.992)	-1.02 (± 2.215)	0.02 (± 1.984)

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in hematology parameter of WBC count, platelet count, neutrophils, lymphocytes at Week 24 and Week 52 for treatment arms who started study intervention from Day 1 (Global Cohort)

End point title	Change from Baseline in hematology parameter of WBC count, platelet count, neutrophils, lymphocytes at Week 24 and Week 52 for treatment arms who started study intervention from Day 1 (Global Cohort)[64]

End point description:

Blood samples were collected for the assessment of change from baseline in hematology parameters including WBC count, platelet count, neutrophils, lymphocytes. Baseline was defined as the latest pre-dose assessment with a non-missing value, including those from unscheduled visits. Change from Baseline was calculated by subtracting the post dose visit value from the Baseline value. The analysis was performed on Safety Set. Fifteen participants in Placebo group received active treatment of Tofacitinib mistakenly from Week 4 instead of Week 12 as planned. They were added with the Tofacitinib arm in safety analysis. Only those participants with data available at the specified data points were analyzed.

End point type	Secondary

End point timeframe:

Baseline (Day 1), Week 24 and Week 52

Notes:

[64] - 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: The endpoints are different for the different parts of the study.

End point values	GSK3196165 90mg + csDMARD (Global Cohort)	GSK3196165 150mg + csDMARD (Global Cohort)	Tofacitinib 5mg + csDMARD (Global Cohort)	
Subject group type	Reporting group	Reporting group	Subject analysis set	
Number of subjects analysed	497	480	255	
Units: Giga cells per liter (10^9/L)				
arithmetic mean (standard deviation)				
Lymphocytes, Week 24	0.004 (± 0.5092)	-0.017 (± 0.5188)	2.215 (± 0.5294)	
Lymphocytes, Week 52	0.001 (± 0.5679)	-0.012 (± 0.5487)	-0.143 (± 0.5739)	
Neutrophils, Week 24	-0.508 (± 1.7714)	-0.647 (± 2.0762)	-1.135 (± 2.2376)	
Neutrophils, Week 52	-0.594 (± 1.8490)	-0.788 (± 2.1627)	-1.022 (± 2.4346)	
Platelets, Week 24	-16.4 (± 61.73)	-21.0 (± 56.36)	-32.0 (± 63.74)	

Platelets, Week 52	-24.9 (± 66.31)	-22.0 (± 63.94)	-37.6 (± 70.56)	
Leukocytes, Week 24	-0.50 (± 1.818)	-0.66 (± 2.129)	-1.17 (± 2.269)	
Leukocytes, Week 52	-0.59 (± 1.976)	-0.80 (± 2.346)	-1.22 (± 2.465)	

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in hematology parameter of WBC count, platelet count, neutrophils, lymphocytes at Week 24 and Week 52 (Global Cohort)

End point title	Change from Baseline in hematology parameter of WBC count, platelet count, neutrophils, lymphocytes at Week 24 and Week 52 (Global Cohort)[65]

End point description:

Blood samples were collected for the assessment of change from baseline in hematology parameters including WBC count, platelet count, neutrophils, lymphocytes. Baseline was defined as the latest pre-dose assessment with a non-missing value, including those from unscheduled visits. Change from Baseline was calculated by subtracting the post dose visit value from the Baseline value. For safety assessments baseline is interpreted as Week 12. The analysis was performed on the Safety Set. Only those participants with data available at the specified data points were analyzed.

End point type	Secondary

End point timeframe:

Baseline (Week 12), Week 24 and Week 52

Notes:

[65] - 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: The endpoints are different for the different parts of the study.

End point values	Placebo+csDMARD and GSK3196165 90mg+csDMARD (Global Cohort)	Placebo +csDMARD and GSK3196165 150mg +csDMARD (Global Cohort)	Placebo +csDMARD and Tofacitinib 5mg +csDMARD (Global Cohort)	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	80	74	64	
Units: Giga cells per liter (10^9/L)				
arithmetic mean (standard deviation)				
Lymphocytes, Week 24	-0.072 (± 0.4236)	0.014 (± 0.5442)	-0.042 (± 0.5563)	
Lymphocytes, Week 52	-0.085 (± 0.5077)	-0.071 (± 0.5098)	-0.243 (± 0.6030)	
Neutrophils, Week 24	-0.582 (± 1.6685)	-0.255 (± 2.1106)	-0.745 (± 1.9306)	
Neutrophils, Week 52	-0.605 (± 1.8343)	-0.288 (± 2.2031)	-0.617 (± 2.1111)	
Platelets, Week 24	-11.6 (± 58.77)	-13.6 (± 40.78)	-36.1 (± 62.88)	
Platelets, Week 52	-17.8 (± 39.56)	-21.1 (± 44.72)	-27.8 (± 72.75)	
Leukocytes, Week 24	-0.64 (± 1.669)	-0.25 (± 2.204)	-0.84 (± 2.093)	

Leukocytes, Week 52	-0.65 (± 2.148)	-0.38 (± 2.259)	-0.94 (± 2.134)	

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in hematology parameter of hemoglobin at Week 12 (Global Cohort)

End point title	Change from Baseline in hematology parameter of hemoglobin at Week 12 (Global Cohort)[66]

End point description:

Blood samples were collected for the assessment of change from baseline in hematology parameters hemoglobin level. Baseline was defined as the latest pre-dose assessment with a non-missing value, including those from unscheduled visits. Change from Baseline was calculated by subtracting the post dose visit value from the Baseline value. For the purpose of all analyses up to week 12, the placebo arms were pooled into a single placebo arm to primarily serve as a reference for the comparison of active treatment arms. The analysis was performed on the Safety Set. Fifteen participants in Placebo group received active treatment of Tofacitinib mistakenly from Week 4 instead of Week 12 as planned. They were added with the Tofacitinib arm in safety analysis. Only those participants with data available at the specified data points were analyzed.

End point type	Secondary

End point timeframe:

Baseline (Day 1) and Week 12

Notes:

[66] - 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: The endpoints are different for the different parts of the study.

End point values	GSK3196165 90mg + csDMARD (Global Cohort)	GSK3196165 150mg + csDMARD (Global Cohort)	Tofacitinib 5mg + csDMARD (Global Cohort)	Pooled Placebo (Global Cohort)
Subject group type	Reporting group	Reporting group	Subject analysis set	Subject analysis set
Number of subjects analysed	492	489	267	231
Units: Grams per liter (g/L)				
arithmetic mean (standard deviation)	0.8 (± 7.50)	0.1 (± 7.57)	0.4 (± 8.53)	-1.0 (± 7.57)

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in hematology parameter of hemoglobin at Week 24 and Week 52 for treatment arms who started study intervention from Day 1 (Global Cohort)

End point title	Change from Baseline in hematology parameter of hemoglobin at Week 24 and Week 52 for treatment arms who started study intervention from Day 1 (Global Cohort)[67]

End point description:

Blood samples were collected for the assessment of change from baseline in hematology parameters

hemoglobin level. Baseline was defined as the latest pre-dose assessment with a non-missing value, including those from unscheduled visits. Change from Baseline was calculated by subtracting the post dose visit value from the Baseline value. The analysis was performed on the Safety Set. Fifteen participants in Placebo group received active treatment of Tofacitinib mistakenly from Week 4 instead of Week 12 as planned. They were added with the Tofacitinib arm in safety analysis. Only those participants with data available at the specified data points were analyzed.

End point type	Secondary

End point timeframe:

Baseline (Day 1), Week 24 and Week 52

Notes:

[67] - 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: The endpoints are different for the different parts of the study.

End point values	GSK3196165 90mg + csDMARD (Global Cohort)	GSK3196165 150mg + csDMARD (Global Cohort)	Tofacitinib 5mg + csDMARD (Global Cohort)	
Subject group type	Reporting group	Reporting group	Subject analysis set	
Number of subjects analysed	497	479	255	
Units: Grams per liter (g/L)				
arithmetic mean (standard deviation)				
Week 24	0.5 (± 8.89)	1.0 (± 8.57)	1.9 (± 9.23)	
Week 52	0.6 (± 10.83)	0.0 (± 10.12)	1.0 (± 10.35)	

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in hematology parameter of hemoglobin at Week 24 and Week 52 for placebo switched arms (Global Cohort)

End point title	Change from Baseline in hematology parameter of hemoglobin at Week 24 and Week 52 for placebo switched arms (Global Cohort)[68]

End point description:

Blood samples were collected for the assessment of change from baseline in hematology parameters hemoglobin level. Baseline was defined as the latest pre-dose assessment with a non-missing value, including those from unscheduled visits. Change from Baseline was calculated by subtracting the post dose visit value from the Baseline value. For safety assessments baseline is interpreted as Week 12. The analysis was performed on the Safety Set. Only those participants with data available at the specified data points were analyzed.

End point type	Secondary

End point timeframe:

Baseline (Week 12), Week 24 and Week 52

Notes:

[68] - 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: The endpoints are different for the different parts of the study.

End point values	Placebo+csDMARD and GSK3196165 90mg+csDMARD (Global Cohort)	Placebo +csDMARD and GSK3196165 150mg +csDMARD (Global Cohort)	Placebo +csDMARD and Tofacitinib 5mg +csDMARD (Global Cohort)	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	79	74	64	
Units: Grams per liter (g/L)				
arithmetic mean (standard deviation)				
Week 24	1.2 (± 6.36)	1.2 (± 6.10)	3.2 (± 9.01)	
Week 52	0.8 (± 7.96)	1.8 (± 8.99)	2.1 (± 10.14)	

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in clinical chemistry parameter of aspartate aminotransferase (AST), alanine aminotransferase (ALT), alkaline phosphatase (AP), Gamma-Glutamyl transpeptidase (GGT) at Week 12 (Global Cohort)

End point title	Change from Baseline in clinical chemistry parameter of aspartate aminotransferase (AST), alanine aminotransferase (ALT), alkaline phosphatase (AP), Gamma-Glutamyl transpeptidase (GGT) at Week 12 (Global Cohort)[69]

End point description:

Blood samples were collected for the assessment of clinical chemistry parameters including aspartate aminotransferase (AST), alanine aminotransferase (ALT), alkaline phosphatase (AP) and gamma-glutamyl transferase (GGT) levels. Baseline was defined as the latest pre-dose assessment with a non-missing value, including those from unscheduled visits. Change from Baseline was calculated by subtracting the post dose visit value from the Baseline value. For the purpose of all analyses up to week 12, the placebo arms were pooled into a single placebo arm to primarily serve as a reference for the comparison of active treatment arms. The analysis was performed on the Safety Set. Fifteen participants in Placebo group received active treatment of Tofacitinib mistakenly from Week 4 instead of Week 12 as planned. They were added with the Tofacitinib arm in safety analysis. Only those participants with data available at the specified data points were analyzed.

End point type	Secondary

End point timeframe:

Baseline (Day 1) and Week 12

Notes:

[69] - 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: The endpoints are different for the different parts of the study.

End point values	GSK3196165 90mg + csDMARD (Global Cohort)	GSK3196165 150mg + csDMARD (Global Cohort)	Tofacitinib 5mg + csDMARD (Global Cohort)	Pooled Placebo (Global Cohort)
Subject group type	Reporting group	Reporting group	Subject analysis set	Subject analysis set
Number of subjects analysed	511	504	273	231
Units: International units per liter (IU/L)				
arithmetic mean (standard deviation)				
AP	-1.3 (± 19.79)	0.4 (± 28.71)	-5.1 (± 19.95)	-1.6 (± 22.96)
ALT	0.8 (± 14.14)	1.2 (± 13.49)	3.0 (± 15.73)	0.3 (± 15.88)
AST	1.3 (± 8.34)	2.0 (± 11.35)	3.8 (± 12.23)	-0.1 (± 8.73)
GGT	-1.5 (± 20.77)	0.3 (± 44.60)	-1.1 (± 17.60)	-1.7 (± 25.38)

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in clinical chemistry parameter of AST, ALT, AP, GGT at Week 24 and Week 52 for treatment arms who started study intervention from Day 1 (Global Cohort)

End point title	Change from Baseline in clinical chemistry parameter of AST, ALT, AP, GGT at Week 24 and Week 52 for treatment arms who started study intervention from Day 1 (Global Cohort)[70]

End point description:

Blood samples were collected for the assessment of clinical chemistry parameters including AST, ALT, AP and GGT levels. Baseline was defined as the latest pre-dose assessment with a non-missing value, including those from unscheduled visits. Change from Baseline was calculated by subtracting the post dose visit value from the Baseline value. The analysis was performed on the Safety Set. Fifteen participants in Placebo group received active treatment of Tofacitinib mistakenly from Week 4 instead of Week 12 as planned. They were added with the Tofacitinib arm in safety analysis. Only those participants with data available at the specified data points were analyzed.

End point type	Secondary

End point timeframe:

Baseline (Day 1), Week 24 and Week 52

Notes:

[70] - 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: The endpoints are different for the different parts of the study.

End point values	GSK3196165 90mg + csDMARD (Global Cohort)	GSK3196165 150mg + csDMARD (Global Cohort)	Tofacitinib 5mg + csDMARD (Global Cohort)	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	497	480	257	
Units: International units per liter (IU/L)				
arithmetic mean (standard deviation)				
AP, Week 24	-0.3 (± 23.40)	0.6 (± 20.47)	-7.9 (± 24.03)	
AP, Week 52	0.3 (± 20.20)	1.4 (± 22.40)	-5.1 (± 23.34)	
ALT, Week 24	1.0 (± 18.23)	4.6 (± 63.38)	4.1 (± 21.70)	
ALT, Week 52	-0.1 (± 14.16)	2.0 (± 16.35)	3.7 (± 15.33)	
AST, Week 24	1.2 (± 9.71)	3.8 (± 45.20)	4.2 (± 13.20)	
AST, Week 52	1.0 (± 8.08)	2.0 (± 11.47)	3.9 (± 11.17)	
GGT, Week 24	-1.2 (± 25.56)	0.5 (± 32.53)	-1.6 (± 16.76)	
GGT, Week 52	-1.0 (± 24.25)	0.2 (± 22.40)	-0.1 (± 17.49)	

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in clinical chemistry parameter of AST, ALT, AP, GGT at Week 24 and Week 52 for placebo switched arms (Global Cohort)

End point title	Change from Baseline in clinical chemistry parameter of AST, ALT, AP, GGT at Week 24 and Week 52 for placebo switched arms (Global Cohort)[71]

End point description:

Blood samples were collected for the assessment of clinical chemistry parameters including AST, ALT, AP and GGT levels. Baseline was defined as the latest pre-dose assessment with a non-missing value, including those from unscheduled visits. Change from Baseline was calculated by subtracting the post dose visit value from the Baseline value. For safety assessments baseline is interpreted as Week 12. The analysis was performed on the Safety Set. Only those participants with data available at the specified data points were analyzed.

End point type	Secondary

End point timeframe:

Baseline (Week 12), Week 24 and Week 52

Notes:

[71] - 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: The endpoints are different for the different parts of the study.

End point values	Placebo+csDMARD and GSK3196165 90mg+csDMARD (Global Cohort)	Placebo +csDMARD and GSK3196165 150mg +csDMARD (Global Cohort)	Placebo +csDMARD and Tofacitinib 5mg +csDMARD (Global Cohort)	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	83	74	64	
Units: International units per liter (IU/L)				
arithmetic mean (standard deviation)				
AP, Week 24	-0.3 (± 15.77)	-3.5 (± 19.93)	-2.8 (± 23.41)	
AP, Week 52	-2.8 (± 19.07)	-1.6 (± 27.58)	-2.7 (± 26.76)	
ALT, Week 24	-0.2 (± 14.86)	0.2 (± 14.15)	6.4 (± 15.92)	
ALT, Week 52	1.0 (± 20.01)	0.7 (± 13.66)	7.8 (± 24.01)	
AST, Week 24	-0.2 (± 10.16)	1.4 (± 6.42)	5.0 (± 9.96)	
AST, Week 52	1.3 (± 14.54)	2.2 (± 7.07)	7.0 (± 16.92)	
GGT, Week 24	0.8 (± 20.15)	-2.0 (± 18.05)	0.0 (± 25.57)	
GGT, Week 52	-2.1 (± 15.84)	-1.1 (± 16.29)	0.8 (± 23.66)	

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in clinical chemistry parameter of total bilirubin at Week 12 (Global Cohort)

End point title	Change from Baseline in clinical chemistry parameter of total bilirubin at Week 12 (Global Cohort)[72]

End point description:

Blood samples were collected for the assessment of clinical chemistry parameter total bilirubin level. Baseline was defined as the latest pre-dose assessment with a non-missing value, including those from unscheduled visits. Change from Baseline was calculated by subtracting the post dose visit value from

the Baseline value. For the purpose of all analyses up to week 12, the placebo arms were pooled into a single placebo arm to primarily serve as a reference for the comparison of active treatment arms. The analysis was performed on the Safety Set. Fifteen participants in Placebo group received active treatment of Tofacitinib mistakenly from Week 4 instead of Week 12 as planned. They were added with the Tofacitinib arm in safety analysis. Only those participants with data available at the specified data points were analyzed.

End point type	Secondary

End point timeframe:

Baseline (Day 1) and Week 12

Notes:

[72] - 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: The endpoints are different for the different parts of the study.

End point values	GSK3196165 90mg + csDMARD (Global Cohort)	GSK3196165 150mg + csDMARD (Global Cohort)	Tofacitinib 5mg + csDMARD (Global Cohort)	Pooled Placebo (Global Cohort)
Subject group type	Reporting group	Reporting group	Subject analysis set	Subject analysis set
Number of subjects analysed	506	499	271	231
Units: Micromoles per liter (umol/L)				
arithmetic mean (standard deviation)	0.3 (± 2.84)	0.5 (± 2.68)	0.5 (± 3.11)	0.2 (± 2.78)

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in clinical chemistry parameter of total bilirubin at Week 24 and Week 52 for placebo switched arms (Global Cohort)

End point title	Change from Baseline in clinical chemistry parameter of total bilirubin at Week 24 and Week 52 for placebo switched arms (Global Cohort)[73]

End point description:

Blood samples were collected for the assessment of clinical chemistry parameter total bilirubin level. Baseline was defined as the latest pre-dose assessment with a non-missing value, including those from unscheduled visits. Change from Baseline was calculated by subtracting the post dose visit value from the Baseline value. For safety assessments baseline is interpreted as Week 12. The analysis was performed on the Safety Set. Only those participants with data available at the specified data points were analyzed.

End point type	Secondary

End point timeframe:

Baseline (Week 12), Week 24 and Week 52

Notes:

[73] - 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: The endpoints are different for the different parts of the study.

End point values	Placebo+csDMARD and GSK3196165 90mg+csDMARD (Global Cohort)	Placebo +csDMARD and GSK3196165 150mg +csDMARD (Global Cohort)	Placebo +csDMARD and Tofacitinib 5mg +csDMARD (Global Cohort)	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	81	73	64	
Units: Micromoles per liter (umol/L)				
arithmetic mean (standard deviation)				
Week 24	0.3 (± 3.07)	0.3 (± 2.06)	0.4 (± 2.79)	
Week 52	-0.1 (± 2.88)	0.6 (± 2.44)	0.4 (± 2.20)	

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in clinical chemistry parameter of total bilirubin at Week 24 and Week 52 for treatment arms who started study intervention from Day 1 (Global Cohort)

End point title	Change from Baseline in clinical chemistry parameter of total bilirubin at Week 24 and Week 52 for treatment arms who started study intervention from Day 1 (Global Cohort)[74]

End point description:

Blood samples were collected for the assessment of clinical chemistry parameter total bilirubin level. Baseline was defined as the latest pre-dose assessment with a non-missing value, including those from unscheduled visits. Change from Baseline was calculated by subtracting the post dose visit value from the Baseline value. The analysis was performed on the Safety Set. Fifteen participants in Placebo group received active treatment of Tofacitinib mistakenly from Week 4 instead of Week 12 as planned. They were added with the Tofacitinib arm in safety analysis. Only those participants with data available at the specified data points were analyzed.

End point type	Secondary

End point timeframe:

Baseline (Day 1), Week 24 and Week 52

Notes:

[74] - 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: The endpoints are different for the different parts of the study.

End point values	GSK3196165 90mg + csDMARD (Global Cohort)	GSK3196165 150mg + csDMARD (Global Cohort)	Tofacitinib 5mg + csDMARD (Global Cohort)	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	496	477	256	
Units: Micromoles per liter (umol/L)				
arithmetic mean (standard deviation)				
Week 24	0.5 (± 2.66)	0.5 (± 2.78)	0.6 (± 2.73)	
Week 52	0.3 (± 2.66)	0.6 (± 2.80)	0.9 (± 2.83)	

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in clinical chemistry parameter of albumin at Week 24 and Week 52 for treatment arms who started study intervention from Day 1 (Global Cohort)

End point title	Change from Baseline in clinical chemistry parameter of albumin at Week 24 and Week 52 for treatment arms who started study intervention from Day 1 (Global Cohort)[75]

End point description:

Blood samples were collected for the assessment of clinical chemistry parameter albumin level. Baseline was defined as the latest pre-dose assessment with a non-missing value, including those from unscheduled visits. Change from Baseline was calculated by subtracting the post dose visit value from the Baseline value. The analysis was performed on the Safety Set. Fifteen participants in Placebo group received active treatment of Tofacitinib mistakenly from Week 4 instead of Week 12 as planned. They were added with the Tofacitinib arm in safety analysis. Only those participants with data available at the specified data points were analyzed.

End point type	Secondary

End point timeframe:

Baseline (Day 1), Week 24 and Week 52

Notes:

[75] - 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: The endpoints are different for the different parts of the study.

End point values	GSK3196165 90mg + csDMARD (Global Cohort)	GSK3196165 150mg + csDMARD (Global Cohort)	Tofacitinib 5mg + csDMARD (Global Cohort)	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	497	479	257	
Units: Grams per liter (g/L)				
arithmetic mean (standard deviation)				
Week 24	0.2 (± 2.72)	0.3 (± 2.59)	1.6 (± 2.95)	
Week 52	0.3 (± 2.77)	0.3 (± 2.88)	1.3 (± 3.03)	

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in clinical chemistry parameter of albumin at Week 12 (Global Cohort)

End point title	Change from Baseline in clinical chemistry parameter of albumin at Week 12 (Global Cohort)[76]

End point description:

Blood samples were collected for the assessment of clinical chemistry parameter albumin level. Baseline was defined as the latest pre-dose assessment with a non-missing value, including those from unscheduled visits. Change from Baseline was calculated by subtracting the post dose visit value from the Baseline value. For the purpose of all analyses up to week 12, the placebo arms were pooled into a single placebo arm to primarily serve as a reference for the comparison of active treatment arms. The analysis was performed on the Safety Set. Fifteen participants in Placebo group received active treatment of Tofacitinib mistakenly from Week 4 instead of Week 12 as planned. They were added with the Tofacitinib arm in safety analysis. Only those participants with data available at the specified data points were analyzed.

End point type	Secondary

End point timeframe:

Baseline (Day 1) and Week 12

Notes:

[76] - 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: The endpoints are different for the different parts of the study.

End point values	GSK3196165 90mg + csDMARD (Global Cohort)	GSK3196165 150mg + csDMARD (Global Cohort)	Tofacitinib 5mg + csDMARD (Global Cohort)	Pooled Placebo (Global Cohort)
Subject group type	Reporting group	Reporting group	Subject analysis set	Subject analysis set
Number of subjects analysed	511	504	273	231
Units: Grams per liter (g/L)				
arithmetic mean (standard deviation)	0.1 (± 2.56)	0.1 (± 2.49)	1.1 (± 2.60)	-0.3 (± 2.72)

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in lipid profile parameter of total cholesterol at Week 12 (Global Cohort)

End point title	Change from Baseline in lipid profile parameter of total cholesterol at Week 12 (Global Cohort)[77]

End point description:

Blood samples were collected for the assessment of lipid profile of total cholesterol levels. Baseline was defined as the latest pre-dose assessment with a non-missing value, including those from unscheduled visits. Change from Baseline was calculated by subtracting the post dose visit value from the Baseline value. For the purpose of all analyses up to week 12, the placebo arms were pooled into a single placebo arm to primarily serve as a reference for the comparison of active treatment arms. Blood samples were collected at indicated time points per schedule of assessment in protocol. Objectives and Endpoints section incorrectly states that Change from baseline in key laboratory parameters at Week 12 was a secondary objective, however for lipid panel, there is no corresponding time point in schedule of assessment. Consequently, the objective that can be assessed for the lipid panel is Week 4 and not Week 12 as no data collected. Week 4 is not pre-specified time point to report.

End point type	Secondary

End point timeframe:

Baseline (Day 1) and Week 12

Notes:

[77] - 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: The endpoints are different for the different parts of the study.

End point values	GSK3196165 90mg + csDMARD (Global Cohort)	GSK3196165 150mg + csDMARD (Global Cohort)	Tofacitinib 5mg + csDMARD (Global Cohort)	Pooled Placebo (Global Cohort)
Subject group type	Reporting group	Reporting group	Subject analysis set	Subject analysis set
Number of subjects analysed	0[78]	0[79]	0[80]	0[81]
Units: Millimoles per liter (mmol/L)				
arithmetic mean (standard deviation)	()	()	()	()

Notes:

[78] - Data was not collected as there is no corresponding time point in schedule of activity of Protocol.

[79] - Data was not collected as there is no corresponding time point in schedule of activity of Protocol.

[80] - Data was not collected as there is no corresponding time point in schedule of activity of Protocol.

[81] - Data was not collected as there is no corresponding time point in schedule of activity of Protocol.

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in clinical chemistry parameter of albumin at Week 24 and Week 52 for placebo switched arms (Global Cohort)

End point title	Change from Baseline in clinical chemistry parameter of albumin at Week 24 and Week 52 for placebo switched arms (Global Cohort)[82]

End point description:

Blood samples were collected for the assessment of clinical chemistry parameter albumin level. Baseline was defined as the latest pre-dose assessment with a non-missing value, including those from unscheduled visits. Change from Baseline was calculated by subtracting the post dose visit value from the Baseline value. For safety assessments baseline is interpreted as Week 12. The analysis was performed on the Safety Set. Only those participants with data available at the specified data points were analyzed.

End point type	Secondary

End point timeframe:

Baseline (Week 12), Week 24 and Week 52

Notes:

[82] - 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: The endpoints are different for the different parts of the study.

End point values	Placebo+csDMARD and GSK3196165 90mg+csDMARD (Global Cohort)	Placebo +csDMARD and GSK3196165 150mg +csDMARD (Global Cohort)	Placebo +csDMARD and Tofacitinib 5mg +csDMARD (Global Cohort)	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	83	74	64	
Units: Grams per liter (g/L)				
arithmetic mean (standard deviation)				
Week 24	0.1 (± 2.33)	0.6 (± 2.13)	2.5 (± 2.99)	
Week 52	-0.0 (± 2.87)	0.9 (± 2.64)	2.1 (± 3.22)	

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in lipid profile parameter of total cholesterol at Week 52 for placebo switched arms (Global Cohort)

End point title	Change from Baseline in lipid profile parameter of total cholesterol at Week 52 for placebo switched arms (Global Cohort)[83]

End point description:

Blood samples were collected for the assessment of lipid profile of total cholesterol levels. Baseline was defined as the latest pre-dose assessment with a non-missing value, including those from unscheduled visits. Change from Baseline was calculated by subtracting the post dose visit value from the Baseline value. For safety assessments baseline is interpreted as Week 12. The analysis was performed on the Safety Set. Only those participants with data available at the specified data points were analyzed.

End point type	Secondary

End point timeframe:

Baseline (Week 12) and Week 52

Notes:

[83] - 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: The endpoints are different for the different parts of the study.

End point values	Placebo+csDMARD and GSK3196165 90mg+csDMARD (Global Cohort)	Placebo +csDMARD and GSK3196165 150mg +csDMARD (Global Cohort)	Placebo +csDMARD and Tofacitinib 5mg +csDMARD (Global Cohort)	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	71	66	55	
Units: Millimoles per liter (mmol/L)				
arithmetic mean (standard deviation)	0.198 (± 0.9586)	0.255 (± 0.8086)	0.691 (± 0.9233)	

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in lipid profile parameter of total cholesterol at Week 24 for placebo switched arms (Global Cohort)

End point title	Change from Baseline in lipid profile parameter of total cholesterol at Week 24 for placebo switched arms (Global Cohort)[84]

End point description:

Blood samples were collected for the assessment of lipid profile of total cholesterol levels. Baseline was defined as the latest pre-dose assessment with a non-missing value, including those from unscheduled visits. Change from Baseline was calculated by subtracting the post dose visit value from the Baseline value. Blood samples were collected at indicated time points per schedule of assessment in protocol. Objectives and Endpoints section incorrectly states that Change from baseline in key laboratory parameters at Week 24 was a secondary objective, however for lipid panel, there is no corresponding time point in schedule of assessment. Consequently, the objective that can be assessed for the lipid panel is Week 16 and not Week 24 as no data collected. Week 16 is not pre-specified time point to report.

End point type	Secondary

End point timeframe:

Baseline (Week 12) and Week 24

Notes:

[84] - 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: The endpoints are different for the different parts of the study.

End point values	Placebo+csDMARD and GSK3196165 90mg+csDMARD (Global Cohort)	Placebo +csDMARD and GSK3196165 150mg +csDMARD (Global Cohort)	Placebo +csDMARD and Tofacitinib 5mg +csDMARD (Global Cohort)	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	0[85]	0[86]	0[87]	
Units: Millimoles per liter (mmol/L)				
arithmetic mean (standard deviation)	()	()	()	

Notes:

[85] - Data was not collected as there is no corresponding time point in schedule of activity of Protocol.

[86] - Data was not collected as there is no corresponding time point in schedule of activity of Protocol.

[87] - Data was not collected as there is no corresponding time point in schedule of activity of Protocol.

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in lipid profile parameter of total cholesterol at Week 24 for treatment arms who started study intervention from Day 1 (Global Cohort)

End point title	Change from Baseline in lipid profile parameter of total cholesterol at Week 24 for treatment arms who started study intervention from Day 1 (Global Cohort)[88]

End point description:

Blood samples were collected for the assessment of lipid profile of total cholesterol levels. Baseline was defined as the latest pre-dose assessment with a non-missing value, including those from unscheduled visits. Change from Baseline was calculated by subtracting the post dose visit value from the Baseline value. Blood samples were collected at indicated time points per schedule of assessment in protocol. Objectives and Endpoints section incorrectly states that Change from baseline in key laboratory parameters at Week 24 was a secondary objective, however for lipid panel, there is no corresponding time point in schedule of assessment. Consequently, the objective that can be assessed for the lipid panel is Week 16 and not Week 24 as no data collected. Week 16 is not pre-specified time point to report.

End point type	Secondary

End point timeframe:

Baseline (Day 1) and Week 24

Notes:

[88] - 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: The endpoints are different for the different parts of the study.

End point values	GSK3196165 90mg + csDMARD (Global Cohort)	GSK3196165 150mg + csDMARD (Global Cohort)	Tofacitinib 5mg + csDMARD (Global Cohort)	
Subject group type	Reporting group	Reporting group	Subject analysis set	
Number of subjects analysed	0[89]	0[90]	0[91]	
Units: Millimoles per liter (mmol/L)				
arithmetic mean (standard deviation)	()	()	()	

Notes:

[89] - Data was not collected as there is no corresponding time point in schedule of activity of Protocol.

[90] - Data was not collected as there is no corresponding time point in schedule of activity of Protocol.

[91] - Data was not collected as there is no corresponding time point in schedule of activity of Protocol.

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in lipid profile parameter of total cholesterol at Week 52 for treatment arms who started study intervention from Day 1 (Global Cohort)

End point title	Change from Baseline in lipid profile parameter of total cholesterol at Week 52 for treatment arms who started study intervention from Day 1 (Global Cohort)[92]

End point description:

Blood samples were collected for the assessment of lipid profile of total cholesterol levels. Baseline was defined as the latest pre-dose assessment with a non-missing value, including those from unscheduled visits. Change from Baseline was calculated by subtracting the post dose visit value from the Baseline value. The analysis was performed on the Safety Set. Fifteen participants in Placebo group received active treatment of Tofacitinib mistakenly from Week 4 instead of Week 12 as planned. They were added with the Tofacitinib arm in safety analysis. Only those participants with data available at the specified data points were analyzed.

End point type	Secondary

End point timeframe:

Baseline (Day 1) and Week 52

Notes:

[92] - 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: The endpoints are different for the different parts of the study.

End point values	GSK3196165 90mg + csDMARD (Global Cohort)	GSK3196165 150mg + csDMARD (Global Cohort)	Tofacitinib 5mg + csDMARD (Global Cohort)	
Subject group type	Reporting group	Reporting group	Subject analysis set	
Number of subjects analysed	438	437	226	
Units: Millimoles per liter (mmol/L)				
arithmetic mean (standard deviation)	0.121 (± 0.8198)	0.129 (± 0.8076)	0.402 (± 0.8794)	

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in lipid profile parameter of low-density lipoprotein (LDL) cholesterol, high-density lipoprotein (HDL)-cholesterol at Week 12 (Global Cohort)

End point title	Change from Baseline in lipid profile parameter of low-density lipoprotein (LDL) cholesterol, high-density lipoprotein (HDL)-cholesterol at Week 12 (Global Cohort)[93]

End point description:

Blood samples were collected for assessment of fasting lipid profile including LDL cholesterol, HDL cholesterol levels. Baseline was defined as latest pre-dose assessment with a non-missing value, including those from unscheduled visits. Change from Baseline was calculated by subtracting post dose visit value from Baseline value. For purpose of all analyses up to week 12, placebo arms were pooled into a single placebo arm to primarily serve as a reference for the comparison of active treatment arms. Blood samples were collected at indicated time points per schedule of assessment in protocol. Objectives and Endpoints section incorrectly states that Change from baseline in key laboratory parameters at Week 12 was a secondary objective, however for lipid panel, there is no corresponding time point in schedule of assessment. Consequently, the objective that can be assessed for lipid panel is Week 4 and not Week 12 as no data collected. Week 4 is not pre-specified time point to report.

End point type	Secondary

End point timeframe:

Baseline (Day 1) and Week 12

Notes:

[93] - 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: The endpoints are different for the different parts of the study.

End point values	GSK3196165 90mg + csDMARD (Global Cohort)	GSK3196165 150mg + csDMARD (Global Cohort)	Tofacitinib 5mg + csDMARD (Global Cohort)	Pooled Placebo (Global Cohort)
Subject group type	Reporting group	Reporting group	Subject analysis set	Subject analysis set
Number of subjects analysed	0[94]	0[95]	0[96]	0[97]
Units: Millimoles per liter (mmol/L)				
arithmetic mean (standard deviation)	()	()	()	()

Notes:

[94] - Data was not collected as there is no corresponding time point in schedule of activity of Protocol.

[95] - Data was not collected as there is no corresponding time point in schedule of activity of Protocol.

[96] - Data was not collected as there is no corresponding time point in schedule of activity of Protocol.

[97] - Data was not collected as there is no corresponding time point in schedule of activity of Protocol.

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in lipid profile parameter of LDL cholesterol, high-density lipoprotein-cholesterol at Week 24 for treatment arms who started study intervention from Day 1 (Global Cohort)

End point title	Change from Baseline in lipid profile parameter of LDL cholesterol, high-density lipoprotein-cholesterol at Week 24 for treatment arms who started study intervention from Day 1 (Global Cohort)[98]

End point description:

Blood samples were collected for the assessment of fasting lipid profile including LDL cholesterol, HDL cholesterol levels. Baseline was defined as the latest pre-dose assessment with a non-missing value, including those from unscheduled visits. Change from Baseline was calculated by subtracting the post dose visit value from the Baseline value. Blood samples were collected at indicated time points per schedule of assessment in protocol. Objectives and Endpoints section incorrectly states that Change from baseline in key laboratory parameters at Week 24 was a secondary objective, however for lipid panel, there is no corresponding time point in schedule of assessment. Consequently, the objective that can be assessed for the lipid panel is Week 16 and not Week 24 as no data collected. Week 16 is not pre-specified time point to report.

End point type	Secondary

End point timeframe:

Baseline (Day 1) and Week 24

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: The endpoints are different for the different parts of the study.

End point values	GSK3196165 90mg + csDMARD (Global Cohort)	GSK3196165 150mg + csDMARD (Global Cohort)	Tofacitinib 5mg + csDMARD (Global Cohort)	
Subject group type	Reporting group	Reporting group	Subject analysis set	
Number of subjects analysed	0[99]	0[100]	0[101]	
Units: Millimoles per liter (mmol/L)				
arithmetic mean (standard deviation)	()	()	()	

Notes:

[99] - Data was not collected as there is no corresponding time point in schedule of activity of Protocol.

[100] - Data was not collected as there is no corresponding time point in schedule of activity of Protocol.

[101] - Data was not collected as there is no corresponding time point in schedule of activity of Protocol.

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in lipid profile parameter of LDL cholesterol, high-density lipoprotein-cholesterol at Week 24 for placebo switched arms (Global Cohort)

End point title	Change from Baseline in lipid profile parameter of LDL cholesterol, high-density lipoprotein-cholesterol at Week 24 for placebo switched arms (Global Cohort)[102]

End point description:

Blood samples were collected for the assessment of fasting lipid profile including LDL cholesterol, HDL cholesterol levels. Baseline was defined as the latest pre-dose assessment with a non-missing value, including those from unscheduled visits. Change from Baseline was calculated by subtracting the post dose visit value from the Baseline value. Blood samples were collected at indicated time points per schedule of assessment in protocol. Objectives and Endpoints section incorrectly states that Change from baseline in key laboratory parameters at Week 24 was a secondary objective, however for lipid panel, there is no corresponding time point in schedule of assessment. Consequently, the objective that can be assessed for the lipid panel is Week 16 and not Week 24 as no data collected. Week 16 is not pre-specified time point to report.

End point type	Secondary

End point timeframe:

Baseline (Week 12) and Week 24

Notes:

[102] - 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: The endpoints are different for the different parts of the study.

End point values	Placebo+csDMARD and GSK3196165 90mg+csDMARD (Global Cohort)	Placebo +csDMARD and GSK3196165 150mg +csDMARD (Global Cohort)	Placebo +csDMARD and Tofacitinib 5mg +csDMARD (Global Cohort)	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	0[103]	0[104]	0[105]	
Units: Millimoles per liter (mmol/L)				
arithmetic mean (standard deviation)	()	()	()	

Notes:

[103] - Data was not collected as there is no corresponding time point in schedule of activity of Protocol.

[104] - Data was not collected as there is no corresponding time point in schedule of activity of Protocol.

[105] - Data was not collected as there is no corresponding time point in schedule of activity of Protocol.

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in lipid profile parameter of LDL cholesterol, high-density lipoprotein-cholesterol at Week 52 for placebo switched arms who started study intervention from Week 12 (Global Cohort)

End point title	Change from Baseline in lipid profile parameter of LDL cholesterol, high-density lipoprotein-cholesterol at Week 52 for placebo switched arms who started study intervention from Week 12 (Global Cohort)[106]

End point description:

Blood samples were collected for the assessment of fasting lipid profile including LDL cholesterol, HDL cholesterol levels. Baseline was defined as the latest pre-dose assessment with a non-missing value, including those from unscheduled visits. Change from Baseline was calculated by subtracting the post dose visit value from the Baseline value. The analysis was performed on the Safety Set. Only those participants with data available at the specified data points were analyzed.

End point type	Secondary

End point timeframe:

Baseline (Week 12) and Week 52

Notes:

[106] - 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: The endpoints are different for the different parts of the study.

End point values	Placebo+csDMARD and GSK3196165 90mg+csDMARD (Global Cohort)	Placebo +csDMARD and GSK3196165 150mg +csDMARD (Global Cohort)	Placebo +csDMARD and Tofacitinib 5mg +csDMARD (Global Cohort)	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	71	66	55	
Units: Millimoles per liter (mmol/L)				
arithmetic mean (standard deviation)				
HDL Cholesterol, Direct, n=71,66,55	-0.041 (± 0.2841)	0.045 (± 0.2769)	0.135 (± 0.3094)	
LDL Cholesterol, n=71,65,55	0.188 (± 0.7796)	0.184 (± 0.6039)	0.495 (± 0.7375)	

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in lipid profile parameter of LDL cholesterol, high-density lipoprotein-cholesterol at Week 52 for treatment arms who started study intervention from Day 1 (Global Cohort)

End point title	Change from Baseline in lipid profile parameter of LDL cholesterol, high-density lipoprotein-cholesterol at Week 52 for treatment arms who started study intervention from Day 1 (Global Cohort)[107]

End point description:

Blood samples were collected for the assessment of fasting lipid profile including LDL cholesterol, HDL cholesterol levels. Baseline was defined as the latest pre-dose assessment with a non-missing value, including those from unscheduled visits. Change from Baseline was calculated by subtracting the post dose visit value from the Baseline value. The analysis was performed on the Safety Set. Fifteen participants in Placebo group received active treatment of Tofacitinib mistakenly from Week 4 instead of

Week 12 as planned. They were added with the Tofacitinib arm in safety analysis. Only those participants with data available at the specified data points were analyzed.

End point type	Secondary

End point timeframe:

Baseline (Day 1) and Week 52

Notes:

[107] - 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: The endpoints are different for the different parts of the study.

End point values	GSK3196165 90mg + csDMARD (Global Cohort)	GSK3196165 150mg + csDMARD (Global Cohort)	Tofacitinib 5mg + csDMARD (Global Cohort)	
Subject group type	Reporting group	Reporting group	Subject analysis set	
Number of subjects analysed	438	437	226	
Units: Millimoles per liter (mmol/L)				
arithmetic mean (standard deviation)				
HDL Cholesterol, Direct, n=438,437,226	0.026 (± 0.2415)	0.010 (± 0.2812)	0.157 (± 0.3184)	
LDL Cholesterol, n=432,436,226	0.076 (± 0.6971)	0.093 (± 0.6396)	0.191 (± 0.7423)	

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in lipid profile parameter of triglycerides at Week 52 for treatment arms who started study intervention from Day 1 (Global Cohort)

End point title	Change from Baseline in lipid profile parameter of triglycerides at Week 52 for treatment arms who started study intervention from Day 1 (Global Cohort)[108]

End point description:

Blood samples was collected for the assessment of change from baseline in fasting lipid profile triglycerides levels. Baseline was defined as the latest pre-dose assessment with a non-missing value, including those from unscheduled visits. Change from Baseline was calculated by subtracting the post dose visit value from the Baseline value. The analysis was performed on the Safety Set. Fifteen participants in Placebo group received active treatment of Tofacitinib mistakenly from Week 4 instead of Week 12 as planned. They were added with the Tofacitinib arm in safety analysis. Only those participants with data available at the specified data points were analyzed.

End point type	Secondary

End point timeframe:

Baseline (Day 1) and Week 52

Notes:

[108] - 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: The endpoints are different for the different parts of the study.

End point values	GSK3196165 90mg + csDMARD (Global Cohort)	GSK3196165 150mg + csDMARD (Global Cohort)	Tofacitinib 5mg + csDMARD (Global Cohort)	
Subject group type	Reporting group	Reporting group	Subject analysis set	
Number of subjects analysed	438	437	226	
Units: Millimoles per liter (mmol/L)				
arithmetic mean (standard deviation)	0.045 (± 0.5902)	0.054 (± 0.5970)	0.117 (± 0.6444)	

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in lipid profile parameter of triglycerides at Week 12 (Global Cohort)

End point title	Change from Baseline in lipid profile parameter of triglycerides at Week 12 (Global Cohort)[109]

End point description:

Blood samples was collected for the assessment of change from baseline in fasting lipid profile triglycerides levels. Baseline was defined as the latest pre-dose assessment with a non-missing value, including those from unscheduled visits. Change from Baseline was calculated by subtracting the post dose visit value from the Baseline value. For the purpose of all analyses up to week 12, the placebo arms were pooled into a single placebo arm to primarily serve as a reference for the comparison of active treatment arms. Blood samples were collected at indicated time points as per schedule of assessment in the protocol. The Objectives and Endpoints section incorrectly states that Change from baseline in key laboratory parameters at Week 12 was a secondary objective, however for the lipid panel, there is no corresponding time point in the schedule of assessment. Consequently, the only objective that can be assessed for the lipid panel is Week 4 and not at Week 12.

End point type	Secondary

End point timeframe:

Baseline (Day 1) and Week 12

Notes:

[109] - 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: The endpoints are different for the different parts of the study.

End point values	GSK3196165 90mg + csDMARD (Global Cohort)	GSK3196165 150mg + csDMARD (Global Cohort)	Tofacitinib 5mg + csDMARD (Global Cohort)	Pooled Placebo (Global Cohort)
Subject group type	Reporting group	Reporting group	Subject analysis set	Subject analysis set
Number of subjects analysed	0[110]	0[111]	0[112]	0[113]
Units: Millimoles per liter (mmol/L)				
arithmetic mean (standard deviation)	()	()	()	()

Notes:

[110] - Data was not collected as there is no corresponding time point in schedule of activity of Protocol.

[111] - Data was not collected as there is no corresponding time point in schedule of activity of Protocol.

[112] - Data was not collected as there is no corresponding time point in schedule of activity of Protocol.

[113] - Data was not collected as there is no corresponding time point in schedule of activity of Protocol.

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in lipid profile parameter of triglycerides at Week 24 for treatment arms who started study intervention from Day 1 (Global Cohort)

End point title	Change from Baseline in lipid profile parameter of triglycerides at Week 24 for treatment arms who started study intervention from Day 1 (Global Cohort)[114]

End point description:

Blood samples was collected for the assessment of change from baseline in fasting lipid profile triglycerides levels. Baseline was defined as the latest pre-dose assessment with a non-missing value, including those from unscheduled visits. Change from Baseline was calculated by subtracting the post dose visit value from the Baseline value. Blood samples were collected at indicated time points per schedule of assessment in protocol. Objectives and Endpoints section incorrectly states that Change from baseline in key laboratory parameters at Week 24 was a secondary objective, however for lipid panel, there is no corresponding time point in schedule of assessment. Consequently, the objective that can be assessed for the lipid panel is Week 16 and not Week 24 as no data collected. Week 16 is not pre-specified time point to report.

End point type	Secondary

End point timeframe:

Baseline (Day 1) and Week 24

Notes:

[114] - 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: The endpoints are different for the different parts of the study.

End point values	GSK3196165 90mg + csDMARD (Global Cohort)	GSK3196165 150mg + csDMARD (Global Cohort)	Tofacitinib 5mg + csDMARD (Global Cohort)	
Subject group type	Reporting group	Reporting group	Subject analysis set	
Number of subjects analysed	0[115]	0[116]	0[117]	
Units: Millimoles per liter (mmol/L)				
arithmetic mean (standard deviation)	()	()	()	

Notes:

[115] - Data was not collected as there is no corresponding time point in schedule of activity of Protocol.

[116] - Data was not collected as there is no corresponding time point in schedule of activity of Protocol.

[117] - Data was not collected as there is no corresponding time point in schedule of activity of Protocol.

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in lipid profile parameter of triglycerides at Week 24 for placebo switched arms (Global Cohort)

End point title	Change from Baseline in lipid profile parameter of triglycerides at Week 24 for placebo switched arms (Global Cohort)[118]

End point description:

Blood samples was collected for the assessment of change from baseline in fasting lipid profile triglycerides levels. Baseline was defined as the latest pre-dose assessment with a non-missing value, including those from unscheduled visits. Change from Baseline was calculated by subtracting the post dose visit value from the Baseline value. Blood samples were collected at indicated time points per schedule of assessment in protocol. Objectives and Endpoints section incorrectly states that Change from baseline in key laboratory parameters at Week 24 was a secondary objective, however for lipid panel, there is no corresponding time point in schedule of assessment. Consequently, the objective that can be assessed for the lipid panel is Week 16 and not Week 24 as no data collected. Week 16 is not pre-specified time point to report.

End point type	Secondary

End point timeframe:

Baseline (Week 12) and Week 24

Notes:

[118] - 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: The endpoints are different for the different parts of the study.

End point values	Placebo+csDMARD and GSK3196165 90mg+csDMARD (Global Cohort)	Placebo +csDMARD and GSK3196165 150mg +csDMARD (Global Cohort)	Placebo +csDMARD and Tofacitinib 5mg +csDMARD (Global Cohort)	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	0[119]	0[120]	0[121]	
Units: Millimoles per liter (mmol/L)				
arithmetic mean (standard deviation)	()	()	()	

Notes:

[119] - Data was not collected as there is no corresponding time point in schedule of activity of Protocol.

[120] - Data was not collected as there is no corresponding time point in schedule of activity of Protocol.

[121] - Data was not collected as there is no corresponding time point in schedule of activity of Protocol.

Statistical analyses

No statistical analyses for this end point

Secondary: Number of participants with National Cancer Institute-Common terminology criteria for adverse events (NCI-CTCAE)>=Grade 3 hematological/clinical chemistry abnormalities (Global Cohort)

End point title	Number of participants with National Cancer Institute-Common terminology criteria for adverse events (NCI-CTCAE)>=Grade 3 hematological/clinical chemistry abnormalities (Global Cohort)[122]

End point description:

Number of participants with NCI-CTCAE >=Grade 3 hematological/clinical chemistry abnormalities were summarized. Hematological and Clinical chemistry parameters were summarized according to the NCI-CTCAE, version 5.0: Grade 1: mild; Grade 2: moderate; Grade 3: severe; Grade 4: life-threatening or disabling. Higher grade indicates more severity. Data is presented for only those parameters for which participants had worst case >=Grade 3 shifts from Baseline. Fifteen participants in Placebo group received active treatment of Tofacitinib mistakenly from Week 4 instead of Week 12 as planned. They were added with the Tofacitinib arm in safety analysis. The analysis was performed on the Safety Set that includes all randomized participants who received at least one dose of study treatment. Pooled Placebo collected data till Week 12. Placebo switched arms collected data from Week 12 to 59. Experimental arm collected data from Day 01 to Week 59.

End point type	Secondary

End point timeframe:

Up to Week 59

Notes:

[122] - 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: The endpoints are different for the different parts of the study.

End point values	GSK3196165 90mg + csDMARD (Global Cohort)	GSK3196165 150mg + csDMARD (Global Cohort)	Tofacitinib 5mg + csDMARD (Global Cohort)	Pooled Placebo (Global Cohort)
Subject group type	Reporting group	Reporting group	Subject analysis set	Subject analysis set
Number of subjects analysed	545	539	286	255
Units: Participants				
Alanine aminotransferase increased,Total,Grade 3	4	5	4	1
Aspartate aminotransferase increased,Total,Grade3	2	3	1	1
Anemia, Total, Grade 3	3	5	2	2
Lymphocyte count decreased, Grade 3	9	11	9	3
Neutrophil count decreased, Total, Grade 3	3	3	2	2
Lymphocyte count decreased, Grade 4	0	0	9	0
Hypertriglyceridemia, Total, Grade 3	10	0	2	0
Aspartate aminotransferase increased,Total,Grade4	0	2	0	0
Alanine aminotransferase increased, Total, Grade 4	0	2	0	0
Creatinine increased, Total, Grade 4	1	0	0	0
Chronic Kidney Disease, Total, Grade 3	0	1	2	0
Chronic Kidney Disease, Total, Grade 4	1	0	0	0
Hemoglobin increased, Total, Grade 3	1	0	0	0
White blood cell decreased, Total, Grade 3	2	0	0	0
Neutrophil count decreased, Total, Grade 4	2	1	0	0
Hypertriglyceridemia, Total, Grade 4	1	0	0	0

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in lipid profile parameter of triglycerides at Week 52 for placebo switched arms who started study intervention from Week 12 (Global Cohort)

End point title	Change from Baseline in lipid profile parameter of triglycerides at Week 52 for placebo switched arms who started study intervention from Week 12 (Global Cohort)[123]

End point description:

Blood samples was collected for the assessment of change from baseline in fasting lipid profile triglycerides levels. Baseline was defined as the latest pre-dose assessment with a non-missing value, including those from unscheduled visits. Change from Baseline was calculated by subtracting the post dose visit value from the Baseline value. The analysis was performed on the Safety Set. Only those participants with data available at the specified data points were analyzed.

End point type	Secondary

End point timeframe:

Baseline (Week 12) and Week 52

Notes:

[123] - 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: The endpoints are different for the different parts of the study.

End point values	Placebo+csDMARD and GSK3196165 90mg+csDMARD (Global Cohort)	Placebo +csDMARD and GSK3196165 150mg +csDMARD (Global Cohort)	Placebo +csDMARD and Tofacitinib 5mg +csDMARD (Global Cohort)	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	71	66	55	
Units: Millimoles per liter (mmol/L)				
arithmetic mean (standard deviation)	0.111 (± 0.4371)	0.034 (± 0.5246)	0.129 (± 0.5816)	

Statistical analyses

No statistical analyses for this end point

Secondary: Number of participants with anti-GSK3196165 antibodies (Global Cohort)

End point title	Number of participants with anti-GSK3196165 antibodies (Global Cohort)[124]

End point description:

Serum samples were collected for the determination of anti-GSK3196165 antibodies (ADA) using a validated electrochemiluminescence (ECL) immunoassay. The assay involved screening, confirmation and titration steps. If serum samples tested positive in the screening assay, they were considered 'potentially positive' and were further analyzed for the specificity using the confirmation assay. Samples that confirmed positive in the confirmation assay were reported as 'positive'. The analysis was performed on the Safety set. Fifteen participants in Placebo group received active treatment of Tofacitinib mistakenly from Week 4 instead of Week 12 as planned. They were added with the Tofacitinib arm in safety analysis.

End point type	Secondary

End point timeframe:

Up to Week 52

Notes:

[124] - 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: The endpoints are different for the different parts of the study.

End point values	GSK3196165 90mg + csDMARD (Global Cohort)	GSK3196165 150mg + csDMARD (Global Cohort)	Placebo+csDMARD and GSK3196165 90mg+csDMARD (Global Cohort)	Placebo +csDMARD and GSK3196165 150mg +csDMARD (Global Cohort)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	545	539	91	89
Units: Participants	6	6	3	1

End point values	Placebo +csDMARD and Tofacitinib 5mg +csDMARD (Global Cohort)	Tofacitinib 5mg + csDMARD (Global Cohort)		

Subject group type	Reporting group	Subject analysis set		
Number of subjects analysed	75	286		
Units: Participants	0	0		

Statistical analyses

No statistical analyses for this end point

Secondary: Concentrations of Granulocyte-macrophage colony stimulating factor (GM-CSF) autoantibody (Global Cohort)

End point title	Concentrations of Granulocyte-macrophage colony stimulating factor (GM-CSF) autoantibody (Global Cohort)[125]

End point description:

Blood samples were collected for markers which may influence rheumatoid arthritis. Concentrations of GM-CSF autoantibodies was determined. The analysis was performed on the Safety Set. Fifteen participants in Placebo group received active treatment of Tofacitinib mistakenly from Week 4 instead of Week 12 as planned. They were added with the Tofacitinib arm in safety analysis.

End point type	Secondary

End point timeframe:

At baseline

Notes:

[125] - 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: The endpoints are different for the different parts of the study.

End point values	GSK3196165 90mg + csDMARD (Global Cohort)	GSK3196165 150mg + csDMARD (Global Cohort)	Placebo+csDMARD and GSK3196165 90mg+csDMARD (Global Cohort)	Placebo +csDMARD and GSK3196165 150mg +csDMARD (Global Cohort)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	545	539	91	89
Units: Microgram per liter (ug/L)				
arithmetic mean (standard deviation)	201.587 (± 519.9638)	193.911 (± 402.0018)	217.622 (± 399.6172)	267.669 (± 642.5823)

End point values	Placebo +csDMARD and Tofacitinib 5mg +csDMARD (Global Cohort)	Tofacitinib 5mg + csDMARD (Global Cohort)		
Subject group type	Reporting group	Subject analysis set		
Number of subjects analysed	75	286		
Units: Microgram per liter (ug/L)				
arithmetic mean (standard deviation)	252.209 (± 671.7397)	189.505 (± 344.7866)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in Health Assessment Questionnaire Disability Index (HAQ-DI) at Week 12 (Asia Cohort)

End point title	Change from Baseline in Health Assessment Questionnaire Disability Index (HAQ-DI) at Week 12 (Asia Cohort)[126]

End point description:

Health Assessment Questionnaire-Disability Index (HAQ-DI) is 20-question instrument that assesses degree of difficulty in accomplishing tasks in eight functional areas:dressing and grooming, arising, eating, walking, hygiene, reach, grip and common daily activities. Overall HAQ-DI score is sum of domain scores divided by number of domains answered. The score ranges from 0 to 3 where 0=least difficulty and 3=extreme difficulty. Higher overall score indicates greater disability. A negative change from baseline indicates an improvement. Baseline was defined as latest pre-dose assessment with a non-missing value, including from unscheduled visits. Change from Baseline was calculated by subtracting post dose value from Baseline.Placebo arms were pooled into single placebo arm to primarily serve as reference for comparison of active treatment arms. Analysis was performed on ITT-Supplementary Asia Cohort set. Participants with data available at indicated timepoints are analyzed.

End point type	Secondary

End point timeframe:

Baseline (Day 1) and Week 12

Notes:

[126] - 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: The endpoints are different for the different parts of the study.

End point values	GSK3196165 90mg + csDMARD (Asia Cohort)	GSK3196165 150mg + csDMARD (Asia Cohort)	Tofacitinib 5mg + csDMARD (Asia Cohort)	Pooled Placebo (Asia Cohort)
Subject group type	Reporting group	Reporting group	Reporting group	Subject analysis set
Number of subjects analysed	46	42	19	21
Units: Scores on a scale				
arithmetic mean (standard deviation)	-0.22 (± 0.479)	-0.25 (± 0.537)	-0.47 (± 0.281)	0.02 (± 0.577)

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of participants achieving CDAI total score <=10 (CDAI LDA) at Week 24 and Week 52 for treatment arms who started study intervention from Day 1 (Asia Cohort)

End point title	Percentage of participants achieving CDAI total score <=10 (CDAI LDA) at Week 24 and Week 52 for treatment arms who started study intervention from Day 1 (Asia Cohort)[127]

End point description:

Clinical Disease Activity Index (CDAI) total score is a composite score consisting of the sum of Swollen Joint Count 28 (SJC28), Tender Joint Count 28 (TJC28), Patient's Global Assessment of Arthritis Disease Activity (PtGA) (visual analogue scale [VAS] with values from 0=best to 100=worst) and Physician Global Assessment of Arthritis Disease Activity (PhGA) (VAS with values from 0=best to 100=worst). PtGA and PhGA are transformed to a 0-10 scale before computing the CDAI total score. CDAI total score ranges from 0 to 76 with higher values representing higher disease activity. Low disease activity (LDA) is achieved when CDAI total score <=10. Percentage values are rounded off. The analysis was performed on all randomized Asia Cohort participants who received study intervention from Day 01 to

Week 52. Participants with data available at indicated timepoints are analyzed.

End point type	Secondary

End point timeframe:

Week 24 and Week 52

Notes:

[127] - 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: The endpoints are different for the different parts of the study.

End point values	GSK3196165 90mg + csDMARD (Asia Cohort)	GSK3196165 150mg + csDMARD (Asia Cohort)	Tofacitinib 5mg + csDMARD (Asia Cohort)	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	38	43	17	
Units: Percentage of participants				
number (not applicable)				
Week 24, n=38,43,17	21.0	19.0	53.0	
Week 52, n-3,32,15	45.0	41.0	47.0	

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of participants achieving Clinical disease activity index (CDAI) total score less than or equal to (<=)10 [CDAI Low disease activity (LDA)] at Week 12 (Asia Cohort)

End point title	Percentage of participants achieving Clinical disease activity index (CDAI) total score less than or equal to (<=)10 [CDAI Low disease activity (LDA)] at Week 12 (Asia Cohort)[128]

End point description:

Clinical Disease Activity Index (CDAI) total score is a composite score consisting of the sum of Swollen Joint Count 28 (SJC28), Tender Joint Count 28 (TJC28), Patient's Global Assessment of Arthritis Disease Activity (PtGA) (visual analogue scale [VAS] with values from 0=best to 100=worst) and Physician Global Assessment of Arthritis Disease Activity (PhGA) (VAS with values from 0=best to 100=worst). PtGA and PhGA are transformed to a 0-10 scale before computing the CDAI total score. CDAI total score ranges from 0 to 76 with higher values representing higher disease activity. Low disease activity (LDA) is achieved when CDAI total score <=10. For the purpose of all analyses up to week 12, the placebo arms were pooled into single placebo arm to primarily serve as reference for the comparison of active treatment arms. Percentage values are rounded off. The analysis was performed on ITT-Supplementary Asia Cohort set. Participants with data available at indicated timepoints are analyzed.

End point type	Secondary

End point timeframe:

Week 12

Notes:

[128] - 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: The endpoints are different for the different parts of the study.

End point values	GSK3196165 90mg + csDMARD (Asia Cohort)	GSK3196165 150mg + csDMARD (Asia Cohort)	Tofacitinib 5mg + csDMARD (Asia Cohort)	Pooled Placebo (Asia Cohort)
Subject group type	Reporting group	Reporting group	Reporting group	Subject analysis set
Number of subjects analysed	45	43	19	21
Units: Percentage of participants	13	12	58	19

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of participants achieving CDAI total score <=2.8 (CDAI Remission) at Week 12 (Asia Cohort)

End point title	Percentage of participants achieving CDAI total score <=2.8 (CDAI Remission) at Week 12 (Asia Cohort)[129]

End point description:

Clinical Disease Activity Index (CDAI) total score is a composite score consisting of the sum of Swollen Joint Count 28 (SJC28), Tender Joint Count 28 (TJC28), Patient's Global Assessment of Arthritis Disease Activity (PtGA) (visual analogue scale [VAS] with values from 0=best to 100=worst) and Physician Global Assessment of Arthritis Disease Activity (PhGA) (VAS with values from 0=best to 100=worst). PtGA and PhGA are transformed to a 0-10 scale before computing the CDAI total score. CDAI total score ranges from 0 to 76 with higher values representing higher disease activity. CDAI remission is achieved when CDAI total score <=2.8. For the purpose of all analyses up to week 12, the placebo arms were pooled into single placebo arm to primarily serve as reference for the comparison of active treatment arms. Percentage values are rounded off. The analysis was performed on ITT-Supplementary Asia Cohort set. Participants with data available at indicated timepoints are analyzed.

End point type	Secondary

End point timeframe:

Week 12

Notes:

[129] - 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: The endpoints are different for the different parts of the study.

End point values	GSK3196165 90mg + csDMARD (Asia Cohort)	GSK3196165 150mg + csDMARD (Asia Cohort)	Tofacitinib 5mg + csDMARD (Asia Cohort)	Pooled Placebo (Asia Cohort)
Subject group type	Reporting group	Reporting group	Reporting group	Subject analysis set
Number of subjects analysed	45	43	19	21
Units: Percentage of participants				
number (not applicable)	2.0	0.0	11.0	0.0

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of participants achieving CDAI total score <=10 (CDAI LDA) at Week 24 and Week 52 for placebo switched arms (Asia Cohort)

End point title	Percentage of participants achieving CDAI total score <=10

	(CDAI LDA) at Week 24 and Week 52 for placebo switched arms (Asia Cohort)[130]

End point description:

Clinical Disease Activity Index (CDAI) total score is a composite score consisting of the sum of Swollen Joint Count 28 (SJC28), Tender Joint Count 28 (TJC28), Patient's Global Assessment of Arthritis Disease Activity (PtGA) (visual analogue scale with values from 0=best to 100=worst) and Physician Global Assessment of Arthritis Disease Activity (PhGA) (visual analogue scale with values from 0=best to 100=worst). PtGA and PhGA are transformed to a 0-10 scale before computing the CDAI total score. CDAI total score ranges from 0 to 76 with higher values representing higher disease activity. Low disease activity (LDA) is achieved when CDAI total score <=10. Percentage values are rounded off. The analysis was performed on all randomized Asia Cohort participants who switched from placebo to study intervention at Week 12. Participants with data available at indicated timepoints are analyzed.

End point type	Secondary

End point timeframe:

Week 24 and Week 52

Notes:

[130] - 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: The endpoints are different for the different parts of the study.

End point values	Placebo + csDMARD and GSK3196165 90mg + csDMARD (Asia Cohort)	Placebo + csDMARD and GSK3196165 150mg + csDMARD (Asia Cohort)	Placebo + csDMARD and Tofacitinib 5mg + csDMARD (Asia Cohort)	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	6	6	7	
Units: Percentage of participants				
number (not applicable)				
Week 24, n=6,6,7	33.0	33.0	43.0	
Week 52, n=4,6,5	75.0	67.0	40.0	

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of participants achieving CDAI total score <=2.8 (CDAI Remission) at Week 24 and Week 52 for treatment arms who started study intervention from Day 1 (Asia Cohort)

End point title	Percentage of participants achieving CDAI total score <=2.8 (CDAI Remission) at Week 24 and Week 52 for treatment arms who started study intervention from Day 1 (Asia Cohort)[131]

End point description:

Clinical Disease Activity Index (CDAI) total score is a composite score consisting of the sum of Swollen Joint Count 28 (SJC28), Tender Joint Count 28 (TJC28), Patient's Global Assessment of Arthritis Disease Activity (PtGA) (visual analogue scale with values from 0=best to 100=worst) and Physician Global Assessment of Arthritis Disease Activity (PhGA) (visual analogue scale with values from 0=best to 100=worst). PtGA and PhGA are transformed to a 0-10 scale before computing the CDAI total score. CDAI total score ranges from 0 to 76 with higher values representing higher disease activity. CDAI remission is achieved when CDAI total score <=2.8. Percentage values are rounded off. The analysis was performed on all randomized Asia Cohort participants who received study intervention from Day 01 to Week 52. Participants with data available at indicated timepoints are analyzed.

End point type	Secondary

End point timeframe:

Week 24 and Week 52

Notes:

[131] - 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: The endpoints are different for the different parts of the study.

End point values	GSK3196165 90mg + csDMARD (Asia Cohort)	GSK3196165 150mg + csDMARD (Asia Cohort)	Tofacitinib 5mg + csDMARD (Asia Cohort)	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	38	43	17	
Units: Percentage of participants				
number (not applicable)				
Week 24, n=38,43,17	0.0	7.0	24.0	
Week 52, n=31,32,15	6.0	16.0	13.0	

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of participants achieving CDAI total score <=2.8 (CDAI Remission) at Week 24 and Week 52 for placebo switched arms (Asia Cohort)

End point title	Percentage of participants achieving CDAI total score <=2.8 (CDAI Remission) at Week 24 and Week 52 for placebo switched arms (Asia Cohort)[132]

End point description:

Clinical Disease Activity Index (CDAI) total score is a composite score consisting of the sum of Swollen Joint Count 28 (SJC28), Tender Joint Count 28 (TJC28), Patient's Global Assessment of Arthritis Disease Activity (PtGA) (visual analogue scale with values from 0=best to 100=worst) and Physician Global Assessment of Arthritis Disease Activity (PhGA) (visual analogue scale with values from 0=best to 100=worst). PtGA and PhGA are transformed to a 0-10 scale before computing the CDAI total score. CDAI total score ranges from 0 to 76 with higher values representing higher disease activity. CDAI remission is achieved when CDAI total score <=2.8. Percentage values are rounded off. The analysis was performed on all randomized Asia Cohort participants who switched from placebo to study intervention at Week 12. Participants with data available at indicated timepoints are analyzed.

End point type	Secondary

End point timeframe:

Week 24 and Week 52

Notes:

[132] - 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: The endpoints are different for the different parts of the study.

End point values	Placebo + csDMARD and GSK3196165 90mg + csDMARD (Asia Cohort)	Placebo + csDMARD and GSK3196165 150mg + csDMARD (Asia Cohort)	Placebo + csDMARD and Tofacitinib 5mg + csDMARD (Asia Cohort)	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	6	6	7	
Units: Percentage of participants				
number (not applicable)				
Week 24, n=6,6,7	0.0	0.0	0.0	

Week 52, n=4,6,5	25.0	0.0	20.0	

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of participants achieving 50%/70% improvement in American College of Rheumatology Criteria(ACR50/70) at Week 12 (Asia Cohort)

End point title	Percentage of participants achieving 50%/70% improvement in American College of Rheumatology Criteria(ACR50/70) at Week 12 (Asia Cohort)[133]

End point description:

ACR50/70 is calculated as 50%/70% improvement from Baseline in Tender Joint Count 68 (TJC68) and Swollen Joint Count 66 (SJC66) and 50%/70% improvement in 3 of the following 5 measures:Patient's Global Assessment of Arthritis Disease Activity (PtGA), Physician Global Assessment of Arthritis Disease Activity (PhGA) [VAS with values from 0=best to 100=worst), Patient Assessment of Arthritis Pain (VAS with values from 0=no pain and 100=most severe pain), Health Assessment Questionnaire-Disability Index (HAQ-DI) (ranges from 0 = least difficulty to 3 = extreme difficulty) and an acute-phase reactant (high sensitivity C-reactive Protein mg/L (hsCRP)]. For the purpose of all analyses up to week 12, placebo arms were pooled into single placebo arm to primarily serve as reference for comparison of active treatment arms. Percentage values are rounded off. The analysis was performed on ITT-Supplementary Asia Cohort set. Participants with data available at indicated timepoints are analyzed.

End point type	Secondary

End point timeframe:

Week 12

Notes:

[133] - 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: The endpoints are different for the different parts of the study.

End point values	GSK3196165 90mg + csDMARD (Asia Cohort)	GSK3196165 150mg + csDMARD (Asia Cohort)	Tofacitinib 5mg + csDMARD (Asia Cohort)	Pooled Placebo (Asia Cohort)
Subject group type	Reporting group	Reporting group	Reporting group	Subject analysis set
Number of subjects analysed	44	42	19	21
Units: Percentage of participants				
number (not applicable)				
ACR50	11.0	12.0	53.0	0.0
ACR70	5.0	2.0	16.0	0.0

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of participants achieving ACR20/50/70 at Week 24 and Week 52 for treatment arms who started study intervention from Day 1 (Asia Cohort)

End point title	Percentage of participants achieving ACR20/50/70 at Week 24

	and Week 52 for treatment arms who started study intervention from Day 1 (Asia Cohort)[134]

End point description:

ACR20/50/70 is calculated as a 20%/50%/70% improvement from Baseline in Tender Joint Count 68 (TJC68) and Swollen Joint Count 66 (SJC66) and a 20%/50%/70% improvement in 3 of the following 5 measures: Patient's Global Assessment of Arthritis Disease Activity (PtGA) (visual analogue scale (VAS) with values from 0=best to 100=worst), Physician Global Assessment of Arthritis Disease Activity (PhGA) [VAS with values from 0=best to 100=worst], Patient Assessment of Arthritis Pain (VAS with values from 0=no pain and 100=most severe pain), Health Assessment Questionnaire-Disability Index (HAQ- DI) (ranges from 0 to 3 where 0 = least difficulty and 3 = extreme difficulty) and an acute-phase reactant [high sensitivity C-reactive Protein mg/L (hsCRP)]. Percentage values are rounded off. The analysis was performed on all randomized Asia Cohort participants who received study intervention from Day 01 to Week 52. Participants with data available at indicated timepoints are analyzed.

End point type	Secondary

End point timeframe:

Week 24 and Week 52

Notes:

[134] - 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: The endpoints are different for the different parts of the study.

End point values	GSK3196165 90mg + csDMARD (Asia Cohort)	GSK3196165 150mg + csDMARD (Asia Cohort)	Tofacitinib 5mg + csDMARD (Asia Cohort)	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	37	42	17	
Units: Percentage of participants				
number (not applicable)				
ACR20, Week 24, n=37,42,17	54.0	55.0	19.0	
ACR20, Week 52, n=30,31,15	63.0	77.0	87.0	
ACR50, Week 24, n=37,42,17	19.0	24.0	53.0	
ACR50, Week 52, n=30,31,15	37.0	48.0	53.0	
ACR70, Week 24, n=37,42,17	8.0	7.0	29.0	
ACR70, Week 52, n=30,31,15	13.0	10.0	27.0	

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of participants achieving ACR20/50/70 at Week 24 and Week 52 for placebo switched arms (Asia Cohort)

End point title	Percentage of participants achieving ACR20/50/70 at Week 24 and Week 52 for placebo switched arms (Asia Cohort)[135]

End point description:

ACR20/50/70 is calculated as a 20%/50%/70% improvement from Baseline in Tender Joint Count 68 (TJC68) and Swollen Joint Count 66 (SJC66) and a 20%/50%/70% improvement in 3 of the following 5 measures: Patient's Global Assessment of Arthritis Disease Activity (PtGA) (visual analogue scale (VAS) with values from 0=best to 100=worst), Physician Global Assessment of Arthritis Disease Activity (PhGA) [VAS with values from 0=best to 100=worst], Patient Assessment of Arthritis Pain (VAS with values from 0=no pain and 100=most severe pain), Health Assessment Questionnaire-Disability Index (HAQ- DI) (ranges from 0 to 3 where 0 = least difficulty and 3 = extreme difficulty) and an acute-phase reactant [high sensitivity C-reactive Protein mg/L (hsCRP)]. Percentage values are rounded off. The analysis was performed on all randomized Asia Cohort participants who switched from placebo to study intervention at Week 12. Participants with data available at indicated timepoints are analyzed.

End point type	Secondary

End point timeframe:

Week 24 and Week 52

Notes:

[135] - 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: The endpoints are different for the different parts of the study.

End point values	Placebo + csDMARD and GSK3196165 90mg + csDMARD (Asia Cohort)	Placebo + csDMARD and GSK3196165 150mg + csDMARD (Asia Cohort)	Placebo + csDMARD and Tofacitinib 5mg + csDMARD (Asia Cohort)	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	6	6	7	
Units: Percentage of participants				
number (not applicable)				
ACR20, Week 52, n=4,6,6	75.0	33.0	67.0	
ACR50, Week 24, n=6,6,7	0.0	0.0	43.0	
ACR50, Week 52, n=4,6,6	50.0	17.0	67.0	
ACR70, Week 24, n=6,6,7	0.0	0.0	14.0	
ACR70, Week 52, n=4,6,6	50.0	17.0	17.0	
ACR20, Week 24, n=6,6,7	33.0	17.0	38.0	

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of participants achieving Disease Activity Score using 28 joint count and C-Reactive Protein (DAS28-CRP) <=3.2 (DAS28-CRP LDA) at Week 12 (Asia Cohort)

End point title	Percentage of participants achieving Disease Activity Score using 28 joint count and C-Reactive Protein (DAS28-CRP) <=3.2 (DAS28-CRP LDA) at Week 12 (Asia Cohort)[136]

End point description:

The DAS28-CRP is a measure of RA disease activity calculated using Tender Joint Count 28 (TJC28), Swollen Joint Count 28 (SJC28), C-reactive protein (CRP) (in mg/L), Patient's Global Assessment of Arthritis Disease Activity (PtGA) (visual analogue scale with values from 0=best to 100=worst). DAS28-CRP scores range from 1.0 to 9.4, where lower scores indicate less disease activity. Low disease activity (LDA) is achieved when DAS28-CRP greater than or equal to (<=)3.2. A negative change from baseline in DAS28-CRP indicates an improvement. For the purpose of all analyses up to week 12, the placebo arms were pooled into a single placebo arm to primarily serve as a reference for the comparison of active treatment arms. Percentage values are rounded off. The analysis was performed on ITT-Supplementary Asia Cohort set. Participants with data available at indicated timepoints are analyzed.

End point type	Secondary

End point timeframe:

Week 12

Notes:

[136] - 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: The endpoints are different for the different parts of the study.

End point values	GSK3196165 90mg + csDMARD (Asia Cohort)	GSK3196165 150mg + csDMARD (Asia Cohort)	Tofacitinib 5mg + csDMARD (Asia Cohort)	Pooled Placebo (Asia Cohort)
Subject group type	Reporting group	Reporting group	Reporting group	Subject analysis set
Number of subjects analysed	45	42	19	21
Units: Percentage of participants				
number (not applicable)	16.0	21.0	58.0	10.0

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of participants achieving DAS28 Erythrocyte Sedimentation Rate (ESR) <=3.2 (DAS28-ESR LDA) at Week 12 (Asia Cohort)

End point title	Percentage of participants achieving DAS28 Erythrocyte Sedimentation Rate (ESR) <=3.2 (DAS28-ESR LDA) at Week 12 (Asia Cohort)[137]

End point description:

The DAS28-ESR is a measure of RA disease activity calculated using Tender Joint Count 28 (TJC28), Swollen Joint Count 28 (SJC28), Erythrocyte sedimentation rate (ESR) (in millimeter [mm]/hour[hr]), Patient's Global Assessment of Arthritis Disease Activity (PtGA) (visual analogue scale with values from 0=best to 100=worst). DAS28-ESR scores range from 1.0 to 9.4, where lower scores indicate less disease activity. Low disease activity (LDA) is achieved when DAS28-ESR<=3.2. A negative change from baseline in DAS28-ESR indicates an improvement. For the purpose of all analyses up to week 12, the placebo arms were pooled into a single placebo arm to primarily serve as a reference for the comparison of active treatment arms. Percentage values are rounded off. The analysis was performed on ITT-Supplementary Asia Cohort set. Participants with data available at indicated timepoints are analyzed.

End point type	Secondary

End point timeframe:

Week 12

Notes:

[137] - 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: The endpoints are different for the different parts of the study.

End point values	GSK3196165 90mg + csDMARD (Asia Cohort)	GSK3196165 150mg + csDMARD (Asia Cohort)	Tofacitinib 5mg + csDMARD (Asia Cohort)	Pooled Placebo (Asia Cohort)
Subject group type	Reporting group	Reporting group	Reporting group	Subject analysis set
Number of subjects analysed	45	43	19	21
Units: Percentage of participants				
number (not applicable)	20.0	9.0	47.0	10.0

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of participants achieving DAS28-ESR <=3.2 (DAS28-ESR LDA) at Week 24 and Week 52 for treatment arms who started study intervention

from Day 1 (Asia Cohort)

End point title	Percentage of participants achieving DAS28-ESR <=3.2 (DAS28-ESR LDA) at Week 24 and Week 52 for treatment arms who started study intervention from Day 1 (Asia Cohort)[138]

End point description:

The DAS28-ESR is a measure of RA disease activity calculated using Tender Joint Count 28 (TJC28), Swollen Joint Count 28 (SJC28), Erythrocyte sedimentation rate (ESR) (in millimeter [mm]/hour[hr]), Patient's Global Assessment of Arthritis Disease Activity (PtGA) (visual analogue scale with values from 0=best to 100=worst). DAS28-ESR scores range from 1.0 to 9.4, where lower scores indicate less disease activity. Low disease activity (LDA) is achieved when DAS28-ESR<=3.2. A negative change from baseline in DAS28-ESR indicates an improvement. Percentage values are rounded off. The analysis was performed on all randomized Asia Cohort participants who received study intervention from Day 01 to Week 52. Participants with data available at indicated timepoints are analyzed.

End point type	Secondary

End point timeframe:

Week 24 and Week 52

Notes:

[138] - 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: The endpoints are different for the different parts of the study.

End point values	GSK3196165 90mg + csDMARD (Asia Cohort)	GSK3196165 150mg + csDMARD (Asia Cohort)	Tofacitinib 5mg + csDMARD (Asia Cohort)	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	38	43	17	
Units: Percentage of participants				
number (not applicable)				
Week 24, n=38,43,17	16.0	16.0	47.0	
Week 52, n=28,30,15	25.0	20.0	47.0	

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of participants achieving DAS28-CRP <=3.2 (DAS28-CRP LDA) at Week 24 and Week 52 for treatment arms who started study intervention from Day 1 (Asia Cohort)

End point title	Percentage of participants achieving DAS28-CRP <=3.2 (DAS28-CRP LDA) at Week 24 and Week 52 for treatment arms who started study intervention from Day 1 (Asia Cohort)[139]

End point description:

The DAS28-CRP is a measure of RA disease activity calculated using Tender Joint Count 28 (TJC28), Swollen Joint Count 28 (SJC28), C-reactive protein (CRP) (in mg/L), Patient's Global Assessment of Arthritis Disease Activity (PtGA) (visual analogue scale with values from 0=best to 100=worst). DAS28-CRP scores range from 1.0 to 9.4, where lower scores indicate less disease activity. Low disease activity (LDA) is achieved when DAS28-CRP greater than or equal to (<=)3.2. A negative change from baseline in DAS28-CRP indicates an improvement. Percentage values are rounded off. The analysis was performed on all randomized Asia Cohort participants who received study intervention from Day 01 to Week 52. Participants with data available at indicated timepoints are analyzed.

End point type	Secondary

End point timeframe:

Week 24 and Week 52

Notes:

[139] - 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: The endpoints are different for the different parts of the study.

End point values	GSK3196165 90mg + csDMARD (Asia Cohort)	GSK3196165 150mg + csDMARD (Asia Cohort)	Tofacitinib 5mg + csDMARD (Asia Cohort)	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	38	43	17	
Units: Percentage of participants				
number (not applicable)				
Week 24, n=38,43,17	24.0	21.0	53.0	
Week 52, n=31,32,15	39.0	34.0	67.0	

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of participants achieving DAS28-CRP <=3.2 (DAS28-CRP LDA) at Week 24 and Week 52 for placebo switched arms (Asia Cohort)

End point title	Percentage of participants achieving DAS28-CRP <=3.2 (DAS28-CRP LDA) at Week 24 and Week 52 for placebo switched arms (Asia Cohort)[140]

End point description:

The DAS28-CRP is a measure of RA disease activity calculated using Tender Joint Count 28 (TJC28), Swollen Joint Count 28 (SJC28), C-reactive protein (CRP) (in mg/L), Patient's Global Assessment of Arthritis Disease Activity (PtGA) (visual analogue scale with values from 0=best to 100=worst). DAS28-CRP scores range from 1.0 to 9.4, where lower scores indicate less disease activity. Low disease activity (LDA) is achieved when DAS28-CRP greater than or equal to (<=)3.2. A negative change from baseline in DAS28-CRP indicates an improvement. Percentage values are rounded off. The analysis was performed on all randomized Asia Cohort participants who switched from placebo to study intervention at Week 12. Participants with data available at indicated timepoints are analyzed.

End point type	Secondary

End point timeframe:

Week 24 and Week 52

Notes:

[140] - 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: The endpoints are different for the different parts of the study.

End point values	Placebo + csDMARD and GSK3196165 90mg + csDMARD (Asia Cohort)	Placebo + csDMARD and GSK3196165 150mg + csDMARD (Asia Cohort)	Placebo + csDMARD and Tofacitinib 5mg + csDMARD (Asia Cohort)	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	6	6	7	
Units: Percentage of participants				
number (not applicable)				
Week 24, n=6,6,7	33.0	33.0	43.0	

Week 52, n=4,6,6	75.0	50.0	67.0	

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of participants achieving DAS28-ESR <=3.2 (DAS28-ESR LDA) at Week 24 and Week 52 for placebo switched arms (Asia Cohort)

End point title	Percentage of participants achieving DAS28-ESR <=3.2 (DAS28-ESR LDA) at Week 24 and Week 52 for placebo switched arms (Asia Cohort)[141]

End point description:

The DAS28-ESR is a measure of RA disease activity calculated using Tender Joint Count 28 (TJC28), Swollen Joint Count 28 (SJC28), Erythrocyte sedimentation rate (ESR) (in millimeter [mm]/hour[hr]), Patient's Global Assessment of Arthritis Disease Activity (PtGA) (visual analogue scale with values from 0=best to 100=worst). DAS28-ESR scores range from 1.0 to 9.4, where lower scores indicate less disease activity. Low disease activity (LDA) is achieved when DAS28-ESR<=3.2. A negative change from baseline in DAS28-ESR indicates an improvement. Percentage values are rounded off. The analysis was performed on all randomized Asia Cohort participants who switched from placebo to study intervention at Week 12. Participants with data available at indicated timepoints are analyzed.

End point type	Secondary

End point timeframe:

Week 24 and Week 52

Notes:

[141] - 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: The endpoints are different for the different parts of the study.

End point values	Placebo + csDMARD and GSK3196165 90mg + csDMARD (Asia Cohort)	Placebo + csDMARD and GSK3196165 150mg + csDMARD (Asia Cohort)	Placebo + csDMARD and Tofacitinib 5mg + csDMARD (Asia Cohort)	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	6	6	7	
Units: Percentage of participants				
number (not applicable)				
Week 24, n=6,6,7	33.0	0.0	29.0	
Week 52, n=4,6,6	50.0	0.0	17.0	

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of participants achieving DAS28-CRP <2.6 (DAS28-CRP Remission) at Week 12 (Asia Cohort)

End point title	Percentage of participants achieving DAS28-CRP <2.6 (DAS28-CRP Remission) at Week 12 (Asia Cohort)[142]

End point description:

The DAS28-CRP is a measure of RA disease activity calculated using Tender Joint Count 28 (TJC28), Swollen Joint Count 28 (SJC28), C-reactive protein (CRP) (in mg/L), Patient's Global Assessment of Arthritis Disease Activity (PtGA) (visual analogue scale with values from 0=best to 100=worst). DAS28-CRP scores range from 1.0 to 9.4, where lower scores indicate less disease activity. Remission is achieved when DAS28-CRP less than (<)2.6. A negative change from baseline in DAS28-CRP indicates an improvement. For the purpose of all analyses up to week 12, the placebo arms were pooled into a single placebo arm to primarily serve as a reference for the comparison of active treatment arms. Percentage values are rounded off. The analysis was performed on ITT-Supplementary Asia Cohort set. Participants with data available at indicated timepoints are analyzed.

End point type	Secondary

End point timeframe:

Week 12

Notes:

[142] - 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: The endpoints are different for the different parts of the study.

End point values	GSK3196165 90mg + csDMARD (Asia Cohort)	GSK3196165 150mg + csDMARD (Asia Cohort)	Tofacitinib 5mg + csDMARD (Asia Cohort)	Pooled Placebo (Asia Cohort)
Subject group type	Reporting group	Reporting group	Reporting group	Subject analysis set
Number of subjects analysed	45	42	19	21
Units: Percentage of participants				
number (not applicable)	11.0	5.0	42.0	10.0

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of participants achieving DAS28 ESR <2.6 (DAS28-ESR Remission) at Week 12 (Asia Cohort)

End point title	Percentage of participants achieving DAS28 ESR <2.6 (DAS28-ESR Remission) at Week 12 (Asia Cohort)[143]

End point description:

The DAS28-ESR is a measure of RA disease activity calculated using Tender Joint Count 28 (TJC28), Swollen Joint Count 28 (SJC28), Erythrocyte sedimentation rate (ESR) (in mm/hr), Patient's Global Assessment of Arthritis Disease Activity (PtGA) (visual analogue scale with values from 0=best to 100=worst). DAS28-ESR scores range from 1.0 to 9.4, where lower scores indicate less disease activity. Remission is achieved when DAS28-ESR <2.6. A negative change from baseline in DAS28-ESR indicates an improvement. For the purpose of all analyses up to week 12, the placebo arms were pooled into a single placebo arm to primarily serve as a reference for the comparison of active treatment arms. Percentage values are rounded off. The analysis was performed on ITT-Supplementary Asia Cohort set. Participants with data available at indicated timepoints are analyzed.

End point type	Secondary

End point timeframe:

Week 12

Notes:

[143] - 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: The endpoints are different for the different parts of the study.

End point values	GSK3196165 90mg + csDMARD (Asia Cohort)	GSK3196165 150mg + csDMARD (Asia Cohort)	Tofacitinib 5mg + csDMARD (Asia Cohort)	Pooled Placebo (Asia Cohort)
Subject group type	Reporting group	Reporting group	Reporting group	Subject analysis set
Number of subjects analysed	45	43	19	21
Units: Percentage of participants				
number (not applicable)	2.0	2.0	21.0	0.0

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of participants achieving DAS28-CRP <2.6 (DAS28-CRP Remission) at Week 24 and Week 52 for treatment arms who started study intervention from Day 1 (Asia Cohort)

End point title	Percentage of participants achieving DAS28-CRP <2.6 (DAS28-CRP Remission) at Week 24 and Week 52 for treatment arms who started study intervention from Day 1 (Asia Cohort)[144]

End point description:

The DAS28-CRP is a measure of RA disease activity calculated using Tender Joint Count 28 (TJC28), Swollen Joint Count 28 (SJC28), C-reactive protein (CRP) (in mg/L), Patient's Global Assessment of Arthritis Disease Activity (PtGA) (visual analogue scale with values from 0=best to 100=worst). DAS28-CRP scores range from 1.0 to 9.4, where lower scores indicate less disease activity. Remission is achieved when DAS28-CRP less than (<)2.6. A negative change from baseline in DAS28-CRP indicates an improvement. Percentage values are rounded off. The analysis was performed on all randomized Asia Cohort participants who received study intervention from Day 01 to Week 52. Participants with data available at indicated timepoints are analyzed.

End point type	Secondary

End point timeframe:

Week 24 and Week 52

Notes:

[144] - 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: The endpoints are different for the different parts of the study.

End point values	GSK3196165 90mg + csDMARD (Asia Cohort)	GSK3196165 150mg + csDMARD (Asia Cohort)	Tofacitinib 5mg + csDMARD (Asia Cohort)	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	38	43	17	
Units: Percentage of participants				
number (not applicable)				
Week 24, n=38,43,17	13.0	19.0	41.0	
Week 52, n=31,32,15	19.0	25.0	53.0	

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of participants achieving DAS28 ESR <2.6 (DAS28-ESR Remission) at at Week 24 and Week 52 for treatment arms who started study intervention from Day 1 (Asia Cohort)

End point title	Percentage of participants achieving DAS28 ESR <2.6 (DAS28-ESR Remission) at at Week 24 and Week 52 for treatment arms who started study intervention from Day 1 (Asia Cohort)[145]

End point description:

The DAS28-ESR is a measure of RA disease activity calculated using Tender Joint Count 28 (TJC28), Swollen Joint Count 28 (SJC28), Erythrocyte sedimentation rate (ESR) (in mm/hr), Patient's Global Assessment of Arthritis Disease Activity (PtGA) (visual analogue scale with values from 0=best to 100=worst). DAS28-ESR scores range from 1.0 to 9.4, where lower scores indicate less disease activity. Remission is achieved when DAS28-ESR <2.6. A negative change from baseline in DAS28-ESR indicates an improvement. Percentage values are rounded off. The analysis was performed on all randomized Asia Cohort participants who received study intervention from Day 01 to Week 52. Participants with data available at indicated timepoints are analyzed.

End point type	Secondary

End point timeframe:

Week 24 and Week 52

Notes:

[145] - 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: The endpoints are different for the different parts of the study.

End point values	GSK3196165 90mg + csDMARD (Asia Cohort)	GSK3196165 150mg + csDMARD (Asia Cohort)	Tofacitinib 5mg + csDMARD (Asia Cohort)	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	38	43	17	
Units: Percentage of participants				
number (not applicable)				
Week 24, n=38,43,17	8.0	12.0	29.0	
Week 52, n=28,30,15	7.0	17.0	20.0	

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of participants achieving DAS28 ESR <2.6 (DAS28-ESR Remission) at Week 24 and Week 52 for placebo switched arms (Asia Cohort)

End point title	Percentage of participants achieving DAS28 ESR <2.6 (DAS28-ESR Remission) at Week 24 and Week 52 for placebo switched arms (Asia Cohort)[146]

End point description:

The DAS28-ESR is a measure of RA disease activity calculated using Tender Joint Count 28 (TJC28), Swollen Joint Count 28 (SJC28), Erythrocyte sedimentation rate (ESR) (in mm/hr), Patient's Global Assessment of Arthritis Disease Activity (PtGA) (visual analogue scale with values from 0=best to 100=worst). DAS28-ESR scores range from 1.0 to 9.4, where lower scores indicate less disease activity. Remission is achieved when DAS28-ESR <2.6. A negative change from baseline in DAS28-ESR indicates an improvement. Percentage values are rounded off. The analysis was performed on all randomized Asia Cohort participants who switched from placebo to study intervention at Week 12. Participants with data available at indicated timepoints are analyzed.

End point type	Secondary

End point timeframe:

Week 24 and Week 52

Notes:

[146] - 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: The endpoints are different for the different parts of the study.

End point values	Placebo + csDMARD and GSK3196165 90mg + csDMARD (Asia Cohort)	Placebo + csDMARD and GSK3196165 150mg + csDMARD (Asia Cohort)	Placebo + csDMARD and Tofacitinib 5mg + csDMARD (Asia Cohort)	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	6	6	7	
Units: Percentage of participants				
number (not applicable)				
Week 24, n=6,6,7	0.0	0.0	0.0	
Week 52, n=4,6,6	25.0	0.0	17.0	

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of participants achieving DAS28-CRP <2.6 (DAS28-CRP Remission) at Week 24 and Week 52 for placebo switched arms (Asia Cohort)

End point title	Percentage of participants achieving DAS28-CRP <2.6 (DAS28-CRP Remission) at Week 24 and Week 52 for placebo switched arms (Asia Cohort)[147]

End point description:

The DAS28-CRP is a measure of RA disease activity calculated using Tender Joint Count 28 (TJC28), Swollen Joint Count 28 (SJC28), C-reactive protein (CRP) (in mg/L), Patient's Global Assessment of Arthritis Disease Activity (PtGA) (visual analogue scale with values from 0=best to 100=worst). DAS28-CRP scores range from 1.0 to 9.4, where lower scores indicate less disease activity. Remission is achieved when DAS28-CRP less than (<)2.6. A negative change from baseline in DAS28-CRP indicates an improvement. Percentage values are rounded off. The analysis was performed on all randomized Asia Cohort participants who switched from placebo to study intervention at Week 12. Participants with data available at indicated timepoints are analyzed.

End point type	Secondary

End point timeframe:

Week 24 and Week 52

Notes:

[147] - 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: The endpoints are different for the different parts of the study.

End point values	Placebo + csDMARD and GSK3196165 90mg + csDMARD (Asia Cohort)	Placebo + csDMARD and GSK3196165 150mg + csDMARD (Asia Cohort)	Placebo + csDMARD and Tofacitinib 5mg + csDMARD (Asia Cohort)	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	6	6	7	

Units: Percentage of participants				
number (not applicable)				
Week 24, n=6,6,7	33.0	0.0	29.0	
Week 52, n=4,6,6	50.0	17.0	17.0	

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of participants achieving a good/moderate European league against rheumatism (EULAR) response at Week 12 (Asia Cohort)

End point title	Percentage of participants achieving a good/moderate European league against rheumatism (EULAR) response at Week 12 (Asia Cohort)[148]

End point description:

DAS28-CRP and DAS28-ESR scores were categorized using EULAR response criteria. Response was defined based on combination of current DAS28 score and improvement in current score relative to Baseline. The definition of no response, moderate response and good response was; DAS28 <=3.2 and DAS28 decrease from Baseline (>1.2:good response, >0.6 to <=1.2:moderate response, <=0.6:no response); DAS28 >3.2 to <=5.1 and DAS28 decrease from Baseline (>1.2:moderate response, >0.6 to <=1.2:moderate response, <=0.6:no response) and DAS28 >5.1 and DAS28 decrease from Baseline (>1.2:moderate response, >0.6 to <=1.2:no response, <=0.6:no response). If the post-Baseline DAS28-CRP score was missing, then corresponding EULAR category was set to missing. Placebo arms were pooled into single arm to serve as reference for comparison to active treatment arms. Percentage values are rounded off. Analysis was performed on ITT-Supplementary Asia Cohort with data available at indicated timepoints are analyzed.

End point type	Secondary

End point timeframe:

Week 12

Notes:

[148] - 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: The endpoints are different for the different parts of the study.

End point values	GSK3196165 90mg + csDMARD (Asia Cohort)	GSK3196165 150mg + csDMARD (Asia Cohort)	Tofacitinib 5mg + csDMARD (Asia Cohort)	Pooled Placebo (Asia Cohort)
Subject group type	Reporting group	Reporting group	Reporting group	Subject analysis set
Number of subjects analysed	44	41	19	21
Units: Percentage of participants				
number (not applicable)	66.0	61.0	84.0	33.0

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of participants achieving a good/moderate EULAR response at Week 24 and Week 52 for treatment arms who started study intervention from Day 1 (Asia Cohort)

End point title	Percentage of participants achieving a good/moderate EULAR

	response at Week 24 and Week 52 for treatment arms who started study intervention from Day 1 (Asia Cohort)[149]

End point description:

DAS28-CRP and DAS28-ESR scores were categorized using EULAR response criteria. Response was defined based on combination of current DAS28 score and improvement in current score relative to Baseline. The definition of no response, moderate response and good response was as; DAS28 <=3.2 and DAS28 decrease from Baseline (>1.2:good response, >0.6 to <=1.2:moderate response, <=0.6:no response); DAS28 >3.2 to <=5.1 and DAS28 decrease from Baseline (>1.2:moderate response, >0.6 to <=1.2:moderate response, <=0.6:no response) and DAS28 >5.1 and DAS28 decrease from Baseline (>1.2:moderate response, >0.6 to <=1.2:no response, <=0.6:no response). If the post-Baseline DAS28-CRP score was missing, then the corresponding EULAR category was set to missing. Percentage values are rounded off. The analysis was performed on all randomized Asia Cohort participants who received study intervention from Day 01 to Week 52. Participants with data available at indicated timepoints are analyzed.

End point type	Secondary

End point timeframe:

Week 24 and Week 52

Notes:

[149] - 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: The endpoints are different for the different parts of the study.

End point values	GSK3196165 90mg + csDMARD (Asia Cohort)	GSK3196165 150mg + csDMARD (Asia Cohort)	Tofacitinib 5mg + csDMARD (Asia Cohort)	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	37	42	17	
Units: Percentage of participants				
number (not applicable)				
Week 24, n=37,42,17	65.0	64.0	94.0	
Week 52, n-30,31,15	70.0	84.0	100.0	

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of participants achieving a good/moderate EULAR response at Week 24 and Week 52 for placebo switched arms (Asia Cohort)

End point title	Percentage of participants achieving a good/moderate EULAR response at Week 24 and Week 52 for placebo switched arms (Asia Cohort)[150]

End point description:

DAS28-CRP and DAS28-ESR scores were categorized using EULAR response criteria. Response was defined based on combination of current DAS28 score and improvement in current score relative to Baseline. The definition of no response, moderate response and good response was as; DAS28 <=3.2 and DAS28 decrease from Baseline (>1.2:good response, >0.6 to <=1.2:moderate response, <=0.6:no response); DAS28 >3.2 to <=5.1 and DAS28 decrease from Baseline (>1.2:moderate response, >0.6 to <=1.2:moderate response, <=0.6:no response) and DAS28 >5.1 and DAS28 decrease from Baseline (>1.2:moderate response, >0.6 to <=1.2:no response, <=0.6:no response). If the post-Baseline DAS28-CRP score was missing, then the corresponding EULAR category was set to missing. Percentage values are rounded off. The analysis was performed on all randomized Asia Cohort participants who received study intervention from Week 12 to Week 52. Participants with data available at indicated timepoints are analyzed.

End point type	Secondary

End point timeframe:

Week 24 and Week 52

Notes:

[150] - 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: The endpoints are different for the different parts of the study.

End point values	Placebo + csDMARD and GSK3196165 90mg + csDMARD (Asia Cohort)	Placebo + csDMARD and GSK3196165 150mg + csDMARD (Asia Cohort)	Placebo + csDMARD and Tofacitinib 5mg + csDMARD (Asia Cohort)	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	6	6	7	
Units: Percentage of participants				
number (not applicable)				
Week 24, n=6,6,7	50.0	50.0	100.0	
Week 52, n=4,6,6	100.0	100.0	100.0	

Statistical analyses

No statistical analyses for this end point

Secondary: Number of participants achieving ACR/EULAR remission at Week 24 and Week 52 for treatment arms who started study intervention from Day 1 (Asia Cohort)

End point title	Number of participants achieving ACR/EULAR remission at Week 24 and Week 52 for treatment arms who started study intervention from Day 1 (Asia Cohort)[151]

End point description:

Boolean-based ACR/EULAR remission is achieved if all of the following requirements are met at the same timepoint: Tender Joint Count 68 (TJC68) <= 1, Swollen Joint Count 66 (SJC66) <= 1, high sensitivity C-reactive Protein (hsCRP) <= 1mg/dl and patient's global assessment of disease activity (PtGA) <= 10. The analysis was performed on all randomized Asia Cohort participants who received study intervention from Day 01 to Week 52. Participants with data available at indicated timepoints are analyzed.

End point type	Secondary

End point timeframe:

Week 24 and Week 52

Notes:

[151] - 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: The endpoints are different for the different parts of the study.

End point values	GSK3196165 90mg + csDMARD (Asia Cohort)	GSK3196165 150mg + csDMARD (Asia Cohort)	Tofacitinib 5mg + csDMARD (Asia Cohort)	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	38	43	17	
Units: Participants				
Week 24, n=38,43,17	0	0	3	
Week 52, n=31,32,15	0	2	2	

Statistical analyses

No statistical analyses for this end point

Secondary: Number of participants achieving ACR/EULAR remission at Week 12 (Asia Cohort)

End point title	Number of participants achieving ACR/EULAR remission at Week 12 (Asia Cohort)[152]

End point description:

Boolean-based ACR/EULAR remission is achieved if all of the following requirements are met at the same timepoint: Tender Joint Count 68 (TJC68) <= 1, Swollen Joint Count 66 (SJC66) <= 1, high sensitivity C-reactive Protein (hsCRP) <= 1mg/dl and patient's global assessment of disease activity (PtGA) <= 10. For the purpose of all analyses up to week 12, the placebo arms were pooled into a single placebo arm to primarily serve as a reference for the comparison of active treatment arms. The analysis was performed on ITT-Supplementary Asia Cohort set. Participants with data available at indicated timepoints are analyzed.

End point type	Secondary

End point timeframe:

Week 12

Notes:

[152] - 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: The endpoints are different for the different parts of the study.

End point values	GSK3196165 90mg + csDMARD (Asia Cohort)	GSK3196165 150mg + csDMARD (Asia Cohort)	Tofacitinib 5mg + csDMARD (Asia Cohort)	Pooled Placebo (Asia Cohort)
Subject group type	Reporting group	Reporting group	Reporting group	Subject analysis set
Number of subjects analysed	45	42	19	21
Units: Participants	2	0	2	0

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of participants achieving no radiographic progression (mTSS <= 0.5) at Week 24 and Week 52 for treatment arms who started study intervention from Day 1 (Asia Cohort)

End point title	Percentage of participants achieving no radiographic progression (mTSS <= 0.5) at Week 24 and Week 52 for treatment arms who started study intervention from Day 1 (Asia Cohort)[153]

End point description:

Van der Heijde mTSS is utilized for scoring radiographs of hands and feet in rheumatoid arthritis. This method includes 16 areas of erosions, and 15 areas for joint space narrowing (JSN) in each hand, and 6 areas for erosions and 6 areas JSN in each foot. The total mTSS score is the sum of erosion (maximum

of 280) and JSN (maximum of 168) scores. The score range from 0 to 448 for mTSS with higher values representing higher disease activity. No radiographic progression is defined as a change from Baseline in van der Heijde mTSS score of <=0.5. Percentage values are rounded off. The analysis was performed on all randomized Asia Cohort participants who received study intervention from Day 01 to Week 52. Participants with data available at indicated timepoints are analyzed.

End point type	Secondary

End point timeframe:

Week 24 and Week 52

Notes:

[153] - 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: The endpoints are different for the different parts of the study.

End point values	GSK3196165 90mg + csDMARD (Asia Cohort)	GSK3196165 150mg + csDMARD (Asia Cohort)	Tofacitinib 5mg + csDMARD (Asia Cohort)	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	6	5	2	
Units: Percentage of participants				
Week 24, n=6,5,2	83	60	50	
Week 52, n=5,3,2	40	100	50	

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of participants achieving no radiographic progression Van der Heijde modified total sharp scores (mTSS) <= 0.5) at Week 12 (Asia Cohort)

End point title	Percentage of participants achieving no radiographic progression Van der Heijde modified total sharp scores (mTSS) <= 0.5) at Week 12 (Asia Cohort)[154]

End point description:

Van der Heijde mTSS is utilized for scoring radiographs of hands and feet in rheumatoid arthritis. This method includes 16 areas of erosions, and 15 areas for joint space narrowing (JSN) in each hand, and 6 areas for erosions and 6 areas JSN in each foot. The total mTSS score is the sum of erosion (maximum of 280) and JSN (maximum of 168) scores. The score range from 0 to 448 for mTSS with higher values representing higher disease activity. No radiographic progression is defined as a change from Baseline in van der Heijde mTSS score of <=0.5. For the purpose of all analyses up to week 12, the placebo arms were pooled into a single placebo arm to primarily serve as a reference for the comparison of active treatment arms. Percentage values are rounded off. The analysis was performed on ITT-Supplementary Asia Cohort set. Participants with data available at indicated timepoints are analyzed.

End point type	Secondary

End point timeframe:

Week 12

Notes:

[154] - 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: The endpoints are different for the different parts of the study.

End point values	GSK3196165 90mg + csDMARD (Asia Cohort)	GSK3196165 150mg + csDMARD (Asia Cohort)	Tofacitinib 5mg + csDMARD (Asia Cohort)	Pooled Placebo (Asia Cohort)
Subject group type	Reporting group	Reporting group	Reporting group	Subject analysis set
Number of subjects analysed	9	6	3	2
Units: Percentage of participants	67	67	67	50

Statistical analyses

No statistical analyses for this end point

Secondary: Number of participants achieving ACR/EULAR remission at Week 24 and Week 52 for placebo switched arms (Asia Cohort)

End point title	Number of participants achieving ACR/EULAR remission at Week 24 and Week 52 for placebo switched arms (Asia Cohort)[155]

End point description:

Boolean-based ACR/EULAR remission is achieved if all of the following requirements are met at the same timepoint: Tender Joint Count 68 (TJC68) <= 1, Swollen Joint Count 66 (SJC66) <= 1, high sensitivity C-reactive Protein (hsCRP) <= 1mg/dl and patient's global assessment of disease activity (PtGA) <= 10. The analysis was performed on all randomized Asia Cohort participants who switched from placebo to study intervention at Week 12. Participants with data available at indicated timepoints are analyzed.

End point type	Secondary

End point timeframe:

Week 24 and Week 52

Notes:

[155] - 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: The endpoints are different for the different parts of the study.

End point values	Placebo + csDMARD and GSK3196165 90mg + csDMARD (Asia Cohort)	Placebo + csDMARD and GSK3196165 150mg + csDMARD (Asia Cohort)	Placebo + csDMARD and Tofacitinib 5mg + csDMARD (Asia Cohort)	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	6	6	7	
Units: Participants				
Week 24, n=6,6,7	0	0	1	
Week 52, n=4,6,6	0	0	0	

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of participants achieving no radiographic progression (mTSS <= 0.5) at Week 24 and Week 52 for placebo switched arms (Asia Cohort)

End point title	Percentage of participants achieving no radiographic progression (mTSS <= 0.5) at Week 24 and Week 52 for

	placebo switched arms (Asia Cohort)[156]

End point description:

Van der Heijde mTSS is utilized for scoring radiographs of hands and feet in rheumatoid arthritis. This method includes 16 areas of erosions, and 15 areas for joint space narrowing (JSN) in each hand, and 6 areas for erosions and 6 areas JSN in each foot. The total mTSS score is the sum of erosion (maximum of 280) and JSN (maximum of 168) scores. The score range from 0 to 448 for mTSS with higher values representing higher disease activity. No radiographic progression is defined as a change from Baseline in van der Heijde mTSS score of <=0.5. Percentage values are rounded off. The analysis was performed on all randomized Asia Cohort participants who switched from placebo to study intervention at Week 12. Participants with data available at indicated timepoints are analyzed.

End point type	Secondary

End point timeframe:

Week 24 and Week 52

Notes:

[156] - 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: The endpoints are different for the different parts of the study.

End point values	Placebo + csDMARD and GSK3196165 90mg + csDMARD (Asia Cohort)	Placebo + csDMARD and GSK3196165 150mg + csDMARD (Asia Cohort)	Placebo + csDMARD and Tofacitinib 5mg + csDMARD (Asia Cohort)	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	1	1	0[157]	
Units: Percentage of participants				
Week 24, n=1,1,0	0	100		
Week 52, n=1,1,0	0	100		

Notes:

[157] - No participant was analyzed at the timepoints Week 24 and Week 52.

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in CDAI total score at Week 12 (Asia Cohort)

End point title	Change from Baseline in CDAI total score at Week 12 (Asia Cohort)[158]

End point description:

Clinical Disease Activity Index (CDAI) total score is a composite score consisting of sum of Swollen Joint Count 28 (SJC28), Tender Joint Count 28 (TJC28), Patient's Global Assessment of Arthritis Disease Activity (PtGA) and Physician Global Assessment of Arthritis Disease Activity (PhGA) (VAS with values from 0=best to 100=worst). PtGA and PhGA are transformed to a 0-10 scale . CDAI total score ranges from 0 to 76 with higher values representing higher disease activity. Low disease activity (LDA) is achieved when CDAI total score <=10. Baseline was defined as latest pre-dose assessment with a NMV, including from unscheduled visits. Change from Baseline was calculated by subtracting PDV from BV. For the purpose of analyses up to week 12, the placebo arms were pooled into single placebo arm to primarily serve as reference for comparison of active treatment arms. Analysis was performed on ITT-Supplementary Asia Cohort with data available at indicated timepoints were analyzed.

End point type	Secondary

End point timeframe:

Baseline (Day 1) and week 12

Notes:

[158] - 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: The endpoints are different for the different parts of the study.

End point values	GSK3196165 90mg + csDMARD (Asia Cohort)	GSK3196165 150mg + csDMARD (Asia Cohort)	Tofacitinib 5mg + csDMARD (Asia Cohort)	Pooled Placebo (Asia Cohort)
Subject group type	Reporting group	Reporting group	Reporting group	Subject analysis set
Number of subjects analysed	44	42	19	21
Units: Scores on a scale				
arithmetic mean (standard deviation)	-13.75 (± 10.935)	-10.91 (± 11.649)	-19.47 (± 12.718)	-4.38 (± 8.640)

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in CDAI total score at Week 24 and Week 52 for placebo switched arms (Asia Cohort)

End point title	Change from Baseline in CDAI total score at Week 24 and Week 52 for placebo switched arms (Asia Cohort)[159]

End point description:

Clinical Disease Activity Index (CDAI) total score is a composite score consisting of sum of Swollen Joint Count 28 (SJC28), Tender Joint Count 28 (TJC28), Patient's Global Assessment of Arthritis Disease Activity (PtGA) and Physician Global Assessment of Arthritis Disease Activity (PhGA) (VAS with values from 0=best to 100=worst). PtGA and PhGA are transformed to a 0-10 scale . CDAI total score ranges from 0 to 76 with higher values representing higher disease activity. Low disease activity (LDA) is achieved when CDAI total score <=10. Baseline was defined as latest pre-dose assessment with a NMV, including from unscheduled visits. Change from Baseline was calculated by subtracting PDV from BV. For efficacy assessments baseline is interpreted as Day 1. Analysis was performed on participants who received study intervention from Week 12 to Week 52 IN Asia Cohort with data available at indicated timepoints were analyzed.

End point type	Secondary

End point timeframe:

Baseline (Day 1), Week 24 and Week 52

Notes:

[159] - 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: The endpoints are different for the different parts of the study.

End point values	Placebo + csDMARD and GSK3196165 90mg + csDMARD (Asia Cohort)	Placebo + csDMARD and GSK3196165 150mg + csDMARD (Asia Cohort)	Placebo + csDMARD and Tofacitinib 5mg + csDMARD (Asia Cohort)	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	6	6	7	
Units: Scores on a scale				
arithmetic mean (standard deviation)				
Week 24, n=6,6,7	-8.78 (± 6.086)	-12.28 (± 10.842)	-20.47 (± 12.133)	
Week 52, n=4,6,5	-16.28 (± 5.351)	-17.47 (± 11.166)	-23.18 (± 13.070)	

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in CDAI total score at Week 24 and Week 52 for treatment arms who started study intervention from Day 1 (Asia Cohort)

End point title	Change from Baseline in CDAI total score at Week 24 and Week 52 for treatment arms who started study intervention from Day 1 (Asia Cohort)[160]

End point description:

Clinical Disease Activity Index (CDAI) total score is a composite score consisting of sum of Swollen Joint Count 28 (SJC28), Tender Joint Count 28 (TJC28), Patient's Global Assessment of Arthritis Disease Activity (PtGA) and Physician Global Assessment of Arthritis Disease Activity (PhGA) (VAS with values from 0=best to 100=worst). PtGA and PhGA are transformed to a 0-10 scale . CDAI total score ranges from 0 to 76 with higher values representing higher disease activity. Low disease activity (LDA) is achieved when CDAI total score <=10. Baseline was defined as latest pre-dose assessment with a NMV, including from unscheduled visits. Change from Baseline was calculated by subtracting PDV from BV. Analysis was performed on participants who received study intervention from Day 01 to Week 52 IN Asia Cohort with data available at indicated timepoints were analyzed.

End point type	Secondary

End point timeframe:

Baseline (Day 1), Week 24 and Week 52

Notes:

[160] - 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: The endpoints are different for the different parts of the study.

End point values	GSK3196165 90mg + csDMARD (Asia Cohort)	GSK3196165 150mg + csDMARD (Asia Cohort)	Tofacitinib 5mg + csDMARD (Asia Cohort)	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	37	42	17	
Units: Scores on a scale				
arithmetic mean (standard deviation)				
Week 24, n=37,42,17	-15.27 (± 12.329)	-13.39 (± 10.575)	-21.44 (± 11.208)	
Week 52, n=30,31,15	-18.29 (± 13.199)	-19.35 (± 13.923)	-23.21 (± 12.303)	

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in DAS28-CRP/DAS28-ESR at Week 12 (Asia Cohort)

End point title	Change from Baseline in DAS28-CRP/DAS28-ESR at Week 12 (Asia Cohort)[161]

End point description:

DAS28-CRP and DAS28-ESR are measure of RA disease activity calculated using Swollen Joint Count 28 (SJC28), Tender Joint Count 28 (TJC28), high sensitivity C-reactive Protein (hsCRP in mg/L)/Erythrocyte sedimentation rate (ESR) [ESR in milimeter/hour (mm/hr)] and patient's global assessment of disease activity (PtGA) transformed to a 0-10 scale. Total score approximate range 0-9.4, with higher scores indicating more disease activity. Baseline was defined as latest pre-dose assessment with a non-missing value, including those from unscheduled visits. Change from Baseline was calculated by subtracting post dose visit value from Baseline value. For the purpose of all analyses up to week 12, the placebo arms

were pooled into a single placebo arm to primarily serve as a reference for the comparison of active treatment arms. The analysis was performed on ITT-Supplementary Asia Cohort set. Participants with data available at indicated timepoints are analyzed.

End point type	Secondary

End point timeframe:

Baseline (Day 1) and Week 12

Notes:

[161] - 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: The endpoints are different for the different parts of the study.

End point values	GSK3196165 90mg + csDMARD (Asia Cohort)	GSK3196165 150mg + csDMARD (Asia Cohort)	Tofacitinib 5mg + csDMARD (Asia Cohort)	Pooled Placebo (Asia Cohort)
Subject group type	Reporting group	Reporting group	Reporting group	Subject analysis set
Number of subjects analysed	44	42	19	21
Units: Scores on a scale				
arithmetic mean (standard deviation)				
DAS28-CRP, n=44,41,19,21	-1.26 (± 1.034)	-1.05 (± 0.968)	-2.27 (± 1.089)	-0.47 (± 0.950)
DAS28-ESR, n=44,42,19,21	-1.33 (± 1.023)	-1.11 (± 0.964)	-2.15 (± 1.161)	-0.40 (± 0.937)

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in DAS28-CRP/DAS28-ESR at Week 24 and Week 52 for treatment arms who started study intervention from Day 1 (Asia Cohort)

End point title	Change from Baseline in DAS28-CRP/DAS28-ESR at Week 24 and Week 52 for treatment arms who started study intervention from Day 1 (Asia Cohort)[162]

End point description:

DAS28-CRP and DAS28-ESR are measure of RA disease activity calculated using Swollen Joint Count 28 (SJC28), Tender Joint Count 28 (TJC28), high sensitivity C-reactive Protein (hsCRP in mg/L)/Erythrocyte sedimentation rate (ESR) [ESR in milimeter/hour (mm/hr)] and patient's global assessment of disease activity (PtGA) transformed to a 0-10 scale. Total score approximate range 0-9.4, with higher scores indicating more disease activity. Baseline was defined as latest pre-dose assessment with a non-missing value, including those from unscheduled visits. Change from Baseline was calculated by subtracting post dose visit value from Baseline value. The analysis was performed on all randomized Asia Cohort participants who received study intervention from Day 01 to Week 52. Participants with data available at indicated timepoints are analyzed.

End point type	Secondary

End point timeframe:

Baseline (Day 1), Week 24 and Week 52

Notes:

[162] - 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: The endpoints are different for the different parts of the study.

End point values	GSK3196165 90mg + csDMARD (Asia Cohort)	GSK3196165 150mg + csDMARD (Asia Cohort)	Tofacitinib 5mg + csDMARD (Asia Cohort)	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	37	42	17	
Units: Scores on a scale				
arithmetic mean (standard deviation)				
DAS28-CRP, Week 24, n=37,42,17	-1.41 (± 1.221)	-1.28 (± 1.086)	-2.29 (± 1.037)	
DAS28-CRP, Week 52, n=30,31,15	-1.63 (± 1.353)	-1.82 (± 1.262)	-2.47 (± 1.253)	
DAS28-ESR, Week 24, n=37,42,17	-1.50 (± 1.153)	-1.27 (± 1.121)	-2.30 (± 1.246)	
DAS28-ESR, Week 52, n=28,29,15	-1.76 (± 1.358)	-1.84 (± 1.303)	-2.42 (± 1.318)	

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in DAS28-CRP/DAS28-ESR at Week 24 and Week 52 for placebo switched arms (Asia Cohort)

End point title	Change from Baseline in DAS28-CRP/DAS28-ESR at Week 24 and Week 52 for placebo switched arms (Asia Cohort)[163]

End point description:

DAS28-CRP and DAS28-ESR are measure of RA disease activity calculated using Swollen Joint Count 28 (SJC28), Tender Joint Count 28 (TJC28), high sensitivity C-reactive Protein (hsCRP in mg/L)/Erythrocyte sedimentation rate (ESR) [ESR in milimeter/hour (mm/hr)] and patient's global assessment of disease activity (PtGA) transformed to a 0-10 scale. Total score approximate range 0-9.4, with higher scores indicating more disease activity. Baseline was defined as latest pre-dose assessment with a non-missing value, including those from unscheduled visits. Change from Baseline was calculated by subtracting post dose visit value from Baseline value. For efficacy assessments baseline is interpreted as Day 1. The analysis was performed on all randomized Asia Cohort participants who switched from placebo to study intervention at Week 12. Participants with data available at indicated timepoints are analyzed.

End point type	Secondary

End point timeframe:

Baseline (Day 1), Week 24 and Week 52

Notes:

[163] - 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: The endpoints are different for the different parts of the study.

End point values	Placebo + csDMARD and GSK3196165 90mg + csDMARD (Asia Cohort)	Placebo + csDMARD and GSK3196165 150mg + csDMARD (Asia Cohort)	Placebo + csDMARD and Tofacitinib 5mg + csDMARD (Asia Cohort)	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	6	6	7	
Units: Scores on a scale				
arithmetic mean (standard deviation)				
DAS28-CRP, Week 24, n=6,6,7	-1.27 (± 1.171)	-1.08 (± 0.852)	-2.14 (± 1.242)	

DAS28-CRP, Week 52, n=4,6,6	-2.24 (± 1.200)	-1.52 (± 1.005)	-2.63 (± 1.244)	
DAS28-ESR, Week 24, n=6,6,7	-0.91 (± 1.216)	-0.99 (± 0.897)	-2.06 (± 1.053)	
DAS28-ESR, Week 52, n=4,6,6	-1.82 (± 1.183)	-1.46 (± 0.912)	-2.48 (± 1.186)	

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in Van der Heijde mTSS at Week 24 and Week 52 for treatment arms who started study intervention from Day 1 (Asia Cohort)

End point title	Change from Baseline in Van der Heijde mTSS at Week 24 and Week 52 for treatment arms who started study intervention from Day 1 (Asia Cohort)[164]

End point description:

Van der Heijde mTSS is utilized for scoring radiographs of hands and feet in rheumatoid arthritis. This method includes 16 areas of erosions, and 15 areas for joint space narrowing (JSN) in each hand, and 6 areas for erosions and 6 areas JSN in each foot. The total mTSS score is the sum of erosion (maximum of 280) and JSN (maximum of 168) scores. The score range from 0 to 448 for mTSS with higher values representing higher disease activity. Baseline was defined as latest pre-dose assessment with a non-missing value, including those from unscheduled visits. Change from Baseline was calculated by subtracting post dose visit value from Baseline value. The analysis was performed on all randomized Asia Cohort participants who received study intervention from Day 01 to Week 52. Participants with data available at indicated timepoints are analyzed.

End point type	Secondary

End point timeframe:

Baseline (Day 1), Week 24 and Week 52

Notes:

[164] - 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: The endpoints are different for the different parts of the study.

End point values	GSK3196165 90mg + csDMARD (Asia Cohort)	GSK3196165 150mg + csDMARD (Asia Cohort)	Tofacitinib 5mg + csDMARD (Asia Cohort)	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	6	5	2	
Units: Scores on a scale				
arithmetic mean (standard deviation)				
Week 24, n=6,5,2	-0.08 (± 0.665)	5.60 (± 10.922)	0.50 (± 0.707)	
Week 52, n=5,3,2	1.40 (± 1.673)	0.00 (± 0.000)	0.50 (± 0.707)	

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in Van der Heijde mTSS at Week 24 and Week 52 for placebo switched arms (Asia Cohort)

End point title	Change from Baseline in Van der Heijde mTSS at Week 24 and Week 52 for placebo switched arms (Asia Cohort)[165]

End point description:

Van der Heijde mTSS is utilized for scoring radiographs of hands and feet in rheumatoid arthritis. This method includes 16 areas of erosions, and 15 areas for joint space narrowing (JSN) in each hand, and 6 areas for erosions and 6 areas JSN in each foot. The total mTSS score is the sum of erosion (maximum of 280) and JSN (maximum of 168) scores. The score range from 0 to 448 for mTSS with higher values representing higher disease activity. Baseline was defined as latest pre-dose assessment with a non-missing value, including those from unscheduled visits. Change from Baseline was calculated by subtracting post dose visit value from Baseline value. For efficacy assessments baseline is interpreted as Day 1. The analysis was performed on all randomized Asia Cohort participants who switched from placebo to study intervention at Week 12. Participants with data available at indicated timepoints are analyzed.

End point type	Secondary

End point timeframe:

Baseline (Day 1), Week 24 and Week 52

Notes:

[165] - 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: The endpoints are different for the different parts of the study.

End point values	Placebo + csDMARD and GSK3196165 90mg + csDMARD (Asia Cohort)	Placebo + csDMARD and GSK3196165 150mg + csDMARD (Asia Cohort)	Placebo + csDMARD and Tofacitinib 5mg + csDMARD (Asia Cohort)	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	1[166]	1[167]	0[168]	
Units: Scores on a scale				
arithmetic mean (standard deviation)				
Week 24, n=1,1,0	0.50 (± 0)	0.00 (± 0)	()	
Week 52, n=1,1,0	0.50 (± 0)	0.00 (± 0)	()	

Notes:

[166] - Standard deviation data was not derived as only one participant was analyzed.

[167] - Standard deviation data was not derived as only one participant was analyzed.

[168] - No participant was analyzed at the timepoints Week 24 and Week 52.

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in Van der Heijde mTSS at Week 12 (Asia Cohort)

End point title	Change from Baseline in Van der Heijde mTSS at Week 12 (Asia Cohort)[169]

End point description:

Van der Heijde mTSS is utilized for scoring radiographs of hands and feet in rheumatoid arthritis. This method includes 16 areas of erosions, and 15 areas for joint space narrowing (JSN) in each hand, and 6 areas for erosions and 6 areas JSN in each foot. The total mTSS score is the sum of erosion (maximum of 280) and JSN (maximum of 168) scores. The score range from 0 to 448 for mTSS with higher values representing higher disease activity. Baseline was defined as latest pre-dose assessment with a non-missing value, including those from unscheduled visits. Change from Baseline was calculated by subtracting post dose visit value from Baseline value. For the purpose of all analyses up to week 12, the placebo arms were pooled into a single placebo arm to primarily serve as a reference for the comparison of active treatment arms. The analysis was performed on ITT-Supplementary Asia Cohort set. Participants with data available at indicated timepoints are analyzed.

End point type	Secondary

End point timeframe:

Baseline (Day 1) and Week 12

Notes:

[169] - 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: The endpoints are different for the different parts of the study.

End point values	GSK3196165 90mg + csDMARD (Asia Cohort)	GSK3196165 150mg + csDMARD (Asia Cohort)	Tofacitinib 5mg + csDMARD (Asia Cohort)	Pooled Placebo (Asia Cohort)
Subject group type	Reporting group	Reporting group	Reporting group	Subject analysis set
Number of subjects analysed	9	6	3	2
Units: Scores on a scale				
arithmetic mean (standard deviation)	1.22 (± 2.476)	3.42 (± 7.889)	0.33 (± 0.577)	0.25 (± 0.354)

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in HAQ-DI at Week 24 and Week 52 for treatment arms who started study intervention from Day 1 (Asia Cohort)

End point title	Change from Baseline in HAQ-DI at Week 24 and Week 52 for treatment arms who started study intervention from Day 1 (Asia Cohort)[170]

End point description:

HAQ-DI is a 20-question instrument that assesses the degree of difficulty of a participant in accomplishing tasks in eight functional areas: dressing and grooming, arising, eating, walking, hygiene, reach, grip and common daily activities. Overall HAQ-DI score was computed as sum of the domain scores divided by the number of domains answered. The total possible score ranges from 0 to 3 where 0 = least difficulty and 3 = extreme difficulty. Higher overall score indicates greater disability. A negative change from baseline indicates an improvement. Baseline was defined as latest pre-dose assessment with a non-missing value, including those from unscheduled visits. Change from Baseline was calculated by subtracting post dose visit value from Baseline value. The analysis was performed on all randomized Asia Cohort participants who received study intervention from Day 01 to Week 52. Participants with data available at indicated timepoints are analyzed.

End point type	Secondary

End point timeframe:

Baseline (Day 1) and Week 24

Notes:

[170] - 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: The endpoints are different for the different parts of the study.

End point values	GSK3196165 90mg + csDMARD (Asia Cohort)	GSK3196165 150mg + csDMARD (Asia Cohort)	Tofacitinib 5mg + csDMARD (Asia Cohort)	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	38	42	17	
Units: Scores on a scale				
arithmetic mean (standard deviation)				
HAQ-Disability Index, Week 24, n=38,42,17	-0.25 (± 0.569)	-0.29 (± 0.524)	-0.48 (± 0.266)	

HAQ-Disability Index, Week 52, n=32,31,15	-0.36 (± 0.573)	-0.40 (± 0.604)	-0.59 (± 0.483)	

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in HAQ-DI at Week 24 and Week 52 for placebo switched arms (Asia Cohort)

End point title	Change from Baseline in HAQ-DI at Week 24 and Week 52 for placebo switched arms (Asia Cohort)[171]

End point description:

HAQ-DI is a 20-question instrument that assesses degree of difficulty of a participant in accomplishing tasks in eight functional areas: dressing and grooming, arising, eating, walking, hygiene, reach, grip and common daily activities. Overall HAQ-DI score was computed as sum of domain scores divided by number of domains answered. Total possible score ranges from 0 to 3 where 0=least difficulty and 3=extreme difficulty. Higher overall score indicates greater disability. Negative change from baseline indicates an improvement. Baseline was defined as latest pre-dose assessment with a non-missing value, including those from unscheduled visits. Change from Baseline was calculated by subtracting post dose visit value from Baseline value. For efficacy assessments baseline is interpreted as Day 1. Analysis was performed on all randomized Asia Cohort participants who switched from placebo to study intervention at Week 12. Participants with data available at indicated timepoints are analyzed.

End point type	Secondary

End point timeframe:

Baseline (Day 1) and Week 52

Notes:

[171] - 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: The endpoints are different for the different parts of the study.

End point values	Placebo + csDMARD and GSK3196165 90mg + csDMARD (Asia Cohort)	Placebo + csDMARD and GSK3196165 150mg + csDMARD (Asia Cohort)	Placebo + csDMARD and Tofacitinib 5mg + csDMARD (Asia Cohort)	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	6	6	7	
Units: Scores on a scale				
arithmetic mean (standard deviation)				
HAQ-Disability Index, Week 24, n=6,6,7	-0.33 (± 0.921)	-0.02 (± 0.436)	-0.46 (± 0.431)	
HAQ-Disability Index, Week 52, n=4,6,7	-0.19 (± 1.139)	-0.19 (± 0.438)	-0.52 (± 0.442)	

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in Arthritis pain VAS at Week 24 and Week 52 for

treatment arms who started study intervention from Day 1 (Asia Cohort)

End point title	Change from Baseline in Arthritis pain VAS at Week 24 and Week 52 for treatment arms who started study intervention from Day 1 (Asia Cohort)[172]

End point description:

For the Arthritis Pain VAS, participants assess the severity of their current arthritis pain using a continuous visual analogue scale (VAS) with anchors at "0" (no pain) and "100" (most severe pain). A negative change from baseline indicates an improvement. Baseline was defined as the latest pre-dose assessment with a non-missing value, including those from unscheduled visits. Change from Baseline was calculated by subtracting the post dose visit value from the Baseline value. The analysis was performed on all randomized Asia Cohort participants who received study intervention from Day 01 to Week 52. Participants with data available at indicated timepoints are analyzed.

End point type	Secondary

End point timeframe:

Baseline (Day 1) and Week 24 and Week 52

Notes:

[172] - 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: The endpoints are different for the different parts of the study.

End point values	GSK3196165 90mg + csDMARD (Asia Cohort)	GSK3196165 150mg + csDMARD (Asia Cohort)	Tofacitinib 5mg + csDMARD (Asia Cohort)	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	38	42	17	
Units: Scores on a scale				
arithmetic mean (standard deviation)				
Week 24, n=38,42,17	-24.4 (± 22.90)	-25.2 (± 25.71)	-32.9 (± 25.97)	
Week 52, n=32,31,15	-30.4 (± 26.98)	-27.9 (± 23.51)	-33.0 (± 23.04)	

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in Arthritis pain VAS at Week 12 (Asia Cohort)

End point title	Change from Baseline in Arthritis pain VAS at Week 12 (Asia Cohort)[173]

End point description:

For the Arthritis Pain VAS, participants assess the severity of their current arthritis pain using a continuous visual analogue scale (VAS) with anchors at "0" (no pain) and "100" (most severe pain). A negative change from baseline indicates an improvement. Baseline was defined as the latest pre-dose assessment with a non-missing value, including those from unscheduled visits. Change from Baseline was calculated by subtracting the post dose visit value from the Baseline value. For the purpose of all analyses up to week 12, the placebo arms were pooled into a single placebo arm to primarily serve as a reference for the comparison of active treatment arms. The analysis was performed on ITT-Supplementary Asia Cohort set. Participants with data available at indicated timepoints are analyzed.

End point type	Secondary

End point timeframe:

Baseline (Day 1) and Week 12

Notes:

[173] - 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: The endpoints are different for the different parts of the study.

End point values	GSK3196165 90mg + csDMARD (Asia Cohort)	GSK3196165 150mg + csDMARD (Asia Cohort)	Tofacitinib 5mg + csDMARD (Asia Cohort)	Pooled Placebo (Asia Cohort)
Subject group type	Reporting group	Reporting group	Reporting group	Subject analysis set
Number of subjects analysed	46	42	19	21
Units: Scores on a scale				
arithmetic mean (standard deviation)	-20.0 (± 22.57)	-18.0 (± 25.37)	-21.2 (± 22.91)	-1.8 (± 21.00)

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in Short form (SF)-36 physical component scores at Week 12 (Asia Cohort)

End point title	Change from Baseline in Short form (SF)-36 physical component scores at Week 12 (Asia Cohort)[174]

End point description:

SF-36 survey evaluates health-related quality of life, covering physical functioning(PF),bodily pain(BP),role limitations due to physical/emotional issues,general health(GH),mental health,social functioning,vitality. Each of 8 domains is scored using average, 0-100; higher score represents better health.PCS was aggregated across the domains and scaled to T-score with mean of 50 and SD of 10; higher score represents better health.PCS is primarily derived from 4 domains(PF,role-physical,BP,GH) representing overall physical health.Positive change from baseline, reported using T-score change, indicates improvement in overall physical health.Quality Metric software was used for scoring.Baseline was defined as most recent pre-dose NMV, including unscheduled visits.CB=subtracting PD value from BV.For analysis up to week 12, placebo arms were pooled into single arm to serve as reference for active treatment arm comparison.ITT set was analyzed using multiple imputation to manage missing

End point type	Secondary

End point timeframe:

Baseline (Day 1) and Week 12

Notes:

[174] - 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: The endpoints are different for the different parts of the study.

End point values	GSK3196165 90mg + csDMARD (Asia Cohort)	GSK3196165 150mg + csDMARD (Asia Cohort)	Tofacitinib 5mg + csDMARD (Asia Cohort)	Pooled Placebo (Asia Cohort)
Subject group type	Reporting group	Reporting group	Reporting group	Subject analysis set
Number of subjects analysed	45	42	19	21
Units: T-Score				
arithmetic mean (standard deviation)	4.051 (± 6.1927)	3.040 (± 5.8359)	8.312 (± 6.6143)	0.222 (± 4.5222)

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in Arthritis pain VAS at Week 24 and Week 52 for placebo switched arms (Asia Cohort)

End point title	Change from Baseline in Arthritis pain VAS at Week 24 and Week 52 for placebo switched arms (Asia Cohort)[175]

End point description:

For the Arthritis Pain VAS, participants assess the severity of their current arthritis pain using a continuous visual analogue scale (VAS) with anchors at "0" (no pain) and "100" (most severe pain). A negative change from baseline indicates an improvement. Baseline was defined as the latest pre-dose assessment with a non-missing value, including those from unscheduled visits. Change from Baseline was calculated by subtracting the post dose visit value from the Baseline value. For efficacy assessments baseline is interpreted as Day 1. The analysis was performed on all randomized Asia Cohort participants who switched from placebo to study intervention at Week 12. Participants with data available at indicated timepoints are analyzed.

End point type	Secondary

End point timeframe:

Baseline (Day 1) and Week 24 and Week 52

Notes:

[175] - 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: The endpoints are different for the different parts of the study.

End point values	Placebo + csDMARD and GSK3196165 90mg + csDMARD (Asia Cohort)	Placebo + csDMARD and GSK3196165 150mg + csDMARD (Asia Cohort)	Placebo + csDMARD and Tofacitinib 5mg + csDMARD (Asia Cohort)	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	6	6	7	
Units: Scores on a scale				
arithmetic mean (standard deviation)				
Week 24, n=6,6,7	-14.2 (± 20.71)	-13.5 (± 27.57)	-27.0 (± 21.86)	
Week 52, n=4,6,7	-32.3 (± 14.45)	-21.8 (± 34.17)	-34.4 (± 27.50)	

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in SF-36 domain scores at Week 12 (Asia Cohort)

End point title	Change from Baseline in SF-36 domain scores at Week 12 (Asia Cohort)[176]

End point description:

SF-36 survey assessed health-related quality of life, covering physical functioning, bodily pain, role limitations due to physical/emotional issues, general health, mental health, social functioning, and vitality. MCS consists of four domains (MH, vitality, SF, role-emotional), and PCS consists of four domains (PF, role-physical, BP, GH).Individual question items were totaled within items under various sections, and these domain scores were then scaled from 0 to 100, with higher scores indicating better health. Positive changes from the baseline indicated improvements. Scoring of SF-36 utilized Quality Metric software. Baseline=latest pre-dose assessment with NMV, including those from unscheduled visits. CB=subtracting PD visit value from BV. For analysis up to week 12, placebo arms were pooled into single arm to serve as reference for active treatment arm comparison. Analysis was performed on ITT-Supplementary Asia Cohort set with data available at indicated timepoints are analyzed.

End point type	Secondary

End point timeframe:

Baseline (Day 1) and Week 12

Notes:

[176] - 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: The endpoints are different for the different parts of the study.

End point values	GSK3196165 90mg + csDMARD (Asia Cohort)	GSK3196165 150mg + csDMARD (Asia Cohort)	Tofacitinib 5mg + csDMARD (Asia Cohort)	Pooled Placebo (Asia Cohort)
Subject group type	Reporting group	Reporting group	Reporting group	Subject analysis set
Number of subjects analysed	45	42	19	21
Units: Scores on a scale				
arithmetic mean (standard deviation)				
Bodily Pain, n=45,42,19,21	12.64 (± 13.888)	7.93 (± 14.984)	23.42 (± 22.741)	1.62 (± 18.712)
General Health, n=45,42,19,21	6.33 (± 17.092)	2.86 (± 13.448)	9.16 (± 15.174)	-4.05 (± 14.928)
Mental Health, n=45,42,19,21	4.00 (± 17.340)	1.43 (± 14.579)	1.32 (± 14.419)	0.24 (± 13.179)
Physical Function, n=45,42,19,21	8.67 (± 15.537)	8.10 (± 17.355)	14.74 (± 19.037)	1.90 (± 18.740)
Role Emotional, n=45,42,19,21	5.93 (± 20.150)	7.54 (± 23.268)	7.89 (± 21.957)	2.38 (± 25.020)
Role Physical, n=45,42,19,21	8.89 (± 16.722)	8.33 (± 23.494)	20.07 (± 30.730)	2.98 (± 19.924)
Social Function, n=45,42,19,21	3.06 (± 20.670)	8.63 (± 20.379)	13.82 (± 19.937)	0.00 (± 16.298)
Vitality, n=45,42,19,21	7.22 (± 20.684)	8.48 (± 15.849)	9.54 (± 20.023)	2.08 (± 11.238)

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in SF-36 mental component scores (MCS) at Week 12 (Asia Cohort)

End point title	Change from Baseline in SF-36 mental component scores (MCS) at Week 12 (Asia Cohort)[177]

End point description:

SF-36 survey evaluates health-related quality of life, covering physical functioning,bodily pain,role limitations due to physical/emotional issues,general health,mental health(MH),social functioning(SF),vitality. Each of 8 domains is scored using average, 0-100; higher score represents

was aggregated across the domains and scaled to T-score with mean of 50 and SD of 10; higher score represents better health.MCS is primarily derived from 4 domains(SF,MH,vitality,role-emotional) representing overall mental health.Positive change from baseline, reported using T-score change, indicates improvement in overall mental health.Quality Metric software was used for scoring.Baseline was defined as most recent pre-dose NMV, including unscheduled visits.CB=subtracting PD value from BV.For analysis up to week 12, placebo arms were pooled into single arm to serve as reference for active treatment arm comparison.ITT set was analyzed using multiple imputation to manage missing data.

End point type	Secondary

End point timeframe:

Baseline (Day 1) and Week 12

Notes:

[177] - 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: The endpoints are different for the different parts of the study.

End point values	GSK3196165 90mg + csDMARD (Asia Cohort)	GSK3196165 150mg + csDMARD (Asia Cohort)	Tofacitinib 5mg + csDMARD (Asia Cohort)	Pooled Placebo (Asia Cohort)
Subject group type	Reporting group	Reporting group	Reporting group	Subject analysis set
Number of subjects analysed	45	42	19	21
Units: T-Score				
arithmetic mean (standard deviation)	1.529 (± 9.2379)	2.197 (± 8.4871)	1.149 (± 7.6184)	0.392 (± 7.0528)

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in SF-36 physical component scores at Week 24 and Week 52 for treatment arms who started study intervention from Day 1 (Asia Cohort)

End point title	Change from Baseline in SF-36 physical component scores at Week 24 and Week 52 for treatment arms who started study intervention from Day 1 (Asia Cohort)[178]

End point description:

SF-36 survey evaluates health-related quality of life, covering physical functioning(PF), bodily pain(BP), role limitations due to physical/emotional issues, general health(GH), MH, SF, vitality. Each domains is scored using average, 0-100; higher score represents better health. PCS was aggregated across domains and scaled to T-score with mean of 50 and SD of 10; higher score represents better health. PCS is primarily derived from 4 domains(PF, role-physical, BP, GH) representing overall physical health. Positive change from baseline, reported using T-score change, indicates improvement in overall physical health. Quality Metric software was used for scoring. Baseline was defined as latest pre-dose assessment with a non-missing value, including from unscheduled visits. Change from Baseline was calculated by subtracting post dose value from Baseline value. ITT set was analyzed using multiple imputation to manage missing data.

End point type	Secondary

End point timeframe:

Baseline (Day 1), Week 24 and Week 52

Notes:

[178] - 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: The endpoints are different for the different parts of the study.

End point values	GSK3196165 90mg + csDMARD (Asia Cohort)	GSK3196165 150mg + csDMARD (Asia Cohort)	Tofacitinib 5mg + csDMARD (Asia Cohort)	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	37	42	17	
Units: T-Score				
arithmetic mean (standard deviation)				
Week 24, n=37,42,17	4.220 (± 7.5564)	3.362 (± 5.9357)	7.826 (± 9.0545)	
Week 52, n=31,31,15	4.646 (± 6.7378)	5.328 (± 5.8824)	9.942 (± 5.7938)	

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in SF-36 mental component scores at Week 24 and Week 52 for treatment arms who started study intervention from Day 1 (Asia Cohort)

End point title	Change from Baseline in SF-36 mental component scores at Week 24 and Week 52 for treatment arms who started study intervention from Day 1 (Asia Cohort)[179]

End point description:

SF-36 survey evaluates health-related quality of life, covering physical functioning, bodily pain, role limitations due to physical/emotional issues, general health, mental health(MH), social functioning(SF), vitality. Each of 8 domains is scored using average, 0-100; higher score represents better health. MCS was aggregated across the domains and scaled to T-score with mean of 50 and SD of 10; higher score represents better health. MCS is primarily derived from 4 domains(SF, MH, vitality, role-emotional) representing overall mental health. Positive change from baseline, reported using T-score change, indicates improvement in overall mental health. Quality Metric software was used for scoring. Baseline was defined as latest pre-dose assessment with a non-missing value, including those from unscheduled visits. Change from Baseline was calculated by subtracting post dose visit value from Baseline value. ITT set was analyzed using multiple imputation to manage missing data.

End point type	Secondary

End point timeframe:

Baseline (Day 1), Week 24 and Week 52

Notes:

[179] - 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: The endpoints are different for the different parts of the study.

End point values	GSK3196165 90mg + csDMARD (Asia Cohort)	GSK3196165 150mg + csDMARD (Asia Cohort)	Tofacitinib 5mg + csDMARD (Asia Cohort)	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	37	42	17	
Units: T-Score				
arithmetic mean (standard deviation)				
Week 24, n=37,42,17	-0.157 (± 8.7537)	2.741 (± 6.6865)	0.071 (± 8.0170)	
Week 52, n=31,31,15	3.837 (± 9.6474)	0.918 (± 10.3466)	1.923 (± 9.4063)	

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in SF-36 domain scores at Week 24 and Week 52 for treatment arms who started study intervention from Day 1 (Asia Cohort)

End point title	Change from Baseline in SF-36 domain scores at Week 24 and Week 52 for treatment arms who started study intervention from Day 1 (Asia Cohort)[180]

End point description:

SF-36 survey assessed health-related quality of life, covering physical functioning, bodily pain, role limitations due to physical/emotional issues, general health, mental health, social functioning, and vitality. MCS consists of four domains (MH,vitality,SF,role-emotional), and PCS consists of four domains (PF,role-physical,BP,GH).Individual question items were totaled within items under various sections, and these domain scores were then scaled from 0 to 100, with higher scores indicating better health. Positive changes from the baseline indicated improvements. Scoring of SF-36 utilized Quality Metric software. Baseline was defined as most recent pre-dose non-missing value, including unscheduled visits. Change from baseline was calculated by subtracting post dose value from Baseline value. Participants who received study intervention from Day 1 to Week 52 in Asia Cohort with data available at indicated timepoints were analyzed.

End point type	Secondary

End point timeframe:

Baseline (Day 1), Week 24 and Week 52

Notes:

[180] - 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: The endpoints are different for the different parts of the study.

End point values	GSK3196165 90mg + csDMARD (Asia Cohort)	GSK3196165 150mg + csDMARD (Asia Cohort)	Tofacitinib 5mg + csDMARD (Asia Cohort)	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	37	42	17	
Units: Scores on a scale				
arithmetic mean (standard deviation)				
Bodily Pain, Week 24, n=37,42,17	13.43 (± 18.292)	8.88 (± 13.862)	30.59 (± 25.048)	
Bodily Pain, Week 52, n=31,31,15	16.77 (± 17.333)	16.97 (± 16.956)	30.20 (± 23.035)	
General Health, Week 24, n=37,42,17	4.97 (± 19.591)	4.19 (± 14.101)	2.41 (± 12.037)	
General Health, Week 52, n=31,31,15	5.74 (± 17.216)	4.13 (± 14.509)	10.87 (± 13.958)	
Mental Health, Week 24, n=37,42,17	0.68 (± 18.226)	4.17 (± 13.521)	2.65 (± 9.701)	
Mental Health, Week 52, n=31,31,15	7.42 (± 18.343)	1.29 (± 17.510)	6.00 (± 17.341)	
Physical Function, Week 24, n=37,42,17	6.08 (± 18.264)	10.60 (± 17.916)	14.71 (± 20.269)	

Physical Function, Week 52, n=31,31,15	10.00 (± 17.512)	11.29 (± 17.367)	21.67 (± 17.491)	
Role Emotional, Week 24, n=37,42,17	1.58 (± 22.209)	8.53 (± 19.259)	9.80 (± 25.215)	
Role Emotional, Week 52, n=31,31,15	9.41 (± 20.609)	8.87 (± 23.267)	11.11 (± 21.973)	
Role Physical, Week 24, n=37,42,17	8.45 (± 24.572)	8.63 (± 20.332)	18.01 (± 40.437)	
Role Physical, Week 52, n=31,31,15	13.31 (± 18.381)	12.90 (± 23.768)	21.67 (± 30.969)	
Social Function, Week 24, n=37,42,17	2.70 (± 18.194)	8.63 (± 16.904)	3.68 (± 37.699)	
Social Function, Week 52, n=31,31,15	10.48 (± 20.941)	5.24 (± 22.770)	11.67 (± 28.530)	
Vitality, Week 24, n=37,42,17	5.07 (± 22.040)	8.04 (± 15.937)	4.78 (± 25.342)	
Vitality, Week 52, n=31,31,15	11.49 (± 22.308)	6.05 (± 21.377)	11.25 (± 23.170)	

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in SF-36 physical component scores at Week 24 and Week 52 for placebo switched arms (Asia Cohort)

End point title	Change from Baseline in SF-36 physical component scores at Week 24 and Week 52 for placebo switched arms (Asia Cohort)[181]

End point description:

SF-36 survey evaluates health-related quality of life, covering physical functioning(PF), bodily pain(BP), role limitations due to physical/emotional issues, general health(GH), MH, SF, vitality. Each domains is scored using average, 0-100; higher score represents better health. PCS was aggregated across domains and scaled to T-score with mean of 50 and SD of 10; higher score represents better health. PCS is primarily derived from 4 domains(PF, role-physical, BP, GH) representing overall physical health. Positive change from baseline, reported using T-score change, indicates improvement in overall physical health. Quality Metric software was used for scoring. Baseline was defined as latest pre-dose assessment with a non-missing value, including from unscheduled visits. Change from Baseline was calculated by subtracting post dose value from Baseline value. ITT set was analyzed using multiple imputation to manage missing data. For efficacy assessments baseline is interpreted as Day 1.

End point type	Secondary

End point timeframe:

Baseline (Day 1), Week 24 and Week 52

Notes:

[181] - 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: The endpoints are different for the different parts of the study.

End point values	Placebo + csDMARD and GSK3196165 90mg + csDMARD (Asia Cohort)	Placebo + csDMARD and GSK3196165 150mg + csDMARD (Asia Cohort)	Placebo + csDMARD and Tofacitinib 5mg + csDMARD (Asia Cohort)	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	6	6	7	
Units: T-Score				
arithmetic mean (standard deviation)				

Week 24, n=6,6,7	1.762 (± 5.8183)	1.675 (± 6.9009)	5.544 (± 5.4800)	
Week 52, n=4,6,7	3.818 (± 3.4904)	3.268 (± 4.8182)	7.024 (± 6.0185)	

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in SF-36 mental component scores at Week 24 and Week 52 for placebo switched arms (Asia Cohort)

End point title	Change from Baseline in SF-36 mental component scores at Week 24 and Week 52 for placebo switched arms (Asia Cohort)[182]

End point description:

SF-36 survey evaluates health-related quality of life, covering PF, BP, role limitations due to physical/emotional issues, GH, mental health(MH), social functioning(SF), vitality. Each domains is scored using average, 0-100; higher score represents better health. MCS was aggregated across domains and scaled to T-score with mean of 50 and SD of 10; higher score represents better health. MCS is primarily derived from 4 domains(SF, MH, vitality, role-emotional) representing overall mental health. Positive change from baseline, reported using T-score change, indicates improvement in overall mental health. Quality Metric software was used for scoring. Baseline was defined as latest pre-dose assessment with a non-missing value, including those from unscheduled visits. Change from Baseline was calculated by subtracting post dose visit value from Baseline value. ITT set was analyzed using multiple imputation to manage missing data. For efficacy assessments baseline is interpreted as Day 1.

End point type	Secondary

End point timeframe:

Baseline (Day 1), Week 24 and Week 52

Notes:

[182] - 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: The endpoints are different for the different parts of the study.

End point values	Placebo + csDMARD and GSK3196165 90mg + csDMARD (Asia Cohort)	Placebo + csDMARD and GSK3196165 150mg + csDMARD (Asia Cohort)	Placebo + csDMARD and Tofacitinib 5mg + csDMARD (Asia Cohort)	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	6	6	7	
Units: T-Score				
arithmetic mean (standard deviation)				
Week 24, n=6,6,7	3.158 (± 8.1659)	3.950 (± 5.3971)	4.889 (± 8.1905)	
Week 52, n=4,6,7	-0.028 (± 9.4600)	-1.940 (± 8.3373)	2.401 (± 6.1426)	

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in SF-36 domain scores at Week 24 and Week 52 for placebo switched arms (Asia Cohort)

End point title	Change from Baseline in SF-36 domain scores at Week 24 and Week 52 for placebo switched arms (Asia Cohort)[183]

End point description:

SF-36 is a health-related survey that assesses quality of life covering 8 domains: physical functioning(PF),bodily pain(BP),role limitations due to physical/emotional problems,general health(GH),mental health(MH),social functioning(SF),vitality. The MCS consists of 4 domains (SF,MH,vitality,role-emotional) and PCS consists of 4 domains (PF,role-physical,BP,GH). The individual question items are first summed, then domain scores are weighted to a scale between 0 to 100, where higher score represents better health. Positive change from baseline indicates an improvement. Quality Metric software was used for scoring for SF-36. Baseline was defined as latest pre-dose assessment with a non-missing value, including those from unscheduled visits. Change from Baseline was calculated by subtracting post dose value from Baseline value. For efficacy assessments baseline is interpreted as Day 1. ITT set was analyzed for participants with data available at the indicated time points.

End point type	Secondary

End point timeframe:

Baseline (Day 1), Week 24 and Week 52

Notes:

[183] - 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: The endpoints are different for the different parts of the study.

End point values	Placebo + csDMARD and GSK3196165 90mg + csDMARD (Asia Cohort)	Placebo + csDMARD and GSK3196165 150mg + csDMARD (Asia Cohort)	Placebo + csDMARD and Tofacitinib 5mg + csDMARD (Asia Cohort)	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	6	6	7	
Units: Scores on a scale				
arithmetic mean (standard deviation)				
Bodily Pain, Week 24, n=6,6,7	18.83 (± 23.017)	12.17 (± 26.180)	18.00 (± 23.951)	
Bodily Pain, Week 52, n=4,6,7	13.50 (± 26.889)	12.83 (± 37.280)	23.00 (± 20.905)	
General Health, Week 24, n=6,6,7	-3.83 (± 14.689)	0.83 (± 16.558)	-1.29 (± 12.148)	
General Health, Week 52, n=4,6,7	5.00 (± 14.697)	-0.83 (± 13.934)	0.57 (± 18.911)	
Mental Health, Week 24, n=6,6,7	9.17 (± 13.197)	5.83 (± 12.813)	14.29 (± 5.345)	
Mental Health, Week 52, n=4,6,7	1.25 (± 13.769)	-2.50 (± 16.355)	6.43 (± 7.480)	
Physical Function, Week 24, n=6,6,7	0.01 (± 17.887)	2.50 (± 15.732)	25.71 (± 18.356)	
Physical Function, Week 52, n=4,6,7	2.51 (± 18.925)	5.83 (± 10.205)	21.43 (± 15.738)	
Role Emotional, Week 24, n=6,6,7	11.11 (± 24.532)	9.72 (± 16.171)	15.48 (± 40.379)	
Role Emotional, Week 52, n=4,6,7	0.00 (± 11.785)	-2.78 (± 21.515)	11.91 (± 27.154)	
Role Physical, Week 24, n=6,6,7	13.54 (± 15.520)	7.29 (± 10.013)	15.18 (± 21.907)	
Role Physical, Week 52, n=4,6,7	9.38 (± 14.878)	1.04 (± 14.479)	16.96 (± 25.697)	
Social Function, Week 24, n=6,6,7	-2.08 (± 20.026)	4.17 (± 6.455)	3.57 (± 17.252)	

Social Function, Week 52, n=4,6,7	3.13 (± 31.250)	-6.25 (± 15.309)	10.71 (± 18.298)	
Vitality, Week 24, n=6,6,7	3.13 (± 11.693)	11.46 (± 14.479)	15.18 (± 8.733)	
Vitality, Week 52, n=4,6,7	4.69 (± 23.593)	8.33 (± 6.455)	8.93 (± 14.815)	

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in Functional assessment of chronic illness therapy (FACIT)-Fatigue at Week 12 (Asia Cohort)

End point title	Change from Baseline in Functional assessment of chronic illness therapy (FACIT)-Fatigue at Week 12 (Asia Cohort)[184]

End point description:

The Functional Assessment of Chronic Illness Therapy (FACIT)-fatigue is a validated patient-reported measure of 13 statements regarding the feeling of fatigue. The total score ranges from 0 to 52 with higher values representing a lower fatigue and a better quality of life. A positive change from baseline in FACIT-fatigue indicates an improvement. Baseline was defined as latest pre-dose assessment with a non-missing value, including those from unscheduled visits. Change from Baseline was calculated by subtracting post dose visit value from Baseline value. For the purpose of all analyses up to week 12, the placebo arms were pooled into a single placebo arm to primarily serve as a reference for the comparison of active treatment arms. The analysis was performed on ITT-Supplementary Asia Cohort set. Participants with data available at indicated timepoints are analyzed.

End point type	Secondary

End point timeframe:

Baseline (Day 1) and Week 12

Notes:

[184] - 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: The endpoints are different for the different parts of the study.

End point values	GSK3196165 90mg + csDMARD (Asia Cohort)	GSK3196165 150mg + csDMARD (Asia Cohort)	Tofacitinib 5mg + csDMARD (Asia Cohort)	Pooled Placebo (Asia Cohort)
Subject group type	Reporting group	Reporting group	Reporting group	Subject analysis set
Number of subjects analysed	46	42	19	21
Units: Scores on a scale				
arithmetic mean (standard deviation)	2.4 (± 8.01)	4.0 (± 6.58)	6.4 (± 7.64)	0.3 (± 9.00)

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in FACIT-Fatigue at Week 24 and Week 52 for treatment arms who started study intervention from Day 1 (Asia Cohort)

End point title	Change from Baseline in FACIT-Fatigue at Week 24 and Week 52 for treatment arms who started study intervention from Day 1 (Asia Cohort)[185]

End point description:

The Functional Assessment of Chronic Illness Therapy (FACIT)-fatigue is a validated patient-reported measure of 13 statements regarding the feeling of fatigue. The total score ranges from 0 to 52 with higher values representing a lower fatigue and a better quality of life. A positive change from baseline in FACIT-fatigue indicates an improvement. Baseline was defined as latest pre-dose assessment with a non-missing value, including those from unscheduled visits. Change from Baseline was calculated by subtracting post dose visit value from Baseline value. The analysis was performed on all randomized Asia Cohort participants who received study intervention from Day 01 to Week 52. Participants with data available at indicated timepoints are analyzed.

End point type	Secondary

End point timeframe:

Baseline (Day 1), Week 24 and Week 52

Notes:

[185] - 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: The endpoints are different for the different parts of the study.

End point values	GSK3196165 90mg + csDMARD (Asia Cohort)	GSK3196165 150mg + csDMARD (Asia Cohort)	Tofacitinib 5mg + csDMARD (Asia Cohort)	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	38	42	17	
Units: Scores on a scale				
arithmetic mean (standard deviation)				
Week 24, n=38,42,17	1.9 (± 9.22)	4.7 (± 5.96)	5.1 (± 10.18)	
Week 52, n=32,31,15	3.3 (± 8.91)	5.3 (± 7.65)	7.7 (± 8.91)	

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in FACIT-Fatigue at Week 24 and Week 52 for placebo switched arms (Asia Cohort)

End point title	Change from Baseline in FACIT-Fatigue at Week 24 and Week 52 for placebo switched arms (Asia Cohort)[186]

End point description:

The Functional Assessment of Chronic Illness Therapy (FACIT)-fatigue is a validated patient-reported measure of 13 statements regarding the feeling of fatigue. The total score ranges from 0 to 52 with higher values representing a lower fatigue and a better quality of life. A positive change from baseline in FACIT-fatigue indicates an improvement. Baseline was defined as latest pre-dose assessment with a non-missing value, including those from unscheduled visits. Change from Baseline was calculated by subtracting post dose visit value from Baseline value. For efficacy assessments baseline is interpreted as Day 1. The analysis was performed on all randomized Asia Cohort participants who switched from placebo to study intervention at Week 12. Participants with data available at indicated timepoints are analyzed.

End point type	Secondary

End point timeframe:

Baseline (Day 1), Week 24 and Week 52

Notes:

[186] - 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: The endpoints are different for the different parts of the study.

End point values	Placebo + csDMARD and GSK3196165 90mg + csDMARD (Asia Cohort)	Placebo + csDMARD and GSK3196165 150mg + csDMARD (Asia Cohort)	Placebo + csDMARD and Tofacitinib 5mg + csDMARD (Asia Cohort)	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	6	6	7	
Units: Scores on a scale				
arithmetic mean (standard deviation)				
Week 24, n=6,6,7	6.3 (± 5.16)	1.3 (± 4.93)	3.0 (± 10.17)	
Week 52, n=4,6,7	4.0 (± 6.16)	2.2 (± 1.94)	2.0 (± 7.94)	

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) (Asia Cohort)

End point title	Number of participants with adverse events (AEs), serious adverse events (SAEs) and adverse events of special interest (AESI) (Asia Cohort)[187]

End point description:

AE is defined as any untoward medical occurrence in a clinical study participant, temporally associated with use of a study intervention, whether or not considered related to study intervention. SAEs are defined as any untoward medical occurrence that, at any dose: results in death, cause life threatening events which requires inpatient hospitalization or prolongation of existing hospitalization, results in persistent disability or incapacity and birth defect or congenital anomaly. Protocol defined AESIs were included. The analysis was performed on Safety Set that includes all randomized participants who received at least one dose of study treatment. Pooled Placebo collected data from Day 01 to Week 12. Placebo switched arms collected data from Week 12 to 59. Experimental arms collected data from Day 01 to Week 59.

End point type	Secondary

End point timeframe:

Up to Week 59

Notes:

[187] - 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: The endpoints are different for the different parts of the study.

End point values	GSK3196165 90mg + csDMARD (Asia Cohort)	GSK3196165 150mg + csDMARD (Asia Cohort)	Tofacitinib 5mg + csDMARD (Asia Cohort)	Pooled Placebo (Asia Cohort)
Subject group type	Reporting group	Reporting group	Reporting group	Subject analysis set
Number of subjects analysed	47	49	19	23
Units: Participants				
AE	37	43	18	14
SAE	5	4	2	1
AESI	4	6	2	0

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in hematology parameter of WBC count, platelet count, neutrophils, lymphocytes at Week 24 and Week 52 for treatment arms who started study intervention from Day 1 (Asia Cohort)

End point title	Change from Baseline in hematology parameter of WBC count, platelet count, neutrophils, lymphocytes at Week 24 and Week 52 for treatment arms who started study intervention from Day 1 (Asia Cohort)[188]

End point description:

Blood samples were collected for the assessment of change from baseline in hematology parameters including WBC count, platelet count, neutrophils, lymphocytes. Baseline was defined as latest pre-dose assessment with a non-missing value, including those from unscheduled visits. Change from Baseline was calculated by subtracting post dose visit value from Baseline value. The analysis was performed on Safety Set participants who received study intervention from Day 01 to Week 52. Only those participants with data available at the specified data points were analyzed.

End point type	Secondary

End point timeframe:

Baseline (Day 1), Week 24 and Week 52

Notes:

[188] - 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: The endpoints are different for the different parts of the study.

End point values	GSK3196165 90mg + csDMARD (Asia Cohort)	GSK3196165 150mg + csDMARD (Asia Cohort)	Tofacitinib 5mg + csDMARD (Asia Cohort)	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	38	43	17	
Units: Giga cells per liter (10^9/L)				
arithmetic mean (standard deviation)				
WBC count, Week 24, n=38,43,17	-0.42 (± 1.780)	-0.56 (± 1.467)	-0.26 (± 3.492)	
WBC count, Week 52, n=29,28,16	-0.60 (± 1.538)	-0.50 (± 1.338)	-1.30 (± 1.207)	
Platelet count, Week 24, n=38,43,17	-24.8 (± 61.57)	-8.0 (± 39.63)	-3.2 (± 74.58)	
Platelet count, Week 52, n=29,28,16	-27.4 (± 54.86)	-24.5 (± 53.19)	-28.6 (± 51.39)	
Neutrophils, Week 24, n=38,43,17	-0.632 (± 1.7911)	-0.737 (± 1.3842)	-0.829 (± 1.7091)	
Neutrophils, Week 52, n=29,28,16	-0.794 (± 1.6493)	-0.475 (± 1.1881)	-0.828 (± 1.2338)	
Lymphocytes, Week 24, n=38,43,17	0.107 (± 0.3436)	0.114 (± 0.2605)	0.454 (± 1.7675)	
Lymphocytes, Week 52, n=29,28,16	0.129 (± 0.3706)	-0.002 (± 0.2894)	-0.414 (± 0.3126)	

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in hematology parameter of white blood cell (WBC) count, platelet count, neutrophils, lymphocytes at Week 12 (Giga cells per liter) (Asia Cohort)

End point title	Change from Baseline in hematology parameter of white blood cell (WBC) count, platelet count, neutrophils, lymphocytes at Week 12 (Giga cells per liter) (Asia Cohort)[189]

End point description:

Blood samples were collected for the assessment of change from baseline in hematology parameters including WBC count, platelet count, neutrophils, lymphocytes. Baseline was defined as latest pre-dose assessment with a non-missing value, including those from unscheduled visits. Change from Baseline was calculated by subtracting post dose visit value from Baseline value. For the purpose of all analyses up to week 12, the placebo arms were pooled into a single placebo arm to primarily serve as a reference for the comparison of active treatment arms. The analysis was performed on the Safety Set. Only those participants with data available at the specified data points were analyzed.

End point type	Secondary

End point timeframe:

Baseline (Day 1) and Week 12

Notes:

[189] - 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: The endpoints are different for the different parts of the study.

End point values	GSK3196165 90mg + csDMARD (Asia Cohort)	GSK3196165 150mg + csDMARD (Asia Cohort)	Tofacitinib 5mg + csDMARD (Asia Cohort)	Pooled Placebo (Asia Cohort)
Subject group type	Reporting group	Reporting group	Reporting group	Subject analysis set
Number of subjects analysed	45	43	19	21
Units: Giga cells per liter (10^9/L)				
arithmetic mean (standard deviation)				
WBC count, n=45,43,19,21	-0.48 (± 1.369)	-0.35 (± 1.699)	-1.25 (± 1.038)	-0.18 (± 1.518)
Platelet count, n=45,43,19,21	-17.8 (± 51.99)	-20.4 (± 44.57)	-22.9 (± 50.17)	5.7 (± 48.47)
Neutrophils, n=45,43,19,21	-0.654 (± 1.3274)	-0.473 (± 1.5847)	-1.316 (± 1.0213)	-0.352 (± 1.2533)
Lymphocytes, n=45,43,19,21	0.094 (± 0.3241)	0.069 (± 0.3391)	0.070 (± 0.4069)	0.117 (± 0.4069)

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in hematology parameter of WBC count, platelet count, neutrophils, lymphocytes at Week 24 and Week 52 (Asia Cohort)

End point title	Change from Baseline in hematology parameter of WBC count, platelet count, neutrophils, lymphocytes at Week 24 and Week 52 (Asia Cohort)[190]

End point description:

Blood samples were collected for the assessment of change from baseline in hematology parameters including WBC count, platelet count, neutrophils, lymphocytes. Baseline was defined as latest pre-dose assessment with a non-missing value, including those from unscheduled visits. Change from Baseline was calculated by subtracting post dose visit value from Baseline value. For safety assessments baseline is interpreted as Week 12. The analysis was performed on Safety Set participants who switched from placebo to study intervention at Week 12. Only those participants with data available at the specified data points were analyzed.

End point type	Secondary

End point timeframe:

Baseline (Week 12), Week 24 and Week 52

Notes:

[190] - 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: The endpoints are different for the different parts of the study.

End point values	Placebo + csDMARD and GSK3196165 90mg + csDMARD (Asia Cohort)	Placebo + csDMARD and GSK3196165 150mg + csDMARD (Asia Cohort)	Placebo + csDMARD and Tofacitinib 5mg + csDMARD (Asia Cohort)	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	6	6	7	
Units: Giga cells per liter (10^9/L)				
arithmetic mean (standard deviation)				
WBC count, Week 24, n=6,6,7	-0.10 (± 1.404)	-1.10 (± 0.729)	-0.53 (± 1.559)	
WBC count, Week 52, n=4,5,6	-0.28 (± 0.544)	-0.08 (± 1.057)	0.85 (± 1.285)	
Platelet count, Week 24, n=6,6,7	-33.5 (± 39.29)	1.2 (± 45.66)	-54.4 (± 72.52)	
Platelet count, Week 52, n=4,5,6	-33.8 (± 48.88)	-27.4 (± 49.23)	-62.7 (± 67.67)	
Neutrophils, Week 24, n=6,6,7	0.042 (± 1.1970)	-1.153 (± 0.8378)	-0.599 (± 1.6470)	
Neutrophils, Week 52, n=4,5,6	-0.205 (± 0.3770)	-0.040 (± 0.6118)	1.305 (± 1.0918)	
Lymphocytes, Week 24, n=6,6,7	-0.160 (± 0.2929)	0.185 (± 0.3747)	0.030 (± 0.4946)	
Lymphocytes, Week 52, n=4,5,6	0.093 (± 0.1962)	0.092 (± 0.3667)	-0.568 (± 0.5136)	

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in hematology parameter of hemoglobin at Week 12 (Asia Cohort)

End point title	Change from Baseline in hematology parameter of hemoglobin at Week 12 (Asia Cohort)[191]

End point description:

Blood samples was collected for the assessment of hematology parameters. Baseline was defined as latest pre-dose assessment with a non-missing value, including those from unscheduled visits. Change from Baseline was calculated by subtracting post dose visit value from Baseline value. For the purpose of all analyses up to week 12, the placebo arms were pooled into a single placebo arm to primarily serve as a reference for the comparison of active treatment arms. The analysis was performed on the Safety Set. Only those participants with data available at the specified data points were analyzed.

End point type	Secondary

End point timeframe:

Baseline (Day 1) and Week 12

Notes:

[191] - 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: The endpoints are different for the different parts of the study.

End point values	GSK3196165 90mg + csDMARD (Asia Cohort)	GSK3196165 150mg + csDMARD (Asia Cohort)	Tofacitinib 5mg + csDMARD (Asia Cohort)	Pooled Placebo (Asia Cohort)
Subject group type	Reporting group	Reporting group	Reporting group	Subject analysis set
Number of subjects analysed	45	43	19	21
Units: Grams per liter (g/L)				
arithmetic mean (standard deviation)	2.3 (± 8.44)	0.0 (± 8.45)	1.4 (± 5.70)	-1.7 (± 7.31)

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in hematology parameter of hemoglobin at Week 24 and Week 52 for treatment arms who started study intervention from Day 1 (Asia Cohort)

End point title	Change from Baseline in hematology parameter of hemoglobin at Week 24 and Week 52 for treatment arms who started study intervention from Day 1 (Asia Cohort)[192]

End point description:

Blood samples was collected for the assessment of hematology parameters. Baseline was defined as latest pre-dose assessment with a non-missing value, including those from unscheduled visits. Change from Baseline was calculated by subtracting post dose visit value from Baseline value. The analysis was performed on Safety Set participants who received study intervention from Day 01 to Week 52. Only those participants with data available at the specified data points were analyzed.

End point type	Secondary

End point timeframe:

Baseline (Day 1), Week 24 and Week 52

Notes:

[192] - 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: The endpoints are different for the different parts of the study.

End point values	GSK3196165 90mg + csDMARD (Asia Cohort)	GSK3196165 150mg + csDMARD (Asia Cohort)	Tofacitinib 5mg + csDMARD (Asia Cohort)	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	38	43	17	
Units: Grams per liter (g/L)				
arithmetic mean (standard deviation)				
Week 24, n=38,43,17	3.2 (± 10.72)	-0.8 (± 9.81)	2.4 (± 8.97)	
Week 52, n=29,28,15	1.9 (± 10.65)	-1.8 (± 9.95)	2.4 (± 9.76)	

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in hematology parameter of hemoglobin at Week 24 and Week 52 for placebo switched arms (Asia Cohort)

End point title	Change from Baseline in hematology parameter of hemoglobin at Week 24 and Week 52 for placebo switched arms (Asia Cohort)[193]

End point description:

Blood samples was collected for the assessment of hematology parameters. Baseline was defined as latest pre-dose assessment with a non-missing value, including those from unscheduled visits. Change from Baseline was calculated by subtracting post dose visit value from Baseline value. For safety assessments baseline is interpreted as Week 12. The analysis was performed on Safety Set participants who switched from placebo to study intervention at Week 12. Only those participants with data available at the specified data points were analyzed.

End point type	Secondary

End point timeframe:

Baseline (Week 12), Week 24 and Week 52

Notes:

[193] - 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: The endpoints are different for the different parts of the study.

End point values	Placebo + csDMARD and GSK3196165 90mg + csDMARD (Asia Cohort)	Placebo + csDMARD and GSK3196165 150mg + csDMARD (Asia Cohort)	Placebo + csDMARD and Tofacitinib 5mg + csDMARD (Asia Cohort)	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	6	6	7	
Units: Grams per liter (g/L)				
arithmetic mean (standard deviation)				
Week 24, n=6,6,7	-0.5 (± 7.94)	-1.2 (± 8.77)	3.3 (± 4.68)	
Week 52, n=4,5,6	-0.5 (± 6.35)	-1.0 (± 11.51)	2.5 (± 7.23)	

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in clinical chemistry parameter of aspartate aminotransferase (AST), alanine aminotransferase (ALT), alkaline phosphatase (AP), Gamma-Glutamyl transpeptidase (GGT) at Week 12 (Asia Cohort)

End point title	Change from Baseline in clinical chemistry parameter of aspartate aminotransferase (AST), alanine aminotransferase (ALT), alkaline phosphatase (AP), Gamma-Glutamyl transpeptidase (GGT) at Week 12 (Asia Cohort)[194]

End point description:

Blood samples were collected for the assessment of clinical chemistry parameters including aspartate aminotransferase (AST), alanine aminotransferase (ALT), alkaline phosphatase (AP) and gamma-glutamyl transferase (GGT) levels. Baseline was defined as the latest pre-dose assessment with a non-missing value, including those from unscheduled visits. Change from Baseline was calculated by subtracting the post dose visit value from the Baseline value. For the purpose of all analyses up to week 12, the placebo arms were pooled into a single placebo arm to primarily serve as a reference for the

comparison of active treatment arms. The analysis was performed on the Safety Set. Only those participants with data available at the specified data points were analyzed.

End point type	Secondary

End point timeframe:

Baseline (Day 1) and Week 12

Notes:

[194] - 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: The endpoints are different for the different parts of the study.

End point values	GSK3196165 90mg + csDMARD (Asia Cohort)	GSK3196165 150mg + csDMARD (Asia Cohort)	Tofacitinib 5mg + csDMARD (Asia Cohort)	Pooled Placebo (Asia Cohort)
Subject group type	Reporting group	Reporting group	Reporting group	Subject analysis set
Number of subjects analysed	46	43	19	21
Units: International units per liter (IU/L)				
arithmetic mean (standard deviation)				
Aspartate Aminotransferase	3.5 (± 13.14)	2.0 (± 5.29)	2.9 (± 4.82)	0.8 (± 8.26)
Alanine Aminotransferase	2.1 (± 16.90)	2.5 (± 7.49)	0.0 (± 7.85)	2.8 (± 16.44)
Alkaline Phosphatase	-1.9 (± 14.73)	-1.0 (± 11.52)	-4.2 (± 15.44)	-0.6 (± 16.52)
Gamma-Glutamyl Transpeptidase	-3.0 (± 10.95)	0.7 (± 12.28)	-3.5 (± 14.69)	2.6 (± 12.52)

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in clinical chemistry parameter of AST, ALT, AP, GGT at Week 24 and Week 52 for treatment arms who started study intervention from Day 1 (Asia Cohort)

End point title	Change from Baseline in clinical chemistry parameter of AST, ALT, AP, GGT at Week 24 and Week 52 for treatment arms who started study intervention from Day 1 (Asia Cohort)[195]

End point description:

Blood samples were collected for the assessment of clinical chemistry parameters including AST, ALT, AP and GGT levels. Baseline was defined as the latest pre-dose assessment with a non-missing value, including those from unscheduled visits. Change from Baseline was calculated by subtracting the post dose visit value from the Baseline value. The analysis was performed on Safety Set participants who received study intervention from Day 01 to Week 52. Only those participants with data available at the specified data points were analyzed.

End point type	Secondary

End point timeframe:

Baseline (Day 1), Week 24 and Week 52

Notes:

[195] - 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: The endpoints are different for the different parts of the study.

End point values	GSK3196165 90mg + csDMARD (Asia Cohort)	GSK3196165 150mg + csDMARD (Asia Cohort)	Tofacitinib 5mg + csDMARD (Asia Cohort)	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	38	43	17	
Units: International units per liter (IU/L)				
arithmetic mean (standard deviation)				
AST. Week 24, n=38,43,17	0.1 (± 10.02)	2.1 (± 6.20)	3.2 (± 7.27)	
AST. Week 52, n=29,28,16	0.9 (± 8.65)	1.2 (± 5.34)	4.2 (± 10.58)	
ALT, Week 24, n=38,43,17	-1.0 (± 16.19)	2.5 (± 8.56)	-0.2 (± 4.22)	
ALT, Week 52, n=29,28,16	-2.3 (± 15.36)	-0.4 (± 5.95)	2.0 (± 19.78)	
AP, Week 24, n=38,43,17	-0.3 (± 15.15)	0.3 (± 16.64)	-5.6 (± 15.14)	
AP, Week 52, n=29,28,16	-5.7 (± 15.00)	-6.3 (± 18.37)	-5.1 (± 21.76)	
GGT, Week 24, n=38,43,17	-4.4 (± 9.83)	0.7 (± 16.68)	-5.0 (± 17.60)	
GGT, Week 52, n=29,28,16	-6.8 (± 10.38)	-2.1 (± 12.53)	1.4 (± 20.96)	

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in clinical chemistry parameter of AST, ALT, AP, GGT at Week 24 and Week 52 for placebo switched arms (Asia Cohort)

End point title	Change from Baseline in clinical chemistry parameter of AST, ALT, AP, GGT at Week 24 and Week 52 for placebo switched arms (Asia Cohort)[196]

End point description:

Blood samples were collected for the assessment of clinical chemistry parameters including AST, ALT, AP and GGT levels. Baseline was defined as the latest pre-dose assessment with a non-missing value, including those from unscheduled visits. Change from Baseline was calculated by subtracting the post dose visit value from the Baseline value. For safety assessments baseline is interpreted as Week 12. The analysis was performed on Safety Set participants who switched from placebo to study intervention at Week 12. Only those participants with data available at the specified data points were analyzed.

End point type	Secondary

End point timeframe:

Baseline (Week 12), Week 24 and Week 52

Notes:

[196] - 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: The endpoints are different for the different parts of the study.

End point values	Placebo + csDMARD and GSK3196165 90mg + csDMARD (Asia Cohort)	Placebo + csDMARD and GSK3196165 150mg + csDMARD (Asia Cohort)	Placebo + csDMARD and Tofacitinib 5mg + csDMARD (Asia Cohort)	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	6	6	7	
Units: International units per liter (IU/L)				
arithmetic mean (standard deviation)				
AST, Week 24, n=6,6,7	-0.5 (± 2.43)	-4.0 (± 9.14)	4.3 (± 4.07)	
AST, Week 52, n=4,5,6	1.3 (± 2.36)	-1.2 (± 1.64)	2.6 (± 5.41)	

ALT, Week 24, n=6,6,7	0.5 (± 2.43)	-14.0 (± 25.91)	1.7 (± 7.36)	
ALT, Week 52, n=4,5,6	6.0 (± 6.98)	-4.0 (± 5.92)	-2.0 (± 8.75)	
AP, Week 24, n=6,6,7	-0.3 (± 7.74)	-6.0 (± 12.57)	0.0 (± 26.44)	
AP, Week 52, n=4,5,6	-10.5 (± 18.16)	1.6 (± 4.98)	-13.6 (± 21.48)	
GGT, Week 24, n=6,6,7	-1.3 (± 5.75)	-10.8 (± 23.23)	-6.0 (± 12.94)	
GGT, Week 52, n=4,5,6	3.0 (± 6.78)	-4.0 (± 12.53)	-7.6 (± 15.45)	

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in clinical chemistry parameter of total bilirubin at Week 12 (Asia Cohort)

End point title	Change from Baseline in clinical chemistry parameter of total bilirubin at Week 12 (Asia Cohort)[197]

End point description:

Blood samples were collected for the assessment of clinical chemistry parameter total bilirubin level. Baseline was defined as the latest pre-dose assessment with a non-missing value, including those from unscheduled visits. Change from Baseline was calculated by subtracting the post dose visit value from the Baseline value. For the purpose of all analyses up to week 12, the placebo arms were pooled into a single placebo arm to primarily serve as a reference for the comparison of active treatment arms. The analysis was performed on the Safety Set. Only those participants with data available at the specified data points were analyzed.

End point type	Secondary

End point timeframe:

Baseline (Day 1) and Week 12

Notes:

[197] - 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: The endpoints are different for the different parts of the study.

End point values	GSK3196165 90mg + csDMARD (Asia Cohort)	GSK3196165 150mg + csDMARD (Asia Cohort)	Tofacitinib 5mg + csDMARD (Asia Cohort)	Pooled Placebo (Asia Cohort)
Subject group type	Reporting group	Reporting group	Reporting group	Subject analysis set
Number of subjects analysed	46	43	19	21
Units: Micromoles per liter (umol/L)				
arithmetic mean (standard deviation)	0.2 (± 2.32)	0.1 (± 2.64)	1.1 (± 4.71)	-0.1 (± 2.68)

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in clinical chemistry parameter of total bilirubin at Week 24 and Week 52 for treatment arms who started study intervention from Day 1 (Asia Cohort)

End point title	Change from Baseline in clinical chemistry parameter of total

	bilirubin at Week 24 and Week 52 for treatment arms who started study intervention from Day 1 (Asia Cohort)[198]

End point description:

Blood samples were collected for the assessment of clinical chemistry parameter total bilirubin level. Baseline was defined as the latest pre-dose assessment with a non-missing value, including those from unscheduled visits. Change from Baseline was calculated by subtracting the post dose visit value from the Baseline value. The analysis was performed on the Safety Set. Only those participants with data available at the specified data points were analyzed.

End point type	Secondary

End point timeframe:

Baseline (Day 1), Week 24 and Week 52

Notes:

[198] - 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: The endpoints are different for the different parts of the study.

End point values	GSK3196165 90mg + csDMARD (Asia Cohort)	GSK3196165 150mg + csDMARD (Asia Cohort)	Tofacitinib 5mg + csDMARD (Asia Cohort)	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	38	43	17	
Units: Micromoles per liter (umol/L)				
arithmetic mean (standard deviation)				
Week 24, n=38,43,17	0.3 (± 2.60)	0.2 (± 2.82)	0.3 (± 2.79)	
Week 52, n=29,28,16	0.7 (± 2.69)	1.6 (± 4.75)	1.6 (± 2.85)	

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in clinical chemistry parameter of total bilirubin at Week 24 and Week 52 for placebo switched arms (Asia Cohort)

End point title	Change from Baseline in clinical chemistry parameter of total bilirubin at Week 24 and Week 52 for placebo switched arms (Asia Cohort)[199]

End point description:

Blood samples were collected for the assessment of clinical chemistry parameter total bilirubin level. Baseline was defined as the latest pre-dose assessment with a non-missing value, including those from unscheduled visits. Change from Baseline was calculated by subtracting the post dose visit value from the Baseline value. For safety assessments baseline is interpreted as Week 12. The analysis was performed on Safety Set participants who switched from placebo to study intervention at Week 12. Only those participants with data available at the specified data points were analyzed.

End point type	Secondary

End point timeframe:

Baseline (Week 12), Week 24 and Week 52

Notes:

[199] - 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: The endpoints are different for the different parts of the study.

End point values	Placebo + csDMARD and GSK3196165 90mg + csDMARD (Asia Cohort)	Placebo + csDMARD and GSK3196165 150mg + csDMARD (Asia Cohort)	Placebo + csDMARD and Tofacitinib 5mg + csDMARD (Asia Cohort)	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	6	6	7	
Units: Micromoles per liter (umol/L)				
arithmetic mean (standard deviation)				
Week 24, n=6,6,7	-0.7 (± 1.97)	3.2 (± 3.54)	0.3 (± 2.75)	
Week 52, n=4,5,5	0.0 (± 1.41)	22.0 (± 2.00)	0.0 (± 1.41)	

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in clinical chemistry parameter of albumin at Week 12 (Asian Cohort)

End point title	Change from Baseline in clinical chemistry parameter of albumin at Week 12 (Asian Cohort)[200]

End point description:

Blood samples was collected for the assessment of clinical chemistry parameter albumin. Baseline was defined as latest pre-dose assessment with a non-missing value, including those from unscheduled visits. Change from Baseline was calculated by subtracting post dose visit value from Baseline value. For the purpose of all analyses up to week 12, the placebo arms were pooled into a single placebo arm to primarily serve as a reference for the comparison of active treatment arms. The analysis was performed on the Safety Set. Only those participants with data available at the specified data points were analyzed.

End point type	Secondary

End point timeframe:

Baseline (Day 1) and Week 12

Notes:

[200] - 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: The endpoints are different for the different parts of the study.

End point values	GSK3196165 90mg + csDMARD (Asia Cohort)	GSK3196165 150mg + csDMARD (Asia Cohort)	Tofacitinib 5mg + csDMARD (Asia Cohort)	Pooled Placebo (Asia Cohort)
Subject group type	Reporting group	Reporting group	Reporting group	Subject analysis set
Number of subjects analysed	46	43	19	21
Units: Grams per liter (g/L)				
arithmetic mean (standard deviation)	0.8 (± 2.99)	-0.2 (± 2.26)	2.1 (± 2.51)	-0.5 (± 2.68)

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in clinical chemistry parameter of albumin at Week 24 and Week 52 for treatment arms who started study intervention from Day

1 (Asia Cohort)

End point title	Change from Baseline in clinical chemistry parameter of albumin at Week 24 and Week 52 for treatment arms who started study intervention from Day 1 (Asia Cohort)[201]

End point description:

Blood samples was collected for the assessment of clinical chemistry parameter albumin. Baseline was defined as latest pre-dose assessment with a non-missing value, including those from unscheduled visits. Change from Baseline was calculated by subtracting post dose visit value from Baseline value. The analysis was performed on Safety Set participants who received study intervention from Day 01 to Week 52. Only those participants with data available at the indicated timepoints were analyzed.

End point type	Secondary

End point timeframe:

Baseline (Day 1), Week 24 and Week 52

Notes:

[201] - 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: The endpoints are different for the different parts of the study.

End point values	GSK3196165 90mg + csDMARD (Asia Cohort)	GSK3196165 150mg + csDMARD (Asia Cohort)	Tofacitinib 5mg + csDMARD (Asia Cohort)	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	38	43	17	
Units: Grams per liter (g/L)				
arithmetic mean (standard deviation)				
Week 24, n=38,43,17	0.8 (± 2.81)	0.3 (± 2.90)	1.4 (± 4.01)	
Week 52, n=29,28,16	1.0 (± 2.54)	0.2 (± 2.47)	2.6 (± 3.50)	

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in lipid profile parameter of total cholesterol at Week 24 for treatment arms who started study intervention from Day 1 (Asia Cohort)

End point title	Change from Baseline in lipid profile parameter of total cholesterol at Week 24 for treatment arms who started study intervention from Day 1 (Asia Cohort)[202]

End point description:

Blood samples were collected for the assessment of lipid profile of total cholesterol levels. Baseline was defined as the latest pre-dose assessment with a non-missing value, including those from unscheduled visits. Change from Baseline was calculated by subtracting the post dose visit value from the Baseline value. Blood samples were collected at indicated time points per schedule of assessment in protocol. Objectives and Endpoints section incorrectly states that Change from baseline in key laboratory parameters at Week 24 was a secondary objective, however for lipid panel, there is no corresponding time point in schedule of assessment. Consequently, the objective that can be assessed for the lipid panel is Week 16 and not Week 24 as no data collected. Week 16 is not pre-specified time point to report.

End point type	Secondary

End point timeframe:

Baseline (Day 1) and Week 24

Notes:

[202] - 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: The endpoints are different for the different parts of the study.

End point values	GSK3196165 90mg + csDMARD (Asia Cohort)	GSK3196165 150mg + csDMARD (Asia Cohort)	Tofacitinib 5mg + csDMARD (Asia Cohort)	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	0[203]	0[204]	0[205]	
Units: Millimoles per liter (mmol/L)				
arithmetic mean (standard deviation)	()	()	()	

Notes:

[203] - Data was not collected as there is no corresponding time point in schedule of activity of Protocol.

[204] - Data was not collected as there is no corresponding time point in schedule of activity of Protocol.

[205] - Data was not collected as there is no corresponding time point in schedule of activity of Protocol.

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in lipid profile parameter of total cholesterol at Week 12 (Asia Cohort)

End point title	Change from Baseline in lipid profile parameter of total cholesterol at Week 12 (Asia Cohort)[206]

End point description:

Blood samples were collected for the assessment of lipid profile of total cholesterol levels. Baseline was defined as the latest pre-dose assessment with a non-missing value, including those from unscheduled visits. Change from Baseline was calculated by subtracting the post dose visit value from the Baseline value. For the purpose of all analyses up to week 12, the placebo arms were pooled into a single placebo arm to primarily serve as a reference for the comparison of active treatment arms. Blood samples were collected at indicated time points as per schedule of assessment in the protocol. The Objectives and Endpoints section incorrectly states that Change from baseline in key laboratory parameters at Week 12 was a secondary objective, however for the lipid panel, there is no corresponding time point in the schedule of assessment. Consequently, the only objective that can be assessed for the lipid panel is Week 4 and not at Week 12.

End point type	Secondary

End point timeframe:

Baseline (Day 1) and Week 12

Notes:

[206] - 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: The endpoints are different for the different parts of the study.

End point values	GSK3196165 90mg + csDMARD (Asia Cohort)	GSK3196165 150mg + csDMARD (Asia Cohort)	Tofacitinib 5mg + csDMARD (Asia Cohort)	Pooled Placebo (Asia Cohort)
Subject group type	Reporting group	Reporting group	Reporting group	Subject analysis set
Number of subjects analysed	0[207]	0[208]	0[209]	0[210]
Units: Millimoles per liter (mmol/L)				
arithmetic mean (standard deviation)	()	()	()	()

Notes:

[207] - Data was not collected as there is no corresponding time point in schedule of activity of Protocol.

[208] - Data was not collected as there is no corresponding time point in schedule of activity of Protocol.

[209] - Data was not collected as there is no corresponding time point in schedule of activity of Protocol.

[210] - Data was not collected as there is no corresponding time point in schedule of activity of Protocol.

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in clinical chemistry parameter of albumin at Week 24 and Week 52 for placebo switched arms (Asia Cohort)

End point title	Change from Baseline in clinical chemistry parameter of albumin at Week 24 and Week 52 for placebo switched arms (Asia Cohort)[211]

End point description:

Blood samples was collected for the assessment of clinical chemistry parameter albumin. Baseline was defined as latest pre-dose assessment with a non-missing value, including those from unscheduled visits. Change from Baseline was calculated by subtracting post dose visit value from Baseline value. For safety assessments baseline is interpreted as Week 12. The analysis was performed on Safety Set participants who switched from placebo to study intervention at Week 12. Only those participants with data available at the indicated timepoints were analyzed.

End point type	Secondary

End point timeframe:

Baseline (Week 12), Week 24 and Week 52

Notes:

[211] - 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: The endpoints are different for the different parts of the study.

End point values	Placebo + csDMARD and GSK3196165 90mg + csDMARD (Asia Cohort)	Placebo + csDMARD and GSK3196165 150mg + csDMARD (Asia Cohort)	Placebo + csDMARD and Tofacitinib 5mg + csDMARD (Asia Cohort)	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	6	6	7	
Units: Grams per liter (g/L)				
arithmetic mean (standard deviation)				
Week 24, n=6,6,7	0.3 (± 3.01)	1.2 (± 1.83)	2.1 (± 2.54)	
Week 52, n=4,5,5	0.3 (± 1.71)	2.0 (± 1.58)	3.8 (± 3.70)	

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in lipid profile parameter of total cholesterol at Week 52 for treatment arms who started study intervention from Day 1 (Asia Cohort)

End point title	Change from Baseline in lipid profile parameter of total cholesterol at Week 52 for treatment arms who started study intervention from Day 1 (Asia Cohort)[212]

End point description:

Blood samples were collected for the assessment of lipid profile of total cholesterol levels. Baseline was defined as the latest pre-dose assessment with a non-missing value, including those from unscheduled visits. Change from Baseline was calculated by subtracting the post dose visit value from the Baseline value. The analysis was performed on the Safety Set participants who received study intervention from Day 01 to Week 52. Only those participants with data available at the specified data points were analyzed.

End point type	Secondary

End point timeframe:

Baseline (Day 1) and Week 52

Notes:

[212] - 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: The endpoints are different for the different parts of the study.

End point values	GSK3196165 90mg + csDMARD (Asia Cohort)	GSK3196165 150mg + csDMARD (Asia Cohort)	Tofacitinib 5mg + csDMARD (Asia Cohort)	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	29	29	16	
Units: Millimoles per liter (mmol/L)				
arithmetic mean (standard deviation)	-0.166 (± 0.8128)	0.146 (± 0.5227)	0.743 (± 0.7569)	

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in lipid profile parameter of total cholesterol at Week 52 for placebo switched arms (Asia Cohort)

End point title	Change from Baseline in lipid profile parameter of total cholesterol at Week 52 for placebo switched arms (Asia Cohort)[213]

End point description:

Blood samples were collected for the assessment of lipid profile of total cholesterol levels. Baseline was defined as the latest pre-dose assessment with a non-missing value, including those from unscheduled visits. Change from Baseline was calculated by subtracting the post dose visit value from the Baseline value. For safety assessments baseline is interpreted as Week 12. The analysis was performed on Safety Set participants who switched from placebo to study intervention at Week 12. Only those participants with data available at the indicated timepoints were analyzed.

End point type	Secondary

End point timeframe:

Baseline (Week 12) and Week 52

Notes:

[213] - 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: The endpoints are different for the different parts of the study.

End point values	Placebo + csDMARD and GSK3196165 90mg + csDMARD (Asia Cohort)	Placebo + csDMARD and GSK3196165 150mg + csDMARD (Asia Cohort)	Placebo + csDMARD and Tofacitinib 5mg + csDMARD (Asia Cohort)	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	4	5	5	
Units: Millimoles per liter (mmol/L)				
arithmetic mean (standard deviation)	0.085 (± 0.4905)	0.318 (± 1.4969)	0.816 (± 0.5924)	

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in lipid profile parameter of total cholesterol at Week 24 for placebo switched arms (Asia Cohort)

End point title	Change from Baseline in lipid profile parameter of total cholesterol at Week 24 for placebo switched arms (Asia Cohort)[214]

End point description:

Blood samples were collected for the assessment of lipid profile of total cholesterol levels. Baseline was defined as the latest pre-dose assessment with a non-missing value, including those from unscheduled visits. Change from Baseline was calculated by subtracting the post dose visit value from the Baseline value. Blood samples were collected at indicated time points per schedule of assessment in protocol. Objectives and Endpoints section incorrectly states that Change from baseline in key laboratory parameters at Week 24 was a secondary objective, however for lipid panel, there is no corresponding time point in schedule of assessment. Consequently, the objective that can be assessed for the lipid panel is Week 16 and not Week 24 as no data collected. Week 16 is not pre-specified time point to report.

End point type	Secondary

End point timeframe:

Baseline (Week 12) and Week 24

Notes:

[214] - 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: The endpoints are different for the different parts of the study.

End point values	Placebo + csDMARD and GSK3196165 90mg + csDMARD (Asia Cohort)	Placebo + csDMARD and GSK3196165 150mg + csDMARD (Asia Cohort)	Placebo + csDMARD and Tofacitinib 5mg + csDMARD (Asia Cohort)	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	0[215]	0[216]	0[217]	
Units: Millimoles per liter (mmol/L)				
arithmetic mean (standard deviation)	()	()	()	

Notes:

[215] - Data was not collected as there is no corresponding time point in schedule of activity of Protocol.

[216] - Data was not collected as there is no corresponding time point in schedule of activity of Protocol.

[217] - Data was not collected as there is no corresponding time point in schedule of activity of Protocol.

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in lipid profile parameter of LDL cholesterol, high-density lipoprotein-cholesterol at Week 24 for placebo switched arms (Asia Cohort)

End point title	Change from Baseline in lipid profile parameter of LDL cholesterol, high-density lipoprotein-cholesterol at Week 24 for placebo switched arms (Asia Cohort)[218]

End point description:

Blood samples were collected for the assessment of fasting lipid profile including LDL cholesterol, HDL cholesterol levels. Baseline was defined as the latest pre-dose assessment with a non-missing value, including those from unscheduled visits. Change from Baseline was calculated by subtracting the post dose visit value from the Baseline value. For safety assessments baseline is interpreted as Week 12. Blood samples were collected at indicated time points per schedule of assessment in protocol. Objectives and Endpoints section incorrectly states that Change from baseline in key laboratory parameters at Week 24 was a secondary objective, however for lipid panel, there is no corresponding time point in schedule of assessment. Consequently, the objective that can be assessed for the lipid panel is Week 16 and not Week 24 as no data collected. Week 16 is not pre-specified time point to report.

End point type	Secondary

End point timeframe:

Baseline (Week 12) and Week 24

Notes:

[218] - 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: The endpoints are different for the different parts of the study.

End point values	Placebo + csDMARD and GSK3196165 90mg + csDMARD (Asia Cohort)	Placebo + csDMARD and GSK3196165 150mg + csDMARD (Asia Cohort)	Placebo + csDMARD and Tofacitinib 5mg + csDMARD (Asia Cohort)	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	0[219]	0[220]	0[221]	
Units: Millimoles per liter (mmol/L)				
arithmetic mean (standard deviation)	()	()	()	

Notes:

[219] - Data was not collected as there is no corresponding time point in schedule of activity of Protocol.

[220] - Data was not collected as there is no corresponding time point in schedule of activity of Protocol.

[221] - Data was not collected as there is no corresponding time point in schedule of activity of Protocol.

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in lipid profile parameter of LDL cholesterol, high-density lipoprotein-cholesterol at Week 24 for treatment arms who started study intervention from Day 1 (Asia Cohort)

End point title	Change from Baseline in lipid profile parameter of LDL cholesterol, high-density lipoprotein-cholesterol at Week 24 for treatment arms who started study intervention from Day 1 (Asia Cohort)[222]

End point description:

Blood samples were collected for the assessment of fasting lipid profile including LDL cholesterol, HDL cholesterol levels. Baseline was defined as the latest pre-dose assessment with a non-missing value, including those from unscheduled visits. Change from Baseline was calculated by subtracting the post dose visit value from the Baseline value. Blood samples were collected at indicated time points per schedule of assessment in protocol. Objectives and Endpoints section incorrectly states that Change from baseline in key laboratory parameters at Week 24 was a secondary objective, however for lipid

panel, there is no corresponding time point in schedule of assessment. Consequently, the objective that can be assessed for the lipid panel is Week 16 and not Week 24 as no data collected. Week 16 is not pre-specified time point to report.

End point type	Secondary

End point timeframe:

Baseline (Day 1) and Week 24

Notes:

[222] - 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: The endpoints are different for the different parts of the study.

End point values	GSK3196165 90mg + csDMARD (Asia Cohort)	GSK3196165 150mg + csDMARD (Asia Cohort)	Tofacitinib 5mg + csDMARD (Asia Cohort)	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	0[223]	0[224]	0[225]	
Units: Millimoles per liter (mmol/L)				
arithmetic mean (standard deviation)	()	()	()	

Notes:

[223] - Data was not collected as there is no corresponding time point in schedule of activity of Protocol.

[224] - Data was not collected as there is no corresponding time point in schedule of activity of Protocol.

[225] - Data was not collected as there is no corresponding time point in schedule of activity of Protocol.

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in lipid profile parameter of low-density lipoprotein (LDL) cholesterol, high-density lipoprotein-cholesterol at Week 12 (Asia Cohort)

End point title	Change from Baseline in lipid profile parameter of low-density lipoprotein (LDL) cholesterol, high-density lipoprotein-cholesterol at Week 12 (Asia Cohort)[226]

End point description:

Blood samples were collected for assessment of fasting lipid profile including LDL cholesterol, HDL cholesterol levels. Baseline was defined as latest pre-dose assessment with a non-missing value, including those from unscheduled visits. Change from Baseline was calculated by subtracting post dose visit value from Baseline value. For purpose of all analyses up to week 12, placebo arms were pooled into a single placebo arm to primarily serve as a reference for the comparison of active treatment arms. Blood samples were collected at indicated time points per schedule of assessment in protocol. Objectives and Endpoints section incorrectly states that Change from baseline in key laboratory parameters at Week 12 was a secondary objective, however for lipid panel, there is no corresponding time point in schedule of assessment. Consequently, the objective that can be assessed for lipid panel is Week 4 and not Week 12 as no data collected. Week 4 is not pre-specified time point to report.

End point type	Secondary

End point timeframe:

Baseline (Day 1) and Week 12

Notes:

[226] - 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: The endpoints are different for the different parts of the study.

End point values	GSK3196165 90mg + csDMARD (Asia Cohort)	GSK3196165 150mg + csDMARD (Asia Cohort)	Tofacitinib 5mg + csDMARD (Asia Cohort)	Pooled Placebo (Asia Cohort)
Subject group type	Reporting group	Reporting group	Reporting group	Subject analysis set
Number of subjects analysed	0[227]	0[228]	0[229]	0[230]
Units: Millimoles per liter (mmol/L)				
arithmetic mean (standard deviation)	()	()	()	()

Notes:

[227] - Data was not collected as there is no corresponding time point in schedule of activity of Protocol.

[228] - Data was not collected as there is no corresponding time point in schedule of activity of Protocol.

[229] - Data was not collected as there is no corresponding time point in schedule of activity of Protocol.

[230] - Data was not collected as there is no corresponding time point in schedule of activity of Protocol.

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in lipid profile parameter of LDL cholesterol, high-density lipoprotein-cholesterol at Week 52 for treatment arms who started study intervention from Day 1 (Asia Cohort)

End point title	Change from Baseline in lipid profile parameter of LDL cholesterol, high-density lipoprotein-cholesterol at Week 52 for treatment arms who started study intervention from Day 1 (Asia Cohort)[231]

End point description:

Blood samples were collected for the assessment of fasting lipid profile including LDL cholesterol, HDL cholesterol levels. Baseline was defined as the latest pre-dose assessment with a non-missing value, including those from unscheduled visits. Change from Baseline was calculated by subtracting the post dose visit value from the Baseline value. The analysis was performed on the Safety Set participants who received study intervention from Day 01 to Week 52. Only those participants with data available at the specified data points were analyzed.

End point type	Secondary

End point timeframe:

Baseline (Day 1) and Week 52

Notes:

[231] - 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: The endpoints are different for the different parts of the study.

End point values	GSK3196165 90mg + csDMARD (Asia Cohort)	GSK3196165 150mg + csDMARD (Asia Cohort)	Tofacitinib 5mg + csDMARD (Asia Cohort)	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	29	29	16	
Units: Millimoles per liter (mmol/L)				
arithmetic mean (standard deviation)				
LDL Cholesterol, n=28,29,16	-0.258 (± 0.7697)	0.076 (± 0.4614)	0.334 (± 0.4170)	
HDL Cholesterol, n=29,29,16	-0.044 (± 0.2490)	-0.012 (± 0.2779)	0.146 (± 0.3082)	

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in lipid profile parameter of LDL cholesterol, high-density lipoprotein-cholesterol at Week 52 for placebo switched arms (Asia Cohort)

End point title	Change from Baseline in lipid profile parameter of LDL cholesterol, high-density lipoprotein-cholesterol at Week 52 for placebo switched arms (Asia Cohort)[232]

End point description:

Blood samples were collected for the assessment of fasting lipid profile including LDL cholesterol, HDL cholesterol levels. Baseline was defined as the latest pre-dose assessment with a non-missing value, including those from unscheduled visits. Change from Baseline was calculated by subtracting the post dose visit value from the Baseline value. For safety assessments baseline is interpreted as Week 12. The analysis was performed on Safety Set participants who switched from placebo to study intervention at Week 12. Only those participants with data available at the indicated timepoints were analyzed.

End point type	Secondary

End point timeframe:

Baseline (Week 12) and Week 52

Notes:

[232] - 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: The endpoints are different for the different parts of the study.

End point values	Placebo + csDMARD and GSK3196165 90mg + csDMARD (Asia Cohort)	Placebo + csDMARD and GSK3196165 150mg + csDMARD (Asia Cohort)	Placebo + csDMARD and Tofacitinib 5mg + csDMARD (Asia Cohort)	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	4	5	5	
Units: Millimoles per liter (mmol/L)				
arithmetic mean (standard deviation)				
LDL Cholesterol, n=4,5,5	0.218 (± 0.5604)	0.094 (± 1.2936)	0.438 (± 0.4544)	
HDL Cholesterol, n=4,5,5,	0.000 (± 0.1089)	0.042 (± 0.2400)	0.226 (± 0.2204)	

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in lipid profile parameter of triglycerides at Week 24 for placebo switched arms (Asia Cohort)

End point title	Change from Baseline in lipid profile parameter of triglycerides at Week 24 for placebo switched arms (Asia Cohort)[233]

End point description:

Blood samples was collected for the assessment of change from baseline in fasting lipid profile triglycerides levels. Baseline was defined as the latest pre-dose assessment with a non-missing value, including those from unscheduled visits. Change from Baseline was calculated by subtracting the post dose visit value from the Baseline value. Blood samples were collected at indicated time points per schedule of assessment in protocol. Objectives and Endpoints section incorrectly states that Change from baseline in key laboratory parameters at Week 24 was a secondary objective, however for lipid panel, there is no corresponding time point in schedule of assessment. Consequently, the objective that can be assessed for the lipid panel is Week 16 and not Week 24 as no data collected. Week 16 is not

pre-specified time point to report.

End point type	Secondary

End point timeframe:

Baseline (Week 12) and Week 24

Notes:

[233] - 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: The endpoints are different for the different parts of the study.

End point values	Placebo + csDMARD and GSK3196165 90mg + csDMARD (Asia Cohort)	Placebo + csDMARD and GSK3196165 150mg + csDMARD (Asia Cohort)	Placebo + csDMARD and Tofacitinib 5mg + csDMARD (Asia Cohort)	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	0[234]	0[235]	0[236]	
Units: Millimoles per liter (mmol/L)				
arithmetic mean (standard deviation)	()	()	()	

Notes:

[234] - Data was not collected as there is no corresponding time point in schedule of activity of Protocol.

[235] - Data was not collected as there is no corresponding time point in schedule of activity of Protocol.

[236] - Data was not collected as there is no corresponding time point in schedule of activity of Protocol.

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in lipid profile parameter of triglycerides at Week 24 for treatment arms who started study intervention from Day 1 (Asia Cohort)

End point title	Change from Baseline in lipid profile parameter of triglycerides at Week 24 for treatment arms who started study intervention from Day 1 (Asia Cohort)[237]

End point description:

Blood samples was collected for the assessment of change from baseline in fasting lipid profile triglycerides levels. Baseline was defined as the latest pre-dose assessment with a non-missing value, including those from unscheduled visits. Change from Baseline was calculated by subtracting the post dose visit value from the Baseline value. Blood samples were collected at indicated time points per schedule of assessment in protocol. Objectives and Endpoints section incorrectly states that Change from baseline in key laboratory parameters at Week 24 was a secondary objective, however for lipid panel, there is no corresponding time point in schedule of assessment. Consequently, the objective that can be assessed for the lipid panel is Week 16 and not Week 24 as no data collected. Week 16 is not pre-specified time point to report.

End point type	Secondary

End point timeframe:

Baseline (Day 1) and Week 24

Notes:

[237] - 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: The endpoints are different for the different parts of the study.

End point values	GSK3196165 90mg + csDMARD (Asia Cohort)	GSK3196165 150mg + csDMARD (Asia Cohort)	Tofacitinib 5mg + csDMARD (Asia Cohort)	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	0[238]	0[239]	0[240]	
Units: Millimoles per liter (mmol/L)				
arithmetic mean (standard deviation)	()	()	()	

Notes:

[238] - Data was not collected as there is no corresponding time point in schedule of activity of Protocol.

[239] - Data was not collected as there is no corresponding time point in schedule of activity of Protocol.

[240] - Data was not collected as there is no corresponding time point in schedule of activity of Protocol.

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in lipid profile parameter of triglycerides at Week 12 (Asia Cohort)

End point title	Change from Baseline in lipid profile parameter of triglycerides at Week 12 (Asia Cohort)[241]

End point description:

Blood samples was collected for the assessment of fasting lipid profile triglycerides levels. Baseline was defined as the latest pre-dose assessment with a non-missing value, including those from unscheduled visits. Change from Baseline was calculated by subtracting the post dose visit value from the Baseline value. For the purpose of all analyses up to week 12, the placebo arms were pooled into a single placebo arm to primarily serve as a reference for the comparison of active treatment arms. Blood samples were collected at indicated time points per schedule of assessment in protocol. Objectives and Endpoints section incorrectly states that Change from baseline in key laboratory parameters at Week 12 was a secondary objective, however for lipid panel, there is no corresponding time point in schedule of assessment. Consequently, the objective that can be assessed for the lipid panel is Week 4 and not Week 12 as no data collected. Week 4 is not pre-specified time point to report.

End point type	Secondary

End point timeframe:

Baseline (Day 1) and Week 12

Notes:

[241] - 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: The endpoints are different for the different parts of the study.

End point values	GSK3196165 90mg + csDMARD (Asia Cohort)	GSK3196165 150mg + csDMARD (Asia Cohort)	Tofacitinib 5mg + csDMARD (Asia Cohort)	Pooled Placebo (Asia Cohort)
Subject group type	Reporting group	Reporting group	Reporting group	Subject analysis set
Number of subjects analysed	0[242]	0[243]	0[244]	0[245]
Units: Millimoles per liter (mmol/L)				
arithmetic mean (standard deviation)	()	()	()	()

Notes:

[242] - Data was not collected as there is no corresponding time point in schedule of activity of Protocol.

[243] - Data was not collected as there is no corresponding time point in schedule of activity of Protocol.

[244] - Data was not collected as there is no corresponding time point in schedule of activity of Protocol.

[245] - Data was not collected as there is no corresponding time point in schedule of activity of Protocol.

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in lipid profile parameter of triglycerides at Week 52 for treatment arms who started study intervention from Day 1 (Asia Cohort)

End point title	Change from Baseline in lipid profile parameter of triglycerides at Week 52 for treatment arms who started study intervention from Day 1 (Asia Cohort)[246]

End point description:

Blood samples was collected for the assessment of change from baseline in fasting lipid profile triglycerides levels. Baseline was defined as the latest pre-dose assessment with a non-missing value, including those from unscheduled visits. Change from Baseline was calculated by subtracting the post dose visit value from the Baseline value. The analysis was performed on Safety Set participants who switched from placebo to study intervention at Week 12. Only those participants with data available at the indicated timepoints were analyzed.

End point type	Secondary

End point timeframe:

Baseline (Day 1) and Week 52

Notes:

[246] - 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: The endpoints are different for the different parts of the study.

End point values	GSK3196165 90mg + csDMARD (Asia Cohort)	GSK3196165 150mg + csDMARD (Asia Cohort)	Tofacitinib 5mg + csDMARD (Asia Cohort)	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	29	29	16	
Units: Millimoles per liter (mmol/L)				
arithmetic mean (standard deviation)	0.443 (± 1.4807)	0.180 (± 0.4439)	0.345 (± 0.6262)	

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in lipid profile parameter of triglycerides at Week 52 for placebo switched arms (Asia Cohort)

End point title	Change from Baseline in lipid profile parameter of triglycerides at Week 52 for placebo switched arms (Asia Cohort)[247]

End point description:

Blood samples was collected for the assessment of change from baseline in fasting lipid profile triglycerides levels. Baseline was defined as the latest pre-dose assessment with a non-missing value, including those from unscheduled visits. Change from Baseline was calculated by subtracting the post dose visit value from the Baseline value. For safety assessments baseline is interpreted as Week 12. The analysis was performed on Safety Set participants who switched from placebo to study intervention at Week 12. Only those participants with data available at the indicated timepoints were analyzed.

End point type	Secondary

End point timeframe:

Baseline (Week 12) and Week 52

Notes:

[247] - 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: The endpoints are different for the different parts of the study.

End point values	Placebo + csDMARD and GSK3196165 90mg + csDMARD (Asia Cohort)	Placebo + csDMARD and GSK3196165 150mg + csDMARD (Asia Cohort)	Placebo + csDMARD and Tofacitinib 5mg + csDMARD (Asia Cohort)	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	4	5	5	
Units: Millimoles per liter (mmol/L)				
arithmetic mean (standard deviation)	-0.288 (± 0.7348)	0.398 (± 0.6266)	0.328 (± 0.5965)	

Statistical analyses

No statistical analyses for this end point

Secondary: Number of participants with National Cancer Institute-Common terminology criteria for adverse events (NCI-CTCAE)>=Grade 3 hematological/clinical chemistry abnormalities (Asia Cohort)

End point title	Number of participants with National Cancer Institute-Common terminology criteria for adverse events (NCI-CTCAE)>=Grade 3 hematological/clinical chemistry abnormalities (Asia Cohort)[248]

End point description:

Number of participants with NCI-CTCAE >=Grade 3 hematological/clinical chemistry abnormalities were summarized. Hematological and Clinical chemistry parameters were summarized according to the NCI-CTCAE, version 5.0: Grade 1: mild; Grade 2: moderate; Grade 3: severe; Grade 4: life-threatening or disabling. Higher grade indicates more severity. Data is presented for only those parameters for which participants had worst case >=Grade 3 shifts from Baseline. The analysis was performed on the Safety Set that includes all randomized participants who received at least one dose of study treatment. Pooled Placebo collected data till Week 12. Placebo switched arms collected data from Week 12 to 59. Experimental arm collected data from Day 01 to Week 59.

End point type	Secondary

End point timeframe:

Up to Week 59

Notes:

[248] - 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: The endpoints are different for the different parts of the study.

End point values	GSK3196165 90mg + csDMARD (Asia Cohort)	GSK3196165 150mg + csDMARD (Asia Cohort)	Tofacitinib 5mg + csDMARD (Asia Cohort)	Placebo + csDMARD and GSK3196165 90mg + csDMARD (Asia Cohort)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	47	49	19	6
Units: Participants				
Cholesterol - high, Total, Grade 3	1	0	0	0
Lymphocyte count decreased, Total, Grade 3	1	1	2	0

Hypertriglyceridemia, Total, Grade 3	1	1	1	0

End point values	Placebo + csDMARD and GSK3196165 150mg + csDMARD (Asia Cohort)	Placebo + csDMARD and Tofacitinib 5mg + csDMARD (Asia Cohort)	Pooled Placebo (Asia Cohort)	
Subject group type	Reporting group	Reporting group	Subject analysis set	
Number of subjects analysed	8	8	23	
Units: Participants				
Cholesterol - high, Total, Grade 3	0	0	0	
Lymphocyte count decreased, Total, Grade 3	0	0	0	
Hypertriglyceridemia, Total, Grade 3	0	0	0	

Statistical analyses

No statistical analyses for this end point

Secondary: Concentrations of Granulocyte-macrophage colony stimulating factor (GM-CSF) autoantibody (Asia Cohort)

End point title	Concentrations of Granulocyte-macrophage colony stimulating factor (GM-CSF) autoantibody (Asia Cohort)[249]

End point description:

Blood samples were collected for markers which may influence rheumatoid arthritis. Concentrations of GM-CSF autoantibodies was determined. The analysis was performed on the Safety Set. Only those participants with data available at the specified time points were analyzed.

End point type	Secondary

End point timeframe:

At baseline

Notes:

[249] - 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: The endpoints are different for the different parts of the study.

End point values	GSK3196165 90mg + csDMARD (Asia Cohort)	GSK3196165 150mg + csDMARD (Asia Cohort)	Tofacitinib 5mg + csDMARD (Asia Cohort)	Placebo + csDMARD and GSK3196165 90mg + csDMARD (Asia Cohort)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	1[250]	0[251]	0[252]	0[253]
Units: Microgram per liter (ug/L)				
arithmetic mean (standard deviation)	526.0 (± 0)	()	()	()

Notes:

[250] - Standard Deviation was not derived as only one participant was analyzed.

[251] - No participants were analyzed at the timepoint.

[252] - No participants were analyzed at the timepoint.

[253] - No participants were analyzed at the timepoint.

End point values	Placebo + csDMARD and GSK3196165 150mg + csDMARD (Asia Cohort)	Placebo + csDMARD and Tofacitinib 5mg + csDMARD (Asia Cohort)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	0[254]	0[255]		
Units: Microgram per liter (ug/L)				
arithmetic mean (standard deviation)	()	()		

Notes:

[254] - No participants were analyzed at the timepoint.

[255] - No participants were analyzed at the timepoint.

Statistical analyses

No statistical analyses for this end point

Secondary: Number of participants with anti-GSK3196165 antibodies (Asia Cohort)

End point title	Number of participants with anti-GSK3196165 antibodies (Asia Cohort)[256]

End point description:

Serum samples were collected for the determination of anti- GSK3196165 antibodies (ADA) using a validated electrochemiluminescence (ECL) immunoassay. The assay involved screening, confirmation and titration steps. If serum samples tested positive in the screening assay, they were considered 'potentially positive' and were further analyzed for the specificity using the confirmation assay. Samples that confirmed positive in the confirmation assay were reported as 'positive'. Confirmed positive ADA samples were further characterized in the titration assay to quasi-quantitate the amount of ADA in the sample. Additionally, confirmed positive ADA samples were also tested in a validated neutralizing antibody assay to determine the potential neutralizing activity of the ADA.

End point type	Secondary

End point timeframe:

Up to Week 59

Notes:

[256] - 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: The endpoints are different for the different parts of the study.

End point values	GSK3196165 90mg + csDMARD (Asia Cohort)	GSK3196165 150mg + csDMARD (Asia Cohort)	Tofacitinib 5mg + csDMARD (Asia Cohort)	Placebo + csDMARD and GSK3196165 90mg + csDMARD (Asia Cohort)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	47	49	19	6
Units: Participants	0	0	0	0

End point values	Placebo + csDMARD and GSK3196165	Placebo + csDMARD and Tofacitinib 5mg		

	150mg + csDMARD (Asia Cohort)	+ csDMARD (Asia Cohort)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	8	9		
Units: Participants	0	0		

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) for placebo switched arms (Global Cohort)

End point title	Number of participants with adverse events (AEs), serious adverse events (SAEs) and adverse events of special interest (AESI) for placebo switched arms (Global Cohort)[257]

End point description:

An AE is any untoward medical occurrence in a clinical study participant, temporally associated with the use of a study intervention, whether or not considered related to the study intervention. A SAE is any untoward medical occurrence that, is life-threatening, requires inpatient hospitalization or prolongation of existing hospitalization, results in persistent disability/incapacity and/or can result in death. The analysis was performed on Safety Set of switched arms that collected data from Week 12 to 59.

End point type	Secondary

End point timeframe:

Week 12 to Week 59

Notes:

[257] - 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: The endpoints are different for the different parts of the study.

End point values	Placebo+csDMARD and GSK3196165 90mg+csDMARD (Global Cohort)	Placebo +csDMARD and GSK3196165 150mg +csDMARD (Global Cohort)	Placebo +csDMARD and Tofacitinib 5mg +csDMARD (Global Cohort)	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	85	80	67	
Units: Participants				
Participants with AE	54	52	45	
Participants with SAE	5	3	2	
Participants with AESI	6	12	3	

Statistical analyses

No statistical analyses for this end point

Secondary: Number of participants with National Cancer Institute-Common terminology criteria for adverse events (NCI-CTCAE)>=Grade 3 hematological/clinical chemistry abnormalities for placebo switched arms (Global

Cohort)

End point title	Number of participants with National Cancer Institute-Common terminology criteria for adverse events (NCI-CTCAE)>=Grade 3 hematological/clinical chemistry abnormalities for placebo switched arms (Global Cohort)[258]

End point description:

Number of participants with NCI-CTCAE >=Grade 3 hematological/clinical chemistry abnormalities were summarized. Hematological and Clinical chemistry parameters were summarized according to the NCI-CTCAE, version 5.0: Grade 1: mild; Grade 2: moderate; Grade 3: severe; Grade 4: life-threatening or disabling. Higher grade indicates more severity. Data is presented for only those parameters for which participants had worst case >=Grade 3 shifts from Baseline. The analysis was performed on Safety Set of switched arms that collected data from Week 12 to 59.

End point type	Secondary

End point timeframe:

Week 12 to Week 59

Notes:

[258] - 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: The endpoints are different for the different parts of the study.

End point values	Placebo+csDMARD and GSK3196165 90mg+csDMARD (Global Cohort)	Placebo +csDMARD and GSK3196165 150mg +csDMARD (Global Cohort)	Placebo +csDMARD and Tofacitinib 5mg +csDMARD (Global Cohort)	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	85	80	67	
Units: Participants				
Anemia, Total, Grade 3	0	2	1	
Lymphocyte count decreased, Grade 3	1	0	2	
Neutrophil count decreased, Total, Grade 3	0	1	0	
Lymphocyte count decreased, Grade 4	0	0	1	
Hypertriglyceridemia, Total, Grade 3	0	1	0	

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) for placebo switched arms (Asia Cohort)

End point title	Number of participants with adverse events (AEs), serious adverse events (SAEs) and adverse events of special interest (AESI) for placebo switched arms (Asia Cohort)[259]

End point description:

An AE is any untoward medical occurrence in a clinical study participant, temporally associated with the use of a study intervention, whether or not considered related to the study intervention. A SAE is any untoward medical occurrence that, is life-threatening, requires inpatient hospitalization or prolongation of existing hospitalization, results in persistent disability/incapacity and/or can result in death. The analysis was performed on Safety Set of switched arms that collected data from Week 12 to 59.

End point type	Secondary

End point timeframe:

Week 12 to Week 59

Notes:

[259] - 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: The endpoints are different for the different parts of the study.

End point values	Placebo + csDMARD and GSK3196165 90mg + csDMARD (Asia Cohort)	Placebo + csDMARD and GSK3196165 150mg + csDMARD (Asia Cohort)	Placebo + csDMARD and Tofacitinib 5mg + csDMARD (Asia Cohort)	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	6	8	8	
Units: Participants				
Participants with AE	6	5	7	
Participants with SAE	0	1	0	
Participants with AESI	0	0	0	

Statistical analyses

No statistical analyses for this end point

Secondary: Number of participants with National Cancer Institute-Common terminology criteria for adverse events (NCI-CTCAE)>=Grade 3 hematological/clinical chemistry abnormalities for placebo switched arms (Asia Cohort)

End point title	Number of participants with National Cancer Institute-Common terminology criteria for adverse events (NCI-CTCAE)>=Grade 3 hematological/clinical chemistry abnormalities for placebo switched arms (Asia Cohort)[260]

End point description:

Number of participants with NCI-CTCAE >=Grade 3 hematological/clinical chemistry abnormalities were summarized. Hematological and Clinical chemistry parameters were summarized according to the NCI-CTCAE, version 5.0: Grade 1: mild; Grade 2: moderate; Grade 3: severe; Grade 4: life-threatening or disabling. Higher grade indicates more severity. Data is presented for only those parameters for which participants had worst case >=Grade 3 shifts from Baseline. The analysis was performed on Safety Set of switched arms that collected data from Week 12 to 59.

End point type	Secondary

End point timeframe:

Week 12 to Week 59

Notes:

[260] - 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: The endpoints are different for the different parts of the study.

End point values	Placebo + csDMARD and GSK3196165 90mg + csDMARD (Asia Cohort)	Placebo + csDMARD and GSK3196165 150mg + csDMARD (Asia Cohort)	Placebo + csDMARD and Tofacitinib 5mg + csDMARD (Asia Cohort)	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	6	8	8	
Units: Participants				
Cholesterol - high, Total, Grade 3	0	0	0	
Lymphocyte count decreased, Total, Grade 3	0	0	0	
Hypertriglyceridemia, Total, Grade 3	0	0	0	

Statistical analyses

No statistical analyses for this end point

Adverse events information

Timeframe for reporting adverse events:

For Global and Asia cohorts, Pooled Placebo arm collected during the timeframe Week 0 to Week 12. Placebo switched to active treatment arms collected during the timeframe Week 12 to Week 59. Experimental arms collected during from Week 0 to Week 59.

Adverse event reporting additional description:

Fifteen participants in Placebo group received active treatment of Tofacitinib mistakenly from Week 4 instead of Week 12 as planned. They were added with the Tofacitinib arm in safety analysis.

Assessment type	Systematic

Dictionary used

Dictionary name	v25.0
Dictionary version	25.0

Reporting groups

Reporting group title	GSK3196165 90mg + csDMARD (Global Cohort)

Reporting group description:

Participants in Global Cohort received GSK3196165 90 mg subcutaneous (SC) injection once weekly for 52 weeks in combination with conventional synthetic disease-modifying antirheumatic drugs (csDMARD).

Reporting group title	GSK3196165 150mg + csDMARD (Global Cohort)

Reporting group description:

Participants in Global Cohort received GSK3196165 150 mg subcutaneous (SC) injection once weekly for 52 weeks in combination with csDMARD.

Reporting group title	Tofacitinib 5mg + csDMARD (Global Cohort)

Reporting group description:

Participants in Global Cohort received Tofacitinib 5mg capsule, orally, twice daily (BID) in combination with csDMARD plus placebo injection weekly to maintain the blind for 52 weeks

Reporting group title	Pooled Placebo (Global Cohort)

Reporting group description:

Participants received Placebo weekly SC injection in combination with csDMARD until Week 12. The placebo arms are pooled into a single placebo arm.

Reporting group title	Placebo+csDMARD and GSK3196165 90mg+csDMARD (Global Cohort)

Reporting group description:

Participants in Global Cohort received Placebo weekly SC injection in combination with csDMARD for 12 weeks. At week 12, participants were switched from placebo to GSK3196165 90 mg, SC injection, once weekly in combination with csDMARD until 52 weeks

Reporting group title	Placebo +csDMARD and GSK3196165 150mg +csDMARD (Global Cohort)

Reporting group description:

Participants in Global Cohort received Placebo weekly SC injection in combination with csDMARD for 12 weeks. At week 12, participants were switched from placebo to GSK3196165 150 mg, SC injection, once weekly in combination with csDMARD until 52 weeks

Reporting group title	Placebo +csDMARD and Tofacitinib 5mg +csDMARD (Global Cohort)

Reporting group description:

Participants in Global Cohort received Placebo capsule BID in combination with csDMARD for 12 weeks. At week 12, participants were switched from placebo capsule to Tofacitinib 5mg, capsule, orally, BID in combination with csDMARD plus placebo injection to maintain the blind for 52 weeks.

Reporting group title	GSK3196165 90mg + csDMARD (Asia Cohort)

Reporting group description:

Participants in Asia Cohort received GSK3196165 90 mg subcutaneous (SC) injection once weekly for 52 weeks in combination with csDMARD.

Reporting group title	GSK3196165 150mg + csDMARD (Asia Cohort)

Reporting group description:

Participants in Asia Cohort received GSK3196165 150 mg subcutaneous (SC) injection once weekly for 52 weeks in combination with csDMARD.

Reporting group title	Tofacitinib 5mg + csDMARD (Asia Cohort)

Reporting group description:

Participants in Asia Cohort received Tofacitinib 5mg capsule, orally, twice daily (BID) in combination with csDMARD plus placebo injection weekly to maintain the blind for 52 weeks

Reporting group title	Pooled Placebo (Asian Cohort)

Reporting group description:

Participants received Placebo weekly SC injection in combination with csDMARD until Week 12. The placebo arms are pooled into a single placebo arm.

Reporting group title	Placebo + csDMARD and GSK3196165 90mg + csDMARD (Asia Cohort)

Reporting group description:

Participants in Asia Cohort received Placebo weekly SC injection in combination with csDMARD for 12 weeks. At week 12, participants were switched from placebo to GSK3196165 90 mg, SC injection, once weekly in combination with csDMARD until 52 weeks

Reporting group title	Placebo + csDMARD and GSK3196165 150mg + csDMARD (Asia Cohort)

Reporting group description:

Participants in Asia Cohort received Placebo weekly SC injection in combination with csDMARD for 12 weeks. At week 12, participants were switched from placebo to GSK3196165 150 mg, SC injection, once weekly in combination with csDMARD until 52 weeks

Reporting group title	Placebo + csDMARD and Tofacitinib 5mg + csDMARD (Asia Cohort)

Reporting group description:

Participants in Asia Cohort received Placebo capsule BID in combination with csDMARD for 12 weeks. At week 12, participants were switched from placebo capsule to Tofacitinib 5mg, capsule, orally, BID in combination with csDMARD plus placebo injection to maintain the blind for 52 weeks.

Serious adverse events	GSK3196165 90mg + csDMARD (Global Cohort)	GSK3196165 150mg + csDMARD (Global Cohort)	Tofacitinib 5mg + csDMARD (Global Cohort)
Total subjects affected by serious adverse events			
subjects affected / exposed	44 / 545 (8.07%)	43 / 539 (7.98%)	31 / 286 (10.84%)
number of deaths (all causes)	5	6	2
number of deaths resulting from adverse events			
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Adenocarcinoma of colon			
subjects affected / exposed	0 / 545 (0.00%)	0 / 539 (0.00%)	1 / 286 (0.35%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Breast cancer			
subjects affected / exposed	0 / 545 (0.00%)	0 / 539 (0.00%)	1 / 286 (0.35%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac myxoma			

subjects affected / exposed	0 / 545 (0.00%)	1 / 539 (0.19%)	0 / 286 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastric cancer			
subjects affected / exposed	0 / 545 (0.00%)	1 / 539 (0.19%)	0 / 286 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Colorectal adenoma			
subjects affected / exposed	1 / 545 (0.18%)	0 / 539 (0.00%)	0 / 286 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Chronic lymphocytic leukaemia			
subjects affected / exposed	0 / 545 (0.00%)	0 / 539 (0.00%)	1 / 286 (0.35%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Invasive ductal breast carcinoma			
subjects affected / exposed	0 / 545 (0.00%)	1 / 539 (0.19%)	0 / 286 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Invasive lobular breast carcinoma			
subjects affected / exposed	0 / 545 (0.00%)	2 / 539 (0.37%)	0 / 286 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lung neoplasm			
subjects affected / exposed	1 / 545 (0.18%)	0 / 539 (0.00%)	0 / 286 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Metastases to liver			
subjects affected / exposed	0 / 545 (0.00%)	1 / 539 (0.19%)	0 / 286 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pancreatic carcinoma metastatic			

subjects affected / exposed	0 / 545 (0.00%)	0 / 539 (0.00%)	1 / 286 (0.35%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Rectal adenocarcinoma			
subjects affected / exposed	0 / 545 (0.00%)	0 / 539 (0.00%)	1 / 286 (0.35%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Transitional cell carcinoma			
subjects affected / exposed	0 / 545 (0.00%)	0 / 539 (0.00%)	0 / 286 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Uterine leiomyoma			
subjects affected / exposed	0 / 545 (0.00%)	0 / 539 (0.00%)	0 / 286 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vascular disorders			
Circulatory collapse			
subjects affected / exposed	0 / 545 (0.00%)	0 / 539 (0.00%)	0 / 286 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Deep vein thrombosis			
subjects affected / exposed	0 / 545 (0.00%)	1 / 539 (0.19%)	0 / 286 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General disorders and administration site conditions			
Death			
subjects affected / exposed	1 / 545 (0.18%)	0 / 539 (0.00%)	0 / 286 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Fatigue			
subjects affected / exposed	1 / 545 (0.18%)	0 / 539 (0.00%)	0 / 286 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Pyrexia			
subjects affected / exposed	0 / 545 (0.00%)	0 / 539 (0.00%)	1 / 286 (0.35%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Sudden death			
subjects affected / exposed	0 / 545 (0.00%)	1 / 539 (0.19%)	0 / 286 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
Immune system disorders			
Secondary amyloidosis			
subjects affected / exposed	0 / 545 (0.00%)	0 / 539 (0.00%)	1 / 286 (0.35%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Reproductive system and breast disorders			
Endometrial hyperplasia			
subjects affected / exposed	1 / 545 (0.18%)	0 / 539 (0.00%)	0 / 286 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hydrosalpinx			
subjects affected / exposed	1 / 545 (0.18%)	0 / 539 (0.00%)	0 / 286 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Menopausal symptoms			
subjects affected / exposed	0 / 545 (0.00%)	1 / 539 (0.19%)	0 / 286 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ovarian cyst			
subjects affected / exposed	1 / 545 (0.18%)	0 / 539 (0.00%)	0 / 286 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Uterine polyp			
subjects affected / exposed	1 / 545 (0.18%)	0 / 539 (0.00%)	0 / 286 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Endometriosis			
subjects affected / exposed	0 / 545 (0.00%)	0 / 539 (0.00%)	0 / 286 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Uterine cyst			
subjects affected / exposed	0 / 545 (0.00%)	0 / 539 (0.00%)	0 / 286 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			
Interstitial lung disease			
subjects affected / exposed	0 / 545 (0.00%)	0 / 539 (0.00%)	0 / 286 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pleural cyst			
subjects affected / exposed	0 / 545 (0.00%)	0 / 539 (0.00%)	0 / 286 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pulmonary embolism			
subjects affected / exposed	0 / 545 (0.00%)	2 / 539 (0.37%)	0 / 286 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pleural effusion			
subjects affected / exposed	0 / 545 (0.00%)	1 / 539 (0.19%)	0 / 286 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pulmonary fibrosis			
subjects affected / exposed	0 / 545 (0.00%)	1 / 539 (0.19%)	0 / 286 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Product issues			
Device dislocation			
subjects affected / exposed	1 / 545 (0.18%)	0 / 539 (0.00%)	0 / 286 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	0 / 545 (0.00%)	0 / 539 (0.00%)	0 / 286 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
International normalised ratio increased			
subjects affected / exposed	0 / 545 (0.00%)	0 / 539 (0.00%)	1 / 286 (0.35%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Transaminases increased			
subjects affected / exposed	0 / 545 (0.00%)	0 / 539 (0.00%)	0 / 286 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Injury, poisoning and procedural complications			
Ankle fracture			
subjects affected / exposed	1 / 545 (0.18%)	0 / 539 (0.00%)	1 / 286 (0.35%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Incisional hernia			
subjects affected / exposed	0 / 545 (0.00%)	1 / 539 (0.19%)	0 / 286 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Joint injury			
subjects affected / exposed	0 / 545 (0.00%)	1 / 539 (0.19%)	0 / 286 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Overdose			
subjects affected / exposed	0 / 545 (0.00%)	1 / 539 (0.19%)	0 / 286 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
Tendon rupture			

subjects affected / exposed	0 / 545 (0.00%)	0 / 539 (0.00%)	1 / 286 (0.35%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Spinal compression fracture			
subjects affected / exposed	0 / 545 (0.00%)	1 / 539 (0.19%)	1 / 286 (0.35%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Skin laceration			
subjects affected / exposed	1 / 545 (0.18%)	0 / 539 (0.00%)	0 / 286 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Tibia fracture			
subjects affected / exposed	0 / 545 (0.00%)	1 / 539 (0.19%)	0 / 286 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Wound dehiscence			
subjects affected / exposed	0 / 545 (0.00%)	1 / 539 (0.19%)	0 / 286 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Congenital, familial and genetic disorders			
Developmental hip dysplasia			
subjects affected / exposed	0 / 545 (0.00%)	0 / 539 (0.00%)	0 / 286 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac disorders			
Acute myocardial infarction			
subjects affected / exposed	2 / 545 (0.37%)	0 / 539 (0.00%)	0 / 286 (0.00%)
occurrences causally related to treatment / all	1 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Angina unstable			
subjects affected / exposed	0 / 545 (0.00%)	1 / 539 (0.19%)	0 / 286 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Atrial fibrillation			
subjects affected / exposed	1 / 545 (0.18%)	1 / 539 (0.19%)	0 / 286 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac arrest			
subjects affected / exposed	0 / 545 (0.00%)	0 / 539 (0.00%)	0 / 286 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Sinus node dysfunction			
subjects affected / exposed	1 / 545 (0.18%)	0 / 539 (0.00%)	0 / 286 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pericardial effusion			
subjects affected / exposed	0 / 545 (0.00%)	1 / 539 (0.19%)	0 / 286 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Myocardial infarction			
subjects affected / exposed	1 / 545 (0.18%)	0 / 539 (0.00%)	0 / 286 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nervous system disorders			
Cerebrovascular accident			
subjects affected / exposed	1 / 545 (0.18%)	0 / 539 (0.00%)	0 / 286 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cerebral infarction			
subjects affected / exposed	0 / 545 (0.00%)	1 / 539 (0.19%)	0 / 286 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Facial paralysis			
subjects affected / exposed	1 / 545 (0.18%)	0 / 539 (0.00%)	0 / 286 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ischaemic stroke			

subjects affected / exposed	0 / 545 (0.00%)	0 / 539 (0.00%)	1 / 286 (0.35%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Seizure			
subjects affected / exposed	0 / 545 (0.00%)	0 / 539 (0.00%)	1 / 286 (0.35%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Paraparesis			
subjects affected / exposed	0 / 545 (0.00%)	0 / 539 (0.00%)	1 / 286 (0.35%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Syncope			
subjects affected / exposed	0 / 545 (0.00%)	0 / 539 (0.00%)	1 / 286 (0.35%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Subarachnoid haemorrhage			
subjects affected / exposed	1 / 545 (0.18%)	1 / 539 (0.19%)	0 / 286 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 1	0 / 0
Transient ischaemic attack			
subjects affected / exposed	0 / 545 (0.00%)	0 / 539 (0.00%)	0 / 286 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lacunar infarction			
subjects affected / exposed	0 / 545 (0.00%)	0 / 539 (0.00%)	0 / 286 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	0 / 545 (0.00%)	1 / 539 (0.19%)	1 / 286 (0.35%)
occurrences causally related to treatment / all	0 / 0	0 / 1	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Iron deficiency anaemia			

subjects affected / exposed	1 / 545 (0.18%)	0 / 539 (0.00%)	1 / 286 (0.35%)
occurrences causally related to treatment / all	0 / 1	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Neutropenia			
subjects affected / exposed	0 / 545 (0.00%)	0 / 539 (0.00%)	0 / 286 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Eye disorders			
Glaucoma			
subjects affected / exposed	0 / 545 (0.00%)	0 / 539 (0.00%)	1 / 286 (0.35%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ulcerative keratitis			
subjects affected / exposed	1 / 545 (0.18%)	0 / 539 (0.00%)	0 / 286 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Acute abdomen			
subjects affected / exposed	1 / 545 (0.18%)	0 / 539 (0.00%)	0 / 286 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Duodenal ulcer			
subjects affected / exposed	0 / 545 (0.00%)	0 / 539 (0.00%)	0 / 286 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Duodenal ulcer perforation			
subjects affected / exposed	1 / 545 (0.18%)	0 / 539 (0.00%)	0 / 286 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Enteritis			
subjects affected / exposed	0 / 545 (0.00%)	1 / 539 (0.19%)	0 / 286 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Large intestine polyp			

subjects affected / exposed	0 / 545 (0.00%)	0 / 539 (0.00%)	0 / 286 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Inguinal hernia			
subjects affected / exposed	0 / 545 (0.00%)	0 / 539 (0.00%)	1 / 286 (0.35%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastric ulcer			
subjects affected / exposed	0 / 545 (0.00%)	0 / 539 (0.00%)	1 / 286 (0.35%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Peritoneal adhesions			
subjects affected / exposed	1 / 545 (0.18%)	0 / 539 (0.00%)	0 / 286 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Mesenteric cyst			
subjects affected / exposed	0 / 545 (0.00%)	1 / 539 (0.19%)	0 / 286 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatobiliary disorders			
Acute hepatic failure			
subjects affected / exposed	0 / 545 (0.00%)	1 / 539 (0.19%)	0 / 286 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
Bile duct stone			
subjects affected / exposed	1 / 545 (0.18%)	0 / 539 (0.00%)	0 / 286 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cholecystitis acute			
subjects affected / exposed	2 / 545 (0.37%)	0 / 539 (0.00%)	0 / 286 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cholelithiasis			

subjects affected / exposed	0 / 545 (0.00%)	0 / 539 (0.00%)	1 / 286 (0.35%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatic steatosis			
subjects affected / exposed	0 / 545 (0.00%)	0 / 539 (0.00%)	1 / 286 (0.35%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal and urinary disorders			
Calculus urinary			
subjects affected / exposed	0 / 545 (0.00%)	1 / 539 (0.19%)	0 / 286 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
IgA nephropathy			
subjects affected / exposed	0 / 545 (0.00%)	1 / 539 (0.19%)	0 / 286 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Musculoskeletal and connective tissue disorders			
Intervertebral disc degeneration			
subjects affected / exposed	0 / 545 (0.00%)	0 / 539 (0.00%)	1 / 286 (0.35%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Back pain			
subjects affected / exposed	0 / 545 (0.00%)	1 / 539 (0.19%)	0 / 286 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Joint destruction			
subjects affected / exposed	1 / 545 (0.18%)	0 / 539 (0.00%)	0 / 286 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lumbar spinal stenosis			
subjects affected / exposed	1 / 545 (0.18%)	0 / 539 (0.00%)	0 / 286 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Osteoporotic fracture			
subjects affected / exposed	0 / 545 (0.00%)	0 / 539 (0.00%)	1 / 286 (0.35%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Osteoarthritis			
subjects affected / exposed	4 / 545 (0.73%)	4 / 539 (0.74%)	1 / 286 (0.35%)
occurrences causally related to treatment / all	0 / 4	0 / 4	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Rheumatoid arthritis			
subjects affected / exposed	1 / 545 (0.18%)	2 / 539 (0.37%)	1 / 286 (0.35%)
occurrences causally related to treatment / all	0 / 1	0 / 2	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Spinal osteoarthritis			
subjects affected / exposed	0 / 545 (0.00%)	1 / 539 (0.19%)	0 / 286 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Synovial cyst			
subjects affected / exposed	0 / 545 (0.00%)	1 / 539 (0.19%)	0 / 286 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Synovitis			
subjects affected / exposed	0 / 545 (0.00%)	0 / 539 (0.00%)	0 / 286 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Tenosynovitis			
subjects affected / exposed	1 / 545 (0.18%)	0 / 539 (0.00%)	0 / 286 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Soft tissue disorder			
subjects affected / exposed	0 / 545 (0.00%)	0 / 539 (0.00%)	0 / 286 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			

COVID-19			
subjects affected / exposed	1 / 545 (0.18%)	2 / 539 (0.37%)	0 / 286 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Appendicitis			
subjects affected / exposed	0 / 545 (0.00%)	2 / 539 (0.37%)	0 / 286 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Escherichia sepsis			
subjects affected / exposed	0 / 545 (0.00%)	0 / 539 (0.00%)	1 / 286 (0.35%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Diverticulitis			
subjects affected / exposed	0 / 545 (0.00%)	1 / 539 (0.19%)	0 / 286 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
COVID-19 pneumonia			
subjects affected / exposed	5 / 545 (0.92%)	5 / 539 (0.93%)	7 / 286 (2.45%)
occurrences causally related to treatment / all	0 / 5	0 / 5	0 / 7
deaths causally related to treatment / all	0 / 1	0 / 2	0 / 1
Herpes simplex			
subjects affected / exposed	0 / 545 (0.00%)	1 / 539 (0.19%)	0 / 286 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Herpes zoster			
subjects affected / exposed	0 / 545 (0.00%)	1 / 539 (0.19%)	0 / 286 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lower respiratory tract infection			
subjects affected / exposed	0 / 545 (0.00%)	0 / 539 (0.00%)	0 / 286 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumocystis jirovecii pneumonia			

subjects affected / exposed	1 / 545 (0.18%)	0 / 539 (0.00%)	1 / 286 (0.35%)
occurrences causally related to treatment / all	1 / 1	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia			
subjects affected / exposed	2 / 545 (0.37%)	1 / 539 (0.19%)	2 / 286 (0.70%)
occurrences causally related to treatment / all	0 / 2	1 / 1	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia bacterial			
subjects affected / exposed	1 / 545 (0.18%)	0 / 539 (0.00%)	0 / 286 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pyelonephritis			
subjects affected / exposed	1 / 545 (0.18%)	0 / 539 (0.00%)	0 / 286 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Postoperative wound infection			
subjects affected / exposed	0 / 545 (0.00%)	0 / 539 (0.00%)	0 / 286 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Post procedural infection			
subjects affected / exposed	0 / 545 (0.00%)	1 / 539 (0.19%)	0 / 286 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pyelonephritis acute			
subjects affected / exposed	0 / 545 (0.00%)	0 / 539 (0.00%)	1 / 286 (0.35%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Sepsis			
subjects affected / exposed	1 / 545 (0.18%)	0 / 539 (0.00%)	0 / 286 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Septic shock			

subjects affected / exposed	0 / 545 (0.00%)	0 / 539 (0.00%)	1 / 286 (0.35%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Urinary tract infection			
subjects affected / exposed	0 / 545 (0.00%)	0 / 539 (0.00%)	0 / 286 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia cryptococcal			
subjects affected / exposed	0 / 545 (0.00%)	0 / 539 (0.00%)	0 / 286 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metabolism and nutrition disorders			
Dehydration			
subjects affected / exposed	1 / 545 (0.18%)	0 / 539 (0.00%)	0 / 286 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	Pooled Placebo (Global Cohort)	Placebo+csDMARD and GSK3196165 90mg+csDMARD (Global Cohort)	Placebo +csDMARD and GSK3196165 150mg +csDMARD (Global Cohort)
Total subjects affected by serious adverse events			
subjects affected / exposed	6 / 255 (2.35%)	5 / 85 (5.88%)	3 / 80 (3.75%)
number of deaths (all causes)	0	1	1
number of deaths resulting from adverse events			
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Adenocarcinoma of colon			
subjects affected / exposed	0 / 255 (0.00%)	0 / 85 (0.00%)	0 / 80 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Breast cancer			
subjects affected / exposed	0 / 255 (0.00%)	0 / 85 (0.00%)	0 / 80 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac myxoma			

subjects affected / exposed	0 / 255 (0.00%)	0 / 85 (0.00%)	0 / 80 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastric cancer			
subjects affected / exposed	0 / 255 (0.00%)	0 / 85 (0.00%)	0 / 80 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Colorectal adenoma			
subjects affected / exposed	1 / 255 (0.39%)	0 / 85 (0.00%)	0 / 80 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Chronic lymphocytic leukaemia			
subjects affected / exposed	0 / 255 (0.00%)	0 / 85 (0.00%)	0 / 80 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Invasive ductal breast carcinoma			
subjects affected / exposed	0 / 255 (0.00%)	0 / 85 (0.00%)	0 / 80 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Invasive lobular breast carcinoma			
subjects affected / exposed	0 / 255 (0.00%)	0 / 85 (0.00%)	0 / 80 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lung neoplasm			
subjects affected / exposed	0 / 255 (0.00%)	0 / 85 (0.00%)	0 / 80 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metastases to liver			
subjects affected / exposed	0 / 255 (0.00%)	0 / 85 (0.00%)	0 / 80 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pancreatic carcinoma metastatic			

subjects affected / exposed	0 / 255 (0.00%)	0 / 85 (0.00%)	0 / 80 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Rectal adenocarcinoma			
subjects affected / exposed	0 / 255 (0.00%)	0 / 85 (0.00%)	0 / 80 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Transitional cell carcinoma			
subjects affected / exposed	0 / 255 (0.00%)	0 / 85 (0.00%)	1 / 80 (1.25%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Uterine leiomyoma			
subjects affected / exposed	0 / 255 (0.00%)	0 / 85 (0.00%)	0 / 80 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vascular disorders			
Circulatory collapse			
subjects affected / exposed	0 / 255 (0.00%)	1 / 85 (1.18%)	0 / 80 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
Deep vein thrombosis			
subjects affected / exposed	0 / 255 (0.00%)	0 / 85 (0.00%)	0 / 80 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General disorders and administration site conditions			
Death			
subjects affected / exposed	0 / 255 (0.00%)	0 / 85 (0.00%)	0 / 80 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Fatigue			
subjects affected / exposed	0 / 255 (0.00%)	0 / 85 (0.00%)	0 / 80 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Pyrexia			
subjects affected / exposed	0 / 255 (0.00%)	0 / 85 (0.00%)	0 / 80 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Sudden death			
subjects affected / exposed	0 / 255 (0.00%)	0 / 85 (0.00%)	0 / 80 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Immune system disorders			
Secondary amyloidosis			
subjects affected / exposed	0 / 255 (0.00%)	0 / 85 (0.00%)	0 / 80 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Reproductive system and breast disorders			
Endometrial hyperplasia			
subjects affected / exposed	0 / 255 (0.00%)	0 / 85 (0.00%)	0 / 80 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hydrosalpinx			
subjects affected / exposed	0 / 255 (0.00%)	0 / 85 (0.00%)	0 / 80 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Menopausal symptoms			
subjects affected / exposed	0 / 255 (0.00%)	0 / 85 (0.00%)	0 / 80 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ovarian cyst			
subjects affected / exposed	0 / 255 (0.00%)	0 / 85 (0.00%)	0 / 80 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Uterine polyp			
subjects affected / exposed	0 / 255 (0.00%)	0 / 85 (0.00%)	0 / 80 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Endometriosis			
subjects affected / exposed	0 / 255 (0.00%)	0 / 85 (0.00%)	0 / 80 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Uterine cyst			
subjects affected / exposed	0 / 255 (0.00%)	0 / 85 (0.00%)	0 / 80 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			
Interstitial lung disease			
subjects affected / exposed	0 / 255 (0.00%)	1 / 85 (1.18%)	0 / 80 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pleural cyst			
subjects affected / exposed	0 / 255 (0.00%)	0 / 85 (0.00%)	1 / 80 (1.25%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pulmonary embolism			
subjects affected / exposed	0 / 255 (0.00%)	0 / 85 (0.00%)	0 / 80 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pleural effusion			
subjects affected / exposed	0 / 255 (0.00%)	0 / 85 (0.00%)	0 / 80 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pulmonary fibrosis			
subjects affected / exposed	0 / 255 (0.00%)	0 / 85 (0.00%)	0 / 80 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Product issues			
Device dislocation			
subjects affected / exposed	0 / 255 (0.00%)	0 / 85 (0.00%)	0 / 80 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	1 / 255 (0.39%)	0 / 85 (0.00%)	0 / 80 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
International normalised ratio increased			
subjects affected / exposed	0 / 255 (0.00%)	0 / 85 (0.00%)	0 / 80 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Transaminases increased			
subjects affected / exposed	1 / 255 (0.39%)	0 / 85 (0.00%)	0 / 80 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Injury, poisoning and procedural complications			
Ankle fracture			
subjects affected / exposed	0 / 255 (0.00%)	0 / 85 (0.00%)	0 / 80 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Incisional hernia			
subjects affected / exposed	0 / 255 (0.00%)	0 / 85 (0.00%)	0 / 80 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Joint injury			
subjects affected / exposed	0 / 255 (0.00%)	0 / 85 (0.00%)	0 / 80 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Overdose			
subjects affected / exposed	0 / 255 (0.00%)	0 / 85 (0.00%)	0 / 80 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Tendon rupture			

subjects affected / exposed	0 / 255 (0.00%)	0 / 85 (0.00%)	0 / 80 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Spinal compression fracture			
subjects affected / exposed	0 / 255 (0.00%)	0 / 85 (0.00%)	0 / 80 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Skin laceration			
subjects affected / exposed	0 / 255 (0.00%)	0 / 85 (0.00%)	0 / 80 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Tibia fracture			
subjects affected / exposed	0 / 255 (0.00%)	0 / 85 (0.00%)	0 / 80 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Wound dehiscence			
subjects affected / exposed	0 / 255 (0.00%)	0 / 85 (0.00%)	0 / 80 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Congenital, familial and genetic disorders			
Developmental hip dysplasia			
subjects affected / exposed	0 / 255 (0.00%)	0 / 85 (0.00%)	0 / 80 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac disorders			
Acute myocardial infarction			
subjects affected / exposed	0 / 255 (0.00%)	0 / 85 (0.00%)	0 / 80 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Angina unstable			
subjects affected / exposed	0 / 255 (0.00%)	0 / 85 (0.00%)	0 / 80 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Atrial fibrillation			
subjects affected / exposed	0 / 255 (0.00%)	0 / 85 (0.00%)	0 / 80 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac arrest			
subjects affected / exposed	0 / 255 (0.00%)	0 / 85 (0.00%)	1 / 80 (1.25%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Sinus node dysfunction			
subjects affected / exposed	0 / 255 (0.00%)	0 / 85 (0.00%)	0 / 80 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pericardial effusion			
subjects affected / exposed	0 / 255 (0.00%)	0 / 85 (0.00%)	0 / 80 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Myocardial infarction			
subjects affected / exposed	0 / 255 (0.00%)	0 / 85 (0.00%)	0 / 80 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nervous system disorders			
Cerebrovascular accident			
subjects affected / exposed	0 / 255 (0.00%)	0 / 85 (0.00%)	0 / 80 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cerebral infarction			
subjects affected / exposed	0 / 255 (0.00%)	0 / 85 (0.00%)	0 / 80 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Facial paralysis			
subjects affected / exposed	0 / 255 (0.00%)	0 / 85 (0.00%)	0 / 80 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ischaemic stroke			

subjects affected / exposed	0 / 255 (0.00%)	0 / 85 (0.00%)	0 / 80 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Seizure			
subjects affected / exposed	0 / 255 (0.00%)	0 / 85 (0.00%)	0 / 80 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Paraparesis			
subjects affected / exposed	0 / 255 (0.00%)	0 / 85 (0.00%)	0 / 80 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Syncope			
subjects affected / exposed	0 / 255 (0.00%)	0 / 85 (0.00%)	0 / 80 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Subarachnoid haemorrhage			
subjects affected / exposed	0 / 255 (0.00%)	0 / 85 (0.00%)	0 / 80 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Transient ischaemic attack			
subjects affected / exposed	0 / 255 (0.00%)	1 / 85 (1.18%)	0 / 80 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lacunar infarction			
subjects affected / exposed	0 / 255 (0.00%)	0 / 85 (0.00%)	0 / 80 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	0 / 255 (0.00%)	1 / 85 (1.18%)	0 / 80 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Iron deficiency anaemia			

subjects affected / exposed	0 / 255 (0.00%)	0 / 85 (0.00%)	0 / 80 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Neutropenia			
subjects affected / exposed	0 / 255 (0.00%)	0 / 85 (0.00%)	0 / 80 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Eye disorders			
Glaucoma			
subjects affected / exposed	0 / 255 (0.00%)	0 / 85 (0.00%)	0 / 80 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ulcerative keratitis			
subjects affected / exposed	0 / 255 (0.00%)	0 / 85 (0.00%)	0 / 80 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Acute abdomen			
subjects affected / exposed	0 / 255 (0.00%)	0 / 85 (0.00%)	0 / 80 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Duodenal ulcer			
subjects affected / exposed	0 / 255 (0.00%)	1 / 85 (1.18%)	0 / 80 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Duodenal ulcer perforation			
subjects affected / exposed	0 / 255 (0.00%)	0 / 85 (0.00%)	0 / 80 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Enteritis			
subjects affected / exposed	0 / 255 (0.00%)	0 / 85 (0.00%)	0 / 80 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Large intestine polyp			

subjects affected / exposed	0 / 255 (0.00%)	0 / 85 (0.00%)	0 / 80 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Inguinal hernia			
subjects affected / exposed	0 / 255 (0.00%)	0 / 85 (0.00%)	0 / 80 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastric ulcer			
subjects affected / exposed	0 / 255 (0.00%)	0 / 85 (0.00%)	0 / 80 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Peritoneal adhesions			
subjects affected / exposed	0 / 255 (0.00%)	0 / 85 (0.00%)	0 / 80 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Mesenteric cyst			
subjects affected / exposed	0 / 255 (0.00%)	0 / 85 (0.00%)	0 / 80 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatobiliary disorders			
Acute hepatic failure			
subjects affected / exposed	0 / 255 (0.00%)	0 / 85 (0.00%)	0 / 80 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bile duct stone			
subjects affected / exposed	0 / 255 (0.00%)	0 / 85 (0.00%)	0 / 80 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cholecystitis acute			
subjects affected / exposed	0 / 255 (0.00%)	0 / 85 (0.00%)	0 / 80 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cholelithiasis			

subjects affected / exposed	0 / 255 (0.00%)	0 / 85 (0.00%)	0 / 80 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatic steatosis			
subjects affected / exposed	0 / 255 (0.00%)	0 / 85 (0.00%)	0 / 80 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal and urinary disorders			
Calculus urinary			
subjects affected / exposed	0 / 255 (0.00%)	0 / 85 (0.00%)	0 / 80 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
IgA nephropathy			
subjects affected / exposed	0 / 255 (0.00%)	0 / 85 (0.00%)	0 / 80 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Musculoskeletal and connective tissue disorders			
Intervertebral disc degeneration			
subjects affected / exposed	0 / 255 (0.00%)	0 / 85 (0.00%)	0 / 80 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Back pain			
subjects affected / exposed	0 / 255 (0.00%)	0 / 85 (0.00%)	0 / 80 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Joint destruction			
subjects affected / exposed	0 / 255 (0.00%)	0 / 85 (0.00%)	0 / 80 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lumbar spinal stenosis			
subjects affected / exposed	0 / 255 (0.00%)	0 / 85 (0.00%)	0 / 80 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Osteoporotic fracture			
subjects affected / exposed	0 / 255 (0.00%)	0 / 85 (0.00%)	0 / 80 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Osteoarthritis			
subjects affected / exposed	1 / 255 (0.39%)	0 / 85 (0.00%)	1 / 80 (1.25%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Rheumatoid arthritis			
subjects affected / exposed	0 / 255 (0.00%)	2 / 85 (2.35%)	0 / 80 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Spinal osteoarthritis			
subjects affected / exposed	0 / 255 (0.00%)	0 / 85 (0.00%)	0 / 80 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Synovial cyst			
subjects affected / exposed	0 / 255 (0.00%)	0 / 85 (0.00%)	0 / 80 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Synovitis			
subjects affected / exposed	1 / 255 (0.39%)	0 / 85 (0.00%)	0 / 80 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Tenosynovitis			
subjects affected / exposed	0 / 255 (0.00%)	0 / 85 (0.00%)	0 / 80 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Soft tissue disorder			
subjects affected / exposed	0 / 255 (0.00%)	0 / 85 (0.00%)	0 / 80 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			

COVID-19			
subjects affected / exposed	0 / 255 (0.00%)	0 / 85 (0.00%)	0 / 80 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Appendicitis			
subjects affected / exposed	0 / 255 (0.00%)	0 / 85 (0.00%)	0 / 80 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Escherichia sepsis			
subjects affected / exposed	0 / 255 (0.00%)	0 / 85 (0.00%)	0 / 80 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Diverticulitis			
subjects affected / exposed	0 / 255 (0.00%)	0 / 85 (0.00%)	0 / 80 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
COVID-19 pneumonia			
subjects affected / exposed	0 / 255 (0.00%)	0 / 85 (0.00%)	0 / 80 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Herpes simplex			
subjects affected / exposed	0 / 255 (0.00%)	0 / 85 (0.00%)	0 / 80 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Herpes zoster			
subjects affected / exposed	0 / 255 (0.00%)	0 / 85 (0.00%)	0 / 80 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lower respiratory tract infection			
subjects affected / exposed	0 / 255 (0.00%)	0 / 85 (0.00%)	0 / 80 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumocystis jirovecii pneumonia			

subjects affected / exposed	0 / 255 (0.00%)	0 / 85 (0.00%)	0 / 80 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia			
subjects affected / exposed	0 / 255 (0.00%)	0 / 85 (0.00%)	1 / 80 (1.25%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia bacterial			
subjects affected / exposed	0 / 255 (0.00%)	0 / 85 (0.00%)	0 / 80 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pyelonephritis			
subjects affected / exposed	0 / 255 (0.00%)	0 / 85 (0.00%)	0 / 80 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Postoperative wound infection			
subjects affected / exposed	0 / 255 (0.00%)	1 / 85 (1.18%)	0 / 80 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Post procedural infection			
subjects affected / exposed	0 / 255 (0.00%)	0 / 85 (0.00%)	0 / 80 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pyelonephritis acute			
subjects affected / exposed	0 / 255 (0.00%)	0 / 85 (0.00%)	0 / 80 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Sepsis			
subjects affected / exposed	0 / 255 (0.00%)	0 / 85 (0.00%)	0 / 80 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Septic shock			

subjects affected / exposed	0 / 255 (0.00%)	0 / 85 (0.00%)	0 / 80 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Urinary tract infection			
subjects affected / exposed	1 / 255 (0.39%)	0 / 85 (0.00%)	0 / 80 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia cryptococcal			
subjects affected / exposed	0 / 255 (0.00%)	0 / 85 (0.00%)	0 / 80 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metabolism and nutrition disorders			
Dehydration			
subjects affected / exposed	0 / 255 (0.00%)	0 / 85 (0.00%)	0 / 80 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	Placebo +csDMARD and Tofacitinib 5mg +csDMARD (Global Cohort)	GSK3196165 90mg + csDMARD (Asia Cohort)	GSK3196165 150mg + csDMARD (Asia Cohort)
Total subjects affected by serious adverse events			
subjects affected / exposed	2 / 67 (2.99%)	5 / 47 (10.64%)	4 / 49 (8.16%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events			
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Adenocarcinoma of colon			
subjects affected / exposed	0 / 67 (0.00%)	0 / 47 (0.00%)	0 / 49 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Breast cancer			
subjects affected / exposed	0 / 67 (0.00%)	0 / 47 (0.00%)	0 / 49 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac myxoma			

subjects affected / exposed	0 / 67 (0.00%)	0 / 47 (0.00%)	0 / 49 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastric cancer			
subjects affected / exposed	0 / 67 (0.00%)	0 / 47 (0.00%)	0 / 49 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Colorectal adenoma			
subjects affected / exposed	0 / 67 (0.00%)	0 / 47 (0.00%)	0 / 49 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Chronic lymphocytic leukaemia			
subjects affected / exposed	0 / 67 (0.00%)	0 / 47 (0.00%)	0 / 49 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Invasive ductal breast carcinoma			
subjects affected / exposed	0 / 67 (0.00%)	0 / 47 (0.00%)	0 / 49 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Invasive lobular breast carcinoma			
subjects affected / exposed	0 / 67 (0.00%)	0 / 47 (0.00%)	0 / 49 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lung neoplasm			
subjects affected / exposed	0 / 67 (0.00%)	0 / 47 (0.00%)	0 / 49 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metastases to liver			
subjects affected / exposed	0 / 67 (0.00%)	0 / 47 (0.00%)	0 / 49 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pancreatic carcinoma metastatic			

subjects affected / exposed	0 / 67 (0.00%)	0 / 47 (0.00%)	0 / 49 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Rectal adenocarcinoma			
subjects affected / exposed	0 / 67 (0.00%)	0 / 47 (0.00%)	0 / 49 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Transitional cell carcinoma			
subjects affected / exposed	0 / 67 (0.00%)	0 / 47 (0.00%)	0 / 49 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Uterine leiomyoma			
subjects affected / exposed	0 / 67 (0.00%)	1 / 47 (2.13%)	0 / 49 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vascular disorders			
Circulatory collapse			
subjects affected / exposed	0 / 67 (0.00%)	0 / 47 (0.00%)	0 / 49 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Deep vein thrombosis			
subjects affected / exposed	0 / 67 (0.00%)	0 / 47 (0.00%)	0 / 49 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General disorders and administration site conditions			
Death			
subjects affected / exposed	0 / 67 (0.00%)	0 / 47 (0.00%)	0 / 49 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Fatigue			
subjects affected / exposed	0 / 67 (0.00%)	0 / 47 (0.00%)	0 / 49 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Pyrexia			
subjects affected / exposed	0 / 67 (0.00%)	0 / 47 (0.00%)	0 / 49 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Sudden death			
subjects affected / exposed	0 / 67 (0.00%)	0 / 47 (0.00%)	0 / 49 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Immune system disorders			
Secondary amyloidosis			
subjects affected / exposed	0 / 67 (0.00%)	0 / 47 (0.00%)	0 / 49 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Reproductive system and breast disorders			
Endometrial hyperplasia			
subjects affected / exposed	0 / 67 (0.00%)	0 / 47 (0.00%)	0 / 49 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hydrosalpinx			
subjects affected / exposed	0 / 67 (0.00%)	0 / 47 (0.00%)	0 / 49 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Menopausal symptoms			
subjects affected / exposed	0 / 67 (0.00%)	0 / 47 (0.00%)	0 / 49 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ovarian cyst			
subjects affected / exposed	0 / 67 (0.00%)	0 / 47 (0.00%)	0 / 49 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Uterine polyp			
subjects affected / exposed	0 / 67 (0.00%)	0 / 47 (0.00%)	0 / 49 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Endometriosis			
subjects affected / exposed	0 / 67 (0.00%)	1 / 47 (2.13%)	0 / 49 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Uterine cyst			
subjects affected / exposed	0 / 67 (0.00%)	1 / 47 (2.13%)	0 / 49 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			
Interstitial lung disease			
subjects affected / exposed	0 / 67 (0.00%)	0 / 47 (0.00%)	1 / 49 (2.04%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pleural cyst			
subjects affected / exposed	0 / 67 (0.00%)	0 / 47 (0.00%)	0 / 49 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pulmonary embolism			
subjects affected / exposed	0 / 67 (0.00%)	0 / 47 (0.00%)	0 / 49 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pleural effusion			
subjects affected / exposed	0 / 67 (0.00%)	0 / 47 (0.00%)	0 / 49 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pulmonary fibrosis			
subjects affected / exposed	0 / 67 (0.00%)	0 / 47 (0.00%)	0 / 49 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Product issues			
Device dislocation			
subjects affected / exposed	0 / 67 (0.00%)	0 / 47 (0.00%)	0 / 49 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	0 / 67 (0.00%)	0 / 47 (0.00%)	0 / 49 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
International normalised ratio increased			
subjects affected / exposed	0 / 67 (0.00%)	0 / 47 (0.00%)	0 / 49 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Transaminases increased			
subjects affected / exposed	0 / 67 (0.00%)	0 / 47 (0.00%)	0 / 49 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Injury, poisoning and procedural complications			
Ankle fracture			
subjects affected / exposed	0 / 67 (0.00%)	0 / 47 (0.00%)	0 / 49 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Incisional hernia			
subjects affected / exposed	0 / 67 (0.00%)	0 / 47 (0.00%)	0 / 49 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Joint injury			
subjects affected / exposed	0 / 67 (0.00%)	0 / 47 (0.00%)	0 / 49 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Overdose			
subjects affected / exposed	0 / 67 (0.00%)	0 / 47 (0.00%)	0 / 49 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Tendon rupture			

subjects affected / exposed	0 / 67 (0.00%)	0 / 47 (0.00%)	0 / 49 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Spinal compression fracture			
subjects affected / exposed	0 / 67 (0.00%)	0 / 47 (0.00%)	1 / 49 (2.04%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Skin laceration			
subjects affected / exposed	0 / 67 (0.00%)	0 / 47 (0.00%)	0 / 49 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Tibia fracture			
subjects affected / exposed	0 / 67 (0.00%)	0 / 47 (0.00%)	0 / 49 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Wound dehiscence			
subjects affected / exposed	0 / 67 (0.00%)	0 / 47 (0.00%)	0 / 49 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Congenital, familial and genetic disorders			
Developmental hip dysplasia			
subjects affected / exposed	0 / 67 (0.00%)	1 / 47 (2.13%)	0 / 49 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac disorders			
Acute myocardial infarction			
subjects affected / exposed	0 / 67 (0.00%)	0 / 47 (0.00%)	0 / 49 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Angina unstable			
subjects affected / exposed	0 / 67 (0.00%)	0 / 47 (0.00%)	0 / 49 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Atrial fibrillation			
subjects affected / exposed	0 / 67 (0.00%)	0 / 47 (0.00%)	0 / 49 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac arrest			
subjects affected / exposed	0 / 67 (0.00%)	0 / 47 (0.00%)	0 / 49 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Sinus node dysfunction			
subjects affected / exposed	0 / 67 (0.00%)	0 / 47 (0.00%)	0 / 49 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pericardial effusion			
subjects affected / exposed	0 / 67 (0.00%)	0 / 47 (0.00%)	0 / 49 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Myocardial infarction			
subjects affected / exposed	0 / 67 (0.00%)	0 / 47 (0.00%)	0 / 49 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nervous system disorders			
Cerebrovascular accident			
subjects affected / exposed	0 / 67 (0.00%)	0 / 47 (0.00%)	0 / 49 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cerebral infarction			
subjects affected / exposed	0 / 67 (0.00%)	0 / 47 (0.00%)	0 / 49 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Facial paralysis			
subjects affected / exposed	0 / 67 (0.00%)	0 / 47 (0.00%)	0 / 49 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ischaemic stroke			

subjects affected / exposed	0 / 67 (0.00%)	0 / 47 (0.00%)	0 / 49 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Seizure			
subjects affected / exposed	0 / 67 (0.00%)	0 / 47 (0.00%)	0 / 49 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Paraparesis			
subjects affected / exposed	0 / 67 (0.00%)	0 / 47 (0.00%)	0 / 49 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Syncope			
subjects affected / exposed	0 / 67 (0.00%)	0 / 47 (0.00%)	0 / 49 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Subarachnoid haemorrhage			
subjects affected / exposed	0 / 67 (0.00%)	0 / 47 (0.00%)	0 / 49 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Transient ischaemic attack			
subjects affected / exposed	0 / 67 (0.00%)	0 / 47 (0.00%)	0 / 49 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lacunar infarction			
subjects affected / exposed	0 / 67 (0.00%)	1 / 47 (2.13%)	0 / 49 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	0 / 67 (0.00%)	0 / 47 (0.00%)	0 / 49 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Iron deficiency anaemia			

subjects affected / exposed	0 / 67 (0.00%)	0 / 47 (0.00%)	0 / 49 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Neutropenia			
subjects affected / exposed	0 / 67 (0.00%)	0 / 47 (0.00%)	1 / 49 (2.04%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Eye disorders			
Glaucoma			
subjects affected / exposed	0 / 67 (0.00%)	0 / 47 (0.00%)	0 / 49 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ulcerative keratitis			
subjects affected / exposed	0 / 67 (0.00%)	0 / 47 (0.00%)	0 / 49 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Acute abdomen			
subjects affected / exposed	0 / 67 (0.00%)	0 / 47 (0.00%)	0 / 49 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Duodenal ulcer			
subjects affected / exposed	0 / 67 (0.00%)	0 / 47 (0.00%)	0 / 49 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Duodenal ulcer perforation			
subjects affected / exposed	0 / 67 (0.00%)	0 / 47 (0.00%)	0 / 49 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Enteritis			
subjects affected / exposed	0 / 67 (0.00%)	0 / 47 (0.00%)	0 / 49 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Large intestine polyp			

subjects affected / exposed	1 / 67 (1.49%)	0 / 47 (0.00%)	0 / 49 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Inguinal hernia			
subjects affected / exposed	0 / 67 (0.00%)	0 / 47 (0.00%)	0 / 49 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastric ulcer			
subjects affected / exposed	0 / 67 (0.00%)	0 / 47 (0.00%)	0 / 49 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Peritoneal adhesions			
subjects affected / exposed	0 / 67 (0.00%)	0 / 47 (0.00%)	0 / 49 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Mesenteric cyst			
subjects affected / exposed	0 / 67 (0.00%)	0 / 47 (0.00%)	0 / 49 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatobiliary disorders			
Acute hepatic failure			
subjects affected / exposed	0 / 67 (0.00%)	0 / 47 (0.00%)	0 / 49 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bile duct stone			
subjects affected / exposed	0 / 67 (0.00%)	0 / 47 (0.00%)	0 / 49 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cholecystitis acute			
subjects affected / exposed	0 / 67 (0.00%)	0 / 47 (0.00%)	0 / 49 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cholelithiasis			

subjects affected / exposed	0 / 67 (0.00%)	0 / 47 (0.00%)	0 / 49 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatic steatosis			
subjects affected / exposed	0 / 67 (0.00%)	0 / 47 (0.00%)	0 / 49 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal and urinary disorders			
Calculus urinary			
subjects affected / exposed	0 / 67 (0.00%)	0 / 47 (0.00%)	0 / 49 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
IgA nephropathy			
subjects affected / exposed	0 / 67 (0.00%)	0 / 47 (0.00%)	0 / 49 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Musculoskeletal and connective tissue disorders			
Intervertebral disc degeneration			
subjects affected / exposed	0 / 67 (0.00%)	0 / 47 (0.00%)	0 / 49 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Back pain			
subjects affected / exposed	0 / 67 (0.00%)	0 / 47 (0.00%)	0 / 49 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Joint destruction			
subjects affected / exposed	0 / 67 (0.00%)	0 / 47 (0.00%)	0 / 49 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lumbar spinal stenosis			
subjects affected / exposed	0 / 67 (0.00%)	0 / 47 (0.00%)	0 / 49 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Osteoporotic fracture			
subjects affected / exposed	0 / 67 (0.00%)	0 / 47 (0.00%)	0 / 49 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Osteoarthritis			
subjects affected / exposed	0 / 67 (0.00%)	0 / 47 (0.00%)	0 / 49 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Rheumatoid arthritis			
subjects affected / exposed	0 / 67 (0.00%)	0 / 47 (0.00%)	0 / 49 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Spinal osteoarthritis			
subjects affected / exposed	0 / 67 (0.00%)	0 / 47 (0.00%)	0 / 49 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Synovial cyst			
subjects affected / exposed	0 / 67 (0.00%)	0 / 47 (0.00%)	0 / 49 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Synovitis			
subjects affected / exposed	0 / 67 (0.00%)	0 / 47 (0.00%)	0 / 49 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Tenosynovitis			
subjects affected / exposed	0 / 67 (0.00%)	0 / 47 (0.00%)	0 / 49 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Soft tissue disorder			
subjects affected / exposed	0 / 67 (0.00%)	0 / 47 (0.00%)	1 / 49 (2.04%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			

COVID-19			
subjects affected / exposed	0 / 67 (0.00%)	1 / 47 (2.13%)	0 / 49 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Appendicitis			
subjects affected / exposed	0 / 67 (0.00%)	0 / 47 (0.00%)	0 / 49 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Escherichia sepsis			
subjects affected / exposed	0 / 67 (0.00%)	0 / 47 (0.00%)	0 / 49 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Diverticulitis			
subjects affected / exposed	0 / 67 (0.00%)	0 / 47 (0.00%)	0 / 49 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
COVID-19 pneumonia			
subjects affected / exposed	0 / 67 (0.00%)	0 / 47 (0.00%)	0 / 49 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Herpes simplex			
subjects affected / exposed	0 / 67 (0.00%)	0 / 47 (0.00%)	0 / 49 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Herpes zoster			
subjects affected / exposed	0 / 67 (0.00%)	0 / 47 (0.00%)	0 / 49 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lower respiratory tract infection			
subjects affected / exposed	1 / 67 (1.49%)	0 / 47 (0.00%)	0 / 49 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumocystis jirovecii pneumonia			

subjects affected / exposed	0 / 67 (0.00%)	0 / 47 (0.00%)	0 / 49 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia			
subjects affected / exposed	0 / 67 (0.00%)	0 / 47 (0.00%)	1 / 49 (2.04%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia bacterial			
subjects affected / exposed	0 / 67 (0.00%)	0 / 47 (0.00%)	0 / 49 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pyelonephritis			
subjects affected / exposed	0 / 67 (0.00%)	0 / 47 (0.00%)	0 / 49 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Postoperative wound infection			
subjects affected / exposed	0 / 67 (0.00%)	0 / 47 (0.00%)	0 / 49 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Post procedural infection			
subjects affected / exposed	0 / 67 (0.00%)	0 / 47 (0.00%)	0 / 49 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pyelonephritis acute			
subjects affected / exposed	0 / 67 (0.00%)	1 / 47 (2.13%)	0 / 49 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Sepsis			
subjects affected / exposed	0 / 67 (0.00%)	0 / 47 (0.00%)	0 / 49 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Septic shock			

subjects affected / exposed	0 / 67 (0.00%)	0 / 47 (0.00%)	0 / 49 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Urinary tract infection			
subjects affected / exposed	0 / 67 (0.00%)	0 / 47 (0.00%)	0 / 49 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia cryptococcal			
subjects affected / exposed	0 / 67 (0.00%)	0 / 47 (0.00%)	0 / 49 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metabolism and nutrition disorders			
Dehydration			
subjects affected / exposed	0 / 67 (0.00%)	0 / 47 (0.00%)	0 / 49 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	Tofacitinib 5mg + csDMARD (Asia Cohort)	Pooled Placebo (Asian Cohort)	Placebo + csDMARD and GSK3196165 90mg + csDMARD (Asia Cohort)
Total subjects affected by serious adverse events			
subjects affected / exposed	2 / 19 (10.53%)	1 / 23 (4.35%)	0 / 6 (0.00%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events			
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Adenocarcinoma of colon			
subjects affected / exposed	0 / 19 (0.00%)	0 / 23 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Breast cancer			
subjects affected / exposed	0 / 19 (0.00%)	0 / 23 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac myxoma			

subjects affected / exposed	0 / 19 (0.00%)	0 / 23 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastric cancer			
subjects affected / exposed	0 / 19 (0.00%)	0 / 23 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Colorectal adenoma			
subjects affected / exposed	0 / 19 (0.00%)	0 / 23 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Chronic lymphocytic leukaemia			
subjects affected / exposed	0 / 19 (0.00%)	0 / 23 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Invasive ductal breast carcinoma			
subjects affected / exposed	0 / 19 (0.00%)	0 / 23 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Invasive lobular breast carcinoma			
subjects affected / exposed	0 / 19 (0.00%)	0 / 23 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lung neoplasm			
subjects affected / exposed	0 / 19 (0.00%)	0 / 23 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metastases to liver			
subjects affected / exposed	0 / 19 (0.00%)	0 / 23 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pancreatic carcinoma metastatic			

subjects affected / exposed	0 / 19 (0.00%)	0 / 23 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Rectal adenocarcinoma			
subjects affected / exposed	0 / 19 (0.00%)	0 / 23 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Transitional cell carcinoma			
subjects affected / exposed	0 / 19 (0.00%)	0 / 23 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Uterine leiomyoma			
subjects affected / exposed	0 / 19 (0.00%)	0 / 23 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vascular disorders			
Circulatory collapse			
subjects affected / exposed	0 / 19 (0.00%)	0 / 23 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Deep vein thrombosis			
subjects affected / exposed	0 / 19 (0.00%)	0 / 23 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General disorders and administration site conditions			
Death			
subjects affected / exposed	0 / 19 (0.00%)	0 / 23 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Fatigue			
subjects affected / exposed	0 / 19 (0.00%)	0 / 23 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Pyrexia			
subjects affected / exposed	0 / 19 (0.00%)	0 / 23 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Sudden death			
subjects affected / exposed	0 / 19 (0.00%)	0 / 23 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Immune system disorders			
Secondary amyloidosis			
subjects affected / exposed	0 / 19 (0.00%)	0 / 23 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Reproductive system and breast disorders			
Endometrial hyperplasia			
subjects affected / exposed	0 / 19 (0.00%)	0 / 23 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hydrosalpinx			
subjects affected / exposed	0 / 19 (0.00%)	0 / 23 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Menopausal symptoms			
subjects affected / exposed	0 / 19 (0.00%)	0 / 23 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ovarian cyst			
subjects affected / exposed	0 / 19 (0.00%)	0 / 23 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Uterine polyp			
subjects affected / exposed	0 / 19 (0.00%)	0 / 23 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Endometriosis			
subjects affected / exposed	0 / 19 (0.00%)	0 / 23 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Uterine cyst			
subjects affected / exposed	0 / 19 (0.00%)	0 / 23 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			
Interstitial lung disease			
subjects affected / exposed	0 / 19 (0.00%)	0 / 23 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pleural cyst			
subjects affected / exposed	0 / 19 (0.00%)	0 / 23 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pulmonary embolism			
subjects affected / exposed	0 / 19 (0.00%)	0 / 23 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pleural effusion			
subjects affected / exposed	0 / 19 (0.00%)	0 / 23 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pulmonary fibrosis			
subjects affected / exposed	0 / 19 (0.00%)	0 / 23 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Product issues			
Device dislocation			
subjects affected / exposed	0 / 19 (0.00%)	0 / 23 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	0 / 19 (0.00%)	0 / 23 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
International normalised ratio increased			
subjects affected / exposed	0 / 19 (0.00%)	0 / 23 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Transaminases increased			
subjects affected / exposed	0 / 19 (0.00%)	0 / 23 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Injury, poisoning and procedural complications			
Ankle fracture			
subjects affected / exposed	0 / 19 (0.00%)	0 / 23 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Incisional hernia			
subjects affected / exposed	0 / 19 (0.00%)	0 / 23 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Joint injury			
subjects affected / exposed	0 / 19 (0.00%)	0 / 23 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Overdose			
subjects affected / exposed	0 / 19 (0.00%)	0 / 23 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Tendon rupture			

subjects affected / exposed	0 / 19 (0.00%)	0 / 23 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Spinal compression fracture			
subjects affected / exposed	0 / 19 (0.00%)	0 / 23 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Skin laceration			
subjects affected / exposed	0 / 19 (0.00%)	0 / 23 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Tibia fracture			
subjects affected / exposed	0 / 19 (0.00%)	0 / 23 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Wound dehiscence			
subjects affected / exposed	0 / 19 (0.00%)	0 / 23 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Congenital, familial and genetic disorders			
Developmental hip dysplasia			
subjects affected / exposed	0 / 19 (0.00%)	0 / 23 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac disorders			
Acute myocardial infarction			
subjects affected / exposed	0 / 19 (0.00%)	0 / 23 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Angina unstable			
subjects affected / exposed	0 / 19 (0.00%)	0 / 23 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Atrial fibrillation			
subjects affected / exposed	0 / 19 (0.00%)	0 / 23 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac arrest			
subjects affected / exposed	0 / 19 (0.00%)	0 / 23 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Sinus node dysfunction			
subjects affected / exposed	0 / 19 (0.00%)	0 / 23 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pericardial effusion			
subjects affected / exposed	0 / 19 (0.00%)	0 / 23 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Myocardial infarction			
subjects affected / exposed	0 / 19 (0.00%)	0 / 23 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nervous system disorders			
Cerebrovascular accident			
subjects affected / exposed	0 / 19 (0.00%)	0 / 23 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cerebral infarction			
subjects affected / exposed	0 / 19 (0.00%)	1 / 23 (4.35%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Facial paralysis			
subjects affected / exposed	0 / 19 (0.00%)	0 / 23 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ischaemic stroke			

subjects affected / exposed	0 / 19 (0.00%)	0 / 23 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Seizure			
subjects affected / exposed	0 / 19 (0.00%)	0 / 23 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Paraparesis			
subjects affected / exposed	0 / 19 (0.00%)	0 / 23 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Syncope			
subjects affected / exposed	0 / 19 (0.00%)	0 / 23 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Subarachnoid haemorrhage			
subjects affected / exposed	0 / 19 (0.00%)	0 / 23 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Transient ischaemic attack			
subjects affected / exposed	0 / 19 (0.00%)	0 / 23 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lacunar infarction			
subjects affected / exposed	0 / 19 (0.00%)	0 / 23 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	0 / 19 (0.00%)	0 / 23 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Iron deficiency anaemia			

subjects affected / exposed	0 / 19 (0.00%)	0 / 23 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Neutropenia			
subjects affected / exposed	0 / 19 (0.00%)	0 / 23 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Eye disorders			
Glaucoma			
subjects affected / exposed	0 / 19 (0.00%)	0 / 23 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ulcerative keratitis			
subjects affected / exposed	0 / 19 (0.00%)	0 / 23 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Acute abdomen			
subjects affected / exposed	0 / 19 (0.00%)	0 / 23 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Duodenal ulcer			
subjects affected / exposed	0 / 19 (0.00%)	0 / 23 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Duodenal ulcer perforation			
subjects affected / exposed	0 / 19 (0.00%)	0 / 23 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Enteritis			
subjects affected / exposed	0 / 19 (0.00%)	0 / 23 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Large intestine polyp			

subjects affected / exposed	0 / 19 (0.00%)	0 / 23 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Inguinal hernia			
subjects affected / exposed	0 / 19 (0.00%)	0 / 23 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastric ulcer			
subjects affected / exposed	0 / 19 (0.00%)	0 / 23 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Peritoneal adhesions			
subjects affected / exposed	0 / 19 (0.00%)	0 / 23 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Mesenteric cyst			
subjects affected / exposed	0 / 19 (0.00%)	0 / 23 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatobiliary disorders			
Acute hepatic failure			
subjects affected / exposed	0 / 19 (0.00%)	0 / 23 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bile duct stone			
subjects affected / exposed	0 / 19 (0.00%)	0 / 23 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cholecystitis acute			
subjects affected / exposed	0 / 19 (0.00%)	0 / 23 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cholelithiasis			

subjects affected / exposed	0 / 19 (0.00%)	0 / 23 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatic steatosis			
subjects affected / exposed	0 / 19 (0.00%)	0 / 23 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal and urinary disorders			
Calculus urinary			
subjects affected / exposed	0 / 19 (0.00%)	0 / 23 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
IgA nephropathy			
subjects affected / exposed	0 / 19 (0.00%)	0 / 23 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Musculoskeletal and connective tissue disorders			
Intervertebral disc degeneration			
subjects affected / exposed	0 / 19 (0.00%)	0 / 23 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Back pain			
subjects affected / exposed	0 / 19 (0.00%)	0 / 23 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Joint destruction			
subjects affected / exposed	0 / 19 (0.00%)	0 / 23 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lumbar spinal stenosis			
subjects affected / exposed	0 / 19 (0.00%)	0 / 23 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Osteoporotic fracture			
subjects affected / exposed	0 / 19 (0.00%)	0 / 23 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Osteoarthritis			
subjects affected / exposed	0 / 19 (0.00%)	0 / 23 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Rheumatoid arthritis			
subjects affected / exposed	0 / 19 (0.00%)	0 / 23 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Spinal osteoarthritis			
subjects affected / exposed	0 / 19 (0.00%)	0 / 23 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Synovial cyst			
subjects affected / exposed	0 / 19 (0.00%)	0 / 23 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Synovitis			
subjects affected / exposed	0 / 19 (0.00%)	0 / 23 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Tenosynovitis			
subjects affected / exposed	0 / 19 (0.00%)	0 / 23 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Soft tissue disorder			
subjects affected / exposed	0 / 19 (0.00%)	0 / 23 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			

COVID-19			
subjects affected / exposed	1 / 19 (5.26%)	0 / 23 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Appendicitis			
subjects affected / exposed	0 / 19 (0.00%)	0 / 23 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Escherichia sepsis			
subjects affected / exposed	0 / 19 (0.00%)	0 / 23 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Diverticulitis			
subjects affected / exposed	0 / 19 (0.00%)	0 / 23 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
COVID-19 pneumonia			
subjects affected / exposed	0 / 19 (0.00%)	0 / 23 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Herpes simplex			
subjects affected / exposed	0 / 19 (0.00%)	0 / 23 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Herpes zoster			
subjects affected / exposed	0 / 19 (0.00%)	0 / 23 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lower respiratory tract infection			
subjects affected / exposed	0 / 19 (0.00%)	0 / 23 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumocystis jirovecii pneumonia			

subjects affected / exposed	0 / 19 (0.00%)	0 / 23 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia			
subjects affected / exposed	0 / 19 (0.00%)	0 / 23 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia bacterial			
subjects affected / exposed	0 / 19 (0.00%)	0 / 23 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pyelonephritis			
subjects affected / exposed	0 / 19 (0.00%)	0 / 23 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Postoperative wound infection			
subjects affected / exposed	0 / 19 (0.00%)	0 / 23 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Post procedural infection			
subjects affected / exposed	0 / 19 (0.00%)	0 / 23 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pyelonephritis acute			
subjects affected / exposed	0 / 19 (0.00%)	0 / 23 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Sepsis			
subjects affected / exposed	0 / 19 (0.00%)	0 / 23 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Septic shock			

subjects affected / exposed	0 / 19 (0.00%)	0 / 23 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Urinary tract infection			
subjects affected / exposed	0 / 19 (0.00%)	0 / 23 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia cryptococcal			
subjects affected / exposed	1 / 19 (5.26%)	0 / 23 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metabolism and nutrition disorders			
Dehydration			
subjects affected / exposed	0 / 19 (0.00%)	0 / 23 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	Placebo + csDMARD and GSK3196165 150mg + csDMARD (Asia Cohort)	Placebo + csDMARD and Tofacitinib 5mg + csDMARD (Asia Cohort)	
Total subjects affected by serious adverse events			
subjects affected / exposed	1 / 8 (12.50%)	0 / 8 (0.00%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events			
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Adenocarcinoma of colon			
subjects affected / exposed	0 / 8 (0.00%)	0 / 8 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Breast cancer			
subjects affected / exposed	0 / 8 (0.00%)	0 / 8 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac myxoma			

subjects affected / exposed	0 / 8 (0.00%)	0 / 8 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastric cancer			
subjects affected / exposed	0 / 8 (0.00%)	0 / 8 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Colorectal adenoma			
subjects affected / exposed	0 / 8 (0.00%)	0 / 8 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Chronic lymphocytic leukaemia			
subjects affected / exposed	0 / 8 (0.00%)	0 / 8 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Invasive ductal breast carcinoma			
subjects affected / exposed	0 / 8 (0.00%)	0 / 8 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Invasive lobular breast carcinoma			
subjects affected / exposed	0 / 8 (0.00%)	0 / 8 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lung neoplasm			
subjects affected / exposed	0 / 8 (0.00%)	0 / 8 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metastases to liver			
subjects affected / exposed	0 / 8 (0.00%)	0 / 8 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pancreatic carcinoma metastatic			

subjects affected / exposed	0 / 8 (0.00%)	0 / 8 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Rectal adenocarcinoma			
subjects affected / exposed	0 / 8 (0.00%)	0 / 8 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Transitional cell carcinoma			
subjects affected / exposed	0 / 8 (0.00%)	0 / 8 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Uterine leiomyoma			
subjects affected / exposed	0 / 8 (0.00%)	0 / 8 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vascular disorders			
Circulatory collapse			
subjects affected / exposed	0 / 8 (0.00%)	0 / 8 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Deep vein thrombosis			
subjects affected / exposed	0 / 8 (0.00%)	0 / 8 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
General disorders and administration site conditions			
Death			
subjects affected / exposed	0 / 8 (0.00%)	0 / 8 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Fatigue			
subjects affected / exposed	0 / 8 (0.00%)	0 / 8 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Pyrexia			
subjects affected / exposed	0 / 8 (0.00%)	0 / 8 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Sudden death			
subjects affected / exposed	0 / 8 (0.00%)	0 / 8 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Immune system disorders			
Secondary amyloidosis			
subjects affected / exposed	0 / 8 (0.00%)	0 / 8 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Reproductive system and breast disorders			
Endometrial hyperplasia			
subjects affected / exposed	0 / 8 (0.00%)	0 / 8 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hydrosalpinx			
subjects affected / exposed	0 / 8 (0.00%)	0 / 8 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Menopausal symptoms			
subjects affected / exposed	0 / 8 (0.00%)	0 / 8 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ovarian cyst			
subjects affected / exposed	0 / 8 (0.00%)	0 / 8 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Uterine polyp			
subjects affected / exposed	0 / 8 (0.00%)	0 / 8 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Endometriosis			
subjects affected / exposed	0 / 8 (0.00%)	0 / 8 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Uterine cyst			
subjects affected / exposed	0 / 8 (0.00%)	0 / 8 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory, thoracic and mediastinal disorders			
Interstitial lung disease			
subjects affected / exposed	0 / 8 (0.00%)	0 / 8 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pleural cyst			
subjects affected / exposed	0 / 8 (0.00%)	0 / 8 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pulmonary embolism			
subjects affected / exposed	0 / 8 (0.00%)	0 / 8 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pleural effusion			
subjects affected / exposed	0 / 8 (0.00%)	0 / 8 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pulmonary fibrosis			
subjects affected / exposed	0 / 8 (0.00%)	0 / 8 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Product issues			
Device dislocation			
subjects affected / exposed	0 / 8 (0.00%)	0 / 8 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	0 / 8 (0.00%)	0 / 8 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
International normalised ratio increased			
subjects affected / exposed	0 / 8 (0.00%)	0 / 8 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Transaminases increased			
subjects affected / exposed	0 / 8 (0.00%)	0 / 8 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Injury, poisoning and procedural complications			
Ankle fracture			
subjects affected / exposed	0 / 8 (0.00%)	0 / 8 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Incisional hernia			
subjects affected / exposed	0 / 8 (0.00%)	0 / 8 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Joint injury			
subjects affected / exposed	0 / 8 (0.00%)	0 / 8 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Overdose			
subjects affected / exposed	0 / 8 (0.00%)	0 / 8 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Tendon rupture			

subjects affected / exposed	0 / 8 (0.00%)	0 / 8 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Spinal compression fracture			
subjects affected / exposed	0 / 8 (0.00%)	0 / 8 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Skin laceration			
subjects affected / exposed	0 / 8 (0.00%)	0 / 8 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Tibia fracture			
subjects affected / exposed	0 / 8 (0.00%)	0 / 8 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Wound dehiscence			
subjects affected / exposed	0 / 8 (0.00%)	0 / 8 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Congenital, familial and genetic disorders			
Developmental hip dysplasia			
subjects affected / exposed	0 / 8 (0.00%)	0 / 8 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac disorders			
Acute myocardial infarction			
subjects affected / exposed	0 / 8 (0.00%)	0 / 8 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Angina unstable			
subjects affected / exposed	0 / 8 (0.00%)	0 / 8 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Atrial fibrillation			
subjects affected / exposed	0 / 8 (0.00%)	0 / 8 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac arrest			
subjects affected / exposed	0 / 8 (0.00%)	0 / 8 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Sinus node dysfunction			
subjects affected / exposed	0 / 8 (0.00%)	0 / 8 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pericardial effusion			
subjects affected / exposed	0 / 8 (0.00%)	0 / 8 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Myocardial infarction			
subjects affected / exposed	0 / 8 (0.00%)	0 / 8 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nervous system disorders			
Cerebrovascular accident			
subjects affected / exposed	0 / 8 (0.00%)	0 / 8 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cerebral infarction			
subjects affected / exposed	0 / 8 (0.00%)	0 / 8 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Facial paralysis			
subjects affected / exposed	0 / 8 (0.00%)	0 / 8 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ischaemic stroke			

subjects affected / exposed	0 / 8 (0.00%)	0 / 8 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Seizure			
subjects affected / exposed	0 / 8 (0.00%)	0 / 8 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Paraparesis			
subjects affected / exposed	0 / 8 (0.00%)	0 / 8 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Syncope			
subjects affected / exposed	0 / 8 (0.00%)	0 / 8 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Subarachnoid haemorrhage			
subjects affected / exposed	0 / 8 (0.00%)	0 / 8 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Transient ischaemic attack			
subjects affected / exposed	0 / 8 (0.00%)	0 / 8 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lacunar infarction			
subjects affected / exposed	0 / 8 (0.00%)	0 / 8 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	0 / 8 (0.00%)	0 / 8 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Iron deficiency anaemia			

subjects affected / exposed	0 / 8 (0.00%)	0 / 8 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Neutropenia			
subjects affected / exposed	0 / 8 (0.00%)	0 / 8 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Eye disorders			
Glaucoma			
subjects affected / exposed	0 / 8 (0.00%)	0 / 8 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ulcerative keratitis			
subjects affected / exposed	0 / 8 (0.00%)	0 / 8 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
Acute abdomen			
subjects affected / exposed	0 / 8 (0.00%)	0 / 8 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Duodenal ulcer			
subjects affected / exposed	0 / 8 (0.00%)	0 / 8 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Duodenal ulcer perforation			
subjects affected / exposed	0 / 8 (0.00%)	0 / 8 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Enteritis			
subjects affected / exposed	0 / 8 (0.00%)	0 / 8 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Large intestine polyp			

subjects affected / exposed	0 / 8 (0.00%)	0 / 8 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Inguinal hernia			
subjects affected / exposed	0 / 8 (0.00%)	0 / 8 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastric ulcer			
subjects affected / exposed	0 / 8 (0.00%)	0 / 8 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Peritoneal adhesions			
subjects affected / exposed	0 / 8 (0.00%)	0 / 8 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Mesenteric cyst			
subjects affected / exposed	0 / 8 (0.00%)	0 / 8 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatobiliary disorders			
Acute hepatic failure			
subjects affected / exposed	0 / 8 (0.00%)	0 / 8 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bile duct stone			
subjects affected / exposed	0 / 8 (0.00%)	0 / 8 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cholecystitis acute			
subjects affected / exposed	0 / 8 (0.00%)	0 / 8 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cholelithiasis			

subjects affected / exposed	0 / 8 (0.00%)	0 / 8 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatic steatosis			
subjects affected / exposed	0 / 8 (0.00%)	0 / 8 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal and urinary disorders			
Calculus urinary			
subjects affected / exposed	0 / 8 (0.00%)	0 / 8 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
IgA nephropathy			
subjects affected / exposed	0 / 8 (0.00%)	0 / 8 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Musculoskeletal and connective tissue disorders			
Intervertebral disc degeneration			
subjects affected / exposed	0 / 8 (0.00%)	0 / 8 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Back pain			
subjects affected / exposed	0 / 8 (0.00%)	0 / 8 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Joint destruction			
subjects affected / exposed	0 / 8 (0.00%)	0 / 8 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lumbar spinal stenosis			
subjects affected / exposed	0 / 8 (0.00%)	0 / 8 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Osteoporotic fracture			
subjects affected / exposed	0 / 8 (0.00%)	0 / 8 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Osteoarthritis			
subjects affected / exposed	0 / 8 (0.00%)	0 / 8 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Rheumatoid arthritis			
subjects affected / exposed	0 / 8 (0.00%)	0 / 8 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Spinal osteoarthritis			
subjects affected / exposed	0 / 8 (0.00%)	0 / 8 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Synovial cyst			
subjects affected / exposed	0 / 8 (0.00%)	0 / 8 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Synovitis			
subjects affected / exposed	0 / 8 (0.00%)	0 / 8 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Tenosynovitis			
subjects affected / exposed	0 / 8 (0.00%)	0 / 8 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Soft tissue disorder			
subjects affected / exposed	0 / 8 (0.00%)	0 / 8 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			

COVID-19			
subjects affected / exposed	0 / 8 (0.00%)	0 / 8 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Appendicitis			
subjects affected / exposed	0 / 8 (0.00%)	0 / 8 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Escherichia sepsis			
subjects affected / exposed	0 / 8 (0.00%)	0 / 8 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diverticulitis			
subjects affected / exposed	0 / 8 (0.00%)	0 / 8 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
COVID-19 pneumonia			
subjects affected / exposed	0 / 8 (0.00%)	0 / 8 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Herpes simplex			
subjects affected / exposed	0 / 8 (0.00%)	0 / 8 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Herpes zoster			
subjects affected / exposed	0 / 8 (0.00%)	0 / 8 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lower respiratory tract infection			
subjects affected / exposed	0 / 8 (0.00%)	0 / 8 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumocystis jirovecii pneumonia			

subjects affected / exposed	0 / 8 (0.00%)	0 / 8 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia			
subjects affected / exposed	0 / 8 (0.00%)	0 / 8 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia bacterial			
subjects affected / exposed	0 / 8 (0.00%)	0 / 8 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pyelonephritis			
subjects affected / exposed	0 / 8 (0.00%)	0 / 8 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Postoperative wound infection			
subjects affected / exposed	0 / 8 (0.00%)	0 / 8 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Post procedural infection			
subjects affected / exposed	0 / 8 (0.00%)	0 / 8 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pyelonephritis acute			
subjects affected / exposed	0 / 8 (0.00%)	0 / 8 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Sepsis			
subjects affected / exposed	0 / 8 (0.00%)	0 / 8 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Septic shock			

subjects affected / exposed	0 / 8 (0.00%)	0 / 8 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urinary tract infection			
subjects affected / exposed	0 / 8 (0.00%)	0 / 8 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia cryptococcal			
subjects affected / exposed	0 / 8 (0.00%)	0 / 8 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metabolism and nutrition disorders			
Dehydration			
subjects affected / exposed	0 / 8 (0.00%)	0 / 8 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

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

Non-serious adverse events	GSK3196165 90mg + csDMARD (Global Cohort)	GSK3196165 150mg + csDMARD (Global Cohort)	Tofacitinib 5mg + csDMARD (Global Cohort)
Total subjects affected by non-serious adverse events			
subjects affected / exposed	233 / 545 (42.75%)	208 / 539 (38.59%)	105 / 286 (36.71%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Skin papilloma			
subjects affected / exposed	0 / 545 (0.00%)	0 / 539 (0.00%)	0 / 286 (0.00%)
occurrences (all)	0	0	0
Uterine leiomyoma			
subjects affected / exposed	0 / 545 (0.00%)	0 / 539 (0.00%)	0 / 286 (0.00%)
occurrences (all)	0	0	0
Vascular disorders			
Hypertension			
subjects affected / exposed	30 / 545 (5.50%)	31 / 539 (5.75%)	19 / 286 (6.64%)
occurrences (all)	32	32	20
General disorders and administration site conditions			

Injection site reaction			
subjects affected / exposed	42 / 545 (7.71%)	47 / 539 (8.72%)	5 / 286 (1.75%)
occurrences (all)	112	137	7
Application site rash			
subjects affected / exposed	0 / 545 (0.00%)	0 / 539 (0.00%)	0 / 286 (0.00%)
occurrences (all)	0	0	0
Vaccination site pain			
subjects affected / exposed	0 / 545 (0.00%)	0 / 539 (0.00%)	0 / 286 (0.00%)
occurrences (all)	0	0	0
Respiratory, thoracic and mediastinal disorders			
Dyspnoea			
subjects affected / exposed	0 / 545 (0.00%)	0 / 539 (0.00%)	0 / 286 (0.00%)
occurrences (all)	0	0	0
Cough			
subjects affected / exposed	0 / 545 (0.00%)	0 / 539 (0.00%)	0 / 286 (0.00%)
occurrences (all)	0	0	0
Epistaxis			
subjects affected / exposed	0 / 545 (0.00%)	0 / 539 (0.00%)	0 / 286 (0.00%)
occurrences (all)	0	0	0
Psychiatric disorders			
Insomnia			
subjects affected / exposed	0 / 545 (0.00%)	0 / 539 (0.00%)	0 / 286 (0.00%)
occurrences (all)	0	0	0
Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	0 / 545 (0.00%)	0 / 539 (0.00%)	0 / 286 (0.00%)
occurrences (all)	0	0	0
Aspartate aminotransferase increased			
subjects affected / exposed	0 / 545 (0.00%)	0 / 539 (0.00%)	0 / 286 (0.00%)
occurrences (all)	0	0	0
Blood beta-D-glucan increased			
subjects affected / exposed	0 / 545 (0.00%)	0 / 539 (0.00%)	0 / 286 (0.00%)
occurrences (all)	0	0	0
Blood creatine phosphokinase increased			

subjects affected / exposed	0 / 545 (0.00%)	0 / 539 (0.00%)	0 / 286 (0.00%)
occurrences (all)	0	0	0
Blood glucose increased			
subjects affected / exposed	0 / 545 (0.00%)	0 / 539 (0.00%)	0 / 286 (0.00%)
occurrences (all)	0	0	0
Blood pressure increased			
subjects affected / exposed	0 / 545 (0.00%)	0 / 539 (0.00%)	0 / 286 (0.00%)
occurrences (all)	0	0	0
Blood lactate dehydrogenase increased			
subjects affected / exposed	0 / 545 (0.00%)	0 / 539 (0.00%)	0 / 286 (0.00%)
occurrences (all)	0	0	0
Electrocardiogram T wave inversion			
subjects affected / exposed	0 / 545 (0.00%)	0 / 539 (0.00%)	0 / 286 (0.00%)
occurrences (all)	0	0	0
Electrocardiogram abnormal			
subjects affected / exposed	0 / 545 (0.00%)	0 / 539 (0.00%)	0 / 286 (0.00%)
occurrences (all)	0	0	0
Gamma-glutamyltransferase increased			
subjects affected / exposed	0 / 545 (0.00%)	0 / 539 (0.00%)	0 / 286 (0.00%)
occurrences (all)	0	0	0
Lipids abnormal			
subjects affected / exposed	0 / 545 (0.00%)	0 / 539 (0.00%)	0 / 286 (0.00%)
occurrences (all)	0	0	0
Low density lipoprotein increased			
subjects affected / exposed	0 / 545 (0.00%)	0 / 539 (0.00%)	0 / 286 (0.00%)
occurrences (all)	0	0	0
Liver function test increased			
subjects affected / exposed	0 / 545 (0.00%)	0 / 539 (0.00%)	0 / 286 (0.00%)
occurrences (all)	0	0	0
Lymphocyte count decreased			
subjects affected / exposed	0 / 545 (0.00%)	0 / 539 (0.00%)	0 / 286 (0.00%)
occurrences (all)	0	0	0
Protein urine present			

subjects affected / exposed	0 / 545 (0.00%)	0 / 539 (0.00%)	0 / 286 (0.00%)
occurrences (all)	0	0	0
Neutrophil count increased			
subjects affected / exposed	0 / 545 (0.00%)	0 / 539 (0.00%)	0 / 286 (0.00%)
occurrences (all)	0	0	0
Monocyte count decreased			
subjects affected / exposed	0 / 545 (0.00%)	0 / 539 (0.00%)	0 / 286 (0.00%)
occurrences (all)	0	0	0
White blood cell count decreased			
subjects affected / exposed	0 / 545 (0.00%)	0 / 539 (0.00%)	0 / 286 (0.00%)
occurrences (all)	0	0	0
White blood cell count increased			
subjects affected / exposed	0 / 545 (0.00%)	0 / 539 (0.00%)	0 / 286 (0.00%)
occurrences (all)	0	0	0
Injury, poisoning and procedural complications			
Cartilage injury			
subjects affected / exposed	0 / 545 (0.00%)	0 / 539 (0.00%)	0 / 286 (0.00%)
occurrences (all)	0	0	0
Joint injury			
subjects affected / exposed	0 / 545 (0.00%)	0 / 539 (0.00%)	0 / 286 (0.00%)
occurrences (all)	0	0	0
Spinal fracture			
subjects affected / exposed	0 / 545 (0.00%)	0 / 539 (0.00%)	0 / 286 (0.00%)
occurrences (all)	0	0	0
Cardiac disorders			
Bundle branch block right			
subjects affected / exposed	0 / 545 (0.00%)	0 / 539 (0.00%)	0 / 286 (0.00%)
occurrences (all)	0	0	0
Sinus bradycardia			
subjects affected / exposed	0 / 545 (0.00%)	0 / 539 (0.00%)	0 / 286 (0.00%)
occurrences (all)	0	0	0
Ventricular tachycardia			
subjects affected / exposed	0 / 545 (0.00%)	0 / 539 (0.00%)	0 / 286 (0.00%)
occurrences (all)	0	0	0
Nervous system disorders			

Headache			
subjects affected / exposed	33 / 545 (6.06%)	19 / 539 (3.53%)	13 / 286 (4.55%)
occurrences (all)	36	23	15
Cervicobrachial syndrome			
subjects affected / exposed	0 / 545 (0.00%)	0 / 539 (0.00%)	0 / 286 (0.00%)
occurrences (all)	0	0	0
Dizziness			
subjects affected / exposed	0 / 545 (0.00%)	0 / 539 (0.00%)	0 / 286 (0.00%)
occurrences (all)	0	0	0
Post herpetic neuralgia			
subjects affected / exposed	0 / 545 (0.00%)	0 / 539 (0.00%)	0 / 286 (0.00%)
occurrences (all)	0	0	0
Transient ischaemic attack			
subjects affected / exposed	0 / 545 (0.00%)	0 / 539 (0.00%)	0 / 286 (0.00%)
occurrences (all)	0	0	0
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	35 / 545 (6.42%)	19 / 539 (3.53%)	8 / 286 (2.80%)
occurrences (all)	41	20	9
Lymphopenia			
subjects affected / exposed	33 / 545 (6.06%)	38 / 539 (7.05%)	24 / 286 (8.39%)
occurrences (all)	45	57	32
Leukopenia			
subjects affected / exposed	0 / 545 (0.00%)	0 / 539 (0.00%)	0 / 286 (0.00%)
occurrences (all)	0	0	0
Eye disorders			
Scleritis			
subjects affected / exposed	0 / 545 (0.00%)	0 / 539 (0.00%)	0 / 286 (0.00%)
occurrences (all)	0	0	0
Gastrointestinal disorders			
Abdominal discomfort			
subjects affected / exposed	0 / 545 (0.00%)	0 / 539 (0.00%)	0 / 286 (0.00%)
occurrences (all)	0	0	0
Abdominal pain			
subjects affected / exposed	0 / 545 (0.00%)	0 / 539 (0.00%)	0 / 286 (0.00%)
occurrences (all)	0	0	0
Irritable bowel syndrome			

subjects affected / exposed	0 / 545 (0.00%)	0 / 539 (0.00%)	0 / 286 (0.00%)
occurrences (all)	0	0	0
Diarrhoea			
subjects affected / exposed	0 / 545 (0.00%)	0 / 539 (0.00%)	0 / 286 (0.00%)
occurrences (all)	0	0	0
Constipation			
subjects affected / exposed	0 / 545 (0.00%)	0 / 539 (0.00%)	0 / 286 (0.00%)
occurrences (all)	0	0	0
Abdominal pain upper			
subjects affected / exposed	0 / 545 (0.00%)	0 / 539 (0.00%)	0 / 286 (0.00%)
occurrences (all)	0	0	0
Nausea			
subjects affected / exposed	0 / 545 (0.00%)	0 / 539 (0.00%)	0 / 286 (0.00%)
occurrences (all)	0	0	0
Salivary gland mass			
subjects affected / exposed	0 / 545 (0.00%)	0 / 539 (0.00%)	0 / 286 (0.00%)
occurrences (all)	0	0	0
Hepatobiliary disorders			
Hepatic function abnormal			
subjects affected / exposed	0 / 545 (0.00%)	0 / 539 (0.00%)	0 / 286 (0.00%)
occurrences (all)	0	0	0
Skin and subcutaneous tissue disorders			
Drug eruption			
subjects affected / exposed	0 / 545 (0.00%)	0 / 539 (0.00%)	0 / 286 (0.00%)
occurrences (all)	0	0	0
Pruritus			
subjects affected / exposed	0 / 545 (0.00%)	0 / 539 (0.00%)	0 / 286 (0.00%)
occurrences (all)	0	0	0
Rash			
subjects affected / exposed	0 / 545 (0.00%)	0 / 539 (0.00%)	0 / 286 (0.00%)
occurrences (all)	0	0	0
Renal and urinary disorders			
Renal impairment			
subjects affected / exposed	0 / 545 (0.00%)	0 / 539 (0.00%)	0 / 286 (0.00%)
occurrences (all)	0	0	0
Musculoskeletal and connective tissue disorders			

Rheumatoid arthritis			
subjects affected / exposed	41 / 545 (7.52%)	40 / 539 (7.42%)	20 / 286 (6.99%)
occurrences (all)	51	53	23
Back pain			
subjects affected / exposed	0 / 545 (0.00%)	0 / 539 (0.00%)	0 / 286 (0.00%)
occurrences (all)	0	0	0
Spinal osteoarthritis			
subjects affected / exposed	0 / 545 (0.00%)	0 / 539 (0.00%)	0 / 286 (0.00%)
occurrences (all)	0	0	0
Osteoarthritis			
subjects affected / exposed	0 / 545 (0.00%)	0 / 539 (0.00%)	0 / 286 (0.00%)
occurrences (all)	0	0	0
Neck pain			
subjects affected / exposed	0 / 545 (0.00%)	0 / 539 (0.00%)	0 / 286 (0.00%)
occurrences (all)	0	0	0
Musculoskeletal stiffness			
subjects affected / exposed	0 / 545 (0.00%)	0 / 539 (0.00%)	0 / 286 (0.00%)
occurrences (all)	0	0	0
Spondylolisthesis			
subjects affected / exposed	0 / 545 (0.00%)	0 / 539 (0.00%)	0 / 286 (0.00%)
occurrences (all)	0	0	0
Infections and infestations			
Urinary tract infection			
subjects affected / exposed	34 / 545 (6.24%)	39 / 539 (7.24%)	19 / 286 (6.64%)
occurrences (all)	47	45	24
Upper respiratory tract infection			
subjects affected / exposed	0 / 545 (0.00%)	0 / 539 (0.00%)	0 / 286 (0.00%)
occurrences (all)	0	0	0
Nasopharyngitis			
subjects affected / exposed	28 / 545 (5.14%)	33 / 539 (6.12%)	15 / 286 (5.24%)
occurrences (all)	33	43	15
COVID-19			
subjects affected / exposed	49 / 545 (8.99%)	32 / 539 (5.94%)	27 / 286 (9.44%)
occurrences (all)	51	35	27
Gingivitis			

subjects affected / exposed	0 / 545 (0.00%)	0 / 539 (0.00%)	0 / 286 (0.00%)
occurrences (all)	0	0	0
Herpes zoster			
subjects affected / exposed	0 / 545 (0.00%)	0 / 539 (0.00%)	0 / 286 (0.00%)
occurrences (all)	0	0	0
Influenza			
subjects affected / exposed	0 / 545 (0.00%)	0 / 539 (0.00%)	0 / 286 (0.00%)
occurrences (all)	0	0	0
Sinusitis			
subjects affected / exposed	0 / 545 (0.00%)	0 / 539 (0.00%)	0 / 286 (0.00%)
occurrences (all)	0	0	0
Pneumonia			
subjects affected / exposed	0 / 545 (0.00%)	0 / 539 (0.00%)	0 / 286 (0.00%)
occurrences (all)	0	0	0
Pharyngitis			
subjects affected / exposed	0 / 545 (0.00%)	0 / 539 (0.00%)	0 / 286 (0.00%)
occurrences (all)	0	0	0
Metabolism and nutrition disorders			
Hyperlipidaemia			
subjects affected / exposed	0 / 545 (0.00%)	0 / 539 (0.00%)	0 / 286 (0.00%)
occurrences (all)	0	0	0
Hypercholesterolaemia			
subjects affected / exposed	0 / 545 (0.00%)	0 / 539 (0.00%)	0 / 286 (0.00%)
occurrences (all)	0	0	0
Diabetes mellitus			
subjects affected / exposed	0 / 545 (0.00%)	0 / 539 (0.00%)	0 / 286 (0.00%)
occurrences (all)	0	0	0
Hypertriglyceridaemia			
subjects affected / exposed	0 / 545 (0.00%)	0 / 539 (0.00%)	0 / 286 (0.00%)
occurrences (all)	0	0	0
Hypokalaemia			
subjects affected / exposed	0 / 545 (0.00%)	0 / 539 (0.00%)	0 / 286 (0.00%)
occurrences (all)	0	0	0

Non-serious adverse events	Pooled Placebo (Global Cohort)	Placebo+csDMARD and GSK3196165 90mg+csDMARD (Global Cohort)	Placebo +csDMARD and GSK3196165 150mg +csDMARD (Global Cohort)

Total subjects affected by non-serious adverse events subjects affected / exposed	3 / 255 (1.18%)	28 / 85 (32.94%)	31 / 80 (38.75%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps) Skin papilloma subjects affected / exposed occurrences (all)	0 / 255 (0.00%) 0	0 / 85 (0.00%) 0	0 / 80 (0.00%) 0
Uterine leiomyoma subjects affected / exposed occurrences (all)	0 / 255 (0.00%) 0	0 / 85 (0.00%) 0	0 / 80 (0.00%) 0
Vascular disorders Hypertension subjects affected / exposed occurrences (all)	0 / 255 (0.00%) 0	0 / 85 (0.00%) 0	0 / 80 (0.00%) 0
General disorders and administration site conditions Injection site reaction subjects affected / exposed occurrences (all)	3 / 255 (1.18%) 3	5 / 85 (5.88%) 8	10 / 80 (12.50%) 15
Application site rash subjects affected / exposed occurrences (all)	0 / 255 (0.00%) 0	0 / 85 (0.00%) 0	0 / 80 (0.00%) 0
Vaccination site pain subjects affected / exposed occurrences (all)	0 / 255 (0.00%) 0	0 / 85 (0.00%) 0	0 / 80 (0.00%) 0
Respiratory, thoracic and mediastinal disorders Dyspnoea subjects affected / exposed occurrences (all)	0 / 255 (0.00%) 0	0 / 85 (0.00%) 0	0 / 80 (0.00%) 0
Cough subjects affected / exposed occurrences (all)	0 / 255 (0.00%) 0	0 / 85 (0.00%) 0	0 / 80 (0.00%) 0
Epistaxis subjects affected / exposed occurrences (all)	0 / 255 (0.00%) 0	0 / 85 (0.00%) 0	0 / 80 (0.00%) 0
Psychiatric disorders Insomnia			

subjects affected / exposed	0 / 255 (0.00%)	0 / 85 (0.00%)	0 / 80 (0.00%)
occurrences (all)	0	0	0
Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	0 / 255 (0.00%)	0 / 85 (0.00%)	0 / 80 (0.00%)
occurrences (all)	0	0	0
Aspartate aminotransferase increased			
subjects affected / exposed	0 / 255 (0.00%)	0 / 85 (0.00%)	0 / 80 (0.00%)
occurrences (all)	0	0	0
Blood beta-D-glucan increased			
subjects affected / exposed	0 / 255 (0.00%)	0 / 85 (0.00%)	0 / 80 (0.00%)
occurrences (all)	0	0	0
Blood creatine phosphokinase increased			
subjects affected / exposed	0 / 255 (0.00%)	0 / 85 (0.00%)	0 / 80 (0.00%)
occurrences (all)	0	0	0
Blood glucose increased			
subjects affected / exposed	0 / 255 (0.00%)	0 / 85 (0.00%)	0 / 80 (0.00%)
occurrences (all)	0	0	0
Blood pressure increased			
subjects affected / exposed	0 / 255 (0.00%)	0 / 85 (0.00%)	0 / 80 (0.00%)
occurrences (all)	0	0	0
Blood lactate dehydrogenase increased			
subjects affected / exposed	0 / 255 (0.00%)	0 / 85 (0.00%)	0 / 80 (0.00%)
occurrences (all)	0	0	0
Electrocardiogram T wave inversion			
subjects affected / exposed	0 / 255 (0.00%)	0 / 85 (0.00%)	0 / 80 (0.00%)
occurrences (all)	0	0	0
Electrocardiogram abnormal			
subjects affected / exposed	0 / 255 (0.00%)	0 / 85 (0.00%)	0 / 80 (0.00%)
occurrences (all)	0	0	0
Gamma-glutamyltransferase increased			
subjects affected / exposed	0 / 255 (0.00%)	0 / 85 (0.00%)	0 / 80 (0.00%)
occurrences (all)	0	0	0
Lipids abnormal			

subjects affected / exposed	0 / 255 (0.00%)	0 / 85 (0.00%)	0 / 80 (0.00%)
occurrences (all)	0	0	0
Low density lipoprotein increased			
subjects affected / exposed	0 / 255 (0.00%)	0 / 85 (0.00%)	0 / 80 (0.00%)
occurrences (all)	0	0	0
Liver function test increased			
subjects affected / exposed	0 / 255 (0.00%)	0 / 85 (0.00%)	0 / 80 (0.00%)
occurrences (all)	0	0	0
Lymphocyte count decreased			
subjects affected / exposed	0 / 255 (0.00%)	0 / 85 (0.00%)	0 / 80 (0.00%)
occurrences (all)	0	0	0
Protein urine present			
subjects affected / exposed	0 / 255 (0.00%)	0 / 85 (0.00%)	0 / 80 (0.00%)
occurrences (all)	0	0	0
Neutrophil count increased			
subjects affected / exposed	0 / 255 (0.00%)	0 / 85 (0.00%)	0 / 80 (0.00%)
occurrences (all)	0	0	0
Monocyte count decreased			
subjects affected / exposed	0 / 255 (0.00%)	0 / 85 (0.00%)	0 / 80 (0.00%)
occurrences (all)	0	0	0
White blood cell count decreased			
subjects affected / exposed	0 / 255 (0.00%)	0 / 85 (0.00%)	0 / 80 (0.00%)
occurrences (all)	0	0	0
White blood cell count increased			
subjects affected / exposed	0 / 255 (0.00%)	0 / 85 (0.00%)	0 / 80 (0.00%)
occurrences (all)	0	0	0
Injury, poisoning and procedural complications			
Cartilage injury			
subjects affected / exposed	0 / 255 (0.00%)	0 / 85 (0.00%)	0 / 80 (0.00%)
occurrences (all)	0	0	0
Joint injury			
subjects affected / exposed	0 / 255 (0.00%)	0 / 85 (0.00%)	0 / 80 (0.00%)
occurrences (all)	0	0	0
Spinal fracture			

subjects affected / exposed	0 / 255 (0.00%)	0 / 85 (0.00%)	0 / 80 (0.00%)
occurrences (all)	0	0	0
Cardiac disorders			
Bundle branch block right			
subjects affected / exposed	0 / 255 (0.00%)	0 / 85 (0.00%)	0 / 80 (0.00%)
occurrences (all)	0	0	0
Sinus bradycardia			
subjects affected / exposed	0 / 255 (0.00%)	0 / 85 (0.00%)	0 / 80 (0.00%)
occurrences (all)	0	0	0
Ventricular tachycardia			
subjects affected / exposed	0 / 255 (0.00%)	0 / 85 (0.00%)	0 / 80 (0.00%)
occurrences (all)	0	0	0
Nervous system disorders			
Headache			
subjects affected / exposed	0 / 255 (0.00%)	4 / 85 (4.71%)	5 / 80 (6.25%)
occurrences (all)	0	5	6
Cervicobrachial syndrome			
subjects affected / exposed	0 / 255 (0.00%)	0 / 85 (0.00%)	0 / 80 (0.00%)
occurrences (all)	0	0	0
Dizziness			
subjects affected / exposed	0 / 255 (0.00%)	0 / 85 (0.00%)	0 / 80 (0.00%)
occurrences (all)	0	0	0
Post herpetic neuralgia			
subjects affected / exposed	0 / 255 (0.00%)	0 / 85 (0.00%)	0 / 80 (0.00%)
occurrences (all)	0	0	0
Transient ischaemic attack			
subjects affected / exposed	0 / 255 (0.00%)	0 / 85 (0.00%)	0 / 80 (0.00%)
occurrences (all)	0	0	0
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	0 / 255 (0.00%)	1 / 85 (1.18%)	4 / 80 (5.00%)
occurrences (all)	0	1	4
Lymphopenia			
subjects affected / exposed	0 / 255 (0.00%)	8 / 85 (9.41%)	3 / 80 (3.75%)
occurrences (all)	0	9	5
Leukopenia			

subjects affected / exposed	0 / 255 (0.00%)	0 / 85 (0.00%)	0 / 80 (0.00%)
occurrences (all)	0	0	0
Eye disorders			
Scleritis			
subjects affected / exposed	0 / 255 (0.00%)	0 / 85 (0.00%)	0 / 80 (0.00%)
occurrences (all)	0	0	0
Gastrointestinal disorders			
Abdominal discomfort			
subjects affected / exposed	0 / 255 (0.00%)	0 / 85 (0.00%)	0 / 80 (0.00%)
occurrences (all)	0	0	0
Abdominal pain			
subjects affected / exposed	0 / 255 (0.00%)	0 / 85 (0.00%)	0 / 80 (0.00%)
occurrences (all)	0	0	0
Irritable bowel syndrome			
subjects affected / exposed	0 / 255 (0.00%)	0 / 85 (0.00%)	0 / 80 (0.00%)
occurrences (all)	0	0	0
Diarrhoea			
subjects affected / exposed	0 / 255 (0.00%)	0 / 85 (0.00%)	0 / 80 (0.00%)
occurrences (all)	0	0	0
Constipation			
subjects affected / exposed	0 / 255 (0.00%)	0 / 85 (0.00%)	0 / 80 (0.00%)
occurrences (all)	0	0	0
Abdominal pain upper			
subjects affected / exposed	0 / 255 (0.00%)	0 / 85 (0.00%)	0 / 80 (0.00%)
occurrences (all)	0	0	0
Nausea			
subjects affected / exposed	0 / 255 (0.00%)	0 / 85 (0.00%)	0 / 80 (0.00%)
occurrences (all)	0	0	0
Salivary gland mass			
subjects affected / exposed	0 / 255 (0.00%)	0 / 85 (0.00%)	0 / 80 (0.00%)
occurrences (all)	0	0	0
Hepatobiliary disorders			
Hepatic function abnormal			
subjects affected / exposed	0 / 255 (0.00%)	0 / 85 (0.00%)	0 / 80 (0.00%)
occurrences (all)	0	0	0
Skin and subcutaneous tissue disorders			

Drug eruption			
subjects affected / exposed	0 / 255 (0.00%)	0 / 85 (0.00%)	0 / 80 (0.00%)
occurrences (all)	0	0	0
Pruritus			
subjects affected / exposed	0 / 255 (0.00%)	0 / 85 (0.00%)	0 / 80 (0.00%)
occurrences (all)	0	0	0
Rash			
subjects affected / exposed	0 / 255 (0.00%)	0 / 85 (0.00%)	0 / 80 (0.00%)
occurrences (all)	0	0	0
Renal and urinary disorders			
Renal impairment			
subjects affected / exposed	0 / 255 (0.00%)	0 / 85 (0.00%)	0 / 80 (0.00%)
occurrences (all)	0	0	0
Musculoskeletal and connective tissue disorders			
Rheumatoid arthritis			
subjects affected / exposed	0 / 255 (0.00%)	3 / 85 (3.53%)	5 / 80 (6.25%)
occurrences (all)	0	4	7
Back pain			
subjects affected / exposed	0 / 255 (0.00%)	0 / 85 (0.00%)	0 / 80 (0.00%)
occurrences (all)	0	0	0
Spinal osteoarthritis			
subjects affected / exposed	0 / 255 (0.00%)	0 / 85 (0.00%)	0 / 80 (0.00%)
occurrences (all)	0	0	0
Osteoarthritis			
subjects affected / exposed	0 / 255 (0.00%)	0 / 85 (0.00%)	0 / 80 (0.00%)
occurrences (all)	0	0	0
Neck pain			
subjects affected / exposed	0 / 255 (0.00%)	0 / 85 (0.00%)	0 / 80 (0.00%)
occurrences (all)	0	0	0
Musculoskeletal stiffness			
subjects affected / exposed	0 / 255 (0.00%)	0 / 85 (0.00%)	0 / 80 (0.00%)
occurrences (all)	0	0	0
Spondylolisthesis			
subjects affected / exposed	0 / 255 (0.00%)	0 / 85 (0.00%)	0 / 80 (0.00%)
occurrences (all)	0	0	0
Infections and infestations			

Urinary tract infection			
subjects affected / exposed	0 / 255 (0.00%)	2 / 85 (2.35%)	6 / 80 (7.50%)
occurrences (all)	0	3	6
Upper respiratory tract infection			
subjects affected / exposed	0 / 255 (0.00%)	5 / 85 (5.88%)	4 / 80 (5.00%)
occurrences (all)	0	5	5
Nasopharyngitis			
subjects affected / exposed	0 / 255 (0.00%)	5 / 85 (5.88%)	1 / 80 (1.25%)
occurrences (all)	0	7	1
COVID-19			
subjects affected / exposed	0 / 255 (0.00%)	3 / 85 (3.53%)	4 / 80 (5.00%)
occurrences (all)	0	3	4
Gingivitis			
subjects affected / exposed	0 / 255 (0.00%)	0 / 85 (0.00%)	0 / 80 (0.00%)
occurrences (all)	0	0	0
Herpes zoster			
subjects affected / exposed	0 / 255 (0.00%)	0 / 85 (0.00%)	0 / 80 (0.00%)
occurrences (all)	0	0	0
Influenza			
subjects affected / exposed	0 / 255 (0.00%)	0 / 85 (0.00%)	0 / 80 (0.00%)
occurrences (all)	0	0	0
Sinusitis			
subjects affected / exposed	0 / 255 (0.00%)	0 / 85 (0.00%)	0 / 80 (0.00%)
occurrences (all)	0	0	0
Pneumonia			
subjects affected / exposed	0 / 255 (0.00%)	0 / 85 (0.00%)	0 / 80 (0.00%)
occurrences (all)	0	0	0
Pharyngitis			
subjects affected / exposed	0 / 255 (0.00%)	0 / 85 (0.00%)	0 / 80 (0.00%)
occurrences (all)	0	0	0
Metabolism and nutrition disorders			
Hyperlipidaemia			
subjects affected / exposed	0 / 255 (0.00%)	0 / 85 (0.00%)	0 / 80 (0.00%)
occurrences (all)	0	0	0
Hypercholesterolaemia			

subjects affected / exposed	0 / 255 (0.00%)	0 / 85 (0.00%)	0 / 80 (0.00%)
occurrences (all)	0	0	0
Diabetes mellitus			
subjects affected / exposed	0 / 255 (0.00%)	0 / 85 (0.00%)	0 / 80 (0.00%)
occurrences (all)	0	0	0
Hypertriglyceridaemia			
subjects affected / exposed	0 / 255 (0.00%)	0 / 85 (0.00%)	0 / 80 (0.00%)
occurrences (all)	0	0	0
Hypokalaemia			
subjects affected / exposed	0 / 255 (0.00%)	0 / 85 (0.00%)	0 / 80 (0.00%)
occurrences (all)	0	0	0

Non-serious adverse events	Placebo +csDMARD and Tofacitinib 5mg +csDMARD (Global Cohort)	GSK3196165 90mg + csDMARD (Asia Cohort)	GSK3196165 150mg + csDMARD (Asia Cohort)
Total subjects affected by non-serious adverse events			
subjects affected / exposed	23 / 67 (34.33%)	28 / 47 (59.57%)	39 / 49 (79.59%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Skin papilloma			
subjects affected / exposed	0 / 67 (0.00%)	0 / 47 (0.00%)	0 / 49 (0.00%)
occurrences (all)	0	0	0
Uterine leiomyoma			
subjects affected / exposed	0 / 67 (0.00%)	0 / 47 (0.00%)	0 / 49 (0.00%)
occurrences (all)	0	0	0
Vascular disorders			
Hypertension			
subjects affected / exposed	0 / 67 (0.00%)	0 / 47 (0.00%)	5 / 49 (10.20%)
occurrences (all)	0	0	5
General disorders and administration site conditions			
Injection site reaction			
subjects affected / exposed	0 / 67 (0.00%)	2 / 47 (4.26%)	5 / 49 (10.20%)
occurrences (all)	0	5	6
Application site rash			
subjects affected / exposed	0 / 67 (0.00%)	0 / 47 (0.00%)	0 / 49 (0.00%)
occurrences (all)	0	0	0
Vaccination site pain			

subjects affected / exposed	0 / 67 (0.00%)	0 / 47 (0.00%)	3 / 49 (6.12%)
occurrences (all)	0	0	4
Respiratory, thoracic and mediastinal disorders			
Dyspnoea			
subjects affected / exposed	0 / 67 (0.00%)	0 / 47 (0.00%)	1 / 49 (2.04%)
occurrences (all)	0	0	1
Cough			
subjects affected / exposed	0 / 67 (0.00%)	2 / 47 (4.26%)	3 / 49 (6.12%)
occurrences (all)	0	2	3
Epistaxis			
subjects affected / exposed	0 / 67 (0.00%)	0 / 47 (0.00%)	0 / 49 (0.00%)
occurrences (all)	0	0	0
Psychiatric disorders			
Insomnia			
subjects affected / exposed	0 / 67 (0.00%)	0 / 47 (0.00%)	0 / 49 (0.00%)
occurrences (all)	0	0	0
Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	0 / 67 (0.00%)	4 / 47 (8.51%)	1 / 49 (2.04%)
occurrences (all)	0	6	1
Aspartate aminotransferase increased			
subjects affected / exposed	0 / 67 (0.00%)	5 / 47 (10.64%)	1 / 49 (2.04%)
occurrences (all)	0	10	1
Blood beta-D-glucan increased			
subjects affected / exposed	0 / 67 (0.00%)	0 / 47 (0.00%)	0 / 49 (0.00%)
occurrences (all)	0	0	0
Blood creatine phosphokinase increased			
subjects affected / exposed	0 / 67 (0.00%)	2 / 47 (4.26%)	2 / 49 (4.08%)
occurrences (all)	0	3	2
Blood glucose increased			
subjects affected / exposed	0 / 67 (0.00%)	3 / 47 (6.38%)	2 / 49 (4.08%)
occurrences (all)	0	4	3
Blood pressure increased			
subjects affected / exposed	0 / 67 (0.00%)	0 / 47 (0.00%)	0 / 49 (0.00%)
occurrences (all)	0	0	0

Blood lactate dehydrogenase increased			
subjects affected / exposed	0 / 67 (0.00%)	3 / 47 (6.38%)	1 / 49 (2.04%)
occurrences (all)	0	4	1
Electrocardiogram T wave inversion			
subjects affected / exposed	0 / 67 (0.00%)	0 / 47 (0.00%)	0 / 49 (0.00%)
occurrences (all)	0	0	0
Electrocardiogram abnormal			
subjects affected / exposed	0 / 67 (0.00%)	0 / 47 (0.00%)	0 / 49 (0.00%)
occurrences (all)	0	0	0
Gamma-glutamyltransferase increased			
subjects affected / exposed	0 / 67 (0.00%)	0 / 47 (0.00%)	0 / 49 (0.00%)
occurrences (all)	0	0	0
Lipids abnormal			
subjects affected / exposed	0 / 67 (0.00%)	0 / 47 (0.00%)	0 / 49 (0.00%)
occurrences (all)	0	0	0
Low density lipoprotein increased			
subjects affected / exposed	0 / 67 (0.00%)	1 / 47 (2.13%)	1 / 49 (2.04%)
occurrences (all)	0	2	1
Liver function test increased			
subjects affected / exposed	0 / 67 (0.00%)	0 / 47 (0.00%)	0 / 49 (0.00%)
occurrences (all)	0	0	0
Lymphocyte count decreased			
subjects affected / exposed	0 / 67 (0.00%)	6 / 47 (12.77%)	6 / 49 (12.24%)
occurrences (all)	0	13	9
Protein urine present			
subjects affected / exposed	0 / 67 (0.00%)	0 / 47 (0.00%)	0 / 49 (0.00%)
occurrences (all)	0	0	0
Neutrophil count increased			
subjects affected / exposed	0 / 67 (0.00%)	0 / 47 (0.00%)	0 / 49 (0.00%)
occurrences (all)	0	0	0
Monocyte count decreased			
subjects affected / exposed	0 / 67 (0.00%)	3 / 47 (6.38%)	1 / 49 (2.04%)
occurrences (all)	0	4	1
White blood cell count decreased			

subjects affected / exposed	0 / 67 (0.00%)	2 / 47 (4.26%)	0 / 49 (0.00%)
occurrences (all)	0	7	0
White blood cell count increased			
subjects affected / exposed	0 / 67 (0.00%)	0 / 47 (0.00%)	0 / 49 (0.00%)
occurrences (all)	0	0	0
Injury, poisoning and procedural complications			
Cartilage injury			
subjects affected / exposed	0 / 67 (0.00%)	0 / 47 (0.00%)	0 / 49 (0.00%)
occurrences (all)	0	0	0
Joint injury			
subjects affected / exposed	0 / 67 (0.00%)	0 / 47 (0.00%)	0 / 49 (0.00%)
occurrences (all)	0	0	0
Spinal fracture			
subjects affected / exposed	0 / 67 (0.00%)	0 / 47 (0.00%)	0 / 49 (0.00%)
occurrences (all)	0	0	0
Cardiac disorders			
Bundle branch block right			
subjects affected / exposed	0 / 67 (0.00%)	0 / 47 (0.00%)	0 / 49 (0.00%)
occurrences (all)	0	0	0
Sinus bradycardia			
subjects affected / exposed	0 / 67 (0.00%)	0 / 47 (0.00%)	0 / 49 (0.00%)
occurrences (all)	0	0	0
Ventricular tachycardia			
subjects affected / exposed	0 / 67 (0.00%)	0 / 47 (0.00%)	0 / 49 (0.00%)
occurrences (all)	0	0	0
Nervous system disorders			
Headache			
subjects affected / exposed	5 / 67 (7.46%)	1 / 47 (2.13%)	3 / 49 (6.12%)
occurrences (all)	5	3	3
Cervicobrachial syndrome			
subjects affected / exposed	0 / 67 (0.00%)	0 / 47 (0.00%)	0 / 49 (0.00%)
occurrences (all)	0	0	0
Dizziness			
subjects affected / exposed	0 / 67 (0.00%)	0 / 47 (0.00%)	4 / 49 (8.16%)
occurrences (all)	0	0	6
Post herpetic neuralgia			

subjects affected / exposed	0 / 67 (0.00%)	0 / 47 (0.00%)	0 / 49 (0.00%)
occurrences (all)	0	0	0
Transient ischaemic attack			
subjects affected / exposed	0 / 67 (0.00%)	0 / 47 (0.00%)	0 / 49 (0.00%)
occurrences (all)	0	0	0
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	2 / 67 (2.99%)	4 / 47 (8.51%)	7 / 49 (14.29%)
occurrences (all)	2	4	8
Lymphopenia			
subjects affected / exposed	4 / 67 (5.97%)	0 / 47 (0.00%)	5 / 49 (10.20%)
occurrences (all)	5	0	12
Leukopenia			
subjects affected / exposed	0 / 67 (0.00%)	1 / 47 (2.13%)	3 / 49 (6.12%)
occurrences (all)	0	1	8
Eye disorders			
Scleritis			
subjects affected / exposed	0 / 67 (0.00%)	0 / 47 (0.00%)	0 / 49 (0.00%)
occurrences (all)	0	0	0
Gastrointestinal disorders			
Abdominal discomfort			
subjects affected / exposed	0 / 67 (0.00%)	0 / 47 (0.00%)	0 / 49 (0.00%)
occurrences (all)	0	0	0
Abdominal pain			
subjects affected / exposed	0 / 67 (0.00%)	0 / 47 (0.00%)	0 / 49 (0.00%)
occurrences (all)	0	0	0
Irritable bowel syndrome			
subjects affected / exposed	0 / 67 (0.00%)	0 / 47 (0.00%)	0 / 49 (0.00%)
occurrences (all)	0	0	0
Diarrhoea			
subjects affected / exposed	0 / 67 (0.00%)	2 / 47 (4.26%)	2 / 49 (4.08%)
occurrences (all)	0	2	2
Constipation			
subjects affected / exposed	0 / 67 (0.00%)	0 / 47 (0.00%)	0 / 49 (0.00%)
occurrences (all)	0	0	0
Abdominal pain upper			

subjects affected / exposed	0 / 67 (0.00%)	0 / 47 (0.00%)	0 / 49 (0.00%)
occurrences (all)	0	0	0
Nausea			
subjects affected / exposed	0 / 67 (0.00%)	3 / 47 (6.38%)	1 / 49 (2.04%)
occurrences (all)	0	3	1
Salivary gland mass			
subjects affected / exposed	0 / 67 (0.00%)	0 / 47 (0.00%)	0 / 49 (0.00%)
occurrences (all)	0	0	0
Hepatobiliary disorders			
Hepatic function abnormal			
subjects affected / exposed	0 / 67 (0.00%)	0 / 47 (0.00%)	3 / 49 (6.12%)
occurrences (all)	0	0	3
Skin and subcutaneous tissue disorders			
Drug eruption			
subjects affected / exposed	0 / 67 (0.00%)	0 / 47 (0.00%)	1 / 49 (2.04%)
occurrences (all)	0	0	1
Pruritus			
subjects affected / exposed	0 / 67 (0.00%)	3 / 47 (6.38%)	0 / 49 (0.00%)
occurrences (all)	0	3	0
Rash			
subjects affected / exposed	0 / 67 (0.00%)	0 / 47 (0.00%)	0 / 49 (0.00%)
occurrences (all)	0	0	0
Renal and urinary disorders			
Renal impairment			
subjects affected / exposed	0 / 67 (0.00%)	0 / 47 (0.00%)	0 / 49 (0.00%)
occurrences (all)	0	0	0
Musculoskeletal and connective tissue disorders			
Rheumatoid arthritis			
subjects affected / exposed	6 / 67 (8.96%)	3 / 47 (6.38%)	0 / 49 (0.00%)
occurrences (all)	7	4	0
Back pain			
subjects affected / exposed	0 / 67 (0.00%)	1 / 47 (2.13%)	1 / 49 (2.04%)
occurrences (all)	0	1	1
Spinal osteoarthritis			
subjects affected / exposed	0 / 67 (0.00%)	0 / 47 (0.00%)	0 / 49 (0.00%)
occurrences (all)	0	0	0

Osteoarthritis			
subjects affected / exposed	0 / 67 (0.00%)	0 / 47 (0.00%)	0 / 49 (0.00%)
occurrences (all)	0	0	0
Neck pain			
subjects affected / exposed	0 / 67 (0.00%)	0 / 47 (0.00%)	0 / 49 (0.00%)
occurrences (all)	0	0	0
Musculoskeletal stiffness			
subjects affected / exposed	0 / 67 (0.00%)	0 / 47 (0.00%)	0 / 49 (0.00%)
occurrences (all)	0	0	0
Spondylolisthesis			
subjects affected / exposed	0 / 67 (0.00%)	0 / 47 (0.00%)	0 / 49 (0.00%)
occurrences (all)	0	0	0
Infections and infestations			
Urinary tract infection			
subjects affected / exposed	1 / 67 (1.49%)	1 / 47 (2.13%)	4 / 49 (8.16%)
occurrences (all)	1	1	6
Upper respiratory tract infection			
subjects affected / exposed	1 / 67 (1.49%)	4 / 47 (8.51%)	7 / 49 (14.29%)
occurrences (all)	1	4	10
Nasopharyngitis			
subjects affected / exposed	5 / 67 (7.46%)	2 / 47 (4.26%)	1 / 49 (2.04%)
occurrences (all)	8	2	1
COVID-19			
subjects affected / exposed	8 / 67 (11.94%)	2 / 47 (4.26%)	5 / 49 (10.20%)
occurrences (all)	8	2	5
Gingivitis			
subjects affected / exposed	0 / 67 (0.00%)	0 / 47 (0.00%)	2 / 49 (4.08%)
occurrences (all)	0	0	2
Herpes zoster			
subjects affected / exposed	0 / 67 (0.00%)	0 / 47 (0.00%)	2 / 49 (4.08%)
occurrences (all)	0	0	2
Influenza			
subjects affected / exposed	0 / 67 (0.00%)	0 / 47 (0.00%)	1 / 49 (2.04%)
occurrences (all)	0	0	1
Sinusitis			

subjects affected / exposed	0 / 67 (0.00%)	0 / 47 (0.00%)	0 / 49 (0.00%)
occurrences (all)	0	0	0
Pneumonia			
subjects affected / exposed	0 / 67 (0.00%)	0 / 47 (0.00%)	0 / 49 (0.00%)
occurrences (all)	0	0	0
Pharyngitis			
subjects affected / exposed	0 / 67 (0.00%)	0 / 47 (0.00%)	0 / 49 (0.00%)
occurrences (all)	0	0	0
Metabolism and nutrition disorders			
Hyperlipidaemia			
subjects affected / exposed	0 / 67 (0.00%)	1 / 47 (2.13%)	2 / 49 (4.08%)
occurrences (all)	0	2	2
Hypercholesterolaemia			
subjects affected / exposed	0 / 67 (0.00%)	1 / 47 (2.13%)	1 / 49 (2.04%)
occurrences (all)	0	2	1
Diabetes mellitus			
subjects affected / exposed	0 / 67 (0.00%)	0 / 47 (0.00%)	0 / 49 (0.00%)
occurrences (all)	0	0	0
Hypertriglyceridaemia			
subjects affected / exposed	0 / 67 (0.00%)	0 / 47 (0.00%)	0 / 49 (0.00%)
occurrences (all)	0	0	0
Hypokalaemia			
subjects affected / exposed	0 / 67 (0.00%)	0 / 47 (0.00%)	4 / 49 (8.16%)
occurrences (all)	0	0	7

Non-serious adverse events	Tofacitinib 5mg + csDMARD (Asia Cohort)	Pooled Placebo (Asian Cohort)	Placebo + csDMARD and GSK3196165 90mg + csDMARD (Asia Cohort)
Total subjects affected by non-serious adverse events			
subjects affected / exposed	18 / 19 (94.74%)	10 / 23 (43.48%)	6 / 6 (100.00%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Skin papilloma			
subjects affected / exposed	1 / 19 (5.26%)	0 / 23 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Uterine leiomyoma			
subjects affected / exposed	0 / 19 (0.00%)	0 / 23 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0

Vascular disorders			
Hypertension			
subjects affected / exposed	1 / 19 (5.26%)	2 / 23 (8.70%)	0 / 6 (0.00%)
occurrences (all)	1	2	0
General disorders and administration site conditions			
Injection site reaction			
subjects affected / exposed	0 / 19 (0.00%)	0 / 23 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Application site rash			
subjects affected / exposed	1 / 19 (5.26%)	0 / 23 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Vaccination site pain			
subjects affected / exposed	1 / 19 (5.26%)	0 / 23 (0.00%)	0 / 6 (0.00%)
occurrences (all)	2	0	0
Respiratory, thoracic and mediastinal disorders			
Dyspnoea			
subjects affected / exposed	1 / 19 (5.26%)	0 / 23 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Cough			
subjects affected / exposed	1 / 19 (5.26%)	0 / 23 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Epistaxis			
subjects affected / exposed	0 / 19 (0.00%)	0 / 23 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Psychiatric disorders			
Insomnia			
subjects affected / exposed	0 / 19 (0.00%)	0 / 23 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	1 / 19 (5.26%)	1 / 23 (4.35%)	0 / 6 (0.00%)
occurrences (all)	1	1	0
Aspartate aminotransferase increased			
subjects affected / exposed	1 / 19 (5.26%)	0 / 23 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Blood beta-D-glucan increased			

subjects affected / exposed	0 / 19 (0.00%)	0 / 23 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Blood creatine phosphokinase increased			
subjects affected / exposed	2 / 19 (10.53%)	0 / 23 (0.00%)	1 / 6 (16.67%)
occurrences (all)	2	0	1
Blood glucose increased			
subjects affected / exposed	0 / 19 (0.00%)	0 / 23 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Blood pressure increased			
subjects affected / exposed	0 / 19 (0.00%)	0 / 23 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Blood lactate dehydrogenase increased			
subjects affected / exposed	0 / 19 (0.00%)	0 / 23 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Electrocardiogram T wave inversion			
subjects affected / exposed	0 / 19 (0.00%)	0 / 23 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
Electrocardiogram abnormal			
subjects affected / exposed	0 / 19 (0.00%)	0 / 23 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
Gamma-glutamyltransferase increased			
subjects affected / exposed	0 / 19 (0.00%)	0 / 23 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	2
Lipids abnormal			
subjects affected / exposed	1 / 19 (5.26%)	0 / 23 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Low density lipoprotein increased			
subjects affected / exposed	1 / 19 (5.26%)	0 / 23 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Liver function test increased			
subjects affected / exposed	2 / 19 (10.53%)	0 / 23 (0.00%)	0 / 6 (0.00%)
occurrences (all)	2	0	0
Lymphocyte count decreased			

subjects affected / exposed	1 / 19 (5.26%)	2 / 23 (8.70%)	0 / 6 (0.00%)
occurrences (all)	1	3	0
Protein urine present			
subjects affected / exposed	1 / 19 (5.26%)	0 / 23 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Neutrophil count increased			
subjects affected / exposed	0 / 19 (0.00%)	0 / 23 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Monocyte count decreased			
subjects affected / exposed	1 / 19 (5.26%)	0 / 23 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
White blood cell count decreased			
subjects affected / exposed	1 / 19 (5.26%)	0 / 23 (0.00%)	1 / 6 (16.67%)
occurrences (all)	1	0	1
White blood cell count increased			
subjects affected / exposed	0 / 19 (0.00%)	0 / 23 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Injury, poisoning and procedural complications			
Cartilage injury			
subjects affected / exposed	0 / 19 (0.00%)	0 / 23 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
Joint injury			
subjects affected / exposed	1 / 19 (5.26%)	0 / 23 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Spinal fracture			
subjects affected / exposed	0 / 19 (0.00%)	0 / 23 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Cardiac disorders			
Bundle branch block right			
subjects affected / exposed	1 / 19 (5.26%)	0 / 23 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Sinus bradycardia			
subjects affected / exposed	1 / 19 (5.26%)	0 / 23 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Ventricular tachycardia			

subjects affected / exposed	0 / 19 (0.00%)	0 / 23 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Nervous system disorders			
Headache			
subjects affected / exposed	0 / 19 (0.00%)	0 / 23 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Cervicobrachial syndrome			
subjects affected / exposed	1 / 19 (5.26%)	0 / 23 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Dizziness			
subjects affected / exposed	0 / 19 (0.00%)	1 / 23 (4.35%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Post herpetic neuralgia			
subjects affected / exposed	1 / 19 (5.26%)	0 / 23 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Transient ischaemic attack			
subjects affected / exposed	0 / 19 (0.00%)	0 / 23 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	1 / 19 (5.26%)	1 / 23 (4.35%)	0 / 6 (0.00%)
occurrences (all)	1	1	0
Lymphopenia			
subjects affected / exposed	0 / 19 (0.00%)	0 / 23 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Leukopenia			
subjects affected / exposed	0 / 19 (0.00%)	0 / 23 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Eye disorders			
Scleritis			
subjects affected / exposed	1 / 19 (5.26%)	0 / 23 (0.00%)	0 / 6 (0.00%)
occurrences (all)	2	0	0
Gastrointestinal disorders			
Abdominal discomfort			
subjects affected / exposed	0 / 19 (0.00%)	0 / 23 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Abdominal pain			

subjects affected / exposed	0 / 19 (0.00%)	0 / 23 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Irritable bowel syndrome			
subjects affected / exposed	0 / 19 (0.00%)	0 / 23 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Diarrhoea			
subjects affected / exposed	1 / 19 (5.26%)	0 / 23 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Constipation			
subjects affected / exposed	1 / 19 (5.26%)	0 / 23 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Abdominal pain upper			
subjects affected / exposed	0 / 19 (0.00%)	0 / 23 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Nausea			
subjects affected / exposed	0 / 19 (0.00%)	2 / 23 (8.70%)	0 / 6 (0.00%)
occurrences (all)	0	2	0
Salivary gland mass			
subjects affected / exposed	0 / 19 (0.00%)	0 / 23 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Hepatobiliary disorders			
Hepatic function abnormal			
subjects affected / exposed	0 / 19 (0.00%)	0 / 23 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Skin and subcutaneous tissue disorders			
Drug eruption			
subjects affected / exposed	1 / 19 (5.26%)	0 / 23 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Pruritus			
subjects affected / exposed	0 / 19 (0.00%)	0 / 23 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Rash			
subjects affected / exposed	1 / 19 (5.26%)	0 / 23 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Renal and urinary disorders			

Renal impairment			
subjects affected / exposed	1 / 19 (5.26%)	0 / 23 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Musculoskeletal and connective tissue disorders			
Rheumatoid arthritis			
subjects affected / exposed	0 / 19 (0.00%)	0 / 23 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Back pain			
subjects affected / exposed	1 / 19 (5.26%)	0 / 23 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Spinal osteoarthritis			
subjects affected / exposed	0 / 19 (0.00%)	0 / 23 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
Osteoarthritis			
subjects affected / exposed	0 / 19 (0.00%)	0 / 23 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
Neck pain			
subjects affected / exposed	1 / 19 (5.26%)	0 / 23 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Musculoskeletal stiffness			
subjects affected / exposed	1 / 19 (5.26%)	0 / 23 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Spondylolisthesis			
subjects affected / exposed	0 / 19 (0.00%)	0 / 23 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
Infections and infestations			
Urinary tract infection			
subjects affected / exposed	0 / 19 (0.00%)	1 / 23 (4.35%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Upper respiratory tract infection			
subjects affected / exposed	3 / 19 (15.79%)	2 / 23 (8.70%)	1 / 6 (16.67%)
occurrences (all)	8	2	1
Nasopharyngitis			
subjects affected / exposed	2 / 19 (10.53%)	0 / 23 (0.00%)	0 / 6 (0.00%)
occurrences (all)	2	0	0
COVID-19			

subjects affected / exposed	1 / 19 (5.26%)	0 / 23 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Gingivitis			
subjects affected / exposed	1 / 19 (5.26%)	0 / 23 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Herpes zoster			
subjects affected / exposed	1 / 19 (5.26%)	0 / 23 (0.00%)	1 / 6 (16.67%)
occurrences (all)	1	0	1
Influenza			
subjects affected / exposed	1 / 19 (5.26%)	0 / 23 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Sinusitis			
subjects affected / exposed	0 / 19 (0.00%)	0 / 23 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Pneumonia			
subjects affected / exposed	0 / 19 (0.00%)	0 / 23 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
Pharyngitis			
subjects affected / exposed	0 / 19 (0.00%)	0 / 23 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Metabolism and nutrition disorders			
Hyperlipidaemia			
subjects affected / exposed	1 / 19 (5.26%)	0 / 23 (0.00%)	2 / 6 (33.33%)
occurrences (all)	1	0	2
Hypercholesterolaemia			
subjects affected / exposed	1 / 19 (5.26%)	0 / 23 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Diabetes mellitus			
subjects affected / exposed	1 / 19 (5.26%)	0 / 23 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Hypertriglyceridaemia			
subjects affected / exposed	0 / 19 (0.00%)	0 / 23 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Hypokalaemia			
subjects affected / exposed	1 / 19 (5.26%)	0 / 23 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0

Non-serious adverse events	Placebo + csDMARD and GSK3196165 150mg + csDMARD (Asia Cohort)	Placebo + csDMARD and Tofacitinib 5mg + csDMARD (Asia Cohort)	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	5 / 8 (62.50%)	7 / 8 (87.50%)	
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Skin papilloma			
subjects affected / exposed	0 / 8 (0.00%)	0 / 8 (0.00%)	
occurrences (all)	0	0	
Uterine leiomyoma			
subjects affected / exposed	1 / 8 (12.50%)	0 / 8 (0.00%)	
occurrences (all)	1	0	
Vascular disorders			
Hypertension			
subjects affected / exposed	0 / 8 (0.00%)	1 / 8 (12.50%)	
occurrences (all)	0	1	
General disorders and administration site conditions			
Injection site reaction			
subjects affected / exposed	0 / 8 (0.00%)	0 / 8 (0.00%)	
occurrences (all)	0	0	
Application site rash			
subjects affected / exposed	0 / 8 (0.00%)	0 / 8 (0.00%)	
occurrences (all)	0	0	
Vaccination site pain			
subjects affected / exposed	0 / 8 (0.00%)	0 / 8 (0.00%)	
occurrences (all)	0	0	
Respiratory, thoracic and mediastinal disorders			
Dyspnoea			
subjects affected / exposed	0 / 8 (0.00%)	1 / 8 (12.50%)	
occurrences (all)	0	1	
Cough			
subjects affected / exposed	0 / 8 (0.00%)	0 / 8 (0.00%)	
occurrences (all)	0	0	
Epistaxis			
subjects affected / exposed	0 / 8 (0.00%)	1 / 8 (12.50%)	
occurrences (all)	0	2	

Psychiatric disorders			
Insomnia			
subjects affected / exposed	2 / 8 (25.00%)	0 / 8 (0.00%)	
occurrences (all)	2	0	
Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	0 / 8 (0.00%)	1 / 8 (12.50%)	
occurrences (all)	0	1	
Aspartate aminotransferase increased			
subjects affected / exposed	0 / 8 (0.00%)	1 / 8 (12.50%)	
occurrences (all)	0	1	
Blood beta-D-glucan increased			
subjects affected / exposed	0 / 8 (0.00%)	1 / 8 (12.50%)	
occurrences (all)	0	1	
Blood creatine phosphokinase increased			
subjects affected / exposed	0 / 8 (0.00%)	1 / 8 (12.50%)	
occurrences (all)	0	1	
Blood glucose increased			
subjects affected / exposed	0 / 8 (0.00%)	0 / 8 (0.00%)	
occurrences (all)	0	0	
Blood pressure increased			
subjects affected / exposed	0 / 8 (0.00%)	1 / 8 (12.50%)	
occurrences (all)	0	1	
Blood lactate dehydrogenase increased			
subjects affected / exposed	0 / 8 (0.00%)	0 / 8 (0.00%)	
occurrences (all)	0	0	
Electrocardiogram T wave inversion			
subjects affected / exposed	0 / 8 (0.00%)	0 / 8 (0.00%)	
occurrences (all)	0	0	
Electrocardiogram abnormal			
subjects affected / exposed	0 / 8 (0.00%)	0 / 8 (0.00%)	
occurrences (all)	0	0	
Gamma-glutamyltransferase increased			

subjects affected / exposed	0 / 8 (0.00%)	0 / 8 (0.00%)	
occurrences (all)	0	0	
Lipids abnormal			
subjects affected / exposed	0 / 8 (0.00%)	0 / 8 (0.00%)	
occurrences (all)	0	0	
Low density lipoprotein increased			
subjects affected / exposed	1 / 8 (12.50%)	0 / 8 (0.00%)	
occurrences (all)	1	0	
Liver function test increased			
subjects affected / exposed	0 / 8 (0.00%)	0 / 8 (0.00%)	
occurrences (all)	0	0	
Lymphocyte count decreased			
subjects affected / exposed	1 / 8 (12.50%)	3 / 8 (37.50%)	
occurrences (all)	4	4	
Protein urine present			
subjects affected / exposed	0 / 8 (0.00%)	0 / 8 (0.00%)	
occurrences (all)	0	0	
Neutrophil count increased			
subjects affected / exposed	0 / 8 (0.00%)	1 / 8 (12.50%)	
occurrences (all)	0	2	
Monocyte count decreased			
subjects affected / exposed	0 / 8 (0.00%)	0 / 8 (0.00%)	
occurrences (all)	0	0	
White blood cell count decreased			
subjects affected / exposed	0 / 8 (0.00%)	0 / 8 (0.00%)	
occurrences (all)	0	0	
White blood cell count increased			
subjects affected / exposed	0 / 8 (0.00%)	1 / 8 (12.50%)	
occurrences (all)	0	1	
Injury, poisoning and procedural complications			
Cartilage injury			
subjects affected / exposed	0 / 8 (0.00%)	0 / 8 (0.00%)	
occurrences (all)	0	0	
Joint injury			

subjects affected / exposed	0 / 8 (0.00%)	0 / 8 (0.00%)	
occurrences (all)	0	0	
Spinal fracture			
subjects affected / exposed	0 / 8 (0.00%)	1 / 8 (12.50%)	
occurrences (all)	0	1	
Cardiac disorders			
Bundle branch block right			
subjects affected / exposed	0 / 8 (0.00%)	0 / 8 (0.00%)	
occurrences (all)	0	0	
Sinus bradycardia			
subjects affected / exposed	0 / 8 (0.00%)	0 / 8 (0.00%)	
occurrences (all)	0	0	
Ventricular tachycardia			
subjects affected / exposed	0 / 8 (0.00%)	1 / 8 (12.50%)	
occurrences (all)	0	1	
Nervous system disorders			
Headache			
subjects affected / exposed	0 / 8 (0.00%)	1 / 8 (12.50%)	
occurrences (all)	0	1	
Cervicobrachial syndrome			
subjects affected / exposed	0 / 8 (0.00%)	0 / 8 (0.00%)	
occurrences (all)	0	0	
Dizziness			
subjects affected / exposed	1 / 8 (12.50%)	0 / 8 (0.00%)	
occurrences (all)	1	0	
Post herpetic neuralgia			
subjects affected / exposed	0 / 8 (0.00%)	0 / 8 (0.00%)	
occurrences (all)	0	0	
Transient ischaemic attack			
subjects affected / exposed	1 / 8 (12.50%)	0 / 8 (0.00%)	
occurrences (all)	1	0	
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	0 / 8 (0.00%)	1 / 8 (12.50%)	
occurrences (all)	0	1	
Lymphopenia			

subjects affected / exposed	0 / 8 (0.00%)	0 / 8 (0.00%)	
occurrences (all)	0	0	
Leukopenia			
subjects affected / exposed	0 / 8 (0.00%)	0 / 8 (0.00%)	
occurrences (all)	0	0	
Eye disorders			
Scleritis			
subjects affected / exposed	0 / 8 (0.00%)	0 / 8 (0.00%)	
occurrences (all)	0	0	
Gastrointestinal disorders			
Abdominal discomfort			
subjects affected / exposed	1 / 8 (12.50%)	0 / 8 (0.00%)	
occurrences (all)	1	0	
Abdominal pain			
subjects affected / exposed	0 / 8 (0.00%)	1 / 8 (12.50%)	
occurrences (all)	0	1	
Irritable bowel syndrome			
subjects affected / exposed	0 / 8 (0.00%)	1 / 8 (12.50%)	
occurrences (all)	0	1	
Diarrhoea			
subjects affected / exposed	0 / 8 (0.00%)	1 / 8 (12.50%)	
occurrences (all)	0	1	
Constipation			
subjects affected / exposed	1 / 8 (12.50%)	0 / 8 (0.00%)	
occurrences (all)	1	0	
Abdominal pain upper			
subjects affected / exposed	0 / 8 (0.00%)	1 / 8 (12.50%)	
occurrences (all)	0	1	
Nausea			
subjects affected / exposed	0 / 8 (0.00%)	0 / 8 (0.00%)	
occurrences (all)	0	0	
Salivary gland mass			
subjects affected / exposed	0 / 8 (0.00%)	1 / 8 (12.50%)	
occurrences (all)	0	1	
Hepatobiliary disorders			

Hepatic function abnormal			
subjects affected / exposed	1 / 8 (12.50%)	0 / 8 (0.00%)	
occurrences (all)	1	0	
Skin and subcutaneous tissue disorders			
Drug eruption			
subjects affected / exposed	0 / 8 (0.00%)	0 / 8 (0.00%)	
occurrences (all)	0	0	
Pruritus			
subjects affected / exposed	0 / 8 (0.00%)	0 / 8 (0.00%)	
occurrences (all)	0	0	
Rash			
subjects affected / exposed	0 / 8 (0.00%)	0 / 8 (0.00%)	
occurrences (all)	0	0	
Renal and urinary disorders			
Renal impairment			
subjects affected / exposed	0 / 8 (0.00%)	0 / 8 (0.00%)	
occurrences (all)	0	0	
Musculoskeletal and connective tissue disorders			
Rheumatoid arthritis			
subjects affected / exposed	0 / 8 (0.00%)	0 / 8 (0.00%)	
occurrences (all)	0	0	
Back pain			
subjects affected / exposed	0 / 8 (0.00%)	1 / 8 (12.50%)	
occurrences (all)	0	1	
Spinal osteoarthritis			
subjects affected / exposed	0 / 8 (0.00%)	0 / 8 (0.00%)	
occurrences (all)	0	0	
Osteoarthritis			
subjects affected / exposed	0 / 8 (0.00%)	0 / 8 (0.00%)	
occurrences (all)	0	0	
Neck pain			
subjects affected / exposed	0 / 8 (0.00%)	0 / 8 (0.00%)	
occurrences (all)	0	0	
Musculoskeletal stiffness			
subjects affected / exposed	0 / 8 (0.00%)	0 / 8 (0.00%)	
occurrences (all)	0	0	

Spondylolisthesis			
subjects affected / exposed	0 / 8 (0.00%)	0 / 8 (0.00%)	
occurrences (all)	0	0	
Infections and infestations			
Urinary tract infection			
subjects affected / exposed	0 / 8 (0.00%)	0 / 8 (0.00%)	
occurrences (all)	0	0	
Upper respiratory tract infection			
subjects affected / exposed	2 / 8 (25.00%)	2 / 8 (25.00%)	
occurrences (all)	2	2	
Nasopharyngitis			
subjects affected / exposed	0 / 8 (0.00%)	0 / 8 (0.00%)	
occurrences (all)	0	0	
COVID-19			
subjects affected / exposed	1 / 8 (12.50%)	0 / 8 (0.00%)	
occurrences (all)	1	0	
Gingivitis			
subjects affected / exposed	0 / 8 (0.00%)	0 / 8 (0.00%)	
occurrences (all)	0	0	
Herpes zoster			
subjects affected / exposed	0 / 8 (0.00%)	0 / 8 (0.00%)	
occurrences (all)	0	0	
Influenza			
subjects affected / exposed	0 / 8 (0.00%)	0 / 8 (0.00%)	
occurrences (all)	0	0	
Sinusitis			
subjects affected / exposed	0 / 8 (0.00%)	1 / 8 (12.50%)	
occurrences (all)	0	1	
Pneumonia			
subjects affected / exposed	0 / 8 (0.00%)	0 / 8 (0.00%)	
occurrences (all)	0	0	
Pharyngitis			
subjects affected / exposed	0 / 8 (0.00%)	1 / 8 (12.50%)	
occurrences (all)	0	1	
Metabolism and nutrition disorders			

Hyperlipidaemia			
subjects affected / exposed	0 / 8 (0.00%)	1 / 8 (12.50%)	
occurrences (all)	0	1	
Hypercholesterolaemia			
subjects affected / exposed	1 / 8 (12.50%)	0 / 8 (0.00%)	
occurrences (all)	1	0	
Diabetes mellitus			
subjects affected / exposed	0 / 8 (0.00%)	0 / 8 (0.00%)	
occurrences (all)	0	0	
Hypertriglyceridaemia			
subjects affected / exposed	1 / 8 (12.50%)	0 / 8 (0.00%)	
occurrences (all)	1	0	
Hypokalaemia			
subjects affected / exposed	0 / 8 (0.00%)	0 / 8 (0.00%)	
occurrences (all)	0	0	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
22 May 2019	Correction of contraceptive requirements for Women of Child Bearing Potential (WOCBP) and additional clarifications.
21 January 2020	To detail revised risks, entry and stopping criteria following the update to comparator drug (tofacitinib) label. To introduce new medical device safety reporting wording, required in dvance of roll out of pre-filled syringes to this study. Other minor corrections and clarifications.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported