Clinical trial results:
A Randomized, Double-Blind, Parallel-Group, Phase 3 Study to Demonstrate Equivalence in Efficacy and Safety of CT-P13 Compared with Remicade when Co-administered with Methotrexate in Patients with Active Rheumatoid Arthritis

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	2010-018646-31
Trial protocol	SK LV GB PT IT AT LT ES BG
Global end of trial date	10 July 2012

Results information

Result version number	v1 (current)
This version publication date	23 December 2016
First version publication date	23 December 2016

Trial information

Trial identification

Sponsor protocol code	CT-P13-3.1

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, 22014
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	09 July 2014
Is this the analysis of the primary completion data?	Yes
Primary completion date	10 July 2012
Global end of trial reached?	Yes
Global end of trial date	10 July 2012
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To demonstrate that CT P13 was equivalent to Remicade up to Week 30, in terms of efficacy as determined by clinical response according to the American College of Rheumatology (ACR) definition of a 20% improvement (ACR20).

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	13 December 2010
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: 143
Country: Number of subjects enrolled	Portugal: 1
Country: Number of subjects enrolled	Romania: 19
Country: Number of subjects enrolled	Slovakia: 8
Country: Number of subjects enrolled	Spain: 8
Country: Number of subjects enrolled	United Kingdom: 9
Country: Number of subjects enrolled	Austria: 7
Country: Number of subjects enrolled	Bulgaria: 32
Country: Number of subjects enrolled	Italy: 8
Country: Number of subjects enrolled	Latvia: 10
Country: Number of subjects enrolled	Lithuania: 28
Country: Number of subjects enrolled	Philippines: 72
Country: Number of subjects enrolled	Bosnia and Herzegovina: 13
Country: Number of subjects enrolled	Jordan: 1
Country: Number of subjects enrolled	Ukraine: 109

Country: Number of subjects enrolled	Chile: 42
Country: Number of subjects enrolled	Colombia: 31
Country: Number of subjects enrolled	Mexico: 40
Country: Number of subjects enrolled	Peru: 25
Worldwide total number of subjects	606
EEA total number of subjects	273

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)	564
From 65 to 84 years	42
85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

Male or female patients aged 18 to 75 years old, inclusive, who had been diagnosed with RA according to the revised 1987 ACR classification criteria

Period 1

Period 1 title	Phase III (overall period)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator, Monitor

Arms

Are arms mutually exclusive?	Yes
Arm title	CT-P13

Arm description: -

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)

Investigational medicinal product name	Remicade
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Powder for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Remicade (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	Remicade

Arm description: -

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

Dosage and administration details:

Remicade (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	CT-P13	Remicade
Started	302	304
Completed	233	222
Not completed	69	82
Consent withdrawn by subject	16	21
Adverse event, non-fatal	36	48
Protocol violation	3	3
Death	-	1
Pregnancy	-	1
Lost to follow-up	4	2
Lack of efficacy	10	6

Baseline characteristics

Reporting groups	
Reporting group title	CT-P13
Reporting group description: -	
Reporting group title	Remicade
Reporting group description: -	

Reporting group values	CT-P13	Remicade	Total
Number of subjects	302	304	606
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	50	
full range (min-max)	18 to 75	21 to 74	-
Gender categorical Units: Subjects			
Female	245	256	501
Male	57	48	105

End points

End points reporting groups

Reporting group title	CT-P13
Reporting group description: -	
Reporting group title	Remicade
Reporting group description: -	
Subject analysis set title	All Randomized population
Subject analysis set type	Intention-to-treat
Subject analysis set description:	
All randomized subjects were included in All Randomized Subjects	

Subject analysis set title	Safety population
Subject analysis set type	Safety analysis
Subject analysis set description:	
All randomized subjects who received a complete or partial dose of IMP were included in the Safety Analysis Set	
Subject analysis set title	Pharmacokinetic population
Subject analysis set type	Sub-group analysis
Subject analysis set description:	
All subjects who received a dose of IMP during the 30 week blinded study period with at least one PK sample.	

Subject analysis set title	Pharmacodynamic population
Subject analysis set type	Sub-group analysis
Subject analysis set description:	
All subjects who received a dose of IMP during the 30 week blinded study periodwith at least one PK sample.	

Subject analysis set title	Per-protocol population up to Week 30
Subject analysis set type	Sub-group analysis
Subject analysis set description:	
All subjects who did not have any major protocol deviations .	

Subject analysis set title	Per-protocol population up to Week 54
Subject analysis set type	Sub-group analysis
Subject analysis set description:	
All subjects who did not have any major protocol deviations .	

Primary: ACR20 Criteria at Weeks 30 (All-randomized Population)

End point title	ACR20 Criteria at Weeks 30 (All-randomized Population)
End point description:	
Proportion of Patients Achieving Clinical Response According to the ACR20 Criteria at Weeks 30	
End point type	Primary
End point timeframe:	
Day 210 (Week 30)	

End point values	CT-P13	Remicade		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	302[1]	304[2]		
Units: percentage				
number (confidence interval 95%)	60.9 (55.17 to 66.46)	58.9 (53.12 to 64.47)		

Notes:

[1] - All-Randomized Population

[2] - All-Randomized Population

Statistical analyses

Statistical analysis title	ACR20 Criteria at Week 30

Statistical analysis description:

Analysis Method: StatXact Version 8 or higher and PROC BINOMIAL
Treatment group: treatment group, Covariates: region and C-reactive protein category
Point estimates: The proportion of patients achieving clinical response defined as a 20% improvement according to ACR criteria at Week 30 was analyzed by the exact binomial approach, calculating a point estimate and 95% CI for the difference in proportion between the 2 treatment groups

Comparison groups	CT-P13 v Remicade
Number of subjects included in analysis	606
Analysis specification	Pre-specified
Analysis type	equivalence[3]
Parameter estimate	Difference in proportion
Point estimate	0.02
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.06
upper limit	0.1

Notes:

[3] - Equivalence margin: -15% - 15%

Primary: ACR20 Criteria at Weeks 30 (Per-Protocol Population)

End point title	ACR20 Criteria at Weeks 30 (Per-Protocol Population)

End point description:

Proportion of Patients Achieving Clinical Response According to the ACR20 Criteria at Weeks 30

End point type	Primary

End point timeframe:

Day 210 (Week 30)

End point values	CT-P13	Remicade		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	248[4]	251[5]		
Units: percentage				
number (confidence interval 95%)	73.4 (67.43 to 78.78)	70.1 (64.04 to 75.71)		

Notes:
[4] - Per-protocol Population
[5] - Per-Protocol Population

Statistical analyses

Statistical analysis title	ACR20 Criteria at Week 30
Comparison groups	CT-P13 v Remicade
Number of subjects included in analysis	499
Analysis specification	Pre-specified
Analysis type	equivalence[6]
Parameter estimate	Difference in proportion
Point estimate	0.03
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.05
upper limit	0.11

Notes:
[6] - Equivalence margin: -15% - 15%

Adverse events

Adverse events information	
Timeframe for reporting adverse events: Day 434(Week 62); up to EOS	
Assessment type	Systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	13.1

Reporting groups	
Reporting group title	CT-P13
Reporting group description: -	
Reporting group title	Remicade
Reporting group description: -	

Serious adverse events	CT-P13	Remicade	
Total subjects affected by serious adverse events			
subjects affected / exposed	42 / 302 (13.91%)	31 / 300 (10.33%)	
number of deaths (all causes)	0	1	
number of deaths resulting from adverse events	0	0	
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Breast cancer			
subjects affected / exposed	0 / 302 (0.00%)	1 / 300 (0.33%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cervix carcinoma stage 0			
subjects affected / exposed	0 / 302 (0.00%)	1 / 300 (0.33%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Colon neoplasm			
subjects affected / exposed	0 / 302 (0.00%)	1 / 300 (0.33%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ovarian cancer			
subjects affected / exposed	1 / 302 (0.33%)	0 / 300 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Ovarian cancer metastatic			
subjects affected / exposed	0 / 302 (0.00%)	1 / 300 (0.33%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal neoplasm			
subjects affected / exposed	1 / 302 (0.33%)	0 / 300 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Salivary gland adenoma			
subjects affected / exposed	1 / 302 (0.33%)	0 / 300 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vascular disorders			
Deep vein thrombosis			
subjects affected / exposed	2 / 302 (0.66%)	0 / 300 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypertension			
subjects affected / exposed	1 / 302 (0.33%)	0 / 300 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Thrombophlebitis			
subjects affected / exposed	1 / 302 (0.33%)	0 / 300 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Surgical and medical procedures			
Hip arthroplasty			
subjects affected / exposed	0 / 302 (0.00%)	1 / 300 (0.33%)	
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			
Pyrexia			

subjects affected / exposed	0 / 302 (0.00%)	1 / 300 (0.33%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Sudden death			
subjects affected / exposed	0 / 302 (0.00%)	1 / 300 (0.33%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Immune system disorders			
Anaphylactic reaction			
subjects affected / exposed	3 / 302 (0.99%)	0 / 300 (0.00%)	
occurrences causally related to treatment / all	3 / 3	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Anaphylactic shock			
subjects affected / exposed	1 / 302 (0.33%)	0 / 300 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Drug hypersensitivity			
subjects affected / exposed	0 / 302 (0.00%)	1 / 300 (0.33%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Reproductive system and breast disorders			
Cervical dysplasia			
subjects affected / exposed	0 / 302 (0.00%)	1 / 300 (0.33%)	
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	2 / 302 (0.66%)	0 / 300 (0.00%)	
occurrences causally related to treatment / all	1 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metrorrhagia			
subjects affected / exposed	1 / 302 (0.33%)	1 / 300 (0.33%)	
occurrences causally related to treatment / all	0 / 1	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

Uterine haemorrhage			
subjects affected / exposed	1 / 302 (0.33%)	0 / 300 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Investigations			
Blood glucose increased			
subjects affected / exposed	0 / 302 (0.00%)	1 / 300 (0.33%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Electrocardiogram T wave abnormal			
subjects affected / exposed	1 / 302 (0.33%)	0 / 300 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Investigation			
subjects affected / exposed	0 / 302 (0.00%)	1 / 300 (0.33%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Injury, poisoning and procedural complications			
Contusion			
subjects affected / exposed	1 / 302 (0.33%)	0 / 300 (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 / 302 (0.00%)	1 / 300 (0.33%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Humerus fracture			
subjects affected / exposed	1 / 302 (0.33%)	0 / 300 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infusion related reaction			
subjects affected / exposed	2 / 302 (0.66%)	3 / 300 (1.00%)	
occurrences causally related to treatment / all	2 / 2	3 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	

Tendon rupture			
subjects affected / exposed	1 / 302 (0.33%)	0 / 300 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac disorders			
Acute coronary syndrome			
subjects affected / exposed	0 / 302 (0.00%)	1 / 300 (0.33%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Atrial fibrillation			
subjects affected / exposed	0 / 302 (0.00%)	1 / 300 (0.33%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Myocardial infarction			
subjects affected / exposed	1 / 302 (0.33%)	0 / 300 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pericarditis			
subjects affected / exposed	0 / 302 (0.00%)	1 / 300 (0.33%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nervous system disorders			
Carpal tunnel syndrome			
subjects affected / exposed	0 / 302 (0.00%)	1 / 300 (0.33%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cerebrovascular accident			
subjects affected / exposed	0 / 302 (0.00%)	1 / 300 (0.33%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cerebrovascular disorder			
subjects affected / exposed	1 / 302 (0.33%)	0 / 300 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Lumbar radiculopathy			
subjects affected / exposed	0 / 302 (0.00%)	1 / 300 (0.33%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Migraine			
subjects affected / exposed	0 / 302 (0.00%)	2 / 300 (0.67%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Blood and lymphatic system disorders			
Neutropenia			
subjects affected / exposed	1 / 302 (0.33%)	0 / 300 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ear and labyrinth disorders			
Tympanic membrane perforation			
subjects affected / exposed	1 / 302 (0.33%)	0 / 300 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Eye disorders			
Uveitis			
subjects affected / exposed	2 / 302 (0.66%)	0 / 300 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	1 / 302 (0.33%)	0 / 300 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastritis			
subjects affected / exposed	0 / 302 (0.00%)	1 / 300 (0.33%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hiatus hernia			

subjects affected / exposed	0 / 302 (0.00%)	1 / 300 (0.33%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Inguinal hernia			
subjects affected / exposed	1 / 302 (0.33%)	0 / 300 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Irritable bowel syndrome			
subjects affected / exposed	0 / 302 (0.00%)	1 / 300 (0.33%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatobiliary disorders			
Cholecystitis acute			
subjects affected / exposed	0 / 302 (0.00%)	1 / 300 (0.33%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal and urinary disorders			
Nephrolithiasis			
subjects affected / exposed	1 / 302 (0.33%)	0 / 300 (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			
Intervertebral disc disorder			
subjects affected / exposed	0 / 302 (0.00%)	1 / 300 (0.33%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Musculoskeletal chest pain			
subjects affected / exposed	1 / 302 (0.33%)	0 / 300 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Osteoarthritis			
subjects affected / exposed	0 / 302 (0.00%)	1 / 300 (0.33%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

Osteochondrosis			
subjects affected / exposed	1 / 302 (0.33%)	0 / 300 (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 / 302 (0.66%)	1 / 300 (0.33%)	
occurrences causally related to treatment / all	1 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Appendicitis			
subjects affected / exposed	0 / 302 (0.00%)	2 / 300 (0.67%)	
occurrences causally related to treatment / all	0 / 0	1 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Arthritis bacterial			
subjects affected / exposed	0 / 302 (0.00%)	1 / 300 (0.33%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cellulitis			
subjects affected / exposed	1 / 302 (0.33%)	0 / 300 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Coxsackie myocarditis			
subjects affected / exposed	0 / 302 (0.00%)	1 / 300 (0.33%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Disseminated tuberculosis			
subjects affected / exposed	2 / 302 (0.66%)	0 / 300 (0.00%)	
occurrences causally related to treatment / all	2 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastroenteritis			
subjects affected / exposed	1 / 302 (0.33%)	0 / 300 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Herpes zoster			

subjects affected / exposed	0 / 302 (0.00%)	1 / 300 (0.33%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Joint abscess			
subjects affected / exposed	1 / 302 (0.33%)	0 / 300 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lobar pneumonia			
subjects affected / exposed	1 / 302 (0.33%)	0 / 300 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia			
subjects affected / exposed	3 / 302 (0.99%)	0 / 300 (0.00%)	
occurrences causally related to treatment / all	3 / 3	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pulmonary tuberculosis			
subjects affected / exposed	1 / 302 (0.33%)	0 / 300 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pyoderma			
subjects affected / exposed	1 / 302 (0.33%)	0 / 300 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal abscess			
subjects affected / exposed	0 / 302 (0.00%)	1 / 300 (0.33%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Septic shock			
subjects affected / exposed	0 / 302 (0.00%)	1 / 300 (0.33%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Staphylococcal sepsis			

subjects affected / exposed	0 / 302 (0.00%)	1 / 300 (0.33%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urinary tract infection			
subjects affected / exposed	1 / 302 (0.33%)	0 / 300 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Wound infection staphylococcal			
subjects affected / exposed	1 / 302 (0.33%)	0 / 300 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metabolism and nutrition disorders			
Diabetes mellitus inadequate control			
subjects affected / exposed	1 / 302 (0.33%)	0 / 300 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

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

Non-serious adverse events	CT-P13	Remicade	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	202 / 302 (66.89%)	206 / 300 (68.67%)	
Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	15 / 302 (4.97%)	17 / 300 (5.67%)	
occurrences (all)	18	18	
Nervous system disorders			
Headache			
subjects affected / exposed	14 / 302 (4.64%)	17 / 300 (5.67%)	
occurrences (all)	18	19	
Musculoskeletal and connective tissue disorders			
Rheumatoid arthritis			
subjects affected / exposed	15 / 302 (4.97%)	10 / 300 (3.33%)	
occurrences (all)	21	14	
Infections and infestations			

Bronchitis			
subjects affected / exposed	13 / 302 (4.30%)	17 / 300 (5.67%)	
occurrences (all)	14	20	
Latent tuberculosis			
subjects affected / exposed	27 / 302 (8.94%)	25 / 300 (8.33%)	
occurrences (all)	28	28	
Nasopharyngitis			
subjects affected / exposed	25 / 302 (8.28%)	17 / 300 (5.67%)	
occurrences (all)	34	18	
Upper respiratory tract infection			
subjects affected / exposed	27 / 302 (8.94%)	17 / 300 (5.67%)	
occurrences (all)	35	23	
Urinary tract infection			
subjects affected / exposed	18 / 302 (5.96%)	21 / 300 (7.00%)	
occurrences (all)	23	27	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
04 May 2010	Summary of significant changes includes the following: •Number of sites/countries reduced • Amended administration route for Remicade and methotrexate •Amended E/C 5, 8, 9 • Removed Treatment Phase II and text associated with the study period •Updated PK and PD objectives •Clarified pregnancy testing • For countries with an increased TB prevalence and incidence, secondary endpoint was added •Updated secondary and tertiary safety endpoints •Updated infliximab measurement, immunogenicity testing, PD blood sampling •Amended blood sample and other supplies •Amended vital signs and demographics •Amended salvage retreatment •Other administrative changes
14 June 2010	Summary of significant changes includes the following: •Amended E/C 8 •Corrected Dose-Loading phase •Amended previous and concomitant treatments •Amended hypersensitivity monitoring •Clarified blinding •Clarified weight record •Other administrative changes
10 January 2011	Summary of significant changes includes the following: •Specified methotrexate administration •Amended I/C 9, 10, E/C 2, 5, 6, 8, 9 •Specified the visit window •Extended screening period •Amended EOS radiographs •Amended the secondary efficacy endpoints •Amended the joint damage and joint count •Updated a 15-minute window •Clarified rescreening of IGRA •Clarified a chest x-ray •Removed the COPD assessment •Amended AEs •Clarified sample retention and destruction •Amended the infusion time •Specified protocol analysis population •Updated phone number •Amended the body of the document •Other administrative changes

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported