Clinical trial results:
An Open-Label, Single-Arm, Extension Study to Demonstrate Long-Term Efficacy and Safety of CT-P13 When Co-administered With Methotrexate in Patients With Rheumatoid Arthritis Who Were Treated With Infliximab (Remicade or CT-P13) in Study CT-P13 3.1

Due to the EudraCT – Results system being out of service between 31 July 2015 and 12 January 2016, these results have been published in compliance with revised timelines

Summary

EudraCT number	2011-004468-31
Trial protocol	GB AT ES LV SK LT PL IT
Global end of trial date	12 July 2013

Results information

Result version number	v1 (current)
This version publication date	01 January 2017
First version publication date	01 January 2017

Trial information

Trial identification

Sponsor protocol code	CT-P13 3.2

Additional study identifiers

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

Notes:

Sponsors

Sponsor organisation name	CELLTRION, Inc.
Sponsor organisation address	23, Academy-ro, Yeonsu-gu, Incheon, Korea, Republic of,
Public contact	SuEun Song, CELLTRION, Inc, SuEun.Song@celltrion.com
Scientific contact	Sung Young Lee, CELLTRION, Inc, SungYoung.Lee@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	10 December 2013
Is this the analysis of the primary completion data?	Yes
Primary completion date	12 July 2013
Global end of trial reached?	Yes
Global end of trial date	12 July 2013
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To confirm long-term efficacy and safety of CT-P13.

Protection of trial subjects:

- Hypersensitivity monitoring was performed as following.
• Vital sign: 15 minutes [±5 minutes] before beginning the infusion, at the start of infusion, every 30 minutes [±5 minutes] after the start of infusion, at the end of infusion, and 30, 60, and 120 minutes [±10 minutes] after the end of infusion.
- Throughout the study, patients were monitored for the clinical signs and symptoms of TB.
• Premedications were given for safety of patients
• Emergency equipment and medication were available.
• For patients who experienced or developed life-threatening infusion-related anaphylactic reactions, infliximab treatment was stopped immediately and the patient withdrawn from the study.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	22 February 2012
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	Peru: 11
Country: Number of subjects enrolled	Philippines: 27
Country: Number of subjects enrolled	Bosnia and Herzegovina: 12
Country: Number of subjects enrolled	Bulgaria: 19
Country: Number of subjects enrolled	Italy: 1
Country: Number of subjects enrolled	Latvia: 9
Country: Number of subjects enrolled	Lithuania: 18
Country: Number of subjects enrolled	Poland: 86
Country: Number of subjects enrolled	Romania: 10
Country: Number of subjects enrolled	Slovakia: 4
Country: Number of subjects enrolled	Spain: 4
Country: Number of subjects enrolled	Ukraine: 38
Country: Number of subjects enrolled	United Kingdom: 8
Country: Number of subjects enrolled	Chile: 15
Country: Number of subjects enrolled	Colombia: 12
Country: Number of subjects enrolled	Mexico: 28

Worldwide total number of subjects	302
EEA total number of subjects	159

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)	289
From 65 to 84 years	13
85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

Male or female patients with rheumatoid arthritis (aged 18 to 75 years old based on Study CT-P13 3.1) who had completed the scheduled visits, including the EOS Visit, in Study CT-P13 3.1

Period 1

Period 1 title	Phase III (overall period)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Not blinded

Arms

Are arms mutually exclusive?	Yes
Arm title	Maintenance

Arm description:

maintain treatment with CT-P13 in Study CT-P13 3.2 (Safety population)

Arm type	Experimental
Investigational medicinal product name	CT-P13
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Powder for infusion
Routes of administration	Intravenous use

Dosage and administration details:

CT-P13 (3 mg/kg, IV infusion for 2hr per dose) coadministered MTX between 12.5 to 25 mg/week (oral or parenteral dose) and folic acid (≥5 mg/week, oral dose)

Arm title	Switch

Arm description:

switch from Remicade reference product in Study CT-P13 3.1 to CT-P13 in Study CT-P13 3.2 (Safety population)

Arm type	Active comparator
Investigational medicinal product name	CT-P13
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Powder for infusion
Routes of administration	Intravenous use

Dosage and administration details:

CT-P13 (3 mg/kg, IV infusion for 2hr per dose) coadministered MTX between 12.5 to 25 mg/week (oral or parenteral dose) and folic acid (≥5 mg/week, oral dose)

Number of subjects in period 1	Maintenance	Switch
Started	159	143
Completed	134	127
Not completed	25	16
Physician decision	1	-
Consent withdrawn by subject	4	5
death	1	-
Adverse event, non-fatal	16	8
Lost to follow-up	2	2
Lack of efficacy	1	1

Baseline characteristics

Reporting groups	
Reporting group title	Maintenance
Reporting group description: maintain treatment with CT-P13 in Study CT-P13 3.2 (Safety population)	
Reporting group title	Switch
Reporting group description: switch from Remicade reference product in Study CT-P13 3.1 to CT-P13 in Study CT-P13 3.2 (Safety population)	

Reporting group values	Maintenance	Switch	Total
Number of subjects	159	143	302
Age categorical Units: Subjects			
In utero			0
Preterm newborn infants (gestational age < 37 wks)			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)			0
From 65-84 years			0
85 years and over			0
Age continuous Units: years			
median	50	49	
full range (min-max)	18 to 73	23 to 74	-
Gender categorical Units: Subjects			
Female	126	121	247
Male	33	22	55

End points

End points reporting groups

Reporting group title	Maintenance
Reporting group description: maintain treatment with CT-P13 in Study CT-P13 3.2 (Safety population)	
Reporting group title	Switch
Reporting group description: switch from Remicade reference product in Study CT-P13 3.1 to CT-P13 in Study CT-P13 3.2 (Safety population)	
Subject analysis set title	Intent-to-Treat Population
Subject analysis set type	Intention-to-treat
Subject analysis set description: All subjects enrolled in Study CT-P13 3.2 were included in Intent-to-Treat Subjects.	
Subject analysis set title	Safety Population
Subject analysis set type	Sub-group analysis
Subject analysis set description: All subjects who received a complete or partial dose of IMP were included in the Safety Analysis Set.	
Subject analysis set title	Efficacy Population
Subject analysis set type	Sub-group analysis
Subject analysis set description: All subjects who received at least 1 full dose of IMP and had data for at least 1 efficacy assessment were included in the Efficacy Analysis Set.	

Primary: Treatment-Emergent Serious Adverse Events

End point title	Treatment-Emergent Serious Adverse Events[1]
End point description: Number of Patients with at least one Treatment Emergent Serious Adverse Event	
End point type	Primary
End point timeframe: up to EOS	

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: The End Points such as Treatment-Emergent Serious Adverse Events, Treatment-Emergent Adverse Events, Treatment-Emergent Adverse Events due to infection, Hypersensitivity and infusion-related reactions were described using descriptive statistics.

End point values	Maintenance	Switch		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	159[2]	143[3]		
Units: percentage				
number (not applicable)	7.5	9.1		

Notes:

[2] - Safety population

[3] - Safety population

Statistical analyses

No statistical analyses for this end point

Primary: Hypersensitivity and infusion-related reactions

End point title	Hypersensitivity and infusion-related reactions[4]

End point description:

Number of patients with at least one Treatment Emergent Adverse Event due to hypersensitivity and infusion-related reactions

End point type	Primary

End point timeframe:

up to EOS

Notes:

[4] - 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: The End Points such as Treatment-Emergent Serious Adverse Events, Treatment-Emergent Adverse Events, Treatment-Emergent Adverse Events due to infection, Hypersensitivity and infusion-related reactions were described using descriptive statistics.

End point values	Maintenance	Switch		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	159[5]	143[6]		
Units: percentage				
number (not applicable)	6.3	2.8		

Notes:

[5] - Safety population

[6] - Safety population

Statistical analyses

No statistical analyses for this end point

Primary: Treatment-Emergent Adverse Events

End point title	Treatment-Emergent Adverse Events[7]

End point description:

Number of Patients with at least one Treatment Emergent Adverse Event

End point type	Primary

End point timeframe:

up to EOS

Notes:

[7] - 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: The End Points such as Treatment-Emergent Serious Adverse Events, Treatment-Emergent Adverse Events, Treatment-Emergent Adverse Events due to infection, Hypersensitivity and infusion-related reactions were described using descriptive statistics.

End point values	Maintenance	Switch		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	159[8]	143[9]		
Units: percentage				
number (not applicable)	53.5	53.8		

Notes:

[8] - Safety population

[9] - Safety population

Statistical analyses

No statistical analyses for this end point

Primary: Treatment-Emergent Adverse Events due to infection

End point title	Treatment-Emergent Adverse Events due to infection[10]

End point description:

Number of Patients with at least one Treatment Emergent Adverse Event due to infection

End point type	Primary

End point timeframe:

up to EOS

Notes:

[10] - 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: The End Points such as Treatment-Emergent Serious Adverse Events, Treatment-Emergent Adverse Events, Treatment-Emergent Adverse Events due to infection, Hypersensitivity and infusion-related reactions were described using descriptive statistics.

End point values	Maintenance	Switch		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	159[11]	143[12]		
Units: percentage				
number (not applicable)	31.4	32.9		

Notes:

[11] - Safety population

[12] - Safety population

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information	
Timeframe for reporting adverse events: up to EOS	
Assessment type	Systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	15.1

Reporting groups	
Reporting group title	Maintenance
Reporting group description: -	
Reporting group title	Switch
Reporting group description: -	

Serious adverse events	Maintenance	Switch	
Total subjects affected by serious adverse events			
subjects affected / exposed	12 / 159 (7.55%)	13 / 143 (9.09%)	
number of deaths (all causes)	1	0	
number of deaths resulting from adverse events	0	0	
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Breast cancer stage II			
subjects affected / exposed	0 / 159 (0.00%)	1 / 143 (0.70%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Intestinal T-cell lymphoma			
subjects affected / exposed	0 / 159 (0.00%)	1 / 143 (0.70%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Myeloproliferative disorder			
subjects affected / exposed	0 / 159 (0.00%)	1 / 143 (0.70%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ovarian cancer stage I			
subjects affected / exposed	1 / 159 (0.63%)	0 / 143 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Ovarian cancer stage III			
subjects affected / exposed	0 / 159 (0.00%)	1 / 143 (0.70%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Injury, poisoning and procedural complications			
Femur fracture			
subjects affected / exposed	0 / 159 (0.00%)	1 / 143 (0.70%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Foreign body			
subjects affected / exposed	0 / 159 (0.00%)	1 / 143 (0.70%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Head injury			
subjects affected / exposed	1 / 159 (0.63%)	0 / 143 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hip fracture			
subjects affected / exposed	1 / 159 (0.63%)	0 / 143 (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			
Cerebrovascular disorder			
subjects affected / exposed	0 / 159 (0.00%)	1 / 143 (0.70%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Blood and lymphatic system disorders			
Anaemia megaloblastic			
subjects affected / exposed	0 / 159 (0.00%)	1 / 143 (0.70%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
General disorders and administration site conditions			
Death			

subjects affected / exposed	1 / 159 (0.63%)	0 / 143 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Medical device complication			
subjects affected / exposed	0 / 159 (0.00%)	1 / 143 (0.70%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
Oesophageal perforation			
subjects affected / exposed	0 / 159 (0.00%)	1 / 143 (0.70%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Reproductive system and breast disorders			
Uterine polyp			
subjects affected / exposed	1 / 159 (0.63%)	0 / 143 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory, thoracic and mediastinal disorders			
Interstitial lung disease			
subjects affected / exposed	1 / 159 (0.63%)	0 / 143 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal and urinary disorders			
Pollakiuria			
subjects affected / exposed	1 / 159 (0.63%)	0 / 143 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Musculoskeletal and connective tissue disorders			
Pseudarthrosis			
subjects affected / exposed	1 / 159 (0.63%)	0 / 143 (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	2 / 159 (1.26%)	0 / 143 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Synovial cyst			
subjects affected / exposed	0 / 159 (0.00%)	1 / 143 (0.70%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Wrist deformity			
subjects affected / exposed	1 / 159 (0.63%)	0 / 143 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Abscess limb			
subjects affected / exposed	1 / 159 (0.63%)	0 / 143 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Appendicitis			
subjects affected / exposed	1 / 159 (0.63%)	0 / 143 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dengue fever			
subjects affected / exposed	0 / 159 (0.00%)	1 / 143 (0.70%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infected dermal cyst			
subjects affected / exposed	1 / 159 (0.63%)	0 / 143 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Otitis media			
subjects affected / exposed	0 / 159 (0.00%)	1 / 143 (0.70%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia			

subjects affected / exposed	1 / 159 (0.63%)	0 / 143 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Salpingitis			
subjects affected / exposed	0 / 159 (0.00%)	1 / 143 (0.70%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

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

Non-serious adverse events	Maintenance	Switch	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	31 / 159 (19.50%)	28 / 143 (19.58%)	
Infections and infestations			
Bronchitis			
subjects affected / exposed	5 / 159 (3.14%)	9 / 143 (6.29%)	
occurrences (all)	5	9	
Latent tuberculosis			
subjects affected / exposed	10 / 159 (6.29%)	5 / 143 (3.50%)	
occurrences (all)	10	5	
Upper respiratory tract infection			
subjects affected / exposed	8 / 159 (5.03%)	6 / 143 (4.20%)	
occurrences (all)	9	6	
Urinary tract infection			
subjects affected / exposed	8 / 159 (5.03%)	8 / 143 (5.59%)	
occurrences (all)	9	8	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
30 May 2012	Summary of significant changes includes the following: • Amended the number of study centers/countries • Clarified visit window and visit intervals • Amended Exclusion Criteria 9 • Amended safety endpoints analysis • Clarified ACR core set of variables • Amended the immunogenicity analysis • Clarified monitoring and reporting of AEs • Clarified analysis of serum pregnancy test • Clarified analysis of sample for clinical laboratory assessments • Clarified back-up sample of immunogenicity analysis • Clarified concomitant medications • Amended demography and MH • Clarified SAE data entry • Clarified coding of AEs, MH, previous and concomitant treatments • Added rescue therapy • Added reporting of changes in terms of dose of concomitant medication • Other clarifications and administrative changes

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported