Clinical trial results:
A Multicenter, Open-Label Study to Evaluate the Long Term Efficacy, Safety, and Tolerability of Repeated Administration of Adalimumab in Subjects With Crohn's Disease

Summary

EudraCT number	2013-004034-15
Trial protocol	HU GB DE ES CZ IT SK DK AT BE FR
Global end of trial date	03 November 2017

Results information

Result version number	v1 (current)
This version publication date	31 October 2018
First version publication date	31 October 2018

Trial information

Trial identification

Sponsor protocol code	M14-347

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02185014
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	AbbVie Deutschland GmbH & Co. KG
Sponsor organisation address	AbbVie House, Vanwall Business Park, Vanwall Road, Maidenhead, Berkshire, United Kingdom, SL6-4UB
Public contact	Global Medical Services, AbbVie, 001 800-633-9110,
Scientific contact	Anne Robinson, AbbVie, anne.robinson@abbvie.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	03 November 2017
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	03 November 2017
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The purpose of this study is to evaluate the long term efficacy, safety, and tolerability of repeated administration of adalimumab in subjects with Crohn's disease.

Protection of trial subjects:

Subject and/or his or her representative read and understood the information provided about the study and gave written permission.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	12 August 2014
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	Austria: 6
Country: Number of subjects enrolled	Belgium: 3
Country: Number of subjects enrolled	Canada: 46
Country: Number of subjects enrolled	Czech Republic: 27
Country: Number of subjects enrolled	Denmark: 4
Country: Number of subjects enrolled	France: 6
Country: Number of subjects enrolled	Germany: 9
Country: Number of subjects enrolled	Hungary: 2
Country: Number of subjects enrolled	Israel: 7
Country: Number of subjects enrolled	Italy: 12
Country: Number of subjects enrolled	Netherlands: 12
Country: Number of subjects enrolled	Poland: 22
Country: Number of subjects enrolled	Slovakia: 1
Country: Number of subjects enrolled	Switzerland: 5
Country: Number of subjects enrolled	Ukraine: 8
Country: Number of subjects enrolled	United Kingdom: 6
Country: Number of subjects enrolled	United States: 76
Worldwide total number of subjects	252
EEA total number of subjects	110

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)	245
From 65 to 84 years	7
85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

Subjects who completed Study M14-115 (NCT02185014) were eligible to enroll in this study.

Period 1

Period 1 title	Overall Study (overall period)
Is this the baseline period?	Yes
Allocation method	Not applicable
Blinding used	Not blinded

Arms

Arm title	Adalimumab

Arm description:

Participants received open-label adalimumab 40 mg by subcutaneous injection every other week for 40 weeks.

Arm type	Experimental
Investigational medicinal product name	Adalimumab
Investigational medicinal product code	
Other name	Humira, ABT-D2E7
Pharmaceutical forms	Solution for injection in pre-filled syringe
Routes of administration	Subcutaneous use

Dosage and administration details:

Adalimumab pre-filled syringe, administered by subcutaneous injection

Number of subjects in period 1	Adalimumab
Started	252
Completed	198
Not completed	54
Requires Alternative/Prohibited Therapy	5
Not Specified	4
Adverse event	18
Subject Noncompliance	1
Withdrew consent	8
Lost to follow-up	4
Lack of efficacy	14

Baseline characteristics

Reporting groups	
Reporting group title	Adalimumab
Reporting group description:	
Participants received open-label adalimumab 40 mg by subcutaneous injection every other week for 40 weeks.	

Reporting group values	Adalimumab	Total	
Number of subjects	252	252	
Age categorical			
Units: Subjects			
Age continuous			
Baseline characteristics from lead-in study M14-115			
Units: years			
arithmetic mean	37.5		
standard deviation	± 12.71	-	
Gender categorical			
Baseline characteristics from lead-in study M14-115			
Units: Subjects			
Female	139	139	
Male	113	113	
Ethnicity (NIH/OMB)			
Baseline characteristics from lead-in study M14-115			
Units: Subjects			
Hispanic or Latino	7	7	
Not Hispanic or Latino	0	0	
Unknown or Not Reported	245	245	
Race (NIH/OMB)			
Baseline characteristics from lead-in study M14-115			
Units: Subjects			
American Indian or Alaska Native	0	0	
Asian	10	10	
Native Hawaiian or Other Pacific Islander	0	0	
Black or African American	12	12	
White	229	229	
More than one race	1	1	
Unknown or Not Reported	0	0	
Simplified endoscopic score for crohn's disease (SES-CD) Total Score			
The SES-CD evaluates 4 endoscopic variables in 5 segments assessed during ileocolonoscopy. The SES-CD total score is the sum of the 4 endoscopic variable scores and range from 0 to 56, where higher scores indicate more severe disease. Baseline characteristics from lead-in study M14-115.			
Units: units on a scale			
arithmetic mean	14.2		
standard deviation	± 6.74	-	

End points

End points reporting groups

Reporting group title	Adalimumab

Reporting group description:

Participants received open-label adalimumab 40 mg by subcutaneous injection every other week for 40 weeks.

Primary: Percentage of participants with endoscopic improvement at week 40 in Participants with endoscopic improvement at Week 0

End point title	Percentage of participants with endoscopic improvement at week 40 in Participants with endoscopic improvement at Week 0[1]

End point description:

Endoscopic improvement defined as a simple endoscopic score for Crohn's Disease (SES-CD) score of ≤4 and at least a 2-point reduction compared with Study M14-115 (NCT02185014) Baseline and no subscore greater than 1 in any individual endoscopic variable. The SES-CD evaluates 4 endoscopic variables (ulcer size ranging from 0 [none] to 3 [very large]; ulcerated surface ranging from 0 [none] to 3 [>30%]; affected surface ranging from 0 [none] to 3 [>75%], and narrowing ranging from 0 [none] to 3 [cannot be passed]) in 5 segments assessed during ileocolonoscopy (ileum, right colon, transverse colon, sigmoid and left colon, and rectum). The score for each endoscopic variable is the sum of values obtained for each segment and range from 0 to 15 where higher scores indicate more severe disease. The Total Score is the sum of the 4 endoscopic variable scores and range from 0 to 56, where higher scores indicate more severe disease. Nonresponder imputation (NRI) was used for missing data.

End point type	Primary

End point timeframe:

Week 40

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: Descriptive data are summarized for this end point per protocol.

End point values	Adalimumab			
Subject group type	Reporting group			
Number of subjects analysed	76[2]			
Units: percentage of participants				
number (confidence interval 95%)	31.6 (21.1 to 42.0)			

Notes:

[2] - All subjects with endoscopic improvement at Week 0 in Study M14-347 (end of lead-in Study M14-115)

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Treatment-emergent adverse events (TEAEs) and serious adverse events (TESAEs) were collected from first dose of study drug until 70 days after the last dose of study drug (up to 48 weeks).

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	21.0

Reporting groups

Reporting group title	Adalimumab

Reporting group description:

Participants received open-label adalimumab 40 mg by subcutaneous injection every other week for 40 weeks.

Serious adverse events	Adalimumab		
Total subjects affected by serious adverse events			
subjects affected / exposed	27 / 252 (10.71%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events			
Injury, poisoning and procedural complications			
POST PROCEDURAL HAEMORRHAGE			
subjects affected / exposed	1 / 252 (0.40%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Nervous system disorders			
HEADACHE			
subjects affected / exposed	1 / 252 (0.40%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
General disorders and administration site conditions			
NON-CARDIAC CHEST PAIN			
subjects affected / exposed	1 / 252 (0.40%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Gastrointestinal disorders			
ABDOMINAL PAIN UPPER			

subjects affected / exposed	1 / 252 (0.40%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
CROHN'S DISEASE			
subjects affected / exposed	14 / 252 (5.56%)		
occurrences causally related to treatment / all	0 / 16		
deaths causally related to treatment / all	0 / 0		
ILEAL STENOSIS			
subjects affected / exposed	1 / 252 (0.40%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
INTESTINAL OBSTRUCTION			
subjects affected / exposed	3 / 252 (1.19%)		
occurrences causally related to treatment / all	0 / 3		
deaths causally related to treatment / all	0 / 0		
SMALL INTESTINAL OBSTRUCTION			
subjects affected / exposed	4 / 252 (1.59%)		
occurrences causally related to treatment / all	0 / 4		
deaths causally related to treatment / all	0 / 0		
Renal and urinary disorders			
NEPHROLITHIASIS			
subjects affected / exposed	1 / 252 (0.40%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Musculoskeletal and connective tissue disorders			
INTERVERTEBRAL DISC PROTRUSION			
subjects affected / exposed	1 / 252 (0.40%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Infections and infestations			
ANAL ABSCESS			

subjects affected / exposed	3 / 252 (1.19%)		
occurrences causally related to treatment / all	1 / 3		
deaths causally related to treatment / all	0 / 0		

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

Non-serious adverse events	Adalimumab		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	65 / 252 (25.79%)		
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
ACROCHORDON			
subjects affected / exposed	2 / 252 (0.79%)		
occurrences (all)	2		
GASTROINTESTINAL TRACT ADENOMA			
subjects affected / exposed	1 / 252 (0.40%)		
occurrences (all)	1		
UTERINE LEIOMYOMA			
subjects affected / exposed	1 / 252 (0.40%)		
occurrences (all)	1		
Vascular disorders			
FLUSHING			
subjects affected / exposed	1 / 252 (0.40%)		
occurrences (all)	1		
HOT FLUSH			
subjects affected / exposed	1 / 252 (0.40%)		
occurrences (all)	1		
HYPERTENSION			
subjects affected / exposed	3 / 252 (1.19%)		
occurrences (all)	4		
PERIPHERAL VENOUS DISEASE			
subjects affected / exposed	1 / 252 (0.40%)		
occurrences (all)	3		
General disorders and administration site conditions			

CHEST PAIN				
subjects affected / exposed	2 / 252 (0.79%)			
occurrences (all)	2			
DRUG INTOLERANCE				
subjects affected / exposed	1 / 252 (0.40%)			
occurrences (all)	1			
HYPERTHERMIA				
subjects affected / exposed	1 / 252 (0.40%)			
occurrences (all)	1			
FATIGUE				
subjects affected / exposed	2 / 252 (0.79%)			
occurrences (all)	2			
INFLUENZA LIKE ILLNESS				
subjects affected / exposed	1 / 252 (0.40%)			
occurrences (all)	1			
INJECTION SITE BRUISING				
subjects affected / exposed	1 / 252 (0.40%)			
occurrences (all)	1			
INJECTION SITE PAIN				
subjects affected / exposed	1 / 252 (0.40%)			
occurrences (all)	1			
INJECTION SITE PRURITUS				
subjects affected / exposed	1 / 252 (0.40%)			
occurrences (all)	1			
INJECTION SITE REACTION				
subjects affected / exposed	1 / 252 (0.40%)			
occurrences (all)	2			
NON-CARDIAC CHEST PAIN				
subjects affected / exposed	1 / 252 (0.40%)			
occurrences (all)	1			
OEDEMA PERIPHERAL				
subjects affected / exposed	2 / 252 (0.79%)			
occurrences (all)	2			
PAIN				
subjects affected / exposed	1 / 252 (0.40%)			
occurrences (all)	1			

PERIPHERAL SWELLING			
subjects affected / exposed	1 / 252 (0.40%)		
occurrences (all)	1		
POLYP			
subjects affected / exposed	1 / 252 (0.40%)		
occurrences (all)	1		
PYREXIA			
subjects affected / exposed	7 / 252 (2.78%)		
occurrences (all)	7		
Immune system disorders			
DRUG HYPERSENSITIVITY			
subjects affected / exposed	1 / 252 (0.40%)		
occurrences (all)	1		
SEASONAL ALLERGY			
subjects affected / exposed	1 / 252 (0.40%)		
occurrences (all)	1		
Reproductive system and breast disorders			
BREAST CYST			
subjects affected / exposed	1 / 252 (0.40%)		
occurrences (all)	1		
CERVICAL DYSPLASIA			
subjects affected / exposed	1 / 252 (0.40%)		
occurrences (all)	1		
DYSMENORRHOEA			
subjects affected / exposed	1 / 252 (0.40%)		
occurrences (all)	1		
DYSPAREUNIA			
subjects affected / exposed	1 / 252 (0.40%)		
occurrences (all)	1		
PROSTATITIS			
subjects affected / exposed	1 / 252 (0.40%)		
occurrences (all)	1		
VAGINAL HAEMORRHAGE			
subjects affected / exposed	1 / 252 (0.40%)		
occurrences (all)	1		
VAGINAL DISCHARGE			

subjects affected / exposed	1 / 252 (0.40%)		
occurrences (all)	1		
VULVOVAGINAL DRYNESS			
subjects affected / exposed	1 / 252 (0.40%)		
occurrences (all)	1		
Respiratory, thoracic and mediastinal disorders			
COUGH			
subjects affected / exposed	6 / 252 (2.38%)		
occurrences (all)	8		
NASAL ULCER			
subjects affected / exposed	1 / 252 (0.40%)		
occurrences (all)	1		
EPISTAXIS			
subjects affected / exposed	1 / 252 (0.40%)		
occurrences (all)	1		
OROPHARYNGEAL PAIN			
subjects affected / exposed	2 / 252 (0.79%)		
occurrences (all)	3		
PARANASAL SINUS HYPERSECRETION			
subjects affected / exposed	1 / 252 (0.40%)		
occurrences (all)	1		
RHINITIS ALLERGIC			
subjects affected / exposed	2 / 252 (0.79%)		
occurrences (all)	2		
RHINORRHOEA			
subjects affected / exposed	2 / 252 (0.79%)		
occurrences (all)	2		
SINUS CONGESTION			
subjects affected / exposed	2 / 252 (0.79%)		
occurrences (all)	2		
SINUS PAIN			
subjects affected / exposed	1 / 252 (0.40%)		
occurrences (all)	1		
TONSILLAR HYPERTROPHY			

subjects affected / exposed	1 / 252 (0.40%)		
occurrences (all)	1		
Psychiatric disorders			
ACUTE STRESS DISORDER			
subjects affected / exposed	1 / 252 (0.40%)		
occurrences (all)	1		
ANXIETY			
subjects affected / exposed	4 / 252 (1.59%)		
occurrences (all)	4		
BIPOLAR DISORDER			
subjects affected / exposed	1 / 252 (0.40%)		
occurrences (all)	1		
DEPRESSION			
subjects affected / exposed	4 / 252 (1.59%)		
occurrences (all)	4		
INSOMNIA			
subjects affected / exposed	4 / 252 (1.59%)		
occurrences (all)	4		
MOOD SWINGS			
subjects affected / exposed	1 / 252 (0.40%)		
occurrences (all)	1		
NIGHTMARE			
subjects affected / exposed	1 / 252 (0.40%)		
occurrences (all)	1		
RESTLESSNESS			
subjects affected / exposed	1 / 252 (0.40%)		
occurrences (all)	1		
SLEEP DISORDER			
subjects affected / exposed	1 / 252 (0.40%)		
occurrences (all)	1		
Investigations			
BLOOD BILIRUBIN INCREASED			
subjects affected / exposed	1 / 252 (0.40%)		
occurrences (all)	1		
ALANINE AMINOTRANSFERASE INCREASED			

subjects affected / exposed	1 / 252 (0.40%)			
occurrences (all)	1			
BLOOD CHOLESTEROL INCREASED				
subjects affected / exposed	1 / 252 (0.40%)			
occurrences (all)	1			
BLOOD CREATININE INCREASED				
subjects affected / exposed	1 / 252 (0.40%)			
occurrences (all)	1			
BLOOD TRIGLYCERIDES INCREASED				
subjects affected / exposed	4 / 252 (1.59%)			
occurrences (all)	7			
BLOOD URINE PRESENT				
subjects affected / exposed	3 / 252 (1.19%)			
occurrences (all)	4			
C-REACTIVE PROTEIN INCREASED				
subjects affected / exposed	1 / 252 (0.40%)			
occurrences (all)	1			
CLOSTRIDIUM TEST POSITIVE				
subjects affected / exposed	1 / 252 (0.40%)			
occurrences (all)	1			
LIVER FUNCTION TEST INCREASED				
subjects affected / exposed	2 / 252 (0.79%)			
occurrences (all)	2			
NEUTROPHIL COUNT INCREASED				
subjects affected / exposed	1 / 252 (0.40%)			
occurrences (all)	1			
NITRITE URINE PRESENT				
subjects affected / exposed	1 / 252 (0.40%)			
occurrences (all)	1			
PROTEIN URINE PRESENT				
subjects affected / exposed	1 / 252 (0.40%)			
occurrences (all)	3			
RED BLOOD CELLS URINE				
subjects affected / exposed	1 / 252 (0.40%)			
occurrences (all)	1			
RED BLOOD CELLS URINE POSITIVE				

subjects affected / exposed	1 / 252 (0.40%)		
occurrences (all)	2		
WEIGHT DECREASED			
subjects affected / exposed	1 / 252 (0.40%)		
occurrences (all)	1		
WHITE BLOOD CELL COUNT INCREASED			
subjects affected / exposed	2 / 252 (0.79%)		
occurrences (all)	2		
Injury, poisoning and procedural complications			
ARTHROPOD STING			
subjects affected / exposed	1 / 252 (0.40%)		
occurrences (all)	1		
CONTUSION			
subjects affected / exposed	1 / 252 (0.40%)		
occurrences (all)	1		
CORNEAL ABRASION			
subjects affected / exposed	1 / 252 (0.40%)		
occurrences (all)	1		
LIMB INJURY			
subjects affected / exposed	1 / 252 (0.40%)		
occurrences (all)	1		
POST PROCEDURAL DIARRHOEA			
subjects affected / exposed	1 / 252 (0.40%)		
occurrences (all)	1		
POST PROCEDURAL HAEMORRHAGE			
subjects affected / exposed	1 / 252 (0.40%)		
occurrences (all)	1		
POST-TRAUMATIC NECK SYNDROME			
subjects affected / exposed	1 / 252 (0.40%)		
occurrences (all)	1		
PROCEDURAL HAEMORRHAGE			
subjects affected / exposed	1 / 252 (0.40%)		
occurrences (all)	1		
RIB FRACTURE			

subjects affected / exposed	1 / 252 (0.40%)		
occurrences (all)	1		
ROAD TRAFFIC ACCIDENT			
subjects affected / exposed	1 / 252 (0.40%)		
occurrences (all)	1		
TOOTH FRACTURE			
subjects affected / exposed	1 / 252 (0.40%)		
occurrences (all)	1		
Cardiac disorders			
PALPITATIONS			
subjects affected / exposed	2 / 252 (0.79%)		
occurrences (all)	2		
Nervous system disorders			
BURNING SENSATION			
subjects affected / exposed	1 / 252 (0.40%)		
occurrences (all)	1		
DIZZINESS			
subjects affected / exposed	2 / 252 (0.79%)		
occurrences (all)	2		
HEADACHE			
subjects affected / exposed	12 / 252 (4.76%)		
occurrences (all)	24		
HYPOAESTHESIA			
subjects affected / exposed	1 / 252 (0.40%)		
occurrences (all)	1		
LETHARGY			
subjects affected / exposed	1 / 252 (0.40%)		
occurrences (all)	1		
MIGRAINE			
subjects affected / exposed	2 / 252 (0.79%)		
occurrences (all)	2		
PARAESTHESIA			
subjects affected / exposed	2 / 252 (0.79%)		
occurrences (all)	2		
SCIATICA			

subjects affected / exposed occurrences (all) SPINAL CLAUDICATION subjects affected / exposed occurrences (all) SYNCOPE subjects affected / exposed occurrences (all)	1 / 252 (0.40%) 1 1 / 252 (0.40%) 1 1 / 252 (0.40%) 1		
Blood and lymphatic system disorders ANAEMIA subjects affected / exposed occurrences (all) IRON DEFICIENCY ANAEMIA subjects affected / exposed occurrences (all) LEUKOPENIA subjects affected / exposed occurrences (all) LYMPHADENOPATHY subjects affected / exposed occurrences (all)	 3 / 252 (1.19%) 3 2 / 252 (0.79%) 2 3 / 252 (1.19%) 3 1 / 252 (0.40%) 1		
Eye disorders CATARACT subjects affected / exposed occurrences (all) KERATITIS subjects affected / exposed occurrences (all) VISION BLURRED subjects affected / exposed occurrences (all)	 1 / 252 (0.40%) 1 1 / 252 (0.40%) 1 1 / 252 (0.40%) 1		
Gastrointestinal disorders ABDOMINAL DISTENSION subjects affected / exposed occurrences (all) ABDOMINAL MASS	 2 / 252 (0.79%) 2		

subjects affected / exposed	3 / 252 (1.19%)			
occurrences (all)	3			
ABDOMINAL PAIN				
subjects affected / exposed	12 / 252 (4.76%)			
occurrences (all)	13			
ABDOMINAL PAIN LOWER				
subjects affected / exposed	3 / 252 (1.19%)			
occurrences (all)	3			
ABDOMINAL PAIN UPPER				
subjects affected / exposed	6 / 252 (2.38%)			
occurrences (all)	6			
ABDOMINAL RIGIDITY				
subjects affected / exposed	1 / 252 (0.40%)			
occurrences (all)	1			
ABDOMINAL TENDERNESS				
subjects affected / exposed	2 / 252 (0.79%)			
occurrences (all)	2			
ANAL FISSURE				
subjects affected / exposed	7 / 252 (2.78%)			
occurrences (all)	8			
ANAL FISTULA				
subjects affected / exposed	3 / 252 (1.19%)			
occurrences (all)	6			
ANAL STENOSIS				
subjects affected / exposed	1 / 252 (0.40%)			
occurrences (all)	1			
ANAL ULCER				
subjects affected / exposed	1 / 252 (0.40%)			
occurrences (all)	1			
ANORECTAL DISCOMFORT				
subjects affected / exposed	2 / 252 (0.79%)			
occurrences (all)	2			
ANORECTAL DISORDER				
subjects affected / exposed	1 / 252 (0.40%)			
occurrences (all)	1			
CHEILITIS				

subjects affected / exposed	1 / 252 (0.40%)			
occurrences (all)	1			
CONSTIPATION				
subjects affected / exposed	6 / 252 (2.38%)			
occurrences (all)	6			
CROHN'S DISEASE				
subjects affected / exposed	46 / 252 (18.25%)			
occurrences (all)	59			
DENTAL CARIES				
subjects affected / exposed	2 / 252 (0.79%)			
occurrences (all)	2			
DIARRHOEA				
subjects affected / exposed	7 / 252 (2.78%)			
occurrences (all)	7			
DRY MOUTH				
subjects affected / exposed	1 / 252 (0.40%)			
occurrences (all)	1			
DYSPEPSIA				
subjects affected / exposed	1 / 252 (0.40%)			
occurrences (all)	1			
FLATULENCE				
subjects affected / exposed	1 / 252 (0.40%)			
occurrences (all)	1			
FREQUENT BOWEL MOVEMENTS				
subjects affected / exposed	1 / 252 (0.40%)			
occurrences (all)	1			
GASTROOESOPHAGEAL REFLUX DISEASE				
subjects affected / exposed	1 / 252 (0.40%)			
occurrences (all)	1			
HAEMATOCHEZIA				
subjects affected / exposed	2 / 252 (0.79%)			
occurrences (all)	2			
HAEMORRHOIDS				
subjects affected / exposed	1 / 252 (0.40%)			
occurrences (all)	1			

HIATUS HERNIA				
subjects affected / exposed	1 / 252 (0.40%)			
occurrences (all)	1			
ILEAL STENOSIS				
subjects affected / exposed	1 / 252 (0.40%)			
occurrences (all)	2			
INTESTINAL OBSTRUCTION				
subjects affected / exposed	4 / 252 (1.59%)			
occurrences (all)	4			
INTESTINAL STENOSIS				
subjects affected / exposed	1 / 252 (0.40%)			
occurrences (all)	1			
IRRITABLE BOWEL SYNDROME				
subjects affected / exposed	1 / 252 (0.40%)			
occurrences (all)	1			
LARGE INTESTINE POLYP				
subjects affected / exposed	2 / 252 (0.79%)			
occurrences (all)	2			
MOUTH ULCERATION				
subjects affected / exposed	1 / 252 (0.40%)			
occurrences (all)	1			
MUCOUS STOOLS				
subjects affected / exposed	1 / 252 (0.40%)			
occurrences (all)	1			
NAUSEA				
subjects affected / exposed	15 / 252 (5.95%)			
occurrences (all)	21			
PROCTALGIA				
subjects affected / exposed	1 / 252 (0.40%)			
occurrences (all)	1			
RECTAL DISCHARGE				
subjects affected / exposed	1 / 252 (0.40%)			
occurrences (all)	1			
RECTAL HAEMORRHAGE				
subjects affected / exposed	2 / 252 (0.79%)			
occurrences (all)	3			

SMALL INTESTINAL OBSTRUCTION			
subjects affected / exposed	6 / 252 (2.38%)		
occurrences (all)	6		
TONGUE DRY			
subjects affected / exposed	1 / 252 (0.40%)		
occurrences (all)	1		
TOOTHACHE			
subjects affected / exposed	3 / 252 (1.19%)		
occurrences (all)	3		
VOMITING			
subjects affected / exposed	11 / 252 (4.37%)		
occurrences (all)	12		
Hepatobiliary disorders			
CHOLELITHIASIS			
subjects affected / exposed	1 / 252 (0.40%)		
occurrences (all)	1		
HEPATIC STEATOSIS			
subjects affected / exposed	1 / 252 (0.40%)		
occurrences (all)	1		
HYPERTRANSAMINASAEMIA			
subjects affected / exposed	1 / 252 (0.40%)		
occurrences (all)	1		
Skin and subcutaneous tissue disorders			
ACNE			
subjects affected / exposed	5 / 252 (1.98%)		
occurrences (all)	5		
ALOPECIA			
subjects affected / exposed	1 / 252 (0.40%)		
occurrences (all)	1		
ANGIOEDEMA			
subjects affected / exposed	1 / 252 (0.40%)		
occurrences (all)	1		
DERMATITIS			
subjects affected / exposed	5 / 252 (1.98%)		
occurrences (all)	5		
DERMATITIS ALLERGIC			

subjects affected / exposed	1 / 252 (0.40%)			
occurrences (all)	1			
DERMATITIS CONTACT				
subjects affected / exposed	1 / 252 (0.40%)			
occurrences (all)	1			
DRY SKIN				
subjects affected / exposed	3 / 252 (1.19%)			
occurrences (all)	3			
ECZEMA				
subjects affected / exposed	2 / 252 (0.79%)			
occurrences (all)	2			
ERYTHEMA				
subjects affected / exposed	2 / 252 (0.79%)			
occurrences (all)	2			
MILIARIA				
subjects affected / exposed	1 / 252 (0.40%)			
occurrences (all)	1			
PAPULE				
subjects affected / exposed	1 / 252 (0.40%)			
occurrences (all)	1			
PRURITUS				
subjects affected / exposed	4 / 252 (1.59%)			
occurrences (all)	7			
PRURITUS GENERALISED				
subjects affected / exposed	1 / 252 (0.40%)			
occurrences (all)	2			
PSORIASIS				
subjects affected / exposed	3 / 252 (1.19%)			
occurrences (all)	4			
RASH				
subjects affected / exposed	6 / 252 (2.38%)			
occurrences (all)	6			
RASH GENERALISED				
subjects affected / exposed	1 / 252 (0.40%)			
occurrences (all)	1			
RASH MACULAR				

subjects affected / exposed occurrences (all) RASH PRURITIC subjects affected / exposed occurrences (all) SKIN EXFOLIATION subjects affected / exposed occurrences (all) SKIN LESION subjects affected / exposed occurrences (all) URTICARIA subjects affected / exposed occurrences (all)	1 / 252 (0.40%) 1 1 / 252 (0.40%) 1 1 / 252 (0.40%) 1 1 / 252 (0.40%) 1 1 / 252 (0.40%) 1		
Renal and urinary disorders INCONTINENCE subjects affected / exposed occurrences (all) NEPHROLITHIASIS subjects affected / exposed occurrences (all) POLLAKIURIA subjects affected / exposed occurrences (all) RENAL COLIC subjects affected / exposed occurrences (all)	 1 / 252 (0.40%) 1 2 / 252 (0.79%) 2 1 / 252 (0.40%) 1 2 / 252 (0.79%) 2		
Endocrine disorders THYROID DISORDER subjects affected / exposed occurrences (all)	 1 / 252 (0.40%) 1		
Musculoskeletal and connective tissue disorders ARTHRALGIA subjects affected / exposed occurrences (all) ARTHRITIS	 18 / 252 (7.14%) 20		

subjects affected / exposed	4 / 252 (1.59%)			
occurrences (all)	4			
ARTHROPATHY				
subjects affected / exposed	1 / 252 (0.40%)			
occurrences (all)	1			
BACK PAIN				
subjects affected / exposed	11 / 252 (4.37%)			
occurrences (all)	12			
BURSITIS				
subjects affected / exposed	1 / 252 (0.40%)			
occurrences (all)	1			
FISTULA DISCHARGE				
subjects affected / exposed	1 / 252 (0.40%)			
occurrences (all)	1			
INTERVERTEBRAL DISC PROTRUSION				
subjects affected / exposed	3 / 252 (1.19%)			
occurrences (all)	4			
LUMBAR SPINAL STENOSIS				
subjects affected / exposed	1 / 252 (0.40%)			
occurrences (all)	1			
MUSCLE SPASMS				
subjects affected / exposed	2 / 252 (0.79%)			
occurrences (all)	2			
MUSCULOSKELETAL PAIN				
subjects affected / exposed	3 / 252 (1.19%)			
occurrences (all)	3			
MUSCULOSKELETAL STIFFNESS				
subjects affected / exposed	1 / 252 (0.40%)			
occurrences (all)	1			
PAIN IN EXTREMITY				
subjects affected / exposed	6 / 252 (2.38%)			
occurrences (all)	7			
ROTATOR CUFF SYNDROME				
subjects affected / exposed	1 / 252 (0.40%)			
occurrences (all)	1			

TENDONITIS			
subjects affected / exposed	1 / 252 (0.40%)		
occurrences (all)	1		
Infections and infestations			
ABSCESS			
subjects affected / exposed	2 / 252 (0.79%)		
occurrences (all)	2		
ACUTE SINUSITIS			
subjects affected / exposed	1 / 252 (0.40%)		
occurrences (all)	1		
ANAL ABSCESS			
subjects affected / exposed	9 / 252 (3.57%)		
occurrences (all)	10		
BACTERIAL VAGINOSIS			
subjects affected / exposed	1 / 252 (0.40%)		
occurrences (all)	1		
BACTERIAL VULVOVAGINITIS			
subjects affected / exposed	1 / 252 (0.40%)		
occurrences (all)	1		
BRONCHITIS			
subjects affected / exposed	4 / 252 (1.59%)		
occurrences (all)	5		
CELLULITIS			
subjects affected / exposed	1 / 252 (0.40%)		
occurrences (all)	1		
CONJUNCTIVITIS			
subjects affected / exposed	3 / 252 (1.19%)		
occurrences (all)	4		
CYSTITIS			
subjects affected / exposed	4 / 252 (1.59%)		
occurrences (all)	4		
EAR INFECTION			
subjects affected / exposed	4 / 252 (1.59%)		
occurrences (all)	4		
ECZEMA INFECTED			

subjects affected / exposed	2 / 252 (0.79%)			
occurrences (all)	2			
EPIDIDYMITIS				
subjects affected / exposed	2 / 252 (0.79%)			
occurrences (all)	2			
FUNGAL INFECTION				
subjects affected / exposed	1 / 252 (0.40%)			
occurrences (all)	1			
GASTROENTERITIS				
subjects affected / exposed	2 / 252 (0.79%)			
occurrences (all)	2			
GASTROINTESTINAL INFECTION				
subjects affected / exposed	1 / 252 (0.40%)			
occurrences (all)	1			
GINGIVITIS				
subjects affected / exposed	3 / 252 (1.19%)			
occurrences (all)	3			
HERPES SIMPLEX				
subjects affected / exposed	1 / 252 (0.40%)			
occurrences (all)	1			
HERPES ZOSTER				
subjects affected / exposed	3 / 252 (1.19%)			
occurrences (all)	3			
HORDEOLUM				
subjects affected / exposed	1 / 252 (0.40%)			
occurrences (all)	1			
INFLUENZA				
subjects affected / exposed	4 / 252 (1.59%)			
occurrences (all)	4			
LOCALISED INFECTION				
subjects affected / exposed	1 / 252 (0.40%)			
occurrences (all)	1			
LOWER RESPIRATORY TRACT INFECTION				
subjects affected / exposed	1 / 252 (0.40%)			
occurrences (all)	1			

NASOPHARYNGITIS				
subjects affected / exposed	9 / 252 (3.57%)			
occurrences (all)	10			
ONYCHOMYCOSIS				
subjects affected / exposed	1 / 252 (0.40%)			
occurrences (all)	1			
ORAL CANDIDIASIS				
subjects affected / exposed	1 / 252 (0.40%)			
occurrences (all)	2			
ORAL HERPES				
subjects affected / exposed	4 / 252 (1.59%)			
occurrences (all)	4			
OTITIS EXTERNA				
subjects affected / exposed	1 / 252 (0.40%)			
occurrences (all)	1			
PERIODONTITIS				
subjects affected / exposed	1 / 252 (0.40%)			
occurrences (all)	1			
PHARYNGITIS				
subjects affected / exposed	1 / 252 (0.40%)			
occurrences (all)	1			
PHARYNGITIS STREPTOCOCCAL				
subjects affected / exposed	1 / 252 (0.40%)			
occurrences (all)	1			
PULPITIS DENTAL				
subjects affected / exposed	1 / 252 (0.40%)			
occurrences (all)	1			
RESPIRATORY TRACT INFECTION				
subjects affected / exposed	1 / 252 (0.40%)			
occurrences (all)	1			
RESPIRATORY TRACT INFECTION VIRAL				
subjects affected / exposed	1 / 252 (0.40%)			
occurrences (all)	1			
RHINITIS				

subjects affected / exposed	3 / 252 (1.19%)		
occurrences (all)	3		
SINUSITIS			
subjects affected / exposed	2 / 252 (0.79%)		
occurrences (all)	2		
SUBCUTANEOUS ABSCESS			
subjects affected / exposed	3 / 252 (1.19%)		
occurrences (all)	3		
TONSILLITIS			
subjects affected / exposed	2 / 252 (0.79%)		
occurrences (all)	2		
TOOTH ABSCESS			
subjects affected / exposed	2 / 252 (0.79%)		
occurrences (all)	2		
TOOTH INFECTION			
subjects affected / exposed	2 / 252 (0.79%)		
occurrences (all)	2		
UPPER RESPIRATORY TRACT INFECTION			
subjects affected / exposed	13 / 252 (5.16%)		
occurrences (all)	13		
URINARY TRACT INFECTION			
subjects affected / exposed	9 / 252 (3.57%)		
occurrences (all)	9		
VIRAL INFECTION			
subjects affected / exposed	1 / 252 (0.40%)		
occurrences (all)	1		
VULVOVAGINAL MYCOTIC INFECTION			
subjects affected / exposed	3 / 252 (1.19%)		
occurrences (all)	4		
WOUND INFECTION			
subjects affected / exposed	1 / 252 (0.40%)		
occurrences (all)	1		
Metabolism and nutrition disorders			

DECREASED APPETITE			
subjects affected / exposed	2 / 252 (0.79%)		
occurrences (all)	2		
FOLATE DEFICIENCY			
subjects affected / exposed	1 / 252 (0.40%)		
occurrences (all)	1		
FOOD INTOLERANCE			
subjects affected / exposed	1 / 252 (0.40%)		
occurrences (all)	1		
GOUT			
subjects affected / exposed	1 / 252 (0.40%)		
occurrences (all)	1		
HYPOVITAMINOSIS			
subjects affected / exposed	1 / 252 (0.40%)		
occurrences (all)	1		
IRON DEFICIENCY			
subjects affected / exposed	1 / 252 (0.40%)		
occurrences (all)	1		
VITAMIN B12 DEFICIENCY			
subjects affected / exposed	3 / 252 (1.19%)		
occurrences (all)	3		
VITAMIN D DEFICIENCY			
subjects affected / exposed	1 / 252 (0.40%)		
occurrences (all)	1		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
13 May 2014	The main purpose of this study was to update Crohn's disease flare and inadequate response criteria, update de-escalation and re-escalation criteria, clarify corticosteroid use, clarify inclusion criteria (contraception) and exclusion criteria (tuberculosis), and clarify endpoints and analyses.
04 December 2014	The main purpose of this study was to update the definition of inadequate response and first week when subjects are allowed to dose-escalate and clarifystudy procedures, including procedures required at unscheduled visit .

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported