Clinical trial results:
A Phase III, Multicenter, Randomized, Double-Blind Placebo-Controlled Study to Assess the Efficacy and Safety of Tocilizumab in Subjects With Giant Cell Arteritis

Summary

EudraCT number	2011-006022-25
Trial protocol	IT SE AT DE DK GB PT NL ES BE PL
Global end of trial date	

Results information

Result version number	v1
This version publication date	26 April 2017
First version publication date	26 April 2017

Trial information

Trial identification

Sponsor protocol code	WA28119

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01791153
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	F. Hoffmann-La Roche AG
Sponsor organisation address	Grenzacherstrasse 124, Basel, Switzerland, CH-4070
Public contact	Roche Trial Information Hotline, F. Hoffmann-La Roche AG, 41 61 6878333, global.trial_information@roche.com
Scientific contact	Roche Trial Information Hotline, F. Hoffmann-La Roche AG, 41 61 6878333, global.trial_information@roche.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	Interim
Date of interim/final analysis	11 April 2016
Is this the analysis of the primary completion data?	Yes
Primary completion date	11 April 2016
Global end of trial reached?	No

Notes:

General information about the trial

Main objective of the trial:

The main objective for this study was to evaluate the efficacy of tocilizumab compared to placebo, in combination with a 26-week prednisone taper regimen, in participants with giant cell arteritis (GCA), as measured by the proportion of participants in sustained remission at Week 52 following induction and adherence to the protocol-defined prednisone taper regimen.

Protection of trial subjects:

The study was conducted in accordance with the principles of the "Declaration of Helsinki" and Good Clinical Practice. Approval from the Independent Ethics Committee/Institutional Review Board was obtained before study start and was documented in a letter to the Investigator specifying the date on which the committee met and granted the approval.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	22 July 2013
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	Belgium: 15
Country: Number of subjects enrolled	Canada: 2
Country: Number of subjects enrolled	Denmark: 1
Country: Number of subjects enrolled	France: 14
Country: Number of subjects enrolled	Germany: 78
Country: Number of subjects enrolled	Italy: 29
Country: Number of subjects enrolled	Netherlands: 13
Country: Number of subjects enrolled	Norway: 4
Country: Number of subjects enrolled	Poland: 6
Country: Number of subjects enrolled	Portugal: 3
Country: Number of subjects enrolled	Spain: 12
Country: Number of subjects enrolled	Sweden: 8
Country: Number of subjects enrolled	United Kingdom: 15
Country: Number of subjects enrolled	United States: 50
Worldwide total number of subjects	250
EEA total number of subjects	198

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)	82
From 65 to 84 years	166
85 years and over	2

Subject disposition

Recruitment

Recruitment details:

The study consists of 2 parts: a 52-week double-blind treatment period (Part 1) followed by a 104-week open label long-term follow-up period (Part 2). Results for Part 1 are reported here. Results for Part 2 will be reported by April 2019.

Pre-assignment

Screening details:

Of the 363 participants screened, a total of 251 participants were randomized into the study. One participant who was randomized to the "Tocilizumab q2w + 26 weeks prednisone taper" group withdrew on the same day of randomization and did not receive any study treatment. This participant was not included in any of the study analyses.

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

Arms

Are arms mutually exclusive?	Yes
Arm title	Part 1: Tocilizumab qw + 26 weeks prednisone taper

Arm description:

Participants received tocilizumab at a dose of 162 milligrams (mg) as subcutaneous (SC) injection every week (qw) up to 52 weeks along with prednisone and/or prednisone placebo according to the protocol-defined schedule. Participants received prednisone tapering oral daily doses during the first 26 weeks and prednisone placebo from Week 26 up to Week 52.

Arm type	Experimental
Investigational medicinal product name	Tocilizumab
Investigational medicinal product code	
Other name	RoActemra, Actemra, RO4877533
Pharmaceutical forms	Solution for injection in pre-filled syringe
Routes of administration	Subcutaneous use

Dosage and administration details:

Tocilizumab was administered at a dose of 162 mg as SC injection qw for 52 weeks in Part 1 of the study.

Investigational medicinal product name	Prednisone placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Prednisone placebo was administered daily according to the protocol-defined schedule (from Week 26 to Week 52) in Part 1 of the study.

Investigational medicinal product name	Prednisone
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Prednisone was administered at tapering oral doses daily for 26 weeks according to the protocol-defined schedule in Part 1 of the study.

Arm title	Part 1: Tocilizumab q2w + 26 weeks prednisone taper

Arm description:

Participants received tocilizumab at a dose of 162 mg as SC injection every 2 weeks (q2w) (and tocilizumab placebo q2w starting from Week 2) up to 52 weeks along with prednisone and/or prednisone placebo according to the protocol-defined schedule. Participants received prednisone tapering oral daily doses during the first 26 weeks and prednisone placebo from Week 26 up to Week 52.

Arm type	Experimental
Investigational medicinal product name	Tocilizumab
Investigational medicinal product code	
Other name	RoActemra, Actemra, RO4877533
Pharmaceutical forms	Solution for injection in pre-filled syringe
Routes of administration	Subcutaneous use

Dosage and administration details:

Tocilizumab was administered at a dose of 162 mg as SC injection q2w for 52 weeks in Part 1 of the study.

Investigational medicinal product name	Prednisone
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Prednisone was administered at tapering oral doses daily for 26 weeks according to the protocol-defined schedule in Part 1 of the study.

Investigational medicinal product name	Prednisone placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Prednisone placebo was administered daily according to the protocol-defined schedule (from Week 26 to Week 52) in Part 1 of the study.

Investigational medicinal product name	Tocilizumab placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection in pre-filled syringe
Routes of administration	Subcutaneous use

Dosage and administration details:

Tocilizumab placebo was administered as SC injection q2w (starting from Week 2) for 52 weeks in Part 1 of the study.

Arm title	Part 1: Placebo + 26 weeks prednisone taper

Arm description:

Participants received tocilizumab placebo as SC injection qw up to 52 weeks along with prednisone and/or prednisone placebo according to the protocol-defined schedule. Participants received prednisone tapering oral daily doses during the first 26 weeks and prednisone placebo from Week 26 up to Week 52.

Arm type	Placebo
Investigational medicinal product name	Tocilizumab placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection in pre-filled syringe
Routes of administration	Subcutaneous use

Dosage and administration details:

Tocilizumab placebo was administered as SC injection qw for 52 weeks in Part 1 of the study.

Investigational medicinal product name	Prednisone placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Prednisone placebo was administered daily according to the protocol-defined schedule (from Week 26 to Week 52) in Part 1 of the study.

Investigational medicinal product name	Prednisone
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Prednisone was administered at tapering oral doses daily for 26 weeks according to the protocol-defined schedule in Part 1 of the study.

Arm title	Part 1: Placebo + 52 weeks prednisone taper

Arm description:

Participants received tocilizumab placebo as SC injection qw up to 52 weeks along with prednisone and/or prednisone placebo according to the protocol-defined schedule. Participants received prednisone tapering oral daily doses for 52 weeks.

Arm type	Placebo
Investigational medicinal product name	Tocilizumab placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection in pre-filled syringe
Routes of administration	Subcutaneous use

Dosage and administration details:

Tocilizumab placebo was administered as SC injection qw for 52 weeks in Part 1 of the study.

Investigational medicinal product name	Prednisone placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Prednisone placebo was administered daily according to the protocol-defined schedule in Part 1 of the study.

Investigational medicinal product name	Prednisone
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Prednisone was administered at tapering oral doses daily for 52 weeks according to the protocol-defined schedule in Part 1 of the study.

Number of subjects in period 1	Part 1: Tocilizumab qw + 26 weeks prednisone taper	Part 1: Tocilizumab q2w + 26 weeks prednisone taper	Part 1: Placebo + 26 weeks prednisone taper
Started	100	49	50
Completed	85	41	44
Not completed	15	8	6
Non-Compliance	1	-	-
Consent withdrawn by subject	6	2	2
Physician decision	-	-	-
Adverse event, non-fatal	7	3	2
Lack of efficacy	1	3	2
Protocol deviation	-	-	-

Number of subjects in period 1	Part 1: Placebo + 52 weeks prednisone taper
Started	51
Completed	46
Not completed	5
Non-Compliance	-
Consent withdrawn by subject	1
Physician decision	1
Adverse event, non-fatal	-
Lack of efficacy	2
Protocol deviation	1

Baseline characteristics

Reporting groups	
Reporting group title	Part 1: Tocilizumab qw + 26 weeks prednisone taper
Reporting group description:	
Participants received tocilizumab at a dose of 162 milligrams (mg) as subcutaneous (SC) injection every week (qw) up to 52 weeks along with prednisone and/or prednisone placebo according to the protocol-defined schedule. Participants received prednisone tapering oral daily doses during the first 26 weeks and prednisone placebo from Week 26 up to Week 52.	
Reporting group title	Part 1: Tocilizumab q2w + 26 weeks prednisone taper
Reporting group description:	
Participants received tocilizumab at a dose of 162 mg as SC injection every 2 weeks (q2w) (and tocilizumab placebo q2w starting from Week 2) up to 52 weeks along with prednisone and/or prednisone placebo according to the protocol-defined schedule. Participants received prednisone tapering oral daily doses during the first 26 weeks and prednisone placebo from Week 26 up to Week 52.	
Reporting group title	Part 1: Placebo + 26 weeks prednisone taper
Reporting group description:	
Participants received tocilizumab placebo as SC injection qw up to 52 weeks along with prednisone and/or prednisone placebo according to the protocol-defined schedule. Participants received prednisone tapering oral daily doses during the first 26 weeks and prednisone placebo from Week 26 up to Week 52.	
Reporting group title	Part 1: Placebo + 52 weeks prednisone taper
Reporting group description:	
Participants received tocilizumab placebo as SC injection qw up to 52 weeks along with prednisone and/or prednisone placebo according to the protocol-defined schedule. Participants received prednisone tapering oral daily doses for 52 weeks.	

Reporting group values	Part 1: Tocilizumab qw + 26 weeks prednisone taper	Part 1: Tocilizumab q2w + 26 weeks prednisone taper	Part 1: Placebo + 26 weeks prednisone taper
Number of subjects	100	49	50
Age Categorical Units: Subjects			
Adults (18 to 64 years)	32	17	16
From 65 to 84 years	67	31	34
85 years and over	1	1	0
Age Continuous Units: years			
arithmetic mean	69.5	69.4	69.3
standard deviation	± 8.5	± 8.29	± 8.14
Gender Categorical Units: Subjects			
Female	78	34	38
Male	22	15	12

Reporting group values	Part 1: Placebo + 52 weeks prednisone taper	Total	
Number of subjects	51	250	
Age Categorical Units: Subjects			
Adults (18 to 64 years)	17	82	
From 65 to 84 years	34	166	
85 years and over	0	2	

Age Continuous Units: years			
arithmetic mean	67.8		
standard deviation	± 7.7	-	
Gender Categorical Units: Subjects			
Female	37	187	
Male	14	63	

End points

End points reporting groups

Reporting group title	Part 1: Tocilizumab qw + 26 weeks prednisone taper

Reporting group description:

Participants received tocilizumab at a dose of 162 milligrams (mg) as subcutaneous (SC) injection every week (qw) up to 52 weeks along with prednisone and/or prednisone placebo according to the protocol-defined schedule. Participants received prednisone tapering oral daily doses during the first 26 weeks and prednisone placebo from Week 26 up to Week 52.

Reporting group title	Part 1: Tocilizumab q2w + 26 weeks prednisone taper

Reporting group description:

Participants received tocilizumab at a dose of 162 mg as SC injection every 2 weeks (q2w) (and tocilizumab placebo q2w starting from Week 2) up to 52 weeks along with prednisone and/or prednisone placebo according to the protocol-defined schedule. Participants received prednisone tapering oral daily doses during the first 26 weeks and prednisone placebo from Week 26 up to Week 52.

Reporting group title	Part 1: Placebo + 26 weeks prednisone taper

Reporting group description:

Participants received tocilizumab placebo as SC injection qw up to 52 weeks along with prednisone and/or prednisone placebo according to the protocol-defined schedule. Participants received prednisone tapering oral daily doses during the first 26 weeks and prednisone placebo from Week 26 up to Week 52.

Reporting group title	Part 1: Placebo + 52 weeks prednisone taper

Reporting group description:

Participants received tocilizumab placebo as SC injection qw up to 52 weeks along with prednisone and/or prednisone placebo according to the protocol-defined schedule. Participants received prednisone tapering oral daily doses for 52 weeks.

Primary: Percentage of Participants in Sustained Remission at Week 52 (Tocilizumab + 26 weeks prednisone taper versus Placebo + 26 weeks prednisone taper)

End point title	Percentage of Participants in Sustained Remission at Week 52 (Tocilizumab + 26 weeks prednisone taper versus Placebo + 26 weeks prednisone taper)[1]

End point description:

Remission was defined as the absence of flare and normalization of the C-reactive protein (CRP) (less than [<] 1 milligram per deciliter [mg/dL]). Sustained remission was defined as the absence of flare following induction of remission within 12 weeks of randomization and maintained up to Week 52. Flare was determined by the investigator and was defined as the recurrence of signs or symptoms of GCA and/or erythrocyte sedimentation rate (ESR) greater than or equal to (>/=) 30 millimeters per hour (mm/hr) attributable to GCA. A single CRP elevation (>/=1 mg/dL) was not considered as a sign of flare, unless the CRP remained elevated (>/=1 mg/dL) at the next study visit. Intent-to-treat (ITT) population included all participants randomized into the study who received at least one administration of study drug.

End point type	Primary

End point timeframe:

Week 52

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 primary endpoint evaluated the proportions of patients in sustained remission in the TCZ groups compared to the 26-week placebo group. Therefore, the 52-week placebo group is not included in this analysis.

End point values	Part 1: Tocilizumab qw + 26 weeks prednisone taper	Part 1: Tocilizumab q2w + 26 weeks prednisone taper	Part 1: Placebo + 26 weeks prednisone taper	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	100	49	50	
Units: percentage of participants				
number (not applicable)	56	53.1	14	

Statistical analyses

Statistical analysis title	Statistical Analysis 1

Statistical analysis description:

The treatment groups were compared using a Cochran-Mantel-Haenszel model adjusted for the stratification factor of starting prednisone dose (less than or equal to [</=] 30 mg/day, greater than [>] 30 mg/day).

Comparison groups	Part 1: Tocilizumab qw + 26 weeks prednisone taper v Part 1: Placebo + 26 weeks prednisone taper
Number of subjects included in analysis	150
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001
Method	Cochran-Mantel-Haenszel
Parameter estimate	Difference in response rates
Point estimate	42
Confidence interval	
level	Other: 99.5 %
sides	2-sided
lower limit	18
upper limit	66

Statistical analysis title	Statistical Analysis 2

Statistical analysis description:

The treatment groups were compared using a Cochran-Mantel-Haenszel model adjusted for the stratification factor of starting prednisone dose (</=30 mg/day, >30 mg/day).

Comparison groups	Part 1: Tocilizumab q2w + 26 weeks prednisone taper v Part 1: Placebo + 26 weeks prednisone taper
Number of subjects included in analysis	99
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001
Method	Cochran-Mantel-Haenszel
Parameter estimate	Difference in response rates
Point estimate	39.06

Confidence interval	
level	Other: 99.5 %
sides	2-sided
lower limit	12.46
upper limit	65.66

Secondary: Percentage of Participants in Sustained Remission at Week 52 (Tocilizumab + 26 weeks prednisone taper versus Placebo + 52 weeks prednisone taper)

End point title	Percentage of Participants in Sustained Remission at Week 52 (Tocilizumab + 26 weeks prednisone taper versus Placebo + 52 weeks prednisone taper)[2]

End point description:

Remission was defined as the absence of flare and normalization of the CRP (<1 mg/dL). Sustained remission was defined as the absence of flare following induction of remission within 12 weeks of randomization and maintained up to Week 52. Flare was determined by the investigator and was defined as the recurrence of signs or symptoms of GCA and/or ESR >/=30 mm/hr attributable to GCA. A single CRP elevation (>/=1 mg/dL) was not considered as a sign of flare, unless the CRP remained elevated (>/=1 mg/dL) at the next study visit. ITT population.

End point type	Secondary

End point timeframe:

Week 52

Notes:

[2] - 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 key secondary endpoint evaluated the proportions of patients in sustained remission in the TCZ groups compared to the 52-week placebo group. Therefore, the 26-week placebo group is not included in this analysis.

End point values	Part 1: Tocilizumab qw + 26 weeks prednisone taper	Part 1: Tocilizumab q2w + 26 weeks prednisone taper	Part 1: Placebo + 52 weeks prednisone taper	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	100	49	51	
Units: percentage of participants				
number (not applicable)	56	53.1	17.6	

Statistical analyses

Statistical analysis title	Statistical Analysis 1

Statistical analysis description:

The treatment groups were compared using a Cochran-Mantel-Haenszel model adjusted for the stratification factor of starting prednisone dose (</=30 mg/day, >30 mg/day).

Comparison groups	Part 1: Tocilizumab qw + 26 weeks prednisone taper v Part 1: Placebo + 52 weeks prednisone taper

Number of subjects included in analysis	151
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001
Method	Cochran-Mantel-Haenszel

Statistical analysis title	Statistical Analysis 2

Statistical analysis description:

The treatment groups were compared using a Cochran-Mantel-Haenszel model adjusted for the stratification factor of starting prednisone dose (</=30 mg/day, >30 mg/day).

Comparison groups	Part 1: Tocilizumab qw + 26 weeks prednisone taper v Part 1: Placebo + 52 weeks prednisone taper
Number of subjects included in analysis	151
Analysis specification	Pre-specified
Analysis type	non-inferiority[3]
Parameter estimate	Difference in response rates
Point estimate	38.35
Confidence interval	
level	Other: 99.5 %
sides	2-sided
lower limit	17.89
upper limit	58.81

Notes:

[3] - The tocilizumab group was to be considered as non-inferior to the placebo group if the lower limit of the two-sided 99.5% confidence interval was >/= -22.5%.

Statistical analysis title	Statistical Analysis 3

Statistical analysis description:

The treatment groups were compared using a Cochran-Mantel-Haenszel model adjusted for the stratification factor of starting prednisone dose (</=30 mg/day, >30 mg/day).

Comparison groups	Part 1: Tocilizumab q2w + 26 weeks prednisone taper v Part 1: Placebo + 52 weeks prednisone taper
Number of subjects included in analysis	100
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0002
Method	Cochran-Mantel-Haenszel

Statistical analysis title	Statistical Analysis 4

Statistical analysis description:

The treatment groups were compared using a Cochran-Mantel-Haenszel model adjusted for the stratification factor of starting prednisone dose (</=30 mg/day, >30 mg/day).

Comparison groups	Part 1: Tocilizumab q2w + 26 weeks prednisone taper v Part 1: Placebo + 52 weeks prednisone taper

Number of subjects included in analysis	100
Analysis specification	Pre-specified
Analysis type	non-inferiority[4]
Parameter estimate	Difference in response rates
Point estimate	35.41
Confidence interval	
level	Other: 99.5 %
sides	2-sided
lower limit	10.41
upper limit	60.41

Notes:

[4] - The tocilizumab group was to be considered as non-inferior to the placebo group if the lower limit of the two-sided 99.5% confidence interval was >/= -22.5%.

Secondary: Time to First GCA Disease Flare

End point title	Time to First GCA Disease Flare

End point description:

Flare was determined by the investigator and was defined as the recurrence of signs or symptoms of GCA and/or ESR >/=30 mm/hr attributable to GCA. Participants who withdrew from the study prior to Week 52 were censored from the time of withdrawal. ITT population. Value "99999" in results indicates that data could not be calculated due to low number of participants who had an event.

End point type	Secondary

End point timeframe:

Up to 52 weeks

End point values	Part 1: Tocilizumab qw + 26 weeks prednisone taper	Part 1: Tocilizumab q2w + 26 weeks prednisone taper	Part 1: Placebo + 26 weeks prednisone taper	Part 1: Placebo + 52 weeks prednisone taper
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	100	49	50	51
Units: days				
median (confidence interval 99%)	99999 (99999 to 99999)	99999 (99999 to 99999)	165 (120 to 260)	295 (168 to 99999)

Statistical analyses

Statistical analysis title	Statistical Analysis 1

Statistical analysis description:

The treatment groups were compared using a Cox proportional hazards model adjusted for the stratification factor of starting prednisone dose (</=30 mg/day, >30 mg/day).

Comparison groups	Part 1: Tocilizumab qw + 26 weeks prednisone taper v Part 1: Placebo + 26 weeks prednisone taper

Number of subjects included in analysis	150
Analysis specification	Pre-specified
Analysis type	other
P-value	< 0.0001
Method	Cox proportional hazards model
Parameter estimate	Hazard ratio (HR)
Point estimate	0.23
Confidence interval	
level	Other: 99 %
sides	2-sided
lower limit	0.11
upper limit	0.46

Statistical analysis title	Statistical Analysis 2
Statistical analysis description:	
The treatment groups were compared using a Cox proportional hazards model adjusted for the stratification factor of starting prednisone dose (</=30 mg/day, >30 mg/day).	
Comparison groups	Part 1: Tocilizumab qw + 26 weeks prednisone taper v Part 1: Placebo + 52 weeks prednisone taper
Number of subjects included in analysis	151
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.0011
Method	Cox proportional hazards model
Parameter estimate	Hazard ratio (HR)
Point estimate	0.39
Confidence interval	
level	Other: 99 %
sides	2-sided
lower limit	0.18
upper limit	0.82

Statistical analysis title	Statistical Analysis 3
Statistical analysis description:	
The treatment groups were compared using a Cox proportional hazards model adjusted for the stratification factor of starting prednisone dose (</=30 mg/day, >30 mg/day).	
Comparison groups	Part 1: Tocilizumab q2w + 26 weeks prednisone taper v Part 1: Placebo + 26 weeks prednisone taper
Number of subjects included in analysis	99
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.0001
Method	Cox proportional hazards model
Parameter estimate	Hazard ratio (HR)
Point estimate	0.28

Confidence interval	
level	Other: 99 %
sides	2-sided
lower limit	0.12
upper limit	0.66

Statistical analysis title	Statistical Analysis 4

Statistical analysis description:

The treatment groups were compared using a Cox proportional hazards model adjusted for the stratification factor of starting prednisone dose (</=30 mg/day, >30 mg/day).

Comparison groups	Part 1: Tocilizumab q2w + 26 weeks prednisone taper v Part 1: Placebo + 52 weeks prednisone taper
Number of subjects included in analysis	100
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.0316
Method	Cox proportional hazards model
Parameter estimate	Hazard ratio (HR)
Point estimate	0.48
Confidence interval	
level	Other: 99 %
sides	2-sided
lower limit	0.2
upper limit	1.16

Secondary: Total Cumulative Prednisone Dose

End point title	Total Cumulative Prednisone Dose

End point description:

The median total cumulative prednisone dose over the 52 weeks for each treatment group and the corresponding 95% confidence intervals are presented. ITT Population.

End point type	Secondary

End point timeframe:

Up to 52 weeks

End point values	Part 1: Tocilizumab qw + 26 weeks prednisone taper	Part 1: Tocilizumab q2w + 26 weeks prednisone taper	Part 1: Placebo + 26 weeks prednisone taper	Part 1: Placebo + 52 weeks prednisone taper
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	100	49	50	51
Units: mg				
median (confidence interval 95%)	1862 (1582 to 1942)	1862 (1568 to 2239.5)	3296 (2729.5 to 4023.5)	3817.5 (2817.5 to 4425.5)

Statistical analyses

Statistical analysis title	Statistical Analysis 1

Statistical analysis description:

The treatment groups were compared using a Van Elteren's test stratified by starting prednisone dose (<=30 mg/day, > 30 mg/day).

Comparison groups	Part 1: Tocilizumab qw + 26 weeks prednisone taper v Part 1: Placebo + 26 weeks prednisone taper
Number of subjects included in analysis	150
Analysis specification	Pre-specified
Analysis type	other
P-value	< 0.0001
Method	Van Elteren's test

Statistical analysis title	Statistical Analysis 3

Statistical analysis description:

The treatment groups were compared using a Van Elteren's test stratified by starting prednisone dose (<=30 mg/day, > 30 mg/day).

Comparison groups	Part 1: Tocilizumab q2w + 26 weeks prednisone taper v Part 1: Placebo + 26 weeks prednisone taper
Number of subjects included in analysis	99
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.0003
Method	Van Elteren's test

Statistical analysis title	Statistical Analysis 2

Statistical analysis description:

The treatment groups were compared using a Van Elteren's test stratified by starting prednisone dose (<=30 mg/day, > 30 mg/day).

Comparison groups	Part 1: Tocilizumab qw + 26 weeks prednisone taper v Part 1: Placebo + 52 weeks prednisone taper
Number of subjects included in analysis	151
Analysis specification	Pre-specified
Analysis type	other
P-value	< 0.0001
Method	Van Elteren's test

Statistical analysis title	Statistical Analysis 4

Statistical analysis description:

The treatment groups were compared using a Van Elteren's test stratified by starting prednisone dose (<=30 mg/day, > 30 mg/day).

Comparison groups	Part 1: Tocilizumab q2w + 26 weeks prednisone taper v Part 1: Placebo + 52 weeks prednisone taper
Number of subjects included in analysis	100
Analysis specification	Pre-specified
Analysis type	other
P-value	< 0.0001
Method	Van Elteren's test

Secondary: Change From Baseline in Short Form (SF)-36 Questionnaire Score at Week 52

End point title	Change From Baseline in Short Form (SF)-36 Questionnaire Score at Week 52

End point description:

The SF-36 is a standardized questionnaire used to assess physical functioning and is made up of eight domains: Physical Functioning, Role Physical, Bodily Pain, General Health, Vitality, Social Functioning, Role-Emotional and Mental Health. Transforming and standardizing these domains leads to the calculation of the Physical Component Score (PCS) and Mental Component Score (MCS). The score for a section is an average of the individual question scores, which are scaled 0-100 (100=highest level of functioning). A positive change from baseline indicates improvement. No imputation was used for missing data. Data was set to missing for participants who received escape therapy. ITT population. Here, 'Number of Subject Analysed' signifies the number of participants evaluable for this outcome measure and 'n' signifies the number of participants evaluable at specified time point for different arms, respectively.

End point type	Secondary

End point timeframe:

Baseline, Week 52

End point values	Part 1: Tocilizumab qw + 26 weeks prednisone taper	Part 1: Tocilizumab q2w + 26 weeks prednisone taper	Part 1: Placebo + 26 weeks prednisone taper	Part 1: Placebo + 52 weeks prednisone taper
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	97	49	48	49
Units: units on a scale				
arithmetic mean (standard deviation)				
PCS: Baseline (n=97,49,48,49)	43.1 (± 9.43)	40.62 (± 8)	42.65 (± 10.87)	41.12 (± 9.97)
PCS: Change at Week 52 (n=59,26,9,18)	5.37 (± 7.38)	2.71 (± 8.86)	2.08 (± 12.11)	-2.8 (± 6.98)
MCS: Baseline (n=97,49,48,49)	42.77 (± 12.43)	47.67 (± 12.59)	42.73 (± 12.13)	40.45 (± 13.73)
MCS: Change at Week 52 (n=59,26,9,18)	8.21 (± 10.35)	1.98 (± 7.17)	4.99 (± 7.54)	2.6 (± 10.56)

Statistical analyses

Statistical analysis title	Statistical Analysis 1

Statistical analysis description:

MCS: Change at Week 52: Repeated measures model used for analysis included the following covariates and interactions: treatment, starting prednisone dose (<=30mg/day, >30mg/day), visit, treatment-by-visit interaction, starting dose-by-visit interaction, baseline score and baseline score-by-visit interaction.

Comparison groups	Part 1: Tocilizumab qw + 26 weeks prednisone taper v Part 1: Placebo + 26 weeks prednisone taper
Number of subjects included in analysis	145
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.8067
Method	Repeated measures model
Parameter estimate	Differences in Least Square Means
Point estimate	0.61
Confidence interval	
level	Other: 99 %
sides	2-sided
lower limit	-5.86
upper limit	7.07

Statistical analysis title	Statistical Analysis 2

Statistical analysis description:

MCS: Change at Week 52: Repeated measures model used for analysis included the following covariates and interactions: treatment, starting prednisone dose (<=30mg/day, >30mg/day), visit, treatment-by-visit interaction, starting dose-by-visit interaction, baseline score and baseline score-by-visit interaction.

Comparison groups	Part 1: Tocilizumab qw + 26 weeks prednisone taper v Part 1: Placebo + 52 weeks prednisone taper
Number of subjects included in analysis	146
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.0252
Method	Repeated measures model
Parameter estimate	Differences in Least Square Means
Point estimate	4.44
Confidence interval	
level	Other: 99 %
sides	2-sided
lower limit	-0.69
upper limit	9.56

Statistical analysis title	Statistical Analysis 3

Statistical analysis description:

MCS: Change at Week 52: Repeated measures model used for analysis included the following covariates and interactions: treatment, starting prednisone dose (<=30mg/day, >30mg/day), visit, treatment-by-visit interaction, starting dose-by-visit interaction, baseline score and baseline score-by-visit interaction.

Comparison groups	Part 1: Tocilizumab q2w + 26 weeks prednisone taper v Part 1: Placebo + 26 weeks prednisone taper

Number of subjects included in analysis	97
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.8374
Method	Repeated measures model
Parameter estimate	Differences in Least Square Means
Point estimate	-0.56
Confidence interval	
level	Other: 99 %
sides	2-sided
lower limit	-7.64
upper limit	6.53

Statistical analysis title	Statistical Analysis 4

Statistical analysis description:

MCS: Change at Week 52: Repeated measures model used for analysis included the following covariates and interactions: treatment, starting prednisone dose (<=30mg/day, >30mg/day), visit, treatment-by-visit interaction, starting dose-by-visit interaction, baseline score and baseline score-by-visit interaction.

Comparison groups	Part 1: Tocilizumab q2w + 26 weeks prednisone taper v Part 1: Placebo + 52 weeks prednisone taper
Number of subjects included in analysis	98
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.1468
Method	Repeated measures model
Parameter estimate	Differences in Least Square Means
Point estimate	3.27
Confidence interval	
level	Other: 99 %
sides	2-sided
lower limit	-2.59
upper limit	9.14

Statistical analysis title	Statistical Analysis 5

Statistical analysis description:

PCS: Change at Week 52: Repeated measures model used for analysis included the following covariates and interactions: treatment, starting prednisone dose (<=30mg/day, >30mg/day), visit, treatment-by-visit interaction, starting dose-by-visit interaction, baseline score and baseline score-by-visit interaction.

Comparison groups	Part 1: Tocilizumab qw + 26 weeks prednisone taper v Part 1: Placebo + 26 weeks prednisone taper
Number of subjects included in analysis	145
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.057
Method	Repeated measures model
Parameter estimate	Differences in Least Square Means
Point estimate	4.38

Confidence interval	
level	Other: 99 %
sides	2-sided
lower limit	-1.58
upper limit	10.34

Statistical analysis title	Statistical Analysis 6

Statistical analysis description:

PCS: Change at Week 52: Repeated measures model used for analysis included the following covariates and interactions: treatment, starting prednisone dose (<=30mg/day, >30mg/day), visit, treatment-by-visit interaction, starting dose-by-visit interaction, baseline score and baseline score-by-visit interaction.

Comparison groups	Part 1: Tocilizumab qw + 26 weeks prednisone taper v Part 1: Placebo + 52 weeks prednisone taper
Number of subjects included in analysis	146
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.0024
Method	Repeated measures model
Parameter estimate	Differences in Least Square Means
Point estimate	5.59
Confidence interval	
level	Other: 99 %
sides	2-sided
lower limit	0.86
upper limit	10.32

Statistical analysis title	Statistical Analysis 7

Statistical analysis description:

PCS: Change at Week 52: Repeated measures model used for analysis included the following covariates and interactions: treatment, starting prednisone dose (<=30mg/day, >30mg/day), visit, treatment-by-visit interaction, starting dose-by-visit interaction, baseline score and baseline score-by-visit interaction.

Comparison groups	Part 1: Tocilizumab q2w + 26 weeks prednisone taper v Part 1: Placebo + 26 weeks prednisone taper
Number of subjects included in analysis	97
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.2218
Method	Repeated measures model
Parameter estimate	Differences in Least Square Means
Point estimate	3.04
Confidence interval	
level	Other: 99 %
sides	2-sided
lower limit	-3.43
upper limit	9.51

Statistical analysis title	Statistical Analysis 8

Statistical analysis description:

PCS: Change at Week 52: Repeated measures model used for analysis included the following covariates and interactions: treatment, starting prednisone dose (<=30mg/day, >30mg/day), visit, treatment-by-visit interaction, starting dose-by-visit interaction, baseline score and baseline score-by-visit interaction.

Comparison groups	Part 1: Tocilizumab q2w + 26 weeks prednisone taper v Part 1: Placebo + 52 weeks prednisone taper
Number of subjects included in analysis	98
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.0412
Method	Repeated measures model
Parameter estimate	Differences in Least Square Means
Point estimate	4.25
Confidence interval	
level	Other: 99 %
sides	2-sided
lower limit	-1.14
upper limit	9.64

Secondary: Change From Baseline in Patient Global Assessment (PGA) of Disease Activity Assessed Using Visual Analogue Scale (VAS) at Week 52

End point title	Change From Baseline in Patient Global Assessment (PGA) of Disease Activity Assessed Using Visual Analogue Scale (VAS) at Week 52

End point description:

Participants assessed their current disease activity on a 0-100 millimeter (mm) VAS, where 0 mm = no disease activity and 100 mm = maximum disease activity. A negative change from baseline indicates improvement. ITT population. Here, 'Number of Subjects Analysed' signifies the number of participants evaluable for this outcome measure and 'n' signifies the number of participants evaluable at specified time point for different arms, respectively.

End point type	Secondary

End point timeframe:

Baseline, Week 52

End point values	Part 1: Tocilizumab qw + 26 weeks prednisone taper	Part 1: Tocilizumab q2w + 26 weeks prednisone taper	Part 1: Placebo + 26 weeks prednisone taper	Part 1: Placebo + 52 weeks prednisone taper
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	100	49	49	51
Units: mm				
arithmetic mean (standard deviation)				
Baseline (n=100,49,49,51)	43.61 (± 25.66)	46.65 (± 25.6)	35.73 (± 28.15)	47.78 (± 27.8)
Change at Week 52 (n=60,26,11,18)	-19.68 (± 33.64)	-22.69 (± 22.41)	-8.45 (± 24.81)	-10 (± 35.12)

Statistical analyses

Statistical analysis title	Statistical Analysis 1
Statistical analysis description:	
Change at Week 52: Repeated measures model used for analysis included the following covariates and interactions: treatment, starting prednisone dose (<=30mg/day, >30mg/day), visit, treatment-by-visit interaction, starting dose-by-visit interaction, baseline score and baseline score-by-visit interaction.	
Comparison groups	Part 1: Tocilizumab qw + 26 weeks prednisone taper v Part 1: Placebo + 26 weeks prednisone taper
Number of subjects included in analysis	149
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.0312
Method	Repeated measures model
Parameter estimate	Differences in Least Square Means
Point estimate	-15.6
Confidence interval	
level	Other: 99 %
sides	2-sided
lower limit	-34.3
upper limit	3.1

Statistical analysis title	Statistical Analysis 2
Statistical analysis description:	
Change at Week 52: Repeated measures model used for analysis included the following covariates and interactions: treatment, starting prednisone dose (<=30mg/day, >30mg/day), visit, treatment-by-visit interaction, starting dose-by-visit interaction, baseline score and baseline score-by-visit interaction.	
Comparison groups	Part 1: Tocilizumab qw + 26 weeks prednisone taper v Part 1: Placebo + 52 weeks prednisone taper
Number of subjects included in analysis	151
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.0476
Method	Repeated measures model
Parameter estimate	Differences in Least Square Means
Point estimate	-11.8
Confidence interval	
level	Other: 99 %
sides	2-sided
lower limit	-27.2
upper limit	3.6

Statistical analysis title	Statistical Analysis 3

Statistical analysis description:

Change at Week 52: Repeated measures model used for analysis included the following covariates and interactions: treatment, starting prednisone dose (<=30mg/day, >30mg/day), visit, treatment-by-visit interaction, starting dose-by-visit interaction, baseline score and baseline score-by-visit interaction.

Comparison groups	Part 1: Tocilizumab q2w + 26 weeks prednisone taper v Part 1: Placebo + 26 weeks prednisone taper
Number of subjects included in analysis	98
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.0059
Method	Repeated measures model
Parameter estimate	Differences in Least Square Means
Point estimate	-21.9
Confidence interval	
level	Other: 99 %
sides	2-sided
lower limit	-42.4
upper limit	-1.4

Statistical analysis title	Statistical Analysis 4

Statistical analysis description:

Change at Week 52: Repeated measures model used for analysis included the following covariates and interactions: treatment, starting prednisone dose (<=30mg/day, >30mg/day), visit, treatment-by-visit interaction, starting dose-by-visit interaction, baseline score and baseline score-by-visit interaction.

Comparison groups	Part 1: Tocilizumab q2w + 26 weeks prednisone taper v Part 1: Placebo + 52 weeks prednisone taper
Number of subjects included in analysis	100
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.0081
Method	Repeated measures model
Parameter estimate	Differences in Least Square Means
Point estimate	-18.2
Confidence interval	
level	Other: 99 %
sides	2-sided
lower limit	-35.8
upper limit	-0.5

Secondary: Area Under the Curve From Time Zero to End of Dosing Interval (AUCtau) at Steady State of Tocilizumab

End point title	Area Under the Curve From Time Zero to End of Dosing Interval (AUCtau) at Steady State of Tocilizumab[5]

End point description:

AUCtau is the model-predicted area under the tocilizumab serum concentration versus time curve from time zero to the end of dosing interval. AUCtau is measured in microgram*day per milliliter (mcg*day/mL). Pharmacokinetics (PK)-evaluable population included all participants who received at least one tocilizumab injection and had at least one PK sample with detectable results taken at any time

during the study.

End point type	Secondary

End point timeframe:

Baseline and Week 16 (Predose [Hour 0], 24, 48, 72, 96, and 120 or 144 hours postdose); Weeks 1, 2, 17, and 18 (Predose [Hour 0])

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: This endpoint evaluated the concentrations of TCZ in serum samples and is therefore not applicable for the two treatment arms in which patients received placebo.

End point values	Part 1: Tocilizumab qw + 26 weeks prednisone taper	Part 1: Tocilizumab q2w + 26 weeks prednisone taper		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	100	49		
Units: mcg*day/mL				
arithmetic mean (standard deviation)	499.2 (± 210.4)	227.2 (± 165.4)		

Statistical analyses

No statistical analyses for this end point

Secondary: Maximum Serum Concentration at Steady State (Cmax,ss) of Tocilizumab

End point title	Maximum Serum Concentration at Steady State (Cmax,ss) of Tocilizumab[6]

End point description:

Cmax,ss is maximum model-predicted serum steady state concentration of tocilizumab measured in micrograms per milliliter (mcg/mL). PK-evaluable population.

End point type	Secondary

End point timeframe:

Baseline and Week 16 (Predose [Hour 0], 24, 48, 72, 96, and 120 or 144 hours postdose); Weeks 1, 2, 17, and 18 (Predose [Hour 0])

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: This endpoint evaluated the concentrations of TCZ in serum samples and is therefore not applicable for the two treatment arms in which patients received placebo.

End point values	Part 1: Tocilizumab qw + 26 weeks prednisone taper	Part 1: Tocilizumab q2w + 26 weeks prednisone taper		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	100	49		
Units: mcg/mL				
arithmetic mean (standard deviation)	73 (± 30.4)	19.3 (± 12.8)		

Statistical analyses

No statistical analyses for this end point

Secondary: Minimum Serum Concentration at Steady State (Cmin,ss) of Tocilizumab

End point title	Minimum Serum Concentration at Steady State (Cmin,ss) of Tocilizumab[7]

End point description:

Cmin,ss is minimum model-predicted serum steady state concentration of tocilizumab measured in mcg/mL. PK-evaluable population.

End point type	Secondary

End point timeframe:

Baseline and Week 16 (Predose [Hour 0], 24, 48, 72, 96, and 120 or 144 hours postdose); Weeks 1, 2, 17, and 18 (Predose [Hour 0])

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: This endpoint evaluated the concentrations of TCZ in serum samples and is therefore not applicable for the two treatment arms in which patients received placebo.

End point values	Part 1: Tocilizumab qw + 26 weeks prednisone taper	Part 1: Tocilizumab q2w + 26 weeks prednisone taper		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	100	49		
Units: mcg/mL				
arithmetic mean (standard deviation)	68.1 (± 29.5)	11.1 (± 10.3)		

Statistical analyses

No statistical analyses for this end point

Secondary: Minimum Observed Serum Concentration (Ctrough) of Tocilizumab

End point title	Minimum Observed Serum Concentration (Ctrough) of Tocilizumab[8]

End point description:

Ctrough is minimum observed serum concentration of tocilizumab measured in mcg/mL. PK-evaluable population. Here, 'Number of Subjects Analysed' signifies the number of participants evaluable for this outcome measure and 'n' signifies the number of participants evaluable at specified time point for different arms, respectively.

End point type	Secondary

End point timeframe:

Predose (Hour 0) at Baseline and Week 52

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: This endpoint evaluated the concentrations of TCZ in serum samples and is therefore not applicable for the two treatment arms in which patients received placebo.

End point values	Part 1: Tocilizumab qw + 26 weeks prednisone taper	Part 1: Tocilizumab q2w + 26 weeks prednisone taper		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	99	48		
Units: mcg/mL				
arithmetic mean (standard deviation)				
Baseline (n= 99, 48)	0.07 (± 0.72)	0 (± 0.02)		
Week 52 (n= 72, 33)	67.93 (± 34.4)	12.22 (± 10.02)		

Statistical analyses

No statistical analyses for this end point

Secondary: Serum Interleukin-6 (IL-6) Level

End point title	Serum Interleukin-6 (IL-6) Level

End point description:

Safety population. Here, 'n' signifies the number of participants evaluable at specified time point for different arms, respectively

End point type	Secondary

End point timeframe:

Baseline and Week 52

End point values	Part 1: Tocilizumab qw + 26 weeks prednisone taper	Part 1: Tocilizumab q2w + 26 weeks prednisone taper	Part 1: Placebo + 26 weeks prednisone taper	Part 1: Placebo + 52 weeks prednisone taper
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	100	49	50	51
Units: picograms per milliliter (pg/mL)				
arithmetic mean (standard deviation)				
Baseline (n=91,44,50,47)	8.79 (± 10.01)	16.29 (± 31.23)	12.73 (± 18.04)	8.31 (± 9.47)
Week 52 (n=69,32,28,30)	65.99 (± 84.92)	52.7 (± 33.1)	35.96 (± 149.65)	10.85 (± 15.17)

Statistical analyses

No statistical analyses for this end point

Secondary: Serum Soluble IL-6 Receptor (sIL-6R) Level

End point title	Serum Soluble IL-6 Receptor (sIL-6R) Level

End point description:

Safety population. Here, 'n' signifies the number of participants evaluable at specified time point for different arms, respectively.

End point type	Secondary

End point timeframe:

Baseline and Week 52

End point values	Part 1: Tocilizumab qw + 26 weeks prednisone taper	Part 1: Tocilizumab q2w + 26 weeks prednisone taper	Part 1: Placebo + 26 weeks prednisone taper	Part 1: Placebo + 52 weeks prednisone taper
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	100	49	50	51
Units: nanograms per milliliter (ng/mL)				
arithmetic mean (standard deviation)				
Baseline (n=99,48,50,50)	51.34 (± 61.98)	50.82 (± 63.51)	42.07 (± 11.32)	40.37 (± 10.84)
Week 52 (n=73,33,33,31)	600.53 (± 217.52)	464.3 (± 153.64)	76.44 (± 149.2)	64.8 (± 105.13)

Statistical analyses

No statistical analyses for this end point

Secondary: Erythrocyte Sedimentation Rate (ESR)

End point title	Erythrocyte Sedimentation Rate (ESR)

End point description:

ESR is a laboratory test that provides a non-specific measure of inflammation. The test assesses the rate at which red blood cells fall in a test tube. Normal range is 0-30 mm/hr. A higher rate is consistent with inflammation. Safety population. Here, 'n' signifies the number of participants evaluable at specified time point for different arms, respectively

End point type	Secondary

End point timeframe:

Baseline and Week 52

End point values	Part 1: Tocilizumab qw + 26 weeks prednisone taper	Part 1: Tocilizumab q2w + 26 weeks prednisone taper	Part 1: Placebo + 26 weeks prednisone taper	Part 1: Placebo + 52 weeks prednisone taper
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	100	49	50	51
Units: mm/hr				
median (inter-quartile range (Q1-Q3))				
Baseline (n=99,49,50,51)	19 (10 to 35)	15 (10 to 30)	23 (9 to 36)	20 (8 to 38)
Week 52 (n=76,35,35,33)	3 (2 to 5)	5 (2 to 7)	20 (11 to 36)	24 (10 to 37)

Statistical analyses

No statistical analyses for this end point

Secondary: C-Reactive Protein (CRP) Level

End point title	C-Reactive Protein (CRP) Level

End point description:

The test for CRP is a laboratory measurement for evaluation of an acute phase reactant of inflammation through the use of an ultrasensitive assay. A decrease in the level of CRP indicates reduction in inflammation and therefore improvement. Safety population. Here, 'n' signifies the number of participants evaluable at specified time point for different arms, respectively.

End point type	Secondary

End point timeframe:

Baseline and Week 52

End point values	Part 1: Tocilizumab qw + 26 weeks prednisone taper	Part 1: Tocilizumab q2w + 26 weeks prednisone taper	Part 1: Placebo + 26 weeks prednisone taper	Part 1: Placebo + 52 weeks prednisone taper
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	100	49	50	51
Units: milligrams per liter (mg/L)				
median (inter-quartile range (Q1-Q3))				
Baseline (n=100,49,50,51)	3.67 (1.02 to 9.26)	4.52 (1.55 to 9.75)	3.64 (1.2 to 9.59)	3.56 (1.17 to 7.24)
Week 52 (n=76,35,35,33)	0.3 (0.2 to 0.59)	0.33 (0.2 to 0.72)	4.9 (2.25 to 9.25)	8.12 (2.02 to 14.4)

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants With Anti-Tocilizumab Antibodies

End point title	Percentage of Participants With Anti-Tocilizumab Antibodies

End point description:

All samples were tested by screening assay, and those samples that were positive were further analyzed by a confirmation assay to confirm specificity. Percentage of participants who has a positive confirmation assay result any time after the initial drug administration with a negative confirmation assay result at baseline was reported. Safety population included all participants who received at least one administration of study drug and provided at least one post-dose safety assessment. Here, 'Number of Subjects Analysed' signifies the number of participants evaluable for this outcome measure.

End point type	Secondary

End point timeframe:

Baseline up to Week 52

End point values	Part 1: Tocilizumab qw + 26 weeks prednisone taper	Part 1: Tocilizumab q2w + 26 weeks prednisone taper	Part 1: Placebo + 26 weeks prednisone taper	Part 1: Placebo + 52 weeks prednisone taper
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	95	46	49	47
Units: percentage of participants				
number (not applicable)	1.1	6.5	2	2.1

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information	
Timeframe for reporting adverse events:	
Up to 52 weeks	
Adverse event reporting additional description:	
Safety population	
Assessment type	Non-systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	19.0

Reporting groups	
Reporting group title	Part 1: Tocilizumab qw + 26 weeks prednisone taper
Reporting group description:	
Participants received tocilizumab at a dose of 162 mg as SC injection qw for 52 weeks along with prednisone and/or prednisone placebo according to the protocol-defined schedule. Participants received prednisone tapering oral daily doses during the first 26 weeks.	
Reporting group title	Part 1: Tocilizumab q2w + 26 weeks prednisone taper
Reporting group description:	
Participants received tocilizumab at a dose of 162 mg as SC injection q2w for 52 weeks along with prednisone and/or prednisone placebo according to the protocol-defined schedule. Participants received prednisone tapering oral daily doses during the first 26 weeks.	
Reporting group title	Part 1: Placebo + 26 weeks prednisone taper
Reporting group description:	
Participants received tocilizumab placebo as SC injection for 52 weeks along with prednisone and/or prednisone placebo according to the protocol-defined schedule. Participants received prednisone tapering oral daily doses during the first 26 weeks.	
Reporting group title	Part 1: Placebo + 52 weeks prednisone taper
Reporting group description:	
Participants received tocilizumab placebo as SC injection for 52 weeks along with prednisone and/or prednisone placebo according to the protocol-defined schedule. Participants received prednisone tapering oral daily doses for 52 weeks.	

Serious adverse events	Part 1: Tocilizumab qw + 26 weeks prednisone taper	Part 1: Tocilizumab q2w + 26 weeks prednisone taper	Part 1: Placebo + 26 weeks prednisone taper
Total subjects affected by serious adverse events			
subjects affected / exposed	15 / 100 (15.00%)	7 / 49 (14.29%)	11 / 50 (22.00%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events			
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Breast cancer			
subjects affected / exposed	0 / 100 (0.00%)	0 / 49 (0.00%)	1 / 50 (2.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Malignant melanoma			

subjects affected / exposed	0 / 100 (0.00%)	0 / 49 (0.00%)	0 / 50 (0.00%)
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 adenoma			
subjects affected / exposed	0 / 100 (0.00%)	1 / 49 (2.04%)	0 / 50 (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			
Hypertension			
subjects affected / exposed	0 / 100 (0.00%)	0 / 49 (0.00%)	1 / 50 (2.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Temporal arteritis			
subjects affected / exposed	1 / 100 (1.00%)	1 / 49 (2.04%)	1 / 50 (2.00%)
occurrences causally related to treatment / all	0 / 2	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Deep vein thrombosis			
subjects affected / exposed	1 / 100 (1.00%)	0 / 49 (0.00%)	0 / 50 (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
Hypertensive crisis			
subjects affected / exposed	2 / 100 (2.00%)	0 / 49 (0.00%)	0 / 50 (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
Dry gangrene			
subjects affected / exposed	0 / 100 (0.00%)	1 / 49 (2.04%)	0 / 50 (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
Immune system disorders			
Drug hypersensitivity			
subjects affected / exposed	1 / 100 (1.00%)	0 / 49 (0.00%)	0 / 50 (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
Hypersensitivity			

subjects affected / exposed	0 / 100 (0.00%)	1 / 49 (2.04%)	0 / 50 (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
Respiratory, thoracic and mediastinal disorders			
Nasal inflammation			
subjects affected / exposed	0 / 100 (0.00%)	0 / 49 (0.00%)	1 / 50 (2.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Oropharyngeal pain			
subjects affected / exposed	0 / 100 (0.00%)	0 / 49 (0.00%)	1 / 50 (2.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Asthma			
subjects affected / exposed	0 / 100 (0.00%)	0 / 49 (0.00%)	0 / 50 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Dyspnoea exertional			
subjects affected / exposed	0 / 100 (0.00%)	0 / 49 (0.00%)	0 / 50 (0.00%)
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	1 / 100 (1.00%)	0 / 49 (0.00%)	0 / 50 (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
Pulmonary embolism			
subjects affected / exposed	1 / 100 (1.00%)	0 / 49 (0.00%)	0 / 50 (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
Dyspnoea			
subjects affected / exposed	0 / 100 (0.00%)	1 / 49 (2.04%)	0 / 50 (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
Psychiatric disorders			

Anxiety			
subjects affected / exposed	1 / 100 (1.00%)	0 / 49 (0.00%)	0 / 50 (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
Stress			
subjects affected / exposed	1 / 100 (1.00%)	0 / 49 (0.00%)	0 / 50 (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			
Hepatic enzyme increased			
subjects affected / exposed	0 / 100 (0.00%)	0 / 49 (0.00%)	0 / 50 (0.00%)
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			
Postoperative wound complication			
subjects affected / exposed	0 / 100 (0.00%)	0 / 49 (0.00%)	1 / 50 (2.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Alcohol poisoning			
subjects affected / exposed	1 / 100 (1.00%)	0 / 49 (0.00%)	0 / 50 (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
Laceration			
subjects affected / exposed	1 / 100 (1.00%)	0 / 49 (0.00%)	0 / 50 (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
Tendon rupture			
subjects affected / exposed	1 / 100 (1.00%)	0 / 49 (0.00%)	0 / 50 (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
Meniscus injury			
subjects affected / exposed	0 / 100 (0.00%)	1 / 49 (2.04%)	0 / 50 (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			
Aortic valve stenosis			
subjects affected / exposed	0 / 100 (0.00%)	0 / 49 (0.00%)	0 / 50 (0.00%)
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 failure			
subjects affected / exposed	0 / 100 (0.00%)	0 / 49 (0.00%)	0 / 50 (0.00%)
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 failure chronic			
subjects affected / exposed	0 / 100 (0.00%)	0 / 49 (0.00%)	0 / 50 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Supraventricular tachycardia			
subjects affected / exposed	1 / 100 (1.00%)	0 / 49 (0.00%)	0 / 50 (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
Tachyarrhythmia			
subjects affected / exposed	1 / 100 (1.00%)	0 / 49 (0.00%)	0 / 50 (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
Nervous system disorders			
Paraesthesia			
subjects affected / exposed	0 / 100 (0.00%)	0 / 49 (0.00%)	1 / 50 (2.00%)
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 / 100 (0.00%)	0 / 49 (0.00%)	1 / 50 (2.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Transient ischaemic attack			
subjects affected / exposed	0 / 100 (0.00%)	0 / 49 (0.00%)	0 / 50 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Headache			
subjects affected / exposed	1 / 100 (1.00%)	0 / 49 (0.00%)	0 / 50 (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
Thrombotic stroke			
subjects affected / exposed	0 / 100 (0.00%)	1 / 49 (2.04%)	0 / 50 (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
Eye disorders			
Glaucoma			
subjects affected / exposed	0 / 100 (0.00%)	0 / 49 (0.00%)	1 / 50 (2.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cataract			
subjects affected / exposed	0 / 100 (0.00%)	0 / 49 (0.00%)	0 / 50 (0.00%)
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			
Gastritis erosive			
subjects affected / exposed	0 / 100 (0.00%)	0 / 49 (0.00%)	1 / 50 (2.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Stomatitis			
subjects affected / exposed	0 / 100 (0.00%)	0 / 49 (0.00%)	1 / 50 (2.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Diarrhoea			
subjects affected / exposed	1 / 100 (1.00%)	0 / 49 (0.00%)	0 / 50 (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
Renal and urinary disorders			
Renal impairment			

subjects affected / exposed	0 / 100 (0.00%)	0 / 49 (0.00%)	0 / 50 (0.00%)
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			
Arthralgia			
subjects affected / exposed	0 / 100 (0.00%)	0 / 49 (0.00%)	1 / 50 (2.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Fibromyalgia			
subjects affected / exposed	0 / 100 (0.00%)	0 / 49 (0.00%)	0 / 50 (0.00%)
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 / 100 (0.00%)	0 / 49 (0.00%)	0 / 50 (0.00%)
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 pain			
subjects affected / exposed	1 / 100 (1.00%)	0 / 49 (0.00%)	0 / 50 (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
Infections and infestations			
Erysipelas			
subjects affected / exposed	0 / 100 (0.00%)	0 / 49 (0.00%)	1 / 50 (2.00%)
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			
subjects affected / exposed	1 / 100 (1.00%)	0 / 49 (0.00%)	1 / 50 (2.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastroenteritis			
subjects affected / exposed	1 / 100 (1.00%)	0 / 49 (0.00%)	0 / 50 (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

Genital herpes zoster			
subjects affected / exposed	0 / 100 (0.00%)	0 / 49 (0.00%)	0 / 50 (0.00%)
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	1 / 100 (1.00%)	0 / 49 (0.00%)	0 / 50 (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
Respiratory tract infection			
subjects affected / exposed	0 / 100 (0.00%)	0 / 49 (0.00%)	0 / 50 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cellulitis			
subjects affected / exposed	1 / 100 (1.00%)	1 / 49 (2.04%)	0 / 50 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Chronic sinusitis			
subjects affected / exposed	1 / 100 (1.00%)	0 / 49 (0.00%)	0 / 50 (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 haemophilus			
subjects affected / exposed	1 / 100 (1.00%)	0 / 49 (0.00%)	0 / 50 (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 / 100 (1.00%)	0 / 49 (0.00%)	0 / 50 (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
Urinary tract infection			
subjects affected / exposed	1 / 100 (1.00%)	0 / 49 (0.00%)	0 / 50 (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
Urosepsis			

subjects affected / exposed	1 / 100 (1.00%)	0 / 49 (0.00%)	0 / 50 (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
Cholangitis infective			
subjects affected / exposed	0 / 100 (0.00%)	1 / 49 (2.04%)	0 / 50 (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
Metabolism and nutrition disorders			
Hypokalaemia			
subjects affected / exposed	0 / 100 (0.00%)	0 / 49 (0.00%)	0 / 50 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hyponatraemia			
subjects affected / exposed	0 / 100 (0.00%)	1 / 49 (2.04%)	0 / 50 (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

Serious adverse events	Part 1: Placebo + 52 weeks prednisone taper		
Total subjects affected by serious adverse events			
subjects affected / exposed	13 / 51 (25.49%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events			
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Breast cancer			
subjects affected / exposed	0 / 51 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Malignant melanoma			
subjects affected / exposed	1 / 51 (1.96%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Ovarian adenoma			

subjects affected / exposed	0 / 51 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Vascular disorders			
Hypertension			
subjects affected / exposed	0 / 51 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Temporal arteritis			
subjects affected / exposed	1 / 51 (1.96%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Deep vein thrombosis			
subjects affected / exposed	0 / 51 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Hypertensive crisis			
subjects affected / exposed	0 / 51 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Dry gangrene			
subjects affected / exposed	0 / 51 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Immune system disorders			
Drug hypersensitivity			
subjects affected / exposed	0 / 51 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Hypersensitivity			
subjects affected / exposed	0 / 51 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Respiratory, thoracic and mediastinal			

disorders				
Nasal inflammation				
subjects affected / exposed	0 / 51 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Oropharyngeal pain				
subjects affected / exposed	0 / 51 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Asthma				
subjects affected / exposed	1 / 51 (1.96%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Dyspnoea exertional				
subjects affected / exposed	1 / 51 (1.96%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Pleural effusion				
subjects affected / exposed	0 / 51 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Pulmonary embolism				
subjects affected / exposed	0 / 51 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Dyspnoea				
subjects affected / exposed	0 / 51 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Psychiatric disorders				
Anxiety				
subjects affected / exposed	0 / 51 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			

Stress			
subjects affected / exposed	0 / 51 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Investigations			
Hepatic enzyme increased			
subjects affected / exposed	1 / 51 (1.96%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Injury, poisoning and procedural complications			
Postoperative wound complication			
subjects affected / exposed	0 / 51 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Alcohol poisoning			
subjects affected / exposed	0 / 51 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Laceration			
subjects affected / exposed	0 / 51 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Tendon rupture			
subjects affected / exposed	0 / 51 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Meniscus injury			
subjects affected / exposed	0 / 51 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Cardiac disorders			
Aortic valve stenosis			

subjects affected / exposed	1 / 51 (1.96%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Cardiac failure				
subjects affected / exposed	1 / 51 (1.96%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Cardiac failure chronic				
subjects affected / exposed	1 / 51 (1.96%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Supraventricular tachycardia				
subjects affected / exposed	0 / 51 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Tachyarrhythmia				
subjects affected / exposed	0 / 51 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Nervous system disorders				
Paraesthesia				
subjects affected / exposed	0 / 51 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Syncope				
subjects affected / exposed	0 / 51 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Transient ischaemic attack				
subjects affected / exposed	1 / 51 (1.96%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Headache				

subjects affected / exposed	0 / 51 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Thrombotic stroke			
subjects affected / exposed	0 / 51 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Eye disorders			
Glaucoma			
subjects affected / exposed	0 / 51 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Cataract			
subjects affected / exposed	1 / 51 (1.96%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Gastrointestinal disorders			
Gastritis erosive			
subjects affected / exposed	0 / 51 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Stomatitis			
subjects affected / exposed	0 / 51 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Diarrhoea			
subjects affected / exposed	0 / 51 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Renal and urinary disorders			
Renal impairment			
subjects affected / exposed	1 / 51 (1.96%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		

Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	0 / 51 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Fibromyalgia			
subjects affected / exposed	1 / 51 (1.96%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Osteoarthritis			
subjects affected / exposed	1 / 51 (1.96%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Tendon pain			
subjects affected / exposed	0 / 51 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Infections and infestations			
Erysipelas			
subjects affected / exposed	0 / 51 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Pneumonia			
subjects affected / exposed	0 / 51 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Gastroenteritis			
subjects affected / exposed	2 / 51 (3.92%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Genital herpes zoster			
subjects affected / exposed	1 / 51 (1.96%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		

Herpes zoster			
subjects affected / exposed	2 / 51 (3.92%)		
occurrences causally related to treatment / all	2 / 2		
deaths causally related to treatment / all	0 / 0		
Respiratory tract infection			
subjects affected / exposed	1 / 51 (1.96%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Cellulitis			
subjects affected / exposed	0 / 51 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Chronic sinusitis			
subjects affected / exposed	0 / 51 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Pneumonia haemophilus			
subjects affected / exposed	0 / 51 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Pyelonephritis			
subjects affected / exposed	0 / 51 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Urinary tract infection			
subjects affected / exposed	0 / 51 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Urosepsis			
subjects affected / exposed	0 / 51 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Cholangitis infective			

subjects affected / exposed	0 / 51 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Metabolism and nutrition disorders			
Hypokalaemia			
subjects affected / exposed	1 / 51 (1.96%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Hyponatraemia			
subjects affected / exposed	0 / 51 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		

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

Non-serious adverse events	Part 1: Tocilizumab qw + 26 weeks prednisone taper	Part 1: Tocilizumab q2w + 26 weeks prednisone taper	Part 1: Placebo + 26 weeks prednisone taper
Total subjects affected by non-serious adverse events			
subjects affected / exposed	87 / 100 (87.00%)	44 / 49 (89.80%)	47 / 50 (94.00%)
Vascular disorders			
Haematoma			
subjects affected / exposed	5 / 100 (5.00%)	3 / 49 (6.12%)	3 / 50 (6.00%)
occurrences (all)	5	3	3
Hypertension			
subjects affected / exposed	12 / 100 (12.00%)	6 / 49 (12.24%)	4 / 50 (8.00%)
occurrences (all)	14	6	4
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	5 / 100 (5.00%)	3 / 49 (6.12%)	5 / 50 (10.00%)
occurrences (all)	8	3	5
Fatigue			
subjects affected / exposed	8 / 100 (8.00%)	5 / 49 (10.20%)	8 / 50 (16.00%)
occurrences (all)	8	6	8
Non-cardiac chest pain			

subjects affected / exposed	1 / 100 (1.00%)	2 / 49 (4.08%)	1 / 50 (2.00%)
occurrences (all)	2	2	1
Oedema peripheral			
subjects affected / exposed	16 / 100 (16.00%)	12 / 49 (24.49%)	8 / 50 (16.00%)
occurrences (all)	17	16	10
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	6 / 100 (6.00%)	3 / 49 (6.12%)	7 / 50 (14.00%)
occurrences (all)	6	3	8
Dyspnoea			
subjects affected / exposed	3 / 100 (3.00%)	3 / 49 (6.12%)	1 / 50 (2.00%)
occurrences (all)	3	3	1
Dyspnoea exertional			
subjects affected / exposed	1 / 100 (1.00%)	0 / 49 (0.00%)	3 / 50 (6.00%)
occurrences (all)	1	0	3
Epistaxis			
subjects affected / exposed	3 / 100 (3.00%)	1 / 49 (2.04%)	4 / 50 (8.00%)
occurrences (all)	3	1	4
Oropharyngeal pain			
subjects affected / exposed	7 / 100 (7.00%)	4 / 49 (8.16%)	4 / 50 (8.00%)
occurrences (all)	9	4	5
Psychiatric disorders			
Anxiety			
subjects affected / exposed	2 / 100 (2.00%)	1 / 49 (2.04%)	6 / 50 (12.00%)
occurrences (all)	2	2	6
Depression			
subjects affected / exposed	3 / 100 (3.00%)	2 / 49 (4.08%)	3 / 50 (6.00%)
occurrences (all)	3	2	3
Insomnia			
subjects affected / exposed	4 / 100 (4.00%)	1 / 49 (2.04%)	4 / 50 (8.00%)
occurrences (all)	4	1	4
Sleep disorder			
subjects affected / exposed	1 / 100 (1.00%)	3 / 49 (6.12%)	1 / 50 (2.00%)
occurrences (all)	1	4	1
Investigations			

Alanine aminotransferase increased			
subjects affected / exposed	5 / 100 (5.00%)	2 / 49 (4.08%)	2 / 50 (4.00%)
occurrences (all)	5	2	2
Injury, poisoning and procedural complications			
Fall			
subjects affected / exposed	7 / 100 (7.00%)	2 / 49 (4.08%)	2 / 50 (4.00%)
occurrences (all)	11	2	2
Cardiac disorders			
Palpitations			
subjects affected / exposed	2 / 100 (2.00%)	2 / 49 (4.08%)	4 / 50 (8.00%)
occurrences (all)	2	2	6
Nervous system disorders			
Dizziness			
subjects affected / exposed	6 / 100 (6.00%)	10 / 49 (20.41%)	6 / 50 (12.00%)
occurrences (all)	9	11	9
Headache			
subjects affected / exposed	27 / 100 (27.00%)	10 / 49 (20.41%)	16 / 50 (32.00%)
occurrences (all)	40	20	24
Paraesthesia			
subjects affected / exposed	4 / 100 (4.00%)	2 / 49 (4.08%)	4 / 50 (8.00%)
occurrences (all)	4	2	4
Tremor			
subjects affected / exposed	0 / 100 (0.00%)	0 / 49 (0.00%)	3 / 50 (6.00%)
occurrences (all)	0	0	3
Ear and labyrinth disorders			
Vertigo			
subjects affected / exposed	2 / 100 (2.00%)	1 / 49 (2.04%)	3 / 50 (6.00%)
occurrences (all)	2	1	3
Eye disorders			
Cataract			
subjects affected / exposed	5 / 100 (5.00%)	1 / 49 (2.04%)	3 / 50 (6.00%)
occurrences (all)	5	1	3
Dry eye			
subjects affected / exposed	1 / 100 (1.00%)	3 / 49 (6.12%)	1 / 50 (2.00%)
occurrences (all)	1	3	1
Gastrointestinal disorders			

Abdominal pain upper			
subjects affected / exposed	3 / 100 (3.00%)	3 / 49 (6.12%)	3 / 50 (6.00%)
occurrences (all)	3	3	3
Constipation			
subjects affected / exposed	0 / 100 (0.00%)	1 / 49 (2.04%)	3 / 50 (6.00%)
occurrences (all)	0	1	6
Diarrhoea			
subjects affected / exposed	12 / 100 (12.00%)	3 / 49 (6.12%)	8 / 50 (16.00%)
occurrences (all)	13	3	12
Dyspepsia			
subjects affected / exposed	0 / 100 (0.00%)	0 / 49 (0.00%)	4 / 50 (8.00%)
occurrences (all)	0	0	5
Nausea			
subjects affected / exposed	8 / 100 (8.00%)	2 / 49 (4.08%)	5 / 50 (10.00%)
occurrences (all)	11	2	7
Vomiting			
subjects affected / exposed	2 / 100 (2.00%)	2 / 49 (4.08%)	2 / 50 (4.00%)
occurrences (all)	2	2	3
Skin and subcutaneous tissue disorders			
Alopecia			
subjects affected / exposed	5 / 100 (5.00%)	7 / 49 (14.29%)	3 / 50 (6.00%)
occurrences (all)	5	7	3
Dry skin			
subjects affected / exposed	2 / 100 (2.00%)	3 / 49 (6.12%)	0 / 50 (0.00%)
occurrences (all)	2	4	0
Ecchymosis			
subjects affected / exposed	0 / 100 (0.00%)	2 / 49 (4.08%)	1 / 50 (2.00%)
occurrences (all)	0	2	1
Night sweats			
subjects affected / exposed	1 / 100 (1.00%)	3 / 49 (6.12%)	1 / 50 (2.00%)
occurrences (all)	1	3	1
Pruritus			
subjects affected / exposed	2 / 100 (2.00%)	4 / 49 (8.16%)	1 / 50 (2.00%)
occurrences (all)	2	4	1
Rash			

subjects affected / exposed	7 / 100 (7.00%)	5 / 49 (10.20%)	4 / 50 (8.00%)
occurrences (all)	7	5	7
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	13 / 100 (13.00%)	8 / 49 (16.33%)	10 / 50 (20.00%)
occurrences (all)	13	10	11
Back pain			
subjects affected / exposed	14 / 100 (14.00%)	7 / 49 (14.29%)	7 / 50 (14.00%)
occurrences (all)	16	14	8
Bursitis			
subjects affected / exposed	1 / 100 (1.00%)	4 / 49 (8.16%)	2 / 50 (4.00%)
occurrences (all)	1	4	2
Muscle spasms			
subjects affected / exposed	4 / 100 (4.00%)	6 / 49 (12.24%)	6 / 50 (12.00%)
occurrences (all)	4	9	6
Musculoskeletal pain			
subjects affected / exposed	12 / 100 (12.00%)	6 / 49 (12.24%)	5 / 50 (10.00%)
occurrences (all)	13	7	7
Myalgia			
subjects affected / exposed	9 / 100 (9.00%)	4 / 49 (8.16%)	4 / 50 (8.00%)
occurrences (all)	9	4	5
Neck pain			
subjects affected / exposed	6 / 100 (6.00%)	1 / 49 (2.04%)	2 / 50 (4.00%)
occurrences (all)	7	1	3
Osteoarthritis			
subjects affected / exposed	7 / 100 (7.00%)	2 / 49 (4.08%)	3 / 50 (6.00%)
occurrences (all)	7	3	3
Pain in extremity			
subjects affected / exposed	8 / 100 (8.00%)	5 / 49 (10.20%)	5 / 50 (10.00%)
occurrences (all)	8	7	5
Infections and infestations			
Bronchitis			
subjects affected / exposed	8 / 100 (8.00%)	4 / 49 (8.16%)	5 / 50 (10.00%)
occurrences (all)	9	4	5
Conjunctivitis			

subjects affected / exposed	4 / 100 (4.00%)	1 / 49 (2.04%)	4 / 50 (8.00%)
occurrences (all)	5	1	4
Cystitis			
subjects affected / exposed	7 / 100 (7.00%)	0 / 49 (0.00%)	2 / 50 (4.00%)
occurrences (all)	13	0	4
Gastroenteritis			
subjects affected / exposed	3 / 100 (3.00%)	4 / 49 (8.16%)	4 / 50 (8.00%)
occurrences (all)	3	4	4
Nasopharyngitis			
subjects affected / exposed	29 / 100 (29.00%)	12 / 49 (24.49%)	9 / 50 (18.00%)
occurrences (all)	39	15	12
Oral herpes			
subjects affected / exposed	4 / 100 (4.00%)	5 / 49 (10.20%)	3 / 50 (6.00%)
occurrences (all)	4	5	3
Pharyngitis			
subjects affected / exposed	4 / 100 (4.00%)	0 / 49 (0.00%)	1 / 50 (2.00%)
occurrences (all)	4	0	1
Rhinitis			
subjects affected / exposed	6 / 100 (6.00%)	4 / 49 (8.16%)	2 / 50 (4.00%)
occurrences (all)	6	4	2
Sinusitis			
subjects affected / exposed	3 / 100 (3.00%)	4 / 49 (8.16%)	1 / 50 (2.00%)
occurrences (all)	4	4	1
Upper respiratory tract infection			
subjects affected / exposed	10 / 100 (10.00%)	6 / 49 (12.24%)	5 / 50 (10.00%)
occurrences (all)	10	7	5
Urinary tract infection			
subjects affected / exposed	10 / 100 (10.00%)	4 / 49 (8.16%)	2 / 50 (4.00%)
occurrences (all)	15	5	4
Metabolism and nutrition disorders			
Hypercholesterolaemia			
subjects affected / exposed	2 / 100 (2.00%)	3 / 49 (6.12%)	0 / 50 (0.00%)
occurrences (all)	2	3	0

Non-serious adverse events	Part 1: Placebo + 52 weeks prednisone taper		
Total subjects affected by non-serious			

adverse events subjects affected / exposed	44 / 51 (86.27%)		
Vascular disorders Haematoma subjects affected / exposed occurrences (all) Hypertension subjects affected / exposed occurrences (all)	 1 / 51 (1.96%) 1 4 / 51 (7.84%) 6		
General disorders and administration site conditions Asthenia subjects affected / exposed occurrences (all) Fatigue subjects affected / exposed occurrences (all) Non-cardiac chest pain subjects affected / exposed occurrences (all) Oedema peripheral subjects affected / exposed occurrences (all)	 0 / 51 (0.00%) 0 3 / 51 (5.88%) 3 3 / 51 (5.88%) 3 6 / 51 (11.76%) 9		
Respiratory, thoracic and mediastinal disorders Cough subjects affected / exposed occurrences (all) Dyspnoea subjects affected / exposed occurrences (all) Dyspnoea exertional subjects affected / exposed occurrences (all) Epistaxis subjects affected / exposed occurrences (all) Oropharyngeal pain	 3 / 51 (5.88%) 3 3 / 51 (5.88%) 3 0 / 51 (0.00%) 0 0 / 51 (0.00%) 0		

subjects affected / exposed	8 / 51 (15.69%)		
occurrences (all)	12		
Psychiatric disorders			
Anxiety			
subjects affected / exposed	1 / 51 (1.96%)		
occurrences (all)	1		
Depression			
subjects affected / exposed	1 / 51 (1.96%)		
occurrences (all)	1		
Insomnia			
subjects affected / exposed	4 / 51 (7.84%)		
occurrences (all)	4		
Sleep disorder			
subjects affected / exposed	1 / 51 (1.96%)		
occurrences (all)	1		
Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	0 / 51 (0.00%)		
occurrences (all)	0		
Injury, poisoning and procedural complications			
Fall			
subjects affected / exposed	2 / 51 (3.92%)		
occurrences (all)	3		
Cardiac disorders			
Palpitations			
subjects affected / exposed	2 / 51 (3.92%)		
occurrences (all)	2		
Nervous system disorders			
Dizziness			
subjects affected / exposed	8 / 51 (15.69%)		
occurrences (all)	9		
Headache			
subjects affected / exposed	12 / 51 (23.53%)		
occurrences (all)	26		
Paraesthesia			

subjects affected / exposed occurrences (all) Tremor subjects affected / exposed occurrences (all)	4 / 51 (7.84%) 4 3 / 51 (5.88%) 3		
Ear and labyrinth disorders Vertigo subjects affected / exposed occurrences (all)	 1 / 51 (1.96%) 1		
Eye disorders Cataract subjects affected / exposed occurrences (all) Dry eye subjects affected / exposed occurrences (all)	 4 / 51 (7.84%) 5 1 / 51 (1.96%) 1		
Gastrointestinal disorders Abdominal pain upper subjects affected / exposed occurrences (all) Constipation subjects affected / exposed occurrences (all) Diarrhoea subjects affected / exposed occurrences (all) Dyspepsia subjects affected / exposed occurrences (all) Nausea subjects affected / exposed occurrences (all) Vomiting subjects affected / exposed occurrences (all)	 4 / 51 (7.84%) 4 4 / 51 (7.84%) 4 5 / 51 (9.80%) 6 1 / 51 (1.96%) 1 4 / 51 (7.84%) 5 3 / 51 (5.88%) 3		
Skin and subcutaneous tissue disorders			

Alopecia subjects affected / exposed occurrences (all)	5 / 51 (9.80%) 5		
Dry skin subjects affected / exposed occurrences (all)	0 / 51 (0.00%) 0		
Ecchymosis subjects affected / exposed occurrences (all)	3 / 51 (5.88%) 4		
Night sweats subjects affected / exposed occurrences (all)	1 / 51 (1.96%) 1		
Pruritus subjects affected / exposed occurrences (all)	1 / 51 (1.96%) 1		
Rash subjects affected / exposed occurrences (all)	2 / 51 (3.92%) 2		
Musculoskeletal and connective tissue disorders			
Arthralgia subjects affected / exposed occurrences (all)	8 / 51 (15.69%) 11		
Back pain subjects affected / exposed occurrences (all)	10 / 51 (19.61%) 12		
Bursitis subjects affected / exposed occurrences (all)	1 / 51 (1.96%) 1		
Muscle spasms subjects affected / exposed occurrences (all)	4 / 51 (7.84%) 6		
Musculoskeletal pain subjects affected / exposed occurrences (all)	2 / 51 (3.92%) 2		
Myalgia			

subjects affected / exposed	4 / 51 (7.84%)		
occurrences (all)	5		
Neck pain			
subjects affected / exposed	4 / 51 (7.84%)		
occurrences (all)	4		
Osteoarthritis			
subjects affected / exposed	3 / 51 (5.88%)		
occurrences (all)	3		
Pain in extremity			
subjects affected / exposed	5 / 51 (9.80%)		
occurrences (all)	7		
Infections and infestations			
Bronchitis			
subjects affected / exposed	5 / 51 (9.80%)		
occurrences (all)	5		
Conjunctivitis			
subjects affected / exposed	1 / 51 (1.96%)		
occurrences (all)	1		
Cystitis			
subjects affected / exposed	3 / 51 (5.88%)		
occurrences (all)	8		
Gastroenteritis			
subjects affected / exposed	3 / 51 (5.88%)		
occurrences (all)	4		
Nasopharyngitis			
subjects affected / exposed	13 / 51 (25.49%)		
occurrences (all)	17		
Oral herpes			
subjects affected / exposed	2 / 51 (3.92%)		
occurrences (all)	2		
Pharyngitis			
subjects affected / exposed	3 / 51 (5.88%)		
occurrences (all)	3		
Rhinitis			
subjects affected / exposed	3 / 51 (5.88%)		
occurrences (all)	3		

Sinusitis subjects affected / exposed occurrences (all)	2 / 51 (3.92%) 2		
Upper respiratory tract infection subjects affected / exposed occurrences (all)	7 / 51 (13.73%) 9		
Urinary tract infection subjects affected / exposed occurrences (all)	4 / 51 (7.84%) 7		
Metabolism and nutrition disorders Hypercholesterolaemia subjects affected / exposed occurrences (all)	1 / 51 (1.96%) 1		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
19 October 2012	The inclusion criteria related to the requirement for a history of ESR >/=50 mm/hr and active disease according to an ESR >/=30 mm/hr were clarified; The exclusion criteria were revised to exclude only major ischemic events unrelated to GCA and a new exclusion criterion added to exclude participants who received pulsed methylprednisolone within 6 weeks of baseline; The criteria concerning re-screening and retesting for laboratory inclusion/exclusion criteria were outlined; The definition of remission was clarified; All participants were made eligible for transition from Part 1 to Part 2 of the study; The status of prednisone as an investigational medicinal product (IMP) during Part 1 of the study was clarified; The protocol was aligned with the Sponsor's memorandum on "Implementing immunoglobulin (Ig)E Assay for tocilizumab Immunogenicity Testing" and immunogenicity testing for participants who discontinued treatment with tocilizumab was added; Collection of information on prior medications and electrocardiograms (ECGs) was simplified; Visit windows were revised to increase flexibility and participant retention; Collection of laboratory assessments was clarified; Information on tocilizumab syringe labels was standardized with that of drug supply; Lipid-lowering agents were added to the list of permitted concomitant non-investigational medicinal products (NIMPs).
08 February 2013	Following Food and Drug Administration (FDA) feedback the definition of relapsing participants was updated to include those with active disease despite at least 2 consecutive weeks of treatment with >/=40 mg/day prednisone (or equivalent) at any time; Following FDA feedback the key secondary endpoint defining a comparison of the proportion of participants in sustained remission at Week 52 in the tocilizumab groups versus the placebo group with 52-week prednisone taper was added; The terminology of the dual assessors was changed; Addition of a ribonucleic acid (RNA) blood sample and serum sample for biomarkers at unscheduled visit; Addition of an exclusion criterion specifying that previous treatment with tofacitinib was not permitted; Timing of the collection of the immunogenicity samples was amended.
22 January 2014	To better reflect clinical practice where CRP is replacing ESR in several health centers, the requirement for a CRP >/=2.45 mg/dL for participants where a historical ESR value was unavailable was added; Removal of the requirement of ESR >/=30 mm/hr or CRP >/=1 mg/dL to confirm active disease in participants with a positive temporal artery biopsy within 6 weeks of baseline; Definition of flare was modified to allow the clinical assessor to consider an elevated ESR as disease flare in the absence of GCA signs and symptoms if, in their opinion, it was attributable to GCA; Further clarification of the definition of new-onset GCA was made; Clarification to the concomitant therapy section on the use of intra-arterial (IA), intravenous (IV) and intramuscular (IM) glucocorticoids; The time window required for a latent tuberculosis test to be performed prior to initiation of study drug treatment was increased form 3 weeks to 6 weeks.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported