

**Clinical trial results:****A Phase 3, Randomized, Open-label, Parallel-group, Multicenter Trial to Evaluate the Safety and Efficacy of Infliximab (REMICADE®) in Pediatric Subjects with Moderately to Severely Active Ulcerative Colitis****Summary**

EudraCT number	2006-000410-20
Trial protocol	DK BE IT NL
Global end of trial date	24 June 2010

Results information

Result version number	v1 (current)
This version publication date	15 July 2016
First version publication date	15 July 2016

Trial information**Trial identification**

Sponsor protocol code	C0168T72
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Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT00336492
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Centocor BV
Sponsor organisation address	Einsteinweg 101, 2333 , CB Leiden, Netherlands,
Public contact	Clinical Registry Group, Centocor BV, ClinicalTrialsEU@its.jnj.com
Scientific contact	Clinical Registry Group, Centocor BV, ClinicalTrialsEU@its.jnj.com

Notes:

Paediatric regulatory details

Is trial part of an agreed paediatric investigation plan (PIP)	Yes
EMA paediatric investigation plan number(s)	EMEA-000240-PIP01-50
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?	Yes

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	24 June 2010
Is this the analysis of the primary completion data?	No
Global end of trial reached?	Yes
Global end of trial date	24 June 2010
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The primary objectives of this study were to evaluate the efficacy of a 3-dose induction regimen of infliximab in inducing clinical response, as measured by the Mayo score, in pediatric participants with moderately to severely active UC, and to evaluate the safety profile of infliximab during induction and maintenance treatment.

Protection of trial subjects:

This study was conducted in accordance with the ethical principles that have their origin in the Declaration of Helsinki and that are consistent with Good Clinical Practices and applicable regulatory requirements. Known instances of nonconformance were documented and are not considered to have had an impact on the overall conclusions of this study. Safety was evaluated based on the variables like Adverse events, Clinical laboratory tests (hematology, serum chemistry), Vital sign measurements, Physical examinations, Tuberculosis testing, Antinuclear antibodies/anti-double-stranded DNA antibodies.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	25 August 2006
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	Belgium: 3
Country: Number of subjects enrolled	Canada: 20
Country: Number of subjects enrolled	Netherlands: 5
Country: Number of subjects enrolled	United States: 32
Worldwide total number of subjects	60
EEA total number of subjects	8

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)	15
Adolescents (12-17 years)	45
Adults (18-64 years)	0
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

A total of 60 pediatric participants were enrolled at 23 investigational sites in North America and Europe.

Pre-assignment

Screening details:

A total of 60 participants were enrolled and included in the primary efficacy endpoint analysis and the safety analyses. At Week 8, 45 participants were randomized to 1 of 2 maintenance treatment regimens.

Period 1

Period 1 title	Induction Regimen
Is this the baseline period?	Yes
Allocation method	Non-randomised - controlled
Blinding used	Not blinded

Blinding implementation details:

Open label

Arms

Arm title	Infliximab 5 mg/kg
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Arm description:

All subjects treated at Week 0.

Arm type	Experimental
Investigational medicinal product name	Infliximab
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Powder for injection
Routes of administration	Intravenous use

Dosage and administration details:

infliximab 5 mg/kg administered at Weeks 0, 2, and 6

Number of subjects in period 1	Infliximab 5 mg/kg
Started	60
Completed	45
Not completed	15
Adverse Event	4
Other	5
Lack of efficacy	6

Period 2

Period 2 title	Maintenance Treatment Regimen
Is this the baseline period?	No
Allocation method	Randomised - controlled
Blinding used	Not blinded

Arms

Are arms mutually exclusive?	No
Arm title	Infliximab 5 mg/kg q8 wks

Arm description:

Infliximab was administered as 5 milligram per kilogram [mg/kg] in a maintenance treatment regimen every 8 weeks (q8w) through Week 46.

Arm type	Experimental
Investigational medicinal product name	Infliximab
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Powder for solution for injection
Routes of administration	Intravenous use

Dosage and administration details:

Infliximab was administered as 5 milligram per kilogram [mg/kg] in a maintenance treatment regimen every 8 weeks (q8w) through Week 46.

Arm title	Infliximab 5 mg/kg q12 wks
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Arm description:

Infliximab was administered as 5 milligram per kilogram [mg/kg] in a maintenance treatment regimen every 12 weeks (q12w) through Week 42.

Arm type	Experimental
Investigational medicinal product name	Infliximab
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Powder for solution for injection
Routes of administration	Intravenous use

Dosage and administration details:

Infliximab was administered as 5 milligram per kilogram [mg/kg] in a maintenance treatment regimen every 12 weeks (q12w) through Week 42.

Arm title	Not Randomized Group
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Arm description:

Participants who were not randomized at Week 8.

Arm type	No intervention
No investigational medicinal product assigned in this arm	

Number of subjects in period 2	Infliximab 5 mg/kg q8 wks	Infliximab 5 mg/kg q12 wks	Not Randomized Group
Started	22	23	15
Completed	18	12	0
Not completed	4	11	15
Adverse Event	3	6	4
Other	-	1	5
Lack of efficacy	1	4	6

Baseline characteristics

Reporting groups

Reporting group title Infliximab 5 mg/kg

Reporting group description:

All subjects treated at Week 0.

Reporting group values	Infliximab 5 mg/kg	Total	
Number of subjects	60	60	
Title for AgeCategorical Units: subjects			
Children (2-11 years)	15	15	
Adolescents (12-17 years)	45	45	
Adults (18-64 years)	0	0	
From 65 to 84 years	0	0	
85 years and over	0	0	
Title for AgeContinuous Units: years			
arithmetic mean	13.4		
standard deviation	± 3.1	-	
Title for Gender Units: subjects			
Female	32	32	
Male	28	28	

End points

End points reporting groups

Reporting group title	Infliximab 5 mg/kg
Reporting group description:	All subjects treated at Week 0.
Reporting group title	Infliximab 5 mg/kg q8 wks
Reporting group description:	Infliximab was administered as 5 milligram per kilogram [mg/kg] in a maintenance treatment regimen every 8 weeks (q8w) through Week 46.
Reporting group title	Infliximab 5 mg/kg q12 wks
Reporting group description:	Infliximab was administered as 5 milligram per kilogram [mg/kg] in a maintenance treatment regimen every 12 weeks (q12w) through Week 42.
Reporting group title	Not Randomized Group
Reporting group description:	Participants who were not randomized at Week 8.

Primary: The Number of Participants With Clinical Response at Week 8

End point title	The Number of Participants With Clinical Response at Week 8 ^[1]
End point description:	Range is 0 to 12 points, where 0 is the least disease activity, and 12 is the most disease activity. Clinical response at Week 8 is defined as a decrease from baseline in the Mayo score (based on symptoms of ulcerative colitis) by greater than or equal to (\geq) 30% and \geq 3 points, with a decrease in the rectal bleeding subscore \geq 1 or a rectal bleeding subscore of 0 or 1. Treatment failure rules (patients who discontinued study agent due to lack of therapeutic effect, had a colectomy or ostomy, or had protocol-prohibited medication changes) were applied to determine the final clinical response status for each patient.
End point type	Primary
End point timeframe:	Week 8
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: No statistical analysis has been planned for this endpoint.

End point values	Infliximab 5 mg/kg			
Subject group type	Reporting group			
Number of subjects analysed	60			
Units: Participants	44			

Statistical analyses

No statistical analyses for this end point

Secondary: The Number of Participants With Pediatric Ulcerative Colitis Activity Index (PUCAI) Remission at Week 54

End point title	The Number of Participants With Pediatric Ulcerative Colitis
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End point description:

Range is 0 to 85 points, where 0 is the least disease activity, and 85 is the most disease activity. Remission is a score less than (<) 10. In addition to the PUCAI remission status, treatment failure rules (patients who discontinued study agent due to lack of therapeutic effect, had a colectomy or ostomy, had protocol-prohibited medication changes, or stepped up) were applied to determine the final PUCAI.

End point type Secondary

End point timeframe:

Week 54

End point values	Infliximab 5 mg/kg q8 wks	Infliximab 5 mg/kg q12 wks		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	21	22		
Units: Participants	8	4		

Statistical analyses

Statistical analysis title Statistical Analysis 1

Statistical analysis description:

Statistical Analysis 1 for The Number of Participants With Pediatric Ulcerative Colitis Activity Index (PUCAI) Remission at Week 54.

Comparison groups	Infliximab 5 mg/kg q8 wks v Infliximab 5 mg/kg q12 wks
Number of subjects included in analysis	43
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.146
Method	Chi-squared

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Week 0 through Week 54

Assessment type	Non-systematic
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Dictionary used

Dictionary name	WHOART
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Dictionary version	NA
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Reporting groups

Reporting group title	Subjects Not Randomized at Week 8
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Reporting group description:

Infliximab was administered as 5 milligram per kilogram [mg/kg] at Weeks 0, 2, and 6.

Reporting group title	Infliximab 5 mg/kg q12 wks
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Reporting group description:

Infliximab was administered as 5 milligram per kilogram [mg/kg] in a maintenance treatment regimen every 12 weeks (q12w) through Week 42.

Reporting group title	Infliximab 5 mg/kg q8 wks
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Reporting group description:

Infliximab was administered as 5 milligram per kilogram [mg/kg] in a maintenance treatment regimen every 8 weeks (q8w) through Week 46.

Serious adverse events	Subjects Not Randomized at Week 8	Infliximab 5 mg/kg q12 wks	Infliximab 5 mg/kg q8 wks
Total subjects affected by serious adverse events			
subjects affected / exposed	5 / 15 (33.33%)	5 / 23 (21.74%)	4 / 22 (18.18%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events			
Blood and lymphatic system disorders			
Anemia			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 15 (0.00%)	0 / 23 (0.00%)	1 / 22 (4.55%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Immune system disorders			
Cellulitis			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 15 (0.00%)	0 / 23 (0.00%)	1 / 22 (4.55%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infection			

alternative assessment type: Systematic			
subjects affected / exposed	0 / 15 (0.00%)	0 / 23 (0.00%)	1 / 22 (4.55%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infection Viral			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 15 (0.00%)	0 / 23 (0.00%)	1 / 22 (4.55%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Neutropenia			
subjects affected / exposed	1 / 15 (6.67%)	0 / 23 (0.00%)	0 / 22 (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
Gastrointestinal disorders			
Colitis Ulcerative			
subjects affected / exposed	4 / 15 (26.67%)	3 / 23 (13.04%)	2 / 22 (9.09%)
occurrences causally related to treatment / all	0 / 4	0 / 3	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pancreatitis			
subjects affected / exposed	0 / 15 (0.00%)	0 / 23 (0.00%)	1 / 22 (4.55%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			
Pharyngitis			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 15 (0.00%)	1 / 23 (4.35%)	0 / 22 (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
Pneumonia Lobar			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 15 (6.67%)	0 / 23 (0.00%)	0 / 22 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Renal and urinary disorders			
Urinary Tract Infection			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 15 (0.00%)	1 / 23 (4.35%)	0 / 22 (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

Frequency threshold for reporting non-serious adverse events: 4 %

Non-serious adverse events	Subjects Not Randomized at Week 8	Infliximab 5 mg/kg q12 wks	Infliximab 5 mg/kg q8 wks
Total subjects affected by non-serious adverse events			
subjects affected / exposed	12 / 15 (80.00%)	23 / 23 (100.00%)	21 / 22 (95.45%)
Vascular disorders			
Flushing			
subjects affected / exposed	0 / 15 (0.00%)	1 / 23 (4.35%)	1 / 22 (4.55%)
occurrences (all)	0	1	2
Hemorrhoids			
subjects affected / exposed	1 / 15 (6.67%)	0 / 23 (0.00%)	0 / 22 (0.00%)
occurrences (all)	1	0	0
General disorders and administration site conditions			
Chest Pain			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 15 (6.67%)	1 / 23 (4.35%)	0 / 22 (0.00%)
occurrences (all)	1	2	0
Chills			
subjects affected / exposed	1 / 15 (6.67%)	0 / 23 (0.00%)	0 / 22 (0.00%)
occurrences (all)	1	0	0
Cyst (Type Unknown)			
subjects affected / exposed	0 / 15 (0.00%)	0 / 23 (0.00%)	1 / 22 (4.55%)
occurrences (all)	0	0	1
Edema			
subjects affected / exposed	0 / 15 (0.00%)	1 / 23 (4.35%)	0 / 22 (0.00%)
occurrences (all)	0	1	0
Edema Peripheral			

subjects affected / exposed occurrences (all)	0 / 15 (0.00%) 0	1 / 23 (4.35%) 1	0 / 22 (0.00%) 0
Fatigue subjects affected / exposed occurrences (all)	0 / 15 (0.00%) 0	1 / 23 (4.35%) 1	1 / 22 (4.55%) 1
Pain subjects affected / exposed occurrences (all)	1 / 15 (6.67%) 1	4 / 23 (17.39%) 4	0 / 22 (0.00%) 0
Immune system disorders			
Cellulitis subjects affected / exposed occurrences (all)	0 / 15 (0.00%) 0	1 / 23 (4.35%) 1	0 / 22 (0.00%) 0
ESR Increased subjects affected / exposed occurrences (all)	0 / 15 (0.00%) 0	1 / 23 (4.35%) 1	0 / 22 (0.00%) 0
Fever subjects affected / exposed occurrences (all)	1 / 15 (6.67%) 1	1 / 23 (4.35%) 1	6 / 22 (27.27%) 7
Herpes Simplex subjects affected / exposed occurrences (all)	0 / 15 (0.00%) 0	0 / 23 (0.00%) 0	1 / 22 (4.55%) 1
Infection subjects affected / exposed occurrences (all)	0 / 15 (0.00%) 0	1 / 23 (4.35%) 1	0 / 22 (0.00%) 0
Infection Bacterial alternative assessment type: Systematic subjects affected / exposed occurrences (all)	1 / 15 (6.67%) 2	0 / 23 (0.00%) 0	0 / 22 (0.00%) 0
Inflammation subjects affected / exposed occurrences (all)	1 / 15 (6.67%) 1	0 / 23 (0.00%) 0	0 / 22 (0.00%) 0
Influenza subjects affected / exposed occurrences (all)	0 / 15 (0.00%) 0	2 / 23 (8.70%) 2	1 / 22 (4.55%) 1
Influenza-Like Symptoms			

subjects affected / exposed	0 / 15 (0.00%)	2 / 23 (8.70%)	0 / 22 (0.00%)
occurrences (all)	0	2	0
Leukopenia			
subjects affected / exposed	0 / 15 (0.00%)	1 / 23 (4.35%)	0 / 22 (0.00%)
occurrences (all)	0	1	0
Moniliasis			
subjects affected / exposed	0 / 15 (0.00%)	1 / 23 (4.35%)	1 / 22 (4.55%)
occurrences (all)	0	1	1
Neutropenia			
subjects affected / exposed	0 / 15 (0.00%)	0 / 23 (0.00%)	1 / 22 (4.55%)
occurrences (all)	0	0	1
Neutrophilia			
subjects affected / exposed	0 / 15 (0.00%)	1 / 23 (4.35%)	0 / 22 (0.00%)
occurrences (all)	0	1	0
Respiratory, thoracic and mediastinal disorders			
Asthma			
subjects affected / exposed	0 / 15 (0.00%)	1 / 23 (4.35%)	0 / 22 (0.00%)
occurrences (all)	0	1	0
Bronchitis			
subjects affected / exposed	0 / 15 (0.00%)	0 / 23 (0.00%)	2 / 22 (9.09%)
occurrences (all)	0	0	2
Cold-Like Symptoms			
subjects affected / exposed	0 / 15 (0.00%)	1 / 23 (4.35%)	0 / 22 (0.00%)
occurrences (all)	0	1	0
Coughing			
subjects affected / exposed	1 / 15 (6.67%)	3 / 23 (13.04%)	2 / 22 (9.09%)
occurrences (all)	1	3	3
Dyspnea			
subjects affected / exposed	0 / 15 (0.00%)	1 / 23 (4.35%)	2 / 22 (9.09%)
occurrences (all)	0	1	2
Pharyngitis			
subjects affected / exposed	3 / 15 (20.00%)	4 / 23 (17.39%)	4 / 22 (18.18%)
occurrences (all)	3	5	6
Respiratory Tract Allergic Reaction			

subjects affected / exposed occurrences (all)	0 / 15 (0.00%) 0	0 / 23 (0.00%) 0	1 / 22 (4.55%) 1
Rhinitis subjects affected / exposed occurrences (all)	0 / 15 (0.00%) 0	0 / 23 (0.00%) 0	1 / 22 (4.55%) 3
Sinusitis alternative assessment type: Systematic subjects affected / exposed occurrences (all)	1 / 15 (6.67%) 1	0 / 23 (0.00%) 0	2 / 22 (9.09%) 2
Stridor subjects affected / exposed occurrences (all)	0 / 15 (0.00%) 0	0 / 23 (0.00%) 0	1 / 22 (4.55%) 1
Throat Tightness subjects affected / exposed occurrences (all)	1 / 15 (6.67%) 1	0 / 23 (0.00%) 0	0 / 22 (0.00%) 0
Upper Respiratory Tract Infection alternative assessment type: Systematic subjects affected / exposed occurrences (all)	1 / 15 (6.67%) 2	6 / 23 (26.09%) 9	7 / 22 (31.82%) 12
Psychiatric disorders Anxiety subjects affected / exposed occurrences (all)	1 / 15 (6.67%) 1	0 / 23 (0.00%) 0	0 / 22 (0.00%) 0
Depression subjects affected / exposed occurrences (all)	0 / 15 (0.00%) 0	0 / 23 (0.00%) 0	1 / 22 (4.55%) 1
Insomnia subjects affected / exposed occurrences (all)	0 / 15 (0.00%) 0	0 / 23 (0.00%) 0	1 / 22 (4.55%) 1
Thinking Abnormal subjects affected / exposed occurrences (all)	1 / 15 (6.67%) 1	0 / 23 (0.00%) 0	0 / 22 (0.00%) 0
Congenital, familial and genetic disorders Congenital Anomaly Nos			

subjects affected / exposed occurrences (all)	0 / 15 (0.00%) 0	0 / 23 (0.00%) 0	1 / 22 (4.55%) 1
Cardiac disorders			
Cyanosis			
subjects affected / exposed occurrences (all)	0 / 15 (0.00%) 0	0 / 23 (0.00%) 0	1 / 22 (4.55%) 1
Pallor			
subjects affected / exposed occurrences (all)	0 / 15 (0.00%) 0	1 / 23 (4.35%) 1	0 / 22 (0.00%) 0
Palpitation			
subjects affected / exposed occurrences (all)	0 / 15 (0.00%) 0	1 / 23 (4.35%) 1	0 / 22 (0.00%) 0
Nervous system disorders			
Dizziness			
subjects affected / exposed occurrences (all)	0 / 15 (0.00%) 0	0 / 23 (0.00%) 0	1 / 22 (4.55%) 1
Headache			
alternative assessment type: Systematic			
subjects affected / exposed occurrences (all)	2 / 15 (13.33%) 2	3 / 23 (13.04%) 5	3 / 22 (13.64%) 6
Hyperkinesia			
subjects affected / exposed occurrences (all)	0 / 15 (0.00%) 0	1 / 23 (4.35%) 1	1 / 22 (4.55%) 1
Muscle Contractions Involuntary			
subjects affected / exposed occurrences (all)	0 / 15 (0.00%) 0	1 / 23 (4.35%) 1	0 / 22 (0.00%) 0
Blood and lymphatic system disorders			
Anemia			
alternative assessment type: Systematic			
subjects affected / exposed occurrences (all)	0 / 15 (0.00%) 0	2 / 23 (8.70%) 2	4 / 22 (18.18%) 4
Antinuclear Factor Test Positive			
subjects affected / exposed occurrences (all)	0 / 15 (0.00%) 0	1 / 23 (4.35%) 1	0 / 22 (0.00%) 0
Thrombocythemia			
alternative assessment type: Systematic			

subjects affected / exposed occurrences (all)	0 / 15 (0.00%) 0	2 / 23 (8.70%) 2	0 / 22 (0.00%) 0
Ear and labyrinth disorders			
Otitis			
subjects affected / exposed occurrences (all)	0 / 15 (0.00%) 0	1 / 23 (4.35%) 1	0 / 22 (0.00%) 0
Otitis Media			
subjects affected / exposed occurrences (all)	0 / 15 (0.00%) 0	0 / 23 (0.00%) 0	1 / 22 (4.55%) 1
Eye disorders			
Conjunctivitis			
alternative assessment type: Systematic			
subjects affected / exposed occurrences (all)	0 / 15 (0.00%) 0	1 / 23 (4.35%) 2	0 / 22 (0.00%) 0
Glaucoma			
subjects affected / exposed occurrences (all)	0 / 15 (0.00%) 0	0 / 23 (0.00%) 0	1 / 22 (4.55%) 1
Gastrointestinal disorders			
Abdominal Pain			
alternative assessment type: Systematic			
subjects affected / exposed occurrences (all)	3 / 15 (20.00%) 3	2 / 23 (8.70%) 2	3 / 22 (13.64%) 3
Blood in Stool			
alternative assessment type: Systematic			
subjects affected / exposed occurrences (all)	1 / 15 (6.67%) 1	1 / 23 (4.35%) 1	0 / 22 (0.00%) 0
Colitis Ulcerative			
alternative assessment type: Systematic			
subjects affected / exposed occurrences (all)	1 / 15 (6.67%) 1	15 / 23 (65.22%) 25	7 / 22 (31.82%) 8
Diarrhea			
subjects affected / exposed occurrences (all)	0 / 15 (0.00%) 0	1 / 23 (4.35%) 1	1 / 22 (4.55%) 1
Diarrhea Bloody			
subjects affected / exposed occurrences (all)	0 / 15 (0.00%) 0	0 / 23 (0.00%) 0	1 / 22 (4.55%) 1

Gastritis			
subjects affected / exposed	0 / 15 (0.00%)	0 / 23 (0.00%)	1 / 22 (4.55%)
occurrences (all)	0	0	1
Nausea			
subjects affected / exposed	0 / 15 (0.00%)	1 / 23 (4.35%)	2 / 22 (9.09%)
occurrences (all)	0	1	3
Stomatitis Ulcerative			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 15 (0.00%)	0 / 23 (0.00%)	2 / 22 (9.09%)
occurrences (all)	0	0	3
Vomiting			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 15 (6.67%)	2 / 23 (8.70%)	1 / 22 (4.55%)
occurrences (all)	1	3	2
Hepatobiliary disorders			
Hepatic Enzymes Increased			
subjects affected / exposed	0 / 15 (0.00%)	2 / 23 (8.70%)	0 / 22 (0.00%)
occurrences (all)	0	3	0
Hepatic Function Abnormal			
subjects affected / exposed	0 / 15 (0.00%)	1 / 23 (4.35%)	0 / 22 (0.00%)
occurrences (all)	0	1	0
SGOT Increased			
subjects affected / exposed	0 / 15 (0.00%)	1 / 23 (4.35%)	0 / 22 (0.00%)
occurrences (all)	0	1	0
SGPT Increased			
subjects affected / exposed	0 / 15 (0.00%)	1 / 23 (4.35%)	0 / 22 (0.00%)
occurrences (all)	0	1	0
Skin and subcutaneous tissue disorders			
Acne			
subjects affected / exposed	0 / 15 (0.00%)	1 / 23 (4.35%)	0 / 22 (0.00%)
occurrences (all)	0	1	0
Alopecia			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 15 (0.00%)	0 / 23 (0.00%)	1 / 22 (4.55%)
occurrences (all)	0	0	1
Dermatitis			

subjects affected / exposed	0 / 15 (0.00%)	0 / 23 (0.00%)	1 / 22 (4.55%)
occurrences (all)	0	0	1
Eczema			
subjects affected / exposed	0 / 15 (0.00%)	0 / 23 (0.00%)	2 / 22 (9.09%)
occurrences (all)	0	0	2
Onychocryptosis			
subjects affected / exposed	0 / 15 (0.00%)	1 / 23 (4.35%)	0 / 22 (0.00%)
occurrences (all)	0	1	0
Onychomycosis			
subjects affected / exposed	0 / 15 (0.00%)	1 / 23 (4.35%)	0 / 22 (0.00%)
occurrences (all)	0	1	0
Pruritus			
subjects affected / exposed	0 / 15 (0.00%)	0 / 23 (0.00%)	1 / 22 (4.55%)
occurrences (all)	0	0	8
Psoriasis			
subjects affected / exposed	0 / 15 (0.00%)	1 / 23 (4.35%)	0 / 22 (0.00%)
occurrences (all)	0	1	0
Rash			
subjects affected / exposed	0 / 15 (0.00%)	1 / 23 (4.35%)	2 / 22 (9.09%)
occurrences (all)	0	1	2
Rash Pustular			
subjects affected / exposed	0 / 15 (0.00%)	0 / 23 (0.00%)	1 / 22 (4.55%)
occurrences (all)	0	0	1
Skin Lesion			
subjects affected / exposed	0 / 15 (0.00%)	0 / 23 (0.00%)	1 / 22 (4.55%)
occurrences (all)	0	0	1
Sweating Increased			
subjects affected / exposed	0 / 15 (0.00%)	1 / 23 (4.35%)	0 / 22 (0.00%)
occurrences (all)	0	1	0
Urticaria			
subjects affected / exposed	0 / 15 (0.00%)	0 / 23 (0.00%)	1 / 22 (4.55%)
occurrences (all)	0	0	4
Verruca			
subjects affected / exposed	0 / 15 (0.00%)	1 / 23 (4.35%)	0 / 22 (0.00%)
occurrences (all)	0	1	0
Renal and urinary disorders			

Hematuria			
subjects affected / exposed	0 / 15 (0.00%)	1 / 23 (4.35%)	0 / 22 (0.00%)
occurrences (all)	0	1	0
Urinary Tract Infection			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 15 (0.00%)	2 / 23 (8.70%)	1 / 22 (4.55%)
occurrences (all)	0	2	2
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	0 / 15 (0.00%)	0 / 23 (0.00%)	1 / 22 (4.55%)
occurrences (all)	0	0	1
Back Pain			
subjects affected / exposed	0 / 15 (0.00%)	1 / 23 (4.35%)	1 / 22 (4.55%)
occurrences (all)	0	2	2
Bone Development Abnormal			
subjects affected / exposed	0 / 15 (0.00%)	0 / 23 (0.00%)	1 / 22 (4.55%)
occurrences (all)	0	0	1
Joint Stiffness			
subjects affected / exposed	0 / 15 (0.00%)	0 / 23 (0.00%)	1 / 22 (4.55%)
occurrences (all)	0	0	1
Joint Swelling			
subjects affected / exposed	0 / 15 (0.00%)	1 / 23 (4.35%)	0 / 22 (0.00%)
occurrences (all)	0	1	0
Osteopenia			
subjects affected / exposed	0 / 15 (0.00%)	1 / 23 (4.35%)	0 / 22 (0.00%)
occurrences (all)	0	1	0
Sprain			
subjects affected / exposed	0 / 15 (0.00%)	0 / 23 (0.00%)	1 / 22 (4.55%)
occurrences (all)	0	0	1
Metabolism and nutrition disorders			
Hypokalemia			
subjects affected / exposed	1 / 15 (6.67%)	0 / 23 (0.00%)	0 / 22 (0.00%)
occurrences (all)	1	0	0
Malnutrition			
subjects affected / exposed	1 / 15 (6.67%)	0 / 23 (0.00%)	0 / 22 (0.00%)
occurrences (all)	1	0	0

Serum Iron Decreased subjects affected / exposed occurrences (all)	0 / 15 (0.00%) 0	0 / 23 (0.00%) 0	1 / 22 (4.55%) 1
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More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
01 March 2007	The first amendment included clarifications about the conduct of the study and minor editorial changes. The major changes were as follows. Statements were added to describe postmarketing reports that link the occurrence of hepatosplenic T-cell lymphoma (HSTCL) with the concomitant use of immunomodulators in adolescent and young adult patients with Crohn's disease. The required use of such immunomodulators concomitantly with infliximab during the study was removed. Planned enrollment was increased from 40 to 60 participants. Participants who had failed only treatment with 5-ASA compounds were allowed to enter the study. The definition of a positive study was modified and the primary analysis was revised. Intervals were changed between screening and the diagnosis of UC and between screening and the discontinuation or use of specific medications or therapies. The Pediatric Ulcerative Colitis Activity Index (PUCAI) was added as a measure of efficacy to be assessed at every visit at which a partial Mayo score was obtained and the major secondary endpoints were modified. The number of sigmoidoscopies required during the study was reduced. A DMC was added. Criteria for screening laboratory test results were revised
04 February 2008	The second amendment included modifications to concomitant medication and exclusion criteria, particularly with regard to corticosteroid use, along with minor editorial changes.
16 October 2008	The third amendment updated the text about HSTCL to be consistent with both the informed consent form and the April 2008 risk update document.

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.

No notable study limitations were identified by the sponsor.

Notes: