ClinicalTrials.gov Protocol and Results Registration System (PRS) Receipt
Release Date: 10/20/2014

ClinicalTrials.gov ID: NCT00887341

Study Identification

Unique Protocol ID:	ML22254
Brief Title:	A Study Comparing Infusion Rates of Tocilizumab in Patients With Moderate to Severe Rheumatoid Arthritis
Official Title:	Phase II Multi-centre, Randomized, Parallel Group, Pilot Trial to Compare the Incidence of Tocilizumab Related Infusion Reactions in Moderate to Severe RA Patients When Infusion is Made Over 1 Hour Against 31 Minutes
Secondary IDs:	2008-006443-39

Study Status

Record Verification:	October 2014
Overall Status:	Completed
Study Start:	May 2009
Primary Completion:	December 2010 [Actual]
Study Completion:	December 2010 [Actual]

Sponsor/Collaborators

Sponsor:	Hoffmann-La Roche
Responsible Party:	Sponsor
Collaborators:	

Oversight

FDA Regulated?:	No
IND/IDE Protocol?:	No

Review Board:	Approval Status: Approved Approval Number: Unkown Board Name: Comite Etic d'Investigacio Clinica Board Affiliation: Hospital Germans Trias i Pujol Phone: +34 93 497 8956 Email: ceic.germanstrias@gencat.net
Data Monitoring?:	
Plan to Share Data?:	
Oversight Authorities:	Spain: Ministry of Health

Study Description

Brief Summary:	This 2 arm study will compare the incidence of tocilizumab-related infusion reactions, using 2 different infusion times, in patients with moderate to severe rheumatoid arthritis who have shown an inadequate response to DMARDs (Disease Modifying Anti Rheumatic Drugs) or anti-TNFs.Patients will be randomized to one of 2 groups, to receive tocilizumab 8mg/kg iv every 4 weeks either a)over a 1h infusion time for all administrations or b) a 1h infusion time for the first administration, followed by a 31 minute infusion time for subsequent administrations (unless drug-related infusion reactions occur).The anticipated time on study treatment is 3-12 months, and the target sample size is <100 individuals.
Detailed Description:	

Conditions

Conditions:	Rheumatoid Arthritis
Keywords:	

Study Design

Study Type:	Interventional
Primary Purpose:	Treatment
Study Phase:	Phase 2
Intervention Model:	Parallel Assignment
Number of Arms:	2
Masking:	Open Label
Allocation:	Randomized
Endpoint Classification:	Safety/Efficacy Study

Enrollment: 76 [Actual]

Arms and Interventions

Arms	Assigned Interventions
Experimental: 1	Drug: tocilizumab [RoActemra/Actemra] 8mg/kg iv every 4 weeks for 6 infusions; first infusion 1h duration, subsequent infusions 31 minutes duration
Active Comparator: 2	Drug: tocilizumab [RoActemra/Actemra] 8mg/kg iv every 4 weeks for 6 infusions; each infusion 1h duration

Outcome Measures

[See Results Section.]

Eligibility

Minimum Age: 18 Years

Maximum Age:

Gender: Both

Accepts Healthy Volunteers?: No

Criteria: Inclusion Criteria:

- adult patients, >=18 years of age;
- active moderate or severe rheumatoid arthritis;
- active disease for >6 months;
- inadequate response to a stable dose of non-biologic DMARDs or antiTNFs.

Exclusion Criteria:

- rheumatic autoimmune disease other than rheumatoid arthritis;
- prior history of, or current inflammatory joint disease other than rheumatoid arthritis;
- major surgery (including joint surgery) within 8 weeks prior to screening, or planned major surgery within 6 months following enrollment.

Contacts/Locations

Study Officials: Clinical Trials
Study Director

Hoffmann-La Roche

Locations: Spain

San Sebastian de los Reyes, Madrid, Spain, 28702

Alcala de Henares, Madrid, Spain, 28805

Palma de Mallorca, Islas Baleares, Spain, 07014

Alzira, Valencia, Spain, 46600

San Juan, Valencia, Spain, 03550

Madrid, Madrid, Spain, 28031

Madrid, Madrid, Spain, 28935

Gijon, Asturias, Spain, 33394

Vigo, Pontevedra, Spain, 36204

Zaragoza, Zaragoza, Spain, 50009

Torrelavega, Cantabria, Spain, 39300

Badalona, Barcelona, Spain, 08915

Mollet del Valles, Barcelona, Spain, 08100

Vigo, Pontevedra, Spain, 36214

Valenica, Valencia, Spain, 46009

Galdakao, Vizcaya, Spain, 48960

Hospitalet de Llobregat, Barcelona, Spain, 08906

Menorca, Islas Baleares, Spain, 07701

Avila, Avila, Spain, 05071

Oviedo, Asturias, Spain, 33006

Castellon, Castellon, Spain, 12004

Vitoria, Alava, Spain, 01009

Palma de Mallorca, Islas Baleares, Spain, 07198

Villajoyosa, Alicante, Spain, 03570

References

Citations:

Links:

Study Data/Documents:

Study Results

Participant Flow

Reporting Groups

	Description
Tocilizumab, 1 Hour Infusions	Participants received tocilizumab 8 milligrams per kilogram (mg/kg) via intravenous (IV) infusion (over 1 hour), once every 4 weeks for 6 infusions (up to 24 weeks).
Tocilizumab, 31 Minute Infusions	Participants received tocilizumab 8 mg/kg via IV infusion, once every 4 weeks for 6 infusions (up to 24 weeks). The first infusion was 1 hour; the remaining 5 infusions were administered over a period of 31 minutes as long as no infusion reactions occurred. If an infusion reaction occurred, 1 hour infusions were used for all subsequent remaining infusions.

Overall Study

	Tocilizumab, 1 Hour Infusions	Tocilizumab, 31 Minute Infusions
Started	37	39
Completed	35	36
Not Completed	2	3
Refused treatment	1	0
Withdrawal by Subject	1	1
Adverse Event	0	1
Lost to Follow-up	0	1

Baseline Characteristics

Analysis Population Description

Intent-to-treat (ITT) Population: all participants enrolled in the study who had been randomly assigned to one of the two study treatments and received at least one dose of study drug.

Reporting Groups

	Description
Tocilizumab, 1 Hour Infusions	Participants received tocilizumab 8 mg/kg via IV infusion (over 1 hour), once every 4 weeks for 6 infusions (up to 24 weeks).
Tocilizumab, 31 Minute Infusions	Participants received tocilizumab 8 mg/kg via IV infusion, once every 4 weeks for 6 infusions (up to 24 weeks). The first infusion was 1 hour; the remaining 5 infusions were administered over a period of 31 minutes as long as no infusion reactions occurred. If an infusion reaction occurred, 1 hour infusions were used for all subsequent remaining infusions.

Baseline Measures

	Tocilizumab, 1 Hour Infusions	Tocilizumab, 31 Minute Infusions	Total
Number of Participants	37	39	76
Age, Continuous [units: years] Mean (Standard Deviation)	52.65 (12.71)	52.46 (10.47)	52.55 (11.54)
Gender, Male/Female [units: participants]			
Female	35	28	63
Male	2	11	13

Outcome Measures

1. Primary Outcome Measure:

Measure Title	Percentage of Participants With an Infusion Reaction Within 24 Hours After Infusion
Measure Description	An infusion reaction was defined as any adverse event (AE) that occurred during the infusion or during the 24 hours following the infusion.
Time Frame	Screening, Baseline, and Weeks 4, 8, 12, 16, 20, and 24
Safety Issue?	Yes

Analysis Population Description

ITT Population

Reporting Groups

	Description
Tocilizumab, 1 Hour Infusions	Participants received tocilizumab 8 mg/kg via IV infusion (over 1 hour), once every 4 weeks for 6 infusions (up to 24 weeks).
Tocilizumab, 31 Minute Infusions	Participants received tocilizumab 8 mg/kg via IV infusion, once every 4 weeks for 6 infusions (up to 24 weeks). The first infusion was 1 hour; the remaining 5 infusions were administered over a period of 31 minutes as long as no infusion reactions occurred. If an infusion reaction occurred, 1 hour infusions were used for all subsequent remaining infusions.

Measured Values

	Tocilizumab, 1 Hour Infusions	Tocilizumab, 31 Minute Infusions
Number of Participants Analyzed	37	39
Percentage of Participants With an Infusion Reaction Within 24 Hours After Infusion [units: percentage of participants]	29.7	17.9

Statistical Analysis 1 for Percentage of Participants With an Infusion Reaction Within 24 Hours After Infusion

Statistical Analysis Overview	Comparison Groups	Tocilizumab, 1 Hour Infusions, Tocilizumab, 31 Minute Infusions
	Comments	[Not specified]
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]

Statistical Test of Hypothesis	P-Value	0.238
	Comments	[Not specified]
	Method	Chi-squared
	Comments	[Not specified]

2. Secondary Outcome Measure:

Measure Title	Percentage of Participants Discontinuing Tocilizumab in Response to an AE or Serious AE (SAE)
Measure Description	
Time Frame	Weeks 4, 8, 12, 16, 20 and Final Visit

Safety Issue?	No

Analysis Population Description
ITT Population

Reporting Groups

	Description
Tocilizumab, 1 Hour Infusions	Participants received tocilizumab 8 mg/kg via IV infusion (over 1 hour), once every 4 weeks for 6 infusions (up to 24 weeks).
Tocilizumab, 31 Minute Infusions	Participants received tocilizumab 8 mg/kg via IV infusion, once every 4 weeks for 6 infusions (up to 24 weeks). The first infusion was 1 hour; the remaining 5 infusions were administered over a period of 31 minutes as long as no infusion reactions occurred. If an infusion reaction occurred, 1 hour infusions were used for all subsequent remaining infusions.

Measured Values

	Tocilizumab, 1 Hour Infusions	Tocilizumab, 31 Minute Infusions
Number of Participants Analyzed	37	39
Percentage of Participants Discontinuing Tocilizumab in Response to an AE or Serious AE (SAE) [units: percentage of participants]	2.7	0.0

3. Secondary Outcome Measure:

Measure Title	Percentage of Participants Discontinuing Tocilizumab for Any Reason
Measure Description	
Time Frame	Weeks 4, 8, 12, 16, 20 and Final Visit
Safety Issue?	No

Analysis Population Description
ITT Population

Reporting Groups

	Description
Tocilizumab, 1 Hour Infusions	Participants received tocilizumab 8 mg/kg via IV infusion (over 1 hour), once every 4 weeks for 6 infusions (up to 24 weeks).

	Description
Tocilizumab, 31 Minute Infusions	Participants received tocilizumab 8 mg/kg via IV infusion, once every 4 weeks for 6 infusions (up to 24 weeks). The first infusion was 1 hour; the remaining 5 infusions were administered over a period of 31 minutes as long as no infusion reactions occurred. If an infusion reaction occurred, 1 hour infusions were used for all subsequent remaining infusions.

Measured Values

	Tocilizumab, 1 Hour Infusions	Tocilizumab, 31 Minute Infusions
Number of Participants Analyzed	37	39
Percentage of Participants Discontinuing Tocilizumab for Any Reason [units: percentage of participants]	2.7	2.6

4. Secondary Outcome Measure:

Measure Title	Percentage of Participants With a Reduction of at Least 1.2 Units on the Disease Activity Scale Based on 28-Joint Count (DAS28) by Visit
Measure Description	DAS28 calculated from the number of swollen joints and tender joints using the 28-joint count, the erythrocyte sedimentation rate (ESR) (millimeters per hour [mm/hr]) and Patient's Global Assessment of Disease (participant-rated arthritis activity assessment) with transformed scores ranging 0 to 10; higher scores indicated greater affectation due to disease activity. DAS28 less than or equal to (≤)3.2 equals (=) low disease activity, DAS28 greater than (>)3.2 to 5.1 = moderate to high disease activity; DAS28 less than (<) 2.6 = remission. A reduction of at least 1.2 units was considered a clinically significant difference.
Time Frame	Weeks 4, 8, 12, 16, 20 and Final Visit
Safety Issue?	No

Analysis Population Description

ITT Population

Reporting Groups

	Description
Tocilizumab, 1 Hour Infusions	Participants received tocilizumab 8 mg/kg via IV infusion (over 1 hour), once every 4 weeks for 6 infusions (up to 24 weeks).
Tocilizumab, 31 Minute Infusions	Participants received tocilizumab 8 mg/kg via IV infusion, once every 4 weeks for 6 infusions (up to 24 weeks). The first infusion was 1 hour; the remaining 5 infusions were administered over a period of 31 minutes as long as no infusion reactions occurred. If an infusion reaction occurred, 1 hour infusions were used for all subsequent remaining infusions.

Measured Values

	Tocilizumab, 1 Hour Infusions	Tocilizumab, 31 Minute Infusions
Number of Participants Analyzed	37	39
Percentage of Participants With a Reduction of at Least 1.2 Units on the Disease Activity Scale Based on 28-Joint Count (DAS28) by Visit [units: percentage of participants]		
Week 4	56.7	61.9
Week 8	58.6	74.1
Week 12	77.8	92.3
Week 16	88.5	88.0
Week 20	88.9	84.0
Final visit	80.8	91.7

5. Secondary Outcome Measure:

Measure Title	Percentage of Participants Achieving a DAS28 Score <3.2 by Visit
Measure Description	DAS28 calculated from the number of swollen joints and tender joints using the 28-joint count, the ESR (mm/hr), and Patient's Global Assessment of Disease (participant-rated arthritis activity assessment) with transformed scores ranging 0 to 10; higher scores indicated greater affectation due to disease activity. DAS28 ≤3.2=low disease activity, DAS28 >3.2 to 5.1=moderate to high disease activity; DAS28 <2.6=remission.
Time Frame	Weeks 4, 8, 12, 16, 20 and Final Visit
Safety Issue?	No

Analysis Population Description

ITT Population

Reporting Groups

	Description
Tocilizumab, 1 Hour Infusions	Participants received tocilizumab 8 mg/kg via IV infusion (over 1 hour), once every 4 weeks for 6 infusions (up to 24 weeks).

	Description
Tocilizumab, 31 Minute Infusions	Participants received tocilizumab 8 mg/kg via IV infusion, once every 4 weeks for 6 infusions (up to 24 weeks). The first infusion was 1 hour; the remaining 5 infusions were administered over a period of 31 minutes as long as no infusion reactions occurred. If an infusion reaction occurred, 1 hour infusions were used for all subsequent remaining infusions.

Measured Values

	Tocilizumab, 1 Hour Infusions	Tocilizumab, 31 Minute Infusions
Number of Participants Analyzed	37	39
Percentage of Participants Achieving a DAS28 Score <3.2 by Visit [units: percentage of participants]		
Week 4	22.2	32.0
Week 8	25.0	60.0
Week 12	46.9	77.1
Week 16	59.4	77.1
Week 20	68.8	79.4
Final visit	64.3	80.6

6. Secondary Outcome Measure:

Measure Title	Percentage of Participants Achieving a DAS28 Score <2.6 (Remission)
Measure Description	DAS28 calculated from the number of swollen joints and tender joints using the 28-joint count, the ESR (mm/hr) and Patient's Global Assessment of Disease (participant-rated arthritis activity assessment) with transformed scores ranging 0 to 10; higher scores indicated greater affectation due to disease activity. DAS28 ≤3.2=low disease activity, DAS28 >3.2 to 5.1=moderate to high disease activity; DAS28 <2.6=remission.
Time Frame	Weeks 4, 8, 12, 16, 20 and Final Visit
Safety Issue?	No

Analysis Population Description

ITT population

Reporting Groups

	Description
Tocilizumab, 1 Hour Infusions	Participants received tocilizumab 8 mg/kg via IV infusion (over 1 hour), once every 4 weeks for 6 infusions (up to 24 weeks).
Tocilizumab, 31 Minute Infusions	Participants received tocilizumab 8 mg/kg via IV infusion, once every 4 weeks for 6 infusions (up to 24 weeks). The first infusion was 1 hour; the remaining 5 infusions were administered over a period of 31 minutes as long as no infusion reactions occurred. If an infusion reaction occurred, 1 hour infusions were used for all subsequent remaining infusions.

Measured Values

	Tocilizumab, 1 Hour Infusions	Tocilizumab, 31 Minute Infusions
Number of Participants Analyzed	37	39
Percentage of Participants Achieving a DAS28 Score <2.6 (Remission) [units: percentage of participants]		
Week 4	11.1	20.0
Week 8	18.8	34.3
Week 12	34.4	57.1
Week 16	40.6	51.4
Week 20	56.3	58.8
Final visit	46.4	74.2

7. Secondary Outcome Measure:

Measure Title	DAS28 Score by Visit
Measure Description	DAS28 calculated from the number of swollen joints and tender joints using the 28-joint count, the ESR (mm/hr) and Patient's Global Assessment of Disease (participant-rated arthritis activity assessment) with transformed scores ranging 0 to 10; higher scores indicated greater affectation due to disease activity. DAS28 ≤3.2=low disease activity, DAS28 >3.2 to 5.1=moderate to high disease activity; DAS28 <2.6=remission. Last observation carried forward (LOCF) visit took the last non-missing post-baseline available value.
Time Frame	Weeks 4, 8, 12, 16, 20, and Final Visit
Safety Issue?	No

Analysis Population Description

ITT Population; n (number)=number of participants analyzed for the specified parameter at a given visit.

Reporting Groups

	Description
Tocilizumab, 1 Hour Infusions	Participants received tocilizumab 8 mg/kg via IV infusion (over 1 hour), once every 4 weeks for 6 infusions (up to 24 weeks).
Tocilizumab, 31 Minute Infusions	Participants received tocilizumab 8 mg/kg via IV infusion, once every 4 weeks for 6 infusions (up to 24 weeks). The first infusion was 1 hour; the remaining 5 infusions were administered over a period of 31 minutes as long as no infusion reactions occurred. If an infusion reaction occurred, 1 hour infusions were used for all subsequent remaining infusions.

Measured Values

	Tocilizumab, 1 Hour Infusions	Tocilizumab, 31 Minute Infusions
Number of Participants Analyzed	37	38
DAS28 Score by Visit [units: units on a scale] Mean (Standard Deviation)		
Baseline visit (n=36,38)	5.75 (1.18)	5.32 (1.14)
Week 4 (n=36,25)	4.28 (1.33)	3.62 (1.27)
Week 8 (n=32,35)	4.14 (1.54)	3.05 (1.20)
Week 12 (n=32,35)	3.30 (1.32)	2.66 (1.04)
Week 16 (n=32,35)	3.07 (1.50)	2.64 (1.18)
Week 20 (n=32,34)	2.78 (1.33)	2.41 (1.22)
Final visit (n=28,31)	2.72 (1.40)	2.19 (1.06)
LOCF visit (n=37,38)	2.92 (1.56)	2.37 (1.13)

8. Secondary Outcome Measure:

Measure Title	Percentage of Participants Achieving American College of Rheumatology 20 Percent (%) Improvement (ACR20 Response)

Measure Description	ACR20 response defined as an improvement of ≥20% in swollen joint count (SJC; 66 joints) and tender joint count (TJC; 68 joints) as well as ≥20% improvement in at least 3 of the following 5 remaining ACR assessments: Patient Global Assessment of Pain; Patient Global Assessment of Disease Activity; Physician Global Assessment of Disease Activity; Health Assessment Questionnaire - Disability Index (HAQ-DI); and acute phase reactive factors (ESR or C-Reactive Protein [CRP])
Time Frame	Weeks 4, 8, 12, 16, 20 and Final Visit
Safety Issue?	No

Analysis Population Description

ITT Population

Reporting Groups

	Description
Tocilizumab, 1 Hour Infusions	Participants received tocilizumab 8 mg/kg via IV infusion (over 1 hour), once every 4 weeks for 6 infusions (up to 24 weeks).
Tocilizumab, 31 Minute Infusions	Participants received tocilizumab 8 mg/kg via IV infusion, once every 4 weeks for 6 infusions (up to 24 weeks). The first infusion was 1 hour; the remaining 5 infusions were administered over a period of 31 minutes as long as no infusion reactions occurred. If an infusion reaction occurred, 1 hour infusions were used for all subsequent remaining infusions.

Measured Values

	Tocilizumab, 1 Hour Infusions	Tocilizumab, 31 Minute Infusions
Number of Participants Analyzed	37	39
Percentage of Participants Achieving American College of Rheumatology 20 Percent (%) Improvement (ACR20 Response) [units: percentage of participants]		
Week 4	26.5	48.5
Week 8	51.5	59.4
Week 12	60.0	69.7
Week 16	74.2	60.6
Week 20	81.8	54.5
Final visit	70.6	64.7

Statistical Analysis 1 for Percentage of Participants Achieving American College of Rheumatology 20 Percent (%) Improvement (ACR20 Response)

Statistical Analysis Overview	Comparison Groups	Tocilizumab, 1 Hour Infusions, Tocilizumab, 31 Minute Infusions
	Comments	Week 4
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]

Statistical Test of Hypothesis	P-Value	0.121
	Comments	[Not specified]
	Method	Chi-squared
	Comments	[Not specified]

Statistical Analysis 2 for Percentage of Participants Achieving American College of Rheumatology 20 Percent (%) Improvement (ACR20 Response)

Statistical Analysis Overview	Comparison Groups	Tocilizumab, 1 Hour Infusions, Tocilizumab, 31 Minute Infusions
	Comments	Week 8
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]

Statistical Test of Hypothesis	P-Value	0.809
	Comments	[Not specified]
	Method	Chi-squared
	Comments	[Not specified]

Statistical Analysis 3 for Percentage of Participants Achieving American College of Rheumatology 20 Percent (%) Improvement (ACR20 Response)

Statistical Analysis Overview	Comparison Groups	Tocilizumab, 1 Hour Infusions, Tocilizumab, 31 Minute Infusions
	Comments	Week 12
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]

Statistical Test of Hypothesis	P-Value	0.367
	Comments	[Not specified]

	Method	Chi-squared
	Comments	[Not specified]

Statistical Analysis 4 for Percentage of Participants Achieving American College of Rheumatology 20 Percent (%) Improvement (ACR20 Response)

Statistical Analysis Overview	Comparison Groups	Tocilizumab, 1 Hour Infusions, Tocilizumab, 31 Minute Infusions
	Comments	Week 16
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]

Statistical Test of Hypothesis	P-Value	0.339
	Comments	[Not specified]
	Method	Chi-squared
	Comments	[Not specified]

Statistical Analysis 5 for Percentage of Participants Achieving American College of Rheumatology 20 Percent (%) Improvement (ACR20 Response)

Statistical Analysis Overview	Comparison Groups	Tocilizumab, 1 Hour Infusions, Tocilizumab, 31 Minute Infusions
	Comments	Week 20
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]

Statistical Test of Hypothesis	P-Value	0.017
	Comments	[Not specified]
	Method	Chi-squared
	Comments	[Not specified]

Statistical Analysis 6 for Percentage of Participants Achieving American College of Rheumatology 20 Percent (%) Improvement (ACR20 Response)

Statistical Analysis Overview	Comparison Groups	Tocilizumab, 1 Hour Infusions, Tocilizumab, 31 Minute Infusions
	Comments	Final visit
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]

Statistical Test of Hypothesis	P-Value	0.451
	Comments	[Not specified]
	Method	Chi-squared
	Comments	[Not specified]

9. Secondary Outcome Measure:

Measure Title	Percentage of Participants Achieving ACR 50% Improvement (ACR50 Response)
Measure Description	ACR50 response defined as an improvement of ≥50% in SJC (66 joints) and TJC (68 joints) as well as ≥50% improvement in at least 3 of the following 5 remaining ACR assessments: Patient Global Assessment of Pain; Patient Global Assessment of Disease Activity; Physician Global Assessment of Disease Activity; HAQ-DI; and acute phase reactive factors (ESR or CRP).
Time Frame	Weeks 4, 8, 12, 16, 20 and Final Visit
Safety Issue?	No

Analysis Population Description

ITT Population

Reporting Groups

	Description
Tocilizumab, 1 Hour Infusions	Participants received tocilizumab 8 mg/kg via IV infusion (over 1 hour), once every 4 weeks for 6 infusions (up to 24 weeks).
Tocilizumab, 31 Minute Infusions	Participants received tocilizumab 8 mg/kg via IV infusion, once every 4 weeks for 6 infusions (up to 24 weeks). The first infusion was 1 hour; the remaining 5 infusions were administered over a period of 31 minutes as long as no infusion reactions occurred. If an infusion reaction occurred, 1 hour infusions were used for all subsequent remaining infusions.

Measured Values

	Tocilizumab, 1 Hour Infusions	Tocilizumab, 31 Minute Infusions
Number of Participants Analyzed	37	39
Percentage of Participants Achieving ACR 50% Improvement (ACR50 Response) [units: percentage of participants]		
Week 4	11.4	20.6
Week 8	26.5	39.4
Week 12	35.5	47.1

	Tocilizumab, 1 Hour Infusions	Tocilizumab, 31 Minute Infusions
Week 16	53.1	45.5
Week 20	65.6	45.5
Final visit	54.5	45.7

Statistical Analysis 1 for Percentage of Participants Achieving ACR 50% Improvement (ACR50 Response)

Statistical Analysis Overview	Comparison Groups	Tocilizumab, 1 Hour Infusions, Tocilizumab, 31 Minute Infusions
	Comments	Week 4
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]

Statistical Test of Hypothesis	P-Value	0.377
	Comments	[Not specified]
	Method	Chi-squared
	Comments	[Not specified]

Statistical Analysis 2 for Percentage of Participants Achieving ACR 50% Improvement (ACR50 Response)

Statistical Analysis Overview	Comparison Groups	Tocilizumab, 1 Hour Infusions, Tocilizumab, 31 Minute Infusions
	Comments	Week 8
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]

Statistical Test of Hypothesis	P-Value	0.387
	Comments	[Not specified]
	Method	Chi-squared
	Comments	[Not specified]

Statistical Analysis 3 for Percentage of Participants Achieving ACR 50% Improvement (ACR50 Response)

Statistical Analysis Overview	Comparison Groups	Tocilizumab, 1 Hour Infusions, Tocilizumab, 31 Minute Infusions
	Comments	Week 12
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]

Statistical Test of Hypothesis	P-Value	0.304
	Comments	[Not specified]
	Method	Chi-squared
	Comments	[Not specified]

Statistical Analysis 4 for Percentage of Participants Achieving ACR 50% Improvement (ACR50 Response)

Statistical Analysis Overview	Comparison Groups	Tocilizumab, 1 Hour Infusions, Tocilizumab, 31 Minute Infusions
	Comments	Week 16
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]

Statistical Test of Hypothesis	P-Value	0.509
	Comments	[Not specified]
	Method	Chi-squared
	Comments	[Not specified]

Statistical Analysis 5 for Percentage of Participants Achieving ACR 50% Improvement (ACR50 Response)

Statistical Analysis Overview	Comparison Groups	Tocilizumab, 1 Hour Infusions, Tocilizumab, 31 Minute Infusions
	Comments	Week 20
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]

Statistical Test of Hypothesis	P-Value	0.110
	Comments	[Not specified]

	Method	Chi-squared
	Comments	[Not specified]

Statistical Analysis 6 for Percentage of Participants Achieving ACR 50% Improvement (ACR50 Response)

Statistical Analysis Overview	Comparison Groups	Tocilizumab, 1 Hour Infusions, Tocilizumab, 31 Minute Infusions
	Comments	Final visit
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]

Statistical Test of Hypothesis	P-Value	0.504
	Comments	[Not specified]
	Method	Chi-squared
	Comments	[Not specified]

10. Secondary Outcome Measure:

Measure Title	Percentage of Participants Achieving ACR 70% Improvement (ACR70 Response)
Measure Description	ACR70 response defined as an improvement of ≥70% in SJC (66 joints) and TJC (68 joints) as well as ≥70% improvement in at least 3 of the following 5 remaining ACR assessments: Patient Global Assessment of Pain; Patient Global Assessment of Disease Activity; Physician Global Assessment of Disease Activity; HAQ-DI; and acute phase reactive factors (ESR or CRP).
Time Frame	Weeks 4, 8, 12, 16, 20 and Final Visit
Safety Issue?	No

Analysis Population Description

ITT Population

Reporting Groups

	Description
Tocilizumab, 1 Hour Infusions	Participants received tocilizumab 8 mg/kg via IV infusion (over 1 hour), once every 4 weeks for 6 infusions (up to 24 weeks).
Tocilizumab, 31 Minute Infusions	Participants received tocilizumab 8 mg/kg via IV infusion, once every 4 weeks for 6 infusions (up to 24 weeks). The first infusion was 1 hour; the remaining 5 infusions were administered over a period of 31 minutes as long as no infusion reactions occurred. If an infusion reaction occurred, 1 hour infusions were used for all subsequent remaining infusions.

Measured Values

	Tocilizumab, 1 Hour Infusions	Tocilizumab, 31 Minute Infusions
Number of Participants Analyzed	37	39
Percentage of Participants Achieving ACR 70% Improvement (ACR70 Response) [units: percentage of participants]		
Week 4	0.0	2.9
Week 8	12.1	14.7
Week 12	22.6	28.6
Week 16	25.1	28.6
Week 20	33.3	29.4
Final visit	38.2	30.6

Statistical Analysis 1 for Percentage of Participants Achieving ACR 70% Improvement (ACR70 Response)

Statistical Analysis Overview	Comparison Groups	Tocilizumab, 1 Hour Infusions, Tocilizumab, 31 Minute Infusions
	Comments	Week 4
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]

Statistical Test of Hypothesis	P-Value	0.327
	Comments	[Not specified]
	Method	Chi-squared
	Comments	[Not specified]

Statistical Analysis 2 for Percentage of Participants Achieving ACR 70% Improvement (ACR70 Response)

Statistical Analysis Overview	Comparison Groups	Tocilizumab, 1 Hour Infusions, Tocilizumab, 31 Minute Infusions
	Comments	Week 8
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]

Statistical Test of Hypothesis	P-Value	0.786
	Comments	[Not specified]
	Method	Chi-squared
	Comments	[Not specified]

Statistical Analysis 3 for Percentage of Participants Achieving ACR 70% Improvement (ACR70 Response)

Statistical Analysis Overview	Comparison Groups	Tocilizumab, 1 Hour Infusions, Tocilizumab, 31 Minute Infusions
	Comments	Week 12
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]

Statistical Test of Hypothesis	P-Value	0.482
	Comments	[Not specified]
	Method	Chi-squared
	Comments	[Not specified]

Statistical Analysis 4 for Percentage of Participants Achieving ACR 70% Improvement (ACR70 Response)

Statistical Analysis Overview	Comparison Groups	Tocilizumab, 1 Hour Infusions, Tocilizumab, 31 Minute Infusions
	Comments	Week 16
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]

Statistical Test of Hypothesis	P-Value	0.680
	Comments	[Not specified]
	Method	Chi-squared
	Comments	[Not specified]

Statistical Analysis 5 for Percentage of Participants Achieving ACR 70% Improvement (ACR70 Response)

Statistical Analysis Overview	Comparison Groups	Tocilizumab, 1 Hour Infusions, Tocilizumab, 31 Minute Infusions
	Comments	Week 20

	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]

Statistical Test of Hypothesis	P-Value	0.690
	Comments	[Not specified]
	Method	Chi-squared
	Comments	[Not specified]

Statistical Analysis 6 for Percentage of Participants Achieving ACR 70% Improvement (ACR70 Response)

Statistical Analysis Overview	Comparison Groups	Tocilizumab, 1 Hour Infusions, Tocilizumab, 31 Minute Infusions
	Comments	Final Visit
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]

Statistical Test of Hypothesis	P-Value	0.516
	Comments	[Not specified]
	Method	Chi-squared
	Comments	[Not specified]

11. Secondary Outcome Measure:

Measure Title	Percentage of Participants Achieving ACR 90% Improvement (ACR90 Response)
Measure Description	ACR90 response defined as an improvement of ≥90% in SJC (66 joints) and TJC (68 joints) as well as ≥90% improvement in at least 3 of the following 5 remaining ACR assessments: Patient Global Assessment of Pain; Patient Global Assessment of Disease Activity; Physician Global Assessment of Disease Activity; HAQ-DI; and acute phase reactive factors (ESR or CRP).
Time Frame	Weeks 4, 8, 12, 16, 20 and Final Visit
Safety Issue?	No

Analysis Population Description

ITT Population

Reporting Groups

	Description
Tocilizumab, 1 Hour Infusions	Participants received tocilizumab 8 mg/kg via IV infusion (over 1 hour), once every 4 weeks for 6 infusions (up to 24 weeks).
Tocilizumab, 31 Minute Infusions	Participants received tocilizumab 8 mg/kg via IV infusion, once every 4 weeks for 6 infusions (up to 24 weeks). The first infusion was 1 hour; the remaining 5 infusions were administered over a period of 31 minutes as long as no infusion reactions occurred. If an infusion reaction occurred, 1 hour infusions were used for all subsequent remaining infusions.

Measured Values

	Tocilizumab, 1 Hour Infusions	Tocilizumab, 31 Minute Infusions
Number of Participants Analyzed	37	39
Percentage of Participants Achieving ACR 90% Improvement (ACR90 Response) [units: percentage of participants]		
Week 4	0.0	0.0
Week 8	2.9	2.9
Week 12	3.1	5.7
Week 16	3.0	11.1
Week 20	8.8	5.7
Final visit	12.1	11.1

Statistical Analysis 1 for Percentage of Participants Achieving ACR 90% Improvement (ACR90 Response)

Statistical Analysis Overview	Comparison Groups	Tocilizumab, 1 Hour Infusions, Tocilizumab, 31 Minute Infusions
	Comments	Week 8
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]

Statistical Test of Hypothesis	P-Value	0.970
	Comments	[Not specified]
	Method	Chi-squared

	Comments	[Not specified]

Statistical Analysis 2 for Percentage of Participants Achieving ACR 90% Improvement (ACR90 Response)

Statistical Analysis Overview	Comparison Groups	Tocilizumab, 1 Hour Infusions, Tocilizumab, 31 Minute Infusions
	Comments	Week 12
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]

Statistical Test of Hypothesis	P-Value	0.587
	Comments	[Not specified]
	Method	Chi-squared
	Comments	[Not specified]

Statistical Analysis 3 for Percentage of Participants Achieving ACR 90% Improvement (ACR90 Response)

Statistical Analysis Overview	Comparison Groups	Tocilizumab, 1 Hour Infusions, Tocilizumab, 31 Minute Infusions
	Comments	Week 16
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]

Statistical Test of Hypothesis	P-Value	0.184
	Comments	[Not specified]
	Method	Chi-squared
	Comments	[Not specified]

Statistical Analysis 4 for Percentage of Participants Achieving ACR 90% Improvement (ACR90 Response)

Statistical Analysis Overview	Comparison Groups	Tocilizumab, 1 Hour Infusions, Tocilizumab, 31 Minute Infusions
	Comments	Week 20
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]

Statistical Test of Hypothesis	P-Value	0.600
	Comments	[Not specified]
	Method	Chi-squared
	Comments	[Not specified]

Statistical Analysis 5 for Percentage of Participants Achieving ACR 90% Improvement (ACR90 Response)

Statistical Analysis Overview	Comparison Groups	Tocilizumab, 1 Hour Infusions, Tocilizumab, 31 Minute Infusions
	Comments	Final Visit
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]

Statistical Test of Hypothesis	P-Value	0.937
	Comments	[Not specified]
	Method	Chi-squared
	Comments	[Not specified]

12. Secondary Outcome Measure:

Measure Title	C-Reactive Protein (CRP) Levels
Measure Description	CRP is an inflammation marker. High levels of this protein indicate inflammation in diseases such as Rheumatoid Arthritis. CRP is measured in milligrams per liter (mg/L).
Time Frame	Screening, Baseline, Weeks 4, 8, 12, 16, 20, and Final Visit
Safety Issue?	No

Analysis Population Description

ITT Population; n=number of participants assessed for the specified parameter at a given visit.

Reporting Groups

	Description
Tocilizumab, 1 Hour Infusions	Participants received tocilizumab 8 mg/kg via IV infusion (over 1 hour), once every 4 weeks for 6 infusions (up to 24 weeks).

	Description
Tocilizumab, 31 Minute Infusions	Participants received tocilizumab 8 mg/kg via IV infusion, once every 4 weeks for 6 infusions (up to 24 weeks). The first infusion was 1 hour; the remaining 5 infusions were administered over a period of 31 minutes as long as no infusion reactions occurred. If an infusion reaction occurred, 1 hour infusions were used for all subsequent remaining infusions.

Measured Values

	Tocilizumab, 1 Hour Infusions	Tocilizumab, 31 Minute Infusions
Number of Participants Analyzed	37	38
C-Reactive Protein (CRP) Levels [units: mg/L] Mean (Standard Deviation)		
Screening (n=35,38)	9.28 (9.64)	10.76 (11.88)
Baseline (n=30,35)	11.49 (15.39)	13.68 (26.21)
Week 4 (n=37,37)	6.45 (13.52)	4.29 (8.16)
Week 8 (n=34,37)	4.84 (10.98)	1.93 (2.84)
Week 12 (n=33,36)	2.94 (5.80)	1.78 (3.95)
Week 16 (n=35,38)	2.81 (6.86)	2.08 (4.00)
Week 20 (n=34,36)	1.97 (2.52)	2.66 (7.89)
Final visit (n=31,34)	5.42 (13.27)	2.26 (4.57)

13. Secondary Outcome Measure:

Measure Title	Erythrocyte Sedimentation Rate
Measure Description	ESR is an acute phase reactant measured in mm/hr. Reduction in ESR indicates improvement.
Time Frame	Baseline, Weeks 2, 4, 8, 12,16, 20, and 24
Safety Issue?	No

Analysis Population Description

ITT Population; n=number of participants assessed for the specified parameter at a given visit.

Reporting Groups

	Description
Tocilizumab, 1 Hour Infusions	Participants received tocilizumab 8 mg/kg via IV infusion (over 1 hour), once every 4 weeks for 6 infusions (up to 24 weeks).
Tocilizumab, 31 Minute Infusions	Participants received tocilizumab 8 mg/kg via IV infusion, once every 4 weeks for 6 infusions (up to 24 weeks). The first infusion was 1 hour; the remaining 5 infusions were administered over a period of 31 minutes as long as no infusion reactions occurred. If an infusion reaction occurred, 1 hour infusions were used for all subsequent remaining infusions.

Measured Values

	Tocilizumab, 1 Hour Infusions	Tocilizumab, 31 Minute Infusions
Number of Participants Analyzed	37	37
Erythrocyte Sedimentation Rate [units: mm/hr] Mean (Standard Deviation)		
Screening (n=37,37)	37.70 (25.19)	31.19 (18.62)
Baseline (n=30,30)	42.53 (28.60)	30.40 (17.78)
Week 4 (n=36,29)	15.03 (16.16)	11.41 (8.93)
Week 8 (n=33,36)	15.36 (17.06)	8.67 (8.82)
Week 12 (n=32,35)	12.19 (16.63)	6.77 (6.47)
Week 16 (n=33,36)	11.97 (15.39)	6.50 (6.22)
Week 20 (n=33,34)	13.83 (19.91)	6.29 (6.76)
Final visit (n=30,33)	12.00 (13.77)	6.70 (5.59)

14. Secondary Outcome Measure:

Measure Title	HAQ-DI Score by Visit
Measure Description	HAQ-DI is a self-reported, valid assessment of functional disability in rheumatoid arthritis. Assessment based on ability of participants to perform daily activities in 8 categories: dressing, arising, eating, walking, reaching, gripping, hygiene, and carrying out daily activities. HAQ-DI scores range: 0-3: without any difficulty=0, with some difficulty=1, with much difficulty=2, unable to do=3. HAQ-DI total scores expressed as overall mean score with range 0-3: 0-0.25=normal functioning; 0.25-0.5=mild functional limitation; 0.5-1=moderate functional limitation; more than 1=significant functional limitation.
Time Frame	Baseline, Weeks 2, 4, 8, 12, 16, 20 and 24

Safety Issue?	No

Analysis Population Description

ITT Population; n=number of participants assessed for the specified parameter at a given visit.

Reporting Groups

	Description
Tocilizumab, 1 Hour Infusions	Participants received tocilizumab 8 mg/kg via IV infusion (over 1 hour), once every 4 weeks for 6 infusions (up to 24 weeks).
Tocilizumab, 31 Minute Infusions	Participants received tocilizumab 8 mg/kg via IV infusion, once every 4 weeks for 6 infusions (up to 24 weeks). The first infusion was 1 hour; the remaining 5 infusions were administered over a period of 31 minutes as long as no infusion reactions occurred. If an infusion reaction occurred, 1 hour infusions were used for all subsequent remaining infusions.

Measured Values

	Tocilizumab, 1 Hour Infusions	Tocilizumab, 31 Minute Infusions
Number of Participants Analyzed	37	38
HAQ-DI Score by Visit [units: units on a scale] Mean (Standard Deviation)		
Baseline (n=37,37)	1.6 (0.7)	1.4 (0.7)
Week 4 (n=37,37)	1.4 (0.7)	1.0 (0.6)
Week 8 (n=35,37)	1.3 (0.8)	0.9 (0.7)
Week 12 (n=31,36)	1.1 (0.7)	0.8 (0.6)
Week 16 (n=33,38)	1.0 (0.8)	0.8 (0.6)
Week 20 (n=35,37)	1.0 (0.7)	0.8 (0.7)
Final visit (n=35,35)	0.9 (0.8)	0.8 (0.7)

15. Secondary Outcome Measure:

Measure Title	Percentage of Participants With Improvement of at Least 0.22 in HAQ-DI

Measure Description	HAQ-DI is a self-reported, valid assessment of functional disability in rheumatoid arthritis. Assessment based on ability of participants to perform daily activities in 8 categories: dressing, arising, eating, walking, reaching, gripping, hygiene, and carrying out daily activities. HAQ-DI scores range: 0-3: without any difficulty=0, with some difficulty=1, with much difficulty=2, unable to do=3. HAQ-DI total scores expressed as overall mean score with range 0-3: 0-0.25=normal functioning; 0.25-0.5=mild functional limitation; 0.5-1=moderate functional limitation; more than 1=significant functional limitation. An improvement of 0.22 units in HAQ-DI was considered to be a clinically significant improvement.
Time Frame	Weeks 4, 8, 12, 16, 20 and Final Visit
Safety Issue?	No

Analysis Population Description

ITT Population

Reporting Groups

	Description
Tocilizumab, 1 Hour Infusions	Participants received tocilizumab 8 mg/kg via IV infusion (over 1 hour), once every 4 weeks for 6 infusions (up to 24 weeks).
Tocilizumab, 31 Minute Infusions	Participants received tocilizumab 8 mg/kg via IV infusion, once every 4 weeks for 6 infusions (up to 24 weeks). The first infusion was 1 hour; the remaining 5 infusions were administered over a period of 31 minutes as long as no infusion reactions occurred. If an infusion reaction occurred, 1 hour infusions were used for all subsequent remaining infusions.

Measured Values

	Tocilizumab, 1 Hour Infusions	Tocilizumab, 31 Minute Infusions
Number of Participants Analyzed	37	39
Percentage of Participants With Improvement of at Least 0.22 in HAQ-DI [units: percentage of participants]		
Week 4	48.6	48.6
Week 8	62.9	54.3
Week 12	64.5	58.8
Week 16	72.7	52.8
Week 20	68.6	54.3
Final visit	68.6	61.8

Reported Adverse Events

Time Frame	Adverse events were recorded from the date of Screening until the End of Study (24 Weeks)
Additional Description	[Not specified]

Reporting Groups

	Description
Tocilizumab, 1 Hour Infusions	Participants received tocilizumab 8 mg/kg via IV infusion (over 1 hour), once every 4 weeks for 6 infusions (up to 24 weeks).
Tocilizumab, 31 Minute Infusions	Participants received tocilizumab 8 mg/kg via IV infusion, once every 4 weeks for 6 infusions (up to 24 weeks). The first infusion was 1 hour; the remaining 5 infusions were administered over a period of 31 minutes as long as no infusion reactions occurred. If an infusion reaction occurred, 1 hour infusions were used for all subsequent remaining infusions.

Serious Adverse Events

	Tocilizumab, 1 Hour Infusions	Tocilizumab, 31 Minute Infusions
	Affected/At Risk (%)	Affected/At Risk (%)
Total	2/37 (5.41%)	2/39 (5.13%)
Gastrointestinal disorders		
Abdominal pain [A] *	1/37 (2.7%)	0/39 (0%)
Crohn's Disease [A] *	1/37 (2.7%)	0/39 (0%)
Infections and infestations		
Hepatitis [A] *	0/37 (0%)	1/39 (2.56%)
Infection [A] *	0/37 (0%)	1/39 (2.56%)

* Indicates events were collected by non-systematic methods.

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Other Adverse Events

Frequency Threshold Above Which Other Adverse Events are Reported: 0%

	Tocilizumab, 1 Hour Infusions	Tocilizumab, 31 Minute Infusions
	Affected/At Risk (%)	Affected/At Risk (%)
Total	30/37 (81.08%)	26/39 (66.67%)
Blood and lymphatic system disorders		
Anaemia [A] *	1/37 (2.7%)	0/39 (0%)
Leukopenia [A] *	2/37 (5.41%)	0/39 (0%)
Neutropenia [A] *	2/37 (5.41%)	0/39 (0%)
Thrombocytopenia [A] *	0/37 (0%)	1/39 (2.56%)
Ear and labyrinth disorders		
Hypoacusis [A] *	0/37 (0%)	1/39 (2.56%)
Tinnitus [A] *	0/37 (0%)	1/39 (2.56%)
Vertigo [A] *	0/37 (0%)	2/39 (5.13%)
Eye disorders		
Conjunctival hyperaemia [A] *	1/37 (2.7%)	0/39 (0%)
Eye pruritus [A] *	0/37 (0%)	1/39 (2.56%)
Gastrointestinal disorders		
Abdominal discomfort [A] *	1/37 (2.7%)	1/39 (2.56%)
Anal fistula [A] *	1/37 (2.7%)	0/39 (0%)
Aphthous stomatitis [A] *	0/37 (0%)	2/39 (5.13%)
Diarrhoea [A] *	1/37 (2.7%)	1/39 (2.56%)
Haemorrhoids [A] *	1/37 (2.7%)	0/39 (0%)
Nausea [A] *	1/37 (2.7%)	1/39 (2.56%)
Odynophagia [A] *	1/37 (2.7%)	0/39 (0%)
Tongue ulceration [A] *	1/37 (2.7%)	0/39 (0%)

	Tocilizumab, 1 Hour Infusions	Tocilizumab, 31 Minute Infusions
	Affected/At Risk (%)	Affected/At Risk (%)
General disorders		
Asthenia [A] *	2/37 (5.41%)	1/39 (2.56%)
Discomfort [A] *	0/37 (0%)	1/39 (2.56%)
Face oedema [A] *	1/37 (2.7%)	0/39 (0%)
Temperature intolerance [A] *	1/37 (2.7%)	0/39 (0%)
Hepatobiliary disorders		
Hyperbilirubinaemia [A] *	1/37 (2.7%)	0/39 (0%)
Immune system disorders		
Hypersensitivity [A] *	0/37 (0%)	1/39 (2.56%)
Infections and infestations		
Bronchitis [A] *	1/37 (2.7%)	1/39 (2.56%)
Cellulitis [A] *	1/37 (2.7%)	0/39 (0%)
Ear infection [A] *	1/37 (2.7%)	0/39 (0%)
Gastroenteritis [A] *	1/37 (2.7%)	0/39 (0%)
Herpes simplex [A] *	0/37 (0%)	1/39 (2.56%)
Nasopharyngitis [A] *	2/37 (5.41%)	5/39 (12.82%)
Oral herpes [A] *	1/37 (2.7%)	0/39 (0%)
Pharyngitis [A] *	0/37 (0%)	2/39 (5.13%)
Respiratory tract infection [A] *	1/37 (2.7%)	0/39 (0%)
Upper respiratory tract infection [A] *	1/37 (2.7%)	1/39 (2.56%)
Urinary tract infection [A] *	2/37 (5.41%)	2/39 (5.13%)
Viral infection [A] *	0/37 (0%)	1/39 (2.56%)
Injury, poisoning and procedural complications		

	Tocilizumab, 1 Hour Infusions	Tocilizumab, 31 Minute Infusions
	Affected/At Risk (%)	Affected/At Risk (%)
Fall [A] *	0/37 (0%)	1/39 (2.56%)
Investigations		
Alanine aminotransferase increased [A] *	0/37 (0%)	2/39 (5.13%)
Aspartate aminotransferase increased [A] *	0/37 (0%)	1/39 (2.56%)
Aspiration joint [A] *	0/37 (0%)	1/39 (2.56%)
Blood cholesterol increased [A] *	2/37 (5.41%)	0/39 (0%)
Blood creatinine increased [A] *	1/37 (2.7%)	0/39 (0%)
Transaminase increased [A] *	2/37 (5.41%)	0/39 (0%)
Metabolism and nutrition disorders		
Dyslipidaemia [A] *	0/37 (0%)	2/39 (5.13%)
Hypercholesterolaemia [A] *	1/37 (2.7%)	1/39 (2.56%)
Hyperlipidaemia [A] *	1/37 (2.7%)	0/39 (0%)
Hypertriglyceridaemia [A] *	1/37 (2.7%)	0/39 (0%)
Hypoglycaemia [A] *	1/37 (2.7%)	0/39 (0%)
Musculoskeletal and connective tissue disorders		
Arthralgia [A] *	1/37 (2.7%)	0/39 (0%)
Back pain [A] *	1/37 (2.7%)	2/39 (5.13%)
Fibromyalgia [A] *	1/37 (2.7%)	0/39 (0%)
Flank pain [A] *	1/37 (2.7%)	0/39 (0%)
Haemarthrosis [A] *	1/37 (2.7%)	0/39 (0%)
Muscle contracture [A] *	1/37 (2.7%)	0/39 (0%)
Muscle spasms [A] *	0/37 (0%)	1/39 (2.56%)

	Tocilizumab, 1 Hour Infusions	Tocilizumab, 31 Minute Infusions
	Affected/At Risk (%)	Affected/At Risk (%)
Muscular weakness [A] *	1/37 (2.7%)	0/39 (0%)
Musculoskeletal stiffness [A] *	0/37 (0%)	1/39 (2.56%)
Rheumatoid arthritis [A] *	1/37 (2.7%)	0/39 (0%)
Tendonitis [A] *	1/37 (2.7%)	0/39 (0%)
Nervous system disorders		
Amnesia [A] *	1/37 (2.7%)	0/39 (0%)
Aphonia [A] *	0/37 (0%)	1/39 (2.56%)
Dizziness [A] *	4/37 (10.81%)	0/39 (0%)
Headache [A] *	1/37 (2.7%)	2/39 (5.13%)
Sciatica [A] *	0/37 (0%)	1/39 (2.56%)
Tremor [A] *	2/37 (5.41%)	0/39 (0%)
Psychiatric disorders		
Anxiety [A] *	1/37 (2.7%)	1/39 (2.56%)
Depressed mood [A] *	1/37 (2.7%)	0/39 (0%)
Depression [A] *	1/37 (2.7%)	0/39 (0%)
Renal and urinary disorders		
Renal colic [A] *	1/37 (2.7%)	0/39 (0%)
Reproductive system and breast disorders		
Amenorrhoea [A] *	0/37 (0%)	1/39 (2.56%)
Menstrual disorder [A] *	0/37 (0%)	1/39 (2.56%)
Metrorrhagia [A] *	1/37 (2.7%)	0/39 (0%)
Respiratory, thoracic and mediastinal disorders		
Cough [A] *	0/37 (0%)	1/39 (2.56%)

	Tocilizumab, 1 Hour Infusions	Tocilizumab, 31 Minute Infusions
	Affected/At Risk (%)	Affected/At Risk (%)
Dyspnoea [A] *	1/37 (2.7%)	0/39 (0%)
Oropharyngeal pain [A] *	1/37 (2.7%)	0/39 (0%)
Rhinitis allergic [A] *	0/37 (0%)	1/39 (2.56%)
Sneezing [A] *	0/37 (0%)	1/39 (2.56%)
Skin and subcutaneous tissue disorders		
Dermatitis contact [A] *	0/37 (0%)	1/39 (2.56%)
Dyshidrosis [A] *	0/37 (0%)	1/39 (2.56%)
Eczema [A] *	1/37 (2.7%)	1/39 (2.56%)
Pruritus [A] *	0/37 (0%)	1/39 (2.56%)
Skin lesion [A] *	0/37 (0%)	1/39 (2.56%)
Urticaria [A] *	1/37 (2.7%)	0/39 (0%)
Surgical and medical procedures		
Cholecystectomy [A] *	1/37 (2.7%)	0/39 (0%)
Dental implantation [A] *	1/37 (2.7%)	0/39 (0%)
Vascular disorders		
Hypertension [A] *	2/37 (5.41%)	1/39 (2.56%)

* Indicates events were collected by non-systematic methods.
A Term from vocabulary, MedDRA

Limitations and Caveats

[Not specified]

More Information

Certain Agreements:

Principal Investigators are NOT employed by the organization sponsoring the study.

There IS an agreement between the Principal Investigator and the Sponsor (or its agents) that restricts the PI's rights to discuss or publish trial results after the trial is completed.

The study being conducted under this agreement is part of the overall study. Investigator is free to publish in reputable journals or to present at professional conferences the results of the study, but after the first publication or presentation that involves the overall study. Sponsor may request that confidential information be deleted and/or the publication be postponed in order to protect the Sponsor's intellectual property rights.

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