Clinical trial results:
A Randomized, Active-Controlled, Double-Blind, Phase 3 Study to Compare Efficacy and Safety of Two Intravenous Infusion Formulations of Tocilizumab (CT-P47 and RoActemra) when Co-administered with Methotrexate in Patients with Moderate to Severe Active Rheumatoid Arthritis

Summary

EudraCT number	2022-001066-36
Trial protocol	PL
Global end of trial date	23 November 2023

Results information

Result version number	v1 (current)
This version publication date	08 December 2024
First version publication date	08 December 2024

Trial information

Trial identification

Sponsor protocol code	CT-P47 3.1

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT05489224
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	CELLTRION, Inc.
Sponsor organisation address	Cenral-ro 263, Incheon, Korea, Republic of,
Public contact	Clinical Planning 3 Department, CELLTRION, Inc., +82 328504167, JeeHye.Suh@celltrion.com
Scientific contact	Clinical Planning 3 Department, CELLTRION, Inc., +82 328504167, JeeHye.Suh@celltrion.com

Notes:

Paediatric regulatory details

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

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	16 May 2024
Is this the analysis of the primary completion data?	Yes
Primary completion date	29 June 2023
Global end of trial reached?	Yes
Global end of trial date	23 November 2023
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To demonstrate that CT-P47 is equivalent to RoActemra, in terms of efficacy as determined by clinical response according to the change from baseline in disease activity measured by Disease Activity Score using 28 joint counts (DAS28) (Erythrocyte-Sedimentation Rate [ESR]) at Week 12.

Protection of trial subjects:

The study was performed following the ethical principles that have their origin in the Declaration of Helsinki (WMA 2013), the International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use (ICH) harmonised tripartite guideline E6 (R2): Good Clinical Practice (GCP), and all applicable regulations. All investigators agreed to conduct all aspects of this study by national, state, local laws and regulations.
For hypersensitivity monitoring, vital signs (including systolic and diastolic BP, heart rate, respiratory rate, and body temperature) was monitored before beginning of the study drug administration (within 15 minutes) and at 1 hour (±15 minutes) after the end of the study drug administration.
In addition, any type of ECG was performed for hypersensitivity monitoring 1 hour (±15 minutes) after the end of the study drug administration. Emergency equipment, such as adrenaline, antihistamines, corticosteroids, and respiratory support including inhalational therapy, oxygen, and artificial ventilator was available.
For patients who experience anaphylaxis or other serious treatment-related hypersensitivity reaction, study drug was to be stopped immediately and the patient discontinued from the study drug.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	01 September 2022
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	Poland: 471
Worldwide total number of subjects	471
EEA total number of subjects	471

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)	365
From 65 to 84 years	106
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

The recruitment was conducted in 22 study centers in Poland.

Pre-assignment

Screening details:

The screening period was up to 42 days. Male or female patient aged 18-75 years with moderate to severe active rheumatoid arthirits for at least 24 weeks was eligible to be enrolled.

Period 1

Period 1 title	Treatment Period I (Week 0 to Week 24)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator, Monitor, Data analyst, Carer, Assessor

Blinding implementation details:

The investigators, patients, and other predefined personnel from the sponsor and CRO teams remained blinded until the EOS.

Arms

Are arms mutually exclusive?	Yes
Arm title	CT-P47

Arm description:

Patients who were initially randomly assigned to CT-P47 in Treatment Period I

Arm type	Experimental
Investigational medicinal product name	CT-P47
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Multiple dose (8 mg/kg, not exceeding 800 mg/dose) of CT-P47 by IV Q4W, co administered with MTX between 10 to 25 mg/week, oral or parenteral; IM or SC dose (dose and route must be maintained from beginning to end of the study) and folic acid (≥5 mg/week, oral dose)

Arm title	RoActemra

Arm description:

Patients who were initially randomly assigned to RoActemra in Treatment Period I

Arm type	Active comparator
Investigational medicinal product name	EU-approved RoActemra
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Multiple dose (8 mg/kg, not exceeding 800 mg/dose) of EU-approved RoActemra by IV Q4W, co administered with MTX between 10 to 25 mg/week, oral or parenteral; IM or SC dose (dose and route must be maintained from beginning to end of the study) and folic acid (≥5 mg/week, oral dose)

Number of subjects in period 1	CT-P47	RoActemra
Started	234	237
Completed	225	219
Not completed	9	18
Consent withdrawn by subject	6	5
Physician decision	-	1
Adverse event, non-fatal	3	11
Lost to follow-up	-	1

Period 2

Period 2 title	Treatment Period II (Week 24 to Week 52)
Is this the baseline period?	No
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator, Monitor, Data analyst, Carer, Assessor

Blinding implementation details:

The investigators, patients, and other predefined personnel from the sponsor and CRO teams remained blinded until the EOS.

Arms

Are arms mutually exclusive?	Yes
Arm title	CT-P47 Maintenance

Arm description:

All patients who received CT-P47 in Treatment Period I and continued to receive CT-P47 in Treatment Period II

Arm type	Experimental
Investigational medicinal product name	CT-P47
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Multiple dose (8 mg/kg, not exceeding 800 mg/dose) of CT-P47 by IV Q4W, co administered with MTX between 10 to 25 mg/week, oral or parenteral; IM or SC dose (dose and route must be maintained from beginning to end of the study) and folic acid (≥5 mg/week, oral dose)

Arm title	RoActemra Maintenance

Arm description:

Patients who received RoActemra in Treatment Period I and re-randomized to continue RoActemra in Treatment Period II

Arm type	Active comparator
Investigational medicinal product name	EU-approved RoActemra
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Multiple dose (8 mg/kg, not exceeding 800 mg/dose) of EU-approved RoActemra by IV Q4W, co administered with MTX between 10 to 25 mg/week, oral or parenteral; IM or SC dose (dose and route must be maintained from beginning to end of the study) and folic acid (≥5 mg/week, oral dose)

Arm title	Switched to CT-P47

Arm description:

Patients who received RoActemra in Treatment Period I and re-randomized to receive CT-P47 in Treatment Period II

Arm type	Experimental
Investigational medicinal product name	CT-P47
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Multiple dose (8 mg/kg, not exceeding 800 mg/dose) of CT-P47 by IV Q4W, co administered with MTX between 10 to 25 mg/week, oral or parenteral; IM or SC dose (dose and route must be maintained from beginning to end of the study) and folic acid (≥5 mg/week, oral dose)

Number of subjects in period 2	CT-P47 Maintenance	RoActemra Maintenance	Switched to CT-P47
Started	225	109	110
Completed	211	100	102
Not completed	14	9	8
Consent withdrawn by subject	3	3	4
Physician decision	1	-	-
Adverse event, non-fatal	10	5	4
Lost to follow-up	-	1	-

Baseline characteristics

Reporting groups	
Reporting group title	CT-P47
Reporting group description:	
Patients who were initially randomly assigned to CT-P47 in Treatment Period I	
Reporting group title	RoActemra
Reporting group description:	
Patients who were initially randomly assigned to RoActemra in Treatment Period I	

Reporting group values	CT-P47	RoActemra	Total
Number of subjects	234	237	471
Age categorical Units: Subjects			
In utero	0	0	0
Preterm newborn infants (gestational age < 37 wks)	0	0	0
Newborns (0-27 days)	0	0	0
Infants and toddlers (28 days-23 months)	0	0	0
Children (2-11 years)	0	0	0
Adolescents (12-17 years)	0	0	0
Adults (18-64 years)	180	185	365
From 65-84 years	54	52	106
85 years and over	0	0	0
Age continuous Units: years			
arithmetic mean	55.1	54.4	
standard deviation	± 10.98	± 11.61	-
Gender categorical Units: Subjects			
Female	181	180	361
Male	53	57	110
Body Weight on Day 1 Units: Subjects			
<100 kg	208	210	418
≥100 kg	26	27	53
DAS28 (ESR) score at Screening Units: Subjects			
DAS28 (ESR) >5.1	229	230	459
DAS28 (ESR) ≤5.1	5	7	12
Prior biologic use approved for RA treatment Units: Subjects			
Yes	58	62	120
No	176	175	351
Ethnicity Units: Subjects			
Hispanic or Latino	6	4	10
Non-Hispanic or Non-Latino	228	233	461

End points

End points reporting groups

Reporting group title	CT-P47
Reporting group description:	
Patients who were initially randomly assigned to CT-P47 in Treatment Period I	
Reporting group title	RoActemra
Reporting group description:	
Patients who were initially randomly assigned to RoActemra in Treatment Period I	
Reporting group title	CT-P47 Maintenance
Reporting group description:	
All patients who received CT-P47 in Treatment Period I and continued to receive CT-P47 in Treatment Period II	
Reporting group title	RoActemra Maintenance
Reporting group description:	
Patients who received RoActemra in Treatment Period I and re-randomized to continue RoActemra in Treatment Period II	
Reporting group title	Switched to CT-P47
Reporting group description:	
Patients who received RoActemra in Treatment Period I and re-randomized to receive CT-P47 in Treatment Period II	

Primary: Mean Change From Baseline in Disease Activity Score 28 (DAS28) Using Erythrocyte Sedimentation Rate (ESR) at Week 12 - ITT set

End point title	Mean Change From Baseline in Disease Activity Score 28 (DAS28) Using Erythrocyte Sedimentation Rate (ESR) at Week 12 - ITT set

End point description:

The DAS28(ESR) score was derived using the following formulae:
DAS28 (ESR)=(0.56 ×√TJC28)+(0.28 × √SJC28)+(0.70 × ln[ESR])+(0.014 ×GH)
Where:

- TJC28 = number of tender joints (0-28): tender joint count (TJC)
- SJC28 = number of swollen joints (0-28): swollen joint count (SJC)
- ESR = ESR measurement (mm/hour)
- GH = patient's global disease activity measured on VAS (mm: 0-100)

DAS28 (ESR) values could be ranged from 0 to 10 while higher values mean a higher disease activity.

End point type	Primary

End point timeframe:

Week 12

End point values	CT-P47	RoActemra		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	221	225		
Units: score				
least squares mean (standard error)	-3.01 (± 0.121)	-3.00 (± 0.120)		

Statistical analyses

Statistical analysis title	CT-P47 vs. EU-approved RoActemra - 95% CI

Statistical analysis description:

An ANCOVA comparing the change from baseline of DAS28 (ESR) at Week 12 between two treatment groups were conducted considering the treatment as fixed effect, and body weight (<100 kg or ≥100 kg) measured on Day 1, baseline DAS28 (ESR) score and prior biologic use approved for RA treatment (yes or no) as covariates.

Comparison groups	CT-P47 v RoActemra
Number of subjects included in analysis	446
Analysis specification	Pre-specified
Analysis type	equivalence[1]
Parameter estimate	Difference of Least square means
Point estimate	-0.01
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.26
upper limit	0.24

Notes:

[1] - The pre-specified equivalence margin is ±0.6.

Secondary: Mean Change From Baseline in DAS28 (ESR) at Week 24 - ITT set

End point title	Mean Change From Baseline in DAS28 (ESR) at Week 24 - ITT set

End point description:

The DAS28(ESR) score was derived using the following formulae:
DAS28 (ESR)=(0.56 ×√TJC28)+(0.28 × √SJC28)+(0.70 × ln[ESR])+(0.014 ×GH)
Where:

- TJC28 = number of tender joints (0-28): tender joint count (TJC)
- SJC28 = number of swollen joints (0-28): swollen joint count (SJC)
- ESR = ESR measurement (mm/hour)
- GH = patient's global disease activity measured on VAS (mm: 0-100)

DAS28 (ESR) values could be ranged from 0 to 10 while higher values mean a higher disease activity.

End point type	Secondary

End point timeframe:

Week 24

End point values	CT-P47	RoActemra		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	222	223		
Units: score				
arithmetic mean (standard deviation)	-3.858 (± 1.2402)	-3.720 (± 1.3945)		

Statistical analyses

No statistical analyses for this end point

Secondary: Mean Change From Baseline in DAS28 (ESR) at Week 32 - ITT - Treatment Period II subset

End point title	Mean Change From Baseline in DAS28 (ESR) at Week 32 - ITT - Treatment Period II subset

End point description:

The DAS28(ESR) score was derived using the following formulae:
DAS28 (ESR)=(0.56 ×√TJC28)+(0.28 × √SJC28)+(0.70 × ln[ESR])+(0.014 ×GH)
Where:
- TJC28 = number of tender joints (0-28): tender joint count (TJC)
- SJC28 = number of swollen joints (0-28): swollen joint count (SJC)
- ESR = ESR measurement (mm/hour)
- GH = patient's global disease activity measured on VAS (mm: 0-100)

DAS28 (ESR) values could be ranged from 0 to 10 while higher values mean a higher disease activity.

End point type	Secondary

End point timeframe:

Week 32

End point values	CT-P47 Maintenance	RoActemra Maintenance	Switched to CT-P47	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	219	104	105	
Units: score				
arithmetic mean (standard deviation)	-3.921 (± 1.2548)	-3.994 (± 1.1753)	-4.218 (± 1.1380)	

Statistical analyses

No statistical analyses for this end point

Secondary: Mean Change From Baseline in DAS28 (ESR) at Week 52 - ITT - Treatment Period II subset

End point title	Mean Change From Baseline in DAS28 (ESR) at Week 52 - ITT - Treatment Period II subset

End point description:

The DAS28(ESR) score was derived using the following formulae:
DAS28 (ESR)=(0.56 ×√TJC28)+(0.28 × √SJC28)+(0.70 × ln[ESR])+(0.014 ×GH)
Where:
- TJC28 = number of tender joints (0-28): tender joint count (TJC)
- SJC28 = number of swollen joints (0-28): swollen joint count (SJC)
- ESR = ESR measurement (mm/hour)
- GH = patient's global disease activity measured on VAS (mm: 0-100)

DAS28 (ESR) values could be ranged from 0 to 10 while higher values mean a higher disease activity.

End point type	Secondary

End point timeframe:

Week 52

End point values	CT-P47 Maintenance	RoActemra Maintenance	Switched to CT-P47	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	218	103	106	
Units: score				
arithmetic mean (standard deviation)	-4.279 (± 1.1934)	-4.231 (± 1.3046)	-4.376 (± 1.4212)	

Statistical analyses

No statistical analyses for this end point

Secondary: ACR20, ACR50, and ACR70 Response Rate at Week 12 - ITT set

End point title	ACR20, ACR50, and ACR70 Response Rate at Week 12 - ITT set

End point description:

ACR20 is defined as both improvement of 20% in the number of tender and number of swollen joints, and a 20% improvement in the three of the following five criteria: 1) patient global assessment of disease activity, 2) physician global assessment of disease activity, 3) functional ability measure using Health Assessment Questionnaire (HAQ), 4) visual analog pain scale, and 5) erythrocyte sedimentation rate (ESR) or C-reactive protein (CRP). ACR50 and ACR70 are the same instruments with improvement levels defined as 50% and 70% respectively versus 20% for ACR20.

End point type	Secondary

End point timeframe:

Week 12

End point values	CT-P47	RoActemra		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	234	237		
Units: participants				
ACR20	185	175		
ACR50	102	106		
ACR70	46	54		

Statistical analyses

No statistical analyses for this end point

Secondary: ACR20, ACR50, and ACR70 Response Rate at Week 24 - ITT set

End point title	ACR20, ACR50, and ACR70 Response Rate at Week 24 - ITT set

End point description:

ACR20 is defined as both improvement of 20% in the number of tender and number of swollen joints, and a 20% improvement in the three of the following five criteria: 1) patient global assessment of disease activity, 2) physician global assessment of disease activity, 3) functional ability measure using Health Assessment Questionnaire (HAQ), 4) visual analog pain scale, and 5) erythrocyte sedimentation rate (ESR) or C-reactive protein (CRP). ACR50 and ACR70 are the same instruments with improvement

levels defined as 50% and 70% respectively versus 20% for ACR20.

End point type	Secondary

End point timeframe:

Week 24

End point values	CT-P47	RoActemra		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	234	237		
Units: participants				
ACR20	199	189		
ACR50	142	146		
ACR70	100	99		

Statistical analyses

No statistical analyses for this end point

Secondary: ACR20, ACR50, and ACR70 Response Rate at Week 32 - ITT - Treatment Period II subset

End point title	ACR20, ACR50, and ACR70 Response Rate at Week 32 - ITT - Treatment Period II subset

End point description:

ACR20 is defined as both improvement of 20% in the number of tender and number of swollen joints, and a 20% improvement in the three of the following five criteria: 1) patient global assessment of disease activity, 2) physician global assessment of disease activity, 3) functional ability measure using Health Assessment Questionnaire (HAQ), 4) visual analog pain scale, and 5) erythrocyte sedimentation rate (ESR) or C-reactive protein (CRP). ACR50 and ACR70 are the same instruments with improvement levels defined as 50% and 70% respectively versus 20% for ACR20.

End point type	Secondary

End point timeframe:

Week 32

End point values	CT-P47 Maintenance	RoActemra Maintenance	Switched to CT-P47	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	225	109	110	
Units: participants				
ACR20	199	96	98	
ACR50	148	79	77	
ACR70	91	47	61	

Statistical analyses

No statistical analyses for this end point

Secondary: ACR20, ACR50, and ACR70 Response Rate at Week 52 - ITT - Treatment Period II subset

End point title	ACR20, ACR50, and ACR70 Response Rate at Week 52 - ITT - Treatment Period II subset

End point description:

ACR20 is defined as both improvement of 20% in the number of tender and number of swollen joints, and a 20% improvement in the three of the following five criteria: 1) patient global assessment of disease activity, 2) physician global assessment of disease activity, 3) functional ability measure using Health Assessment Questionnaire (HAQ), 4) visual analog pain scale, and 5) erythrocyte sedimentation rate (ESR) or C-reactive protein (CRP). ACR50 and ACR70 are the same instruments with improvement levels defined as 50% and 70% respectively versus 20% for ACR20.

End point type	Secondary

End point timeframe:

Week 52

End point values	CT-P47 Maintenance	RoActemra Maintenance	Switched to CT-P47	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	225	109	110	
Units: participants				
ACR20	211	97	100	
ACR50	174	88	87	
ACR70	123	64	63	

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Adverse events were assessed from the date the patient signed the Informed Consent Form (ICF) until 4 weeks after the last study drug administration (up to 52 weeks [End-of-study visit]).

Adverse event reporting additional description:

Treatment Period I: From Week 0 to prior to the 1st dosing in Treatment Period II.
Treatment Period II: On or after the 1st dosing in Treatment Period II.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	26.0

Reporting groups

Reporting group title	Treatment Period I: CT-P47

Reporting group description:

Patients who were initially randomly assigned to CT-P47 in Treatment Period I

Reporting group title	Treatment Period I: RoActemra

Reporting group description:

Patients who were initially randomly assigned to RoActemra in Treatment Period I

Reporting group title	Treatment Period II: CT-P47 Maintenance

Reporting group description:

Patients who received CT-P47 during Treatment Period I and continued to receive CT-P47 in Treatment Period II

Reporting group title	Treatment Period II: RoActemra Maintenance

Reporting group description:

Patients who were initially randomly assigned to RoActemra at Day 1 (Week 0) and re-randomized (1:1 ratio) at Week 24 to continue to receive RoActemra in Treatment Period II

Reporting group title	Treatment Period II: Switched to CT-P47

Reporting group description:

Patients who were initially randomly assigned to RoActemra at Day 1 (Week 0) and re-randomized (1:1 ratio) at Week 24 to undergo transition to CT-P47 in Treatment Period II

Serious adverse events	Treatment Period I: CT-P47	Treatment Period I: RoActemra	Treatment Period II: CT-P47 Maintenance
Total subjects affected by serious adverse events			
subjects affected / exposed	10 / 234 (4.27%)	9 / 237 (3.80%)	11 / 225 (4.89%)
number of deaths (all causes)	0	0	1
number of deaths resulting from adverse events			
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Pancreatic neoplasm			
subjects affected / exposed	0 / 234 (0.00%)	1 / 237 (0.42%)	0 / 225 (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
Meningioma benign			

subjects affected / exposed	0 / 234 (0.00%)	0 / 237 (0.00%)	0 / 225 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vascular disorders			
Extremity necrosis			
subjects affected / exposed	0 / 234 (0.00%)	1 / 237 (0.42%)	0 / 225 (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
Venous thrombosis limb			
subjects affected / exposed	1 / 234 (0.43%)	0 / 237 (0.00%)	0 / 225 (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
General disorders and administration site conditions			
Peripheral swelling			
subjects affected / exposed	1 / 234 (0.43%)	0 / 237 (0.00%)	0 / 225 (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
Chest pain			
subjects affected / exposed	0 / 234 (0.00%)	0 / 237 (0.00%)	0 / 225 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Reproductive system and breast disorders			
Cervical cyst			
subjects affected / exposed	1 / 234 (0.43%)	0 / 237 (0.00%)	0 / 225 (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
Endometrial hyperplasia			
subjects affected / exposed	0 / 234 (0.00%)	1 / 237 (0.42%)	0 / 225 (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
Rectocele			

subjects affected / exposed	0 / 234 (0.00%)	0 / 237 (0.00%)	1 / 225 (0.44%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Uterine hemorrhage			
subjects affected / exposed	0 / 234 (0.00%)	0 / 237 (0.00%)	0 / 225 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			
Pleural effusion			
subjects affected / exposed	1 / 234 (0.43%)	0 / 237 (0.00%)	0 / 225 (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
Interstitial lung disease			
subjects affected / exposed	0 / 234 (0.00%)	0 / 237 (0.00%)	0 / 225 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pulmonary embolism			
subjects affected / exposed	0 / 234 (0.00%)	0 / 237 (0.00%)	1 / 225 (0.44%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory failure			
subjects affected / exposed	0 / 234 (0.00%)	0 / 237 (0.00%)	1 / 225 (0.44%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Psychiatric disorders			
Schizophrenia			
subjects affected / exposed	1 / 234 (0.43%)	0 / 237 (0.00%)	0 / 225 (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			
Interferon gamma release assay positive			

subjects affected / exposed	0 / 234 (0.00%)	0 / 237 (0.00%)	1 / 225 (0.44%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Injury, poisoning and procedural complications			
Femur fracture			
subjects affected / exposed	0 / 234 (0.00%)	1 / 237 (0.42%)	1 / 225 (0.44%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ankle fracture			
subjects affected / exposed	0 / 234 (0.00%)	0 / 237 (0.00%)	1 / 225 (0.44%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Femoral neck fracture			
subjects affected / exposed	0 / 234 (0.00%)	0 / 237 (0.00%)	0 / 225 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Humerus fracture			
subjects affected / exposed	0 / 234 (0.00%)	0 / 237 (0.00%)	0 / 225 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Radius fracture			
subjects affected / exposed	0 / 234 (0.00%)	0 / 237 (0.00%)	0 / 225 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Tendon rupture			
subjects affected / exposed	0 / 234 (0.00%)	0 / 237 (0.00%)	0 / 225 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Upper limb fracture			
subjects affected / exposed	0 / 234 (0.00%)	0 / 237 (0.00%)	1 / 225 (0.44%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac disorders			

Acute myocardial infarction			
subjects affected / exposed	0 / 234 (0.00%)	1 / 237 (0.42%)	0 / 225 (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
Coronary artery disease			
subjects affected / exposed	0 / 234 (0.00%)	1 / 237 (0.42%)	0 / 225 (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
Coronary artery stenosis			
subjects affected / exposed	0 / 234 (0.00%)	1 / 237 (0.42%)	0 / 225 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Myocardial ischaemia			
subjects affected / exposed	0 / 234 (0.00%)	2 / 237 (0.84%)	0 / 225 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Angina pectoris			
subjects affected / exposed	0 / 234 (0.00%)	0 / 237 (0.00%)	1 / 225 (0.44%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Angina unstable			
subjects affected / exposed	0 / 234 (0.00%)	0 / 237 (0.00%)	1 / 225 (0.44%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nervous system disorders			
Monoparesis			
subjects affected / exposed	0 / 234 (0.00%)	1 / 237 (0.42%)	0 / 225 (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
Cerebrovascular disorder			
subjects affected / exposed	0 / 234 (0.00%)	0 / 237 (0.00%)	0 / 225 (0.00%)
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	0 / 234 (0.00%)	0 / 237 (0.00%)	0 / 225 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Syncope			
subjects affected / exposed	0 / 234 (0.00%)	0 / 237 (0.00%)	1 / 225 (0.44%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Inguinal hernia			
subjects affected / exposed	1 / 234 (0.43%)	0 / 237 (0.00%)	0 / 225 (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
Hepatobiliary disorders			
Cholelithiasis			
subjects affected / exposed	0 / 234 (0.00%)	0 / 237 (0.00%)	1 / 225 (0.44%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Skin and subcutaneous tissue disorders			
Dermatitis			
subjects affected / exposed	0 / 234 (0.00%)	0 / 237 (0.00%)	0 / 225 (0.00%)
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			
Bone loss			
subjects affected / exposed	1 / 234 (0.43%)	0 / 237 (0.00%)	0 / 225 (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
Fracture nonunion			
subjects affected / exposed	0 / 234 (0.00%)	0 / 237 (0.00%)	0 / 225 (0.00%)
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 / 234 (0.00%)	0 / 237 (0.00%)	0 / 225 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Rheumatoid arthritis			
subjects affected / exposed	0 / 234 (0.00%)	0 / 237 (0.00%)	0 / 225 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
COVID-19 pneumonia			
subjects affected / exposed	1 / 234 (0.43%)	0 / 237 (0.00%)	0 / 225 (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
Erysipelas			
subjects affected / exposed	0 / 234 (0.00%)	1 / 237 (0.42%)	0 / 225 (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
Lyme disease			
subjects affected / exposed	1 / 234 (0.43%)	0 / 237 (0.00%)	0 / 225 (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
Pyelonephritis			
subjects affected / exposed	1 / 234 (0.43%)	0 / 237 (0.00%)	0 / 225 (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	0 / 234 (0.00%)	1 / 237 (0.42%)	0 / 225 (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
Arthritis bacterial			
subjects affected / exposed	0 / 234 (0.00%)	0 / 237 (0.00%)	0 / 225 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Peritonitis			

subjects affected / exposed	0 / 234 (0.00%)	0 / 237 (0.00%)	1 / 225 (0.44%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Pneumonia			
subjects affected / exposed	0 / 234 (0.00%)	0 / 237 (0.00%)	1 / 225 (0.44%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Sepsis			
subjects affected / exposed	0 / 234 (0.00%)	0 / 237 (0.00%)	0 / 225 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	Treatment Period II: RoActemra Maintenance	Treatment Period II: Switched to CT-P47	
Total subjects affected by serious adverse events			
subjects affected / exposed	8 / 109 (7.34%)	6 / 110 (5.45%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events			
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Pancreatic neoplasm			
subjects affected / exposed	0 / 109 (0.00%)	0 / 110 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Meningioma benign			
subjects affected / exposed	1 / 109 (0.92%)	0 / 110 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vascular disorders			
Extremity necrosis			
subjects affected / exposed	0 / 109 (0.00%)	0 / 110 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Venous thrombosis limb			

subjects affected / exposed	0 / 109 (0.00%)	0 / 110 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
General disorders and administration site conditions			
Peripheral swelling			
subjects affected / exposed	0 / 109 (0.00%)	0 / 110 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Chest pain			
subjects affected / exposed	1 / 109 (0.92%)	0 / 110 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Reproductive system and breast disorders			
Cervical cyst			
subjects affected / exposed	0 / 109 (0.00%)	0 / 110 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Endometrial hyperplasia			
subjects affected / exposed	0 / 109 (0.00%)	0 / 110 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Rectocele			
subjects affected / exposed	0 / 109 (0.00%)	0 / 110 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Uterine hemorrhage			
subjects affected / exposed	0 / 109 (0.00%)	1 / 110 (0.91%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory, thoracic and mediastinal disorders			
Pleural effusion			

subjects affected / exposed	0 / 109 (0.00%)	0 / 110 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Interstitial lung disease			
subjects affected / exposed	0 / 109 (0.00%)	1 / 110 (0.91%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pulmonary embolism			
subjects affected / exposed	0 / 109 (0.00%)	0 / 110 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory failure			
subjects affected / exposed	0 / 109 (0.00%)	0 / 110 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Psychiatric disorders			
Schizophrenia			
subjects affected / exposed	0 / 109 (0.00%)	0 / 110 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Investigations			
Interferon gamma release assay positive			
subjects affected / exposed	0 / 109 (0.00%)	0 / 110 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Injury, poisoning and procedural complications			
Femur fracture			
subjects affected / exposed	0 / 109 (0.00%)	0 / 110 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ankle fracture			

subjects affected / exposed	0 / 109 (0.00%)	1 / 110 (0.91%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Femoral neck fracture			
subjects affected / exposed	1 / 109 (0.92%)	0 / 110 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Humerus fracture			
subjects affected / exposed	1 / 109 (0.92%)	0 / 110 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Radius fracture			
subjects affected / exposed	1 / 109 (0.92%)	0 / 110 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Tendon rupture			
subjects affected / exposed	1 / 109 (0.92%)	0 / 110 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Upper limb fracture			
subjects affected / exposed	0 / 109 (0.00%)	0 / 110 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac disorders			
Acute myocardial infarction			
subjects affected / exposed	0 / 109 (0.00%)	0 / 110 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Coronary artery disease			
subjects affected / exposed	0 / 109 (0.00%)	0 / 110 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Coronary artery stenosis			

subjects affected / exposed	0 / 109 (0.00%)	0 / 110 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Myocardial ischaemia			
subjects affected / exposed	0 / 109 (0.00%)	0 / 110 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Angina pectoris			
subjects affected / exposed	0 / 109 (0.00%)	0 / 110 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Angina unstable			
subjects affected / exposed	0 / 109 (0.00%)	0 / 110 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nervous system disorders			
Monoparesis			
subjects affected / exposed	0 / 109 (0.00%)	0 / 110 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cerebrovascular disorder			
subjects affected / exposed	0 / 109 (0.00%)	1 / 110 (0.91%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Headache			
subjects affected / exposed	0 / 109 (0.00%)	1 / 110 (0.91%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Syncope			
subjects affected / exposed	0 / 109 (0.00%)	0 / 110 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			

Inguinal hernia			
subjects affected / exposed	0 / 109 (0.00%)	0 / 110 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatobiliary disorders			
Cholelithiasis			
subjects affected / exposed	0 / 109 (0.00%)	0 / 110 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Skin and subcutaneous tissue disorders			
Dermatitis			
subjects affected / exposed	0 / 109 (0.00%)	1 / 110 (0.91%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Musculoskeletal and connective tissue disorders			
Bone loss			
subjects affected / exposed	0 / 109 (0.00%)	0 / 110 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Fracture nonunion			
subjects affected / exposed	0 / 109 (0.00%)	1 / 110 (0.91%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Osteoarthritis			
subjects affected / exposed	1 / 109 (0.92%)	0 / 110 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Rheumatoid arthritis			
subjects affected / exposed	0 / 109 (0.00%)	1 / 110 (0.91%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
COVID-19 pneumonia			

subjects affected / exposed	0 / 109 (0.00%)	0 / 110 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Erysipelas			
subjects affected / exposed	0 / 109 (0.00%)	0 / 110 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lyme disease			
subjects affected / exposed	0 / 109 (0.00%)	0 / 110 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pyelonephritis			
subjects affected / exposed	0 / 109 (0.00%)	0 / 110 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urosepsis			
subjects affected / exposed	0 / 109 (0.00%)	0 / 110 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Arthritis bacterial			
subjects affected / exposed	1 / 109 (0.92%)	0 / 110 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Peritonitis			
subjects affected / exposed	0 / 109 (0.00%)	0 / 110 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia			
subjects affected / exposed	0 / 109 (0.00%)	0 / 110 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Sepsis			

subjects affected / exposed	1 / 109 (0.92%)	0 / 110 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Frequency threshold for reporting non-serious adverse events: 3 %

Non-serious adverse events	Treatment Period I: CT-P47	Treatment Period I: RoActemra	Treatment Period II: CT-P47 Maintenance
Total subjects affected by non-serious adverse events			
subjects affected / exposed	139 / 234 (59.40%)	143 / 237 (60.34%)	95 / 225 (42.22%)
Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	36 / 234 (15.38%)	49 / 237 (20.68%)	30 / 225 (13.33%)
occurrences (all)	40	56	36
Aspartate aminotransferase increased			
subjects affected / exposed	12 / 234 (5.13%)	18 / 237 (7.59%)	14 / 225 (6.22%)
occurrences (all)	14	21	17
Blood creatine phosphokinase MB increased			
subjects affected / exposed	0 / 234 (0.00%)	0 / 237 (0.00%)	11 / 225 (4.89%)
occurrences (all)	0	0	15
Blood creatine phosphokinase increased			
subjects affected / exposed	0 / 234 (0.00%)	0 / 237 (0.00%)	7 / 225 (3.11%)
occurrences (all)	0	0	8
Gamma-glutamyltransferase increased			
subjects affected / exposed	0 / 234 (0.00%)	0 / 237 (0.00%)	4 / 225 (1.78%)
occurrences (all)	0	0	5
Transaminases increased			
subjects affected / exposed	6 / 234 (2.56%)	10 / 237 (4.22%)	5 / 225 (2.22%)
occurrences (all)	8	11	5
Vascular disorders			
Hypertension			
subjects affected / exposed	9 / 234 (3.85%)	12 / 237 (5.06%)	2 / 225 (0.89%)
occurrences (all)	9	12	2
Nervous system disorders			

Headache			
subjects affected / exposed	7 / 234 (2.99%)	9 / 237 (3.80%)	0 / 225 (0.00%)
occurrences (all)	9	9	0
Blood and lymphatic system disorders			
Leukopenia			
subjects affected / exposed	20 / 234 (8.55%)	25 / 237 (10.55%)	18 / 225 (8.00%)
occurrences (all)	24	29	26
Lymphopenia			
subjects affected / exposed	9 / 234 (3.85%)	13 / 237 (5.49%)	0 / 225 (0.00%)
occurrences (all)	10	16	0
Neutropenia			
subjects affected / exposed	19 / 234 (8.12%)	23 / 237 (9.70%)	14 / 225 (6.22%)
occurrences (all)	21	27	18
Thrombocytopenia			
subjects affected / exposed	9 / 234 (3.85%)	8 / 237 (3.38%)	0 / 225 (0.00%)
occurrences (all)	11	9	0
Immune system disorders			
Hypersensitivity			
subjects affected / exposed	3 / 234 (1.28%)	8 / 237 (3.38%)	0 / 225 (0.00%)
occurrences (all)	5	9	0
Infections and infestations			
Bronchitis			
subjects affected / exposed	0 / 234 (0.00%)	0 / 237 (0.00%)	2 / 225 (0.89%)
occurrences (all)	0	0	2
Latent tuberculosis			
subjects affected / exposed	0 / 234 (0.00%)	0 / 237 (0.00%)	16 / 225 (7.11%)
occurrences (all)	0	0	16
Nasopharyngitis			
subjects affected / exposed	18 / 234 (7.69%)	20 / 237 (8.44%)	8 / 225 (3.56%)
occurrences (all)	19	23	8
Oral herpes			
subjects affected / exposed	0 / 234 (0.00%)	0 / 237 (0.00%)	4 / 225 (1.78%)
occurrences (all)	0	0	4
Pharyngitis			
subjects affected / exposed	9 / 234 (3.85%)	4 / 237 (1.69%)	5 / 225 (2.22%)
occurrences (all)	9	4	5
Upper respiratory tract infection			

subjects affected / exposed	50 / 234 (21.37%)	40 / 237 (16.88%)	16 / 225 (7.11%)
occurrences (all)	57	48	19
Metabolism and nutrition disorders			
Hypercholesterolaemia			
subjects affected / exposed	16 / 234 (6.84%)	19 / 237 (8.02%)	0 / 225 (0.00%)
occurrences (all)	16	20	0
Hyperlipidaemia			
subjects affected / exposed	8 / 234 (3.42%)	5 / 237 (2.11%)	0 / 225 (0.00%)
occurrences (all)	8	5	0

Non-serious adverse events	Treatment Period II: RoActemra Maintenance	Treatment Period II: Switched to CT-P47	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	54 / 109 (49.54%)	50 / 110 (45.45%)	
Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	13 / 109 (11.93%)	15 / 110 (13.64%)	
occurrences (all)	15	19	
Aspartate aminotransferase increased			
subjects affected / exposed	8 / 109 (7.34%)	9 / 110 (8.18%)	
occurrences (all)	9	11	
Blood creatine phosphokinase MB increased			
subjects affected / exposed	7 / 109 (6.42%)	5 / 110 (4.55%)	
occurrences (all)	9	6	
Blood creatine phosphokinase increased			
subjects affected / exposed	1 / 109 (0.92%)	3 / 110 (2.73%)	
occurrences (all)	1	4	
Gamma-glutamyltransferase increased			
subjects affected / exposed	4 / 109 (3.67%)	1 / 110 (0.91%)	
occurrences (all)	4	1	
Transaminases increased			
subjects affected / exposed	1 / 109 (0.92%)	4 / 110 (3.64%)	
occurrences (all)	1	4	
Vascular disorders			

Hypertension			
subjects affected / exposed	5 / 109 (4.59%)	1 / 110 (0.91%)	
occurrences (all)	5	1	
Nervous system disorders			
Headache			
subjects affected / exposed	0 / 109 (0.00%)	0 / 110 (0.00%)	
occurrences (all)	0	0	
Blood and lymphatic system disorders			
Leukopenia			
subjects affected / exposed	8 / 109 (7.34%)	12 / 110 (10.91%)	
occurrences (all)	8	16	
Lymphopenia			
subjects affected / exposed	0 / 109 (0.00%)	0 / 110 (0.00%)	
occurrences (all)	0	0	
Neutropenia			
subjects affected / exposed	8 / 109 (7.34%)	12 / 110 (10.91%)	
occurrences (all)	9	15	
Thrombocytopenia			
subjects affected / exposed	0 / 109 (0.00%)	0 / 110 (0.00%)	
occurrences (all)	0	0	
Immune system disorders			
Hypersensitivity			
subjects affected / exposed	0 / 109 (0.00%)	0 / 110 (0.00%)	
occurrences (all)	0	0	
Infections and infestations			
Bronchitis			
subjects affected / exposed	4 / 109 (3.67%)	3 / 110 (2.73%)	
occurrences (all)	4	3	
Latent tuberculosis			
subjects affected / exposed	3 / 109 (2.75%)	5 / 110 (4.55%)	
occurrences (all)	3	5	
Nasopharyngitis			
subjects affected / exposed	2 / 109 (1.83%)	4 / 110 (3.64%)	
occurrences (all)	2	4	
Oral herpes			
subjects affected / exposed	4 / 109 (3.67%)	2 / 110 (1.82%)	
occurrences (all)	4	2	

Pharyngitis			
subjects affected / exposed	4 / 109 (3.67%)	4 / 110 (3.64%)	
occurrences (all)	4	4	
Upper respiratory tract infection			
subjects affected / exposed	10 / 109 (9.17%)	8 / 110 (7.27%)	
occurrences (all)	11	10	
Metabolism and nutrition disorders			
Hypercholesterolaemia			
subjects affected / exposed	0 / 109 (0.00%)	0 / 110 (0.00%)	
occurrences (all)	0	0	
Hyperlipidaemia			
subjects affected / exposed	0 / 109 (0.00%)	0 / 110 (0.00%)	
occurrences (all)	0	0	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
07 July 2022	Summary of significant changes included the following: •Numeric rating scale (NRS) was changed to visual analogue scale (VAS) •Added low-density lipoprotein cholesterol in the laboratory testing •Other editorial changes.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported