Clinical trial results:
A Randomized, Active-Controlled, Double-Blind, Phase 3 Study to Compare Efficacy and Safety of CT-P17 with Humira when Co-administered with Methotrexate in Patients with Moderate to Severe Active Rheumatoid Arthritis

Summary

EudraCT number	2018-001690-25
Trial protocol	HU LT BG PL
Global end of trial date	24 April 2020

Results information

Result version number	v1 (current)
This version publication date	09 July 2021
First version publication date	09 July 2021

Trial information

Trial identification

Sponsor protocol code	CT-P17-3.1

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT03789292
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	CELLTRION, Inc.
Sponsor organisation address	23, Academy-ro, Yeonsu-gu/Incheon Metropolitan City, Korea, Republic of,
Public contact	MoonSun Choi, Celltrion, Inc, +82 328505757, moonsun.choi@celltrion.com
Scientific contact	SungHyun Kim, Celltrion, Inc, +82 328505778, sunghyun.kim@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	24 April 2020
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	24 April 2020
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The primary objective of this study is to demonstrate that CT-P17 is equivalent to Humira, in terms of efficacy as determined by clinical response according to the American College of Rheumatology (ACR) definition of a 20% improvement (ACR 20) at Week 24.

Protection of trial subjects:

Hypersensitivity/allergic reactions will be assessed prior to the study drug administration and 1 hour (±10 minutes) after the end of the study drug administration by additional vital sign measurements including BP, heart and respiratory rates, and body temperature.

In addition, hypersensitivity will be monitored by routine continuous clinical monitoring including patient-reported signs and symptoms. In case of hypersensitivity, emergency medication and equipment, such as adrenaline, antihistamines, corticosteroids, and respiratory support including inhalational therapy, oxygen, and artificial ventilation must be available and any types of ECG can be performed.
For patients who experience or develop life threatening treatment-related anaphylactic reactions, study drug must be stopped immediately and the patient withdrawn from the study.

Background therapy:

Methotrexate was co-administered by oral or parenteral at a dose of between 12.5 to 25 mg/week, or 10 mg/week if intolerant to a higher dose, throughout the study.
Folic acid was co-administered at a dosage of at least 5 mg/week by oral dose throughout the duration of study.

Evidence for comparator:

CT-P17 has been developed as a proposed biosimilar product of Humira (adalimumab), a recombinant humanized monoclonal antibody. The purpose of this study is to show that there are no clinical meaningful differences between the two products.

Actual start date of recruitment	26 November 2018
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: 462
Country: Number of subjects enrolled	Bulgaria: 39
Country: Number of subjects enrolled	Hungary: 34
Country: Number of subjects enrolled	Lithuania: 9
Country: Number of subjects enrolled	Peru: 51
Country: Number of subjects enrolled	Ukraine: 53

Worldwide total number of subjects	648
EEA total number of subjects	544

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)	536
From 65 to 84 years	112
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

First patient randomly assigned to treatment: 05 December 2018.
The study was conducted at 52 study centers in Poland, Ukraine, Peru, Bulgaria, Hungary and Lithuania.

Pre-assignment

Screening details:

Male or female patients with moderate to severe active RA diagnosed according to the 2010 ACR/EULAR classification criteria, despite previous treatment with MTX over at least 12 weeks.

Pre-assignment period milestones

Number of subjects started	800[1]
Number of subjects completed	648

Pre-assignment subject non-completion reasons

Reason: Number of subjects	Inclusion/exclusion criteria not met: 126
Reason: Number of subjects	Consent withdrawn by subject: 24
Reason: Number of subjects	Other: 2

Notes:

[1] - The number of subjects reported to have started the pre-assignment period are not the same as the worldwide number enrolled in the trial. It is expected that these numbers will be the same.
Justification: The 'Number of subjects reported to have started the pre-assignment period' means subjects who consented to participate in this trial through the Screening procedure. If these subjects meet Inclusion and Exclusion criteria defined by the protocol, they can be randomized which will have study drug administration. For this reason, 800 patients were screened and of these 648 patients were met Inclusion and Exclusion criteria and randomized to each arm.

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	CT-P17

Arm description:

CT-P17 (Adalimumab) every 2 weeks from Week 0 to Week 24

Arm type	Experimental
Investigational medicinal product name	CT-P17
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection in pre-filled syringe
Routes of administration	Subcutaneous use

Dosage and administration details:

40mg every 2 weeks, co-administered with MTX; 12.5–25 mg/week or 10 mg/week if intolerant to a higher dose and folic acid (≥5 mg/week).

Arm title	Humira

Arm description:

Humira (Adalimumab) every 2 weeks from Week 0 to Week 24

Arm type	Active comparator
Investigational medicinal product name	EU-approved Humira
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection in pre-filled syringe
Routes of administration	Subcutaneous use

Dosage and administration details:

40mg every 2 weeks, co-administered with MTX; 12.5–25 mg/week or 10 mg/week if intolerant to a higher dose and folic acid (≥5 mg/week).

Number of subjects in period 1	CT-P17	Humira
Started	324	324
Completed	303	305
Not completed	21	19
Physician decision	1	-
Consent withdrawn by subject	9	8
Adverse event, non-fatal	7	8
Other	1	2
Lost to follow-up	2	-
Protocol deviation	1	1

Period 2

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

Arms

Are arms mutually exclusive?	Yes
Arm title	CT-P17 maintenance

Arm description:

Patients who received CT-P17 during Treatment Period 1 and continued to receive CT-P17 in Treatment Period 2 (from Week 26 to Week 48).

Arm type	Experimental
Investigational medicinal product name	CT-P17
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection in pre-filled syringe
Routes of administration	Subcutaneous use

Dosage and administration details:

40mg every 2 weeks, co-administered with MTX; 12.5–25 mg/week or 10 mg/week if intolerant to a higher dose and folic acid (≥5 mg/week).

Arm title	Humira maintenance

Arm description:

Patients who received Humira during Treatment Period 1 and re-randomized to Humira in Treatment Period 2 (from Week 26 to Week 48).

Arm type	Active comparator
Investigational medicinal product name	EU-approved Humira
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection in pre-filled syringe
Routes of administration	Subcutaneous use

Dosage and administration details:

40mg every 2 weeks, co-administered with MTX; 12.5–25 mg/week or 10 mg/week if intolerant to a higher dose and folic acid (≥5 mg/week).

Arm title	Switched to CT-P17

Arm description:

Patients who received Humira during Treatment Period 1 and re-randomized to CT-P17 in Treatment Period 2 (from Week 26 to Week 48).

Arm type	Experimental
Investigational medicinal product name	CT-P17
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection in pre-filled syringe
Routes of administration	Subcutaneous use

Dosage and administration details:

40mg every 2 weeks, co-administered with MTX; 12.5–25 mg/week or 10 mg/week if intolerant to a higher dose and folic acid (≥5 mg/week).

Number of subjects in period 2	CT-P17 maintenance	Humira maintenance	Switched to CT-P17
Started	303	153	152
Completed	287	147	143
Not completed	16	6	9
Physician decision	1	-	-
Consent withdrawn by subject	9	2	2
Adverse event, non-fatal	3	3	6
Other	3	1	-
Lost to follow-up	-	-	1

Baseline characteristics

Reporting groups	
Reporting group title	CT-P17
Reporting group description:	
CT-P17 (Adalimumab) every 2 weeks from Week 0 to Week 24	
Reporting group title	Humira
Reporting group description:	
Humira (Adalimumab) every 2 weeks from Week 0 to Week 24	

Reporting group values	CT-P17	Humira	Total
Number of subjects	324	324	648
Age categorical Units: Subjects			
Adults (18-64 years)	269	282	551
From 65-84 years	55	42	97
Age continuous Units: years			
median	53.5	54.0	
full range (min-max)	18 to 75	19 to 75	-
Gender categorical Units: Subjects			
Female	249	265	514
Male	75	59	134

End points

End points reporting groups

Reporting group title	CT-P17
Reporting group description:	
CT-P17 (Adalimumab) every 2 weeks from Week 0 to Week 24	
Reporting group title	Humira
Reporting group description:	
Humira (Adalimumab) every 2 weeks from Week 0 to Week 24	
Reporting group title	CT-P17 maintenance
Reporting group description:	
Patients who received CT-P17 during Treatment Period 1 and continued to receive CT-P17 in Treatment Period 2 (from Week 26 to Week 48).	
Reporting group title	Humira maintenance
Reporting group description:	
Patients who received Humira during Treatment Period 1 and re-randomized to Humira in Treatment Period 2 (from Week 26 to Week 48).	
Reporting group title	Switched to CT-P17
Reporting group description:	
Patients who received Humira during Treatment Period 1 and re-randomized to CT-P17 in Treatment Period 2 (from Week 26 to Week 48).	

Primary: Proportion of Patients with an ACR20 Response at Week 24

End point title	Proportion of Patients with an ACR20 Response at Week 24
End point description:	
End point type	Primary
End point timeframe:	
Week 24	

End point values	CT-P17	Humira		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	324	324		
Units: Responder	268	268		

Statistical analyses

Statistical analysis title	Proportion of ACR20 responder
Statistical analysis description:	
The proportion of patients achieving clinical response (responder/non-responder) according to ACR20 criteria at Week 24 was analyzed as a primary endpoint. The analysis was conducted by the exact binomial approach using a Farrington-Manning score method (Chan and Zhang, 1999; Inverting two one-sided test), and the 95% CI for the difference in proportion between the 2 treatment groups was produced.	
Comparison groups	CT-P17 v Humira

Number of subjects included in analysis	648
Analysis specification	Pre-specified
Analysis type	equivalence[1]
Parameter estimate	Treatment difference (%) and 95% CI
Point estimate	0
Confidence interval	
level	95 %
sides	2-sided
lower limit	-5.94
upper limit	5.94

Notes:

[1] - Predefined equivalence margin: -15% to 15%

Secondary: Proportion of Patients with ACR50 and ACR70 Response at Week 24

End point title	Proportion of Patients with ACR50 and ACR70 Response at Week 24

End point description:

End point type	Secondary

End point timeframe:

Week 24

End point values	CT-P17	Humira		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	324	324		
Units: Responder				
ACR50	195	206		
ACR70	132	144		

Statistical analyses

No statistical analyses for this end point

Secondary: Proportion of Patients with ACR20, ACR50 and ACR70 Response at Week 52

End point title	Proportion of Patients with ACR20, ACR50 and ACR70 Response at Week 52

End point description:

End point type	Secondary

End point timeframe:

Week 52

End point values	CT-P17 maintenance	Humira maintenance	Switched to CT-P17	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	303	153	152	
Units: Responder				
ACR20	244	119	125	
ACR50	201	95	101	
ACR70	135	75	72	

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in DAS28 (CRP) at Week 24

End point title	Change from Baseline in DAS28 (CRP) at Week 24

End point description:

End point type	Secondary

End point timeframe:

Week 24

End point values	CT-P17	Humira		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	324	324		
Units: Score				
arithmetic mean (standard deviation)	-2.738 (± 1.1911)	-2.734 (± 1.2052)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in DAS28 (CRP) at Week 52

End point title	Change from Baseline in DAS28 (CRP) at Week 52

End point description:

End point type	Secondary

End point timeframe:

Week 52

End point values	CT-P17 maintenance	Humira maintenance	Switched to CT-P17	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	303	153	152	
Units: Score				
arithmetic mean (standard deviation)	-2.945 (± 1.1273)	-3.074 (± 1.1926)	-2.983 (± 1.2529)	

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information	
Timeframe for reporting adverse events:	
From the date the patient signed the ICF until 4 weeks after the last drug administration (up to 52 weeks)	
Adverse event reporting additional description:	
TP1 groups: Treatment-emergent adverse events reported from Week 0 to Week 26 pre-dose TP2 groups: Treatment-emergent adverse events reported from Week 26 to Week 52	
Assessment type	Systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	22.0

Reporting groups	
Reporting group title	TP1: CT-P17
Reporting group description:	
CT-P17 (Adalimumab) every 2 weeks from Week 0 to Week 24	
Reporting group title	TP1: Humira
Reporting group description:	
Humira (Adalimumab) every 2 weeks from Week 0 to Week 24	
Reporting group title	TP2: CT-P17 maintenance
Reporting group description:	
Patients who received CT-P17 during Treatment Period 1 and continued to receive CT-P17 in Treatment Period 2 (from Week 26 to Week 48).	
Reporting group title	TP2: Humira maintenance
Reporting group description:	
Patients who received Humira during Treatment Period 1 and re-randomized to Humira in Treatment Period 2 (from Week 26 to Week 48).	
Reporting group title	TP2: Switched to CT-P17
Reporting group description:	
Patients who received Humira during Treatment Period 1 and re-randomized to CT-P17 in Treatment Period 2 (from Week 26 to Week 48).	

Serious adverse events	TP1: CT-P17	TP1: Humira	TP2: CT-P17 maintenance
Total subjects affected by serious adverse events			
subjects affected / exposed	12 / 324 (3.70%)	19 / 324 (5.86%)	6 / 303 (1.98%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events			
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Uterine leiomyoma			
subjects affected / exposed	0 / 324 (0.00%)	1 / 324 (0.31%)	0 / 303 (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
Breast cancer			

subjects affected / exposed	1 / 324 (0.31%)	0 / 324 (0.00%)	0 / 303 (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
Benign muscle neoplasm			
subjects affected / exposed	1 / 324 (0.31%)	0 / 324 (0.00%)	0 / 303 (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
Basal cell carcinoma			
subjects affected / exposed	0 / 324 (0.00%)	0 / 324 (0.00%)	0 / 303 (0.00%)
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			
Hypertension			
subjects affected / exposed	0 / 324 (0.00%)	1 / 324 (0.31%)	0 / 303 (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
Surgical and medical procedures			
Cataract operation			
subjects affected / exposed	0 / 324 (0.00%)	1 / 324 (0.31%)	0 / 303 (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
Polypectomy			
subjects affected / exposed	0 / 324 (0.00%)	1 / 324 (0.31%)	0 / 303 (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
Reproductive system and breast disorders			
Endometriosis			
subjects affected / exposed	0 / 324 (0.00%)	0 / 324 (0.00%)	0 / 303 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Endometrial hyperplasia			
subjects affected / exposed	0 / 324 (0.00%)	0 / 324 (0.00%)	1 / 303 (0.33%)
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, thoracic and mediastinal disorders			
Rheumatoid lung			
subjects affected / exposed	0 / 324 (0.00%)	1 / 324 (0.31%)	1 / 303 (0.33%)
occurrences causally related to treatment / all	0 / 0	1 / 1	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Injury, poisoning and procedural complications			
Extradural haematoma			
subjects affected / exposed	0 / 324 (0.00%)	0 / 324 (0.00%)	0 / 303 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Femur fracture			
subjects affected / exposed	0 / 324 (0.00%)	1 / 324 (0.31%)	0 / 303 (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
Injury			
subjects affected / exposed	1 / 324 (0.31%)	0 / 324 (0.00%)	0 / 303 (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
Limb crushing injury			
subjects affected / exposed	0 / 324 (0.00%)	0 / 324 (0.00%)	1 / 303 (0.33%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Skin laceration			
subjects affected / exposed	1 / 324 (0.31%)	0 / 324 (0.00%)	0 / 303 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Tendon rupture			
subjects affected / exposed	0 / 324 (0.00%)	0 / 324 (0.00%)	1 / 303 (0.33%)
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			
Supraventricular tachycardia			

subjects affected / exposed	0 / 324 (0.00%)	1 / 324 (0.31%)	0 / 303 (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
Angina unstable			
subjects affected / exposed	0 / 324 (0.00%)	0 / 324 (0.00%)	0 / 303 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nervous system disorders			
Amyotrophic lateral sclerosis			
subjects affected / exposed	1 / 324 (0.31%)	0 / 324 (0.00%)	0 / 303 (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
Carotid artery occlusion			
subjects affected / exposed	0 / 324 (0.00%)	0 / 324 (0.00%)	0 / 303 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ischaemic stroke			
subjects affected / exposed	0 / 324 (0.00%)	0 / 324 (0.00%)	0 / 303 (0.00%)
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 / 324 (0.00%)	1 / 324 (0.31%)	0 / 303 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood and lymphatic system disorders			
Neutropenia			
subjects affected / exposed	1 / 324 (0.31%)	1 / 324 (0.31%)	1 / 303 (0.33%)
occurrences causally related to treatment / all	1 / 1	1 / 1	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Eye disorders			
Vitreous haemorrhage			
subjects affected / exposed	0 / 324 (0.00%)	1 / 324 (0.31%)	0 / 303 (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

Retinal vein thrombosis			
subjects affected / exposed	0 / 324 (0.00%)	0 / 324 (0.00%)	0 / 303 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	1 / 324 (0.31%)	0 / 324 (0.00%)	0 / 303 (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
Hepatobiliary disorders			
Hepatic failure			
subjects affected / exposed	1 / 324 (0.31%)	0 / 324 (0.00%)	0 / 303 (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
Nonalcoholic fatty liver disease			
subjects affected / exposed	1 / 324 (0.31%)	0 / 324 (0.00%)	0 / 303 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal and urinary disorders			
Acute kidney injury			
subjects affected / exposed	1 / 324 (0.31%)	0 / 324 (0.00%)	0 / 303 (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
Musculoskeletal and connective tissue disorders			
Myositis			
subjects affected / exposed	0 / 324 (0.00%)	1 / 324 (0.31%)	0 / 303 (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
Rheumatoid arthritis			
subjects affected / exposed	0 / 324 (0.00%)	1 / 324 (0.31%)	0 / 303 (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
Infections and infestations			
Breast abscess			

subjects affected / exposed	0 / 324 (0.00%)	0 / 324 (0.00%)	0 / 303 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bronchitis			
subjects affected / exposed	0 / 324 (0.00%)	1 / 324 (0.31%)	0 / 303 (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
Cellulitis			
subjects affected / exposed	1 / 324 (0.31%)	0 / 324 (0.00%)	0 / 303 (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
Chronic tonsillitis			
subjects affected / exposed	0 / 324 (0.00%)	1 / 324 (0.31%)	0 / 303 (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
Epididymitis			
subjects affected / exposed	0 / 324 (0.00%)	1 / 324 (0.31%)	0 / 303 (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
Erysipelas			
subjects affected / exposed	1 / 324 (0.31%)	0 / 324 (0.00%)	0 / 303 (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
Gastroenteritis rotavirus			
subjects affected / exposed	1 / 324 (0.31%)	0 / 324 (0.00%)	0 / 303 (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
Lower respiratory tract infection			
subjects affected / exposed	0 / 324 (0.00%)	1 / 324 (0.31%)	0 / 303 (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
Otitis media acute			

subjects affected / exposed	1 / 324 (0.31%)	0 / 324 (0.00%)	0 / 303 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia			
subjects affected / exposed	0 / 324 (0.00%)	0 / 324 (0.00%)	2 / 303 (0.66%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pulmonary tuberculosis			
subjects affected / exposed	0 / 324 (0.00%)	1 / 324 (0.31%)	0 / 303 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pyelonephritis acute			
subjects affected / exposed	0 / 324 (0.00%)	1 / 324 (0.31%)	0 / 303 (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
Tuberculosis			
subjects affected / exposed	0 / 324 (0.00%)	1 / 324 (0.31%)	0 / 303 (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

Serious adverse events	TP2: Humira maintenance	TP2: Switched to CT-P17	
Total subjects affected by serious adverse events			
subjects affected / exposed	3 / 152 (1.97%)	5 / 152 (3.29%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events			
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Uterine leiomyoma			
subjects affected / exposed	0 / 152 (0.00%)	0 / 152 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Breast cancer			
subjects affected / exposed	0 / 152 (0.00%)	0 / 152 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Benign muscle neoplasm			
subjects affected / exposed	0 / 152 (0.00%)	0 / 152 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Basal cell carcinoma			
subjects affected / exposed	1 / 152 (0.66%)	0 / 152 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vascular disorders			
Hypertension			
subjects affected / exposed	0 / 152 (0.00%)	0 / 152 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Surgical and medical procedures			
Cataract operation			
subjects affected / exposed	0 / 152 (0.00%)	0 / 152 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Polypectomy			
subjects affected / exposed	0 / 152 (0.00%)	0 / 152 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Reproductive system and breast disorders			
Endometriosis			
subjects affected / exposed	0 / 152 (0.00%)	1 / 152 (0.66%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Endometrial hyperplasia			
subjects affected / exposed	0 / 152 (0.00%)	0 / 152 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory, thoracic and mediastinal disorders			
Rheumatoid lung			

subjects affected / exposed	0 / 152 (0.00%)	0 / 152 (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			
Extradural haematoma			
subjects affected / exposed	1 / 152 (0.66%)	0 / 152 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Femur fracture			
subjects affected / exposed	0 / 152 (0.00%)	0 / 152 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Injury			
subjects affected / exposed	0 / 152 (0.00%)	0 / 152 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Limb crushing injury			
subjects affected / exposed	0 / 152 (0.00%)	0 / 152 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Skin laceration			
subjects affected / exposed	0 / 152 (0.00%)	0 / 152 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Tendon rupture			
subjects affected / exposed	0 / 152 (0.00%)	0 / 152 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac disorders			
Supraventricular tachycardia			
subjects affected / exposed	0 / 152 (0.00%)	0 / 152 (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	1 / 152 (0.66%)	0 / 152 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nervous system disorders			
Amyotrophic lateral sclerosis			
subjects affected / exposed	0 / 152 (0.00%)	0 / 152 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Carotid artery occlusion			
subjects affected / exposed	0 / 152 (0.00%)	1 / 152 (0.66%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ischaemic stroke			
subjects affected / exposed	0 / 152 (0.00%)	1 / 152 (0.66%)	
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 / 152 (0.00%)	0 / 152 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Blood and lymphatic system disorders			
Neutropenia			
subjects affected / exposed	0 / 152 (0.00%)	0 / 152 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Eye disorders			
Vitreous haemorrhage			
subjects affected / exposed	0 / 152 (0.00%)	0 / 152 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Retinal vein thrombosis			

subjects affected / exposed	0 / 152 (0.00%)	1 / 152 (0.66%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	0 / 152 (0.00%)	0 / 152 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatobiliary disorders			
Hepatic failure			
subjects affected / exposed	0 / 152 (0.00%)	0 / 152 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nonalcoholic fatty liver disease			
subjects affected / exposed	0 / 152 (0.00%)	0 / 152 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal and urinary disorders			
Acute kidney injury			
subjects affected / exposed	0 / 152 (0.00%)	0 / 152 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Musculoskeletal and connective tissue disorders			
Myositis			
subjects affected / exposed	0 / 152 (0.00%)	0 / 152 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Rheumatoid arthritis			
subjects affected / exposed	0 / 152 (0.00%)	0 / 152 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Breast abscess			

subjects affected / exposed	0 / 152 (0.00%)	1 / 152 (0.66%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bronchitis			
subjects affected / exposed	0 / 152 (0.00%)	0 / 152 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cellulitis			
subjects affected / exposed	0 / 152 (0.00%)	0 / 152 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Chronic tonsillitis			
subjects affected / exposed	0 / 152 (0.00%)	0 / 152 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Epididymitis			
subjects affected / exposed	0 / 152 (0.00%)	0 / 152 (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 / 152 (0.00%)	0 / 152 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastroenteritis rotavirus			
subjects affected / exposed	0 / 152 (0.00%)	0 / 152 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lower respiratory tract infection			
subjects affected / exposed	0 / 152 (0.00%)	0 / 152 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Otitis media acute			

subjects affected / exposed	0 / 152 (0.00%)	0 / 152 (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 / 152 (0.00%)	0 / 152 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pulmonary tuberculosis			
subjects affected / exposed	0 / 152 (0.00%)	0 / 152 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pyelonephritis acute			
subjects affected / exposed	0 / 152 (0.00%)	0 / 152 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Tuberculosis			
subjects affected / exposed	0 / 152 (0.00%)	0 / 152 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

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

Non-serious adverse events	TP1: CT-P17	TP1: Humira	TP2: CT-P17 maintenance
Total subjects affected by non-serious adverse events			
subjects affected / exposed	96 / 324 (29.63%)	118 / 324 (36.42%)	50 / 303 (16.50%)
Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	11 / 324 (3.40%)	17 / 324 (5.25%)	8 / 303 (2.64%)
occurrences (all)	12	18	10
Aspartate aminotransferase increased			
subjects affected / exposed	4 / 324 (1.23%)	12 / 324 (3.70%)	4 / 303 (1.32%)
occurrences (all)	4	13	5
Blood and lymphatic system disorders			

Leukopenia			
subjects affected / exposed	10 / 324 (3.09%)	9 / 324 (2.78%)	8 / 303 (2.64%)
occurrences (all)	17	12	10
Neutropenia			
subjects affected / exposed	13 / 324 (4.01%)	17 / 324 (5.25%)	15 / 303 (4.95%)
occurrences (all)	19	24	19
General disorders and administration site conditions			
Injection site reaction			
subjects affected / exposed	16 / 324 (4.94%)	23 / 324 (7.10%)	1 / 303 (0.33%)
occurrences (all)	27	73	1
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	5 / 324 (1.54%)	3 / 324 (0.93%)	2 / 303 (0.66%)
occurrences (all)	5	3	2
Infections and infestations			
Latent tuberculosis			
subjects affected / exposed	12 / 324 (3.70%)	15 / 324 (4.63%)	0 / 303 (0.00%)
occurrences (all)	12	15	0
Nasopharyngitis			
subjects affected / exposed	17 / 324 (5.25%)	20 / 324 (6.17%)	6 / 303 (1.98%)
occurrences (all)	21	24	7
Pharyngitis			
subjects affected / exposed	12 / 324 (3.70%)	10 / 324 (3.09%)	4 / 303 (1.32%)
occurrences (all)	12	12	4
Upper respiratory tract infection			
subjects affected / exposed	18 / 324 (5.56%)	22 / 324 (6.79%)	10 / 303 (3.30%)
occurrences (all)	20	24	11
Urinary tract infection			
subjects affected / exposed	15 / 324 (4.63%)	15 / 324 (4.63%)	9 / 303 (2.97%)
occurrences (all)	17	17	9

Non-serious adverse events	TP2: Humira maintenance	TP2: Switched to CT-P17	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	35 / 152 (23.03%)	33 / 152 (21.71%)	
Investigations			
Alanine aminotransferase increased			

subjects affected / exposed	1 / 152 (0.66%)	7 / 152 (4.61%)	
occurrences (all)	1	7	
Aspartate aminotransferase increased			
subjects affected / exposed	1 / 152 (0.66%)	4 / 152 (2.63%)	
occurrences (all)	1	4	
Blood and lymphatic system disorders			
Leukopenia			
subjects affected / exposed	0 / 152 (0.00%)	7 / 152 (4.61%)	
occurrences (all)	0	9	
Neutropenia			
subjects affected / exposed	6 / 152 (3.95%)	8 / 152 (5.26%)	
occurrences (all)	7	12	
General disorders and administration site conditions			
Injection site reaction			
subjects affected / exposed	4 / 152 (2.63%)	1 / 152 (0.66%)	
occurrences (all)	28	1	
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	3 / 152 (1.97%)	5 / 152 (3.29%)	
occurrences (all)	3	5	
Infections and infestations			
Latent tuberculosis			
subjects affected / exposed	1 / 152 (0.66%)	0 / 152 (0.00%)	
occurrences (all)	1	0	
Nasopharyngitis			
subjects affected / exposed	5 / 152 (3.29%)	3 / 152 (1.97%)	
occurrences (all)	6	3	
Pharyngitis			
subjects affected / exposed	4 / 152 (2.63%)	3 / 152 (1.97%)	
occurrences (all)	4	4	
Upper respiratory tract infection			
subjects affected / exposed	11 / 152 (7.24%)	6 / 152 (3.95%)	
occurrences (all)	11	9	
Urinary tract infection			
subjects affected / exposed	5 / 152 (3.29%)	3 / 152 (1.97%)	
occurrences (all)	6	3	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
14 December 2018	Summary of significant changes included the following: • Changed the number of study centers and countries. • Added usability endpoint and assessment. • Added definition of usability population. • Added site visit (at Week 6). • Added details for usability assessment and self-injection. • Clarified training from home injection to self-injection. • Other administrative changes.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

Limitations of the trial such as small numbers of subjects analysed or technical problems leading to unreliable data.

Due to the COVID-19 pandemic, some study procedures (affecting week 48 and EOS visits only) were amended as per US FDA and EMA guidance, to prioritise subject safety and data validity.

Notes: