Clinical trial results:
A Phase III, Open-label, Single-arm, Multiple-dose Study to Evaluate Usability of Subcutaneous Auto-injector of CT-P17 in Patients with Moderate to Severe Active Rheumatoid Arthritis

Summary

EudraCT number	2019-000660-25
Trial protocol	PL
Global end of trial date	23 April 2020

Results information

Result version number	v1 (current)
This version publication date	17 November 2021
First version publication date	17 November 2021

Trial information

Trial identification

Sponsor protocol code	CT-P17_3.2

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT04171414
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	MinJi Ma, Celltrion, '+82 328505780, minji.ma@celltrion.com
Scientific contact	SungHyun Kim, Celltrion, '+82 328504100, 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	23 April 2020
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	23 April 2020
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To evaluate usability of CT-P17 auto-injector (AI) assessed by patients at Week 4.

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: -

Actual start date of recruitment	13 August 2019
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Poland: 62
Worldwide total number of subjects	62
EEA total number of subjects	62

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	0

months)	
Children (2-11 years)	0
Adolescents (12-17 years)	0
Adults (18-64 years)	56
From 65 to 84 years	6
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

First patient first visit: 13 August 2019.
This study was conducted at 5 study centers in Poland.

Pre-assignment

Screening details:

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

Pre-assignment period milestones

Number of subjects started	73[1]
Number of subjects completed	62

Pre-assignment subject non-completion reasons

Reason: Number of subjects	Inclusion/exclusion criteria not met: 8
Reason: Number of subjects	Consent withdrawn by subject: 3

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 subject number is correct who has started screening activities.

Period 1

Period 1 title	Treatment Period (overall period)
Is this the baseline period?	Yes
Allocation method	Non-randomised - controlled
Blinding used	Not blinded

Arms

Arm title	CT-P17

Arm description:

CT-P17 (Adalimumab) EOW 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 pen
Routes of administration	Solution for injection

Dosage and administration details:

40mg EOW, 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
Started	62
Completed	60
Not completed	2
Adverse event, serious fatal	1
Consent withdrawn by subject	1

Baseline characteristics

Reporting groups	
Reporting group title	CT-P17
Reporting group description:	
CT-P17 (Adalimumab) EOW from Week 0 to Week 24.	

Reporting group values	CT-P17	Total	
Number of subjects	62	62	
Age categorical Units: Subjects			
In utero	0	0	
Preterm newborn infants (gestational age < 37 wks)	0	0	
Newborns (0-27 days)	0	0	
Infants and toddlers (28 days-23 months)	0	0	
Children (2-11 years)	0	0	
Adolescents (12-17 years)	0	0	
Adults (18-64 years)	56	56	
From 65-84 years	6	6	
85 years and over	0	0	
Gender categorical Units: Subjects			
Female	42	42	
Male	20	20	

End points

End points reporting groups

Reporting group title	CT-P17
Reporting group description:	
CT-P17 (Adalimumab) EOW from Week 0 to Week 24.	

Primary: The usability as assessed by patients rating using PRE- and POST-Self-Injection Assessment Questionnaire (SIAQ) at Week 4

End point title	The usability as assessed by patients rating using PRE- and POST-Self-Injection Assessment Questionnaire (SIAQ) at Week 4[1]
End point description:	
End point type	Primary
End point timeframe:	
Week 4	
Notes:	
[1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point. Justification: Summarized using descriptive statistics	

End point values	CT-P17			
Subject group type	Reporting group			
Number of subjects analysed	62			
Units: Domain Score				
arithmetic mean (standard deviation)				
Feelings about self-injections (PRE)	8.00 (± 2.131)			
Feelings about self-injections (POST)	8.16 (± 2.036)			
Self-confidence (PRE)	6.55 (± 1.859)			
Self-confidence (POST)	7.07 (± 1.616)			
Self-image (POST)	8.39 (± 2.079)			
Pain and skin reactions during or after the inject	9.59 (± 0.968)			
Ease of use of the self-injection device (POST)	8.70 (± 1.457)			
Satisfaction with self-injection (PRE)	8.27 (± 1.669)			
Satisfaction with self-injection (POST)	8.23 (± 1.191)			

Statistical analyses

No statistical analyses for this end point

Secondary: Patient’s rating of PRE- and POST-SIAQ at Weeks 0, 2, and 24

End point title	Patient’s rating of PRE- and POST-SIAQ at Weeks 0, 2, and 24
End point description:	
Here result from week 24 was uploaded	

End point type	Secondary

End point timeframe:

Weeks 0,2,24

End point values	CT-P17			
Subject group type	Reporting group			
Number of subjects analysed	60			
Units: Domain Score				
arithmetic mean (standard deviation)				
Feelings about self-injections (PRE)	8.88 (± 2.034)			
Feelings about self-injections (POST)	8.97 (± 1.888)			
Self-confidence (PRE)	7.21 (± 1.556)			
Self-confidence (POST)	7.44 (± 1.840)			
Self-image (POST)	9.04 (± 1.533)			
Pain and skin reactions during or after the inject	9.60 (± 0.841)			
Ease of use of the self-injection device (POST)	9.35 (± 1.057)			
Satisfaction with self-injection (PRE)	8.83 (± 1.868)			
Satisfaction with self-injection (POST)	8.95 (± 1.023)			

Statistical analyses

No statistical analyses for this end point

Secondary: Observer’s rating of successful self-injection using self-injection assessment checklist at Weeks 0, 2, 4, and 24

End point title	Observer’s rating of successful self-injection using self-injection assessment checklist at Weeks 0, 2, 4, and 24

End point description:

End point type	Secondary

End point timeframe:

Week 0,2,4,24

End point values	CT-P17			
Subject group type	Reporting group			
Number of subjects analysed	62			
Units: count of participants				
Week 0, Successful Self-Injection	62			
Week 0, Overall Successful Self-Injection	62			
Week 2, Successful Self-Injection	62			
Week 2, Overall Successful Self-Injection	62			

Week 4, Successful Self-Injection	62			
Week 4, Overall Successful Self-Injection	62			
Week 24, Successful Self-Injection	60			
Week 24, Overall Successful Self-Injection	60			

Statistical analyses

No statistical analyses for this end point

Secondary: Mean for actual values and change from baseline in DAS28 (CRP and ESR)

End point title	Mean for actual values and change from baseline in DAS28 (CRP and ESR)

End point description:

End point type	Secondary

End point timeframe:

Week 8,16,24

End point values	CT-P17			
Subject group type	Reporting group			
Number of subjects analysed	62			
Units: score				
arithmetic mean (standard deviation)				
CRP, Baseline	5.248 (± 0.8415)			
CRP, Week 8, Change from baseline	-2.560 (± 1.1223)			
CRP, Week 16, Change from baseline	-2.795 (± 1.2381)			
CRP, Week 24, Change from baseline	-3.111 (± 1.1109)			
ESR, Baseline	6.190 (± 0.7360)			
ESR, Week 8, Change from baseline	-3.287 (± 1.3525)			
ESR, Week 16, Change from baseline	-3.495 (± 1.4695)			
ESR, Week 24, Change from baseline	-3.799 (± 1.4287)			

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 EOS/ED visit	
Assessment type	Systematic
Dictionary used	
Dictionary name	MedDRA
Dictionary version	22.0
Reporting groups	
Reporting group title	CT-P17

Reporting group description: -

Serious adverse events	CT-P17		
Total subjects affected by serious adverse events			
subjects affected / exposed	3 / 62 (4.84%)		
number of deaths (all causes)	1		
number of deaths resulting from adverse events	1		
Gastrointestinal disorders			
Lower gastrointestinal haemorrhage			
subjects affected / exposed	1 / 62 (1.61%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 1		
Reproductive system and breast disorders			
Cervical polyp			
subjects affected / exposed	1 / 62 (1.61%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Infections and infestations			
Tooth infection			
subjects affected / exposed	1 / 62 (1.61%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		

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

Non-serious adverse events	CT-P17		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	30 / 62 (48.39%)		
Nervous system disorders			
Headache			
subjects affected / exposed	2 / 62 (3.23%)		
occurrences (all)	2		
General disorders and administration site conditions			
Influenza like illness			
subjects affected / exposed	2 / 62 (3.23%)		
occurrences (all)	2		
Injection site reaction			
subjects affected / exposed	2 / 62 (3.23%)		
occurrences (all)	2		
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	2 / 62 (3.23%)		
occurrences (all)	2		
Hepatobiliary disorders			
Hyperbilirubinaemia			
subjects affected / exposed	2 / 62 (3.23%)		
occurrences (all)	4		
Infections and infestations			
Upper respiratory tract infection			
subjects affected / exposed	13 / 62 (20.97%)		
occurrences (all)	13		
Urinary tract infection			
subjects affected / exposed	3 / 62 (4.84%)		
occurrences (all)	3		
Nasopharyngitis			
subjects affected / exposed	2 / 62 (3.23%)		
occurrences (all)	2		
Pharyngitis			
subjects affected / exposed	2 / 62 (3.23%)		
occurrences (all)	2		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
11 November 2019	Summary of significant changes included the following: - Changed number of planned study population - Included anaphylactic reactions as AESI. - Differentiated the definition from the Safety Population. - Deleted time limitation regarding report of all AEs related to hypersensitivity and allergic reactions - Updated details regarding IGRA and active TB

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.

During the latter half of the study period, the COVID-19 pandemic broke out. For the majority of patients, only EOS visit was affected, the adjusted procedure including remote follow-up was conducted.

Notes: