Clinical trial results:
A Randomized, Double-Blind, Parallel-Group, Phase 3 Study to Demonstrate Noninferiority in Efficacy and to Assess Safety of CT-P13 Compared to Remicade in Patients With Active Crohn's Disease

Summary

EudraCT number	2013-004497-10
Trial protocol	BE HU GB IT ES RO DK NL
Global end of trial date	15 February 2017

Results information

Result version number	v1 (current)
This version publication date	02 March 2018
First version publication date	02 March 2018

Trial information

Trial identification

Sponsor protocol code	CT-P13 3.4

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02096861
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	Clinical Operations Management Department, CELLTRION, Inc., +82 328506724, SuEun.Song@celltrion.com
Scientific contact	Clinical Planning Department, CELLTRION, Inc., +82 328506532, 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	08 December 2017
Is this the analysis of the primary completion data?	Yes
Primary completion date	11 January 2016
Global end of trial reached?	Yes
Global end of trial date	15 February 2017
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To demonstrate that CT-P13 (Remsima) is non-inferior to Remicade at Week 6 (Dose 3), in terms of efficacy, as determined by the CDAI-70 response rate

Protection of trial subjects:

Additional vital signs including blood pressure, heart and respiratory rates, and temperature were measured to monitor for possible hypersensitivity reactions on each dosing day and recorded at the following time points:

• 15 minutes (± 5 minutes) before the beginning of the study drug infusion
• At the start of the study drug infusion (± 5 minutes)
• Every 30 minutes (± 5 minutes) after the start of the study drug infusion
• At the end of the study drug infusion (± 5 minutes) and 30, 60, and 120 minutes (± 10 minutes) after the end of the study drug infusion

In addition, hypersensitivity wasmonitored by routine continuous clinical monitoring, which had to be performed after the patient had rested quietly for at least 5 minutes in the supine position. Emergency equipment, such as adrenaline, antihistamines, corticosteroids, and respiratory support including inhalational therapy, oxygen, and artificial ventilator, had to be available. For patients who experienced or developed life-threatening infusion-related anaphylactic reactions, study drug was stopped immediately and the patient withdrawn from the study.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	01 July 2014
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	Netherlands: 3
Country: Number of subjects enrolled	Poland: 5
Country: Number of subjects enrolled	Romania: 8
Country: Number of subjects enrolled	Belgium: 2
Country: Number of subjects enrolled	Denmark: 1
Country: Number of subjects enrolled	France: 5
Country: Number of subjects enrolled	Germany: 2
Country: Number of subjects enrolled	Hungary: 11
Country: Number of subjects enrolled	Italy: 12
Country: Number of subjects enrolled	Russian Federation: 50
Country: Number of subjects enrolled	Korea, Republic of: 54

Country: Number of subjects enrolled	Ukraine: 32
Country: Number of subjects enrolled	Israel: 26
Country: Number of subjects enrolled	United States: 3
Country: Number of subjects enrolled	Brazil: 2
Country: Number of subjects enrolled	Mexico: 4
Worldwide total number of subjects	220
EEA total number of subjects	49

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)	216
From 65 to 84 years	4
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

First patient randomly assigned to treatment: 19 September 2014
A total of 99 study centers were initiated in 4 geographical regions (Europe, North America, Latin America, and Asia Pacific)

Pre-assignment

Screening details:

Key Inclusion Criteria
1. Patient is male or female between 18 to 75 years old, inclusive
2. Patient has a diagnosis of CD according to CDAI 220 - 450 points for least 12 weeks prior to randomisation
3. Patient has not responded despite a full and adequate therapy/intolerant/has contraindications with corticosteroid and/or immunosuppressant

Pre-assignment period milestones

Number of subjects started	308[1]
Intermediate milestone: Number of subjects	Subject screened: 308
Intermediate milestone: Number of subjects	Enrolled: 220
Number of subjects completed	220

Pre-assignment subject non-completion reasons

Reason: Number of subjects	Screening Failure: 88

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.

Period 1

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

Blinding implementation details:

Data analyst became unblinded at Week 6 for reporting purpose. Other members were remained blinded.

Arms

Are arms mutually exclusive?	Yes
Arm title	CT-P13

Arm description:

Patients who were randomized to CT-P13-CT-P13 or CT-P13-Remicade treatment groups at Week0

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

Dosage and administration details:
CT-P13 (5 mg/kg) by intravenous (IV) infusion administered as a 2 hour IV infusion per dose

Arm title	Remicade

Arm description:
Patients who were randomized to Remicade-Remicade or Remicade-CT-P13 treatment groups at Week0

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

Dosage and administration details:
Remicade (5 mg/kg) by intravenous (IV) infusion administered as a 2 hour IV infusion per dose

Number of subjects in period 1	CT-P13	Remicade
Started	111	109
Completed	92	88
Not completed	19	21
Non-responder at Week 14	9	8
PATIENT NON COMPLIENCE	1	-
Consent withdrawn by subject	-	1
Physician decision	-	1
Disease progression	2	4
Adverse event, non-fatal	4	6
Lost to follow-up	1	-
Protocol deviation	2	1

Period 2

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

Arms

Are arms mutually exclusive?	Yes

Arm title	CT-P13 - CT-P13

Arm description:

CT-P13 followed by CT-P13 from Week 30

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

Dosage and administration details:

CT-P13 (5 mg/kg) by intravenous (IV) infusion administered as a 2 hour IV infusion per dose

Arm title	CT-P13 - Remicade

Arm description:

CT-P13 followed by Remicade from Week 30

Arm type	Experimental
Investigational medicinal product name	Remicade
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Powder for concentrate for solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Remicade (5 mg/kg) by intravenous (IV) infusion administered as a 2 hour IV infusion per dose

Arm title	Remicade - Remicade

Arm description:

Remicade followed by Remicade from Week 30

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

Dosage and administration details:

Remicade (5 mg/kg) by intravenous (IV) infusion administered as a 2 hour IV infusion per dose

Arm title	Remicade - CT-P13

Arm description:

Remicade followed by CT-P13 from Week 30

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

Dosage and administration details:

CT-P13 (5 mg/kg) by intravenous (IV) infusion administered as a 2 hour IV infusion per dose

Number of subjects in period 2	CT-P13 - CT-P13	CT-P13 - Remicade	Remicade - Remicade
Started	48	44	41
Completed	44	40	37
Not completed	4	4	4
Consent withdrawn by subject	-	1	-
Disease progression	1	2	1
PATIENT WENT ABROAD SO ESV WAS NOT DONE	-	1	-
Pregnancy	-	-	1
Lost to follow-up	2	-	2
Protocol deviation	1	-	-

Number of subjects in period 2	Remicade - CT-P13
Started	47
Completed	45
Not completed	2
Consent withdrawn by subject	-
Disease progression	-
PATIENT WENT ABROAD SO ESV WAS NOT DONE	-
Pregnancy	-
Lost to follow-up	2
Protocol deviation	-

Baseline characteristics

Reporting groups	
Reporting group title	CT-P13
Reporting group description:	
Patients who were randomized to CT-P13-CT-P13 or CT-P13-Remicade treatment groups at Week0	
Reporting group title	Remicade
Reporting group description:	
Patients who were randomized to Remicade-Remicade or Remicade-CT-P13 treatment groups at Week0	

Reporting group values	CT-P13	Remicade	Total
Number of subjects	111	109	220
Age categorical Units: Subjects			
Adults (18-64 years)	108	108	216
From 65-84 years	3	1	4
Age continuous Units: years			
median	35	32	
full range (min-max)	18 to 69	18 to 69	-
Gender categorical Units: Subjects			
Female	48	49	97
Male	63	60	123

Subject analysis sets	
Subject analysis set title	CT-P13 - CT-P13
Subject analysis set type	Intention-to-treat
Subject analysis set description:	
The number of patients who randomized to CT-P13-CT-P13 treatment group at Week 0. CT-P13 followed by CT-P13 from Week 30	
Subject analysis set title	CT-P13 - Remicade
Subject analysis set type	Intention-to-treat
Subject analysis set description:	
The number of patients who randomized to CT-P13-Remicade treatment group at Week 0. CT-P13 followed by Remicade from Week 30	
Subject analysis set title	Remicade - Remicade
Subject analysis set type	Intention-to-treat
Subject analysis set description:	
The number of patients who randomized to Remicade-Remicade treatment group at Week 0. Remicade followed by Remicade from Week 30	
Subject analysis set title	Remicade - CT-P13
Subject analysis set type	Intention-to-treat
Subject analysis set description:	
The number of patients who randomized to Remicade-CT-P13 treatment group at Week 0. Remicade followed by CT-P13 from Week 30	

Reporting group values	CT-P13 - CT-P13	CT-P13 - Remicade	Remicade - Remicade
Number of subjects	56	55	54
Age categorical Units: Subjects			
Adults (18-64 years)	54	54	53
From 65-84 years	2	1	1
Age continuous Units: years			
median	39	31	31
full range (min-max)	19 to 68	18 to 69	18 to 69
Gender categorical Units: Subjects			
Female	27	21	28
Male	29	34	26

Reporting group values	Remicade - CT-P13		
Number of subjects	55		
Age categorical Units: Subjects			
Adults (18-64 years)	55		
From 65-84 years	0		
Age continuous Units: years			
median	35		
full range (min-max)	19 to 63		
Gender categorical Units: Subjects			
Female	21		
Male	34		

End points

End points reporting groups

Reporting group title	CT-P13
Reporting group description:	
Patients who were randomized to CT-P13-CT-P13 or CT-P13-Remicade treatment groups at Week0	
Reporting group title	Remicade
Reporting group description:	
Patients who were randomized to Remicade-Remicade or Remicade-CT-P13 treatment groups at Week0	
Reporting group title	CT-P13 - CT-P13
Reporting group description:	
CT-P13 followed by CT-P13 from Week 30	
Reporting group title	CT-P13 - Remicade
Reporting group description:	
CT-P13 followed by Remicade from Week 30	
Reporting group title	Remicade - Remicade
Reporting group description:	
Remicade followed by Remicade from Week 30	
Reporting group title	Remicade - CT-P13
Reporting group description:	
Remicade followed by CT-P13 from Week 30	
Subject analysis set title	CT-P13 - CT-P13
Subject analysis set type	Intention-to-treat
Subject analysis set description:	
The number of patients who randomized to CT-P13-CT-P13 treatment group at Week 0. CT-P13 followed by CT-P13 from Week 30	
Subject analysis set title	CT-P13 - Remicade
Subject analysis set type	Intention-to-treat
Subject analysis set description:	
The number of patients who randomized to CT-P13-Remicade treatment group at Week 0. CT-P13 followed by Remicade from Week 30	
Subject analysis set title	Remicade - Remicade
Subject analysis set type	Intention-to-treat
Subject analysis set description:	
The number of patients who randomized to Remicade-Remicade treatment group at Week 0. Remicade followed by Remicade from Week 30	
Subject analysis set title	Remicade - CT-P13
Subject analysis set type	Intention-to-treat
Subject analysis set description:	
The number of patients who randomized to Remicade-CT-P13 treatment group at Week 0. Remicade followed by CT-P13 from Week 30	

Primary: CDAI-70

End point title	CDAI-70
End point description:	
Proportion of patients achieving response according to CDAI-70 criteria at Week 6	
End point type	Primary
End point timeframe:	
At Week 6	

End point values	CT-P13	Remicade		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	111	109		
Units: Participant	77	81		

Statistical analyses

Statistical analysis title	Primary efficacy endpoint - CDAI-70 response rate
Comparison groups	CT-P13 v Remicade
Number of subjects included in analysis	220
Analysis specification	Pre-specified
Analysis type	non-inferiority[1]
Parameter estimate	Difference in response rate
Point estimate	-4.9
Confidence interval	
level	Other: 97.5 %
sides	1-sided
lower limit	-17

Notes:

[1] - Non-inferiority margin is -20%.

Secondary: CDAI-70

End point title	CDAI-70
End point description:	
Proportion of patients achieving response according to CDAI-70 criteria at Week 30	
End point type	Secondary
End point timeframe:	
At Week 30	

End point values	CT-P13	Remicade		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	111	109		
Units: Participants	85	82		

Statistical analyses

No statistical analyses for this end point

Secondary: CDAI-70

End point title	CDAI-70

End point description:

Proportion of patients achieving response according to CDAI-70 criteria at Week 54

End point type	Secondary

End point timeframe:

At Week 54

End point values	CT-P13 - CT-P13	CT-P13 - Remicade	Remicade - Remicade	Remicade - CT-P13
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	56	55	54	55
Units: Participants	44	39	38	42

Statistical analyses

No statistical analyses for this end point

Secondary: Clinical remission

End point title	Clinical remission

End point description:

Proportion of patients achieving clinical remission at Week 6

End point type	Secondary

End point timeframe:

At Week 6

End point values	CT-P13	Remicade		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	111	109		
Units: Participants	47	49		

Statistical analyses

No statistical analyses for this end point

Secondary: Clinical remission

End point title	Clinical remission

End point description:

Proportion of patients achieving clinical remission at Week 30

End point type	Secondary

End point timeframe:

At Week 30

End point values	CT-P13	Remicade		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	111	109		
Units: Participants	61	62		

Statistical analyses

No statistical analyses for this end point

Secondary: Clinical remission

End point title	Clinical remission

End point description:

Proportion of patients achieving clinical remission at Week 54

End point type	Secondary

End point timeframe:

At Week 54

End point values	CT-P13 - CT-P13	CT-P13 - Remicade	Remicade - Remicade	Remicade - CT-P13
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	56	55	54	55
Units: Participants	35	32	29	33

Statistical analyses

No statistical analyses for this end point

Secondary: Short Inflammatory Bowel Disease Questionnaire

End point title	Short Inflammatory Bowel Disease Questionnaire

End point description:

End point type	Secondary

End point timeframe:

Baseline

End point values	CT-P13	Remicade		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	111	109		
Units: score				
arithmetic mean (standard deviation)	34.3 (± 10.92)	33.9 (± 9.27)		

Statistical analyses

No statistical analyses for this end point

Secondary: Short Inflammatory Bowel Disease Questionnaire

End point title	Short Inflammatory Bowel Disease Questionnaire

End point description:

End point type	Secondary

End point timeframe:

At Week 6

End point values	CT-P13	Remicade		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	107[2]	107[3]		
Units: score				
arithmetic mean (standard deviation)	46.4 (± 10.86)	45.8 (± 12.54)		

Notes:

[2] - The number of patients who had SIBDQ score at Week 6

[3] - The number of patients who had SIBDQ score at Week 6

Statistical analyses

No statistical analyses for this end point

Secondary: Short Inflammatory Bowel Disease Questionnaire

End point title	Short Inflammatory Bowel Disease Questionnaire

End point description:

End point type	Secondary

End point timeframe:

At Week 30

End point values	CT-P13	Remicade		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	92[4]	88[5]		
Units: score				
arithmetic mean (standard deviation)	51.1 (± 11.96)	52.5 (± 10.68)		

Notes:

[4] - The number of patients who had SIBDQ score at Week 30

[5] - The number of patients who had SIBDQ score at Week 30

Statistical analyses

No statistical analyses for this end point

Secondary: Short Inflammatory Bowel Disease Questionnaire

End point title	Short Inflammatory Bowel Disease Questionnaire

End point description:

Arithmetic mean value of SIBDQ by 4 treatment groups

End point type	Secondary

End point timeframe:

Baseline

End point values	CT-P13 - CT-P13	CT-P13 - Remicade	Remicade - Remicade	Remicade - CT-P13
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	56	55	54	55
Units: score				
arithmetic mean (standard deviation)	34.7 (± 10.61)	33.8 (± 11.31)	33.3 (± 9.77)	34.5 (± 8.81)

Statistical analyses

No statistical analyses for this end point

Secondary: Short Inflammatory Bowel Disease Questionnaire

End point title	Short Inflammatory Bowel Disease Questionnaire

End point description:

End point type	Secondary

End point timeframe:

At Week 54

End point values	CT-P13 - CT-P13	CT-P13 - Remicade	Remicade - Remicade	Remicade - CT-P13
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	45[6]	41[7]	37[8]	47[9]
Units: score				
arithmetic mean (standard deviation)	54.4 (± 10.28)	54.1 (± 11.07)	52.6 (± 11.35)	51.2 (± 11.26)

Notes:

[6] - The number of patients who had SIBDQ score at Week 54

[7] - The number of patients who had SIBDQ score at Week 54

[8] - The number of patients who had SIBDQ score at Week 54

[9] - The number of patients who had SIBDQ score at Week 54

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information	
Timeframe for reporting adverse events:	
Up to End-of-Study Visit (8 weeks after Week 54 infusion)	
Adverse event reporting additional description:	
Adverse events was based on Treatment Emergent (Serious) Adverse Event	
Assessment type	Systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	19.1

Reporting groups	
Reporting group title	CT-P13 - CT-P13
Reporting group description:	
CT-P13 followed by CT-P13 from Week 30	
Reporting group title	CT-P13 - Remicade
Reporting group description:	
CT-P13 followed by Remicade from Week 30	
Reporting group title	Remicade - Remicade
Reporting group description:	
Remicade followed by Remicade from Week 30	
Reporting group title	Remicade - CT-P13
Reporting group description:	
Remicade followed by CT-P13 from Week 30	

Serious adverse events	CT-P13 - CT-P13	CT-P13 - Remicade	Remicade - Remicade
Total subjects affected by serious adverse events			
subjects affected / exposed	4 / 56 (7.14%)	4 / 55 (7.27%)	4 / 54 (7.41%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Injury, poisoning and procedural complications			
Infusion related reaction			
subjects affected / exposed	0 / 56 (0.00%)	0 / 55 (0.00%)	1 / 54 (1.85%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Road traffic accident			
subjects affected / exposed	0 / 56 (0.00%)	0 / 55 (0.00%)	1 / 54 (1.85%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nervous system disorders			

Syncope			
subjects affected / exposed	0 / 56 (0.00%)	0 / 55 (0.00%)	0 / 54 (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
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	1 / 56 (1.79%)	0 / 55 (0.00%)	0 / 54 (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
General disorders and administration site conditions			
Generalised oedema			
subjects affected / exposed	0 / 56 (0.00%)	0 / 55 (0.00%)	1 / 54 (1.85%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	0 / 56 (0.00%)	1 / 55 (1.82%)	0 / 54 (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
Anal fissure			
subjects affected / exposed	1 / 56 (1.79%)	0 / 55 (0.00%)	1 / 54 (1.85%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Anal fistula			
subjects affected / exposed	0 / 56 (0.00%)	0 / 55 (0.00%)	1 / 54 (1.85%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Constipation			
subjects affected / exposed	0 / 56 (0.00%)	0 / 55 (0.00%)	0 / 54 (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
Duodenal ulcer haemorrhage			

subjects affected / exposed	0 / 56 (0.00%)	0 / 55 (0.00%)	0 / 54 (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
Gastritis haemorrhagic			
subjects affected / exposed	0 / 56 (0.00%)	0 / 55 (0.00%)	0 / 54 (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
Haematochezia			
subjects affected / exposed	0 / 56 (0.00%)	0 / 55 (0.00%)	0 / 54 (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
Haemorrhoids			
subjects affected / exposed	1 / 56 (1.79%)	0 / 55 (0.00%)	0 / 54 (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
Lower gastrointestinal haemorrhage			
subjects affected / exposed	0 / 56 (0.00%)	0 / 55 (0.00%)	0 / 54 (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
Hepatobiliary disorders			
Hepatitis			
subjects affected / exposed	0 / 56 (0.00%)	1 / 55 (1.82%)	0 / 54 (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			
Abscess intestinal			
subjects affected / exposed	0 / 56 (0.00%)	0 / 55 (0.00%)	0 / 54 (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
Acute sinusitis			
subjects affected / exposed	0 / 56 (0.00%)	1 / 55 (1.82%)	0 / 54 (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
Anal abscess			

subjects affected / exposed	1 / 56 (1.79%)	0 / 55 (0.00%)	0 / 54 (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
Cellulitis			
subjects affected / exposed	0 / 56 (0.00%)	1 / 55 (1.82%)	0 / 54 (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
Peritoneal tuberculosis			
subjects affected / exposed	1 / 56 (1.79%)	0 / 55 (0.00%)	0 / 54 (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
Tuberculous pleurisy			
subjects affected / exposed	0 / 56 (0.00%)	0 / 55 (0.00%)	0 / 54 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	Remicade - CT-P13		
Total subjects affected by serious adverse events			
subjects affected / exposed	7 / 55 (12.73%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events	0		
Injury, poisoning and procedural complications			
Infusion related reaction			
subjects affected / exposed	0 / 55 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Road traffic accident			
subjects affected / exposed	0 / 55 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Nervous system disorders			
Syncope			

subjects affected / exposed	1 / 55 (1.82%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	0 / 55 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
General disorders and administration site conditions			
Generalised oedema			
subjects affected / exposed	0 / 55 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	0 / 55 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Anal fissure			
subjects affected / exposed	0 / 55 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Anal fistula			
subjects affected / exposed	0 / 55 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Constipation			
subjects affected / exposed	1 / 55 (1.82%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Duodenal ulcer haemorrhage			
subjects affected / exposed	1 / 55 (1.82%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		

Gastritis haemorrhagic				
subjects affected / exposed	1 / 55 (1.82%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Haematochezia				
subjects affected / exposed	1 / 55 (1.82%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Haemorrhoids				
subjects affected / exposed	0 / 55 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Lower gastrointestinal haemorrhage				
subjects affected / exposed	1 / 55 (1.82%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Hepatobiliary disorders				
Hepatitis				
subjects affected / exposed	0 / 55 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Infections and infestations				
Abscess intestinal				
subjects affected / exposed	1 / 55 (1.82%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Acute sinusitis				
subjects affected / exposed	0 / 55 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Anal abscess				
subjects affected / exposed	0 / 55 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			

Cellulitis			
subjects affected / exposed	0 / 55 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Peritoneal tuberculosis			
subjects affected / exposed	0 / 55 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Tuberculous pleurisy			
subjects affected / exposed	1 / 55 (1.82%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		

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

Non-serious adverse events	CT-P13 - CT-P13	CT-P13 - Remicade	Remicade - Remicade
Total subjects affected by non-serious adverse events			
subjects affected / exposed	37 / 56 (66.07%)	36 / 55 (65.45%)	36 / 54 (66.67%)
Investigations			
Aspartate aminotransferase increased			
subjects affected / exposed	1 / 56 (1.79%)	1 / 55 (1.82%)	0 / 54 (0.00%)
occurrences (all)	1	1	0
Blood creatine phosphokinase increase			
subjects affected / exposed	1 / 56 (1.79%)	1 / 55 (1.82%)	4 / 54 (7.41%)
occurrences (all)	1	1	5
Gamma-glutamyltransferase increased			
subjects affected / exposed	3 / 56 (5.36%)	1 / 55 (1.82%)	0 / 54 (0.00%)
occurrences (all)	3	1	0
Injury, poisoning and procedural complications			
Infusion related reaction			
subjects affected / exposed	8 / 56 (14.29%)	2 / 55 (3.64%)	5 / 54 (9.26%)
occurrences (all)	13	2	7
Nervous system disorders			

Dizziness			
subjects affected / exposed	2 / 56 (3.57%)	0 / 55 (0.00%)	0 / 54 (0.00%)
occurrences (all)	2	0	0
Headache			
subjects affected / exposed	3 / 56 (5.36%)	1 / 55 (1.82%)	2 / 54 (3.70%)
occurrences (all)	3	1	2
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	5 / 56 (8.93%)	5 / 55 (9.09%)	5 / 54 (9.26%)
occurrences (all)	5	5	5
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	3 / 56 (5.36%)	8 / 55 (14.55%)	5 / 54 (9.26%)
occurrences (all)	3	9	7
Diarrhoea			
subjects affected / exposed	1 / 56 (1.79%)	3 / 55 (5.45%)	3 / 54 (5.56%)
occurrences (all)	2	3	3
Frequent bowel movements			
subjects affected / exposed	1 / 56 (1.79%)	3 / 55 (5.45%)	0 / 54 (0.00%)
occurrences (all)	2	4	0
Nausea			
subjects affected / exposed	0 / 56 (0.00%)	3 / 55 (5.45%)	3 / 54 (5.56%)
occurrences (all)	0	4	3
Pyrexia			
subjects affected / exposed	0 / 56 (0.00%)	3 / 55 (5.45%)	0 / 54 (0.00%)
occurrences (all)	0	3	0
Skin and subcutaneous tissue disorders			
Rash			
subjects affected / exposed	0 / 56 (0.00%)	1 / 55 (1.82%)	3 / 54 (5.56%)
occurrences (all)	0	1	4
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	3 / 56 (5.36%)	1 / 55 (1.82%)	4 / 54 (7.41%)
occurrences (all)	4	1	5
Infections and infestations			

Gastroenteritis			
subjects affected / exposed	1 / 56 (1.79%)	1 / 55 (1.82%)	1 / 54 (1.85%)
occurrences (all)	1	1	1
Influenza			
subjects affected / exposed	2 / 56 (3.57%)	1 / 55 (1.82%)	1 / 54 (1.85%)
occurrences (all)	3	1	1
Upper respiratory tract infection			
subjects affected / exposed	3 / 56 (5.36%)	1 / 55 (1.82%)	0 / 54 (0.00%)
occurrences (all)	3	1	0

Non-serious adverse events	Remicade - CT-P13		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	40 / 55 (72.73%)		
Investigations			
Aspartate aminotransferase increased			
subjects affected / exposed	3 / 55 (5.45%)		
occurrences (all)	3		
Blood creatine phosphokinase increase			
subjects affected / exposed	3 / 55 (5.45%)		
occurrences (all)	3		
Gamma-glutamyltransferase increased			
subjects affected / exposed	1 / 55 (1.82%)		
occurrences (all)	1		
Injury, poisoning and procedural complications			
Infusion related reaction			
subjects affected / exposed	4 / 55 (7.27%)		
occurrences (all)	4		
Nervous system disorders			
Dizziness			
subjects affected / exposed	4 / 55 (7.27%)		
occurrences (all)	4		
Headache			
subjects affected / exposed	3 / 55 (5.45%)		
occurrences (all)	3		
Blood and lymphatic system disorders			

Anaemia			
subjects affected / exposed	4 / 55 (7.27%)		
occurrences (all)	4		
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	4 / 55 (7.27%)		
occurrences (all)	6		
Diarrhoea			
subjects affected / exposed	0 / 55 (0.00%)		
occurrences (all)	0		
Frequent bowel movements			
subjects affected / exposed	1 / 55 (1.82%)		
occurrences (all)	1		
Nausea			
subjects affected / exposed	0 / 55 (0.00%)		
occurrences (all)	0		
Pyrexia			
subjects affected / exposed	1 / 55 (1.82%)		
occurrences (all)	1		
Skin and subcutaneous tissue disorders			
Rash			
subjects affected / exposed	0 / 55 (0.00%)		
occurrences (all)	0		
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	4 / 55 (7.27%)		
occurrences (all)	4		
Infections and infestations			
Gastroenteritis			
subjects affected / exposed	3 / 55 (5.45%)		
occurrences (all)	3		
Influenza			
subjects affected / exposed	5 / 55 (9.09%)		
occurrences (all)	6		
Upper respiratory tract infection			

subjects affected / exposed occurrences (all)	0 / 55 (0.00%) 0		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
01 December 2014	Summary of significant changes included the following: • Patient who has a Stoma (e.g., ileostomy or colostomy) within 6 months prior to randomization cannot enrolled in this study • Deletion of Cav, Swing, Degree of fluctuation as PK enpoints • Revision of the wording on margin justification, and define the population for primary efficacy analysis • Biomarker analysis was added as tertiary endoint • Deletion of time to loss of response up to and including Week 54 in the Week 13 responders as endpoint. • To define per-protocol definition in regarding to major deviations • Other administrative changes
22 December 2014	Summary of significant changes included the following: • To exclude patients who have been administered with any TNFα inhibitors.
10 February 2015	Summary of significant changes included the following: • Deleted PK time point after Week 22 • To exclude enteral or parenteral nutrition use during the study

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported